

Embryogenesis:

starts with the fertilization of the ovum (or egg) by sperm → zygote

1-The zygote undergoes rapid mitotic divisions and cellular differentiation, leading to development of an embryo.

It's always asymmetric, having an "animal pole" (future ectoderm and mesoderm) and a "vegetal pole" (future endoderm).

2- Cleavage: is cell division with no significant growth, producing a cluster of cells that is the same size as the original zygote → morula 30 cells.

3- Blastocyst: A thin-walled hollow structure that contains a cluster of cells(100 cells). It possesses:

a- **embryoblast**- inner cell (central) mass → subsequently forms the embryo

By 2nd week, embryoblast forms two cavities yolk sac(lined by hypoblast cells) & amniotic cavity (lined by epiblast)

the point where the two cavities hit forms bilaminar (two layered) germ disk which is composed of:

-epiblast (primary ectoderm)

-hypoblast (primary endoderm) → embryo proper

b- **trophoblast**- an outer layer of cells → forms the placenta.

Embryoblast implants in the uterus's endometrium @day 5 of gestation.

4- Epiblast (single layered) @ day 16 → **gastrula** (3 layered).

By 3 wks, formation of primitive streak & primitive knot at the caudal end of the epiblast.

5- Gastrula: cells migrate to the interior of the blastula forming three germ layers: the ectoderm, mesoderm and endoderm.

6- neural plates: induced by the formation of notochord (precursor to vertebral column- formed by budding from the primitive knot)

folding up of the **ectoderm**, one on either side of the middle line of neural plates in front of the primitive streak.

7- Neural tube: (precursor to nervous system) a closed canal formed by:

mesoderm condensation → folding of the neural plates sides → then fusion in the middle line deepening the groove.

9- neural crest cells: ectodermal cells detach from each neural fold before the neural groove is closed. Migrate through the embryo to form variety of cells & tissues

When the neural tube is closed, the cephalic end of the neural groove exhibits several dilatations, which assume the form of three vesicles.

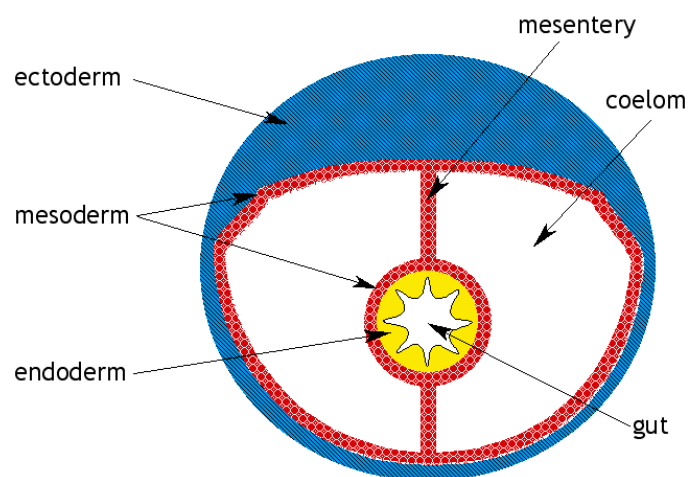
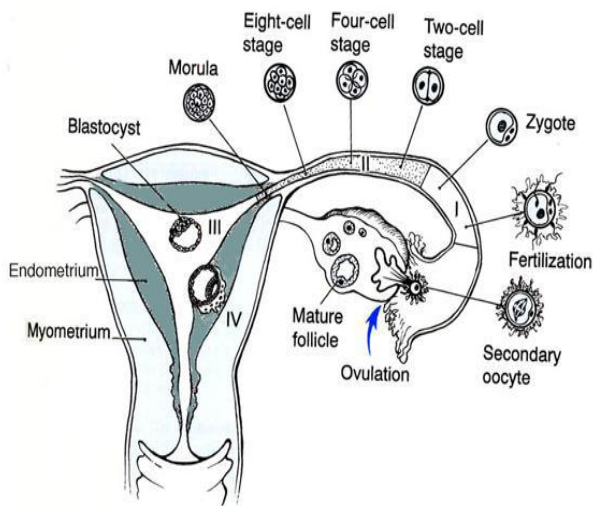
These constitute the three primary cerebral vesicles, and correspond respectively to the future **forebrain** , **midbrain**, and **hindbrain**

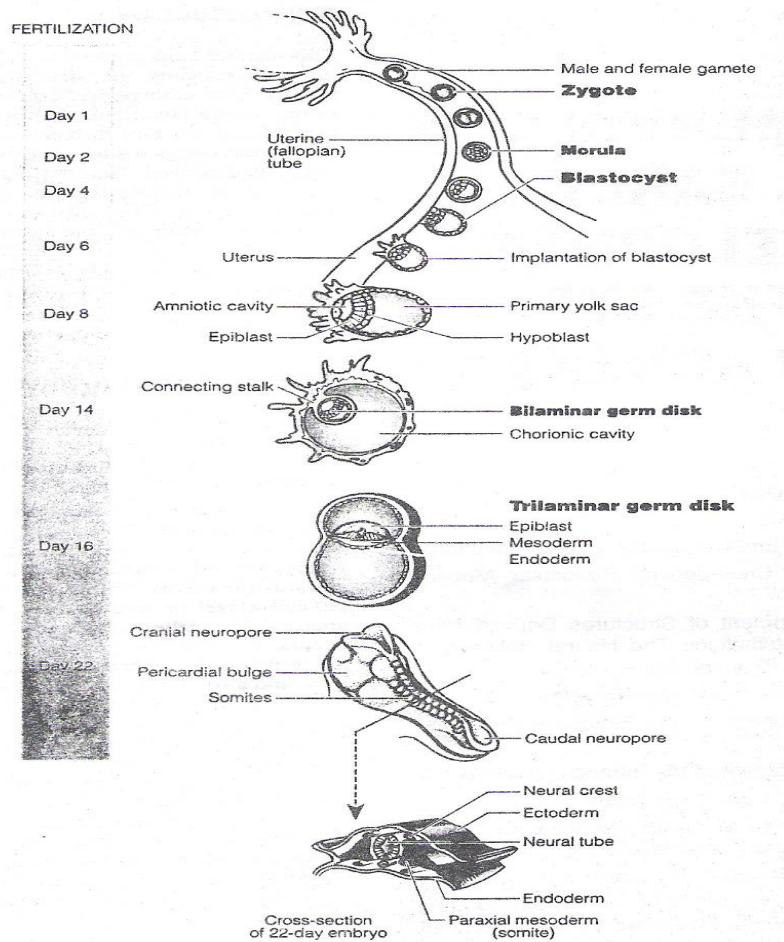
Dorsal = anterior

Ventral = posterior

Rostral = superior, head

Caudal = inferior, tail





Summary of embryologic events occurring in the first 3 weeks following fertilization.

Eye is formed from three embryonic tissue:

1- Ectoderm

a) Ectoderm of neural tube (neuroectoderm) → retina, optic nerve fibers, iris.

b) Surface ectoderm → corneal & conjunctival epithelium, lens, lacrimal & tarsal glands.

2- Mesenchyme (mesoderm) → corneal stroma, sclera, choroid, iris, ciliary muscle, parts of vitreous, muscles lining anterior chamber.

Steps of development:

1- Ectodermal diverticulum from the lateral aspect of the forebrain. By 22 days of gestation.

2- Diverticulum grows out laterally toward the sides of the head.

3- a) Optic vesicles: dilated end of diverticulum- which invaginates & sinks below the surface ectoderm to form double layered optic cup.

b) The proximal portion restricts to form optic stalk.

When the optic vesicle reaches the surface ectoderm, the lens vesicle will develop.

c) Lens placode: a thickening of small area of surface ectoderm- which evaginates & sinks below the surface ectoderm to form Lens vesicle. by 27 days.

4- Inferior edge of optic cup is deficient & continuous with the Optic (choroidal) fissure: a groove in the inferior aspect of the optic stalk.

5- Vascular mesenchyme: grows inside the optic fissure taking hyaloids artery with them. By 33 days.

6- Optic canal: a narrow tube inside the optic stalk formed by 7th week by narrowing & closure of optic fissure margins around the artery.

Failure of the fissure to close results in coloboma which may include pupil, ciliary body, choroid and optic nerve.

7- By 5th week → lens vesicle separates from surface ectoderm & lies within the mouth of the optic cup where edges will form pupil later.

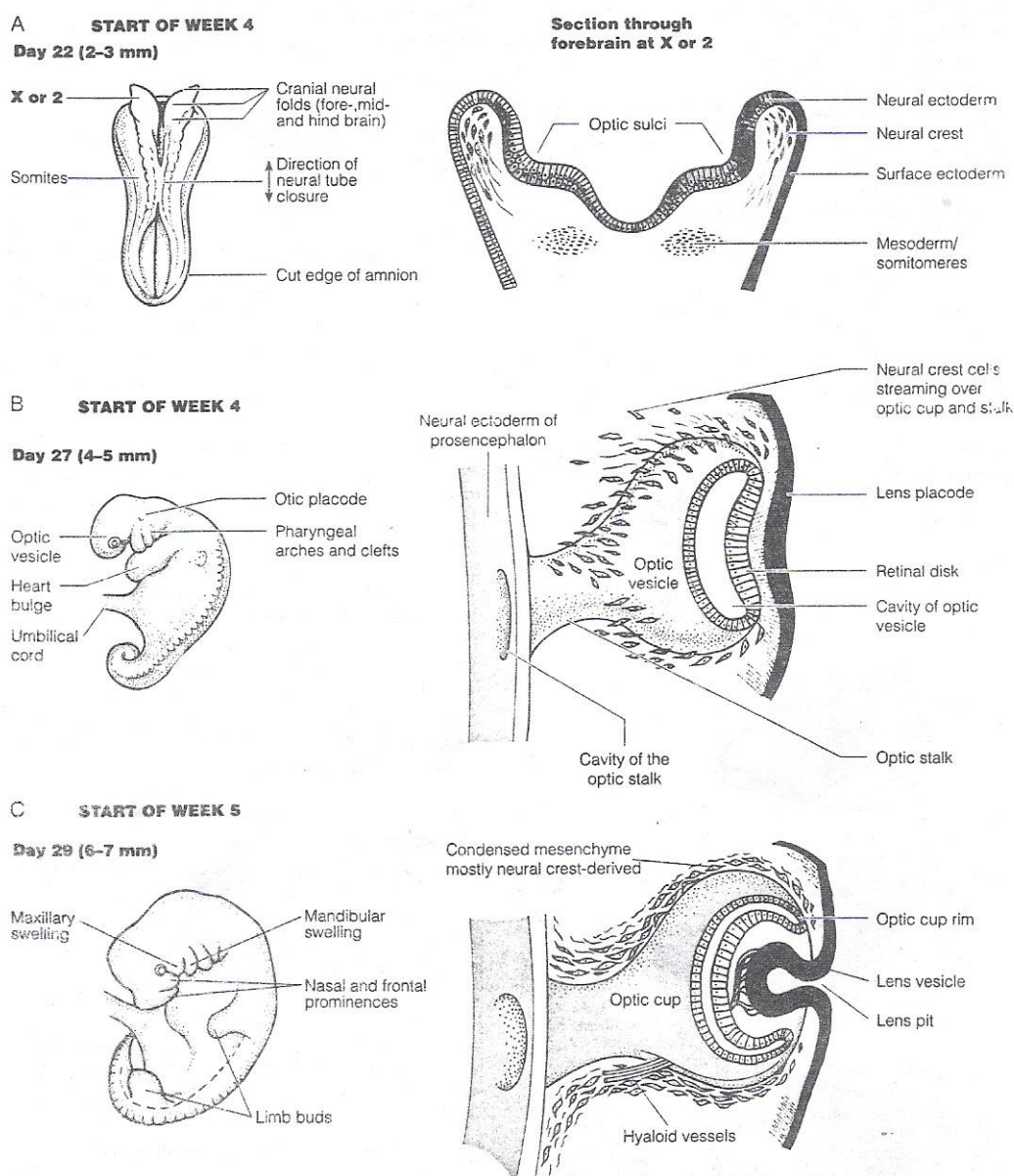


Fig. 2.3. Diagrammatic summary of ocular embryonic development from day 22 to week 8. The external appearance of the whole embryo at the equivalent period is shown on the left. The various 'germ layers' are color coded to illustrate their origin and final contribution to the eye and periocular tissues.

Diagrammatic summary of ocular embryonic development from 3 to 8 weeks

Development of the retina:

Retina consists of two layers developed from optic cup: pigmented layer and neural layer and inter-retinal space between them that is continuous through the optic stalk with the 3rd ventricle.

1- **Pigmented layer** (external): single columnar layer with pigment granules in its cytoplasm formed from the outer thinner layer of optic cup. By 6th week.

2- **Neural layer** (internal): formed from inner layer of optic cup. Start by 40 days continue until 7th month.

a) Anterior 1/5th of inner layer → a layer of columnar cells.

It's the region of the cup that overlaps the lens & doesn't differentiate into nervous tissue.

Extends forward with the pigmented epithelium of the outer layer onto the posterior surface of the developing ciliary body & iris.

b) Posterior 4/5th of the inner layer of optic cup → undergoes cellular proliferation forming outer nuclear zone, inner marginal zone, and devoid of nuclei.

Cells of nuclear zone invades marginal zone by 130 days:

i- Inner neuroblastic layer → form ganglion cells, amacrine cells, Muller body fibers.

ii- Outer neuroblastic layer → form horizontal, rod, and cone bipolar nerve cells & rod and cones cells.

Inner layer of optic cup: small non-nervous portion near the cup edge and large photosensitive portion

Separated by Ora serrata (weavy line).

The cavity of optic vesicle is continuous through optic canal with the cavity of diencephalon (later 3rd ventricle)

Early in development: Outermost layer of nuclear zone has cilia which are continuous with the ciliated ependymal cells of 3rd ventricle.

By 7th week, cilia of nuclear zone disappear & are replaced by the outer segment of rods & cones during the 4th month.

All layers of retina are fused & detached by 8th month.

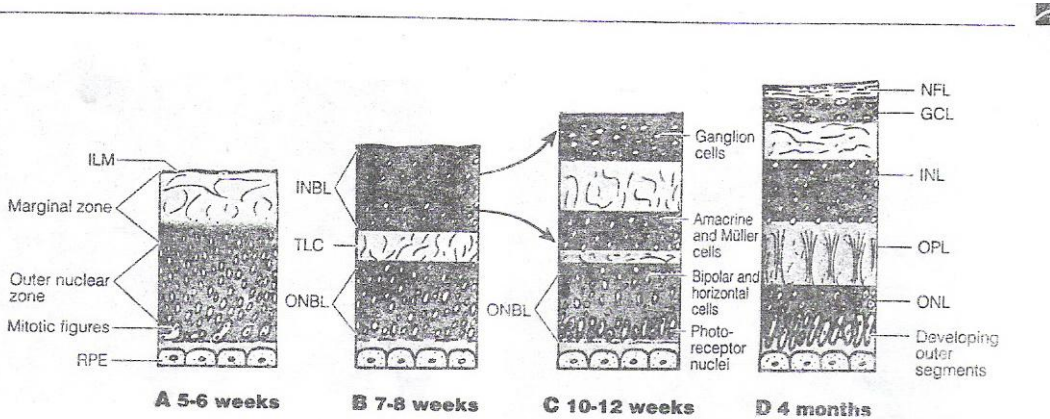


Fig. 27. (A-D) Summary of early retinal morphogenesis in the human eye. Arrows indicate major patterns of cell movements. ILM, inner limiting membrane; RPE, retinal pigment epithelium; INBL, inner neuroblastic layer; ONBL, outer neuroblastic layer; TLC, transient layer of Chievitz; NFL, nerve fiber layer; GCL, ganglion cell layer; INL, inner nuclear layer; OPL, outer plexiform layer; ONL, outer nuclear layer.

Summary of retinal development

Macular area & Fovea centralis:

- 1- Macula develops as a localized increase of superimposed nuclei in the ganglion cell layer lateral to optic disc.
 - 2- By 7th month, Fovea centralis is formed, a central shallow depression formed by peripheral displacement of ganglion cells.
 - 3- Foveal cones decrease in width in their inner segment while elongate in outer segment which increases foveal cone density.
- at birth, ganglion cells are reduced to one layer in fovea.
 - 1st to 3rd month after birth, no ganglion cells cover the cone nuclei in centre of the fovea.

Optic nerve:

1- Ganglion cells of the retina develop axons that converge to a point where the optic stalk leaves the posterior of optic cup.

2- Axons pass among the cells of the inner layer of optic stalk.

3- Inner layer encroaches on the cavity of the stalk until the inner & outer layer fuse.

4- Cells of optic stalk form neurological supporting cells to the axons.

Cavity of the stalk disappears.

5- Stalk & optic axons form the optic nerve.

Just before birth → optic nerve starts to myelinate and continues after birth.

6- Optic chiasma → formed by partial decussation of the axons of the two optic nerves.

7- Hyaloid artery & vein → becomes central artery & vein of the retina.

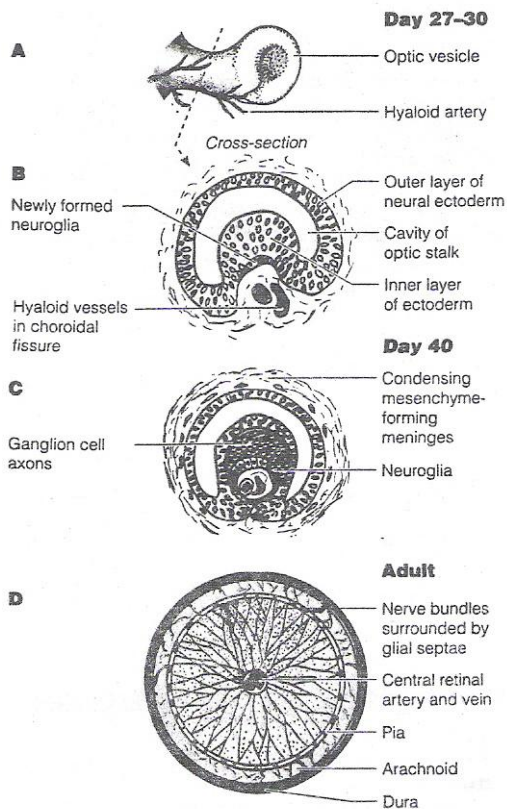


Fig. 2.10. Diagram summarizing the major events in the development of the optic stalk and optic nerve.

The lens:

- 1- Lens placode → by thickening of surface ectoderm. At 22 days, it overlies optic vesicle.
 - 2- Lens vesicle → by invaginating & sinking of placode below surface ectoderm. It consists of single layer of cells covered by basal lamina.
 - 3- Primary lens fibers → transparent lens fibers formed by elongation of cells of posterior wall and loss of their nuclei.
 - 4- Lens vesicle becomes obliterated. Lengthening of the cells occurs at the centre of posterior wall first and then projects forward into lens cavity.
 - 5- Nuclei of the lens fibers move anteriorly within the cells to form a line convex forward → nuclear bow.
 - 6- The primary lens fiber become attached to the apical surface of the anterior lens epithelium.
- Secondary lens fibers → additional lens fibers that are formed by the division of the anterior epithelial cells of the equator.

New secondary lens fibers will be formed throughout life.

Basal ends of the fibers remain attached to the basal lamina while their apical ends extend anteriorly around the primary fibers beneath the capsule.

So, lens fibers are laid down concentrically and lens on section has laminated appearance.

7- Lens enlarges as new lens fibers are added.

8- Fiber distribution:

a) None of the fibers runs completely from the anterior to the posterior surface of the lens.

b) The end of fibers comes into apposition at sites referred to as sutures.

c) Fibers run in a curved course from the sutures on the anterior surface to those on the posterior surface.

d) No fiber run from pole to pole. Fibers that begin near the pole on one surface ends near the peripheral extremist on the other & vice versa.

e) Anterior suture line is shaped like an upright Y that is inverted on the posterior aspect.

f) Because of hyaloids artery supply → rapid fetal lens growth.

Hyaloids artery form a **plexus** on the posterior surface of lens capsule (nearly spherical, soft, reddish tinted)

9- By time of birth →

Anterior posterior diameter of lens is nearly the same of an adult.

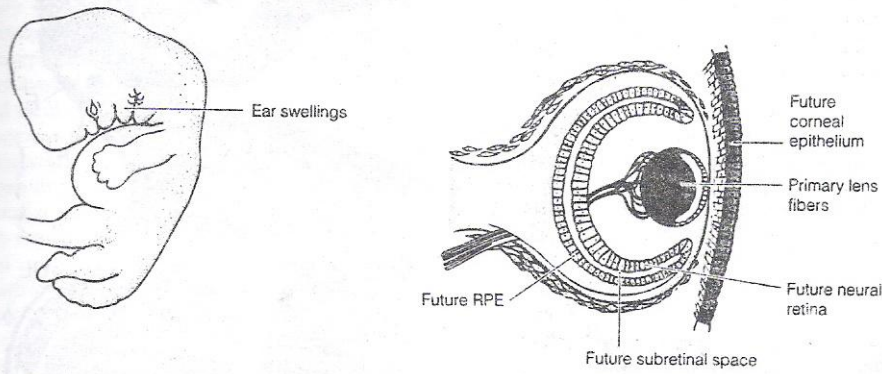
Equatorial diameter → $\frac{2}{3}$ of an adult.

Equatorial diameter continues to grow because of continuous production of secondary lens fibers.

Lens capsule → formed from the mesenchyme surrounding the lens, receives blood supply from hyaloids artery.

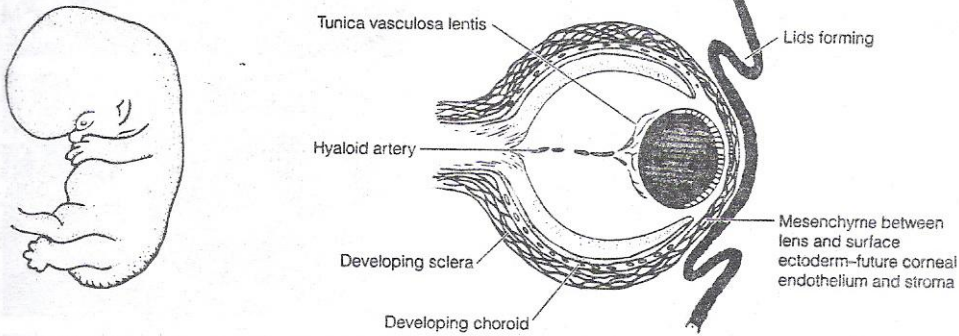
D **START OF WEEK 6**

Day 37 (8-11 mm)



E **START OF WEEK 7**

Day 44 (13-17 mm)



F **WEEK 8 (20-30 mm)**

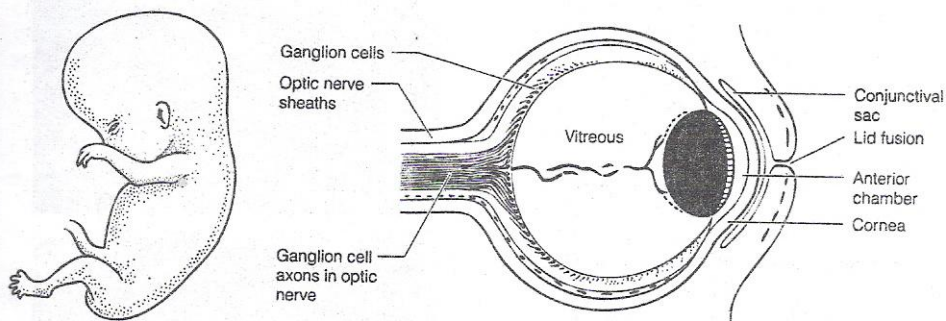


Fig. 2.3. Continued.

Ciliary body & suspensory ligaments of the lens:

1- The mesenchyme (at the edge of the cup) → differentiate into:

- a) connective tissue of ciliary body.
- b) smooth ciliary muscle fiber of ciliary muscle.
- c) suspensory ligaments of lens.

2- Edge of optic cup (two layered neuroectoderm) → posterior surface of ciliary muscle (two epithelial layer covering ciliary body). Then extend onto the posterior surface of pupillary membrane.

3- Mesenchyme on the anterior surface of the lens → condenses to form pupillary membrane.

4- Pupillary membrane + neuroectoderm from edge of optic cup → form Iris.

5- Pigment cells of neuroectoderm → form sphincter & dilator muscle of pupil.

6- Mesenchyme forms the connective tissue & blood vessels of the Iris.

Pigment cells derived from neuroectoderm → penetrate sphincter muscle & entre the connective tissue.

Pupillary membrane → first attached to pupil edge. Later, begins to separate from the iris because of the mesenchyme split but remains attached to the front

8th month it degenerate & disappear.

Anterior chamber:

Arises as a slit in the mesenchyme posterior to the Iris & anterior to lens.

Anterior & posterior chambers communicate when pupillary membrane disappears and pupil is formed and aqueous humor fills them.

Vitreous body:

1- Primitive- primary vitreous → consist of a network of delicate cytoplasmic processes.

Derived from → ectodermal cells of lens + neuroectoderm of retinal layer of optic cup.

Mesenchyme that entre the cup through choroidal fissure contains many vascular elements including vasa hyaloidea propria

2- Definitive- secondary vitreous → arises between the primitive vitreous + retina.

develops from the retina.

Starts as a homogenous gel that increases in volume rapidly & pushes the primitive vitreous anteriorly to behind the lens.

Hyalocytes → derived from mesenchyme around hyaloids vessels. Migrates into definitive vitreous.

Later hyaloids vessels atrophy & disappear leaving the acellular hyaloids canal.

3- Tertiary vitreous → large number of collagen fibers develop with formation of zonular fibers which extend between the ciliary processes & lens capsule.

The cornea:

Induced by lens & optic cup

1- corneal epithelium → from surface ectoderm

Substantia propria + endothelium → from mesenchyme

Sclera:

Out fibrous coat of the eyeball

From condensation of mesenchyme outside the optic cup. It first forms near the future insertion of the rectus muscles.

Choroid:

Inner vascular coat of eyeball

From mesenchyme surrounding the optic vesicle with contribution of cranial neural crest cells.

Extraocular muscles:

4 rectus muscles & superior & inferior oblique

From mesenchyme in the region of the eyeball

Starts as single mass of mesenchyme and later separate into distinctive muscles.

First at their insertion & later at their origins.

Levator palpebrae superioris → is formed last, splitting from the mesenchyme that forms superior rectus muscle

During development, EOM, become associated with the 3rd, 4th, 6th cranial nerves.

Eyelids:

Develop as folds of surface ectoderm above + below the cornea.

3rd month → they become united

5th month → start to separate

7th month → complete separation

Conjunctival sac → formed in front of cornea while eyelids are fused.

Connective tissue + tarsal plates → formed from mesenchyme core of eyelids

Orbicularis oculi muscle → formed from mesenchyme of second pharyngeal arch which invades the eyelids & supplied by 7th cranial nerve.

Cilia (eyelashes):

Develop as epithelial buds from surface ectoderm

1st arise in upper eyelid & arrange in 2-3 rows one behind the other.

Ciliary glands (moll & zeis) → grow out from ciliary follicles

Tarsal glands (meibomian glands) → develop as columns of ectodermal cells from the lid margin

Lacrimal glands → form as a series of ectodermal buds that grow separately from the superior fornix at the conjunctiva into the underlying mesenchyme

The buds later unite → form secretory units & multiple ducts of the gland

After development of levator palbrae superioris → gland is divided into **orbital & palpebral**

Tears are produced 3rd month after birth

Lacrimal sac & Nasolacrimal duct:

1- solid cord at ectodermal cells between the lateral nasal process & maxillary process of the face.

2- cord is canalized to form the nasolacrimal duct. Superior end dilates to form lacrimal sac.

3- lacrimal duct formed by cellular proliferation.

Orbit:

Orbital bones → From mesenchyme that encircles optic vesicle.

Medial wall → from lateral nasal process

Lateral + inferior wall → from maxillary process

Superior wall → mesenchymal capsule of forebrain

Posterior orbit → from bones of base of the skull

Bones of orbit form in membrane except those from base of the skull which develop cartilage

6th month of gestation, anterior half eyeball projects beyond orbital opening

Postnatal growth:

1- Eyeball → increase in size rapidly during first years of life, then slow down, then increase again at puberty.

2- Cornea → reaches adult size by age of two.

3- Iris → increase in stromal pigmentation during first few years.

4- Lens → grow rapidly after birth & continue to grow throughout life.

5- At birth → eyes are hypermetropic.

As anteroposterior axes increase in length it becomes emmetrope.

More increase in axial length is balanced by flattening of lens as growth proceeds.