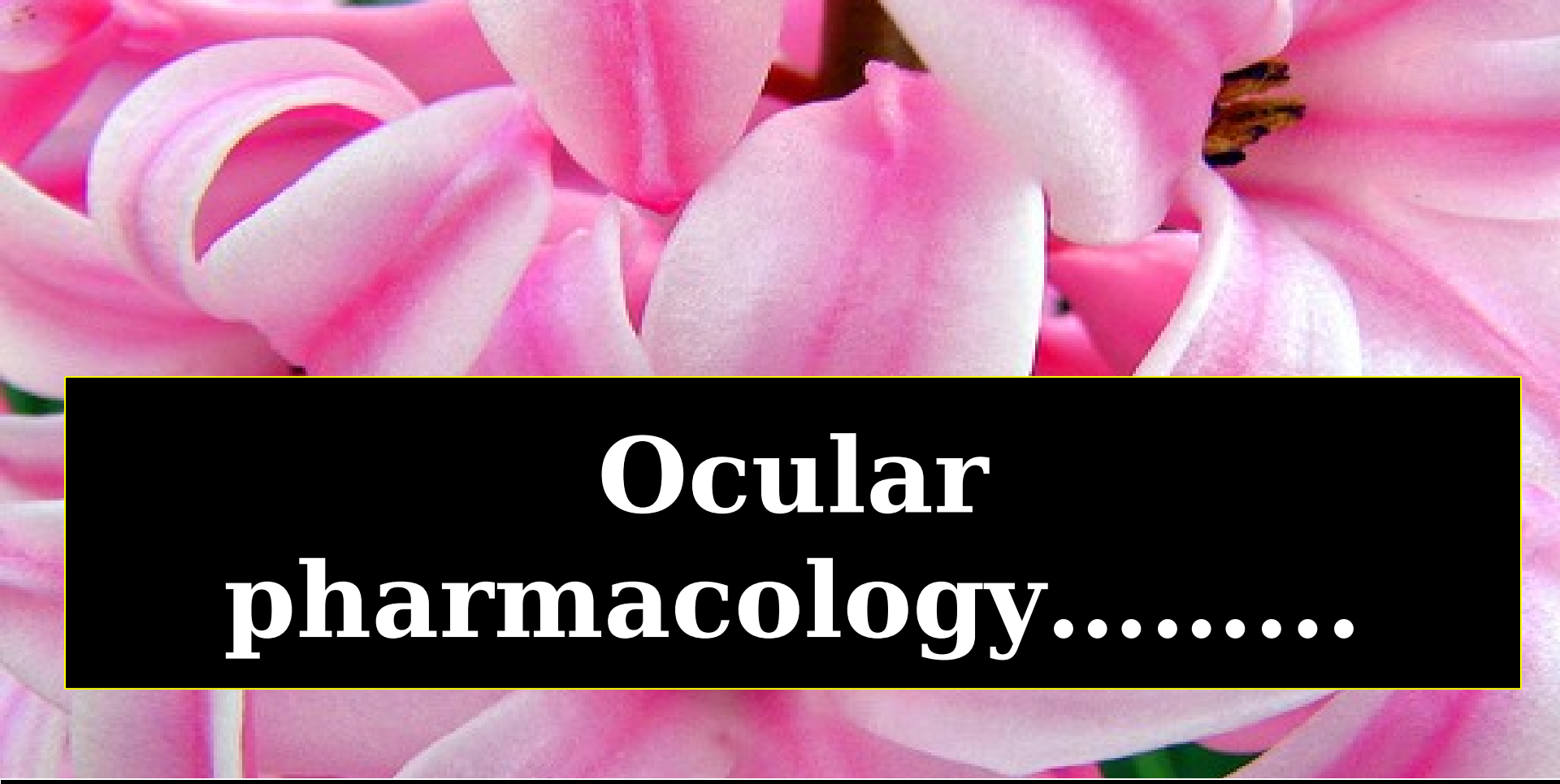
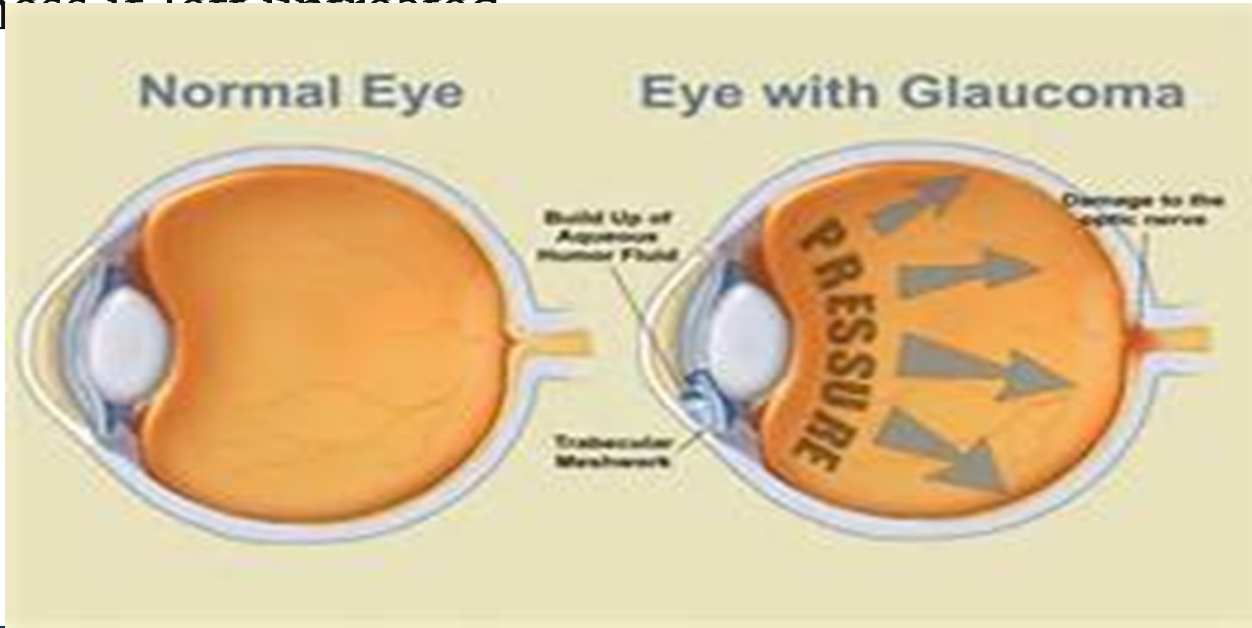


Ocular pharmacology……

Glaucoma……

- Has been called the "silent thief of sight
- **Glaucoma' are a group of ocular disorders that lead to an optic neuropathy characterized by**
  - changes in the optic nerve head (optic disk)
  - associated with loss of visual sensitivity and field.
  - irreversible blindness if left untreated



Glaucoma……

- **Two major types of glaucoma have been identified**:

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I. Open angle-Glaucoma:

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- Is the most common type of glaucoma and known as “sneak thief of sight

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- Can appear suddenly and is often painful

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- Visual loss can progress quickly

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  - **decreased aqueous outflow and/or**

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  - **increased aqueous production**.

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- However, **the discomfort often leads patients to seek medical attention** before permanent damage occurs

- However, **the discomfort often leads patients to seek medical attention** before permanent damage occurs

Glaucoma……

II. Closed angle-Glaucoma

II. Closed angle-Glaucoma

- closure of the angle between the iris and cornea obstructs outflow of aqueous humor
  - Functional block b/n the iris and the lens
  - Increase resistance to aqueous flow from P/C to A/C
  - narrowing or closure of the anterior chamber(A/C) angle

closure of the angle between the iris and cornea obstructs outflow of aqueous humor
Functional block b/n the iris and the lens
Increase resistance to aqueous flow from P/C to A/C
narrowing or closure of the anterior chamber(A/C) angle

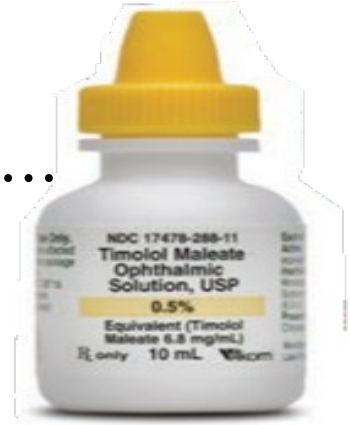
Clinical presentation

- **Symptoms:**
  - Irritability, photophobia, epiphora, severe eye and headache pain blurred vision, redness of the eye, nausea and vomiting and intermittent eye ache at night.
  - Loss of vision in the affected eye.
  - Coloured haloes or bright rings around lights

Pharmacology of Glaucoma…

I. Beta-blockers

- Topical beta-blockers are **the drugs most often prescribed to treat glaucoma**



➢ **Timolol (Timoptic, Betimol) has been** …

- the **standard beta-blocker** for years.

➢ **Newer nonselective drugs include** ….

- **levobunolol (Betagan),**
- **carteolol (Ocupress), and**
- **metipranolol (OptiPranolol).**



➢ A few studies suggest some are more beneficial than timolol with similar side effects.

Cont…..

- **Selective beta-blockers include:**
  - **Betaxolol (Betoptic) and**
  - **levobetaxolol (Betaxon)**
- Have **fewer adverse effects on the heart** than the nonselective beta-blockers
- **They slow progression more than timolol, but timolol is more effective at lowering IOP**

Cont…..

- **MOA:**
  - They lower the pressure inside the eye **by inhibiting the production of aqueous humor**
  - They **cause less eye irritation** than many other glaucoma medications
- **Selective: Betazolol 0.5% one drop BID**
- **Non-selective: Timolol 0.25-0.5% one drop daily** and **Metipranolol 0.3% one drop BID are the drug of choice for treatment of glaucoma**

Cont…..

Side effects

- **Systemic effects** include reduced sexual drive, fatigue, depression, anxiety, and breathing difficulties, lower heart rate and reduce blood pressure and can worsen severe asthma or other lung diseases.
- **Local effects** include dry eyes, corneal anesthesia, blepharitis, blurred vision, and, rarely, conjunctivitis, uveitis, and keratitis

II. Prostaglandins…….

- Are hormone-like substances that help to **Open up blood vessels**.

MOA:

- Drugs that resemble prostaglandins **increase outflow of aqueous** humor which helps reduce intraocular pressure(IOP)

- **Latanoprost 0.005% solution one drop every night**
- **Travoprost 0.004% solution one drop every night**
- **Bimatoprost 0.001-0.03% solution one drop every night**

- **Iridectomy** (laser or surgical) is the definitive treatment of CAG and if no response for therapy.

Cont…..

- **Significant and sustainable IOP lowering effect than Timolol**
- Increase uveoscleral outflow by 50%
- **Latanoprost** was the **first prostaglandin** to be approved as first-line treatment for elevated eye pressure

Side Effects

- No effect on the heart rate and safe for people with asthma but **cause itching, redness, and burning during administration, muscle and joint pain** may also occur and may **permanently change eye color from blue or green to brown.**

III. Carbonic Anhydrase Inhibitors…..

- CAIs decrease eye pressure by **reducing** the aqueous humor production.
  - They are indicated **when other drugs do not work**.
  - They may be **combined** with other medications.
- CAIs may also **improve blood flow** in the retina and optic nerve …thus can keep the disease from getti



- **Topical:**

Brintholamide 5% suspension BID/TID

Dortholamide 2% solution BID/TID

- **Local adverse effects include** transient burning and stinging, ocular discomfort and transient blurred vision, tearing, and, rarely, conjunctivitis, lid reactions, and photophobia, fatigue, stinging in the eye, using dorzolamide

Cont…..

- Oral medications
  - **Acetazolamide 125mg, 250mg PO BID/QID**
  - **Methazolamide 25mg, 50mg PO BID/TID**
  - **Dichlorphenamide** (Daranide)
    - More effective than eye drops, but cause **more side effects** and **rarely used for long-term treatment**
- **Side effects**
  - About 10% of patients report **fatigue, stinging** in the eye, and **loss of appetite**
  - **Taste changes** can occur

Cont…..

- The **very unpleasant S/E of oral forms** include
  - Frequent urination, depression, stomach problems, fatigue, wt loss, sexual dysfunction, and failure to thrive (in infants)
- Long-term use of the oral forms can cause **serious anemia** and **kidney problems** . . . .in rare cases

IV Adrenergic Agonists…..

- Activate muscles in the eye that dilate pupils …
  - thus increase outflow of aqueous fluid.
- **Alpha 2-adrenergic** agonists

MOA

  - **reduce production** of aqueous humor
  - **increase outflow** through the uveoscleral pathway
  - (the alternative channel to the trabecular meshwork).
- **Agents….**
  - **Apraclonidine (Iopidine)** …..is used for the **short term**
  - **brimonidine (Alphagan**) … effective for **long-term therapy**

Cont…..

- Safer than other drugs during **pregnancy** and for **patients with asthma**
- **Side Effects**. . . . are **dry mouth** and **altered taste**
  - **Allergic reaction**. . . red and itching eyes and lids
  - Brimonidine causes less of an allergic response
  - But it can cause **lethargy** and **mild low blood pressure**

Miotics (Parasympatomimetics

- **Cholinergic agonists narrow the iris muscles** and **constrict the pupil**
  - This pulls the iris away from the trabecular meshwork, allowing the aqueous humor to flow out through the drainage channels
- **Pilocarpine**
  - Was the **most widely used anti-glaucoma drug before timolol** was introduced
  - It is the preferred **miotic**

Cont…..

- **Carbachol** is another miotic
- **Epinephrine** and its derivatives
  - Epinephrine is now rarely prescribed because of side effects
- **Dipivefrin** is **a newer form of epinephrine**
  - **remains inactive until it reacts with enzymes in the cornea**
  - It is effective in low doses and causes few systemic side effects

Administering Eye Drops. …..

- The following are some recommended steps:
  - If you use both ointments and eye drops, take the eye drops first
  - Wash your hands before applying eye drops
  - Hold the bottle upside down
  - Tilt your head back and, with one hand, pull the lower eyelid down to form a pocket
  - With your other hand, hold the bottle as close as possible to your eye
  - Don’t let the bottle directly touch your eye or eyelid
  - After you have placed the drop, close your eye or press your index finger against the corner of the eye near your nose
  - Gently move the lower lid upward until the eye is closed
  - **Keep your eye closed for at least 1 minute**
    - This prevents the drop from draining out

Cont…

- Do not let the bottle directly touch your eye or eyelid.
- After you have placed the drop, close your eye or press your index finger against the corner of the eye near your nose.
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Topical Drugs Used in the Treatment of Open-Angle Glaucoma			
Drug	Pharmacologic Properties	Common Brand Names	Mechanism of Action
Beta-Adrenergic blocking agents			
• Betaxolol	Relative $_1$-selective	• Generic	All reduce aqueous production of ciliary body
		• Betoptic-S	
• Carteolol	Nonselective, intrinsic sympathomimetic activity	• Generic	
• Levobunolol	Nonselective	• Betagan	
• Metipranolol	Nonselective	• OptiPranolol	
• Timolol	Nonselective	• Timoptic, Betimol, Istalol	
		• Timoptic-XE	
Nonspecific adrenergic agonists			
• Dipivefrin	Prodrug	Propine	Increased aqueous humor outflow
Alpha-2 Adrenergic agonists			
• Apraclonidine	Specific $_2$-agonists	Iopidine	Both reduce aqueous humor production; brimonidine known to also increase uveoscleral outflow; only brimonidine has primary indication
• Brimonidine		Alphagan P	

Topical Drugs Used in the Treatment of Open-Angle Glaucoma

Drug	Pharmacologic Properties	Common Brand Names	Mechanism of Action
Cholinergic agonists direct acting			
Carbachol	Irreversible	Carboptic, Isopto Carbachol	All increase aqueous humor outflow through trabecular meshwork
Pilocarpine	Irreversible	Isopto Carpine, Pilocar	
		Pilopine HS	
Cholinesterase inhibitors			
Echothiophate		Phospholine Iodide	
Carbonic anhydrase inhibitors			
Topical			
Brinzolamide	Carbonic anhydrase	Azopt	All reduce aqueous humor production of ciliary body
Dorzolamide	type II inhibition	Trusopt	
Systemic			
Acetazolamide		Generic	
		Injection	
		Diamox Sequels	
Methazolamide		Generic	

Topical Drugs Used in the Treatment of Open-Angle Glaucoma

Drug	Pharmacologic Properties	Common Brand Names	Mechanism of Action
Prostaglandin analogs			
Latanoprost	Prostaglandin F_2 analog	Xalatan	Increases aqueous uveoscleral outflow and to a lesser extent trabecular outflow
Bimatoprost	Prostamide analog	Lumigan	
Travoprost		Travatan Z	
Combinations			
Timolol-dorzolamide		Cosopt	
Timolol-brimonidine		Combigan	

[a] Use of nasolacrimal occlusion will increase the number of patients successfully treated with longer dosage intervals.

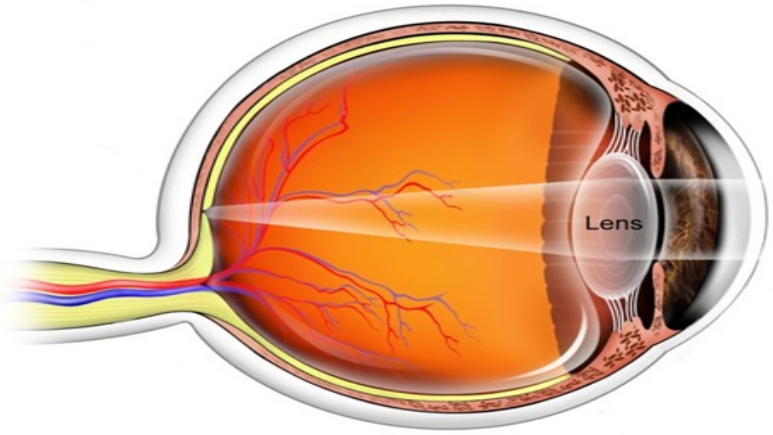
1. CATARACT

- **The primary function of the ocular lens is to transmit light and to focus it on the retina.**
- **A cataract occurs when the lens loses its clarity** such that visual acuity is compromised
- Cataracts can result from **genetic, metabolic, nutritional, or environmental insults** or can be secondary to other ocular or systemic conditions, such as **diabetes**

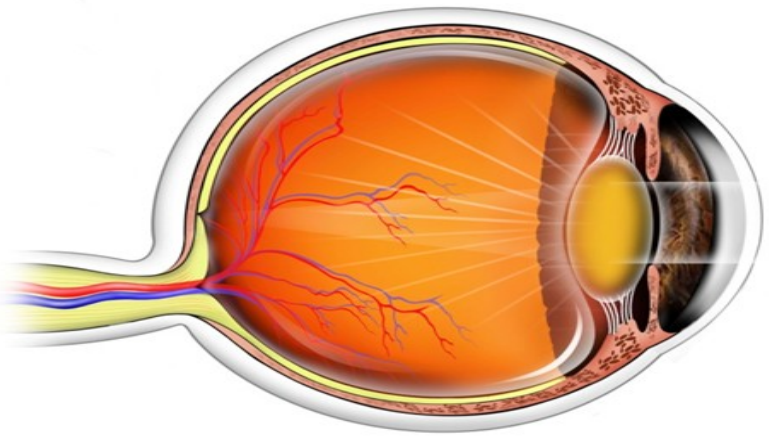


Cont..

- **The most important risk factor is age**
  - Age-related cataract constitutes the great majority of all cataracts
- **Cataract remains the leading cause of blindness globally**



Normal lens
(Clear leans)



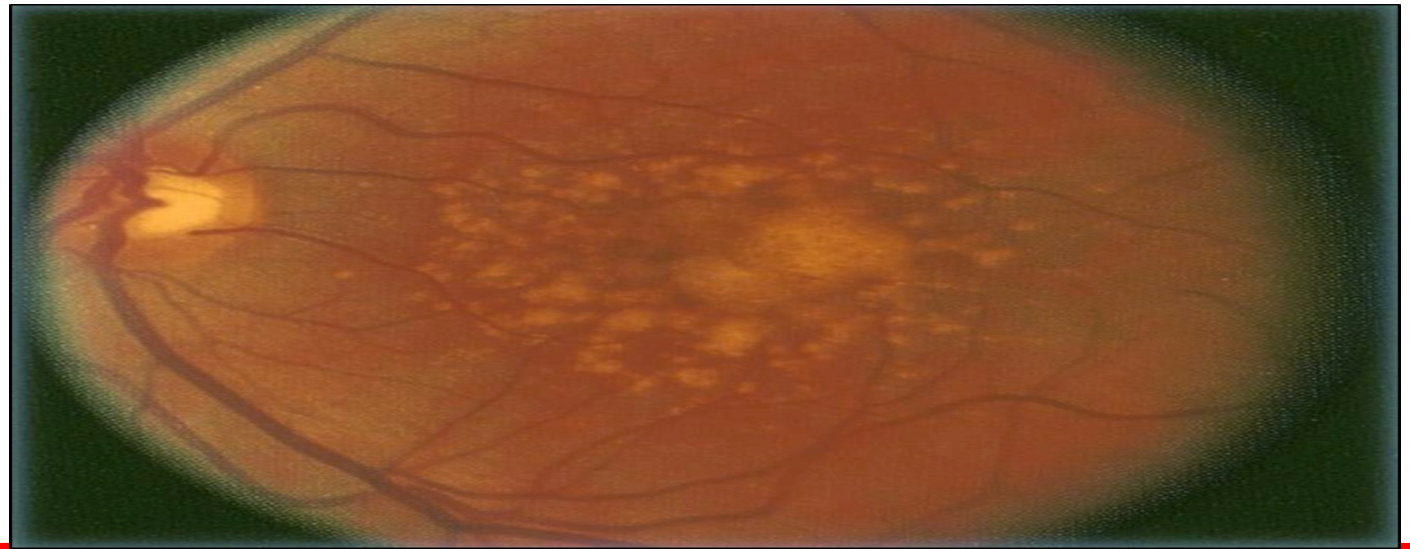
Cataract
(Cloudy lens)

CATARACT: TREATMENT

- There are **no medications or eye drops to treat cataracts**
- Cataracts **never get better** on their own
- Treatment for cataract is **surgery to remove the cloudy lens** and **replace it with clear artificial lens**
- The surgery is usually performed on an outpatient basis under local anesthesia
- **Cataract surgery is one of the most cost-effective health interventions**

3. Age-related Macular Degeneration

- AMD causes **progressive damage to the macula**, the small area in the retina responsible for sharp and central vision
  - The major risks for AMD are **age** and **family history**
- **AMD causes central vision loss**
  - Central vision is critical for reading and recognizing faces
- **AMD is the leading cause of irreversible blindness in industrialized countries**



Cont…



Normal vision



Macular degeneration

Cont…

- **Dry AMD** is characterized by
  - **Progressive atrophy of the retinal pigment epithelium,**
  - Accumulation of retinal metabolic products, and
  - Loss of retinal photoreceptor function
- **Wet AMD** is characterized by
  - **Bleeding underneath the retina**
  - Treated by injection of **anti-Vascular Endothelial Growth Factor antibodies** into the eye

AMD: TREATMENT

- Injections directly into the eye for treatment of the "wet" form of AMD include:
  1. **Lucentis,**
  2. **Macugen**
  3. **Eylea**

- **MOA**
  - Works by inhibiting proteins called **vascular endothelial growth factor (VEGF)**
    - **VEGF stimulates the growth of new blood vessels in the body**

Lucentis (ranibizumab)

- FDA approved in June 2006 **for treating the more advanced or "wet" form** of macular degeneration
- **Is the colorectal cancer treatment drug**

Lucentis (2)

- VEGF promotes the growth of **abnormal blood vessels** in the back of the eye (retina) . . . . . contributes to development of macular degeneration
- **Administered through monthly injections into the eye**
- Has rare adverse reactions to it mainly associated with the injection itself

Macugen (Pegaptanib sodium)

- FDA approved in December 2004
- **Administered through injections into the eye every 6 weeks**
- Helps to **slow the rate of vision loss for many AMD patients**
- Fewer serious S/Es such as a **detached retina** or **endophthalmitis** reported
- However, less serious S/Es. . . . **eye floater and discomfort**. . . . . occurred in up to 40 percent of patients

Eylea…

- FDA approved in November 2011 and inhibits the action of VEGF in wet (neovascular) AMD
- Also **known as VEGF Trap-Eye**
- After **3 initial monthly injections** into the eye, it is administered **every 8 weeks**
- Side effects and benefits reported were similar to those of Lucentis