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CANCER

AND ITS

NON-SURGICAL TREATMENT

BY

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NEW YORK

WILLIAM WOOD AND COMPANY

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PREFACE

An attempt has been made in the following pages to study cancer from all its angles and aspects, except that of operative surgery, which latter has been exploited heretofore, quite to the exclusion of any possible medical consideration of the disease.

It has been a difficult task to compress within a certain compass sufficient data, and to make each chapter satisfactorily full and clear, so that all would be understood. For the amount which has been written concerning cancer in books and periodicals is so enormous that the process has entailed an amount of reading and study hardly imaginable.

As will be seen, the work of Dr. James Ewing, one of the most competent and careful pathological scientists living, has been drawn on very largely, along certain lines, with his kind personal permission. It was not intended to slight the views of other pathologists, but Dr. Ewing's masterly work on neoplastic diseases covered the pathological ground so completely, and presented various subjects in such a definite and seemingly conclusive manner, and embraced so much of the work of others, that it was thought best to adhere largely to his descriptions and statements.

It was not considered wise or necessary to attempt any illustrations, either clinical or histological, as these have appeared so abundantly in other works accessible in the libraries.

Nor was it thought desirable to dwell too long on the various attempts which have been made to control cancer by many different means, such as various sera, etc., or the theories on which their employment was based. Some good results have been claimed from many of them, but there are few reliable statements or data in regard to end results. Also no attention has been paid to surgical procedures, except an analysis of the end results, as far as could be obtained; the surgical books on

cancer which were consulted amply supply all needed information as to details and technique of operations.

The aim of this book has been to establish on firm scientific grounds the proofs of the constitutional nature of cancer, now so widely accepted, and to illustrate freely the value of this thesis by successful cases.

In selecting cases for report the effort has been to select and present them in such a manner as would give a satisfactory presentation of the disease carcinosis, as it sresults or products affect various portions of the human economy, to which products, or local manifestations, the name of cancer is usually given. All this is in opposition to the more recent views as to its purely local nature, and to the idea that excision or removal in any way of the local lesions of the disease can possibly effect a radical cure of cancer, which experience, sustained by mortality statistics, has shown to be no longer tenable.

The comparison is constantly made between tuberculosis and cancer, as indicating the radical difference in results between an intelligent and faithful application of medical principles and treatment, and surgery, in handling these two ormidable enemies of the human race; for the mortality of the former has declined about thirty per cent in the last twenty years, under wise medical care, while that of cancer has risen about thirty per cent, in the same period, under surgical domination. While no absolute statement can yet be made statistically as to the reduction of mortality by a properly directed dietetic, hygienic, and medicinal treatment of cancer, the clinical portion of this work furnishes data from which may be judged some of its results. It is confidently asserted that when the principles and practice here laid down are fully understood, widely accepted, and generally acted upon, there will be shown a reduction in the mortality of cancer which will be conclusive and gratifying.

I would like to repeat what I have said in my former books, and elsewhere in this, as a word of caution in regard to the medical treatment of cancer. Namely, that this is not to be entered upon lightly or without due consideration. For,

although when rightly carried out long enough, the results obtained far exceed any that can be otherwise secured, on the other hand a lax, or careless, or too brief employment of the measures enjoined can only end in disappointment. It takes a great deal of time, patience, and careful thought, as well as resolute will, to fully succeed along this line of practice. Also such a perfect acquaintance with, and confidence in the principles on which it is based, as will beget a like confidence in the patient to enable one to pursue the tedious treatment sufficiently long to secure the result desired.

No attempt has been made to furnish a full bibliography regarding cancer, which would be so enormous, and is very fully presented in other writings on this disease, and reference is only made, as far as possible, in the form of footnotes, to the matter actually consulted. In securing much of this I am greatly indebted to my former associate, Dr. Edward Preble, whose references I have worked into the text.

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CANCER

CHAPTER I

NATURE OF CANCER

Cancer, with its cause and proper treatment, is still one of the greatest problems before the medical profession. No disease has in late years received more attention than cancer, and concerning no disease has there been more diligent search to find out its nature and cause, and yet to many it is still a great mystery, and most writers both recent and older, say that we know nothing as to its cause.

Tuberculosis, which at one time seemed to threaten even the existence of the race, with its constantly rising mortality has sunk into relative insignificance, as we have learned its true nature and conquered some of the causes of its ravages, and reduced its mortality about 30 per cent since 1900, by careful medical treatment.

Syphilis, under various names, forms, and aspects, was formerly much more of a menace than now; in earlier years it caused veritable epidemics but is now well understood and controlled.

Leprosy is less of a terror than in earlier times, since it has been definitely shown not to be contagious, and is now slowly diminishing in frequency.

Small pox no longer rages, and yellow fever and the plague, and hook worm disease, have been hunted down and largely controlled by scientific study and the application of proper sanitary and medical measures. And so on, as to malaria and many of the ills which afflict mankind.

But cancer has held its own and has even increased in frequency in civilized countries, until now it looms large as a national or even universal scourge: it has been estimated to cause the death of half a million of persons yearly, among the civilized people of the earth, and untold misery and suffering to many times this number. In the United States with over 80,000 deaths from the disease last year, the mortality has risen nearly 30 per cent, about the same proportion as the death rate of tuberculosis has fallen.

And all this has occurred in spite of the earnest, faithful, and intelligent labors of innumerable research workers, the sacrifice of countless animal lives, and the expenditure of vast sums of money, together with the best endeavors of surgeons, more skilled than ever before in the history of medicine.

Much, however, has already been established by scientific research, but still more earnest thought, observation, and endeavor are necessary in seeking most diligently for the nature and cause of cancer, both in the laboratory, as well as clinically in practice; for there must be some cause of the disease and also some reason for its steady increase in morbidity and mortality.

But it is never to be forgotten that as Pope says: "The proper study of mankind is man," and the true base upon which all real advance as to the nature, treatment, and prevention of the malady can ever rest must be founded upon clinical observation, with proper laboratory research, on cancer as it appears in the human being, rather than on animal experimentation. To effect this we must study the patient in all relations of life, his diet and mode of living, the constitution and class of subjects in which the disease is most apt to manifest itself, the chemico-physiologic actions going on in the system, etc., both before and during the existence of the malady, and by synthesis and deduction understand what is wrong and endeavor to correct it. As all this is done intelligently and faithfully the malignant process is seen to yield, even in cases more or less advanced. This is no easy task, and great patience and perseverance on the part of

both physician and patient are necessary, as in the case of tuberculosis.

To understand the study of the true nature of cancer it is well first to consider what scientific laboratory research and clinical observation have already determined negatively and positively in regard to its nature and character. First as to *negative* propositions.

1. Cancer is *not* wholly due to traumatic causes; although these may play some part in its occurrence in certain localities and cases, when other causes exist, as in syphilis, tuberculosis, gout, etc.

2. It is pretty conclusively decided that cancer is *not* caused by a micro-organism or parasite; although various forms of these have been seen in connection with the disease, but none have been conclusively shown to convey it to another living being.

3. It is known clinically and experimentally that cancer is *not* contagious. Surgeons, pathologists, and nurses have never contracted the disease from the practice of their profession, nor can human cancer be conveyed to animals by inoculation.

4. *Nor* is it hereditary in any appreciable degree, as Life Insurance statistics have repeatedly shown; although certain rare instances have been reported where such seemed to be the case and some tendency in that direction has been demonstrated in regard to tumors in certain strains of mice.

5. Occupation has *not* any very great influence on the occurrence of cancer; although it has been claimed to be more frequent in some pursuits than in others; but a careful study of these instances shows that in the former there are elements which demonstrate constitutional causes, which we shall see lead up to the disease.

6. Cancer is *not* altogether a disease of older years; although its incidence is increased with advancing age.

7. Cancer does *not* especially belong to or effect any particular sex, race or class of persons. It is, however, more frequent in females than in males, although of late years the proportion in the latter is steadily increasing.

8. Cancer is *not* confined to any climate, location, or section of the earth, but has been observed in all countries and climates, though with different frequency according to the mode of life there.

9. It is thus seen that no single or definite cause of cancer has been demonstrated, in spite of the immense amount of laboratory effort which has been expended in this direction. Nor is it at all likely that such will ever be found, as experimental and other investigations have covered almost every possible line of research, with only *negative* results as to any definite cause.

But while laboratory and other investigations have not demonstrated any single cause of cancer, and have yielded only negative results, they have, by elimination, cleared the way for a study of its causes along other lines, which are bright with promise. They have established certain facts which confirm the views which from time to time have been briefly expressed by surgeons and those who were best acquainted with cancer, and which are daily gaining wider acceptance. These are, that, because of its constant recurrence after removal, and from the failure of surgery to check its rising mortality, it must be of a constitutional nature, intimately associated with dietary or nutritional elements, with greater or less failure of some of the organs relating to life processes, the details of which will appear later. These *positive* results of laboratory investigation are encouraging.

1. We know now that the local mass, which we call cancer, represents but a deviation from the normal life and action of certain ordinary cells of the body. These once normal cells, for some reason difficult to understand, take on an abnormal or morbid action, with a continued tendency to a malignancy which invades contiguous tissues, and even distant parts, and in the end tends to destroy life.

2. There is some reason to believe that this diseased action often first takes place in what is known as "embryonic rests," or pre-natal, wrongly placed tissue elements. But these

latter are shown to exist in every individual in many localities, and few of them ever take on this malignant activity, and as no adequate explanation has been determined for this action, this basis of malignity is not now generally accepted. Moreover, in a large share of instances no such connection has been observed microscopically.

3. Microscopic study has shown that there is a certain change in the polarity of cells about to become cancer-genetic, with an altered relation of the centresome to the nucleus. These changes have been well attributed to an alteration in the enzyme of the cell, which further depends upon its nutrition, as influenced by faulty metabolism of food elements.

4. The blood in advancing cancer has repeatedly been shown to exhibit many manifest changes, which indicate vital alterations in the action of the organs which form blood, and so control the nutrition of the body and its cells.

5. The exclusion of all other possible causes leads us naturally to look to a disordered metabolism as a cause of the disturbed action of the hitherto normal cells; and we find much to confirm this view both in laboratory studies on the bio-chemistry of cancer, and also in clinical and statistical observations, as will be studied later.

6. Laboratory and clinical evidence demonstrate that the secretions and excretions of the body, both in early and late stages of cancer, exhibit departures from normal which deserve consideration. Although none of these have as yet been established as pathognomonic of cancer, they all indicate metabolic disturbances which influence the nutrition of the cellular elements, and so these secretory and excretory disturbances are of importance in connection with its causation.

7. As all healthy cells of the body, by their catabolism and anabolism, contribute a hormone or something to the general circulation, so experimental evidence shows that the cells of the cancer mass itself, when fully developed, secrete a hormone or something which is poisonous to animals, and which probably hastens the lethal progress of the disease.

8. Repeated laboratory experiences have demonstrated, in a most remarkable manner, the absolute controlling effect of diet on the development of inoculated cancer in mice and rats, so that the process was inhibited almost entirely by vegetable feeding.

All of these points will be elaborated fully in the following pages.

It is thus seen that as laboratory experiences have eliminated the local nature of cancer, they have also, in a measure, established the fact that there are medical aspects of the disease which further studies will show to be of the utmost importance. All this tends to demonstrate the constitutional origin of cancer, that is, its relation to or dependence upon deranged metabolism and nutrition, which are now recognized as the basis of many diseases of more or less serious character. But clinical and statistical studies come in with overwhelming force to confirm the correctness of the position.

1. It is recognized that under medical neglect the mortality from cancer has steadily and greatly increased in the United States, in late years, in spite of the prodigious advances of surgical attempts at control during the same time. This is also true of all countries from which we have any accurate statistics. We know, also, that tuberculosis, as a result of careful medical attention, has decreased in mortality by almost as great a percentage as cancer has increased. The same is reported by reliable observers all over the civilized world.

2. Any number of observers, in many lands, have recorded the almost total absence of cancer among aborigines, living simple lives, largely vegetarian. They have also shown the definite increase of the disease, and of its mortality, in proportion to the adoption by natives of the customs and diet of modern civilization.

3. This increase of cancer mortality seems to depend largely upon the altered conditions of life attending advanced civilization, particularly along the lines of self indulgence in eating and drinking, together with indolence.

4. Statistics from many countries show that a per capita increase in the consumption of meat, coffee, and alcoholic beverages, appears to be coincident with a very great and proportionately greater augmentation in the mortality of cancer.

5. Clinical observation has time and again shown the specific effect of nerve strain and shock in the development of cancer; and there seems to be little question but that the enormous nerve strain of modern life is an element of importance in this direction, both through metabolic disturbance and by direct action on living cells, as is seen in other diseased conditions.

6. At present no clear demonstration is possible of the direct method by which errors of metabolism effect the changes in cells to which we give the name malignant, any more than we know how other alterations in the body are produced; such as arterial degeneration, bone changes, obesity, etc., which are recognized as due to metabolic derangement.

7. The results which have been observed in connection with the starvation of cancer, by ligation of vessels, illustrate the relation of the blood supply to growing cancer.

8. Finally, the repeated observation and report of the spontaneous disappearance of cancer, by careful and competent medical men, shows that conditions of the system may arise which are antagonistic to malignant growth, even when it has begun to take place; just as other wrong conditions of the system arose which favored the aberrant and malignant action of previously normal cells, resulting in the mass which we call cancer, a product of previous disordered systemic action.

Having stated now the fundamental propositions upon which the thesis of the constitutional origin and nature of cancer rests, which will be more fully developed in later chapters, we may briefly consider some general questions relative to the subject.

First it may be remarked that our studies do not relate to oncology in general, but only to the two main groups of malignant neoplasms, commonly known as carcinoma and sarcoma: although unquestionably all tumors, of which Ewing, gives a list of over twenty, have relations to nutrition, which even Ewing

recognizes. In our consideration also the ordinary epithelioma of the skin is excluded, although carcinoma is likewise an epithelial degeneration, but mainly of glandular epithelium.

The histology of the two will be considered in a separate chapter.

We come then to the question "What is the real nature of cancer?"

Alas! All scientific, experimental and clinical investigations have failed to settle the question, and the medical profession is still divided as to the answer. Pathologists and surgeons still cling to a local origin and nature, while evidence comes from all sides of the acceptance by medical men of a constitutional nature of the disease, and all must acknowledge that "all evidence points to the conclusion that cancer is to be considered as a pathological disturbance of the normal cell life from some unknown cause"—this last phrase is repeated almost universally by writers on cancer.

It would carry us too far from the practical side of our subject, even if we were at all able, to present or analyze the vast number of contributions which have been made to the pathological histology of cancer, and the changes which take place in the transformation of normal cells into those of malignant character: the amount of microscopic work which has been done along this line can hardly be imagined and the literature relating to it is enormous. Some of it will be presented in a later chapter.

Ewing[1] defines carcinoma as "a tumor process characterized by atypical and destructive proliferations of epithelium," and emphasizes the lawless overgrowth of neoplastic structures which show variable but pronounced grades of anaplasia, or the alteration in cell character which constitutes malignancy. He states that "in some cases carcinoma has developed after excision of wholly benign fibro-adenoma," and the immense number of cases of recurrent cancer after operations shows that we must look further than surgery if we wish to stay the progress of the formidable disease.

[1] EWING, "Neoplastic Diseases." Philadelphia, 1919, p. 27.

Leo Loeb[1] has recently made a most interesting study of the causes of cancer, which is full of evidence and suggestions looking toward an acceptance of the views set forth in these pages, and is well worthy of careful consideration. Although the article relates largely to experimental cancer in lower animals, the deductions appearing here and there are equally or more reasonably applicable to cancer in human subjects. He says, for instance: "Thus we may assume that abnormal metabolic processes or other conditions which retard development at a certain place, and at a critical period of development, may cause embryonal malformations, teratomata, or mixed tumors." Again: "It is therefore possible that while in the majority of cancers repeated stimulation of tissues leads to a long continued or even perpetual increase in the intensity of those metabolic processes which cause cell proliferation and cell movements, in certain sarcomata the same effect is produced through a constantly acting extraneous, chemical growth stimulus, supplied by micro-organisms and not, as in the case of the majority of cancers through their own metabolism of the cancer cells."

Later on he says: "The basis of this transformation in cell equilibrium may be conceived as a change in cell metabolism, during which substances are produced which maintain the alteration in cell metabolism on which the acceleration in growth and the increase in motility depend. It is conceivable that in certain cases a similar constant alteration is produced through a stimulus reaching the cell from an extraneous source; a micro-organism might perhaps be able to supply such a stimulus."

We shall see in later chapters that while it is universally acceded that cancer is not parasitic or conveyed directly by micro-organisms, it is recognized that the latter produce diseases in the system by virtue of their bio-plastic composition, acting largely as a foreign protein in the tissues, as will appear in a subsequent chapter, which concides with the propositions upon which this work is based. It is interesting to find pure scientists,

[1] LOEB, *Amer. Jour. Med. Sci.*, June, 1920.

formerly advocates of the purely local nature of cancer, of late referring to metabolism, and the changes produced in the tissues by perverted nutrition.

It would be useless to attempt to present the many theories which have been advanced relating to cellular metaplasia, or even to detail all the more or less accepted facts as to the manner in which normal cells change and degenerate into those of a malignant character: but some of the principal facts may be of service in understanding somewhat of the mode of development of malignant tissue from that which has been normal.

The statement of Virchow, "Omnis cellula e cellula," that is, "Where a cell arises there a cell must have previously existed, just as an animal can spring only from an animal and a plant from a plant," forms the basis of all study on the genesis of cancer and all tumor formation. Karyokinesis, or indirect nuclear or cell division, is at the bottom of all growth, both normal and malignant, and the two classes of growth differ only in their methods and activity. In healthy tissues cell proliferation proceeds in an orderly manner, forming homologous structures, as when the hairs and nails are constantly produced from newly formed cells at the root, and the result of this new-growth is removed mechanically, as they are cut from time to time.

In the case of the skin, the epidermal layers are pushed forward, and finally exfoliated as useless epithelial debris.

With the cells composing other, or internal structures, however, the process is different. For here, while each normal cell produces others of homologous structure, and the different parts of the system are kept in active service, through anabolism, the older or effete cells are removed by catabolism; the elements of which they are composed are thus split up into their component parts, and carried off by the blood or lymph-stream, and are then either discharged as effete substances or reutilized in the system along physiological lines.

But the process relating to malignant formation, as in cancer, is again different. We have seen that the cells in this disease

have lost their controlling influence, and no longer tend to an homologous action leading to the formation of new normal tissue, but have taken a heterologous course, wild and unrestrained, and serve no useful purpose in the organism, but in the end lead to their own destruction and that of the individual.

In other words, while the ordinary, healthy body cells of the economy all have their functions to perform, such as those of a contracting muscle or a secreting gland, the cancer cell, having broken away from its accustomed control, expends all its energies simply on growth, which soon becomes over-growth with all its well-known evil results.

A great deal of thought, study and speculation have been given in regard to the behaviour of the cells themselves, and strong arguments are adduced for a local pathology, that is, to regarding the cells as autonomous beings, possessed of morphological and physiological independence.

But, on the other hand, we must recognize that there is some restraining influence which causes the great mass of cells to reproduce those of homologous structure into useful tissues, in an orderly manner, and only very rarely some of them to break loose and form tumors which may become malignant and even destroy life. How this restraining influence is modified or lost is, of course, a part of the problem of cancer. Those who maintain their autogenous character lay great stress on the polarity of the cells, and the relation of the centrosome to the nucleus, indicating a change in the polar axis in cells about to become cancer-genetic, as does Ewing,[1] in his recent classical study of pre-cancerous lesions. But whatever changes are observed microscopically we must recognize that the cells themselves must be influenced ultimately by that mysterious force which we call life, which ends with its extinction from the body as a whole, and which is eventually related to nerve action. We must also recognize that the cells everywhere depend for their life and activity upon the blood in which they are bathed, and from whence they draw their sustenance; and

[1] EWING, *Medical Record*, 1914, lxxxvi, p. 951.

this blood is renewed day by day from the food and drink taken.

Students of cancer are more and more recognizing and acknowledging that "all these phenomena, apparently so different, are merely protean manifestations of one common process which underlies and is the cause of them all, to wit, cell growth and proliferation." The particular outcome of the process in any given case is due to the influence of conditions of nutrition—understanding by this term the whole of the material changes wrought in the organism through its relations with the surrounding world. This being so it is easy to understand how, under favorable conditions, certain cells may take an independent action, growing and multiplying without regard to the requirements of adjacent tissues and of the organism as a whole.

Nels Quevli[1] has written a remarkable and most interesting book, showing the intelligence of the cells of plants and animals in building up various structures, and while not devoted to pathological states, explains in a measure how cells once starting on a wild, unrestrained, heterologous, and destructive course can go on propagating and influencing others to join with them. What the cause is which induces one or more cells to begin this course of morbid action is as yet undetermined, but it appears that irritation, whether mechanical or chemical, is the most likely incentive to this first departure from normal life.

In the case of sarcoma mechanical injury is most commonly seen, and in cancer of the breast many believe that a blow first excites the process. In deeper structures this is commonly not recognizable, nor so likely, and chemical or nutritional irritants probably start the process, in one otherwise prepared for it.

There seems to be some reason to support the view advocated by Williams,[2] that tumor formation and growth are but forms of agamogenesis, or non-sexual reproduction of cells, distinctly related to the decline in growth of the body in general. Hence

[1] NELS QUEVLI, "Cell Intelligence, etc." The Colwell Press, Minneapolis, 1917.

[2] WILLIAMS, "The Natural History of Cancer." New York, 1908.

while the forces of growth, development, and reproduction are in greatest activity, the tendency to this disease is relatively small; but when growth declines and nutrition is relatively low the cells undergo gemmation, owing to perverted nutriment, and thus hyperplasia and not inflammation is the starting point of every neoplasm. The histology and chemistry of cancer will be considered in later chapters.

The essence of our study thus far has been that in every instance what is called malignant disease is but an aberrant action of originally normal body cells. That, as normal cells find their nutriment in the circulating blood, so some pathological change in this latter causes them to take on an abnormal action, and they no longer develop homologous cells, capable of forming normal tissue, but heterologous elements which have a natural tendency to break down and exert a destructive influence on adjoining cells of any kind; and in this process they secrete a hormone, or substance, which is prejudicial to the system and tends to destroy life.

Thus it is seen that the disease under consideration is not a mysterious something from without, of whose cause we know nothing; for it is not parasitic or contagious, but it is simply a perverted operation of internal organs, including the endocrinous glands, whose *product*, variously manifested, we call cancer. We all recognize such an explanation for many diseased conditions, such as gout, arteriosclerosis, rickets, osteo-malacia, obesity, etc., but are slow in acknowledging the internal derangements which lead up to the disease we are studying. It is interesting to note that the founders of the index catalogue of the Government Library placed cancer among metabolic diseases, where it still stands, and also that in the very recent "Loose-leafed Living Medicine" published by Nelson, it is still placed there, with gout, diabetes, etc.

CHAPTER II

FREQUENCY AND GEOGRAPHICAL DISTRIBUTION OF CANCER

Cancer in man has been observed in all portions of the globe, but in greatly different degrees of frequency, according to varying conditions of life. Growths, benign and malignant, occur also in animals, birds, and fishes, though also with greatly varying frequency under different conditions, the frequency being particularly increased by domestication; tumors are, however, rarely found in mollusks, reptiles, or amphibians, living their normal life.

Considerable interest has been excited by the study of tumors occasionally found in vegetable oragnisms, presenting increased growth and proliferation of cells, and some have endeavored to show that they are related to cancer as occurring in the human being.[1] Some of these are quite local and benign, as galls, due to the operation of insects, or of cryptogamic origin, some remain quite local and relatively benign, others extend and spread and affect the health and life of the plant. But no sufficient proof has ever been produced to show that they have any real relation to human cancer.

There are, however, other tumors, especially on trees, which do afford interesting analogies to the growth of benign and malignant tumors in man, but present no evidence of any true connection; of these Williams[2] has made a most interesting study. He shows that such are derived from abnormally evolving buds, and remarks: "Thus the origin of buds, as well as their subsequent development, is chiefly determined by the conditions of nutrition. Whenever there is excess of nutritive materials, capable

[1] ERWIN V. SMITH, U. S. Department of Agriculture, Bureau of Plant Industry. *Bulletin No.* 255, 1912.

[2] WILLIAMS, "The Natural History of Cancer." New York, 1908, pp. 115–128.

of being utilized for growth by the cells of the part, there buds arise;" and many of the specimens of abnormal growths, or excrescences, which he observed occurred on trees situated where their roots rested in soil highly charged with sewage matter. While all these studies confirm in a measure what may be observed in human cancer, *they do not*, of course, establish any true relationship between tumors in vegetable organisms and carcinoma in man; they only show that where there is cell life, in the animal or vegetable kingdom, there are agencies which can cause cells to proliferate unwisely and uselessly, if not harmfully, under conditions which careful observation and study can recognize and overcome.

Cancer has been styled a disease of civilization, like tuberculosis, although of quite a different nature, which relationship will be considered in the next chapter. Interesting studies have been repeatedly made in regard to the increased death rate from the former, in England, coincident with a diminished mortality of the latter, in accordance with nutritional changes which have taken place in certain populations, and the same has occurred in the United States, as mentioned in the previous chapter.

Williams,[1] who quotes largely from the accurate statistics which have long been carefully recorded in England, states that: "While tubercle has declined with great rapidity, cancer has increased at a still faster rate, and these inversely related changes are still in active progress. In illustration of these remarks it may be mentioned that during the last half of the nineteenth century the cancer mortality for England tripled; while during the same period the tubercle death rate declined to the extent of nearly one-half. Unless some great change in the national health takes place, of which there is at present no well marked indication, cancer will ere long claim more victims than phthisis, as is already the case in many localities—*e.g.* Hampstead, Clifton, Bath, etc." In New York City the actual number of deaths from cancer, as reported by the Board of Health,

[1] WILLIAMS, *loc. cit.*, p. 58.

exceeded those from tuberculosis during certain five weeks in 1920, and during the last six months of the year there were actually 22 more deaths recorded from cancer than from tuberculosis.[1]

All statistics from various localities, show that cancer has certainly increased in mortality very greatly of late years, and in the United States the rate has kept pace with and steadily exceeded that from kidney disease, heart disease, and apoplexy, which are recognized not as local diseases but of internal origin. Some have attempted to claim that this increase is only apparent, and is due to greater accuracy in diagnosis, and the prolonging of more lives to an age when cancer is more common, but there is no doubt in the minds of those who have studied the figures of the Mortality Tables of the United States Census Bureau that the increase is certainly very real; and unless measures other than those thus far employed are more universally adopted the death rate at the end of the century will be appalling.

It is impossible even to give a comprehensive idea of the immense amount of work which has been given to the study of the statistics of cancer in various parts of the world, as collected in the remarkable works of Williams, Jacob Wolff[2] and F. L. Hoffman,[3] from which I shall quote freely, as also from others; a synopsis of some of the recorded facts and figures may be given in order to properly understand our subject.

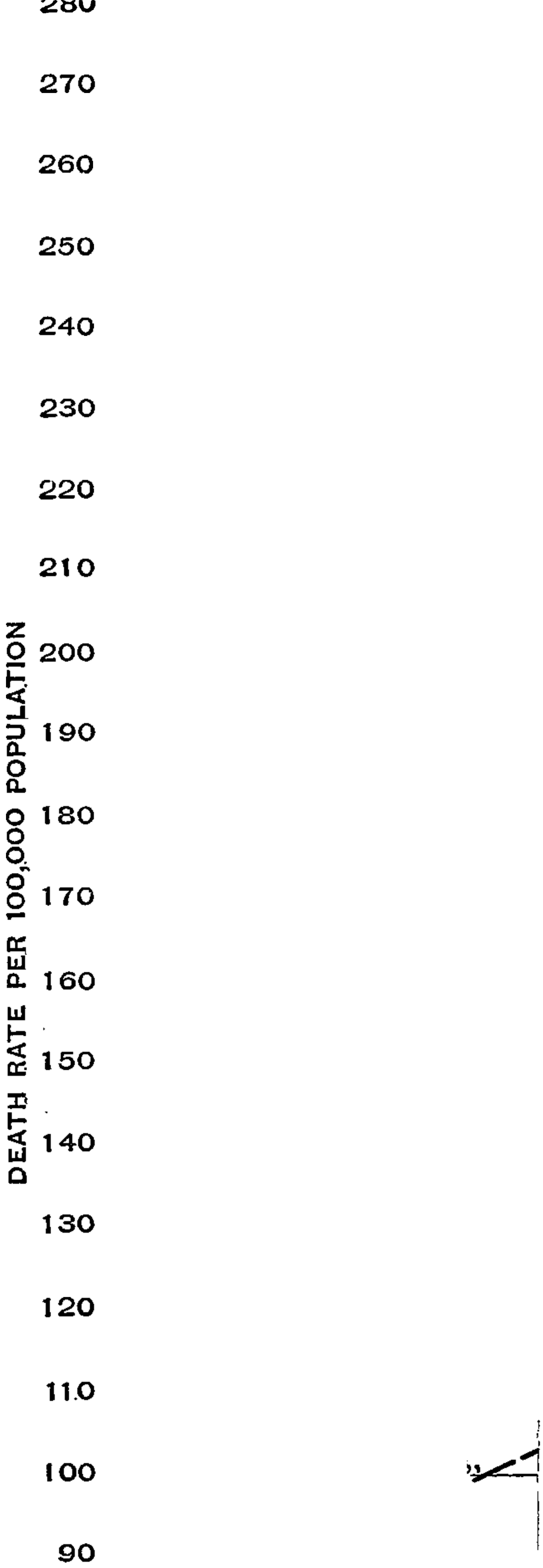
England and Wales present the most satisfactory field for the study of the progress of cancer, as the national vital statistics have been remarkably well kept since 1840: even at that time, under the able direction of William Farr, they had already acquired a well deserved reputation for reliability, as Williams remarks.

In that year, 1840, there died of malignant disease in England and Wales, 1 in 5,646 of the total population, 1 in 129 of the

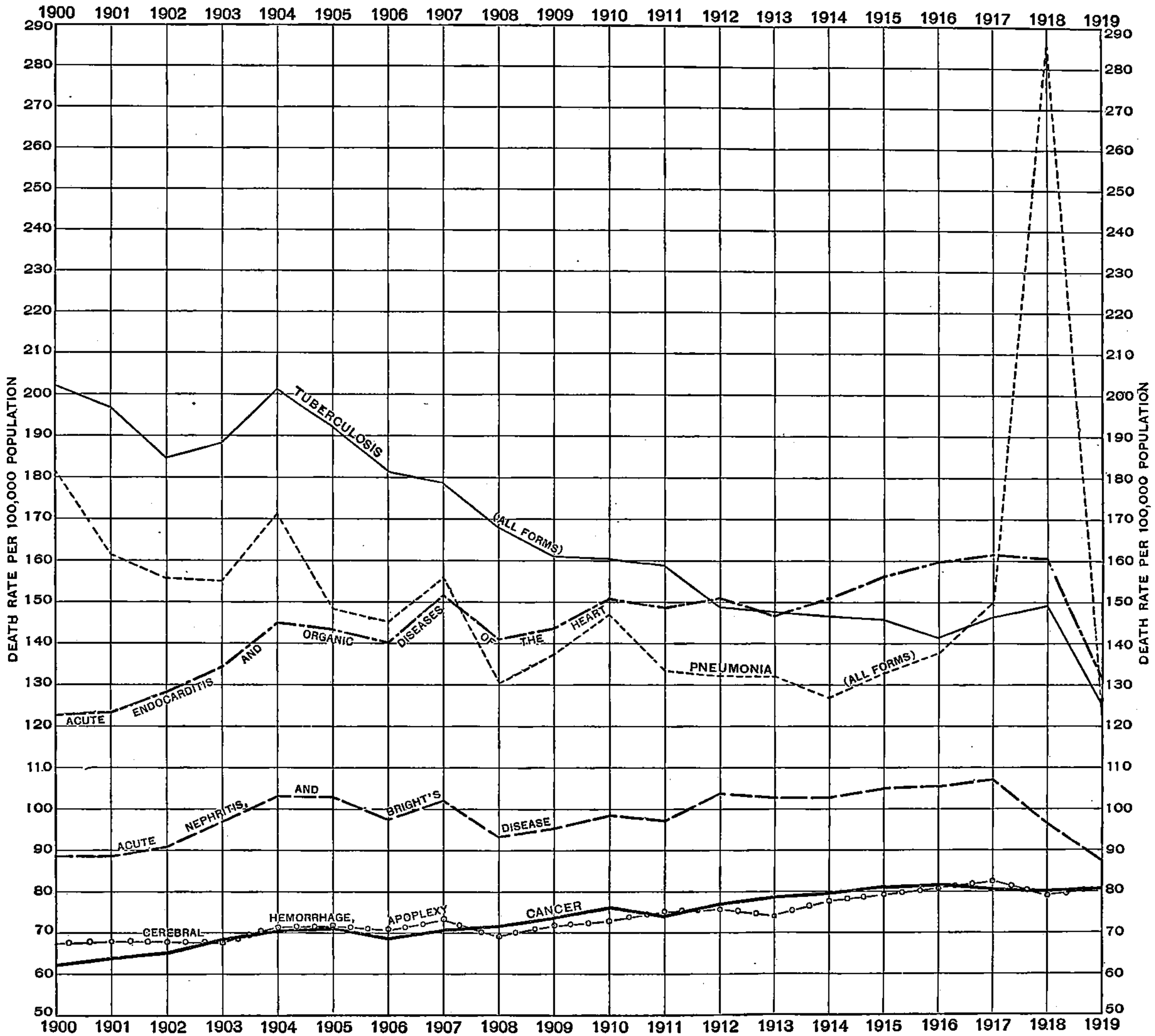
[1] Bulkley, Medical Record, New York, January 29, 1921.

[2] Jabob Wolfe, "Lehre von der Krebs Krankheit." Jena, 1911.

[3] F. L. Hoffman, "The Mortality from Cancer throughout the World." Newark, 1915.



The Death R
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DEATH RATE PER 100,000 POPULATION
TUBERCULOSIS (ALL FORMS)
ACUTE ENDOCARDITIS AND ORGANIC DISEASES OF THE HEART
PNEUMONIA (ALL FORMS)
ACUTE NEPHRITIS, AND BRIGHT'S DISEASE
CEREBRAL HEMORRHAGE, APOPLEXY
CANCER

total mortality, or 177 per million living. In 1905 the deaths due to this cause were 1 in 1,131 of the total population, 1 in 17 of the total mortality, or 885 per million living: thus, while the population has only a little more than doubled, the cancer death rate million had increased five-fold.

Objections have been constantly raised that this alleged increase in the mortality from cancer is not real, but may be accounted for on these grounds: 1. Mere increase of population; 2. The average age of the population having advanced, giving more persons of a cancer age; and 3. Improved diagnosis and more careful death certification. As these are vital questions, which are often brought forward, and almost always mentioned when I have spoken before many medical audiences, I will give as briefly as possible the conclusive evidences to the contrary, which Williams has presented by figures and tables in many pages of his instructive book; this proof will apply also to references which will be made regarding the increased mortality from cancer in other countries. I will quote from Williams.

1. *Increasing Population.*—This has already been answered by the figures already given.

2. *Increase of Average Longevity, Giving more Persons of a Cancer Age.*—To this it may be answered. "The saving of life in modern times has been mainly confined to the pre-cancerous years of existence, the death rate of males over 35 and of females over 45 has remained almost stationary, while the numbers attaining old age have decreased. Hence only an infinitesimal fraction of the increased cancer mortality can be thus accounted for. Moreover, an increase in the cancer mortality is by no means a necessary corollary of the survival of augmented numbers to the cancer age, as the Irish mortality statistics show."

3. *Improved Diagnosis and more Careful Death Certification.* "If improved diagnosis and death certification have caused additions to the cancer total—which I do not deny—the same conditions have also caused subtractions from it. Thus, as the Registrar General tells us in his fifty-fifth Report, that even up to the year 1880, such common diseases as "fibroid tumor,

polypus, and lupus" were usually classed as cancer. In like manner many other morbid states, formerly classed as cancerous, are now relegated to other categories: " the basis of this claim is also easily refuted by statistics from many countries.

Williams[1] has given some interesting tables showing that the increase in the cancer death in England has not been largely due to the improved diagnosis or registration of the disease in "inaccessible regions," one of which may be presented:

Males per 100 deaths from malignant disease			Females per 100 deaths from malignant disease		
	1897	1900		1897	1900
Stomach	20.6	20.5	Uterus	23.5	22.5
Liver	14.2	13.9	Breast	15.5	15.8
Rectum	8.6	9.0	Stomach	11.3	13.8
Tongue and mouth	6.3	6.8	Liver	13.2	14.3
Intestine (*ex* rectum)	6.3	7.0	Rectum	5.2	5.2
Œsophagus	5.7	5.4	Intestine (*ex* rectum)	5.2	5.7
Bladder	3.3	2.8	Ovary	1.7	1.7
Jaws	3.0	2.3	Œsophagus	1.4	1.3
Neck	2.7	2.3	Tongue and mouth	1.3	0.6
Pharynx, tonsils, etc.	2.3	2.2	Bladder	0.8	0.9
Larynx and trachea	1.8	2.0	Jaws	0.6	0.6
Testis and penis	1.5	1.5	Neck	0.6	0.5
	76.3	75.7		82.3	82.9
All others	23.7	24.3	All others	17.7	17.1
	100.0	100.0		100.0	100.0

Hoffman[2] has given an interesting table showing the Cancer Mortality from the records of the Prudential Insurance Co. of America from 1891 to 1913. While the deaths from cancer in 1891 formed 3 per cent of the total mortality in 1891, it had risen steadily to 6.1 per cent of all deaths in 1913.

[1] WILLIAMS, *loc. cit.*, p. 55.
[2] HOFFMAN, *loc. cit.*, p. 321.

In the United States, however, there appears to have been some increase in the deaths from cancer affecting "inaccessible regions" as shown in the following table:

DEATHS FROM CANCER IN RELATION TO SEX

Location		1911	1912	1913	1914	1915	1916	1917	Increase
Buccal cavity	Male	1,402	1,465	1,628	1,878	1,738	1,730	1,846	404
	Female	325	373	338	392	385	361	356	31
Stomach and liver	Male	8,698	9,215	9,749	10,122	10,915	11,481	11,384	2,686
	Female	8,667	9,302	10,018	9,767	10,306	10,999	11,140	2,473
Peritoneum and intestines	Male	2,464	2,459	2,811	2,903	3,156	3,286	3,416	952
	Female	3,360	3,464	3,814	3,842	4,176	4,430	4,508	1,148
Female genital organs		6,707	7,089	7,706	8,152	8,120	8,898	8,464	1,757
Breast	Male	74	75	78	88	64	97	84	10
	Female	4,190	4,356	4,514	5,335	5,099	5,461	5,338	1,148
Skin	Male	1,011	1,079	1,128	1,242	1,221	1,294	1,373	362
	Female	608	664	597	715	734	768	740	132
Other organs	Male	3,876	4,171	4,651	5,049	5,424	6,156	6,395	2,519
	Female	2,646	2,819	2,896	2,935	3,246	3,659	3,575	933

But wherever the increase in mortality may occur, in internal or external cancer, it only shows the unfortunate results of the past and even present modes of regarding and treating cancer, in that with all the immense amount of research and surgical skill that have been applied to the disease its ravages still increase in an appalling manner.

"The proportionate localization ratios shows that there has been special increase in the "inaccessible" manifestations of the disease; and this is very noticeable in such organs as the stomach and liver, which comprise the great majority of this form of disease." Dr. Williams also gives many illustrations to show the fallacy of the objections which have been raised as to the reliability of the figures which have been presented everywhere, in many countries, regarding the increase in cancer mortality.

Hoffman has collected an enormous amount of statistics from official sources in regard to cancer mortality all over the

world, which show a remarkable difference in different localities, both as to the actual mortality and its increase over different periods.

COMPARATIVE MORTALITY PROM CANCER IN EUROPEAN COUNTRIES
1896–1910

RATE PER 100,000 POPULATION

	1896–1900	1901–1905	1906–1910
Hungary	30.7	39.1	43.6
Italy	50.9	55.2	63.6
Ireland	58.1	68.5	78.8
Austria	68.9	74.7	78.3
German Empire	70.8	77.7	84.2
Scotland	77.1	84.8	99.7
England and Wales	80.1	86.7	94.0
Norway	85.7	94.0	96.6
Holland	91.9	97.8	103.5
France (cities)	97.3	92.1	102.7
Denmark (cities)	118.9	129.1	137.3
Switzerland	127.4	128.3	125.9
Combined average	79.8	85.7	92.3

"The high cancer death rate of Switzerland is not the result of an increase of population ages over 45. According to the most recent cancer returns this proportion was 22.16 per cent of the population in Switzerland, 22.85 per cent in Denmark, 21.36 per cent for England and Wales and 18.89 per cent for the United States."

Cancer is known to differ in frequency in different parts of the world, and the following figures are given by Hoffman[1] in regard to Australasia, Asia, and Africa.

[1] HOFFMAN, *loc. cit.*, pp. 136–138.

Australasia

Mortality Rate Per 100,000 Population

Hawaii	40.7
Northern Territory (Australia)	44.9
Western Australia	59.0
Queensland	63.2
Tasmania	65.3
New South Wales	73.1
New Zealand	75.2
South Australia	76.4
Victoria	83.4

Asia

Ceylon	5.6
Hongkong	8.1
Penang	10.3
India (Calcutta)	11.7
Singapore	12.6
Philippine Islands (Manilla)	27.3
Shanghai (Europeans)	55.3
Japan	60.2

Africa

Mauritius	9.3
Sierra Leone	13.2
Natal	32.9
Algeria (European)	34.1
Transvaal	34.4
Cape Colony (cities)	56.2

It will be noticed by these figures that cancer mortality is greater where Europeans congregate, for, as will be seen in the next chapter, cancer is decidedly a disease of civilization, while the natives, living as natives in these same countries, are rarely affected.

Mortality Rate per 100,000 Population

	1881	1913
Twenty American cities	49.6	89.3
Ten English cities	57.3	106.9
Fifteen German cities	72.1	119.3
French cities	89.9	104.5
Seven Italian cities	83.7	96.2

The following table given by Hoffman[1] of the relative frequency of cancer deaths in the various cities of the world is interesting.

[1] Hoffman, *loc. cit.*, p. 225.

International Statistics of Cancer Mortality 1908–1912
Rate Per 100,000 Population

Calcutta	11.0	Liverpool	96.6
Constantinople	34.8	Madrid	96.7
Rio Janeiro	42.5	Rome	100.5
Osaka	55.9	Glascow	102.1
Tokio	73.6	Budapest	102.6
New York	77.1	Hamburg	105.4
Chicago	78.9	Paris	110.8
Philadelphia	85.3	London	111.7
Buenos Ayres	85.5	Amsterdam	116.7
Petrograd	85.6	Vienna	128.9
Sydney	90.1	Berlin	133.5
Moscow	94.8	Copenhagen	161.3

In the United States the deaths from cancer vary also greatly in different cities. In the following table are given the figures from the five year period ending with 1910.

Mortality Rate per 100,000 Population

Savannah	47.1	Denver	77.9
Memphis	48.7	St. Louis	78.4
Augusta, Ga	49.1	Bor. Manhattan and Bronx	78.4
Seattle	50.2	Columbus	79.5
Charleston	53.6	Hoboken	80.7
Jersey City	60.5	Philadelphia	81.9
Louisville	61.1	New Orleans	82.2
Cleveland	62.9	Buffalo	84.0
Detroit	64.5	Omaha	85.7
Minneapolis	65.3	Baltimore	85.8
Pittsburg	66.4	District of Columbia	86.0
Nashville	68.0	Springfield (Mass.)	86.9
Milwaukee	68.4	Rochester, N. Y	88.2
Brooklyn	68.9	Dayton	88.5
Indianapolis	70.4	New Haven	89.8
St. Paul	71.1	Hartford	91.9
Kansas City	71.1	Cincinnati	93.0
Richmond	73.9	Los Angeles	94.9
Greater New York	74.1	Providence	96.9
Chicago	76.5	Boston	99.4
Newark	76.9	San Francisco	102.5

Cancer mortality also differs materially in the various registration states of the Union, in regard to cities and rural districts, as shown by the United States Mortality Statistics for 1917 (the last table published).

CANCER MORTALITY PER 100,000 POPULATION IN 1917

States	Cities	Rural districts	States	Cities	Rural districts
California	120.5	83.1	New York	91.2	101.4
Maine	119.1	101.8	Indiana	89.9	89.8
Maryland	107.5	73.8	Kentucky	89.5	45.8
Massachusetts	106.0	116.5	Kansas	88.9	62.5
New Hampshire	105.6	105.1	New Jersey	82.3	86.9
Rhode Island	101.7	67.8	Colorado	81.5	51.8
Montana	100.9	45.1	Tennessee	76.8	40.1
Missouri	99.7	58.4	Utah	70.8	44.2
Vermont	99.5	109.0	Washington	70.7	46.9
Minnesota	98.3	76.1	Virginia	70.6	48.6
Connecticut	97.3	92.0	North Carolina	70.2	40.6
Ohio	97.2	86.5	South Carolina	69.5	33.9
Wisconsin	94.5	77.6			
Michigan	92.8	86.2	Average	92.0	71.8
Pennsylvania	91.4	67.3			

Space does not permit of a very full consideration of the wonderful statistics contained in this great volume of Hoffman's, which is worthy of much study, but some points may be mentioned.

It is not a little interesting to note the discrepancy which exists between the mortality from cancer in the cities, (those of 10,000 or more inhabitants) as against that in rural districts.

In a very few instances the mortality in the latter exceeded, and in a few it almost equalled that in the former, but in most instances and in the general average the rural districts showed a far better per cent.

It may be claimed that the larger number of cancer deaths per 100,000 in the cities resulted from the number of cases going there for treatment, but if this were the case it would be expected that the results of operations would reduce the relative mortality below that found in rural districts, where surgical opportunities were less favorable; especially is this true when we consider the large population of the cities, which should reduce the proportion of deaths to the 100,000.

An interesting study has been made by Williams[1] of the relative number of deaths from cancer among men and women, and he gives the following table.

INCREASE OF MALIGNANT DISEASE AMONG MALES AND FEMALES PER MILLION LIVING

Period	Cancer death rate		Sex ratio
	Male	Female	
1851–1860	195	434	1–2.2
1861–1870	244	523	1–2.1
1871–1880	315	622	1–1.9
1881–1890	430	739	1–1.7
1891–1900	597	903	1–1.5
1900–1905	723	997	1–1.3

"It thus appears that, although there has been a great increase of malignant disease in both sexes during the last half century, and although at the present time more women are affceted than men, yet the malady has augmented much more rapidly among the latter than among the former. Moreover, it is noticeable that the average age of English women is *higher than that of men*, so that the death rates, as given above, are unduly favorable to the female sex."

In the United States the ratio between the sexes seems to be about constant, as is seen in the following table.

RELATION OF CANCER TO SEX

	1911	1912	1913	1914	1915	1916	1917
Females	26,499	28.067	29,883	31,138	32,066	34,576	34,121
Males	17,525	18,464	20,045	21,282	22,518	24,024	24,498
Difference	8,974	9,603	9,838	9,856	9,548	10,552	9,623

[1] WILLIAMS, *loc. cit.*, p. 57.

Cancer is relatively less frequent among certain classes of individuals than among others, and all evidence seems to point to a lessened mortality from this disease in accordance with certain conditions of life.

Thus, among the Jews, while divergent statements have been made in regard to the relative per cent of mortality from cancer among Jews and non-Jews, there is a very considerable unanimity of experience that cancer of the uterus is very much less common among the former than among the latter; in the statistics from Budapest for several years, the ratio of deaths from uterine carcinoma to all carcinomas was about one-third, for Jews. When the greater length of life is considered, and the greater frequency of marriage and prolific child-bearing are realized, this very much smaller proportion of deaths from the disease in this location is the more remarkable.

Some observers, however, have claimed a larger proportion of cancer deaths among the Jews than among others, but as these statements have been analyzed by Williams[1] and Hoffman[2] it would appear that the evidence of greater longevity, together with the social position *of different groups of Jews* in different localities, would account for the diversity of opinions expressed. The concensus of opinion seems to be that orthodox Jews, especially of the poorer class, observing their ritual life are much less subject to cancer than the rest of any population.

The negro race presents also a striking instance of the difference in the mortality from cancer under varying conditions. Quoting from Williams[3] "In their native African homes the ancestors of the negro slaves of the United States, like other similarly situated savages, are believed to have been almost exempt from malignant tumors. . . . Transplanted to the United States, and having lived there in slavery for over two centuries, these negroes have been found to have acquired greatly increased liability to cancer, to which, however, they

[1] WILLIAMS, *loc. cit.*, p. 16ff.
[2] HOFFMAN, *loc. cit.*, p. 147ff.
[3] WILLIAMS, *loc. cit.*, p. 14.

were very much less prone than their white masters." This is clearly shown by the 1917 United States Mortality Statistics. The North American Indians afford, also, an illustration of relative immunity from cancer in their native state, with increased mortality under changed conditions of life. These, and other here mentioned facts, will be more fully considered in subsequent chapters on "Civilization and Cancer," and "Diet and Cancer."

Cancer is thus seen to be a wide spread and increasingly fatal disease, in spite of prodigious efforts to check its progress by extensive and intensive laboratory study, and increasingly bold and skillful surgery. Of late there has also been strenuous work put forth along the line of the education of the profession and laity by various societies in regard to the early recognition of the disease and the necessity for immediate surgical operation. As we have seen in the previous chapter, and as will appear later, all this is based on the erroneous supposition that cancer is a wholly local affection, and that the early and complete removal of the particular local manifestation of the disease will effect its *cure*.

The fallacy of this latter supposition has been abundantly proven by every one who has seen much of cancer for many years, and by the steadily rising mortality which has been set forth in the preceding pages.

For a hundred and more years candid physicians and surgeons of great prominence have briefly voiced the opinion that cancer was certainly not a purely local disease, but that back of it all there was some constitutional disturbance, details of which will appear in a later chapter. In the study of the chemistry and metabolism of cancer there will appear the grounds upon which its study and proper treatment are to be based.

It is strange that the medical profession should be so slow in accepting, or unwilling to accept and act upon the suggestions along this line which have been thrown out from time to time for many years by many men who were well acquainted with

cancer, and who felt and expressed their inability to cope with this distressing and fatal disease. But light begins to shine, and from all over the country in medical societies, book reviews and by personal letters, come the encouraging statements of those who accept the line of thought and action in regard to cancer set forth in these pages.

The writer is well aware that there have been many clever attempts to discredit the value of the statistics which have been thus far available for the study of the progress of cancer throughout the world. These relate principally to the greater care exercised by governments and individual physicians in regard to accuracy of records, etc. But until better statistics are procured it is but reasonable to work with those we have, and any criticisms can hardly affect the fact that under the past treatment of cancer the death rate has most certainly increased with a steady and really alarming rapidity, especially when compared with the steady decrease in the mortality from tuberculosis. Whatever the surgeon may have accomplished in regard to "cancer in the individual," no progress has been made, but rather the reverse has occured, in regard to "cancer of the race," either by surgical activity or by the immense amount of labor and money which has been bestowed upon laboratory work.

CHAPTER III

RELATIONS OF CIVILIZATION, SO-CALLED, TO CANCER

Civilization has been defined as a "reclamation of mankind from the savage state, and instruction in the arts and refinements of cultivated life," also "a condition of organization, enlightenment, and progress." The term, being derived from the Latin civis, a citizen, originally implied the urbanization of rural or nomadic peoples. But modern so-called civilization is quite a different affair, and involves modes of life which are far away from the simplicity of living of earlier times which conduces to perfect health.

In the sense of culture and refinement, civilization *per se* can hardly be associated with disease, for in many urban communities the standards of life have been simple, and gluttony, debauchery, and intemperance have been regarded as vices of a lower class of people, and have often been discountenanced. In regard to urbanization of nomadic races, this has been going on for thousands of years, but there has never been a "cancer problem" until recently, within a generation. Even today, in the Italian peninsula, where civilization has flourished for some 4000 years, or since the days of the Etruscans, cancer has hardly become a menace to the entire people, and its incidence is still relatively low and without great tendency to increase. On the other hand, there are some reasons for believing that cancer may have occurred more or less frequently in past centuries. Civilization was not very far advanced in England in the days of John Arderne, who flourished about 1300, but not only does his description of rectal cancer show a wide experience, but he states clearly that he had seen many deaths from this cause, and not a single recovery.

While modern civilization, so called has its advantages, it has also its disadvantages. All recognize that the mortality of tuberculosis had been steadily increasing of late years, from the evil effects of over crowding, bad sanitation, and erroneous life, until wiser methods of treatment have more recently succeeded in arresting its rising progress, and greater care has lessened its death rate immensely, almost 30 per cent since 1900.

Cancer incidence has also been steadily increasing of late years all over the world, under advancing civilization, and the death rate has not diminished, but has steadily and alarmingly increased in the same proportion as that of tuberculosis has declined. The deaths from cancer have increased so surely and persistently that unless something occurs to arrest the continued progress of the disease, cancer will soon outstrip tuberculosis in its morbidity and mortality. For the death rate of the two have approached each other almost 60 per cent since 1900; while tuberculosis mortality in the United States has steadily dropped from 201.9 per 100,000 population to 141.6, or 29.8 per cent, that of cancer has risen from 63 per 100,000 in 1900 to 81.8 in 1916, or 29.84 per cent. Since that date it has fallen a trifle, possibly owing to a better understanding of the nature and proper treatment of the disease. But in New York City the registered deaths from cancer actually outstripped those from tuberculosis in the period from July 1st to December 31st, 1920; the deaths from the latter were only 2,669 against 2,691 from cancer, which were 22 in excess.

The rational deduction from this steady increase would seem to be that we should inquire as to whether there has not been something radically wrong in our conception of the nature of cancer and its treatment up to the present time. Moreover, not only is cancer of high and increasing incidence and mortality in most civilized countries, but it also shows a marked tendency to attack primitive and previously immune races, within a comparatively short time after they have lived among the civilized whites and adopted their customs.

But this seems to be only one aspect of a much larger problem. What is true of cancer is true also of a dozen other conditions which are known collectively as "white men's diseases." As such may be mentioned appendicitis, arteriosclerosis, cardio-vascular diseases (which now lead the list of causes of death), renal disease, diabetes, so-called uric acid disease or atypical gout, metasyphilis, insanity, neurasthenia, dental caries, pyorrhœa, etc. Other conditions which may be mentioned in the same connection are low birth rate and race suicide, sexual anæsthesia, increased tendency to divorce and abandonment of wives, the assumption of man's activities by women, and much else which points to a profound upheaval in the white race. It has been shown that the Nordic races, which have for many centuries dominated the world, are in process of extinction. They have been the world's great conquerors, colonists, and civilizers, but as Woodruff has shown, cannot persist racially in tropical and sub-tropical countries.

From what we know of historical pathology man was originally immune to disease, and only when a race had arrived at a period of decadence did it become subject to the latter. It is conceivable that with species as with individuals, longevity varies. Thus, we can conceive that what is called civilization "ages" a race, just as a certain kind of living "ages" an individual. The latter is an optimistic view, because it suggests that regeneration is possible. For centuries it has been preached and taught that a return to primitive customs, so far as these are rational, living in the open and in touch with Nature, a simple diet, a life of moderate activity, etc., act as a preventive of disease, and a cure for disease not too far advanced. This has been abundantly proven in regard to tuberculosis, in spite of the continued presence of the bacilli.

We must now analyze what is known as civilization, and isolate the factors in it which may have special reference to the incidence of cancer, for the human being influenced by so-called modern civilization differs materially from the primitive man in many respects. The chief elements relating to life are food,

sleep, neurotic influences, housing, clothing, occupation, habits of life, reproduction, etc.

Food.—This will be more fully considered in a later chapter, but some general points may be considered. The more primitive types of men, and even some classes of white men today, are seldom exposed to a constant surfeit of food. But the prosperous city man has manifold temptations to eat and drink wrongly and immoderately, and all recognize that over-eating is a most common error. The appetite is often increased by stimulants before or during meals, and the three or less simple meals daily, of the more primitive or sensible person, are often increased to four or five. The Englishman is famed for his capacity to eat as compared with other civilized men, but he offsets this in part by his habits of exercise and sport. When this type of man becomes too old for an active life, but continues to eat, he suffers from certain well-defined symptoms, which yield when he readjusts himself. Later we shall see that, as far as relates to cancer, this gluttony involves largely the consumption of much meat, or some form of protein, for without plenty of these substances over-eating is hardly conceivable.

Sleep.—Those who see much of chronic disease, and study the tendency of the times, recognize that in so-called highly civilized communities the customs in regard to sleep are far different from those of some years ago, and entirely different from those of the primitive man. Late and irregular bed hours are the rule, rather than the exception, and the rest and refreshment from "Nature's sweet restorer" are often far from what could be desired, or from what was secured by primitive man. As contributory to be deranged blood current which causes cancer, this may be of significance.

Neurotic Influences.—Closely connected with the last mentioned element are the nervous conditions appearing with modern civilization, as compared with those of the primitive man. The uncivilized man is dominated heavily by custom and traditional beliefs, and in adhering to his tribal customs he escapes cancer to a very large extent. He must be quite free

from ambition, as we understand the term, for with him this is limited to proficiency in war and hunting, as shown by his collection of trophies and spoils of war. His responsibility is similarly limited to playing his proper role in tribal life. He has few worries, limited perhaps to fear of famine, earthquakes, etc. He is almost always a fatalist, and this prevents him from worry. He is also free from sympathy, and is usually indifferent to the woes of others. Of anything like home life he has no conception, his hut being chiefly a place of refuge in inclement weather and a protection from other accidents. That it is a place to enjoy life would never occur to him. The uncivilized man works when he must work, and whatever there is of routine drudgery is done by women. If we contrast this life with that of the so-called civilized people, with their constant anxieties, rush and whirl of life, seeking wealth and pleasure, the differences appear to be extreme and conducive to disease.

Clothing.—In regard to this there is not much to say, except that the corset has often been accused of being a factor in the causation of cancer of the breast. But we know that the vagaries of clothing have much to do with diseases of other kinds in civilized life, and it is possible that some influence therefrom may ultimately be traced in regard to cancer.

Occupation.—The contrast between the occupation of those in highly civilized life and those living primitive lives is very striking, and we know that there are many occupational diseases, and that some of them undoubtedly have some bearing on the question under discussion. Chimney-sweeps' cancer was once a very serious menace in England some years ago, now averted by mechanical cleaning of chimneys. Workers in tar, petroleum, and certain analin chemicals are said to be subject to epithelial cancer, and the disastrous results following careless exposure to *x*-rays, both in those who manufacture them and those who employ them therapeutically, are well known to all. Sailors and those much exposed to the elements are subject to epithelioma of the face and hands. But, as stated elsewhere, these local degenerations of epithelial elements are

not included in our study of cancer as a disease, as they are amenable to local measures of treatment, which experience shows is not the case in true cancer of internal organs, in which there is abundant evidence of deep constitutional causes, often of long standing. Undoubtedly some occupations which lead to erroneous modes of living, such as indulgence in alcohol or faulty hygienic conditions, etc. may be shown to have an etiologic relation to cancer.

Habits of Life.—These, such as excessive or faulty eating and drinking, indolence, and irregularities of many kinds, certainly have a very great bearing on the production of cancer, as will appear elsewhere.

Reproduction.—With primitive man, as with animals, this is a normal process, an integral part of life, most cherished, as it should be, throughout the world. But the differences between so-called civilized and primitive types of human beings are very marked here. The reproductive life of the latter is simple, the women usually bearing a child every second or third year, during the reproductive cycle. In this way the reproductive organs are constantly being normally occupied. The mothers suckle their children normally. In a sophisticated people, who are not necessarily worthy to be called civilized, birth control, abortion, contraception, etc., are all practiced, while venereal diseases flourish.

It is not necessary to go to primitive people to visualize the remarkable change which has come over some of the white women within comparatively recent times. Very large families have been succeeded by moderate, and these again by very small families, or none at all. Here civilization, in the proper significance of the term has been at fault, as shown by the attitude of the cultivated woman toward reproduction. Apparently she is satisfied to produce only the number necessary to make up for the losses by death. In ability to withstand the shock of labor, lack of expulsive force, necessitating artificial aids to labor, inability or unwillingness to nurse her child, the great increase in cases of sexual indifference, the frequency of

vaginismus, late marriage and frequent divorce and desertion, are all something recent. The net result is that the uterus and breasts of the modern civilized woman have but little to do, and are active in an extremely small portion of the reproductive cycle. This disuse should result in some form of disease or degeneration, and cancerous disease of these organs has shown a steady and remarkable increase during later years. In Sweden and some other countries, where large families are the rule, cancer of these organs is rare as compared with that of the stomach and other organs.

We will now consider some of the evidence from statistics that the morbidity and mortality of cancer have increased to such a degree in countries and localities where the influence of the white man and his customs of life have entered largely, that there can be hardly any doubt but that what is called modern civilization has had very much to do with this increase. It is therefore, upon the recognition and rectification of these factors in its production that the true prophylaxis and cure of cancer rest, even as has been the case in the treatment of tuberculosis.

Abundant testimony has come from all over the world that cancer is very rare among aborigines, living simple, mainly vegetarian, lives. Supporting this is the vast amount of evidence collected in the admirable works of Williams, Hoffman, and Wolff, already referred to and from which we will quote largely: Hoffman is particularly impressive in 470 pages of tabular statistics, taken largely from official records throughout the world.

In New Zealand, according to Hislop and Fenwick, where the general death rate is the lowest in the world, cancer is on the increase as civilization advances. In the great majority of cases the alimentary canal is the seat of invasion, even in women: all the patients were hearty eaters, taking also very much strong tea many times daily.

The Polynesians and the Melanesians seem to be peculiarly exempt from cancer. Sir William McGregor, although he had operated several times on whites in the Fiji Islands, never

remembers operating for cancer on a Polynesian or Melanesian, who are practically vegetarians. He never saw a case of cancer in British Guiana in 9½ years, and then saw an encephaloid cancer of the tibia in a Papuan, who for 7 or 8 years had lived practically a European life, eating canned Australian meat daily.

In Australia cancer is reported to be very infrequent among the natives and Wolff gives a very striking table in regard to the progress of cancer among the native born and foreigners, as follows:

OF 100,000 LIVING THERE DIED OF CANCER IN AUSTRALIA

Year	Number of inhabitants	Native born	English	Other Nationalities
1851	403,889	....	28.0	14.0
1861	1,153,973	5.6	30.5	19.0
1871	1,168,377	9.7	56.7	25.0
1881	2,252,167	16.8	72.9	32.6
1891	3,183,237	19.8	119.8	45.9
1901	3,771,715	22.6	203.1	57.3

He remarks: "We see from this comparison in what a great degree the death rate from cancer has increased in foreigners as compared to the native born, in whom disease has remained about stationary, when the increase in population is considered." Another writer remarks that when native Australians mingle with foreigners as servants or employees, and adopt their diet and customs, cancer occurs more frequently in them. Much the same has been reported in regard to other peoples and nationalities.

In regard to Africa, Williams quotes Dr. Madden of Cairo, who says: "The concensus of opinion among medical men in Egypt is, that cancer is never found, either in male or female, among the black races of that country. Of 19,529 deaths among natives of Cairo in 1891, only 19 were due to cancer, (females 10, males 9) or 1 in 1, 028." In England during the

same year the proportion was 1 : 29 deaths from all causes. In the Islands of Lagos, on the West Coast of Africa, Dr. Johnson, in 14 years' practice there saw five cases of cancer in natives, all of whom lived as Europeans. In southern Africa, "among Boers and Europeans, who are large flesh eaters, malignant tumors are common; but among the natives, who are mainly vegetarians, these tumors are so rare as to be almost unknown."

Renner reports interestingly in regard to cancer among the descendants of liberated Africans or Creoles, in Sierra Leone, Africa. During 30 years, from 1870 to 1900, there were but 20 cases of malignant disease recorded among 22,453 admitted to the Colonial Hospital: in the next 10 years there were 26 among a total of 10,163 general cases, a low but steady gain in cancer incidence, with the advancing influence of the white man. Every case of cancer recorded was in a Creole, living like a European, and not a single case among the aborigines.

In India all writers agree that cancer is rare among the natives living simple lives, although some have claimed that the disease is more common than previously supposed; but its incidence there still bears no relation to that in many other countries, and an analysis of some recent reports explains in an interesting and curious manner the reasons for the diversity of opinion as to the actual frequency of the disease.

Thus, Benratt collected a total of only 1,700 cases of cancer from 5 years' statistics of 15 Mission Hospitals and 34 Government Hospitals, representing of course many million inhabitants, whereas in New York City alone, according to the weekly Bulletins of the Board of Health, there were 2,670 deaths from cancer in the first six months of 1920: a striking illustration of the relative rarity of cancer in India. Moreover, of these 1,700 cases in India over 1,200 were about the mouth, a very large share or almost all of them arising from the very common habit, in men and women, of chewing betel, which contains much calcium, which latter is one of the salts incriminated in the causation of cancer.

Sandwith also attempts to show that cancer is prevalent in

India, but refers to only 2,000 cases reported in the hospitals there in 3 years, also among many millions of people, and he refers to the betel chewing cancer and the "kangri burn" on the abdomen of men, from the charcoal furnace worn for warmth; many have doubted if the latter were true carcinoma, but only an obstinate local dermatitis; such peculiar local disorders certainly vitiate any deduction which could be drawn from such statistics as to the occurrence of true, deep cancer in India. Against all claims as to the frequency of cancer in India may be mentioned the fact, stated in the table in the previous chapter, that the death rate from cancer in Calcutta was only 11.8 per 100,000; this is shown in the Imperial Cancer Research scheme, where it is stated that the principal form is that of the buccal cavity, attributed to the betel chewing by every native, it consisting of tobacco, betel leaves, areca nut, and a little slacked lime.

In China all observers agree that cancer is very uncommon among the bulk of the people, but frequent enough among Europeans there resident. Hoffman gives some interesting tables, one of which may be quoted.

MORTALITY FROM CANCER PER 100,000, IN HONGKONG, CHINA, BY RACE, 1901–1910

YEAR	CIVIL EUROPEANS	CHINESE
1901–1905	49.0	5.4
1906–1910	52.7	5.5

In Shanghai the cancer mortality among Foreigners had risen in 1914 to 97.9 per 100.000 residents.

Even in Manilla, Philippine Islands, the mortality per 100,000 among the Chinese was only 18.8 against 50.6 for the white population, and 27.0 for the Philippinos, who naturally mingle much with the whites and follow in their ways.

In Japan cancer is much more prevalent than in any other of the Far East countries, and from 1899 to 1911, the mortality had risen from 44.0 to 66.9 per 100,000 population. In the cities it was still greater, in Tokio 72.8 and in Kyoto 85.1, showing clearly the baneful influence of so-called modern civilization.

In regard to the general occurrence of cancer in the Far East, I may add a bit of personal observation. During a rather extensive trip, I was unable to see or even hear of any cancer, although I met a large number of very intelligent medical men and made diligent inquiry regarding the same. As I wished to verify my views in regard to the rarity of the occurrence of cancer among those who lived on a rice or other vegetarian diet, I visited very many civil, military, and mission hospitals, with a total of many thousand patients, and ministering to many millions of population: in Japan, Korea, China, the Philippines, India, Siam, and Egypt, I met the same response, that cancer was rarely seen among those vegetarian nations.

In the Near East we have relatively little information as to the prevalence of cancer. But only very recently a medical missionary, who has long been connected with the medical college and hospital in Beirut, Syria, told me that cancer was practically unknown among the thousands of patients who flock there from all over the Near East; he adding that they were all largely vegetarians. We are told that cancer is rare among Mohammedans, who live simple lives and avoid alcohol, and in the preceding chapter we saw that the cancer death rate in Constantinople was 34.8 per 100,000 population; and of these the Mohammedans had but 22.6, while the highest rate was among the Greeks, who had 56.1 per 100.000.

Brazil, especially in the equatorial regions, is credited with having the lowest cancer death record of any portion of the Western Hemisphere, with a death rate in 1903 of only 4 per 100,000: in Rio Janeiro it was about 26 per 100,000, showing, of course, the effect of civilization. In Uruguay cancer is comparatively common, the death rate in 1897 being 47 per 100,000 while in Argentina, where very much meat is eaten, the rate in 1900 was 91 per 100,000

In Mexico cancer is said to be fairly common among those of European descent: in the city of Mexico the death rate in 1913 was 48.2 per 100,000, but the females were far in excess of the males, 69.4 to 23.7. In Nicaragua it was 10.6, in British Hon-

duras, 14.7, in Venezuela, 14.7, in Jamaica, 18.4, and in the British West Indies, 20.9 per 100,000.

In Canada the mortality from cancer seems to vary with the intensity of civilization, that for the rural district of British Columbia being 30.3, in the Province of Ontario, 69.4, and in the city of Toronto, 81.9 per 100,000, while among the aborigines of Canada it is reported that the disease is very infrequent.

In Iceland, according to Stephanson, who was specially requested by Dr. H. C. Ross to inquire into the prevalence of cancer among the Eskimos, he reported that he had found none among them whatever.

An interesting study of the effects of modern civilization upon the mortality from cancer may be made from an examination of its increase in certain localities, a few of which will suffice.

In France, cancer mortality in 1892 was 88, and in 1905 it was 100.2 per 100,000 inhabitants, while in Paris it had risen from 97.2 in 1881 to 112.4 in 1912.

In Germany deaths from cancer increased from 53.5 in 1891 to 90 per 100,000 living in 1912, and in Berlin from 64.6 in 1881 to 132.8 in 1912, that is it has more than doubled in proportion to the living inhabitants.

In Holland the mortality from cancer rose from 57.6 per 100,000 in 1881 to 109.5 in 1903. In Amsterdam the rise was from 72.2 to 114.8 in the same period.

In Belgium the rise in the mortality of cancer was from 59.4 per 100,000 in 1903 to 71.3 in 1912. In Antwerp it was from 47.6 in 1896 to 90.9 in 1912, and in Brussels it rose from 88.2 per 100,000 living in 1901 to 106.2 in 1912.

In Italy the death rate from cancer was 21 per 100,000 in 1880, and 1912 it was 64.7. In Rome it had risen from 79.1 in 1898 to 99.6 per 100,000 in 1912.

Space does not permit of the evidence which has been so carefully collected by Williams, Hoffman, and Wolff to show the inter-relation of tuberculosis and cancer to the conditions of life in various localities, but a careful study of the statistics which

Williams gives warrants the rather remarkable statement which he makes as follows:

"Such an examination shows that the cancer mortality is the *lowest* where the struggle for existence is the hardest, the density of the population greatest, the tubercle mortality highest, the birth rate highest, the average duration of life shortest the infantile and general mortality highest, and where sanitation is least perfect, in short among the industrial classes in our large towns; whereas among the wealthy and well-to-do where the standard of health is at its best, and life is easiest, and all conditions are just the reverse of the foregoing, there the cancer mortality is *highest*."

These are strong words, and may be contested by some, but a very careful consideration of the facts and statistics collected by Williams will convince the impartial student that they are not far from the truth.

All are familiar with the clinical history of tuberculosis. When from unsanitary surroundings, poor nourishment, and overwork, together with deficient oxygen, the patient's health fails, there comes a time when a focus of tuberculosis is discovered, and, unless checked by a reversal of the conditions inducing the depression of health, the disease becomes fatal.

With cancer, however, the clinical history is quite the reverse. The subjects of beginning cancer are commonly seen to be in apparently excellent health: they are often ruddy and blooming in appearance, and can hardly be made to believe that the dire disease has actually begun in them.

The two diseases represent exactly two opposite phases of nutrition, both induced by the fundamentally different conditions of life pertaining to advanced civilization. In the former there is commonly under-nourishment with overwork, while in the latter there is habitually an over-nourishment with under-work. In the period from 1881 to 1890, Dr. Latham, Registrar General, found the death rate from cancer in England to be more than twice as great among well-to-do men having no specific occupation, as it was among occupied males in general,

the mortality ratios being 96 for the former as against only 44 for the latter.

If it were necessary a mass of evidence could be adduced to show that cancer is a disease of "hypernutrition," as Williams remarks. This does not mean that normal nutrition can be overdone, if all the contributing factors are correct. But the complex of modern civilization, with all its temptations and errors in regard to eating and drinking and living, together with its nervous strain felt everywhere, and the absence of sufficient and proper physical exercise, has produced such a disturbance in the normal metabolism and nutrition, that, under some slight provocation a heterologous growth of certain tissue cells results, with malignant tendencies, instead of the normal, homologous, and stabile structures which compose healthy tissues: and this departure from normal cell action, we call cancer. What these disturbances are will appear in subsequent chapters.

The fact remains that while cancer is very infrequent among primitive people, and among animals living in a state of nature, it has been shown to increase very steadily in morbidity and mortality with the intensity of human civilization, and also among animals as they become domesticated, or kept under unusual conditions, as in Zoological Gardens and laboratories. There cannot, therefore, be any other conclusion than that this dire disease depends largely upon the conditions developed by or associated with our artificial existence, to which is given the name of "modern civilization."

CHAPTER IV

HISTO-PATHOLOGY OF CANCER

The histology of cancer is a vast subject, which of late years has occupied the attention of a great number of earnest and faithful workers, and it is quite impossible even to consider much of it in a single chapter. But the endeavor will be made to present sufficient of the details to help to an understanding of the subject before us.

Dr. Ewing's monumental work,[1] of over one thousand pages, well demonstrates the vastness of the subject and the difficulties of the study, and presents many conflicting views on many points, but with clear judgment in regard to them; it is indeed a mine of knowledge, from which I shall freely draw.

The term cancer has sometimes been employed to designate any rebellious tumor, or neo-plastic growth, of which Ewing gives a list of twenty-three. But in our present study we con ide only carcinoma and sarcoma, the former a disease of erratic epithelial structure, the latter disorder of the connective tissue type. Epithelioma, or as Ewing designates it, "epidermoid carcinoma," affecting the skin, is not, in the main, included in our study of cancer as a disease, for reasons to be stated later, but much has been learned of the behavior of diseased epithelial cells from its microscopial study, and it will be first considered.

Cutaneous epithelioma represents a disordered or vicious growth of the epithelium of the epidermis, or of the glands and follicles. Ewing makes two main histological types. 1. Hornifying cancroid, or acanthoma, and 2. Basal cell carcinoma. Krompecher named the two varieties. 1. *Epithelioma baso-cellare*, and 2. *Epithelioma spinocellare*, according to the layers of the skin in which each is supposed to originate, and this division and nomenclature is commonly adopted. These

[1] EWING, "Neoplastic Diseases." Philadelphia, 1919.

two forms differ materially in their clinical and histological features, the first being relatively benign, and seldom metastasizing, while the second is far more virulent and destructive; it is of much more rapid growth, and tends greatly to metastisize, as seen especially when it occurs on mucous surfaces.

Baso-cell, or Tubular Epithelioma.—This, the mildest form of epithelial degeneration, arises from the basal-cells of the Malpighian layer and of the ducts of the sweat, hair, and sebaceous follicles.

Microscopically it is characterized by the prolongation into the lower tissues of plugs or masses of epithelial elements, resembling the basal-cells of the epidermis, small, polyhedral or spindle, with relatively large vesicular nuclei, minute nucleoli, and scanty cytoplasm: no epithelial pearls are present, and the cells invade the surrounding tissue in groups. In fact the cells show some approach to those of an endothelial type, and some observers have maintained that these growths are really endotheliomata. These tumors are strikingly different from the ordinary forms of cancer, and represent the small, superficial, slow growths in the skin, that appear upon the face, nose, ears, and upper lip, and are relatively amenable to careful and proper local treatment: the *x*-ray generally removes them, often with inappreciable scar, as also radium, and thorium paste. But, on the other hand, when wrongly treated, as for instance with nitrate of silver or otherwise, they may become very destructive, invading large areas and extending deeply (rodent ulcer, Jacob's ulcer), but rarely metastasize.

Spino-cellular, or Lobular Epithelioma (the Acanthoma of Ewing).—This is of quite a different character. The tumor here is composed of large cells, with a relatively great amount of protoplasm, and well formed nuclei: the latter frequently show mitotic figures. The cells distinctly preserve the epithelial type, in form and characteristics, and intercellular union in the form of prickle cells is present. Epithelial pearls, due to the inherent tendency of the cells to the normal life history of spine cells, are a special feature of these tumors. The growth of the

lesions is rapid, and metastases are of frequent occurrence, even in distant parts, as the liver and bone-marrow. Ewing says that "this tumor arises from previously normal epithelium, after a period of over-nutrition and overgrowth, during which the sub-epithelial tissues become altered and less resistant. Lymphocytic infiltration, swelling with mucoid or other forms of degeneration, followed by atrophy of elastic tissue and chronic œdema or fibrosis, usually but not always precede the downward growth of epithelium." These latter descriptions of acanthoma apply equally or even more truly to epidermoid cancer of the tongue and mouth.

Gastric Cancer.—Here as elsewhere the epithelial element of cancer is stikingly manifest, as the enormous number of epithelial elements lining the pyloric and peptic glands afford an ample source of malignant degeneration, under the varying influences of substances presented for digestion. Cancer may develop in any portion of the stomach, but the region of the pylorus and lesser curvature are the parts most affected, in even up to 75 per cent of the cases. Ewing distinguishes six types of the disease, but the two principal forms are adenocarcinoma and scirrhus: the question of the relation of peptic ulcers to carcinoma is still a disputed one, various observers place the relation from 2 or 3 per cent to over 50 per cent of ulcers of the stomach which develop into carcinoma. We will not here attempt to discuss the immense subject of gastric cancer, but briefly consider the two principal forms of the disease. All recognize, however, that simple ulcers in other localities, as in the mouth, can and do take a malignant character, and there is no reason why those in the stomach should not do the same, under the continued and often repeated irritation of food, with a continuance of the constitutional condition which lies at the bottom of all cancer.

Adeno-carcinoma of the Stomach.—The structure of gastric adeno-carcinoma presents somewhat orderly imitations of the gastric tubule. The originating tubes become much elongated, bifurcated and sacculated, and the tumors are composed of such alveoli compactly grouped, with little stroma. The cells are

cylindrical or cubital, the cytoplasm clear, and the nuclei hyperchromatic. The lumina of the alveoli are usually small, or they may be distended with mucus and exudate, or secondary alveoli may form within the acinus. The adeno-carcinomas are regularly embedded in the submucosa, which may be widely infiltrated, and in the muscularis, which is usually perforated; but extensions to the lymphnodes may be long delayed. All these growths are comparatively solid on section, resembling medullary carcinoma, but some show accumulation of mucus, and areas of fatty degeneration, hemorrhage, and necrosis.

Scirrhus Carcinoma.—This is a slowly progressive type of the disease, which is characterized by its wider extent, more cellular, of fibroid nature, and frequent metastasis. The entire organ may be involved, and greatly reduced in size by cicatricial contraction. The pylorus and other areas of mucosa may be eroded over a wide extent, and pyloric stenosis is common, but there is seldom destructive ulceration.

Ewing regards it as thoroughly attested that carcinoma of the stomach arises from the previous normal glands, through a process beginning as localized overgrowth, and that this takes place primarily in the epithelial cells, which usually show preliminary disturbances of over-nutrition and excessive function, as was mentioned in cutaneous epithelioma. There is, however, a considerable gap between the ordinary condition of inflammatory overgrowth and definite adeno-carcinoma in the stomach, and this gap appears to be bridged, if at all, by a rather sharp morphological change which is established rapidly. The single glands and minute groups of glands exhibit a pronounced alteration, while surrounded by normal or slightly altered tubules. The original cancerous area may be single or composed of multiple foci, which later fuse together. From this area of origin the tumor tends to grow from its own elements.

The enormous supply of lymphatics in the stomach play a most important part in the extension of cancer and in metastasis elsewhere, and the impossibility of absolutely eradicating all

slightly affected nodes explains in part the unsatisfactory ultimate results of surgical procedure.

But cancer of the stomach also extends itself, and involves adjoining tissues by its well known tendency to advance into any organ or part contiguous to it, for cancer respects no anatomical divisions. Cancer may also spread through the vascular system, as when it ulcerates into a vein, and as the blood vessels of the stomach communicate directly with the portal system, the liver is most commonly affected. When the disease has advanced so as to involve the peritoneum, free cancer cells may be scattered over the general peritoneal cavity and even be found upon the anterior surface of the rectum.

Carcinoma of the Intestine.—This differs greatly in frequency in different portions of the intestinal tract, from being very rare in the duodenum, more common in the colon, and most frequent in the sigmoid flexure and in the rectum: it may occur in younger persons than cancer in other locations. The histopathology is much the same as in carcinoma of other mucous surfaces, adeno-carcinoma predominating.

The disease arises usually in a circumscribed area of mucosa, in which the glands become enlarged, the lining cells hypertrophied and multiplied, and bifurcated. The neoplastic alveoli soon break through the muscularis mucosæ, and extend along the submucosa, often reaching the surface at lateral points, and thus extending the lesion, or penetrating the muscularis along lymph and blood vessels. In the early stages of most cases, and in some instances throughout the disease, there is a gradual extension of the area of origin by the progressive transformation of normal into neo-plastic alveoli. Intestinal polypi play an important part in the histogenesis of cancer in the large intestine.

As in cancer in all other localities, continued local irritation is probably the effective agent in the actual localization of the diseased process in the intestinal tube. Thus, the largest number of cancers occur in the sigmoid flexure and rectum, where the fecal matter is more solid, and may be retained for some time,

while it is least frequent, or very rare, in the descending colon, which is empty much of the time, and again more common in the transverse colon. The pendant cecum, at the other end of the colon, which first receives irritating and other substances from the ilium, and where there is often an accumulation, and also the appendix, are frequent sites of cancer in the intestine.

Cancer of the Rectum and Anus.—In 1914 this caused the death of 2,171 persons in the registration district of the United States, 4.1 per cent of all carcinomas, or 3.3 persons per 100,000 population. Over 80 per cent are due to adeno-carcinoma, and a small percentage to epithelioma, beginning at the anus. Within the rectum, as in the case of the urinary bladder, polypi, which are quite abundant, appear to be the starting point of the malignant disease. The anatomical form of the carcinoma varies extremely. The polyps may be very small, very numerous, widely distributed, and the entire mucosa hyperplastic, or they may be large and less numerous. The carcinomatous process usually begins in a single polyp, involving others later: as a rule, one or more of the polyps are malignant, the others benign. In structure the tumors show various types, malignant adenoma, adeno-carcinoma, and alveolar carcinoma. Ulcer of the rectum may degenerate into a carcinoma, but it is not thought that hemorrhoids have any great predominating cause. Constipation, with the urgent efforts of the rectum to relieve itself, is certainly a very important element in its causation.

Carcinoma of the pancreas is not infrequent, as a primary or secondary disease, it representing 1.3 per cent of all deaths from carcinoma in the United States in 1914, with a rate of one person per 100,000 population.

The location of the tumor is usually in the head of the pancreas, or extending diffusely over most of the organ, and the tail is rarely affected. Two main types of pancreatic carcinoma are observed: 1. Cylindrical cell adeno-carcinoma, arising from the ducts, and 2. Carcinoma simplex, arising from the parenchyma. The structure of adeno-carcinoma is composed of papillary outgrowths and alveoli, lined by cylindrical or

cuboidal cells. The local extensions of the tumor have been traced through ducts, lymphatics, and nerve trunks. Carcinoma of the parenchyma produces a more diffuse, rapidly growing tumor, which is firm or soft according to the proportion of fibrous tissue. The cells are small or large, granular, hydropic, or fatty, resembling those of the pancreatic alveoli. The cell borders are often indistinct, and the vesicular nuclei occupy most of the cell. Nucleoli are poorly developed, and the relatively large size of the nuclei is often a notable feature. Large mononuclear giant cells may appear in numbers, and also in metastases. The origin of this tumor has been traced, in an early case, to the pancreatic alveoli, and the transformation of gland cells into tumor cells has been sketched in detail. Extensions throughout the pancreas occur early and travel fast by ducts, lymphatics, blood vessels, nerve trunks and alveolar spaces. The islands of Langerhans are usually hypertrophied, and may be much increased in number, showing many transitions from secreting to island tissue.

Carcinoma of the Liver.—Primary cancerous disease of this organ is very rare, but from its connection with and approximation to other organs the deaths from cancer of the liver and the gall bladder caused the death of 9.8 persons per 100,000 living in the United States in 1914, a little over one-half of the number being attributed to cancer of the stomach.

Considerable difference of opinion exists in regard to hepatoma, or tumors in general which affect the liver, and their connection with cirrhosis, and it is difficult to present a concise statement in regard to carcinoma of this organ; Ewing makes seven varieties of neo-plastic hyperplasia.

Primary cancer of the liver undoubtedly begins as an adenoma, with angiocholitis proliferans as an antecedent. It has also been shown that there is a uniform gradation between nodular hyperplasia, multiple adenoma, and multiple carcinoma. During the transition the cells may retain the granular character of liver cells, while staining more intensely with basic dyes, or they may lose granules and pigment and assume

a transparent, embryonal character. Nuclear hypertrophy and hyper-chromatism are very constant, multi-nucleated giant-cells appear, and mitosis and amitosis are frequent.

Notable changes in the nuclei are often seen in neighboring liver tissue, forming a feature of collateral hyperplasia.

Secondary cancer of the liver may affect a large portion or the whole of the organ. The liver may be greatly increased in size, extending an inch or more below the costal cartilages, and its edge irregularly nodular. The whole surface becomes studded with white, carcinomatous masses. The microscopical structure shows extensive replacement of parenchyma by adenomatous and carcinomatous nodules. The process begins with hypertrophy and hyperplasia of cell groups, within the acinus, and apparently at any point within the lobule. These cell groups enlarge, forming nodules, which rapidly encroach upon the remaining parenchyma, with atrophy. The tumor cells are of large size, forming thickened liver cords, or the nuclei multiply actively, and numerous smaller cells resu t. Peculiar forms of nuclear division, chiefly of the amitotic type are observed: giant and syncytial masses often appear. Fatty degeneration may be prominent, and liquefaction may be added. The cells may be arranged in small regular alveoli, with a fine lumen, or the lumen may be wide, and the lining cells low cuboidal. Many transitions from adenoma to adeno-carcinoma are observed.

Carcinoma of the gall bladder and ducts exhibits about the best proof of the local disease developing as the result of long continued local irritation, some having claimed that in as high as 75 per cent of cases gall stones were found. But on the other hand in about 4,000 operations at the Mayo clinic on the gall bladder and biliary ducts, only about 2.25 per cent were for malignant conditions. Furthermore the innumerable successful operations for cholelithiasis, where no cancer existed, show that even this prolonged local irritation is not sufficient to induce the disease, unless the constitutional conditions exist which predispose to cancer: for we know that there may be

immense concretions of gall stones, dating back for years, even 25, without cancer, and symptoms of gall stones are said to be absent in the majority of cases of carcinoma of the gall bladder. Aside from minor variations the established disease presents two main structural types: 1. Adeno-carcinoma, and 2. Alveolar carcinoma.

Adeno-carcinoma is the most frequent form and produces papillary and scirrhous growths, and become universal in certain cases, which run the course of bulky and widespread gelatinous carcinoma. They early tend to perforate the wall and extend to the peritoneum.

In the scirrhous type extensive new growth of fibrous tissue surrounds the isolated adenomatous alveoli in the gall bladder, but in the lymph nodes and liver the cells grow more rapidly and fibrosis is wanting: the extent of the fibrosis is often remarkable.

Alveolar carcinoma in the gall bladder presents the usual features of this neo-plastic process. The most malignant growths are composed largely of pseudo-alveoli of small cuboidal or rounded cells. Others show many traces of adeno-carcinomatous structure, and the frequent transition of one type into the other indicates that both arise from the same glandular structure in the mucosa.

Squamous cell carcinomata, pure or associated with cylindrical cell carcinoma, are not infrequently observed, in which the squamous characters with pearls and spinecells may be found.

Cancer of the Ampulla of Vater.—Carcinoma arises in the corrugated mucosa of this structure, and at the duodenal papilla, but except in very early cases it is very difficult to determine the exact origin of the tumors. The tumors are small, villous or papillary growths, or diffuse infiltrations of the wall. Columnar cell adeno-carcinoma is the type almost always observed: the architecture is villous, fungoid, or infiltrating, without much variation in structure, with alveoli lined by smaller cubical or rounded cells.

Carcinoma of the Kidney.—The term hypernephroma, or adrenal rest tumor, has of late years been applied to all malignant tumors of the kidney, but Ewing rejects that name, and very clearly differentiates real carcinomatous tumors of the kidney, arising from its own epithelial elements. He discusses adrenal disease separately, under seven sub-divisions, as affecting the cortical or medullary divisions of the organ.

Malignant tumors of renal epithelium appear in two main forms: 1. Papillary adeno-carcinoma, and 2. Alveolar carcinoma. In general it may be stated that the two forms of carcinoma accord with the two chief groups of adenoma, from which many of them arise.

1. *Papillary adeno-carcinoma* is the most frequent of renal growths, of which three forms are recognized: (*a*) Papillary adenoma and carcinoma with clear or glassy cells: (*b*) Papillary adeno-carcinoma, or carcinoma with granular cells, and: (*c*) Malignant tumors arising from simple cystadenoma.

The first of these produces large, single, less often multiple, yellowish, circumscribed, vascular or hemorrhagic tumors, composed of villous or thin papillary strands of connective tissue, lined by one layer of cubical or cylindrical, clear, fatty epithelium.

The second form appears as multiple, solid, whitish and cellular growths, less distinctly encapsulated, commonly free from hemorrhage and composed of numerous branching strands of connective tissue, lined by one or several layers of opaque, granular epithelium, free from fat.

The third group includes cystadenomas which have become malignant.

In advanced and fatal cases these tumors become very large, destroying most of the kidney, and undergoing further necrosis, hemorrhage and cystic softening. They extend by continuity to kidney, renal pelvis with hydro-nephrosis, adrenal, lymph-nodes, and abdominal walls, and they invade the renal and other veins, often very early. Metastases are very frequent in the lungs, liver, and bones, chiefly in ribs, spine, skull, scapula,

and long bones, sometimes even 8 to 10 years after removal of the primary tumor.

2. *Alveolar Adeno-carcinoma.*—In this group are included the majority of malignant alveolar tumors of the renal epithelium. They are clearly separable from the carcinoma with clear cells, from papillary carcinoma, and from adrenal growths. The structure is uniformly alveolar or tubular, adult in type, and resembles the renal parenchyma. These tumors probably originate from well-differentiated renal blastema or from adult cortical tubules. These neoplasms may arise from any portion of the kidney, and may be located chiefly in the cortex or pelvis, which are widely distended, or beneath the capsule, or they may be extra-renal. Most of the tumors reach considerable and sometimes large dimensions. Fatty changes, hemorrhage, and necrosis are not prominent, but the solid, lobulated, opaque texture serves to distinguish them from adrenal growths and papillary carcinoma: small cysts containing gelatinous material are not infrequent. The highly malignant tumors infiltrate the kidney diffusely, perforate the pelvis and capsule, invade both veins and lymphatics, and produce metastases in many organs.

Carcinoma of the Urinary Bladder.—The deaths from carcinoma of the bladder were 1.5 persons per 100,000 in the United States in 1914, half more than those from the pancreas. Carcinoma of the bladder seems somewhat of a mystery. Its inception does not seem to be traced to any one cause of continued local irritation, as in the gall bladder, intestines, mouth, etc., but simply to the liability, from unknown cause, of the sluggish tendency of certain cells to take on malignant action; it is the best illustration of chronic inflammation affording the basis for malignant transformation of epidermic cells.

Vesical calculi are charged as the irritative cause, in proportions varying greatly with different authors, up to 30 per cent of the cases; but in Judd's series of 111 malignant growths they were present in only two cases. On the other hand, we know of vesical calculi existing for even 25 years without the production of cancer, and this disease is relatively seldom found in the

multitudinous cases in which stones are removed from the kidney, ureters, or bladder.

Chronic cystitis is also charged as a cause, as it naturally exists when cancer is found surgically. But the same argument pertains as in regard to calculi, seeing the large numbers of subjects having chronic cystitis for years without carcinomatous developments.

Papillomata, however, and mucous polyps, are very frequent in the bladder, and while many of them are benign, which have lasted 18, 30, and even 60 years, it is claimed that in 25 per cent. of cases they become malignant after a variable period; while some few of them are malignant from the first, and occasionally the removal of a benign papilloma will be followed by the development of carcinoma. Adeno-carcinoma may also be found in the bladder, though rarely.

Signs of malignancy in papillomas include much variation in the size and type of the cells, and extensive and irregular overgrowth, but the most important indications may be found in the pedicle, which is seldom accessible in operative material. Downward growth of the convoluted epithelium, invading the pedicle and subjacent tissue, is the chief factor in local recurrence and malignancy. There is reason to believe that chronic inflammation with œdema and round cell infiltration facilitate this downward growth and renders it posible, without any great change in the growth capacities or morphology of the cells. Frankly malignant papillomas exhibit throughout the atypical and lawless growth of carcinoma. Primary cancer of the bladder is thought to be relatively rare.

Secondary invasion of the bladder from the prostate, rectum, and uterus, etc., is not uncommon, and the differential diagnosis between this and primary tumor is often difficult, and at times impossible.

Cancer of the prostate caused the death of 1.2 persons in 100,000 population in the United States in 1914, and the proportion of cancerous disease in operative cases of prostatic trouble has been stated at from 16.5 to 21 per cent. The common form

of malignant disease of the prostate is adeno-carcinoma, although scirrhus carcinoma, and squamous epithelioma or acanthoma may occur.

The typical adeno-carcinoma presents large spaces filled with masses of atypical cells, forming numerous secondary alveoli. The size of the cells varies from large, clear, prostatic epithelium to small, granular, acidophile cells, and the carcinomas derived from them present corresponding varieties. The simplest form of adeno-carcinoma is the structure usually observed in the suspicious and pre-cancerous areas of chronic hypertrophy, but compact groups of small alveoli, as in malignant adenoma, also occur in these cases, and occasionally multiple layers of atypical cells completely fill the alveolus, and the structure passes directly into solid carcinoma. Pure adeno-carcinoma is doubtless not so active and aggressive as alvelolar carcinoma, and its presence probably signifies that a preliminary period of relatively slow growth has preceded the more malignant carcinoma with which it is usually associated.

Carcinoma of the prostate presents many variations in structure. A pseudo-alveolar type is assumed where very numerous, small groups of cells, inclosing a definite lumen, are closely packed together, and infiltrate the stroma, gland, capsule, and nodes. This is really a more malignant form adeno-carcinoma.

The prostate is very richly supplied with lymphatics, which play an important part in connection with the disease. They anastomose with the rectal vessels, also with the bladder, and there are very rich connections with the seminal vesicles, and with the general lymphatic system, and involvement of the thoracic and cervical nodes are not infrequently observed. Various organs have been involved, liver, kidneys, adrenals, pancreas, peritoneum, lungs, pleura, dura, brain, heart, thyroid, and spleen. The bones are also attacked, and it has been estimated that about 70 per cent of prostatic carcinoma cause skeletal metastases; the spinal column, pelvis, long bones, skull, ribs, sternum, scapule and clavicle have been thus affected.

Carcinoma of the Uterus.—In the United States, registration area, in 1914, there were 7,470 deaths from cancer of the uterus: this was 14.3 per cent of all deaths from carcinoma, and 11.3 persons per 100,000 population. Other statistics have placed the frequency much higher, up to 15.59 per cent of the total cancer deaths in both sexes, and as high as 30 to 38 per cent of all those occurring in women.

Two main histological and clinical varieties of uterine carcinoma are recognized: 1. Squamous cell carcinoma of the cervix, and 2. Glandular carcinoma of the body. The vaginal portion of the cervix is almost exclusively the seat of epidermoid carcinoma: in the cervical canal the two types meet and intermingle, while glandular carcinoma, or malignant adenoma, predominates in the corpus.

Cervical Carcinoma.—In cervical carcinoma, which forms at least 90 per cent of uterine carcinoma, two histological types of structure appear, epidermoid carcinoma and adeno-carcinoma, but the two types are often combined. The most frequent presents cords of pavement epithelium in which neither alveoli, pearls, spine cells, nor hornification are demonstrable. Rarely adult acanthoma is observed, with abundance of pearls and much hornification. These structures usually affect the portio vaginalis and ulcerate early.

The established tumor is usually composed of columns of transitional epithelium, with cells of large dimensions, polyhedral or rounded, without a trace of pearl formation or keratosis; giant cells are commonly frequent. The stroma is usually scanty, vascular, and infiltrated by mononuclear or eosinophile leukocytes. Evidently this structure is produced by the growth of the epithelial layer as a whole, which, in order to accommodate its enlarged dimensions, becomes variously folded, incurved, or everted, thus resulting in a bulky tumor of essentially papillary type. This structure produces the majority of the papillary or cauliflower, superficial, or deep tumors of the cervix. Their histogenesis has been traced to the stratified epithelium lining the cervical canal and the ducts of the glands. This metaplasia

may extend to the endometrium, where changes occur in many cases of cervical carcinoma. Adeno-carcinoma, reproducing the alveoli of the cervical glands, occurs in a small proportion of cervical carcinomas.

Carcinoma of the Corpus Uteri.—The histogenesis of corpus carcinoma presents many difficulties, and in spite of much labor the exact origin of the different histological types remains uncertain. Ewing recognizes four forms of disease.

1. Malignant adenoma, the most frequent type, presents greatly enlarged and elongated alveoli, giant reproductions of the uterine glands, lined by several compact layers of cuboidal and cylindrical cells. The cell bodies are usually paler than the normal lining cells, but the large hyperchromatic nuclei give a dark staining character to the gland linings.

2. Papillary adeno-carcinoma is a form assumed by certain tumors which probably arise from superficial cells or adenoid forms. They may closely resemble in structure and gross appearance the coarser papillomas of the bladder, but are usually diffuse and compact. Various stages of malignant transformation of benign polyps are observed.

3. Alveolar carcinoma is rare in the uterus, but some tumors early show solid masses of cells forming alveoli, and smaller cell groups infiltrating spaces and vessels.

4. Squamous cells may form a prominent element in adeno-carcinoma of the corpus, and in rare cases they predominate over the glandular structure, and produce a true adeno-acanthoma. While in many cases neither spine cells nor keratohyaline granules are demonstrable, in others both these criteria or true squamous epithelium are present, and pearl formation is added.

The frequent association of adeno-carcinoma with myoma suggests that the originating glands may be in some way connected with a myomatous area, or other developmental anomally. From 10 to 25 per cent of corpus carcinoma are said to be associated with myomas.

Carcinoma of the Breast.—In the United States registration area during 1914, there were 5,423 deaths from cancer of the

breast out of a mortality of 52,420 from cancer in general, something over 10 per cent, and 17.4 per cent, of the total deaths from cancer in women.

Cancer of the breast has very naturally been the object of histological study more than that of any other organ, and great diversity of opinion exists in regard to many points concerning it: it is quite impossible in the present writing to compass the subject at all fully, but the attempt will be made to give enough to render the subject fairly clear. It is interesting to realize that as Ribbert says: "No one has ever seen a beginning carcinoma of the breast," nor, it might be added, in any other location.

Ewing says: "While there are several well defined forms of mammary cancer, the specific features characterize chiefly the early forms of the disease. Arising under markedly different conditions of a wide variety, the anatomical distinctions are often obliterated when the disease is fully established and the local lymphatics are invaded. On chiefly anatomical features the disease may be considered under the following forms," according to Ewing: "1. Adeno-carcinoma, arising chiefly in cysts of ducts or sweat glands: 2. Duct-carcinoma, arising from the lining cells of ducts: and 3. Acinar-carcinoma, arising from the epithelium of the acini; of these main groups there are several sub-divisions, such as gelatinous or mucous carcinoma, fibro-carcinoma, and carcino-sarcoma, while striking clinical features stamp certain cases of the disease as highly specific." We will briefly consider the main divisions.

Adeno-carcinoma.—This is characterized by its origin chiefly in cysts of chronic mastitis, by the markedly circumscribed character of the growth, the bulky local tumor often produced, the long immunity of the lymph nodes, the relatively favorable prognosis, and the specific structure. But certain cases are much more malignant, and produce bulky tumors invading much of the breast, perforating the skin as fungous masses, and early involving the lymphatics in various directions. Everywhere epithelium predominates over stroma.

The gross appearance, transitional types, and minute structure point clearly to the origin of these tumors from the papillary ingrowth of mammary cysts. From the study of the groups of tumor, Ewing concludes that the lacteal ducts produce most of the low papillary and glandular adeno-carcinomas, with cuboidal, clear cells, while the sweat glands give rise chiefly to papillary and villous adeno-carcinomas, with cylindrical cells of acidophile character.

Duct-carcinoma.—Carcinoma arising in the interlobular and large ducts produces tumors of characteristic gross and microscopical structure, and somewhat peculiar clinical course. The tumor usually begins near the nipple and affects the central portions of the gland, or it may first appear in any portion of the breast. Eventually it tends to invade the entire organ, with marked fibrosis and reduction in size. In the more malignant forms the organ may be considerably enlarged by diffuse growth, in which case the typical gross features may be lost. Very extensive involvement of the skin and subcutaneous tissue, extending even beyond the breasts is a striking feature in some cases. The structure presents marked proliferation of the lining cells, first of the larger, then of the smaller ducts, or *vice versa*. The origin of this form of mammary carcinoma has been satisfactorily traced to the lining cells of the interlobular ducts.

As a rule the cells of duct-carcinoma are clear, and as they become more atypical, the cytoplasm becomes less prominent.

Acinar-carcinoma.—This develops in the malignant transformation of fibro-adenoma, it occurs in rare cases of small alveolar-carcinoma, and it produces a type of fibro-carcinoma. These tumors are characterized in general by a diffuse growth and lack of encapsulation, by absence of the specific gross features of many duct cancers, and by a structure in which small alveoli predominate, while the cells are usually small, and lack the pavement form and clear cytoplasm of the duct epithelium. In some cases of productive mastitis, and possibly in otherwise unaltered breasts, the acinar epithelium may give rise to a

malignant form of scirrhus, or fibro-carcinoma. About the unaltered layer and the interlobular ducts the acini become increased in number and break up into many small groups of atypical cells, with hyperchromatic nuclei. The connective tissue is much increased and soon becomes fibrous, while the tumor cells are compressed into narrow rows or small groups. Many cases of primary scirrhus develop in this manner, and the process is fully malignant.

Paget's Disease.—This is a specific, chronic, progressive disease of the epithelium of the mammary nipple and adjoining skin, which is closely related to and almost invariably followed by carcinoma. Some cases appear to represent an extension of duct- or sweat-gland carcinoma into the epidermis, others a primary precancerous affection, limited chiefly or exclusively to the epidermis.

The earliest changes have been located in the squamous epithelium of the nipple, or in the milk ducts below the nipple, but it is doubtful if the earliest stages of the process have been yet observed. In the epidermis characteristic "Paget cells" appear as swollen, rounded, clear staining, hydropic cells, single or in groups, with hyper-chromatic nuclei, often in mitosis. The Malpighian layer containing these cells is usually thickened and the papillæ elongated: the corium is commonly rich in plasma-cells. There is still much discussion in regard to the true nature of Paget's disease, whether it is primary or secondary to the carcinoma of adenoid growth, which is apt to follow it.

As in all cancer the lymphatic system plays an important part, both in its dissemination in the breast and in the involvement of other organs. The permeation theory of Handley has become pretty widely accepted, mainly for the extension of the disease within the organ; this relates to a growth of cancer cells along lymphatic vessels, rather than to a conveyance of them in the lymph stream. We know, however, that cancer in every location spreads by continuity of tissue, cancer cells having, as it were, the power of persuading adjoining cells to take on the same morbid action.

The chief mode of extension to other and distant parts is undoubtedly through the lymphatics and also in a measure through blood vessels, mainly through the veins, the cancer cells having gained access to the latter through the thoracic duct, or possibly by the penetration of a vein by the disease. This method is almost exclusively followed in the highly malignant tumors, fibro-carcinoma, acinar-carcinoma, and adeno-carcinoma.

In advanced cancer of the breast almost every portion of the body may be affected, and the following list of the relative frequency of different parts affected has been given, Gross, Ewing: lungs, liver, bones, brain, ovary, opposite breast, dura mater, kidneys, retro-peritoneal nodes, uterus, and other organs. The bones most frequently involved are the sternum and ribs, femur, vertebral column, cranium, humerus, and clavicle. The main lymphatic line of dissemination is that which leads through the sheaths of the muscles to the axillary region, which is the largest and drains all parts of the gland. Another set of lymphatic vessels passes to the glands of the anterior mediastinum, and others pass upward over the clavicle and invade the supraclavicular glands, while still others stretch across to the other breast.

Sarcoma.—While conventionally sarcoma is often spoken of as cancer, and is commonly included in the statistics of cancer, it is quite a different disease, histologically as well as clinically, from carcinoma as just presented. Some statistics place its frequency at about 14.5 per cent of cases of malignant disease but it is probably much less. It is apt to occur at a far earlier period of life, and malignant tumors occurring before 20 years of age are practically all sarcomas; while carcinoma is very rarely seen before that age, although sarcoma may also occur much later in life.

The subject of the histology of sarcoma is rather a mixed one, as there are so many different types, according to the tissues involved. Thus, Ewing says: "According to histogenesis sarcoma may be classified as fibro-plastic, angio-sarcoma,

chondro-sarcoma, osteo-sarcoma, lipo-sarcoma, myo-sarcoma, myxo-sarcoma, lympho-sarcoma, and glio-sarcoma." It would take us far beyond the proper limits of this chapter, and be unnecessary for the understanding of our subject to attempt in any way to analyze the facts concerning all the manifestations of the disease to which the name of sarcoma is attached. We will, therefore, only briefly outline the general characteristics of the sarcomatous neoplasm as given by Ewing, leaving until later the consideration of its development, which is undoubtedly due to much the same deranged constitutional conditions as cause carcinoma. There is, however, this difference between these two forms of neoplastic growths, namely, that sarcoma seems to arise from single or brief traumatic incidents, while in carcinoma the cause of the primary location of the malignant disease in any particular place may be from repeated or long continued local injury or excitation.

Sarcoma is a malignant tumor composed of cells of the connective tissue type. Sarcomas are chiefly histoid tumors, that is, resembling in structure, or composed of, or developed from one of the tissues of the body. In general the structure of sarcoma presents an imperfect development of the tissue of origin, as indicated in the various forms of the disease already mentioned: its cells are usually larger and always numerous. "It seems high probable," says Ewing, "that sarcomas, like carcinomas, arise through exaggerated and regenerative overgrowth of tissue cells."

While in many cases the cells of origin are adult, theoretical considerations suggest that in some instances they are embryonal. While according to cell form, sarcomas may be divided into spindle-cell, round-cell, and giant-cell groups, he believes that these terms convey little information, and unless the tissue of origin be stated, no significant diagnosis has been reached. The controlling factor in the structure of sarcoma is found in the natural tendencies of the cells of origin to reproduce the mother tissue.

The stroma of sarcoma is derived from remnants of pre-

existing tissue, from blood vessels appropriated for the nutrition of the tumor, or new formed as an integral part of the neoplasm, and from the specific intercellular substances derived from the tumor-cells. The blood vessels form the most important part of the stroma, and are of various forms and sources. Such vessels may be venous, arterial, or capillary, and their walls are composed of adult normal cells. As the tumor develops the adventitia of the vessels is lost in the stroma of the neoplasm, and eventually nothing but a swollen endothelial cell separates the blood current from tumor-tissue, leading to interstitial hemorrhage.

Spindle-cell sarcoma is the most common, and represents the purest form of fibro-plastic neoplasm. The structure falls into two main classes which differ also in their clinical features: 1. Small and 2. Large spindle-cell sarcoma. The spindle-cells of either type resemble fusiform fibro-blasts. They are much smaller than normal fibro-blasts, and more densely packed in the smaller cell growths, but reach very large dimensions and are loosely arranged in the large-cell type. The cytoplasm is granular, opaque, and acidophile, the nuclei vesicular and provided with one or more small nucleoli. In many soft, vascular tumors the cells are polymorphous, small and large spindle, polyhedral, and rounded cells appearing in foci or throughout. Such growths are often called round-cell sarcoma, but a true round-cell sarcoma of fibro-blastic origin probably does not occur.

Round-cell and giant-cell sarcoma are much less common, and affect deeper organs. In the stomach they are reported as constituting about 1 per cent of all gastric tumors, and have been observed in the œsophagus, intestines, uterus, etc. The most important aspect of sarcoma is probably its relation to the bones, where it produces great ravages, originating in the periosteum, commonly with the history of a mechanical injury. This great subject can hardly be well considered here.

Sarcomas in general have very few lymphatics, and metastases are not as common as in carcinoma, although they are observed in the advanced stage of most sarcomas. Their

extension to other parts is mainly through the blood vessels and through fascial planes, along vessels and nerves, and directly through the soft tissues.

ANAPLASIA

This term, unlike metaplasia, has a specific bearing on malignant tumors. The normal parent cells give rise to tumor-cells which bear some relationship to the former, both morphologically and physiologically. Thus sarcomata which arise from the chromatophiles of the skin consist of cells which can produce melanin. In addition to resemblances of this kind there are notable differences; and all alterations which confer malignancy on the tumor-cells such as unlimited growth, absence of all function, abnormal cell division, etc. are summed up by von Hansemann under the term anaplasia. One of the most significant of these is the tendency to degenerate, and here the terms anaplasia and metaplasia may be confusing. As the cell loses its differentiating attributes it takes on an independent existence. In cancer, etc. "every cell is for itself" and there is no altruism or commonwealth. Anaplasia means "lessened differentiation and increased power of independent existence."

The term *heteroplasia* has but little use in tumor genesis and it may readily be confused with heterotopia. The heteroplasias of authors correspond to apparent heterotopias, such as the occurrence of islets of gastric tissue in the œsophagus; these, since they are limited to certain areas of the body, are doubtless congenital.

Other terms sometimes found in connection with malignant tumor growth are kataplasia, alloplasia and dysplasia. All such terms are confusing, often overlap, etc, and individually have at times quite unusual meanings, as when anaplasia is applied to plastic surgery, dysplasia to a congenital malformation, etc. Their applicability to cancer genesis and retrograde changes seems uncalled for.

THE CANCER CELL AND SOME OF ITS PROPERTIES

The cancer cell, by which term is understood the aggregation of cells which makes up the morbid growth, may be studied

from a number of angles. These include the histology of the cells and the architecture of the tumor, the chemical composition, the dynamics of the cells—their mode of multiplication, the action on the surrounding tissues, and the reaction of the environment to the cancer process—the metabolism of the cancer as distinguished from that of the individual as a whole, during the active period of growth; also the regressive changes, and finally the products of the cells from first to last, both during the active period and after secondary changes have set in.

The subjects of anatomical structure and cell multiplication may be studied to advantage jointly. It is not necessary to consider such aspects as are fully covered in textbooks on cancer. Of the isolated cancer cell we know but little, and the expression is commonly found that a single cancer cell presents nothing to characterize it or to distinguish it from normal epithelial cells, except for a certain biological misbehavior. It is claimed that while the normal cell swells up in saline solution the cancer cell shrinks, which claim, if true, appears to point to some physico-chemical peculiarity involving osmosis. It is also claimed that a cancer cell dissolves in the serum of its host, but not in the serum of a sound subject. This fact appears to point to the formation of a lysin in the blood of the patient. Such facts, if facts they are, are of the utmost interest, but do not seem to have led to any practical conclusions or to have opened up any new field of research. It may be added that cancer cells can be transplanted in animals and give rise to tumors of the same sort, while normal epithelium cannot act thus, but grows normally, as in skin grafts.

When cancer cells are considered in the aggregate they present a certain absence of standardisation or departure from the normal, which has been termed anaplasia and which is elsewhere considered because of its theoretical character; for this chapter deals as far as possible with facts.

The next subject for consideration is the segmentation of the cell, that is as to its method of multiplication. Much has been

written of karyokinesis and mitotic changes in cancer cells, but apparently these may be summed up in a few words; dissociation of the chromatin in the two nuclei which result from segmentation, so that one contains much more chromatin than the other; and reduced mitosis, such as is seen in other pathological processes; also multipolar mitosis and the formation of giant-cells. The practical significance of these departures has not thus far been significant, either for practical ends or for opening up new lines in research. It has been claimed, for example, in the Mayo laboratory, that in the division of a cancer or cancer-genetic cell a new cell is formed without a chromosome, the latter becoming thus an autocratic or parasitic cell; but others hold that the nuclei of different cancer-genetic cells conjugate to produce new individual cells which are cancerous. These two views may be made to coincide without much effort, but the speculative element enters strongly into the subject of cancer-genetic cells, which are presumably normal until altered by some force from without. Of these beginnings we know nothing. It may be that one cancer cell can corrupt normal cells and compel them to share its behavior, or that an entire breed of cancer cells may be generated synchronously from normal cells. The opinion at present seems to be in favor of the normal character of the cells which give rise to cancer.

To pass from speculation to fact there is every reason to believe that cancer cells may lie fallow in the tissues until roused to activity by some unknown force. This has been seen for example in the margin of a gastric ulcer. But a cancer which is inactive, presenting only the histological appearance of the disease, may not be a cancer in a clinical sense, as in so-called benign cancer of the appendix.

The cancer cell is technically a modified epithelial cell which resembles closely the epithelial cells from which it springs, but which tends to depart from a standard model, giving rise to the expression anaplasia already mentioned. To call it an embryonal cell involves a contradiction, for it is a property of embryonal cells to develop into finished and adult cells, and this is not

seen in cancer but rather in teratomata. Its tendencies are in fact to regression and degeneration, as will be shown later, all such retrograde alterations having nothing in common with so-called anaplasia.

The predisposing and exciting factors in the genesis of cancer will be discussed in full elsewhere. It seems enough to state in this connection that nothing can run wild in nature unless some natural check is withdrawn, and that a study of what inhibits cancer growth in the subject who escapes the disease should be as profitable as any one of the exciting causes—for the rapid diffusion of cancer today argues that the protection enjoyed for centuries is being withdrawn. Since cancer develops from normal epithelial cells which have a characteristic arrangement, it is commonly said that the first step in the formation of a cancer is a penetration of cells through the basement membrane, or other limiting connective tissue formation. Aside from this, cancer also develops along the lines of benign epithelial growths —papilloma and adenoma—this being true of cancer of the skin and mucosæ. There is either an outgrowth or an infolding of the epithelium, in the latter case ending in infiltration of the subepithelial connective tissue.

It was formerly taught that the cancer cell secreted a histolytic substance which to some extent dissolved the surrounding tissues; but at the present day we find this procedure reserved for tumors made up of decidual cells. The subject of locomotive properties of cancer cells is no longer emphasized today, save in connection with retrograde metastases in the lymph-tracts, which make it necessary to assume that the cancer cell can force itself against the lymph-current. But even this might be explained by ordinary *vis a tergo*, and the latter seems to be the only mechanism understood to exist today, the energy of cell growth being sufficient to explain the invasion of the neighboring tissues. Cancer cells select the path of least resistance, which explains why they first enter the interstices of the surrounding cellular tissue and the preformed lymph channels. But it is difficult to understand the different behavior of cancer

and sarcoma when these tumors come in contact with bone, as at the base of the skull: for while the sarcoma wears away the bone mechanically, cancer penetrates into the latter, infecting and softening it. This behavior once more suggests either a special penetrating force or the formation of enzymes which can attack the connective tissue.

According to the Mayos there is in incipient cancer the formation of an acid-reacting fluid which tends to spread through the body and is a forerunner of cachexia. This statement is not readily harmonized with the claim that in the latter condition the alkalinity of the body has become increased. An initial acidity must give way eventually to an opposite state. But these subjects belong properly under the chemistry of cancer.

We next have to consider the action of cancer on the connective tissues and the reaction of the latter to the cancer mass. The latter contains a varying amount of stroma, none of which it forms itself. In sarcoma, where the stroma is always slight, it may be formed from the tumor cells, but this is not the case with carcinoma. The cells of the latter, as stated, invade interstices and move along the lymph channels from the very start, and then, according as defense reaction does or does not develop, we see opposite types of cancer arise with all gradations between.

As it infiltrates its periphery, cancer at the same time compels the latter to deliver tribute in the shape of a stroma of supporting tissue containing blood vessels. This is the chief action of the growth. When there is a pronounced reaction this is practically inflammatory in character, and must be interpreted in part as a defense reaction. It is in evidence between cell clusters, as well as in the circumference of the new growth, and not only walls off the surrounding tissues like a coffer dam, but, since it may manifest contractive properties, it compresses the tumor cells both from within and without, and doubtless obliterates or contracts the lymph spaces and thus prevents metastases. So intense is this reaction in special cases that the new connective cells have ended in the formation of sarcoma-

tous tissue. The barrier formed doubtless bears some analogy to that which develops after removal of a cancer by the cautery, or the use of caustic pastes; it is also claimed that the beneficial effects of irradiation are brought about by increased production of stroma. Where the reaction is slight or absent we have the so-called soft or medullary cancer, which is now admitted to present a certain amount of stroma, this differentiating it largely from rapidly growing sarcoma. But in soft cancer no "cofferdam"—to quote Murphy—forms, and infiltration and metastases have no natural check.

In this general outline of cancer the cutaneous form is not necessarily included, owing to its lower malignancy and clinical pecularities, which tend to make of it more of a surgical affection; this form of growth has not shown the increased frequency and mortality which is exhibited by the mammary uterine, gastric, buccal and other forms. Again in cutaneous epithelioma, although a predisposition is necessary, the exciting cause is usually in evidence to a much greater degree than in other cancers.

In regard to the defense reaction on the part of the connective tissue, some doubt exists as to the formation of the almost cartilage-like substance produced in extreme forms of scirrhous cancer. This sort of reaction is not seen under any other circumstances, hence, it may be well to ascribe it to the action of the tumor, rather than the reaction of the sound tissues. It has been assumed that a special secretion of the cancer cell can generate this sclerogenic tissue, and it has received the name of "desmoplastic secretion." According to Murphy loose cellular tissue, filled with adipose, is unable to form a protective barrier. The relations of cancer to inflammation are discussed elsewhere but it may be remarked here that in some stromas the process is purely inflammatory, while in others this feature is not in evidence. We may infer that in inflammatory stroma there will be some contraction with compression of cancer cell groups, as already suggested.

The relations between the parenchyma and stroma in cancer

tissue may differ notably. In some cases of so-called organoid cancer the correlation may approximate that of normal glands, etc. In scirrhus, the stroma may greatly preponderate over the parenchyma, while at the other extreme the tissue approaches the histioid type, in which the cellular element greatly preponderates over the stroma. The supply of blood vessels is at best very poor, with resulting sluggishness of the circulation, and since the stroma supports the vessels, cancer which is deficient in this respect is prone to necrotic changes. Aside from this factor there is another which has the same result—the compression of the central cells by the rapid accumulation of peripheral cells.

In reviewing the histo-pathology of carcinoma and sarcoma we are struck with the similarity in the accepted descriptions of the changes which take place in the cells which constitute cancer in any and every region. In all of them there is an irregular, atypical, abnormal development, which results in a malignity tending to perpetuate itself and extend, until, if not checked, the process destroys life.

The reason for this malignant action, which must first start in some individual cell or cells, has never been explained, and it is universally stated that we do not know the cause of cancer. But there is no mystery in the disease, and the real cancer problem is cleared up when we study the bio-chemistry of the disease, as will appear in other chapters. Elsewhere, also, there are presented the negative results of laboratory, experimental, and clinical research, and how one is forced by them, and by many positive reasons, to turn to faulty metabolism for the explanation of the erroneous actions of the cells. Ewing and others repeatedly mention "atypical, over-nourished cells" in connection with cancer in many locations. The fact that in practically every part of the human frame where epidermic cells are found, there is a liability for them to become diseased, either primarily or secondarily, would seem to point to some common cause or agent capable of reaching every cell in the

body, and this, of course, is found in the blood, which we will later see is profoundly affected in these diseases. This has been studied mainly as to its cellular constituents, but very little in regard to its plasma, in which the cells are bathed, and from which they receive their right or wrong pabulum.

That no specific changes in the blood which are pathognomonic of cancer have as yet been determined, is not singular or negatively conclusive. How little do we know in the matter of the absolute blood changes belonging to many diseased conditions, which are treated with more or less success, osteomalacia, ricketts, arthritis deformans, arterio-sclerosis, or many affections non-inflammatory or non-infective. Who can even say what is the active resisting power by which the very large proportion of the multitudes in whom the tubercle bacillus finds lodgment, escape serious results from the same? If the erratic, malignant behaviour of the originally normal body cells, resulting in cancer, does not come from erroneous nutrition, as accomplished by anabolism and catabolism, which will be discussed later, what other possible explanation can be offered?

CHAPTER V

BIO-CHEMISTRY OF CANCER

Much labor has been expended in endeavoring to discover in tumor tissue the secret of malignancy, but thus far all efforts have failed to identify the presence of any specific morbid substance which answers all requirements.

Ewing has given a chapter upon this subject, and while it does not appear to lead to any striking advance in our practical knowledge of the nature of cancer, the interesting and valuable researches recorded warrant their presentation.

"*Constitution of Tumor Proteins.*—The conception that tumor proteins must differ in essential respects from those of normal tissues has not been demonstrated by chemical methods. The nature of the problem involved appears to have presented itself in different forms in the minds of investigators who have attacked the problem.

"A different distribution of normal proteins from that of normal tissues has been demonstrated in tumor tissues by Pétry, Wolff, and Beebe, who found a higher content in nucleo-protein, more uncoagulable protein, and less globulin and albumen. It is probable that these results depend on the over-growth of cell nuclei, degenerative and autolytic processes, and œdema. Nucleohiston is present only in lymph-nodes among normal tissues and its presence in lymphatic metastases of tumors originally free from this protein, indicates that metastatic tumors receive chemical impress from the tissue in which they are growing. Although nucleohiston is absent in primary carcinoma of the breast and in the testis, Beebe found this substance in lymph-node metastases of mammary cancer, and Bang in the lymphatic metastases of testicular carcinoma. Nucleohiston gives a preciptiate when calcium chloride is added to a watery solution of the tumor.

"Direct chemical analysis of the split products of cancer proteins by Wolff yielded a high proportion (35 per cent) of glutaminic acid, while Bergell and Dorpinghaus found excess of alanin, phenylalanin, asparaginic acid, and diamino acids. Yet these results conflicted with those of Pétry, Neuberg, and Beebe.

"Resistance to peptic, and susceptibility to tryptic digestion, was said by Blumenthal and Wolff to distinguish tumor from normal tissues. Yet their results were not uniform and were probably determined by the increased amount of nucleo-proteid in some of the tumors.

"Excess of potassium and defiency in calcium in rapidly growing tumors, free from necrosis, and the opposite relations in slowly growing or old necrotic tumors, have been demonstrated by Beebe and by Clowes.

"Pentose was greatly increased in fibro-carcinoma of the breast, in comparison with the amount in the normal breast, in cases studied by Beebe and Shäffer. These authors also found that the pentose content in different tumors varied, and bore no relation to the nucleoprotein or to the presence of degeneration.

"Lactic acid appears in tumors, according to Fulci, in considerable quantities. It is more abundant in epithelial than in connective tissue growths, and increases in the more malignant, actively growing tumors. Its formation is dependent on metabolic activity of the tumor-cells, its source is the blood carbohydrates and possibly the proteins. It appears to have no relation to cachexia.

"Of the total phosphorus of the normal liver, B. Wolter found 28.68 per cent as phosphatid phosphorus; in the tumor-free portions of the liver with primary carcinoma 22.04 per cent, and in the tumor nodules, 16.28 per cent while the protein phosphorus in the same materials ran 20 per cent, 25.5 per cent, and 26.70 per cent. In 0.0634 gms. of dried-tumor substance he found 1.40 per cent of cholesterin.

"Tryptophan was markedly increased in an epidermoid

carcinoma of the skin, and in an hepatic carcinoma, over the proprotions found in a normal skin and liver, in cases studied by Fasal, but this substance was absent in fibro-carcinoma.

"*Fats*.—The chemistry of tumor fats has been studied extensively in renal and adrenal tumors. In general it appears from Bossart's work that actively growing tumors, free from degeneration, contain little fat and much lecithin, while with degeneration and necrosis free fats replace lecithin.

"Purin bodies were found by Wells and Long in about the same form and amount as in normal tissue, and less abundantly than the nuclear content would suggest. The purin enzymes were also identical with those of normal tissues, guanase being constantly present, and adénase absent.

"The delicate methods of immunological studies indicate that there are biological differences between certain tumor-tissues, which are probably based on chemical distinctions, but the results obtained in this field are not decisive. Following Michaelis' failure to produce specific immune bodies against mouse cells, Beebe, working with purified nucleoproteids of a leukemic spleen, produced a serum which agglutinated and emulsified cells of the spleen and those of a lympho-sarcoma, but acted feebly and only in strong concentration on cells and nucleoproteids of normal spleen and other tissues, as well as of cancer and spindle-cell sarcoma.

"*Tumor Ferments*.—The study of special ferments in tumors by Buxton and Shaffer demonstrated no distinct difference in quantity or quality from equivalent normal tissues. Weil, using the viscosimeter found more proteolytic activity in certain cellular tumors than in normal tissues, but was not prepared to say that the difference did not depend on leucocytes. Aberhalden however, concluded that extracts of tumor-tissue and those of normal tissue split certain polypetids in a different manner. Extracts of normal mouse liver cleave certain polypeptids slowly, while those of mouse tumors act much more quickly. In comparing the extracts of mouse and human tumors with those of normal tissues, he found differences in the split products of the

proteins after the action of these ferments. Comparing the peptolytic action of normal and tumor-tissue from lower animals on peptone, Abderhalden and Medigreceanu found occasional but no striking differences.

"Autolysis is often observed to proceed more rapidly in certain tumor tissues than in normal tissues, but it is probable that all such differences depend on the more cellular character, and presence of degenerating tissue, œdema, leucocytes, and bacteria. It is extremely difficult to obtain normal tissue which may safely be compared with tumor-tissue in this respect.

"The increased activity of autolysis is well illustrated in Yoshimoto's experiments, in which an hepatic carcinoma yielded 7.2 gms. of nitrogen in the split products, as compared with 4.8 gms. in equivalent units of normal liver. With a mammary carcinoma the difference was even greater. In the tumor autolysate purin nitrogen was reduced, while that of diamino-acids, peptone, and ammonia was increased in proportion.

"It is commonly believed, on the basis of Jacoby's experiments, that autolytic ferments have a high degree of specificity for the proteins of the organs in which the ferments are found. Blumenthal and Wolff have reported that when measured amounts of tumor-tissue and of normal tissue are autolized separately in one series, and conjointly in another the autolysis is always greater in the conjoined series. They conclude that the tumor ferments attack the normal tissues and exhibit a heterolytic property. On this basis rests the claim that infiltrative growth and cachexia depend on the heterolytic activities of the tumor ferments. Baer and Ettinger demonstrated a proteolytic activity in cancerous ascitic fluid, which failed to appear with ascitic fluid from other sources, but Kepinow, and Hess and Saxl were unable to verify any of these observations. The possible presence of bacteria, necrosis, or post-mortem decomposition has apparently not been considered, although Neuberg has subsequently denied that bacteria or leucocytes have any influence on the results.

"The milky character of carcinomatous ascitic fluid is

ascribed by Wolff to the presence of chlorestin-acid-ester, combined with euglobulin. In a series of cancerous and other ascitic fluids Weil demonstrated occasional but inconstant hemolytic and hemaglutinative properties, abundance of complement in two cancer cases, and some antitryptic action, but no constant distinction between the cancerous and non-cancerous fluids. Signs of active autolysis in a peritoneal exudate, accompanying ovarian carcinoma, are reported by Umber, who found increase in non-coagulable nitrogen, albumose, leucin, and tyrosin. Eppinger reports similar findings. In a bloody cancerous exudate K. Wiener demonstrated an ereptic ferment, but any tryptic ferment present was masked by the blood. In this fluid were traces of histidin and arginin.

"J. W. Vaughan has obtained a striking relation between anaphylactic sensibility of guinea pigs inoculated with tumor residue and the lymphocytosis excited by the inoculation. Animals receiving the water-soluble residue of cancer cells, after their extraction with alkalized alcohol, or a vaccine of tumor-cell emulsion, after extraction with alcohol, showed in many cases very high lymphocytosis, and in such sensitized animals anaphylactic death was readily produced. The sensitization was quite transitory, lasting only during the 4 to 10 hour period of lymphocytosis, and the author interprets the result as depending on the action of lymphocytic ferments on the tumor cells.

"*Wasserman Reaction in Cancer*.—The results obtained with the Wasserman reaction in cancer patients varied very widely. Caan secured positive reactions in 41 per cent of 85 cases; 6 out of 7 lip carcinomas, in 9 per cent of breast tumors, and in 17 per cent of gastro-enteric tumors. All of these cases were free from clinical signs of syphilis. A Foerster secured 36 negatives in 37 cases, and Noguchi 38 in 39, while F. J. Fox reports 5 positive in 210 cases of cancer. Positive reactions in patients with cerebral tumors, free from syphilis, appear to be not uncommon (Cohn).

"*Antitryptic Power of the Blood.*—Blood serum has long been known to inhibit the action of certain ferments. Brieger and Trebing first found that the serum of cancer patients inhibits very markedly the action of trypsin. Using various technical methods, these authors, followed by Bergman and Meyer, Herzfeld, Roche, and others, showed that in about 90 per cent of cancers there was a marked increase in the antitryptic power of the blood serum but that considerable increase occured also in many other diseases, especially in those attended with leucocytosis (Weins, Schlect). Weil by an exact quantative method determined that the "antitrypsin" is increased in some cancer cases beyond that observed in any other diseases, while in other cases it failed to fall as low as the ratio observed in other diseases. All authors agree that the failure of an increase is rather strong evidence against the existence of established malignant disease. Brieger regarded the phenomenon as a sign of cachexia and an immunity reaction against excessive amounts of proteolytic ferments derived from tumor cells. Wiens and Schlecht trace a close connection with leucocytosis. Weil points out that the exact nature of the inhibiting substance is undetermined, and that no specific relation to trypsin need necessarily exist, since blood serum also inhibits saponin. Among 57 cases of cancer and 3 of sarcoma S. M. Lewin found much increased antitryptic power in 57. He could not refer the antiferment action to leucocytes, but attributed it to a reaction to proteolytic ferments discharged into the blood from degenerating tumor tissue.

"*Stammler's Reaction.*—Most tumor extracts exhibit a slight or distinct opalescence. Stammler observed that the addition of cancer serum clears up this opalescence, with the formation of a slight precipitate, while most normal sera fail to act in this manner.

"*Ransohoff's Test.*—Ransohoff observed that the injection of 3–5 c.c. of blood serum from cancer patients in guinea pigs, which had previously been sensitized by 1 c.c. of such sera, caused none or very weak anaphylactic reaction, while normal

human serum produced the usual violent reaction. Since the same immunity followed sensitization by tumor extract, he concluded that the immunizing substance of the serum was derived from the tumor. In a series of 50 cancer cases 92 per cent gave a positive reaction, while the test was always negative in other conditions."

We may now discuss the chemical composition and the metabolism of the cancer cell. Individual analyses have shown a great variability in the kind of tissue-protein found in the cancer cell, one or more members of the amino-acid group being present perhaps in great excess. But if we pursue the subject further there is a fair amount of agreement between the proteins of cancer and normal proteins. There is no constantly present fact to stand out like the high percentage of lipoids in hyper-nephroma. Variations depend on a number of factors such as the proteins in the tissue from which the growth arises, the age of the cancer—for in the older ones autolytic products are added to those of ordinary metabolism, etc. As far as possible we are writing of young and rapidly growing cancer cells. Of fresh cancer cells we only know from experiments *in vitro* that amino-acids are excreted in double the amount found in ordinary tissues; this find apparently explains the presence of the acid medium said to occur in the field of proliferation. Another reason for different results in protein analysis is said to be the retention of this product in the veins, owing to sluggish circulation. In young cancer cells the production of katabolic substances is too slight to be readily appreciable by ordinary tests, so that considerable amounts of amino-acids, along with proteoses, speak for autolysis. The metabolism of cancer *per se* must not be confounded with the metabolism of the individual, to be studied later, for the latter is studied through the urine, while even the most delicate tests of the urine would give no idea of the metabolism of the tumor itself, and the same is possibly true of blood studies. Few facts under organic chemistry have any practical bearing. Accumulation of glycogen apparently signifies only the filling of a void, as seen

in deposits of fat in cellular tissue. Of possible significance is the increase of cholesterol, to be discussed later. Cancer protein is attacked by trypsin while normal tissues are practically immune. It is commonly stated that cancer cells exhibit striking efficiency in the utilization of nitrogen for building purposes. They contain only about half the amount found in ordinary epithelium yet make it answer. This fact should be contrasted with another—the double production of katabolic amino-acid by cancer cells. Of great importance is the fact that the water content of rapidly growing cancer cells is high. In general all statements as to increase of nucleins, purin bodies, and various amino-acids should be rejected as applying to cancer in general, however they may apply to a particular case. It is not claimed that any of the data cited above are specific for cancer, for very similar finds are seen in other malignant growths, and even in certain benign tumors.

In regard to autolytic changes which indicate that some sort of retrograde alteration has begun, no one knows just when and how this is brought about. The tendency of many cancers, like those of the cervix, is to very early softening—the latter in fact is one of the earliest diagnostic symptoms, although this is found only in certain kinds of epithelioma which tend to early ulceration. Ordinarily softening occurs much later and as a result of several factors—compression of central cells, interference with nutrition through poor supply of blood, etc. Presumably autolysis does not begin until after necrosis has occurred, and the latter may be molecular or occur in mass, with resulting atrophy of cancer cells or the formation of ulceration, or areas of degeneration.

The inorganic material of cancer cells is of small interest in comparison to the large amount of literature and the many generalizations which have been made on the subject. Young cancer cells are poor in calcium and the latter tends to increase until in old cancers calcification may result. They contain at the outset much more potash than lime—in the proportion of 2 : 1 or 3 : 2. Later the potassium tends to diminish and

the old cancer is very poor in it. Sodium is present in larger amount than potassium and apparently persists to the last with little or no change. Phosphorus is present in proportion to the amount of nuclein in the tumor. Certain minerals which are not constituents of the body as selenium and uranium salts have a selective attraction for cancer tissue. The magnesium content of cancer is naturally feeble, but we find no accurate figures for sulphur or other mineral content.

An extraordinary number of active substances have been described as cancer products. These have been studied through the behavior of cancer extracts for the most part. The amino-acids of katabolism are not included here although some of them show activity, in being able to inhibit cancer cell growth in experiment. Fresh cancer extract contains a variety of enzymes such as are found in ordinary tissue cells, and some show marked proteolytic powers with normal tissues, which suggests the old belief that cancer digested its way to some extent through sound tissues. Loeper claims that the proteolytic enzyme enters the blood and can lower the azotemic coefficient of the same. Cancer-juice can digest more peptone or rather produce more amino-acid than other and normal tissues. The products of autolytic enzymes have been summed up as autolysates, and some of these are doubtless toxic, as shown by their ability to cause hemolysis. The enzyme of growing cancer cells has been pronounced to be erepsine. Lumiere has announced that young cancer cell extract is toxic to small animals, although many experiments along this line have given negative results. Cancer extracts have proved toxic to protozoa. It must be said emphatically of autolytic cancer extracts that they are not in the least specific, and that they are identical with those produced when a large benign tumor like a fibroma undergoes necrosis. Such extracts also produce hemolysis. Possible lysin formation has been mentioned.

The supposed desmoplastic substance has already been mentioned. It is formed clearly from the young, growing, tumor cell and of its nature nothing is known.

Finally, for the sake of completeness, we may mention that cancer of glandular and endocrinic organs can produce the special secretions and hormones of these organs, so that cancer may actually be seen in the role of a physiological organ. The mucous gland cancer may produce mucus ("colloid" matter is really of this nature), the liver cancer cell has not become anaplastic and still secretes bile, the cancer cell of the thyroid produces thyroidin and the adrenal cell adrenalin. In addition to the normal functions these cancerous secretions can set up diseases such as follow excess of internal secretion. But phenomena of this kind are very rare and merely curiosities of medicine. That ordinary cancer cells produce bodies worthy to be called hormones has not been definitely proven, though widely accepted, but it is possible that the decidual cell which produces chorioepithelioma may secrete a substance of this kind, as shown by the changes in the corpora lutea in that affection; on the other hand, the claim is equally made that irregularities in the secretion of lutein are responsible for the genesis of these tumors.

While no specific or definite information leading to a knowledge of the true nature of cancer is afforded by these or other accessible researches, there runs through many of them a thread of thought which is important.

It will be noticed how many of these studies relate to the disintegration of protein, to protolytic ferments, to nuclein, to lymphocytosis, to autolytic action, etc., all of which go to confirm the thesis on which our study is based. Namely that errors in the blood content are the true cause of cancer, and it will be worth while to consider some of these matters more fully.

We have always held that errors in regard to protein cleavage is at the root of cancer, and that while this substance is necessary in building up the individual elements composing the system, an excess of animal protein decomposes wrongly, while that from the vegetable kingdom assimilates perfectly, and can supply all the wants of the system. This is seen in animals, where those who live from the ground are free from cancer, also

native aborigines, who subsist mainly on vegetable products, escape, but the latter readily acquire cancer when living with Europeans and partaking largely of animal food.

Few realize what nuclein is and the enormous part which it plays in the organism. Some one has said that "nuclein is life," for it forms part of every cell in the animal or vegetable kingdom. It exists in every cell in the body and is the controlling element in the nucleus of each cell, and exists in the primordial cell from which every organism is formed. It would carry us too far to attempt to discuss the cell changes involved in amitosis and mitosis, and the operation of the centrosomes and chromosomes in effecting the reproduction of cells in normal tissues.

Ewing says[1]: "Tumor cells exhibit a wide variety of alterations which have been subjected to close scrutiny, but which it is difficult to interpret and classify. These changes affect both the nucleus and the cytoplasm. In the highly developed tumor-cell the nucleus may be distinguished by five elements: 1. Nuclein, a nucleo-protein, composing the chromatin, which appears in densely basic staining clumps, normally arranged along the periphery of the nucleus, or as an intra-nuclear network. 2. Paranuclein, an acidophile substance composing the nucleoli. 3. Linin, or plastin, an achromatic substance, forming an intranuclear network. 4. Amphipyrenin, which some authors describe as constituting the nuclear membrane. 5. Nuclear fluid; filling the meshes of the nuclear network.

"As compared with normal cells all these nuclear structures may be much more abundant in tumor cells. In giant cells, especially those of myogenous origin, and in various sarcomas and epitheliomas, the nuclei reach astonishing proportions from hyperhypertrophy, chiefly of nuclein. In epitheliomas great excess and multiplicity of paranuclein bodies is somewhat characteristic, while in endotheliomas the nuclei are relatively small.

"Shrinkage and pyknosis of nuclei occur in degenerating and necrosing areas of many tumors. Wide distension, from inhibi-

[1] EWING, "Neoplastic Diseases." Philadelphia, 1919, p. 46.

tion of fluids, may accompany hydropic degeneration of the cytoplasm. Rarefaction of nuclein masses may result in a pale, diffuse stain of the thickened chromatic network. Or the chromatin may appear in very thin strands eventually disappearing in complete karyolysis. A common appearance in carcinomas is the presence of several discrete blocks of chromatin, lying irregularly in a nucleus devoid of chromatic membrane. The various stages of karyorrhexis may be followed in degenerating or necrosing cells. The fragments of chromatin thus resulting may be scattered in the cytoplasm and remain pyknotic or become vacuolated or surrounded by cytoplasmic vacuoles, or become dissolved. Extrusion of chromatin into the cytoplasm may result in the appearance of many basophile granules in the cell. The chromatin or linin may break up into many fine rings within the nucleus, and then be discharged into the cytoplasm."

It is unnecessary to follow this interesting study further, to which a number of pages are devoted, but enough has been given to show how the active properties of the cells change and become distorted when they take on their riotous action.

Now what is the cause of this disastrous, wild, unnatural behaviour of living cells which should be performing their normal functions of mitosis, and reproduction of healthy cells to take their place in the tissues? Why do not these morbid changes take place in the earlier years of life? Why do they persist in their mad career, inducing many other cells to join in riotous action? Why does the process go on until a pernicious anæmia destroys life? These and other matters will be considered more fully in later chapters, but the single answer to all of them may be given here.

All the cells of the body depend for their constant nourishment on the circulating blood, and lymph, and I cannot do better here than to use some of the practical and sane thoughts given to us by Dr. Robert Bell[1] of London, who has done so much to establish the constitutional relation of cancer, in

[1] BELL, "Cancer, Its Cause and Treatment without Operation. London, 1913, p. 176.

spite of the opposition of those adhering to the present surgical views.

Says Dr. Bell: "The cancer cell is primarily a normal cell that has rebelled against the persistent ill usage it has been subjected to. In consequence of this it has gradually parted with its loyalty to those physiological laws which hitherto have regulated its cycle of life. We know it of old as an active, prolific, versatile, and adaptable cell. It can be successfully transplanted from one individual to another, and it is even capable of taking up a novel position, and carrying on its existence within a muscle, for example, when it has been carried into such a structure through a wound.

"Is it to be wondered at them, that, as we know to our cost, a cell may, and does frequently throw off its allegiance to those laws which govern healthy cell metabolism, and take up a new *rôle* of existence and adopt cannibal proclivities, which it does when it develops into a cancer cell. Now, if the various cells and organs of the body are for a lengthened period to derive their nourishment from a vitiated blood supply, no matter what the pollution consists of, is it reasonable to expect that they will be able to continue in healthy vigor, and be competent to carry on their various functions satisfactorily? Need we wonder if then physiological harmony is seriously interfered with, and that a spirit of mutiny should arise—just as in an army, for instance, when the food supply is considered defective—and that if matters are not speedily rectified this mutiny should spread till eventually the whole fabric is overthrown?" It is quite possible to suppose that the organs or cells which create the nuclein, which other cells seize on and use as their controlling agent, do not then afford a perfect nuclein, and the vicious circle is continued until death ends the scene. Later on the elements which combine to make the vitiated blood stream will be considered.

An interesting suggestion as to why cancerous changes in cells do not ordinarily occur in the earlier years of life, is made in the remarkable book on the study of "Induced Cell-repro-

duction and Cancer," by Hugh Campbell Ross, with others, in regard to the reason for the non-early development of cancer.[1]

We know that in certain tissues, cells are continually dying and being replaced, so that it is evident that birth and death must be going on incessantly in the body. What happens to the dead cells? They, of course, liquefy and become disorganized, and their constituents are presumably excreted or converted into other compounds. While this is happening, it seems probable that some of the products of the remains of the dead cells may be absorbed by their neighbors, for it must be remembered that the diffusion of substances into living cells appears to be a physical process over which they have no control. Many cells live only a very short time, the length of their lives varying perhaps in different parts of the body, so that the remains of dead cells are probably always present in the body fluids. In this connection, however, we have to keep in mind the physiological curve expressing the relationship between katabolism and anabolism. There are only three stages of life, if it is regarded from this point of view, the first terminating at about the thirtieth year, when man reaches his prime, and up to which period cellular birth must preponderate over its death rate. For some years it may be suggested that katabolism and anabolism remain balanced; and that after the age of 40, quite physiologically, so that nothing occurs to make one aware of it physically, these conditions begin to be reversed, and more of the products of katabolism—that is, the remains of dead cells—tend to exist in the body fluids than was the case before middle age.

"Here we have a fact incidental to the cancer period, which suggests the possibility that these products of katabolism may in some way predispose to the onset of malignancy. Thus, some certain morphological (chemical) element in a dead cell may be the agent. For the sake of argument it may be derived

[1] Ross., "Induced Cell-production and Cancer." Philadelphia, 1911, p. 361. Also "Further Researches." Vol. I, II.

from either the cytoplasm, the cell wall, the nuclear wall, or the lining, or it may be the chromatin itself."

The age factor has always been one of the problems of cancer, and few have attempted to explain it, other than that it belongs to the declining years, when active constructive metabolism has ceased, and degenerative changes are prone to occur. This may, therefore, be a rational explanation of the actual process by means of which certain cells in different parts of the body take on that virulent action to which we give the name of cancer, when the other contributing agents, to be considered later, exist in the economy.

CHAPTER VI

DIAGNOSIS OF CANCER

Various societies for the prevention of cancer have of late years made strenuous endeavors to educate the medical profession and laity in regard to its early recognition, with a view to reaching the disease by the prompt surgical removal of the discovered local lesion. If the early recognition of cancer is important from a surgical point of view, it is manifestly of even greater importance from a medical aspect, inasmuch as prophylaxis is always more desirable than cure. Too much attention and thought therefore can hardly be paid both to the early detection of the first signs of a cancerous growth and to the recognition of the constitutional conditions which lead up to the disease, as will be developed in subsequent chapters. For experience has shown that if these systemic conditions can be fully met and overcome by proper measures, the process inducing the wrong cell action which resulted in the malignant disease, will be reversed, and absorption of the wrongly formed cells will result.

When the disease has lasted some time, and there is a larger mass of disordered cells, it is naturally less easy to effect such an absorption, and when by longer continuance there is glandular involvement or metastasis to other parts, it is, of course, more difficult for the revitalized blood stream to affect them all. Moreover, as the disease progresses all these foci of degenerated cells must give forth products of their catabolistic and anabolistic changes (which cannot be the same as the hormone resulting from the disintegration of normal, healthy cells) poisoning the system and disintegrating the blood, and the task of regenerating the blood stream, from which all cells derive their sustenance, becomes still harder. But, as will appear from the cases recorded later, even in advanced cancer and in recurrences

after surgical removal it is possible to effect changes which are often most remarkable.

It is readily seen, therefore, how essential it is in any attempt at a medical treatment of cancer to begin at the earliest possible moment the work of changing the constitutional conditions of the system upon which the malignant process depends. It is seen also how erroneous it is to simply watch and observe a patient, as is often done, to see if the lesion suspected to be a beginning cancer will develop further; for of course, the longer the systemic disorder continues the more foci of disease will develop, and the harder it will be to reverse the faulty metabolism and to induce a healthy action in the diseased tissues.

Even the smallest mass which can be found in a woman's breast has not been formed in a day, or a week, or a month, but the thousands of deranged cells of which it is composed have been accumulating perhaps for months, and the disordered blood condition producing them naturally dates back much longer.

Furthermore, if by chance an operation has been performed to remove one or more of the diseased portions, how unreasonable it is to leave the patient with the same proclivities to cancer, which so constantly re-develop either in or near the original site, or in other locations, when this tendency to recurrence can be checked by proper medical attention.

Over one hundred years ago the great English surgeon Abernethy[1] wrote very pointedly in regard to this. Says he: "There can be no subject which I think more likely to interest the mind of the surgeon than that of an endeavor to amend and alter that state of a cancerous constitution. The best timed and best conducted operation brings with it nothing but disgrace, if the diseased propensities of the constitution are active and powerful. It is after an operation that, in my opinion, we are most particularly incited to regulate the constitution, lest the disease should be revived or renewed by its disturbance." In later chapters we shall see what these

[1] ABERNETHY, "Surgical Observations on Tumors." London, 1816, p. 221.

disturbances are and what measures should be adopted to alter them.

It will be impossible in the present compass to go as fully into the diagnosis of cancer in different localities as could be desired, and reference must be made to some of the many *surgical works* on the disease, where these are elaborated. For unfortunately, although, as will be seen, while cancer is rightly a medical and not a surgical affection, medical men have not heretofore interested themselves in it to any great degree, but have left its description as well as treatment to the surgeons. But a brief presentation of some of the salient points will help in grasping the subject under discussion.

In the preceding chapter we have seen that the actual beginning of the histological cell disturbance which eventuates in the tumor which we call cancer, is somewhat uncertain, and undoubtedly the disease has been going on in individual cells long, long before their accumulation has formed a mass large enough to suffice for detection. Thus too often there is already such a general carcinosis habit of body developed that surgeons agree that at least 50 per cent of true cancer cases (excluding cutaneous epithelioma) come to them when too late for successful operation: moreover the proportion of cases which remain ultimately well for a long period of years is exceedingly small. Hence, the very great importance of recognizing at the earliest possible moment both the local manifestation of the disease and especially the constitutional elements leading up to cancer, as described in other chapters.

In regard to the actual appearances, or recognizable local symptoms which may be discovered by sight and touch, we may briefly take up the disease as it affects various organs or portions of the body. We will begin with epithelioma of the skin, which, however, being such a peculiarly local affection, often readily amenable to correct local treatment, especially if taken early, is not considered in this book as true cancer, and is but little influenced by internal medical measures.

Epithelioma of the Skin.—Synonyms: Epithelial cancer; Epidermoid carcinoma; Cancroide; Rodent ulcer. The forms and appearances of epithelioma, both baso-cellular and spino-cellular, in different degrees and stages vary so greatly that those unacquainted with the disease may fail to appreciate the lesion: cases also differ greatly in their malignity. The beginning is always very small, and commonly its real nature is not recognized until it has lasted some time. The disease may start from a mole or wart, or from a hardened sebaceous congretion, or it begins unrecognized as a scaly patch, which exhibits a raw and frequently slightly bleeding surface, whenever the crust is picked or rubbed off. Soon greater infiltration is manifested and more ulceration: in the progress of the disease, small pearly, rather translucent tubercles, hard and cartilaginous, are commonly formed, often as a ring around the margin. When irritated by injudicious treatment the edge becomes hard, infiltrated, and elevated, the ulcer extends and deepens, and great destruction of tissues, even of the bones, may result (Rodent ulcer, Jacobs' ulcer, Noli me tangere). In occasional instances the disease may remain quiescent for years, slowly increasing so as to cover a large area.

Epithelioma is a disease of middle or advanced age, and is relatively infrequent, forming about 2 per cent of 30,000 miscellaneous skin cases analyzed. In the beginning it may be confounded with eczema or horny seborrhœa, and in later stages with lupus or the later manifestations of syphilis. Many syphilitic lesions, even the chancre, when occurring on the skin, have occasionally been excised as epithelioma.

Epithelioma of the mucous membranes is quite a different affair, and is rightly called by Ewing epidermoid carcinoma, for it is characterized almost invariably by metastases in the lymphatics and other tissues.

Epidermoid Carcinoma of the Lip and Buccal Cavity.—On the lip the disease begins very insidiously, in a crack or fissure, and most commonly in smokers, and as the sore refuses to heal, more or less of an almost cartilaginous hardness forms, and with it a

greater or less involvement of sub-maxillary glands. When not too greatly irritated it may progress slowly, and not ulcerate much, but the tendency is to increase in size, ultimately producing great destruction and tending to destroy life, if the progress is not checked by a relatively early and complete treatment. Unfortunately involvement of the glands too often follows surgical removal and the patient succumbs.

Cancer of the Tongue.—This is generally a most serious affair, of which the diagnosis is often very difficult in its earlier stages; quite innocent abrasions or ulcerations of the tongue may pass into cancer, and leucoplakia is found to be a frequent pre-cancerous condition. The very early diagnosis of cancer of the tongue is often most difficult, and yet most important, both from a medical and a surgical aspect, for, as Butlin[1] remarks: "There is ample evidence to prove that many forms of the disease in which cancer appears, are in the first instance, and even for a time after their first appearance, simple, non-cancerous affections. But the great interest in relation to them is to study carefully the manner in which each of them becomes carcinomatous, and above all to strive to arrive by the most careful study, at the signs by which the actual development of carcinoma in each of them may be perceived."

The sore place, no matter what its origin, whether from an apthous sore, or a jagged tooth, or a leucoplakia, or a syphilitic lesion, *is at first, not at all suggestive* of malignant disease, and it is extremely difficult to be certain just when it has become carcinomatous, and it is precisely in this stage that exactly right medical treatment is most effective as will be mentioned later: but if irritated by ill advised treatment, as by nitrate of silver, it slowly enlarges, the base ulcerates and the edges harden, more or less adenopathy develops, and it has entered the carcinomatous stage. The later progress is generally much more rapid, and if untreated it can end life in eighteen months, and the end results of surgical operation are most unsatisfactory, glandular recurrence being almost universal.

[1] Butlin, Henry T., "Diseases of the Tongue." Philadelphia, 1885, p. 270.

The later developments of cancer lesions on the tongue are very varied, but as a rule almost unmistakable, and can hardly be briefly described. There is a raw, granulating surface, with rolled edges, upon a greatly hardened base, and giving off considerable fetid pus. Later in the disease the malignant process has often spread to adjoining parts. the tongue is more or less immovable, rendering mastication and deglutition almost impossible, and the pain may be very great; death results from inanition rather than from the cancerous cachexia found with cancer elsewhere.

The mouth lesions are to be differentiated from: 1. Aphthous stomatitis; 2. Simple ulceration of the tongue; 3. Syphilitic lesions, including chancre; 4. Leukoplakia, and 5. Tubercular lesions.

Carcinoma of the Cheek.—The disease is also difficult of definite recognition in its very early stages in this locality as well as on the tongue, and the diagnosis is much the same as in that location. The lesion is very apt to develop upon patches of leucoplakia, and is very often found opposite the back teeth, and may be from roughened tooth surfaces and possibly from amalgum fillings. Some pain in eating generally first calls attention to the relatively innocent lesion. Presently more or less hardness occurs over a definite, limited area, moderate ulceration then appears, with some sub-maxillary glandular enlargement. As the disease increases the ulceration increases, the jaws stiffen and proper mastication is difficult, and when fully established the progress is more rapid. The disease, however, is apt to be rather sluggish and does not affect the glands as much as tongue cancer.

Carcinoma of the Palate presents an eroded surface, with hard edges, which may extend over the tonsils and uvula. It is relatively rare, and is seldom diagnosed until too late for any surgical operation, which later is most unsatisfactory, owing largely to the involvement of deep lymphatics. It should be carefully diagnosticated from syphilitic lesions.

Cancer of the Œsophagus.—The early diagnosis of cancer in this location is difficult indeed. The first symptom is generally dysphagia, in swallowing hard pieces of food, the attacks being temporary, increasing in severity, until even liquid foods are resisted and regurgitation occurs: the material brought up is distinguished from stomach contents by its alkalinity and by the absence of gastric juice and the products of digestion. As the disease advances there is distinct pain, sometimes of very severe character, especially after taking food. Coughing is often a symptom, and occasionally loss of voice and dyspnœa, from paralysis of the recurrent laryngeal nerves. Emaciation occurs from inability to take proper nourishment.

Accurate diagnosis may be finally established by the *x*-ray, showing the tumor and often dilatations of the œsophagus above it. A direct view of the growth may be obtained by the œsophagoscope, and bougies, if carefully used, will detect obstructions produced by the tumor.

Cancer of the Stomach presents very great difficulty of early diagnosis as such, so that thus far it is agreed that about 50 per cent of the cases are fully diagnosed only when it is already too late to expect any permanent beneficial results from surgery; how very important it is, therefore, to recognize and thoroughly treat the antecedents of this insidious affection. The early symptoms are commonly pain or discomfort in the epigastric region, loss of appetite, vomiting, loss of weight, and general weakness. But some cases give practically no symptoms until the disease is far advanced. In other instances there is a long history of obstinate dyspepsia, in others, a sudden attack from indiscretion in diet will first disclose that there is an ulcer preceding cancer, or an already developed neoplasm. The constant absence or great reduction of hydrochloric acid and the presence of lactic acid are strongly indicative of cancer, as also the well known Boas' tests, and the discovery of the Boas-Oppler bacillus.

The *x*-ray is often of service when a cancerous mass has formed, and careful auscultatory percussion will often discover

the lesion, but may not until the tumor is of some size. When pain is experienced in this prodedure the diagnosis is more probable. In its late and fatal stages, however, from which mortality figures are taken, the diagnosis is relatively easy; in all recent statistics the mortality of cancer of the stomach and liver forms about 40 per cent of the total deaths from cancer, and these are increasing in men more than in women. It is a disease of adult life, about 90 per cent of all patients being between the ages of 40 and 70, and only about 2 per cent before the age of 30 years.

Cancer of the Intestine.—Here the early diagnosis is even more perplexing, and is rarely established early, or until the diseased mass has greatly advanced, and even a stricture has formed. Indefinite and more or less colicky pain, not necessarily associated with digestion, together with flatulence, causing abdominal distension, are usually premonitory signs. There is almost always irregular action of the bowels, generally constipation, alternated with diarrhœa. When there is obstruction caused by the tumor formed, the action of the intestines may be spasmodic and intussusception may occur, with great pain.

Naturally the recognition of a tumor in the intestine is very difficult until it has attained some size, and even very careful palpation and percussion may fail to distinguish between it and fecal retention, which latter, however, may aid diagnosis, as indicating an obstruction. The *x*-ray, if rightly interpreted, can help in a measure. The character of the feces may be an aid, when carefully examined microscopically. Blood, occult or visible in the stools, should always be suggestive of cancer, either of the stomach or intestinal tract, and, of course, if pieces or particles of neoplastic growth are found the diagnosis is assured. While piles are not commonly associated with cancer of the rectum, any hardening of them or ulceration should always be suggestive and indicate closer examination.

Cancer of the Pancreas.—Pain in the epigastric region, often radiating to the back, is one of the earliest signs of cancer of the pancreas, and is very constant. Jaundice occurs early and the

liver and gall bladder are greatly enlarged, with ascites, as carcinoma, commonly at the head of the pancreas, obstructs the common bile duct. Later in the disease there is apt to be glycosuria and stools containing free fat and undigested meat particles. By this time the tumor can be palpated in a good proportion of cases. Cachexia usually sets in pretty early and is rapid in progress, and metastases, which are abundant, aid in destroying life.

Cancer of the Liver.—The early diagnosis of primary cancer of the liver, which is very rare, is well nigh impossible, and later the symptoms depend on the extent of the disease and the general weakness, etc. Jaundice is present fairly early and is continuous, and commonly ascites at some stage of the disease.

When the liver is much affected secondarily the margin can generally be easily felt, even below the line of the ribs, and is often hard and knotty.

Carcinoma of the Gall Bladder.—This is more easily determined, as there is usually a previous history of gall stones, but in many cases the malignant disease has not been recognized until after an operation for the latter.

Pain and tenderness over the gall bladder occur in over half the cases, and the tumor can be discovered, sooner or later, in most instances, generally when it is too late for a successful operation. Jaundice is common, and ascites in 25 per cent of cases. Vomiting and diarrhœa are not uncommon during some stage, in most instances. Jaundice is generally present, often due to the presence of gall stones, before the development of the carcinoma: ascites occurs late, due to secondary metastases in the abdomen.

Carcinoma of the Kidney.—Hæmaturia, even as very small clots, is very commonly the first sign of this disease, and may vary very greatly as to frequency, amount, and character during the period of the disease; it does not occur especially after exercise, as in renal calculus, but may appear in the morning urine. Pain is not generally an early symptom, but later is of a dragging character in the lumbar region, running down the

thigh, and may be very severe. Cachexia is not a marked symptom until late in the disease, and is then rather due to metastases; these, however, are not commonly recognized, except it is stated the bones are not infrequently affected, and renal carcinoma should be suspected in a patient with hematuria and cachexia when bone disease is found in the extremities.

Naturally the existence of a tumor of the kidney cannot be felt until the disease has well progressed, but the *x*-ray may help in a diagnosis before that time. Cystoscopy, showing a bleeding from one ureter aids also, if renal calculus can be excluded.

Carcinoma of the Urinary Bladder.—Here, also, hematuria is commonly the first symptom in a large share of the cases. There may be only a few small clots, and not constant, or a considerable amount of blood, well mixed with the urine. It appears without cause, and not especially connected with exercise, and is often seen in the morning urine. Frequent urination is a common accompaniment, even in early stages. Pain, or an uncomfortable sensation, frequently is early and continuous. Competent cystoscopic examination will commonly establish the diagnosis, even in early cases.

Carcinoma of the Prostate.—The early diagnosis of cancer in this locality is very difficult if not impossible, so closely related is it to hypertrophy of this organ that it is difficult to determine with certainty when a malignant process has started. There is naturally an increase in the symptoms belonging to the benign enlargement, but with the addition of pain, which may be the first symptom, increasing as the disease progresses. It may be referred to the penis, testes, bladder, thighs, etc. Digital examination, from the rectum, may detect malignancy by the stony hardness, which may affect a part or the whole of the gland. It is stated that about 70 per cent of prostatic carcinomas cause bone disease, so that the discovery of such in one with much trouble in the prostate might be a diagnostic help.

Carcinoma of the Uterus.—This is a most important subject which merits the closest attention. For, as it is recognized that fully one-half of the cases which apply for surgical relief are

inoperable when first seen by the surgeon, so for the medical treatment the chances are very much better the earlier the disease can be recognized. But, as will be shown in the final chapter, cancer can be thus cured even when surgically inoperable, and when this fact is widely known physicians and patients will look for the earlier symptoms and recognize the disease sooner, when the terror of the knife is replaced by the hope of other relief. Space does not admit of the elaboration of details in diagnosis to the fullest extent desirable, and reference may well be made to the many excellent descriptions which have been put forth as arguments for surgical procedures. The conditions are so different in cancer of the cervix and that of the body of the uterus, that they will be considered separately.

Carcinoma of the Cervix.—It is doubtful if any one has ever seen and recognized the absolutely first beginning of cervical uterine cancer, it is so insidious. As in epithelioma in other locations, the earliest condition observed is a superficial erosion or possibly an indefinite papular élevation, either of which may be perfectly benign and disappear under mild measures. For it is stated that two-thirds of the cancers of the cervix are epitheliomas, and only one-third adeno-carcinoma of this canal. Practically there are no subjective symptoms during the very early stage, but all authorities agree that the first indications that attract a patient's attention are: 1. Irregular bleeding, and 2. Abnormal discharge from the vagina; but it is recognized that when these occur the malignant disease is already established. This bleeding may be very slight, and when this occurs apart from menstruation, attention should always be paid to it, and a competent examination and treatment be given. Later in the disease this is a conspicuous feature. The vaginal discharge, which later is such a characteristic symptom, is, of course, very slight at first, until some ulceration has taken place, but at any rate if there is an appreciable change in a leucorrheal discharge, discolored with blood, and peculiarly offensive, it is significant, more or less, of beginning trouble, and should be attended to. There is usually no pain in the early stage, and

the patient often seems in such perfect health that it is difficult to convince one that a serious danger threatens.

As the disease progresses there occurs more and more ulceration, with exuberant granulations, to which the name of cauliflower excrescence has been given. Later this increases, often to a great degree, and the adjoining vaginal tissue is involved. By this time there has developed a hardness to the touch, so different from the normal condition of the cervix that it is almost pathognomic. Still later the uterus is found to be more or less fixed, with also an infiltration of the broad ligaments. There may be urinary and rectal symptoms, owing to the extension of the disease, and metastases are developing elsewhere. As the disease progresses pain is a marked feature, in the back, thighs, and some in the uterus itself. By this time the case is certainly inoperable, but, as will be seen later, even in very late stages, the disease can be overcome by exactly the proper internal treatment, dietary and other, with sufficient and correct vaginal douches.

Carcinoma of the Fundus.—The diagnosis of this condition is still more difficult, and commonly is not made until the disease is far advanced. Irregular bleeding and altered vaginal discharge are farily early symptoms, but these also occur in connection with a myoma, or fibro-myoma, and endometritis. When the discharge is fetid and mixed with blood it is significant.

Pain is not a marked symptom, even rather late in the disease, as the uterus is relatively insensitive; although uterine colic, as though expulsion of the diseased mass was attempted, may occur early, and there may be considerable pain late, when ulceration has occurred, or invasion of sensitive adjoining structures has taken place. Cancer of the body of the uterus does not, as a rule, greatly enlarge the size, and external palpation or vaginal examination, digital or otherwise, does not establish much. Taylor[1] states that : "probably 75 per cent, at least, of the cases of carcinoma of the cervix uteri, and of the fundus uteri are inoperable at the time that they are seen by

[1] TAYLOR, "Cancer, Its Study and Prevention." Philadelphia, 1915, p. 157.

competent surgeons; that is they have passed the stage when the uterus can be removed with any hope of permanently curing the patient."

Carcinoma of the Breast.—Although occurring in such an accessible region there is no means of knowing just when the diseased process has begun, or how long it has lasted before it is seen by the physician. For the tendency to cancer has existed long before there is any definite, recognizable inward or outward lesion; the process has unquestionably begun in a single cell or group of cells of microscopic character, and some time has always elapsed before a tumor has formed which can be discovered by palpation. It is for this reason that surgeons have been urging the removal of every tumor, however small, in women over 35 years of age, lest they should become malignant. All the more necessary is it to recognize and treat instantly and *very thoroughly by medical measures, each and every breast tumor*, as experience has abundantly shown that under the correct dietary and medical treatment many tumors, which had been recognized clinically as early carcinoma by able surgeons, have disappeared and remained absent for many years, as will appear later.

The first symptom of carcinoma which attracts the attention of the patient and sooner or later leads one to seek medical advice, is a tumor, in three-quarters of the cases. This is discovered accidentally by the patient, often in bathing, and may be very small, or even of some size before it is noticed. Quite commonly, perhaps in a quarter of the cases, there is a little darting pain, running from the breast to the shoulder or down the arm, just enough to call attention to the developing lesion: later, of course, when there is pressure on nerves or œdema of the arm, the pain may be a really troublesome feature, and in recurrent cancer of the breast, after operation, it is often most agonizing. In rare cases the patient will first notice an axillary adenopathy, and this may be detected by careful manipulation in perhaps fifty per cent of cases when first coming for treatment. In a few cases retraction of the

nipple will be the first sign noticed, and still more rarely discharge from the nipple.

The carcinomatous tumor is by no means easy of early recognition with certainty in quite a proportion of cases: there are always chronic mastitis, cysts, simple adenoma, fibro-adenoma, etc., etc., to consider. When well developed there is a certain hardness, often with rather sharp nodular margins of the tumor mass, which are quite characteristic, but by this time there is commonly also adenopathy, either in the axilla or in the anterior pectoral fold. It is to be remembered, however, that lymphatic glandular enlargement is not necessarily or always indicative of cancerous infection, for the glands are often enlarged in leukemia, tuberculosis, pus infection, and many other conditions. When the lymph-nodes in the axilla or elsewhere are fixed, their diagnostic value is of greater importance for cancer, or when the supra clavicular glands are palpable.

Retraction of the nipple, when the growth is located nearby, and dimpling of the skin, or "pig skin" appearance, are pretty certain signs, but the latter may occur in chronic mastitis, tuberculosis, and syphilis. Oedema of the arm is a late sign, especially after operations, and may prove a distressing feature. When ulceration occurs, later in the disease, the diagnosis of cancer, of course, is relatively easy, although the amount and character of the ulceration vary greatly in different cases. In some it may be soft luxuriant, bleeding easily, while in others there is a brawny hardness around, with a larger or smaller area of raw surface; when extensive, the odor is commonly very characteristic. It must never be forgotten, however, that a good share of the ulceration and pus discharge in advanced cancer is largely due to the action of the omnipresent pus cocci, which find a suitable nidus for their development and operation.

As the disease progresses, with greater or less involvement of other parts, there are many symptoms pointing to other organs which are dependent on the invading carcinosis. Thus, by

the rather ready involvement of the mediastinal and other lymphatic glands, there will be cough and great discomfort within the chest. Neuritic pains in the neck and elsewhere occur, from pressure or involvement of the nerve sheaths. Bony swelling on the sternum or ribs, with much pain are not uncommon. Cachexia develops pretty rapidly after the disease has reached this stage, and the patient dies from exhaustion.

Since breast tumors are largely a law to themselves a study of them jointly should be of interest. The benign growths of younger women are fibro-epithelial and are circumscribed or more or less diffuse. The diffuse form or fibro-adenoma type, is often due to traumatism and is known to follow mastitis. These benign growths have all the properties of benign tumors in general, but the rule of surgical procedure is to remove them, and their removal, with microscopic demonstration of benignity, is sometimes followed by the development of true carcinoma. Fibro- or adeno-sarcoma may show anaplasia in the connective tissue with tendency to malignancy. The properties are partly those of benign and partly of malignant growths —under the latter head is rapid growth. For these the breast is commonly amputated, and in advanced cases the complete cancer operation is performed and recovery is then expected, but with many disappointments.

The corresponding type of epithelial tumor is the cyst-adenoma, which is said to present a type of cancerous malignity of low grade in about 15 per cent only (papillary form 50 per cent). According to circumstances, as in fibro-sarcoma, the breast may be amputated or the radical cancer operation may be performed, and as in the preceding, the out look is then fairly good. Compared with cancer proper these tumors are rare. The semi-benign sarcoma is however more common than the typically malignant one.

In regard to cancer of the breast it is now known to be as common in the negress as in the white woman, as abundantly shown in statistics. The foreign born of various nationalities in the United States are twice as commonly affected as the

natives. It is not uncommon in the Chinese, and Kerr of Canton did 11 breast operations in a year out of 30 cancer operations of all kinds. Cantlie states that of 114 cases of cancer in native Chinese 38 were mammary. In regard to heredity this has been seen in as high as 33 per cent, although in other material it has been very small. The element of heredity affects all breast tumors, including those of the male. The married woman and multipara are considerably more predisposed than the opposite type, as is the woman who nurses her own infants, and some very high percentages are given for those predisposed. The age period corresponds with the involution of the gland.

The general average of histories of traumatism is only about 14 per cent. Although it is often stated that the single trauma tends to cause sarcoma and not cancer, the latter has sometimes followed at once upon an injury. According to Gilliam but one case in 400 arises from the scar left by an injury. In male breast cancer the element of trauma is not to be ignored, and there seems to be unanimity that trauma is a prominent factor, and cancer in the male has followed the absorption of hematoma from a bruise. Mastitis is known to be a factor in both sexes and in about 22 per cent there is a direct history of puerperal mastitis. Cancer has frequently arisen in the scar of suppurative mastitis. The question of transition of benign to malignant is a vexed one here as elsewhere. In one form of cyst adenoma, known as the papillary, one-half of the cases may be depended on to become malignant, and varying lower percentages in others.

The encephaloid cancer of old authors is rare and appears in younger women, and the disease may pursue an acute course, simulate mastitis, and even suppurate. The longest survival is about a year, and metastases occur by both routes at an early period. "Simple cancer" makes up a per cent of 15 or 18, and the two forms together make about 20 per cent. This form is midway in type between encephaloid or medullary and scirrhous cancer. The latter is attended by much proliferation of connective tissue which retracts and compresses the epithelia,

thus limiting their proliferation. This may perhaps be regarded as a natural conservative attempt at cure, and in the higher types of scirrhus the affection is often brought to a relative standstill. This form seems to occur by preference in the feeble or slender, elderly subject. It is in these cases that the knife has sometimes done harm by lighting up the disease. Some of these cases bear a great resemblance to chronic atrophic mastitis.

Malignant adenoma is a rarer form of malignancy, which gives a good per cent of operation recoveries because the axillary glands are seldom involved. Halsted says that operation cures 75 per cent. The form of cancer in question may be traced to mastitis and benign growths in many cases.

In the acute cancer of the breast of Volkmann there is a distinction from encephaloid, because both forms are represented —there may be an acute type of scirrhus as well. As a rule mastitis is simulated at the outset, and the diagnosis may be very difficult. The condition is very rare. Fever may be present and the toxemia is profound and both types of metastasis occur early. Moore saw a case run its entire fatal course in 2 weeks and others are on record which took but 2 or 3 months to destroy life.

Incomplete operations have sometimes cured early cases of cancer. In early, nonadherent cases so good a surgeon as Warren of Boston claims but 17 per cent of real recoveries, while in adherent cases only 5 per cent. On the other hand, with the axilla not yet involved Warren claims 64 per cent cures (most of these were very likely examples of semimalignant cancer or tumors). Bloodgood admits but 7 per cent recoveries when the axillary glands are involved.

After high claims had been made by surgeons of 3 years or more survival Barker traced a number of 3 year survivors, finding that 30 per cent of these succumbed to cancer sooner or later. Smith traced out many cases of operative recovery, and found that only 17 per cent of alleged cures were really cured (Mastin in Wood's Handbook).

Multiple Primary Cancer.—This subject is of great importance, as adherents of the local origin state that such cases would be much more common if cancer were constitutional; not only is it very rare but in some of the cases it is difficult to show that one of the tumors is not secondary.

Recently a double primary cancer—stomach and rectum—was reported by Letulle and Jaquelin, and it was naturally very difficult to disprove the claim that the rectal cancer was not secondary, as several ways of transmission are known. The patient, a man of 68, died only 11 days after admission to the clinic. The entire wall of the stomach was in a state of carcinosis and the process had extended along the peritoneum to the diaphragm, pleura and lungs. In addition gland metastases involved the posterior abdominal nodes, secondarily attacking the kidneys. The cancer found in the rectal ampulla was pronounced primary, despite the extensive secondary deposits. The intestine from stomach to rectum was intact while the rectal cancer close to the anus was extensive. No path could be discovered for the secondary involvement of the rectum, through abdominal movements, as already mentioned.

Moreover, the two cancers were of different type, that of the stomach showing none of the usual cylindrical epithelium, while the rectal cancer was a pure cylindroma which presented the same type of cell as its environment. The gastric cancer showed small cells and extensive colloid degeneration. The rectal cancer was in the ulcerative stage and was associated with a marked inflammatory reaction; but, despite this none of the usual metastases of rectal cancer were discovered, a fact of great significance. The question is raised as to whether in multiple primary cancer both foci or all foci metastasize. Neither peritoneal or lymphnode metastases having occurred from the rectal lesion, this might be regarded as evidence of secondary origin, but the negative evidence and histological differences seem to leave no doubt as to diagnosis.

We have seen that cancer shows every sign of being a consti-

tutional affection, in which, as in gout or rheumatism, the actual manifestation of the disease begins in some one location, as when the great toe is stepped on or bruised. In carcinoma the disordered cells of a part produce a center of malignant tissue, and these diseased cells seem to have acquired the property of continuing their mad career and inducing other neighboring cells to take on the same action until a tumor is formed, the *local product of the disease* carcinosis, and to this local lesion we give the name of cancer. This sequence of events is best illustrated in cancer of the tongue and buccal cavity, where from an innocent abrasion of the mucous membrane by a ragged tooth, there will develop a malignant mass, which, if wrongly treated, or even left alone, progresses with fearful certainty to the destruction of life. It is as irrational to believe cancer to be a purely local disease, and that a blow on the breast or prolonged irritation of any kind anywhere can induce true cancer, without an underlying constitutional cause, as it is to believe that stepping on the great toe can induce an attack of gout, although this occurrence may be the first sign which leads to the recognition of the gouty state.

CHAPTER VII

PROGNOSIS OF CANCER

When left entirely to itself, and under unfavorable circumstances, the prognosis of cancer, in any and all locations, is most distressing, and most authorities agree that, unless the patient is carried off otherwise, 90 per cent of those once attacked with cancer succumb to the disease, whether treated or not: and, as has been mentioned, all statistics show that the mortality of the disease has been steadily rising in every country, especially during the past 20 years of increasing surgical activity.

Fortunately the United States statistical report for 1918 shows that the mortality for that year had fallen a trifle, so that it was 79.8 persons in the 100,000 population, against 81.6 in 1917; due perhaps to greater enlightenment in regard to the medical *versus* the surgical treatment of the disease.

The prognosis of cancer varies, of course, very greatly with the case, the location of the disease, its duration before treatment, and the method and skill employed. As thus far the reports are mainly in regard to surgery, and latterly radium and *x*-ray, and as these reports are often so conflicting, it is very difficult to give briefly what may reasonably be expected in regard to the disease as it affects various regions. For as yet there are no reliable data as to the relative mortality of cases under medical treatment. But Dr. J. Aebli[1] by tabulating the cancer mortality in Switzerland, between 1900 and 1915, and for 23 years before, gives us some idea of the natural course of of the disease in general. His tabulated cases of those patients who had been operated on, and those left under ordinary medical, not special, treatment, show apparently that operative procedures either lessen the life expectancy or have such a

[1] Aebli. Schweitz. Med. Wochenschr., October 14, 1920.

slight influence in prolonging life, that it may be regarded as negligible. How far a properly guided medical treatment may affect prognosis will appear later.

As already stated we exclude epithelioma of the skin, which commonly yields such excellent results, especially when taken early and rightly, under quite a variety of external measures, and from which local disease no judgment should be made regarding true cancer affecting deeper organs.

Cancer of the breast, which is the most accessible of these latter, both for early recognition and radical treatment, should afford perhaps the best field for estimating the prognosis of the disease, and here we may abstract from Ewing,[1] an unprejudiced, scientific student. After quoting reported statistics of recurrences occurring from 7 to 25 years after operation, and referring to the occasional later appearance of the disease in the other, unoperated breast, and the statement that the average duration of life in untreated cases was placed by Paget at 4 years by Odekop at 29 months, and by Sprengel at 27 months, he says:

"1. The figures (4 years—27 months) are too divergent to permit accurate conclusions regarding the natural duration of mammary cancer. The attempt to establish an average duration of this disease should be replaced by the systensic classification of cases, according to the factors known to influence prognosis.

"2. The comparison of operated and unoperated cases is sophistical. The choice of operable cases tends to throw into the untreated class the majority of rapid and unfavorable cases.

"3. Statistics favor the conclusion that operation in the whole shortens life in recurrent cases, although sometimes rendering it more tolerable. Handley's recurrent cases lived 29.6 months, while in the above series the duration of life was 27, 29, 34, and 48 months respectively. This conclusion is strengthened by theoretical considerations, as well as by observations on the rapid course of many recurrent cases. It is clearly proven in many

[1] EWING, "Neoplastic Diseases." Philadelphia, 1919, pp. 521, 522.

instances by the increasing anaplasia exhibited in the structure of recurrent cases.

"4. The high proportion of clinical cures from the modern operation has resulted largely from the earlier recognition of cancer, and the inclusion of a large number of minute carcinomas or precancerous lesions in the operated class.

"5. The choice of therapeutic measures should not be made under the impression that the duration of the untreated cases is 27 months, and that 40 per cent of the operated cases are cured. Since the duration of the disease may vary from 16 weeks to 25 years, and the favorable results of operation from 0 to 100 per cent, the first essential in treatment is accurate diagnosis and prognosis of each individual case.

"6. In estimating the economic importance of the surgical treatment of mammary cancer there must be charged up the cost of acquiring surgical skill, and the deplorable conditions following local recurrence. There can be no doubt that operation shortens life and aggravates the terminal suffering in the great majority of recurrent cases. Most of those who deal with the great number of these unfortunate patients would welcome a judicious limitation of the scope of operability in this disease.

"From clinical and pathological studies I have drawn the impression that in dealing with mammary cancer surgery meets with more peculiar difficulties and uncertanities than with almost any other form of the disease. The anatomical types of the disease are so numerous, the variations in clinical course so wide, the paths of dissemination so free and diverse, the difficulties of determining the actual conditions so complex, and the sacrifice of tissue so great, as to render impossible in a majority of cases a reasonably accurate adjustment of means to ends.

"The scope of the operative field having apparently reached a limit, the chief hope for a reduction in the mortality from mammary carcinoma lies in its prevention and earlier diagnosis." Most of those who have had the best opportunity of

watching cancer for many years, especially its recurrences, will I think, agree with Dr. Ewing in his judgment.

Carcinoma of the Uterus.—Here also, in the case of cervical carcinoma, which forms over 80 per cent of the cases, one would expect that, from the relative ease of an early diagnosis of the cervix by inspection, and the comparative accessibility of the diseased tissue, the prognosis would be correspondingly good. But there are no data accessible to show the natural duration of cancer in this region, because in so large a proportion of the cases the disease is neglected until it has attained formidable proportions. Taylor[1] states that "Probably 75 per cent, *at least* of the cases of carcinoma of the cervix uteri and of the fundus uteri are inoperable at the time that they are seen by competent surgeons; that is, they have passed the stage when the uterus can be removed with any hope of permanently curing the patient."

Ewing[2] states: "The mortality from uterine cancer is very high. Jacobson, from an elaborate analysis, shows that of the women who enjoy the services of the best American operators, 35 per cent are inoperable, the operative mortality is 15.17 per cent: after 5 years, 8.39 per cent are well, and 1 per cent of the total are permanently cured . . . From the economical standpoint it must be considered that a competent Wertheim operation is beyond the reach of a great majority of the population, and that all the phases of the cost of acquiring technical skill should be counted in estimating its utility. Because of these considerations a marked change has occurred during the last few years in the aspects of surgical treatment of uterine cancer, most surgeons preferring to reduce the scope of operability, and others abandoning operations for uterine cancer, in favor of radium and *x*-ray treatment."

Cancer of the Lip.—In this situation also the lesion is readily seen and accessible for operation, and the prognosis varies immensely with the case, and the time and character of the

[1] Taylor, "Cancer, its Study and Prevention." New York, 1915, p. 157.
[2] Ewing, *loc. cit.*, p. 541.

treatment. The reports of different operators also differ greatly, according as they relate to early or late cases. While some claim that there are not over 25 per cent of permanent cures of all cancers in this location, others who take only early cases claim as high as 90 per cent, which is undoubtedly extravagant. When left entirely alone, and constantly exposed to the ordinary irritation of smoking, eating and drinking, and atmospheric influences, the disease, when once developed, tends very certainly to a steady increase until it is entirely inoperable; but if protected or carefully handled it may be quiescent even for some years. Under most careful medical treatment, external and internal, many cases of unquestioned early cancer of the lip subside entirely, and remain well indefinitely, as we have repeatedly observed, even the enlarged glands disappearing. It is recognized that early surgical operations on the lip are successful in proportion to the care exercised in removing lymphatic glands which are or may become affected. Much has been claimed for radium, and also *x*-rays, but end results after a lapse of time have not been generally reported.

Cancer of the Tongue and Mouth.—Here again the lesions which are or may become cancerous are easy of inspection and moderately accessible for operation, but the prognosis is far from satisfactory. When left alone, Butlin says that there is but one end, death. Ewing states that "The clinical course of buccal cancer is usually progressive and terminates fatally in an average period of 2 years." "More rapid courses are commonly observed in lingual cases, 6 to 12 months, and in tonsillar 6 to 10 months." Taylor says that the end results of operation are unsatisfactory, the chance is less than for epithelioma in most other locations. The immediate operative mortality is very large, even up to 25 to 36 per cent by some operators, but the best modern surgery has reduced this very considerably. As will be seen later most careful medical treatment can hold the disease in check for a long period, and obtain a certain fair percentage of cures. However radical the operation, the lymphatic connections in this locality are so enormous and deep, that even

if the disease does not recur in the previous site, sooner or later it may appear in the glands, with ulceration and great distress. Radium promises better results than surgery in many of the cases of cancer of the tongue and buccal cavity, but very careful and complete medical treatment, with the addition of radium, can accomplish more, as will be seen in a later chapter.

Cancer of the Alimentary Tract.—The prognosis varies very greatly with the location of the trouble, the period at which it is discovered and treated, and the treatment employed. The United States report for 1918, gives a mortality from cancer of the intestines at 6.7 persons per 100,000, against 6.8 persons in 1917. Unchecked the disease in every location tends to a fatal termination, and unfortunately the statistics furnished by surgery are far from encouraging. There are no statistics available as to the average duration of life in these cases, partly for the reason that it is next to impossible to determine with certainty just when the diseased process begins, and a very considerable proportion of the cases have already advanced so far when seen by the surgeon, that they are practically inoperable; the immediate operative mortality is high in many locations, even up to 50 per cent. Cancer of the large intestine is apt to be less malignant, and with better end results than in the small intestine: it is stated by Taylor that the average course of carcinoma of the large intestine, without operation, is from 2 to 4 years, but malignant cases may terminate fatally in 6 months. The best modern surgery has reduced the operative mortality very considerably. The average duration of life after the formation of an artificial anus is stated to be approximately one and a half years.

Carcinoma of the Rectum.—The prognosis of cancer in this locality is very unfavorable. The operative mortality of all cases is stated to be from 15 to 20 per cent, and recurrence after operation is not infrequent.

Cancer of the Stomach.—It is difficult to secure any adequate data regarding the prognosis of cancer of the stomach, except the statement that it is fatal in from 2 to 4 years, when not

operated on, and that the number of patients thus treated who are permanently cured is small, although the total number of cases is very great, and steadily increasing. In the United States Report for 1914, there were 12,768 deaths from this cause, or 19.3 persons per 100,000, and in the 1918 Report the number was 15,844, or 19.4 persons per 100,000 population. As in so many other situations the definite symptoms of cancer which warrant interference are so uncertain, and the disease is so slow in fully establishing itself, that in most instances there has already occurred such an involvement of the lymphatics, liver, and other organs, that by the time the patient sees a competent surgeon it is practically too late to expect a permanent cure of the disease. Ewing has collected data respecting curability by surgical procedure, and expresses the opinion that "of selected operable cases about 20 per cent may be surgically cured." But he gives also other less favorable statistics, where of 480 operations only 8 patients were known to be alive after 3 or 4 years, quoting also Friedenwald, who reports "from 1,000 cases, 266 operations, 138 exploratory, 9 gastrectomies, one living over 18 months, but all dying of the disease." Advanced surgery has reduced the operative mortality from 68 per cent to 35, 25, 17, and even 13 per cent has been claimed.

Cancer of the Liver and Gall Bladder.—Here the prognosis is even more unfavorable, 4 to 6 months is stated as the duration of life with primary cases of the liver, but in secondary involvement the progress may be much slower: practically no operations are feasible. Cancer of the gall bladder is said to terminate in from 6 months to a year after it has become established, and while occasionally operated on there are very few cures, except in cases where carcinoma has been discovered accidentally in removing gall stones.

Carcinoma of the Kidney.—Here the prognosis is also most unfavorable, not only is the operative mortality high, but there are many deaths from metastases, although some fully successful cases are reported.

Carcinoma of the Bladder and Prostate.—In these cases the prognosis depends upon the extent of the growth before operation. Small papillomatous cancers of the bladder can often be removed successfully, both by complete surgical operation and by careful use of the high frequency current. It is stated that the average duration of life after the first symptoms of carcinoma of the bladder is under 3 years. In carcinoma of the prostate Taylor says "This is unfavorable even if the case is seen at an operable stage. In most cases there is an early recurrence. There is, however, definite prolongation of life and an increase of comfort, obtained by operation in many cases."

In studying the prognosis of cancer one is struck with the similarity of statements, just as in the case of the histo-pathology of the disease in various locations. Cancer wherever situated is one and the same disorderly and virulent action of certain cells of the body, mainly of the epithelial elements, which when left to itself tends to a fatal termination in a period from a few months to a few years. In every location it is acknowledged that the surgical excision of a diseased portion, with more or less removal of adjoining parts and lymphatics, has relatively little to do with really checking the progress of the disease, while the operative mortality varies from 10 to 50 or more per cent, according to the location and severity of the process when operated on, with some other factors.

We have also seen that recurrences *in situ* or involvement of other organs or lymphatics is the rule rather than the exception. While most of these unfortunate occurrences take place largely in the first year or so, there are plenty of recorded instances of recurrences (or, more properly, new developments of cancer,) in all succeeding years, even as late as 25 years after surgical interference.

It is recognized that the aims of surgery in regard to cancer are: 1. To cure the disease: 2. To prolong life: 3. To relieve symptoms.

In regard to the first it is more and more acknowledged,

both by physicians and surgeons, that the surgical removal of the affected parts does not and cannot reach the real cause of the trouble, which all assert to be unknown. Moreover, the steadily rising death rate up to 90 per cent of those once affected, shows the futility of the attempt.

In regard to the prolongation of life by operation, we have mentioned the study by Aebli, that after an analysis of a large number of cases treated surgically and those left with ordinary treatment, that the advantage of the knife cases is inconsiderable, and that of Ewing that secondary operations in cancer of the breast shorten life, while the pain and agony of later recurrences is often beyond description.

As to the relief of symptoms by operation, this is conceivable in a small proportion of instances, but those who have had the opportunity of seeing large numbers of post-operative recurrences will testify that the subsequent distress from them quite overbalances any relief received in the few successful ones. Complete, careful, and long continued dietary, hygienic, and medicinal treatment answers all of these purposes far, far better, as will be shown in succeeding chapters.

CHAPTER VIII

METASTASIS OF CANCER

While cancer is not infectious or contagious, and while human cancer cannot be inoculated on another human subject, or on animals, the disease, first manifested in a single spot can be spread and is spread by metastasis in the same individual to an almost indefinite extent, until there is a general carcinosis which is fatal. For cancer is not a local affection, the lesion or mass to which we give the name of cancer being only the local manifestation or *product* of an antecedent and long continued systemic derangement, just as are those of rickets, arthritis deformans, arteriosclerosis, gout, etc.

This extension or development of the disease, cancer, can occur in four ways: First, by recurrence in or near the site of an operation; Second, by what is known as metastasis, spreading the disease to distant parts and organs, through the lymphatics or blood vessels; Third, by a continuance of action of the same abnormal blood condition which induced the first vicious aberration of previously normal body cells, causing them to produce new or fresh neoplastic growths, instead of forming healthy tissue; and Fourth, by a certain hormone, or poisonous something given off by already existing cancer cells, which aids in exciting other cells to cancerous action. The latter of these agencies has been considered in the chapter on the biochemistry of cancer; the first three are frequently confounded, but are distinct, though closely connected.

Recurrence in or near the site of an operation indicates simply that there has been an incomplete removal of all the morbid tissue, although the remaining portion may be microscopic. The impossibility of determining absolutely the utmost extent of the original lesion, and reaching and removing all possible lymphatic involvements, accounts for the redevelop-

ment of the disease; for it is recognized that even single, minute cancer cells have the power, under existing conditions of the blood, to reproduce their like and renew the disease in any location. Rough handling of tumors before or during operating may force cancer cells into lymphatics, and the opening of main lymphatics and blood vessels during operation is also a source of the spread of the disease.

Metastasis is undoubtedly the cause or means of disseminating cancer, by transferring microscopic cells which have taken on a cancerous action to distant sites, where they pursue their rampant and vicious course, inciting the same action in adjoining cells.

These cancer cells are scattered through the body by 1. The lymphatic system; 2. The venous system; and 3. The arterial system; of these the lymphatic system is generally the first point of entry, although they may gain access also directly through the others. A good knowledge of the distribution and structure of the lymph capillaries, with their single layer of endothelial cells, and the lymph-nodes, will aid greatly in understanding the subject of metastasis in cancer. The enormous and most intimate relation of the lymphatics to all the structures and to every cell in the body, and the immense numbers of lymphatic glands, both external and deep, together with the functions they perform normally, in their effort to protect the health of the individual, explain how readily they become affected in cancer, and how natural it is for metastastic processes to take place through them.

In studying the histo-pathology of cancer we have seen that its morbid cells have no respect for anatomical divisions, but have the power to induce neighboring cells of any tissue to join in their mad career. As the lymphatics have as one of their functions to carry away the results of catabolism from the tissues of the body, these minute carcinomatous cells, or emboli, are readily carried along until stopped by the nearest small lymphatic gland, even as pus cells, or tuberculous or other elements are arrested. But the lymphatic gland suffers in its

struggle to prevent them from passing into the blood. It is believed that the glands do succeed in destroying some proportion of the cancer cells, but commonly the task is too great, and the activity of the retained cancerous elements overcomes their resistance, they pass on and succeeding glands are affected, until ultimately the tumor-cell particles are carried on into the left or right thoracic duct, and thus reach the circulating venous blood. As this passes through the lungs the lymphatic glands there try to arrest them, and the cancerous mediastinal and supra-clavicular nodes result. As cancerous particles pass through the capillaries they lodge in the skin and elsewhere, and create foci for the development of the disease.

Carcinoma may also grow directly into the lumen of a blood vessel, and cancer cells may be washed off into the general circulation. But the argument is advanced that if, cancer were mainly distributed through the vascular system there would be a more general and sudden outburst of cancerous lesions all over the body. Some believe that the blood has certain cytolytic powers, which destroy a portion at least of these elements in its current. But the weight of proof is mainly that cancer is distributed through the lymphatic system. In certain cases a neo-plastic process will ulcerate through a vein, and thus give an abundant supply of infectious material.

Quoting Ewing: "In cancer of the breast Handley has shown that there may be continuous extension of tumor cells through the lymphatics of the deep pectoral fascia to the axillary and supra-clavicular nodes; thence to overlying skin and to humerus; through the deep lymphatics to the ribs, pleura, lung, and spine; across the chest wall to the opposite breast; downward through the abdominal wall to the epigastric regions, and thence by the falciform ligament to the liver; and further to the inguinal region with involvement of lymph-nodes, skin, and femur. Invasion of the humerus occurs at the deltoid insertion, and of the femur at the trochanter, where these bones are closest to the skin, through the deep lymphatics of which the bone invasion follows. The lower leg and forearm bones escape infection,

which is inconsistent with an embolic origin through blood vessels.

"Passing through the deep lymphatics of the chest and abdominal wall the cells enter the pleura and peritoneum, and become implanted on the serous surfaces, and produce superficial infiltrations of the lung, liver, intestines, and ovary. Or the viscera may be invaded through their main lymphatic vessels, giving central tumors. The liver is involved through the lymphatics of the falciform and round ligaments, or by transperitoneal implantation, or by way of portal nodes; the lung by transpleural implantation or through bronchial nodes and hilus. Abdominal invasion by the epigastric route is earlier and more frequent than the thoracic, occurring without thoracic lesions in 12 per cent of all cases. The diaphragm is invaded by the epigastric peritoneal route, and through the descending lymphatics of its crura the retroperitoneal nodes and kidneys are attacked. This process of lymphatic permeation Handley believes is the master process of general dissemination of cancer."

Ewing does not wholly endorse the Handley permeation theory of cancer, namely, that cancer cells grow along the lymphatic vessels centrifugally, by which means the cells excite around the lymphatics an inflammatory reaction, which may result in the destruction of the cancer cells and the replacement of the lymphatic by a fibrous band.

Quoting Ewing further: "The frequency of lymph-node metastases varies with different tumors, with different varieties of the same tumor, and with different positions of the tumor in the same organ, and must be separately considered for each case. Cancer of the breast probably stands high in the list, very few malignant cases of this disease failing to involve the nodes, if allowed to remain more than a few months. Williams found the nodes involved in 73 per cent of 118 cases at first examination, and in 90 per cent of 44 autopsies.

"Epithelioma of the tongue or tonsil very early and nearly constantly invades the lymph-nodes, but here again the type of the tumor is the determining factor. Williams recorded 83 per

cent of 104 lingual cases infected at the first examination, and almost 100 per cent of cases coming to autopsy. Epithelioma of the lower lip invades the lymph-nodes more slowly, but eventually in almost all cases. In 186 cases of cancer of the stomach examined at autopsy by Moore, Cuneo, and Colwell, lymph-nodes were involved in 149.

"The lymph-nodes escape in many cases of uterine cancer, especially with tumors of the fundus. Epithelioma of the skin is slow in reaching the lymph-nodes, and rodent ulcer and adenoid cystic epithelioma are remarkable for the long or permanent immunity of adjoining lymph-nodes. Of 34 malignant tumors of the testis, Butlin found the lymph-nodes free in only 3, but in a series of 19 cases I found several which had not attacked the inguinal nodes. The tumor usually affects first the epigastric nodes.

"Changes in lymph-nodes draining malignant tumors show that the implantation of metastases is preceded by a preparation of the soil. For weeks or months before the actual tumor invasion the regional lymph-nodes may be moderately swollen. During this period many new lymph-nodes may develop in the course of the vessels. On section the swollen lymph-nodes show diffuse hyperplasia with catarrhal exfoliation of sinus epithelium, or multiplication of follicles. It is not uncommon also to find the nodes atrophic and fibrous, or extensively invaded by fat tissue, conditions which reduce their effectiveness as filters. Owing to a variety of causes old changes of the latter class may permit the passage of cancer cells through or around a given group, only to lodge in a more central area. The former class of recent alterations must be referred to the absorption of toxic products from the tumor, autolytic and bacterial. There are no specific histologic features of the precancerous condition of the lymph-nodes, but there are reasons to believe that regressing tumor cells may be found in the sinuses before definite implantation has occurred. As previously noted, Kuster found that in only 2 of 117 cases were the axillary nodes which were removed with breast cancer free from invasion.

"The earliest nodules appear in the sinuses, from which they invade, and compress the pulp with complete atrophy of lymphoid tissue. From this point the cells may invade the capsule and the peripheral lymphatics, blood vessels, fat, or fibrous tissue.

"When the metastatic period is established lymph-node invasion may follow rapidly. In a case of cancer of the breast, a swollen axillary node examined in March showed only inflammatory hyperplasia with no demonstrable tumor in the breast, but in June the entire breast was infiltrated by a flat, diffuse growth, and some axillary nodes were completely replaced by cancer. Since many tumor metastases long remain confined to the regional lymph-nodes and fail to make any headway through the blood stream, it may be assumed that there is a regional and general immunity against implantation. Yet in not a few cases cancer skips the regional nodes and yields distant metastases. According to Gross this occurred in 1 out of 7 cases of breast cancer. With some rapidly growing tumors both local and general susceptibility to metastases exist at a very early period, and in most cases one must conclude that the growth capacities of the cells are of chief importance in determining the fate of cell emboli.

"In not a few cases of advanced cancer the thoracic duct is invaded, an event which commonly leads to wide dissemination by lymph- and blood-stream. One of the striking results of invasion of the thoracic duct is the appearance of enlarged nodes in the supraclavicular region.

"The large serous cavities are penetrated by many pathways, and in the course of a considerable number of tumors, chiefly those of contained organs. The most frequent source of free peritoneal growths is the ovarian adeno-carcinoma, which at any period may rupture its covering and be disseminated throughout the cavity. Its cells rapidly become implanted in the peritoneum, producing miliary or large, solid, papillary, or cystic tumors, with a tendency to ascites. One of the most remarkable forms of peritoneal cancer arises from small adeno-

carcinomas of colon or appendix, which early penetrate the peritoneum, spread rapidly throughout the greater sac and, retaining the large alveolar structure, produce enormous quantities of mucus, greatly distending the abdomen. I have seen gelatinous cancer of the rectum, following an extra-peritoneal route, fill the pelvis, enclosing rectum and bladder, pass up the abdominal parietes in front and retroperitoneal tissues behind, separating liver from diaphragm, inclosing the entire abdominal cavity in a rigid shell 3–5 cm. in thickness, and eventually invading the mesentery and subserous intestinal lymphatics, but without any trace of intra-peritoneal growth.

"Peritoneal invasion is a very common complication in breast cancer, and occurs as Handley shows, often by the way of epigastric lymphatics. From the superficial lymphatics and along the falciform and round ligaments of the liver he has found cancer nodules opening into the peritoneum. Loose cells often become implanted first in Douglas sac or on the ovary. More frequently there is a wide spread permeation of the subperitoneal lymphatics, which may become almost universal. It is associated with active growth of hard fibrous tissue, producing nodules and adhesions. Eventually the entire peritoneum becomes thickened, leathery, and opaque, and the omentum shrinks to a firm, globular, infiltrated mass.

"The peritoneum seems to have very little capacity to destroy cancer cells, so that invasion once accomplished is usually progressive. Gravity and the muscular contraction of stomach, intestines, diaphragm, and parietes assure a general dissemination of cells. These movements may cause the separation of tumor masses which have been found free in the peritoneal and pleural cavities, while the aspirated fluid nearly always contains exfoliated cancer-cells.

"Intrapleural and intrapericardial cancerous invasion occur chiefly by direct invasion from cancer of the breast, bronchi, and lung, with results very similar to those produced by breast cancer in the peritoneum."

Ewing and others state that the removal of tumors which

have been shown to be benign by the microscope is occasionally followed by the appearance of malignant disease, either *in situ* or by metastasis.

There is still something to be said which has not been covered by the above. In rare cases, with and without treatment, the primary tumor may not be followed by metastases, or these may be of very late development; in case of extirpation there may be no recurrence. Nay even partial removals and palliative operations have occasionally seemed to cure cancers which have been termed inoperable. The rationale of these cases is not in the least understood. In some recorded instances of this kind in literature there is no record of a microscopic examination. This so-called benign or semi-malignant behavior of cancer may at times be explained by the histology, for in cancer of the breast some forms are known to be less malignant than others.

We have not yet mentioned spontaneous regression of cancer. A small number of cases are on record, but they teach us nothing. We find the statement that regression is seldom complete, some of the neoplasm remaining behind, but we do not know whether this statement refers to so-called cured cancers, or to the spontaneous regressions just mentioned. The dozen or more of the latter on record were no doubt complete regressions. The fact of regression must not be welcomed too gladly, for this does not exclude the possibility that metastasis has already occurred.

Much could also be said regarding local recurrence. After removal of a growth that is clearly benign in all respects, there may be a malignant recurrence *in situ*. After removal of a primary nodule of cancer there may be a recurrence close by, due evidently to an outstanding focus. These secondary nodules not infrequently spring up in the neighborhood of a primary focus. It is evident that in some of the cases the satellite foci can remain latent over long periods, until roused to activity by some unknown cause.

In regard to metastases, appearance of the disease in the

regional lymph-nodes is the rule, and only now and then do we see cases without this association. It may be early or late in development. Lymph-node metastases must not be confounded with so-called symphathetic or irritative enlargement. This latter condition tends to disappear as soon as the primary growth is removed, while true cancerous metastasis continues to grow. It happens now and then, however, that cancerous lymph-nodes disappear after removal of the primary growth. Biopsy is made by some operators to distinguish between true and pseudo-metastases. The prevalent tendency, however, is to extirpate all the accessible glands, whether normal or otherwise. In certain cases, as in cancer of the tonsil, the regional lymph-nodes suppurate as a result of infection; so that cancer metastasis and septic phlegmon are associated in the same subject. In cancer of the nasal fossæ metastases are as a rule not in evidence, and appear in positive cases very late. At autopsy there are sometimes found metastases in the nodes which are hidden from view, by their deep seat, but these are seldom serious.

Lymph-node metastases are almost inevitable, because as soon as cancer cells break through the basement membrane of glandular structures and the corresponding limiting connective tissue in other situations, they enter directly into the lymph channels, passing from these into the nodes. They continue to infect the secondary nodes and those beyond, sometimes skipping one set of nodes; and in such cases as a rule only one-half of the body is affected. If the cancer cells enter the thoracic duct they readily reach the blood, but in most cases blood metastases are due to direct entry into the veins of the tumor. It sometimes happens that glandular enlargements occur in a region prone to metastases which are not directly induced by cancer, but are exposed to forms of malignancy peculiar to themselves. Thus it may be difficult at times to distinguish between malignant lymph-adenoma of the neck, which is a primary manifestation, and secondary lymph-node metastases due to cancer somewhere in the buccal or neighboring cavities.

Blood metastases do occur in cancer, but many cases which at first sight seem to be due to blood transmission, are found at autopsy to have been examples of transmission along lymph vessels. These blood metastases are seen as a rule in sarcoma and in certain locations of carcinoma. Among the latter are primary cancer of the liver and kidneys and the prostate. Lymph metastases tend to occur in cancer of the skin and mucosæ, where regional lymph-nodes are present. In cancerous propagation along the lymphatics the cancer cells are able to make headway against the lymph stream, and cause so-called retrograde metastases. Cancer cells may circulate in the blood of an individual without causing metastases; and at the other extreme metastasis may result in benign growths, as chondroma of the testes. Indeed normal tissue, as in ordinary thyroid adenoma, may metastasize extensively into the bones and cause lesions which while not technically malignant, require, when possible, surgical removal.

The general rule is that metastases are more malignant than the primary focus, although there are exceptions. If a primary growth makes but little stroma, a bone metastasis may nevertheless contain much new bone tissue. Metastases almost always follow the type of the parent growth, but there may be a falling off in anaplasia, as when metastases of epidermal cancer are found to contain no pearls. In distinction to cancer, malignant teratomata cause metastases which are unlike the parent growth—those of chorioepithelioma. Bone metastases have also appeared at a very late day—thus, when there has been no local recurrence after 5 years in breast tumors, metastases have yet appeared in some of the long bones.

It is very easy for the surgeon to contribute to the production of metastases. In the course of operation he may cause inoculation or transplantation metastasis. Both biopsies and rough handling in examination and operation, as well as the mere use of the knife in laying open blood vessels, invite metastases. It is also claimed that one can also ward off some of the dangers of metastasis by *x*-raying all the lymphatics. This is said to cause

a narrowing of the latter, and it is known that the narrower the vessel the more difficult is it for cancer cells to pass. A factor in metastasis is the character of the tissue for furnishing nutriment in which the cancer cells are arrested. The cancer cell requires a special type of nutriment, and when a metastasis fails to take place it is alleged to be due to this cause. Most metastases in the general blood circulation involve the lungs because of the relative narrowness of the capillaries; but some of them may pass and enter the liver and other viscera. Cancer in the portal area always metastasizes in the liver. Certain organs are quite immune to metastases, for the cancer cells in these regions cause only emboli. Here belong the pancreas, thyroid, cardiac wall, and muscles. Metastases and cachexia are usually associated, but either may occur without the others.

The study of the progress of neo-plastic growths by metastasis is thus seen to be a most interesting one, which throws much light upon the resistance of cancer to surgical measures: which many are beginning to recognize more and more clearly. The part played by the lymphatic system both in the nourishment and metabolism of the body is an enormous one which will be further studied in a later chapter, but which must be briefly considered here in order to understand the relation of what has preceded to cancer.

All are familiar with the lacteals of the stomach and intestines, and the important part they play in carrying the products of digestion into the system through the thoracic duct. Less thought, however, is given to the immense importance of the lymphatic system in removing from the tissues the results of catabolism, or the disintegration of effete body elements, and passing them again into the general circulation through the thoracic duct, for the action upon them of the various organs of the body. From observation upon a case with a lymph fistula it has been estimated that in man the flow of lymph may be equal to from 50 to 100 or 120 c.c. per hour. The lymph glands through their lymph cells, act as the first modifier

of this stream, before it passes through the lungs, mingled with venous blood, for oxidation, arresting foreign elements, such as micro-organisms, as we see in many diseases.

One can readily understand, therefore, how a disturbance in this great circulating system, by disturbing or abrogating the action of its digestive nodes, as well as by blocking its circulation by the inroads of carcinomatous cells, can very seriously affect the nutrition of the body. Also it is evident that the great multiplication of carcinomatous centres, each giving off its poisonous hormone, to be further considered in a later chapter, induces the cachexia of carcinosis, by further deteriorating the blood, as will also be discussed later. It is seen, therefore, that the mere removal of the primary lesion or lump, which we call cancer, by surgery, *x*-ray, or radium, is a small factor in the cure of the disease, if the lymphatics or distant tissues have been invaded. It will be shown later how even less reasonable it is to expect a real cure of the disease if the constitutional disturbances still continue which produced the original tumor, and which will pretty certainly produce others.

CHAPTER IX

MALIGNANCY OF CANCER

In the preceding chapter we have seen how seriously cancer interferes with the action of that most important circulatory system, the lymphatic, upon which so much of the nutritive and metabolic action of the cells depends. Lymph stasis is recognized as an important feature in many other diseased conditions, and disordered action of the protective and blood making function of the lymphatic glands naturally leads to faulty metabolism, and to an incorrect blood current. For we must remember that malignancy is physiologic and not anatomic. We will note later the changes in the blood and secretions taking place both in early and late cancer. Malignancy is also furthered by the derangement produced by metastasis in the various organs, including those concerned in nutrition and blood making, and, finally, by the general toxic action of absorbed tumor products, which is recognized as an important factor in malignancy.

Ewing says: "The general intoxication resulting from tumor growth is a complex subject which has long been recognized as one of the most obscure and important problems in the natural history of malignant tumors. Hemorrhage, mechanical interference with nutrition, pain, the psychical condition, abnormal secretion, destruction of important tissues, the toxic action of products absorbed from degenerating and ulcerating areas, and bacterial infection combine to produce the cachexia of tumors. When the clinical signs of malignancy declare themselves, the conditions exciting them often belong to the past history of the disease and are often irremediable.

"The prediction of the course that a given tumor will take is based upon two sources of information: 1. Anatomical and microscopical diagnosis, and 2. Accumulated experience regard-

ing the usual behavior of tumor of known histological structure. Fortunately, a parallel exists to a very marked degree between the histological structures and the usual clinical course." But he quite insists that the correct interpretation of structure in the light of clinical data requires a very wide experience, not only with the general tendencies of specific structures, but with the observed courses of different tumors, as many will also agree who have had experience with different, or rather indifferent, microscopists.

"A somewhat general estimate of the malignancy of tumors may be based on the distinctions between *adult* and *embryonal* or *anaplastic* growth. It has long been recognized that the greater variation in type between a tumor and its originating tissue, the more malignant the tumor, and Hanseman has effectually emphasized this principle, pointing out that the morphological evidences of anaplastia have a physiological significance, indicating the degree to which the process is freed from growth restraints and from the control of the organism. Yet here is encountered the difficulty of distinguishing between original embryonal qualities and signs of acquired anaplasia. One group of tumors arises from embryonal cells which have lagged behind in development, and such tumors bear an embryonal stamp. The histological signs of this embryonal character are often difficult to distinguish from the signs of anaplasia, and if they are wrongly interpreted an erroneous impression may be drawn of the malignancy of the tumor. The great theoretical value of the distinction between embryonal and anaplastic cells is not, however, equal in practical importance, since both types of tumors, especially the latter, are usually quite malignant. The histological signs of anaplasia are, a cellular character, marked variations in size in either direction from the originating cells, increase of chromatic, nuclear substance, abundance and abnormality of mitoses. and a loss of polarity, and diffuse infiltrative growth of cells. In many instances lack of reaction of the tissues against the infiltration of tumor-cells is a significant feature. Equally

important are the general signs of exalted nutrition and vitality of the cells. Upon these features one may safely base the estimate of growth capacity and potential *malignancy of tumors*."

"The histological signs of malignancy measure the potential malignancy of a tumor, but the clinical course is subject to wide variations from the position of the tumor, hemorrhage, trauma, changes in rate of growth, bacterial infection, etc., any one of which influences may greatly alter the course. With these important limitations it may be asserted that there is a close parallel between histological structure and the malignancy of a tumor.

"The *emaciation* accompanying tumor growths has long been recognized as one of the most significant and obscure of its many features. It may be said to be a constant effect of both very malignant and relatively benign tumors. It occurs early or late, with or without anæmia, though probably always with diminution in the total volume of blood, sometimes with preservation of the fat deposits, and is preceded by distinct muscular weakness. It affects chiefly the muscular system, but also all cellular organs and tissues. Inanition is undoubtedly the chief factor in the loss of weight. Mental depression, leading to distaste of food, the lowering of the digestive capacity, and mechanical obstructions to the alimentary passages, reduce the amount of food absorbed. In six cases of uterine cancer V. Norden calculated the voluntary ingesta at 300 to 1,200 calories.

"*The Blood in Cancer*.—The great majority of malignant tumors are associated throughout most of their course with progressive deterioration in the quality and quantity of the blood. Usually the anemia takes the form of a secondary chlorotic process, with loss of hemoglobin exceeding the reduction of cells, low hemoglobin index, and slight leucocytosis. In a notable group of cancers of the stomach the anemia dominates the clinical picture, and takes a secondary, pernicious form.

"The absorption of hemolytic agents from ulcerated and

infected surfaces, and from necrosing areas of closed tumors, is a chief factor in producing anemia. Maragliano, Kullman, Bard, Polk and many others have demonstrated the presence of hemolytic properties in the blood of cancer. Elsberg found that normal red cells injected beneath the skin of cancerous subjects were soon hemolyzed, yielding a characteristic discoloration of the skin, and he proposed this method as a diagnostic test for carcinoma. In extracts of degenerating and necrosing tumors Weil demonstrated thermolabile and thermostabile hemolysins, not differing from those obtained from necrosing normal organs. Clinical effects of such hemolysins were observed by Bard, who pointed out that in cancerous pleuritic exudates the red cells are often hemolyzed, while in other bloody pleural fluids the red cells are intact.

"The specific gravity of the blood in most cases does not differ from that of the other forms of secondary anæmia, but in well-established cachexia the specific gravity has often been found remarkably low. The albumins of both plasma and serum are distinctly low in such cases (Gravitz). In a case of gastric cancer Wendelstadt and Bleibtreu found 0.70 gm., instead of the normal 2 to 2.25 gms., in 100 gms. blood-serum.

"*Leucocytosis* was early recognized as a very frequent condition in cancer, having been described post-mortem by Andral in 1823, and in the circulating blood by Lucke and Virchow about 1867 . . . Ulceration or other inflammatory complications are the most definite causes of leucocytosis in cancer, and the resulting hemorrhage adds to the increase of white cells seen in bleeding and necrosing tumors. Bacterial infection, local and general, may intensify the effects of absorption of tissue toxins and loss of blood.

"*The total quantity of Blood* in cases of malignant tumor varies greatly, but as Louis showed in 1846, it is usually much diminished. *The regeneration of the blood* in cancer has been found by Bierfreund to require much longer time than in other surgical conditions, and in progressive cases the hemoglobin seldom reaches the ratio existing before operation.

"*Alkalescence of the Blood.*—Determination of the alkalescence of the blood have yielded results which differ with the methods employed and the particular factors brought into consideration. Klemperer found a reduced amount of carbonic acid in the blood in advanced cancer. Peiper tritrating the whole blood, found very low grades of alkalescence in advanced cachexia, and Rumpf, Limbeck, and others, dealing with the whole blood, obtained uniform diminution of alkali in advanced cases.

"*Influence of Cancer on Digestion.*—The absence of free hydrochloric acid in the gastric contents of cancer of the stomach, discovered by Van der Velden in 1879, and thoroughly investigated by many later writers, stands as a prime factor in the anemia and mal-nutrition of this disease. In all but from 10 to 13 per cent of such cases free hydrochloric acid is missing (Richter). When cancer is grafted on simple ulcer the early stages of the process may be marked by the excess of free hydrochloric acid belonging to the former condition, but as a rule, this excess declines and eventually disappears, sometimes suddenly, as the disease progresses (Rosenheim, Schneider). In most cases the loss occurs early in the disease (Riegel). . . . In other cancers, not involving the stomach, a simlar deficiency of hydrochloric acid occurs, so that it seems necessary to assume that malignant disease exerts some general influence which affects gastric secretion, even in the absence of severe anemia and cachexia.

"As a result of diminished digestive capacity, disturbances of motility, and retarded absorption, abnormal fermentative processes become established, and various bacterial species find a favorable soil. The products of fermentation include lactic, butyric, and acetic acids, alcohol, and protein decomposition products. Boas at one time claimed that the presence of lactic acid in the stomach contents was specific of carcinoma, and appeared at an early stage, when stagnation and loss of free hydrochloric acid did not exist, but it has since been shown that the presence of lactic acid is dependent upon impaired

motility and deficiency of hydrochloric acid (Strauss, Wagner, Seelig). Since these conditions are present in very early cancer, and since, as Sick has shown, formation of lactic acid is favored by decomposition products of cancer tissue, the test for lactic acid is of considerable diagnostic value.

"*Intestinal digestion* suffers in many ways from malignant tumors of the gastrio-intestinal tract and its accessory glands. With gastric cancer the discharge of abnormal digestive putrefactive and bacterial products into the intestine tends to incite disorder throughout the entire course of digestion, and Wasbutski, Kast, and others have shown that intestinal decomposition occurs, especially with loss of free hydrochloric acid and active fermentation in the stomach. The main effects of tumors of the intestinal tract are the result of stenosis and ulceration, and either of these conditions in pronounced form has a prompt influence on general nutrition. Excessive indicanuria tells of absorption of putrefactive products in stenosis, and formation of fistulous tracts may complicate and terminate the course, without much influence on the extent of this absorption.

"*Blood in the Stools* offers a means of diagnosis in ulcerating tumors, and constitutes a serious source of anæmia. Acholic stools results from cancerous stenosis of the common duct, and impaired digestion of fats follows destruction of the pancreas and obstruction of its duct. Tumors of the liver, bile passages, pancreas, cecum, and rectum produce various important clinical types of disease. Here it may only be said that all of these conditions tend to produce cachexia through the combination of very numerous factors, which must be analyzed for each case, and the variety of which reveals the very complex nature of tumor cachexia.

"*Changes in the Urine.*—Specific alterations in the urine have not been demonstrated, but its composition varies according to general rules. Uric acid may be increased without relation to leucocytosis. Ammonia nitrogen has not been found to show any variations other than those dependent upon digestion and nutrition. Herter found high ammonia in the coma of gastric cancer.

"Rest nitrogen, chiefly amino-acids, is higher than in some abnormal states, and increases with the progress of the disease (Setti). Salkowski has drawn attention to an increase in the colloidal nitrogen precipitable by alcohol, in cancer. This fraction corresponds partly to the amino-acids (Wolff). Later Salkowski estimated the nitrogen precipitated by lead-acetate, after the removal of phosphates by alkaline barium chloride, finding that this nitrogen fraction is greatly increased in cancer. The nitrogen estimated by Salkowski probably includes the oxyproteic acids and polypeptids.

"An increase of unoxidized sulphur has also been observed by M. Weiss and others, and Salomon and Saxl have demonstrated such a notable and uniform increase in oxidizable neutral sulphur as to indicate its value in diagnosis. Lehman points out that the results of this test depend largely on the diet, without the control of which the examination is useless. From observations in this field Saxl concludes that various analytic methods demonstrate the occurrence in notably increased amounts of protein derivatives, chiefly oxyproteic acids, which escape the normal transformation into urea. In general he finds a somewhat specific disturbance of metabolism in cancer, marked by a nearly constant excess in total metabolism, relative reduction in urea formation, increased ammonia excretion and increase of protein derivatives which fail of oxidation into urea. In no other disease, except certain special intoxications, is the internal oxidation of protein so much disturbed as in cancer. Saxl goes on to show that the disturbance of oxidation is probably due to accumulation in the system of rhodan, an oxidation product of hydrocyanic acid, since this substance is increased in the urine in cancer, and when administered to man reproduces the typical metabolic disturbances of cancer. The basis of this theory remains to be verified.

"Products of putrefaction are found in increased quantities in the urine of advanced cancer, but the exact source of the substances has not been fully determined. Indican, phenol, aromatic oxyacids, and ethereal sulphates have been estimated

by several observers, who attribute their presence to intestinal putrefaction, to decomposition of secretions, and to destruction of tumor tissue. That intestinal putrefaction is not the sole source is indicated by the considerable quantities of such substances observed with decomposing tumors of the breast and uterus (Brieger, Haberlin, Hennige). Leviwn finds excess of aromatic acids in patients with nitrogen loss, but not with those showing nitrogen retention, and concludes that these substances are derived from the toxic destruction of tumor and tissue proteins, and not wholly from intestinal putrefaction.

"*Acidosis of Cancer.*—The acetone bodies in cancer follow the same rules as in other conditions. Their presence in the urine bears no relation to the growth of cancer as such, and their substances are absent in the early stages of the disease, and when the patient is well fed (Waldvogel). With the advent of protein loss and cachexia, acetone and diacetic acid commonly appear in the urine, and beta-oxybutyric acid is added in severe inanition. It is not entirely clear that cancer coma is purely an acid intoxication, and it seems probable that the rapid burning of tissue fats and proteins, of which acidosis is only one result, may be responsible for some of the sudden terminations of malignant tumors. Von Noorden's observation of considerable quantities of lactic acid in the urine of two cases suggests that the acidosis of cancer may involve hepatic disturbance as well as pure acidemia.

"*Albuminuria* occurs in most cases of cancerous cachexia, but is absent in early stages of the disease. According to Muller it occurs in 35 to 72 per cent of all cases of carcinoma. In cancer of the alimentary tract albumoses are very often present (Ury, Lilienthal), either by direct absorption of digestive products through the ulcerated surface (Maixner) or from the disintergration of tumor tissues (Pacanowski)."

Cancer Cachexia.—The statement by Woglom in the article "Neoplasms" in Wood's Handbook, which throws doubt on the existence of special malignant tumor cachexia is a good example of how authorities constantly overlook certain points

when generalizing on malignancy. A tumor with its primary manifestation and often large lymph or blood metastases, etc., requires nourishment and will go to any length to take it from the body tissues. This shows that the innate impulse to limitless and lawless growth is quite independent of a rich blood supply or excess of nutrition. Cancer anemia is developed often in a high degree, yet the growth is not arrested; and the general breakdown of the organism must be charged chiefly to the absorption of much or most of the nutrient material by the growth of the tumor. Wood in his article on "Cancer" in "Wood's Reference Handbook of the Medical Sciences" states that cancer cachexia is the sum of all the injurious consequences of the disease, including pallor, emaciation, loss of appetite, and asthenia. It is not a specific manifestation, for it does not differ from the cachexia in chronic hemorrhagic affections and chronic suppurations, but it is seen more frequently with cancer than with any other affection. Of two theories one is that the tumor takes the nutriment intended for the body while the other holds that the tumor secretes a toxic sustance—not *per se*, but as a result of degenerative processes. Cachexia cannot precede cancer although this was once held to be the case. It is most significant that it can disappear when the growth is removed, to return with recurrence of the growth. It cannot be due to sepsis, although the latter can coexist. Wood is inclined to blame it on a special tendency of cancer cells to undergo degeneration and presumably to form noxious substances. Cachexia is often associated in appearance wth metastases, the latter being held to undergo rapid degenerative alterations. A large breast tumor may not show any cachectic accompaniment.

Anyone who carefully considers this remarkable study of the elements of malignancy in cancer, abstracted from the most careful and elaborate analysis of the matter by Dr. Ewing, a pure scientist, and other laboratory workers, must be struck with the constant recurrence of references to metabolism, nutrition,

the character of the blood and the action of the various organs concerned in the operation of the human system, etc., and wonders why there should be any doubt in regard to the constitutional nature of cancer. The link that is missing in the evidence undoubtedly relates to the question as to whether the various systemic changes observed in cancer patients are a cause or an effect of the disease.

The unfortunate part of all such laboratory study is, that it always relates largely, or almost entirely, to conditions found in patients where the malignant process has been going on for some time, and there has been so little minute searching for the clinical and bio-chemical conditions existing in those with very early cancer, or even in those predisposed to it by hereditary influence. Also that so little attention has been devoted or to the study and observation of those inclined to it by habits of life or surroundings, which have been found later in those who have already developed the disease: (for instance, obseity is recognized as being of great importance in connection with recurrences of cancer of the breast), as also the many points of living, which are brought out in later chapters.

Looking at the question from a common sense and scientific standpoint, it is recognized that there must be a cause for everything, and that the gross disturbances of the system associated with cancer, ending fatally if unchecked, must have a definite cause, although thus far all surgical writers affirm that no cause is known. It is inconceivable and impossible to believe that the misbehaviour of a cell, or a small group of cells, in any of the various parts of the body can, without cause, excite a malignant process which ultimately becomes so destructive, unless the cause which first induced the cell misbehaviour has also existed throughout the whole course of the trouble. In other words, the theory of a purely local nature of the disease is quite untenable. We have already seen that a parasitic cause is rejected by all who have laboriously studied the question, etc. True it is that cancer first manifests itself in one particular spot,

remaining there and increasing, but that is so with other diseases.

As will be seen in later chapters, there are so many features pointing unmistakably to the constitutional character of cancer (endorsed by so many surgeons and physicians), including its control by dietary, hygienic, and medicinal measures, that it need not be any longer declared that we know nothing of its cause.

There are still unfortunately many other affections, such as pernicious anæmia and other diseases of the blood (which remind one of the pathogenesis of cancer), of which this is still said, but, as in the case of tuberculosis we now know that restored metabolism and corrected nutrition will even overcome the harmful influence of the ever present tubercle bacilli. So in the case of cancer much the same measures, along somewhat different lines, can and do overcome the carcinosis or cancerous dyscrasia, even in established cases, if intelligently and long persisted in.

CHAPTER X

METABOLISM OF CANCER

In former chapters we have considered the histo-pathology, the bio-chemistry, metastasis, and malignancy of cancer, and we will now examine the data in regard to the metabolism of the system leading up to these conditions. There will be necessarily some little repetition of what has preceded, in order to grasp intelligently the basic facts of the true pathogenesis of the disease.

The common opinion, and statement, is that nothing is known in regard to the cause of cancer. Long continued and abundant laboratory and clinical research have about decided certain *negative* questions in regard to the disease, so that in a measure the field is cleared for the study of some of its possible basic causes.

Thus, all are pretty well agreed that, 1. Cancer is *not* contagious or infectious: 2. It is *not* caused by a micro-organism or parasite: 3. It is *not* wholly due to local injury: 4. It does *not* appertain to any particular occupation: 5. It is *not* hereditary to any great degree: 6. It does *not* especially belong to or affect any particular sex, race, or class of persons: 7. It is *not* confined to any location or section of the earth: 8. It is *not* wholly a disease of old age. By exclusion, therefore, we are left to conclude that it develops from some cause pertaining to the individual, to the manner in which the tissues are developed, nutrified and changed, and these we know are effected by certain systemic processes to which has been given the name metabolism, with its two divisions, catabolism and anabolism.

It is not a little strange that the efforts of the various agencies engaged in Cancer Research have not been directed to this aspect of the question, and to a clinical and other study of the

effect of diet and mode of life in producing cancer, of which evidence appears in these pages, instead of so much microscopic study of tissues and animal experimentation.

W. Roger Williams[1] in 1894, wrote: "Do cancers, and other neoplasms, arise, as John Hunter and Johannes Müller maintained, through a modification of a formative process: or, are they the outcome of the inflammatory process, owing to the presence of micro-organisms, or some other sources of irritation? In other words are they, *directly* or *indirectly*, due to the intrusion of some irritant, *ab extra?* I incline to the former alternative: and I think the future will see decided reaction in this direction. . . . In the genesis of neoplasms, as in the genesis of other organic structures, I believe that we must take into consideration two factors—the *cells* whence they originate, and the *force* that regulates cellular activities."

Of late years considerable attention has been paid to the possible influence of "embryonic rests," or pre-natal, wrongly placed *tissue elements*, in the causation of cancer, and Ewing[2] has shown that various neoplastic growths in many different situations may have some relation to embryonic rests; but as these are now known to exist in every one at birth, and even in large numbers, it does not explain why one or more of them take on malignancy only in later periods of life. Nor are cancerous lesion always or commonly associated with such.

Some have attributed cancer to independent cell action, relating to a changed polarity in the cells, etc. But it is inconceivable that a cell or cells can, of their own volition start out on a rampant course, and pursue it with increasing severity, even until death results, without some definite cause, which rationally would seem to be the vitiated character of the blood by which they were nourished.

So in all these studies, histologic, bio-chemic, etc., we are forced to look back to a faulty metabolism, which furnishes

[1] WILLIAMS, "Diseases of the Breast, with Special Reference to Cancer." London, 1894, p. 138.

[2] EWING, "Neoplastic Diseases." New York, 1919, p. 94.

nutriment improper to the satisfactory growth of certain cells which compose the organism. This is often shown by the marvellous restorative effect of treatment based on this thesis, both in early cancer, even with developed adenopathy, which recedes and remains absent without surgical aid, and in the great benefits often seen in well developed, and even in post-operative, recurrent cancer, as will be detailed later. We will now consider some of the evidences of faulty metabolism as observed in cancer patients.

That the blood shows great changes in advanced cancer is recognized by all, and is clinically manifested by the intense cachexia and anæmia commonly present, and always strongly marked toward the end. When then examined there is found to be a marked reduction of red cells, low hæmoglobin index, and distinct leucocytosis, with greatly diminished alkalescence. Some consideration of this subject has already been given in the preceding chapter, which need not be repeated here. The interesting and valuable experiments of Hugh Campbell Ross[1] and others have thrown light on the changes which take place in the cells of the blood and tissues, as mentioned in the last chapter. His studies explain also in a measure the continuance of the morbid process in the blood and tissues where the disease has been carried by metastasis.

The reported changes in the blood have varied with the location of the malignant disease, according as it may interfere mechanically or otherwise with the function of other organs, which fact naturally obscures the question of the true relationship of the blood to cancer. Thus, it is stated that in cancer of the liver and pancreas there is always leucocytosis and glycogen, and that "cancer appears to interfere greatly with the function of the liver as a destroyer of intestinal toxins, they, passing into the general circulation, probably cause the glycogen reaction and at least part of the leucocytosis."

There are also other microscopical alterations in the blood in

[1] Ross, "Induced Cell Reproduction and Cancer." Philadelphia, 1911, pp. 349ff.

late cancer. Thus degenerative changes in the leucocytes are common, with derangement in the normal proportion of their different forms, as also changes in the erethrocytes, with nucleated red cells and megalocytes in severest cases.

Price Jones,[1] in a study of the blood in 30 cases of cancer (9 of the breast), found the red cells diminished on an average of 6 per cent, the white blood cells increased 38 per cent, lymphocytes increased by 10 per cent, large mononuclear cells increased 164 per cent, and polynuclears 42 per cent. Burnham states that in the severe grades of anæmia with malignant disease poikilocytosis is marked, and nucleated cells of both normoblastic and megaloblastic type may be present. The red corpuscles may be reduced to 2,500,000, and exceptionally to 1,000,000. Cohnreich in a very technical study of blood from cancer subjects, observed very great increase in the resisting power of the red blood cells to osmotic tension, in regard to their hæmoglobin, which he believed to be of diagnostic value in doubtful cases.

O. C. Gruner[2] has gone further than many others, and has attempted to demonstrate the possibility of an "exact diagnosis of latent cancer" by means of the blood. He says: "Every gradation of blood state, be it physiological or para-physiological, is faithfully reflected in morphological characters, so that the blood provides an expression of the final effect of a number of circumstances which have been gradually converging at different velocities, toward that spot on the highway of our neighbor's life, called 'the present moment.'"

"The para-physiological states differ from the physiological only in their being *deflections* from routine metabolic tendencies. These deflections are manifested in the substrata of the various orders of cells, and concern the proteins, carbohydrates, fat, and salts. They are, in their turn, traceable to a series of sequent influences contributed by a number of synchronous factors provided by the *tout ensemble* of the organs and tissues of which

[1] JONES, "Archives Middlesex Hospital." London, 1911, p. 72.
[2] GRUNER, "The Exact Diagnosis of Latent Cancer." Philadelphia, 1919, p. 2.

our body is composed. Functional inadequacies or errors in the ductless glands, in the sympathetic nervous system, and even in the mental state are contributory . . . Pathology, and therefore physiology, must advance beyond the cellular doctrine to perceive 'elements' more fundamental, if more elusive.

"Once we grasp the existence of deeper principles, the more surely shall we see that every other diagnostic problem can yield to the same mode of attack. The precision is gained only at the expense of a thousand fold increase of depth of knowledge concerning the intimate processes of physiology. The relation between every organ and the composition of the blood must be worked out. However simple the technique may appear, or however few the immediate data acquired, the fact remains that there is a need of so detailed complex of knowledge that the fullest intellectual energies will be taxed before it is achieved."

It is impossible to present briefly even the salient features of his interesting study, which is pretty technical. After comparing blood from a cancer patient with that from those with many other forms of disease, he presents tables and illustrations showing the differences along many lines, and believes that with sufficient patience and care, with knowledge and experience in hæmotology, it can be discovered if a patient has cancer before an operation, or if the tendency to cancer still exists thereafter.

Unfortunately there have been relatively few satisfactory studies of the plasma of the blood in cancer or other diseases. And yet the condition of this fluid must be of the utmost importance, inasmuch as from it are derived, not only the solid constituents of the blood, but also those of the entire system, about 8 per cent of it being serum albumen and serum globulin, together with certain salts, sugar, fatty matter, and gases. It also holds in solution inorganic salts, phosphates, carbonates, sulphates, and chlorides, the latter often varying greatly, and being chiefly responsible for the isotonic relation of cells and serum. A high percentage of chlorides is usual in anæmias, such as that of cancer. The reaction should be alkaline, but in

cancerous cachexia a diminution of carbonic acid, a constantly diminishing alkalinity, and an increase of acid principle in the blood have been fully demonstrated, pointing in all probability to the existence of an acid intoxication.

It must be remembered that the whole volume of the blood has constantly added to it, through the absorbent veins and lymphatics, quantities of partially assimilated substances, which have not yet undergone the transformation produced in them by all the various organs of the body: for instance the proteins have been but imperfectly split up into their end products, the amino-acids, urea, etc. Thus far the gastric, intestinal, and lymphatic glands are the only agencies which have acted upon the various crude substances, as is seen by the difference in composition of the venous and arterial blood.

When we consider the large size of the abdominal aorta and the relatively small size of the arterial branches given off to the kidneys, by which the poisonous elements are filtered off, we appreciate that the purification of the blood stream by that organ, by which nearly all of the nitrogen waste is eliminated, must be very slow. It has been estimated that of the total quantity of blood sent out of the heart in a minute, only about 5 per cent may pass through the kidneys.

The formation of the corpuscular elements of the blood, also, must be greatly interfered with when metastases occur in the blood-forming and blood-destroying organs, the lymphatic tissue, bone marrow, spleen, and liver; for it has been estimated that the total duration of life of each individual red corpuscle cannot exceed ten days. It seems also that the toxic hormone or secretion from the cells of a cancerous mass, has a distinctive, harmful action on the blood: for after surgical removal of a malignant tumor there is often observed an increase of hæmoglobin, as I have witnessed, also a high leucocytosis has disappeared after the surgical removal of a scirrhus of the breast, only to return again with recurrence of the tumor. Abderhalden[1] states that in from 2 to 3 weeks after the operative

[1] ABDERHALDEN, "Defensive Ferments." New York, 1914.

removal of cancer, certain defensive ferments can no longer be found in the serum of the blood.

Many laboratory studies have been made upon the chemistry of cancer tissue, some of them detailed in former chapters, seeking to determine the nature of the toxins produced by cancer growth, and its experimental effect on animals, but thus far no great results have been obtained. It has been observed, however, by Gruner[1] that when cancer-juice is injected intravenously a marked lymphocytosis arises, which is followed by the appearance of large mast-cell myelocytes in the blood. The cancer juice is supposed to be auto-toxic in cancer patients, and comprises toxic albuminoids, which, being in quantities too great to be quickly neutralized, poison the system, especially the blood and the hæmopoietic organs.

It is hardly possible to draw a line between the blood and nutrition in the precancerous period and in latent cancer on the one hand, and in the early stages of cancer on the other: nor between the latter period and the period of cachexia. The metabolism in cancer tissue must not be confounded with the metabolism of the cancerous individual. The blood is believed to contain antibodies which can protect it from cancer, somewhat as the pregnant woman is protected against chorioepithelioma of the uterus. As soon as delivery has occurred she continues, as a rule, to enjoy protection, but in the exceptional case she develops this form of malignancy. The source of the protection may lie in the ovary, for when this disease develops there is said to be some disturbance in the production or retention of lutein substance. In cancer we may suppose that a similar mechanism is at work, and that the failure of protection may coincide with the disappearance of some substance from the blood.

The work in the Mayo clinic in regard to cholesterol appears to show that this substance is in excess in subjects who later develop cancer, while it is also thought that sugar tolerance is diminished under the same conditions.

[1] GRUNER, "Biology of the Blood Cells." 1913, pp. 153, 260.

The exhaustive studies of the blood by Gruner suggest that the bloood count may show departures from normal while cancer, although present, is inactive, and this implies that similar alterations may occur before the development of cancer has occurred at all. His meaning is not altogether clear but he teaches that *cancer, the disease, precedes cancer the local manifestation.* There is also a poverty of blood in calcium and an excess of potassium, according to some laboratory workers.

The presence of hemolysins, enzymes, toxins, lysins, etc. has been mentioned. The question of antibodies, generated in response to the presence of cancer, has thus far not been mentioned. There is enough evidence of antibody formation to suggest that cancer protein differs somewhat from tissue protein. Injection of virulent cancer material has been found to generate some antibody substance, but the formation is low and inconstant, and the specificity is not marked. That antibodies exist in health and give natural immunity is not proven. Normal serum does not dissolve a cancer cell, while cancer serum does. Much has been written on blood cholesterol in cancer, and the excess present before the occurrence of the tumor suggests defective oxidation; Luden believes that radium benefits because it antagonizes this lipoid excess.

There are certain facts of interest concerning cancer anemia. It is twofold in character, and either due to hemorrhage or toxemia, in the latter case being caused by the hemolysins formed in the growth. In rare cases anemia may not develop at all, as has been noted in cancer of the œsophagus; or a veritable pernicious anemia may be set up. In many cases of anemia hemorrhage is the cause, nor is it necessary that this be manifest, for some of the worst cases may follow occult hemorrhage. In such cases not the clinical history nor symptoms, but the characteristic blood count of hemorrhage is decisive.

In order for cancer products to cause cachexia it is not necessary for nutrition to suffer first, although this is the rule. Cachexia is called the sum of all the ill consequences of cancer

to the general system. It is said not to be specific, and to differ in no essential from the cachexiæ of chronic suppuration, chronic loss of blood, tuberculosis, etc., but cancer is the most frequent cause and produces the most typical form. Authorities differ as to the operation of one of the factors, to wit, the withdrawal of the body nutriment in order to feed the cancer. Wood does not mention it, although others regard this as the most essential cause, the next being absorption of toxic matter after secondary changes have occurred. A third factor is anemia. In certain cases sepsis is a complication. Still another is local interference with vital functions. The action of mental depression at the hopelessness of recovery, and the doom of months of suffering, is sometimes given as a factor. Cachexia clinically is characterized chiefly by pallor and emaciation, with marked weakness. The patient as a rule has no appetite and it is not easy to feed him. It is not now believed that cachexia has ever preceded cancer, although this view was once held.

Cachexia may follow the primary tumor or may not appear until the metastases have begun. Sometimes removal of the primary growth has led to the disappearance of the cachexia, the latter reappearing with recurrence or metastases. As a rule cachexia and metastases coexist, but either may be present without the other. Cachexia never seems to check or arrest the growth of the primary or secondary tumors. These continue to enlarge until the last. For the same reason cancer may very rarely appear in the course of cachexia from some other cause—tuberculosis for example. Even when all outside nutriment is cut off the tumor growth proceeds.

The metabolism of the cachectic individual is said not to differ in any way from the metabolism in cachexias from other causes. While according to the Mayos freshly growing cancer is attended by production of acid (increased amino-acids?) which extends through the organism and is a factor in cachexia production, it seems none the less true that after cachexia is once present the acid content of the body is lessened, and the

blood alkalinity increased. This occurs in any cachexia, and incidentally is shown by diminished hydrochloric acid in the stomach. Demineralization also occurs, all of the saline content diminishing except the chlorides.

Cachexia however only kills about one patient out of three, for the occurrence of numerous complications, which vary with the seat of the disease, is the cause of the majority of deaths—these are very numerous and include hemorrhage, inanition from obstruction, sepsis, albuminuria, pneumonia, meningitis, the results of operation and so on.

We will now consider some of the data which have been recorded in regard to the secretions and excretions, including the internal secretions, in cancer patients, as they furnish the means of understanding human metabolism.

Beebe[1] has said: "No phase of metabolism has been described as cancerous which does not have a counterpart in non-cancerous conditions. This applies to such questions as the nutritive relations between the cancer cells and the normal body tissue, to the nitrogenous balance, retention or elimination of sodium chloride, the excretion of acetone, the relation of ammonia excertion, and a possible acidosis." He adds, however: "Diet doubtless forms an important part in the growth of cancer, possibly even in the origin of the disease." It is encouraging to find that this able and careful laboratory investigator recognizes, in a measure, the basic cause of diet, towards which all evidence points so strongly, although its definite connection may not yet have been established by laboratory methods.

The urine has been the object of much study in connection with cancer, as it would naturally be expected to reflect the metabolic changes in this disease, as it does in others. While many departures from the normal are constantly observed, and while under complete volumetric analysis of the urine of a cancer subject, it is rarely if ever found to be that of perfect health, it cannot be said that any definite and specific changes

[1] BEEBE, *New York Medical Journal*, 1910, p. 1058.

have been established which may not be found in those without cancer; although there have been several who have so asserted and have even claimed to have found diagnostic signs of cancer in the urine.

But minute, repeated, volumetric analysis is often of great service in guiding the nutrition and medication of these patients, and gross urinary errors are constantly met with which may have the greatest bearing on the case in hand, as indicating very important metabolic disturbance; and treatment, to be thoroughly effectual, must be based on the study and recognition of these elements, and adjusted accordingly.

It must be remembered that while the kidneys are one of the main excretory agents of the system, carrying off daily in health between 6 and 7 grains of solid matter for each pound of body weight, their secretion, the urine, is very complex in its composition of over a dozen ingredients, and can afford invaluable indications as to the systemic derangements existing and their necessary correction in cancer. As the urine comes directly from the arterial blood, and there are only two layers of epithelial cells in the Malpighian tufts, between the interior of the capillaries and the uriniferous tubes, through which the urinary elements filtrate, I have been accustomed to call the kidneys the judge and jury as to the condition of the blood; when the urine is most carefully analyzed volumetrically and its indications correctly interpreted. This does not relate to the presence of sugar, albumin, or casts, but to the other various constituents. For while the products of the assimilation and dissimilation of the simple carbohydrates and fats pass off by the lungs, generally without harm, those of the protein and salts are eliminated by the kidneys, and as is known, may be the cause of various systemic derangements. From the study of hundreds of complete volumetric analyses in scores of cancer patients, both in the very early and late stages of the disease, I have found that this excretion, almost invariably, exhibits departures from normal which are significant and helpful to know and act upon.

First to be mentioned is the relation of the *total solids*

excreted daily to the body weight of the individual: for it is evident that a person weighing 200 lb. should pass off more than a smaller person. In one very interesting case of cancer of the breast, in a stout, flabby lady, near 55, in private practice, the total quantity of the urine, measured daily for weeks, was always far below the normal amount, and in spite of diet and active medication it seemed almost impossible, for a long time to raise the total daily quantity of solids excreted in the urine, to more than one-half of that called for by weight of the patient. In cancer I seek to have the daily output somewhat above that of a normal individual, and find the disease improve accordingly.

The following table represents fairly well the total solids that should pass daily in order to maintain a healthy equilibrium.

Body weight, pounds	Total urinary solids, grains	Body weight, pounds	Total urinary solids, grains
90	500	150	920
95	535	155	955
100	570	160	990
105	605	165	1,025
110	640	170	1,060
115	675	175	1,095
120	710	180	1,130
125	745	185	1,165
130	780	190	1,200
135	815	195	1,235
140	850	200	1,270
145	885	205	1,305

These figures do not represent much active exercise, and with increased bodily exertion the solids passed should be more. This table was really constructed for women, and men should excrete perhaps one-tenth more than women: there are also less urinary solids passed with advancing years, and about 5 per cent may be deducted from each 10 years after forty.

The estimation of the total solids is easy with Haines' modification of Häser's method. *Multiply the last two figures of the specific gravity of the total daily urine by the number of ounces voided in 24 hours, and add 10 per cent to the product.* Thus, if the amount passed in 24 hr. was 36 oz. with a specific gravity of 1,021, it would be $36 \times 21 = 756 + 10$ per cent $= 832$ gr. of solids in the whole amount of urine excreted that day. By comparing this figure with the table it can be readily ascertained if the amount is above or below the normal standard for the body weight of the patient as judged by the exact weight and age.

For many years I have employed this method of determining the urinary output in hundreds of patients with various diseases of the skin and cancer, and have found it of inestimable value. It is understood, of course, that by dietary and therapeutical measures the urinary solids are to be brought up to and maintained at or above normal.

As before remarked in regard to the elements in the study of the disease, it would be very desirable to have a knowledge of the urine in pre-cancerous stages, and also in very early cancer, likewise after surgical operations, that we might better understand the metabolic changes which lead up to malignant disease. But unfortunately these are very few, if they exist at all, and almost all the studies on the urine have been made in advanced cancer, and often when the disease has affected vital organs, or when by its own poison it has disturbed the workings of the economy. For, as will be shortly noticed in regard to bowel action, deficient body elimination, often of long standing, is most certainly at the bottom of cancer, although subjects will often appear in blooming health before the insidious process has been detected.

The *acidity* of the urine, as measured by the oxalic acid and phenophthalein test is also of the greatest importance. This is not difficult or tedious of application, and has been used daily in my laboratory for years: the litmus test is of relatively little value in comparison with an actual chemical measurement. Thus with an average normal standard of 285 to 300, we not

infrequently find an acidity of 500 or 600, or even 1,000, and I have known it 1,200; or it may sink to 200 or 100, or even be strongly alkaline. As this urine comes directly from the substances circulating in the arterial blood, which the kidneys are striving, often in vain, to remove or keep down, it, most surely, must make a great difference to nutrition whether the alkalescence of the blood is normal, as reported by the urine at 300, or whether the acid element is doubled or even quadrupled. In cancer I have striven to keep the urinary acidity, by diet and remedies, a little below normal, as it has been shown that the blood in the disease exhibits a constantly increasing tendency to diminished alkalescence, or, wrongly called, increased acidity. We know the result of acidosis in diabetes.

Proteid metabolism has been found by many observers to be greatly disturbed in cancer, and dependent on this many deviations from normal are found in the urine.

A number of studies have been made upon the nitrogen partition in the urine of cancer patients by Einhorn, Kahn, and Rosenblum,[1] also by de Bloeme,[2] Sweet, and others, showing and increase in colloid nitrogen to more than double the normal amount, increased elimination of xanthin, oxyproteic acid, and urinary ammonia, together with many other changes which show that disintegration of the protein elements is very imperfect and often defective. An interesting statement is made by Blumenthal,[3] that the oxyproteic acids are increased even in very early cancer, and independently of the size of the tumor and degree of cachexia, showing them to have some specificity for cancer, because they have not been found in other forms of malignancy. He also states that urobilin is increased in a large proportion of cases of cancer, especially when cachexia is setting in, and is a grave symptom.

Reid,[4] who has confirmed many of these matters reported

[1] Einhorn, Kahn and Rosenblum, Archiv. f. Verdauungsekr., 1911, p. 557.
[2] Dr. Bloeme, Munch. Med. Wochenschr., 1914, p. 1718.
[3] Blumenthal, Handh. d. Spezial, Path. d. Harns., 1913, p. 263.
[4] Reid, Cancer Research Lab., *Manchester Med. Chron.*, Nov., 1912; April, 1914.

by others, says: "I have found an increase of amino-acid nitrogen in practically every case of cancer I have examined. . . . .Hence we can only infer that in cancer, the liver, while not involved in the disease, is still unable, for some reason, to perform its function in synthetizing urea. The organ is functionally injured, no lesions having been found to explain its insufficiency; or possibly cancerous subjects form proteids which the liver is unable to deal with, so they are excreted unchanged, or nearly so. "Degres[1] has made confirmatory studies along these lines, and found the nitrogen disintegration very imperfect, with increase of the ammonia fraction of nitrogen and increased elimination of xanthin bases. He states that: "the toxicity of the urine is increased, apparently as the result of the presence of substances which have not been fully oxidized."

The *urea* is almost invariably diminished, often very greatly, as I have verified time and again, in many cases.

Sulphur elements have been recorded as exhibiting notable changes in the urine of cancer patients. These are, a great increase in neutral (unoxidized) sulphur, and a considerable excess of sulpho-cyanic acid, together with an increase in sulphates and indican, which I have constantly observed.

The chlorides, on the other hand, are as a rule diminished in the urine of cancer, especially in its late stages, when there is inanition or kidney insufficiency: and probably any change in these has only a relation to the nutrition of the patients, for the chlorides come from the food, and are commonly an index of the amount of nutriment absorbed. Robin[2] finds some relation between the excretion of chlorine and nitrogen, according to the stage in which the system is affected by cancer.

The phosphates are known to be increased in the urine of cancer subjects, although irregularly and in an inverse ratio to the chlorides. As inanition increases there is a greater autolysis of cellular structures, and the nuclei yield an excess

[1] DEGRES, *Gaz. Med. de Paris*, 1913, p. 400.
[2] ROBIN, *Bull.* Gen. de Therapeutique, 1913, clxvi, p. 433.

of phosphates, which are excreted in the urine. A more or less general demineralization of the system through the urine has been observed by several, and has been recognized as a significant matter, which is of special importance when we consider what an important part minerals take in the nourishment of cell life.

While the changes which have been observed in the urine in connection with cancer are not wholly pathognomonic, but occur in connection with other diseased states of the system, so that few if any of them can be accepted as diagnostic, or productive of malignant disease, they all have a certain significance, as indicating the metabolic changes which accompany and, as we believe, have much to do with its nature and etiology: and, as stated before, a careful, systematic, and frequently repeated volumetrical analysis of the urine certainly assists greatly in the proper management of these cases, when the departures from normal are carefully studied and correctly interpreted, and acted upon intelligently.

The saliva, by its action, constitutes a very important element in the process of digestion, and consequently has its influence on metabolism and the genesis of cancer. Far too little attention has been paid scientifically to this secretion, in ordinary life or in disease, although there have been laboratory studies on its physiological action. And yet the experience of Mr. Fletcher and others have demonstrated wonderful results from perfect mastication and thorough insalivation, and a careful consideration of the processes of digestion must convince every one of the importance of this secretion in connection with nutrition, both in health and disease. In Mr. Fletcher's case he was able to reduce his own body weight over fifty pounds, largely abdominal fat, solely by very perfect and prolonged mastication. Many have observed a connection between obesity and cancer. The unsatisfactory ultimate results of operations on cancer occurring in fat subjects is well known, and often dwelt upon by the late Dr. John B. Murphy, and the perfect transformation of carbohydrates and fatty sub-

stances by the proper and sufficient use of the salivary secretion may prove to be an important element in the prophylaxis and cure of cancer. The salivary secretion has been found by me to be so constantly acid, and often strongly so, even in very early cancer, and almost invariably in cancer of the buccal cavity, that I cannot but believe that this condition has some bearing upon the subject which we are studying. Not only have I observed it in dozens of patients in my office, but in the New York Skin and Cancer Hospital I have had hundreds of testings made and recorded, as a daily routine, quarter of an hour before eating and quarter of an hour after eating, and rarely is it other than acid, until altered by treatment. As dietary and other treatment, with proper mastication, is carried on rightly, followed by improvement in the cancer mass, the saliva returns to its normal alkalinity, but with a tendency to relapse into an acid condition when there is any laxness in the measures employed.

It is interesting in this connection that Dr. W. J. Mayo has called our attention to the fact that cancer is apt to develop in regions exhibiting an acid reaction. Thus, while it is frequent in the acid stomach it is absent in the alkaline duodenum, and again common in the acid colon: it is also frequent in the bladder under certain acid conditions.

It is to be remembered that the saliva, which amounts in health to between one and two quarts daily, varying with the food, etc., is not wholly for the purpose of lubricating the mouth and facilitating deglution, but its enzymes, ptyalin and maltase, effect radical and important changes in the starchy matter consumed. It is also to be remembered that the latter cannot be acted upon by the acid stomach secretions, but, if the salivary digestion has been imperfect; through insufficient or imperfect mastication, such carbonaceous substances must be passed on to the influence of the pancreatic fluid in the small intestine. Hence there follows delayed and imperfect digestion, faulty metabolism, deranged nutrition, and possibly tumor growth. The importance, therefore, of very slow eating,

very thorough mastication, and perfect insalivation cannot be too strongly insisted on, both as an element in the prevention of cancer and also as a curative measure, when it has developed.

Imperfect intestinal elimination is constantly observed in cancer cases, both habitually both before and in the very early, formative period, and also later, even before any recourse to morphine, which, of course, heightens the trouble. In questioning these patients closely, and recording their statements, I have been so struck with the almost invariable history of constipation, or at least imperfect intestinal elimination, that I cannot help feeling very strongly the probability that the toxins produced by the millions of micro-organisms generated through intestinal stasis and fecal putrefaction, play a great part in the production of that blood dyscrasia which culminates in the formation of the malignant growth. Sir Arbuthnot Lane, of London, has emphasized the fact that one of the terminal results of intestinal stasis may be cancer. Dr. Robert Bell,[1] of London, also, originally a surgeon operating largely on cancer, is most strong on this subject, and says: "During a period, now extending over 20 years, that I have devoted special attention to this subject, with ample opportunity at my command for observation, I have never met with a single instance where constipation did not exist, and, moreover, had not been in evidence for a lengthened period prior to the manifestation of the disease," and he dwells at some length on the necessity of a daily and *complete* evacuation of the bowels.

I, myself, am even more strenuous in regard to this matter, and spend much time making the subject clear to patients, and, as in the case of the urine I endeavor to have the solid urinary excreta a little above normal, and the acidity also even below normal, so with the intestinal excreta, I prefer that they shall be in excess rather than possibly deficient. Under a proper vegetarian diet there is less likelihood of trouble, but even then there should be at least one full, free movement of normal character daily, and certainly one immediately after breakfast.

[1] BELL, Cancer, Its Cause and Treatment without Operation. London, 1913.

The internal secretions, so called, have also been the subject of much research and speculation of late years, in regard to their influence on metabolism and the life processes of the economy, and many studies have been made concerning their connection with cancer, so that there seems to be little doubt but that the secretions of the ductless glands in common have much to do with regulating the metabolism of the cells. We know, for instance, that disease of the pituitary body produces bone disease, resulting in gigantism: that thyroid derangement results in myxœdema: and that disease of the supra-renal capsules gives rise to Addison's disease, or bronzed skin. It is not impossible, therefore, that the derangement of secretion of one or more of these, or other organs, may be an element in the disordered action of certain epithelial cells, resulting in cancer. Harrower calls attention to the fact that cancer is essentially a disease of that period of life when certain of the endocrinous glands lose their normal functions, this loss entailing related changes in the whole chain of interrelated functions of the ductless glands.

The Thymus Gland.—This is a ductless gland of early extra-uterine life, slowly retrograding, until by the twentieth year scarcely a vestige of glandular tissue remains. It originates in the entoderm and begins its fœtal existence as a typical gland. Into this epithelial structure mesodermic cells grow and differentiate into lymphatic tissue (Bailey).[1] Forbes Ross,[2] in his interesting and instructive book, makes some reasonable suggestions as to its influence in protecting young life from cancer. He administered thymus gland tablets to some inoperable cancer cases and was appalled at the colossal increase of growth which followed; in two or three weeks the tumors had quadrupled in size and the conditions of the patients were very much worse. The same occurred when he gave calcium salts freely to other similar cases. He reasoned that in early life calcium was freely used in the ossification of bones, over

[1] BAILEY, A Text-book of Histology. New York, 1910, p. 153.
[2] ROSS, Cancer, the Problem of Its Genesis and Treatment. London, 1912.

which process the thymus presided. He calls attention to the fact that mesoblastic tissue disease, sarcoma, is far more common in early life than epiblastic, or epithelial neo-plasms, and that in adult life sarcoma is very liable to originate from bony structures, having relation to calcium. His study of the relations of the four principal salts of the body, calcium, magnesium, sodium, and potassium, to disease is very suggestive.

The pituitary gland is also an organ whose internal secretion has to do with cellular action, as already alluded to in its connection with gigantism, and therefore with the handling of calcium in the system. But I have been unable to find any satisfactory reports of its action in relation to cancer.

The thyroid is now recognized as playing an important part in assisting metabolism, and like the adrenals and pituitary, its complete removal with the para-thyroids, in animals, is followed by death. While the study of the hormones is still in its infancy, there seems to be no question but that the endocrinous glands act conjointly, one influencing the other, and that together they exert a very great influence in the life processes of the body, and on the behaviour of its component cells. The thyroid has been shown to be one of the main factors, in the post-thymus period, in the management of calcium within the body, which mineral is believed to be an element in cancer, and it also enhances the metabolism of toxic wastes, which are etiological factors in this disease. Many have reported favorably on the effect of thyroid feeding in this disease, and after an experience with it in many cases, I am convinced that it has been one of the means which contributed to the good results obtained. Bell is particularly strong on this subject, and reports many cases where the results were most striking, believing that the thyroid has a peculiar and particular control over epidermic cells.

The internal secretions of the *testicles* and *ovaries* are also thought to have some share in metabolic processes, and observations have been made in regard to their influence in cancer.

Thus, Cahen[1] reported that Beatson's operation of removal of the ovaries for inoperable cancer of the breast, first done in 1896, has been repeated by many, so that Lott has reported 96 cases, including his own. Of these in 23.2 per cent the operation caused a distinct improvement in the cancer. In 15 cases the improvement persisted for a year, in four cases for 4½ years, and in one case for over 5 years. Cahen operated on seven women with remarkable results: in two cases, life was prolonged 4 and 6 years respectively. Others, however, have shown by statistics, that damage to the ovaries by disease, or their removal by operation, greatly increases the proclivity to cancer.

Several writers have connected cancer with the waning of the sexual powers, and the suggestion is made by Sherrington and Copeman[2] that in the period which antedates the cancer age, the reproductive glands by means of internal secretions are able to inhibit the growth of cancer.

Whitman of the Dennison Research Fund, has published a new view of cancer which seems merely a verbal one and does not interfere with any of the older ones. His articles have appeared in the *Journal of Cancer Research* during 1919 and 1920. His mutation theory agrees to some extent with Von Hansemann's anaplasia. Since all biological units undergo mutation as a phase of evolution he thinks the cancer cell is no exception. The mutation theory, however, applies to all tumor cells and accounts well for the change of a benign to a malignant tumor. He thinks heterotopic rests may be more inclined to mutation than normal cells, hence the importance of heterotopia in cancer. In regard to cancer being a disease of civilisation this is intelligible because nearly all cancer nations represent much mixture of blood, and animal experiment shows that pure strains are much less liable to cancer than mixed strains. He thinks that excess and diminution of food articles in the diet may start mutation but only in a secondary way. Chronic irritation is

[1] Cahen, *Deut. Zeitschr. f. Chir.*, 1909, cxix, p. 415.
[2] Sherrington and Copeman, *Brit. Med. Jour.*, 1910, ii, p. 787.

doubtless the main cause of mutation, especially when it disturbs mitotic processes. Of special irritants he mentions arsenic, tar, soot paraffin, radium and *x*-rays. Radiation is known to determine altered mitosis.

He is strong on the pre-existence doctrine, that "cancer exists long before there is any evidence of it." "The cancerous disease is present before the cancer." While this seems to imply a constitutional origin the author possibly refers to local pre-existence, although he nowhere says so.

He denies that there is a "cancer age," and shows by curves that cancer does increase directly with age—more centenarians would have it than nonagenarians, for example. There is no foundation for any other teaching. Under diet he forms an axiom—"a cell feeds but is not fed." That is, it looks out for its own food and cannot be forcibly nourished.

In looking back over what has been observed and recorded in regard to the excretions, and secretions, including those of the ductless glands, we see that very strong evidence has accumulated to show that they have an intimate connection with the development of cancer, as was to be expected, since they are very important factors in connection with metabolism, upon the proper performance of which, in its catabolism, and anabolism cell life and health depend.

We have also seen that while there have not been demonstrated any definite and specific changes in the bio-chemistry of tumors or the blood, and no specific enzymes, hormone, or poison secreted by cancer cells, which can directly cummunicate the disease to another, there is evidence that the disordered cells secrete a something which deranges the blood, and, with other causes related to metastasis, ultimately tends to end life: for the blood in advancing cancer undergoes very radical degenerative changes, some of which improve decidedly when a cancerous mass is removed surgically, but return with the regrowth of the tumor.

We have further seen that the urine manifests alterations

which indicate the trend of the deranged protein and mineral metabolism, and that the saliva has an abnormal acidity which both indicates and produces a disturbed amylaceous digestion.

Lastly there is evidence that the internal secretions of many organs, probably through their influence on metabolism, are factors in connection with the genesis and cure of cancer. Dr. Little[1] well says: "Cancer is a disease of disordered nutrition, as a result of which cells revert to a primitive stage which permits reproduction. The disordered nutrition is due to relative hypofunction of the ductless glands."

In later chapters we shall consider the basic causes of this deranged nutrition, which, as has been already intimated, has much to do with diet and the various elements of life which tend to induce functional and other derangements of the system, many of which are included in and influenced by the various elements related to what we term the advance of civilization.

[1] LITTLE, *Boston Med. Jour.*, 1914, p. 587.

CHAPTER XI

MEDICAL ASPECTS OF CANCER

In view of all that has preceded, the medical aspects of cancer loom very large in comparison to the prevailing view of its being a local disease, which requires only the surgical removal of a tumor; for this latter in reality is only the *local product* of an erroneous life process which has existed with an increasingly deleterious force, for a greater or shorter length of time. In other words, carcinosis, or cancer as a disease has existed long before the local manifestation can be discovered. This same constitutional derangement, continuing to operate, unless checked by proper measures, accounts for the almost constant recurrence of the neoplasm, and for the ultimate death from the disease, in 90 per cent of those who have been affected with cancer.

In a recent President's address before the American Surgical Association Dr. William J. Mayo spoke in regard to the internal causation of cancer in a manner which should attract serious attention. Few have had a wider acquaintance with the surgical aspects of the disease than he, and few others know better than he how relatively impotent surgical procedures are to stay the steadily increasing mortality from cancer. A few of his words may be quoted, as they confirm so strongly the views I have held, and those by which I have practised for 40 years and more, with results which I have seldom, if ever, have had cause to regret. For, of course, while there has been a certain mortality, it has been so much less than that generally accepted, life has been so greatly prolonged and patients have experienced so very much less pain than is commonly expected, that an unprejudiced observer who had watched all the cases could not fail to be satisfied that the right course was being pursued, although

with much yet to learn concerning the cure and prophylaxis of cancer.

Speaking of the prophylaxis of cancer, mainly from its surgical aspects in regard to early operation, Dr. Mayo[1] says: "Cancer of the stomach forms nearly one-third of all cancers, of the human body. So far as I know this is not true of the lower animals, nor of uncivilized man. . . . It is not possible, therefore, that there is something in the habit of civilized man, in the cooking or other preparation of his food, which acts to produce the pre-cancerous condition? . . . Within the last 100 years four times as much meat is taken as before that time. If flesh foods are not broken up, decomposition results and active poisons are thrown into an organ not intended for their reception, and which has not time to adapt itself to the new function."

In conclusion he says: "Where cancer in the human is frequent, a close study of the habits of civilized man as contrasted with primitive races and lower animals, where similar lesions are conspicuously rare, may be of value," and finally, "the prophylaxis depends, first, on a change in these cancer producing habits, and, second, on the early removal of all pre-cancerous lesions and sources of chronic irritation."

It is strange that the medical profession has been so slow in accepting, or unwilling to accept and act upon the suggestions along this line which have been thrown out from time to time, for very many years, a hundred and more, by surgeons of prominence well acquainted with cancer, and who felt their inability to cope with this distressing and fatal disease.

That all may know that Dr. Mayo is not alone in his impression that "there is something in the habits of civilized man . . . which acts to produce the pre-cancerous condition," I must briefly refer to some of the leading surgeons of the past, who, from time to time, with more or less emphasis, have claimed that the disease is constitutional, and that it depends largely on diet and mode of life: later I shall hope to present sound grounds for such belief.

[1] MAYO, Annals of Surgery, June, 1914, p. 805.

Abernethy, the great English surgeon, who wrote in 1816, has already been referred to in a previous chapter, as saying: "The best timed and best conducted operation brings with it nothing but disgrace, if the diseased propensities of the constitution are active and powerful," saying that "after an operation we are most particularly incited to regulate the constitution, lest the disease should be revived or renewed by its disturbance."

Walshe, in 1815, in his classical work on cancer, gives numerous references to the constitutional nature of cancer, original or quoted from recognized authorities, as well as expressions in regard to the futility of expecting that surgical interference could cure the real disease in any great proportion of cases. He says: "It would in theory appear that the removal of a tumor cannot in itself cure the disease, as the local formation is but a symptom of the general vice of the economy. . . . This tissue being, as the normal textures, the seat of nutrition, is, like them susceptible of its disordered actions." He even quotes Galen as holding this view. He also mentions the effect of diet on the disease.

Lambe, in 1815, wrote clearly in regard to the causation of cancer from luxurious living, and adduced strong proof to show the effect of diet in curing cases of undoubted cancer of the breast and uterus, the diagnosis of which had been confirmed by prominent surgeons of the day, several of whom endorsed the vegetarian diet.

Sir Astley Cooper, in 1825, said: "The cause of the disease (cancer of the breast) is supposed to be some accidental blow or the pressure of a part of the dress: but although a blow may produce a swelling on the bosom, yet that swelling will not be of a scirrhous nature unless some defective state of the constitution disposes to malignant action. If the constitution be good the effects of the blow are speedily dissipated: but if the constitution be faulty, the swelling grows into a formidable disease."

Sir James Paget, that prince of surgeons and pathologists, in 1854, comes out very strongly for the constitutional origin of

cancer, when he says twice in his "Lectures on Surgical Pathology," that cancers are: "local manifestations of certain specific morbid states of the blood:" and again he says: "I believe it to be constitutional, in the sense of having its origin and chief support in the blood . . . the existence of the morbid material in the blood, whether in the rudimental or effective state, constitutes the general predisposition to cancer."

The late Dr. Willard Parker, one of New York's great surgeons, in a study of 397 cases of cancer of the breast, observed from 1830 to 1880, wrote very strongly in regard to the constitutional relations of cancer. In considering its etiology he places first, luxurious living and particularly excess in animal food. He says: "Cancer is to a great degree one of the final results of a long-continued course of error in diet, and a strict dietetic regimen is, therefore, the chief factor in the treatment, preventative and curative." He further says: "In regard to the effect of abstemiousness on cancer I can speak with great positiveness, that a vegetable, or at least a very bland diet, does check the progress of the disease, and in some cases, now under treatment, has been attended by an alleviation of symptoms; and in a few instances even by a recession of the growth."

If it were necessary, any amount of further corroborative evidence could be presented, collected from old and recent literature, giving the experience and views of practical men who have observed and studied cancer and know of what they speak. Often these are fugitive observations, like those of Dr. Mayo, others have written largely on the subject, often in complete journal articles and also in number of books, such as those of Forbes Ross and Robert Bell, already alluded to. Some of these have often presented quite opposite views as to the real cause and nature of the systemic disturbances leading up to cancer, and their remedy, all, however, agree as to there being a basic constitutional origin of the disease. Moreover, the trend of all is to establish very firmly the thesis that cancer is no longer to be looked upon as a purely local affection, of unknown cause, but that it is the final result of a

disturbance of equilibrium in the system, generally of long continuance. This induces certain cells, first in some particular locality, to take on an abnormal, vicious action, which is perpetuated by the continuance of the same systemic condition which induced the first aberration from a normal state of life and function.

But these many fugitive and other observations and studies have never attracted the attention they deserve, and it would sometimes seem as if they were deliberately ignored, and that scientists and practitioners had combined to recognize only the local nature and treatment of cancer. The truth is that very little serious effort has ever before been made to assemble all the evidence of the constitutional nature of the disease, and by synthesis and deduction to establish a basis for the recognition and proper treatment of the constitutional elements involved in the ultimate causation, continuance, increase, and recurrence of the cancer lesion.

The glamor of surgery during the last two decades, has excluded from the minds of the medical profession and laity much thought of the medical aspects and treatment of cancer; and the reasons are not difficult to discover.

Under previous medical care, with no sound reason advanced, and with no definite plan of treatment elaborated, these cases had commonly been seen to go from bad to worse, until the disease was considered incurable, and the patient was then left to die under morphia, which only increased the disease, by further deranging the secretions and excretions. As the local manifestation of the disease appeared to be the real seat of the trouble from which it spread through adjoining glands, which could be recognized, it was very natural that the surgeons believed that by removing the offending tumor early the malady could be checked, and soon they learned, or thought they did, that by also extirpating the neighboring enlarged glands the work would be effective. But they forgot or did not know that elements of the disease lingered in the deeper lymphatic vessels and glands, which were not removable.

Then, the immediate results of well conducted surgical operations often seemed to be favorable, for at time at least, with the possible expectation that with a recurrence of the malady there was still hope that further operations might succeed in eradicating the disease. But we have already quoted Ewing, from the observation and view of a scientific student of very wide experience, in saying that he believed that secondary operations on cancer only shortened life, and we know that after them the pain and distress of recurrent lesions are excessive, and the case generally hopeless. However, for the last two decades surgery has had full sway, and the medical man has practically kept his hands off from cancer and referred these cases at once to the surgeon, with the result often mentioned that 90 per cent of those once affected die of the disease, unless carried off otherwise. Whereas by the practice of great patience and acumen the mortality of tuberculosis has been reduced nearly 30 per cent since 1900, and that of cancer has advanced by almost the same percentage. It is certainly time for the medical man, in view of what has preceded and will follow, to see if great patience and similar acumen will not enable him to check this constantly rising mortality, and effect something commensurate with what has been accomplished in tuberculosis.

On the Mortality chart furnished each year by the United States authorities, there are several other chronic diseases, whose steadily rising mortality during the last twenty years may well excite the alarm of the medical profession, and incite it to more intelligent and earnest efforts to control their morbidity and mortality. These are heart disease, kidney disease, and apoplexy. The deaths from the first of these—heart disease—now exceed those from tuberculosis, having risen from 128.1 persons per 100,000, to 197.7, the others having risen also about 15 and 25 per cent. All these three are recognized as having much to do with diet and mode of living, and it is reasonable to suppose that cancer, whose advancing mortality has outstripped that of these three, should be of

somewhat the same general cause. The dietary, hygenic, and medical treatment suitable for the latter should also avail towards the prophylaxis of these three serious affections.

There could hardly be a more eloquent argument for the application of medical perspicacity and acumen to the study and treatment of cancer than the results of the same which have been applied to tuberculosis with such wonderful results. Because science and clinical study have not been able thus far to point to the single cause of cancer, to discover a single remedy, or to lay out a treatment which will always be successful, there is no reason for doubting that we are on the right track, when every sign points that way.

Nor is there any wisdom, or sagacity, but only mis-conception, error, and obstinacy, in questioning the correctness of the medical aspect of cancer simply because we are constrained to accept and acknowledge that there are other elements which may act as coadjutors in producing the local lesions of the disease. We have always been taught that there are primary and also secondary, or exciting, causes of many affections, and we have seen in previous chapters that various causes of irritation may be, and are, the exciting cause of the local development of the neoplasm in any particular region. Thus, no one doubts that a jagged tooth induces a cancer on the tongue, a smoker's pipe may be responsible for cancer of the lip, betel nut chewing causes cancer of the mouth, a blow on the breast may be followed by a cancer, retained gall stones or irritating feces may be the exciting cause of cancer of the gall bladder and intestine, many sarcomas undoubtedly owe their origin to a single blow on a bony structure, etc. But how often do these accidents, if we may so call them, occur without any such result following, and how continually are there injuries of all sorts, and even prolonged irritating agencies acting without cancer resulting.

A remarkable confirmation of the fact that cancer is not solely the result of traumatism is found in the extreme rarity of the disease on the extremities, which are so often injured, or after

the damage to tissues caused by surgical operations in general: and also that carcinoma is unknown as the result of skin grafting, although it is these same epidemic elements which are the original seat of the disease.

There must, therefore, be some occult, if you please, process going on in the system, which lays the foundation, so to speak, for the morbid response of the cells to such irritants, something which so alters their nutrition that disturbance of their integrity results, and instead of pursuing their normal course of homologous reproduction, or fulfilling their sécretory powers, they take on a new, heterologous formation and begin a wild, unrestrained, and destructive course, with the well known results. This primary or basic cause is found in the disordered nutriment which they receive through blood which has been deranged in various ways and by various causes. In several chapters some of the causes leading to these derangements are pointed out.

Even in regard to the possible influence of the endocrinous glands the same argument holds good. Namely, that those organs not receiving the exactly proper pabulum, or blood supply, either fail in their activity or produce an inadequate or improper secretion, incapable of effecting the correct interchange of tissue elements, represented by metabolism.

The effect of diet will be considered later in another chapter, but a word may be said with advantage here. As all cells are formed and nourished rightly or wrongly, by what goes into the mouth, there can be no question but that diet must be of supreme importance in connection with cancer, and this, indeed, is the first or basic element to be considered in its treatment, without this being correct cancer is a hopeless disease.

CHAPTER XII

NOSOLOGY AND RELATIONS OF CANCER

The only method by which we can comprehend the nature of cancer is by a system of comparing its phenomena with those of other processes, not only pathological but normal. In this way we can form an idea not only as to what cancer is but what it is not.

Normal Growth and Development.—The energy of growth of a malignant disease has often been compared to that of the embryo, and it is stated that in the natural process of growth this energy is superior to that in the malignant; inasmuch as the embryo starting from a single ovum, the weight of which can be computed, increases its weight more rapidly than a tumor, concerning the beginnings of which we know nothing. Furthermore in a fetus, in the embryonal stage, processes like infiltration of connective tissue by epithelium may be seen to occur, exactly as in cancer, although this is only temporary.

To turn to another chapter in embryology there is a strong resemblance between the growth of cancer and that of the trophoblastic tissue which nourishes the embryo at its earliest stages. At a later period, after the formation of the chorion, the syncytial cells exhibit properties which in many ways resemble cancer cells. These decidual cells will be discussed under chorio-epithelioma. It is enough to state here that both embryonal and fetal tissues behave to some extent like carcinoma, so that the latter cannot be regarded as anything absolutely foreign to the economy. While cancer proper is distantly related to these processes, numerous malignant, non-cancerous growths are much more closely related, and this is the germ of the idea that cancer is something added to to the simpler and more primitive types of malignancy. The latter are rare and show no tendency to increased incidence;

they are local and not constitutional, surgical and not medical. Cancer is an entity of which malignancy is a pronounced attribute, but it is something more.

Epithelium in its Normal and Pathological Expressions.—Cancer is an epithelial formation and it is necessary to compare it with both normal and pathological growth. Epithelium of the skin, mucosæ, and glandular organs is in constant change; it is being shed and renewed continually. Save for the blood corpuscules there is no other tissue in the body in which this rotation is clearly in evidence. Differences between cancerous and ordinary epithelial cells have already been mentioned, including the fact that cancer tissue of certain animals can be implanted and form tumors of its own kind in suitable soil in animals of the same class; but while epithelial reproduction is seen in human skin-grafting, tumor formation does not take place. The cancer cells awaken some reaction in strange tissues, so that a stroma with blood vessels is formed to nourish the new growth. This desmoplastic function is one of the most striking attributes of the cancer cell, but as will appear later, it also resides in non-cancerous epithelium. Thus cancer is often antedated by the formation of the two leading forms of benign epithelial tumor, papilloma and adenoma. These are a connecting link between hyper-plastic and neoplastic processes, and represent an outgrowth of epithelium. They are peculiar in that they form no true stroma, being nourished from the subjacent corium and submucous elements. Papillomata are plainly due, for the most part, to some form of local irritation, and the agencies which cause their appearance also cause cancer. In a certain per cent of cases they are changed to malignant tumors, or else malignancy pre-exists in a certain number. Adenomata, on the other hand, represent an ingrowth of epithelium into the sub-epithelium, and presumably are of heterotopic origin, in part. The epithelium in ordinary adenoma is desmoplastic, and a considerable stroma may be formed. As in the case of papilloma there is a tendency to develop into cancer.

An interesting feature of papilloma is the tendency to recur after extirpation. This property then is not primarily cancerous but resides in the epithelium of the benign growth. But it is not so easy to make straightway a difference between papilloma and epithelioma. Some adenomata result from irritation, while not all papillomata have self-evident causes. The two forms must often co-exist clinically. We see papilloma develop in the cystic cavity of certain adenomas; and for a papilloma to become highly malignant there must be an ingrowth of epithelium into the sub-epithelial structure.

By using certain agents which stain epithelium, it has been possible to cause, in laboratory animals, epithelial neoplasms which are not cancerous.

If epithelium *per se* had any tendency to become cancerous without any other component it should appear in wound healing in the elderly. But in all processes of repair it is very exceptional, even in the aged for the scar of an ordinary wound to develop cancer, and perhaps only in patients with the peculiar condition of metabolism pre-disposing thereto.

Transitional forms between adenoma and cancer are well known; in malignant adenoma, so-called, there may be no immediate change in anatomical structure. The growth rate may be very rapid so that the basement membrane may be defective or absent, yet this need not amount to malignancy. It is known that in malignant adenoma the epithelium may force itself through a basement membrane. In adeno-carcinoma, so-called, the original structure of the adenoma may be recognizable, not because of residual tissue but because the newly formed cells make an abortive attempt to form an organoid tumor. In these cases the stroma and even a lumen suggesting a normal gland may be formed, but there is never a new formed basement membrane. Adenoma changing to cancer is evidently quite distinct from a primary adeno-carcinoma, which is better termed a cylindroma or columnar cell cancer, to avoid this source of confusion.

Benign Tumors.—Having entered a little permaturely into the consideration of epithelial tumors, we may in passing allude to tumors as a whole, without reference to the malignant component. It may be said of them as a class that they contain wholly normal tissue in a large minority. Grown *in vitro* there is little difference in the character of the cells, whether these proceed from benign or malignant growths. All tumors are autonomous and autocratic, and not amenable to the ordinary laws of growth, development, and repair. A tumor is less organized than normal tissues, and the less the degree of organization the greater the tendency to malignancy. There is a radical difference in the plan of growth, for a benign tumor expands from within like an onion, without any effort to infiltrate the evironment, while a malignant growth grows from the periphery and infiltrates outlying tissues. It has often been shown that benign growths, taken *en masse*, exhibit all the phenomena of so-called malignancy; although the individual neo-plasm may be either one or the other. If we take all tumors in common the only causal factor common to all alike is irritation or injury.

As already intimated a tumor is autonomous and independent of laws which regulate the individual. If the subject starve, the growth is not inhibited; but lest the idea of autonomy be carried too far it is well to remember that if the subject dies the tumor dies at once. The subject's hair may perhaps grow after death but not his tumor.

Of other facts to notice, one is that in neoplastic growth of glandular tissue, ducts are never formed. Tumors never develop a special nerve supply although they must be under the influence of vasomotor nerves. Their blood supply is in general poor, outside of certain angiomata.

To state that tumor cells are embryonic is an error, for by an embryonic cell we understand one which can develop into something higher.

Inflammation.—The relations between cancer and ordinary inflammation are numerous and varied. Cancer invasion seems able to set up inflammation in connection with certain stroma

formation, so that here the neoplasm figures as the cause of a fibro-plastic process. On the other hand, chronic inflammation seems to be a common cause of cancer; in mammary cancer, for example, it is claimed at the Mayo clinic that a previous chronic mastitis is the essential forerunner of cancer of the breast. In many cancers there seems to be an inflammatory component from the clinical standpoint; for the application of a soothing and antiphlogistic regimen will cause a prompt disappearance of some of the more distressing symptoms. A sarcoma may exceptionally start up a zone of peripheral inflammation, while conversely in the intense connective tissue reaction about a cancerous growth, sarcoma has been known to develop. In the most acute known types of cancer it is almost impossible to state where inflammation begins and malignancy leaves off. Large sarcomatous tumors are hot to the touch. Pre-cancerous lesions are very largely chronic inflammations. Leucoplakia is technically a superficial glossitis. Many skin cancers develop upon a basis of chronic dermatitis, and in general any irritant which can set up a dermatitis, with secondary hyperkeratosis, should be able to cause an epithelioma. Myeloma or giant, cell sarcoma, formerly so-called, is now recognized as a chronic osteitis. Numerous growths which clinically are sarcoma are in reality granulomata and probably of infectious origin. The numerous types of lymph-node tumors and so-called leucomas stand, like certain sarcomas, midway between neoplasms and infections.

Keratoses.—Cancer has numerous points of contact with the hyper- and parakeratoses. The disease psoriasis, which is histologically an invasion of the corium by the epithelial cells with accompanying elongation of the papillæ, has several curious analogies with cancer. It affects the healthiest of subjects as well as others, and has an irresistible tendency to reappear after recession due to treatment. It cannot be cured by local or internal treatment, but on a vegetarian diet, plus a sort of physical training, it may be held in check. It is claimed that psoriatic athletes are often free from eruption during

active training, but the lesions reappear when training stops. But psoriasis is seldom a precursor of cancer. The condition known as acanthosis nigricans, a rare form of skin disease, may be secondary to or at least associated with visceral cancer, the nature of this association being quite obscure. In arsenical tylosis, so-called, which develops in certain subjects under the continued administration of arsenic, epithelioma occasionally develops, despite the old belief that arsenic is a preventive of cancer. The relations of senile keratosis to epithelioma are well known. This does not exhaust the list, for in dermatitis due to the irritation of paraffin, etc., a hyperkeratosis precedes the development of cancer. Histologically the resemblance between a common corn or a wart and an epithelioma is so striking, that failure of the latter to develop in these familiar affections is puzzling. A few such cases are on record, but when we consider the universality of corns and warts, we are forced to believe that the fingers and toes are almost immune to cancer from irritation.

Sarcoma.—The points of dissimilarity between cancer and sarcoma are numerous and often striking. While they share the essential features of malignancy, cancer is far more common and greatly on the increase, while sarcoma makes up but 2 or 3 per cent of all tumors, and is not known to be increasing greatly. No one has ever claimed that sarcoma is a constitutional or diathetic affection, but among those who make this claim for cancer are the editors of the "Index Medicus," who have always classed cancer among metabolic and diathetic diseases; while sarcoma is placed under tumors, hence is made a surgical affection. Sarcoma is much more apt to occur before 40, and cancer after 40. Multiple primary sarcoma is not uncommon, while multiple primary cancer is almost a curiosity. Cancer has more stroma than sarcoma and is often organoid in character, while sarcoma is poor in stroma and mostly histioid. Cancer manufactures its stroma from the connective tissues which it invades, while sarcoma is said to form its stroma from its own cells. Early sarcoma may show no tendency to

invade the surrounding tissues while cancer invades from the very outset. Sarcoma is more apt to metastasize by the blood route, and cancer by the lymphatics.

The two growths attack by preference different structures: with sarcoma it is the bones and periosteum, fascias, ligaments, and tendons, and next to these the brain, gonads, and skin. With cancer it is the female breast and uterus, the stomach and colon, the mouth and skin. Thus the latter is the only structure in which both affections occur in numbers, but cutaneous cancers are to some extent a special type which differs from the true cancers in a number of ways. Both affections, primary cancer and sarcoma, are rare in the liver and intestines, and muscles. Each is rare in structures in which the other is common. Cancer seems able to provoke the formation of sarcoma in rare cases, through the intense connective tissue reaction; while sarcoma is not known to produce carcinoma. When serially transplanted in the laboratory, mouse cancer has eventually resulted in sarcoma, but the opposite has not been noted.

Cancer often causes the tissues around it to put up a defense reaction, but such behavior is much less in evidence in sarcoma. Sarcoma follows at times upon a pronounced injury, like a blow; this is rarely seen in cancer, if at all only in the breast. Cancer habitually follows chronic irritation, while sarcoma does not exhibit such behavior. Sarcoma shades into conditions like lymphoma and leucoma, and granulation tumors, while cancer shows no such affiliations. Sarcoma naturally agrees histologically with the tissues that develop from the mesoblast, while cancer, developing from the epi- and hypo-blast, is akin to the benign epithelial growths. Sarcoma, while even more malignant than cancer, is yet often amenable go relatively mild measures of treatment, such as Coley's toxins and exsection of the large arterial trunk which supplies it; it is also more amenable to radiation therapy than most cancer. Cancer causes the cachexia which bears its name, while in sarcoma it is said that only a high degree of anemia results. The rarer forms of

malignancy like chorio-epithelioma, hypher-nephroma, endothelioma, are more like sarcoma than cancer. In teratoma both tissues may be seen side by side. The position of melanoma—whether cancer or sarcoma—is not yet settled.

Chorio-epithelioma.—By this term two separate affections are understood, of which one develops in connection with child-birth, the other is associated with teratomata. The decidual cell, to begin with, shows certain properties not seen in the cancer cell. In normal pregnancy it infiltrates the uterus like a malignant growth, and even enters the blood-vessels and may be arrested in the pulmonary capillaries, without causing metastases. Pathologically the same cell, without apparent cause, multiplies into a vesicular mole, and with or without this step the chorionic cells, which persist in the uterus after abortion or labor, may become malignant and cause early metastases in the lungs. The latter may result even in the absence of a primary focus in the uterus. Yet despite its high malignancy it is evident that chorio-epithelioma has a greater tendency towards regression than any other malignant growth. The only explanation of all these facts is the presence or absence of some antibody which holds the decidual cell in check. In pregnancy the woman seems in no danger, but only afterwards, although the risk is not great. This affection occurs only after conception, according to standard writers, but cases occur very rarely in which previous conception has not been shown.

Ordinary cancer of the corpus uteri differs radically from chorio-epithelioma. The former is fairly common, occurs in elderly women who have never borne any, or have borne but one child, and is much less malignant than the average cancer; chorio-epithelioma occurs in comparatively young women who have borne children rapidly. Cancer metastasizes slowly and by the regional lymphatics, while the other growth metastasizes early and by the blood route. There is no better demonstration that chorio-epithelioma is not a form of cancer. There are other dissimilarities, for chorio-epithelioma stands in

some relation to the ovary, the amount of lutein material being augmented; but whether this is cause or effect is not yet known.

Malignant Teratomata and Cancer.—Teratomata are always congenital and undoubtedly originate from misplaced embryonal cells, while cancer has this origin only in a small per cent, as far as is known. The cells from which teratomata develop apparently do not come from the individual proper but either from the trophoblast, which is of fetal origin, or from a so-called autosite or remains of a unioval twin birth. The malignant element of a teratoma is indistinguishable from ordinary chorio-epithelioma, this, too, originating in fetal tissues.

Teratoma, unlike cancer, differs from the tissues in which it originates, and the functions of the parent cell are handed down in a much higher degree than in cancer. The malignant tumors of the endocrine organs which cause the formation of hormones, and the results of their physiological action are largely teratomata. The metastases of a teratoma are cherioepitheliomatous. Cancer can never be produced experimentally from embryonal tissues, but inoculation of the latter readily produces teratoma. Better than any other growth the latter can illustrate the formation of malignant out of benign growths. While teratomata may originate anywhere, they have their peculiar sites for development, which differ largely from those of cancer, although in both the ovary is a favorite site. Teratoma is purely local and must be removed surgically, as the bones, skin, teeth, hair, etc., which they contain can undergo neither regression nor softening. Somewhat akin to teratomata are mixed tumors which contain cancerous, in association with some connective tissue growth. The congenital cancers, and those which develop in connection with congenital malformations, such as branchiogenous cancer, apparently have little in common with typical cancer. Any cancer which occurs in subjects well below the cancer age may be regarded as congenital, and purely local, without any element of general predisposition.

Relations of Cancer to Certain Constitutional Diseases.—There can hardly be a doubt that the rapid diffusion of certain forms of cancer stands in some relationship to other and constitutional or diathetic affections which are rapidly increasing, and which are especially dependent on modern white civilization, so that they are jointly spoken of as "white men's diseases." That these affections are not racial but due to the mode of life is apparent from the fact that aboriginal peoples become subject to them as soon as they begin to lead the lives of white men, and after some generations are as much if not more subject to the said affections than the whites themselves. This subject has not been intensely studied and we can only scratch at the surface of it in these pages. Some of these affections bear little resemblance to others, yet the same causal factors may enter into them.

Dental Caries.—This condition is primarily a demineralization of the teeth—a decalcification—which is almost universal among modern civilized whites, in distinction to the immunity of the native black, and to a less extent the American Indian. The explanation of its dependence on acid secretions throws us back to the problem of acid fermentation as a factor, but this kind of speculation throws no light on the diffusion of the disease in modern man, as distinguished from prehistoric man, whose teeth simply wore out but did not decay. The common sense explanation is that with modern cookery, and the choice of certain soft foods, the teeth have too little to do and undergo regressive changes. But some primitive types of man were bolters of their food, and it is to be inferred that they developed caries as a natural result, while those whose food had to be chewed before it could be swallowed retained their teeth, as not a few do today. That a hereditary or cumulative element is involved seems to be shown by the fact that caries is really a disease of childhood and adolescenec and that after maturity the condition, while present, is much slower in evolution. The teeth which have weathered the first few decades of life do not give much trouble, with the exception of the wisdom teeth.

Pyorrhea-alveolaris replaces caries as a menace in the later decades. The two exclude each other apparently, because in pyorrhea the reaction is alkaline, while in caries it is acid. Pyorrhea has also shown a remarkable increase in civilized white men. It may be compared in some ways with the normal senile retraction of the gums and loosening of the teeth, but is quite distinct from this process, appearing during maturity and having a distinct pathological mechanism. Both affections are aggravated by the lodging of food particles between the teeth, due to imperfect alignment. In perfect dentures this lodgment can hardly occur. We see, therefore, in these dental affections the operation of several factors—evolution of the cranium, disuse of the teeth, the consumption of food softened by cookery and perhaps without proper mineralization, and various local factors.

There is an important relationship between the teeth and endocrine glands, and perhaps with the vitamines. Some dentists isolate thyroid, pituitary and adrenal types of teeth, and we know that in scorbutus the gums bear the brunt of the disease, so that the teeth loosen and fall out. If civilization means a strain on the endocrine apparatus, as is claimed by those who seek the simplest and most universal explanation of the spread of diseases, it would not be difficult to formulate a theory to show such relationship between defective internal secretions and the pathology of the teeth.

Before going further we may speculate a little on the possibility of common factors between the spread of caries and that of cancer. Victims of the latter are often, if not commonly, of apparently, remarkable physical soundness, with well preserved teeth, and caries is preeminently a disease of adolescence, so that there is little analogy between the affections themselves. Robust people, well preserved and with good teeth are by no means immune from pyorrhea. But we are not interested in comparing the diseases themselves but only the common causal factors.

That an evolutionary factor is concerned in the spread of

some cancers is not impossible. While parous women suffer more from cancer of the breast and cervix than the single women, it must be remembered that when women were continually breeding and nursing infants and raised large families cancer of these organs was far less common than today. Where limitation of families is the rule, as in most civilized countries, cancer appears to flourish, as in Holland and France. The one and two child system of today means for most of the woman's life the breast and uterus are idle. The fact that the woman who has borne children is more menaced than the single and nulliparous woman, may be explained by the handicap of past mastitis, cervical lacreation, and other local factors, but back of all may be the factor of disuse, with the tendency to earlier involutional changes long before the menopause. The inability of so many young women to nurse their children points more than any other factor to evolutionary causal moments, and suggests that the time may come when the maternal functions will be greatly in abeyance as a racial characteristic, and that sterility, abortion, low natality, etc., will rapidly increase. Another evolutionary development is female sexual frigidity, which according to Havelock Ellis is a development of the past 150 years. Vaginismus, not known before Marion Sims' discovery, is now extremely common. Rapid increase of divorce may also be mentioned in the same connection. Hence he would be a bold man who should deny that there is some correlation between increase of cancer of the breast and uterus on the one hand, and all of the race suicidal factors just enumerated on the other.

Another factor which may be compared with disuse deserves mention; a disuse of the muscles, or lack of exercise. Despite numerous faddish, modern activities, the normal woman of the past was very different from the modern woman; she was one of the busiest of beings, who really worked and did not play at work. She was on her feet most of the time and doubtless walked miles a day in her household, climbing stairs included. Her metabolism was also constantly stimulated by gestation and

lactation, and there was little chance for the development of sluggish metabolism and its attendent diseases. The modern, well-to-do woman lies abed late, has servants, gets about with a car, and must burn up a relatively small amount of food, including bonbons, with which she is tempted. Much the same line of argument pertains to cancer in men.

In regard to cancer in other localities, some of this line of thought may not hold in regard to the considerable increase in cancer of the stomach in women, a fact most difficult to explain and which we will not attempt in this connection. Woman is somewhat immune to buccal cancer, or has been in the past. At one time it was unusual to see a cancer of the tongue in women. As shown by the frequency of smoker's cancer and betel-nut, or buyo (Philippine cancer) irritation plays a great role in this location. Three causes of cancer in the buccal area are said to be responsible for the rapid increase in the male—tobacco, syphilis, and alcohol, to which may be added the consumption of hot tea and coffee. None of these factors obtain in primitive people but buyo cancer shows that there is no natural immunity to the disease. The word civilization hardly fits the introduction of bad habits into a primitive community, and sophistication seems a much better term. The betel chewer is a sophisticated person at least, for he, or she, has a vice which like tobacco, whiskey, and venery leads to disease. We have digressed a good deal from the subject of caries and pyorrhea as a white man's disease, and will next speak of:

Early Baldness and Canities.—These affections are eminently of the class which we are discussing, and are set down to evolutionary factors, hair being no longer a necessity. The white man seems to have been the only hairy man among the primitive peoples, and at one time is believed to have inhabited the cold countries and to have been covered from head to foot. With the need for such a protective covering no longer apparent, he would naturally lose it as he began more and more to clothe himself. The darker races must have lost their hirsute covering at a much earlier period, as far as the face, body and limbs are

concerned, but on the other hand do not suffer from baldness of the scalp or canities until very old. The problems of the hair, of the head, beard, and general surface must be kept separate, being under different conditions. Thus in the white man, the beard and facial hair in general is largely a sexual characteristic while the scalp hair in women has similar significance.

In regard to baldness the type differs in man and woman, introducing another sex element. The growth and distribution of hair is intimately associated with the endocrine organs, as is seen in mild sex confusion. Premature baldness and greyness also run in families and are often inherited. In regard to the mechanism of baldness it stands in some relationship to a hidebound state of the scalp. This, the most important feature in baldness, is barely mentioned by authors. In senile baldness the hair first turns grey, but this is not seen in the premature form. The general use of the Derby hat has been accused as responsible in part for early baldness, which, if true, is an example of the effects of civilization or sophistication. This is like attributing cancer of the breast to the use of corsets—it cannot be proved or disproved. Enough has been said to point out evolutionary factors and disuse of the hair which no longer has any office to perform, or disuse of the muscles which corrugate the scalp; endocrine factors disturbing the hair growth; effects of civilization as seen in the rigid hat, etc. Baldness seems far more common in the high-brow type of man than in the more primitive white men, and in this way be the consequence of increased mental activity—resulting from ambition, from business competition, worry, etc. This factor must be reckoned with in white men's diseases—anxiety for the future. Since many athletes suffer from early baldness it can hardly be attributed to slow or defective metabolism. Not much appears to be known about early greying of the hair, save that an emotional factor is present at times and that it may be familial and hereditary. It stands in some relationship to depigmentation of the skin, which places it among the affections influenced by internal secretions.

Other affections rapidly increasing in the past 50 years among

civilized or sophisticated whites are arteriosclerosis, cardiovascular disease in general, nephritis, appendicitis, diabetes, so-called atypical gout or uric acid disease, neurasthenia, insanity, metasyphilitic affections, sexual shortcomings of various kinds etc. The same causal factors can be detected in all, plus other factors.

Arteriosclerosis.—The affection thus called is believed to be rapidly increasing as a so-called malady of civilization, and some evidence of its precocious appearance is a natural consequence of this diffusion. Its occurrence in those who work at hard manual labor is not known to be on the increase, but it now prevails more in the brain worker and sedentary persons. The cancer subject, although he may have a high blood pressure proportional to his age, is said to be remarkably exempt from a high degree of arteriosclerosis, and the per cent of the latter, found in a series of autopsies on cancer victims, was found to be not above 15. Nevertheless, it is more than likely that the causal factors of the two maladies partly coincide. According to Bishop the typical arteriosclerotic subject here in the United States is rugged and sound and of good stock, who has an unusual capacity for work and is not sensible of fatigue. He works incessantly and he constantly assumes responsibilities which he must then fulfil. He, no doubt, eats to excess and often his diet is unbalanced. Syphilis as a factor may be excluded as causing other types of arterial disease, although in some cases, such as coronary sclerosis, both factors seem to be present. The arteriosclerotic improves under mental rest, moderate physical exercise and restriction of diet, with elimination of protein. The nervous and endocrine factors are very evident in arteriosclerosis, apparently much more than in cancer, and in many cases there is a history of some infection such as typhoid and septicemia. The cancer subject often is immune to infectious diseases, or else has had the good fortune to escape them. Closely related to arteriosclerosis is one form of kidney disease which is not due to the ordinary types of nephritis, although classed among them. At one time cancer was attributed to a

nervous element—worry, sickness and death in the family, and business reverses—but it is questionable if it is not only natural in people of the cancer age to have encountered losses and reverses. Although these nervous disturbances can derange metabolism, and so produce the erroneous blood current which leads up to the wrong action of cells ending in cancer.

ETIOLOGICAL FACTORS IN CANCER

The Congenital, Hereditary, and Familial Element.—In seeking to arrive at the causal nexus of disease this is perhaps the first element to investigate. If we argue that man ascended from the lower forms of life by evolution or mutations, the fact that morbid growths occur in insects, fishes and amphibia, to say nothing of warm-blooded animals, will tend to show that the malady is inseparable from the growth of all highly organized life. The local origin of cancer in the frog, according to Kopsch, appears to be a very simple matter. Certain nematode worms in the larval state cause what are known as worm nodes, and a secretion or excretion of these larvæ is able to start up almost every form of neoplasm known to man. There are no typical growths, but adenoma, carcinoma, sarcoma, etc., are seen to be represented in the microscopic slides of these tumors. Whether any other irritant can induce the genesis of these tumors does not appear. As far as we know there is no predisposition involved, but, of course, this has not been investigated yet, and perhaps is impossible of discovery. In the so-called cancer-like tumors of the thyroid in certain genera of fishes, the genesis of the tumor is very dissimilar from the preceding, and seems to depend on something in the water, as in the case of human goitre. In mammals, with the exception of mice and rats used in laboratory experiments, we have but little knowledge of malignant disease. As far as we know it attacks domestic animals much more than those in a wild state, flesh eaters oftener than herbivora, and stall-fed horses, etc., more frequently than animals which run wild. This is exactly what we should expect from a study of cancer in man.

There is no reason to believe that primitive man suffered to any extent from cancer, and even the earliest civilizations, although much like our own in some respects, are not accused of producing this malady on a large scale: this also holds good for medieval civilization, after the passing of the Dark Ages. Flocking to cities, commingling of races, wide spread luxury and sophistication of the people, were apparently incapable of producing cancer, or other of the so-called white man's diseases. Whatever, today is responsible for the rapid increase of cancer must also be responsible for the multiplication of a dozen other morbid conditions, which as far as is known did not prevail in former civilizations. These conditions have little in common, aside from their community of origin. Hence those who seek for a formula which simplifies everything, explain all these affections by the theory of evolution or mutation. The entire subject is covered in the section on the relation of cancer to other constitutional affections.

In regard to the immediate inheritance of cancer patients, who are themselves prone to appear particularly healthy, it may be stated that the ancestry is by no means always as sound as might be inferred. While many ancestors of a cancer patient may have been healthy and long lived, there are often among the collateral ascendants cases of tuberculosis or psychoses. But not many of the families of cancer subjects have been studied to date.

If we assume that cancer is a matter of individual soil rather than of active causes, it should show the same degree of heredity as is seen in other racial scourges, like gout. But the inheritance of cancer is a very unstable quantity. In some figures quite a respectable percentage of heredity is in evidence, while in other material the element seems quite lacking. If we judge by averages, the inherited contingent is relatively small and doubtful. But that cancer families do rarely exist, is undoubted, although but few good examples are on record. In such families, with numerous cases in three or four generations, we note a tendency to early incidence and to attack,

in unusual, and often the same localities. In this way familial cancer simulates racial cancer. In other words, increase of cancer in a single strain of mankind imitates increase in the community, and may, of course, be due to similar, continued modes of life.

The sudden increase of cancer in a community is sufficient evidence that heredity can play but a slight role therein. It also eliminates slow evolutionary processes, and causes us to think of mutations, either of the tissue cells or of individual human beings. In a relatively short time mankind has passed from a non-cancerous to a cancerous race. Only a few years ago cancer was almost a medical curiosity—a special visitation on some unfortunate wight; today with the odds of developing cancer are shortened to something like 8 to 1 for middle-aged subjects, the malady is one which dominates most others.

There is no better illustration of the difference between hereditary and congenital disease.than is offered in this affection The congenital element in cancer differs from the inherited factor. Students of cancer as a racial malady, which is rapidly increasing, find but little to interest them in the study of congenital cancer. The latter naturally affects young subjects, and hence is extremely rare. No one knows the real age limit in congenital cases, but there is a suspicion that most instances of cancer in the young who are well below the lower limit of the cancer age, are congenital. Since the rapid diffusion of cancer causes it to appear in younger and younger subjects, a border line arises in which it is impossible to distinguish between congenital and spontaneous cancer. In such cases much depends on the locality. If the latter is one in which the adult is commonly attacked, like the rectum, we should be able to exclude the congenital factor. If the liver, where primary cancer is extremely rare, the latter may be accused. It has been said that cancer in early life is always an example of a mixed tumor, and hence congenital. The same holds good for cancer which develops in association with some congenital malformation, even if at a late date. Moreover, all malignant

tumors known to develop from misplaced embryonal "rests" while very seldom cancerous, are naturally congenital. Malignant growths which originate at any time of life in congenital nevi, may in a way be regarded as congenital.

Heterotopia.—Before leaving this subject another, that of heterotopia—should be considered more fully. While it may be associated with hereditary and congenital components, it may also exist in the absence of such factors. It may enter into the subject of wound repair and inflammatory sequelæ. In its relation with embryology it may exhibit wide differences. Thus, in the very period of development the trophoblastic cells may be included in the development of the individual. This is hardly possible to prove, but if such cells were to lie latent in the tissues, and then be aroused to proliferate, they should possess much resemblance to cancer growth, being without other function than to grow at will.

The trophoblastic hypothesis receives a demonstration in chorio-epithelioma of the uterus, in which decidual cells, remaining in the uterine wall, are activated to malignant growth by some unknown force, thought to depend on the ovarian secretion. But according to this conception of cancer in general, the latter should behave as a chorio-epithelioma, which, as is elsewhere shown, differs notably from cancer. Chorio-epithelioma also constitutes the malignant component in malignant teratoma, which is also distinct from cancer. In these teratomata, especially those with considerable production of fetal tissues, the presumable source is not the trophoblast; the tumor originates in a twin conception unioval, in which only one individual is produced, abortive remains of the other having been infolded into its tissues. This origin is sometimes unquestionable, and in other cases may be inferred, and the theory explains the majority if not all of the teratomata. By heterotopia authors refer to a displacement of cells which occurs in the course of the ordinary evolution of the fetus in which neither a trophoblast nor a fetal conclusion is concerned.

During the brief embryonal period in which organ-genesis occurs, every opportunity is offered for displacement of the various cells, and confusion of tissues. Many such displacements are transitory, and, owing to some inherent principle, this tendency to displacement is spontaneously corrected. Wherever there has been an infolding of the epiblast, portions of epithelial tissue may be included in the tissues of the mesoblast. In this way certain types of cancer appear to have their origin. That most commonly cited develops in the site of the branchial clefts, a temporary structure of embryonal life. Incomplete development may leave a cyst or fistula, and in middle life a strong, robust man may have cause to develop cancer in that location.

Facts of this sort have given more or less support to the heterotopic theory of cancer genesis. To enumerate all of the possibilities of this origin would be to repeat much of embryology, but not only does cancer commonly develop where such a theory is inadmissible, but, on the other hand, in cases where embryological confusion exists cancer may fail to develop. In addition, the malignant growth in these cases may not be cancerous in the strict sense, but may be a teratoma, sarcoma, hypernephroma, etc. The latter seems to be due to an infolding of the adrenal body by the kidney. It is enough to state that it is recognized that malignant tumors, among which cancer is included, may at times have a heterotopic origin, but that such growths are rare and not increasing, and are local and surgical at first, and, so this aspect does not touch the cancer problem. If, as Ewing emphasizes, cancer of the breast may originate from misplaced sweat glands, we have a heter
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growths and congenital ones. The latter, however, arise comparatively early in life, and a heterotopic factor may or may not be present. As we have already seen, branchiogenic cancer appears as a rule in middle life, although dependent on a marked congenital anticedent. It is asserted that mixed growths in which cancer develops in association with some mesoblastic tissue, usually appear early in life. Such mixed tumors are not classed among the teratomata. After extensive injuries followed by repair it is possible for an acquired heterotopia to occur, and scar cancer may have this factor present.

Metaplasia, Anaplasia, Etc.—These terms are in extensive use to account in part for the genesis of cancer. The term metaplasia originally connected the degradation of a higher to a lower type of tissue, but in epithelial metaplasia it means no more than the appearance of one kind of epithelium in the midst of another. Thus, occasionally a focus of squamous cell cancer is seen in the midst of the columnar epithelium of the stomach, or in the lining of cyst. When this apparent transposition occurs close to a transition point between squamous and columnar epithelium, as in the cervix uteri, we may speak of it as an illustration of heterotopia, and it has been attempted to account for the frequency of cancer of the cervix in this manner. But metaplasia of this sort may be acquired as the result of inflammation, wherein the destruction of the columnar epithelium may be succeeded by the appearance of the squamous form.

Metaplasia does no more than explain the formation of certain types of, cancer, or rather only describes them. In the absence of some efficient cause, like heterotopic displacement, we are

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the cancer cell from a normal or healthy cell. Anaplasia is applicable as a term only to malignant tumor cells, and whatever may characterize the latter, while mutation is universally applicable to living individuals, and is a well known phenomenon in both plant and animal life. Moreover, mutation may be created at will, and mutations will arise from various factors, such as feeding on a special pabulum, crossing of breeds or strains, etc. Malignant cells have usually been regarded as involving regression of higher to lower cell forms, but mutation does not possess such significance, and implies the creation of a new species from an old one. These subjects strike us as academic in the discussion of cancer as a racial plague.

Immunity and Susceptibility.—These terms, one of which implies the other, may be discussed from general and special viewpoints, the latter of which come up under age, site, occupation, race, etc. There seems to be no absolute immunity to cancer anywhere among the metazoa, although the disease may not have been encountered as low as the radiata, mollusks, arthropods, and annelides. Among mankind there is no absolute immunity, despite the fact that in certain races and at certain times of life the disease is extremely rare. The perfect health which can throw off all other maladies does not protect from cancer, and even those who appear supernormally robust seem specially menaced by the disease; although the latter may also, on rare occasions, attack a subject in the terminal stage of tuberculosis or other disease. Perhaps the nearest example of immunity is seen in the leper, who, however, does not usually live far into the cancer age. It was shown, at least for Sweden, that individuals who have been immune from infections in the past, even from the ordinary affections of childhood, were in a majority among cancer victims.

It is the same with the community as with the individual. The more healthy the locality and the lower the death rate, the greater is the tendency to cancer, at least in certain countries, as in England and New Zealand.

In regard to the state of nutrition, the thin subject has a sort of immunity which gives him a better prognosis than the fat subject, or at least this seems true of cancer of the breast, for reasons already mentioned. This does not mean that she is less susceptible to the disease—although she may be. We have no figures to quote, but in New York, at least, the large share of cancer patients are stout, and many flabby.

Subjects with continued high fever are perhaps largely immune for the time being, although this statement is apparently contradicted by the occasional development of cancer in advanced tuberculosis. Erysipelas has some power in restraining the growth of sarcoma, but this may be through its toxin action. Mice heated in an artificial environment cannot be inoculated with cancer.

Dietetic immunity and susceptibility is so important a subject that it will be separately considered. It is of course very difficult to separate the dietetic component from the hygienic, and the entire subject is best considered under the head of the relationship between diet and cancer, and also civilization and cancer, of which dietetics form an important sub-division. It is one thing to discuss the causation of cancer and quite another to consider the cause of the increase of the same. Since cancer is often preceded by some local alteration *in situ*, whatever tends to induce this local change will also cause increased frequency. Local factors will be discussed in due season.

Neoplastic Diathesis.—The plausible statement has been made that this is shown in the small superficial neo-plasms which are usually multiple; thus, one subject may present numerous moles, fleshy, pigmented, hairy, etc., along with nevus araneus, while another may be free from such developments entirely. Aside from the fact that these nevi themselves may become cancerous at times, the further claim is made that in the same subjects there is a greater tendency to neoplastic formation, and that the said individuals are more apt, than others with smooth skins, to develop both benign and malig-

nant growths. We have never seen any statistics bearing on this point. In the same connection may be mentioned senile keratosis and verrucosis.

Endocrinic Factor.—As if by exclusion, the endocrine system has been made responsible for the development of cancer, since it begins to fail in its activities as the cancer age is approached. Nature is believed to exert a check on the development of cancer either by the formation of antibodies in the blood or by local defensive forces, and the withdrawal of this protection may make it possible for certain cell growth stimulants to rouse the certain cells to cancer activity. It does seem that endocrine factors, when the balance is disturbed, may act as excitants of cancer, as is shown by the fact that it is claimed that ovariotomy will inhibit the growth of cancer. It has already been shown that accumulation of lutein material in the ovary makes possible the formation of chorio-epithelioma in the uterus. That thyroid is able at times to retard cancer growth may be due to its ability to reduce the amount of adipose tissue, as obesity is looked on as unfavorable in certain cancers (breast). Secretin has been credited with the comparative immunity of the duodenum. But the only direct evidence of a relationship between endocrinic activity and cancer, is found in the diminished tolerance to glucose usually encountered in subjects of carcinoma; this resource is actually in use in the diagnosis of internal and occult cancer. It also indicates a point in common with diabetes.

Special Immunity and Susceptibility.—These may be racial, chronological, topographical, occupational, etc. There is no true racial immunity, as far as is known, for when the primitive and aboriginal or dark races begin to live the lives of white men, eating their food, sharing their habits and occupations, wearing their clothing, and bearing their responsibilities, they contract cancer like the white men, and their descendants are fully as susceptible as the whites. Indians living on their reservations, enjoy a high degree of immunity, which evidently is not shared by those who live as ordinary whites. A study of these Indians

might give us the entire key to the riddle of cancer, but such has not been made. Are these reservation Indians also immune to other white man's diseases?

It is not necessary to go into the geographical pathology of cancer in this connection as it has already been considered. We may state without contradiction that primitive and pure blooded races, living in a state of nature, are largely immune from cancer, and that this is not wholly a matter of diet, for the more or less carnivorous Eskimos is said to be immune; but he lives largely on fats, and also is said to devour the contents of the stomachs of animals killed, which consist largely of mosses, etc.

But increase in the consumption of protein has been clearly shown by many to be a factor in the production of cancer when man is living in a sophisticated state; in other words, the dietetic factor may loom large in civilized man but not in primitive man. The latter, if he indulge freely in meat, may escape cancer from the absence of other factors. Meat is to be feared chiefly when it cooperates with several other elements which make up the difference between civilized and savage life. The oft quoted figures for cancer in India in 1904 would seem to show that the diet made little difference, the vegetarians even being largely affected. But a study of these and all similar statistics shows that almost all the cases were of cancer in the mouth, and that the chief cause of this was betel chewing, so that diet could exert but a slight controlling influence, or rather none at all, in the presence of such a powerful exciting local cause.

In regard to age incidence, there is a radical difference of opinion as to the existence of a cancer age. According to one view cancer occurs at all ages, very rarely in infancy and childhood, a little more frequently in adolescence, still more frequently in early adult life, but thus far of decidedly rare incidence during that period. Then the frequency advances by leaps and bounds, until we reach the period of old age, when there is an apparent falling off, due in reality to the relatively few people of late cancer age; in truth cancer continues to

increase with years, even to the extreme of longevity. From this angle there is no such thing as a cancer age.

The other view appears to hold that the few cases of cancer in infancy and childhood are congenital, and should not be counted in morbidity. Cases in adolescence even may be found to be atypical, often belonging to the so-called mixed tumors, and hence congenital. All cases occurring up to the age of 35 are infrequent, and simply to be classed as precocious, after the fashion of other diseases, like gout for example, which may begin in early life, although eminently a disease of middle age. The true cancer age begins at 35 or 40, and the disease increases in frequency up to a certain age, when perhaps it slowly declines in its ratio. This latter view of cancer in the aged seems to have been regarded as settled until recently, when a thorough study of tabulations by Whitman appeared to show that there is no period of equilibrium and decline, and that the older a subject the more likely he is to develop cancer.

When the disease is rapidly extending in a community the tendency is to attack persons both younger and older than the typical cancer subject, and there is no doubt that many cases now being published as carcinoma in adolescents and children are such as in the past would have been classed as sarcoma.

There has usually been accepted a law involving age and malignancy, which states that the younger the subject the greater the malignancy. To such a law there are numerous exceptions. Thus, in cancer of the nasal fossæ, which may attack very young subjects, the degree of malignancy in the latter is surprisingly low, while in the aged the course, which should in theory be slow, is very rapid and malignant. As is well known, cancer in this locality is slow to infiltrate the surrounding tissues and seldom causes metastases. The chief peril is seen in extension to the cranial cavity, death commonly being due to meningitis. Cancer of the vault of the pharynx, which originates but a few centimeters further back, also attacks very young subjects in considerable frequency, but is highly malig-

nant in these, as in theory it should be. Examples like these show that cancer in a given locality is apt to be a law to itself.

As already stated, in familial cancer some of the victims are unusually young, and unusual localities may be attacked as well as the ones commonly seen. Cancer among the Hindoos and other peoples of the far East appears to develop much earlier on the average than cancer in the Europeans; this may be due in part to earlier maturity and decline, but the chief factor, as regards the disease in the mouth, is doutedless the custom of betal leaf chewing which is begun in childhood.

The paradoxical fact that a young subject cannot as a rule put up a defence against cancer, while an old and decrepit one makes a vigorous defence, is hard to reconcile with the other fact that cancer develops more frequently in the old subject, and until recently has hardly been associated in the mind with the age of growth and development. If we compare cancer to a fungus growth in a special type of soil, then it should attain its greatest development in the soil in which it naturally grows. Most diseases follow this law but cancer is an exception, and leads to the conclusion that the nature of cancer in the young must be different from that in the old. Yet as we have just seen, cancer may in at least one locality be milder in youth and attain its greatest malignancy in old age.

In regard to immunity of certain organs several questions at once come up. One deals with the existence of serum immunity, which has been vigorously denied, although many speak of it as present in a feeble and inconsistent way, quite unequal for diagnostic and therapeutic usefulness. Our knowledge of the blood in cancer subjects in which the disease is quiescent or just beginning is not extensive, and can hardly be detached from the study of blood states due to cancer. Thus the blood state in cancer had best be studied of itself from all angles.

To return to special organ immunity and susceptibility, this has been denied outright by F. C. Wood, and others. That one organ is frequently attacked while another is usually spared, is capable of other explanations than special susceptibility or

immunity. The chief support of the negative viewpoint is seen in metastasis, for the very organs which escape primary cancer are the ones which are most likely to be affected by secondary cancer, and *vice versa*. Furthermore, carcinoma invades all tissues impartially which are contiguous to it, this fact showing that no tissue is actually immune. The liver is seldom the seat of primary cancer, but one of the chief victims of secondary and metastatic cancer. The apparent immunity of the spleen to metastases is explained by Wood through the peculiarities of its blood supply, which, however, permit of metastases of sarcoma.

Nevertheless there is apparent organ immunity and numerous generalisations have been based on it. Cancer, for example, is much more apt to develop where the reaction is acid, or at least naturally so; as in the stomach and colon, and little liable to appear where the reaction is normally alkaline, as in the duodenum. Its failure to appear primarily in certain organs is readily explained by the absence of epithelium, but this fact can hardly be counted under immunity. Cancer is said to develop where there is an abundant supply of lymphatics, but this anatomical fact bears chiefly on the subject of secondary diffusion. Other generalisations appply to the alleged presence of bacterial activity and decomposition, etc., which does not agree with the facts and is lacking in lucidity.

In regard to organ incidence it would be of great interest to know whether cancer is increasing in all localities, or only in a few of the organs which bear the brunt of the incidence. As long as the stomach and the female breast and uterus furnish the majority of cancers it seems perverse not to speak of susceptibility and immunity. If we turn to some of the primitive folk we may find the breast and uterus almost exempt, while some other organ like the buccal cavity or penis may head the list. Even in some civilized countries, as Sweden, the stomach or entire alimentary tract may furnish the majority of cases, while both uterus and breast are in a decided minority. This arbitrary way of choosing one organ in one part of the

world and another in another region argues either for a special causal nexus for each kind of tumor, or for a general condition that selects a point of minimum resistance.

In some forms of cancer the exciting cause is everything and it is easy to abolish these types, as in chimney sweeps' cancer, which was once very frequent, even heading the lists in some of the old English hospital material. It has been practically stamped out by legislation and improvements in construction. Betel chewing cancer could be stamped out in the same way, as could also smoker's cancer. But buccal cancer and cancer of the scrotum still occur in the absence of these causal factors. In such cases we cannot make use of the term local immunity and susceptibility. It is probable that cancer could be made to appear in almost any locality in one inclined thereto by the blood condition, if there were a sufficient amount of chronic irritation applied, although, it is quite certain that some localities would prove more resistant than others. In the absence of knowledge of predisposing and exciting factors we cannot explain the increase in the incidence of regional cancers. Either of the two factors might increase while the other remains in equilibrium. This subject leads naturally to the local factors in cancer.

Local Factors.—These include pre-cancerous affections and traumatism. They are both discussed very fully in textbooks and we shall not go exhaustively into the subject, for it is evident that cancer which originates in a lesion of any sort or from any form of injury or chronic irritation tends to increase or diminish with the exciting cause. Such cancers are readily preventable if the cause can be removed, and do not enter into the general problem of cancer as a racial malady. Moreover, most of these traumatic cancers, as well as those which originate in preexisting lesions, are of a special histological and clinical type, and many are of low malignancy, with little tendency to metastasize, as in basal cell cancer. Of pre-cancerous conditions we may name benign growths of various kinds including congenital nevi, any form of ulceration (chronic),

low forms of inflammation, demonstrable perhaps only under the microscope, among which belong superficial glossitis, leucoplakia buccalis and analogous lesions on the genitals, burns, scars, and dermatitis with hyperkeratosis following chronic irritation, etc.

Of the severe and malignant types of internal cancer the mammary form is preceded by adenoma and mastitis, gastric cancer by round ulcer, prostatic cancer by hypertrophic prostate (technically an adenoma), cancer of the cervix by laceration and its consequences, etc. These of course explain only part of the morbidity. Cancer of the colon has no such distinct factors to account for its presence, and this seems true of cancer of the œsophagus. Nor are these factors always lucid. It does not increase our practical knowledge to be told that cancer of the breast is practically always preceded by evidence of mastitis; and concerning the development of cancer from benign tumors and leukoplakia, it is very difficult to prove just when a malignant metamorphosis has really occurred, for a papillomatous cancer may at its origin be indistinguishable from benign papilloma. Some 25 or 30 types of cancer originating in other lesions have been isolated.

The evidence of trauma as a factor in cancer is largely of the negative type. Before the cancer age so-called, cancer following traumatism is very hard to prove, and in the recent war, of 200,000 soldiers in the French army either dead or mustered out at a given period, less than 500 developed cancer and not one of these was due to a wound. Of the 500 cases 179 occurred in soldiers between 40 and 45, and most of these were cancers of the stomach. The only organ in which a blow is repeatedly accused of causing cancer is the female breast. On the other hand sarcoma often follows a single blow, fracture, etc.

Certain substances of very different kinds are known or believed to be able to stimulate the multiplication of cells, including cancer cells, just as others are believed to inhibit this growth. So-called oncotropic substances, which have a selective action on cancer cells, especially staining agents,

conceivably belong here, and while some are accused of stimulating, others appear to inhibit the growth of the cells. Some agencies like *x*-rays and radium stimulate in small doses, and inhibit in large doses. It is admitted that to stimulate cell growth it is necessary for the active substance to enter within the cell, where it can disturb karokinesis, but it is not certain that an inhibiting agent must have this property, although it doubtless acts directly in some instances. Among substances said to excite cell growth are cholesterol, potassium salts, pituitrin, indol, and skatol, stains like trypan and sudan red, also many active substances which have caused occupation cancers, like aniline, tar, paraffin, tobacco, betel nut, leaf (really calcium in admixture), and arsenic in internal administration (it must first cause hyperkeratosis) and others. The katabolic or excretory products of the larvæ of certain nematode worms are known to produce cancer in frogs and even in warm-blooded animals (mice).

In addition to many facts there is a world of speculation on this subject, with attempts to show that certain cellular products of a katabolic origin act as manures or fertilizers or catalysts or what not, and thus stimulate cell growth. Certain cells are accused of fertilising other cells and thus producing a cancer cell brood. Cancer soil, so-called, has been likened to a vegetable mold in which cancer grows like a fungus. There is no proof of these claims, but there are many facts which suggest that cancer is at least favored by the presence of certain catabolic substances. As a source of enzyme or hormone-like bodies which have fertilised cancer-genetic cells, lymphocytes have been accused, as well as spermatozoa-like bodies.

In this connection should be mentioned the parasitic theory. As a universal cause this has doubtless been eliminated, but no one can disprove the possibility of incidental cancers of parasitic origin. This has been shown in regard to tumor growth in plants, and there is no reason to doubt that certain bacteria or protozoa may be able to stimulate cell growth in animal cells. The so-called symbiotes-bacteria, believed to enter the tissue

cells and promote normal functioning, may have their pathogenic counterparts. These as yet little known organisms, even the existence of which has not yet been shown beyond doubt, have been associated with the other unknown substances, vitamines—for we cannot prove that vitamines of the kind destroyed by heat are not living beings.

Of substances known to inhibit cell growth are some of the amino-acids, including those produced by the normal metabolism of the cell, and in general tryptophan and tyrosin, calcium salts, trypsin (which digests cancer protein), the toxin of erysipelas, radium and *x*-rays, elevation of temperature in mice experiments, etc. In this class are to be placed also eosin, selenium, uranium salts and silica (as recommended by Czerny), Whatever can produce a fibro-plastic reaction is indirectly a cell inhibitor.

One who studies this chapter, in which an attempt has been made to present some of the observations and thoughts of the many who have been studying "the cancer problem," must be struck both with the difficulty of the task, and the almost hopelessness of trying to come to any definite conclusion in regard to the real cause of carcinoma. If one should seriously heed all the ideas which have been presented, and attempt to act upon them in caring for cancer, he would be puzzled indeed. The writer cannot see much in them which would help in determining any intelligent line of treatment. Everything seems to point to the conclusion that cells are only degenerated normal body cells, which take on their abnormal action from a wrong pabulum, much as we found in the chapter on the histo-pathology and in that on the bio-chemistry of cancer.

We found that the energy of growth of malignant disease had often been compared with that of the embryo, only that of the latter was superior.

We found that the epithelial cells of the body were very active entities, which were constantly changing and disappearing, as their proper function had been discharged; but

that when they became malignant they could serve no useful purpose, as secretion, etc., and with their acquired property of malignancy they ran riot, as it were, infecting other cells and simply dying and acting as a foreign body on which the ordinary forces of catabolism and anabolism could not well act.

We found that benign and malignant neoplasms did not differ, so greatly in their mechanism, but mainly in their behavior. Both seemed to be autonomous and independent of the laws which regulate the individual.

Inflammation was found to be closely related to both. Sarcoma seemed to have somewhat different laws from carcinoma.

We found that cancer had certain relations to constitutional diseases of various kinds, which are on the steady increase among civilized people. It has also probably relations with the endocrinous glands.

Cancer was found to be a disease of the individual, and that heredity played little or no part in its genesis.

While along certain lines immunity and susceptibility seem to be an element in the situation of the local product of the disease cancer, nothing can be learned from the study of these features which helps in the knowledge or treatment of cancer. Except that the disease is peculiarly liable to develop in localities where there is an acid reaction, as in the stomach and colon, which sustains the theory and observation that cancer is in reality an acidosis disease.

We see thus that all evidence points to the constitutional nature of the disease, which slowly develops long before any local manifestation of it can be determined with certainty.

All of which leads to the conclusion which even many surgeons state in their writings, that the surgical removal of a cancer mass does not and cannot cure the disease or insure that there shall not be a recrudescence of the same.

CHAPTER XIII

RELATION OF DIET TO CANCER

For the proper understanding of the relation of food and drink to cancer, and the satisfactory application of the principles involved, it is necessary to bear well in mind the chemistry of the body, and the relation to nutrition of the various elements which contribute to form its tissues and cells, both in health and disease.

The human body is composed of some 15 different primary elements, which are found in the composition of what enters the mouth and lungs. It is understood, of course, that all food is ultimately broken up into its composite organic elements, which are carried by the blood and appropiated by the cells for their formation and nourishment, and to enable them to perform their functions.

Cancer has its foundation in the erroneous formation of previously healthy cells. Throughout all nature it is recognized that plants and animals must have the right food in order to have healthy and vigorous life, and man is no exception. There must be the proper balance in the various elements of nutriment, which ordinarily is found in their surroundings, or is supplied by human intelligence. Wild animals, guided by instinct, select their proper food, and are never sick, but with man matters are different. He does not seem to be guided so much by instinct as by taste, whim, or fancy, or by the influence of others, and so will often indulge in gratifying the taste rather than simply in satisfying the appetite, and the temptations to this, in modern life, are increasingly great. Thus it happens that gross errors are continually committed, leading to various diseases, as we all know. It is to be remembered also than man is the only animal that cooks its food, or attempts to alter or refine it from its

natural state, often very disadvantageously, as will be seen later.

The following table, from Sherman,[1] represents probably as approximately correct an average of the elements composing the human body as can be given.

COMPOSITION OF THE HUMAN BODY

Oxygen	About 65.00 per cent
Carbon	About 18.00 per cent
Hydrogen	About 10.00 per cent
Nitrogen	About 3.00 per cent
Calcium	About 2.00 per cent
Phosphorus	About 1.00 per cent
Potassium	About 0.35 per cent
Sulphur	About 0.25 per cent
Sodium	About 0.15 per cent
Chlorine	About 0.15 per cent
Magnesium	About 0.05 per cent
Iron	About 0.004 per cent
Iodine, Fluorine, Silicon	Very minute quantities

Sherman says: "The so-called inorganic elements exist in the body and take part in its functions in at least three different ways: 1. As the constituents which give rigidity and comparative permanence to the skeleton: 2. As essential elements of the protoplasm of the active tissues: 3. As salts held in solution in the fluids of the body, giving these fluids their characteristic influence upon the elasticity and irritability of muscle and nerve, supplying the material for the acidity or alkalinity of the digestive juices and other secretions, and yet maintaining the neutrality or slight alkalenence of the internal fluids, as well as their osmotic pressure and solvent power."

It would lead us too far from the practical purposes of this writing to attempt to enter into the chemistry of nutrition, which is a most interesting study, or into the intricate processes through which food stuffs, carbohydrates, fats, and protein

[1] SHERMAN, "Chemistry of Food and Nutrition." New York, 1911, p. 260.

substances, pass in the digestive tract before they are broken up into their component parts and enter the blood. But for the proper understanding of the relation of diet to cancer these should be thoroughly grasped, as shown in other books. The relation of the organic salts, especially calcium, magnesium, sodium, and potassium will be considered later.

The actual composition of the body is changing day by day, through the activities of the system, so that it is commonly believed that after some years all the tissues are entirely renewed, and the entire body is composed of new materials. The supplies for this, for the daily wear and tear, and that expended in heat and activity; must be supplied by the diet, together with oxygen through the lungs. For the ordinary requirements of the system, in health, as already suggested, the appetite serves as a proper guide, which should suffice in man, as in wild animals, to preserve the balance of nutrition.

But man has also the power to *gratify the taste*, which must be recognized in our study as distinct from satisfying the appetite; and the refinements of civilization have added so greatly to the temptation of wrong eating, and overeating and drinking, as they have to so many other temptations, that it is questionable if reason, and what is often spoken of as the natural instinct for food, can be trusted in mankind.

It is to be remembered that the advance of civilization, and the facilities of transportation and cold storage, have brought from far and near an innumerable number and variety of articles for food and drink, including condiments, which bear no relation to the relatively few simple articles formerly consumed. Even the fruits which we eat are rarely ripened fully by nature, but are picked more or less green, and undergo an artificial ripening without the action of the sun, which in reality is akin to decay. The effect of cold storage must also in some measure alter meat, poultry, eggs, etc.

In the combination and preparation of articles of food, also, so-called civilization and refinement have made the greatest departure from the simple life of the aborigines, who are largely

free from cancer, and with increasing wealth and ease throughout the civilized world, more and more individuals are sharing in unnecessary and often harmful indulgences: and this is especially true of animal food, the consumption of which has increased so greatly of late, as will be considered further on.

Many other elements likewise enter into the matter of the digestibility and consequent nutritive value of food and drink. Such as nervous conditions, rapid eating, imperfect mastication, heat and cold, character of the air breathed, micro-organisms, etc., and all the various causes which may derange the action of the digestive organs, and so prevent the perfect metabolism between nutrient material and the cells composing the different organs and portions of the human frame.

The organic substances, protein, carbohydrates, and fats, which supply the nutrition of man, are found in various combinations in animal and vegetarian foods, which as a rule contain much of the organic or mineral substances necessary for the system: all of these, with water and its salts, and oxygen, supplied by the lungs, unite through anabolism and catabolism, to build and maintain the human body in health.

It is well known that in order to preserve health and proper weight there must exist in the economy a certain balance or equilibrium between the amount of the ingesta and the excreta. Thus we speak of a nitrogen equilibrium, a carbo-equilibrium, a phosphorus equilibrium, an iron equilibrium, etc., some of which are disturbed continually in ill health and in different diseases, including cancer. Thus we have the carbohydrate equilibrium disturbed in diabetes, the carbohydrates and fats in adiposis, and proteins in gout, etc.

Until quite recently the principles of diet (even if not often carried out in practice) have been established on lines laid down by Carl Voit, of Munich. This eminent physiologist, after observing and studying the actual dietary of various classes of workers, claimed that the adult man of 150 lb., doing moderate muscular work, requires 118 gms. of protein, or albuminous food, 56 gms. of fat, and 500 gms. of carbohydrate, with

a total fuel value of 3,000 Cal., in order to maintain the body in equilibrium.

But the remarkable and scientific experiments of Chittenden[1] have demonstrated beyond question that perfect bodily and nitrogenous equilibrium can be maintained with one-third of the amount of protein called for by the Voit standards, and with a total value in the diet of only about 1,600 Cal., or about one-half of that indicated as necessary by Voit. These experiments were based on a group of five men, of varying age, professors and instructors of Yale, 13 volunteers from the Hospital Corps of the United States Army, and eight students in Yale, all thoroughly trained athletes, 26 in all.

It would be quite beyond the scope of this writing to enter at all in to the intricate questions connected with the metabolism of nitrogenous and other food, but Chittenden has well put the reasons, "Why prominence is given to the establishment of nitrogenous equilibrium and why the proteid intake assumes a greater importance than the daily amount of fats and carbohydrates consumed? Fats and carbohydrates when oxidized in the body are ultimately turned into simple gaseous products, namely carbonic acid and water. Hence, these waste products are easily and quickly eliminated, and cannot exercise much deleterious influence, even when formed in excess. To be sure, there is waste of energy in digesting, absorbing, and oxidizing the fats, and carbohydrates, when they are taken in excessive amounts. Once introduced into the alimentary canal they must be digested, otherwise they will clog the intestines or undergo fermentation, and so cause trouble. Further, when absorbed, they may be transposed into fat and be deposited in the various tissues and organs of the body; a process desirable up to a certain point, but undesirable when such an accumulation renders the body gross and unwieldly.

"With proteid foods, on the other hand, the story is quite different. These substances, when oxidized yield a row of crystalline nitrogenous products which ultimately pass out of

[1] CHITTENDEN, "Physiological Economy in Nutrition." New York, 1904.

the body through the kidneys. Prior to their excretion, however, these products—frequently spoken of as toxins—float about through the body and may exercise more or less of a deleterious influence upon the system, or, being temporarily deposited, may exert some specific or local influence that calls for their speedy removal. Hence the importance of restricting the production of these bodies to the minimal amount, owing to their possible physiological effect, and the part they are liable to play in the causation of many diseased conditions." We have seen in the preceding chapters on the biochemistry of cancer, and metabolism, how constantly a deranged nitrogenous partition occurs in this disease.

When we consider the small share which nitrogen plays in the normal human frame, only 3 per cent, as shown in the table just presented, it is easy to see how an excess of nitrogenous food must necessarily either pass off unassimilated or undergo imperfect cleavage into its ultimate elements, and so derange the general metabolism. Chalmers Watson,[1] and others, have shown in a most remarkable manner, by animal experiments, that an excessive meat diet alters very materially the microscopic structure of the cells of very many organs and portions of the body.

Beneke,[2] who is often quoted, was one of the first to seriously consider the actual diet beneficial in cancer, his observations dating back to 1875, upon material in the service of Esmarch and Oldekop, who treated patients according to his plan. While the diet he gave was not wholly vegetarian, he limited the nitrogenous intake very greatly and reported some very favorable results, with the complete disappearance of some malignant new formations.

Referring now to data presented in a previous chapter concerning the frequency and geographical distribution of cancer, we can understand better, on scientific grounds, some of the reasons why the disease is so steadily increasing in

[1] Watson, "Food and Feeding in Health and Disease." New York, 1913.
[2] Beneke, Berlin. Klin. Wochenschr., March 15, 1880.

civilized communities, and why in some sections of the earth it is less common, while certain aborigines have seemed to be almost immune.

In England vital and other statistics have received very much attention for many years, dating back to 1840, when under the able direction of William Farr, they had acquired a well-deserved reputation for reliability. In England, a few years ago, it was stated that the consumption of what was called butchers' meat had risen to 130 pounds per capita, that is of the total population, men, women and children, in addition to large quantities of fish, game, poultry, rabbits, eggs, cheese, etc. Among the well-to-do the meat consumption has been estimated at between 180 and 330 lb. per year. All this is much more than *double* the amount consumed 50 years ago, and in the same time deaths from cancer have increased *four fold.*

In Ireland, where the meat consumption in 1895 was only 40 lb. per capita, or less than one-third that in England, the cancer death rate is very much lower, not much over one-half: and yet the average age of the population is very high, as the young people emigrate and the older ones stay in the country.

In the United States the mortality from cancer has certainly risen very greatly during the last 50 years, and the consumption of meat has also increased very largely. In 1909, the per capita amount was 215.9 lb. per capita, which, however, had fallen to 201.1 lb. in 1909, in which year the cancer death rate was 73.8 persons per 100,000 living: then in 1914, it was 79.4, and in 1915, 81.1 persons per 100,000.

The United States Report of the Meat Situation, 1916, furnishes some valuable information to aid in this inquiry. According to this I learn that the consumption of meat had recently reached the enormous amount of 172 lb. per capita yearly, a quantity much greater than in England.

The Argentine Republic stands next to England in the consumption of meat with 140 lb. per capita in 1899, and with a cancer mortality of 91 per 100,000, in 1900.

New Zealand exceeds the United States a little, with a meat

consumption of 212.5 lb. per capita in 1902, and an increase in cancer mortality from 32 in 1877–1888, to 60 per 100,000 in 1900, and 71 in 1903. This increase is mainly among British and other residents, whereas the aborigines, living simple lives, are reported as seldom affected.

Australia stands first in the consumption of meat, with the enormous rate of 262.6 lb. per capita in 1902, and the increase of deaths from cancer is most striking. In 1851 the death rate per 100,000 living, was 14, in 1900, 62.6, and in 1913, 75 per 100,000 living. The most striking difference is exhibited between those who are native born, who in 1900 had a cancer death rate of only 22 per 100,000, while the British born had a mortality from cancer of 203, or over nine times as great. A still higher ratio was found among immigrants of some other nationalities. Those who have written there on the subject ascribe this frightful proclivity to cancer to the gluttonous habits of the immigrants, who have meat for breakfast, lunch, dinner, tea, and supper. (MacDonald, Williams.)

Italy, consuming the least quantity of meat, 46.5 lb. per capita, in 1901, had the lowest cancer rate, but the present meat consumption cannot be learned. In Italy, however, the mortality from this disease is steadily rising, from 50.9, per 100,000 from 1860 to 1900, to 63.6 per 100,00, from 1906 to 1910. The cities, however, where travellers bring luxurious living, show a very high death rate from cancer. In 1912, Rome had 99.6, Genoa, 100.7 Turin, 111.6 Milan, 120.7, and Florence, 165.1 deaths from cancer per 100,000 population. The poorer country districts must have a very low cancer death rate, as the general death rate in 1912 from cancer in Italy was only 64.7, in spite of the very high rate in populous cities.

Spain, also, with a very low meat consumption, 49 lb. per capita, had a cancer death rate of only 55.5 persons per 100,000 living in 1912.

But, as I have often tried to show, the real basic cause of neo-plastic growths is due to some one or many derangements of metabolism, inducing a blood current which does not properly

nutrify the body cells, and that derangement is not necessarily due to any one single cause, as meat diet, although that forms a large share of it, and with that wrong all else is wrong.

There are other elements of disturbance besides the nitrogenous mal-assimilation due to the intake of an excessive amount of proteid from the animal kingdom. For cancer is said to have been seen in vegetarians, although I have never personally known of such a case, and Dr. Kellogg of the Battle Creek Sanitarium, has never known of a case developing in one who had strictly followed their regimen. We know, however, that some of the articles from the vegetable kingdom, such as the pulses and nuts, contain a very large proportion of proteid. Thus, dried peas contain 21 per cent, haricot beans, 23, lentils 23.2, dried lima beans 26.4, soy bean flour 39.5, almonds 24, peanuts 25.8, black walnuts 27.6, and butternuts 27.9 per cent of proteid, all of them more than is found in beef and mutton. Thus a large supply of any of these might cause the same nitrogenous error in the blood stream as is induced by meat.

We see, also, that the system can secure all the protein needed for its cells and nuclei from the vegetable kingdom, as the animals do, and somehow, we know not how, vegetable protein seems less obnoxious to nutrition than that which is formed in animal life. Much vegetable protein is also found in many of the ordinary vegetarian foods, which give the following percentages of nitrogen, according to the Experimental Station of the United States Department of Agriculture: oat meal 16.1, macaroni 13.4; Graham flour 13.3; cracked wheat 11.1; shredded wheat 10.5; Zwiebach 9.8; corn meal 9.2; hominy 8.3; rice 8; potato chips 6.8; rye flour 6.8; buckwheat flour 6.4; most of the succulent vegetables contain from 1 to 3 per cent of protein.

Coffee and tea are so widely and almost universally used in civilized countries, and their apparently pleasant effect is so great that few realize that harm may result therefrom; although from time to time their injurious effects, especially along the

line of digestive and nervous affections, are dwelt upon by medical writers. In my own person, on medical advice, I have experienced the most remarkable result in the immediate, absolute, and permanent relief of an obstinate and agonizing spasmodic stomach trouble, solely by abandoning coffee, that I am more than ever convinced of the potency of coffee in creating systemic disorder.

Of late years considerable attention has been paid to the influence of coffee and tea on metabolism, and to the increase of cancer thereby. From a report to the House of Commons, in England, Holland is shown to be the largest consumer of coffee of any country in Europe, and the cancer rate in 1905 was among the highest, 101 in 100,000. Hungary was shown to be the smallest consumer of coffee, and the cancer mortality in 1903, was only 39 per 100,000, or a little over one-third of that in Holland. It may be interesting to know that Thompson[1] states that: "the people of the United States consume one-third of the coffee produced, or more than Germany, Austria, Hungary, France and the United Kingdom combined. On the other hand, England and her colonies consume one-half of the world's output of tea, and the United States but one-fifth of it."

The scientific basis of a possible relationship of the consumption of coffee and tea to the prevalence of cancer may be better understood when we remember that caffeine and theine belong to the xanthin group, and contain exactly the same equivalent of nitrogen as uric acid. A single cup of coffee of fair strength is stated by Hutchinson[2] to contain 1.7 grains of caffeine, and a cup of tea, 1.21 g., so that when indulged in largely much harm may result; also the latter contains an amount of tannic acid, two or three times greater than the former. It is readily seen that as some individuals take large quantities of either of these, much harm can be done: the working class especially often consume enormous amounts of tea, which is kept brewing all day.

[1] THOMPSON, "Practical Dietetics." New York, 1901, p. 256.

[2] HUTCHINSON, "Food and the Principles of Dietetics." New York, 1911, p. 324.

Roberts[1] has very clearly demonstrated, by clever experiments, that tea interferes greatly with the salivary and gastric digestion.

Alcohol, or some of its combinations, has also been shown by several observers to be undoubtedly an element contributory to the causation of cancer. This relates not only to countries or cities where the consumption is greatest or least, but also to various occupations, in which statistics show the more or less abundant use of distilled or fermented drinks, and increased deaths from the same, and also in regard to fewer deaths among total abstainers; and a careful study of the subject makes it pretty clear that the incidence of cancer corresponds in a measure with drinking habits. Cancer mortality is highest among those classes of persons among whom primary or secondary mortality from alcoholism is greatest.

There are so many elements to be taken into consideration in connection with the derangements of metabolism which lead to cancer, that it is difficult to fix upon the precise influence which each may exert. But in watching cancer cases for any length of time it is easy to see the harmful effect when alcoholic beverages are indulged in, and the improvement when all such are absolutely excluded.

We understand, of course, that the body is a vast laboratory, wherein by exceedingly complicated processes, material from the outside world is appropriated to the needs of the economy, and after its use is cast out in very different and elementary or composite forms. To effect the various changes necessary in this material, we have a very considerable number of what are called organs, of secretion and excertion, whose functions are combined in a marvellous manner, which is even yet very imperfectly understood. All these processes seem to be controlled and co-ordinated by the action of the endocrinous or ductless glands, of which we know still less.

The actual procedure by means of which most of these activities are carried on is one of oxidation, by means of the oxygen supplied by the lungs, which constitutes about 65 per cent of the

[1] ROBERTS, "Lectures in Dietetics and Digestion." London, 1886.

human body. Now to make up for the loss of the other 14 elements which form 35 per cent of the body tissues, and to support the necessary activities of the system, mental and physical, it is necessary every day to take in a more or less evenly balanced supply of outside substances, which we call food and drink, and these should contain about the proper proportion of the requisite bodily components. It is easy to see, therefore, how quite unconsciously, through carelessness, errors of judgment, or perverted will, the system may be deprived of some valuable or important elements necessary to supply the blood with exactly proper material for the cells, constantly changing by catabolism and anabolism, or it may receive too great a supply of some particular substance, such as the nitrogenous protein, for it to elaborate. The whole problem of good and bad nutrition is so intimately connected with the real cancer problem that it will be some time before all these matters are satisfactorily worked out. But *labor omnia vincet*, and it is confidently hoped and expected that extended clinical and laboratory work along proper lines, quite different perhaps from those along which it has been commonly done, will ere long throw much more light on the subject.

The difficulty of understanding and applying our present knowledge of nutrition in its relation to cell life, normal and abnormal, is well illustrated in a report from the director of the Imperial Cancer Research Fund, as editorially commented on recently in the Lancet.[1]

"Investigation on the metabolism of cancer cells, their nutrition requirements, their chemical composition, their respiration, have so far failed to reveal any features in which the malignant cell is essentially different from a normal or non-malignant cell . . . So far nothing has been found to show that the mechanism of the growth is in any way different from that of a normal cell. In many respects the likeness between the cancer cell and the normal cell, of the animal in which it originated, is greater than that between the normal cells of

[1] *Lancet*, July 31, 1920, p. 254.

two different animals. The change which takes place when a normal cell becomes malignant is evidently a subtle one, and cannot be expressed in the comparatively crude terms of ferments, toxins, differences in amino-acids, increased affinity for food stuffs, and so on. The nature of this subtle change cannot be stated, and the disability arises from the fact that our knowledge of the normal cell life is yet imperfect, while the phenomena of growth in the normal cell life forms almost a *terra incognita*."

After referring to the mechanism of proliferation of cells in the reparation of damages to the skin, which he says cannot yet be answered, he says, "but they will have to be answered before we can hope to understand how the malignant cells begin to proliferate and how they escape the control which keeps in check the proliferation of the normal cell. The 'cancer problem,' viewed from the aspect, is a biological problem."

We see here again that, while the laboratory is the foundation for scientific medicine, its powers are limited, and, as in the past, we must more or less fall back on careful observation, with inductive and deductive reasoning, together with clinical and other experience, if we would be successful in combatting cancer.

An interesting confirmation of the beneficial results of a low diet and simple life, as regards cancer, is found in certain reports of Commissioners of Prisons and Asylums in England, where the matter has been studied, as given by Russell.[1] Asylums contain an excessive number of persons who have inherited or acquired constitutional weakness, and in many cases tendencies towards consumption or cancer: also many alcoholics who are prone to these maladies. Yet the habits and rules of these institutions reduce the cancer rate much below that of the classes from which they are drawn, and below the rate of both occupied and unoccupied persons."

The same is observed in regard to many religious orders, where the members live a very simple and frugal life, and where

[1] RUSSELL, "Preventable Cancer." London, 1912, p. 96.

cancer is reported to be almost unknown. Personally, I can recall but a single instance among such, a sister of pretty high rank, with cancer of the breast, who, I think, was pretty self indulgent, although I have had very many men and women belonging to such orders under my care for other troubles.

Valuable confirmation of the relation of diet to neo-plastic growth is attributed to Ehrlich, but I cannot find the original reference. He "has shown that mice living upon a rice diet cannot be inoculated with cancer, while mice living on a meat diet can be readily inoculated, cancerous tumors developing quickly and continuing to grow until the animal dies." Ehrlich also found that when mice, with cancerous tumors, the result of inoculation, were placed upon a rice diet, the tumors ceased to grow, and in many cases degenerated and disappeared. This confirms what I have already mentioned, that in an extensive trip through the Far East, I failed to find any cases of cancer, though I visited many hospitals in different countries, ministering to millions of population, and was repeatedly told by intelligent physicians, missionary, civil, and military, that they did not have cancer among rice-eating peoples.

This is further confirmed by experiments made by Sweet, Corson, White, and Saxon.[1] They made a series of experiments on the "influence of certain diets upon the growth of experimental tumors," all with the same results. Of 50 white mice, 25 fed on glutenin and gliadin, and 25 on normal diet, 23 of the 25 on the normal diet acquired tumors, against only 4 in the 25 on glutenin and gliadin. This was repeated on 50 males, with the result of 18 in 25 against 3 in 25 of the latter class: and in a third series of 50 females, the figures were 15 in 25, against 7 in 25. Thus, they found that 75 per cent of 75 mice developed experimentally inoculated tumors when under normal diet, while only 19 per cent of other 75 mice developed such tumors when under a diet of glutenin and gliadin, that is, vegetable proteins. Moreover, the tumors in the latter were in 30 days hardly larger than

[1] Sweet, Corson, White, and Saxon, *Proceed.* Soc. for Exper. Biol. and Med., N. Y., Vol. x, p. 175.

those in the former in 10 days. Rous[1] has recently shown that large growths of certain rat and mouse tumors are checked in their development by underfeeding the host on a special diet.

Kessler[2] has called attention to the disturbance of sulphur partition in cancer patients, in connection with diet, and the desirability of excluding those foods exhibiting an excess of sulphur, giving lists of the same, and indicating a satisfactory diet.

Packard[3] has made a strong argument in regard to the value and importance of the mineral elements contained in plant life, in connection with the disturbances in the elements which had been observed in connection with cancer. He recalls that modern chemistry teaches that the organic principles of the vegetable kingdom are absolutely necessary to the highest degree and type of animal tissue and health, and resistance to disease. Plant life is the connection between the minerals and salts of the earth and animal life, but in the manufacture or refinement, and cooking, of products of the vegetable kingdom, and many of them are largely demineralized. This is especially so in the case of fine white wheat flour, rice, potatoes (in peeling and cooking) etc. So that while animals get plenty of mineral matter in right proportions, from plants and the earth, man gets but little, and while the herbiverous animals are rarely affected with cancer, civilized man is succumbing to it more and more every year. One has often seen animals consume earth, and dogs bury bones to gnaw on later when they have absorbed minerals from the earth. The United States Agricultural Department informs us that in the rough peeling of potatoes, formerly so common, and in the soaking and boiling them, fully 30 per cent (some say 50 per cent) of the nutriment was lost, including all of the valuable potassium and other salts contained in the inner skin.

It is stated that among savage tribes, who are practically free

[1] ROUS, *Journal of Experim. Med.*, Lancaster, Penn., 1914, p. 433.
[2] KESSLER, *New York Med. Journal*, 1912, p. 122.
[3] PACKARD, *Boston Med. & Surgical Journal*, 1912, p. 452.

from cancer, the water in which vegetables are cooked is also consumed as food, thus securing all the salts. It has long been my custom, to have all the water in which all vegetables are boiled for the family, used as the stock for soup, in regard to the vegetable soup given to cancer patients, as will be seen in connection with the diet card furnished, as described in the chapter on Diet in Cancer.

The same idea of mineral starvation has been popularly presented to the public in a startling manner by McCann[1] in a book, which, with a great deal of verbiage, contains a large amount of valuable information concerning nutrition, and its disturbance by erroneous, or worse, preparation and administration of food.

Possibly there are other dietary elements which may also play some part in the causation of cancer, but the demonstrated facts concerning them are so few and uncertain that they need not detain us here, although it is certainly desirable to investigate any and all that seem to have reasonable support. And it is hoped that the future will develop many more facts which will aid in solving more clearly the real cancer problem.

Some of these which have been suggested probably have to do with a local irritant action on the digestive organs, as we have seen that prolonged local irritation undoubtedly plays an important part in the determination of the site and actual time of occurrence of cancerous disease, for instance, in the mouth, from a ragged tooth, etc. Thus, some have ascribed cancer of the mouth, palate, œsophagus, and stomach to hot food or drink, or to stimulating drink, condiments, etc., and it is quite possible or probable that they act as the exciting cause, to start the epithelial cells on their destructive course, when the other elements are favorable to such development.

The increasing frequency of cancer in the mouth, palate, œsophagus, and stomach in men, especially, looks toward an irritating character of the substances which traverse these regions, including alcoholic drinks, and the irritant effect of

[1] McCann, "Starving America." New York, 1912.

tobacco should not be overlooked in regard to cancerous mouth lesions. But of the millions who use tobacco only very few are affected with cancer, and as far as we can see, only those predisposed thereto by some metabolic disturbance, as has been previously considered. It has been already mentioned that I have found the saliva to be acid almost invariably in cancer patients, even in those with early disease, and I think I have never found it otherwise, unless altered by treatment, in those with malignant lesions within the mouth. With this there is a faulty preparation of carbonaceous and fatty foods.

Mayo[1] says: "In civilized man one-third of all cancers are seated in the stomach. This is not known to be the case in uncivilized man, or in animals. There should therefore be something—some one cause—which causes the preponderance. The acid secretion may favor its development, for when we come to the colon, also with an acid secretion, we again meet with cancer, and we seldom see it in the alkaline, small intestine. Gastric ulcer, which may be pre-cancerous, is connected with hyper-acidity.

In Scandanavia cancer of the stomach is remarkably frequent, according to Soëgaard;[2] thus of 1,235 cancer cases in Norway, 73.9 per cent were in that location. In a former chapter we saw that cancer in general was connected with a lowered alkalescence of the blood, and all our studies show hyper-acidity to be related to cancer genesis. Nitrogenous acidity, or uric acid (purim bases, xanthin, etc.) undoubtedly plays a great part in inducing malignant action in tissues, as Haig[3] has so long contended, even in regard to cancer; and the almost invariable occurrence of rheumatic and neuritic symptoms in cancer patients, even in regions far distant from definite lesions, shows this strongly. Such pains, as also the pains in active cancerous lesions are continually found to be controlled by efficient repeated administration doses of aspirin, which also seems to help the cancer itself.

[1] MAYO, "Annals of Surgery." 1914, p. 587.
[2] SOËGAARD, "Zeitschr. für Krebsforsch." 1913, p. 89.
[3] HAIG, "Uric Acid in the Causation of Disease." 7th edition, 1908, p. 420.

Although, as far as I know, there are no scientific observations to prove it, still I cannot help feeling, from a long clinical study of cancer as a disease, that xanthin or some of the purin bases, has to do with the erroneous and erratic action of the cells which result in cancer. We have seen in a previous chapter how the cancer cells change from the form of normal cells, and in the chapter on the bio-chemistry of cancer, that there were changes in their chemical constituents, especially in regard to the nuclei which supply the endogenous purin, and we shall see later how cutting off the supply of exogenous purin checks the disease. We know of uratic deposits in gout and arthritis deformans, and the alteration of the cells lining the vessels in arterio-sclerosis, and it does seem reasonable to believe that long continued irritation of cells by some of the purin bases can excite them to the morbid action which we call cancer. Certainly all the treatment which I have given, dietary and medicinal, with success, is along the lines of modifying or removing elements which tend to the production of uratic features.

There are yet other considerations concerning the relation of diet to cancer, which are worthy of attention. We have mentioned some principal agents which seem unquestionably to have an influence in the production and continuance, and even recurrence of cancer, namely proteids, coffee and tea, and alcoholics. But millions of human beings partake of these with apparent immunity, while in the relatively few they appear to have cancer-genetic powers. This need not surprise or puzzle us any more than do the many other problems in medicine which we are seeking to solve: for we know that the system often reaches a point where certain things, once well borne, are no longer tolerated. We know, for instance, that Port and Madeira wine can certainly cause gout, but with many individuals they may be indulged in freely for some time before this result follows. We must remember that it is not the alcoholic content of this that does the mischief, as much as it is the acids and some other of the 28 elements of which they are composed. Likewise that tobacco may even be abused for a long time,

without apparent ill effects, when suddenly there is a revulsion of the system, and the slightest use of tobacco will be intolerable. Also that many edible substances which have long been well borne, will at a certain time act unfavorably and excite eruptions, urticaria, acne, eczema, etc., and we are only beginning to understand some of the strange conditions associated with anaphylaxis.

Psoriasis also furnishes an illustration which may be of service in understanding the relation of diet to cancer. For psoriasis is characterized by a disordered epithelial growth, which shows both on the surface and manifests itself by epithelial prolongations into the corium, which are quite comparable to the ingrowing cellular masses of some forms of cancer. Moreover, cancer is not very rare in psoriatic patients. In this eruption it has been very clearly demonstrated, clinically and experimentally, that error in nitrogenous metabolism is commonly at the bottom of the disease, and I have repeatedly seen the eruption promptly and entirely disappear simply under an absolute vegetarian diet alone, correctly regulated, excluding also coffee and alcohol, without the use of any medical treatment whatever, internal or external, and then return when these dietary measures were neglected: but, of course, this result cannot always be obtained, and sometimes the eruption will resist during what is claimed to be a vegetarian diet. There must, therefore, be some systemic disturbance which causes nutritive material, at some particular time, thus to derange cell action in the eruptions mentioned, and the same is true in regard to the production of cancer.

Some years ago Braithwaite[1] called attention to the occurrence of cancer among certain people who were vegetarians, and attributed it to the great amount of salt which they consumed. While the objection that salt, which is a prominent constituent of the blood, can be a cause of cancer has been ridiculed, it is quite possible that a great excess of sodium chloride may disturb the salt equilibrium in the blood, by replacing the

[1] BRAITHWAITE, *Lancet*. 1902, Vol. I, p. 400.

potassium which is such a feature in cell life, as shown by Forbes Ross, and also by hindering the excretion of uric acid, as Haig has pointed out. This matter of salt in relation to cancer has recently been agitated strongly by Robinson[1] who gives cases illustrating the advantage of limiting its intake. We do know that the restriction of salt in the diet is an important matter in connection with certain kidney and other conditions of disease.

When we inquire into the cause of the systemic disturbance which tends to such faulty metabolism that the nutrition of cellular structures is deranged, even to the degree of taking on malignant action, we find many elements, more or less connected with what is known as modern civilization, which have been considered in another chapter but may be briefly alluded to here. Williams has shown pretty clearly that wealth, with its tendency to luxury and idleness, greatly increased the proclivity to cancer. Not only is this observed in different countries, but in certain cities the difference is very striking between the cancer mortality in sections which are occupied by the rich and well-to-do, and those in which the poorer classes are herded. Also in England it was found that in one decennium cancer nortality was more than twice as great among the well-to-do men, having no specific occupation, as it was among occupied males in general, the ratio being 96 to 44.

Change in the mode of life, and sudden changes of environment and urbanization have also been found to have a great effect in the production of cancer. As Bell remarks: "Cancer is essentially a disease supervening upon a persistent neglect of hygienic laws."

Finally, nervous conditions unquestionably can and very often do exert a profound influence on the secretions of the various organs of the body, and can so disturb digestion, metabolism, and nutrition that the most varied results may follow. Witness the now well attested fact that sudden fright or grief can cause a complete greyness of the hair, even in a

[1] ROBINSON, *The Medical Record*, Aug. 24, 1920.

very brief time. So that nerve strain, more or less incident to modern life, must be accredited with a certain share in the production of cancer, as many have observed.

It is seen, therefore, that there are many contributing factors in the causation of cancer. But the fact remains that the proper diet must lie at the bottom of all effective medical treatment. We also see that it is not meat eating alone which induces the neo-plastic growth, but that disordered metabolism is the fundamental cause, and this is influenced by diet to such a degree that without this being properly controlled, as will be shown in the chapter on treatment, simple medical or surgical measures can never hope to check its ravages.

CHAPTER XIV

MORTALITY FROM CANCER: ANALYSIS OF SURGICAL STATISTICS

The chapter on the "Frequency and Geographical Distribution of Cancer" was based largely on its mortality, but this may with advantage be briefly alluded to in connection with the resulst of the surgical treatment of the disease.

The total deaths from cancer in the United States each year is estimated at about 80,000, judging from the actual reports from the States which are included in the registration area, as shown by the United States Mortality Reports. In the registration area, covering an estimated 77.8 per cent of the whole population, there were 65,340 deaths from cancer and other malignant tumors, during 1918, and 68,551 in 1919.

Interesting confirmation of the actual and certain increase in the mortality from cancer in the United States is furnished by a study of the table given on page 15 of the Special Report of the Mortality from Cancer in the Registration Area of the United States, for 1914. In 1900, the estimated population of the registration area was 30,765,618, and in 1914, the larger area included a population of 65,989,295, or had a little over doubled; and, whereas in 1910 the cancer deaths were 19.381, in 1914 they were 52.420, that is, the cancer deaths had nearly tripled in these 14 years, while the population had only a little more than doubled.

In New York City, by the Reports of the Board of Health, there were in 1919, 5,124 such deaths, (2,250 males, 2,874 females), with an increase of more than 4.6 per cent over the preceding year. This is remarkable and unexplainable, for in 1918, the increase was less than *one* per cent over those in

1917. This total number of deaths, 5,124, divided by 365 days, makes an average of over 14 deaths daily from malignant neo-plasms, against 13.39 persons dying daily in 1918. The lowest number recorded in any one week in 1918, was 81, or 11.52 persons daily, and the highest was the surprising number of 132, or 18.83 each day, in the week ending December 20th: the next highest week, ending December 6th, gave 119 deaths from cancer, or an average of 17 per day. During the first 6 months of 1920, there were 2,670 deaths from this cause, or 14.59 persons daily. Surely this increase in the reported mortality is not one due as is commonly claimed, to : 1. Increased longevity in general, leading to the existence of more people of the cancerous age; or 2. Improved diagnosis; or 3. More careful death certification: these often alleged causes of the steadily rising mortality could hardly be operative in New York City in 6 months or a year and during the last six months of the year, as we have already mentioned; the recorded cancer deaths were actually 2691, an excess of 22 over those from tuberculosis.

The mortality from cancer varies greatly in different States of the Union, but in almost every instance there has been an increase worthy of note. We will give that per 100,000 population, for 1918 as compared with that in 1911, which is shown in the last Government Report. Maine 107.5 against 98.6: New Hampshire 107.3, 96.8: Massachusetts 107.2, 94.4: California 106.0, 82.6: Vermont shows a decrease, 99.7, 101.0 (but in 1916 it was 114.9 per 100,000): New York State 93.2 against 86.3 per 100,000 population. The lowest rates in 1918, are shown for South Carolina 34.4: North Carolina 43.5: Tennessee 44: Louisiana 46.4: and Utah 50.5. In all the states in which it is given, the death rate is lower among the colored than among the whites, except Kentucky, where it is a trifle higher. The lowest mortality among the colored people was in South Carolina, where it was 27.4 to the 100,000 against 42.3 among the whites.

The cities also vary greatly in the number of reported deaths from cancer, and as a rule show a higher percentage than that

of the state in general. This is owing in part to the number of patients coming for treatment and also to the more complex life of the cities, with the greater temptations, leading to the disturbances of metabolism causing cancer. Thus, the average of 20 large cities gives a rise in the death rate of cancer from 48.6 in 1881 to 1885, to 89.3 per 100,000 living in 1913.

The following table gives the average cancer mortality from 1906 to 1910 per 100,000 in certain American cities:

San Francisco	102.5	Newark	76.9
Boston	99.4	Chicago	76.5
Providence	96.9	Greater New York	74.1
Los Angeles	94.9	Richmond	73.9
Cincinnati	93.0	Kansas City, Mo	71.1
Hartford	91.9	St. Paul	71.1
New Haven	89.8	Indianapolis	70.4
Dayton	88.5	Borough of Brooklyn	68.9
Rochester	88.2	Milwaukee	68.4
Springfield, Mass.	86.9	Nashville	68.0
District of Columbia	86.0	Pittsburgh	66.4
Baltimore	85.8	Minneapolis	65.3
Omaha	85.7	Detroit	64.5
Buffalo	84.0	Cleveland	62.9
New Orleans	82.2	Louisville	61.1
Philadelphia	81.9	Jersey City	60.5
Hoboken	80.7	Charleston	53.6
Columbus	79.5	Seattle	50.2
Manhattan and Bronx	78.4	Augusta, Ga	49.1
St. Louis	78.4	Memphis	48.7
Denver	77.9	Savannah	47.1

It is readily understood that many factors enter into the study and proper understanding of the statistics of the mortality of cancer, such as age, sex, location of the lesion, race, etc., and it is quite impossible in the present writing, or from any data accessible, to make any such analysis in full, but a few points may be mentioned.

Thus, in regard to age, the states which represented the greatest number of deaths from cancer—Maine with 107.5; New Hampshire, 107.3; Vermont, 99.7 (114.9 in 1916)—per 100,000, show that the proportion of individuals 45 years of age or older

was over 27 per cent, compared with 17.7 per cent for Kentucky and 16.2 per cent for Montana, which latter gave almost the lowest mortality for cancer.

The same is somewhat true in regard to sex, although sufficient data are not at hand to show the relative number of males and females in different states. Of the total deaths from cancer in the United States in 1918, 38,619, or 59.1 per cent were females, and 26.721, or 40.9 per cent males, although the male population in the registration area exceeds the female.

We know, of course, that the great preponderance of deaths from cancer in females is due to the disease affecting the breast and uterus, and where females preponderate the total cancer mortality would be higher. The general mortality for cancer has always been higher in females, but that of males is steadily gaining, owing it is thought to the steady increase of deaths from cancer of the stomach, liver, and intestines in males.

The location of the lesion has also a bearing upon the understanding of statistics. Thus, in Norway, for some unexplained reason, cancer of the stomach seems to be extremely common. With a death rate from cancer in general, in 1912, of 104.8 per 100,000 inhabitants (risen from 50.6 in 1886), there is reported by Dr. Soërgaard [1] a mortality of 60 per cent of all to be from cancer of the stomach, while those from the breast and uterus are very few.

In the United States, in 1918, cancer of the stomach and liver caused the death of 23,845 persons, of these 12,208 were males and 11,637 females. The total cancer deaths were 25,780 males, of which almost one-half were from cancer of the stomach and liver, and 36,379 females, of which less than one-third were from this cause. Cancer of the uterus caused 8,043 deaths, and that of the breast, 6,040, a total of 15,043, or 41 per cent of all the cancer deaths in females, and 23 per cent of all deaths from cancer in both sexes.

[1] SOËRGAARD, "Die Krebsform. Norweg. Zeitschr. f. Krebsforcsh." 1913 (HOFFMAN, p. 633).

DEATHS IN THE UNITED STATES REGISTRATION AREA, 1918

Age of decedent	Carcinoma		Sarcoma		Hyper-nephroma	
	Male	Female	Male	Female	Male	Female
All ages.....	24,715	36,780	1,923	1,795	83	44
Under 1 year.....	9	13	22	13	1	1
1 year.....	6	4	32	17	..	..
2 years.....	12	19	26	18	2	2
3 years.....	12	17	23	20	..	..
4 years.....	8	8	19	22	..	3
Under 5 years.....	47	61	122	90	3	6
5 to 9 years.....	27	28	44	41	..	..
10 to 14 years.....	23	17	49	35	..	..
15 to 19 years.....	34	43	75	65	..	1
20 to 24 years.....	81	146	89	58	1	2
25 to 29 years.....	155	386	111	75	2	..
30 to 34 years.....	307	856	104	79	2	1
35 to 39 years.....	611	1,626	126	96	6	1
40 to 44 years.....	1,069	2,719	130	125	15	4
45 to 49 years.....	1,711	3,738	131	167	6	3
50 to 54 years.....	2,602	4,246	172	166	14	5
55 to 59 years.....	3,201	4,695	210	156	13	5
60 to 64 years.....	3,714	4,694	163	172	12	5
65 to 69 years.....	3,759	4,566	141	154	5	5
70 to 74 years.....	3,278	3,856	126	126	1	4
75 to 79 years.....	2,246	2,686	70	109	2	2
80 to 84 years.....	1,106	1,540	38	51	..	..
85 to 89 years.....	481	613	19	23	1	..
90 to 94 years.....	102	178	2	6	..	..
95 to 99 years.....	27	27	..	..	..	..
100 years and over...	6	7	..	..	..	..
Unknown age.....	38	52	1	1	..	..

Race also seems to have something to do with the mortality from cancer, although as statistics develop, it is seen that habits of life in natives modify the death rate, according as these later approach to that of foreigners with whom they come in contact.

Thus, in slavery times the negroes were said to have almost no cancer, when they lived simple lives and worked hard. But

since their freedom, and as they mingled with others, serving in hotels, etc., the death rate has steadily increased.

In studying the latest Mortality Tables of 1918, it is rather surprising to find that in New York City, with a total of 4,985 deaths from cancer, there were only 96 in colored persons: of course no judgment can be formed from this without knowing the relative number of the latter in the city, which cannot be stated; the percentage of total deaths from cancer, among the colored is always very much lower than among the whites, in every state but one in which they are recorded.

The Polynesians and Melanesians seem to be peculiarly exempt from cancer. Sir William McGregor[1], although he had operated several times for cancer in whites in the Fiji Islands, never remembers operating on a Polynesian or Melanesian, who are vegetarians. He never saw a case of cancer in British Guiana in 9½ years, and then saw an encephaloid cancer of the tibia in a Papuan, who for 7 or 8 years had lived practically a European life, eating canned Australian meat daily.

As regards Africa, Williams quotes Dr. Madden[2] of Cairo, who says: "The consensus of opinion among medical men in Egypt is, that cancer is never found, either in male or female, among the black races of that country. These include the Berberines and the Sudanese, who are all Musslemans, and live almost entirely on vegetable diet." Of 19,529 deaths among natives of Cairo in 1891, only 19 were due to cancer (9 males and 10 females) or 1 in 1,028, while in England during the same year the proportion of cancer deaths to total deaths was 1 to 29. In the Islands of Lagos, on the west coast of Africa, Dr. Johnson[3] in 14 years' practice there saw five cases of cancer in natives all of whom lived as Europeans. Renner[4] reports interestingly in regard to cancer among the descendants of liberated Africans or Creoles, in Sierre Leone, Africa. During 30 years, from 1870

[1] McGregor, *Brit. Med. Journ.*, 1900, ii, p. 982.

[2] Madden-quoted by Williams, p. 43, *Brit. Med. Journ.*, 1902, Vol. 2, p. 730.

[3] Johnson, *Brit. Med. Journ.*, 1900, ii, p. 982.

[4] Renner, *Brit. Med. Journ.*, 1910, ii, p. 587; also 1911, i, p. 110.

to 1900, there were but 30 cases recorded of malignant disease among 22,453 admitted to the Colonial Hospital: in the next 10 years there were 26 among a total of 10,163, a slow but steady gain in cancer incidence, with the advancing influence of the white man. More of this evidence will be found in other chapters, and we need not dwell on it longer here.

Realizing, then, that the mortality of cancer is materially and steadily rising, in spite of most diligent research by innumerable honest and capable scientists, with the expenditure of vast sums of money and countless animal lives, and in spite of the work of ardent, earnest, and capable surgeons, to whom all honor is due, but who have failed to stay the terrible progress of the disease, let us briefly study some of the reported statistics in regard to operative interference in cancer.

It may be first stated that this is a most difficult task, so different are the reports from different surgeons. There are many elements which affect the statistics relating to the surgery of cancer, which we will briefly consider in turn.

First, as to the *stage of the disease* at which the operation was performed. We have tried to show that the lesion which we call real cancer is but the *result* of a deranged blood state, probably of long existence, and that the whole trouble is not a purely local process, a something simply to be removed surgically in order to have the patient get well and remain well. For one sees plenty of cases where there were recurrences shortly after removal, even after the very earliest operations possible, especially on the breast and uterus. But the claims put forth that favorable results are conditional on very early operations are so strenuous and persistent that we must perhaps believe that a measure of the favorable results claimed can be thus accounted for. Though, as already mentioned, the excision of lesions which were pronounced microscopically not to be cancerous have been followed by unmistakable cancer. We know, of course, that very late in the disease, and in recurrences, operations are out of the question, and commonly harmful.

It is a little curious, however, that most of the pictures

shown, statistics presented, and arguments advanced by these advocates of early operations, relate to cutaneous epithelioma, mainly about the face, which cause a very small mortality, which would be very much less if the disease were properly cared for at the beginning, for their early recognition is relatively easy. Moreover, those who see much of cutaneous epithelioma know that if rightly handled early, it is generally a comparatively mild affair and relatively easily cured without a surgical operation, as by *x*-ray, radium, certain pastes, etc. And, as already mentioned, it is excluded in our present study of cancer as a disease, for it is really a local epithelial degeneration from external causes. But mortality statistics are greatly influenced by the class of cases which an operator takes, and so if epithelioma of the skin is included the ratio of cures will be higher. Selected cases also always give more favorable statistics.

Second, the *knowledge and skill* of the operator, and the perfection of technique undoubtedly influence surgical statistics. The ordinary practitioner or surgeon cannot hope for as favorable results in many operations for cancer as can those who are past masters in this line, and these latter are the ones who furnish the most favorable statistics.

Third, *the class of cases* operated on affect surgical statistics very greatly. While cutaneous epithelioma of the face, and even of the lip, when well removed, may yield favorable statistics, cancer of the breast, uterus, stomach, intestines, gall bladder, etc., still yield even increasingly unfavorable statistics, as will be presently seen.

Fourth, the *duration of observation* after operation affects very seriously the validity of statistics. Not long ago three years' freedom from the disease was considered the time to regard a cancer as permanently cured. But this time has been lengthened more and more, by the observation of many cases where the disease has recurred even long afterwards, and reliable observers are now very chary in expressing an opinion as to the final cure of cancer; and some surgeons, as Deaver, already quoted, say: "We still do nothing to cure it."

Finally, the *optimism of the reporter* seems often to have something to do with the reliability of surgical statistics. This need hardly be discussed. The older and more experienced the surgeon, the less confident he is of having actually cured cancer with the knife. At a discussion on cancer in the New York Academy of Medicine some years ago, Dr. Robert F. Weir of New York, said that the late Dr. Agnew, a celebrated surgeon of Philadelphia, had remarked just before his death that he doubted if he had ever been justified in an operation upon cancer, and he, Dr. Weir, stated that he could almost say the same. At a recent meeting of a County Medical Association in a neighboring city, a very prominent surgeon, 60 years old, operating over a wide district, said: "Mr. President and Gentlemen: I have done with operations on cancer, and hope that no one will ever ask me again to operate on that disease. I do not know if I have ever done enough good to warrant the operation." A very prominent anesthetist, who has had a very great deal to do with operations on cancer, remarked to me recently that he was struck with the unfortunate results of operations on the disease. Although there are still occasional records of cancer operations reported as successful, there is seldom mention of observation long enough to determine if the disease was eradicated.

Turning now to the actual statistics of operative surgery on cancer, we will find that the percentage of reported cures varies greatly in accordance with the points just stated. It is understood, of course, that no accurate statements can be made in regard to the actual mortality from cancer in any location, partly owing to the paucity of reliable figures, and partly because the stages and extent of the disease differ so greatly in different cases, and the final results vary with the previous duration of the disease and the period of observation after the operation, which is seldom stated.

Cancer or *epithelioma* of the skin presents the best operative statistics of any region, and the claim is made that all cases are curable if operated on early enough and rightly. While this is

not wholly true, it is certain that if all lesions which one chooses to call "pre-cancerous" are thoroughly extirpated very early, and all of them included as cancer in statistics, the percentage of cures can be reported as very high. So that it may be said that, taking all statistics together, including very small as well as large lesions, the favorable results, that is permanent cures of lesions which can truly be called cutaneous epithelioma, may, as some claim, run as high as 75 per cent.

But against this is set the fact that a very large share of these cutaneous epitheliomas taken early and treated by competent persons, are equally amenable to lighter measures, without the horrible disfigurement which one sometimes sees after purely surgical procedures.

Cancer of the lip, when treated early, and skillfully, and radically, including sufficient gland extirpation, also yields a fairly satisfactory result, depending, of course, on the duration and stage of the disease, or amount of involvement of tissue and glands, and the completeness of the operation. But while the lip lesion may remain absent, subsequent recurrence in deep glands is most distressing and hopeless. Thus, while some operators have claimed 75 per cent of cures, Hertzler[1] makes the percentage of permanent cure; "not much over 25 per cent," and Taylor agrees that this is approximately correct, if all operations, by all operators were taken into account. And here again, it may be remarked, if taken early and treated correctly, by proper local and constitutional measures, many of these cases yield without the knife, as will be seen in a later chapter.

When we come, however, to cancer *within the mouth*, on *the tongue*, etc., it is quite a different story, as mentioned in the chapter on prognosis, and the end results of surgery are commonly unsatisfactory. Certain European surgeons have reported an operative mortality in cancer of the tongue as high as 36 per cent, while recurrences are the rule, and really permanent cures

[1]Hertzler, "Treatise on Tumors" quoted by Taylor, "Cancer." Phila. 1915, p. 193.

the very great exception. Of 25 cases reported on by Steiner[1] there were 9 operative deaths, or 36 per cent. Of the 16 that recovered from the operation 9 died within the first year, 4 cases in the second year, and the result in 3 cases was unknown. Of Steiner's 25 cases 12, or nearly 50 per cent, were operated on within the first 3 months of the apparent onset of the disease. Of 51 cases reported by Erlich[2] there were 13 operative deaths, or over 25 per cent, and but five cases were free of recurrence at the end of 5 years.

As before stated, it is extremely difficult to give any true and accurate estimate of the real end results from operative surgery, as ordinarily performed, in cancer affecting various regions. The obvious reason is that most of our statistics are from those who are especially occupied with the disease, and under most favorable hospital facilities; and also certain statistics may be from selected cases. Moreover, operators are naturally inclined to report mainly satisfactory results, and that also too soon after operation to afford a just and fair statement of end results, while the unfavorable aspects are seldom fully presented. Aside then from superficial epitheliomata, about the only location in which there is even a fair chance for the patient under the knife, should be the relatively accessible regions of the breast, uterus, intestines, and rectum, and for these large statistics are on record; but again these are unsatisfactory, as they vary so greatly.

In *cancer of the breast* the statistics are very provoking. Individual operators have claimed as high as 50 and even 75 per cent of cases (Rodman).[3] John B. Murphy,[4] on the other hand, on the basis of end results, states that the plump woman invariably succumbs, and that Paget's disease ends fatally in 90 per cent of the cases.

Hilderbrand mentions 606 operations, in which the percent-

[1] STEINER, Deutch. Zeitschr. f. Chir. Vol. 98. Quoted by Taylor, p. 182.
[2] ERLICH, Arch. f. Klin. Chir. Vol. lxxviii. Quoted by Taylor, p. 182.
[3] RODMAN. *Jour. Amer. Med. Asso.*, Feb. 27, 1915.
[4] MURPHY, Clinics, Aug. 12, Aug. 19, 1913, Dec. 12, Sept. 14, June 14.

tobacco should not be overlooked in regard to cancerous mouth lesions. But of the millions who use tobacco only very few are affected with cancer, and as far as we can see, only those predisposed thereto by some metabolic disturbance, as has been previously considered. It has been already mentioned that I have found the saliva to be acid almost invariably in cancer patients, even in those with early disease, and I think I have never found it otherwise, unless altered by treatment, in those with malignant lesions within the mouth. With this there is a faulty preparation of carbonaceous and fatty foods.

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[2] SOËGAARD, "Zeitschr. für Krebsforsch." 1913, p. 89.
[3] HAIG, "Uric Acid in the Causation of Disease." 7th edition, 1908, p. 420.

Although, as far as I know, there are no scientific observations to prove it, still I cannot help feeling, from a long clinical study of cancer as a disease, that xanthin or some of the purin bases, has to do with the erroneous and erratic action of the cells which result in cancer. We have seen in a previous chapter how the cancer cells change from the form of normal cells, and in the chapter on the bio-chemistry of cancer, that there were changes in their chemical constituents, especially in regard to the nuclei which supply the endogenous purin, and we shall see later how cutting off the supply of exogenous purin checks the disease. We know of uratic deposits in gout and arthritis deformans, and the alteration of the cells lining the vessels in arterio-sclerosis, and it does seem reasonable to believe that long continued irritation of cells by some of the purin bases can excite them to the morbid action which we call cancer. Certainly all the treatment which I have given, dietary and medicinal, with success, is along the lines of modifying or removing elements which tend to the production of uratic features.

There are yet other considerations concerning the relation of diet to cancer, which are worthy of attention. We have mentioned some principal agents which seem unquestionably to have an influence in the production and continuance, and even recurrence of cancer, namely proteids, coffee and tea, and alcoholics. But millions of human beings partake of these with apparent immunity, while in the relatively few they appear to have cancer-genetic powers. This need not surprise or puzzle us any more than do the many other problems in medicine which we are seeking to solve: for we know that the system often reaches a point where certain things, once well borne, are no longer tolerated. We know, for instance, that Port and Madeira wine can certainly cause gout, but with many individuals they may be indulged in freely for some time before this result follows. We must remember that it is not the alcoholic content of this that does the mischief, as much as it is the acids and some other of the 28 elements of which they are composed. Likewise that tobacco may even be abused for a long time,

without apparent ill effects, when suddenly there is a revulsion of the system, and the slightest use of tobacco will be intolerable. Also that many edible substances which have long been well borne, will at a certain time act unfavorably and excite eruptions, urticaria, acne, eczema, etc., and we are only beginning to understand some of the strange conditions associated with anaphylaxis.

Psoriasis also furnishes an illustration which may be of service in understanding the relation of diet to cancer. For psoriasis is characterized by a disordered epithelial growth, which shows both on the surface and manifests itself by epithelial prolongations into the corium, which are quite comparable to the ingrowing cellular masses of some forms of cancer. Moreover, cancer is not very rare in psoriatic patients. In this eruption it has been very clearly demonstrated, clinically and experimentally, that error in nitrogenous metabolism is commonly at the bottom of the disease, and I have repeatedly seen the eruption promptly and entirely disappear simply under an absolute vegetarian diet alone, correctly regulated, excluding also coffee and alcohol, without the use of any medical treatment whatever, internal or external, and then return when these dietary measures were neglected: but, of course, this result cannot always be obtained, and sometimes the eruption will resist during what is claimed to be a vegetarian diet. There must, therefore, be some systemic disturbance which causes nutritive material, at some particular time, thus to derange cell action in the eruptions mentioned, and the same is true in regard to the production of cancer.

Some years ago Braithwaite[1] called attention to the occurrence of cancer among certain people who were vegetarians, and attributed it to the great amount of salt which they consumed. While the objection that salt, which is a prominent constituent of the blood, can be a cause of cancer has been ridiculed, it is quite possible that a great excess of sodium chloride may disturb the salt equilibrium in the blood, by replacing the

[1] BRAITHWAITE, *Lancet*: 1902, Vol. I, p. 400.

potassium which is such a feature in cell life, as shown by Forbes Ross, and also by hindering the excretion of uric acid, as Haig has pointed out. This matter of salt in relation to cancer has recently been agitated strongly by Robinson[1] who gives cases illustrating the advantage of limiting its intake. We do know that the restriction of salt in the diet is an important matter in connection with certain kidney and other conditions of disease.

When we inquire into the cause of the systemic disturbance which tends to such faulty metabolism that the nutrition of cellular structures is deranged, even to the degree of taking on malignant action, we find many elements, more or less connected with what is known as modern civilization, which have been considered in another chapter but may be briefly alluded to here. Williams has shown pretty clearly that wealth, with its tendency to luxury and idleness, greatly increased the proclivity to cancer. Not only is this observed in different countries, but in certain cities the difference is very striking between the cancer mortality in sections which are occupied by the rich and well-to-do, and those in which the poorer classes are herded. Also in England it was found that in one decennium cancer nortality was more than twice as great among the well-to-do men, having no specific occupation, as it was among occupied males in general, the ratio being 96 to 44.

Change in the mode of life, and sudden changes of environment and urbanization have also been found to have a great effect in the production of cancer. As Bell remarks: "Cancer is essentially a disease supervening upon a persistent neglect of hygienic laws."

Finally, nervous conditions unquestionably can and very often do exert a profound influence on the secretions of the various organs of the body, and can so disturb digestion, metabolism, and nutrition that the most varied results may follow. Witness the now well attested fact that sudden fright or grief can cause a complete greyness of the hair, even in a

[1] ROBINSON, *The Medical Record*, Aug. 24, 1920.

very brief time. So that nerve strain, more or less incident to modern life, must be accredited with a certain share in the production of cancer, as many have observed.

It is seen, therefore, that there are many contributing factors in the causation of cancer. But the fact remains that the proper diet must lie at the bottom of all effective medical treatment. We also see that it is not meat eating alone which induces the neo-plastic growth, but that disordered metabolism is the fundamental cause, and this is influenced by diet to such a degree that without this being properly controlled, as will be shown in the chapter on treatment, simple medical or surgical measures can never hope to check its ravages.

CHAPTER XIV

MORTALITY FROM CANCER: ANALYSIS OF SURGICAL STATISTICS

The chapter on the "Frequency and Geographical Distribution of Cancer" was based largely on its mortality, but this may with advantage be briefly alluded to in connection with the resulst of the surgical treatment of the disease.

The total deaths from cancer in the United States each year is estimated at about 80,000, judging from the actual reports from the States which are included in the registration area, as shown by the United States Mortality Reports. In the registration area, covering an estimated 77.8 per cent of the whole population, there were 65,340 deaths from cancer and other malignant tumors, during 1918, and 68,551 in 1919.

Interesting confirmation of the actual and certain increase in the mortality from cancer in the United States is furnished by a study of the table given on page 15 of the Special Report of the Mortality from Cancer in the Registration Area of the United States, for 1914. In 1900, the estimated population of the registration area was 30,765,618, and in 1914, the larger area included a population of 65,989,295, or had a little over doubled; and, whereas in 1910 the cancer deaths were 19.381, in 1914 they were 52.420, that is, the cancer deaths had nearly tripled in these 14 years, while the population had only a little more than doubled.

In New York City, by the Reports of the Board of Health, there were in 1919, 5,124 such deaths, (2,250 males, 2,874 females), with an increase of more than 4.6 per cent over the preceding year. This is remarkable and unexplainable, for in 1918, the increase was less than *one* per cent over those in

1917. This total number of deaths, 5,124, divided by 365 days, makes an average of over 14 deaths daily from malignant neo-plasms, against 13.39 persons dying daily in 1918. The lowest number recorded in any one week in 1918, was 81, or 11.52 persons daily, and the highest was the surprising number of 132, or 18.83 each day, in the week ending December 20th: the next highest week, ending December 6th, gave 119 deaths from cancer, or an average of 17 per day. During the first 6 months of 1920, there were 2,670 deaths from this cause, or 14.59 persons daily. Surely this increase in the reported mortality is not one due as is commonly claimed, to : 1. Increased longevity in general, leading to the existence of more people of the cancerous age; or 2. Improved diagnosis; or 3. More careful death certification: these often alleged causes of the steadily rising mortality could hardly be operative in New York City in 6 months or a year and during the last six months of the year, as we have already mentioned, the recorded cancer deaths were actually 2691, an excess of 22 over those from tuberculosis.

The mortality from cancer varies greatly in different States of the Union, but in almost every instance there has been an increase worthy of note. We will give that per 100,000 population, for 1918 as compared with that in 1911, which is shown in the last Government Report. Maine 107.5 against 98.6: New Hampshire 107.3, 96.8: Massachusetts 107.2, 94.4: California 106.0, 82.6: Vermont shows a decrease, 99.7, 101.0 (but in 1916 it was 114.9 per 100,000): New York State 93.2 against 86.3 per 100,000 population. The lowest rates in 1918, are shown for South Carolina 34.4: North Carolina 43.5: Tennessee 44: Louisiana 46.4: and Utah 50.5. In all the states in which it is given, the death rate is lower among the colored than among the whites, except Kentucky, where it is a trifle higher. The lowest mortality among the colored people was in South Carolina, where it was 27.4 to the 100,000 against 42.3 among the whites.

The cities also vary greatly in the number of reported deaths from cancer, and as a rule show a higher percentage than that

of the state in general. This is owing in part to the number of patients coming for treatment and also to the more complex life of the cities, with the greater temptations, leading to the disturbances of metabolism causing cancer. Thus, the average of 20 large cities gives a rise in the death rate of cancer from 48.6 in 1881 to 1885, to 89.3 per 100,000 living in 1913.

The following table gives the average cancer mortality from 1906 to 1910 per 100,000 in certain American cities:

San Francisco	102.5	Newark	76.9
Boston	99.4	Chicago	76.5
Providence	96.9	Greater New York	74.1
Los Angeles	94.9	Richmond	73.9
Cincinnati	93.0	Kansas City, Mo.	71.1
Hartford	91.9	St. Paul	71.1
New Haven	89.8	Indianapolis	70.4
Dayton	88.5	Borough of Brooklyn	68.9
Rochester	88.2	Milwaukee	68.4
Springfield, Mass.	86.9	Nashville	68.0
District of Columbia	86.0	Pittsburgh	66.4
Baltimore	85.8	Minneapolis	65.3
Omaha	85.7	Detroit	64.5
Buffalo	84.0	Cleveland	62.9
New Orleans	82.2	Louisville	61.1
Philadelphia	81.9	Jersey City	60.5
Hoboken	80.7	Charleston	53.6
Columbus	79.5	Seattle	50.2
Manhattan and Bronx	78.4	Augusta, Ga	49.1
St. Louis	78.4	Memphis	48.7
Denver	77.9	Savannah	47.1

It is readily understood that many factors enter into the study and proper understanding of the statistics of the mortality of cancer, such as age, sex, location of the lesion, race, etc., and it is quite impossible in the present writing, or from any data accessible, to make any such analysis in full, but a few points may be mentioned.

Thus, in regard to age, the states which represented the greatest number of deaths from cancer—Maine with 107.5; New Hampshire, 107.3; Vermont, 99.7 (114.9 in 1916)—per 100,000, show that the proportion of individuals 45 years of age or older

was over 27 per cent, compared with 17.7 per cent for Kentucky and 16.2 per cent for Montana, which latter gave almost the lowest mortality for cancer.

The same is somewhat true in regard to sex, although sufficient data are not at hand to show the relative number of males and females in different states. Of the total deaths from cancer in the United States in 1918, 38,619, or 59.1 per cent were females, and 26.721, or 40.9 per cent males, although the male population in the registration area exceeds the female.

We know, of course, that the great preponderance of deaths from cancer in females is due to the disease affecting the breast and uterus, and where females preponderate the total cancer mortality would be higher. The general mortality for cancer has always been higher in females, but that of males is steadily gaining, owing it is thought to the steady increase of deaths from cancer of the stomach, liver, and intestines in males.

The location of the lesion has also a bearing upon the understanding of statistics. Thus, in Norway, for some unexplained reason, cancer of the stomach seems to be extremely common. With a death rate from cancer in general, in 1912, of 104.8 per 100,000 inhabitants (risen from 50.6 in 1886), there is reported by Dr. Soërgaard [1] a mortality of 60 per cent of all to be from cancer of the stomach, while those from the breast and uterus are very few.

In the United States, in 1918, cancer of the stomach and liver caused the death of 23,845 persons, of these 12,208 were males and 11,637 females. The total cancer deaths were 25,780 males, of which almost one-half were from cancer of the stomach and liver, and 36,379 females, of which less than one-third were from this cause. Cancer of the uterus caused 8,043 deaths, and that of the breast, 6,040, a total of 15,043, or 41 per cent of all the cancer deaths in females, and 23 per cent of all deaths from cancer in both sexes.

[1] SOËRGAARD, "Die Krebsform. Norweg. Zeitschr. f. Krebsforcsh." 1913 (HOFFMAN, p. 633).

DEATHS IN THE UNITED STATES REGISTRATION AREA, 1918

Age of decedent	Carcinoma		Sarcoma		Hyper-nephroma	
	Male	Female	Male	Female	Male	Female
All ages.....	24,715	36,780	1,923	1,795	83	44
Under 1 year.....	9	13	22	13	1	1
1 year.....	6	4	32	17	..	..
2 years.....	12	19	26	18	2	2
3 years.....	12	17	23	20	..	..
4 years.....	8	8	19	22	..	3
Under 5 years.....	47	61	122	90	3	6
5 to 9 years.....	27	28	44	41	..	..
10 to 14 years.....	23	17	49	35	..	..
15 to 19 years.....	34	43	75	65	..	1
20 to 24 years.....	81	146	89	58	1	2
25 to 29 years.....	155	386	111	75	2	..
30 to 34 years.....	307	856	104	79	2	1
35 to 39 years.....	611	1,626	126	96	6	1
40 to 44 years.....	1,069	2,719	130	125	15	4
45 to 49 years.....	1,711	3,738	131	167	6	3
50 to 54 years.....	2,602	4,246	172	166	14	5
55 to 59 years.....	3,201	4,695	210	156	13	5
60 to 64 years.....	3,714	4,694	163	172	12	5
65 to 69 years.....	3,759	4,566	141	154	5	5
70 to 74 years.....	3,278	3,856	126	126	1	4
75 to 79 years.....	2,246	2,686	70	109	2	2
80 to 84 years.....	1,196	1,540	38	51	..	..
85 to 89 years.....	481	613	19	23	1	..
90 to 94 years.....	102	178	2	6	..	..
95 to 99 years.....	27	27	..	..	..	..
100 years and over...	6	7	..	..	..	..
Unknown age.....	38	52	1	1	..	..

Race also seems to have something to do with the mortality from cancer, although as statistics develop, it is seen that habits of life in natives modify the death rate, according as these later approach to that of foreigners with whom they come in contact.

Thus, in slavery times the negroes were said to have almost no cancer, when they lived simple lives and worked hard. But

since their freedom, and as they mingled with others, serving in hotels, etc., the death rate has steadily increased.

In studying the latest Mortality Tables of 1918, it is rather surprising to find that in New York City, with a total of 4,985 deaths from cancer, there were only 96 in colored persons: of course no judgment can be formed from this without knowing the relative number of the latter in the city, which cannot be stated; the percentage of total deaths from cancer, among the colored is always very much lower than among the whites, in every state but one in which they are recorded.

The Polynesians and Melanesians seem to be peculiarly exempt from cancer. Sir William McGregor[1], although he had operated several times for cancer in whites in the Fiji Islands, never remembers operating on a Polynesian or Melanesian, who are vegetarians. He never saw a case of cancer in British Guiana in 9½ years, and then saw an encephaloid cancer of the tibia in a Papuan, who for 7 or 8 years had lived practically a European life, eating canned Australian meat daily.

As regards Africa, Williams quotes Dr. Madden[2] of Cairo, who says: "The consensus of opinion among medical men in Egypt is, that cancer is never found, either in male or female, among the black races of that country. These include the Berberines and the Sudanese, who are all Musslemans, and live almost entirely on vegetable diet." Of 19,529 deaths among natives of Cairo in 1891, only 19 were due to cancer (9 males and 10 females) or 1 in 1,028, while in England during the same year the proportion of cancer deaths to total deaths was 1 to 29. In the Islands of Lagos, on the west coast of Africa, Dr. Johnson[3] in 14 years' practice there saw five cases of cancer in natives all of whom lived as Europeans. Renner[4] reports interestingly in regard to cancer among the descendants of liberated Africans or Creoles, in Sierre Leone, Africa. During 30 years, from 1870

[1] McGregor, *Brit. Med. Journ.*, 1900, ü, p. 982.

[2] Madden-quoted by Williams, p. 43, *Brit. Med. Journ.*, 1902, Vol. 2, p. 730.

[3] Johnson, *Brit. Med. Journ.*, 1900, ii, p. 982.

[4] Renner, *Brit. Med. Journ.*, 1910, ii, p. 587; also 1911, i, p. 110.

to 1900, there were but 30 cases recorded of malignant disease among 22,453 admitted to the Colonial Hospital: in the next 10 years there were 26 among a total of 10,163, a slow but steady gain in cancer incidence, with the advancing influence of the white man. More of this evidence will be found in other chapters, and we need not dwell on it longer here.

Realizing, then, that the mortality of cancer is materially and steadily rising, in spite of most diligent research by innumerable honest and capable scientists, with the expenditure of vast sums of money and countless animal lives, and in spite of the work of ardent, earnest, and capable surgeons, to whom all honor is due, but who have failed to stay the terrible progress of the disease, let us briefly study some of the reported statistics in regard to operative interference in cancer.

It may be first stated that this is a most difficult task, so different are the reports from different surgeons. There are many elements which affect the statistics relating to the surgery of cancer, which we will briefly consider in turn.

First, as to the *stage of the disease* at which the operation was performed. We have tried to show that the lesion which we call real cancer is but the *result* of a deranged blood state, probably of long existence, and that the whole trouble is not a purely local process, a something simply to be removed surgically in order to have the patient get well and remain well. For one sees plenty of cases where there were recurrences shortly after removal, even after the very earliest operations possible, especially on the breast and uterus. But the claims put forth that favorable results are conditional on very early operations are so strenuous and persistent that we must perhaps believe that a measure of the favorable results claimed can be thus accounted for. Though, as already mentioned, the excision of lesions which were pronounced microscopically not to be cancerous have been followed by unmistakable cancer. We know, of course, that very late in the disease, and in recurrences, operations are out of the question, and commonly harmful.

It is a little curious, however, that most of the pictures

shown, statistics presented, and arguments advanced by these advocates of early operations, relate to cutaneous epithelioma, mainly about the face, which cause a very small mortality, which would be very much less if the disease were properly cared for at the beginning, for their early recognition is relatively easy. Moreover, those who see much of cutaneous epithelioma know that if rightly handled early, it is generally a comparatively mild affair and relatively easily cured without a surgical operation, as by *x*-ray, radium, certain pastes, etc. And, as already mentioned, it is excluded in our present study of cancer as a disease, for it is really a local epithelial degeneration from external causes. But mortality statistics are greatly influenced by the class of cases which an operator takes, and so if epithelioma of the skin is included the ratio of cures will be higher. Selected cases also always give more favorable statistics.

Second, the *knowledge and skill* of the operator, and the perfection of technique undoubtedly influence surgical statistics. The ordinary practitioner or surgeon cannot hope for as favorable results in many operations for cancer as can those who are past masters in this line, and these latter are the ones who furnish the most favorable statistics.

Third, *the class of cases* operated on affect surgical statistics very greatly. While cutaneous epithelioma of the face, and even of the lip, when well removed, may yield favorable statistics, cancer of the breast, uterus, stomach, intestines, gall bladder, etc., still yield even increasingly unfavorable statistics, as will be presently seen.

Fourth, the *duration of observation* after operation affects very seriously the validity of statistics. Not long ago three years' freedom from the disease was considered the time to regard a cancer as permanently cured. But this time has been lengthened more and more, by the observation of many cases where the disease has recurred even long afterwards, and reliable observers are now very chary in expressing an opinion as to the final cure of cancer; and some surgeons, as Deaver, already quoted, say: "We still do nothing to cure it."

Finally, the *optimism of the reporter* seems often to have something to do with the reliability of surgical statistics. This need hardly be discussed. The older and more experienced the surgeon, the less confident he is of having actually cured cancer with the knife. At a discussion on cancer in the New York Academy of Medicine some years ago, Dr. Robert F. Weir of New York, said that the late Dr. Agnew, a celebrated surgeon of Philadelphia, had remarked just before his death that he doubted if he had ever been justified in an operation upon cancer, and he, Dr. Weir, stated that he could almost say the same. At a recent meeting of a County Medical Association in a neighboring city, a very prominent surgeon, 60 years old, operating over a wide district, said: "Mr. President and Gentlemen: I have done with operations on cancer, and hope that no one will ever ask me again to operate on that disease. I do not know if I have ever done enough good to warrant the operation." A very prominent anesthetist, who has had a very great deal to do with operations on cancer, remarked to me recently that he was struck with the unfortunate results of operations on the disease. Although there are still occasional records of cancer operations reported as successful, there is seldom mention of observation long enough to determine if the disease was eradicated.

Turning now to the actual statistics of operative surgery on cancer, we will find that the percentage of reported cures varies greatly in accordance with the points just stated. It is understood, of course, that no accurate statements can be made in regard to the actual mortality from cancer in any location, partly owing to the paucity of reliable figures, and partly because the stages and extent of the disease differ so greatly in different cases, and the final results vary with the previous duration of the disease and the period of observation after the operation, which is seldom stated.

Cancer or *epithelioma* of the skin presents the best operative statistics of any region, and the claim is made that all cases are curable if operated on early enough and rightly. While this is

not wholly true, it is certain that if all lesions which one chooses to call "pre-cancerous" are thoroughly extirpated very early, and all of them included as cancer in statistics, the percentage of cures can be reported as very high. So that it may be said that, taking all statistics together, including very small as well as large lesions, the favorable results, that is permanent cures of lesions which can truly be called cutaneous epithelioma, may, as some claim, run as high as 75 per cent.

But against this is set the fact that a very large share of these cutaneous epitheliomas taken early and treated by competent persons, are equally amenable to lighter measures, without the horrible disfigurement which one sometimes sees after purely surgical procedures.

Cancer of the lip, when treated early, and skillfully, and radically, including sufficient gland extirpation, also yields a fairly satisfactory result, depending, of course, on the duration and stage of the disease, or amount of involvement of tissue and glands, and the completeness of the operation. But while the lip lesion may remain absent, subsequent recurrence in deep glands is most distressing and hopeless. Thus, while some operators have claimed 75 per cent of cures, Hertzler[1] makes the percentage of permanent cure; "not much over 25 per cent," and Taylor agrees that this is approximately correct, if all operations, by all operators were taken into account. And here again, it may be remarked, if taken early and treated correctly, by proper local and constitutional measures, many of these cases yield without the knife, as will be seen in a later chapter.

When we come, however, to cancer *within the mouth*, on *the tongue*, etc., it is quite a different story, as mentioned in the chapter on prognosis, and the end results of surgery are commonly unsatisfactory. Certain European surgeons have reported an operative mortality in cancer of the tongue as high as 36 per cent, while recurrences are the rule, and really permanent cures

[1]HERTZLER, "Treatise on Tumors" quoted by Taylor, "Cancer." Phila. 1915, p. 193.

the very great exception. Of 25 cases reported on by Steiner[1] there were 9 operative deaths, or 36 per cent. Of the 16 that recovered from the operation 9 died within the first year, 4 cases in the second year, and the result in 3 cases was unknown. Of Steiner's 25 cases 12, or nearly 50 per cent, were operated on within the first 3 months of the apparent onset of the disease. Of 51 cases reported by Erlich[2] there were 13 operative deaths, or over 25 per cent, and but five cases were free of recurrence at the end of 5 years.

As before stated, it is extremely difficult to give any true and accurate estimate of the real end results from operative surgery, as ordinarily performed, in cancer affecting various regions. The obvious reason is that most of our statistics are from those who are especially occupied with the disease, and under most favorable hospital facilities; and also certain statistics may be from selected cases. Moreover, operators are naturally inclined to report mainly satisfactory results, and that also too soon after operation to afford a just and fair statement of end results, while the unfavorable aspects are seldom fully presented. Aside then from superficial epitheliomata, about the only location in which there is even a fair chance for the patient under the knife, should be the relatively accessible regions of the breast, uterus, intestines, and rectum, and for these large statistics are on record; but again these are unsatisfactory, as they vary so greatly.

In *cancer of the breast* the statistics are very provoking. Individual operators have claimed as high as 50 and even 75 per cent of cases (Rodman).[3] John B. Murphy,[4] on the other hand, on the basis of end results, states that the plump woman invariably succumbs, and that Paget's disease ends fatally in 90 per cent of the cases.

Hilderbrand mentions 606 operations, in which the percent-

[1] Steiner, Deutch. Zeitschr. f. Chir. Vol. 98. Quoted by Taylor, p. 182.
[2] Erlich, Arch. f. Klin. Chir. Vol. lxxviii. Quoted by Taylor, p. 182.
[3] Rodman. *Jour. Amer. Med. Asso.*, Feb. 27, 1915.
[4] Murphy, Clinics, Aug. 12, Aug. 19, 1913, Dec. 12, Sept. 14, June 14.

survival percentages were 18 and 55 per cent—the latter in favor of the rayed series. Other series have been published to the same effect.

Next to prophylaxis may be considered recurrent cancer, but he only states that with the number of the recurrences the resistance to the rays increases. The first recurrence is more amenable to treatment than the second, and the second than the third. From this angle the possibility of keeping the patient alive indefinitely is not good.

In the treatment of inoperable cases the results are far better than was once the case. The figures of Seitz and Wintz are unusually good, amounting, it is claimed, to 50 per cent of cures; while Duane and Greenough report 55 per cent "improved." Sittenfeld cannot claim such good results. A certain per cent are brought back to the operable stage. In the treatment of the cachectic patient, which is practically left to the *x*-ray men, failure is the rule, yet now and then a result is obtained in the most hopeless cases, which is encouraging. There is daengr that the rays may injure the blood cells and, hence, frequent blood tests must be made.

He emphasizes the need of standardization in the employment of *x*-rays, this includes filtration, focal distance, time, penetration and other factors affecting both the quantity and quality of the rays.

Sittenfeld has recently[1] reported very interestingly on "New Roentgentherapy in Cancer," after a visit to several medical centers in Germany. He states that the technique has undergone great changes there, and that the new type of inductor or transformer develops hard rays capable of penetrating the entire body. Three standard types of tubes are now in use, the Lilienfeld tube, the Müller Slide, and the Furstenau Coolidge tube. These led to the study of accurate measurement of dosage and ray absorption in the deeper tissues. He gives interesting technical details and also clinical data of value relating to work in Berlin, Erlangen, and Freiburg, which

[1] SITTENFELD, *Journ. of the A. M. A.*, January 8, 1921.

cannot be dwelt upon here, but which seem of decided importance, and he speaks of the results obtained as astoundingly favorable. At the Cancer Institute in Berlin he saw in one day 35 patients with cancer of the breast who had reported for observation, who had been radiated 2, 3, or 4 years previously, nearly all of them with gratifying results. His reports in regard to cancer of the uterus at Freiburg were also remarkable. He refers the advantage to more powerful Roengten-ray apparatus, and with it new tubes to accept a high-tension voltage.

Dr. Stevens[1] after considering surgery, electric heat and the value of the *x*-rays for the lymphatics, also emphasizes the crudeness of the Roentgen technique at the hands of the average practitioner with his own equipment. With many of these men the rays are primarily for radiography. In this kind of work benefit must often be due to accident. Again, a good picture machine may be quite unsuited for raying malignant growths. Ordinary gas tubes are entirely insufficient for deep rayings, which require a Coolidge tube, a special tube holder, etc. A Roentgen specialist naturally has to give his entire time to his specialty, which fact militates against his acquisition of knowlege of other methods, or of cancer as a disease.

Not so many years ago the methods against cancer were very simple and crude. Diseased tissues were cut away regardless of the site or character of the tumor, and if the case was frankly inoperable, either nothing was done at all, or an attempt was made to give some relief with the knife, too often with sadly unfortunate results, as to subsequent pain and length of life. Today a merely palliative operation is seldom or never practiced, because it is known to hasten the end. The *x*-ray has undoubtedly done much good in many directions, and has come to stay, but it certainly has its limitations and it is futile to suppose that it alone can ever be regarded as a cure for cancer, any more than can surgery, as abundantly appears elsewhere.

[1] STEVENS, *Medical Record*, November 13, 1920.

Radium.—We will now consider radium, whose rays and action many consider to be the same, or much the same, as those of the *x*-ray, but which has shown itself to be of much greater service in malignant disease in general, for reasons which will appear in its consideration. Unfortunately by the unwise exploitation of some operators, its powers have been greatly exaggerated, and the public has gotten to believe, it would seem, that it has miraculous powers against cancer, to the terrible disappointment of multitudes of sufferers. At the best its operation is only local, like *x*-rays and surgery, and again unfortunately, the mortality rate in the United States has risen just as steadily since the introduction of radium—and in New York City, where it is probably used more largely than anywhere else, the increase in the death rate from cancer is still greater, and in recent weeks has even exceeded that from tuberculosis.

The Memorial Hospital in this city, which now has probably the largest amount of radium in any Institution, has for 6 years given very great attention to this line of treatment of cancer, and with a very large clinic, and an active and intelligent staff of workers has done much to place its use on a firm basis and to formulate and demonstrate the most satisfactory modes of its employment; though all acknowledge that there is need yet of far greater advance before its true value and the proper technique and application can be fully established.

In 1917 there was published a book on "Radium Therapy in Cancer at the Memorial Hospital in New York," covering the previous 2 years of its use. In this was given at some length an interesting, though technical, and valuable consideration of the "Physical Considerations Relative to the Application of Radium," by Dr. Failla, E.E., A.M., who has had charge of the laboratory and the physical handling of the element from the beginning to the present time, and to whom, I believe, much credit is due for its successful use—Dr. H. H. Janeway being director of the radium department has devised and directed the actual employment of the same, Dr. Ewing collaborating

clinically and pathologically in the hospital work. This is not the place to enter on the physics of radium and reference to this book may be made.

During the last 4 years the work with radium has been steadily and energetically pushed, with a very large amount of material, and later will be presented material regarding the present status and scope of radium treatment at the Memorial Hospital, taken from the manuscript of the forthcoming report of the Hospital, kindly loaned by Dr. Janeway. We will first consider some of the earlier and later works on radium by others, which have combined to place this form of treatment on its present basis. Space does not permit of going very far back, nor even covering a tithe of the material which could be presented.

Howard Kelly, writing with Dr. Neill, Jr.,[1] says that he has used radium for over 11 years and claims to have been the first to cure uterine cancer by this means. This was a recurrent uterine cancer in a patient on whom he, had himself operated for the same the year before. She was treated for 3 weeks and has remained well since. Since that time he has worked with Burnam, Lewis, Neill, Jr., Robnett, O'Brien, and Lantsberry. During this time he has seen a remarkable change in the attitude of the profession toward radium. There is fake radium in the market he says—which may explain some non-successes—and that he himself has been victimized, so that all radium should be tested before use. Large quantities, from half a gram to a gram and a half, give better results than smaller, and the latter are known to be dangerous. He mentions using now the emanation in minute capillary tubes, such as are used so largely in the Memorial Hospital. Kelly states that at present a radium expert can cure a cervical cancer, and he and John Clark are committed to the belief that 5 years from now there will be no more surgery for cancer of the uterus. The involved parametria and outlying nodules may be felt through the rectum and radium needles or emanation may be

[1] KELLY and NEILL, JR., *Amer. Journ. of Surg.*, December, 1919.

carried into these foci; under the knife recurrences invariably begin in the latter. Recurrent cancer in the vaginal vault, he says, is "made for radium" treatment, and when seen early enough these may be wiped out, never to return. Routine examination of patients may therefore help to treat recurrences without delay, for a massive recurrence is practically incurable.

Kelly does not like the too common use of the term palliative treatment in connection with radium. The objective is curative treatment and many cures have been accomplished, to say nothing of the great extension of life in some so-called incurable cases. This is worthy of a better name he says, than palliative, which seems to connote relief from certain symptoms. He says that we must not forget that radium and surgery can do team work in individual cases.

In the *American Journal of Roentgenology* for January, 1920 are clinical papers by Clarke and Keene of Philadelphia and Samuel of New Orleans, with other data in discussion by Stacy of the Mayo clinic.

Clarke and Keene control a material of 209 cases of cancer of the uterus which go back as far as 1913. Of this 111 patients are known to have died, and 25 others cannot be traced. It is known that 73 are still living, and the number of survivors have steadily increased, year by year. At the end of 1914 there was but one survivor for the year, while there were 34 survivors for the year 1918 alone. The original survivor is the most remarkable of all, for the woman had chorio-epithelioma which had ruptured into the peritoneal cavity. Death from hemorrhage was averted only by supra-vaginal hysterectomy. Six weeks later there was another profuse hemorrhage from the vagina, the growth having reappeared as a large fixed mass in the left side of the pelvis. Radium was applied and strange to relate, the case was cured and remained well for 5 years.

Samuels of New Orleans is frankly pessimistic. He does not understand why his results were not as good as those of some other men. He tabulates 126 cases of cancer of the uterus. But a small number are alive after a 2-year interval;

all apparently did well for the first 8 to 12 months. Recurrences cannot be treated with radium, for this aggravates them in the majority of cases. At the end of the quiescent period, when nothing can be seen or felt, the woman mentions abdominal pain, and recurrence is found to follow. Cases in which the Perry cautery had been applied did not do well under radium.

Stacy, of the Mayo clinic, mentioned a series of 79 cases of cancer of the uterus treated with radium—of these 54 have been traced. All lived longer than 1½ years and 25 per cent were still alive, mostly after more than 2 years. In the treatment of 24 cases of recurrence results had not been good. Of 16 traced, three are living after from 2 to 3 years.

Racasen[1] began the radium treatment in 1913 and has had many cases of 3, 4, and 5 year cures. But in 30 to 40 per cent of his 400 cases thus treated in the same manner radium has failed, and he is seeking for the reasons. The cases sent home to die had sometimes surprised him by coming back to the clinic greatly improved and even at times clinically cured; in such cases there had been evidently a cumulative action of the radium. As accessory measures he has heated the splenic area by diathermy, because the products of the spleen are cancrolytic and leucocytosis is set up. He has also injected colloidal copper into the vein in the hope of making the growth more radio-sensitive. He likewise applied copper sulphate locally, 10 per cent before radium treatment to prevent secondary infection.

In breast cancer, a field where some experts are not so very sanguine, Kelly states that all depends upon the dose. Spraying with radium is enough for lymphosarcoma, but for cancer we must have intensive treatment, comparable to sledge hammer blows, inflicted directly on the lesion in the breast. These blows must follow each other in timed succession, always on the proper spot. Herein Kelly presents a paradox. He says that early cancer belongs to surgery, while utterly inoperable cases may do remarkably well under radium. Since

[1] Racasen, Abstr. from *Journ. Amer. Med. Assn.*, April 16, 1920.

metastases are not influenced by radium the authors do not attempt treatment if there are intra-thoracic deposits, and mention the use of *x*-rays only in connection with diagnosis.

Young and Frontz[1] of Johns Hopkins, report the results of treatment of 66 cases of cancer of the prostate. There is no mention of total figures, but in 12 cases, three which received only external treatment did not improve, while the balance, in which radium was applied both externally and internally there was more or less improvement.

At the Radium Institute of London radium[2] is being used in a most conservative manner.

Operable cancer is not treated there at all, with the exception, of course, of rodent ulcer and the few cases in which operation is refused. At least 70 per cent of the cases treated are very far advanced, with extensive dissemination of the disease.

About 20 to 25 per cent of all the cancers treated are mammary, including all varieties, whether acute or chronic. Prognosis in the encephaloid type is very bad, especially in the young woman of corpulent habit. But little benefit is obtained here—a slight retardation has been seen from screening the periphery. In the chronic atrophic form the radium strongly reinforces Nature, by producing the so-called curative fibrosis. Between these two extremes all gradations are seen, and the success obtained varies with the amount of curative fibrosis produced. The cancerous alveoli contract and the cells degenerate.

The percentage of cancer of the uterus is not given, but apparently these cases are not numerous and of the border line type, which promise the patient a chance of benefit. In the inoperable case the benefit is very rapid and almost always forthcoming. The growth diminishes in size, ulcers heal, discharge and hemorrhage cease and the rate of growth is slowed up. The young and corpulent do badly, and results after the menopause are not favorable. Under the most

[1] Young and Frontz, *Journal of Urology*, Vol. i, p. 505.
[2] *Radium*, September, 1920.

favorable conditions the progress of the growth is arrested and the patient may survive, 3, 4, 5, or more years, but she cannot be regarded as cured. If the uterus is fixed, with extension into the parametria, not much can be done. Recurrence in the vagina after hysterectomy sometimes improves remarkably. In the cauliflower type the mass must first be excised. To get the best results the patient should be around 50 years of age, with intact septa between the bladder and rectum, and not much periuterine infiltration. Of intraoral cases the greater number are in an advanced stage when first seen, the resources of surgery having been exhausted. As a whole the results have been disappointing, especially in ulcerated cases. Massive implication of lymph-nodes may be reduced in size, and involvement of the skin and ulceration prevented.

The rectum and vagina are both very sensitive to the action of radium, a fact which must interfere somewhat with its use. In cancer of the rectum a colostomy must as a rule be performed before treatment with radium. In the bladder, especially in the female, good results are obtainable, largely because the radium can be introduced through the urethra and the bladder may also be treated through the vagina.

In cancer of the prostate life has been prolonged for 2 or 3 years in certain cases. In cancer of the œsophagus relief, while decided, is only temporary. In the stomach radium is now used by allowing the patient to swallow a radium tube held by a string. Results are not stated.

To contrast with the above are the statements of a radium expert of great experience; Boggs,[1] who is a prolific writer, insists that there should be specialists in malignant disease who should not be wedded to any one plan but be familiar with the indications of all. If there is an immediate recurrence after an apparent radium cure, it is a sign that some technical error has been committed. Much depends on a smooth and even radium scar, which should be pliable. In common with other radium men he recommends the treatment especially for cancer

[1] Boggs, *Journal of Radiology*, Jan., 1920.

of the lower lip. In its first stage 90 per cent recover without deformity, while more advanced cases are curable and all are benefited. In contrast to surgery the dreaded scar recurrence is not seen. If there are no palpable glands, 50 per cent of cases recover and if the glands are palpable 25 per cent only, as far as gland recurrence goes. In intraoral cancer brilliant results have been seen, while others are disappointing. If the knife is used radium should follow. Boggs recommends associated treatment in these cases—electrocoagulation, radium, and *x*-rays.

Since but 15 per cent of cancers of the cervix can be helped by surgical operation there should be a field for radium here. In 40 per cent of operable cancers of the cervix the pelvic lymph-nodes are not involved, while in inoperable cases the per cent involved is from 30 to 50. Hence, metastases or their absence do not fix the indications, and the pelvis should be *x*-rayed in every case. Of late radium has been inserted into the cervical canal for cancer in that locality, and the recurrences so common in knife cases are not seen in anything like the same frequency. Radium will clinically cure a third of the inoperable cancers of the cervix and give the patient two or three years of health, but sooner or later recurrence is apt to occur. In the incurable case pain, discharge and hemorrhage may be arrested.

Boggs appears to prefer heat in intraoral and pharyngeal cancer, and in this he is supported by numerous London specialists, who use diathermy in preference to radium. Boggs recommends electrocoagulation in preference to the knife, because the blood vessels are not opened and metastases are averted. He even prefers *x*-rays to radium in the oro-pharyngeal cancer, both *per se* and when used with heat. He would always use the *x*-rays when ulceration has exposed the muscles.

He quotes Schmidt, who states that while radium will preserve life for 2 or 3 years, recurrence usually results, although the suffering then is much less than when the knife has been used. Franck of Mt. Sinai uses brief intensive radium before excision of cervical cancer, and then goes back to radium again.

Boggs has in the past 19 years seen over 1,500 cases of mammary cancer and would never perform the ultraradical operation. All of our resources put together are not solving the problem of cancer of the breast, but in 80 per cent of cases radium can palliate, with prolongation of life from 1 to 5 years. In another set of cases surgery and radium combined are useful. Since the introduction of radium treatment there are no more morphine eaters among those thus treated.

In 1917 Professor Ewing[1] collected much information concerning the results of radium treatment of cancer. He has found no exaggerated statements of benefit, so that the optimism of the public was not inspired by the medical profession who have used the remedy.

In all localities where the knife is preëminently unsatisfactory, as the cervix, antrum and pharynx, tongue, prostate, etc., the operability should have its limits reduced, and radium be given a trial. But to overtreat with radium causes a host of accidents —severe and profound pain, sloughing, perforations, infection and intoxication. It is claimed that areas which have been exposed to radium are unfavorable for surgery. Radium is a locally acting remedy like the knife and can never be regarded as a general cure for cancer.

In regard to operability and the treatment of operative cancer by radium, the accumulated evidence seems to justify its trial in the early and circumscribed case. But it is evident that there should be in such cases some special contraindication to the use of the knife. On account of the great mutilation in operations in the intraoral and certain other localities, with high operative death rate in some, radium might be a substitute for the knife, but only the expert radium man should apply this treatment. The matter had better be settled at once, (apparently it has been settled in favor of using heat, at least in the minds of a number of throat surgeons). The cervix uteri is a promising field for radium treatment of operable cases, and Ewing believed that in the future radium will be used in certain

[1] EWING, *Amer. Journal of Roentg*, 1918, v. 413.

classes of early and localized cancers. There are conditions of *morale* to be considered. Patients are not afraid of radium as they are of the knife, and do not procrastinate so much when they realize the circumstances. The medical man himself hesitates on the same account. Again, pre-cancerous lesions in great variety are curable by radium, and the hesitation of the patient will not be so great, for the prospect of surgical removal of warts, moles, polypi, etc., favors procrastination.

Many details of interest should be generally known. Thus in cancer involving bone, radium is usually resisted, although this is by no means a contraindication to its use here. Some radium experts are looking forward to a deeper action of radium and a greater projection of its rays (Ewing does not mention the fact that the *x*-rays have a very great advantage here).

Ewing has never personally seen the phenomenon of the stimulation of cancer cell growth by weak doses of radium, but cites a few who claim to have observed this result. He gives considerable space to the overdosage. Granulation tissue of long standing heals very poorly after the tumor cells have been destroyed, and the tumor ought by rights to be attacked before there is much accumulation of this sort, for in the latter case the defense reaction of the connective usually set up by radium does not occur. This dense fibrous tissue appears to interfere with the destruction of the cancer cells by radium. When this kind of cicatricial tissue is rayed, an indolent ulcer is apt to develop. These sores will not heal and form irritable areas that are more or less crippling from the great pain and tenderness which may coexist. When a tumor becomes infected with streptococci radium is said to be unable to cope with the situation, which antagonizes also the success of the treatment. The early history of radium exhibition shows the number and variety and severity of the accidents caused.

Cameron[1] of Pittsburgh has recently published notes of interest on the use of radiation in cancer. He goes into certain refinements of radium selection. The supply of blood to the

[1] CAMERON, *Radium*, Vol. iv, 1914.

area and its lymphatic drainage capacity must be considered. One must bear in mind the structure and embryological origin of the tissues involved, for there is a special response in each of the three layers. One must know the patient's local and constitutional resistance to the cancerous invasion. Especially within the mouth one is apt to be dealing with syphilis as well as cancer. One may be able to increase the immunity, but may also diminish what there is of natural immunity. One has to deal for the most part with border line, advanced, and terminal cases, and there has usually been a history of the use of various remedies, such as surgery, caustic pastes, *x*-raying (perhaps excessive), etc., which tends to alter the tissues to be treated.

In cancer of the lip one should know whether the growth originated on the mucous or cutaneous surface. Cancer of the buccal surface of the cheek is a different proposition from cancer of the antrum, and cancer of the cervix uteri from cancer of the fundus of the same. The indication for radium naturally involves those of associated methods, as electrocoagulation, *x*-rays, etc. Some cases do best under radium alone, others under radium and surgery, others again under *x*-rays and radium or fulguration and radium.

The drawbacks of extensive surgery are excessive hemorrhage, failure to close blood vessels, failure to hinder lymphatic drainage, violent handling of the tumor, prolonged anesthesia and of course great mutilation, high primary mortality, and percentage recurrence despite all care (with the evils of scar recurrence). Radium is without these drawbacks. Surgery removes the diseased tissue at a great cosmetic cost and radium does the same without cost or appreciable loss of healthy tissue. The medical man would doubtless prefer radium for a member of his own family. Cameron realizes that his judgment on the proper method for treating cancer of the cervix will antagonize many but adheres to it—(but is open to statistical proofs to the contrary).

He differs from some authors in his advice to build up th

cancer patient by diet and nourishing food, for it has been claimed that to give such patients eggs and milk is like feeding fire with fuel. He lays stress on fresh air, rest and local care of the lesion. Indifference to the local lesion is incomprehensible and favors mixed infection. During the radium reaction period raw surfaces may become angry and the patient should be warned. We must avoid burning the mucosa of the mouth, although this is well nigh impossible, and irritating the rectum and vagina: in the case of the latter a gauze pack is used for distending it and contains the radium tubes: the bladder is fitted with a retention catheter to prevent its distension. In working on the endometrium a persistent discharge may be set up, and in the case of the cervix extensive radiations may cause adhesions with contractions. Antiseptic douches are then indicated. With low white cell blood count in cancer cases smaller doses frequently applied are substituted for larger ones, in a few prolonged treatments. Radium in the uterus may cause nausea, perhaps as a reflex from the uterus to the stomach.

Side by side with successes obtained by deep radiation should be mentioned others, in which the course of successful raying of uterine fibroids the most malignant form of cancer has been roused to activity. It is not known whether the cancer growth originated within the area of the fibroid as an example of malignant degeneration, or in the normal intact mucosa of the corpus uteri. Monnard[1] reported three personal cases of this type. From a study of these cases there can be little doubt but that the soft rays required in the treatment of the fibroid stimulated latent cancer or cancer-genetic cells to furious proliferation. The malignity was so intense that one uterus became fixed in 72 hours. The same consequences might occur in any locality where latent cancer cells preexisted, but such cases seem to be very rare, and it is said by authorities that malignant degeneration of fibroids is usually acute.

"The Mechanism of the Action of Radium on Tumor Tissue"

[1] MORNARD, Societé de Chirurgie, 1919, xlv, p. 1553.

has been discussed by Levin.[1] He mentions the selective action of the rays on the tumor-cells which is in no sense caustic. Side by side with the degenerative changes in the cell we see the connective-tissue reaction. To determine which is first, experiments were made on crown gall in plants where a connective-tissue reaction is out of the question. The rays arrest the growth of the crown gall and hence the action on tumor-cells is no doubt a direct one. These cells in malignant disease are short lived and before they undergo spontaneous degeneration the usual multiplication into two daughter cells is prevented. This being the case it is difficult to prove that the degenerative changes would not occur of themselves. But when radium is used the process is much more extensive and intensive. Another point, when the cells as a result of radium, or spontaneously, lose their malignancy through inability to proliferate, the connective-tissue reaction would be apt to occur itself. We see this illustrated in the evolution of a scirrhus cancer; and when a piece of cancer is implanted in the tissues the connective-tissue reaction also occurs. But in speaking of sterilizing the cells and thereby preventing proliferation it must not be forgotten that a cell may be merely "stunned." It lives in a sort of suspended animation and after a time may be able to proliferate. Raying normal tissues and benign tumors never produces a connective-tissue reaction, so that there is a direct connection between this reaction and malignancy.

In a bone metastasis we may also see a connective-tissue reaction characterized by the formation of osteo-plastic tissue. But this is not always seen. In the more unfavorable kind of metastasis there is no new bone formed and on the contrary the bone is rapidly destroyed. Levin does not believe that one treatment can possibly destroy all the cancer cells.

Much speculation has been indulged in, in regard to the mode of action of both *x*-rays and radium, some of it is probably correct, some may be modified by further experience. We may quote a bit from the article of Levin previously referred to.

[1] LEVIN, *Amer. Journ. of Roentgenology*, November, 1920.

"The action of radium and *x*-rays when analyzed shows little difference, and only such as could be explained by the physical difference in the genesis of the rays. The action is exerted both on the tumor and on the connective tissue. On the former the action may be stimulating, inhibiting and destructive, while on the latter one sees both stimulating and destructive activity. Moreover in acting on the connective tissue there is a secondary action on the cells which attacks them from without. In other words, not only may they inhibit or destroy the cells directly but they also destroy them indirectly, through the contraction of the new fibro-plastic connective tissue. These forms of activity should be reviewed in more detail."

The stimulating action of weak rays is well known, and is sufficient to cause *x*-ray cancer of the skin in the predisposed. There is no doubt, outside of this class of cases, that soft rays can stimulate cancer or cancer-genetic cells to growth, and it has been the great aim of cancer radiologists to eliminate this danger by using hard rays with protective screenings. The danger from radium seems greater in the clinic than the danger from *x*-rays, which latter are a greater menace to the operator than to the patient, a number of operators having died from *x*-ray burns. But that rays of either kind may do harm to patients is evident from the cases already mentioned, which could be reinforced by others.

Next to the stimulating action on the cells should be mentioned the inhibitive, or to use a more expressive term, the sterilizing action. The cancer cell is notably short lived, but breeds rapidly before its death. The rays are able to put a stop to proliferation without causing any visible change in the appearance of the cell; and if this sterilizing action is maintained the cancer cells may die a natural death, without having undergone any destruction. Levin and Joseph (*loc. cit.*) claim to have been the first to isolate this form of activity of radium in human cancer, although it is known to occur in experimental mouse cancer. It is, of course, understood that when the cells

are actually destroyed by the rays the sterilizing action must have preceded the destructive changes. The authors call this activity clinical inhibition, because the growth is arrested without actual morphologic change. A case is cited of a cancer of the breast, with autopsy, in which the cancer cells showed no morphological change and no metastases. The growth which had been inoperable was completely arrested clinically. The same phenomena were studied in a melanotic cancer with metastases, the progress of which was arrested by radium.

Coming to the destructive action on the cells, the morphological changes have been described in great detail by many pathologists. Such changes are known to be primary and not due secondarily to the effects of the connective-tissue reaction, but since both processes occur side by side it is not a simple matter to prove the existence of a direct destructive action. Levin and Joseph however have seen the evidence of direct action long before the secondary changes. In rodent ulcers, moreover, the cells are destroyed without any connective-tissue reaction. In the latter phenomenon the death of a large number of cancer cells makes it possible for new connective tissue to fill the void; but the part played by connective tissue is much more than a passive one, for the round cell infiltration becomes organized into a dense connective tissue not very vascular.

This sclerogenic action plays a great role in walling off the cancer from the sound tissues, and in isolating and strangling the outlying aggregations of cancer cells. It works hand in hand with the direct destructive action upon the cells, but is, in part, of inferior potency, because the microscope shows that intact cancer cells, doubtless able to awaken to activity, are simply held in latency. A merely sterilizing action may not be permanent and the claim that cancer cells are shortlived may not exhaust the situation. This may be true of the young and actively growing cell, but there is much evidence that cancer cells may awaken after years of latency, as in those cells found at times in the margins of gastric ulcers.

There remains only for mention the destructive action of the rays on the sound tissues from high doses, which is tantamount to destructive burns, followed by extensive scarring. The tissues undergo secondary sloughing and the defects are filled in by scar tissue. This accident is not uncommon under unskilled radium treatment, while with *x*-rays the caustic action is more superficial.

As before mentioned, there is about to be issued a report upon "The Present Status and Scope of Radium Therapy" at the Memorial Hospital, and through the kindness of Dr. Janeway I have been able to see the manuscript and to use it as desired. This represents the results of the last 4 years use of this remedy, since the reports of the first 2 years work was reported. He says that since that time the methods formerly used and fully described in that publication have been modified and new ones developed. Chief among these is the imbedding of practically unfiltered emanation within the tumor tissue. This method has proved so useful that it now replaces most of the methods formerly resorted to for the treatment of lesions of the mucous membranes, and either replaces or is used in conjunction with other methods in the treatment of many external tumors.

Also during the past four years well supported conclusions regarding the method of choice for different lesions and regarding a safe and efficient dosage have been reached; in other words, standards for treatment have been created which are reliable, possibly a close approach to the best standards for the methods concerned. Moreover, a knowledge of what can be accomplished by radium in the various forms and stages of malignant growths has been acquired, so that a very accurate prognosis can now be given at the start of the treatment.

This knowledge, attained during the past four years has not been acquired sufficiently early to make it of much value to now record percentages of apparently complete retrogressions. The period covered by this report, like that covered by the preceding one, has been a period of development; an attempt to

discover just what radium is able to accomplish in the cure of cancer; a period in the creation of methods and determination of dosage; and of determining what forms of cancer can be best treated by its use, and to what extent benefited.

Most of the material with which the work was done—at first almost all, and even now most of it—must be classified as the deadwood of other hospitals, most of it ignorantly neglected or unsuccessfully operated on by other physicians and surgeons. A report of percentage of cure upon material of this character is valueless. In the future cases can be intelligently classified at the start of treatment from a standpoint of prognosis, and the proportion of cases in each class apparently cured or benefited can be reported.

The report states that the results of treatment of malignant growths by radium depend so much on the method of application that the use of different methods of application may be considered really as the use of different therapeutical agents. It is frequently stated in surgical literature, in regard to malignant tumors of practically every variety, that radium has been used and failed, but the use of the element, often in indifferent ways although in some instances good, by no means represents the possibilities which may be obtained by this agent, any more than if radium had not been used at all. By patient trial for the past 6 years of one method after another, of various forms of filtration, of different dosage, and finally, of the use of buried emanation, the efficiency of the treatment of many forms of cancer has resulted in a change at this hospital, which justifies the attending staff in turning over to radium treatment some operable as well as inoperable varieties of many malignant tumors. The treatment of operable carcinoma of the larynx by radium is still questioned: but the concensus of opinion is that the surgical sacrifice of the larynx is so great a loss, and the results already obtained by radium are sufficiently so good, as to justify its use before laryngectomy. They justify their use of radium in operable cancer of the rectum, as against the frequent, unfortunate consequences of operation, the loss of

of sphincter control, and the deplorable condition of an artificial anus. They claim much for radium in many other locations, already alluded to, but state that the evidence cannot yet be based upon percentage of cures, but rather on results of individual cases, and upon a certain regularity with which such results can be obtained.

Their view, they believe, is further confirmed by a comparison, especially true of the cases in the border line of operability, of the radium successes and failures, with the disabling deformities of surgical successes, and the pitiable condition of surgical failures. They are certain, from what is seen at the Memorial Hospital that the apparent irresponsibility and the freedom with which attempts are made to excise cancer, too frequently makes the disease immediately worse and unfits it for radium, by which it should have been first treated and to which it subsequently comes, after it is too late. They emphasize the importance of the type of malignant growth as influencing the results of any kind of treatment, and remark that no well informed surgeon would today operate on tumors having pronounced invasive tendencies, but say that for the cure of these cases a general remedy must be awaited. As a local remedy, radium where successful, undeniably involves far less initial damage and far fewer permanent sacrifices than does the knife.

In regard to cancer of the breast they state that in operable tumors which have refused surgical operation, the results of radium alone or combined with *x*-ray, have been good enough to greatly broaden their use in this field; as only 4 per cent of carcinomas of the breast, when surgically attacked after involvement of the axillary glands, remain well for any length of time.

The report goes at some length into the technical principles employed in radium therapy at the Memorial Hospital, and refers to the former study by Dr. Failla, already alluded to. Considerable attention is paid to the employment of radium emanation and also an active deposit from it, instead of the substance itself, which avoids the possible loss of any of the radium by accident or theft. It is believed that from this

active deposit are derived the radiations of most therapeutic value. The details of all this are too technical and lengthy to be given here, and those interested are referred to the publication previously mentioned and the report of the Memorial Hospital about to appear, and also to an article by Dr. Failla[1] giving further information as to the making of appliances, filtration, and measurement of dosage.

Dr. Janeway[2] has personally reported in recent years upon cases treated with radium, which may be briefly alluded to. He gives results in 24 cases of cancer of the lip treated by this means. There was one series of six cases with cancer of the lip during the years 1915 and 1916. One had not been traced, and there had been but one recurrence up to January 1, 1918. The remainder, 18 had all been treated within a year, and three have died, all advanced cases. He believes that results justify the use of radium in operable lower lip cases, especially if taken early. If lymphatic nodes have already formed it is best to dissect them out and use radium in the wound. The emanation is recommended filtered through the thinnest material, as 1 mm. of platinum, or enclosed in 0.5 mm. of silver for other work.

Later[3] he reported on four patients with cancer of the uterus treated with radium, one of whom was apparently well 2 years after treatment, one was well 1 year after treatment, one well for 2 years, when recurrence and metastases occurred, and the fourth did not improve. Glass emanation tubes, unfiltered, were imbedded in the mass, while filtered tubes were also used.

Dr. Janeway[4] about the same time made a remarkable study on the treatment of uterine cancer by radium which is worthy of most careful attention, as he gives a careful analysis of surgical results and a full study of reports on the use of radium by many observers, with a very extensive bibliography. He gives careful histories of 30 cases, of which there were 17 cases of car-

[1] FAILLA, Radium technique, etc. *Radium*, June, 1920.
[2] JANEWAY, *Journ. Amer. Med. Assn.*, April 13, 1918.
[3] JANEWAY, *Radium*, November, 1919.
[4] JANEWAY, *Surgery, Gynecology and Obstetrics*. September, 1919.

cinoma of the cervix, and of these 12 clinically cured, 3⅓ years to 6 months after treatment: four cases of recurrent carcinoma of the crevix, 2 clinically cured 16 and 25 months after treatment, one improved; four cases of carcinoma of the fundus, two improved for a period of 2 years, and two clinically cured: and five cases of carcinoma of the external genitals, three clinically cured 21 to 16 months after treatment, 1 improved, 1 unimproved.

While there were some recurrences, even shortly after the use of radium, he says that "Our present evidence indicates that radium destroys the disease at this site to a greater distance than the knife is capable of removing it, and does this with no risk or inconvenience to the patient and only a small tax on the skill of the surgeon."[1]

Two cases of cancer of the tongue treated with radium are reported by him. The first patient, a woman of 36 had pyorrhœa and several ulcers on the tongue. Two of these on the tip healed spontaneously, but one on the right margin grew worse, showing the character of malignancy, and the microscope showed epidermoid cancer. There was but slight infiltration and no lymph-node hyperplasia. Three small tubes were buried directly in the ulcer and others applied directly upon it in a mold of dental modelling compound, for an hour only. In 3 weeks there was no trace of the lesion. Another patient, a man of 70, heavy smoker, no teeth, had a small ulcer on the right side of the tongue for 18 months, increasing slowly and becoming painful; base was slightly indurated, but there was no mention of adenopathy, nor of biopsy. The radium was applied by means of a dental molding for 2 hours, and glass tubes embedded in the floor. The ulcer healed, but left an induration which was treated by embedding, and there was no evidence of the disease three months later.

There was also reported the case of a man with cancer of the right tonsil with infiltration of deep nodes, clinically cured with one treatment of buried emanation. There was micro-

[1] JANEWAY, *Amer. Journ. of Radiology*, February, 1920.

scopic diagnosis. Six tubes were embedded in the mass, and healing followed with complete disappearance of the mass, and eventually the swelling of the lymph nodes vanished. A case of primary carcinoma of the antrum in a woman aged 59 was reported, clinically cured by one treatment of unfiltered radium. There was a swelling of the right cheek, and within the mouth the superior alveolar process of the right side was felt to be swollen, suggesting downward displacement of the antrum. In the bucco-gingival sulcus there protruded a small ulcerated mass breaking through from the cavity. The microscope revealed epithelioma. The external carotids were ligated on both sides of the neck, and the right antral cavity laid open by removing the superior alveolar process. Fifty millicuries, unfiltered, in glass tubes were placed in the center of the antrum and surrounded by packing and left in place 48 hours. The operation was followed by radium inflammation and an attack of lobar pneumonia, but she recovered.

In writing and studying these and other accounts of the action of *x*-rays and radium in malignant disease, one is struck by several points presented:

1. The claim that both are similar in action, requiring only a better understanding, especially in regard to the former, of the strength, modes of application, filtering, dosage, etc.

2. That many observers recognize that both methods of radiation are only local measures, like the knife, and that one cannot expect thereby to cure the disease permanently; one of them at least speaks of looking for a general remedy to reach certain cases.

3. All recognize that much involvement of lymphatic glands, or metastases, precludes expectation of permanent success.

4. Very many emphasize the grave imperfection of much that is done by inexperienced workers, and the great necessity of standardization as to equipment, filtration, dosage, etc.

Looking over all the reports that have been given here and elsewhere, one cannot help feeling things that, as with

surgery, we are still on the wrong track as to the real nature and proper treatment of the disease carcinoma. As in the past, so at present, the eyes of the profession and the laiety are directed solely to the local manifestations or *product* of the disease, and not at its true nature, as has been shown in other pages. The mere removal of the affected area, and its surroundings by surgery, or their disappearance under *x*-rays or radium, leaves unnoticed and uncared for the basic cause of the new formation, and this is very likely to be reproduced somewhere, as all recognize, if the original causes are still at work. Even Ewing[1] from a pathological standpoint, says "by far the most important element"(speaking of cancer of the breast)" "is chronic productive mastitis. The great majority of cancers develop in organs altered by reactive inflammatory processes. Minute histological analysis of the conditions surrounding the beginnings of cancer in chronic mastitis point to mechanical isolation of cell groups in fibro-carcinoma, and irritation by chemically altered secretion and exudate in adeno-carcinoma, as the immediate precursor of a typical overgrowth . . . the disease is satisfactorily accounted for as the liberation of growth tendencies of overnourished and proliferating cells,"—and as has been mentioned elsewhere, he frequently refers to deranged nourishment as a cause of malignant growths, which latter is the entire basis of our thesis in regard to the nature and proper treatment of cancer.

Several of the authors on *x*-ray and radium realizing that these play only a secondary part in the real treatment of cancer, urge that the specialist in malignant disease be not wedded to any one plan of treatment, but that he be familiar with all, and employ them as necessity requires, and should the dietetic, hygienic, and medicinal treatment of cancer become generally adopted, medico-radiation should and probably will form a valuable adjunct in attacking and modifying the local products of the disease.

[1] EWING, "Neoplastic Diseases." Philadelphia, 1919, p. 490.

CHAPTER XVI

BIO-THERAPY OF CANCER

This is a large and important subject which may, by continued scientific research and clinical experience, result in a material advance in the control of cancer, but which at present is considered with suspicion or doubt by a large share of the medical profession, especially by the surgeons. There is no reason, however, why ultimately such treatment may not confirm and support the thesis of the constitutional nature and medical therapeutics of cancer, and why it may not, when perfected, be a rational and efficient aid in the treatment advocated in these pages.

The lines along which attempts have been made for what has been called the biological treatment of cancer are many and varied, and cannot and need not all be considered here. It is difficult indeed even to classify them, as they are of such different characters, based upon quite different ideas or theories regarding the nature and cause of the disease, some of them quite bizarre and erroneous. Literature is full of reports of various experiments and studies, scientific and other, which have been made, largely unsuccessfully, with substances of all kinds, and the nomenclature advanced has been about as wild and confusing as some of the theories.

The various solutions which have been employed and tested parenterally, by intravenous or subcutaneous injections, may possibly be best grouped under three headings, (1) Bacterial, (2) Serous, including human and animal substances, and (3) Cytolytic, from vegetable substances, and with all of them the proposer or advocates have claimed some measure of success, though often slight, in the cure of cancer. To these should

perhaps be added (4) Organotherapy, relating to the employment, generally by the stomach, though often otherwise, of preparations of the endocrinous glands of animals, in one or another form. It would carry us far beyond the practical purpose of this writing to consider separately, or even to mention the name and composition of the various solutions or mixtures which have been employed in connection with the bio-therapy of cancer. But it is interesting, in relation to our studies regarding erroneous protein metabolism in cancer, to note that all of these preparations used parenterally, or most of them, contain a protein substance which is foreign to that ordinarily taken as food. Later we will see the basis of their action in modifying the protein relations in carcinoma.

Some years ago Ewing[1] made a careful study of "The Treatment of Cancer on Bio-logical Principles," giving a summary of sero-therapy to date, including auto- and vaccino-therapy, and we cannot better introduce the subject than by freely abstracting from the same. For we must recognize that while some of them were based on wrong conceptions of the parasitic nature of cancer, or on erroneous theories, the experiments and trials of various means were made mainly by honest and often very skillful investigators, in the earnest desire to find some means of overcoming this dire disease, which surgery failed to control.

Toxin Therapy, Vaccinotherapy, Etc.—That so many different procedures seem to have been of temporary value, at least, in some cases is a fact worthy of attention and analysis. The benefit in these cases should not be too hastily explained away. It is of course possible that simple measures like asepsis may be responsible for slight improvement. But in the case of thyroid extract we have a substance that has repeatedly led to regressive changes in cancer, although it is not a remedy in the ordinary sense. If we could learn the secret of this benefit, it might aid us in our general work in the research for a genuine or specific remedy. In the same connection the author would

[1] Ewing, *New York Medical Journal*, October 12, 1912.

place arsenic. Even recently Czerny had noted that certain cases improve under injections of salvarsan.

Toxin therapy is of course different from sero-therapy, yet some of the sera contain toxic substances. At the time of writing Coley's toxin treatment had been efficacious only against sarcoma, but since the appearance of Ewing's article, at least one cancer has been cured by this method, and Coley has recently reported it. Under toxin treatment come those of Doyen, San Felice, and Schmidt. The first named had as a basis the activities of a micrococcus (*m. neoformans*), the second used the blastomyces, and the third a mould. Ewing does not pause for details, here, but classes all the preceding under a common head. The active principle is secreted by the micro-organisms and is toxic enough to cause fever and general intoxication. Vidal lays stress on the fever-producing properties. In addition to the three just enumerated and Coley's serum, a streptococcus serum was used with the same kind of result by Emmerich and School. The tumors show regression, but as a rule this is limited. Small tumors may disappear. The growing edge resists treatment much more than the center, which is often in a stage of softening.

The treatment of inoperable sarcoma by the mixed toxins of erysipelas and bacillus prodigiosus, introduced by Dr. William B. Coley in 1893, and of which a description of the method and the early results, was published a year later,[1] deserves special mention, as increasing years to the present time have established its value in many cases of the too often hopeless disease, sarcoma. Dr. Coley has repeatedly written on the subject, and for its proper understandings a number of references are here given. There is no apparent reason why "Coley's serum" may not be of value in connection with other proper dietetic and medical treatment.

This method was an outgrowth of a year's experience in treating inoperable malignant tumors with the living cultures

[1] *Transaction Amer. Surg. Ass'n.*, 1894, and *Amer. Jour. of Med. Sciences*, July, 1894.

of the streptococcus of erysipelas, suggested by a considerable number of clinical observations recorded in the literature, in which malignant tumors, particularly sarcoma, had disappeared during or immediately after an intercurrent attack of erysipelas.[1] Dr. Coley's later results, published in 1913, may be found in the Transactions of the Third International Cancer Research Conference, Brussels, of that year. His greatest success with the toxins has been in sarcoma of the long bones. For many years he has constantly advocated the conservative treatment of sarcoma of the long bones, in spite of the almost universal surgical practice of immediate amputation as soon as the diagnosis was made, and in a recent paper on the subject[2] he reported 250 personal cases of this type. Although in a large proportion of these, the disease was far advanced and the condition practically hopeless at the time of observation, 31 patients have remained well for a period of more than 3 years; in 15 of these the tumor was of the periosteal type, a type very rarely cured by high amputation. Up to the present time Dr. Coley has had 17 cases of sarcoma of the long bones in which the limb has been saved, in 11 of which the toxins alone or toxins and curetting were used, and in 6, the toxins supplemented by radium, or radium and *x*-ray.[3]

Theoretically there are strong grounds for advising the use of the toxins after operation for sarcoma—and often-times after operation for carcinoma and melanoma—as a prophylactic measure against recurrence. This use of the toxins has been strongly advocated by Dr. Howard Lilienthal for many years. While there are no large series of cases yet published to definitely prove the value of this procedure, there are a certain amount of data that support this view. It is generally recognized that nearly all cases of sarcoma or teratoma of the testis recur after operation, causing death in 1–3 years. Dr. Coley has now 8 cases of sarcoma of the testis (one a highly malignant,

[1] *Amer. Jour. of Medical Sciences*, March, 1906.
[2] *Transactions of the Amer. Surg. Ass'n.*, 1919.
[3] *Proceedings Royal Society of Medicine*, 1909.

3-times recurrent in three months) in which the toxins were used after operation, and the patients are still free from recurrence 3–12 years after. In nearly 100 cases of sarcoma of the clavicle treated by total excision, reported in the literature, only 5 were apparently cured by operation, while in 5 cases in which the toxins were given in conjunction with excision, 4 of the patients have remained well from 6–12 years after.

As regards the use of the toxins in melanotic sarcoma or melanoma. This type of malignant disease is the most hopeless of all from any form of treatment. Almost no cases have been cured by surgery alone. X-ray and radium have cured few if any cases. Dr. Coley has reported 5 cases apparently cured by the toxins.[1] Three of these were inoperable, *i.e.*, 1, the Greenwood case of Leeds, England (well now 10 years); 2nd, the Lilienthal case, chestwall involving the ribs (well 10 years); 3rd Coley's case, neck, inoperable recurrence (well 6¼ years). In the other cases the toxins were given after operation and the patient are well over 10 years. Coley believes that every melanotic sarcoma should be removed as early and widely as possible and then given prolonged toxin treatment for 6 months to 1 year.[2] Local treatment of the operative area and nearest glandular fields with radium or X-ray should be given.

Another important field for the toxins, in Dr. Coley's opinion, is that of lymphosarcoma in which thus far, surgery has been practically of no avail and the often very brilliant results from radium or *x*-ray have for the most part proved temporary. In his paper on Primary Neoplasms of the Lymphatic Glands, including Hodgkin's Disease.[3] Dr. Coley reports 168 cases, 19 of which have remained well from 3–22 years; he also reports 36 cases successfully treated with the toxins by other men, 30 of which have remained well from 1–17 years.

As regards Dr. Coley's final results up to 1917, a brief report

[1] "Melanotic Cancer," *Trans. Amer. Surg. Ass'n.*, 1916.

[2] End results following total excision. *Clin.* Surg. Assoc., 1920; *Annals of Surgery*, Aug., 1920.

[3] *Trans. of the Amer. Surg. Ass'n.*, 1915.

of the same may be found in an astract of remarks made at a discussion of the Treatment of Inoperable Sarcoma, before the New York Academy of Medicine, April 19, 1917, covering 1,000 cases of all types of sarcoma, and showing that in 95, or almost ten per cent the tumors disappeared as the result of treatment. Of these, 8 remained well and free from recurrence three to five years; 34 from five to ten years; 14 from ten to fifteen years, 7 from fifteen to twenty years; 5 from twenty to twenty-four years; in other words, 68 cases remained well from three to twenty-four years. In five of these cases radium and x-ray were used in addition to the toxins. The diagnosis was confirmed by microscopical examination in all but 10 cases. Dr. Coley's Brussels' paper, 1913, contains a tabulated report of 124 cases of inoperable sarcoma successfully treated by other surgeons, in 110 of which the patients have remained well from one to twenty years, and 87 from three to twenty years.

In vaccino-therapy, as carried out by Coca,[1] regression was frequently seen, but more commonly in the febrile cases. The fact that puncture of the thermic center in canine tumor has been followed by regression appears to show that fever has much to do with regression. According to Ewing heat is without influence on growing cancer cells, but since the date of the paper, raising the temperature of the medium to a certain degree has been found to inhibit the growth of mouse tumors. If heat is the principle involved in these regressions, then we should speak of thermo-therapy.

Under sero-therapy in the strict sense of the word Ewing first mentions the use of convalescent serum. At first it was thought that in cures thus produced specific immune bodies were active, but it was later ascertained that injections of various organ extracts gave the same results. Edel reduced the size of cancers by injecting human placental blood. The same results were obtained with normal blood serum by Arloing and Courmont, injected in a manner not stated. It was thought that the only factor amenable to treatment was the

[1] COCA, *Zeitschr. f. Immunitat. forsch.*, 1911–2, xiii, p. 524.

secondary inflammation about the tumors. In non-specific, or, as they may be termed, normal sera, used by numerous reporters, the mechanism was explained by Vidal in several ways, as follows: (1) The action of the toxic component already mentioned, which also can cause the fever, is called autolytic, acting on the necrotic center; (2) the enzyme component may have a hostile action against the cancer cell (as shown in trypsin); (3) an antibody component, the existence of which is doubtful or rather its action is non-specific; and finally (4) The thermic action which has been attributed to the toxic component.

The author now passes to the autotherapy of cancer and to the treatment based thereon, namely, that of injecting exudates of cancer subjects into cancerous patients. The first clinical fact quoted was the spontaneous cure of mammary cancer after absorption of pleural exudates. The observer was Mackay, 1907, and the cancer was in the most advanced state—*cancer en cuirasse.*

This pointed apparently to the existence of histolytic substances in the exudate. But in a considerable series of spontaneous cures on record there was not one in which an exudate had been absorbed. Hodenpyl then took advantage of the numerous cases of cancerous ascites to experiment on animals. In one case a very extensive recurrent and metastatic breast cancer, including cancer of the liver, in which chylous ascites was present, the disease, severe and generalized as it was, appeared to be undergoing spontaneous cure. The ascitic fluid in this case was used in the treatment of 40 cases of inoperable cancer, and in some of these the initial improvement was remarkable but was not maintained, while the donor of the exudate herself succumbed, not to the disease but because the liver had become completely atrophic as the result of cancerous infiltration. Ewing examined slides from the liver and the evidence of regression of the cancer process was complete. Of the 40 patients treated with this fluid all died but one, in whom the inoperable case became operable and was apparently

cured by removal. Dr. Ill of Newark then encountered a case almost the duplicate of the first, in which death seems to have been due to the excessive accumulation of ascitic fluid. The liver was much as in the first case just mentioned. Shaffer examined both sera but could find no active principles either by chemical or bio-logical tests. Rushmore of Boston had a third case of this type, and the general conclusion was that this serum for some unknown reason can like many others cause some regression in cancer growths. To these three cases and the Mackay case of cure with pleuritic exudate, may be added a fifth by Tuffier which recalls Mackay's. There was *cancer en cuirasse* with pleuritic effusion, and the patient received injections of her own serum plus others of nucleinate of soda, a fever-producing substance. The patient was kept at a febrile-temperature for 3 months and was completely cured. In the other four cases fever was not a factor, nor was there any evidence of toxic activity.

The line of research passed on to the alleged discovery by Freund and Kaminer, that while normal serum dissolves cancer cells the serum of cancerous patients has lost this property. The reactions were practically 100 per cent positive, and hence, this test has sometimes been used in diagnosis. Normal serum is thus seen to contain a cytolytic substance which can be visualized by numerous properties. It does not go through a dialyser, is thermolabile, etc., and may be adherent to the lecithin of the serum. The inhibiting agent in the cancer serum is contained in the euglobulin. The remarkable significance of this discovery is vitiated by the fact that others who followed the Freund-Kaminer technique have obtained very different results. Ewing found that the emulsions made according to the originators were not sterile and could not be sterilized. Simon and Thomas obtained results which completely overturned those of Freund and Kaminer, while each investigator found some added discrepancy, and the whole superstructure had to be given up. No doubt the basic facts were those of autolysis.

Vidal sought to prepare a cytolytic cancer serum based on the principles involved in complement deviation for diagnosis. He studied many tumor and tissue emulsions for the presence of antigens, also making combinations. He prepared specific antisera from the antigens by dog experiments, and added these to the antigens. The resulting serum had the usual effect of temporary regression. Of 100 patients treated no improvement was noted in 50, while among the others were some permanent cures (three). A number of cases were so much benefited as to become operable. Of the actual cures were a cancer of the breast and one of the rectum. While accepting Vidal's facts Ewing is doubtful concerning the explanation. Vidal regards the principle involved as the activity of an amboceptor. Ewing thinks the principle less involved and not differing from that of a toxic serum.

The next line of study is that of vaccination with cancer emulsions. Thus far but few have reported benefit. Coca and Gilman got a surprising result in Manila, but ever afterward the best that could be gotten was marked regression. In 1910 Bertrand showed an almost cured advanced breast case, in which he had vaccinated the subject with dried breast cancer tissue—that is, he had injected emulsions of the same. Other surprising results were seen only in sarcomata. The treatment is not free from danger.

The remarkable cures narrated, few though they are, seem to show that sero-therapy may play a role in cancer therapy. Not all could have been coincidental, spontaneous cure, or if such be the case, then the mechanism employed by Nature was of the sero-therapeutic type. Side by side are many, scores, of partial regressions. The case material used in these instances is always of the worst character, for one cannot experiment on patients with good operative prognosis. The chronic cancer invalid is of course quite another subject than the robust and well-nourished one who is just developing the disease. There is so little to work on in these desperate cases—so little to be done by the reparative forces of the body—that such cures

should command our admiration. The cure of these cases, as Tuffier states, is paradoxical, for we know nothing about cancer immunity. The most promising lead to follow is that of slow, passive immunization by injecting the products of tumors. This is more than suggested by the cures in exudate patients, for, despite laboratory reports, the exudates should contain something which inhibits cancer development. Ewing is sure that the blood of the cancer subject contains some neutralizing anti-body which can also pass into other fluids such as exudates.

This quasi-specific activity differs from the favorable action of many non-specific fluids. It is quite possible to produce a histolytic substance so specific in character that it will simply melt away the cancer cells, even despite the cachectic state of the subject. This is evident from the study of the most striking cases quoted. The tumor itself is where we much look for the cure of the tumor. With this in view many studies of cancer products have been made without regard to the clinical aspect. Among these are glycogen, ferments, etc. This line of work has accomplished little. Cancer nucleo-proteids may offer the best outlook. Instead of tumor-tissue that of very young embryos has been used, after having undergone autolysis. It has been inferred that embryonal and growing tumor-tissues have much in common. Fischera has announced cures no better nor worse than those obtained from various sera. The principle is probably the same. The action of autolysis must set free certain toxins, so that any specific property which originally resided in the fresh cancer or embryonal cell must lose any specificity of action under continuous self digestion.

Reviewing the entire subject the chief drawback is the absence of selection of cases. All cancer looks the same to the surgeon, but to the pathologist they present much individuality, and on the latter basis it may be possible to decide when to use a serum, when a toxin, and when a vaccine, etc. The means for making this selection are not stated but depend on many factors, such for example as the state of the endocrine organs. Blood

examinations might furnish a clue, as well as the presence or absence of a local or general reaction to a provocative injection. Failing in getting a criterion for selection, the next best course would be the combination of a number of resources, such as the use of thyroid or pluri-glandular extracts, polyvalent serum, or vaccine, etc. When the regressive action of one product has run out another might be substituted. Ewing is silent on the combination of seric factors with radium and *x*-rays. It would seem that in the combined methods which are now being endorsed some serum treatment might be added.

Berkeley's Serum.—After the publication of Ewing's paper in 1912 the serum prepared by Berkeley at Cornell, with the help of Beebe, attracted considerable attention. Berkeley wrote several papers and the one we abstract appeared when the author had been working on it 3 years.[1] The quest of the investigators was to find a remedy soluble in the blood and lymph and capable thereby of transportation to all portions of the organism, which could prevent or antagonize the formation of metastases. His inspiration came from von Dungern, Vidal, and Hodenpyl. The possibility of reaching cancer through an antiserum is said to have originated with the first named. Credit is given Beebe for his early work on antithyroid serum. The good work of Hodenpyl was interrupted by his death in 1910.

The author claims successes in a field marked by failures. He attributes success to great pains taken with antigens and with details in general. The present paper deals with clinical results and naturally with less than 3 years experience, permanent ones cannot be supplied. He received from surgeons and others 135 to 140 cases of tumor, from which 25 could be eliminated as doubtful or benign. The others were used in making stock and serum and for treatment. Of 104 cases 15 were so far gone that no treatment was undertaken. Of postoperative recurrences microscopic slides were obtained to make sure of histological malignancy. Since all forms of malignant

[1] BERKELEY, *Medical Record*, April 25, 1914.

tumor are said to have been represented, the paper as a whole cannot refer to cancer alone, but many inoperable and recurrent cancers were mentioned. The serum proper is not discussed, except as above, but the doses—5 to 50 c.c.—were injected intravenously and subcutaneously at intervals of a few days. A member of the New York Board of Health improved the serum by concentrating it. The unmodified serum continued to give an anaphylactic shock of mild type (there were but two cases of severe shock) together with blushing, urticaria, fever, etc. The work of the author seems closely related to that of Vidal as quoted by Ewing; as he uses the complement deviation method.

Some of the cases quoted are as follows: A woman with cancer of the breast, small *per se* but with much axillary imvolvement, had had it removed by Halsted operation. She received an intravenous injection of serum without the slighest reaction. The operation had been difficult and the prognosis could hardly have been favorable, but she was surely well 21 months later, and probably still later. In a second case the tumor of the breast and amount of tissue removed weighed 2 lb. Three years later she was well and working in a department store. A third case in the breast was much like the preceding. An operation was performed, although the mass was ulcerated and the patient cachectic. Serum treatment was followed by a gain of 25 pounds, and 2 years later she was well. A fourth case was cancer of the sigmoid, and a fifth of the uterus, involving the bladder. The results were of the same favorable character. In all of this material the fact of an antecedent operation clouds the issue, as there is no exact proof that the serum produced the given result.

It is not known that Berkeley's serum has any subsequent history. Beebe who sponsored it had announced 1 year later a new method of treatment by "autolysin." This preparation has nothing to do with the autolytic products of cancer degeneration, but is a saline aqueous extract of 12 different vegetable substances.

Autolysin.—The idea of this treatment, introduced by Beebe,[1] which he termed "*autolysin*," originated in the claimed success of a poultice composed of twelve vegetable ingredients, including viola tricolor, colocynth, quassia, rhubarb, etc., used on ulcerated cancers, which was first employed by Horowitz of Budapest. Extracts were made by Beebe from the dry poultice powder and injected hypodermically. The use of the word "autolysin" indicates that the action on the cancer cells is that of a lysin. It is not a serum and should not be termed such. The extract contains vegetable protein, salts and extractives, chlorophyll, chromophyll, and lipoids, and is injected into the arm. From 15 to 90 minims were injected and the act was painful. There should be a marked local reaction which may be extreme, and reaches its maximum in 7 to 10 hours. No typical general reaction follows, although one is occasionally seen, with fever. Such patients are sensitive to vegetable protein, as shown by the coexistence of hay fever. The second injection may cause anaphylactic reaction, if intravenous. There is no doubt that with large enough doses the first injection would always lead to a severe reaction, comparable to acute malaria, but the dose is regulated to prevent this. In second injections anaphylaxis is immediate and may be severe. It can be avoided by using the hypodermic method instead of the intravenous. Or it may be disposed of by adaptation to the point of tolerance.

At a later date than Beebe's paper, H. S. Williams[2] made a more complete study, using the same name, autolysin, for the injection, which Beebe had used, and presumably about the same in composition. In all, about 1,000 cases are said to have been treated throughout the country. One series of nearly 500 is analyzed, and 50, or about 10 per cent, are termed clinical cures, despite the shortness of the interval. But the cases were all hopelessly inoperable, whether recurrences after

[1] BEEBE, *New York Medical Journal*, May 15, 1915. (This was followed by several others, by different writers, in the issue of October 9th.)

[2] WILLIAMS, *New York Medical Journal*, November 13, 1915.

operation or unoperated cases. There was a marked aggregate extension of life, while pain and odor were favorably influenced. In regard to radium and *x*-rays, these resources had been exhausted in a number of the patients before coming under treatment.

The number of physicians to test the method has been reckoned as 138. This number may or may not include the local men who carried out the treatment under Dr. Beebe, for it is said that these 138 men treated but 272 patients while Beebe and staff alone treated nearly 500. The two series added together give a material of between 700 and 800, and even this does not account for the grand total of 1,000 cases mentioned earlier. The deficit is probably found in the 200 cases of very recent reports, separately considered toward the close of the paper. The total number of physicians to treat cases is given as 200. In the final summary by Williams we note the following: effects of the injections may be startlingly apparent, even the first being followed by softening, which should not be too rapid lest the growth break down entirely. Although there may be much swelling and induration at the site of the puncture no abscess is known to have formed. A reaction may occur and should be expected, and failure of one to develop may be followed by an intravenous injection. This is the reverse of what is given in Beebe's paper, in which there is a passage which seems to show that a general reaction seldom occurs. Too rapid breaking down has advantages and disadvantages. Some of the best results have followed rapid breakdown but on the other hand hemorrhage may (rarely) develop. Most of these patients had become morphine addicts, and it becomes possible and advisable to wean them. The softening may be such that it is advisable to scoop out the softened area.

For a while there was a notable silence in literature as to sero-therapeutic remedies for cancer. Whether this was due, as is probable, to the great diffusion of radiation endeavors, or to the relatively unsatisfactory character of bio-therapeutic

measures, or to both causes acting in common, or to some factor which is not yet visible, at any rate it seems true that efforts in this direction have rapidly abated. Fischera[1] writes of the biological treatment of cancer, his article having been composed in 1917 and may be contrasted with the review by Ewing published in 1912. Fischera is himself the originator of the use of autolysates of tumors and miscellaneous tissues including embryonal, and while he seems to retain his enthusiasm for his own methods he seeks to discredit all that had been previously done in the field of biological treatment. His own he calls "histogenetic chemotherapy." He gives an admirable account of the history of biological methods, grouping them into antiparasitic, passive immunization or sero-therapy in the narrow sense, and active immunization or vaccino-therapy. The antiparasitic group of methods was entirely based on the theory that cancer was due to various fungi, moulds, bacteria, etc., so that the treatment is strictly causal. This is not generally remembered. Bra, who seems to have been the first, really believed that a myxomycetes found on certain plants was the cause of cancer. He used killed cultures, filtered, and was followed by others. As usually happens early reports were good. As injections caused fever, Ewing would class it under toxin therapy. Adverse reports caused Bra to seek the same fungus in human association, but his new product has been forgotten for years.

It is otherwise with Schmidt's cancroidin which is still used by the discoverer and others, although officially condemned by Orth, the successor to Virchow. This preparation of cultures of the *mucor racemosus*, the latter being alleged as the cause of cancer, has been in use for years, and is the only one to survive. The persistence of the author has led some of the best men to try it, including Czerny, who associated it with radium to no purpose.

The blastomycetes was accused as a cause by Wlaeff and San Felice, and the preparation made therefrom was given a

[1] FISCHERA, *Journal of Cancer Research*, 1918, III, 303.

good tryout, but the idea is completely extinct. Doyen believed (or pretended to) that the cancer was due to the *micrococcus neoformans*. The remedy produced from the latter was tried out by leading French surgeons and condemned, and along with Doyen's theory has been laid on the shelf.

The apparent successes produced by all of these methods have been explained away by wrong diagnoses, coincidence, psychic influence, better local and general hygiene, and so on. Fischera does not take this view, and Ewing who mentions some of these factors has isolated some cases which pass the tests.

Attempts to cure cancer by passive immunization are summed up in the work of Vidal, who seems to have covered all the possibilities of the method. His work is described by Ewing. Fischera adds that sero-therapy has not fulfilled expectations and has now lost most of its experimental basis. Besides, Jensen was forced to admit that regressions under sero-therapy could be explained sufficiently by spontaneous motivation. Sera are not only non-specific but have no proved efficacy.

Active immunization or vaccino-therapy is dangerous, and it is possible by such means to cause implantation—evidently in animals only—but this prevents a proper study of it. Delbet obtained one positive result by taking a freshly amputated cancer and reducing it to pulp, which was injected under the skin in three or four places. There was no relapse, but as he also used radiation the case cannot be regarded as conclusive.

Aside from a possibility of implantation the method is dangerous on general principles, as is stated in Ewing's review.

Fischera is still at work developing his own method and making new discoveries. There are no clinical cases in his article. He is using autolysates, and filtrates, and ordinary tissues, presumably mostly in the embryonal state. Many of his laboratory colleagues are at work along the same lines. He has shown that certain organs have a greater selective action than others in the lysis of tumors and in provoking a hyperplastic reaction. Emulsions of liver and spleen appear

to be superior to others. He has discovered that large doses have an opposite action to small ones, and may cause the tumors to proliferate. This same behavior is seen with radium and *x*-rays, save that here it is the small dose which is dangerous.

Another important discovery is that the amount given must be in direct proportion to the amount of tumor mass. In other words the action is purely quantitative and not due to enzymes, etc. Koch says the same of his tissue thrombin, in the use of which he has reported such marvellous results in the *Medical Record*, November 3, 1920. Until these latter are confirmed by others, or demonstrated in a good hospital under competent medical supervision, they must be taken with caution and the whole conception and practice has been thoroughly investigated and condemned.

Dr. H. S. Williams, of New York, has continued his work on the relation of protein derangement and its correction in cancer and many other diseased conditions of older years, and has recently presented it very thoroughly and in a manner which commands attention and merits confidence. The subject under the title of "The Proteomorphic Theory" is developed in a large book[1] and in subsequent journal articles[2,3], so definitely as to warrant serious consideration and some little space. These represent in a large measure the ideas promulgated some years ago,[4] but with a greatly extended experience and profound study, as will presently be seen.

The correctness of the theory on which it is based, is demonstrated by accurately recorded blood counts in hundreds of cases, taken before and after sufficient proteal treatment had been given. These latter show by many tables, clearly and remarkably the changes toward normality developed in the blood in a very large share of cases, accompanying the progress-

[1] WILLIAMS, "The Proteomorphic Theory, etc." New York, 1918.

[2] WILLIAMS, *The Medical Record*, November 22, 1919.

[3] WILLIAMS, *The Medical Record*, December 20, 1919.

[4] WILLIAMS, *New York Medical Journal*, October 2, 1914, *American Medicine*, October and November, 1914.

ive improvement in the patient and of the disease, so that this line of thought is certainly one which should be generally accepted if true. The plan of treatment based thereon has also been widely tested in certain public institutions and by hundreds of physicians all over the country, to whom the material has been furnished, and the confirmatory reports fully bear out the statements of Dr. Williams. While the substance has thus far been prepared in and sent out from his laboratory, there is no secrecy in the matter, and the formula by which it is prepared is published, and will shortly be here given, so that it can be made in laboratories of Boards of Health and public institutions, but it has never been commercialized.

The basis of the proteomorphic theory and treatment of cancer rests on the now recognized metabolic or constitutional nature of the disease, as opposed to its purely local character, and the treatment is founded on the action of the blood cells, as altered by the parenteral administration of foreign vegetable proteins, to which is given the name of Proteals.

In order to really understand the plan and scope of this treatment some knowledge should be had of the basic facts upon which it rests, which are very fully presented in Dr. Williams' articles and in his book of over 300 pages. This latter in some parts is pretty hard reading, as he goes so minutely into scientific statements in regard to the character of protein and its dismemberment and synthesis into living tissue, with chemical formulæ. This grasp of the subject can perhaps be best obtained by utilizing freely some of the material which he gives.

1. Certain substances administered hypodermically have been observed to have a definite influence on the clinical progress of persons suffering from inoperable cancer of many types. These substances include extracts of plant products and animal products of many kinds: but they have this point in common—all of them contain protein or the products of partial protein hydrolysis.

2. The observed modification in cancer subjects through administration of these substances include: Alleviation of pain, modification of discharge, modification of the tumor itself, and modification in the general health and mental attitude of the patient.

3. The same protein substances, administered hypodermically, have been observed to benefit markedly cases exhibiting various kinds of metabolic disturbances.

4. The clinical betterment of these cases has been observed to be associated with blood modifications of a definite and predictable character, namely: increase of hemoglobin, increase of number of red corpuscles, increase of large mononuclear leucocytes, increase of eosinophiles, and modification of numbers of polynuclears and small lymphocytes, in the direction of the normal; also with conspicuous qualitative changes in the direction of the normal.

5. Physiological changes, including rises of temperature, quickened pulse, and a chill are not infrequently associated with the administration of some of the remedies in question, suggesting an anaphylactic reaction, not known to be produced by anything but protein or its products. This reaction appears not to be evoked in the same degree by partially hydrolyzed proteins.

6. It has been observed that a condition of immunization appears to be attained sooner or later, after which the patient no longer responds in the same way to a particular protein; but that a change to another protein may bring about a new response, with possibilities of cumulative beneficial effects.

He gives then certain theories on which he explains these observed facts:

1. The essential point of contact between the different substances administered hypodermically is their protein content (either the full molecule or products of partial hydrolysis).

2. Any foreign protein injected into the parenteral system serves as an antigen, and stimulates the defensive mechanism of the body to the production of antibodies, capable of hydrolyzing foreign proteins of various types.

3. Such antibodies are enzymic in character, and both specific and general in nature—that is to say, they hydrolyze the particular protein injected, but also other foreign proteins if present.

4. The proteins of cancer are in a sense foreign proteins, and fall within the scope of action of the enzymes called forth by the medical protein antigens. The degenerative diseases of middle life and old age are usually associated with disturbances of metabolism, involving the parenteral invasion of foreign proteins, or the undue retention or incomplete catabolism of protein end products.

5. The mechanism particularly involved in the production of the protein-hydrolyzing enzymes is the blood-forming mechanism and its products, the white and red corpuscles.

6. The general province of the white corpuscles is to deal with the full-sized protein molecule, or its early cleavage products, and the province of the red corpuscles is to deal with the end products of polypeptid order, including bodies of the hypoxanthin-xanthin-uric acid-urea series.

7. The condition of the abnormal hyperplasia of the cells of various organs of the body, including the blood-forming organs, the coats of the arteries, and the cells of epithelial, endothelial, and connective tissues, may be spoken of as a condition of hyper-proteomorphism, or the cancerous condition. All such conditions are more or less subject to clinical and physiological benefits from the administration of protein antigens—the effect being indirect and conditioned on changes in corpuscular numbers or enzymic activities.

8. Autolyzed cancer cells themselves serve as antigens, stimulating the blood-forming mechanism, but ultimately, in unfavorable cases, leading to the exhaustion and overpowering of this mechanism through over-stimulation, and to the excessive destruction of corpuscles.

9. Protein antigens as a whole may be conveniently spoken of as Proteantigens. Considering the observed action of these proteins in stimulating the increase of the large monocytes, the word Monocytosins may be used as a synonym, or a more gen-

eral and perhaps more appropriate work would be Cytogens. He adheres to the word Proteals in all writings, and considers that the essence of the Proteomorphic theory is the relative action of the white and red corpuscles of the blood just mentioned; namely, that the mononuclear leucocytes are the agents vitally concerned in beginning hydrolysis, and that the red cropuscles are the agents concerned with the completion of decompounding of foreign proteins in the parenteral system.

Dr. Williams seems to have departed very decidedly from the line followed by Dr. Beebe in the composition of the vegetable fluid for injections, and gives very freely and fully his experience in seeking for the best vegetable protein and the mode of preparation of the solution used, which should not be called a serum, as no animal product is used. He gives a list of some five substances which he has mainly used to supply the vegetable protein: alfalfa meal, mustard seed, millet seed, alfalfa seed and rape seed, each with a number to designate them in his laboratory, and then five mixtures of several of these solutions, any or all of which single proteals or compound mixtures he may use singly or combined, as the conditions of the patient or the progress of the case may indicate. He explains that these proteins are really foreign to the organism as foods, and so act efficiently in disintegrating others. He is also experimenting with proteins taken from nine other vegetarian articles, edible, such as oats, potato, wheat, carrot, etc., but apparently has not yet formulated their relative value. He is very clear in regard to the necessity of changing the vegetable protein employed from time to time when immunity seems to be established and when the progress of the case does not seem satisfactory, either from the feelings or state of the patient, or the condition of the neoplasm. This is only quite natural, as in the treatment of any disease a change of remedies now and then may be essential to a successful issue.

Space does not permit of greater elaboration of this most interesting and important subject, and for full details the references given must be consulted. We may, however, say

that for cancer he turns first to a proteal containing alfalfa protein, or a combination of those from alfalfa and millet. "Not infrequently," says he, "I shift from one proteal to another, experimentally, after a few doses; and sometimes I find that an individual patient responds far better to one type of protein than to another, regardless of the type of the malady."

A word may be added in regard to the preparation of proteals, quoting Williams, who calls attention to the different types of protein which have been used. The one (Beebe's autolysin) contains "the unbroken protein molecule; the other contains proteins partially hydrolyzed. The former were used almost exclusively until late in 1916." Since then it appears that he has been seeking to simplify matters and to select the particular vegetable protein, partially digested or hydrolyzed, suitable to different individuals and diseases.

"The essential procedures consist of the extraction of the protein from the ground seed or other vegetable substance by boiling the powdered plant products for from 2 to 4 hours in a very dilute solution of hydrochloric acid (20 to 80 c.c. of a 10 per cent hydrochloric acid in a liter of water, with 50 to 100 gms. of the plant powder): filtering: neutralizing with sodium hydroxide: refiltering: standardizing by the Kjeldahl nitrogen test, so that the solution when used contained 2 per cent of protein: sealing in ampules, and sterilizing for 3 days discontinuously. If properly prepared it makes a perfectly transparent fluid varying in color from amber to claret according to the specific protein content. The partially hydrolyzed protein (alkali albumen, proteose, peptone) does not coagulate on heating but is partly precipitated by alcohol. Nitric acid precipitates it in part, the precipitate being dissolved on boiling, to reprecipitate on cooling (the familiar test for proteoses)."

"Proteals thus prepared are pleasant to administer, and as a rule produce little or no reaction, and in ordinary dosage no conspicuous systemic reaction. No case of anaphylactic shock from their use has been observed by me, or reported, although many thousand ampules of proteals of this character have been

sent from my laboratory, to a large aggregate number of physicians in all parts of the western hemisphere, and administered to a great aggregate number of patients suffering from disturbances of protein metabolism."

"The proteals hitherto used most extensively, as supplied from my laboratory to several hunderd physicians in various parts of the world, are chiefly those made from alfalfa seed, alfalfa meal, mustard seed, rape seed, hemp seed and millet seed."

Dr. Williams is very modest, both in propounding his new theories of immunization and protein disassociation and synthesis, as also in regard to the therapeutic results obtained. But all of his studies represent such vast research and intelligent grasp of the various aspects of metabolism, together with such an immense amount of microscopical work and the exposition of tables of the beneficial changes taking place in the blood elements, that credence should certainly be given to his work and to this additional aid in overcoming cancer. He very properly shows that it is of wide application, as it has been employed by several hundred practising physicians, many of whom have no special knowledge of the disease, many of whom have reported most favorably of the results obtained, and that it may be combined with other methods of treatment.

He says, "One of the greatest merits of the proteal treatment is that it enables isolated physicians, in the remotest hamlets, to do something tangible and definite toward ameliorating the condition of the cancer patient who has passed beyond the reach of the surgeon.

"Thanks to the new treatment the most inexperienced practitioner can do more today for the amelioration of the condition of a late stage, inoperable cancer case, than could hitherto be accomplished by the most experienced practitioner in the best metropolitan cancer hospital." Hitherto, he has been able to supply institutions, and individuals, mainly free, from his private laboratory, to the extent of many thousand average doses, but has also brought the proteals and the methods of

their manufacture and administration to several prominent pharmaceutical houses, and to many Boards of Health, in hopes that the latter will prepare and circulate them as they do ordinary vaccines, diphtheritic antitoxin, etc.

Organotherapy.—Although strictly speaking this hardly belongs here, with bio-therapy as commonly understood, it is really only another expression of the attempt to control cancer by internal measures in place of the knife, etc. Moreover, the influence exercised by the endocrinous glands on metabolism and nutrition, and the more or less benefit from their employment in certain cases of cancer, add indubitable proof to the correctness of the views regarding the constitutional relations and nature of the disease, as unfolded in these pages.

All are aware of the abundant studies and literature on the action and influence of the secretions of the ductless glands on nutrition, and there is, of course, no doubt but that they play an important part in coordinating the life processes of the body, and that disturbance of their action can and does produce disease. This is seen in goiter, cretinism, and myxœdema, from dysthyroidism, Addison's disease from adrenal disorder, and acromegaly and gigantism, from pituitary derangement, etc. Evidence is accumulating that irregularities in the action of these glands have some relation to the disturbed metabolic condition which eventuates in the neoplasms in various regions which we call cancer, but just how this occurs is one of the problems which it will take time and assiduous attention and work to determine. One of the best proofs of the importance of the endocrinous system of glands is that complete extirpation of both adrenals in the higher animals is invariably fatal, and the strange muscular and nervous symptoms which may end in death, which follow the removal of the parathyroids, etc.

The most prominent among the ductless glands of which we have much knowledge in regard to cancer, is, as we all know, the thyroid, which has been pretty clearly shown to have considerable influence over epithelial structures, as is mentioned elsewhere in this writing. Its sometime beneficial influence in

cancer is now well known. Definite and satisfactory knowledge of the relation of other endocrinous glands, or their employment in carcinoma is not accessible, though there have been statements along this line which must be taken with caution until more conclusively proved.

The action of these glands on the system is believed to be through the operation of what has been called a hormone, a chemical substance formed in one organ or part of the body and carried in the blood to another organ or part, which it stimulates to functional activity or secretion. The secretions of some or all of the ductless glands are regarded as hormones, so is secretine, so is carbon dioxide formed in muscle during contraction, which incites the respiratory center to increased activity. It is supposed to be generated in all the cells of the body during catabolism and anabolism, and the cancer cell is no exception; its secretion being abnormal is thought to exert an adverse influence, as the condition of the blood has been found to be improved temporarily after the surgical removal of a cancerous mass, as I have witnessed.

All are familiar with the many preparations made from the ductless glands of animals which have been advocated in the treatment of cancer, many of them without satisfactory scientific basis. There have also been combinations of them presented, and it is possible that in the future pluriglandular extracts may be found of service in this disease.

The various glandular preparations have generally been administered through the stomach, but some of the extracts have been used hypodermically, like the sera, antitoxins, autolysin, the proteals, etc. Space does not allow of our elaborating this subject further, especially as I am not prepared personally to advise concerning the employment of other than thyroid preparations, which I have found satisfactory given by the mouth, as mentioned elsewhere.

In all claimed results from organo-therapy we must, as in connection with some of the other bio-therapeutical remedies mentioned in this chapter, take into consideration the psychical

element, whereby a measure of improvement in the patient's general condition may be produced by the hope engendered from a new remedy. But when the microscope shows a changed and improved blood condition, together with improvement in the local lesion, in the way of diminished secretion and correction of the foul odor, and especially with a diminution in the size of the neoplasm and healing, the total syndrome must be more than a coincidence or a mental delusion.

In looking over this chapter one is struck, as with so many other chapters, by the strong evidence cropping out everywhere in regard to the systemic or constitutional nature of cancer, as opposed to its purely local character, so that the accumulating confirmation of it is so clear that "he that runs may read."

All the studies and experience in bio-therapy are based on an attempt to alter the vital action of the system from within, and not by measures, such as the knife or radiation, directly applied to the local product of the cancerous dyscrasia. Many of the observers remark on changes in the bio-chemical relation of cancer cells, which they hope to alter, and to the removal of those already accumulated into appreciable lesions, which they hope to effect through blood changes produced by various sera, vaccines, etc. But, as far as the reading of hundreds of pages reveals, few if any of them have gone into matters with a care and fullness of microscopical evidence which are conclusive, as has Williams. As previously remarked, his line of reasoning, in his book and journal articles, from known and recognized data regarding digestion and metabolism, and also cyto-chemistry, cyto-genesis, and cyto-lysis, when confirmed as it has been by his own experience in very many cases, as well as in that of many others, seems so conclusive that the principles enunciated cannot be ignored. Personally, I have as yet had experience in the employment of proteals in but few cases, and those were not treated systematically enough to report upon, but I am now employing it and shall certainly test this treatment in future, as

an adjuvant, inasmuch as in principle it is closely allied to that indicated in these pages.

Finally, as hinted by one writer quoted in the last chapter, that on *x*-rays and radium, the student, observer, or specialist in malignant disease should not be tied to any one exact plan of treatment, but as with other diseases, he should know the entire subject so well and be so intelligent and broad minded that he will adopt with care any and every well authenticated means of curing his patient.

CHAPTER XVII

DIETETIC, HYGIENIC, AND MEDICAL TREATMENT OF CANCER. PROPHYLAXIS

It is not a little remarkable that so little serious attention has heretofore been paid to the medical treatment of cancer in standard works on the disease, in view of the occasional strong statements and reports which have appeared from time to time in current literature and in occasional books, dating back for many years, some of which have been quoted in earlier chapters. The value of some of this, of course, may be impaired by imperfect observation and erroneous diagnosis, but there have also been plenty of good men, who knew the disease well, who have reported favorable results, and even the complete disappearance of cancer, under dietetic regimen and proper medical treatment alone, without operative interference of any kind.

But even the recent and best books on the disease have not in the slightest degree alluded to the subject, and a large share or almost all of my patients, I think, have been told strongly by medical men and surgeons, that there was no possible hope in anything but the knife. The laity, therefore, have become so strongly imbued with this idea that it is often difficult for them to see or believe anything different. For, as the drowning man catches at a straw, so the cancer patient hopes against hope that an operation will be permanently successful in this particular case, although the odds are so immeasurably against it. Laboratory studies have always fostered the idea that cancer was wholly a local process, and have supported the surgeons in this stand and in the necessity of operations. This and the glamor of surgery, and its wonderful and often spectac-

ular success along many lines, have created such an obcession in everyone's mind that they believe that almost everything can be accomplished by an operation.

As I have before remarked, from the enormous work which has been done on cancer with the microscope and the test tube, it would seem sometimes that research workers and others have become somewhat myopic, and not far sighted enough to recognize the true value of statistical studies and careful clinical observations. And the medical profession and the laity have had their minds diverted from the gross errors of living which have crept in with modern life, and which are undoubtedly at the bottom of cancer and of many of the other ills, such as kidney disease, heart disease, arteriosclerosis, etc., which cause the death of so large a number of those of middle age.

From what has preceded, in other chapters, it is understood that there is no one definite or demonstrable state of the system which is certainly productive of cancer, and possibly such will never be discovered. But we have seen abundantly that the cancerous subject is profoundly disturbed in regard to metabolism and we have found that this disturbance is occasioned by the wrong action of some of the organs which in health supply the proper nutrition to all the cells of the body. We all know, even from personal experience, what a disturbing element wrong diet can be to the system, and what ills, acute and chronic, are caused thereby.

We see, then, that to understand and rightly treat the systemic condition belonging to cancer, which is indeed its basic factor, one needs to take a very broad view of the complex processes which pertain to metabolism and nutrition. This is indeed a very different proposition from the very simple surgical view, which regards the tumor as a local matter, of absolutely unknown origin, which needs only the knife to end its career. Candid and thoughtful men must recognize that deranged, disturbed, perverted nutrition is the bottom fact of all erroneous growth, whether it be obesity, rickets, or cancer.

Coming down, then, to the actual and practical facts relating

to the dietetic, hygienic, and medicinal treatment of cancer, we readily see that "the real cancer problem" relates to placing the patient in such a normal and ideal state of life that the function of nutrition is performed in an exactly proper manner, as nature intended, and from which man has erred through the manifold temptations incident to an artificial existence.

The requisites of this are fulfilled in three ways, which we will consider in turn: 1. *Dietary regulation*, that is stopping the constant intake of substances which tend to produce the perverted metabolism of cancer, and increasing the intake of just the right food elements of nutrition: 2. *Hygienic adjustment*, that is such a regulation of the various wrong habits or conditions of the patient as will conduce to restore a normal and ideal blood state: and, 3. *Medicinal treatment*, or the proper use of such remedies as will incite the various organs of the body, including the endocrinous glands, to form and eliminate properly the effete elements circulating in the system, and effect the production of a healthy and proper blood stream. It is readily recognized that it is by these means, and along these lines that medical acumen has accomplished such marvellous results in tuberculosis, *reducing* its mortality almost 30 per cent since 1900, in spite of the continued presence of tubercle bacillus, while the death rate of cancer has *risen* almost the same, 30 per cent during the same period.

1. *Dietary Regulation.*—Since first writing on the subject under consideration, medical reviewers, and many others, including the daily press, have spoken as though I regarded meat eating as the sole cause of cancer, and that enforced abstention therefrom was the single element necessary for its prevention and cure. From what appears all through these studies it is readily seen that this is by no means the case. But that I regard animal protein and its faulty partition as a fertile cause of the derangement of metabolism which leads up to and fosters the growth of cancer, is most certainly true, as appears from what has preceded. The question of diet, however, is a much broader one than that, for without this

being correct all other measures are of no avail. For, as in gout, the continuance of over-indulgence in Port and Madeira wine would invalidate any attempt to cure the trouble permanently, so in cancer an excess of animal protein, or even a large amount of vegetable protein, militates against any effort to remove the disease medically: this appears to be true also of coffee and alcohol.

As diet is the basic element upon which all health, good and bad, rests, it is all important that the physician and patient come to a perfect understanding as to how the proper diet in cancer is to be secured and maintained. Moreover, it is well to remember that there is no absolute or definite period during which a rightly directed diet is to be carried out or continued: or rather, there is no fixed time when it may be discontinued, lest errors should induce a recrudescence of the disease, and my patients are made to understand that it is at their own risk that it is to be stopped. For safety from recurrence of cancer the proper diet should be persisted in indefinitely or even permanently; for if the original errors are returned to there is no reason why the disease should not return. Even as in tuberculosis we know that a patient may overcome the disease by fulfilling all the necessary conditions, dietary, hygienic, and medicinal, but that the disease may, and probably will, recur when the patient resumes exactly the same life as before.

It is often difficult to make sure that a patient will adopt and follow faithfully all the necessary procedure for a period long enough to secure perfect results, so obsessed is the medical profession and the laity with the idea that surgery offers the only hope in cancer. But this can certainly be accomplished, and I have many, many patients who have done this even for years or even indefinitely. Some of these, whom I have followed for years, and who remain entirely freed from undoubted cancer, which had been previously diagnosed as such by prominent surgeons, have told me that they have suffered much more distress from the persistent solicitations of their physician, surgeons, or friends, urging an operation, than they had from the

diet and treatment, or from the disease itself, as it slowly vanished under the measures employed.

But as the true facts regarding the ultimate results of operations are becoming known, and as it is more and more accepted that the disease is amenable to rightly directed dietetic, hygienic, and medicinal treatment, patients are coming to the Medical Clinic at the New York Skin and Cancer Hospital, and adhering more and more faithfully to treatment. Thus far, however, these have been largely recurrent cases, where further operations were impossible, or primarily inoperative cases referred to me. To illustrate the satisfactory treatment of early cases, I shall, therefore, have to depend largely upon those observed in private practice during the last 30 or 40 years: for as yet the primary and operative cases in public practice are still referred directly to the surgeons of the hospital for operation.

At first the idea of an absolutely vegetarian diet is distasteful and seemingly impossible to many patients, but when it is patiently explained, and the reasons for its employment and the real benefit to be derived therefrom are made clear, it is readily acquiesced in and carried out very faithfully. Indeed many a patient has asserted that they are more than pleased with the general good feelings resulting from it, and have no desire whatever for meat. At each visit I am particular to inquire about this, and often have patients bring their diet card with them and make sure that all is right, by repeated questioning.

Among the poorer classes especially it has sometimes been hard to make matters clear, and to secure a proper diet for those attending our Medical Clinic for Cancer. Therefore some years ago I prepared a dietary card or folder, with a daily menu, which has long been in very satisfactory use by hundreds of patients in private and public practice, and which is here reprinted.

To make the whole matter of this line of treatment perfectly clear, certain statements in regard to cancer have been presented on the first page, and on the last page some directions as to diet and mode of life, of a practical character, were added, with the daily menu on the inside pages, to which particular

attention is always repeatedly called. At first there were one thousand of this "Green card diet slip," printed, which were given to patients and interested physicians, and then it was somewhat revised and five thousand were issued, which have also been largely distributed to physicians all over the country who have made good use of them for cancer patients.

The complete card, in full, is as follows:

New York Skin and Cancer Hospital, Second Ave. and 19th St.

DIRECTIONS FOR CANCER PATIENTS

1. Cancer is a serious disease which should receive constant medical care from time it is first suspected.

2. "Cancer Specialists," who advertise, should be avoided.

3. Cancer is not contagious, and there is no danger of communicating the disease to others.

4. Cancer is not a disgraceful disease, and there is no reason for being ashamed of it or hiding it.

5. As soon as cancer is suspected, whether there be a lump or sore, or other symptoms, it should be at once cared for by a competent medical man, as the earlier it is rightly treated the more prospect there is of its being cured.

6. Anything suspected to be cancer should not be handled or squeezed, but should be kept from all irirtation, as all this increases and spreads the trouble and renders the cure more difficult.

7. If it is decided that a surgical operation is desirable and wise, this should be done very completely at the earliest possible moment; delay is dangerous.

8. The proper medical treatment of cancer should never be neglected, both at the very beginning, and also long after an operation has been performed, in order to prevent recurrence.

9. It is not necessary to operate on every cancer, *x*-ray and radium are often of value, and the disease can certainly be made to disappear and remain absent under careful and efficient dietetic and medical treatment alone.

10. This treatment consists in an absolutely vegetarian diet, with continuous proper medication, for a long time.

11. To get favorable results this treatment should be kept up faithfully and strictly, until discontinued by the physician.

To assist in carrying out a strictly vegetarian diet, a diet list for cancer is here given, which should be closely adhered to. Coffee, chocolate, and cocoa, as also alcoholic drinks, even beer, are harmful and must be avoided. The rules given at the end of this card are also be strictly observed.

DIET FOR CANCER

First Day

Breakfast

Baked apple
4 ounces Rice
3 ounces Corn bread
1¼ ounces Butter
½ ounce Sugar
Hot water or Postum

Dinner

5 ounces Tapioca soup
3 ounces Baked potatoes
3 ounces Stewed celery
3 ounces Peas
1 ounce Graham bread
1¼ ounces Butter
1 Fresh apple

Supper

4 ounces Rolled oats
2 ounces White bread
1¼ ounces Butter
4 ounces Stewed prunes
¼ ounce Sugar
Very weak tea

Second Day

Breakfast

Orange
4 ounces Hominy
2 ounces Graham toast
1¼ ounces Butter
½ ounce Sugar
Postum

Dinner

ounces Pea soup
ounces Macaroni
ounces String beans
ounces Carrots
5 ounces Bread
1¼ ounces Butter
Dates

Supper

4 ounces Cream of Wheat
2 ounces White bread toast
1¼ ounces Baked apple
2 ounces Crackers
1¼ ounces Butter
¼ ounce Sugar
Very weak tea

Third Day

Breakfast

Banana
4 ounces Pettijohn
2 ounces White bread
1¼ ounces Butter
½ ounce Sugar
Hot water or Postum

Dinner

5 ounces Corn soup
3 ounces Baked potatoes
3 ounces Squash
3 ounces Boiled onions
2 ounces Bread
1¼ ounces Butter
Raisins

Supper

4 ounces Farina
4 ounces Stewed figs
2 ounces Graham crackers
1½ ounces Butter
¼ ounce Sugar
Very weak tea

Fourth Day

Breakfast

Raw apple
4 ounces Cornmeal mush
2 ounces Graham bread
1¼ ounces Butter
½ ounce Sugar
Postum.

Dinner

5 ounces Vegetable soup
4 ounces Baked beans
3 ounces Cauliflower
3 ounces Asparagus
2 ounces Bread
1¼ ounces Butter
Figs

Supper

4 ounces Rice
4 ounces Stewed prunes
2 ounces Graham crackers
1¼ ounces Butter
¼ ounce Sugar
Very weak tea

Fifth Day

Breakfast

Orange
4 ounces Cracked wheat
3 ounces Corn muffins
1¼ ounces Butter
½ ounce Sugar
Hot water or Postum

Dinner

5 ounces Sago soup
4 ounces Spaghetti
3 ounces Lima beans
3 ounces Boiled onions
2 ounces Bread
1¼ ounces Butter
Dates

Supper

4 ounces Cream of wheat
Sliced orange
2 ounces Oatmeal crackers
1¼ ounces Butter
¼ ounce Sugar
Very weak tea

Sixth Day

Breakfast	Dinner
4 ounces Samp	5 ounces Celery soup
2 ounces Graham toast	4 ounces Baked potatoes
1¼ ounces Butter	3 ounces Carrots
½ ounce Sugar	3 ounces Spinach
Postum	2 ounces Bread
	1¼ ounces Butter
	Orange

Supper

4 ounces Wheatena
4 ounces Stewed figs
2 ounces Saltine biscuit
1¼ ounces Butter
¼ ounce Sugar
Very weak tea

Repeat this bill of fare on successive days.

Some interchange of the different articles may be made according to the season and to suit the appetite, or convenience of patients; but in the main this bill of fare should be followed, with occasional substitution of similar articles, if necessary.

Bread, preferably from whole wheat, at least 24 hours old may be taken as desired.

A little old cheese may be grated on the macaroni and spaghetti, but not cooked with it.

One boiled or poached egg may be taken for breakfast every other day, and very fat bacon on the alternate days, unless otherwise directed by the physician.

It is desirable to eat the skin of potatoes, baked or boiled.

Each and every meal should be eaten very slowly, for at least half an hour, *with long chewing*.

One tumbler of water, not iced, is to be taken with each meal, but not when food is in the mouth; also a tumbler full of hot water, one hour before breakfast and one hour before supper.

No milk is to be taken unless specially ordered.

The vegetable soups are to be made from a stock composed of the water in which all vegetables, iucluding potatoes, have been boiled, added to, day by day, kept hot, and allowed to

evaporate; a portion is each day thickened as desired with cereals, farina, sago, vermicelli, etc. No meat stock is to be added.

The cereals are to be boiled with water, three or four hours, and may be cooked in the afternoon and re-heated in the morning, adding more water. Rice, farina, and cream of wheat require only one hour. Chopped dates, figs, raisins, or currants may be added to cereals when desired.

All the cereals are to be served very hot, on hot plates, and eaten with butter and salt to taste (not milk and sugar). They are to be eaten very slowly, with a *fork*, and very well chewed.

The crackers with supper may be varied to suit the taste; they should be eaten dry, with butter, and chewed very thoroughly.

Nothing should be taken between meals, unless especially directed, and the life should be as simple and healthful as possible, with early and long bed hours.

L. Duncan Bulkley, M. D.

This diet was prepared with the assistance of the dietitian of the hospital, and represents an average of 2,100 calories per day, with 140 of vegetable protein. This is calculated for a person of about 150 lb., either in bed or not taking much active exercise. The quantity of each article may, of course, be increased or diminished for lighter or heavier weights, but in the main this menu has sufficed, so that fat persons have come to nearer normal weight and thin persons have gained in weight. I have records of one hospital patient, whose case will be reported later, with a frightful sarcoma of the upper cheek, who completely recovered. She weighed 89½ lb. on entering the hospital, and some months later, when I showed her at my lecture, with the hole perfectly covered with a thick skin graft, she weighed 130 lb., absolutely on this diet alone, with medication.

On the last page of the folder are certain directions which are necessary to have acted upon, and about which I frequently

question patients. An important one is that with regard to slow eating and perfectly masticating and insalivating the food, at each meal, even cereals, for at least half an hour. Note also that the cereals are to be eaten with butter and salt, and not with milk and sugar, and should always be eaten with a fork, and not with a spoon, in order to encourage slow eating and chewing. I have already called attention to this, instancing the remarkable results obtained by Mr. Fletcher, which Dr. Chittenden verified, and the word "fletcherism" is a valuable addition to our vocabulary in explaining this to patients. It is to be remembered that in an earlier chapter the salivary secretion was mentioned as at fault even in early cases of cancer, and this perfect mastication is intended to stimulate the salivary glands and facilitate the change of starchy food into glucose, the first step in digestion, without which later processes must be defective: for the rapid eating of modern days may be one of the contributing basic causes of the perverted nutrition leading up to cancer.

Attention is also called to the preparation of the vegetable soup, which is to be employed in place of the meat stock which is ordinarily used, which latter naturally contains the most poisonous extract of meat, (with which dogs have been killed in the laboratory), or with milk, which is not desirable. This vegetable stock, (made from all the vegetables used by the family), contains all the salts and other valuable extracts from the vegetables, which are commonly thrown away, to the great detriment of nutrition. For we have already seen what an important part mineral salts play in the constitution of the body and its cells. A portion of this vegetable stock for soup is, to be thickened and flavored as desired each day, some butter being added, as also cooked and chopped vegetables, various cereals, macaroni, vermicelli, tapioca, sago, etc. I may add that many patients in private practice have declared that their families pronounced this the best soup thay had ever tasted, to which I, myself, can also bear witness.

Attention has already been called to the great loss of nutritive

elements in the modern or common preparation of many articles of food. The loss of vitamines and minerals in the refinement of wheat flour is also serious, and whole wheat preparations should be more freely used in these cases. Also some one has called attention to the loss of mineral and other substances in the refinement of sugar, and brown sugar and old fashioned molasses, and maple sugar, and honey are more desirable. The United States Agricultural Experiment Bureau tells us that 30 per cent of the nutritive value of potatoes is ordinarily wasted in the common method of roughly peeling and cooking them: the inner skin contains a large amount, indeed about all, of the mineral content and most of the proteids. Hutchinson tells us that: "If a bushel of potatoes were peeled and soaked before being boiled, the loss of nutrients would be equivalent to the amount contained in a pound of beefsteak." For this reason I have advised that the skin of potatoes, baked or boiled, should be eaten.

It will be noticed in the menu that the use of butter is encouraged, a quarter of a pound being given daily, divided into three portions, one at each meal. This quarter of a pound contains 800 calories or one-third of the total amount ordinarily required, and is easily digestible. Hutchinson[1] says: "There is no likelihood of this quantity surpassing the absorptive powers of the intestine," Sugar also is prescribed in reasonable quantity, affording an additional carbohydrate, which is completely oxidyzed under favorable conditions.

It is realized, of course, that this bill of fare can, and undoubtedly will be improved upon. But is was complied with considerable care and thought, and an experience with it now for some years in hundreds of cases, both of cancer and other diseases, shows that it is workable, and it has accomplished results which are often surprising and most gratifying, both in my public and private practice, and also in the hands of other physicians. It was prepared primarily for hospital practice, among the poorer and uneducated classes, of all nationalities,

[1] HUTCHINSON, "Food and the Principle of Dietetics." New York, 1911, p. 12.

and perhaps there are many other articles similar to those named which might be taken with advantage.

Heretofore I have not advised the use of much fruits, especially raw, fearing the acid element in them, but since reading recently, for the first time, all or most of the writings of Dr. Robert Bell of London, I am inclined to believe that they are beneficial, as also more of raw vegetable products, lettuce, celery, tomatoes, etc., also nuts. He likewise advocates the use of cheese and milk much more than I allow: though I have been accustomed to give blood-warm milk, drank pure and alone, without a particle of food with it, full half an hour to an hour before meals, to those who seemed to need more nourishment.

In the former chapter I mentioned the rarity of cancer among vegetarian nations, and I may quote my own personal experience in the matter, as written on my return from visiting many of them. During a rather extensive trip through the Far East I was unable to see or even to hear of any cancer, although I met a large number of medical men, and made diligent inquiry regarding the same. As I wished to verify my views in regard to the rarity of the occurrence of cancer among those who lived on rice or other vegetarian diet, I visited many civil, military, and missionary hospitals, with a total of many thousands of patients, and ministering to many millions of population. In Japan, Korea, China, The Philippines, India, Siam, and Egypt I met with the same response, that cancer was rarely seen among these vegetarian nations.[1]

In India all writers agree that cancer is rare among the inhabitants of warmer country districts, where they live largely on rice and millet, with a little milk and butter and vegetables. They eat meat rarely, the immense majority of the people live a rural life, depending largely upon agriculture for their sustenance.

Of late years some have endeavored to show that cancer was more prevalent in India than previously supposed. But its

[1] BULKLEY, "Cancer, Its Cause and Treatment." New York, 1915, p. 56.

incidence still bears no real relation to that occurring in other countries, and an analysis of some recent reports explains in an interesting and curious manner the reasons, for the diversity of opinion as to the actual frequency of the disease, as has been already mentioned.

Thus Benratt[1] could collect a total of only 1,700 cases of cancer from 5 years' statistics of 15 Mission Hospitals and 34 Government Hospitals in India, representing of course, very many millions of inhabitants, whereas in New York City alone, according to the weekly *Bulletin* of the Board of Health, there were 2,691 deaths from cancer during the *six months* from July 1st to December 31st 1920, in a population of only about six million.

Moreover, of these 1,700 cases reported as cancer by Benratt, there were 1,200 about the mouth, the greater share of these arising from the very common habit of "chewing betel." The substance chewed, or held in the mouth a long time, is composed of tobacco, betel leaves, areca nut, and slaked lime, the mass being held in the cheek, back in the mouth, where the lesions usually occur.

Sandwith[2] also attempts to show that cancer is prevalent in India, but refers to only 2,000 cases reported in the hospitals there, in 3 years, also among many millions of people, and he refers, likewise, to the betel chewing cancer, and to the "kangri burn," on the abdomen of men, from the charcoal furnace worn there for warmth. These peculiar local disorders certainly vitiate any deductions which could be drawn from such statistics. Again Bashford and others have endeavored to overturn the generally accepted view of the rare occurrence of cancer in the Far East, but a careful study of the evidence presented shows much the same inadequacy of proof, and cannot at all weigh against the reports and unprejudiced opinion of most capable medical men who have long lived and practised in those regions, some of whom as medical mission-

[1] BENRATT, *Indian Medical Gazette*, 1908, p. 452.
[2] SANDWITH, *Clinical Journal*, 1910, p. 409.

aries of unusual ability have had most intimate contact and acquaintance with the natives. Not long ago a very bright and strong medical missionary, who has long been connected with the medical college and hospital in Beirut, Syria, told me that cancer was practically unknown among the thousands of patients who flock there from all over the Near East; he adding that they were all largely vegetarians.

2. *Hygienic adjustment*, that is, such a regulation of the various wrong habits or conditions of the patient as will conduce to restore a normal and ideal blood state. We know what this will do for tuberculosis, but strangely enough practically no attention to this is ordinarily applied to cancer. The details may seem simple and homely, but, as close attention to details is most important in antiseptic or aseptic surgery, so in cancer no detail is too small which can have a good or bad effect on the state of the blood current which induces the wrong action of the cells of the body and favors their erratic and destructive course.

As uncontaminated oxygen is essential to give the tuberculosis patient the power to resist the inroads of the tubercle bacillus, so imperfect oxygenation of the material which enters and composes the blood is injurious in cancer. Attention should therefore be paid to ventilation and drainage, and every source of contamination of the atmosphere surrounding these patients should be removed.

Sunlight we know is essential for perfect animal and vegetable life, and must have its effect on the vitality of cancer patients. Unfortunately many of the poor creatures who have to go to hospitals or cancer retreats are seldom fully and perfectly ministered to in regard to either oxygen or sunlight.

Sleep is nature's sweet restorer, and attention should be paid to this, both in the early and late stages of cancer. All know that of late years the errors in regard to this are very gross. The normal 8 hours of sleep should be secured and the avoidance of late bed hours should be insisted on, the patient being in bed and lights out by 10:30 p. m. Early sleep is certainly more refreshing than that begun late and prolonged into the morning

hours. Morphine and all opiates given to secure sleep are certainly harmful, as I have long observed, and they only increase the real disease by interfering with the action of the endocrinous glands, and checking the secretions and excretions, thereby vitiating the blood stream. As remarked elsewhere, when proper treatment of all kinds is carefully carried out they are seldom required, and it is the rarest thing for any of my patients ever to require or have them, even up to a fatal termination of the disease: patients will die peacefully, without an ache or pain; in very many instances opiates previously ordered by others have been abandoned voluntarily and entirely, soon after getting under proper treatment.

Regularity of habits certainly conduces to perfect health, as is exemplified in those in training for athletics, as also in the army and navy.

I insist on perfect regularity of meal hours, rest, sleep, and recreation. Eating between meals, of sweets or of anything, is conductive to more or less disturbances of digestion and metabolic action, and must be prevented.

Recreation is a much misunderstood matter, and should be looked into. For instead of its being a *re*-creation of the vital powers, it is often as *wreck*-creation of them. One can readily overdo recreation. Excessive fatigue certainly interferes with perfect digestion and assimilation, and lowers bodily vigor. Dissipation primarily means a wasting, scattering, or squandering anything, and many a person's health is dissipated by "pursuing pleasure to excess," as the dictionary has it.

Mental and nervous states have also much to do with bad and good digestion and assimilation, and several writers have insisted that great nerve strain and fright have induced cancer. This is quite possible, both by their influence in arresting or delaying digestion, and by direct innervating influence on cell-life, through the sympathetic and vaso-motor nervous systems. In one interesting case of cancer of the breast, to be reported later, I felt pretty certain that prolonged nervous strain, from many deaths and insanity in the family was the predominating cause

of the disease. The effect of nerve influence on digestion was observed a while ago in some cats under *x*-ray examination. When well fed and happy the intestinal peristaltic action progressed perfectly, but when the same cats were then greatly irritated purposely, all intestinal movements ceased.

In attempting, therefore, to control early or late cancer, every possible element which can influence assimilation and disassimilation, or anabolism and catabolism badly, must be carefully guarded against hygienically, if we would place the system in a condition to resist inroads of cancer. All these matters which have been referred to may seem to be homely and trite, but long experience, which is more or less verified by other observers, shows, by the results obtained in overcoming the disease, that they are of importance. And in regard to the points mentioned in regard to both diet and hygiene, they are well worth while, if they can help stay the ever increasing horrors of the morbidity and mortality of cancer, which surgeons acknowledge cannot be accomplished by operations, stating that we know nothing of its cause. And experience has shown, in the hands of a number of practitioners, that with all this care, together with proper internal remedies, this end can be accomplished. Experience also shows that a certain number of patients will gladly follow whatever course is necessary, especially when they see the benefits therefrom in the disappearance of malignant tumors. The tuberculotic patient undergoes any amount of privation and discomfort in the endeavor to overcome the disease.

3. *Medical Treatment.*—This includes the proper use of such remedies as will incite the various organs, including the endocrinous glands, to form and eliminate properly the effete elements circulating in the system, and to effect the production of a healthy and ideal blood stream

Unfortunately the historical path of cancer is strewn with the wrecks of blasted hopes regarding various remedies, quack and other, whose virtues for the cure of the disease have been heralded for a while, only to sink into oblivion, to the sad disappointment of trusting sufferers from the dire malady. Various

serums have been tried, with varying success, partially from psychic reasons, but these too have gone the way of the others. These and also *x*-rays and Radium have been considered in former chapters. The reason of all this failure is found in the fact that many of them were empirical and not founded on a scientific basis. As already intimated, medicinal measures are really valuable only as based on knowledge and experience and on a correct judgment in regard to the result or effect desired to be produced, and in conjunction with proper diet and hygiene as detailed in this chapter.

It must first be clearly appreciated and understood that there is no one remedy or single course of treatment which is to be invariably followed, or is always successful in every case of cancer. And probably there will never be such found, as may be judged from what has preceded in this and other chapters.

In a disease about which there seems to be such uncertainty of opinion as to the absolute, final, and integral cause of the particular deviation from normal tissue growth, and the production of such vicious, destructive cells as in cancer, the remedies which may be required in different cases, to meet varied conditions, are as varied as are the peculiarities of the individual. The treatment requires the utmost diligence and attention to details on the part of both the physician and patient, and over a length of time which it may be difficult to secure. This is quite different from simply performing a relatively brief surgical operation, after which the patient is dismissed, with the vain hope that the disease will not return, but with no precautions taken against recurrence.

Patience and perseverance, with much thought and medical acumen are the first requisites—but before this there must be a thorough belief and confidence in the statements which have been made, the correctness of the theory, and the value of the methods employed. With this there must also be an optimism on the part of the physician which begets a confidence on the part of the patient, which will do much toward reaching the desired result. Unless much time, thought, study, and effort

can be given to each case of cancer, I should deprecate any attempt to treat it medically, and rather risk at once the chances of the best surgery, poor as they are. It was for fear of harm following an incomplete understanding of, and an imperfect or careless carrying out of the line of practice which I had pursued satisfactorily for 30 or 40 years, that I hesitated and delayed so long before urging it generally, for the first time over 6 years ago. But the continued and steady rise in mortality from cancer under the ordinarily accepted treatment, compels me more and more to attempt to make clear whatever study and experience have taught me to be the correct view of its nature and cause, and the approximately correct treatment of the disease carcinosis.

From what has preceded it will be seen at once that rational and right internal treatment must proceed and continue along the lines indicated relating to the bio-chemistry of cancer as a disease, and not simply with reference to its local manifestations as they may appear in various parts of the body, either primarily or as the result of its spreading by metastasis. Some tissue cells have broken loose from their normal physiological state, and have taken on a wrong and rampant action, of a reproductive character, owing to an erroneous metabolism, which has induced a deranged or disordered blood current. This disordered metabolism has, in turn been produced by a multiplicity of causes, including dietary errors, by faulty action of some of the organs of the body, and measures are to be devised and carried out to restore the bodily functions to a normal state.

The first line of treatment, therefore, after the prevention of the introduction into the system of harmful elements, and the providing of suitable material for the building up of healthy body cells, by dietary measures, and removing wrong hygienic features, is then to seek by medicinal agents, to restore the various bodily secretions to the normal.

Constipation, or rather *imperfect intestinal excretion*, has been recognized by many as an important element in the

causation of cancer, by means of the auto-intoxication resulting therefrom; and this condition I have found to exist almost invariably in the subjects of cancer, even long before any special harm therefrom was suspected, and also in the very early stages of the disease, and long before such a derangement has been induced by opiates given for pain. Dr. Bell is even more positive than I am, as to the invariable occurrence of imperfect intestinal excretion, or intestinal stasis, in cancer patients, and of the relation of a stagnant colon to cancer.

Imperfect intestinal excretion is a large subject, about which much has been written, and it is difficult to compass what should be said in regard to it in a brief space: but it is very essential in the medical treatment of cancer to secure what is really an ideal action of the intestinal canal, which, unfortunately, is by no means the common condition found in these patients, and some attention must now be given to this homely subject.

Long experience has taught me that it is not at all enough simply to ask patients if the bowels are regular, which will often be answered in the affirmative, when this is far from being the real truth. Repeatedly it is found, on most careful inquiry, that they endeavor to keep them so by some mineral water or oil, or by some advertised remedies, so that one must question them if such are ever used, or perhaps remedies from another practitioner. And often it occurs that there is not that complete emptying of the rectum which belongs to perfect health, accompanied with that comfortable feeling which all recognize when this has been accomplised, Bell[1] says: "I am convinced that constipation constitutes a most potent predisposing cause to cancer, and is invariably present when cancer crops up. A *complete evacuation* every 24 hours must be insisted upon, for many are under the impression that if their bowels are *moved* once a day, no matter what the character of the stool is, everything is satisfactory in this respect: whereas, in innumerable instances which I have come across, I have, on close questioning, ascertained that the bowel has by no means been

[1] BELL, "Cancer, Its Cause and Treatment without Operation." 1913, p. 197.

thoroughly relieved or emptied at the time. In these instances the character of the stool has been quite sufficient to prove that the feces have been retained for an undue length of time within the colon, the result being that the greater portion of the liquid has been absorbed into the blood, and we know that this cannot occur without interfering sadly with its purity." Colonic absorption is being more and more recognized as the source of various diseases, and the possibilities of fecal retention in this location was most remarkably demonstrated in a case which came under my observation in one of the hospitals of this city. A great solid mass was found in a woman's upper abdomen, and suspecting that it might be cancerous 'an exploratory incision was made, and revealed only an enormously distended transverse colon, between 4 and 5 inches in diameter. This was removed and was said to contain nearly 2 quarts of impacted feces, with an opening through the centre, by means of which the bowels had a regular action, as also free movement induced before the operation.

It is not enough to give general directions to patients in regard to the action of the bowels, or to leave the matter of therapeutic measures to their discretion. Definite and careful directions should be given and the actual remedies directed to be used, together with explict directions as to the exact method of their employment, and careful inquiry should continually be made as to the results. Lorand[1] is very clear and strong upon the ill results from the retained excretory products in the large intestine. "The bacteria of the intestine exert their decomposing action upon any constituents of the food which have escaped digestion by the gastric and intestinal juices. When a person has ingested a large quantity of meat, it may happen that a portion of it will reach the intestine still undigested, and here the bacterial action will very decidedly come into play. The body, however, cannot derive any nutritive benefit from the action of the decomposing bacteria upon the albumen in the large intestine, for, even though the result-

[1] LORAND, "Health through Rational Diet." Philadelphia, 1916, p. 44.

ing products may be absorbed, they are not assimilated in the same manner as other albumenoid nutriments, but on the contrary may exert an injurious and even poisonous action. Indeed the general symptoms occurring after long-continued constipation, such as headache, nausea, mental depression, loss of appetite, etc., may be referred to the absorption of such poisonous products. . .

"During their progress through the intestine, all the fluids and other portions of the food which are capable of being absorbed, are taken up, and, the farther the mass progresses downwards, the more its liquid constituents are given up, until only dry feces remain. The longer the feces remain in the intestine the harder they become. When the diet consists principally of meat, the feces tend to be dry, but with more carbohydrates, especially in the form of sweets, they are more liquid." The absorptive power of the lower intestine is recognized by all, when we remember that patients may be fed by the bowel for weeks and even months, and that medicines, alcohol, and even ether are effcctive when thus administered.

Kidney action, good or bad, has repeatedly been mentioned as an element of great importance in connection with the development and continuance of cancer, and this is a matter which should receive constant and serious consideration in attempting to control cancer. As we recognize that the kidneys are only filters, seeking to remove obnoxious material from the arterial blood, their secretion should be watched, with repeated volumetric analyses, and agencies are to be employed to make it that of health, which is seldom the case. I have had many cases in which the urine was all saved each day, measured and recorded, for months, and even for a year or two, with careful analyses made and recorded weekly, or at stated periods. It is interesting to note how the kidney secretion improves as the cancerous mass improves under most careful medicinal guidance. And the saliva, which has been acid regains its normal alkalinity. The importance of proper salivary action, and through mastication has been considered in a previous chapter.

In regard to the actual medical treatment employed it is difficult to speak clearly and briefly, for during a prolonged course there may be any number and variety of remedies used to meet the varied condition of the patient. But in the New York Skin and Cancer Hospital, and also in private practice, these patients are almost always first given a certain mixture, in varying proportions, which for years has rendered the most admirable service. The mixture is as follows: R. Potassii acetatis ℥i Tinct. nucis vom. ℥iv. Extract. cascar. fld ℥i-℥iv, Extract. rumicis radicis fluid ad ℥iv. The amount of cascara is varied according to the action of the bowels, which should move with it freely twice daily. This commonly acts also somewhat on the urine, but the acetate of potassa may be increased, and other diuretic ingredients added, such as sweet spirits of nitre, digitalis, etc. if needed. This mixture is always taken three times daily, fully half an hour before eating, in one-third tumbler of water.

It is interesting to note that Dr. Forbes Ross,[1] a London cancer surgeon, whose untimely death has deprived us of a valuable scientific worker along our present lines, was an ardent advocate of potassium in the treatment of cancer, whose value he established on bio-chemical as well as on clinical grounds; and he is even more positive in regard to the actual control of the disease by potassium than the present writer has cared to express himself. He, however, pushes the administration of the salt of potassium far, far in excess of that which I have found necessary: this is probably because he had not yet reached the point of the influence of correct diet on cancer. Dr. Ross prefers potassium citrate and potassium phosphate combined, of which he gives as much as from 90 to 180 grains per day. He has related instances of advanced, inoperable cancer in which the results were remarkable, and one of them, a case of cancer of the uterus in a widow aged 59, was quite a counterpart of one which I shall report in the final chapter.

[1] Forbes Ross, "Cancer, the Problem of Its Genesis and Treatment." London, 1912.

Dr. Ross had operated much on cancer, but, realizing the inefficiency of surgery to cure the disease, he wrote very severely in regard to cancer surgery in the opening chapter of his book. After "ten years of constant microscopic, clinical and surgical research" he advanced the hypothesis that "cancer is due to a want of balance in particular mineral salts of the body, and that the disturbance of this balance leads to the disorderly and malignant growth of epithelial cells (epiblastic and hypoblastic) known as carcinoma," and claims that the main disturbance is in regard to the potash balance in the body. By very careful deductive and inductive reasoning, and by actual experimentation and practice, he shows how this answers and explains more of the puzzles and intricacies of the cancer problem than any other hypothesis, and the experience of many others has certainly borne this out in practice.

Dr. Ross makes three references, which in a measure support the potassium theory of cancer.

"1. The old physiological adage, 'potassium is the salt of the tissues, and sodium the salt of the fluids of the body,' still holds good as an absolute physiological truth.

"2. Animal physiology teaches us that the whole range of the animal creation, from an ameba to man, follows the same law, 'Potassium is the salt of the tissue cell.'

"3. Examination of the botanical world brings us face to face with the same identical statement, 'Potassium is the salt of the chemical physiology of the vegetable cell.'"

In regard to the blood cells, Dr. Ross shows the importance fo potash in the following language. "How vitally important potassium salts are to the red corpuscles is shown by the following: One thousand parts of red blood corpuscles are found to contain 688 parts of water, 308 parts of organic solids, and 8 parts of mineral. Of these 8 parts of mineral substances 3.5 are of potassium chlorid, 2.5 are of potassium phosphate, and 0.1 potassium sulphate: the remaining 1.9 parts are divided between the iron, sodium, calcium, and magnesium, comprising the rest of the corpuscles. More than three-quarters

of the total mineral ash of the red corpuscles is, therefore, composed of potassium."

It is not a little satisfactory to find from a surgeon such a microscopic, bio-chemical, and clinical explanation and support for a line of treatment which I have followed for so very many years, solely on clinical grounds. Dr. Ross makes the interesting statement that, having used enormous quantities of potash salts in his practice for 15 years, for various complaints, not one single case of cancer had ever to his knowledge occurred among the clientelle of his own practice; he had, however, constantly been engaged in operating on patients with cancer sent to him by other medical men. I made much the same remark in regard to the absence of cancer among my patients, in one of my lectures, before I had seen the work of Dr. Ross.

The first and basic treatment, therefore, in addition to dietetic and hygienic measures, is a full amount of a potassium salt, of which I prefer the acetate (but Dr. Ross the citrate, phosphate, and sometimes carbonate), as previously mentioned, in combination with cascara and rumex fluid extract. This latter, an extract of the yellow dock root, is one of the old, so called alterative remedies, which I have used for many years, generally in this combination, for certain skin diseases. And it was the disappearance of lumps in the breasts of patients, which had been diagnosticated by surgeons as cancer, while taking this mixture for some skin complaint, that first directed my attention to the disease, very many years ago, and led to my adding cancer to skin diseases, when I founded the New York Skin and Cancer Hospital, about 40 years ago. I have had cancer patients where this mixture, with little variation, has been taken for months, or even years, with occasional alternation with other remedies as required, with most satisfactory results.

But it must not be imagined that this is the only line of treatment necessary in these cases, to meet the different conditions which may lead up to the disturbed metabolism of cancer.

Patients with a cancer of the breast just beginning, will often, or even generally, seem to be in excellent health. They are

ruddy and blooming in appearance, and when the lump is first discovered it is hard indeed to believe that if the erroneous life processes which caused the cancerous lesion to develop are not checked, that patient will before long succumb to the direful disease. Williams[1] remarks that: "Such types are indications of hypernutrition. Such cases show great benefit from thyroid feeding, and Bell reports many instances with surprising results from this remedy, with the entire disappearance of the tumor, in a short time. I often give the thyroid after eating, and also at bedtime, in conjunction with the potassium and rumex mixture, with good result. In patients who are at all obese, and who as a rule do very badly after operation, it is always desirable to reduce the flesh by thyroid at the beginning of the treatment.

Williams[2] remarks: "Cancer patients usually are of a coarse physical type. Those recently attacked never present a cachectic appearance. The small, ill-nourished and over-worked women of the type so familiar in Lancashire and other large industrial centres, are seldom the victims of the disease. Of 75 consecuitive cases, when they first came under observation four were markedly cachectic or sallow (primary 3, recurrent 1) eight were emaciated (primary 6, recurrent 2) and 14 pale (primary 10, recurrent 4): the remaining 49 (primary 39 recurrent 10) were well nourished and healthy looking, seven of them being obese." Of course, with cancerous lesions affecting internal organs, and when the carcinosis, or cancerous habit has already been under way for some time before medical observation, cachexia and loss of weight are often prominent symptoms, as the cancerous lesions themselves also aid in disturbing the processes of metabolism and nutrition, as already explained.

But a most careful study in every particular of all patients affected with cancer, even in very early stages, and probably some time before, will so constantly reveal such various errors of life and derangement of metabolism that these must be looked upon as contributing causes, at least, to the development

[1] WILLIAMS, "The Natural History of Cancer." New York, 1908.
[2] WILLIAMS, "A Monograph on Diseases of the Breast." London, 1894, p. 286.

of the local condition which later becomes malignant. In the same way a patient will appear to be in blooming health just before an attack of acute gout, but sufficient study and analysis some time before would reveal a condition of system which an experienced eye would recognize as a forerunner of the disease. For when these conditions in cancer, whether early or late, are recognized and sufficiently rectified by proper dietetic and medicinal measures, the local cancerous condition not only ceases to develop but actually disappears, without surgical removal, as I have repeatedly shown: and no one doubts but that the threatening attack of gout could be warded off in the same manner. We know what passes for good health is often fictitious, and is quite compatible with even grave disorders of various kinds.

It is readily, seen therefore, that no very definite directions can be given here as to all of the internal medicinal treatment of cancer, other than has been already said. As remarked before there is no one single remedy, nor even any single course of treatment which is to be invariably followed, or is always successful in every case of cancer. Nor will there ever be such, for the palpable reason that the true nature of cancer, as heretofore developed, precludes the possibility of such a thing.

But many articles in the materia medica may very materially assist at times in overcoming the cancerous state. Iron is very often of great service, when properly used, in meeting the cachexia as it develops, and of this I prefer the dialyzed iron, given in pretty full doses in the middle of the meal. Arsenic with it helps somewhat, and Bell speaks very highly of the hypodermic use of atoxyl, every other day, in addition to other treatment. In certain cases I have seen greater improvement when phosphatic preparations were added or substituted for other remedies, as seemed indicated by the nerve condition of the patient. And I find nothing better than what is known as Horsford's acid phosphates, taken freely whenever needed for neurasthenic feelings; and various remedies may be needed to restore and keep the bodily functions in perfect condition.

Cancer is continually found to be connected with rheumatic

symptoms of various kinds, and neuritis, often very severe, away from the neighborhood of the local disease, is not uncommon; so that from first to last I may use aspirin very freely in many cases, and it seems to do the local cancerous lesion good also. I always give it in powder form, in capsules, with hot water, and have it repeated in two hours, or as often as necessary. This is also my main reliance in connection with the pain of the actual cancerous lesion, and it is generally sufficient, when the patient is under full and efficient dietetic hygienic, and medicinal treatment. Morphia is practically never needed then, and it is the very rarest thing for me ever to sanction it, and I have taken it away from very many patients, without complaint

A word more in regard to the bowel action, which should be quite a little more than normal. At the beginning of treatment I very commonly give a certain old pill, the supreme value of which is known to many, it is as follows: R. Extract. colocynth. comp., Massæ hydrargyrii aa Gr. x Pulv. Ipecac. Gr. ij—Div. in Caps. No. iv—take two at night and two on the second night after. In many cases, especially in full blooded persons, I have these repeated each week on exactly the same nights, for some weeks, perhaps, but never more frequently. When taking the mixture of acetate of potassa and rumex, or at other times, I have long found the very best results as to bowel action secured by a tablet now made by several firms, as follows: R. Podophyllin, Cascarin, Aloin, each ¼ gr.: from one to three four or more, may be taken at bedtime, with excellent results.

In giving potassa very freely many fear a bad action on the heart, as the older books say, but never have I found it to be the case, though of course, there is not the slightest objection to administering strophanthus or digitalis at the same time.

Mention was made of the value of thyroid extract in cancer, and some of the other endocrinous extracts have been employed with advantage by a number of observers, alone or in combination. While from my personal experience along this line I am not in a position to speak strongly, except in reference to

thyroid, I cannot but believe that rightly used they can have a beneficial effect in cancer. From my reading and studying I am convinced that all of them have some, almost mysterious, effect on the nutrition and behavior of the cells of the body, as mentioned in regard to myxœdema, Addison's disease, and gigantism. It is quite possible that with a blood stream vitiated by dietary or other errors, and wrong action of the ordinary secretory and excretory glands of the body, the endocrinous glands, in common with other structures, may suffer and so be unable to do their part, whatever that may be, in the balancing or equalizing the general metabolistic powers of the system. In this case the introduction of the normal endocrinous tissue from healthly animals may supply quite the element wanted in the human system, just as ox bile has long been of service in medicine, and the effect of adrenalin on blood vessels is well known.. I think therefore, that the evidence is very strong that preparations from some of the ductless glands of animals may and probably will sometime be an established element in the treatment of cancer, in conjunction of course, with diatetic and other proper measures.

The local medical treatment of cancer often forms an important part, both in the comfort afforded the patient and as a measure of benefit to the diseased part.

In the early stages of breast cancer, keeping the part painted night and morning with a mixture of equal parts of true, imported ichthyol and water appears to help in the disappearance of the lesion, as I have observed in dozens of cases, and have thought that it aided in dispelling the darting pain common in them. In the late cutaneous nodules, developing thickly in cases recurrent after operation, I have seen them fade away, almost magically, under the constant painting with thiol and olive oil each 50 per cent, as in one of the cases to be reported in the final chapter. Sometimes I have used the tincture of iodine, with glycerine, a drachm to the ounce, with equally good results, on unbroken surfaces in early cancer. All of

this local treatment is, of course, in conjunction with complete internal treatment as already indicated, for certainly these, or any other local measure would be powerless alone.

In the terrible, ulcerating surfaces formed, especially in recurrent cancer, the very greatest relief and benefit is continually seen when the harsh, surgical dressing with gauze is replaced by a soothing ointment, thickly spread upon very thin portions of absorbent cotton, and gently laid so as to cover the entire area. This may be covered with gauze held in place by adhesive strips, but I deprecate any thick mass of cotton, or much bandaging. The ointment, softened by a little heat if necessary, is easily spread on thin portions of absorbent cotton, perhaps 3 inches each way, held on the hand and applied with a steel spatula or ordinary table knife. The joy and relief experienced, especially by hospital patients, when this change of dressing is made is very gratifying. The ointment layer should be pretty thick, and so well spread that the fibres of cotton need not touch the sore. This is generally changed twice in the 24 hours or oftener if desired, and being gently removed, fresh portions having been prepared in advance, they are quickly replaced, without having much exposure to the air. I do not have the surfaces treated much otherwise, except under certain circumstances to be mentioned later, but if there is much moisture or suppuration on removing the dressing, the surface may very gently be sopped with a bit of dry absorbent cotton.

The ointment almost invariably used at the hospital, and generally in private practice, is that of calamine and zinc, which I introduced many years ago, and is now well known. R. Acidi carbolici ℈i Pulv. calaminæ prep. ℈iv. Zinci oxidi ʒ ij. Unguent aquæ rosæ ℥iv. When there is much pain a drachm or more of a 4 per cent solution of cocaine is incorporated in the ointment. Sometimes a few grains of acetate of morphine in solution, worked into the ointment serves better. It is surprising to see how the diseased surface will improve under this method of handling, and often, with all other treat-

ment proper, evidence of normal epitheliation will appear in places and increase steadily.

A very considerable share of the suppuration and pain in cancerous raw surfaces is undoubtedly due to the presence and operation of the omnipresent pus bacilli, rather than to the disease itself, for it is out of the question to keep these surfaces aseptic. This may in a measure be obviated by the proper use of antiseptics, though they sometimes seem even to irritate the sore. I have used the peroxide of hydrogen, generally with good effect, applied thus: pouring it out in a saucer, very thin portions of absorbent cotton are very thoroughly soaked in it, and being lifted carefully are made to lie over all the affected surface. In five minutes these are replaced by a second set, remaining on for five or ten minutes, and on their removal the portions of cotton, firmly spread with the calamine and zinc ointment are quickly laid on, without attempting to dry the surface. Latterly I have been using in the same manner chinosol, one tablet in a pint of water with half a teaspoonful of salt in it, with good effect, possibly better than with the peroxide. Sometimes the chinosol solution seems a little strong, and it may be diluted one-half, and then be made stronger if agreeable.

In early cancer of the lip, under proper internal treatment I have repeatedly seen the local lesion entirely disappear, and remain indefinitely absent, under just the right internal and local management, as will be reported in a case or two in the final chapter. For this I have an ointment quite thickly spread upon what I call "a whiff of cotton," and kept on all the time, day and night, even during meals, changing it quickly several times daily. At first this seems to the patient difficult to accomplish, but it is surprising to see how soon they learn to apply it, deftly and perfectly, better than I can myself. The ointment commonly used is as follows: ℞. Ichthyol (imported) ʒss-ʒi Zinci oxidi ʒi Unguent aquæ rosæ ℥i. If the hardness persists I often add a trifle, gr. v-x of well powdered salicylic acid, or pyrogallic acid to the ounce; occasionally if it

is at all irritated, the calamine and zinc ointment, just mentioned, may be alternated with it.

In cancerous lesions within the buccal cavity my constant application for many years has been simply a saturated solution of bi-carbonate of soda, diluted more or less if it seems too strong, but generally it is not, used six times a day, ¼ hr. before and ¼ hr. after each meal. The idea of this is to secure an alkaline condition of the mouth, for the saliva, as before remarked is invariably acid instead of alkaline, and cancer develops in an acid medium, as previously stated. The solution is held in the mouth for some time, a few minutes, and well worked around, with pressure, and repeated twice at each application. The use of it after eating serves to cleanse the mouth of particles of food which might remain and induce an acid fermentation. The results are excellent.

In cancer of the cervix, I have seen, with proper treatment, remarkable results, as in the cases to be later reported, from a simple but effective douche, which I have long used in very many cases. It consists simply of carbolic acid and borax, half to one teaspoonful of the former and two to four of the latter, well dissolved in one *pint* of very hot water, or as hot as can be borne, even up to about 110°. This is used two or three times daily, *not* with an ordinary gravity douche bag, but with a Davison or Alpha *ball syringe*. With the long nozzle deeply inserted, the douche is squirted in with a quick movement, and some force, against the diseased surface, and it is interesting to learn how soon the flow comes away odorless and more and more clear of blood and pus, and finally quite clear. The idea, of coures, is disinfection, with a complete alkalinization of the affected parts, while the heat and sharp impact of the stream stimulates the diseased cells to healthy action. With all this treatment cases of advanced, inoperable cancer have recovered, and remained well for years with proper diet and internal measures.

In the case, to be mentioned, of a sarcoma of the cheek which had left a large opening, with ulcerated surfaces within the

buccal cavity, an extemporized solution was made up and kept continually applied, renewed several times daily, with pledgets of absorbent cotton, from the beginning of treatment, until all was healed and a skin graft inserted, which latter took perfectly, with permanent healing of the opening and good cosmetic results. She was, of course, under thorough internal treatment all the while, and for a long time afterwards, also she was long watched. The lotion referred to was as follows: Acidi carbolici ℥ss Listerine ℥i. Liquor sodae chlor ℥i. Glycerine ℥ss. Aqua hydrogenii dioxidi ad ℥iv M.

The local treatment of epithelomatous lesions of the skin by *x*-ray and radium is considered in another chapter.

We have thus seen that the medical treatment of cancer is no trifling matter, and must be entered upon and faithfully conducted with great patience and perseverance, until long after the local signs of the disease have ceased. How long this must be I cannot possibly tell, but the results amply repay all the work that can possibly be put into it, and a good share of patients are duly appreciative when they are really made to understand what they have escaped.

Early lesions can certainly be dissipated and the patient can, I believe, surely remain well indefinitely under proper conditions of life, as a number of my breast cases were followed 14 to 16 years. In some cases of stomach cancer, so diagnosticated by every test, including *x*-ray, given by able physicians and surgeons, the symptoms all vanished and they seemed well, but of course, some patients where the disease was advanced have died. In a case of apparent cancer of the second kidney, where the removed one was absolutely cancerous microscopically, which will be recorded later, the patient who was in a very bad condition when first seen has lived 4 years, weighing more than ever, working very hard all the time, and, so far as can be seen, perfectly free from his former trouble. Fuller statements will be made in the final chapter.

The whole proper thought about cancer, therefore, is that

the local lesions, which may arise from discoverable local irritation or from some unknown reason, and may develop in any and probably every part of the body, wherever epithelial cells exist, are all one and the same manifestations of one and the same error in nutrition. This latter is the culmination of long standing modes of life which have produced such a condition of the blood current nourishing the tissues, that some cells, under peculiar exciting circumstances, have rebelled against the physiological laws under which they formerly underwent the normal changes of catabolism and anabolism pursued by their healthy and well behaved comrades. Having once started on this abnormal course, and being fed with the same perverted blood stream, they naturally pursue a vicious course until they receive again their proper nourishment, and are possibly influenced by neighboring regenerated cells and leucocytes.

The treatment, therefore, is practically the same for true epithelial cancer in every location, for each lesion is essentially the result of the same internal cause, being specially incited by some local irritation. These vitiated conditions of disordered blood explain equally well the result of metastasis, whereby cells already diseased are carried along until they lodge and form a new focus of irritation, which is fed by the same disordered blood stream until a real palpable neoplasm forms there. This also explains why these metastatic lesions also disappear under proper constitutional treatment, as we constantly see them do in connection with breast cancer, and presumably in deeper metastatases, as the patient recovers from uterine and other manifestations of neoplastic growth.

Sarcoma, which is only a cancerous form of mesoblastic tumor, as Forbes Ross remarks, has repeatedly been found to respond to the same therapeutic measures.

The *prophylaxis* of cancer naturally follows the same lines as already indicated. How early the tendency to the disease carcinosis, or cancerous dyscrasia, can be suspected and guarded against remains to be seen. But I have repeatedly asserted before medical assemblies that if the systemic conditions

mentioned were seriously guarded against, and the "green card diet" had been accurately followed for several years, and persisted in indefinitely, any one would be insured against the development of cancer. This may seem a rash statement, but long observation and study have so thoroughly convinced me of the correctness of the views set forth in these pages that I feel warranted in making it. And I am confirmed in my judgment by the large number of confirmatory letters, which I am receiving from physicians all over the country, telling of the results they have had from following out this line of treatment. Time will show, and it is hoped before long, how far the principles and practice here indicated are correct, by a diminution in the mortality reports of this terrible disease.

CHAPTER XVIII

CLINICAL CONSIDERATIONS AND RESULTS

In the first small book, published 6 years ago, on "Cancer, its cause and treatment," I remarked, "The test of everything lies in the results obtained. Theories, discussions and arguments are unavailing unless results show their truth," and eight cases of undoubted cancer of the breast were then reported, four of them of particular interest, two of the patients I had then followed for 16 years and two for 9 years, all of whom had remained perfectly well without operation.

In the second little book I repeated the same sentences, saying that I could then utter them with stronger emphasis, after 2 years further experience and an immense amount of reading and study, and I then reported nine more illustrative cases, from among many others, all showing remarkable results, some of them dating back 5 years or more. And now after 6 years of specially active work along these lines, added to 40 previous years of moderate devotion to this branch of practice, I call attention to the same words with greatly increased interest and certainty, predicated upon daily experience with the disease and intensive study of literature, with more illustrative cases, making over ninety in all, out of many hundred under observation and treatment.

In the preceding chapters I have endeavored to present the scientific basis for the constitutional nature and treatment of cancer, and I may say that to my knowledge these views have never been effectively refuted, either in discussions before societies or in literature, while the very many most favorable book reviews, and innumerable letters and statements from physicians and surgeons endorsing the views and treatment set forth, have been most satisfying and encouraging.

Dietetic and medical treatment of cancer, in the fullest sense, have never yet been given a fair and really intelligent trial on a scale large enough and long enough to procure general conviction in regard to their value; although for many years past single physicians and surgeons have more or less strongly advocated them. Many cases of cancer and sarcoma have been reported here and there, which have recovered spontaneously, that is without surgical interference, and often greatly to the surprise of the medical attendant. This shows of itself, that under certain conditions or circumstances something may occur in the system which causes the malignant process to cease and the neoplastic mass to subside and disappear, and the cells to return to their normal function. This certainly should be a stimulus to an endeavor to discover what the reason is for this beneficial change, and to seek to accomplish the same by proper medical care. These studies and measures have been given as far as possible in what has preceded.

Before presenting further clinical facts confirming the views presented and the treatment employed, it is but right to state that this line of thought and treatment are not of recent date, and do not represent any suddenly conceived theory of practice. They are simply the growth of experience, dating back over 40 years, as previously mentioned, to casual cases of cancer of the breast, so diagnosticated by capable surgeons, who had urged immediate operations, which were not performed, and which completely disappeared without surgical interference, under dietary and medical treatment given for other complaints. The notes of all these cases were not kept in a manner to be used, but of the eight cases reported in my first book, the first patient came for treatment in 1892, nearly 30 years ago, and the second recorded, in 1894, who were each followed for 16 years, as already mentioned, remaining well, without surgical interference.

In the third volume 18 additional cases of malignant disease thus treated, from among many more, were fully reported, making 35 in all, as samples of neo-plastic disease which had

responded to medical treatment alone in a gratifying manner; this being shown either by a complete cure for years duration, or by great prolongation of life and amelioration of suffering, without the use of an opiate.

In order to save referring to those volumes and that these cases may help to confirm and enforce all that has been said previously, it is but right that their histories should be again recorded in abbreviated form, before reporting some more, from among many others who have come under treatment during the two years since the last publication or who were held over for observation from former years.

The criticism has sometimes been made in public and in print, that in the majority of the cases the diagnosis has rested only on clinical grounds without microscopical proof of its correctness.

To this may be answered: (1) That of the post-operative cases there could be no doubt: (2) That all are now agreed that a biopsy in cancer is always a very questionable procedure, as it surely tends to spread the disease; and it would be especially perilous in such cases as are to undergo medical treatment, and would not be all justified, simply to satisfy so-called scientific curiosity. (3) The vast majority of cancer operations in general are performed without microscopical evidence as to diagnosis. (4) In almost every one of the cases mentioned, if not in all, there had already been the definite opinion of one or several competent physicians and surgeons, that the disease was cancer, and generally an immediate operation had been urged, and in several instances wholly arranged for, but avoided. (5) Constant observation of and contact with cancer patients for forty years and more, in private and public practice, should warrant the present writer in claiming some authority in diagnosing cancer. (6) In regard to cancer of the breast it is claimed or stated by the surgeons that 80 per cent of tumors in that location, in persons over 30 years of age, other than at lactation periods, either are or certainly would be cancer, which would be fatal within 5 years if not surgically removed. The

soundness of this opinion may be judged by the dozens of such tumors which have disappeared and remained absent under careful medical management alone.

In order that a proper knowledge may be had of what can be done by the medical treatment of cancer we will first present abbreviated reports of the cases referred to, and then those of more recent cases, exhibiting various points of special interest.

CASE I.—*Primary cancer of the breast.* Mrs. B. E. C. aged 44, first seen Sept. 19, 1892. In the outer lower segment of the right breast, there was a flat, hard tumor, sharply defined, tender on pressure, first noticed about 2 months previously. A well-known prominent New York surgeon had diagnosed undoubted cancer and strongly urged instant removal. Under complete dietary and medical treatment it had entirely disappeared in 6 months. Four years later she was seen regarding the menopause, and the breast was found perfectly normal, she still continuing the diet. The case was followed for 16 years with no recurrence of the breast tumor.

CASE II.—*Primary cancer of the breast.* Miss B. M. L. aged 45, seen Jan. 4, 1894. Tumor in the upper, outer quadrant of the left breast, sharply defined, with some darting pains. Three medical men, one a surgeon of prominence, had diagnosed it as cancer, and immediate surgical removal had been arranged for the next day, but avoided. In 2 months the lump was recorded as less distinct and flatter, and within 11 months it had entirely disappeared. A month or two later she had some pain in the breast in connection with menstrual disturbance accompanying the menopause, but no trace of the tumor could be found. She was seen at repeated intervals also for 16 years, and the breast was always found perfectly normal.

CASE III.—*Primary cancer of the breast.* Miss J. M. A. aged 45, seen Oct. 12, 1905, a hard working city missionary under great physical strain, had for some months a tumor in the left breast above the nipple, awaking her at night with pain, with also numb, shooting pain in the daytime. She had seen many

medical men, all diagnosing cancer, but had declined the operation urged. Two months later, December 15, there was little to be felt in the breast, and no pain, and on Jan. 5, 1906, both breasts were the same, with no sign of the former tumor. She was repeatedly seen for 9 years to the time of reporting, being very faithful to treatment, and is still in active work now, yet 7 years later, also almost 16 years from the first, with no recurrence of the tumor.

CASE IV.—*Primary cancer of the breast.* Miss G. M. aged 44, a public school teacher, seen first Nov. 13, 1905, had struck the breast in a fall, 16 years before, but the effects passed off and there were no sensations for 7 or 8 years, when she began to have pain, aggravated at menstruation. During the past year there was a lump formed with constant pain, also pain recently in the axilla which kept her from school. A number of medical men had always diagnosed cancer, and one, a surgeon of prominence in one of the large hospitals had strongly pressed for an immediate operation.

When first seen there was a tumor, 2 or 3 in. in diameter in the upper inner segment of the left breast, hard, sharply defined and nodular on the surface, with enlarged glands in the axilla. She had long been constipated and passed only about 60 per cent of the amount of urinary solids proper for her weight. Under very active treatment it was recorded, 4 weeks later, that there had been hardly any sensation in the breast during the previous week, that the tumor had diminished materially in size and hardness, and that she was now out of doors daily, feeling much better. One month later it was recorded that the breast was about the same as the other but having a little caking and absolutely no pain for some time, and she was at her duties in school. On April 7, it was recorded that the lump was all gone and no glands could be detected in the axilla. When reported in 1913, 8 years later, she was still free from trouble, in spite of strenuous and often exhausting work as a public school teacher. A sister had recently died at sixty with cancer of the stomach in a distant country town. It is now

over 7 years still later, and not long ago I heard of her as free from her trouble, 15 years after her first visit.

CASE V.—*Post-operative cancer of the breast.* Miss H. B. aged 61, June 21, 1913. Two years previously a lump appeared in the outer, lower segment of the left breast, which was removed in August, 1911, healing soon, with a good axillary scar, and remained well until 2 months before her visit. A small red spot then appeared near the sternum which enlarged and hardened, with others around the scar until there were a dozen, up to half an inch in diameter, and tense skin between, with minute points developing. Under active treatment including thyroid and *x*-ray, many of the nodules disappeared, although some new ones formed which were removed surgically, under local anæsthesia, the wounds healing kindly. As she lived some distance from the city I did not see her after Oct. 7, 1914, as she wished to take the *x*-ray nearer home, and I, of course urged the continuance of the dietetic and other treatment. In this instance the patient lived completely without pain and without an opiate for almost 16 months at least, when otherwise the disease would have rapidly progressed, possibly to a fatal issue with the pain usual in recurrent cancer.

Two hospital cases, recurrent after operation, were reported to show the benefit that could be given to such in the hospital, which, however, is not equal to that obtained in private cases, where every possible detail can be effectively carried out by intelligent patients.

CASE VI.—*Post-operative cancer of the breast.* Mrs. C. M. aged 38, had an abscess of the right breast 19 years previously, which healed and left a tumor the size of a pigeon's egg. This remained quiescent, until it began to enlarge, 11 months before removal surgically, at the New York Skin and Cancer Hospital, Nov. 14, 1912, it being then the size of a hen's egg, in the inner quadrant. A complete operation was then performed, with dissection of axillary and supra-clavicular glands, and she was discharged Jan. 16, 1913. On Feb. 12, 1914 she

returned, in my service, with an ulceration along the line of incision from the second to the fourth rib, an inch or two wide, with many nodules around, raised and reddened, quite inoperable. The liver extended 2 inches below the edge of the ribs, with a hard nodular margin; the right arm was enormously swollen, hard and helpless.

When she left the hospital, against my wish June 20, 1914, the ulceration had wholly healed, many of the nodules had entirely disappeared, the arm had returned to the normal size of the other, as measured by several in the hospital, and the liver had retracted to only a trifle below the margin of the ribs, with hardly any nodular margin. All this had occurred within about 5½ months, under very disadvantageous circumstances, for she was a very ignorant Polish woman who often rebelled at the diet, and wearied of the routine and the restrictions imposed.

The patient, who attracted a good deal of attention in the hospital, was subjected to careful investigations according to a definite schedule. The *blood* studied weekly showed 3,262,000 erythrocytes on entering, which rose within 2 months to 4,282,000; the leucocytes were 9,000 on entering and 5,200 before leaving, the polynuclear being 69 per cent, fell to 60, etc. The *urine*, volumetrically analyzed every 3 days, was kept free and a little below normal acidity, with rather low specific gravity, etc. The *saliva*, tested and recorded ¼ hr. before and after each meal, was acid at first but became neutral and alkaline. The *weight*, taken weekly, fell a little from the first as desired, but maintained a good level and rose before she left the hospital, cured as she supposed.

One other, a hospital out-patient, was also reported on, where the disease was recurrent after three operations, who in 2½ months showed a change which was remarkable compared with the increasing development of the disease in the two months previous.

CASE VII—*Post-operative cancer of the breast.* Mrs. W. C. aged 45, a hospital out-patient, seen first at my medical clinic

for cancer, on Sept. 17, 1914. Nearly 4 years previously a lump appeared in the left breast, which was removed Jan. 6, 1911. It soon regrew and a complete operation was performed at the New York Skin and Cancer Hospital, May 30, 1911. Two years later there was a return, and she was again operated on at the hospital, May 30, 1914. About 3 months later, 2 months before her visit, there came a swelling on the sternum, and soon another above it, both of which increased rapidly. When seen there was a hard mass in the scar over the sternum about 1½ in. long, raised, reddened, and immovable, and another smaller, an inch or so above, which gave her pain when at housework.

Under active treatment there was immediate improvement, and when last seen, December 7, both lumps had subsided fully one-half, there was no pain at any time, and her general condition was immensely improved, she feeling better than she did 4 or 5 years ago, that is, before the beginning of the cancerous development. She had been working all the time, unusually hard, as janitor of four buildings, and also going out scrubbing and working. She weighed 157½ lb. at first, ran down to 154, and gained to 155½ at the last visit, when she was lost sight of, like so many others. It is often hard indeed to keep patients faithful to the monotony of medical treatment, when the minds of all are so attracted by the glamor of surgery, and its spectacular features.

A fatal case was reported to show the benefits which can be obtained even when a primary case has advanced far beyond the possible aid of surgery.

CASE VIII.—*Primary, far advanced cancer of the breast.* Mrs. M. B. J. widow, aged 68, a private patient, was first seen Feb. 17, 1914. Two years previously she had noticed a lump in the upper part of the right breast, after great and repeated mental distress, from the death of a number of very near relatives and a sister's mental derangement, the great nervous strain having been attended with various bilious attacks, and nervous indigestion. The mass increased steadily in size and

was kept concealed even from her family, until the day before she called, when her family physician who was consulted saw that it was far beyond the possible hope from any operation, in which view a prominent surgeon concurred.

When first seen the whole breast was involved, double the size of the other, like a very large half melon, hard and immovable. There was a rather thick crust, several inches in diameter, adhering to an ulcerating surface, beneath which came a moderate discharge. The axillary glands were enormously enlarged, and also the supra-clavicular, and she was strongly cachetic. She was placed under very complete dietetic and medical treatment, and the breast kept painted with 50 per cent ichthyol in water, the adherent crust not being disturbed. In a very short time the discharge ceased, the protective crust adhering until she passed away peacefully, from exhaustion and pulmonary œdema, on Sept. 9, 1914. On August 5 it was recorded that the breast had done very well, was soft and movable, and not larger than the other breast, with no discharge, and no pain since a short time after beginning treatment. The axillary glands had diminished three-quarters in size, and the supra-clavicular glands were also very much smaller. She never took, or required a particle of morphine or any opiate. The peace and comfort experienced by this lady during 7 months with an enormous inoperable cancer and great cachexia when first seen, was certainly very different from the generally conceived and observed course of cancer.

In the second volume nine additional cases were recorded, which may be synoptized and reported on.

CASE IX.—*Primary cancer of the breast.* Miss T. M. M. aged 37, consulted me Mar. 23, 1916, for a mass in the left breast, which a surgeon of great eminence had diagnosed as cancer, urging most strenuously an immediate operation, saying that from its rapid development she would die within 6 months if not operated on. She had had a neurasthenic breakdown the previous autumn and for some months now had been under very great nervous strain with a father aged 71, slowly dying of

Bright's disease. Two years ago she had suffered severely with uricacidæmia.

The lump in the outer upper, inner quadrant of the left breast was noticed only a month or two before her visit, and had increased rapidly. When first seen there was a mass about 2 inches in diameter, attached to the puckered skin over an area of 1 inch, and there was considerable pain, increased measurably by the rather hard handling of the surgeon just referred to. There were a number of enlarged, hard axillary glands.

Under very active treatment with constant observation every week or two, in 8 months the improvement in her general condition and the breast tumor was very marked. When she then kindly appeared at my lecture at the hospital she said that she "felt a thousand times better." Her color was excellent, she had held her weight, 153 lb., a trifle above that called for by her height and age, and all this in spite of heavy daily office work and very great trouble and anxiety nursing her father for for 13 weeks, who died in October

The breast then was soft, with still a lump, hardly half the original size, the area of attached skin had decreased, with only a slight pimpling and the enlarged axillary glands had disappeared. She went on a trip to Chicago by auto, slept perfectly and had no pain. Ten months after her visit she had a very severe attack of grippe, being in bed 3 weeks in another city, and this with many weeks of neglect of treatment set her back a little and she was lost sight of, 14 months after she had been given but 6 months to live by the surgeon, she being healthy and happy all the time, and never missing a day's work.

CASE X.—*Primary cancer of the breast.* Mrs J. T. T. a farmer's wife, aged 38, seen Aug. 11, 1914. She had been confined with her first child 4 months previously, but had not nursed the baby, and had no trouble with the breast. Four weeks before her visit she noticed a tumor in the upper, outer segment of the left breast, increasing steadily, with considerable pain. There was a mass the size of an egg, hard and well defined, tender on

manipulation with some enlarged axillary glands. Under very active treatment including thyroid and iron and 50 per cent ichthyol locally, with Hebra's diachylon ointment later, the lump disappeared slowly, and just a year subsequently it was recorded that the breast was perfectly normal with no trace of the tumor nor axillary adenopathy. She was again confined of a healthy child June, 1916, and the surgeon who had made the orignal diagnosis of cancer and urged immediate operation, reported the breast perfectly normal. Seen and examined very recently she still remains free from trouble over 7 years after her first visit.

CASE XI.—*Primary cancer of the breast.* Mrs. I. T. G. aged 43, first noticed a lump in the left breast 2 weeks before her first visit May 7, 1905. This had been diagnosed as cancer by at least four medical men, one of them a prominent surgeon in Hartford, who urged immediate operation. When first seen there was a hard, sharply defined mass, 1½ inches in diameter, which gave a darting pain at times and was painful on light handling. With vigorous treatment the change in the tumor was remarkable, and at the end of 8 weeks it was recorded that there was no trace of tumor, that both breasts were alike. She was a large flabby woman, weighing 207½ pounds, of the kind that do so badly after operation. With absolute faithfulness to treatment she weighed 199 pounds 2 years later, with no return of the breast trouble. She was last seen for another difficulty 5½ years after her first visit, and the breast was found perfectly normal.

Some cases of post-operative cancer were reported which showed the stricking benefit of proper medical treatment. But it would be unreasonable to expect any startling effects in patients who had become thoroughly saturated with the poisonous hormone generated by repeated new developments of cancerous tissue, and when there were numerous metastases, not only in internal organs and lymphatic glands, but also with cutaneous nodules, produced in various parts of the skin through capillary infection. And yet in most of the cases there has been

a betterment of condition as to color, weight and so forth, which sometimes seemed to encourage one that the real disease would be conquered. But although life has frequently been prolonged far beyond what might have been expected, and discomfort and distress have often been greatly lessened or entirely abrogated, without a particle of morphine or opiate, we have not yet reached the position of checking and curing far advanced cancer, to a degree at all comparable with what can be accomplished in its early stages; the benefit of this line of treatment, however, was strikingly seen in the following case, recurrent after four operations.

CASE XII.—*Recurrent cancer of the breast.* Mrs. D. S. aged 53, first seen July 6, 1916, in private practice. Over 5 years previously, a small pimple as she called it, appeared on the left side which was left alone until Jan. 21, 1914, when the left breast was removed by a surgeon of prominence and all seemed well for 6 months. There was then some return and a second operation was performed in January, 1915. There was again a return, and a third removal was done in April, and a fourth operation by the same excellent surgeon in August, 1915, but the wound had never healed since. There had never been any attempt at dieting or medical treatment, or any effort to check the cause producing the malignant growth.

Since January, 1916 many cutaneous nodules developed around the open area, which when first seen presented a characteristic ulceration 8 inches long by two or three wide. The axillary glands were enlarged and the left arm, which had been greatly swollen since the first operation was hard, tense, and painful, and of course helpless. Her weight which had been 168 pounds 3 years previously was reduced to 132. She was always constipated and the urine deficient and irritating and frequent at night. She has long suffered from rheumatism and also severe headaches up to the menopause, 7 years before her visit.

Under rigid treatment she began to improve much in her general feelings, the arm became soft and somewhat flabby and

the nodules which had been painted with 50 per cent ichthyol, were less prominent. The urine, which at first was only 26 oz. in 24 hours, with great deficiency in solids, was brought up to 45 oz., with the proportion of solids to her weight about right. The saliva which was very acid became less so, though still acid and scanty and the mouth dry. After about 5 months I find a record that she felt so very well that her friends think that there can not be much the matter with her. There was still considerable ulcerating surface, but painless and with some islands of healing; there were still metastatic nodules in the skin, though fewer, and the arm, though still swollen, was useful, smaller and no longer tense, the flesh shaking when the arm was moved.

The difference between her condition and what she would have been without treatment can hardly be imagined, for within those 5 months she would probably have been in her grave, whereas during all this time she traveled back and forth from her home some distance away in New Jersey, to my office, a happy woman, without pain. Of course she never took any opiate. About this time she fell and broke her hip, and after some months I was asked to go out and see her, and found that the neglect of treatment had allowed the disease to assert itself, and she was in a poor condition and I think she died some weeks later.

CASE XIII.—*Post-operative cancer of the breast.* Mrs. P. A. aged 46, a Bohemian woman came to my medical clinic at the hospital July 26, 1916. She had noticed a lump in her left breast only 2 weeks before it was removed in the New York Skin and Cancer Hospital, 2 years prior to her visit. Three months later the right breast was also removed on account of a lump there. All seemed to go well until about a year later when cutaneous nodules appeared on the chest, around the scar of the former operation, which nodules increased in number and size, until when first seen there were fully fifty of them, forming a veritable *cancer en cuirasse.*

Under active treatment with thiol in olive oil 50 per cent,

painted on night and morning, she improved at once. Later some of the nodules ulcerated but healed shortly when treated with thorium paste, diluted 25 per cent, so that when shown at my lecture something over 4 months later, on passing the hand over the surface there was hardly a trace of the nodules which were once so abundant. All who know anything about the ravages of cancer will realize the difference between her condition then and what it would have been under ordinary circumstances. She had no pain after beginning treatment and no opiate.

CASE XIV.—*Inoperable cancer of the breast.* Miss J. M. aged 53 was transferred to my medical service in the ward of the New York Skin and Cancer Hospital Aug. 26, 1914, as quite inoperable. One year before there occurred an enlargement of the right breast with general hardness, which broke down 9 months later. There was some pain from the beginning which became severe and constant. When first seen there was a great fungous mass, about 6 in. in each diameter, with a profuse and very offensive discharge; she was very weak, with a septic temperature of 101° and over, and complained greatly of pain, for which she was under morphine; there had been no operation.

For a while under active dietary and medicinal treatment of various kinds she seemed to do remarkably well, the color and weight improving, with less pain and very comfortable nights, without any morphine or hypnotic, which she had previously been taking. Shortly her weight, which was 106½ lb. at first, rose to 110¾ lb. and October 28th it had risen to 111¼ lb. By October 10th the wound was secreting very little, she slept well with no opiate, and complained little of pain day or night, and it seemed as if the disease was being overcome, as there was some evidence of cicatrization in places. But she then had several severe hemorrhages, and the hemoglobin which had been 80 dropped to 60 and the red corpuscles to 2,100,000. She rallied however, under an intravenous saline injection and the Murphy drip, with proper medication, so that the hemoglobin rose to 75 per cent and the red corpuscles were actually 4,110,000. But

kidney trouble set in, and with ups and downs she finally succumbed on July 3, 1915, about a year after entering the hospital.

The case was watched with great interest by the attending staff, and careful studies of the blood and volumetric analyess of the urine were made weekly. The urine was generally scanty, running even as low as 9 ounces a day, of fair specific gravity and it was very hard to raise the total solid urinary output to anywhere near the normal standard. The saliva, tested and recorded ¼ hour before and after each meal, was commonly acid, often strongly so, though at periods it would be neutral, and occasionally become alkaline for a while under active treatment. The case was an interesting one, but hopeless from the first, and any other, end could hardly be expected. But certainly life was prolonged and much comfort secured as to sleep, almost total abolition of pain, without morphine, and diminution of the offensive discharge, etc.

Two cases of cancer of the uterus were reported which were of great interest as they were entirely inoperable and have remained well a long time.

CASE XV.—*Inoperable cancer of the uterus.* Mrs. F. L. A. aged 48, seen first on Mar. 21, 1916, had had four children 22, 20, 17 and 12 years of age, also a miscarriage 9 years previous, and the menopause had occurred suddenly 2 years before. She had never had trouble with confinements and never laceration. On February 24 a few drops of bright blood appeared, and she was seen that afternoon by a competent surgeon in a distant city, who sent her to me; he had found an inoperable cancer of great extent, which diagnosis was confirmed by others, who refused to operate. The accompanying pathological report read "About one-third of cervix destroyed, vaginal wall involved, right broad ligament infiltrated, curettings revealed squamous-cell carcinoma in numerous slides. From histological appearance I judge that the cancerous process is developing rapidly." The slides brought to me were submitted to Dr. H. H. Janeway who confirmed them to be "rapidly

growing, malignant epithelioma." Those who saw the patient on February 24 gave the opinion that she would hardly live 6 months.

On June 2, not 3 months after her first visit she was again examined by Dr. Janeway who reported "I find no ulceration whatever on the cervix or vagina, the uterus is movable and of normal size. There are no evidences of any disease remaining which can be detected by examination." On July 7 he wrote "I have examined Mrs. F. L. A. again and find that there has been no return of the evidence of the disease." On October 20 he wrote "Mrs. F. L. A. appears to be absolutely free from disease." This was confirmed by her own surgeon. It is now at the present writing almost 5 years since I first saw her, when she was given hardly 6 months to live. A very recent letter dated Feb. 14, 1921 states that she "still enjoys the best of health," 5 years, less 10 days, from Feb. 24, 1916, when she was given hardly 6 months to live by several competent surgeons and a good pathologist. There is no reason to believe that she will not remain so, as she is an intelligent and most faithful patient. When last seen she weighed 110 lb., her normal weight before her sickness was always 93 lb. During the treatment she traveled back and forth from Bangor, Maine, repeatedly without fatigue.

The medical treatment and voluminous notes can hardly be compressed here, but from first to last she has used the douche of carbolic acid and biborate of soda, as described in the previous chapter, with, of course, complete dietetic and varied medical treatment and one application of radium, 300 millicuries, for 16 hr. On March 25 about 4 months after beginning treatment her hemoglobin showed 80 per cent and red blood cells 4,500,000, leucocytes 5,800, of which polynuclears 64, lymphocytes 27, transitional 8, and eosinophiles 1 per cent, and she was apparently as healthy a woman as is often seen. I realize that all this seems almost incredible, but it can be easily verified by her own surgeon and by many witnesses.

CASE XVI.—*Inoperable cancer of the uterus.* Mrs. H. F. J. aged 52 first seen Aug. 3, 1916. This was a very similar case, also sent from Bangor, Maine. She had three children, 27, 25 and 16 years of age. The menses had been regular up to April 15, then nothing to July 1, when there was a clotted flow, checked by treatment, which had returned in 2 weeks with pain, after an auto ride. On July 14 she was examined by two surgeons who found inoperable cancer of the cervix, which was confirmed by Dr. Janeway on July 31, who reported "cancer of the cervix and vaginal canal with some cauliflower excrescence." She received one application of radium 300 millicuries to the canal and 120 to the cervix for 12 hours.

Not to dwell long on the case, under rigid dietetic and medical treatment and morning and night douches as in the other case, she improved every day and on September 30 reported as quite herself again. On October 20 Dr. Janeway reported that Mrs. H. F. J. was free from disease, although the healing was not quite complete, and reports from her friends 2 or 3 years later state that she seems perfectly well.

A remarkable case of sarcoma was recorded, which yielded to pretty much the same line of dietetic and medical treatment, and was followed for fully 3 years after, remaining well, with a perfect skin graft covering the operative deformity.

CASE XVII.—*Post-operative sarcoma of the jaw.* Miss R. L. aged 19, entered my service in the New York Skin and Cancer Hospital July 24, 1916 weighing 89½ lb., she had formerly weighed 120. The story as given in volume II is a long one and difficult to abstract.

Three years previously a small lump appeared beneath a pigmented mole, which had long existed, an inch or so below the right eye, and grew until about an inch in diameter, movable and painless. She had been submitted to various surgical measures, and radium had been used for 18 hours on March 1, which seemed to light up the trouble terribly. Finally an extensive operation was performed in another hospital, in which the right upper maxilla was removed, together with the

tumor, all of which healed. Four weeks before being seen a pin-hole opening formed in the cicatrix, which increased rapidly in size until admission. The microscopic examination of the portions removed at the operation showed the disease to be sarcoma.

On entering the hospital there was an opening in the right cheek something over an inch in diameter with ulcerated edges, and a mass of ulceration within giving forth a foul odor; from the upper margin of the opening there was a mass of dead bone of the zygoma hanging. She was thin, pale, and cachectic, with 85 per cent hemoglobin and 3,620,000 red corpuscles. She was placed on the same dietary and medical treatment as the carcinomatous cases, and the frequent use of the wash mentioned in the previous chapter, kept continuously applied on pledgets of absorbent cotton, renewed frequently. The change in her general and local condition from the first was something remarkable. The discharge and foul odor from the ulceration ceased shortly, and within a few weeks the cavity and edges of the opening showed a healthy condition, with evidence of cicatrization.

To be brief, she gained daily from the first visit, even several pounds in some weeks, being weighed every week in the same wrapper by several doctors and nurses, who also took great interest in the case. Finally I weighed her myself at 130 pounds which was over that called for by her height and age, and 10 pounds more than she had ever weighed before, and a contrast to the 89½ pounds which she weighed when first seen.

The blood, which was carefully studied weekly, steadily improved, until on September 18 the hemoglobin stood at 95 per cent with 4,600,000 red corpuscles and 8,000 white, and on November 10 the hemoglobin was 100 per cent, and the erythrocytes 4,700,000. On November 14 all evidence of the disease had so completely gone, and the edges of the opening were so perfectly cicatrized, that Dr. Semken prepared a thick flap on the arm, the raw surface of which he lined with a Thiersch graft, and on November 24 he attached this over the

opening, after scarifying its cicatrized edges. Every stitch took perfectly and I showed her at my lecture with excellent cosmetic results. She was watched for a couple of years when she ceased coming to the clinic, but she kept well in every way, the skin-graft remaining perfect.

In the next volume, "The Medical Treatment of Cancer," 18 more cases were reported, which may be more or less fully quoted.

CASE XVIII.—*Primary cancer of the breast.* Mrs. S. J. aged 33, first noticed a lump in the right breast 2 months previous to her visit at my hospital clinic, Feb. 28, 1917. This steadily increased in size until seen, when it was fully an inch and a half in either direction, in about the middle line above the nipple, with sharp rather hard edges, and a small palpable gland in the axilla; she had been having sharp pains, radiating from the breast to the axilla. For future reference I called in the surgeon in attendance, who at once recognized it as carcinoma and strongly urged immediate removal, as the only hope.

She was extremely constipated, the mouth dry and the saliva acid. Being placed on the usual dietary and medical treatment it was recorded in 2 weeks that she felt better than for a year. The lump was materially smaller, though the edges were sharp and nodular. There was no pain, except on extreme exertion in doing her own housework and caring for two small children. She was very faithful to treatment, generally coming every week, and 6 months later it was recorded that the mass had markedly diminished, being about an inch in diameter, very shallow, and with absolutely no pain. Six months still later practically nothing could be felt, no adenopathy. A little over a year after the first visit, a physician visiting the clinic was told that she had cancer, and was asked to tell which breast had been affected. After careful examination he decided that it must have been the left breast, instead of the right, as there was a slight chronic mastitis there. At intervals later, four other physicians and surgeons made the same mistake. Within the first year she had

been pregnant, the child dying soon after birth. She was recently at the clinic, nearly 4 years after her first visit, and there was still nothing in the right breast and no adenopathy; she had given birth to still another living child not long before.

One of my assistants reported to me a similar case, where the cancerous mass had disappeared under the same treatment, and after a year a doctor made the same mistake after examining both breasts.

CASE XIX.—*Primary cancer of the breast.* Mrs. C. M. S. aged 35, a private case, seen first Jan. 15, 1917. Six months before she had had a severe blow on the right breast, which soon enlarged and was painful, it had been poulticed and iodex applied. When first seen there was a lump the size of an English walnut, quite well defined, with darting pain; no axillary glands were felt, though small enlargements developed 2 weeks subsequently, when she had neglected treatment. Two months later the right breast felt almost the same as the left, though there was still a sharp margin in one place. When last seen, about 18 months after the first, the right breast was normal, but there was a little caking in the left breast, and some little feeling in both breasts during menstruation. This was a difficult case to handle, as she had much care, work, and worry, keeping a boarding house, with her mother sick at times. She had gastric disturbance, and was much constipated before treatment.

CASE XX.—*Primary cancer of the breast.* Miss G. D. aged 45, was under treatment for eczema, which had about disappeared, when on Jan. 22, 1917, she called my attention to a large lump in the left breast, which had existed for 6 months or more. It was just above the nipple, the size of an egg, with sharp edges, some adherence to the skin, some glandular enlargement, and sharp pains occasionally. She has been a faithful patient, under frequent observation, and after about a year it was recorded that the lump was not one-half the size, was softer and without any sharp edges, and that the glands could hardly be felt; there was scarcely any pain expect on great exertion. She kept her weight and color well and was very active.

Unfortunately she has not done so well of late, now nearly 4 years after the first; for, in spite of faithful treatment, including *x*-rays and also a period of the Williams' proteal treatment,[1] the mass has remained and rather increased, and also the axillary adenopathy. We can find no reason for the rebelliousness, but it is the rare exception, and only shows that we have not yet reached the desired goal.

CASE XXL—*Primary cancer of the breast.* Mrs. G. K. L. aged 59, wife of a physician, was first seen Aug. 30, 1918. Four years previously a lump was noticed in the inner, upper quadrant of the left breast, after a slight blow some time before. Since then the breast has felt heavy, and gradually the mass increased in size, until it was about 3½ inches in diameter, hard and characteristic, with some enlarged glands in the axilla. Under very strict diet with medication, in 3 months the tumor had diminished one-half the size and was much softer; she had gained 4 pounds was of a good color, and felt better than for a long time. Seen rather recently the breast was entirely normal and the adenopathy gone, 3 years after the first visit.

CASE XXII.—*Primary cancer of the breast.* Miss L. M. aged 55, had noticed a small lump in the left breast 14 months before the first visit, Nov. 4, 1918, which had been kept secret until a week previously. It was painful from the first, the pain increasing as the mass grew, until of late it had caused sleepless nights. When first seen there was a large mass, 2 or 3 inches in diameter, in the upper, inner segment, near the nipple, with a purplish-red, protruding area an inch in diameter. The whole breast was tense and the axillary glands enlarged and painful on handling; there was no supra-clavicular adenopathy. The almost immediate relief to many symptoms from a rigid diet and appropriate medical treatment was surprising. In a week the tenseness of the breast had materially lessened, as also the pain. Two weeks later the purplish color had almost gone and the axillary glands had diminished one-third or more, all verified by a physician who watched the case with me. She was then lost sight of, for

[1] WILLIAMS, "The Proteomorphic Theory, Etc." New York, 1918.

pecuniary reasons, after being charged not to discontinue any of the treatment.

CASE XXIII.—*Late, inoperable cancer of the breast.* Mrs. L. H. aged 36, seen first Sept. 20, 1918, had a lump in the left breast for 14 months, which had gradually increased in size, with darting pain, disturbing sleep for the past 6 weeks, it beginning 2 weeks after a severe blow on the breast. She had seen three surgeons of prominence, who decided that it was too late to operate. When seen there was a large hard mass in the upper, outer segment of the left breast, 2 or 3 inches in diameter, adherent to the skin for an inch or so, with axillary adenopathy, and subsequently some supra-clavicular adenopathy. The saliva was acid and the urine secretion insufficient in its solid ingredients.

For a month or two she did well under active dietetic and medical treatment, gained a little in flesh, and slept well without pain, but had some darting pains in the daytime. As she and her husband were restless under the treatment given, and insisted on an operation, I consented to have the breast and glands removed by "chemical extirpation," as I have had some of my cases so treated at the New York Skin and Cancer Hospital by Dr. Strobel, with good results, as described later, in another place. This was done on October 31, but the skin-grafting was delayed until November 26, owing to the difficulty of reaching the axillary glands. The graft took perfectly over the breast area, giving a smooth, healthy surface, leaving some raw space in the axilla, to be treated later. The slough there separated on December 8, and skin-grafting was done December 13, and took well. Later records state that the axilla also healed.

After this she did well, walking out, and in March went West for several weeks. But some metastases appeared in the skin and glands, for which she had strong radium treatment by Dr. Janeway, with little effect, and she gradually failed in strength, undoubtedly from internal metastases, and died on July 12. The saliva continued acid, and the urinary function was poor to the last, in spite of careful treatment. The disease had

evidently become very wide spread, before coming under treatment, showing, as quoted elsewhere from Dr. Levin, that the bones and other blood-making organs were very early involved.

Some cases were also reported to illustrate what can be done for patients where the disease has recurred after one or more surgical removals.

CASE XXIV.—*Post-operative cancer of the breast.* Miss H. K. aged 45, first seen Dec. 17, 1917, had noticed a lump in the right breast in April, 1915, which was removed surgically within 3 months, with a good axillary operation. About the middle of June, 1917, she noticed a lump in the left breast, in the outer, lower segment. When seen there was a mass the size of an egg, hard and with some irregular nodosities, the glands along the pectoral muscles were enlarged, with some doubtful axillary adenopathy. She was always constipated, and the saliva was acid, the menopause had not yet occurred. Placed on strict diet and proper medication, she was very faithful, though living in a distant city, coming many times to New York for treatment. Within a few months the tumor became materially smaller and soft, and no adenopathy could be detected. Like so many of these cases, she was lost sight of, but there is reason to believe that all treatment was continued and that the disease passed away, for the last record was that she "feels very well indeed."

CASE XXV.—*Post-operative cancer of the breast.*—Mrs. B. E. aged 49, had the right breast removed, by a very complete axillary operation for adeno-carcinoma, by one of the leading surgeons of New York, on Sept. 27, 1916. She had never thought of the breast until 5 or 6 weeks before the operation, the lump beginning the size of a walnut and growing rapidly in extent, with glandular enlargement.

Four months after the operation the surgeon sent her to me, on Jan. 30, 1917, with recurrence in the axilla and a swollen arm, with pain and aching. She had born three children 21, 20, and 13 years of age; the menses had ceased 5 years. She had long had persistent constipation, depending on cathartics

all the time; she had also persistent insomnia for the last year or two, lying awake until 2 or 3 a.m.

She was a very faithful patient, coming weekly from a neighboring town, and for a while seemed to do well, under varied treatment to meet existent conditions, but taking most of the time the mixture of acetate of potassa, nux, cascara, and rumex, often referred to. But in spite of faithful treatment cutaneous nodules kept appearing, though very slowly, and some adenopathy, which painting with ichthyol, as mentioned, and *x*-ray, seemed to control. On October 25 it was recorded that she felt very well, had a great appetite (for the "green card diet") and "sleeps wonderfully, with no nocturnal urination," with which she had formerly been troubled; she never took morphine or any opiate. On November 28 there was "very great improvement," the cutaneous nodules had gone, also certain areas of diffuse redness which had appeared; and the enlarged gland which had formed in the axilla was less.

But 6 or 8 months later the disease seemed to increase, in spite of her diligent attention to every detail of treatment, and slowly signs of internal metastasis occurred, as well as supraclavicular adenopathy and sternal nodes, for which radium emanation tubes were inserted by Dr. H. H. Janeway, without appreciable benefit. Slowly evidence of pulmonary involvement came on, with a cough and distress, and the chest was tapped several times and large amounts of fluid, up to 72 oz., removed. She finally passed away Jan. 19, 1919, 2 years after her first visit, and 2 years and 4 months after the operation.

While the ultimate result was not such as was hoped for, or even expected by the surgeon who performed the relatively early operation, the case illustrates what was referred to in Case XXIII, that probably there was at the time of operation already a far more extensive spread of the disease in the blood-making organs than was suspected. The question also arises as to the effect of traumatism during operation, in spreading the disease through cut lymph- and blood-vessels, and whether thorough dietary and medicinal measures would not have

checked the whole process at the first, as has occurred in so many cases, of which a few illustrations have been given. It was however, a comfort to have her husband, an unusually intelligent gentleman, write to me when announcing her death, "I am fully convinced that you have added considerable to her life, in comfort and length of days."

CASE XXVI.—*Inoperable cancer of the uterus.* Mrs. N. R. M. aged 55, first seen Dec. 27, 1917, had been examined by a number of gynæcologists, who reported inoperable cancer of the uterus, with not over 6 months to live. There was "a great ragged crater, extending back to the rectum, almost into the bladder and laterally to the pelvic wall." All this was confirmed by able New York surgeons, who gave her but a few months to live. For 9 months she had had a profuse, watery vaginal discharge and occasional bleedings, with pain over the pubis, and on entering the hospital the discharge was bloody and offensive. She had always been habitually constipated, and the saliva was found to be very acid.

She was treated as other uterine cases already reported, dietetically and medicinally, and with a vaginal douche of very hot water, one pint, with half a teaspoonful of carbolic acid and two of borax, thrown in deeply and strongly with a Davidson bulb syringe, night and morning and later at noon. Within about a month there was a marked improvement in her looks and feelings. The douche, which was frequently examined, came away clear, with no blood and only with a few shreds, and with no odor. The urine, which had been scanty, increased to quite the normal amount and character, and the saliva became neutral. She slept well most of the time, without much pain in the pubic region, and with no opiate, and it almost seemed as if she would pull through.

But the dullness above the pubis slowly increased, with bowel obstruction and tympanites, the urine became scanty and albuminous, with swollen legs and feet, and other signs of kidney involvement. The blood, which had been in fairly good condition, showed great degeneration, with only 50 per

cent hemoglobin, 1,350,000 erythrocytes, 13,000 leucocytes, of these, 70 per cent polynuclears, 4 transitional, 1 eosinophile. She passed away very peacefully on August 16, without requiring or having taken a particle of morphine or other hypnotic, except occasionally a small dose of chloral and bromide, at night, when sleepless.

When we consider the original condition, and the course of the disease in this patient, with her constant hopefulness and comfort during these 8 months, instead of six months or less, as prophesied, as compared with the agony often suffered, and the morphine commonly required or taken, the benefit of careful medical treatment is clearly seen. With the enormous infiltration of the abdominal viscera, and the great ulceration, the case was, of course, hopeless from the beginning.

CASE XXVII.—*Inoperable cancer of the uterus.* Mrs. T. F. V. aged 64, who came first to my office Nov. 23, 1917, was a very similar case, fatal but with like satisfactory results. She had had backache and vaginal hemorrhage for 3 months before coming under treatment, and had not felt well since June, losing 20 pounds and then weighing 107. Examined by a surgeon in Maine, and a gynæcologist here, she was found to have extensive cauliflower ulceration of the cervix, quite inoperable. She was always constipated, the urine always scanty, and the saliva was very acid.

Under careful dietetic and medical treatment, with the same vaginal douche, as in the other cases, she improved greatly, gained 2 pounds, and "felt like a different person" within a week, coming frequently to the office. She had relatively little pain, never required an opiate, and 2 months from the first she said that she "felt more free from pain during the previous week than for weeks or months." The douche came clear, without blood. Two weeks later she had a strange attack, with suppression of the urine, and became irrational, and was moved to the Hospital. Two weeks later she was perfectly rational, said she had no pain, but wanted to go home to Maine. She reached home in comfort and died peacefully 25 hours after reach-

ing there, Mar. 21, 1918. Thus she lived 4 months in comfort, not taking a particle of morphine or other hypnotic, and died without pain in peaceful sleep, as reported by letter. The case of course was hopeless from the beginning.

CASE XXVIII.—*Cancer of the stomach.* Mr. B. W. aged 56, had been sickly and not working for a year before his first visit, Aug. 30, 1916. He had seen many physicians and surgeons, all diagnosing cancer of the stomach. He had long had pain in the epigastrium, with swelling and hardness.

On examination there was dullness on percussion near the pyloric region, and a mass could be felt. He had chronic constipation, with coated tongue, and was very weak, having lost many pounds. Placed on a rigid diet and strict regulations and instructions as to mastication and living, with medication, he improved greatly, looking and feeling much better at the end of the few visits he made from another city. Seven months later I learned from his brother-in-law, who had first brought him to my office, that the patient was very well and was working again. He may not have had real cancer of the stomach, though so diagnosed by many physicians and surgeons, but the history, and his whole appearance and the objective and clinical symptoms, with his cancerous cachexia and loss of weight, etc., indicated the probable correctness of the diagnosis, and the result certainly was most satisfactory.

CASE XXIX.—*Cancer of the rectum.* Mr. J. R. aged 42, first seen June 13, 1917. Two years and a half previously he had had an operation for ulcer of the stomach, and had had no trouble until November 16, when he was given Russian oil for obstinate constipation. About a month before his visit he was seen by a surgeon of prominence, who diagnosed cancer of the rectum, verified by microscopic findings, and advised an operation, which he refused.

When seen he was rather thin and haggard, having lost a good many pounds, pulse 92 and poor, tongue badly coated. His sleep was disturbed by having to get up three or four times at night for small, thready movements, of which he had from

12 to 15 in 24 hours. On examination there were no external signs of disease and digital examination revealed little, the disease being higher up. Under dietetic and other treatment the stools were soon reduced to 4 in the 24 hr., one of them at night, but still watery and generally with some blood, but no pain. Six months later he was often having formed movements of good size, and had been better every way during the preceding month than for a year, with only slight pain in the rectum occasionally. There was still a little blood passed, but on April 12, after not having called for a month, it was recorded that there was no blood in the passage.

When last seen, nearly a year from the first, he was in about the same condition, feeling well, and had been steadily at work in a dry-goods house, all the time while under treatment. In view of the unsatisfactory results commonly attained by operation, and the distressing condition of a patient when colostomy is performed, the results in this case may be considered satisfactory.

CASE XXX.—*Cancer of the prostate.* B. S. aged 54, had long had an enlarged prostate, with frequent urination day and night. He had lost flesh, especially during the 6 months preceding his first visit, Oct. 25, 1917. He had an earthy cachectic look, was thin and depressed. On examination by a surgeon the prostate was found enlarged, and the inguinal glands on both sides were much affected, forming great masses, visible to the eye, there being no lesions on the penis. Under the green card diet and internal medication there was a great change in a few weeks. The patient felt and looked much better. The glands in the groin had subsided greatly, and shortly thereafter they had quite disappeared, the cachexia was gone, and he had not an ache or a pain. He was lost sight of, and although written to he did not respond, but I learned by the daily paper that he died suddenly, certainly not from his cancer, many months after he was first seen. As in cancer of the stomach, a clinical diagnosis of carcinoma of the prostate is often difficult, but such a result of treatment was certainly

satisfactory, and preferable to surgical interference, with all its uncertainties.

CASE XXXI.—*Cancer of the kidney.*—Mr. H. H. B., aged 55, had been indisposed for a year, his color was bad, and work was difficult to accomplish, he being a clergyman in a far distant town. On Aug. 29, 1916 he passed blood in the urine, which continued, often coagulated, with much pain in the back. The *x*-ray showed nothing, nor cystoscopy, except blood coming from the right ureter. The right kidney was removed on September 1, in another city, and found to be enlarged many times, weighing over 2 pounds, and shown to be cancerous microscopically. He made a good recovery, and had no pain while in bed, 3 weeks, but on walking had pain in the left side, increasing toward afternoon, and making life miserable up to his coming under treatment, Jan. 20, 1917. He then weighed 174½ pounds, and was a large meat eater and very fond of milk and eggs. He had never had any restriction in diet, nor directions as to eating, nor other treatment of any kind.

Under strict "green card" diet and varied medication at frequent office consultations, with voluminous notes, and latterly by correspondence, he has now been under my care for over 4 years. He has been able to do his work all the time, has gained 14½ pounds in weight, and for long periods has been free from pain, although at times when overworked or strained he has pain over the remaining kidney. Notes from time to time record that he was "doing normal work," "stands well the hardest strains," "felt better than for years," "never had so good a color or circulation," etc.

The urine has been watched and actually measured and recorded daily during all this time, and frequently analyzed volumetrically. It has commonly averaged over 50 oz. daily, the various ingredients are generally about normal, except that the urea is apt to be low, owing to his vegetarian diet. He has been, and I believe will be very faithful to treatment, which has certainly prolonged his life and usefulness, and given great comfort and ease. How long it will be necessary to continue

active treatment it is difficult to say. A relapse to his former method of living, and entire neglect of protective treatment, might naturally be expected to again induce again a serious involvement of the remaining kidney. He has, of course, never taken a particle of morphine or other hypnotic, the pains occurring at times being largely relieved by the frequent use of aspirin. A very recent medical letter, 4 years after first visit, reports a continued well being, but full treatment is still continued, as he has repeatedly had threatenings of trouble when careless.

CASE XXXII.—*Cancer of the bladder.* Mr. G. W. H. aged 68, had been under my care for a number of years, for various difficulties, when on Mar. 14, 1914, he brought two specimens of urine with clots of blood and a considerable amount of albumen in the evening sample. There had been no special pain in the back, nor on passing urine. The urine cleared, but 3 days later he was again passing blood and was feeling weak, and thought he had lost 2 pounds in weight. He had to urinate every 2 hours, twice at night; the blood appeared at the end of urination. Blood pressure 160 systolic.

On April 2, he was cystoscoped by Dr. A. R. Stevens, who found the bladder mucosa normal, except near the left ureteric orifice. Just above this there was a small, defined, sessile mass, with small blood vessels over its surface, pretty typical of early carcinoma of the bladder wall. Radical excision was advised, or else fulguration. Declining these very positively he was treated medically for a month, when he yielded to my persuasion and on May 7, Dr. Stevens treated the lesion by fulguration, which was repeated several times. On October 22, he was cystoscoped and no sign of recurrence was seen, only a scar. Later there appeared to be some recurrence which was treated, and repeated cystoscopy by three urologists, showed no signs of recurrence up to the time when his case was reported, nearly 5 years after the first symptoms were observed.

But some time later blood again appeared in the urine and he was found to have a large, elastic prostate ("not carcinoma") and prostatectomy was performed. Being still under constant

observation and medical treatment, he has, however, some trouble with urination, sometimes with a little blood, said to come from the deep urethra, but as far as can be learned, with no recurrence of the bladder trouble, now nearly 7 years since its first appearance. During all this time, under strict regimen and varied medication, he has maintained his general health, color, and weight and has pursued his usual business.

CASE XXXIII.—*Cancer of the tongue.* Mr. K. M. A. aged 59, first seen Sept. 11, 1918, first noticed an irritation of the right side of the tongue, from a broken tooth, in May, and on May 11 it was "operated on with a knife," and healed, so that he went to work on May 20, with no pain for 3 weeks. It then began to ulcerate and "a knife was again used and it was cauterized" on August 5, and he left the hospital on August 11, 5 weeks before his visit to my office. Since that time the trouble had been increasing rapidly, until when first seen the tongue was enormous, filling the buccal cavity, with a large, ulcerative patch, an inch and more wide with sharp, hard edges. The sub-maxillary glands were large, hard, and matted together, and the case was considered inoperable by the surgeons whom he had seen. The saliva was very acid, and the urine contained much indican, also oxalates and phosphates.

Being placed on a rigid diet, with absolutely no smoking, alcohol, coffee, or tea, and with a mixture of acetate of potassa, nux vomica, cascara, and rumex, the improvement began almost at once. He also used as a mouth wash a saturated solution of bi-carbonate of soda, diluted more or less if necessary, held in the mouth for some minutes, quarter of an hour before and after taking food. He could take only liquid food, having great difficulty in swallowing. By the end of 3 months the change was most remarkable. The tongue had greatly diminished in size and the ulceration had actually ceased, though there was still hardness. He swallowed much better, the jaws, which at first opened only a little, opened much wider, he could chew some, and the glands beneath the jaw were much smaller and less adherent, and quite movable, as was verified by two

physicians. He remarked the "great improvement in his condition" and his wife said "the change from the first is marvellous." He still complained of some pain in the neck, running up to the head, but he has never taken any morphine or any anodyne. When seen later the improvement was still more marked.

But, alas, the knife and cauterization had already done their deadly work, and deeper glands and organs became involved, and I was summoned to Brooklyn a month or two later to find the neck enormously swollen, with abscesses forming, though the tongue remained relatively well. I did not hear from him again and I presume that he succumbed to the disease.

In this instance a benign lesion on the tongue, from a ragged tooth, was transformed into a malignant one by injudicious treatment, and is in striking contrast to a case which will be reported later.

CASE XXXIV.—*Cancer of the tonsil.* Mr. F. F. aged 72, came under observation and treatment in my office on Oct. 2, 1918. For 3 months he had felt a pressure of something wrong in the right side of the throat, and on September 3 had had some sort of an operation from within, the nature of which could not be determined. He had seen many physicians and surgeons who advised a complete operation from the outside, that was refused. A Wasserman had been taken and found negative.

On examination the right tonsil was found to be the seat of an ulcerative process, nearly an inch in diameter, very hard to the touch, and sharply defined, with hard edges and considerable inflammatory action of the surrounding parts, reaching almost over to the left tonsil. The glands beneath the jaw were greatly enlarged, the size of a large walnut, but rather movable. The saliva was very acid. He had been in the habit of taking beer twice daily, and smoking, which, of course were stopped, and he was placed on a complete dietetic and medical treatment, with the soda gargle, held a good while in the throat, quarter of an hour before and after each meal.

Under these measures he began to improve from the first, and within two months the ulceration had about ceased, and

much of the adjoining inflammatory action subsided. The hardness had largely gone, but the edges were still sharp and somewhat hard. The gland in the neck had diminished to the size of a small almond. He remarked "I feel all right and have nothing to complain of." A little later it was recorded that there was still slight marginal hardness, but superficial, and the gland was smaller and freely movable. "I feel perfectly well," "find no complaint of any kind."

This patient has been under constant observation and treatment for 2 years more since then reported, working at his regular employment, and has repeatedly used much the same expressions, quite a contrast to the result commonly observed in such cases. But in the last 6 months he being now nearly 75, he has been failing, possibly from neglecting some item of treatment, for he can call from another city but seldom, for financial reasons, and the disease has attacked the other tonsil, with much glandular swelling on the left side, and he will probably succumb to the disease before very long. Over 2 years of comfortable life, however, have been secured in spite of the injury inflicted by "some sort of an operation from within" on Sept. 3, 1918, for if left alone, with the progress the disease was making, he would probably have been in his grave long ago.

CASE XXXV.—*Cancer of the lip.* Mr. W. H. N. an unusually intelligent gentleman aged 45, from Boston, had a slowly growing cancer of the lower lip for several months, for which an immediate radical operation was insisted on by several prominent surgeons there, and by his friends.

When first seen Feb. 6, 1917 there was an oval, epithelioma-tous lesion, just to the left of the medium line, about a half an inch in diameter, and raised a line or so, as characteristic as could be, with possible slight adenopathy below the chin. He was placed on the rigid diet and medication, with no smoking, liquor or beer. The surface was kept covered night and day, even at meal time, with an ointment (℞ Ichthyol ʒss Zinci oleat. ʒss Unguent. aquæ rosæ ʒi). This was spread, with a steel spatula, on the thinnest possible portion of absorbent

cotton, large enough to fully cover the sore, pressed down, so as to make it adhere firmly, and was replaced twice a day or oftener if desired, and the new plaster was to be spread in advance and reapplied instantly, never leaving the sore exposed for a moment. I have used this method in many cases, and it is surprising how deft patients become in keeping on the application, even during meals and at night.

In a week there was a decided change, the mass being much softer, though, of course, still with decided induration. This ointment was changed somewhat from time to time, with occasionally 1 per cent of powdered salicylic or pyrogallic acid added, reverting at times to the first ointment, or to a calamine and zinc ointment, when these seemed a trifle irritating. Nine months later he kindly presented himself at my lecture at the New York Skin and Cancer Hospital with the disease about gone, and gave the physicians a remarkable talk on cancer of the lip and its treatment. He stated that he was a Harvard graduate and had studied medicine a while, and knew what he was talking about, from wide acquaintance with physicians and surgeons, and urged them seriously to follow up the line of medical treatment of cancer if I were called away.

He became deeply interested in war work, traveling over the country for the Government, and I did not see him, but a year later he wrote enthusiastically about his case. Very recently, nearly 4 years after first seeing him, he hailed me in the street, and we spent some time together; the lip was and had long been perfectly well.

CASE XXXVI.—*Cancer of the lip.* An interesting case was overlooked in my previous report, of a Mr. V. F. aged 40, who came to me Oct. 17, 1915. He had a very characteristic cancer of the right side of the lower lip, firm and moderately ulcerated. Under diet and careful medical treatment, internal and external it steadily improved, until on April 10, 1916, it was recorded that it was well, with absolutely no hardness left. A year later another patient with lip cancer looked him up, and the man actually could not remember just where the lesion had been,

so perfectly well was he. He was a butcher, who had been in the habit of consuming much meat, which, of course, was stopped entirely, and replaced by an absolutely vegetarian diet.

We have now reviewed the histories of 36 cases of undoubted cancer, some shown by microscopic examination to be carcinoma, and all of them diagnosed as such by at least one, and often by many other physicians and surgeons, while the cases recurrent after operation are unquestionable. The results of medical treatment speak for themselves. A large share have clinically recovered, some have died, especially those who had had from one to four surgical operations. Some were absolutely hopeless when first seen, but even in the worst cases there has been an amelioration of distressing symptoms and a prolongation of life which have been indeed gratifying. When all this is compared with the ordinary course of cancer cases, it does seem that we are at least on the right track concerning the treatment of this dire disease.

In the second volume I presented a table of the cases which had been observed up to Jan. 1, 1917, to this I will now add those seen in private practice from that date to Jan. 1, 1921, of which full notes are before me. It is understood of course, that not all of them have been under complete and satisfactory dietetic and medical treatment. For many cases were seen but a single time in consultation, many made but one or two visits, and evidently were not satisfied with the outlook; some have wearied with the restraint and the prospect of prolonged treatment, and undoubtedly many have not carried out every item of treatment perfectly; again, some have thought that there was not rapid enough progress, and some have been drawn away by the lure of surgery, hoping that in their case at least it might possibly be successful, and others have been led to try *x*-ray or radium.

But a very considerable proportion of the patients have been faithful to the end, and have warmly appreciated the results obtained. I may truly say that I have not selected my cases, but have always accepted any and every one, however hopeless

it seemed, because from experience I knew that some measure of benefit would be obtained. The cases which have been and will be presented, are assuredly selected from among very many others more or less similar, to illustrate certain features which might help the profession in mastering the disease. In a very few instances indeed have I yielded to the importunity of the patient, the physician, or friends and have acceded to having a surgical operation performed, and I do not by any means deny that this may possibly be advisable, in certain rare cases. But it is in the early cases, which medical men are so apt to think as most suitable for operations, that we find the best, and almost invariably successful, results from medical treatment.

During the past 4 years, from Jan. 1, 1917, to Dec. 31, 1920, there have been in my office recorded histories of cases of malignant disease, as follows: Carcinoma 187, Sarcoma 12, Cutaneous epithelioma 30, a total of 229 cases of neoplastic disease. The hospital material is now excluded, as judgment is better made concerning the more intelligent class of patients seen in private practice than in those met within the Outpatient Department or in Hospital wards, and records are apt to be more accurate. Adding these figures to those given in the second volume on "Cancer, Its Cause and Treatment" we have the following table:

CASES OF NEOPLASTIC DISEASES

Carcinoma	Males	Females	Total
Breast	3	235	238
Uterus	...	22	22
Lip	35	3	38
Tongue and Mouth	41	6	47
Head and Neck	41	14	55
Oesophagus, Stomach, Liver, and Intestine	34	17	51
Kidney, Bladder, and Prostate	5	2	7
Other localities	18	7	25
Epidermoid carcinoma (Epithelioma) of the skin	444	261	705
Sarcoma	25	24	49
Totals	646	591	1237

There are also records of dozens of instances in practice or consultation where carcinoma or sarcoma was suspected or feared, which proved to be simple, innocent affections; such were chronic mastitis or cysts, adenoma, fibroma, lipoma, enchondroma, angioma, etc. benign in character, as also gastric, intestinal, renal, or other disorders, to say nothing of late syphilitic and tubercular lesions, thought to be cancer, and sometimes treated as such; all of these, of course, are excluded from our study, as were also some case papers with the diagnosis "Cancerphobia." This latter term, however, is a good suggestion for the lay mind, harassed by the fear of hereditary transmission, or alarmed through newspaper or other articles, or by occurrences to friends, if considered from a broad medical aspect, and if it will lead to the very early recognition of the existence of the true disease, and its proper treatment.

Epithelioma of the skin, although included with cancer in the Mortality Statistics of the United States, and often elsewhere, is excluded from our present study of carcinosis as a disease, for reasons shortly to be given, and will be only briefly mentioned, with some practical suggestions concerning its treatment.

Carcinoma, or true cancer, has been and will be considered as it affects various organs and localities, together with its different stages. It will be noticed that no attempt is made to differentiate the various forms of deranged cell activity, chemically or microscopically, as discussed by Ewing and others, for in the broadest sense all carcinomata are practically but different manifestations of the same real disease, carcinosis, wherever the neoplasm occurs, just as are the various manifestations of gout, tuberculosis, syphilis, etc. True cancer is simply a departure of normal epithelial cells, mainly of the glands or lining membranes of different organs, from a normal state of life. The forms taken by the neoplasm, as also its histological features, will naturally vary according to the tissue in which it exists, and for other reasons as yet unknown; this is especially observed in regard to sarcoma.

For many years I have observed that those cases of any form

of malignant disease have always done worse after a biopsy, curetting, surgery or any measure breaking the surface and facilitating the entrance of cancerous elements into the blood vessels and lymphatics. While I am glad to take advantage of microscopical studies already made, I do not recall an instance for many years where I have sanctioned a biopsy, as it always does harm, as many now agree.

We have already seen that the beginning of these disturbances can often, but not always, be traced to some local irritation. This disturbs the equilibrium of the cell nuclei, by which means they are induced to change their form and that of the cells, more or less, and to enter upon their erratic and destructive course; this occurs and is continually furthered through errors of metabolism, or by the manner in which they receive and respond to the wrong nutriment offered to them. This latter we found to be partly due to the erroneous pabulum furnished by the food and drink taken, and partly due to the faulty action of the various organs of the body, including the endocrinous glands and the blood making and destroying agencies of the body; for all of these are concerned in producing and purifying the blood stream, from which all the cells of the body secure their nutriment.

Sarcoma will be considered separately, as microscopically it is a different affair, namely a disease of the connective tissue, or mesoblastic elements. But practically it is of the same nature as carcinoma, being also due to faulty nutrition and metabolism, and yielding to practically much the same measures as that disease. Benign neoplastic growths and adiposis are undoubtedly due to wrong nutritive action.

CUTANEOUS EPITHELIOMA

It is not worth while to attempt to analyze the notes of the 705 cases of ordinary cutaneous epithelioma, many of which were small and superficial, and easily cured. Females formed 37 per cent of the patients, which conforms to the proportion of deaths attributed to it in the United States Special Mortality Report on cancer for 1914.

In the United States Mortality Reports for 1918, the deaths from cancer of the skin were put down at 3.4 per cent of all cases of carcinoma, of all kinds in any locality. This seems a very large proportion, but these deaths must have occurred in cases which had been dreadfully maltreated in their earlier stages; for we do continually see certain cases which have been almost maliciously stimulated or goaded on to severe, malignant action by injudicious therapeutic measures. About the worst malpractice is the almost universal employment of nitrate of silver, which should be forbidden by law in these cases. For I can find no personal record of any case which had been properly treated from the beginning and had resulted in death, although I have seen a number of patients where the disease had so far progressed under previous management that they probably ended fatally, in other hands. Quite possibly cases have been reported in the United States Statistics as epithelioma of the lip, tongue, buccal cavity, and even of the cervix uteri, which should be more properly classed as carcinoma of those regions.

Cutaneous epithelioma, especially about the face is excluded from our study of real cancer: (1) Because its cause and treatment are almost entirely local, and so the disease does not greatly concern our general inquiry as to the internal or constitutional cause and treatment of real carcinoma. (2) Because dietary and medicinal measures seem to have relatively little effect on cutaneous epithelioma, except sometimes in the later stages; where the disease has caused great ravages, showing that a cancerous dyscrasia has existed, and (3) Because, if the proper treatment of cutaneous epithelioma is begun early and carried out faithfully, it need never, or exceedingly seldom, acquire such a severity as is often depicted by overzealous surgeons who advocate only the knife. It is not denied, of course, that complete and early excision may cure such a local disease, in many instances, but it is wrong to infer from this that true carcinoma can be successfully treated in this manner, (for even surgeons now agree that this latter is impossible) moreover, the ultimate results of the excision of epithelioma are

often very deforming, whereas if properly treated, early lesions leave practically no scar.

Inasmuch as the border line between superficial and deep misbehaviour of epithelial cells is frequently so indistinct, it is often difficult at first to designate as carcinoma all cases in certain regions that might possibly belong there. On looking over the case papers I find a number in which the first diagnosis was entered as epithelioma, but where the disease proved so malignant in its course that they should certainly be included in the carcinomatous class; these included also cancer of the lip and buccal cavity, likewise certain ones of the face and neck, which from their metatastic tendency, belong to the latter.

In regard to the treatment of cutaneous epithelioma, this must vary greatly according to the stage of the disease and its locality. In my earlier years I employed frequently the Marsden's paste1, consisting of equal parts of arsenious acid and powdered gum acacia, mixed with water in a thick paste at the time of using. This is spread on surgeon's lint, cut to the size of the lesion and held in place. In from 2 to 4 days a distinct line of demarcation around the diseased parts is seen, and poultices are to be then kept applied, changed every few hours, until the resulting slough separates, and repeated, afterwards until good cicatrization results; and often no other dressing is used, even until all is healed. Marsden advises the application of the arsenic paste to be not over 1 square inch at a time. The arsenic seems to have a selective action for the diseased epithelial tissue, and in many cases I had perfect and permanent results, with trifling disfigurement. This is still a useful measure, where others cannot well be employed.

Later I curetted the lesion very thoroughly, and when the bleeding was staunched by pressure, the surface was covered with powdered pyrogallic acid, and in this way I secured some excellent results in 59 cases.[2]

[1]MARSDEN, "A New and Successful Mode of Treating Certain Forms of Cancer." London, 1874, p. 83.

[2]BULKLEY and JANEWAY, "Study of 400 Cases of Epithelioma in Private Practice." *Medical Record*, Mar. 11, 1908.

Early after the introduction of the *x*-ray, in 1903, the disease was almost invariably treated by this means, and even up to the present time I find it the best treatment in certain cases, and in scores or even hundreds of instances the lesion has been seen to slowly melt away and a perfect result to follow, with little or no scar. The results have been commonly permanent, though sometimes slight recurrences have happened, which in turn yielded quickly to the *x*-ray. Some judgment and experience, of course, are necessary, as harm may result from the injudicious or inexperienced use of this two-edged weapon; there should never be a burn. I have thus repeatedly cured epithelioma about the eye, with no harm to the organ. I have always employed the original gas tube, and not the Coolidge tube, as I believed that a prolonged application of the ray is more penetrating and permanently curative, than the short, strong exposure; even as in the use of radium and thorium the action is prolonged, in order to secure benefical affect.

Radium has been exploited much in later years, but I have had relatively little personal experience with it, though I used it some years ago in the Hospital, with a measure of success. I am surprised, in looking over my histories, however, to see how many times it had been previously employed without the expected results, both in epithelioma and in carcinoma and sarcoma cases, while in some instances it is recorded that it seemed to light up the trouble even more. Abundant evidence exists, however, to show that this is a valuable addition to therapeusis, as has been seen in a former chapter.

Of late years, since 1910 and to the present time, I have treated a large number of cases of cutaneous epithelioma with perfect results with a thorium paste, which is a radio-active agent, like radium, and which if judiciously used is capable of effecting wonders in the treatment of many cases of this disease. It is somewhat caustic in its powers, and especially until acquainted fully with its action, it should be employed cautiously. I have reported twice on the subject.[1] The paste is

[1] BULKLEY, "Notes on the Technique of Using Thoruim Paste." Chicago *Medical Recorder*, June 1913.

now called the Semerak paste, made in Chicago after directions by the originator, and obtained through the drug trade. The formula now furnished with each package is as follows: ℞ Lead Sulphate 68.6, Thorium Sulphate 1.5, Didymium Sulphate, 0.25 Sulphuric Acid (U.S.P.) 27.6, Nitric Acid, trace, and moisture by differences 2.05, and is said to be difficult of production. It is radio-active, and a chemist in my office, on reading the formula said that he could photograph with it, taking of course a long time.

It is difficult to give briefly the technique of its use, which occupied many pages in my reports, but a few hints may be of service. As furnished the substance is too acid, and I pour off that which rises to the top, and even use the paste sometimes diluted with a little water; to raw surfaces the latter is always wise. In an early epithelioma, with unbroken skin, the paste may be used in full strength, treated as above, applied with the glass rod furnished, quite over all the surface, and left to dry on; where there is danger of its being rubbed off, a little cotton may be applied, when it is dry, and plaster over it. To do its full work this crust of paste should remain intact for a week, but after five days an application of olive oil, several times each day, may be made, to facilitate its separation. It is then removed gently, and if the epithelioma is still a little raised a second application can be made, and again at a week or 10 days interval, until it has disappeared.

The crust should never be violently torn off, but if there is any suppuration beneath, it should be gently removed and a fresh application made. On raw surfaces the application is painful, and sometimes it is best to soak the surface first with a 4 per cent solution of cocain, on pledgets of absorbent cotton, before making the application. In real raw surfaces it is sometimes well to treat them for awhile with a two per cent watery solution of the paste, on pledgets of absorbent cotton, during the day, and the application at night of a rose ointment with 10 per cent of thorium paste; spread on cotton. To the thickened edges the strong paste may be freely applied.

Finally, some cases of epithelioma do remarkably well with a mild, soothing ointment, spread on very thin layers of absorbent cotton, and kept on continuously, alternating this, perhaps, with occasional applications of the Thorium paste. The ointment which I commonly use is as follows: R Acid Carbolic gr. v, Pulv. Calaminæ prep, ℈ Zinci Oxidi ʒss Unguent. aquæ rosæ ʒi ℳ.

CANCER OF THE BREAST

Of the 238 patients with cancer in the breast, of which three were in males, one primary and two with the disease recurrent after operation; one of these, to be reported later, was a great sufferer after two surgical removals, the last operation being very extensive, with a greatly swollen arm. Of the female cases the right breast was affected 101 times, the left breast 120 times, and both breasts 13 times, and 4 not recorded. Among these there were 12 typical cases of Paget's disease.

There were 121 primary cases, that is, that had never been submitted to surgical removal, though many had had *x*-ray and radium. Of the 117 recurrent cases 86 had been operated on once, 20 twice, four 3 times, two 4 times, and one 5 times, with a continued development of the disease. In many cases the surgical removal had been done almost immediately after the first discovery of the lesion, and in quite a number of these recurrences were observed within 3 months after the operation. The youngest patient was single, aged 26, and the oldest 85 years old, a widow. One hundred and sixty-four were married or widowed, 65 single, and nine unrecorded.

Some few of the patients with primary carcinoma have come under medical treatment within a few days after the first discovery of the tumor, when, of course, there is the best chance for its dissipation; but unfortunately many patients come only when other measures, surgery, *x*-ray, radium, etc. have been exhausted, or when the disease has increased so greatly, with extensive adenopathy that the case has been pronounced by competent surgeons to be wholly inoperable and hopeless. Of the 89

cases of cancer of the breast recorded since the last report 11 are known to have died, although there must have been very many more, as many of those seen only once or twice or in consultation were very far advanced, and must have succumbed soon. There were four known deaths among the primary cases, aged 85, 68, 53, and 36, all far advanced and inoperable. The youngest patient in this series was 25 years of age, the oldest 85; 18 were 40 or less years of age, and the average was 45½ years.

It is a little disappointing that so many patients, 49, were seen but once or twice and that so many are easily discouraged by the common belief in the hopelessness of cancer under any treatment, and of some of them it is recorded that they had been persuaded to try the chances of a surgical operation. But from first to last a very considerable number, some dozens, have been faithful and persisted in treatment, and have been very grateful for the results obtained, in the relief from pain without an opiate, even in advanced and hopeless cases. Of the patients seen since the last full report, 4 years ago, eight are recorded as clinically cured, five very greatly improved and a dozen and more as improved, many being still under treatment. In earlier pages there were a considerable number, 27, of primary cases, some of these were reported as clinically cured for many years: Cases I, II, III, IV, each for 16 years, others for 4 or 5 years, or greatly improved up to the time of reporting, Cases IX, X, XI, XVIII, XIX, XX, XXI, XXII; there were also 11 cases of post-operative cancer, and three inoperable cases, all demonstrating the value of this line of practice.

Perhaps enough cases have already been presented to demonstrate conclusively the truth of the position taken throughout this book, but a few more, from among many others, may be given, which illustrate features not previously shown. First may be mentioned one that occurred some years ago, but which was earlier overlooked.

CASE XXXVII.—*Primary cancer of the breast.* Mrs. H. R. aged 30, had been under my care for acne for some time, when

on Oct. 26, 1904 she called my attention to a characteristic lump about an inch in diameter just below the nipple of the right breast, for which she had consulted her family physician in September, she having had pain in it since July. She was a nervous, excitable woman, under great strain, and indulged a good deal in liquor, and ate freely. Not being willing to have the operation which was advised by her physician, she consulted me and was placed on diet and thorough medical treatment. To be brief, on December 27, it was recorded that there was no pain and that nothing could be felt in the breast, and it was repeatedly recorded, for several months, that the breast remained normal. She is a difficult patient to manage, living high at times and neglecting treatment, and has been under my care off and on to the present moment for various troubles, over 16 years. She continually has high blood pressure, up to 232 systolic and 122 diastolic, with a pulse pressure of 110, but repeated records show that the right breast remains normal.

Once, some 4 years after the disappearance of the mass in the right breast, she had a tumor develop in the left breast, which also subsided under careful treatment, and both breasts examined recently remain perfectly well. She has never been pregnant and still has her menses, at 47 years of age. If she relapses into her former mode of life with the condition of blood arising which first caused the right breast, to be affected, and then, after some years, the left breast to be attacked, she will probably have further recurrences: and experience teaches us what would have been the result from an operation over 16 years ago when the disease first appeared.

CASE XXXVIII.—*Primary cancer of the breast.* Mrs. K. S. aged 28 came for treatment Aug. 14, 1918, with a hard mass in the left breast, the size of an egg, forming for some months and adhering to the lower side of the nipple. Some lymph-nodes were found in the pectoral muscle and some lumpy condition, of chronic mastitis, in the right breast. On December 16, it was recorded that nothing could be felt in the left

breast, and the enlarged glands had disappeared. She has been under constant observation and treatment from the first to the very present time, and remains free from the breast tumor, though she has a little caking of the breast occasionally at the time of the menses, which are regular. She has never been pregnant. She has at times a good deal of rheumatism, so common in these cases. Her weight which was 97½ pounds when first seen has risen to 103 lb. She has been under constant dietetic and medical treatment now for over 2 years, and if she continues on this line of living she will remain free from cancer, as have the others.

CASE XXXIX.—*Primary cancer of the breast.* Mrs. C. W. aged 40 first seen Apr. 18, 1919, never pregnant, regular in menses, had noticed a soreness in the right breast for a year, and slowly a hard, flat mass had developed, 3 by 4 in., across the middle. Under the "green card" diet and the acetate of potassium and rumex mixture this had about disappeared when I last saw her Oct. 7, 1919, and very recently her husband reported that she remained perfectly well.

CASE XL.—*Primary cancer of the breast.* Miss M. H. N. aged 45, had removal of the uterus, for what was called a fibroid, which had caused menorrhagia, in February 1919. In June 1919 a small lump, the size of a bean had appeared in the left breast which had disappeared by August, under some treatment, not surgical. When first seen, Mar. 20, 1920, there was in the left breast, directly beneath the nipple, a moderately movable mass about 1¾ inches in diameter, with one freely movable lymph-node in the axilla. Under complete treatment it was recorded on August 13, that there was no trace of the trouble in the breast, nor of the axillary gland. She still maintains the diet and medicine, and recently it was recorded, that both breasts were normal, with no adenopathy.

CASE XLI.—*Primary cancer of the breast.* Mrs. R. R. a short, stout woman, aged 52, had noticed a small lump in the right breast with twinges of pain, 3 or 4 weeks previous to her visit on Apr. 12, 1920, which a doctor had tried to aspirate

on March 22, and gave her oil to be rubbed in. When seen there was a hard, rectangular mass 3 by 4 inches below the nipple. Under diet and the mixture, with capsules of thyroid, 5 gr. after eating, her weight which was something over 170 lb. at first was reduced to 156½. On October 14, when the breast trouble had disappeared she said that she "felt fine," and when seen again very recently the breast still remained normal. Had the breast been removed surgically there would certainly have been severe recurrence in such a fat, flabby subject.

The oldest patient seen presents some interesting features.

CASE XLII.—*Primary cancer of the breast.* Mrs. S. aged 85, had grip 2 years ago, after which a small lump developed in the left breast pea-size when first noticed. This increased steadily in size and she was treated by *x*-ray for over a year. Radium was then once used for 4 hours. When first seen Sept. 26, 1918, there was a large mass 3 by 4 inches in the center of the left breast, with an ulcerating surface an inch in diameter, just above the nipple, giving off a foul, characteristic odor. As she lived some distance away I did not see her again, but heard from her physician that under the dietary and internal and local treatment given she did "remarkably well." While there was at times pain she was up and did much knitting for the soldiers. She died suddenly just a year later, without the disease having made any progress.

The connection between diabetes mellitus and cancer has been noted by several, and two cases were observed which may be briefly mentioned. They are particularly interesting in the light of a recent article by Julius Friedenwald[1] on "The blood sugar tolerance test as an aid in the diagnosis of gastro-intestinal cancer," although relating to the disease in another locality. If our thesis is correct, that carcinoma wherever located is one and the same disease of aberrant epithelial cells from constitutional causes, and if the evidence which he has collected from literature is true that "hyperglycemia is always present in cancerous patients," this may afford some clue to the disentangle-

[1] FRIEDENWALD, *Amer. Jour. Med. Sci.*, September, 1920. p. 313.

ment of some of the chemic problems connected with cancer. In the first case it seemed as if the largely carbonaceous and saccharine diet which did wonders for the carcinoma, increased the diabetes, and possibly hastened the lethal end.

CASE XLIII.—*Primary cancer of both breasts.* Mrs. W. C. L. aged 40, was first seen Dec. 26, 1918. Three months previous she had first noticed a lump in the right breast the size of a marble, which grew to that of an egg in one month. This had since decreased almost entirely under the "green card" diet given to her by her doctor. Four weeks before her visit a lump appeared in the left breast, which had steadily increased. During all this time she had much rheumatic pain over the chest and arms, she having had two attacks of acute rheumatism, the first at 10 years of age. She had always been a very hearty eater, taking much meat, and had eczema for 15 years; rheumatism and eczema being not uncommon in cancerous patients. On January 21, it was recorded that the mass in the right breast was entirely gone, but that in the left breast remained about the same. When examined on March 13, there was absolutely nothing found in either breast. On April 25, I heard from her physician that she had just died, very suddenly of diabetes, and from the person who made the autopsy I learned that "there was no evidence of malignant disease found in the viscera."

CASE XLIV.—*Post-operative cancer of the breast.* Mrs. F. E. L. aged 62, was first seen Oct. 20, 1917. Two years previously she had noticed a small lump in the left breast, which was removed by a thorough axillary operation the same week, microscopic examination showing carcinoma. In July a supra-clavicular lymph-node was discovered, which was at once removed, and found to be carcinomatous microscopically. When seen there were again glandular nodes over the left clavicle, and a small one in the left axilla, with considerable pain in the left shoulder. Under the largely carbonaceous diet given she developed considerable glycosuria, for which she had been treated abroad before the war, with the result of becoming

and remaining sugar free when she came under my observation and treatment, as shown by several urinalyses. Her saliva was very acid and remained so while I saw her, which was only for a month, when she left for the West, somewhat improved. In August, 1920, I heard that she had recently died, possibly from the diabetes.

Paget's Disease is an interesting and commonly troublesome condition, of which there have been 12 cases, three of them among the last series, and one of these on the glans penis.

CASE XLV.—*Paget's disease of the breast.* Mrs. F. T. aged 32, had had a slowly developing rawness about the left nipple, which had increased steadily for a year, until first seen October 18, 1919. There was then a characteristic, circular, red, raw area, something over an inch in diameter, moist in places and glazed in others. There was no involvement of the mammary gland nor axillary adenopathy. She did well for a while, so that in 3 months there was very little rawness, and some areas of good epidermis. There was still no evidence of deep carcinoma, and no axillary involvement. But at the end of 5 months she became restless and saw a number of surgeons, all of whom advised radium or complete ablation of the breast, and I have not been able to learn the result, as my letter has not been answered. Another case, seen at the same time is worthy of report.

CASE XLVI.—*Paget's disease of the breast.* Mrs. I. W. J. aged 48, came to me Sept. 25, 1919. For about 2 years she had noticed soreness about the right nipple, with rawness, which had gradually increased, until when first seen there was an area affected the size of a half-dollar. It was a little raised, red and glazed over. There was no deep lump in the breast, but some chronic mastitis in the left breast, no axillary adenopathy on either side. Under dietetic and medicinal treatment, including thyroid, and the continued application day and night, first with the calamine and zinc ointment, already referred to, later with the addition to it of half of one drachm of ichthyol to the ounce, the lesion soon largely subsided. On September 28,

it was recorded, that the breast looked better than ever, with only a few small raw points and the days before there had been no raw points on removing the dressing; the chronic mastitis in the left breast had largely disappeared; no axillary adenopathy on either side.

On October 18, as there was still a little rawness in places, and she was restless, and wanted radium, this was applied by a colleague with a patch ⅞ in. square, with 25 mg. of radium element, in shellac, filtered through ½ mm. of platinum, for 90 min., over four areas, so as to cover the entire patch. This applicator had been used effectively in many various conditions for some time, and the result was a perfect healing, with only a little redness and no rawness at all for over 4 months. Seen recently both breasts were in good condition, only a little red, no deep lesion and no adenopathy.

Two recent cases are of interest, not because of any great advance toward a cure, but from the remarkable and steady improvement along many lines which has taken place since beginning treatment.

CASE XLVII.—*Advanced primary cancer of the breast.* Miss B. C. M. aged 52, a hard working and ambitious school teacher, came to my office Sept. 14, 1920. Three years ago a small lump appeared in the outer, upper segment of the right breast, which had been treated for 2 years by an osteopath. A year ago it opened spontaneously and a surgeon wished to remove the whole breast, which was declined. Since then the mass has increased, with active and deep ulceration, which has been treated with disinfectants, but with no other measures.

When first seen the whole breast was hard, presenting a deep, ulcerating surface of about 2 by 3 inches with hard, characteristic edges and profuse, offensive discharge. There were several enlarged axillary glands, somewhat movable. She could bear no ordinary clothing, but came with a loose wrap over the affected breast. She was depressed and anxious, but of good color, and weighed more than that called for by her height and age, namely 160 pounds, which was reduced by treatment to 144

when seen February 5. She had always been constipated, and had piles and an anal fissure, the saliva was very acid, and the sleep very bad from the great pain. Being placed on the acetate and rumex mixture, with cascara, and very strict diet, the change recorded in 2 weeks was remarkable: she slept perfectly, with no pain, no opiate, and the breast appeared better and the discharge lessened, and soon after the hardened edges flattened down, with signs of cicatrization here and there. She was given small doses of thyroid after eating, but this soon disagreed with her, and was changed to 5 grains of apiol after eating, and at bedtime, and from time to time she has had various remedies to meet digestive, rheumatic, nervous, and other symptoms.

The change in her whole condition from the first to her last recent visit is most remarkable in comparison with the previous and usual progress in such cases. She now dresses as usual, is very active, walks much, going upstairs as never before, going out shopping and to the theatre and is very urgent to return to her school duties, from which she has been absent for a year and a half. Her color and appearance are excellent, and she sleeps perfectly. There is still a very considerable mass in the breast, but all is much softer and the ulceration is less in extent and not nearly so deep, and with no fetor. From first to last she has used large quantities of the carbolized calamine and zinc ointment already mentioned, very thickly spread on thin layers of absorbent cotton, changed twice daily, but with no disinfectant, except the little carbolic acid in the ointment. When last seen April 19, 1921, over 7 months after her first call, one could hardly believe that it was the same person, well dressed, bright and active, without a particle of pain, and, as her sister said, "wants to do too much."

The mass still exists in the breast, but is softer and has diminished markedly in size, and the enlarged axillary glands have about disappeared. While the disease is far from being cured, and will require yet many months of treatment, there is reason to hope that the carcinosis habit or dyscrasia is being reached, and with faithful and intelligent perseverance the disease will be

overcome. As in the treatment of tuberculosis, it would be unwise to allow the slighest deviation from the regime which as carried her thus far toward health, for a return to the same conditions which caused the neoplasm to develop would probably induce a recurrence.

CASE XLVIII.—*Post-operative cancer, both breasts.* Mrs. F. D. J. aged 48, first consulted me Nov. 6, 1920, on account of a mass in the right arm which developed 8 months after the removal of both breasts for cancer. This mass had been excised 6 months after its appearance, but soon returned. She had had trouble with the left breast, called mastitis for 10 years, and in November, 1916 a bullet-like lump appeared, and the breast became larger and hard, and in May, 1918 both breasts were removed, as a similar condition had developed in the right breast shortly before. The breast lesions were determined microscopically to be carcinomatous. Since the last operation she had had much pain in the recurrent mass and in the whole right arm, preventing sleep. She had been on the "green card" diet for some time before consulting me, which had had the effect of relieving her chronic constipation and relieving the pain so that she slept. Being placed on the acetate of potassa, etc. mixture she wrote a month later very enthusiastically that she "had been more comfortable then for a long time," slept well with no pain. Her last letter from Los Angeles, Cal., February 23, states that she "has not been so well for many years."

A hospital case, which well illustrates the value of a chemical removal of inoperable breast carcinoma, instead of surgical excision, is worthy of report. The same method of removal was used in CASE XXIII, already reported.

CASE XLIX.—*Inoperable cancer of the breast, with chemical removal.* Mrs. H. L. aged 46, was first seen Jan. 2, 1918. She had had two childern, each nursed a long time, and there was no history of an injury or of mastitis. Six months before coming she had noticed a "hard pimple" by the nipple, which had remained and increased in size pretty rapidly till the time of the

visit. When first seen most of the breast was involved in a hard, scirrhous mass, with deep ulceration and hard, very characteristic everted edges, an inch and a half or more in diameter, with axillary adenopathy, which had been declared entirely inoperable. Being placed on full dietetic and medicinal treatment it was soon decided that the mass would take very long, if it yielded at all to these measures, and it would be better if it could be removed.

But, as for a long time I had not consented to have a breast carcinoma removed by the knife, I decided to have my assistant Dr. C. W. Strobel, remove it by caustic or chemical extirpation, which he had been practicing for many years. This was done on January 25, and on February 12 the raw surface, level with the chest, was skin grafted. All the grafts took well, and by March 20 everything was closed over perfectly, with excellent result. Leaving the hospital she was watched at the clinic for some months and on October 23 was recorded that the scar was excellent, with no sign of recurrence or skin nodules. As is so often the case she became irregular in calling, and in diet and medicine, until about Jan. 2, 1921, when the breast area was found to be in perfect condition, with a soft, supple scar, but there was a small enlarged gland below the right-axilla. She was warned of the danger, and has been faithful to internal dietetic and medicinal measures since, and on April 13, 1921, it was recorded that the breast area was perfect, and the gland had diminished fully one-half, and was very movable, over 3 years after the chemical removal. When we consider what would have been the result of the rapidly growing and deeply ulcerating tumor if left alone, or if subjected to surgical extirpation, this result is extremely satisfactory; and from experience it may be safely predicted that with continued proper care the gland will disappear and she will ultimately be cured of her disease.

A few words may be added in regard to this safe and sane method of the radical removal of breast carcinoma by chemical measures, avoiding the mechanical dissimination of the disease which is so common in surgical procedures: for the caustic

seals the blood and lymph vessels as the destruction of the tumor proceeds. Thus far I have had only half a dozen cases thus treated, but Dr. Strobel claims that of over 50 patients he has so treated there has not been recurrence in over 20 per cent of the cases, even in far advanced, broken down conditions, for I understand that all his cases are of this character. I see no reason, however, why it is not equally applicable to primary cases where there is an urgent desire to remove the offending tumor, provided thorough dietetic and medicinal treatment is also employed for a long time to remove the cause; although I have shown by cases that these latter yield perfectly to this internal treatment alone.

The technique evolved by Dr. Strobel makes this procedure both painless and thorough, and with no operative dangers. The anæsthetic employed almost exclusively is by the hypodermic injection of a tablet of scopolamine-morphine, or hyoscine-morphine an hour before the operation is begun and again half an hour later, sometimes a whiff of an inhalant is required at the beginning; nothing is necessary after the skin is all removed, or at subsequent applications of the caustic paste, about every other day, when also the resulting slough is trimmed off.

He divides the operation into four stages: (1) Denuding the skin, down to the breast tissue with, first an application of carbolic acid, and then by the very free use of stick caustic potash, dampened frequently. (2) The caustic paste of chloride of zinc and flour, equal parts, and water, darkened with powdered charcoal, spread on canton flannel, cut in pieces to fit, is laid over the whole denuded area. As this is removed about every other day there is a slough which is trimmed off, and a new application made. As I have repeatedly witnessed this procedure the patients say there is no pain. (3) When the chest level is reached, generally within 2 weeks, there is a large area, with reddened, inflammatory edges, and an adherent slough, which is kept covered with an emollient ointment, spread on lint, changed several times daily, until it is shed, and a raw, healthy, granulation surface is presented. (4) This is then skin-

grafted thoroughly and properly cared for. Great care must be exercised in confining the chloride of zinc paste to the area to be destroyed, by proper protection and careful nursing, for there is pain indeed if it gets on the skin, which is the reason for darkening it with charcoal.

This method of removal of a cancerous breast seems to be the most rational possible, when combined with thorough and intensive internal measures to prevent the further development of the products of the carcinosis in other places. For there is certainly not the recurrence seen about the healed surface which commonly appears after surgical procedures, nor the swollen arms, so frequently resulting from the latter, and, of course, no operative mortality. When there is already much involvement of the axillary or supra-clavicular or other glands there is, of course danger, of a fresh outbreak or development of the products of the disease somewhere else. But when there is only slight axillary involvement the gland, or few glands, they can be destroyed and enucleated by the very careful use of the caustic stick potash, while the employment of any cutting instrument vitiates the whole proceeding, and invites recurrence.

CASE XLIX.—*Post-operative cancer of the male breast.* Dr. G. J. aged 41, first seen Oct. 20, 1919. Twenty seven months previously he began to have a tense, inflammatory condition of both nipples, and the right one began to discharge. In October 1917, the right breast was excised, but not the axillary contents. Six months ago he noticed the axillary glands enlarged, and then he had a very extensive operation in New York. Shortly there again appeared axillary lumps, and cutaneous manifestations. When seen there was an enormous, elliptical scar from the neck, along the clavicle, to the arm, across the axilla and down the chest to the abdomen. All around the scar on the chest were very numerous cutaneous nodules, and the arm was hard and greatly swollen, 15 in. in circumference compared to 11½ of the other arm. The saliva was very acid. He had had *x*-ray and radium treatment

for the past 6 months, with no relief to the great pain in the arm, which prevented sleep. He was soon lost sight of and nothing has been learned as to the result of the treatment advised.

CANCER OF THE UTERUS

There were 22 cases of cancer of the uterus and vagina and one of the ovary; the latter patient had been submitted to an operation, when two large cysts were found, undergoing malignant change, with involvement of the lower bowel and rectum. Almost all of the cases were post-operative, or had been submitted to curetting, caustics, *x*-ray, radium, etc. There were recently 6 primary cases which had been declared entirely unoperable, each by several surgeons, in three of which the results of treatment were remarkable, to be mentioned later. Only one or two of them had not been previously treated actively, and one of these, a recent case, has shown great improvement in three months. The ages of these patients ran from 33 to 77 years of age, and there were five of 40 or less years, the average age being 50 years.

Ten of the patients were seen only once or twice or in consultation, four or five of the entire number are known to have died, although there were probably many more, and three are clinically cured, while others have been materially benefitted. The two totally inoperable cases, XV and XVI reported 2 years ago are still living and well, fully 5 years after adopting this line of treatment, and another similar case, more remarkable will be recorded.

CASE LI.—*Inoperable cancer of the uterus.* Mrs. W. G. aged 43½ came on Feb. 6, 1919, hardly able to crawl up the single flight of stairs to my office, so great was her pain. For 3 years she had felt badly, with an uneasy pain toward the pubis, keeping her awake at night. In June, 1918, she had increased vaginal discharge, until curetted on October. In October she saw four surgeons in another city, one of them very prominent, all of whom diagnosed inoperable cancer, and she was given not 6 months to live, on morphine, and told that there was no

possible treatment, medical or other, which could possibly help her. On November 15, she went to an advertising cancer sanitarium for 6 weeks and had various treatments. On January 20, she went to a New York Hospital, where exploratory cœliotomy was performed, by a well known surgeon, who found "the uterus hard and adherent to the pelvis, the ureters and bladder involved, and masses of glands in the floor of the pelvis, absolutely inoperable," and was given not 2 months to live.

When first seen there was a great and very offensive vaginal discharge, with intense backache and continual abdominal pain. She was a good deal over weight for her height and age, flabby, always constipated, the urine very deficient in solid constituents, and the saliva very acid.

Being placed on the "green card" diet, with acetate of potasa, nux, cascara, and rumex mixture, and douches of a pint of very hot water with carbolic and sodium biborate night and morning, as previously mentioned, in 8 days she stated that she "felt like a different woman," the backache was much better, and the douche came away still cloudy, but without odor. One month from the first visit she stated that she "felt better than in 2 years," slept perfectly from 10 to 6:30. On April 25, it was recorded that for 2 weeks she had felt absolutely well, "never felt so well in her life," "not an ache or a pain, and had sometimes walked for miles." The urine had been brought up in its solid constituants to about normal, by the use of caffein, 2 gr. after each meal, while continuing the former mixture, and on May 23, it was recorded that she "would never know that she had been sick."

On Mar. 26, 1920, I sent her to the surgeon who had performed the exploratory cœliotomy, 14 months previously, and had given her 2 months to live, and he was naturally amazed, and could hardly believe that she was the same patient, and said "you look like a perfectly healthly woman." Strange to say, the menses, which had been absent for 2 years, appeared on that date quite normally, ceasing after 3 or 4 days, and then

recurred each month, or in 28 days, in the same manner. During this year and a half she had naturally required various remedies to meet different conditions, which need not be detailed here. She neither required or took a particle of morphine nor any hypnotic during the entire period, 18 months after her first visit.

A rather recent case is also of considerable interest, because of the previous history and the unusual and steady gain in 8 months.

CASE LII—*Inoperable cancer of the uterus.* Mrs. G. N. aged 40, first came under my care July 13, 1920. Five and a half years before she had uterine hemorrhage for 2 months. This was actively treated by packing and remedies, until Nov. 22, 1916, when the uterus was removed by a very good operator. After this she was pretty well for a time, but with much sickness in the family, and worry, and trouble with the urine she was much depressed, and on Nov. 24, 1919 went to the same Hospital, when there was found so much return of the disease that she was considered inoperable and was sent to the Memorial hospital for radium treatment. There she had three treatments, but in June it was given up as hopeless. Being placed under strict dietary and therapeutic measures, with a douche two or three times daily she improved steadily, so that the douche came away about clear, the pains had about gone. Being asked to return for examination to the Memorial about February 15, the physician there was greatly surprised to see her so well, as he had expected her decease long before, and he found a hard patch on the side of the vagina, for which he wished to use radium again, which she refused. She had neglected the treatment more or less, and was again constipated and when last seen Mar. 12, 1921, she complained of much pain in the right hip, possibly from bone metastasis, and again had some bloody discharge. But the improvement in her general condition, with gain in flesh and color in these eight months warrants the belief that if she remains perfectly faithful to treatment the disease will be overcome, as in the other cases.

CANCER OF THE LIP

Thirty-eight cases of cancer of lip were recorded, 35 in males and three in females: all the latter were on the upper lip, and mainly on the cutaneous portion, also two of the males, all the other cases in males were on the lower lip. Fourteen patients were seen only once or twice or in consultation, leaving 21 cases more or less satisfactorily treated, although some dropped off or were lost sight of too soon to form any definite judgment concerning them. Of these 21 cases, nine were recorded as clinically cured, four greatly improved, eight improved. Two were known to have died, one from apoplexy and one from hemorrhage from secondary infection in the neck. It is fair to say that most of the cases were in a pretty early, although perfectly characteristic stage, with lesions of not over half or three quarters of an inch in diameter, and there were none of the terrible late cases sometimes seen. The location of the lesions in men were 14 on the right side of the lip, 9 on the left, nine in the middle, and in three instances it was not recorded. Most of the patients were smokers, some used the pipe, but some neither smoked nor used alcoholics. Two striking cases XXXV and XXXVI, have been given to show that, in the early stage, at least, the disease is amenable to correct medical treatment, when faithfully carried out; earlier cauterization, as with nitrate of silver, makes this more difficult.

CANCER OF THE TONGUE AND MOUTH

Forty-seven cases appear here, tongue 16, buccal cavity 11, serious affection of the jaw 17, soft palate, tonsil, and larynx each one. Of the entire number 30 were seen only one or two times, or in consultation. There were only six females in the whole 47. The ages ran from 28, a lady with a serious cancer of the tongue whose case will be detailed later, to 76 years of age. There were but four who were 40 years of age or less, and 10 who were 70 or over and the average of all was 57 years.

The end results of cancer within the mouth are indeed

distressing and show the impotence of our present means of reaching the disease by local measures, and the futility of surgical procedures in this location. Almost all the patients had been subjected to active treatment by surgery, *x*-ray, radium, caustics, or curetting, and many of them were in a pitiable condition when first seen. Ten were known or believed to have died but there must have been many more, and but two of the entire number are recorded as cured, and these were tongue cases. The total amount of misery and suffering from cancer in this locality seems to exceed the total experienced by an equal number of patients with cancer in any other locality, although post-operative cancer of the breast and uterus is often painful beyond measure, in many cases. The enormous and deep lymphatic supply and connections, with their early and almost certain involvement, preclude the expectation of benefit from surgical attempts to check the disease. Good results have been claimed for radium and thermo-therapy within the mouth, and experience would seem to show that the knife and caustics do more harm than good in this region of the body.

But very careful and proper dietary and medical treatment, general and local have been productive of good results to many patients, both in lengthening life and relieving pain, and many cases have records of improvement, and some of great improvement, although naturally but few are recorded as clinically cured; this is not surprising or discouraging, considering the generally hopeless condition of these patients when first seen, commonly in a late stage, and their distressing end: some illustrations will be given.

CANCER OF THE TONGUE

Sixteen cases of cancer of the tongue were recorded, but of these eight were seen only once or twice, or in consultation. Of the cases treated two were clinically cured, one was known to have died, and four probably succumed, so great was amount of disease when last seen. The ages ran from 28 (the only one under 40) to 75 years, the average of all being just 57: there were

four females and 12 males. The disease was located on the right side in 12 cases, on the left in three, and in the middle in one. In several the disease had lasted 2 years, and the most recent case was of 2 months duration. One interesting and fatal case who at first did marvellously well, with the greatest relief to an enormously affected tongue, but who finally sucumbed, has been already reported, Case XXXIII. The good results of gentle and properly directed medical measures, when the case is seen fairly early are well shown in the following case.

CASE LIII.—*Early cancer of the tongue.* Miss B. S. E. aged 75, had been under my care for chronic eczema, some years before she was sent to me by her physician on Mar. 15, 1919, on account of a trouble on the tongue, which he rightly recognized as early cancer. Two months previous she had felt an irritation on the right side of the tongue, which was treated 2 weeks with nitrate of silver, and as a painful ulcer formed, she was using an application of cocaine and boric acid. She had long been constipated but used remedies, the tongue was much coated, the saliva neutral; she was drowsy during the day time, and had lost some weight, it being then 135½ lb.

When first seen there was a painful ulcerated lesion about the middle of the right side of the tongue, nearly the size of a quarter, edges moderately hard, and with some adenopathy under the right jaw. Being placed on full dietetic and medical treatment, with a mouth wash of saturated solution of bicarbonate soda, diluted if necessary, and used very thoroughly ¼ hr. before and ¼ hr. after eating, it is recorded that there was decided improvement in 10 days. The area had cleared off and was less hard, and the pain had decreased. By May 27, it was recorded that the tongue seemed well, there being no hardness and no glandular enlargement could be felt. From that time to the present the tongue has remained practically well, although she has repeatedly had apthous sores in various places, which have yielded to careful medication, and occasionally the original site seems to light up, but never to harden or ulcerate. Seen by Dr. Janeway that summer he confirmed the diagnosis and

remarked upon the satisfactory control of the disease. For a long time there remained a somewhat raised, reddened area in the old site, but never anything like ulceration. She has had quite a good deal of other sickness, much of it rheumatic in character, but when seen Aug. 22, 1920, there was no trace of the former trouble. She has adhered more or less to the diet and medication.

This is a good illustration of the harmfulness of nitrate of silver in driving an innocent lesion on the tongue into a malignant one, and had there been a surgical operation at first, and a continued neglect of proper dietary and internal treatment, the course would probably have been such as is continually seen in these sad cases, such as Case XXXIII.

In the following case there was no history of cauterization, but the disease was far advanced when first seen and proved more rebellious.

CASE LIV.—*Inoperable cancer of the tongue.* Mr. P. E., aged 49, seen first Jan. 27, 1919. For 15 years he had had white patches on the left side of the tongue, and 5 years prior to his visit there were small ulcers within the cheek. Five months before he came the white patches on the left side of the tongue broke down and became ulcerated and bleeding; the whole thing was not painful to any degree, but occasionally he had pain beneath the jaw. His Wasserman had been found negative, he had never smoked much.

When first seen there was a new growth, nearly 3 by 1 inch, on the left side of the tongue, moderately hard, presenting a roughened, fungating surface, with fissures, and some glandular enlargement beneath the jaw, utterly inoperable. Being on complete dietary and other treatment, with the bicarbonate of soda mouth wash six times daily, on March 17, it was recorded that he felt very different, the saliva, which was very acid at first became neutral, he lost the pain in the tongue and side of the head, the ulcer had somewhat healed, the fissure was not one-half the size, and the glands beneath the jaw were decidedly smaller. By Oct. 25, he noticed that the tongue was softer,

though occasionally it bled some, and hardly any glands could be felt beneath the jaw. On Jan. 24, 1920, 1 year from the first, it was recorded that the diseased mass had shrunken considerably in contrast to the first condition, but that there was some lymphatic involvement in the left side of the neck. On Mar. 20, it was recorded that there was still much hardness of the tongue, and not much pain, but he had a great flow of saliva, which, however, was neutral or even a little alkaline. A little later there was great swelling and tenderness on the left side of the face and beneath the jaw, and still later much redness over all the neck, but the tongue remained in much the same fair condition. He was then having piles and passing blood from them, and unfortunately he was then lost sight of. But the relief and benefit which he obtained during the 14 months he was under full dietetic and medical treatment was very great, for which he was very grateful.

There have been several other more or less similar cases. One of these may be narrated to illustrate the evil result of early bad treatment, scraping or cutting, leading to infection of deep lymphatics, which caused a fatal termination 8 months after she was first seen, in spite of very great improvement in the disease on the tongue while under treatment.

CASE LV.—*Advanced cancer of the tongue.* Mrs. S. E. aged 28, first seen on Mar. 18, 1913. Something over 2 years previously there was an irritation on the right side of the tongue, possibly from a rough tooth, and about a year later the left side of the tongue was affected. The right side of the tongue was scraped and burned soon after it first became affected and it had remained increasingly sore ever since. Five or six weeks before her visit she entered one of the New York Hospitals where a negative Wasserman was taken, and a section made from the right side of the tongue, with the report of epithelioma.

When first seen a ragged ulcer extending from near the tip to the base of the tongue, on the right side, with slightly enlarged glands: there was a little trouble on the left side. She

had always been constipated and was dyspeptic, and lately had bad sleep, and was taking aspirin and codein.

Being placed on a strict dietetic and medicinal regime, with a weak mouth wash with carbolic, salicylic acid, borax, and honey, it was recorded on Apr. 8 that there was a "remarkable change." The sore on the right side had diminished largely, and the pain had about gone. On May 8 it was recorded that the sore on the right side of the tongue was largely healed, though there was still hardness, and there was very little adenopathy. On May 22 it was recorded that the right side of the tongue was almost healed, on the left side there was still some ulceration, but not painful on handling. She then took a trip West and neglected treatment and was very constipated, and on June 22 it was recorded that there was a lump in the side of the throat nearly choking her, and that she could not sleep from the great pain and burning in the tongue. On examination there was found sloughing, the left tonsil excavated with a foul smelling discharge, and on the left side of the neck large hard, fixed lymph nodes. Four days later she had a very severe hemorrhage from the spot where the tissue was cut for examination. Four days still later there was a severe cough, showing lung involvement. She was not seen then until Nov. 2, when whole neck was hard and board like; she was greatly emaciated, pulse 140 and died 5 days later, the victim of curetting and biopsy for evident cancer.

CANCER OF THE BUCCAL CAVITY

Carcinoma within the mouth is always a sad and discouraging proposition, for, unless taken very early and treated very wisely, there is commonly a steady progress with deep glandular involvement, which renders a permanent cure almost hopeless; though of late great claims, for temporary benefit at least, have been made for radium and thermo-therapy, as mentioned in another chapter. But the end results of this treatment are as yet unknown. Surgery, it would seem from experience is helpless if not harmful.

There were 31 cases recorded, 17 in the jaw, all males, 11 in the cheek or floor of the mouth, one female, one on the soft palate, one on the tonsil and one in the larynx, all males.

CANCER OF THE JAW

Of the 17 cases of cancer of the jaw, one female, the disease affected the upper jaw in three patients, and all were on the right side, except two on the left. The recognized duration of the disease had been from 3 weeks, in a gentleman aged 65, to be reported, generally from a few months, to some years, even, 16, as in case 64 also to be reported.

CASE LVI.—Mr. G. E. aged 75 noticed a mass on the left side of the lower jaw 3 weeks before his visit, which had shortly ulcerated. When seen Jan. 15, 1915 there was a mass ¾ inch in diameter, adherent to the bone and involving the sulcus of the cheek, with a typically carcinomatous ulceration and enlarged lymph glands in the neck. Under active treatment, with the mouth wash already mentioned there was almost at once a surprising improvement and within a month the mass had largely subsided and healed, with very little swelling of the jaw or adenopathy. Shortly after this he wrote me that the trouble was so nearly well that he would not call, as appointed, promising to come if any unfavorable symptoms developed. I wrote for him not to neglect treatment, and as he was a very intelligent man I cannot but believe that the disease was checked in its incipiency.

CASE LVII.—*Inoperable cancer of lower jaw.* Mr. E. G., aged 70, seen first on Jan. 2, 1919, lived until Apr. 11, 1920 with an enormous amount of malignant disease of the front of the lower jaw, which when first seen threatened to carry him off shortly. For some months he seemed to be doing excellently well, and it was recorded on Feb. 1, that there was steady and great improvement and very little pain or trouble, he finding great relief from aspirin freely given. Also on July 24, the mass was smaller, and he appeared better in every way. He lived some distance from the city, and was probably not very attentive to

all the details of treatment, and soon began to take morphine, though in moderate quantity, until he died Apr. 11, 1920, 15 months after his first visit. After he began to take morphine the disease increased and progressed rapidly.

CANCER OF THE MOUTH

Of the 11 patients with cancer of the soft tissues of the mouth there was one female, aged 54, seen but once, who had undergone three operations, and many *x*-ray treatments which had seemed to aggravate the trouble, and all resulted in an ulcerated mass, opening through the left cheek. In these cases the disease affected the left inner cheek four times, the right cheek four times, the front sub-lingual region three times. One man, aged 69, seen but once, had the trouble 25 years, and had undergone five surgical excisions. There was an ulceration 1 to 2 inches wide in the right side of the mouth, with adenopathy in the neck. When seen quite early lesions inside the mouth often do very well, as in the following case.

CASE. LVIII.—*Cancer of buccal cavity.*—Mr. N. F. E. aged 53, first seen May 12, 1919, with a lesion on the inside of the right cheek, which was to have been operated on surgically the second day following. He had had white patches in the mouth for 25 to 30 years, but experienced no annoyance, until 5 or 6 weeks before his visit when one of them became sore, and it had recently been treated with nitrate of silver. He was in good health, well nourished, and the functions well performed.

When first seen there was a slightly raised, moderately hard mass, a little granular, with a fissure in it. There was no glandular enlargement. No apparent cause for the trouble was found, in the way of bad or rough teeth. Under dietetic and medical treatment, with a soda mouth wash, used quarter of an hour before and after each meal, by June 4, it was recorded that the lesion had materially improved, there was no raw surface, and very little hardness left; the leucopathia was lessening. By Aug. 21 he reported "everything all right," no soreness on eating, as before, and on Oct. 23, he remarked "would not know

it was there." Some little hardness remained on May 19, and as he was somewhat restless under continued treatment I sent him to a good radium man, hoping that would remove the slight remaining hardness. Unfortunately he went to another well known radiologist, and on Oct. 12, 1920, he wrote to me, in answer to my inquiry "It was sad for me, as the disease became more deep seated, glands affected, etc. Now after months of treatment I am suffering more than ever, and while hope is not quite dead, it is nearly so." With the good progress he had previously made one could not but hope and expect that a faithful continuance of the same, which I fear he neglected in a distant city, would have completely overcome his disease.

The case of carcinoma of the soft palate in a man aged 47, seen but once, presented no special interest. He had had a surgical operation 6 months before, with recurrence, for which he had two radium treatments, which did not relieve his great pain. When seen the left side of the soft palate was the seat of a grey sloughing mass of hard tissue, with swelling of the cheek, and he could hardly open the jaws half an inch.

The case of cancer of the right tonsil has been already reported Case XXXIV, with very satisfactory results, although after 21 months of perfect comfort, under fairly faithful treatment, he was failing, at the age of 75; this was from involvement of the deeper lymphatic glands, due possibly to some operative treatment he had had a month before his first visit. The case of cancer of the larynx, in a man aged 48, was of the usual type. He had had laryngotomy performed by one of our best surgeons in New York, 10 months before his visit, when he seemed well for 3 months, but there was then recurrence, for which he had been having three radium treatments by Dr. Janeway.

CANCER OF THE HEAD AND NECK

In this group also are seen many of the sad cases, generally the result of previous bad treatment. Many of these cases were taken from the general group of epithelioma, as in earlier

years they were first entered as such. But careful study of the case papers and of their later history shows that they should properly be regarded as epidermoid-carcinoma of the skin, together with Paget's disease, etc. The hundreds of cases of early and relatively benign epithelioma, largely cured by *x*-rays, thorium, etc., were left under that designation, but in these cases the rebelliousness and often frightful destruction of tissue showed that the carcinomatous habit or diathesis was actually present. There were 55 cases in this class, 14 females and 41 males. The ages ranged from 36 to 83 (three cases under 40) and the large majority were in elderly persons.

CANCER OF THE NOSE

Here were placed 16 cases, eight females and eight males. The ages run from 36 to 78 years, mostly in elderly people, for omitting this young patient the average age was 65 years. Some of the patients had had the trouble for many years, up to 20, and there had been great destruction of tissue, under varied treatment. There were two known deaths, one from "cardiac asthma," and one, a lady of 62 who had had the disease 15 years, with two excisions, and much voilet rays, but who was practically cured by thorium and x-rays, which sometimes irritated; she died at 67 of general debility, not from cancer.

CASE LIX.—*Epidermoid carcinoma of the nose.* K. J. H., aged 36, Aug. 26, 1911, had had a lesion on the left side of the nose for 4 years, which had slowly increased in size to the time of his visit. He had had no special treatment, except cauterization with nitrate of silver, until 2 months previously, when he had radium applied by a well known expert, without apparent effect. He had four applications of thorium paste, and when seen May 1, 1912 there was no trace of the disease, only a slightly depressed normal scar. Two years and four months later he returned with the recurrence of a small superficial lesion in the scar, which was treated with four applications of thorium paste, and when last seen Feb. 27. 1915, there was a perfect scar, but little depressed. Should there possibly be any

slight recurrence, this would yield quite as readily to the paste, as it has in other cases.

In the light of experience of many other serious cases, which began just like this, and that had been cauterized with nitrate of silver, and when we consider the deformity which might result from surgery, especially with a recurrence, the result was eminently satisfactory. In contrast to this may be mentioned the following case:

CASE LX.—*Nose destroyed by epidermoid-carcinoma and treatment.* Mr. H. B. D. E., aged 75, from Yucatan, had had a hard lesion in the nose for 24 years, not ½ an inch in diameter, which was checked slightly by cauterization, and gave no trouble until 1900. Then a paste was used for 40 hrs. and the entire soft parts of the end of the nose sloughed off, leaving an ulcerated area, which received *x*-ray treatment by a well known dermatologist, in 1906 and again in 1909 by another physician. When seen the entire lower part of the nose was gone, leaving a characteristic epitheliomatous mass above. Of course little could be done for such a case, and I was not able to follow it up.

CASE LXI.—*Epidermoid-carcinoma of the nose.* Miss E. G. W., aged 50, seen June 21, 1910, for 2 or 3 years had had epitheliomatous development on the left side of the nose, slowly increasing in size, which had been treated only with ointments, and apparently held in check. When seen there was a dusky red, epitheliomatous mass, about the middle of the left side of the nose. With complete internal treatment and seven mild *x*-ray exposures it was recorded on Aug. 19 that everything had disappeared, which remained so when last seen Apr. 27, 1911, and almost 6 years later I learned from her physician that the cure was perfect.

CANCER OF THE EAR

Eight cases are here recorded, all in males, four on the left ear and four on the right, most of them on the upper edge of the concha. The ages were from 34 to 83; leaving out the youngest the average age was 68; four of them were seen but once. Most

of the patients had had the disease several years, and in several the destruction was very considerable. One patient, aged 66, whose trouble had started on the ridge of the left ear about 2 years previously, which he had picked, had had *x*-ray without effect. He was treated 4 months with thorium paste, in various strengths, with benefit, but becoming restless he was sent to Dr. Kelly, in Baltimore, for radium treatment. After about 4½ months treatment Dr. Kelly wrote me that the disease had been very rebellious to treatment, there being great destruction, and he was still very doubtful about the outcome. When in New York, from a distant city, he had been very faithful to dietetic and medical treatment, but I fear that the neglect of this may account in part for the poor results from radium.

CASE LXII.—*Epidermoid-carcinoma of the ear.* Mr. A. W. E. aged 69, came to the office Oct. 19, 1917, with a characteristic ulcerated epithelial mass, an inch long and half an inch wide, on the top of the pinna of the left ear, which had lasted 3 or 4 months and had been picked, and bled as the crust came off repeatedly. He had had no treatment. Under six applications of the thorium paste the ear became entirely well within 2 months leaving practically no scar, and on Feb. 20 he wrote that it seemed as good as ever. A similar case, in an elderly man, was seen at the New York Skin and Cancer Hospital, treated with thorium paste, with the same result. When first seen there was a large area, over an inch long by half an inch wide, raw and oozing, with characteristic edges. He was shown repeatedly in after years at my clinic, with a perfectly smooth, slightly cicatricial surface, and with no recurrence.

CANCER OF THE FACE

There were 23 cases, five females and 18 males, seen with lesions on the face, forehead, and about the eye, of various degrees of severity, 7 of them being seen only once or twice. Only two clinical cures were recorded, but in many instances great improvement was noted, and possibly a cure.

CASE LXIII.—*Epidermoid cancer at outer canthus of eye.* Mrs. L. V. J. aged 62, came on Mar. 9, 1917, with a lesion ½ of an inch long, at the outer canthus of the left eye, which had existed about a year. She had had no active treatment, only mild ointments. It was moderately raised and of a waxy appearance, a characteristic basal cell epithelioma. She was a large woman, of flabby texture, weighing 221¼ lb., which by strict diet and medication was reduced to 191 lb. in about 5 months. Under nine applications of thorium paste the cancer lesion had entirely disappeared, leaving only a slight red stain and no scar. Where this is compared with the results commonly seen from surgery in this region the result is indeed satisfactory.

CASE LXIV.—*Epidermoid cancer over right eye.* Mrs. S. W. J. aged 74, came on Oct. 15, 1920, on account of an epitheliomatous mass over the right eye fully an inch in diameter, and raised ⅓ of an inch, resulting from a wound 25 years previously, which had never healed. This had not given much trouble, but in 1917 a warty growth had formed which had gradually increased in size and had bled when the crust was knocked off. She then underwent electrical treatment for a year with one physician, and since then high frequency, violet rays, etc. Under six applications of thorium paste it was recorded on December 13 that all disease had entirely gone leaving a very good scar, and when seen later this had so improved under a calamine and zinc ointment that it was hardly noticeable.

A word of caution has already been given in the section on epithelioma, in regard to the employment of the thorium paste, for in inexperienced hands I have seen very serious damage done, as in a patient at my hospital clinic where some outside physician had used it with the result of destroying the left side of the nose almost completely, leaving a great permanent opening.

CANCER OF THE NECK

Nine cases, all males, are placed here, in which the disease appeared primarily on the neck: the ages ranged from 30 to

75 years, with an average of 54 years. Some of them were post-operative, one patient having had five operations, others *x*-rays, and all were rebellious to treatment, but none of them present special interest to report. These eight cases on the neck are in addition to the many others seen where there were secondary lesions in the neck from metastatic involvement, generally from mouth lesions. These latter are often most distressing and quite inoperable; also they are generally seen too late for medical treatment to have any great curative effect, although much benefit has often been obtained by exactly the right internal and local measures.

CANCER OF THE ŒSOPHAGUS, STOMACH, LIVER, AND INTESTINES

With the often distressing forms of cancer seen in these localities, there were 51 patients, 17 females and 34 males. Unfortunately a large number of them were seen only once or twice, or in consultation, and naturally there were very few clinical cures, although improvement or great improvement was recorded in many cases, in regard to comfort, relief from pain without opiates, and lengthening of life. There were only six known deaths, but there must have been very many more, as a number of the patients were in a desperate condition when seen, with advanced cancer pronounced incurable by some of the best surgeons. As the prospects of medical relief become more widely known and accepted, and earlier diagnosis is made, more lives will be saved. The ages of the patients varied somewhat, according to the location of the disease, as will be seen later, but the large majority were well advanced in life.

CANCER OF THE ŒSOPHAGUS

Six cases are found here, two females and four males: their ages ranged from 51 to 65, with an average of almost 60 years. In one of them the upper portion of the œsophagus and larynx were affected, and one at the cardiac portion. One of them, a female, had had gastrostomy performed.

CASE LXV.—*Cancer of the œsophagus.* Mrs. M. B. aged 64, seen Sept. 15, 1920, had already had a gastrostomy performed, and for 5 months had been fed through the opening, maintaining a quite fair condition, though she had lost flesh, from 160 to 105 lb. When seen they were, however, feeding her with animal broth, eggs, and milk, which only favored the development of the cancerous state. This line of feeding was of course stopped and all nutriment was made to come from the vegetable kingdom. She was also receiving codeine, because of a certain amount of digestive pain, this was also stopped and further remedies substituted. This is a very recent case and no judgment can be formed from it. One other case is interesting.

CASE LXVI.—*Cancer of the œsophagus.* Mr. G. M. aged 55, first came under my care July 31, 1919. Eight months previously he began to notice difficulty in swallowing, which had gradually increased. He had been examined by a good stomach specialist, diagnosing œsophageal cancer, and 10 weeks previously he had had a careful study by a hospital physician. The bougie met two obstructions, deep in the œsophagus, and the *x*-ray showed a shadow, 1¼ by 3 in. He had lost 15 lb. and weighed 111, was cachectic, pulse 100, tongue coated, and saliva acid, and had long been constipated.

On September 4, being under full dietetic and medical treatment it was recorded that he felt very well, "very little difficulty in swallowing, now eats finely—was a torture before." On December 8, his weight was 113½ lb., but some evidences of metastasis were occurring, with some dullness in the epigastric region and moderate pain on manipulation. Shortly some manifestations of kidney involvement appeared, with swollen ankles, but during this entire time to February 2, for 6 months from first, he had attended to his duties as sexton of a Jewish Synagogue, and was able to come repeatedly to my office from another city, and was reasonably comfortable, with little difficulty in swallowing.

On Feb. 21, 1920, I was called to another city to see him in consultation with his physician, as the day before he had felt

badly and vomited blood at 4 o'clock that morning, at first red, then black, and it looked as though he would succumb very soon. He was in bed, and a sorry figure; we could find no special cause for the occurrence. There was now pain on percussion over the epigastric region, and apparently some solid mass there, and considerable dullness in the left iliac region, with abdominal cramps, although the bowels had been acting freely all the time, with the mixture he had been taking. Under extra digestive remedies, and minute and often repeated doses of the tincture of colocynth, he improved at once, so that on March 17, his doctor wrote me that "he had improved greatly, walks about the house, and had even been to the Synagogue." He added that he was "amazed at the result of treatment, it is mysterious, if not miraculous." He was able to come and see me several times after this, but the liver became gradually affected, and on June 10, liver dullness extended about 2 in. below the ribs, with some pain on percussion over the epigastric region.

As I have not seen him since I presume that he gradually succumbed to his disease, showing that while very much can be done medically for these patients, greater advances will have to be made before we can expect to cure them all. The patient, however, has had nearly a year of relative comfort and activity, with absolutely no opiate, and stands in striking contrast to the case just before briefly noticed. In her case the gastric tube feeding cannot long sustain life, besides the seriousness of the operation and the constant annoyance of the leaky gastric fistula, only a little less distressing than a colostomy, are to be taken into consideration.

CANCER OF THE STOMACH

There were 28 cases recorded, four females and twenty-four males; in a number of them marked involvement of the liver was noted. Only two patients, males, aged 31 and 36, were under 40 years of age, the oldest was 75 and the average a trifle under 60. There were three between 40 and 50, 11 between

50 and 60, nine between 60 and 70, and three 70 years or over. In 12 of the cases the disease had been recognized more or less definitely from 2 to 7 months, in many of them from 1 to 2 years. Two had had recent gastro-enterostomy, and several had had exploratory operations revealing inoperable cancer of the stomach; the *x*-ray and other diagnostic measures had been employed in many cases, and all the patients, I think, had had the diagnosis confirmed by several physicians and surgeons. X-ray had been employed therapeutically in some cases but I find no mention of radium. Only five of the patients are known to have died, but there were many seen only once or twice, or in consultation, who must have succumbed soon. One of the patients a man aged 56 has been already reported, Case XXVIII as clinically cured, so as to return to and continue at his work.

CASE LXVII.—*Inoperable cancer of the stomach.* Mr. D. F. B. aged 68, was referred to me June 15, 1919, with the history of stomach distress and a tumor in the right upper abdomen, dating back 5 months, with weakness and loss of 10 pounds in weight, and he was pale and cachectic, with great constipation. A firm, nodular mass was found in the upper abdominal cavity, not freely movable, about 2 inches in diameter. Being placed on full dietary and other treatment he returned to his physician, in a distant city, and the nurse wrote me on August 5, that he seemed better, the last 3 weeks, walking further, half a mile without fatigue. Seeing him the same day his weight was 111½ lb., and he appeared much better, with some soreness after the noon meal. The saliva was very acid.

On August 27, he weighed 115¾ lb., seemed very much brighter and better, and it was recorded that the mass in the gastric region seemed far less than at the first visit, though some indefinite nodular masses were found below the ribs, on both sides. The saliva was still very acid.

On September 18, the weight was 117 lb., and he stated that he "felt very well, the same as a year ago," saliva less acid. Examination showed the gastric mass still firm, but less in size. The bowels were acting finely, twice daily. On Sep-

tember 25, he insisted that the mass in the gastric region was all gone, but it could be felt, now somewhat movable. He then went to his home in Florida, in a very different condition from that at first. He had been perfectly comfortable for over 3 months, and his gain in weight was interesting. When he left New York he seemed bright and normal, and wrote repeatedly of his condition. But probably he relaxed in some way as to his diet and treatment, and metastasis undoubtedly occurred. The ordinary drinking water there seemed to disturb him, and his kidneys acted badly, œdema of the feet came on, with also ascites, for which he was tapped. The urine came down to half a pint or a pint daily, and he gradually became worse, until on December 18, he wrote "I won't be here long," and I presume he passed away. While the ultimate result was only what might be expected, the early results of treatment were certainly encouraging, and possibly would have been better if he could have remained here under careful supervision.

CASE LXVIII.—*Cancer of the stomach.* Dr. W. L. T. aged 70, first seen on May 5, 1920, had had digestive trouble for 15 months, with loss of weight the past 4 months; his weight was 159½ pounds, the weight for his height, 6 ft. 2 in., and age, should be 190 pounds. In April he had had 15 deep *x*-ray treatments over the stomach. His bowels had been always constipated, depending upon an enema for 20 years, and the saliva was very acid; his sleep was very bad, lying awake for hours after 2 a.m.

He brought a long and most elaborate and scientific fluoroscopic and other study of his internal condition, by an excellent observer, which need not be all entered here. These showed "carcinoma of the stomach, involving the greater curvature at pars media, with beginning stasis in the stomach." There was free hydrochloric acid, with a total acidity of 18, a trace of lactic acid, also Oppler-Boas bacilli, some pus cells and a few red blood cells. Wasserman negative. The hæmoglobin stood at 57 (Dare), erythrocytes 3.160.000, leucocytes 6.900, polymorph. 82.2 per cent, small lymphocytes 10.3 large lymphocytes 3.8, transitional 2.2, and large mono-nuclear 1.5 per cent.

He was under observation and treatment for only 6 weeks, when he left for the West, but the change in his condition during that time was most gratifying to himself and to me. At the fifth visit he expressed himself as feeling very different, and had still gained a little in weight. He was lively and bright, with improved color, bowels acting well, sleep much better, and saliva neutral. As a doctor he thought he was overcoming his trouble.

There is relatively little of importance to note regarding the other cases of stomach cancer, all giving the same story, having seen many physicians and surgeons, with *x*-ray diagnosis of cancer etc. Four had been operated upon; and two had had exploratory operations. While relatively few were observed long enough to speak definitely of permanent results, it is interesting in studying the case records to note how continually there was a decided change for the better after beginning treatment. But with the general feeling of hopelessness in regard to cancer, and the commonly expressed opinion by surgeons and others that if an operation is not possible there is nothing else that can be done, it is often difficult to persuade patients to be faithful to the necessarily tedious process of dietetic and medicinal treatment; so in a number of instances they shortly dropped off, when feeling better.

CASE LXIX.—*Inoperable cancer of the stomach, omentum etc.* Dr. K. I. M. aged 52, seen Oct. 21, 1920. He had had vague stomach symptoms for many years, but active syndromata, pain and distension, for 1½ years, for which he had had gastric lavage, etc. In January and July the *x*-ray reveated carcinoma at the pylorus, and he had lost 80 lb. since January 1. On August 6 he had an exploratory operation by Dr. Wm. J. Mayo, who found "colloid cancer of the pylorus with metastases to the greater omentum and transverse mesocolon," absolutely inoperable, and he remarked to his medical son "the future of cancer of the stomach is medical." Ascites developed 10 to 14 days after the operation, for which he had been tapped several times. He had been chronically constipated, depending always

on an enema. Of course medical treatment could have no possible chance, in such a condition of advanced carcinosis, and the patient died early in December.

CASE LXX.—*Post-operative cancer of the stomach.* Mr. S. A. W. first seen July 27, 1920. For 4 years he had had great gastric symptoms, much higher acidity as shown by many gastric analyses, also vomiting, so that he could not even retain test food. He had been in the Navy for 24 years, and during the war had made many trips with troops, though a sick man. In February 1919 he had had various tests by Dr. Charles Mayo, with the diagnosis of an operable cancer, and he operated on him, removing a small growth, probably external to the stomach, which was pronounced cancerous, microscopically, and he was given 3 to 6 months to live. He felt better after the operation and returned to army transportation, in 3 months. But the vomiting began again, with intense cramps, and about November 8 he was very weak, weight 104 pounds which had been 165. He then went to the Walter Reed Hospital, and the day after Thanksgiving a gastroenterostomy was performed for cancer of the pylorus, after which he gained up to 150 pounds, 2 months before his visit; this, however, had again run down to 139½ at his visit.

When seen he was in a pretty bad condition, tongue coated and bowels very constipated, depending entirely on enemata, and his sleep was very bad, often not for more than an hour or two on account of gastric pain. Being placed on full dietetic and medicinal treatment, in 1 month it was recorded that he "feels ever so much better in every way, draggy pains gone" The lump over the pylorus was, of course, still present and even visible, 2 to 3 in. in diameter, but not very hard. Much of the time there was no pain and he had good sleep from lying down till morning, with about 5 gr. of potassium bromide and chloral in elixir of lactopeptine; the bowels were acting freely with the mixture given to so many others. Two weeks later no dullness or tumor could be discovered at the pylorus, it seemed to have moved to the left. But there was a mass of mesenteric glands

felt, which were a little painful at times, when standing erect. From his general appearance and feelings it did seem as though with very careful and prolonged treatment the disease might be overcome.

But his duties at the Navy Yard, and various matters prevented him from carrying out everything faithfully. He developed a grippy bronchitis, and then was called to Washington on September 19, and the next I heard of him was in a letter from his wife on October 22 saying that he had died on September 30, as a result of the operation performed on him on the 28th. He lived, however, 1 year and 7 months after he had been given but 3 to 6 months to live, in February, 1919, and while he was under full treatment he was more comfortable than for a long time, with no nausea or vomiting, and practically no pain after he had gotten well under treatment. How much longer he would have lived but for the operation no one knows.

A recent case, observed for 10 months, shows how much can be accomplished under the most absolute and perfect carrying out of every detail of treatment.

CASE LXXI.—*Primary cancer of the stomach.* Mr. V. H. aged 75 came under treatment May 8, 1920, his very intelligent daughter coming with him always and supervising the carrying out of every order given. In September, 1911, he had some operation at one of the New York Hospitals, but on careful inquiry no record could be found as to its nature; there was a large scar of an incision which had been made in the region of the stomach. For the next 7 years he always had abdominal discomfort, with a sense of fullness, though keeping at work, as a time keeper. He had had pain beneath the scars for a year. About 1 month before his visit he had vomiting, and pain in the upper abdomen, for which he applied a hot water bottle which may have caused the ulcerated area 2 or 3 in. in diameter over the scar, which was really the cause of his visit. He had always been much constipated, with poor digestion.

When first seen there could be felt quite a mass beneath the

ulceration, which latter healed completely in a month or so, under the constant application of a soothing ointment. The epigastric mass could then be readily discovered by percussion and palpatation, under which it was a little tender. Within 2 months from the first he declared that he had no trouble with the stomach, no pain or vomiting, and does not yet know of the serious nature of his disease, though his daughter is fully acquainted with it, and keeps him faithful in diet and medication, and he keeps steadily at his work, walking some miles every day to it. He has gained somewhat in weight during these 10 months, though he has had one or two set backs from severe lumbago, which has yielded to treatment. When last seen Mar. 3, 1921, he appeared as healthy and robust as could be desired, but there was still dullness in the epigastric region and a little pain on deep pressure, but absolutely no stomach symptoms.

CANCER OF THE LIVER

In quite a number of cases of cancer in various localities there were very distinct indications of metatastic involvement of the liver, both by clinical symptoms and physical examination, and also by jaundice and ascites, as well as by exploratory operations. In addition to these there were four cases in which the liver was so prominently affected, with no other lesion of cancer elsewhere at the time, that one or two of them at least, were regarded as primary carcinoma of the liver, although this is known to be quite rare. A case or two illustrating the former condition may be first mentioned.

CASE LXXII.—*Cancer of the stomach and liver.* Mr. G. S. aged 59, first seen Aug. 11, 1920, had had stomach trouble for 5 or 6 months, heaviness, pain, vomiting, for which he soon went to a hospital in this city, for observation. He was there nine weeks, under *x*-ray treatment, but the abdomen soon began to swell with fluid, and he was tapped. This aspiration was repeated three times in another hospital, nearly a gallon being drawn off on August 8. When seen, soon after the

tapping, the abdomen seemed very full of metastatic masses, with a large area of dullness over the epigastric region. He was constipated, the urine scanty and milky, and the saliva very acid; he weighed 123½ lb., having come down from 150. Of course little if anything could be expected from diet or medication in such a case, and little if any benefit resulted before he ceased his visits.

CASE LXXIII.—*Cancer of the liver secondary to uterine cancer.* Mrs. G. S. aged 51, seen Feb. 8, 1919, had had the uterus and ovaries removed for carcinoma in June 1914, by an eminent surgeon, whose son at the same time operated also for gall stones, draining the gall bladder. In August 1917, a mass had appeared in the region of the gall bladder, and in November 1917, another prominent surgeon removed a mass of adeno-carcinoma near the liver, the size of a hen's egg. The wound was left open and in December radium was used on it for 8 hr., at the Memorial Hospital. In March 1918, a large dosage of radium was again used, and again in July, all causing much suffering and apparently causing the tumor to grow. In September the wound opened up, and Alpine Sun light was applied, under which the tumor developed externally, as a cauliflower excresence, 2 in. in diameter. On January 8, jaundice appeared. Pain had never ceased since the operation in 1917, and was not controlled by narcotics.

When seen there was a granulating mass over the lower margin of the ribs, 3 or 4 in. in diameter, secreting profusely, and she was in great pain, groaning day and night. She had always been extremely constipated, latterly the movements were very white, and the urine very scanty. The mass was dressed with a soothing calamine and zinc ointment, spread thickly on thin layers of absorbent cotton, which gave great relief. With the diet and medicine given she seemed better, the bowels acting twice daily, and the pains materially lessened by chloral and sodium bromide, in elixir of peptenzyme. But the weakness continued and she passed away peacefully without an opiate about a month later.

CASE LXXIV.—*Cancer of the liver secondary to removal of cancer of the small intestine.* Mrs. R. A. aged 50, was well and hearty until 2 years ago. There was then pain in the upper abdominal region and a prominent surgeon removed an adeno-carcinoma from the ileum, on July 7, 1918. A second and then a third operation was performed, and she was well for a year or so. Then there was pain over the liver and on August 14, an exploratory operation was performed, revealing a large mass over the liver, with nodules, some which were removed and found microscopically to be adeno-carcinoma. When seen in consultation, 10 days later on Aug. 24, 1920, she was in a low condition being fed on a high protein diet, and although she rallied and all thought that she was much better the first week or so, under the measures advised, she succumbed within 2 weeks to the great amount of metatastic encroachment of the disease. The last operation, with partial removal of diseased tissue was a great shock to her system, and undoubtedly hastened the lethal end.

CASE LXXV.—*Primary cancer of the liver.* Mrs K. C. R. aged 66, had always been constipated and with a "torpid liver." Six weeks before my seeing her, when South, she had a severe attack of indigestion after taking some clam broth, with purging and beginning of jaundice. On the way North the case was studied by physicians in Philadelphia and Washington with *x*-ray, blood tests etc., as also in New York, and while no definite diagnosis was made all pointed to be neoplasm in the region of the gall bladder.

When I saw her, May 11, 1914, it was really on account of the terrific itching caused by the jaundice, which nearly drove her crazy, and had been severe from the beginning, the body and limbs being covered with scratch marks. The jaundice was as severe as could be, everywhere, the pulse was 40 and irregular, 64 beats by auscultation, urine scanty and dark yellow.

Under a rice diet and active medication, internal and external, the itching was soon very greatly controlled, so that on May 14 it was recorded that there was very little trouble from it, and

she was sleeping perfectly, and in a few days the stools which, had been white and acholic, were formed and of good color, but the urine was still dark, though with much less bile.

A very careful study of the abdominal region revealed the left lobe of the liver at the costal margin, and the right lobe projecting down to the level of the umbilicus, moving with respiration, irregular in shape, at one place nodular. Beneath the right lobe there was a second, smaller mass in the region of the head of the pancreas. The stools had been curdy, with no bile, but under mercurial purges she had had those of good color at times. Under treatment the urine, which had been scanty, rose to 61 oz. on one day, and had improved in many respects, there being but a trace of albumin, and amorphous urates, but hardly any bile when last seen. She passed from under my observation soon after her skin symptoms had been relieved. There was no history or evidence of any other manifestation of carcinoma from which the liver mass could be a metastasis, and no particular evidence of gall stones, certainly she never passed any. So this case was regarded as probably a primary cancer of the liver.

CASE LXXVI.—*Possible primary cancer of the liver.* A somewhat similar case was that of Mrs. B. I. aged 58, seen Nov. 7, 1919 who was in a very bad condition, with great constipation; much jaundice, very yellow urine, and a mass in the right hypochondrium, and bad stomach symptoms, with belching of much gas. But some time later I learned from her physician that under dietetic and other treatment she was very much better, sitting up. No other cancerous lesion existed, and this appeared also like a primary cancer of the liver.

The case of cancer of the mesentery and that of the omentum presented no particular interest, and were not followed long. That in the mesentery was probably from stomach cancer, the liver being also much affected, over-riding the stomach, with tenderness. There had been an exploratory operation in which the piece removed showed metatastic carcinoma microscopically. The patient with omental disease, a female, exhibited a mass 3 to 4 in. in diameter to the right of the umbilicus, and a

smaller one, about 2 in. in size, on the left side probably from a former cystic adenoma of the right ovary. The case of carcinoma of the sigmoid was followed 3 months and was interesting.

CASE LXXVII.—*Cancer of sigmoid.* Mr. C. H. W. aged 54, living in a distant city, began to be greatly constipated 2 years before he was first seen Oct. 11, 1919. For this he took much salts and other laxatives and had diarrhœa, with blood and mucus. He saw several surgeons and a proctoscopic examination revealed a mass, with ulcerations high up, for which he was given injections of a gallon, with a teaspoonful of salt to the quart. With this he improved and passed no more blood; he was on a mixed diet, with some animal proteins.

When seen he weighed 154 lb. having fallen from 163, and seemed in fair general condition, though the saliva was very acid, the urine acid and of high specific gravity, the tongue white and coated, and he had some diarrhœa. Under careful treatment in three weeks he said that he felt "very well," sleeping finely and seemed in much better condition. Two months later evidence of liver involvment appeared, with sharp pains there, lasting 10 to 15 min., several times daily, decided jaundice set in, and dark yellow urine. On December 1 he was sent to a New York surgeon who found a large sigmoid neoplasm below the true pelvic rim. He was lost sight of some months after first seen, but in the mean time he was very comfortable, with no pain and no opiate.

CANCER OF THE RECTUM

Eight cases of the disease in this location were observed, four females and four males; four of the patients were seen only once, or in consultation. The ages ran from 26 to 55 years, with an average of 40 years. Three of them had had colostomy, one of them two operations, and one had had three. One of the four treated died, as expected, and of the others one is recorded as improved and two as greatly improved. One case has been already reported, Case XXIX, another, of rather recent date, although ultimately fatal, presents great interest.

CASE LXXVI.—*Cancer of the rectum.* Mr. H. A. G. aged 41 came to me on Feb. 18, 1920. He had always been constipated, taking medicine, and for 7 years had had bleeding piles. One year prior to his visit one pile, on the left side, had been removed under local anæsthesia. Three weeks before his visit his family physician had examined him, and found an extensive growth just above and about the anus. He weighed 143 lb, having fallen from 155, was fairly nourished, but of a sallow, cachectic hue, tongue white and coated, saliva very acid, very constipated, and with movements the size of a pencil. Examination showed a hard mass, around and within the anus, with some external piles, easily bleeding. Under full treatment, with ichthyol internally and an astringent ointment, the bleeding ceased and the mass became less hard and smaller.

But a month or so later he had some fever, and I visited him in another city, on April 8, in consultation with his physician. He had complete obstipation, tenesmus, hiccough, and was greatly prostrated and in bed. His physician urged a colostomy, to which I did not agree, and with active treatment, including tincture of colocynth, 2 drops every 10 minutes, he came out all right, so that on April 20, he came again to my office.

On April 27, I sent him to the Memorial Hospital, thinking that radium might perhaps help to melt away the tumor, but it was thought there that it would only overstimulate the growth and make it worse. Some of the masses at the side of the anus softened and were allowed to break and discharge, as I have always found that when such were lanced the wound never healed, but left a raw, increasingly ulcerating surface, giving great pain. There has been very considerable discharge from several of these openings, one or more of them closing.

On August 27, he said that he "never felt better in his life," but on the 28th, he drove his car a while, and that night had a great hemorrhage from that region, and coming from the bathroom fainted and fell unconscious; he was somewhat delirious that night, the bleeding continuing until August 30. His physician then gave him 20 c.c. of Squibb's Thrombo-

plastin in a glass of water, which stopped the bleeding in an hour, but the doctor said that he could not live 2 days, and gave him beef soup and eggs in milk. On September 4, I went to another city to see him, and found him better, quite bright, but weak, pulse 100, he had slept well. I gave him digalen, 5 drops increased slowly to 15, every 3 hours., with a powerful alkaline tonic. On September 15, still in bed, he felt and looked very much better, with much less cachetic appearance. He had had no more hemorrhage and the purulent discharge from the openings was lessened. On October 6 I saw him, sitting up part of the day, and he remarked, as he had often done, that he "had not an ache nor a pain," and on Octover 13 was all day on the porch, "feeling very well."

But the disease progressed internally, and he finally died peacefully on November 11, 9 months after his first visit, and up to the last he declared that he had not an ache nor a pain but only felt so weak. He never required nor took any opiate.

Another case is interesting, although I was not able to follow it many months after there had been great improvement.

CASE LXXIX.—*Cancer of the rectum.* Mrs. B. C. aged 31, with quite an extensive growth in the rectum, and some bleeding piles, had been troubled for a year, and had recently lost 2 pounds; she was greatly constipated, had much gas in the stomach, saliva acid, and had had bad sleep for 2 or 3 months, from pain low down in the back. At first she did remarkably well, and said she felt a 100 per cent better, the bleeding piles being controlled by ichthyol, 10 to 30 drops internally, well diluted in water, half an hour before meals, with the mixture as given to others. But after a few visits she was lost sight of, rebelling as so many do at the dietary restrictions and the protracted treatment, without the immediate cure of her disease.

CANCER OF THE KIDNEY, BLADDER, AND PROSTATE

Relatively few cases of cancer in this region appear here, only 7, two females and five males, two of the kidney, males,

three of the bladder, two females and one male, and two of the prostate. The youngest, a woman of 32 with the disease in the bladder, the oldest a man of 74, with cancer of the prostate. Omitting the youngest patient the average was 61½ years. There were three known deaths, one each with the kidney, bladder, and prostate affected. All the cases were very interesting, one of which, with post-operative cancer of the kidney, Case XXXI, is still living and is very well and flourishing, in very active work, under continued very rigid treatment. His last letter, Dec. 21, 1920, states that he was in the "best of health and condition that I have known for many years," and that nearly 4 years after beginning treatment. If our proposition to patients is correct, that one cannot go down hill in health until one ceases to go up hill, he pretty certainly will not die of cancer if he maintains his present course of living and treatment—which he undoubtedly will do, as he is a very intelligent, educated gentleman and a most faithful patient. One patient with cancer of the bladder has also been reported, Case XXXII, who is still alive 7 years after his first visit, and active in business. A case of cancer of the prostate was likewise reported, Case XXX, in which the disease had apparently disappeared, and he died from some other cause, suddenly, many months after he was first seen.

CASE LXXVIII.—*Suprarenal carcinoma.* Mr. K. C., aged 65, first seen in consultation, in Brooklyn, Oct. 13, 1919. He had had an exploratory laparotomy in a New York Hospital in April, which revealed a "large, inoperable hypernephroma of the right kidney." When seen he was very weak, in bed having lost 50 lb., suffering greatly and under morphine, and it did not seem that he could live 2 weeks. Under full dietetic and other treatment, with considerable aspirin for the pain, I heard from his physician on October 31, that the patient was very well, sitting up and eating at the table, and had no pain, except in the right foot. On November 24, I was amazed to see him and his physician walk into my office, coming from Brooklyn, 6 weeks after my first visit there. He was sleeping

fairly and had taken no morphine since I first saw him, and had very little pain, except when lying down. The bowels had always been much constipated, and he had some troublesome hemorrhoids, for which I gave him ichthyol internally, as mentioned in similar cases, and on December 22, when he called again at the office, they had disappeared.

On Jan. 8, 1920, I saw him in Brooklyn because of terrific pain in the left leg, the one on the opposite side from the hypernephroma, the whole sciatic nerve being tender on pressure, and painful down to the toes. I did not see him again and learned that he died about 6 months after I first saw him, when we did not think he could live 2 weeks, and 14 months after the real trouble was revealed by exploratory laparotomy.

CASE LXXXI.—*Carcinoma of the bladder.* Mrs. C. J. C., aged 72, with cancer of the bladder, seen in consultation in a neighboring city, Sept. 23, 1919. The disease had apparently begun in January, with urinary trouble, and in March and April she had passed some blood, and in July much more, with pain. She was then cystoscoped and a fungating neo-plastic mass was found around and below the ureters. For the last 6 weeks the urine had passed involuntarily, and for 10 days had excoriated the external parts dreadfully. She was always greatly constipated, was very cachectic and nervous, and with intensely acid saliva. I learned that she died suddenly, no cause being given, within 2 weeks after the visit.

CASE LXXXII.—*Carcinoma of the bladder.* Mr. F. C. R., aged 51, first consulted me Sept. 7, 1920. He had had a suprapubic operation for what was called papilloma of the bladder on Jan. 23, 1917, followed by a cauterization of the base, and a 24-hour application of radium 2 weeks later, through the incision, and also in the rectum. He has since had radium used a number of times. His health seemed very much better until, in June, 1918, there were bladder symptoms, and he was unfortunately burned in the bladder, with an electric cautery. On Feb. 15, 1919, the deep cautery was used by a noted urologist "to burn out the ulcer," and since that time until May, he

has been using bladder injections daily, of permanganate of potassium alternated with a solution of nitrate of silver.

At the time of the first consultation he was passing urine every two or three hours in the day and several times at night, and could not hold 3½ oz. in the bladder to secure a specimen for analysis. The urine was of a high specific gravity, with high acidity, and some pus. Placed on full dietetic and medicinal treatment the improvement was marked very shortly. My last note December 21 states that he can retain 8 oz. of urine at one time, and has retained it as long as 6 hours, and usually goes through the night with one evacuation of urine. The total amount passed daily during the preceding 30 days had varied from 35 to 62 oz., with an average of 47½ oz., and he had lost the painful sensation he had had after voiding urine. It is, of course, too soon to make any final judgment of the case, but with other experience in cancer in this and other regions it is reasonable to expect that with absolute faithfulness to treatment he will remain well. He now weighs 181 pounds, which was his normal weight before the trouble begun, he doing his full work as lawyer all the time.

CASE LXXXIII.—*Post-operative cancer of the bladder.* Mrs. B. R., aged 32, was referred to me for treatment by her physician, Oct. 12, 1920. Five years previously she had had something wrong with a pregnancy, and was curetted, and has had hemorrhage and pain with menstruation since. Six weeks previous to her visit she had hysterectomy and ovariotomy performed, and there was then found a cancerous mass on the wall of the bladder which was left, after a biopsy was taken. She had since sharp pain in the left loin. A later communication from a distant city stated that the full dietetic and medicinal treatment had produced "wonderful improvement," and treatment along every line was ordered to be continued.

CANCER IN OTHER LOCALITIES

In this group were placed 25 miscellanous cases of cancerous lesions on various parts of the body, some of them primary

lesions of carcinosis, and some of them the result of metastasis, many of them of very considerable interest. There were seven females and 18 males, whose ages ran from 24 to 80 years, with eight who were 69 or more years old. Four were recorded as having died, and four were cured. These cases relate to carcinoma on the back of the hand, five instances, two from *x*-rays, axilla, shoulder, abdomen, thigh, leg, foot, and nine on the penis. Some of the more interesting cases may be alluded to.

CASE LXXXIV.—Mr. B. H. C., aged 74, seen first on Mar. 10, 1919. He had long had a roughened, warty condition on the back of the right hand, which began to be active about a year before his visit, and for the previous 3 to 4 months had grown to its present state, having been cauterized. When seen there was a patch about an inch in diameter, raised about ⅓ of an inch, hard, with characteristic edges, and covered with a moderate crust, which continually reformed when knocked off. The strong thorium paste was freely applied over all, with a wire vaccination shield to protect the same, which was worn all the time until on August 24, when the surface was normal. There had been about a dozen applications of the paste, at intervals of from one to two weeks, according as the crust formed was still adherent or loose.

CASE LXXXV.—*Cancer of the axilla following removal of same on the hand.* Mr. C. W. R., aged 59, had a warty growth on the back of the right hand, 2 years before his visit July 20, 1917. One year later this, which had grown, was removed surgically, together with glands which had formed in the axilla, in October, 1916. On Feb. 12, 1917, the glands in the axilla, which had returned, were removed, and he had also *x*-ray treatment. When he called the right arm was greatly swollen, and there was an enormous mass of characteristic, ulcerating tissue filling the axilla and keeping the arm more or less extended. The saliva was strongly acid, and the bowels were constipated, he depending on medicine. He was placed on full dietetic and medicinal treatment, but little could be expected in such a condition, and he was soon lost sight of.

CASE LXXXVI.—*Possible primary cancer of the axilla.* Mrs. K. R. A. H., aged 67, first noticed a small enlarged gland in the left axilla, slightly painful, about 7 months before I was consulted May 18, 1920. This was removed surgically on Oct. 20, 1919, 3 or 4 weeks after it was detected; with several courses of *x*-ray treatments thereafter. After the operation the left arm was very much swollen, involving the whole forearm and hand, which has gone down somewhat but not entirely, with *x*-ray treatment, but since being placed on full dietary and medicinal treatment, her son, who is a physician writes that it has returned to normal, which he attributes to the treatment, which "had worked wonders for her, so far." Neither before the operation, nor some months after, have they been able to discover "any other focus of carcinoma in any other organ, and it seems as if the axillary glands were the primary seat."

CASE LXXXVII.—*Metastatic cancer of the hip bone.* Mrs. C. J., aged 37, was first seen April 22, 1920. She had had one exploratory operation at a New York Hospital 3 years previous- She was told that she had a tumor at the neck of the womb, too far gone to operate upon, and was sent to the Memorial Hospital, and apparently cured by 3 or 4 treatments. But for the past several months she had had symptoms pointing to the left hip, with spasmodic pains and contraction of the muscles, and for about 3 weeks had been in bed. She was cachectic, with a poor appetite, pulse 135, and she succumbed within 2 months. There were probably metastases elsewhere as well.

CASE LXXXVIII.—*Carcinoma of the left thigh.* Mrs. S. B., aged 70, two years previous to the visit had injured the back of the middle of the left thigh on a barrel hoop, and the sore had never healed, although treated with ointments, etc. When seen, Apr. 15, 1920 there was a deeply ulcerated mass of cancerous tissue 4 by 6 in. in diameter, on the outside and back of the middle of the left thigh, with hard, typical edges, and two very large and hard, and not painful glands, in the groin. Very much comfort and improvement was realized by careful internal

measures, together with a continuous application of a carbolized calamine and zinc ointment, spread on very thin pledgets of absorbent cotton; but the disease overcame her and she died not so very long after.

There were nine cases of carcinoma of the penis, mainly on the glans, some of which were very severe and distressing; the ages ran from 24 to 76, with an average of 52 years. One of them was particularly interesting, because of its duration and the complete cure by operation, observed nearly five years thereafter.

CASE LXXXIX.—*Carcinoma of the penis.* Mr. H. A. G., aged 47, made his first visit on Aug. 8, 1912. For 3 or 4 years he had had some disease beneath the foreskin, which had become very troublesome 6 months before his visit. It was thought to be syphilitic, and he took mixed treatment for 3 months without result. The lesion was then scraped on June 7 by a specialist in another city, and it was thought that spirochetæ were found in the scrapings, and he was given salvarsan intravenously. On July 4, there was another dose of salvarsan, and the sore seemed to heal up in 10 days, but a week before his visit it was again sore, and was cauterized by his family physician.

When seen there was a characteristic epidermoid carcinoma, involving nearly half the glans, with much infiltration and deeply eroded, and very painful, for which he took morphine. He was treated with an emollient ointment and internal measures for 6 weeks, when the sore was partially healed by September 19, but it was then quite hard and characteristic of epithelioma, with everted edges and abundant granulations. There was no pain and he had abandoned the opiate, sleeping well. On September 25 there was a very complete operation performed, under my direction, with amputation at the base of the penis, and thorough cleaning out of the enlarged glands in both groins. Later he was worried about the former diagnosis of syphilis, and two Wasserman's were taken by two different serologists, and both were negative, and the excised lesion had

been examined microscopically and found to be carcinomatous. On Feb. 3, 1917, he presented himself for examination and there was a perfect result, with no recurrence, four years and 6 months after his first visit. How much of the unfortunate result in this case was due to the mistaken diagnosis and the repeated scraping and cauterization, cannot be decided, but it teaches a lesson.

SARCOMA

There were 46 patients with sarcoma in various locations and with different degrees of severity, whose ages ran from 6 years to eighty. The advanced ages of many of the patients was unexpected, for, leaving out that of the youngest, 6 years, the average age of all was just 50 years, contrary to what is generally expected in sarcoma: there were only 9 of 40 or less years of age.

The youngest patient, a boy of 6, ultimately died with a large tumor over the sacrum; the oldest, aged 80, had a great metastatic mass by the left jaw, from pigmentary lesions above, irritated by shaving, ten years before. There were 11 cases, 7 males and 4 females with the disease in the mouth and jaws, 4 with multiple non-pigmented sarcoma, 1 male and 3 females, and 13 cases of melano-sarcoma, one of them, a most striking case, with comple recovery, has already been recorded, Case XVII: two others are worthy of special record.

CASE XC.—*Melano-sarcoma of the lower leg.* Mrs. L. H., aged 50, seen in a county town, Sept. 1, 1918. For 2 or 3 years there had been developing on the right lower leg, about the middle and outer aspect, a tumor somewhat dark in color, which gave her no particular trouble, except some aching when long standing. She was being treated for an eczema of some duration when this was incidently mentioned. On examination there was a mass about an inch in diameter, raised half an inch or so, and of a dark, purplish color. Dr. H. H. Janeway saw her with me and confirmed the diagnosis of melano-sarcoma and very strongly urged that she go at once to the Memorial Hospital, for radium treatment, predict-

ing that it would prove very serious if neglected or removed surgically, as there were enlarged inguinal glands. This we expected that she should do.

For her eczema, and for this, she was placed under rigid vegetarian diet, and given an acetate of potassa, nux, cascara, and rumex mixture. The next summer I saw her, in the country, and the eczema had vanished, and she thought little of the leg trouble, which was in about the same condition, she had not taken the radium treatment, or any other than as prescribed, as she could not well come to the city. When last seen, on Sept. 19, 1920, over 2 years after the first, the mass was only a little larger, projecting a little further, and had given her no particular annoyance. The result in this case is striking, especially in contrast with the next one.

CASE XCI.—*Melano-sarcoma of the left hip.* Mrs. T. E. J. aged 66, had been treated by me in 1888 for eczema, which yielded shortly and remained well, and then at intervals for other troubles, and then not for a long time. On Feb. 20 1920, she came to me for a minor skin trouble, and rather incidentally mentioned a pigmented lesion on the left hip, which had existed for 5 years; but for the past year it had developed slowly into a flat, slightly raised mass, which annoyed her by itching.

When seen there was a black tumor, about a half an inch in diameter and raised ⅓ inch with a little moisture beneath it, from scratching. As she was a lady of position and means, I disliked to take the responsibility of the case alone, and sent her to a very prominent surgeon for consultation. He recognised it as a melano-sarcoma, with enlarged inguinal glands, and strongly advised immediate removal of the primary growth and the inguinal lymph-nodes, but considered the "out-look as certainly very bad." He operated on March 29, and confirmed the diagnosis by microscopic sections. I saw her socially a few weeks after the operation, she still being confined to her room, when she seemed fairly well, but I learned that she died within 4 months thereafter.

There have now been presented the more or less full clinical histories of over 90 cases of malignant disease, besides the incidental mention of some others; these all are from among still many others of like character mostly all illustrating to a greater or less degree the value of a faithfully carried out proper dietetic, medical, and local treatment, in both early and late cancer.

Among these have been some terrible cases, post-operative and inoperable, which have exhibited the value of this line of procedure in an interesting manner, both in ameliorating suffering and in prolonging life, with some cures, while the results in early cases have been most gratifying.

Among the 91 cases, here recorded, more or less fully, there were 26 known deaths from the disease, besides 3 which were probably fatal, a total of 29 in all. But, of course, there were very many more not traced, among far advanced cases seen once or twice, or in consultation. There were 35 regarded as clinically cured, that is all recognizable signs and symptoms of cancer had disappeared. Some were known to be well and free from disease for 16 years, others for 5 years and more. Many more, of more recent date were recorded as so improved or greatly improved that in the light of experience it is expected that all will go well, if they will continue to follow all directions as conscientiously as has been the case with others. Of those who died such an end was inevitable when first seen, in many of them, but their records show a course very different from that commonly observed in such cases, and most of them passed away peacefully, without pain and not requiring or taking any morphine or opiates.

Among the entire number of patients, 229, with neoplastic disease, recorded during the past 4 years, since statistics were last given, there were 52 known deaths, including the 29 mentioned above, among the histories given. But, as already remarked, there must have been very many more, for it is very difficult in a busy private practice to follow up patients when they do not call as directed. Some of the cases, of course, are too recent to enter at all into statistics.

Of the 24 cases of undoubted primary cancer of the breast whose histories have been given, there were 8 patients who were known to have recovered clinically for over or about the 5-year period, several being watched for about 16 years, perfectly well, and there is no reason to expect recurrence of the cancerous trouble, if with proper care they persist in the measures which have removed the neoplasm. There were also more than that number who had been clinically well from 1 to 4 years, with every prospect of remaining well if they persisted faithfully, as they had done, in all the necessary measures; there are also many others in whom the progress has been favorable up to the present time, which will probably continue, if they are faithful to treatment. All this is on a very different basis from that of surgery, or even of *x*-ray and radium, which may remove more or less of the accessible products of carcinosis, leaving the real cause of the disease to produce new lesions, possibly at a late date; even as tuberculosis will remain absent indefinitely under proper conditions, but will recur with a recurrence or continuance of the elements allowing the first lesions to develop.

Four of the patients with primary cancer of the breast died, one suddenly at 85 years, one at 68, who came with an enormous, absolutely inoperable mass, one aged 53 quite similar, and one, aged 36, with general carcinosis after removal of the breast by chemical procedure, as described already. All of these had been declared inoperable, by surgeons, before coming for treatment. There were 10 post-operative cases detailed, three of them were known to have died, peacefully, without morphine, and four were greatly improved when last seen.

There were six absolutely inoperable cases of cancer of the uterus, of whom three recovered completely, whose histories have been detailed, two now for almost 4 years, and two died, and one is too recent to report on, but improving. Time and space do not permit of analyzing the balance of the cases, which, however, are well worthy of consideration.

Clinical experience, therefore, and the results obtained, con-

firm abundantly what has preceded in regard to the constitutional nature and the value of intense medical treatment, as intimated in the opening sentences of this chapter. Did space permit the number of these illustrative histories could be increased materially, although, naturally, the most striking instances have been selected. Much confirmation could also be given by the written testimony of many physicians and surgeons who have made trial of this mode of procedure, while any amount of testimony could be adduced by those who, in print or otherwise, have acknowledged the futility of surgical operations in really curing cancer. All knowledge and experience, therefore, seems surely to point to the wisdom of not ignoring a proper medical consideration and treatment of the disease carcinosis, and of not simply attempting to attack only its manifestations in different parts of the body, surgically or otherwise, except as an adjunct to proper medical treatment.

CHAPTER XIX

CONCLUSIONS

In the light of all that has been presented in the preceding pages what must be concluded in regard to the nature and proper treatment of cancer? What is the real cancer problem? For it has been abundantly shown by statistics and otherwise that the hitherto accepted theory and view of its purely local nature and treatment have resulted only in a steadily increasing morbidity and mortality of cancer, with all the miseries and uncertainties of surgical operations, and the pain and distress and fatality of recurrent manifestations of the disease; and even the ultimate shortening of life in the average, as claimed by many.

Laboratory research, with its enormous expenditure of time, money, energy, and animal life has proved an utter failure in solving "The Cancer Problem," as far as adding materially to our intrinsic knowledge of the disease, or in the way of lessening its morbidity and mortality. Nor have the various Societies for the study and prevention of cancer accomplished anything practical in regard to its prophylaxis or cure, and have certainly not lessened its ravages.

Propaganda in regard to the necessity for the very early and complete extirpation of all suspected cancerous and pre-cancerous lesions, have been shown by United States statistics to have more than doubled the percentage of deaths, in the year of greater surgical activity which followed this special appeal throughout the country.

During all this period of the intense study of cancer in the laboratory, and of surgical zeal, the mortality of tuberculosis, under wise medical supervision has fallen about 30 per cent, since 1900, while that of cancer has risen by about the same 30

per cent. The mortalities of the two diseases have, therefore, approached one another almost 60 per cent, and at this rate in 20 years more the death curve of the two will have more than crossed one another, unless something occurs to produce a change in the method of handling these two diseases. Indeed, in New York City, during 5 particular weeks, in 1920, the deaths from cancer, according to the weekly reports of the Board of Health, have actually been more than those from tuberculosis, and, as we have seen, during the last 6 months of 1920 the deaths from cancer actually exceeded those from tuberculosis, by *twenty-two*.

What then is to be done? Shall the world go blindly ahead with the accepted dictum that "we know nothing of the cause of cancer," and pursue a course of treatment under which the death rate has so steadily and alarmingly increased, or shall we have minds open to conviction? It is by no means claimed that the goal has been reached, nor that we know fully the real, absolute, and ultimate cause of cancer, any more than we know absolutely the final cause of many other diseases, which are treated more or less successfully. We do know enough now, however, to begin with at least, for nothing could be worse than the commonly recognized and acknowledged 90 per cent of ultimate deaths from the disease in those once affected with cancer, under surgical management, while that of the cases here analyzed has been very much less under medical management.

In order that the subject of the constitutional nature and treatment of cancer might be readily understood and grasped, a synopsis, which I have already repeatedly presented, was given in the first chapter, to cover as far as possible the essential matters to be brought out in later pages. And now in conclusion these are especially referred to as illustrating what the laboratory has furnished negatively and positively, to demonstrate that cancer is not a local disease, but one of constitutional origin and nature, together with the confirmation of this fact from statistical and clinical evidence.

In regard to no other bodily ailment has there been such an

imperious and insistent demand for the establishment of an absolutely definite cause of disease, proven by laboratory research and experimental procedures, as in the case of cancer. This is due to the long prevailing and narrow-minded view which has been held as to its local nature, and until some definite cause is fully proven, the skepticism which has existed will probably still continue to exist, for a while, in the minds of many, namely that no cause can possibly be proved otherwise. It is here frankly acknowledged that the exact and precise metabolic conditions causing this disease have not yet been definitely fixed upon, and possibly will never be capable of actual laboratory demonstration. And yet it has been shown by many cases that by proceeding along this line of study and treatment, results have been obtained in many directions which greatly surpass those commonly seen. And if the many other practitioners who have obtained similar results from proper diet and medical treatment, could speak, it would be thoroughly convincing. Moreover, if the real truth could be told, it would be found that physicians and surgeons pretty unanimously recognize the fact that heretofore the profession has not gotten on the right track concerning the nature and proper treatment of cancer.

It is not at all claimed that "the cancer problem" has been fully solved, but "the real cancer problem" is here presented for further study and elaboration, by close observation upon the human subject, conjoined with proper laboratory work.

As in the treatment of other diseases many remedies and measures may be required, singly, combined, or alternately, each contributing its share to a successful result, so undoubtedly in cancer many different lines of treatment may be used with advantage, conjointly or in succession. While "the day of cancer surgery is past. There is nothing in it," as an eminent pathologist has remarked, it is conceivable that occasions may arise when some surgical procedure is advisable, for the prompt removal of a seriously offending cancerous mass, but not with the expectation of curing the disease: and operative surgery may possibly be called for occasionally, in certain rare cases.

We have seen that the *x*-ray and radium have been effective in causing to disappear, even permanently, certain very local epithelial derangements, such as cutaneous epithelioma, and also that their skillful use may possibly affect some deeper, true cancerous lesions favorably. But when more or less metastasis has taken place they are either helpless or afford only temporary benefit. Moreover, many candid workers along this line acknowledge that their effect is only local, like surgery, and that it does not and cannot reach and remove the real cause of, or cure true carcinoma. But proper radiation does mark a distinct advance in the conflict with cancer, and should certainly be skillfully used when possible, in certain cases, as an adjunct in overcoming some of the local results or products of the carcinosis, carcinomatous dyscrasia, or disease.

In like manner sero-therapy, of one kind or another, has been reliably shown to have had a favorable action in a certain small proportion of cases of cancer, even those which seemed inoperable and hopeless. But one after another of these measures has been abandoned as practically useless or infeasible, and as not at all reaching and removing the true basic cause of the disease. The only possible exception to this is the one last mentioned, by repeated injections of foreign vegetable proteals; this treatment approaches the line of thought presented in these pages, namely the relation of cancer to the imperfect breaking up and assimilation of the elements of protein in the system. So that this line of treatment has also a distinct indication in regard to the disease cancer, or carcinosis, of which the local lesion which we call cancer is the product, and this may and perhaps should be employed in connection with any or all of the other measures which have been found of service.

Organotherapy is still in its infancy and no correct judgment can be yet formed as to what part it may eventually take in checking carcinosis, or removing its manifestations. Undoubtedly the ductless glands play an important part in the conduct of metabolism, and in the life processes of the system, as we have seen in a former chapter, and they seem to have a syner-

getic action on each other; they also affect the operation of the larger organs and the condition of the blood, and consequently influence the healthy or diseased action of all the cells of the body.

But it is not yet determined exactly what part each of the endocrinous glands play, or whether disorder comes from excessive or insufficient action of any or all of them, so that for the present our knowledge of this line of practice is rather experimental and empiric. Thus far, to my knowledge, there is only one of them, the thyroid, which has been widely acknowledged to have any very distinct influence in connection with cancer, and our knowledge of this is almost wholly clinical. But the experience of many, including myself, is that, when rightly used, proper preparations of animal thyroid are of decided service in many cases of cancer, especially in subjects exhibiting adiposity, in whom the disease always tends to do badly. So that thyroid treatment may and should be used in many cases, in conjunction with other proper measures, already indicated; for it acts along the same lines of modifying and restoring to the normal state a blood current which will so nourish all the cells of the body that none of them will rebel and run riot, as in our illustration of a mutiny in a regiment or on shipboard, from insufficient or poorly prepared nutriment. It has been abundantly shown in other chapters, however, that the basic element of the successful treatment of cancer must always rest upon the proper supply of correct alimentation: if this is wrong all other treatment is ineffective.

Having covered all the means thus far commonly employed in the treatment of cancer, and finding such limitations in ultimate service in regard to each and all of them, what conclusion must we finally come to? There is only one. Thus far the profession has not succeeded in checking the morbidity and mortality of the disease because investigators have long been mainly on the wrong track, and our ideas as to the true nature of cancer must be radically changed if we wish to diminish its morbidity and mortality.

Led by honest, industrious, intelligent, and capable pathological workers, cancer has been regarded as a local disease, whereas it has been abundantly shown and declared by any number of good clinical observers that it is a constitutional one, quite as much as is gout, and many other affections. In the latter the derangement of tissues takes an inflammatory form or character, and in the former, cancer, a neoplastic one, both of them from an erroneous pabulum, a faulty blood and lymph stream furnished to the cells. Exactly why this is so we may perhaps never know: indeed we now know little more about the true, actual pathogenesis of gout than we do about that of cancer; but experience has taught us how to reach the former by correct dietetic, hygienic, and medicinal measures, and many of us have learned the same about cancer, with gratifying results, as has been shown in the preceding pages.

The logic of the whole situation is to accept what has been shown to be reasonably correct and of advantage in all lines of procedure, and to adapt them, singly or conjointly, to individual cases, remembering always that probably there never can be any one single or simple cure for cancer, such as quinine for malaria, mercury for syphilis, or even antitoxin for diphtheria (for cancer is not a microbic affection). But back of all other measures there must be a correct diet and mode of living, and correct action of the whole system, furnishing a correct blood stream for the proper nourishment of every cell of the body; for proper nutrition is the basis of health. Then there will be no rebellion or mutiny of cells, with its sad consequences, which are familiar to all.

When exactly the proper nutrition is restored, and the cells receive a correct pabulum, we find that the aggregation of riotous cells, whether in the original lesion of cancer or in metastases, disperse and return to their normal function, as would mutinous soldiers or sailors when their rations were made adequate and attractive. But, as with a return to bad sanitary or dietetic conditions there would be again mutinous action in the latter, even so there will be a recurrence of the

cancerous lesion, if there is a continuance of the same bad blood conditions which first caused certain normal cells to give up their allegiance to physiological control and to combine in neoplastic groups of malignant character.

Therefore, one who would intelligently and successfully treat malignant disease must have broad medical knowledge and experience, with medical acumen, and apply the same vigorously to the study of the individual patient, with patience and great perseverance. He must also keep abreast with advances made in surgery, radiation, serotharapy, thermotherapy, chemical extirpation and any and all measures which may be of service at any time in favorably acting on the immediate products of the disease carcinosis.

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