

# 20.

## PLACODES AND SENSORY DEVELOPMENT

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**READING ASSIGNMENT:** Larsen 3<sup>rd</sup> Edition **Chapter 12, Part 2.** pp.379-389; **Part 3.** pp.390-396; **Chapter 13,** pp.430-432

### SUMMARY

A series of ectodermal thickenings or placodes develop in the cephalic region at the periphery of the neural plate. Placodes are central to the development of the cranial sensory systems in vertebrates and are among the innovations that appeared in the early evolution of vertebrates. There are placodes for the three organs of special sense: olfactory, optic (lens) and otic placodes, and (epibranchial) placodes that give rise to the distal cells of the sensory ganglia of cranial nerves V, VII, IX and X. Placodes (with the possible exception of the olfactory placodes) form under the influence of surrounding cranial tissues. They do not appear to require the presence of neural crest. The mesoderm in the prechordal plate plays a significant role in the initial development of the placodes for the organs of special sense, while the pharyngeal pouch endoderm plays that role in the development of the epibranchial placodes. The development of the organs of special sense is described briefly.

### LEARNING OBJECTIVES

You should be able to:

- a. Give a definition of placodes and describe their evolutionary significance.
- b. Name the different types of placodes, their locations in the developing embryo and their developmental fates.
- c. Discuss the early development of the placodes and some of the possible factors that feature in their development.
- d. Describe the contributions by trigeminal and epibranchial placodes, and by neural crest cells to the ganglia of cranial nerves V, VII, IX, X.
- e. Describe the development of olfactory epithelium, specifically the origin of the olfactory placodal cells, the differentiation of sensory neurons, and the stages in the development of the olfactory nerve (CN I).
- f. Describe the development of the eye, specifically the origin and derivatives of the optic vesicle, and of the lens vesicle; the differentiation of the cells in the mature retina and the development of the optic nerve (CN II).
- g. Describe the development of the structures of the inner ear, specifically the derivatives of the ventral and dorsal components of the otic vesicle, the development of the cochlear duct and of the semicircular canals, and the development of the statoacoustic ganglion and nerve (CN VIII).

## GLOSSARY

**Choroidal fissure:** A groove on the ventral surface of the optic stalk, in which the hyaloid is situated.

**Epibranchial placodes:** Located close to the dorsal ends of the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> pharyngeal grooves.

They will give rise to the distal cell population of the trigeminal ganglion (V), geniculate ganglion (VII), petrosal ganglion (IX), nodose ganglion (X).

**Hyaloid artery:** This artery is a terminal branch of the ophthalmic artery and is located in the choroidal fissure. The artery will develop into the central artery of the retina.

**Hypobranchial placodes:** Located close to the ventral ends of the 2<sup>nd</sup> and 3<sup>rd</sup> pharyngeal grooves.

Found in only two vertebrates to date. Their role is unknown.

**Lens vesicle:** A hollow structure formed by the invagination of the optic placode.

**Olfactory placode:** Gives rise to the sensory receptor cells of the olfactory and vomeronasal epithelia of the nose.

**Ophthalmic trigeminal placode:** Located in an intermediate position- between the otic placode and the epibranchial placodes. This is the ophthalmic component of the future trigeminal ganglion.

**Optic cup:** Develops when the distal face of the otic vesicle forms a depression (optic fissure)

transforming it into a goblet-shaped structure. The hollow lens vesicle sits in the depression of the optic cup. The inner layer of the optic cup becomes the neural retina, while the outer layer becomes the pigment retina.

**Optic placode:** Invaginates and gives rise first to a lens vesicle and subsequently to the lens of the eye.

**Optic stalk:** The structure by which the optic vesicle remains attached to the forebrain.

**Optic vesicle:** An evagination that expands from the wall of the forebrain towards the optic placode.

**Otic pit:** formed as the result of invagination of the otic placode during the 4<sup>th</sup> week, still open to the ectodermal surface.

**Otic placode:** The only remaining placode of the dorsolateral series. Will give rise to the membranous labyrinth of the inner ear and the statoacoustic ganglion of cranial nerve VIII.

**Otic vesicle:** Invagination of the otic placode during the 4<sup>th</sup> week results in the development of an open otic pit and subsequently in a closed otic vesicle.

**Pigment retina:** pigmented epithelium of the retina

**Placodes:** Localized thickened areas of specialized ectoderm that originate from ectoderm at the border between the neural plate/neural crest and the future epidermis in the cephalic region. These structures are essential for the development of sensory components of the peripheral nervous system in vertebrates.

## TEXT

Placodes are localized regions of columnar epithelium that develop from ectoderm between the 10- and 30-somite stage at the border between neural plate/neural crest and the future epidermis. While it has long been held that placodes evolved with the emergence of vertebrates, recent evidence indicates that structures **analogous** to otic, optic and olfactory placodes are present in non-vertebrate chordates, based on the expression of molecular markers and/or the presence of specialized sensory cells. However, no structures homologous to epibranchial placodes have thus far been found in lower chordates, suggesting that these evolved separately in vertebrates.

The following placodes are present (in rostrocaudal sequence): hypophyseal, olfactory, optic (lens), trigeminal, otic, four epibranchial, and possibly two hypobranchial placodes. All placodes have a neural fate, with the exception of the optic placode, which will form the lens of the eye (Table 20-1).

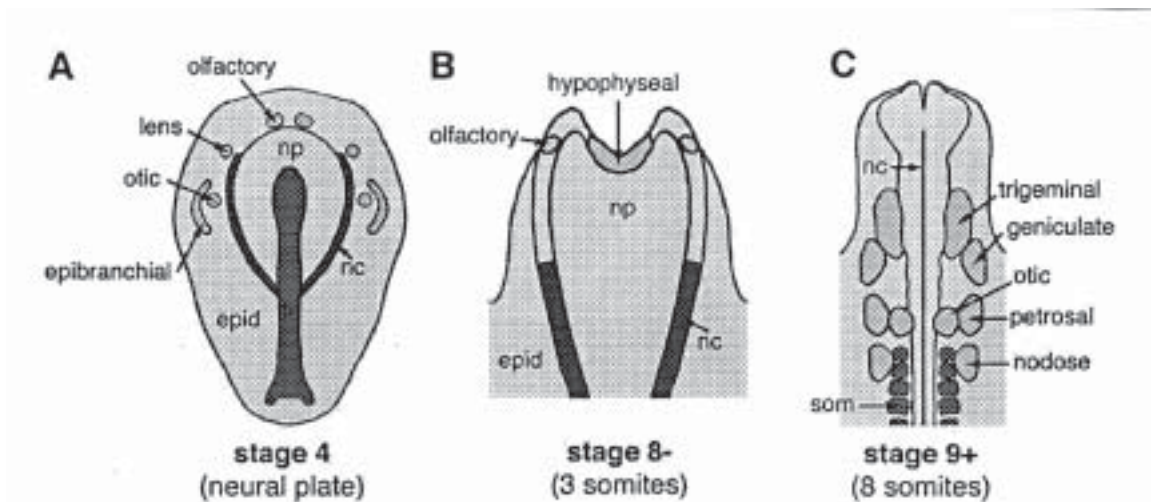
Most organs of special sense are located in the cranial region, which has the advantage of being close to the brain, where the neural integration of all sensory input will occur. Among the organs of

special sense, the organs of olfaction, vision, and hearing and balance originate completely, or in part, as thickened patches of surface ectoderm: olfactory, optic and otic placodes respectively (Fig. 20-1).

Placodal cells will become sensory receptors (membranous labyrinth of inner ear, olfactory epithelium) or bipolar ganglion cells of cranial nerves. As stated before, the optic placode will become the lens of the eye.

Surface ectoderm		Nervous System		ORIGIN OF SENSORY ELEMENTS	ORIGIN OF NERVOUS CONDUCTORS
Ganglionic cell	I	II	OL-FACTION	Placode	Placode
	II		VISION	Neural tube	Neural tube
	III		AUDITION BALANCE	Placode	Placode
	IV		TASTE	Sensory differentiation of certain cells of surface ectodermal covering of tongue	Neural crest (spinal ganglia)
	L M		SPINAL NERVE	PAIN TOUCH	Free nerve endings (L): neural crest. Mesenchymal cells (M)

Table 20-1.

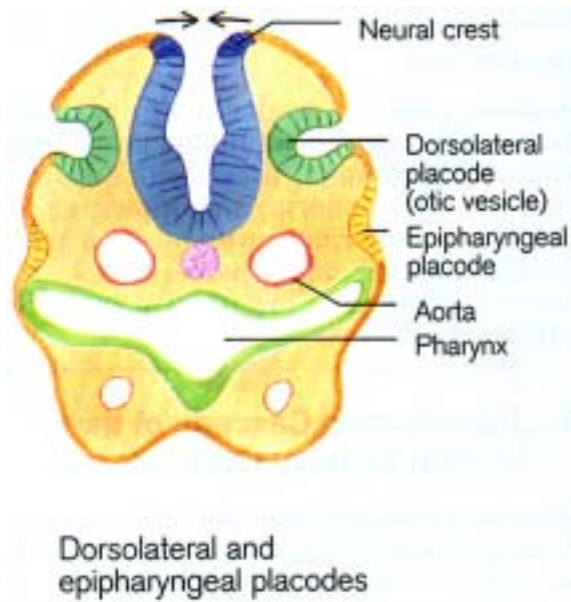


**Fig. 20-1** Cranial placodes fate map to the anterior neural plate border in chick embryos. (A) Neural plate stage fate map. After Rudnick (1944). (B) Neurula stage fate map of the anterior neural folds. After Couly and Le Douarin (1987). (C) Fate map at the 8-somite stage. After D'Amico-Martel and Noden (1983). epid, epidermis; nc, neural crest; np, neural plate; s, primitive streak; som, somites.

## LOCATION OF PLACODES

During early embryonic development placodes are found in the following **locations** (Fig. 20-2, Fig. 20-3):

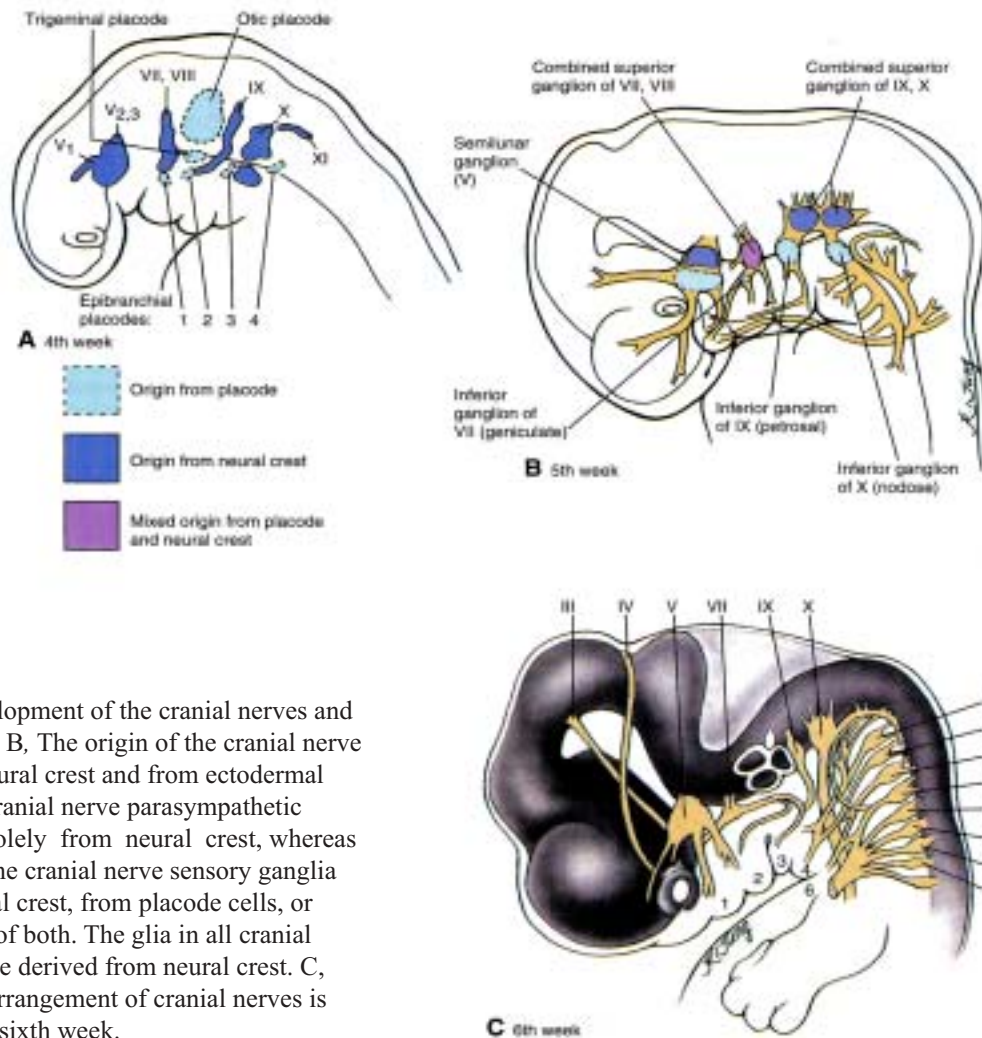
- **Dorsolateral** - along the lateral surface of the developing brain: this the location of the otic placode, a remnant of the lateral line series, which belonged to the dorsolateral group.
- **Intermediate** - between the otic placode area and the epibranchial placodes: this is the location of the ophthalmic component of the trigeminal placode.
- **Epibranchial placode series**- close to the dorsal ends of the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> pharyngeal grooves.
- **In addition**, the olfactory and optic placodes form near the forebrain.
- **Hypobranchial placode series**- in two vertebrates hypobranchial placodes have been found close to the ventral ends of the 2<sup>nd</sup> and 3<sup>rd</sup> pharyngeal grooves. Their role is unknown. It is possible that these placodes have been overlooked in other vertebrates. They will not be discussed further here.



**Fig. 20-2** Classification of placodes.

## DEVELOPMENT OF PLACODES

The first step in placode development is the formation of a horseshoe-shaped preplacodal ectoderm field at the border of the cranial neural plate. Both placodes and neural crest cells are induced at this border in distinct but overlapping domains, with the prospective placodal ectoderm forming lateral to the neural crest. The rostral forebrain does not form neural crest cells. The most rostral placodes: hypophyseal and olfactory, abut the neural plate directly and are incorporated in the outer folds of the anterior neural ridge. The cells in the preplacodal field co-express a specific set of genes (*Six* and *Eya*). *Six* and *Eya* are the only transcripts to be maintained in all developing placodes, while being lost in the interplacodal domains. The role of these transcripts is not clear. Possibly they bestow placodal competence or bias on the ectoderm next to the anterior neural plate, while **during the next step of development** *Pax* gene expression confers specific placodal identities.



**Fig. 20-3** Development of the cranial nerves and their ganglia. A, B, The origin of the cranial nerve ganglia from neural crest and from ectodermal placodes. The cranial nerve parasympathetic ganglia arise solely from neural crest, whereas the neurons in the cranial nerve sensory ganglia arise from neural crest, from placode cells, or from a mixture of both. The glia in all cranial nerve ganglia are derived from neural crest. C, The definitive arrangement of cranial nerves is apparent by the sixth week.

Placodes (with the possible exception of the olfactory placodes) form under the influence of surrounding cranial tissues. They do **not** appear to require the presence of neural crest. All placodes express one or more members of the Pax family of paired class homeobox genes as transcription factors at a relatively early stage in their development.

- **Epibranchial** placodes express *Pax2*, and *Sox3* during early development. These placodes require pharyngeal pouch endoderm as the source of their inductive signal. The signalling molecule BMP-7 has been identified as the mediator of inductive interaction. *In vitro*, this molecule will induce cephalic ectoderm, but not trunk ectoderm, to form placodes.
- The **ophthalmic** trigeminal placode expresses *Pax3* in its early development. It requires for its inductive interaction and maintenance a diffusible signal from the neurectoderm. No signalling molecule has been implicated as yet.
- The **otic** placode expresses *Pax8* early in development and *Pax2*, *Sox3*, and Notch during subsequent developmental stages. Ear-inducing signals probably arise *initially* from mesoderm (both axial and non-axial), and *later* from the hindbrain. FGF-3 has been identified as a secreted growth factor, which is responsible for induction and morphogenesis of the vertebrate inner ear. Ectopic expression of FGF-3 results in formation of ectopic placodes, which express the typical otic placode marker genes. This suggests widespread competence of surface ectoderm to form sensory placodes.

- The **optic** placode expresses *Pax6* in early eye development, later *Pax2*. Neural plate and anterior mesoderm are responsible for lens placode induction. BMP-4 and later BMP-7 are optic cup-derived signals and are needed to maintain eye placode development.
- The **olfactory** placode also expresses *Pax6* early in its development. The anterior mesoderm probably is the most important source for olfactory placode inducing signals. The forebrain may provide reinforcing signals. No signaling molecules have been identified so far.

### DEVELOPMENTAL FATES OF PLACODES

When the first vertebrates arose, one of the new features was the derivation of most sensory components of the peripheral nervous system from two sources:

- Migrating neural crest cells;
- Thickened ectodermal placodes.

The trigeminal and epibranchial placodes invaginate to form **the distal neurons** (sensory) of the

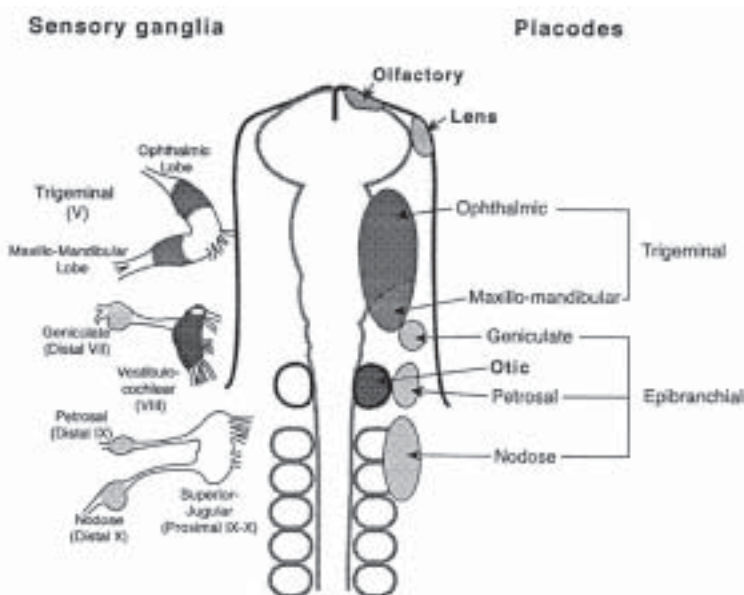
- Trigeminal ganglion (CN V)
- Genuiculate ganglion (CN VII)
- Petrosal ganglion (CN IX)
- Nodose ganglion (CN X)

Once the placodal cells invaginate and initiate neurogenesis the expression of the transcription factors (e.g. *Sox3*) is lost. These neurons are larger than the more **proximally located neural crest-derived neurons** in the ganglia of the branchiomeric cranial nerves (Fig. 20-4).

The **otic** placode invaginates to give rise to the entire membranous labyrinth of the inner ear (cochlea, semicircular canals, utricle, saccule, and endolymphatic duct) and to the neurons of the vestibulo-acoustic ganglion of cranial nerve VIII.

The **optic** placode invaginates and gives rise to the lens of the eye.

The **olfactory** placode gives rise to the ciliated sensory receptor cells of the olfactory (odorant-sensing) and vomeronasal (pheromone-sensing) epithelia of the nose.



**Fig. 20-4** Schematic drawing showing the locations of neural crest and placodal primordia of cranial ganglia in a neurula-stage avian embryo. The ciliary, ethmoidal and sphenopalatine contain parasympathetic second neurons; all the rest are sensory ganglia. The avian acoustic (cochlear) ganglion is homologous to the mammalian spiral ganglion. (From D'Amico-Martel and Noden, 1983.)

## ORGANS OF SPECIAL SENSE

### **Olfactory epithelium**

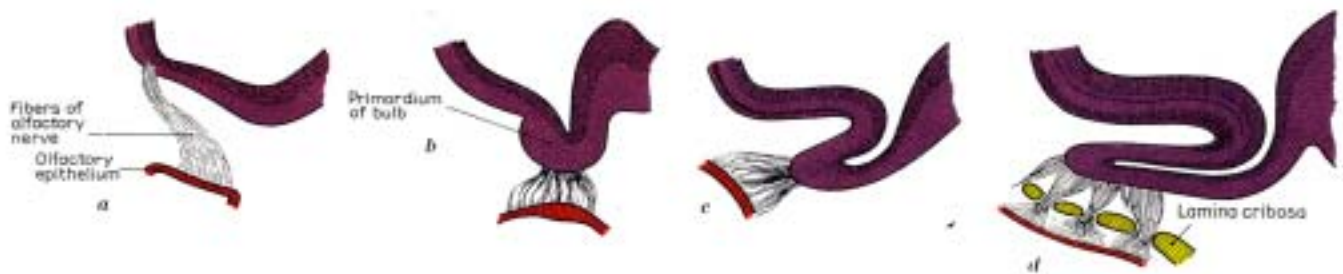
The olfactory placodes are somewhat unique in that they probably do not arise as a localized proliferation of a discrete group of ectodermal cells that are separated from the edge of the neural plate. Rather, the field of olfactory placode precursor cells is continuous with, and adjacent to the field of cells that will later form the telencephalon. The placodal precursor cells are initially located in the lateral anterior neural plate and form as identifiable placodes by anterior convergence. **Thus, it appears that the olfactory placodes originate in the neural plate, rather than the ectoderm.**

As the placode differentiates into olfactory epithelium stratified cell types appear:

- basal cells,
- sensory neurons, and
- glia.

Throughout life the basal cells generate olfactory sensory neurons that migrate to the apical surface of the epithelium. The cell bodies of the olfactory sensory neurons remain in the epithelium, while their axons grow through the olfactory nerve into the differentiating CNS (Fig. 20-5).

The first outgrowth of axons from the olfactory placode involves a transient group of pioneer neurons that prefigure the olfactory pathway before outgrowth of the sensory axons can occur. These pioneers provide the first necessary connection with the CNS and establish an axonal scaffold for the later arriving olfactory neurons.



**Fig. 20-5** Human Embryo

a) about 46 days (17mm), b) about 54 days (25mm), c) about 68 days (45mm), d) about 84 days (78 mm)

### **Eye**

Eye development involves an:

- evagination of the forebrain, and an
- invagination of the optic (lens) placode.

The process begins in the future diencephalic region of the forebrain, even before its neural folds have come together.

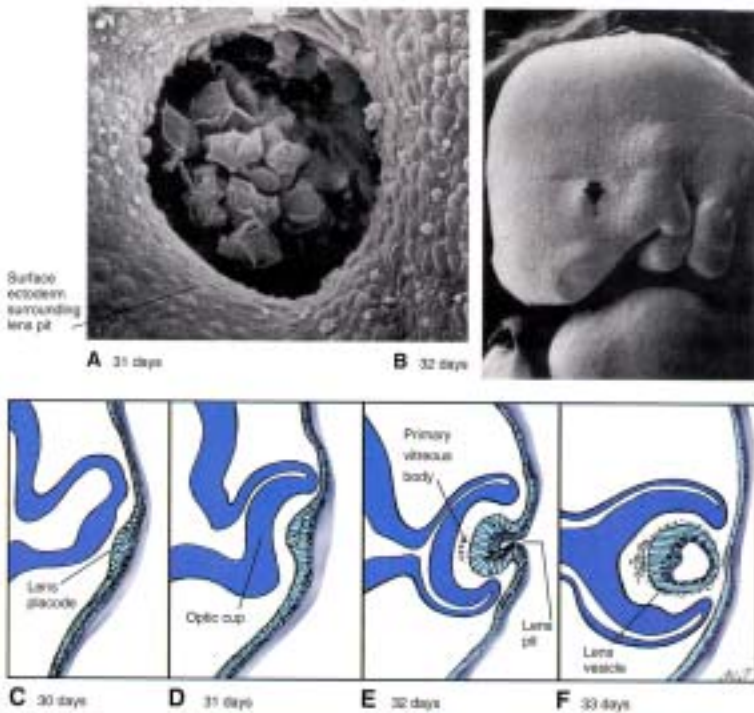
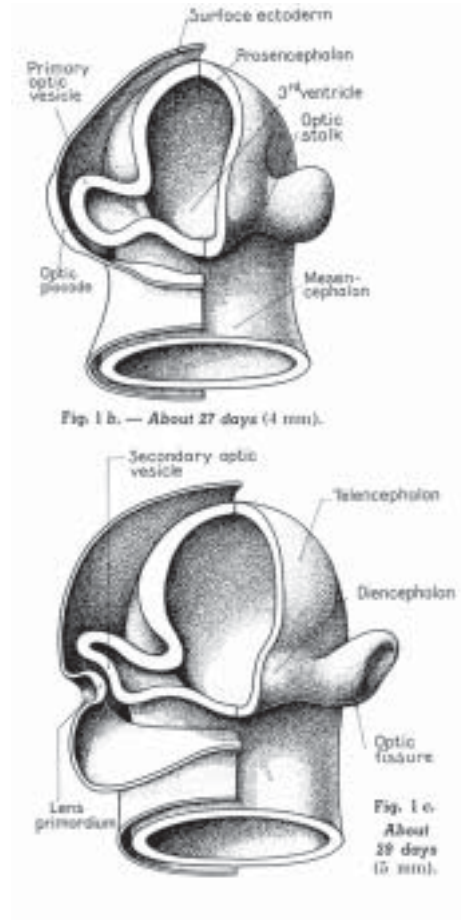
Initially, a single eye field exists in the anterior ridge of the neural plate. This field separates later into two separate optic primordia, under the influence of Shh expressed in the prechordal plate. At that time the expression of the marker gene *Pax6*, a most important transcription factor in lens placode development, is downregulated, and *Pax2* is upregulated.

An **evagination** (the **optic vesicle**) expands from the wall of the forebrain towards the overlying ectoderm, which has formed a placode (optic, lens placode). The optic vesicle remains attached to the forebrain by an **optic stalk**. Once the optic vesicle nears the ectoderm, its distal face forms a depression (optic fissure) transforming the optic vesicle into a goblet-shaped **optic cup** (Fig. 20-6). Contact

between the optic vesicle and the lens ectoderm is responsible for the initiation of lens differentiation, including *crystallin* expression, cell elongation and cell cycle arrest.

The adjacent lens placode simultaneously **invaginates** and forms a hollow lens vesicle that sits in the depression of the optic cup (Fig. 20-7).

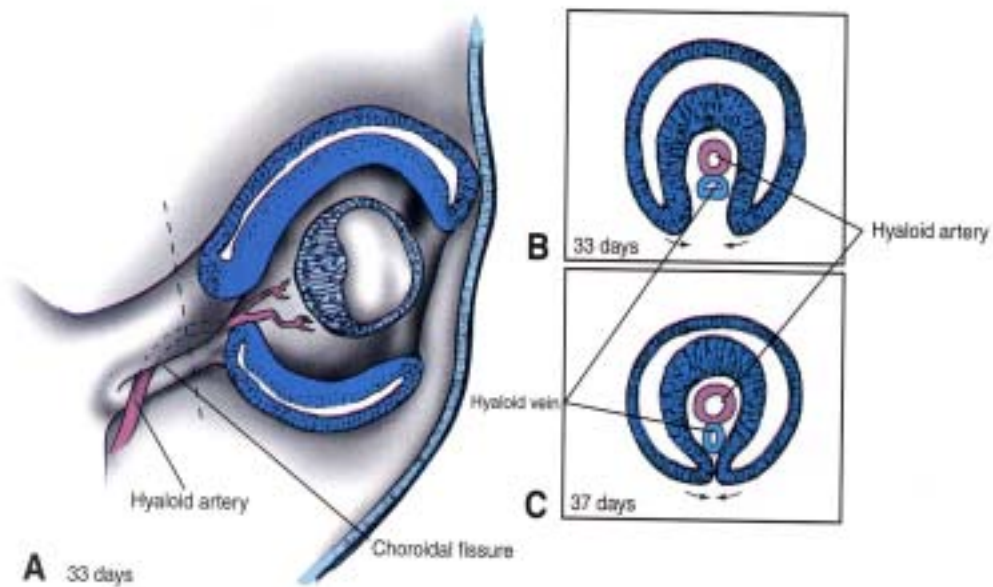
**Fig. 20-6** A. about 27 days (4mm).  
B. About 29 days (5mm).



**Fig. 20-7** Formation of the lens placode and lens vesicle. Contact with the optic cup is necessary for the maintenance and development of the lens placode, although other influences are apparently more important in its induction. A-E, During the fifth week, the lens placode begins to invaginate to form the lens pit (arrow in B). E, F, The invaginating lens placode pinches off to form a lens vesicle enclosed in the optic cup. (A, Photo courtesy of Dr. Arnold Tamarin.)



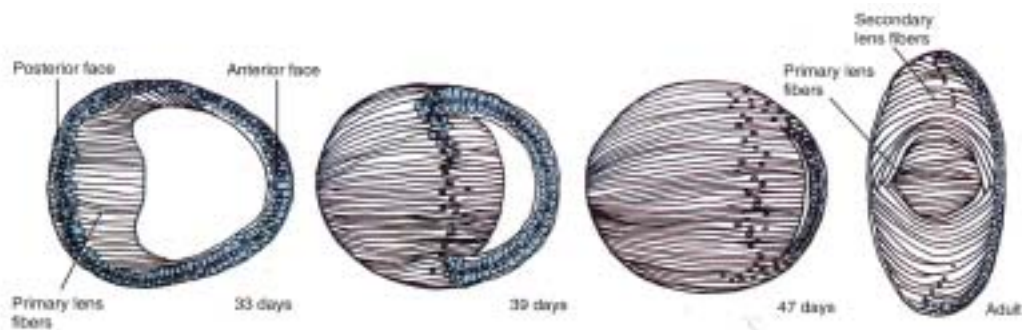
Blood supply to the developing eye is by the hyaloid artery, a terminal branch of the ophthalmic artery. This artery is located in the **choroidal fissure**, a groove on the ventral surface of the optic stalk. The artery will develop into the central artery of the retina. (Fig. 20-8).



**Fig. 20-8 Vascularization of the lens and retina.** *A*, As the lens vesicle detaches from the surface ectoderm, it becomes vascularized by the hyaloid vessels, which gain access to the lens through the choroidal fissure. *B, C*, During the seventh week, the edges of the choroidal fissure fuse together, enclosing the hyaloid artery and vein in the hyaloid canal. When the lens matures, the vessels serving it degenerate, and the hyaloid artery and vein become the central artery and vein of the retina.

DERIVATIVES OF THE COMPONENTS DESCRIBED ABOVE:

The hollow **lens vesicle** will become the solid lens of the eye as the result, first, of an anteroposterior elongation of the posterior cells of the lens vesicle (**primary lens fibers**). During this process of elongation the anterior lens epithelium remains simple. Secondly, during the further expansion of the lens, the anterior epithelium gives rise to **secondary lens fibers**, which will make up most of the mature lens. Programmed removal of nuclei and other organelles from the lens fiber cells ensures that an optically clear structure is created (Fig. 20-9).



**Fig. 20-9 Differentiation of the lens.** The lens develops rapidly in the fifth to seventh weeks as the cells of its posterior wall elongate and differentiate to form the primary lens fibers. Secondary lens fibers begin to form in the third month.

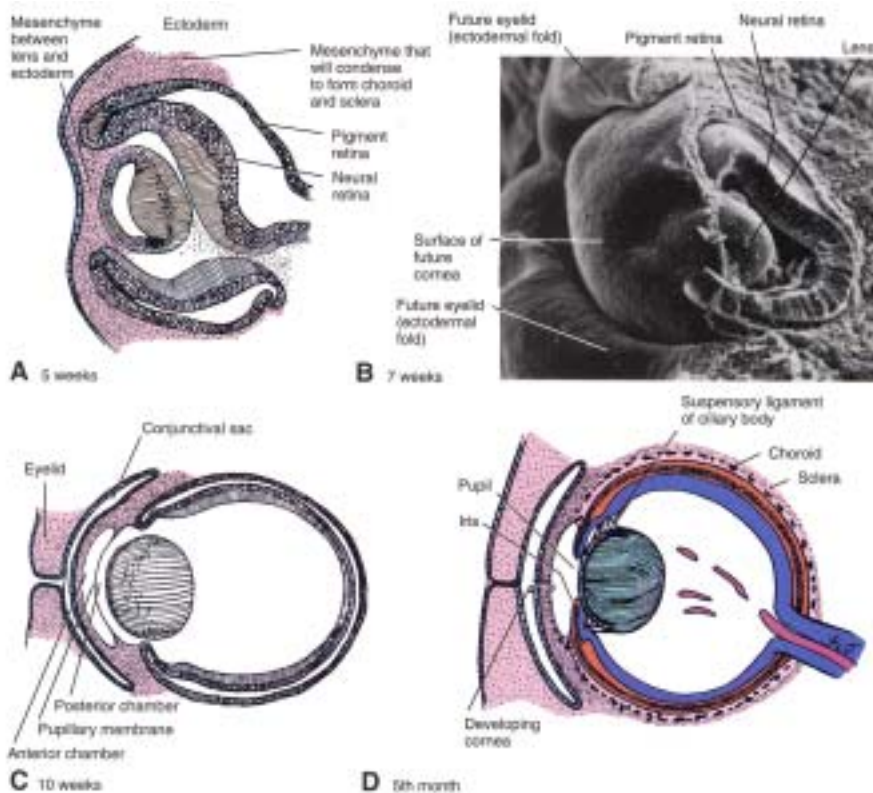
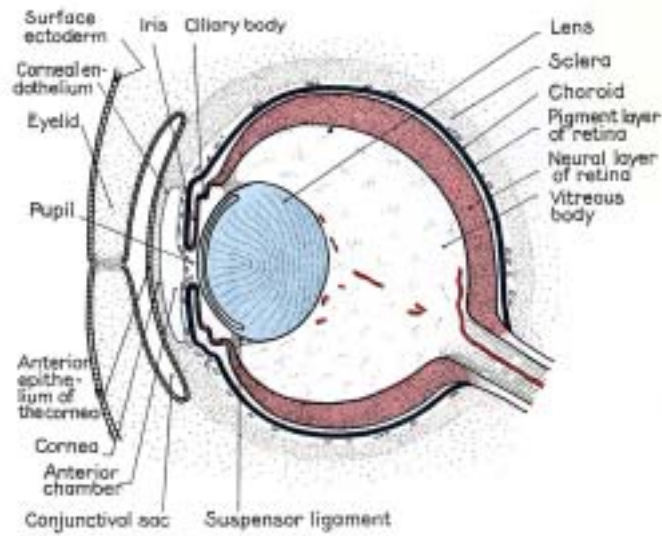
The inner layer of the **optic cup** becomes the **neural retina**, while the outer layer becomes the **pigment retina** (Fig. 20-10). The intraretinal space between the two layers gradually is obliterated, but neural and pigment retina do not fuse completely.

The **neural retina** undergoes further differentiation between the 6<sup>th</sup> week and the 8<sup>th</sup> month to form the cellular layers of the mature **retina**.

Axons from the neural retina grow through the **choroid fissure of the optic stalk** to the brain, converting the optic stalk to the **optic nerve**.

The neural crest-derived mesenchyme that surrounds the optic cup during early development will become the thin inner **choroid** and the fibrous outer **sclera** that surround the globe of the eye (Fig. 20-11).

Fig. 20-10

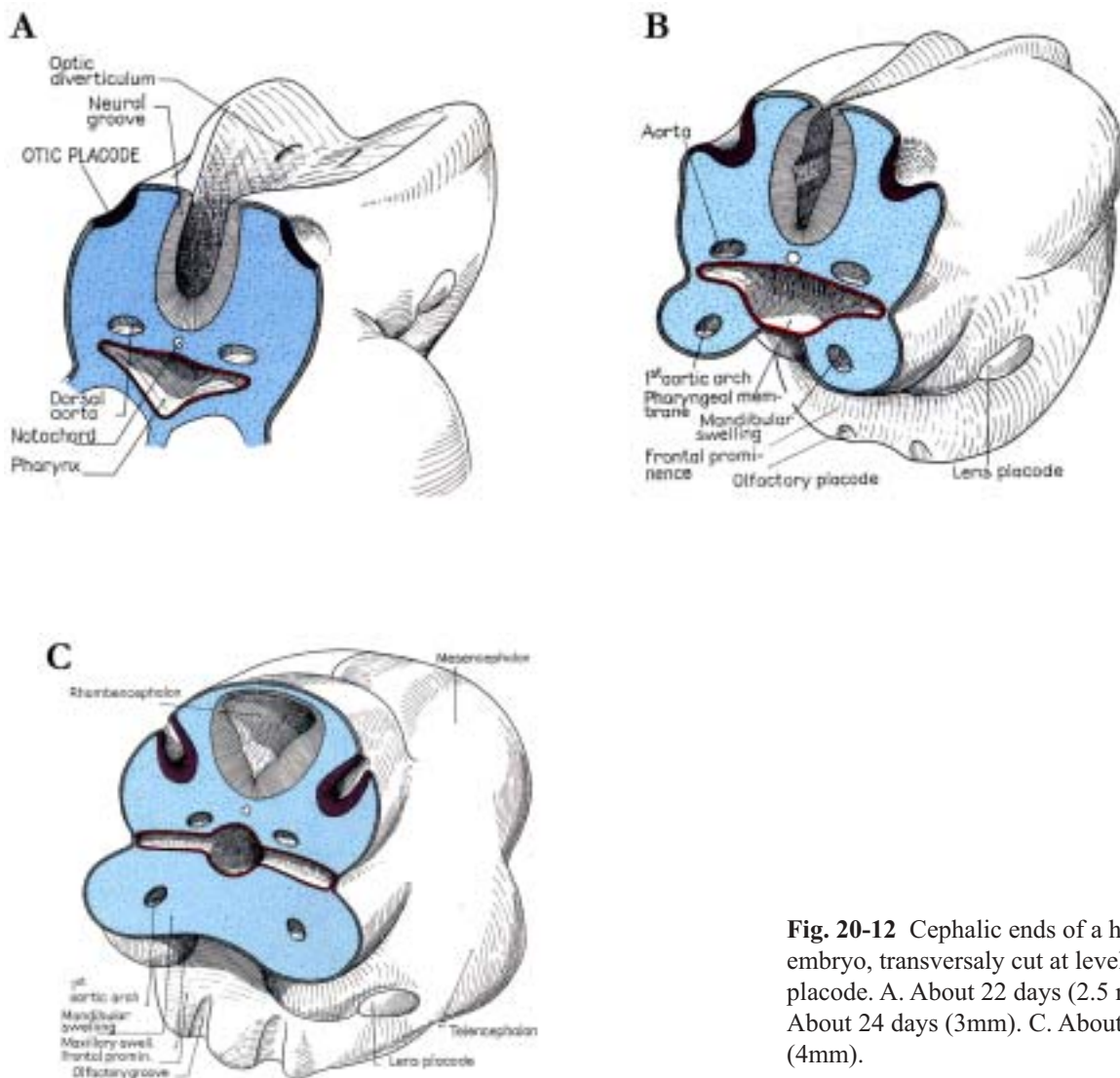


**Fig. 20-11** Development of the anterior and posterior chambers, the eyelids, and the coverings of the optic globe. *A, B*, Mesenchyme surrounds the developing eyeball (optic globe) between the fifth and seventh weeks to form the choroid and sclera. *C, D*, Vacuolization within this mesenchyme in the seventh week forms the anterior chamber. Shortly thereafter, vacuolization in the layer of mesenchyme immediately anterior to the lens forms the posterior chamber. The pupillary membrane, which initially separates the anterior and posterior chambers, breaks down in early fetal life. The upper and lower eyelids form as folds of surface ectoderm. They fuse together by the end of the eighth week and separate again between the fifth and seventh months.

The neural crest derived-mesenchyme between ectoderm and lens will undergo vacuolization, which separates it into an anterior and posterior layer. The fluid-filled space between the two layers is the **anterior chamber** of the eye. The anterior layer will participate in the formation of the **cornea**, while the posterior layer will form the **pupillary membrane** and a secondarily vacuolized space, the **posterior chamber** of the eye.

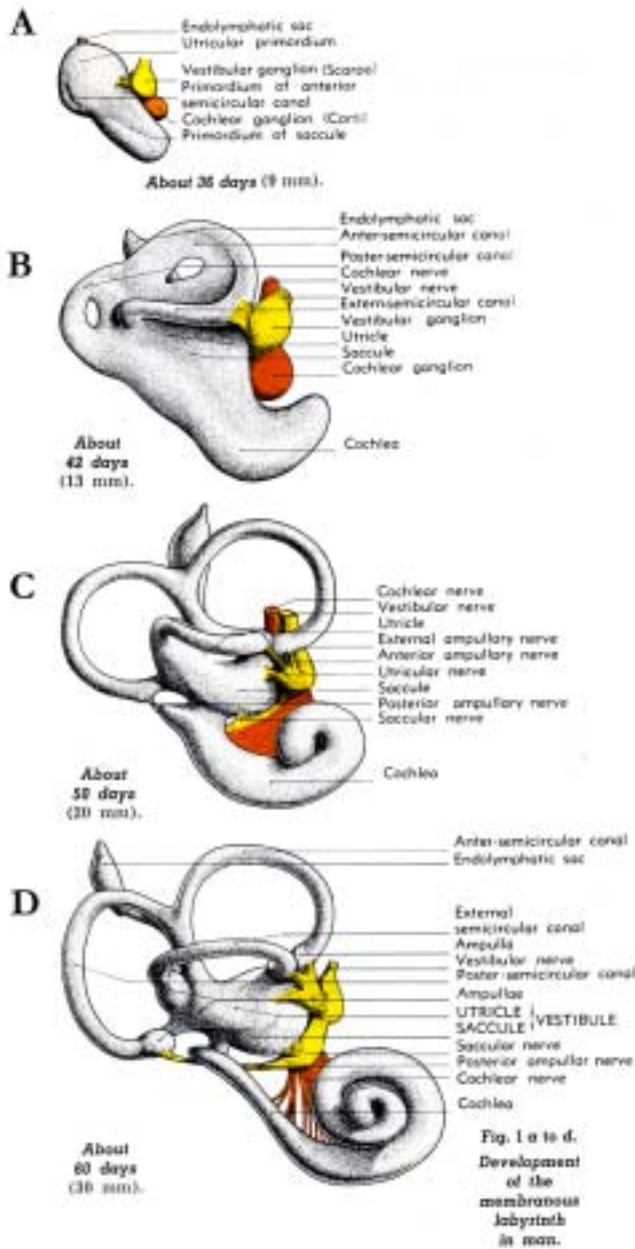
### Inner ear

The otic placode is located close to the hindbrain. Invagination of the placode during the 4<sup>th</sup> week results in an **otic pit** and subsequently in an **otic vesicle** (Fig. 20-12). The otic placode invagination, in which the cellular cytoskeleton plays a limited role, is regulated in part by basal lamina components (e.g. heparan sulphate proteoglycan), which may contribute towards anchoring the otic epithelium to adjacent structures. Some placodal cells migrate out of the vesicular wall to give rise to the **statoacoustic ganglion of CN VIII**.



**Fig. 20-12** Cephalic ends of a human embryo, transversally cut at level of optic placode. A. About 22 days (2.5 mm). B. About 24 days (3mm). C. About 27 days (4mm).

The otic vesicle develops two clearly separable components during further differential growth (Fig. 20-13):



**Fig. 20-13** Development of the membranous labyrinth in man.

for transducing sound vibrations into electrical impulses (sense of hearing). A more detailed description of the histology and function of eye and ear will be given in SBPM/D.

- A ventral, tapered component, **saccule**, which will give rise to the future cochlea and the mature saccule. The **cochlear duct** starts as a tubular outpocketing at the base of the saccule during the 5<sup>th</sup> week. The duct undergoes progressive asymmetrical growth, which results in regular spiral turns that ultimately lead to its snail shell configuration.

- A dorsal component, **utricle**, which will give rise to the future semicircular canals, the mature utricle and the endolymphatic duct. The **semicircular canals** begin as flattened outpocketings of the utricle. The central parts of the walls of these pockets come close together, fuse, and undergo apoptosis, leaving the edges of the pockets intact as the three semicircular canals. Each canal is widened at one of its ends, where it adjoins the utricle. This widening, the **crus ampullare**, contains sensory cells that are similar to those in the walls of the **utricle** and **saccule**. This system of sensory cells is responsible for detection of accelerations and the orientation of the head and thus the **sense of balance**.

Further development of the **cochlear duct** is intimately associated with the development of the surrounding skeleton. The membranous labyrinth becomes encased by the 6<sup>th</sup> and 7<sup>th</sup> weeks in a cartilage shell, the otic capsule. This is the future petrous part of the temporal bone. By the 11<sup>th</sup> week the cochlear duct occupies only a limited segment of the fluid-filled perilymphatic space in the cartilage. This space plays a major role in the transmission of sound vibrations. Some cells of the cochlear duct differentiate to form the spiral organ of Corti, which bears the hair cell receptors responsible