

(a) Diagrammatic view. The vitreous humor is illustrated only in the bottom part of the eyeball.

Head fold of amnion partly covering the fore-brain

Mid-brain

Hind-brain

Nerve ganglion

Auditory vesicle

Heart

Vitelline vein

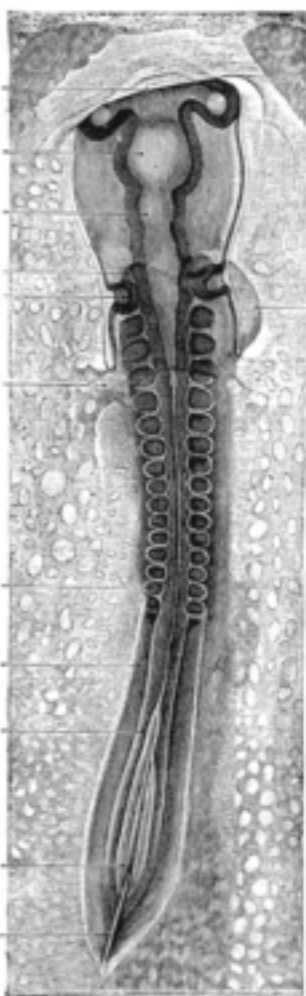
Fourteenth primitive segment

Paraxial mesoderm

Neural fold

Sinus rhomboidalis

Remains of primitive streak



FORMATION OF LENS VESICLE

- The optic vesicle grows laterally and comes in contact with the surface **ectoderm**.
- The surface ectoderm, overlying the optic vesicle becomes thickened to form the **lens placode** , which sinks below the surface and is converted into the **lens vesicle** .
- It is soon separated from the surface ectoderm at (**33rd**) day of gestation.

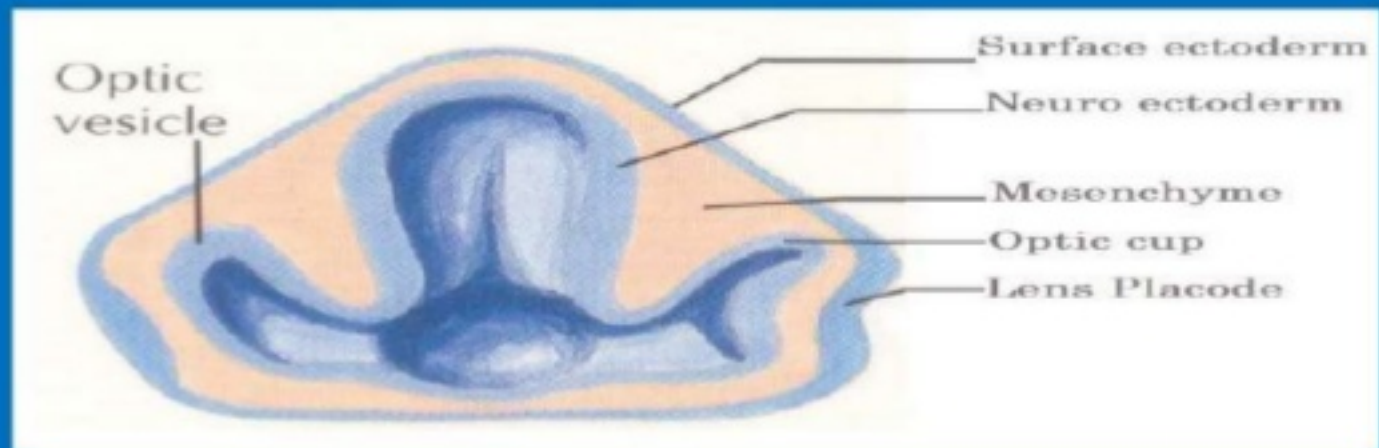
DEVELOPMENT OF THE Eye

- ▶ The development of eyeball can be considered to commence around(**day 22**) when the embryo has eight pairs of somites and is around(**2 mm**) in length.
- ▶ It grows out laterally toward the side of head, and its end slightly dilated to form----- **optic vesicle**.
- ▶ Its proximal part constricted to form----- **optic stalk**
- ▶ The eyeball and its related structures are derived from the following primordial.

1. Optic vesicle: Outgrowth from prosencephalon (a neuroectodermal structure),\

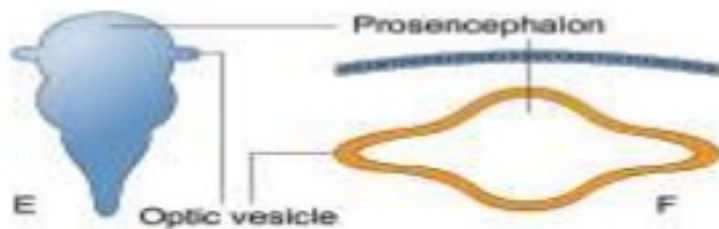
2. Lens placode: a specialised area of surface ectoderm, and the surrounding surface

ectoderm. 3. Mesenchyme: Surrounding the optic vesicle.



FORMATION OF OPTIC VESICLE & OPTIC STALK

- ▶ The area of neural plate which forms the **prosencephalon** develops a linear thickened area on either side (which soon becomes depressed to form optic sulcus).
- ▶ Meanwhile neural plate gets converted into **prosencephalic vesicle**.
- ▶ As the **optic sulcus** deepens, the walls of the prosencephalon overlying the sulcus bulge out to form the **optic vesicle**.
- ▶ The proximal part of the optic vesicle becomes constricted and elongated to form the **optic stalk**.



- How ever such a growth does not take place over the inferior part of the **lens** and therefore, the walls of the cup show deficiency in this part.
- This deficiency extends to some distance along the inferior surface of the optic stalk and is called (*choroidal or fetal fissure*).

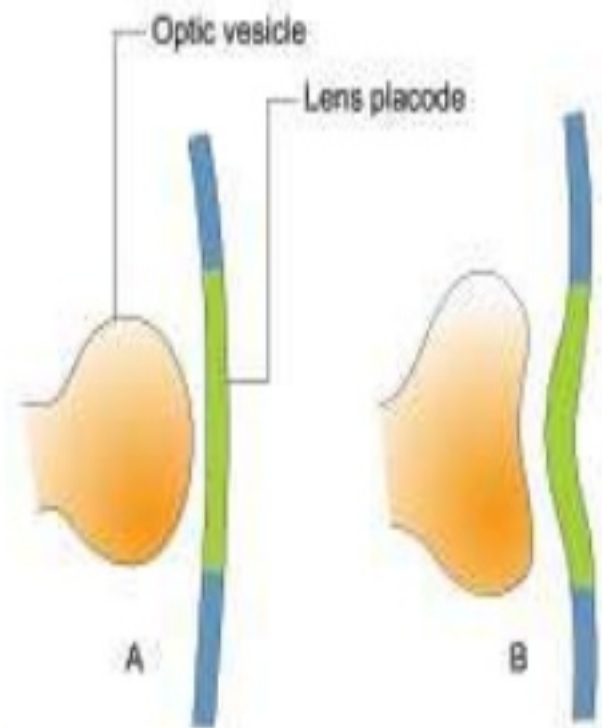
Eye is formed from:

1- Ectoderm

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

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

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



FORMATION OF THE OPTIC CUP:

The **optic vesicle** is converted into a double-layered *optic cup*.

This has happened because the developing lens is invaginated itself into the optic vesicle.

In fact the conversion of the optic vesicle to the optic cup is due to differential growth of the walls of the vesicle.

The margins of optic cup grow over the upper and lateral sides of the lens to enclose it.

➤ With the formation of optic cup, part of the inner vascular layer of mesenchyme is carried into the **cup**, through the choroidal fissure.

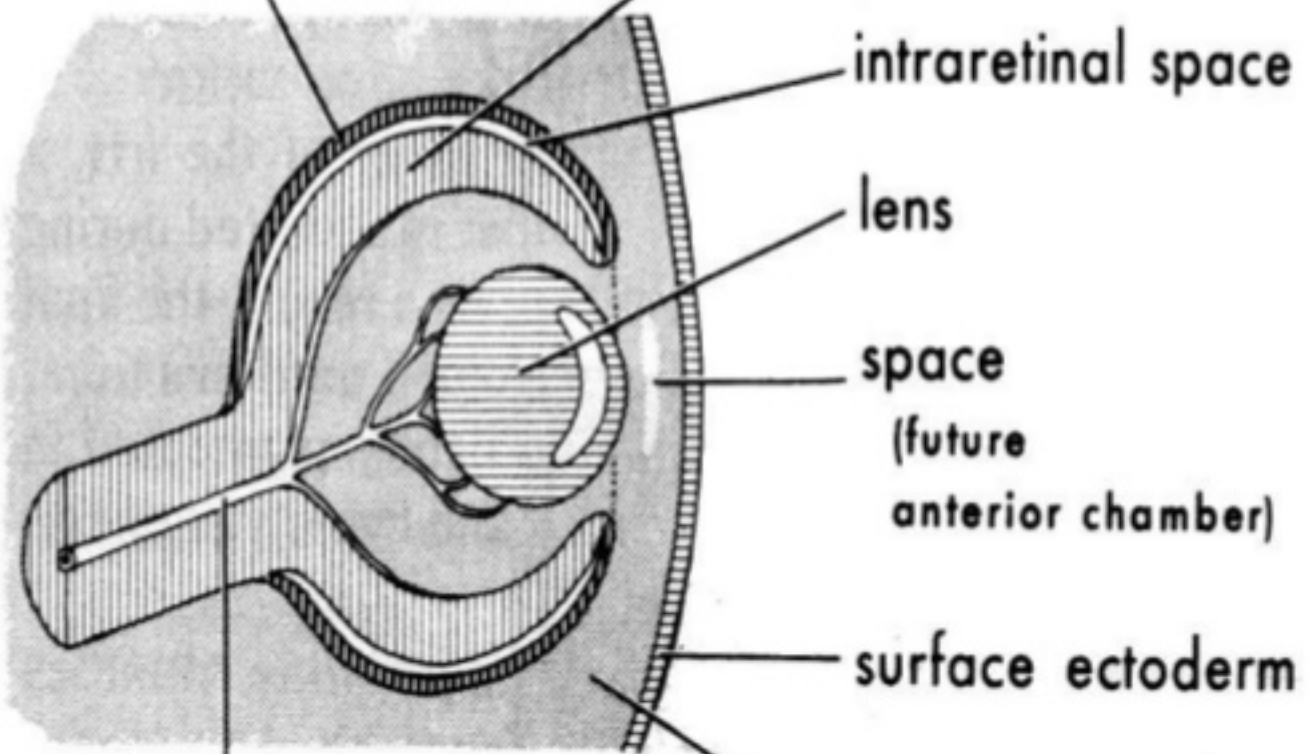
➤ With the closure of this fissure, the portion of mesenchyme which has made its way into the eye is cut off from the surrounding mesenchyme and gives rise to the **hyaloid** system of the vessels.

CHANGES IN THE ASSOCIATED MESENCHYME

- The developing **neural tube** (from which central nervous system develops) is surrounded by mesenchyme, which subsequently condenses to form **meninges**.
- An extension of this mesenchyme also covers the **optic vesicle**.
- Later, this mesenchyme differentiates to form a superficial fibrous layer (corresponding to **dura**) and a deeper vascular layer (corresponding to **pia-arachnoid**).

developing pigment
epithelium of the retina

developing neural
layer of the retina



intraretinal space

lens

space
(future
anterior chamber)

surface ectoderm

hyaloid artery

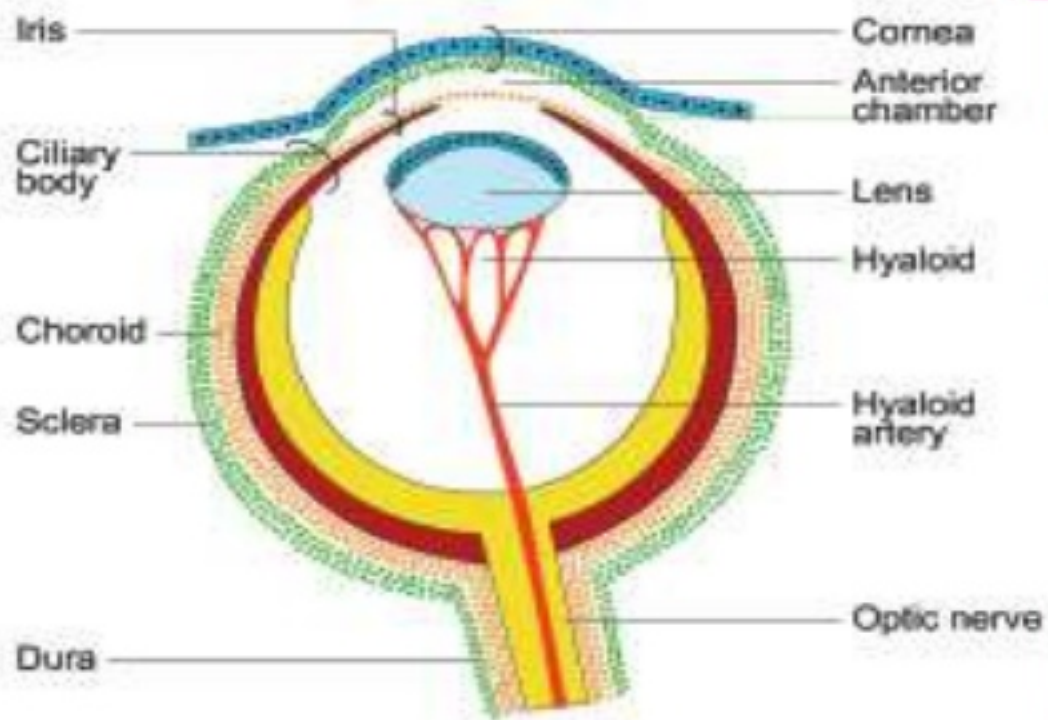
mesoderm

Macular Area and Fovea Centralis

Just after midterm---maculae are first develop as a localized increase of superimposed nuclei in ganglion cell layer, lat to optic disc.

During 7th m there is peripheral displacement of ganglion cell, leaving a central shallow depression, the fovea centralis.

Inner segment of foveal cones decrease in width, but outer segment are elongated



Derivation of various structures of the eyeball.

- ▶ *Sheaths of optic nerve* are formed from the layers of mesenchyme like meninges of other parts of central nervous system.
- ▶ *Myelination of nerve* fibres takes place from brain distally and reaches the **lamina cribrosa** just before birth and stops there.

In some cases, this extends up to around the optic disc and presents as congenital opaque nerve fibres. These develop after birth.

Crystalline lens

The crystalline lens is developed from the surface ectoderm as below :

Lens placode & lens vesicle formation .

- ***1.Primary lens fibres***. The cells of posterior wall of lens vesicle elongate rapidly to form the primary lens Fibres, which obliterate the cavity of lens vesicle.
- The primary lens fibres are formed upto 3rd month of gestation and are preserved as the compact core of lens, known as *embryonic nucleus*.

2. Secondary lens fibres are formed from equatorial cells of anterior epithelium which remain active through out life. Since the secondary lens fibres are laid down concentrically, the lens on section has a laminated appearance.

Depending upon the period of development, the secondary lens fibres are named as below :

- *Fetal nucleus* (3rd to 8th month),
- *Infantile nucleus* (last weeks of fetal life to puberty),.
- *Adult nucleus* (after puberty), and *Cortex* (superficial lens fibres of adult lens)

Lens capsule is a true basement membrane produced by the lens epithelium on its external aspect

Cornea

1. *Epithelium* is formed from the surface ectoderm.
2. *Other layers viz.* endothelium, Descemet's membrane, stroma and Bowman's layer are derived from the fibrous layer of mesenchyme lying anterior to the optic cup .

Sclera

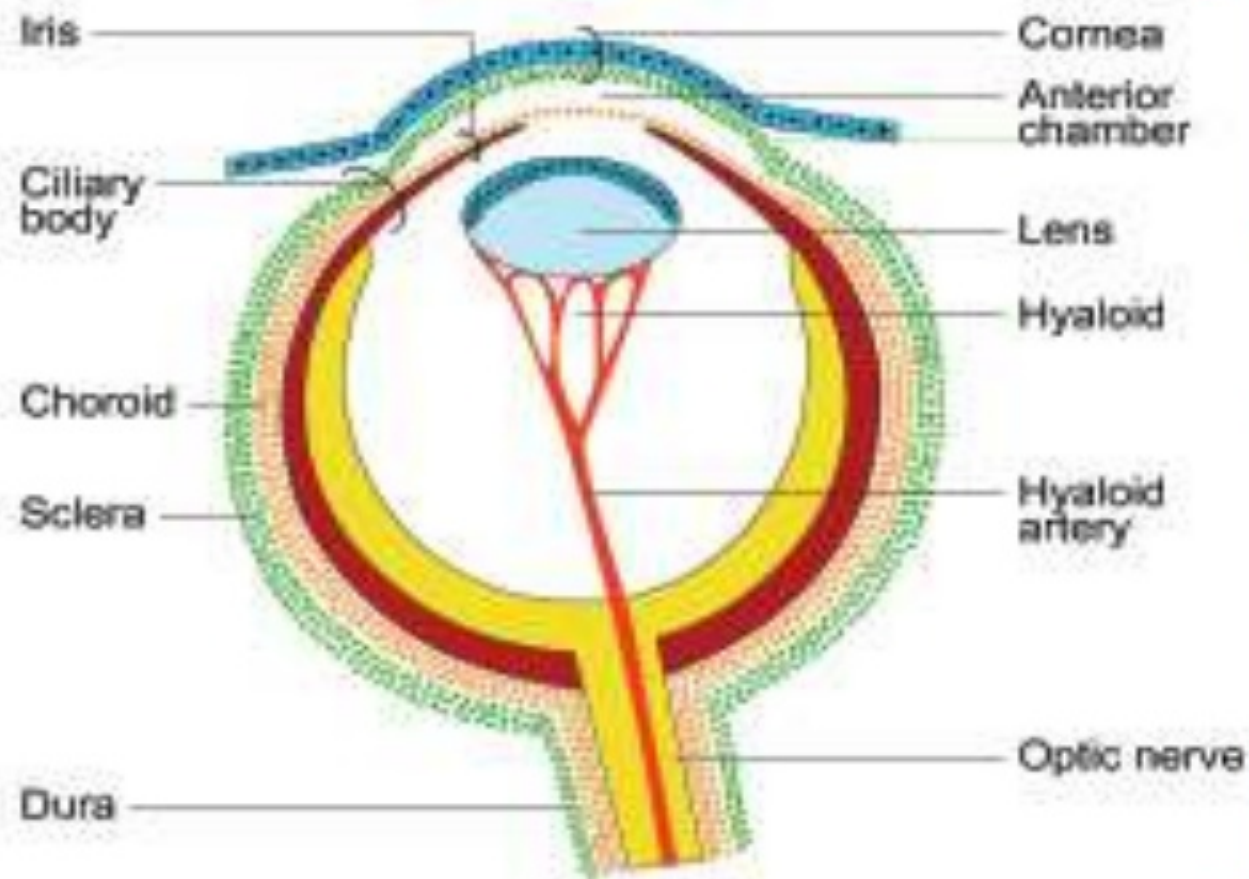
Sclera is developed from the fibrous layer of mesenchyme surrounding the optic cup (corresponding to dura of CNS)

Choroid

It is derived from the inner vascular layer of mesenchyme that surrounds the optic cup.

CILIARY BODY

- The two layers of *epithelium* of ciliary body develop from the anterior part of the two layers of optic cup (neuroectodermal).
- *Stroma of ciliary body*, *ciliary muscle* and *blood vessels* are developed from the vascular layer of Mesenchyme surrounding the optic cup.



Iris

Both layers of *epithelium* are derived from the marginal region of optic cup (neuroectodermal).

Sphincter and *dilator pupillae* muscles are derived from the anterior epithelium (neuroectodermal).

Stroma and *blood vessels* of the iris develop from the *vascular mesenchyme* present *anterior* to the optic cup.

Vitreous

1. *Primary* or *primitive vitreous* is *mesenchymal* in origin and is a vascular structure having the *hyaloid system* of vessels.
2. *Secondary* or *definitive* or *vitreous proper* is secreted by *neuroectoderm* of optic cup.
3. This is an *avascular structure*. When this vitreous fills the cavity, *primitive vitreous* with hyaloid vessels is pushed anteriorly and ultimately disappears.
4. *Tertiary vitreous* is developed from neuroectoderm in the ciliary region and is represented by the ciliary zonules.

Eyelids

Eyelids are formed by reduplication of surface ectoderm **above** and **below** the cornea.

The folds enlarge and their margins meet and fuse with each other. The lids cut off a space called the *conjunctival sac*.

The folds thus formed contain some mesoderm which would form the muscles of the lid and the tarsal plate.

The lids separate after the 7th month of **intra-uterine life**.

Tarsal glands are formed by ingrowth of a regular row of solid columns of ectodermal cells from the lid margins.

Cilia develop as epithelial buds from lid margins.

Conjunctiva

Conjunctiva develops from the ectoderm lining the lids and covering the globe .

Conjunctival glands develop as growth of the basal cells of upper conjunctival fornix.

Fewer glands develop from the lower fornix.

The lacrimal apparatus

Lacrimal gland is formed from about 8 cuneiform epithelial buds which grow by the end of 2nd month of fetal life from the superolateral side of the conjunctival sac .

Lacrimal sac, nasolacrimal duct and canaliculi.

These structures develop from the **ectoderm** of nasolacrimal furrow, It extends from the medial angle of eye to the region of developing mouth.

The ectoderm gets buried to form a **solid cord**, The cord is later canalised. The upper part forms the **lacrimal sac**.

The nasolacrimal duct is derived from the lower part as it forms a secondary connection with the **nasal cavity**.

Some ectodermal buds arise from the medial margins of eyelids.

These buds later canalise to form the **canaliculi**.

Extra ocular muscles

All the extraocular muscles develop in a closely associated manner by mesodermally derived mesenchymal condensation.

This probably corresponds to preotic myotomes, hence the triple nerve supply (III, IV and VI cranial nerves).

STRUCTURES DERIVED FROM THE EMBRYONIC LAYERS

Based on the above description, the various structures derived from the embryonic layers are given below :

1. Surface ectoderm

1. The crystalline lens
2. Epithelium of the cornea
3. Epithelium of the conjunctiva
4. Lacrimal gland
5. Epithelium of eyelids and its derivatives viz., cilia, tarsal glands and conjunctival glands.
6. Epithelium lining the lacrimal apparatus.

2. Neural ectoderm

1. Retina with its pigment epithelium
2. Epithelial layers of ciliary body
3. Epithelial layers of iris
4. Sphincter and dilator pupillae muscles
5. Optic nerve (neuroglia and nervous elements only)
6. Melanocytes
7. Secondary vitreous
8. Ciliary zonules (tertiary vitreous)

3. Associated paraxial mesenchyme

1. Blood vessels of choroid, iris, ciliary vessels, central retinal artery, other vessels.
2. Primary vitreous
3. substantia propria, Descemet's membrane and endothelium of cornea
4. The sclera
5. Stroma of iris
6. Ciliary muscle
7. Sheaths of optic nerve
8. Extraocular muscles
9. Fat, ligaments and other connective tissue structures of the orbit
10. Upper and medial walls of the orbit
11. Connective tissue of the upper eyelid

4. Visceral mesoderm of maxillary process below the eye

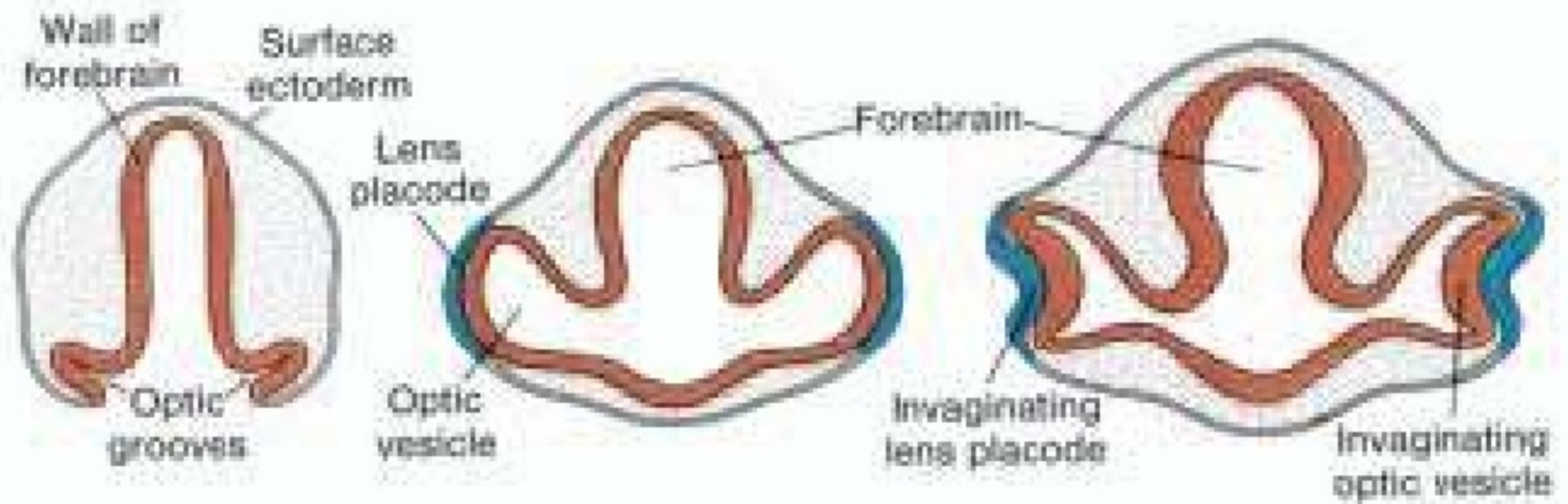
- ▶ Lower and lateral walls of orbit
- Connective tissue of the lower eyelid

Questions

- ▶ 1. DO THE EYE DEVELOPS FROM BOTH NEURAL SURFACE ECTODERM, MESODERM? WHAT DO YOU THINK?
- ▶ 2. MESODERM GIVE RISE TO THESE EXCEPT...
- ▶ A. CORNEAL STROMA.
- ▶ B. ENDOTHEL
- ▶ C. CHORIOD
- ▶ D. IRIS STROMA
- ▶ E. SCLERA.
- ▶ F. EPITH OF CORNEA.

ANSWERS

- ▶ 1. YES....EYE DEVELOPS FROM ALL THESE AS WE MENTION BEFORE.
- ▶ 2. EPITHELIUM OF THE CORNEA.



By 22 days of conception, optic peduncles: a bilateral evagination of the neuroectoderm of the forebrain.

By 27 days, optic vesicles (hollow balls of neuroectoderm connected to the brain- 3rd ventricle- through the hollow optic stalk) reach surface ectoderm and induce formation of lens placode.

Optic vesicles: dilated end of diverticulum- invaginates & sinks below the surface ectoderm to form double layered optic cup.
 Lens placode → lens vesicle.

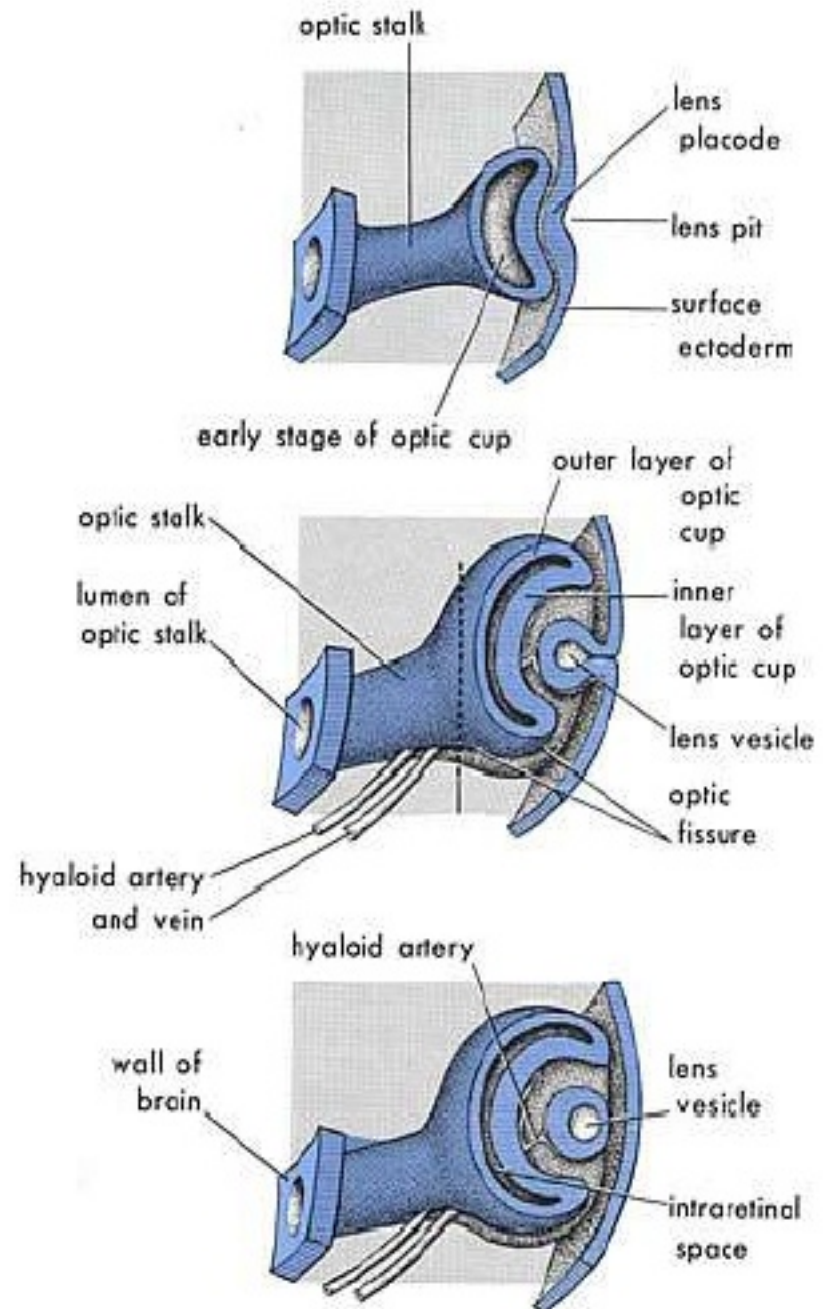
- The proximal portion restricts to form optic stalk
- Inferior edge of optic cup is deficient & continuous with the Optic (choroidal) fissure: a groove in the inferior aspect of the optic stalk.

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

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

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

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



Development of the retina:

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.

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.

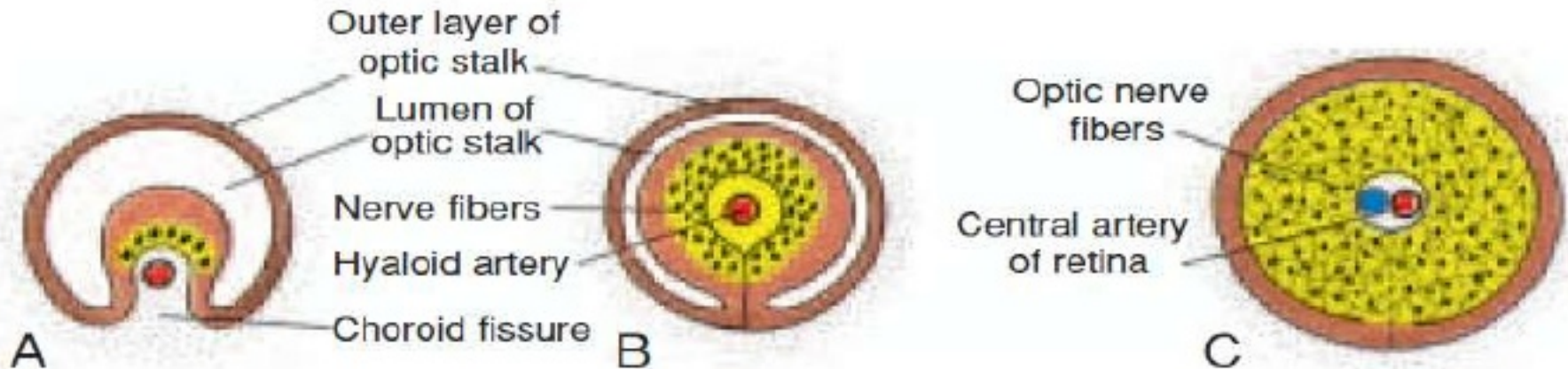
Cells of nuclear zone invades marginal zone by 130 days:

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

Optic nerve:



1- Ganglion cells of the retina develop axons that converge & exit the optic cup through the optic stalk .

2- Inner layer of optic stalk encroaches on the cavity of it until the inner & outer layer fuse and Cavity of the stalk disappears.

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

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

- In the posterior part of optic cup the surrounding fibrous mesenchyme forms **sclera** and **extraocular muscles**,)
- while the vascular layer forms the (**choroid & ciliary body**).

The lens:

1- Lens placode which develops into lens vesicle → a single layer of cells covered by basal lamina formed by invaginating & sinking of placode below surface ectoderm.

2- Primary lens fibers → transparent lens fibers formed by elongation of cells of posterior wall and loss of their nuclei.

Nuclei of the lens fibers move anteriorly within the cells to form a line convex forward → nuclear bow.

3- The primary lens fibers become attached to the apical surface of the anterior lens epithelium.

4- 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 and lens keeps enlarging.

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



"Developing pig eye,
light micrograph. From
right the structures
seen are:

the cornea (brown)

the lens (purple)

the retina (pink)

the choroid (dark
brown line)

the sclera (brown)

The optic nerve (at
centre left).

5- 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.

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

Ciliary body & suspensory ligaments of the lens:

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.

Iris:

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

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

Pigment cells of neuroectoderm → form sphincter & dilator muscle of iris.

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

Anterior chamber:

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

Vitreous body:

1- Primitive- primary vitreous → a network of delicate cytoplasmic processes. Derived from → ectodermal cells of lens + neuroectoderm of retinal layer of optic cup.

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

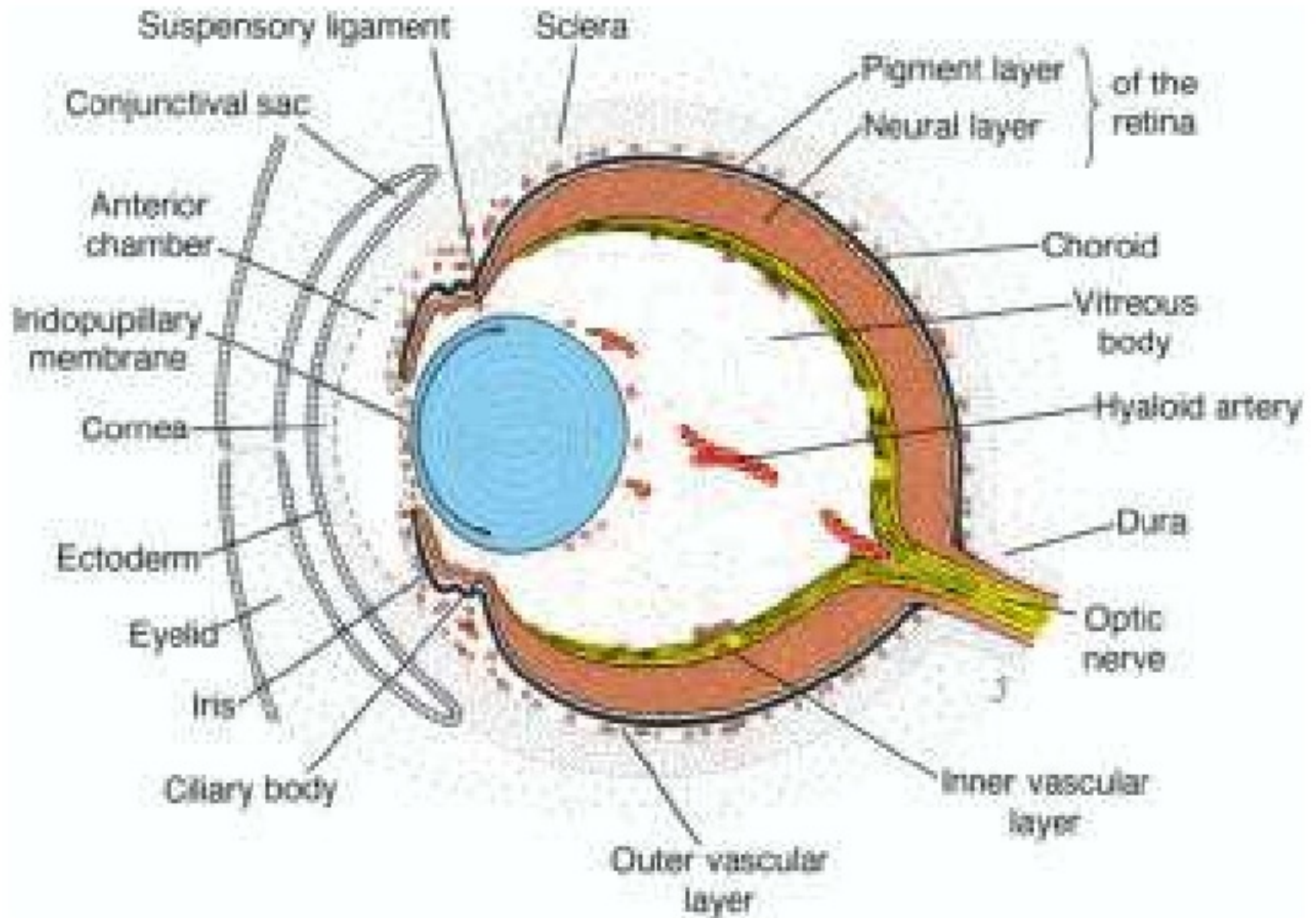
Substantia propia + endothelium → from mesenchyme

Sclera:

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

Choroid:

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



Section through the eye of a 15-week fetus showing the anterior chamber, pupillary membrane, inner and outer vascular layers, choroid, and sclera

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.

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 palpebrae 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

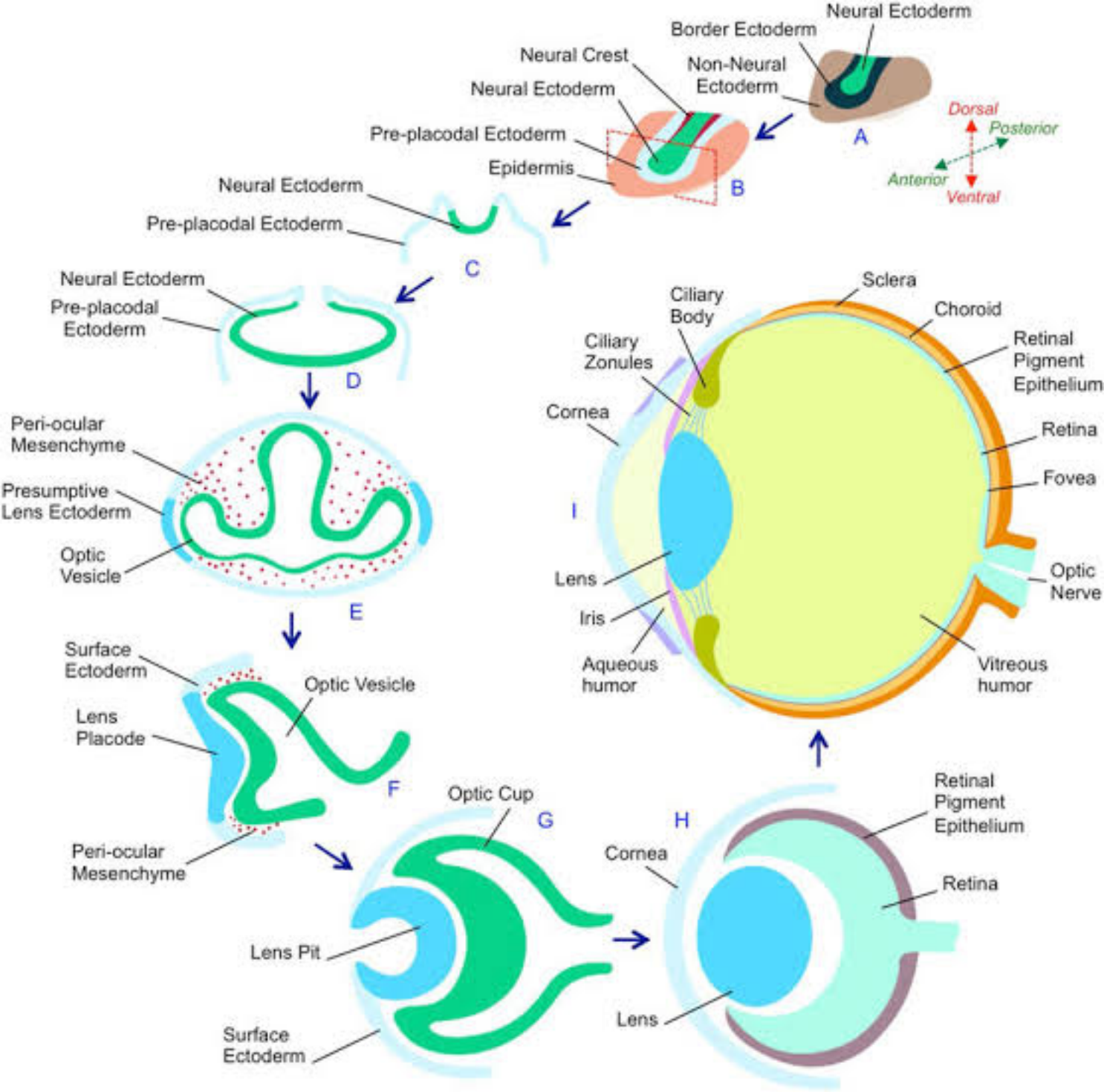
Eye abnormalities related to embryologic phase

- **Coloboma:** the choroid fissure fails to close.
- **The pupillary membrane** *may persist instead of being* resorbed during formation of the anterior chamber.
- **Congenital cataracts:** due to genetic reasons, german measles (rubella) infection between 4-7 week of gestation.
- The **hyaloid artery** may persist to form a cord or cyst.
- In **microphthalmia the eye is too small.** (results from intrauterine infections).

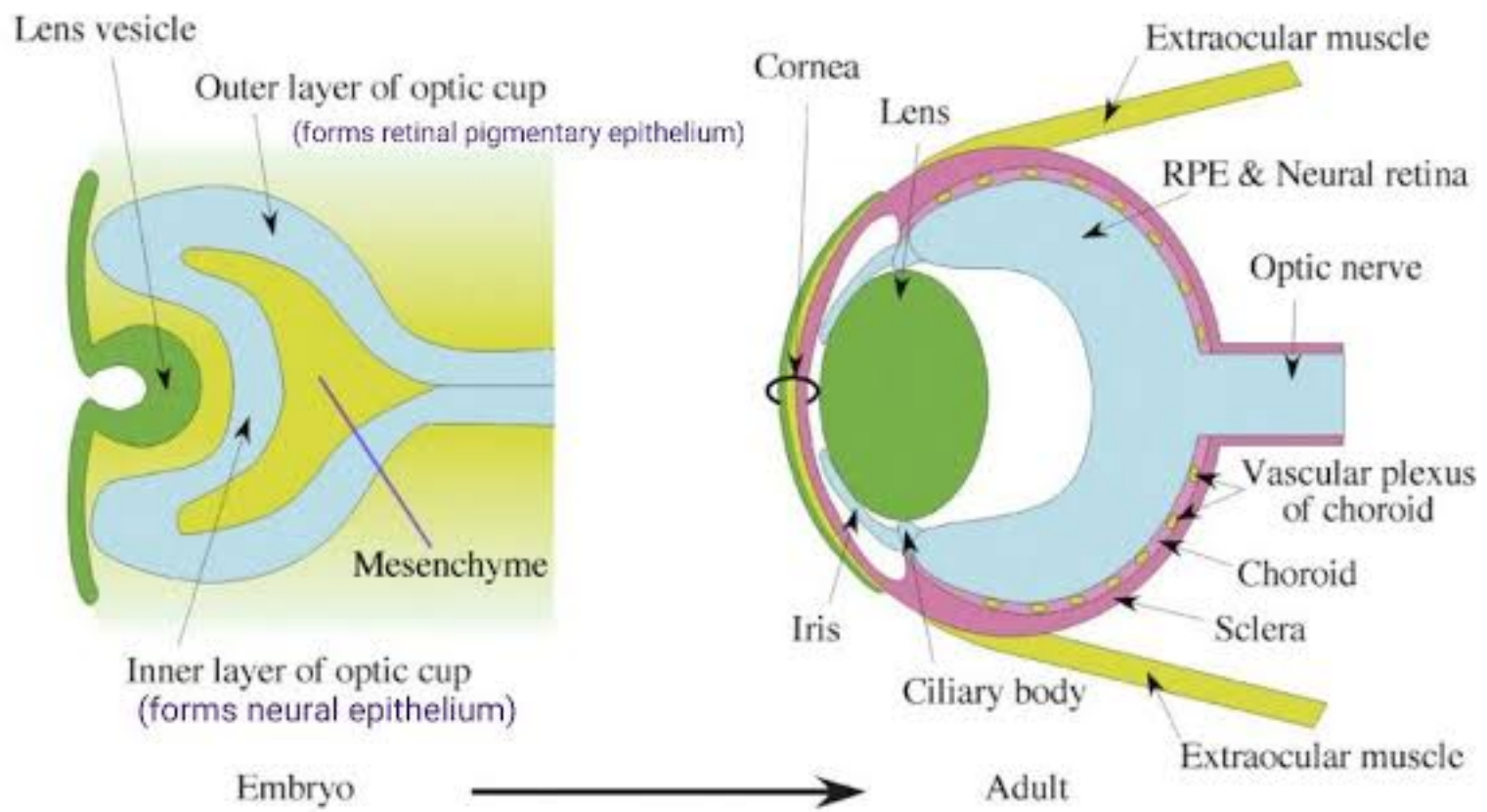
- **Anophthalmia** is absence of the eye.
- **Congenital aphakia** (absence of the lens) and **aniridia** (absence of the iris) are rare anomalies.
- **Cyclopia** (single eye) and **synophthalmia** (fusion of the eyes) are invariably associated with cranial defects in which the cerebral hemispheres are partially or completely merged into a single telencephalic vesicle.
- **Blue sclera.** (thin sclera through which the pigment of choroid can be seen).
- **Anomalies of pigmentation/ albinism.**

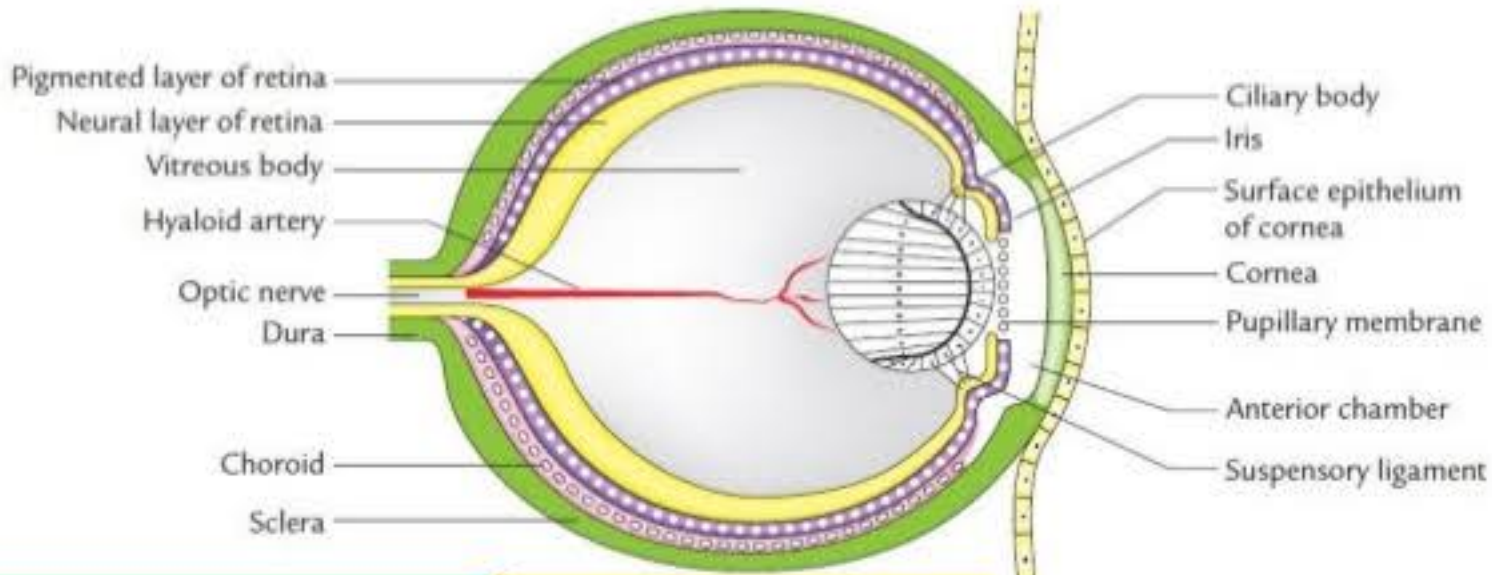
Summary of various part of the eye ball.

Part	Derived from
Lens	Surface ectoderm
Retina	Neuroectoderm (optic cup)
Vitreous	Mesoderm- mesenchyme
Choroid	Mesoderm (infiltrated by neural crest cells?)
Ciliary body	Mesoderm
Ciliary muscles	Mesenchymal cells covering the developing ciliary body (neural crest)
Iris	Mesoderm- mesenchyme
Muscles of the iris	Neuroectoderm (from optic cup)
Sclera	Mesoderm (infiltrated by neural crest cells?)
Cornea	Surface epithelium by ectoderm, substantia propria and inner epithelium by neural crest
Conjunctiva	Surface ectoderm
Blood vessels	mesoderm- mesenchyme
Optic nerve	Neuroectoderm. Its covering (pia, arachnoid and dura) are derived from mesoderm



- neuroectoderm
- surface ectoderm
- neural crest
- mesoderm





Derivatives of optic stalk

Optic nerve

Derivatives of optic cup

- Retina
- Dilator pupillae
- Sphincter pupillae
- Epithelium of the iris
- Epithelium of ciliary body

➤ The fibrous layer of mesenchyme surrounding the anterior part of optic cup forms the **cornea**.

- The corresponding vascular layer of mesenchyme becomes the **iridopupillary membrane**, which in the peripheral region attaches to the anterior part of the optic cup to form the **iris**.
- The central part of this lamina is pupillary membrane which also forms the **tunica vasculosa lentis**.