

Gestational trophoblastic disease GTD

Prepared By
Divya Rani R
Lecturer
Midwifery Dept

Gestational trophoblastic disease

GTD

Definition : It is a clinical term used to indicate three closely related conditions characterized by active abnormal proliferation of trophoblastic cells : :

- ❖ ***hydatidiform mole ,***
- ❖ ***invasive hydatidiform mole and***
- ❖ ***Choriocarcinoma***

Gestational trophoblastic disease

GTD

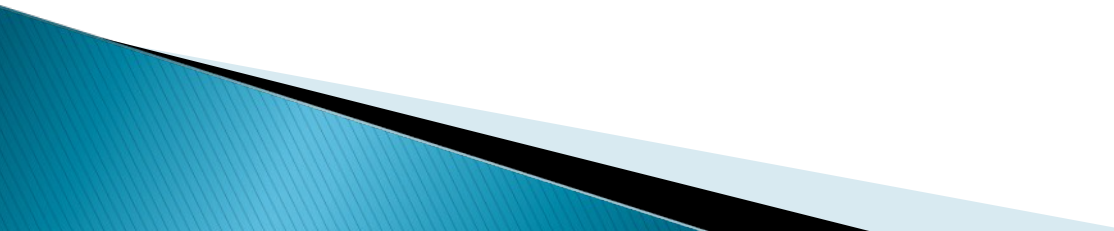
- ▶ **These neoplasms retain certain characteristics of the normal placenta such as invasive tendencies and the ability to make hCG hormone**

Gestational trophoblastic disease

GTD

- ▶ **Pathological classification** :
 - ❖ Hydatidiform mole = 80 % of cases.
 - ❖ Invasive mole = 12-15% of cases.
 - ❖ Choriocarcinoma = 5-8% of cases.
- ▶ **Clinical classification** : The course, and prognosis of the disease accurately reflected by hCG hormone
 - ❖ Benign = 80%
 - ❖ Malignant = 20%

Types of GTD

- ▶ The term *Gestational Trophoblastic Tumors* has been applied the latter three conditions
 - ▶ Arise from the trophoblastic elements
 - ▶ Retain the invasive tendencies of the normal placenta or metastasis
 - ▶ Keep secretion of the human chorionic gonadotropin (hCG)
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Hydatidiform mole

- ▶ The maternal age over 40 years found to have a 5.2-fold increased risk of trophoblastic disease in comparison to the mothers below the age of 35 years.
- ▶ Based on:
 - ✓ Genetic and histopathological features
- ▶ Hydatidiform mole can be subdivided into:
 - ❖ complete and
 - ❖ partial mole

complete moles

- **Genetic features:** One of the most remarkable discoveries about hydatidiform mole has been the demonstration that complete moles have chromosomes exclusively from the paternal side, and the karyotype is nearly always 46,xx and only rarely is 46,XY observed.
- The normal mechanism is for a haploid sperm, 23X, to fertilize an empty egg, and to duplicate itself to form a 46,XX complement. Much less commonly, two spermatozoa, one being 23,X, and the other, 23,Y, can fertilize an empty egg, to give karyotype a 46,XY.

Partial moles

- ▶ **Are triploid in origin with two sets of paternal haploid genes and one set of maternal haploid genes**

Partial moles

- ▶ **They occur, in almost all cases, following dispermic fertilization of an ovum.**
- ▶ **There is usually evidence of a fetus or fetal red blood cells**

partial moles

- ▶ In the partial moles ,the normal finding is a triploid karyotype ,69 chromosomes instead of normal 46. The most common mechanism appears to be fertilization of normal egg by two sperm, giving a complement of 69,XXY.



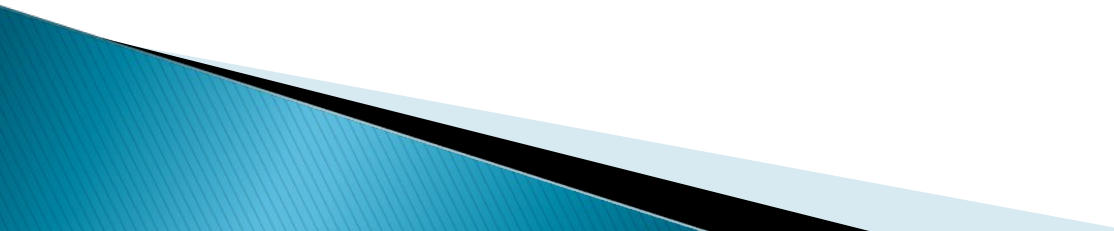
Partial hydatidiform mole

Pathological features

❖ **Complete mole :**

- ❑ **there are numerous edematous vesicles, which looks like a bunch of small clear grapes,**
- ❑ **; usually no fetus, or membranes.,**

Pathological features

- ▶ **microscopically: there are:**
 - **large oedematous enlarged villi ,**
 - **a vascular ,**
 - **with variable degree of trophoblastic hyperplasia.**
 - **carries greater risk of malignancy and requires longer follow up than the partial mole.**
- 

Pathological features

- ❖ **Partial mole:**
 - **Shows a less clear -cut picture ,with the formation of vesicles usually focal ,**
 - **fetus and membranes may present,**
 - **the vesicles have degree of vascularity.**

Pathological features

- ▶ **In general ,the more active trophoblastic appearance the greater the risk of malignancy.**
 - ▶ **So the subsequent management depends more on the hCG results than the histological reports.**
- 

Clinical features

- ❖ **Bleeding : Bleeding in early pregnancy after variable period of amenorrhea is the most common clinical sign of the mole (occurs in 90% of cases), with the passage of the vesicles.**

Clinical featu.....

- ❖ Hyperemesis gravidarum : Occurs into 25% of cases of moles ,and appears more common when the uterus is much enlarged and hCG levels are very high.
- ❖ Uterine enlargement: The uterus is commonly “large for date”in 50% of case of moles ,
- ✓ although, in a small proportion of cases the uterus corresponding to the gestational age or smaller than date. .
- ✓ The fetal parts are not palpable, and fetal heart is absent.

Clinical featu.....

- ❖ Large theca lutein cysts of the ovary are present in “20%” of moles, these may be exaggerated the clinical picture of large for date uterus. These cysts are manifestation of excessive hCG.

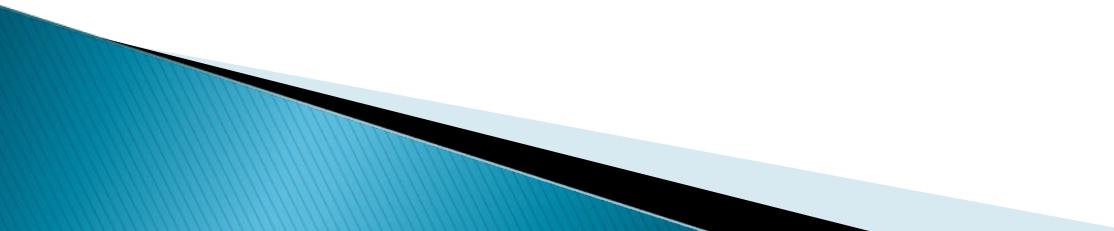
Clinical featu.....

- ▶ Pre-eclampsia :Occur in association with the moles with range widely from 12-54%,these due to differing times of diagnosis, the longer pregnancy progresses ,the greater chance to developing pre-eclampsia. If the signs of pre-eclampsia appears early in pregnancy , the possibility of hydatidiform mole should be looked for with out delay.

Clinical featu.....

- ❖ Hyperthyroidism: Develop in small proportion of women ,and this may be due to thyrotrophic effects of the human chorionic thyrotrophin , which may lead to goitre, fine tremor , tachycardia, and weight loss.
 - ❖ DIC can develop in long-standing hydatidiform moles , when there is embolization of trophoblastic tissue to the lung, leads to thromboplastic substances which stimulate fibrin, and platelet deposition.
- 

Diagnosis of hydatidiform moles

- **History and examination :**
From the history of amenorrhea ,passage of vesicles vaginally with bleeding ;the size and consistency of the uterus.
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Diagnosis..

- **The increasing use of ultrasound in early pregnancy has probably led to the earlier diagnosis of molar pregnancy**

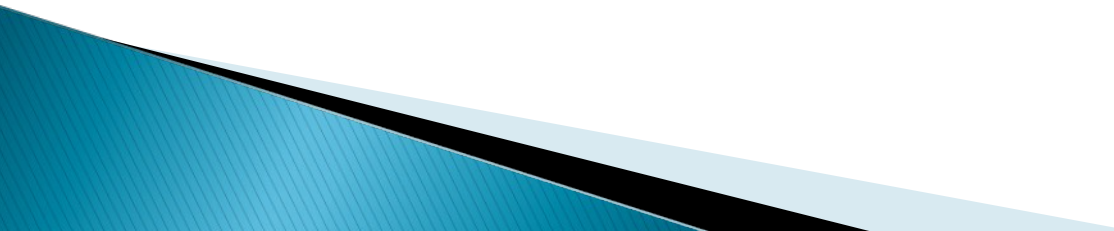
Diagnosis....

- **By the U/S examination can be diagnosed from very early pregnancy ,characterized by “Snow-storm” appearance.**

Diagnosis....

- **By very high levels of serum hCG than the normal singleton pregnancy ,which is diagnostic and prognostic to the course of the disease ,with very short duobling time.**

The risks of hydatidiform mole are:

- **Immediate hemorrhage ,sepsis, or pre-eclampsia; the treatment of these conditions has vastly improved recently.**
 - **Molar metastases :**
- 

- Choriocarcinoma: The most important danger association with the hydatidiform mole is the development of malignant GTD(Invasive mole or choriocarcinoma) in about 10% of cases,

Management

The aim of treatment is to eliminate all trophoblastic tissue from the maternal systems ;

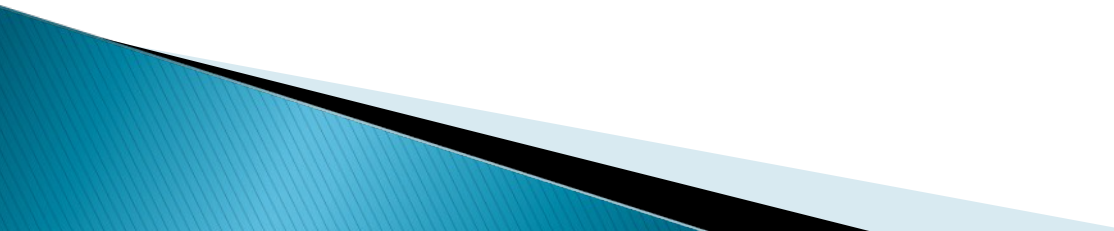
If the hydatidiform mole diagnosed ,steps should be taken to evacuate the uterus, and this achieved by:



Mangement

➤ **Suction & curettage (S&C):** The method of choice even when evacuation large mole

Mangement

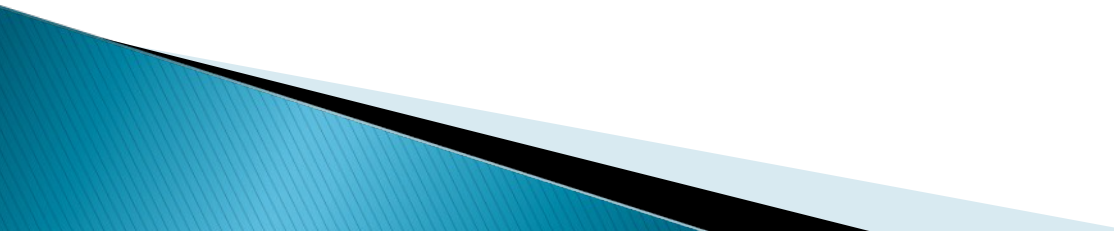
- ▶ **Under Anesthesia**
 - ▶ **Cervix dilation till 12mm.and S&C induced to the uterine cavity.**
 - ▶ **I.V oxytocin infusion is started .**
 - ▶ **S&C started by negative pressure of about 60 to 70mHg.**
 - ▶ **The curette is gently rotated to avoid perforation of the soft uterus, and the majority of the molar tissue is evacuated rapidly ,and the uterine size decreases**
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Mangement

➤ **Uterine
stimulation.**

Mangement

Medical termination of complete molar pregnancies including cervical preparation prior to suction evacuation, should be avoided where possible.



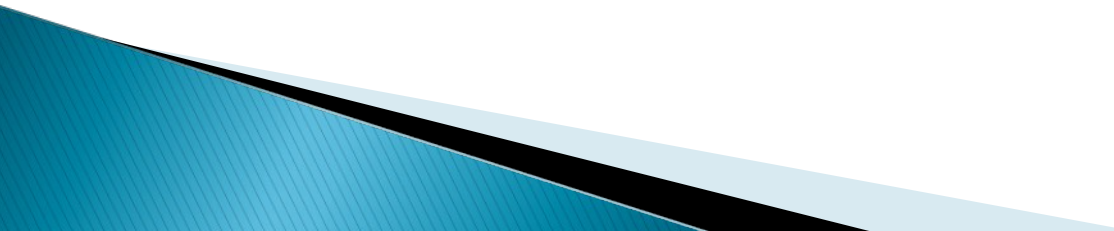
Mangement

- ▶ **The contraction of the myometrium may force tissue into the venous spaces at the site of the placental bed.**
- ▶ **The dissemination of this tissue may lead to the profound deterioration in the woman, with embolic and metastases disease occurring in the lung**

Mangement

➤ ***Surgical:***

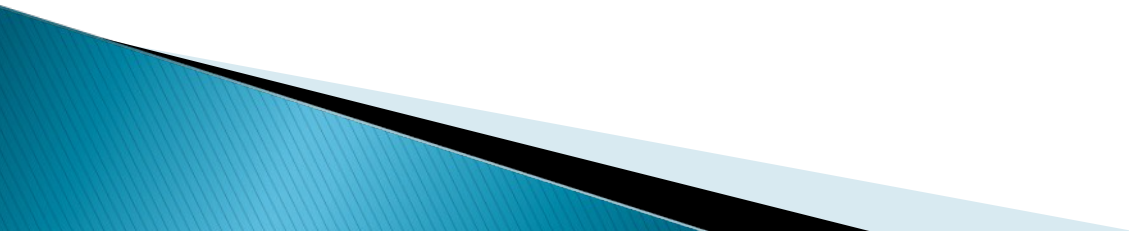
Mangement

- ▶ ***Surgical* : Hysterectomy has been recommended as a suitable method of treating hydatidiform mole in older women who completed their family ,to reduce the risk of post-molar trophoblastic disease**
 - ▶ **Chemotherapy with a single-agent drug**
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Evacuation of partial mole

- ▶ **In partial molar pregnancies where the size of the fetal parts deters the use of suction, medical termination can be used.**

High-risk postmolar trophoblastic tumor



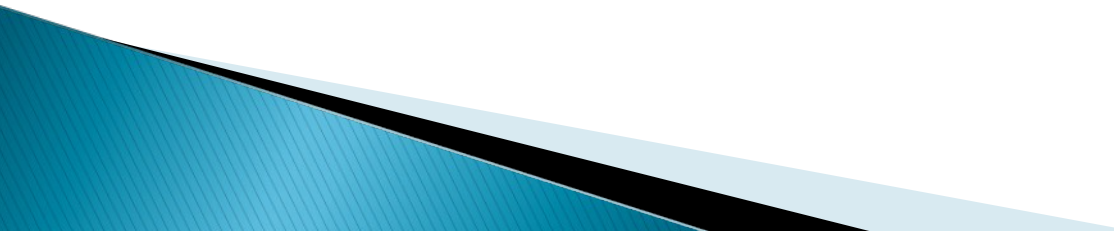
Follow-up

- ▶ **After the uterus has been evacuated :**
 - ✓ About 90% of cases ,the trophoblastic tissue die out completely.
 - ✓ About 10% of cases the trophoblastic tissue does not die out completely and may persist or recur as : **invasive mole** or **choriocarcinoma.**

Follow-up

- ▶ So it is important that women who have had a hydatidiform mole:
- should have close follow-up by *serum hCG levels* after the evacuation of the uterus,
- To ensure early recognition of persistent trophoblastic tissue
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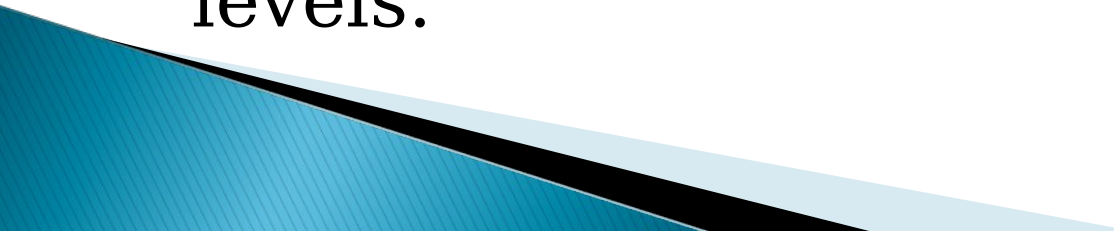
Follow-up

- ▶ After a molar pregnancy ,the hCG levels will usually have returned to non pregnant levels by 4 to 6 weeks after evacuation.
 - ▶ The follow-up is recommended for 2 years in cases of complete moles, and 6 months of cases of partial moles after the evacuation of uterus.
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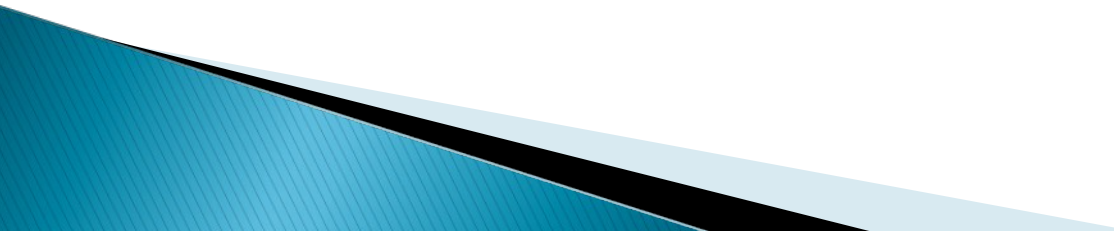
Follow-up

- ▶ Serial quantitative measurement of serum hCG level at weekly intervals, after evacuation of moles till 4 to 5 weeks when the hCG become normal Then every other week .When the titer gets negative the measurements are done every month fore 1 year.

Follow-up

- Indication of chemotherapy after the evacuation of the hydatidiform mole in:
 - ✓ Serum hCG >20000 i.u/L , at any time after evacuation of mole.
 - ✓ Raised hCG at 4 to 6 weeks after evacuation of mole.
 - ✓ Evidence of metastasis ,hepatic,brain,and pulmonary.
 - ✓ Persistent uterine hemorrhage after evacuation of mole with raised hCG levels.
- 

Follow-up

- ▶ To achieve effective follow-up ,the pregnancy is better to be avoided ,and also the use of oral contraceptive pills until the hCG levels returns to normal after the evacuation of the mole.
 - ▶ Early diagnosis of persistent trophoblastic disease ensures a good prognosis and an effective system of follow-up.
- 

Malignant trophoblastic disease

- ▶ **Malignant trophoblastic disease can exist in two forms:**
 - ❖ **Invasive mole = non-metastatic form.**
 - ❖ **Choriocarcinoma = metastatic form .**

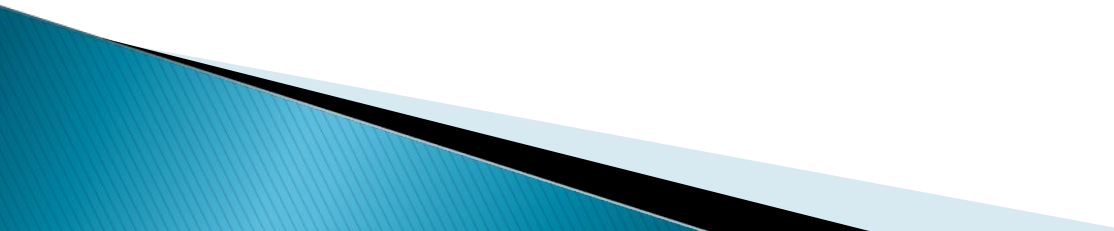
Malignant trophoblastic disease

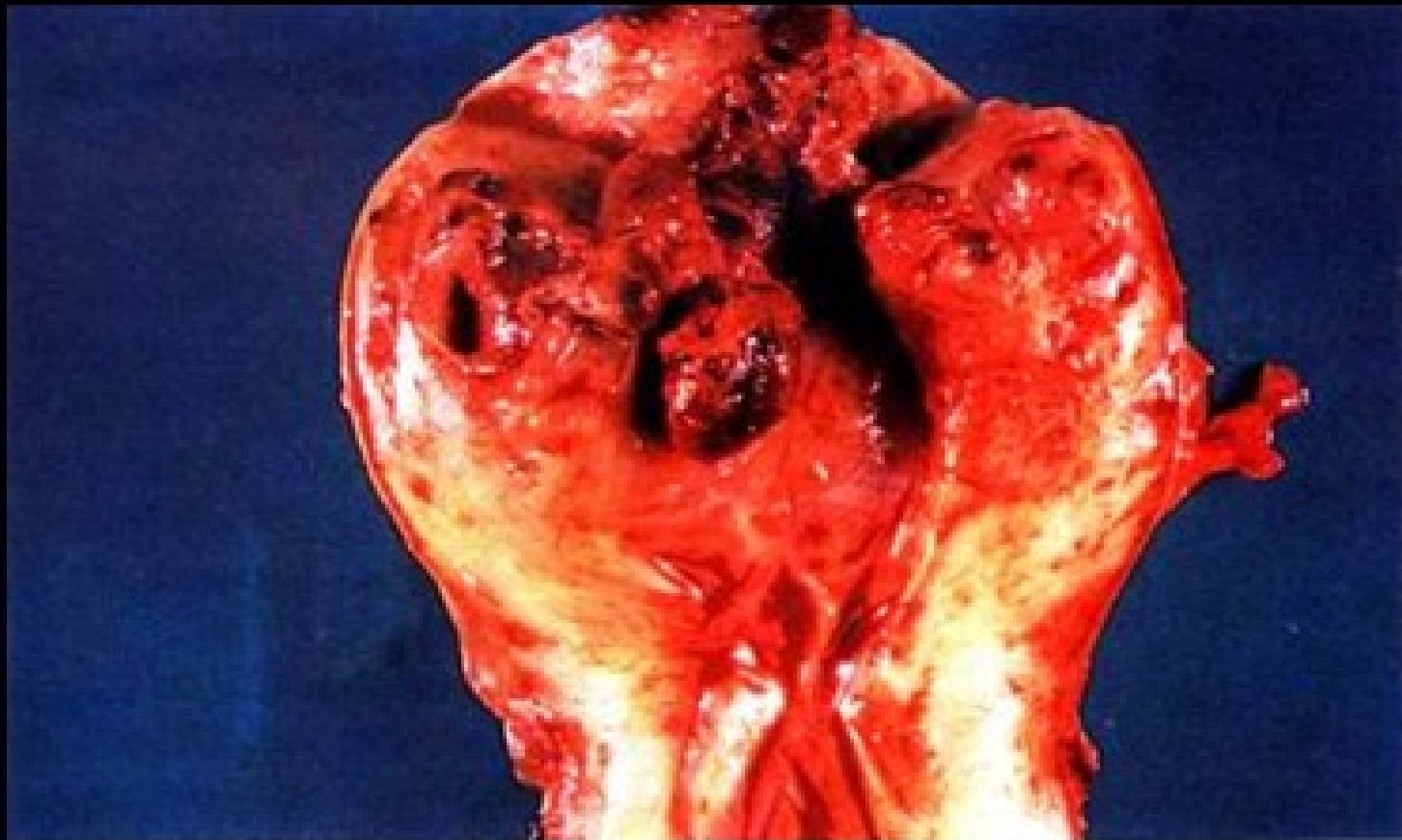
- ▶ **Both treated with the chemotherapy and monitored by hCG tumor marker.**
- ▶ **Choriocarcinoma subdivide into :**
 - **good-prognosis (Low-risk) ,and**
 - **poor- prognosis (High-risk).**

Invasive mole

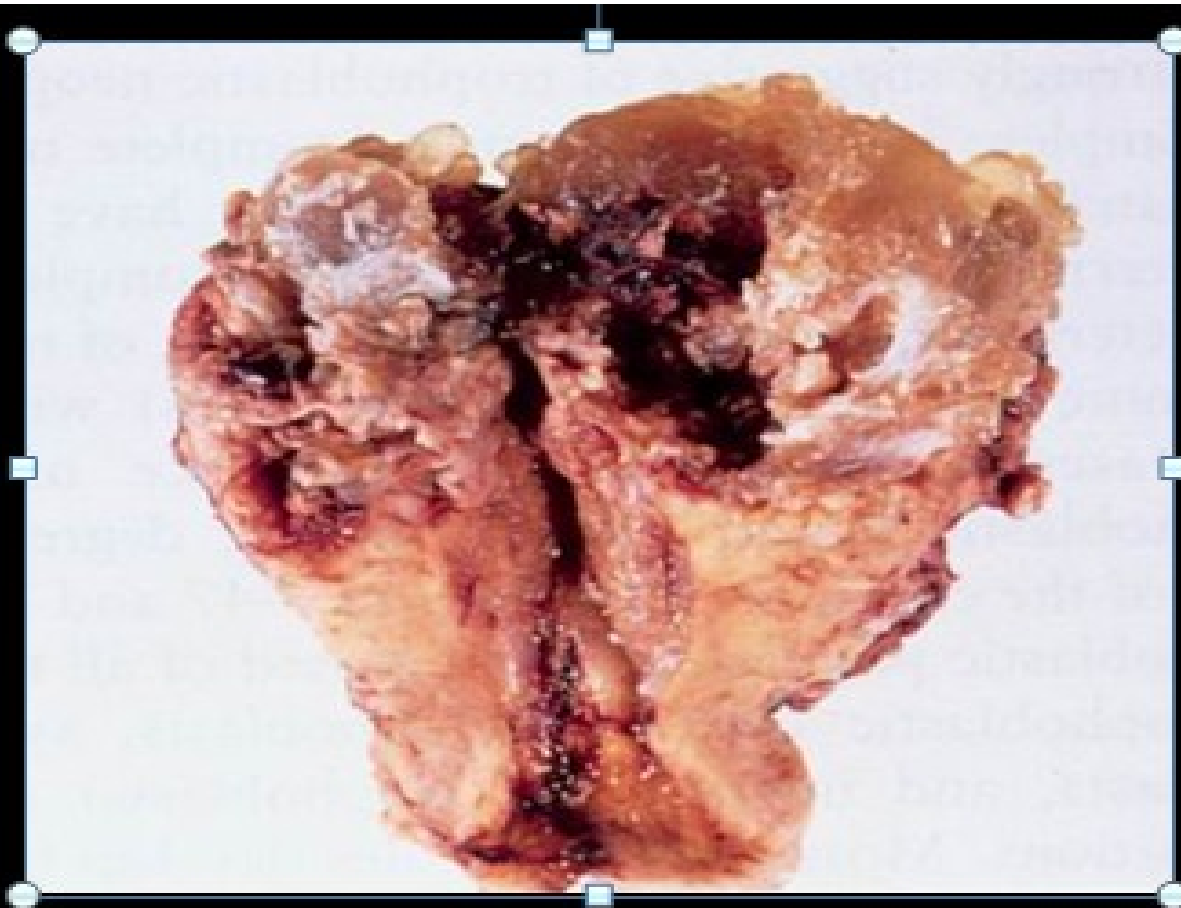
- **The diagnosis of invasive moles or “chorioadenoma ” is applied to the moles characterized by :**
 - **Abnormal penetrativeness and,**
 - **Extensive local invasion, along with**
 - **Excessive trophoblastic proliferation ,**

Invasive mole

- ▶ **The proliferative villi may invade the myometrium ,parametrium or the vaginal wall, although there is rarely evidence of metastasis.**
 - ▶ **The morbidity and mortality of this disease results from the penetration of the tumor through the myometrium and to the pelvic vessels with the resultant hemorrhage .**
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Invasive mole: the tissue invades into the myometrial layer.
No obvious borderline, with obvious bleeding.

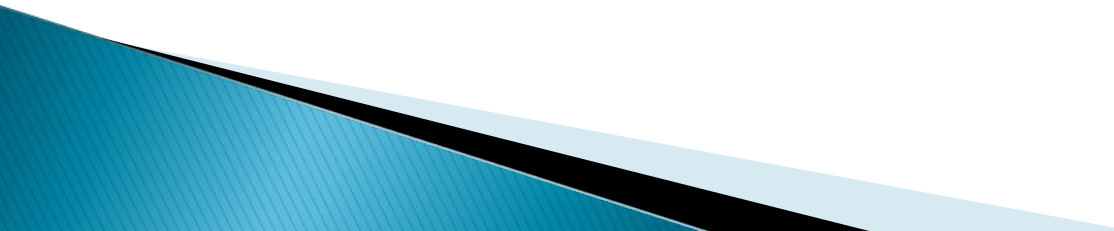


Invasive hydatidiform mole infiltrating the myometrium

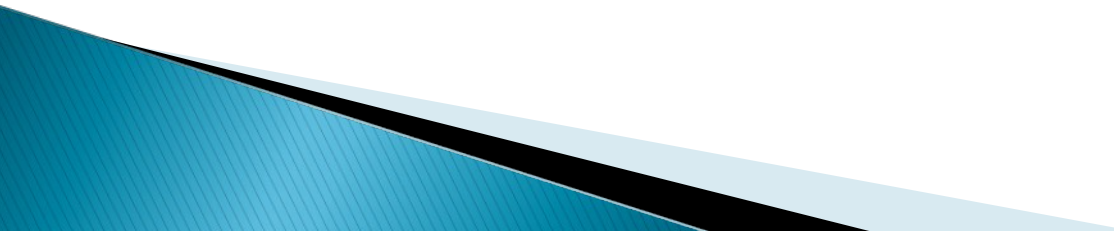
Choriocarcinoma

- **Choriocarcinoma**
subdivide into:
 - **good-prognosis (low risk).**
 - **Poor- Prognosis (High risk).**

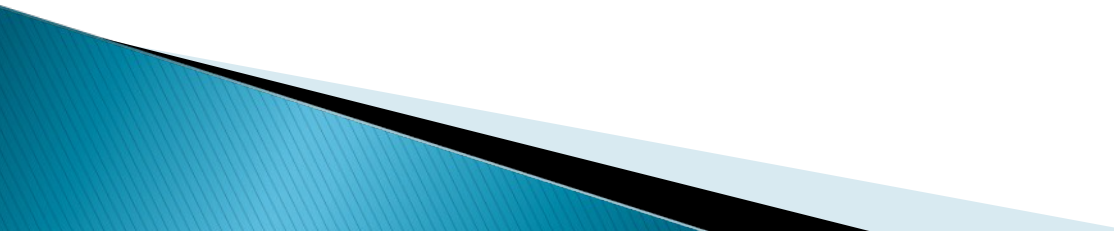
Epidemiology

- ▶ **The antecedent pregnancy is :**
 - ✓ **Hydatidiform mole in about 57% of cases.**
 - ✓ **Normal pregnancy in about 26% of cases.**
 - ✓ **Abortion and ectopic pregnancy in about 17% of cases.**
- 

Epidemiology

- ▶ **The risk of Choriocarcinoma after a hydatidiform mole is about 2-4% which is 1000 times greater than after a normal pregnancy.**
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Epidemiology

- ▶ **Choriocarcinoma is more likely to occur after complete mole .**
 - ▶ **The incidence is in excess in maternal blood group A, and deficit in group O.**
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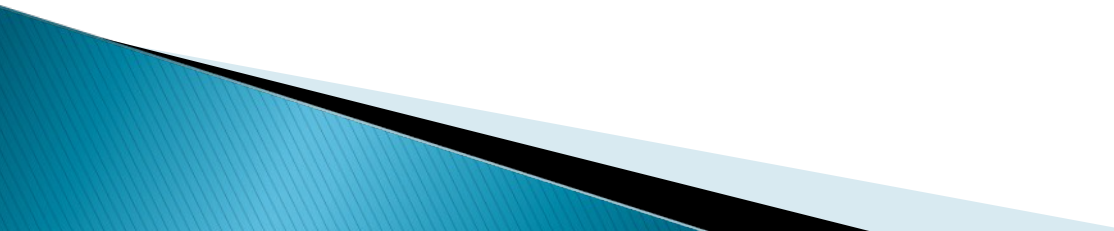
Pathological features

- ▶ **Site: In the uterus 90% of cases; 10 % of cases in the ovaries ,vagina, vulva, lung, liver, and brain.**

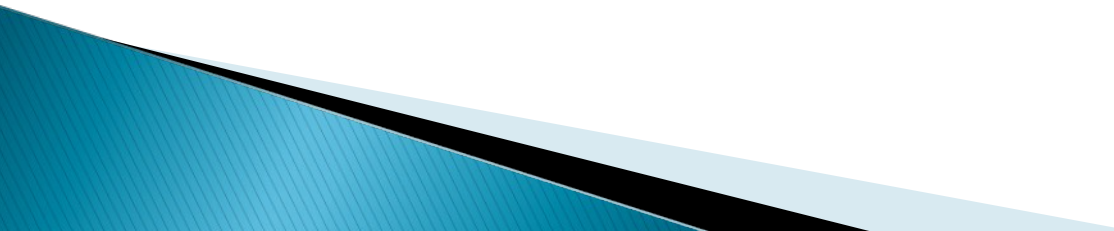
Pathological features

- Macroscopically:
- ✓ Uterus: It may be localized in the form of hemorrhagic polyp or multiple hemorrhagic ,necrotic masses in the cavity.
- ✓ Some times it is present in the uterine wall (intramural) and the cavity is empty.
- Ovaries : May show stromal lutein hyperplasia, and theca-lutein cysts. And may be site of secondaries

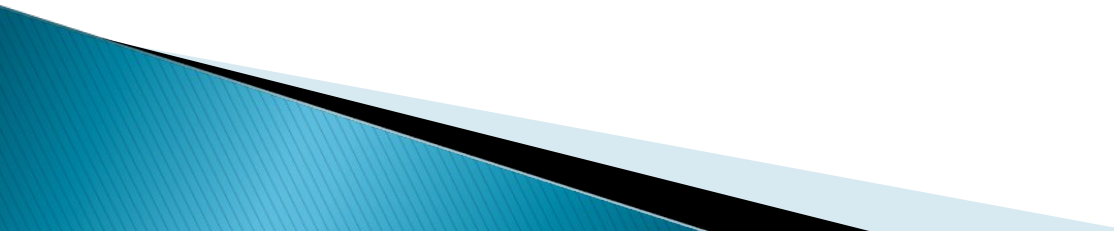
Pathological features

- ▶ **Microscopically:**
 - ✓ **Malignant hyperplasia of both cytotrophoblasts, and syncytiotrophoblasts.**
 - ✓ **Extensive hemorrhage.**
 - ✓ **Absence of villi.**
 - ✓ **Destruction of the surrounding myometrium.**
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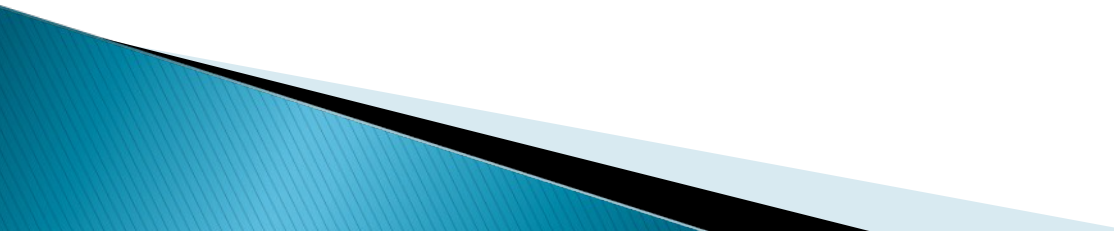
Spread

- ▶ **Direct : Through the myometrium and may end in uterine perforation ,internal hemorrhage, and peritonitis**
 - ▶ **Through the fallopian tubes to the ovaries.**
- 

Spread

- ▶ **Blood : The main method of spread ,and occurs to;**
 - ✓ **Genital : Vagina, vulva, and ovary.**
 - ✓ **Extra genital : Lung, liver, brain, and bones especially skull and spine.**
 - ✓ **The lung is the commonest site for secondaries and haemoptysis may be the presenting symptom.**
- 

Causes of death

- ▶ **Vaginal bleeding.**
 - ▶ **Haemoptysis.**
 - ▶ **Intraperitoneal hemorrhage.**
 - ▶ **Peritonitis.**
 - ▶ **Metastasis to the vital organs e.g,brain.**
 - ▶ **Pulmonary complications.**
- 

Treatment

- ▶ **Prophylaxis: After care of vesicular mole;**
- **D&C after one week of the evacuation.**
- **Monitored for the signs and symptoms of trophoblastic neoplasms by:.**

I. ***serial hCG.***

Active treatment

- I. Non metastatic GTD:**
 - o Methotrexate (antimetabolite) +folinic acid.**
 - o The cytotoxic therapy is controlled by doing CBC,platelet count**
 - o After the the hCG level gets normal ;stop the therapy and follow-up by weekly estimation of hCG levels.**

Active treatment

II. Low metastatic GTD:

- o Methotrexate , or Actinomycin D ,if there is resistance ,change to triple chemotherapy.**

Active treatment

III. High risk metastatic GTD :

- o Triple chemotherapy :
Methotraxate,
Actinomycin D, and
Cytosan.**

Active treatment

- **Surgery:**

- **TAH may be done in patients not desirous of further reproduction.**
- **Irradiation : Whole brain irradiation for cerebral metastases , The whole organ irradiation for hepatic metastases**

Follow-up

- ▶ **After successful therapy ,the hCG levels are obtained :**
 - ✓ **every 2weeks for 3 months,**
 - ✓ **every month for 3months,**
 - ✓ **every 2months for 6 months then every sixes months indefinitely.**

Follow-up

- ▶ **If at any time hCG levels rises, repeat the evaluation , staging ,and chemotherapy.**
 - ▶ **Physical examination, and chest x-ray follow-up at 6 weeks, then every 3months for one year, then every 6 months for one year.**
- 

Future pregnancy

- ▶ **Women who undergo chemotherapy are advised not to conceive for one year after completion of treatment**

**THIS IS THE END OF THE
LECTURE .**



***THANK
YOU ! ! !***

