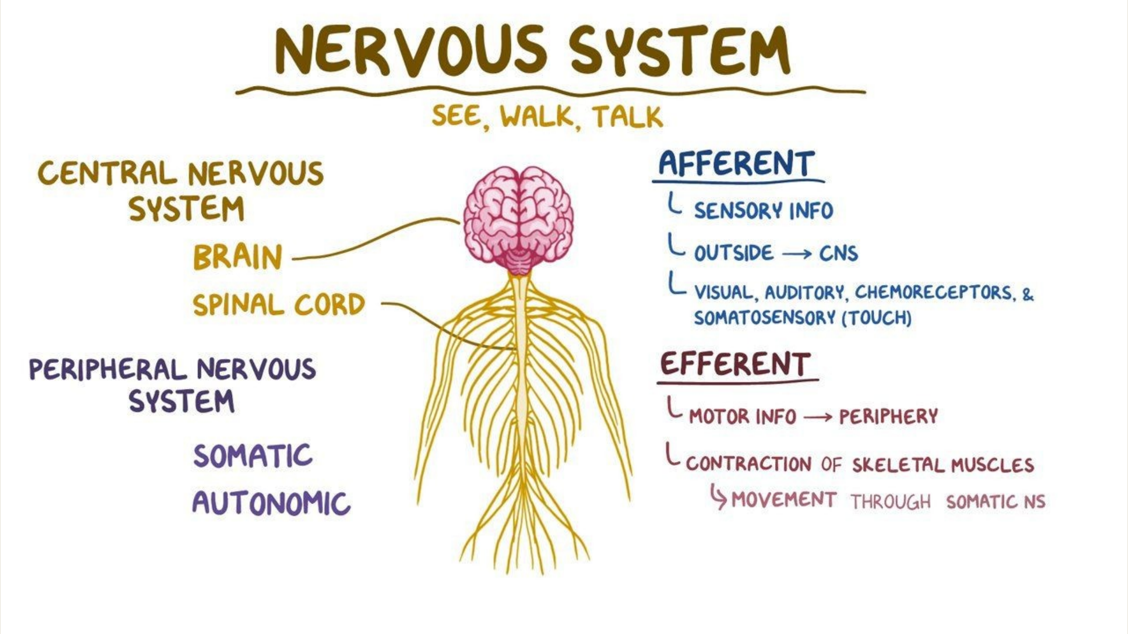
DEVELOPMENT OF NERVOUS SYSTEM AND SENSORIC ORGANS

Functions of nervous system

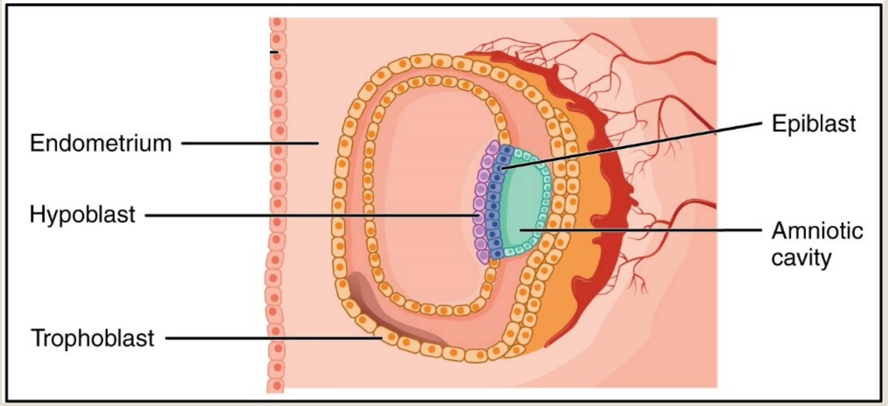
- Control of other body tissues and organs
- Perception of body and limb positition
- Perception of stimuli from the environment and reactions
- Perception of stimuli from body and reactions
- Ability to learn and memory creation

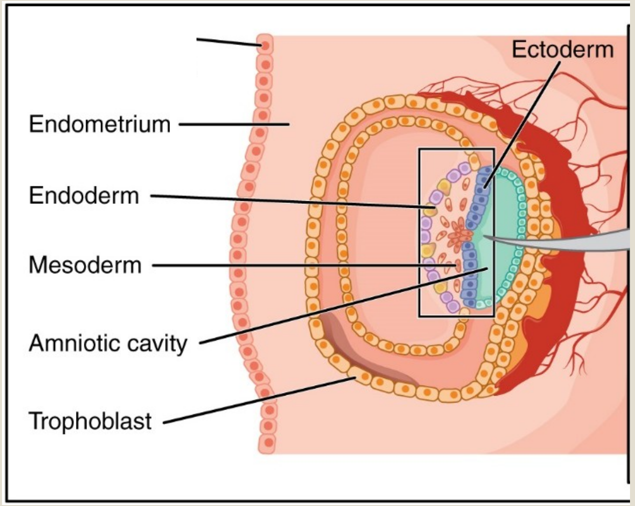


https://www.osmosis.org/learn/Nervous_system_anatomy_and_physiology

Embryonic origin of nervous system

- **Primitive streak** formation in **epiblast** layer of bilaminar disc
- **Epiblast** layer cells **migrate** through primitive streak to space between epiblast and hypoblast, **replacement** of hypoblast cells
- Formation of trilaminar disc:
  - **Endoderm** – inner layer
  - **Mesoderm** – middle layer
  - **Ectoderm** – outer layer
- **Nervous** system forms from **ectoderm**, originally epiblast





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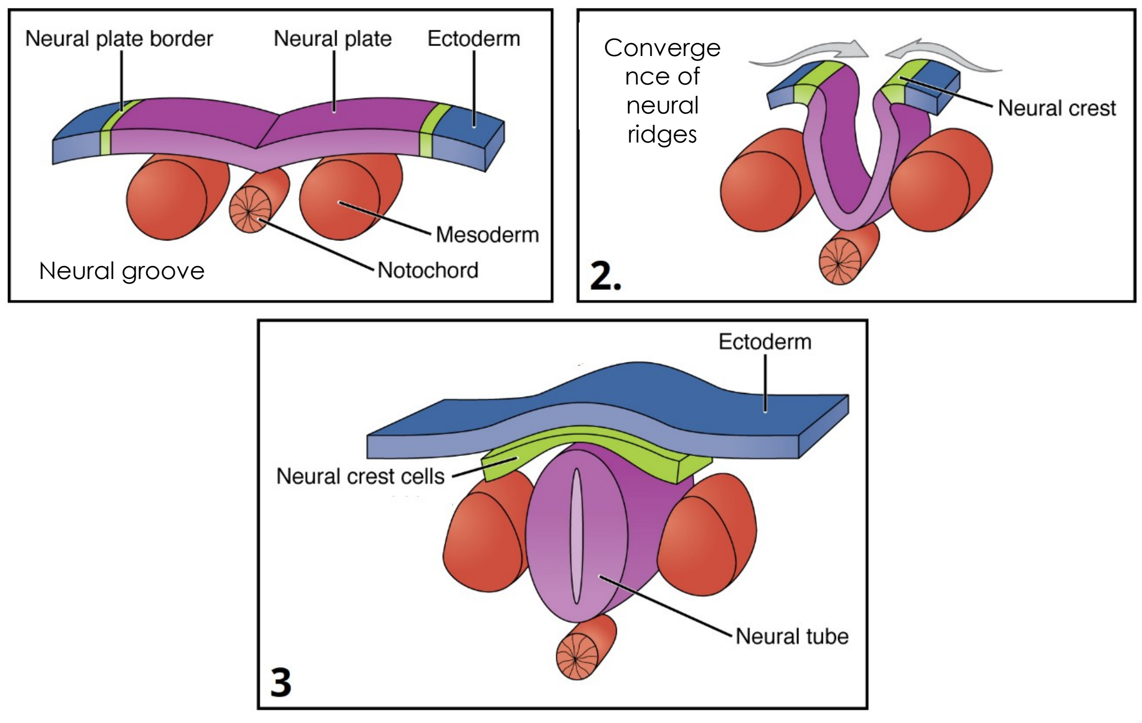
Neurulation

- **Ectoderm** influenced by factors produced by **notochord**
- **adjacent** ectoderm **differentiate** into **neuroectoderm**
- formation of thickened neuroectoderm layer – **neural plate**
- lateraly in neural plate – **neural ridges, neural groove** between them → neural ridges move **towards each other**, **fusion** along midline – formation of **neural tube** (basis for central nervous system)
- **interface** between ectoderm and neuroectoderm – region of **neural tube fusion** – formation of **neural crest** cells population (basis for peripheral nervous system)

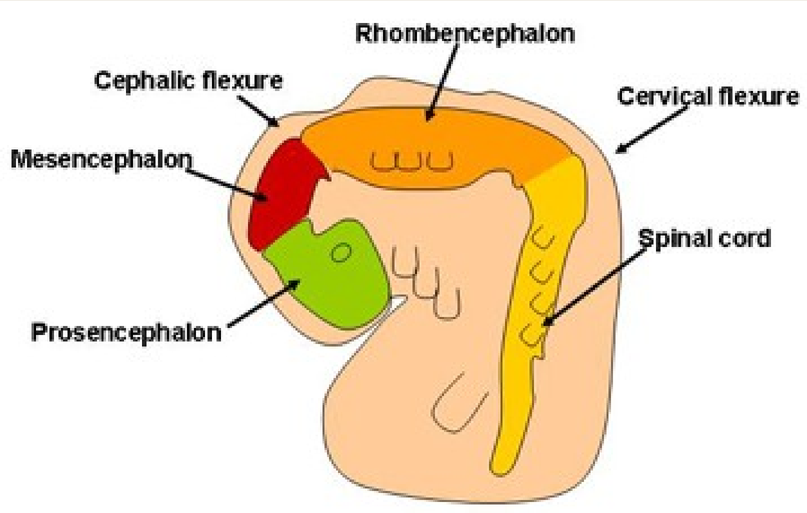


Teach Me Anatomy

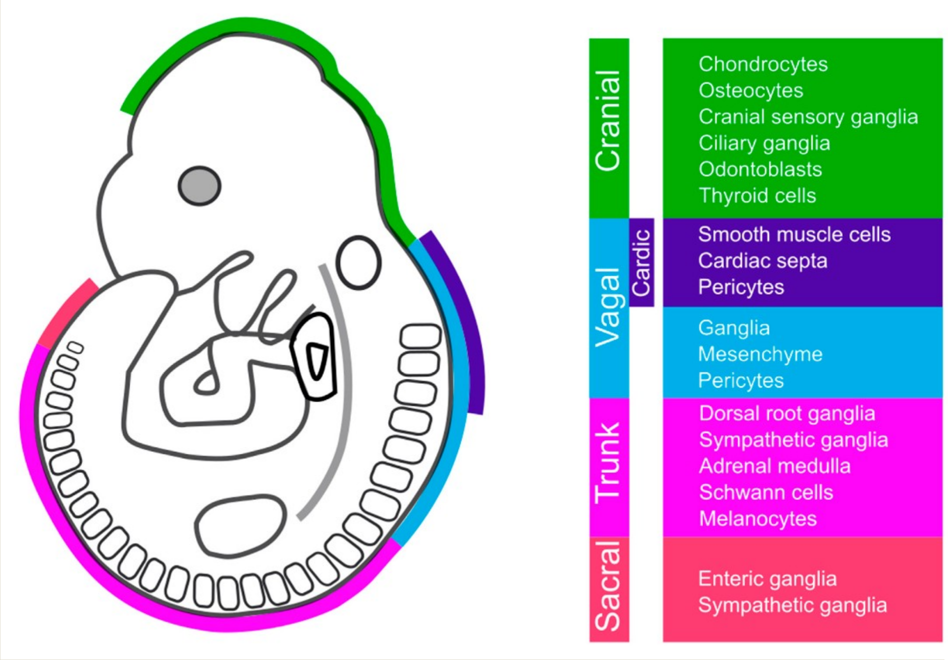
Nervous system

- Structures formed during neurulation:
  - **Neural tube** – basis for development of **central nervous system**
  - **Neural crest** – basis for development of **peripheral nervous system**

- Neural tube:
  - **brain**
  - **Spinal cord**

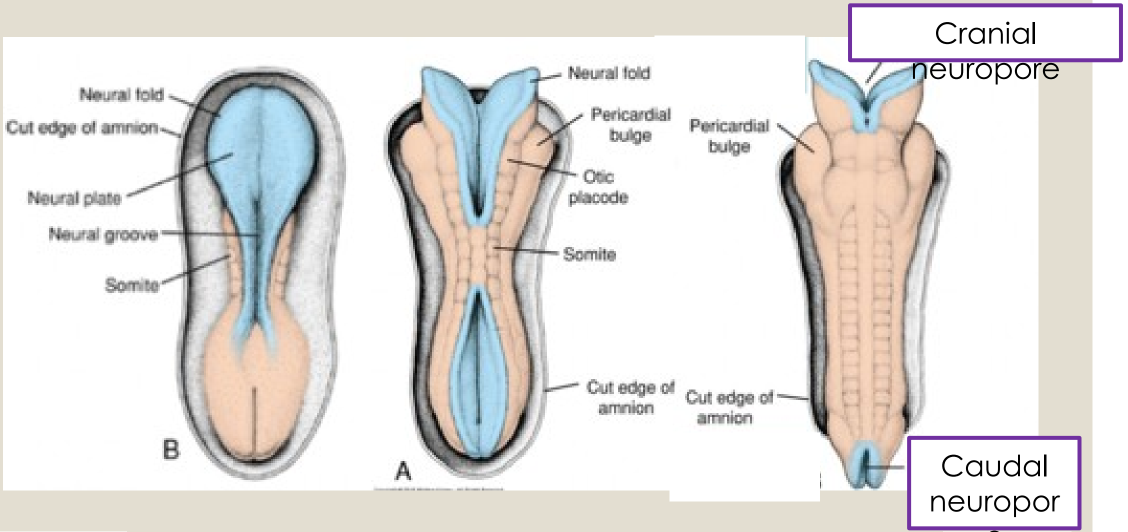


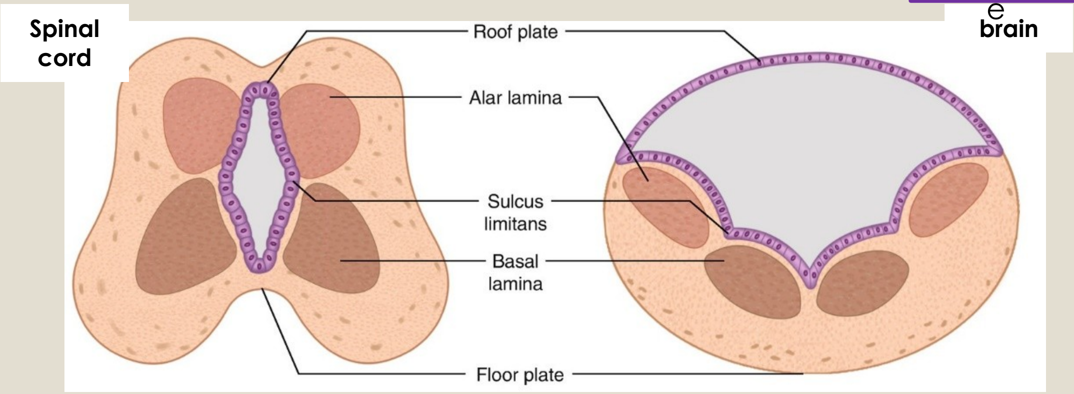
- Neural crest:
  - **Peripheral neurons**
  - **Enteric neurons**
  - **Glial cells**



Development of neural tube

- **brain** forms from **cranial** neural tube, **spinal cord** from **caudal**
- **closing** neural tube from **cranial** region (4. somite) to **caudal** – cranial and caudal parts stay temporarily open, formation of cranial and caudal **neuropores** (communication of neural tube with amnion)
- first **closure** of cranial neuropore, later caudal neuropore
- Enclosed neural tube divided along dorsoventral axis:
  - **Ventral – floor plate,** development influenced by notochord
  - **ventrolateral** – **basal lamina/plate – motor neurons**
  - **dorsolateral** – **alar lamina/plate – sensory neurons**
  - **dorsal – roof plate,** development influenced by surface ectoderm (epidermis)
  - **Sulcus limitans** – divide basal and alar lamina





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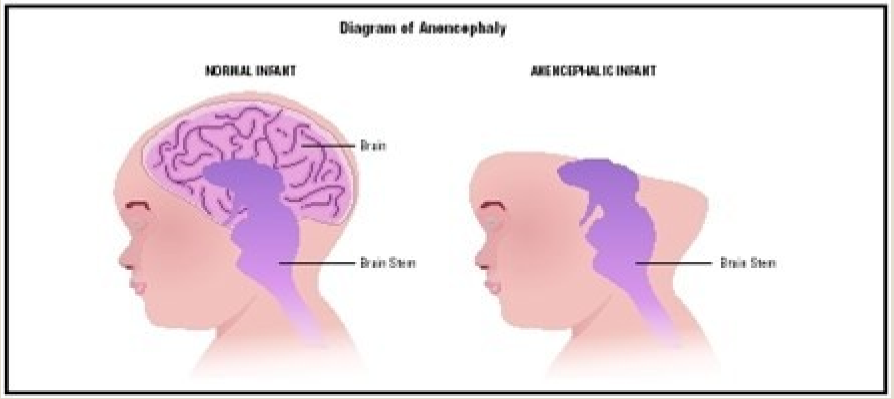
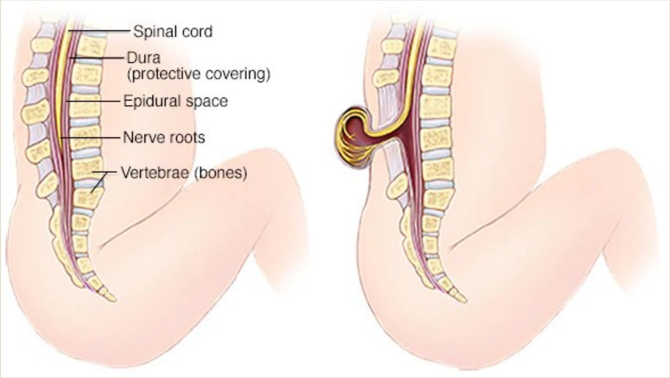
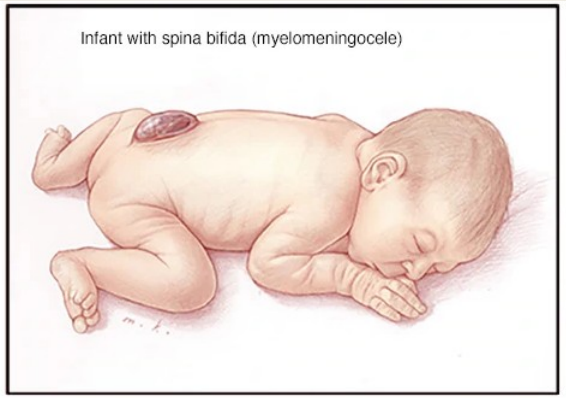
Developmental defects of neural tube closure

- **Anencephaly**
  - Cranial neuropore closure defect
  - Reduced formation of brain, or its part (telencephalon)
  - Often lethal



- **Spina bifida**
  - Defect of caudal neuropore closure
  - Cleft, prolapse of spinal cord
  - surgery



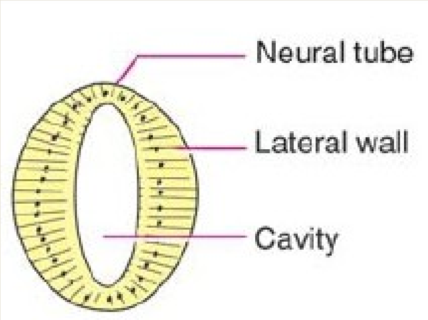


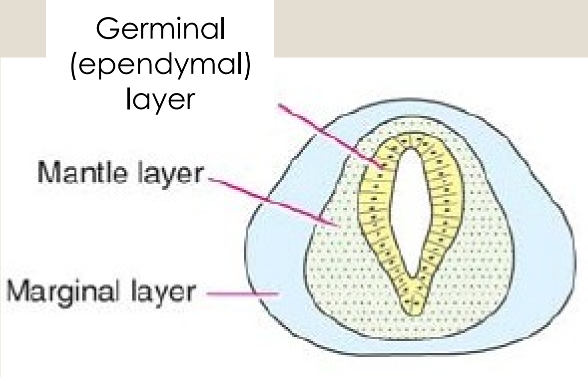
Initial differentiation of neural tube cells

- Neural tube lined by **pseudostratified cylindrical** epithelium

- Neuroepithelium differentiate into two major types of progenitors:
  - **neuronal** progenitors (**neuroblasts**) – formation of central nervous system cells
  - **glial** progenitors (**glioblasts**) – formation of CNS supporting cells

- Neural tube neuroepithelium **differentiate** into 3 basic layers:
  - **Inner (germinal/ventricular) layer** – neural tube cavity lining epithelium
  - **Mantle layer** – spinal cord grey matter
  - **Marginal layer** - periphery



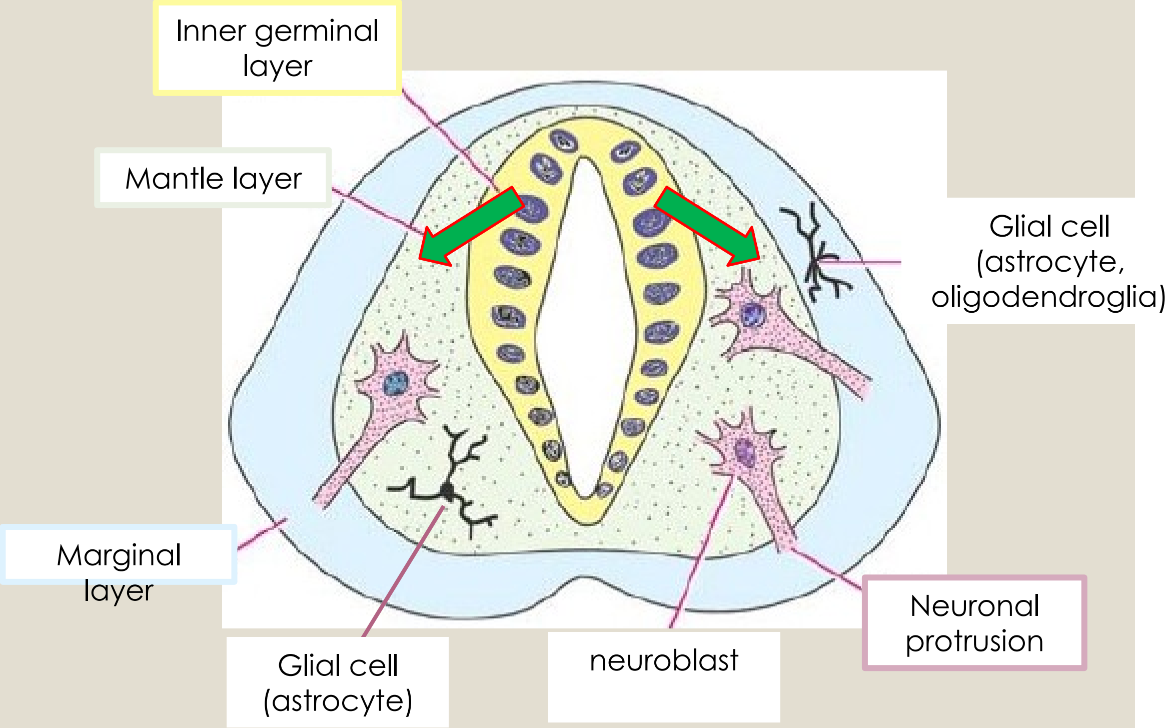


Formation of neural tube layers

- neuroblasts **migrate** from gerrminal inner layer to **mantle** layer
- **neuroblasts** form protrusions from mantle layer lateraly – formation of marginal layer

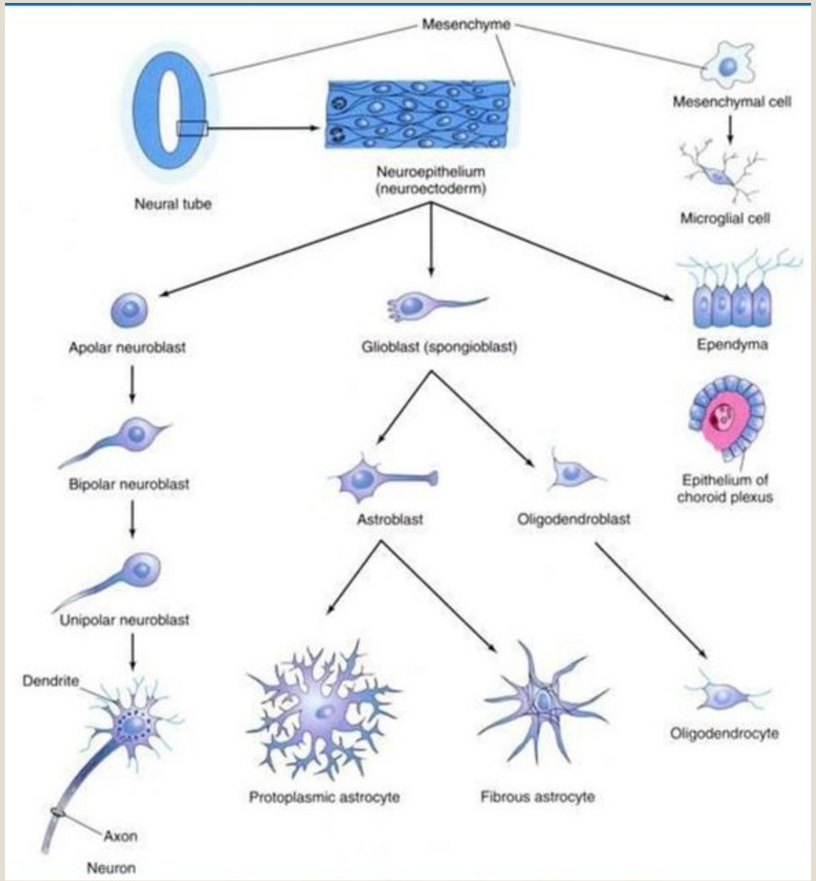
- Cells formed from **glioblasts**:
  - astrocytes – formed in mantle and marginal layer
  - oligodendroglia – especially in marginal layer

- **Neuroepithelial** cells lining cavity **differentiate** to ependymal cells – future **lining** of brain ventricles and spinal cold canal



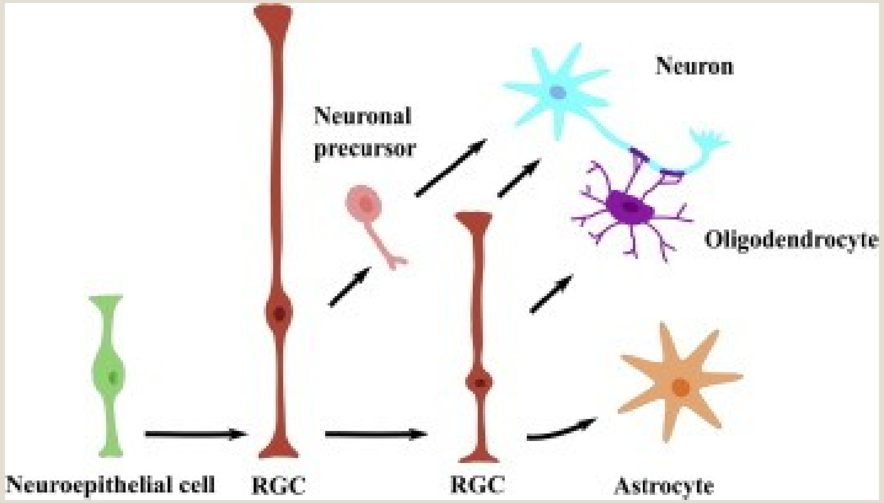
Neural tube wall histogenesis

- Differentiation of neural tube cells – from germinal neuroepithelium
- **Neuroblast** lineage – development of neurons
  - Apolar neuroblast – progenitor without protrusions
  - Bipolar neuroblast – formation of two protrusions
  - Unipolar neuroblast – one protrusion
  - Neuron – formation of one axon, development of dendrites
- **Glioblast** lineage – development of supporting cells
  - Spongioblast – glial cells progenitor
  - Astroblast – astrocytic progenitor (blood-brain barrier)
  - Oligodendroblast – progenitor of oligodendroglia (CNS neurons myelination)
- **ependyma** – epithelial cells forming neural tube lining → important for development of choroid plexus
- mesenchyme – microglia development (nervous system monocytic cells)



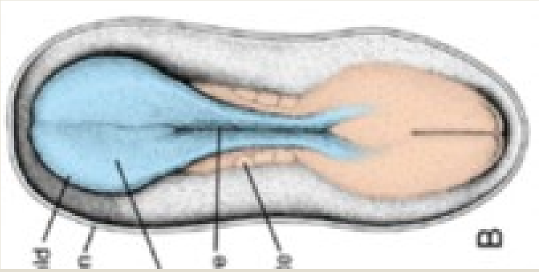
Radial glia

- specialized neural cells (**bipolar** morphology – similiarly to neuroepithelial cells
- **Long protrusions** from ventricular zone (germinal epithelium) to marginal layer
- **supporting** cells for **migration** of immature neurons from germinal epithelium to marginal layers of developing epithelium
- **progenitor** cell for development of:
  - neurons
  - Glial cells
- important for **differentiation** of cells in specific CNS regions

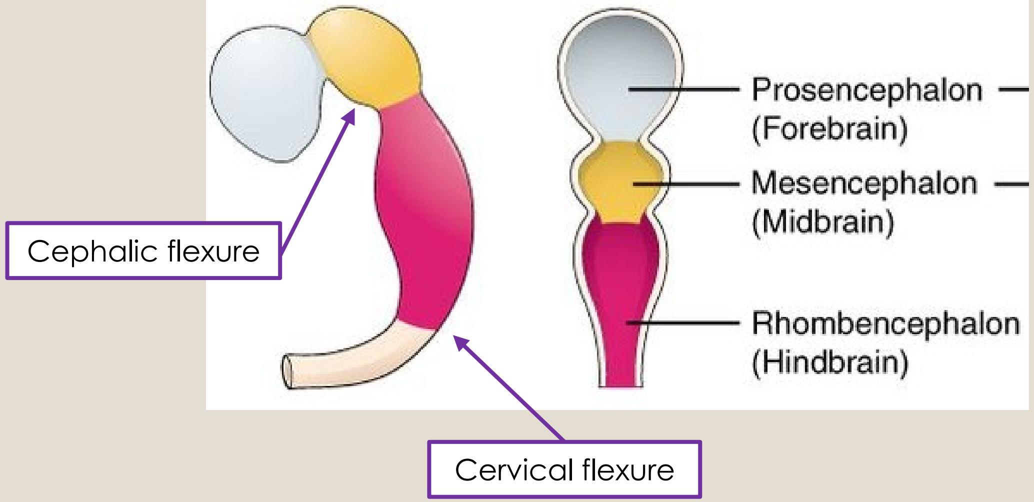


Brain development – primary brain vesicles

- Brain development in cranial region – region of neural plate **extension**
- From neural plate extension, 3 **primary brain vesicles** formed:
  - **prosencephalon** – forebrain
  - **mesencephalon** – midbrain
  - **rhombencephalon** – hindbrain



- Brain compactness and small space for its development →
- Formation of 2 **flexures** of neural tube:
  - **Cervical** – flexure between hindbrain and spinal cord
  - **Cephalic** – ventral flexure in the midbrain region

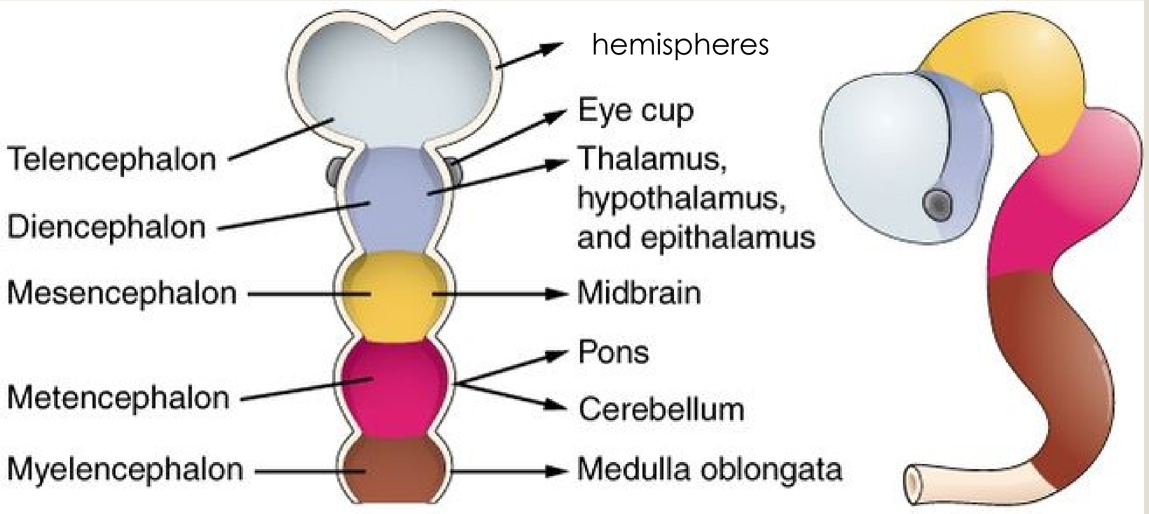


Brain development – secondary brain vesicles

- 3 primary vesicles transform to **5 secondary** brain vesicles

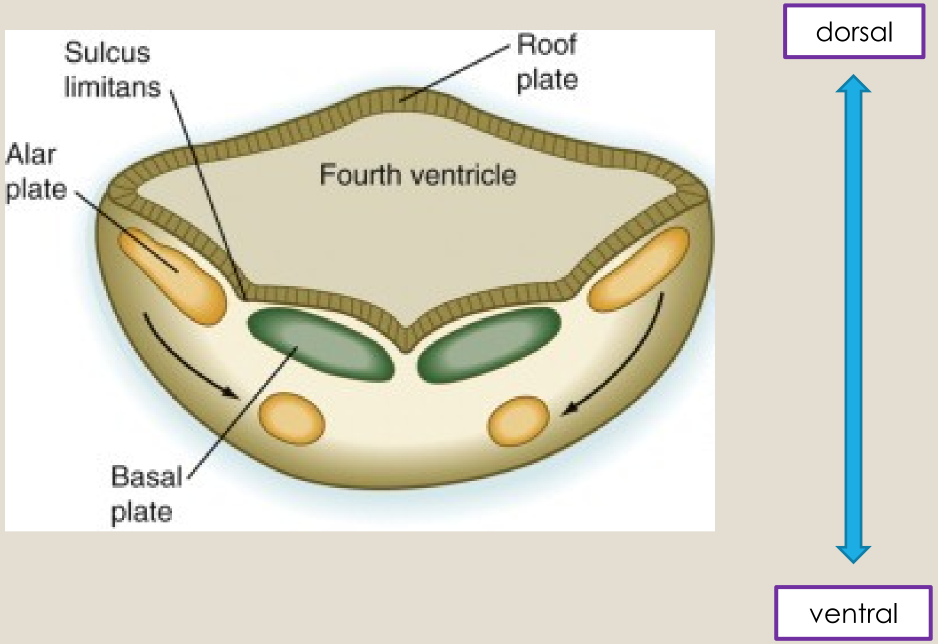
- **Prosencephalon**:
  - Telencephalon – cranial part; brain hemispheres, olfactory lobe
  - Diencephalon – caudal part; eye cups, thalamus, neurohypophysis, epiphysis
- **Mesencephalon** – no division

- **Rhombencephalon**
  - Metencephalon – cranial part; pons Varoli, Cerebellum
  - Myelencephalon – caudal part; Medulla oblongata



Rhombencephalon

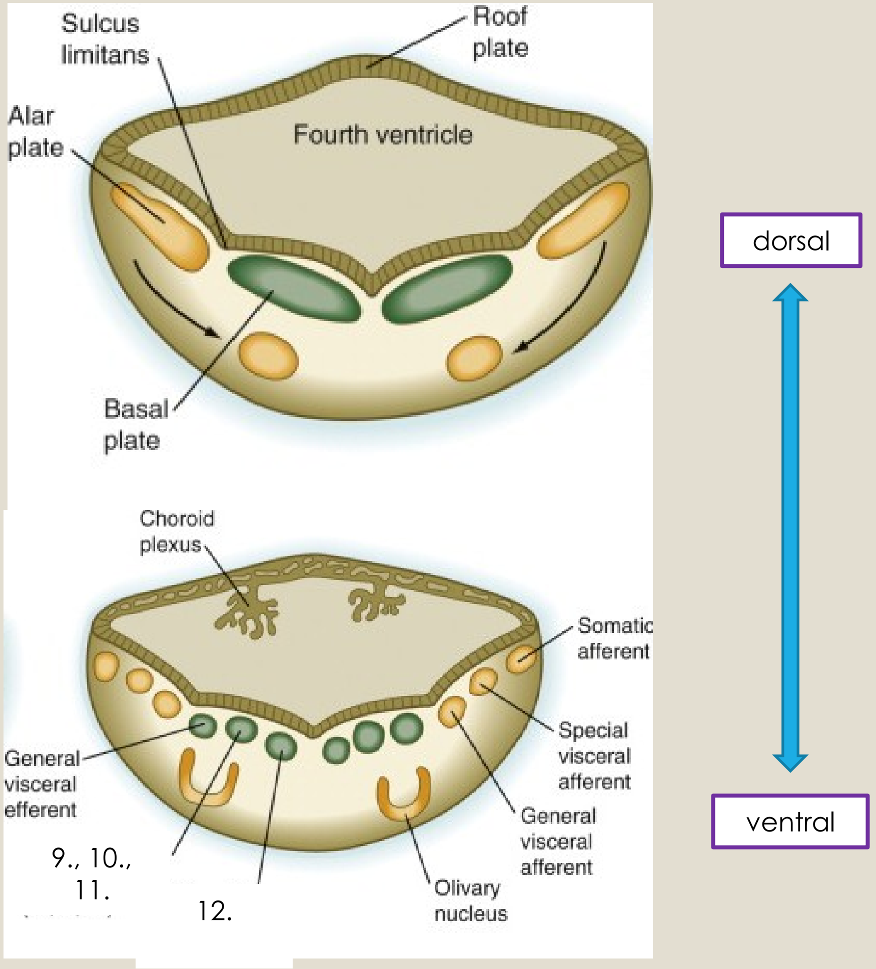
- after **neuropore** closure – **expansion** of lateral rhombencephalic walls **dorsally**
- **roof plates** extend **laterally** and **dorsally** – formation of **diamond-shaped** structure – fourth ventricle
- Brain ventricle covered by thin **ependymal** cell layer
- cranialy – formation of **metencephalon**
- caudally – formation of **myelencephalon**



Sadler, 1990. Langman`s medical embryology

Myelencephalon

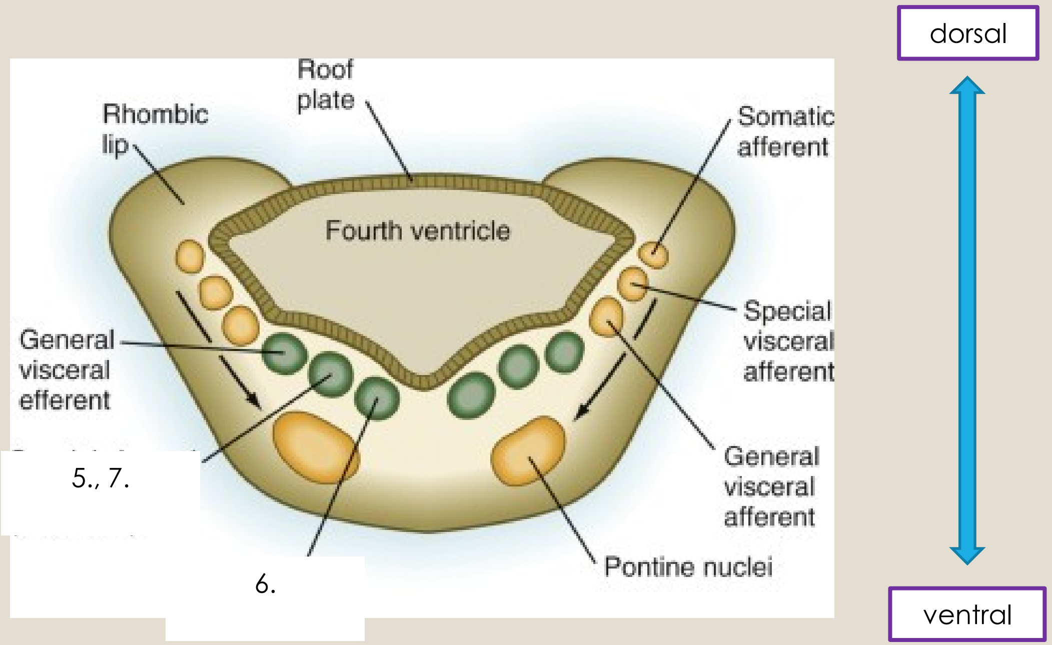
- **myelencephalon –** caudal rhombencephalon
- **myelencephalon** – connection of spinal cord and brain → **Medulla oblongata**
- Extension of walls laterally – alar plates localized laterally, basal plates medially
- Formation of dorsal (roof) and ventral (floor) plates
- **roof plate** compose of one layer of **ependymal** cells covered by cells of developing **vessels** (mesoderm) – **pia mater** (vascular cover closely attached to brain)
- **ependyma** and **pia mater** of **4. ventricle** → **tela choroidea**, **invagination to** 4. ventricle – formation of **choroid plexus** (production of cerebrospinal fluid)
- development of **cranial nerves** - VI. abducens, VII. facial, VIII. vestibulocochlear, IX. glossopharyngeal, X. vagus, XI. accessory, XII. hypoglossal



Sadler, 1990. Langman`s medical embryology

Metencephalon

- **metencephalon –** cranial rhombencephalon
- **metencefalon** – development of dorsally localized Cerebellum and ventrally localized pons Varoli
- develops similarly to myelencephalon – **extension** of walls laterally – alar plates laterally, basal plates medially
- dorsolaterally – formation of **rhombic lips** (basis for Cerebellum)
- Development of V. cranial nerve - **trigeminal**



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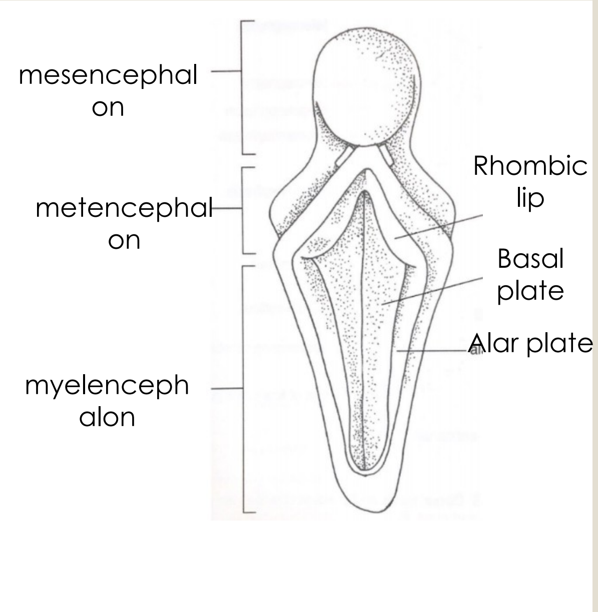
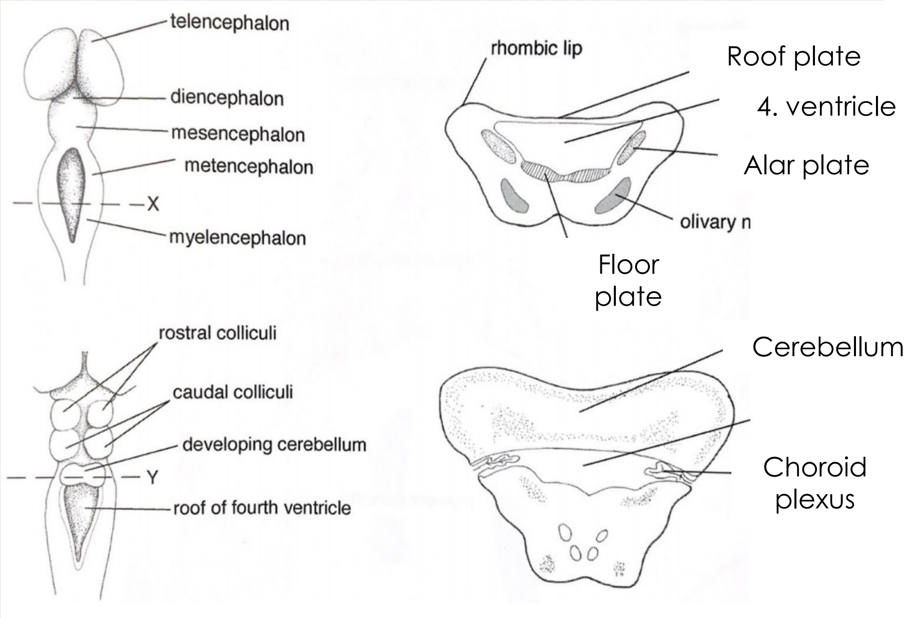
Cerebellum development

- originates in dorsolateral parts of alar plate of rhombencephalon – **rhombic lips**





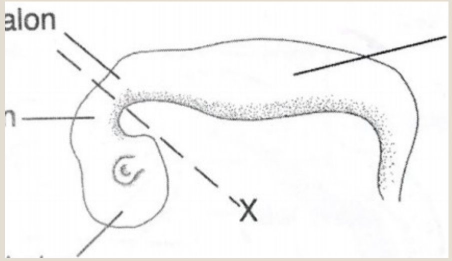
- Rhombic lips come together in mesencephalon region – proliferation of rhombic lip cells – formation of precursors of **cerebellar hemispheres**

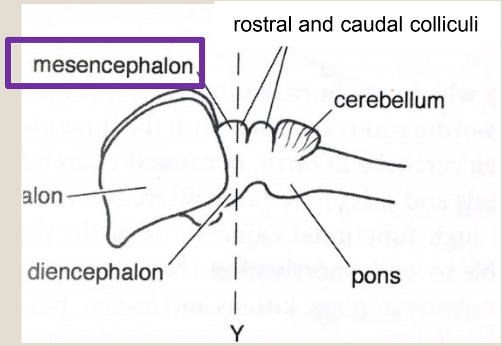
- Further proliferation results in connection and **fusion medially** – **one** cerebellum formed covering 4. ventricle

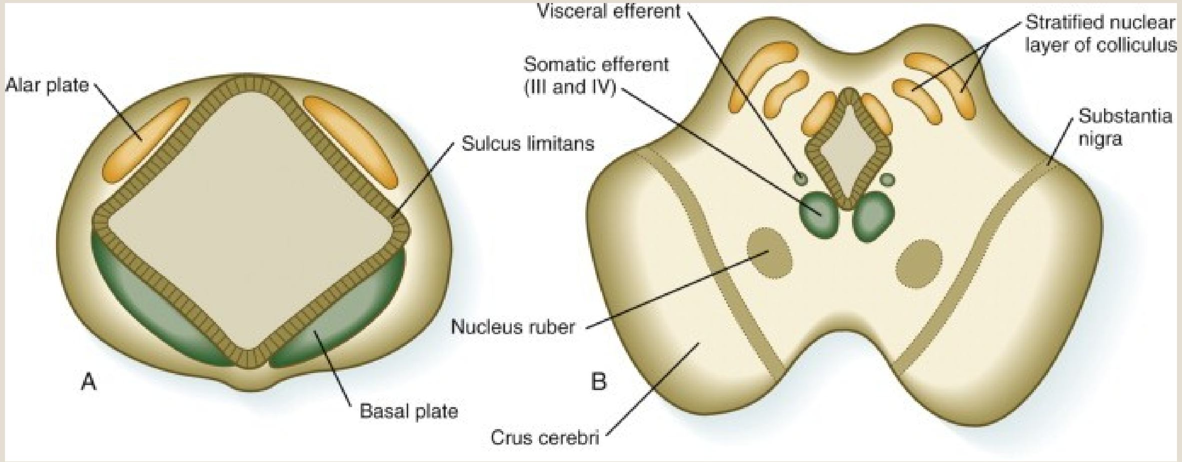
Edited: McGeady et al. Veterinary Embryology. 2009

Mesencephalon

- slight developmental changes compared to other parts
- **medial expansion** of **alar** and **basal plates** – reduction of neural canal – formation of **mesencephalic aquaduct**
- **Basal plate** – formation of **motoric** nuclei of **cranial** nerves (III. oculomotor, IV. trochlear)
- **crura cerebri** – expansion of peripheral parts of basal plate – roots for descending nerves from cereberal cortex to pons and spinal cord
- neuroblasts from **alar plates** settle tectum (dorsal part of mesencephalon) – formation of 4 nuclei (colliculi) with visual and auditory function
- **substancia nigra** – migration of alar cells ventrally (dopamine production), motoric function







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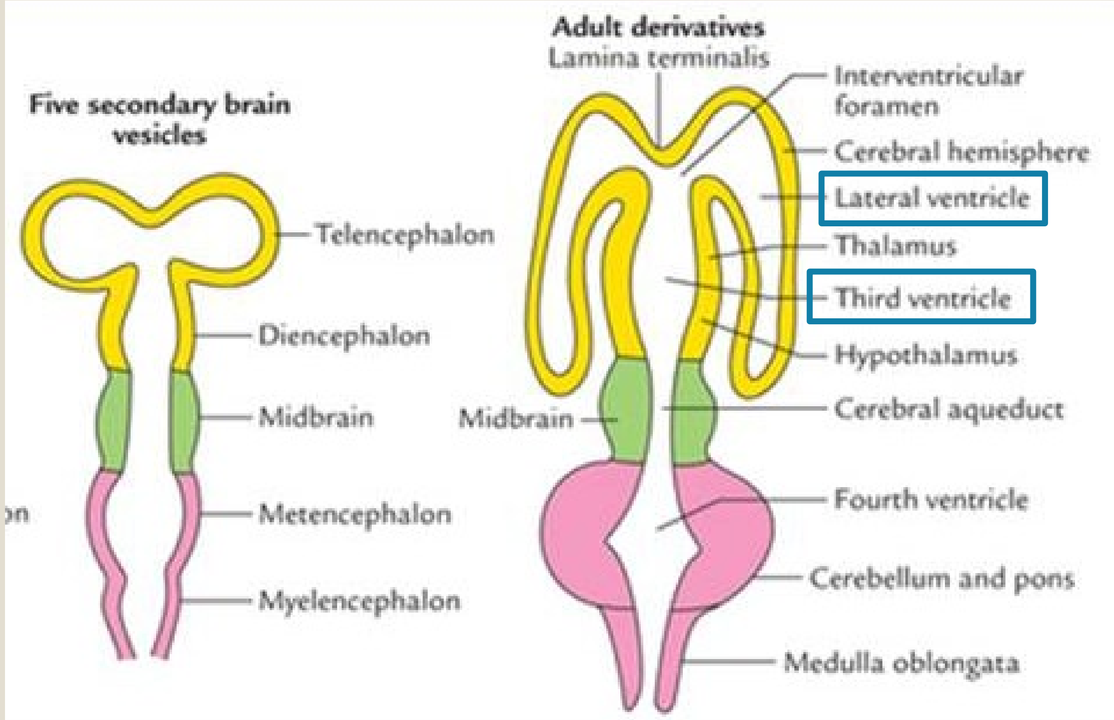
Prosencephalon

- **rostral** part of **brain** – telencephalon rostrally, diencephalon caudally

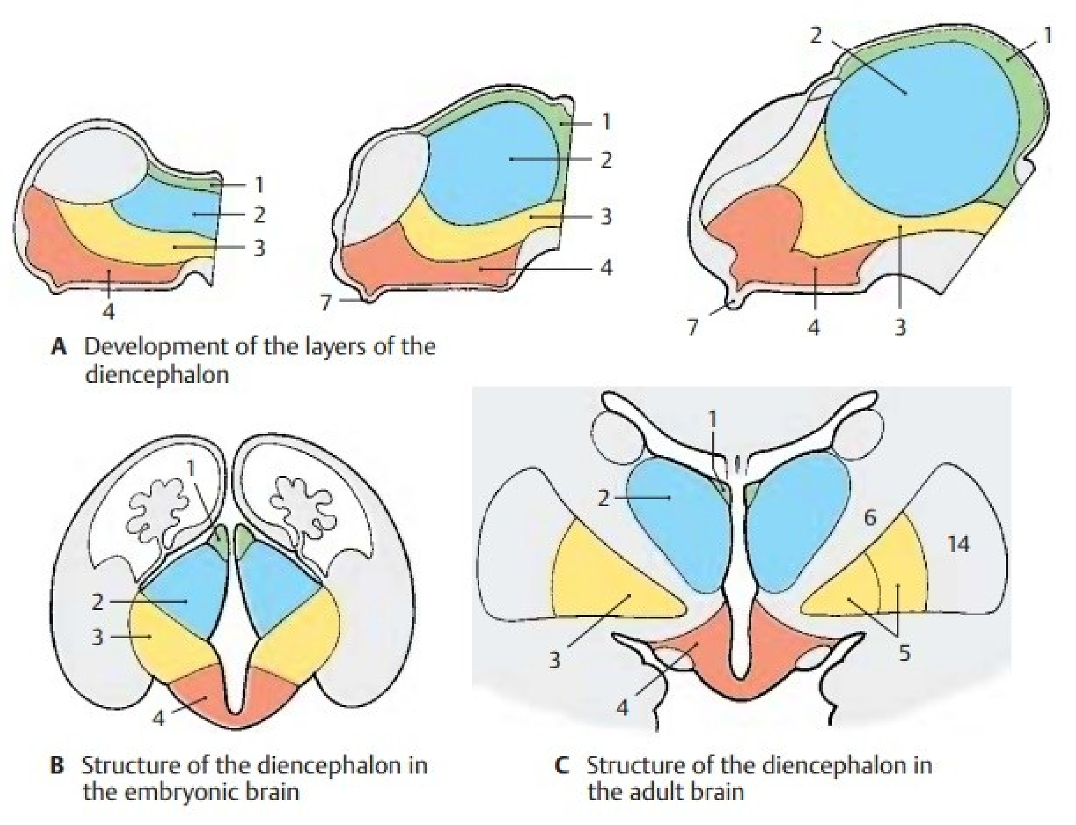
- Prosencephalon:
  - **Telencephalon** – cranial part; hemispheres, olfactory lobe
  - **Diencephalon** – caudal part; eye cups, thalamus, hypothalamus, neurohypophysis, epiphysis

- Cavity of **diencephalon** – **3.** brain ventricle
- Cavity of **telencephalon** – paired **lateral ventricles**



Diencephalon

- Caudal part of forebrain
- Does **not** form basal plates – formation from **alar** and **roof** plates
- Formation of 3 medial protrusions from lateral walls:
  - **dorsally – epithalamus (1)**
  - **middle – dorsal thalamus (2), subthalamus (3)**
  - **ventrally – hypothalamus (4)**
- Growth of **thalamus** (sensoric center of brain) medially to ventricle – reduction of cavity
- **hypothalamus** – center for sleep, digestions, termoregulation, behaviour
- **ventrally** – formation of **neurohypophyseal** infundibulum
- **Caudal** part of **epithalamus** – **epiphysis cerebri –** endocrine gland (melatonin)



A Development of the layers of the diencephalon

B Structure of the diencephalon in the embryonic brain

C Structure of the diencephalon in the adult brain

https://www.brainkart.com/article/Subdivision-of-Diencephalon-s-Structure_14831/

Hypothalamo-hypophysal system

HYPOTHALAMUS

- **Ventral part of diencephalon (tuberal hypothalamus with the pituitary stalk, mammilary bodies) + caudal part of telencephalon (preoptical area)**
- **Symmetrically duplicated parts divided**

by the 3rd ventricle

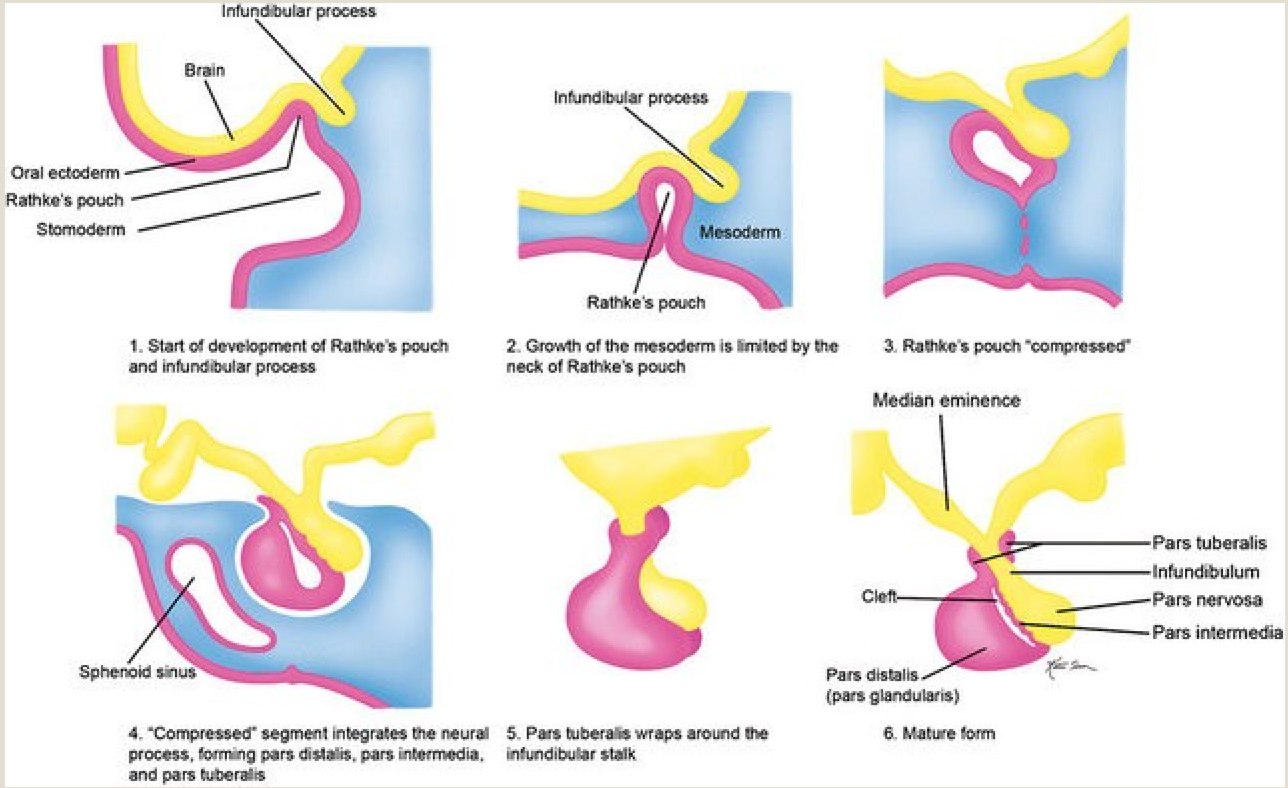
HYPOPHYSIS

Diencephalon – infundibulum

- Neurohypophysis (pars nervosa)

Oral cavity endoderm – Rathke´s pouch

- Adenohypophysis (pars distalis)



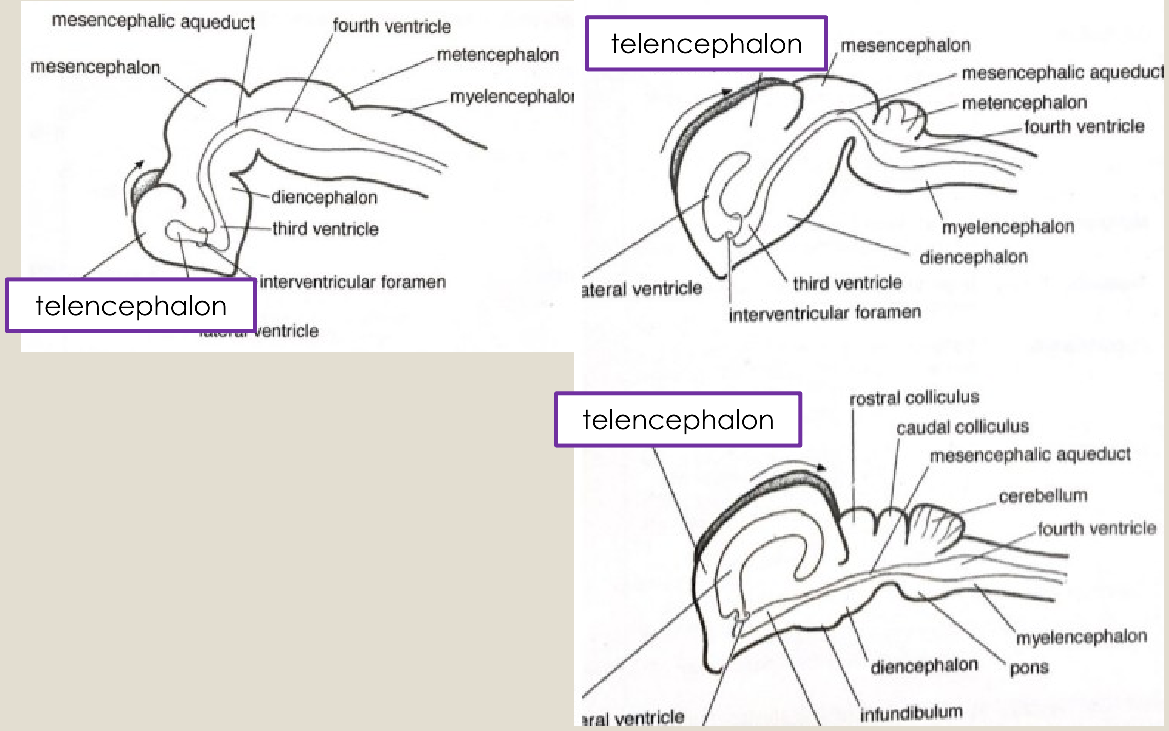
https://www.researchgate.net/publication/273833506_Magnetic_resonance_imaging_of_sellar_and_juxtasellar_abnormalities_in_the_paediatric_population_an_imaging_review/figures?lo=1

Telencephalon

- **The most rostral** brain region – central part lamina terminalis, 2 lateral diverticles – formation of **hemispheres**

- Cavities of lateral diverticles communicate with 3. ventricle of diencephalon
- **expansion** of hemispheres – **reduction** of lateral ventricles and 3. ventricle

- Development of telencephalon – first **rostral** expansion, further **dorsal** expansion, subsequent **caudal** expansion, finally **ventral** expansion – formation of C-shaped hemispheres
- Hemispheres cover diencephalon, mesencephalon and rostral rhombencephalon – formation of **brain cortex**
- Biggest region – development of centers for **learning** and **memory**, **intellect** and **emotions**



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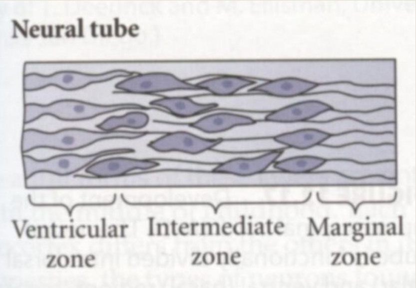
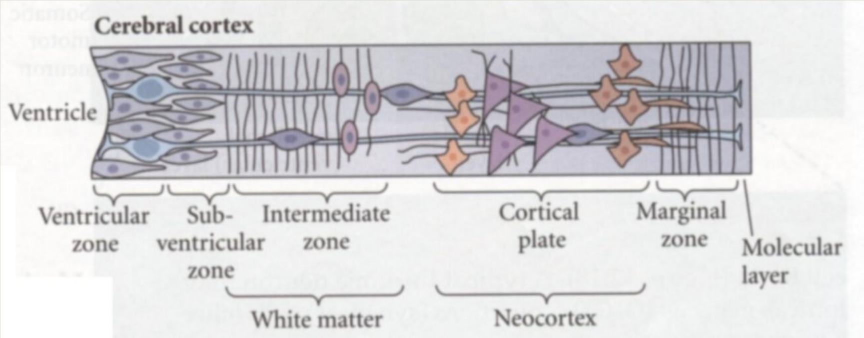
Differentiation of cells in brain cortex

- 3 basic zones – ventricular, intermediate, marginal
- Onset of **cortex formation** – **asymmetric** division of **radial** glial cells – formation of radial glia and neurons
- **Intermediate progenitors** (IP) migrate from ventricular to subventricular zone – **symetric** division of IPs – formation of identical neurons
- **migration** of **IPs** to cortical zone through **intermediate** zone (future **white** matter)
- **Cortical** layer formed of (from inner to outer regions):
  - Fusiform – smaller pyramidal cells, interneurons
  - Inner pyramidal layer – bigger pyramidal neurons
  - Inner granular – dense small granular cells
  - Outer pyramidal – pyramidal cells, short protrusions
  - Outer granular – dense small granular cells
  - molecular – stelate and basket cells



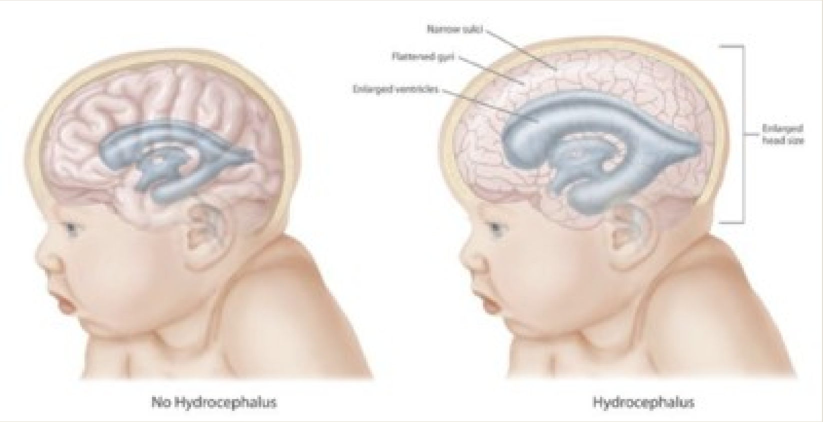


Scott Gilbert. Developmental Biology 10th edition

Developmental defects of brain

- **Macrocephaly**
  - Expansion of individual brain regions
  - Major cause – enhanced proliferation of neurons and glial cells

- **Hydrocephaly**
  - Higher production and accumulation of cerebrospinal fluid in brain, often caused by altered connection between ventricles
  - Enlarged ventricles cause higher pressure in brain
  - lead to headache, problems with balance, double vision, mental changes



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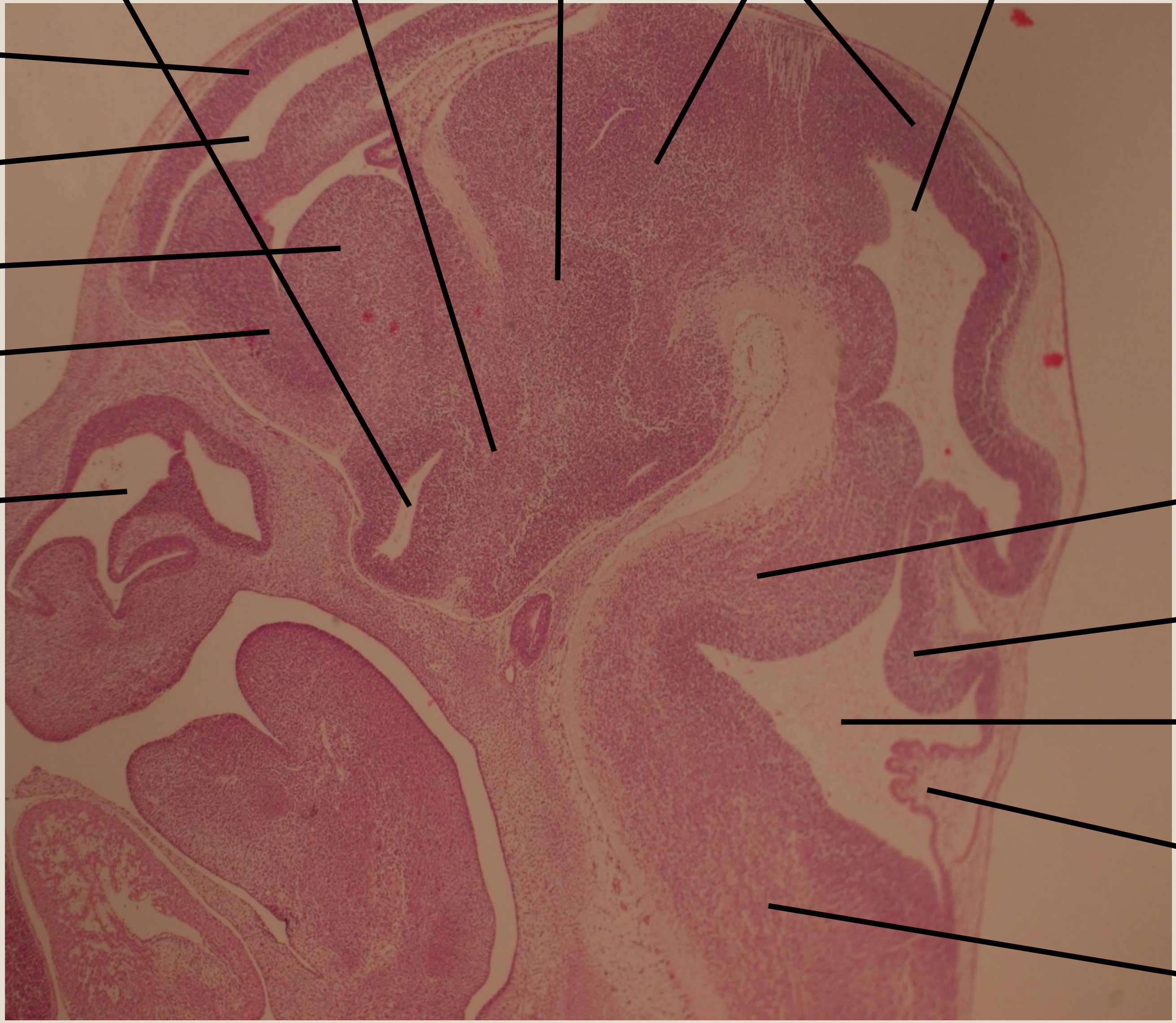


Hypothalamus
Thalamus
Midbrain
Aquaduct of sylvii
Rathke pouch
Cerebral cortex
Lateral Ventricle
Septum
Olfactory bulb
Nasal cavity
Pons
Cerebellum
Fourth Ventricle
Choroid plex
Myelenceph.

Development of spinal cord

- development of spinal cord from neural tube **caudally from** rhombencephalon

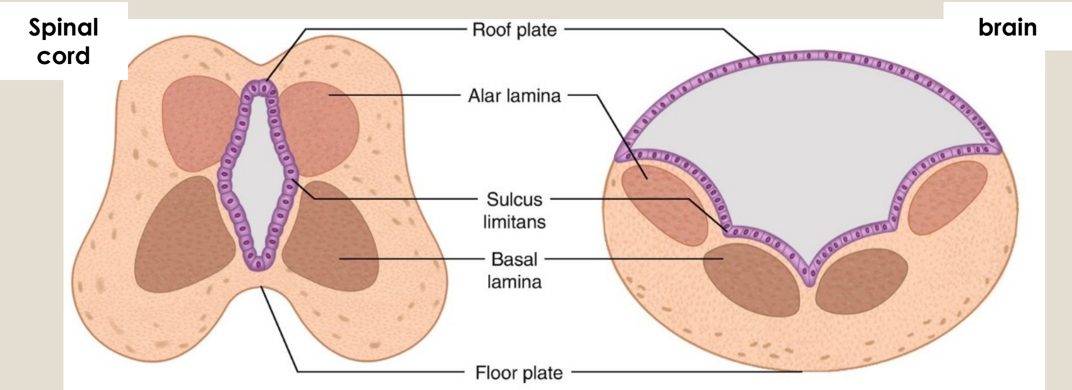
- Enclosed neural tube divided along dorsoventral axis:
  - **Ventral – floor plate,** development influenced by notochord
  - **ventrolateral** – **basal plate – motor neurons**
  - **dorsolateral** – **alar plate – sensory neurons and interneurons**
  - **dorsal – roof plate,** development influenced by surface ectoderm (epidermis)
  - **Sulcus limitans** – divide basal and lateral plates

- alar and basal plates – formed by **proliferation** of neuroblasts **in mantle layer**

- **alar** – formation of **sensory** and **interneurons**

- **basal** – formation of **motoric** neurons

- intensive proliferation, fusion of plates – typical butterfly shape of grey matter



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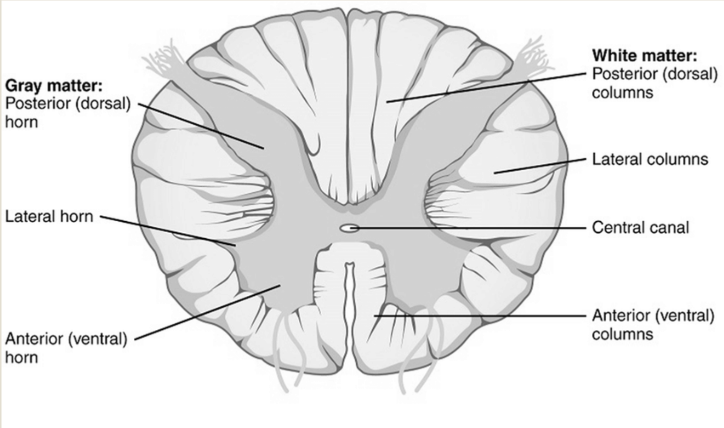
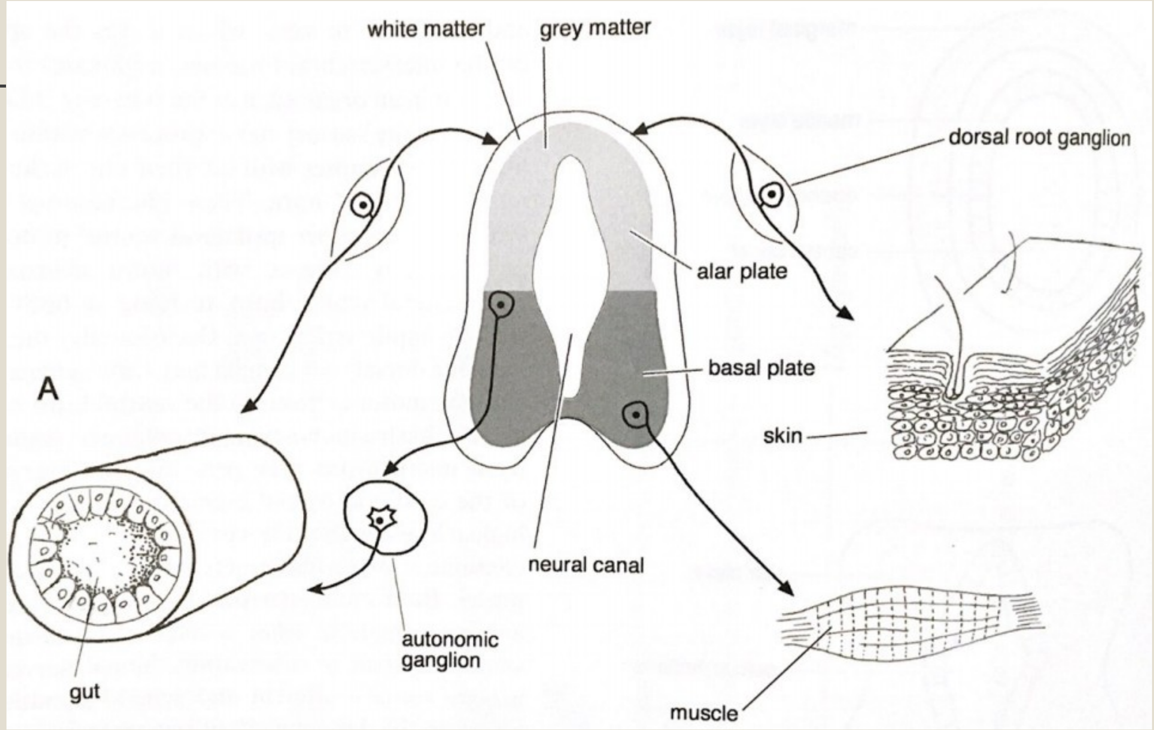


Development of ventral and dorsal spinal cords

- Formation of **motor neurons (basal plate):**
- **Ventral cord** – motor axon outgrows from neuroblast – inervation of **effector** organ (muscle)
- **Lateral cord** – motoric axon outgrows from neuroblast to autonomic ganglion, axons outgrows from axons of autonomic ganglion – inervation of autonomic organ (gut)
- Formation of **sensory neurons (neural crest)**:
- **somatic** neuroblast of dorsal ganglion – one protrusion outgrows towards dorsal spinal cord, other protrusion terminates in somatic sensory receptor (skin)
- **viscelar** neuroblast of dorsal ganglion - one protrusion outgrows towards dorsal spinal cord, other protrusion terminates in visceral sensory receptor (gut)



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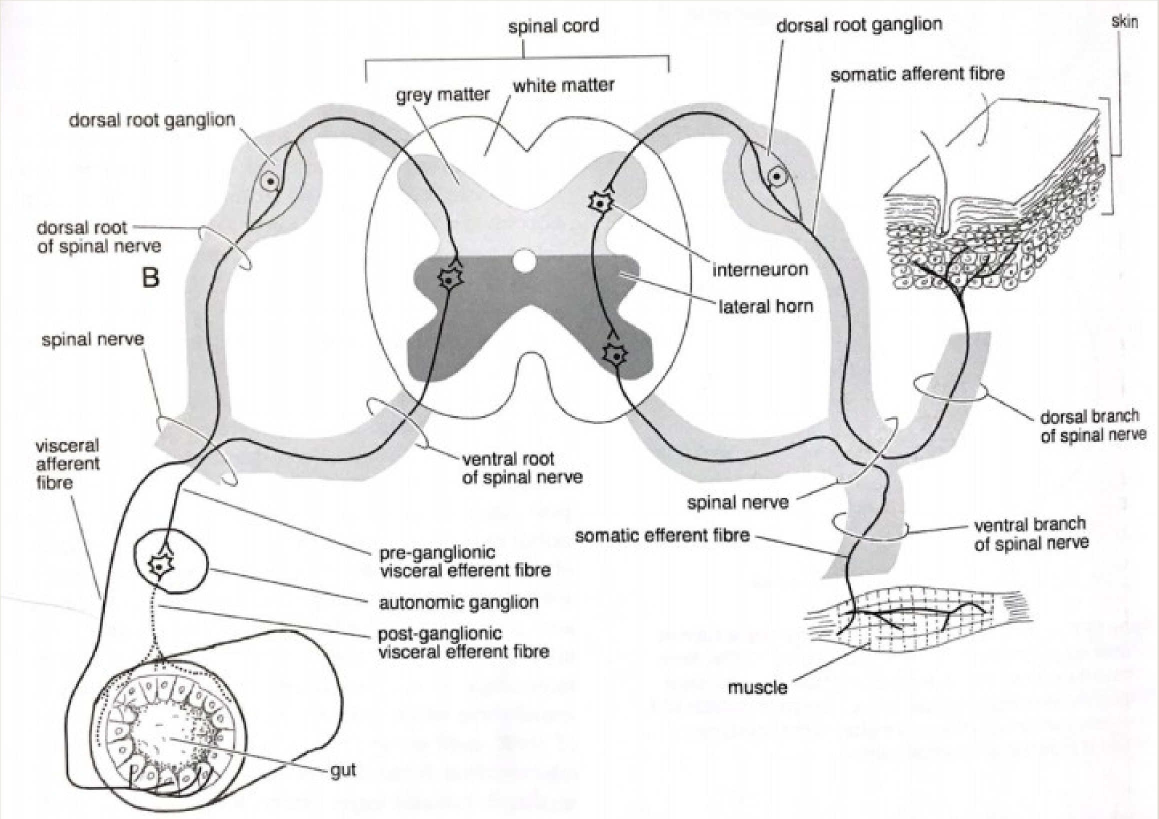
Development of spinal nerves

- **interneurons** – connection between CNS neurons
  - Receive information from sensory neurons or interneurons
  - Transmission of information to motor neurons or interneurons

- **efferent fibers –** lead **signals from CNS** to tissues and organs**, formed** from **basal** plates

- **afferent fibers –** lead **signals from periphery** to CNS**, formed** from **neural crest** cells

- together – **spinal nerve**, formed of **dorsal** (afferent) and **ventral** (efferent) **fibers**



Edited: McGeady et al. Veterinary Embryology. 2009

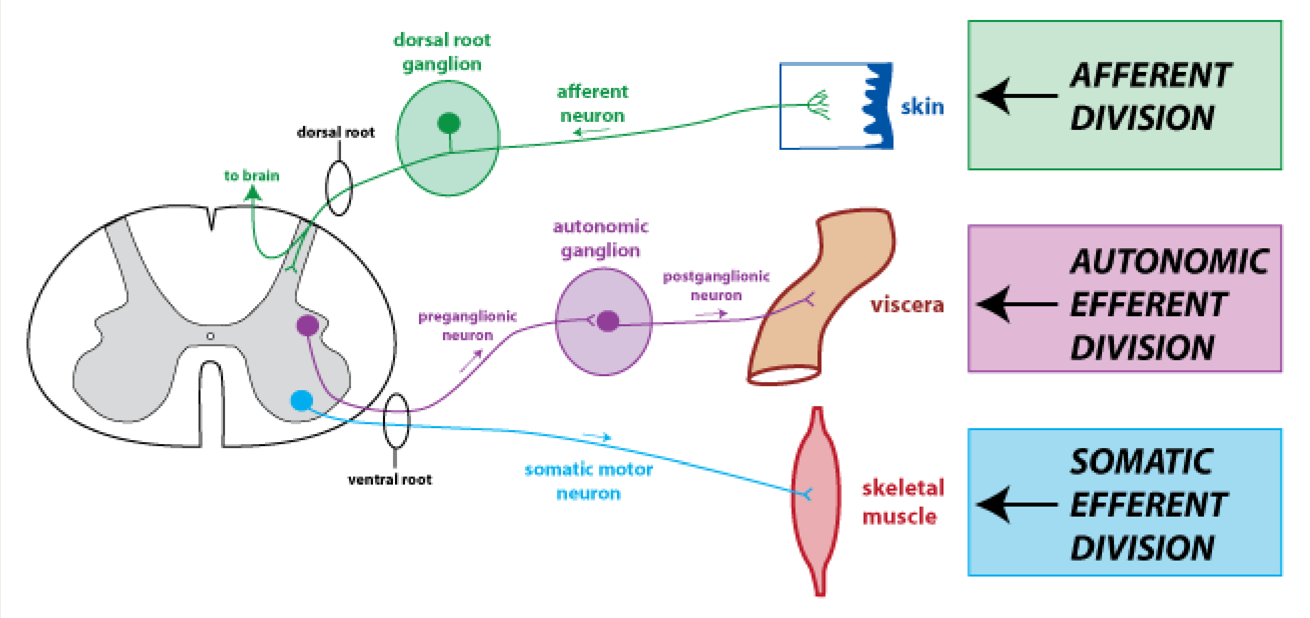
Development of peripheral nervous system

- Nervous system outside the brain and spinal cord:
  - Cranial and spinal nerves
  - Sensory and autonomic ganglia
  - Supporting cells

- **CNS** – efferent somatic and autonomic fibers from basal plates

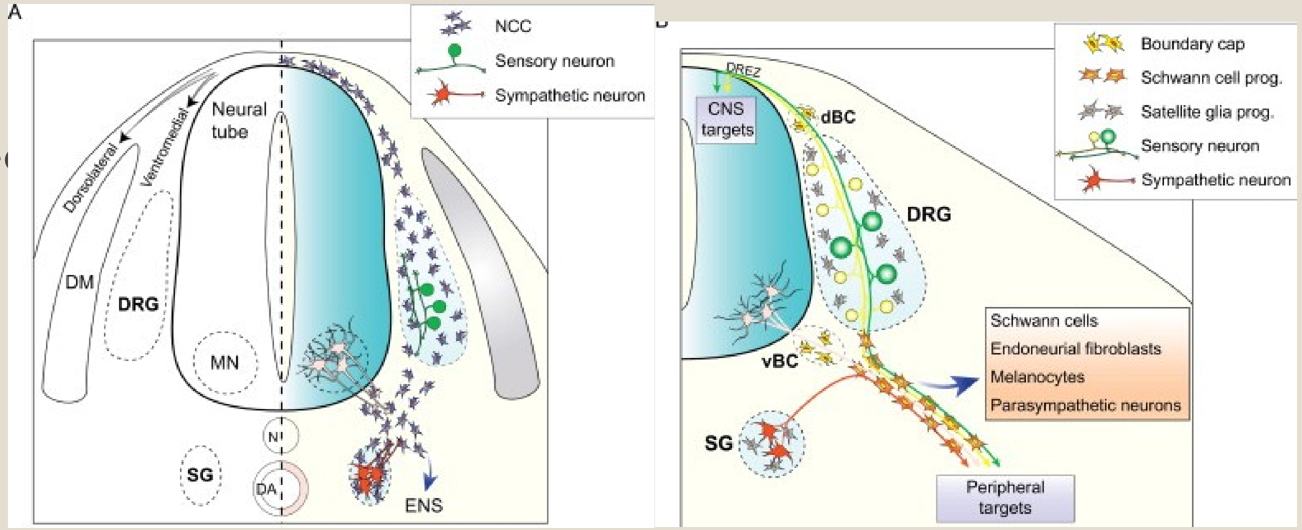
- **Neural crest:**
  - Afferent nerve fibers
  - Postganglionic neurons
  - Spinal, head and autonomic ganglia
  - Glial cells

- **Placodal tissues** (ectodermal placodes of sensory system):
  - part of cranial neurons and ganglia



Development of dorsal root ganglia (DRG)

- **Bodies of neurons** responsible for transmission of sensory information from receptors (termoreceptors, nociceptors, proprioreceptors, chemoreceptors) to CNS
- **Bodies of neurons separated by satellite** glial cells – preventing transmission of signals betwe bodies
- **Trunk neural crest** cells **migrate** ventrally
- migration **terminated medially** from **somites**
- formation of two cell populations:
  - **Sensory neurons**
  - **Glial cells** (Satellite glia, Schwann cells)
- neuron:
  - Dorsomedial outgrowth (neural tube)
  - Ventrolateral outgrowth (connected to developing spinal nerve)



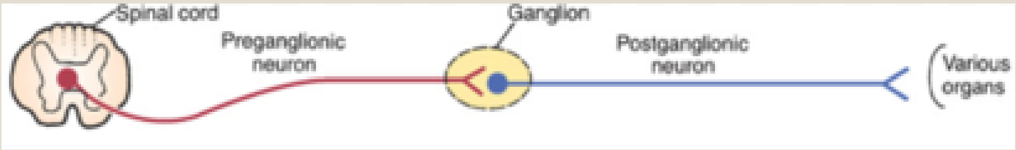
Autonomic nervous system

- General visceral efferent system – involuntary regulation of systems (smooth and cardiac muscles, exocrine and endocrine glands)

- Divided to:
  - **sympathetic**
  - **parasympathetic**

- in contrast with **somatic** efferent system (one neuron), **autonomic** system formed of **two neurons**

- **connection** takes place in **autonomic ganglion** (neural crest)



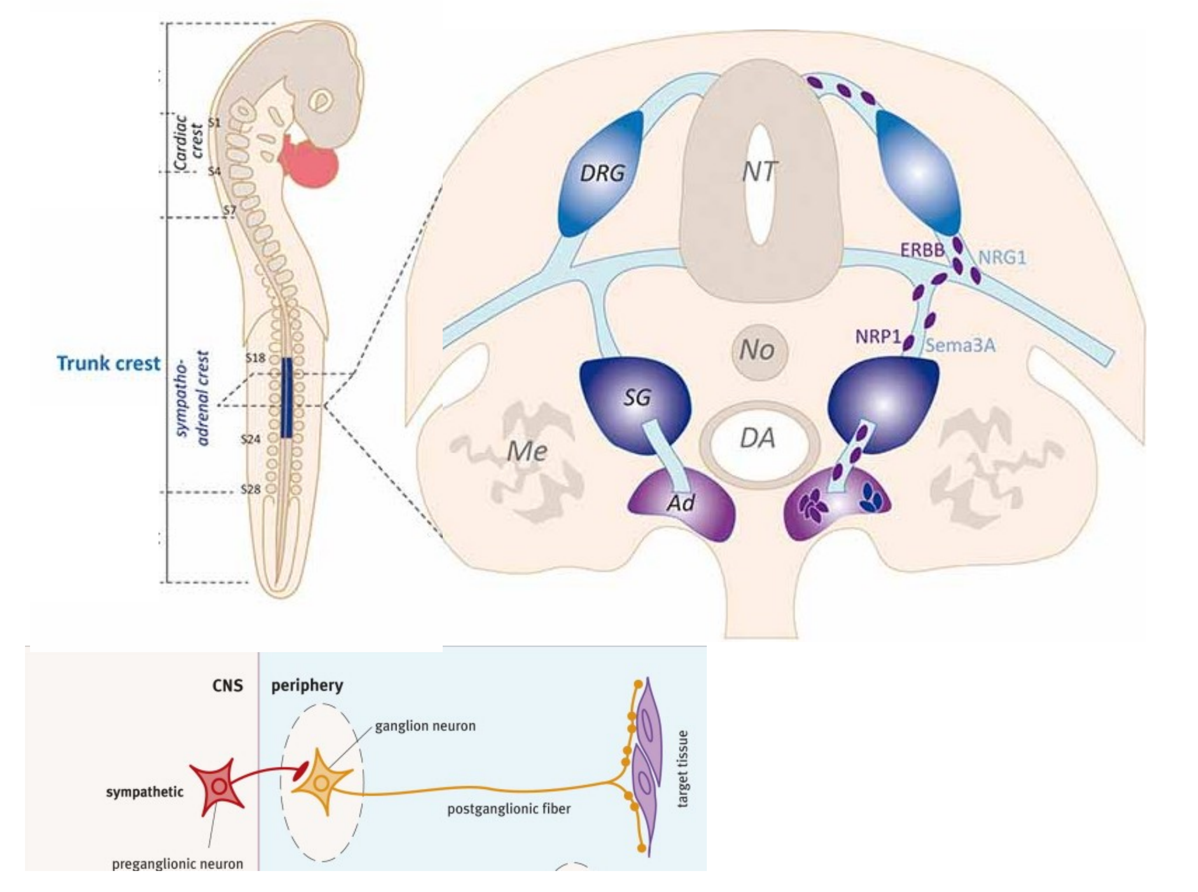
Delloye-Bourgeois and Castellani, 2019. Front Mol Neurosci

Sympathetic nervous system

- Sympathetic system develops:
  - **preganglionic** neurons – **trunk** and **lumbar** spinal cord
  - **postganglionic** neurons and **ganglion** - **sympatoadrenal** population of trunk **neural crest**

- Sympathetic fibers:
  - preganglionic - **short**
  - postganglionic - **long**
  - Ganglia formed **close** to **neural tube**

- Myelination:
  - Myeline sheet formed from Schwann cells
  - Postganlionic axon not myelinated



Delloye-Bourgeois and Castellani, 2019. Front Mol Neurosci

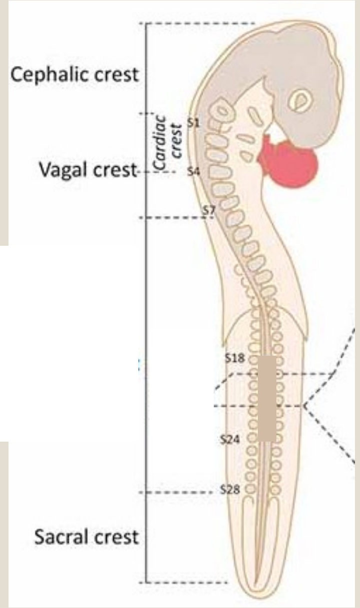
Parasympathetic nervous system

- Parasympathetic system develops:
  - **Preganglionic** axons – brain stem (part of cranial nerves – Oculomotor, Facial, Glossopharyngeal, Vagus)
  - **Ganglia** and **postganglionic neurons** – from cranial, vagal and lumbosacral neural crest

- Parasympathetic ganglia formed **close** to or **directly** in innervated **tissue**

- Parasympathetic fibers:
  - Preganglionic – **long**
  - Postganglionic – **short**

- Myelination:
  - Formation of myeline sheet from Schwann cells
  - Post-ganglionic axon not myelinated

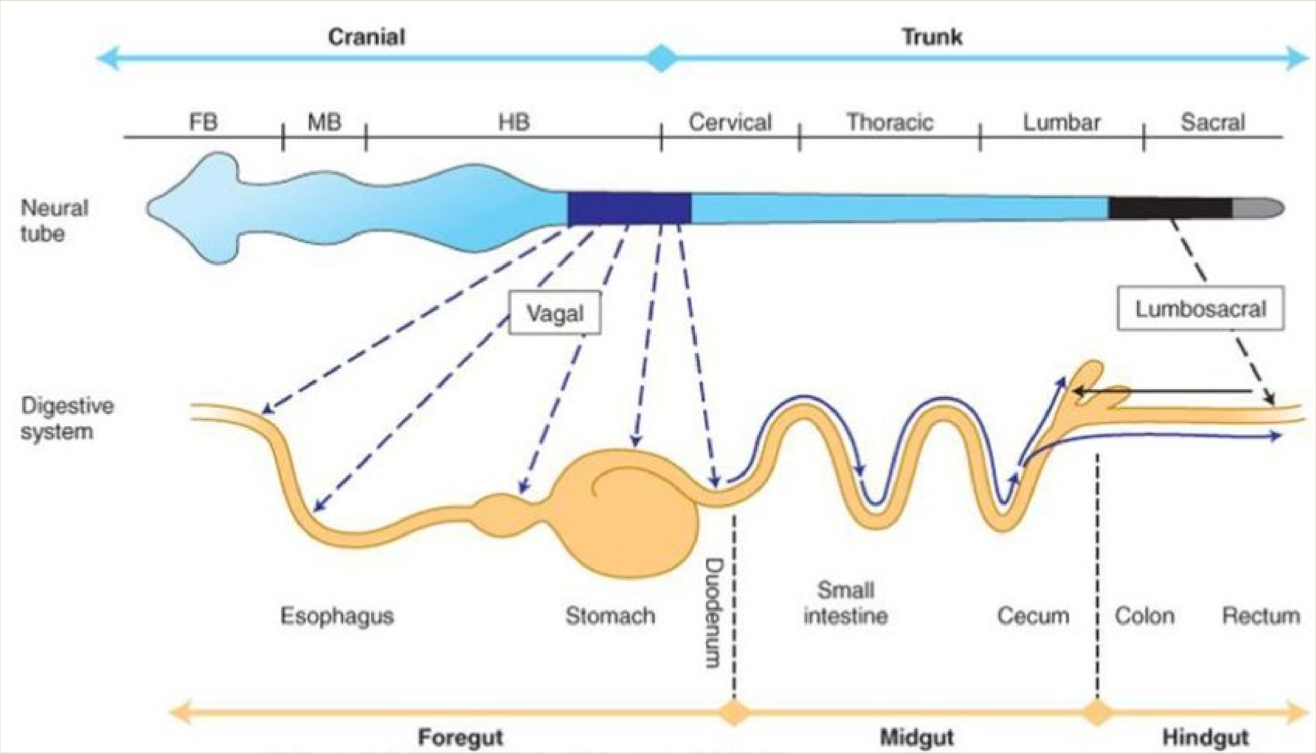


Enteric nervous system

- Control of gut motility, secretion, transport of water and electrolytes, vascularization of mucosa

- Formed from 2 sources:
  - **Vagal neural crest** (hind brain), inervation of almost the whole gut – including first 2/3 of colon
  - **Lumbosacral neural crest**, inervation of last 1/3 of colon and rectum

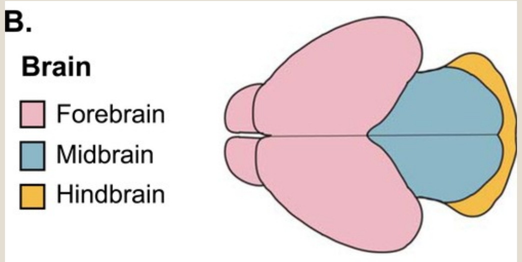
- **Neural crest cells migrate to** wall of developing gut, formation of nerve plexus:
  - submucosa – **Meissner`s** plexus
  - External muscle layer – **Auerbach`s** plexus

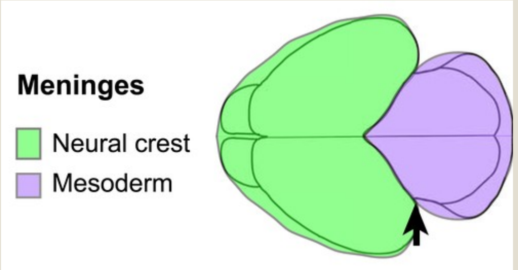


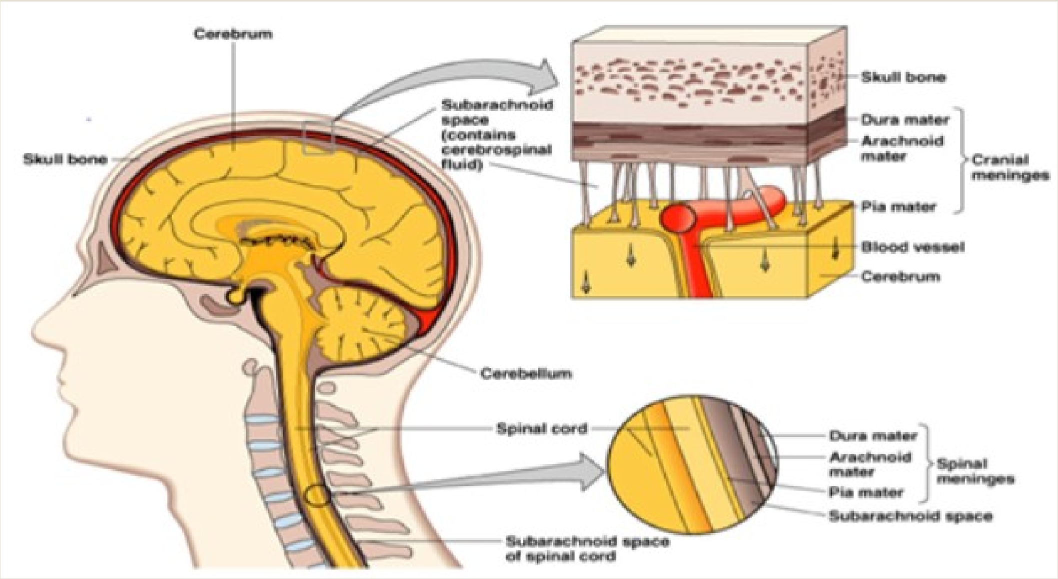
Larsen Human Embryology, 2008

Development of CNS meninges

- neural tissue **protection**, **attachement** to bones (cranium, backbone), **flow** of cerebrospinal fluid
- Origin of meninges – **different** for **brain** and **spinal cord**
  - **Cranial brain** – **neural crest** (forebrain)
  - **Caudal brain** and **spinal cord** – **paraxial mesoderm**
- CNS meninges:
  - Outer layer – **dura mater**
  - Middle layer – **arachnoidea**
  - Inner layer – **pia mater**
- Development from mesenchymal sheath - **primary meninx**
- Differentiation of primary meninx:
  - **Pachymeninx** – dura mater
  - **Leptomeninges** – arachnoidea and pia mater







Dasgubta and Jeong, 2019. Genesis

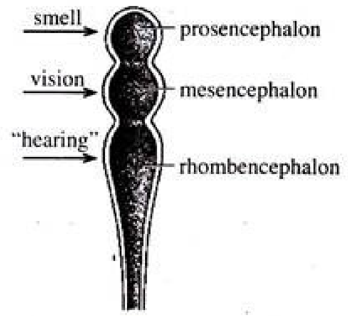


Fig. 5.72 : Diagram of the three-part division of the brain in relation to smell, vision and hearing.

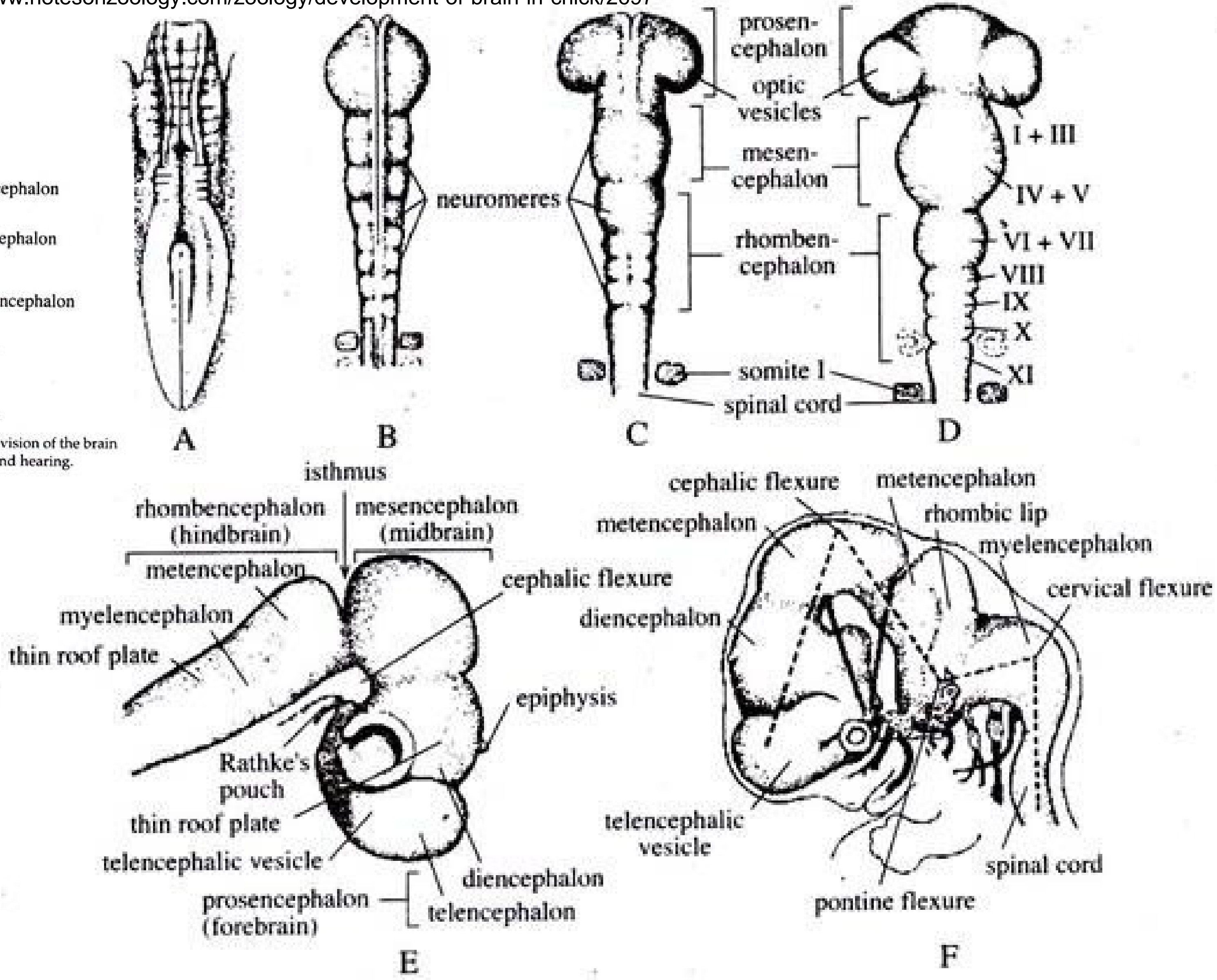
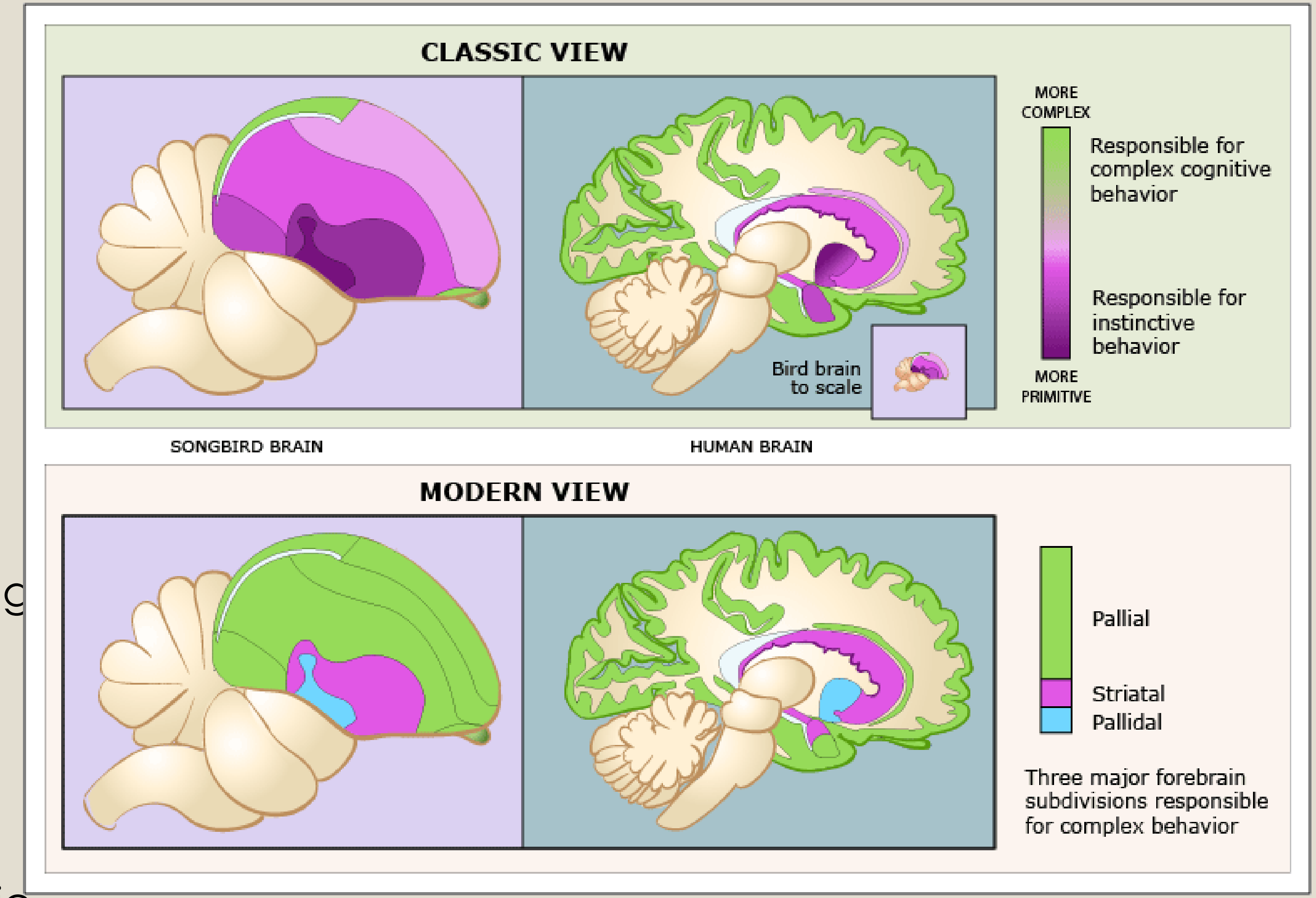


Fig. 5.71 : Early development of the brain in chick showing the tendency to form neural segments or neuromeres. (A) Dorsal view of developing brain of chick embryo with 4 pairs of somites. (B) Dorsal view of primitive brain or encephalon of chick embyo with 7 pairs of somites. (C) Dorsal view of developing brain of chick embryo with 14 pairs of somites. (E) Lateral view of brain of chick embryo about 75 to 80 hours of incubation. (F) Lateral view showing the flexures.

Avian brain

- Early development resembles the mammal brain
- Main difference – lack of neocortex
- In mammals - information flow among brain's layers
- In birds - interconnected nuclei with bands of neurons
- Both microcircuits of info are analogic
- Increased optic region

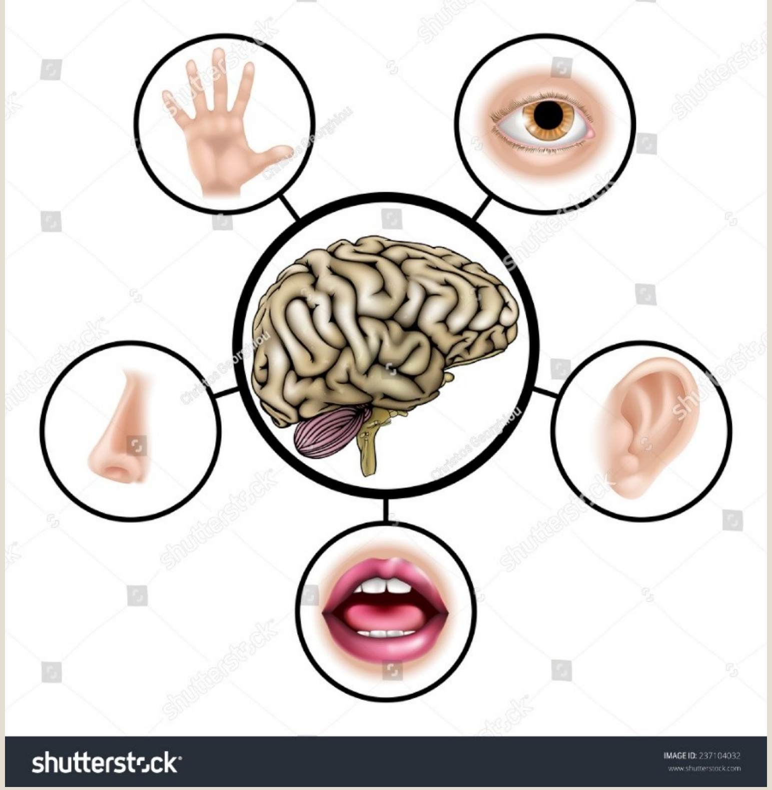


https://medicalxpress.com/news/2015-02-mammalian-avian-brains-corticosensory-microcircuit.html

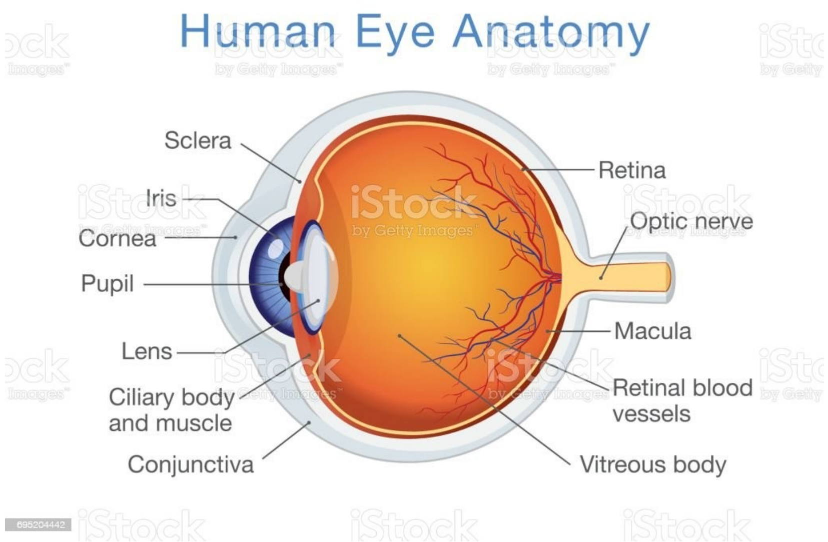
DEVELOPMENT OF SENSORY ORGANS

Functions of sensory organs

- Development of structures specific for perception of stimuli
- Tastes and smells perception
- Sounds perception
- Optical perception
- Water flow perception and electric field perception
- Structures for perceving body position and balancing

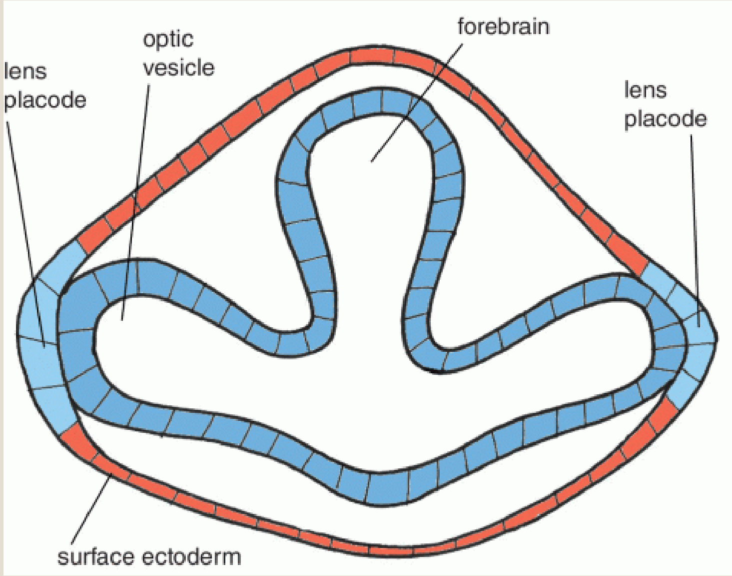


EYE

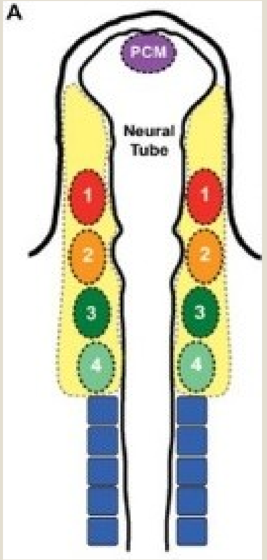

Human Eye Anatomy
Sclera
Iris
Cornea
Pupil
Lens
Ciliary body and muscle
Conjunctiva
Retina
Optic nerve
Macula
Retinal blood vessels
Vitreous body
iStock
by Getty Images
695204442

Embryonic origins of individual eye parts

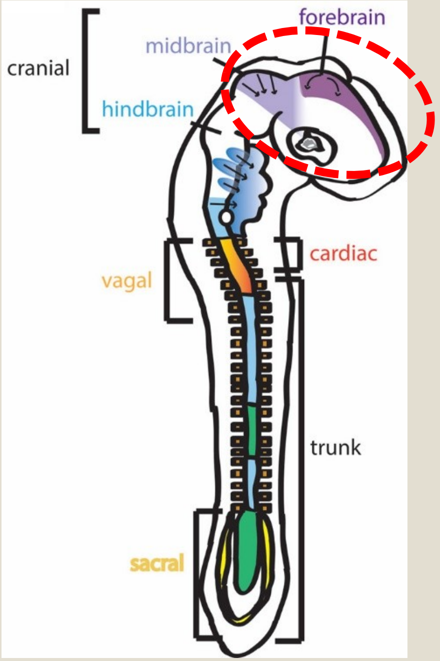
- **Neural epithelium of diencephalon** – retina, iris including smooth muscles, optic nerve, part of vitreous body
- **Surface ectoderm** – lens, cornea, conjunctiva, eyelids, lacrimal duct
- **Prechordal mesoderm** (preotic mesoderm) – external occulomotor muscles
- **Neural crest** (prosencephalon a mesencephalon) – part of epithelium and stroma of cornea, stroma of iris, stroma and muscles of ciliary body, sclera



Veterian Key



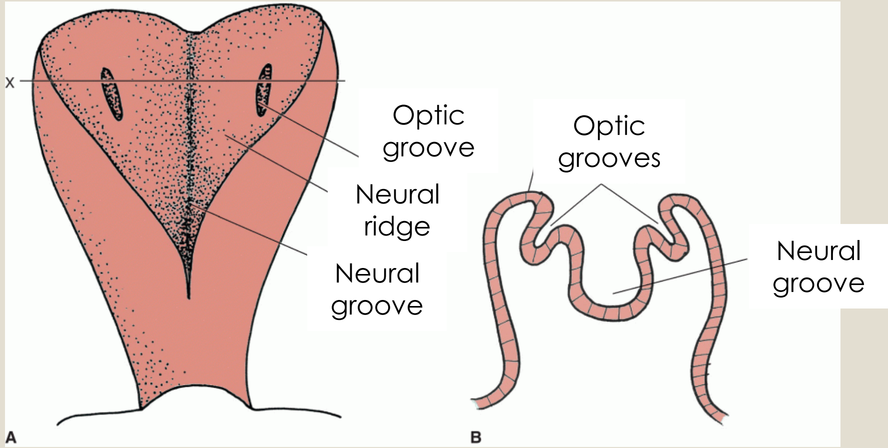
Randolph and Pavlath, 2015

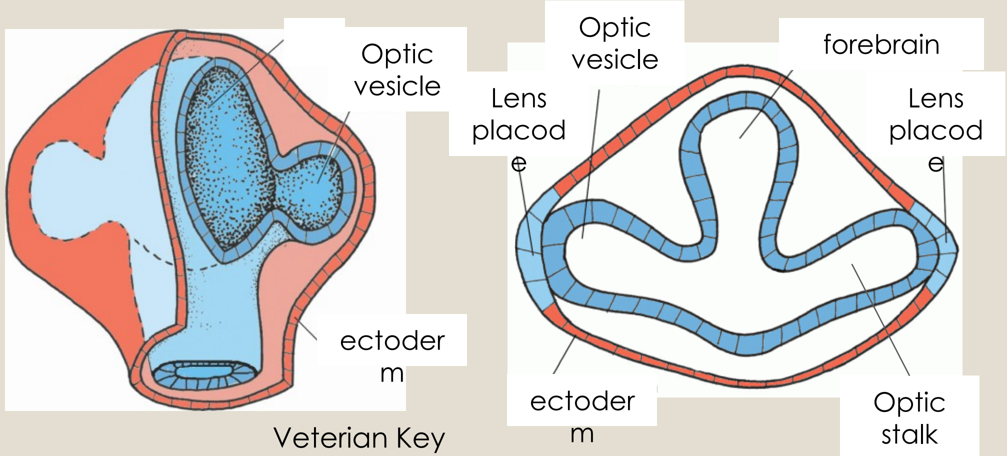


Williams and Bohnsack, 2015.
Birth Defects Res C Embryo Today

Development of optic groove and optic vesicle

- formation of **optic grooves** on both sides of **forebrain** (neural ridges)
- **Enclosure** of neural tube – formation of sacs from grooves – **optic vesicles**
- Optic vesicles grow from forebrain through mesenchyme towards the surface ectoderm
- During growth – connection between forebrain and optic vesicle is **prolonged** – **optic stalk** (basis for optic nerve)
- **interaction** between **optic vesicle** and **surface ectoderm** – induction of **epithelial thickening** (**lens placode**) in ectoderm (lens precursor)

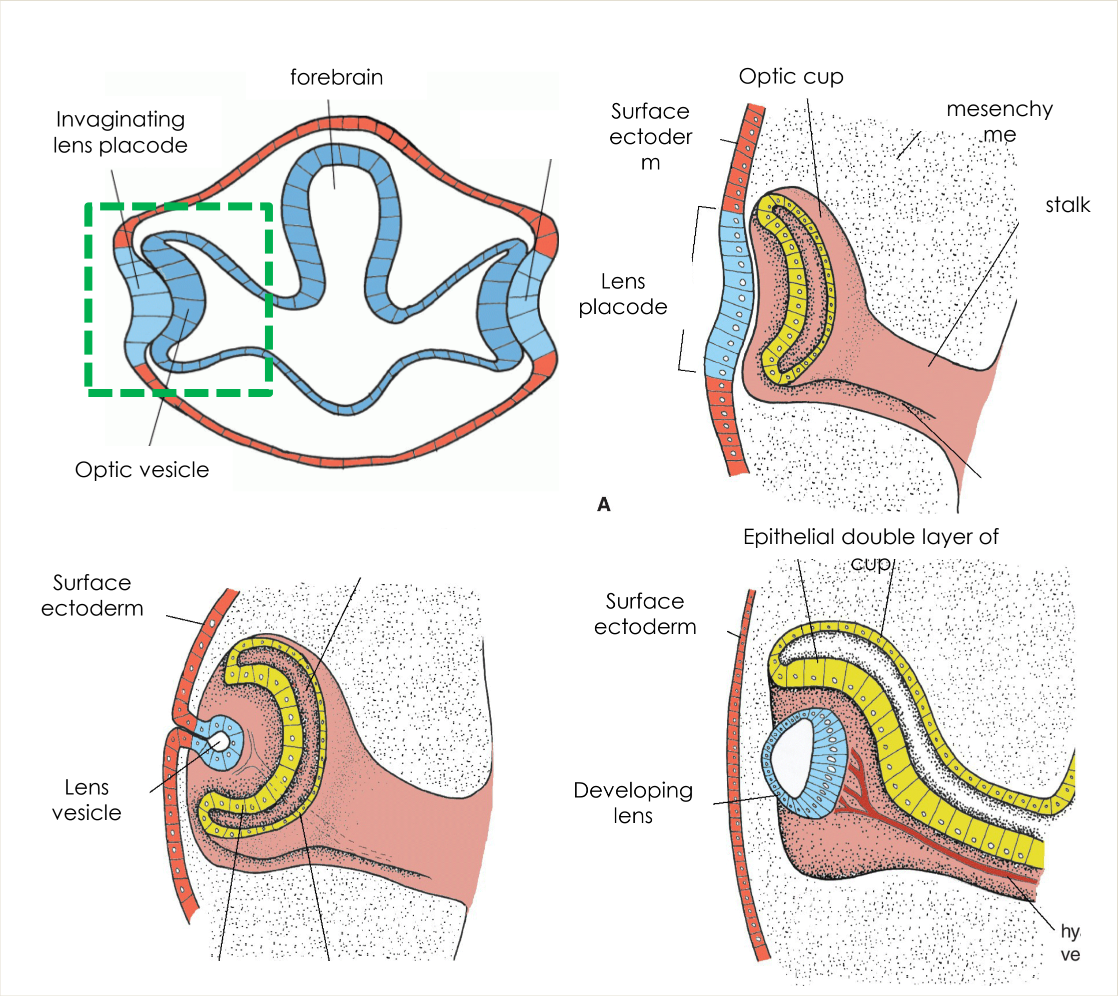




Veterian Key

Development of eye basis

- induction of **invagination epithelium** of **lens placode** – formation of **lens depression**
- from lens placode is formed **circular** structure – further **invagination** – separation of structure from surface ectoderm – formation of **lens vesicle**
- concurrently **invagination** of **optic vesicle** epithelium – formation of **doublelayered** epithelial structure – **optic cup**
- epithelial **double** layer of **optic cup** – basis for development of **retina**



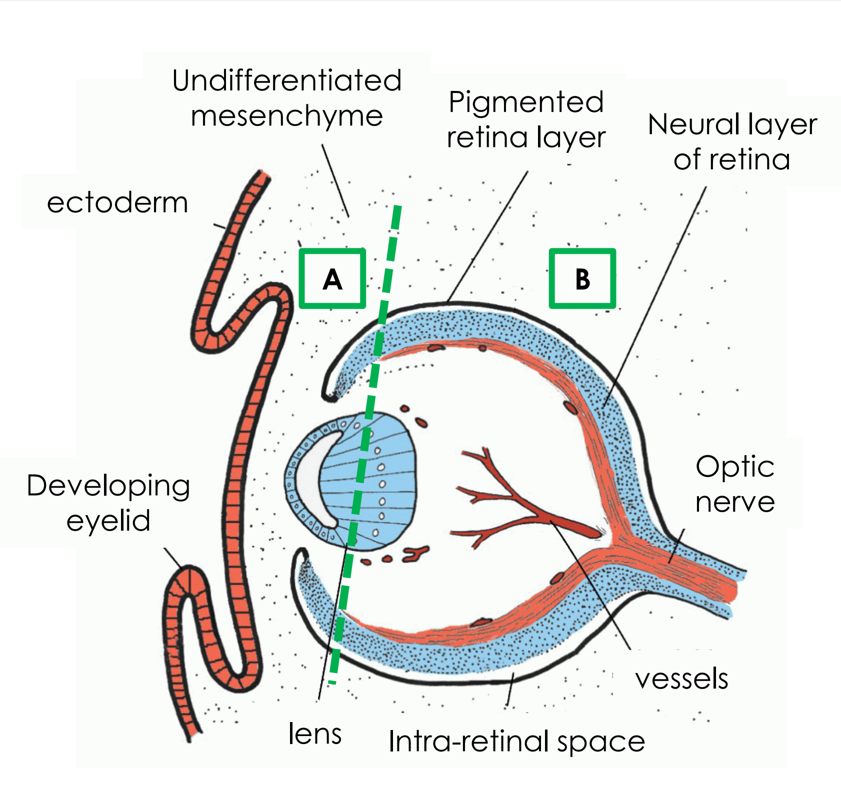
Veterian Key

Development of retina

- basis – **epithelial double layer** (outer thinner, inner thicker) of **optic cup**

- smaller **anterior** (**A**) part – iris and ciliary body
- larger **posterior** (**B**) part - retina

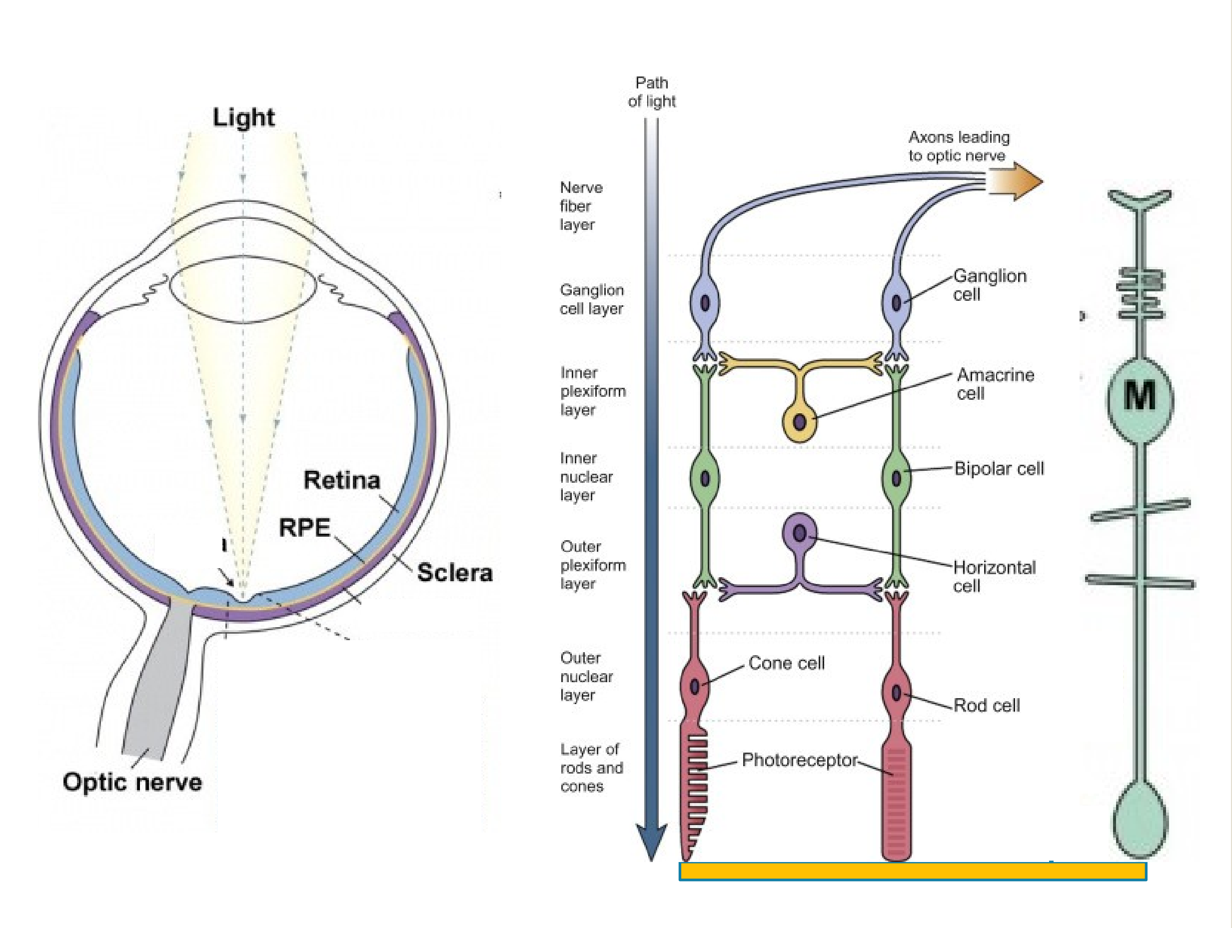
- Posterior part:
  - Inner epithelial layer – **neural** layer of retina (photosensory)
  - Outer epithelial layer – **pigmented** retina layer
  - separated by **intraretinal** space



Veterian Key

Neural retina histogenesis

- layer adjacent to intraretinal space – photoreceptors (**rods** and **cones**)
- **Outer nuclear layer** – bodies of receptor cells
- **Outer plexiform layer** – formation of synapses between photoreceptors and bipolar neurons, horizontal cells (signal integration)
- **Inner nuclear layer** – bipolar, horizontal and amacrine cell bodies (signal transmission to ganglion cells)
- **Inner plexiform layer** – synapses between bipolar, amacrine and ganglion cells
- **Ganglion cell layer** – ganglion cell bodies
- **Nerve fiber layer** – ganglion cell axons
- **Müllerian cell (M)** – glial cell, supporting retinal cell

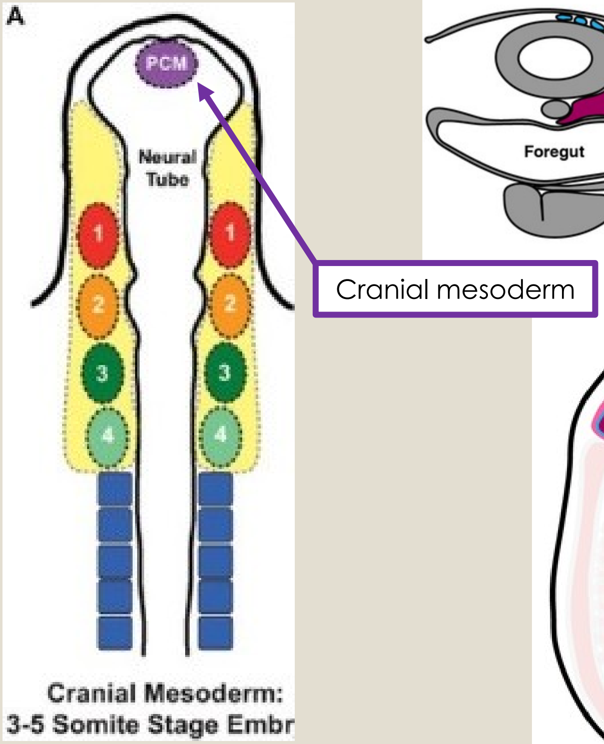


Origin of extraocular muscles

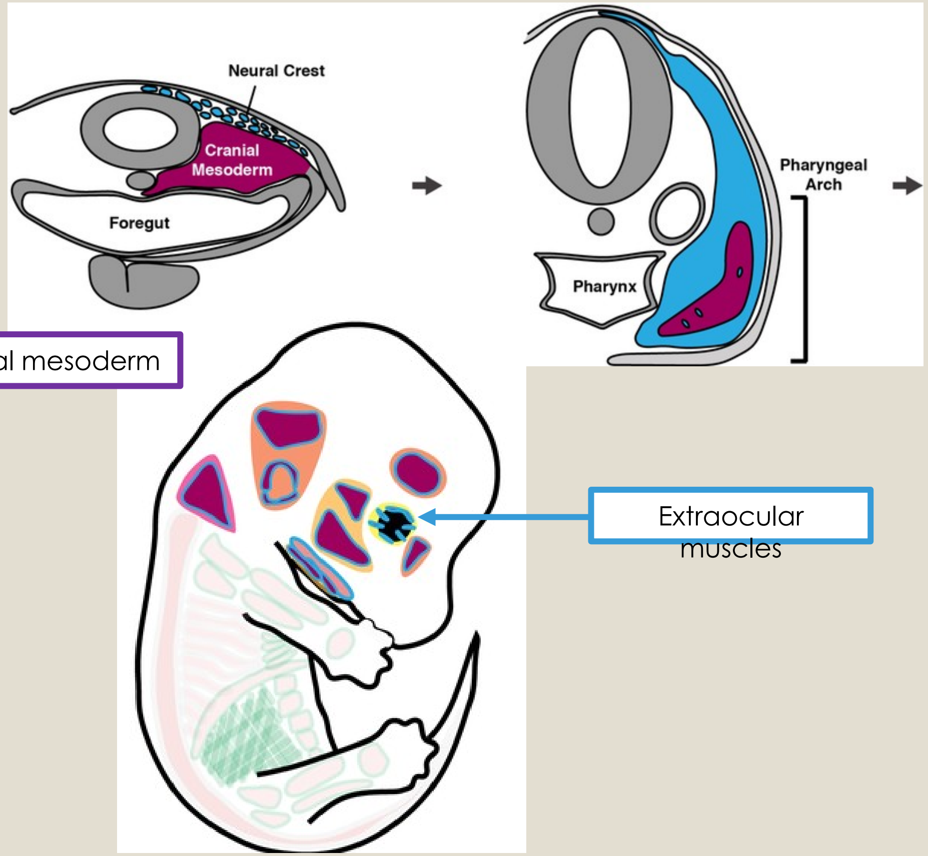
- Extraocular muscles develop from 2 sources:
  - nonsegmented **cranial mesoderm**
  - cranial **neural crest**

- Nonsegmented cranial mesoderm
  - **Muscle cells**

- Cranial neural crest
  - **Muscle connective tissue** (muscle coat)



Randolph and Pavlath, 2015



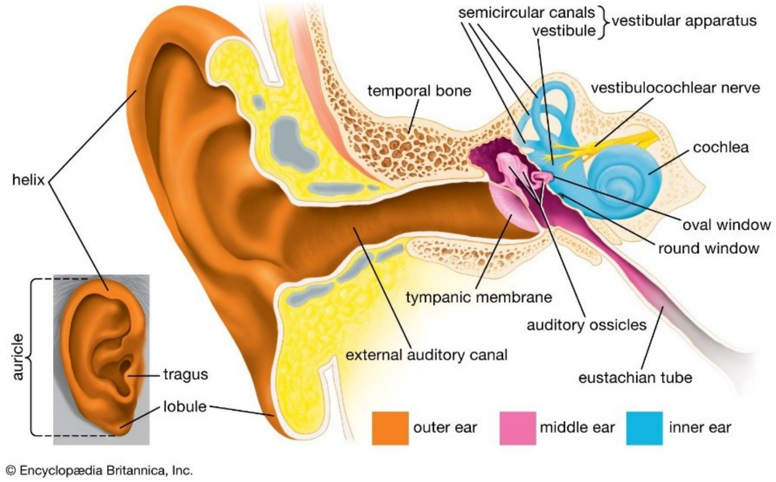
Sefton and Kardon, 2019. Curr Top Dev Biol

Developmental defects of eye

- **Microphthalmia**
  - Congenital eye defect
  - Small and insufficiently developed eye
  - Defect in formation of optic vesicle
  - Unilateral or bilateral

- **Anophthalmia**
  - Congenital eye defect
  - Missing eye, ultrasound often reveals rest of the eye basis inside the head
  - Defective formation of optic vesicle
  - Unilateral or bilateral

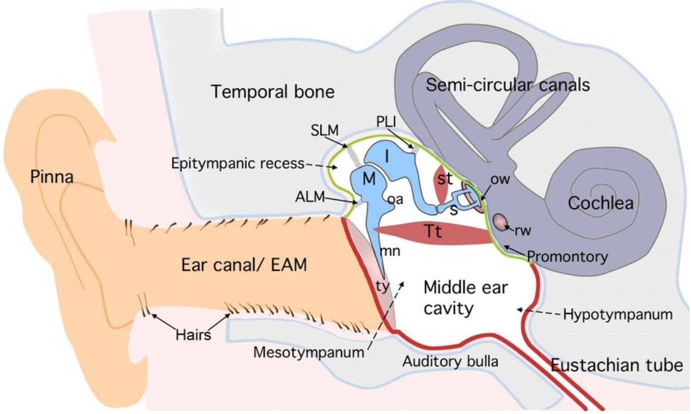
EAR


semicircular canals
vestibule
vestibular apparatus
temporal bone
vestibulocochlear nerve
cochlea
helix
oval window
round window
tympanic membrane
auditory ossicles
external auditory canal
eustachian tube
auricle
tragus
lobule
outer ear
middle ear
inner ear
© Encyclopædia Britannica, Inc.

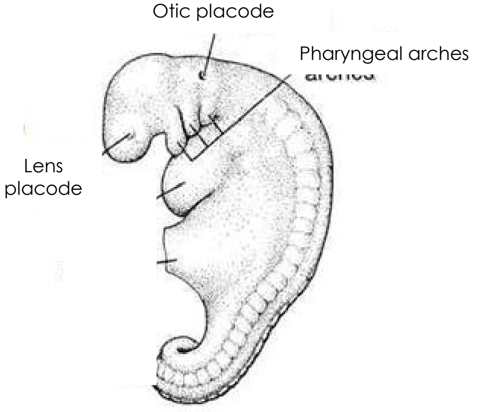
Development of ear

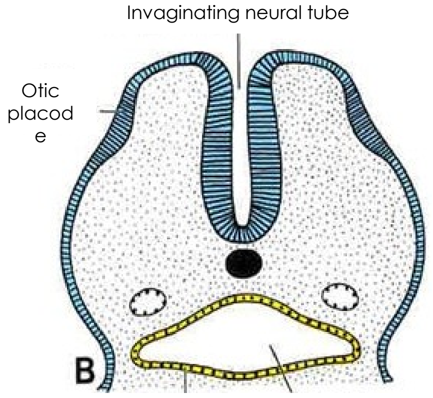
- Ear formed of 3 parts:
  - **external** – auricle, external canal
  - **middle** – middle ear cavity, Eustachian tube, bones and muscles
  - **inner** – saccule, cochlea, organ of Corti

- Ear basis develops:
  - in **region** of **pharyngeal arches** and **hindbrain**
  - formation of **ectodermal thickening** (ear placode)
  - **placode** – basis for development of **inner** ear



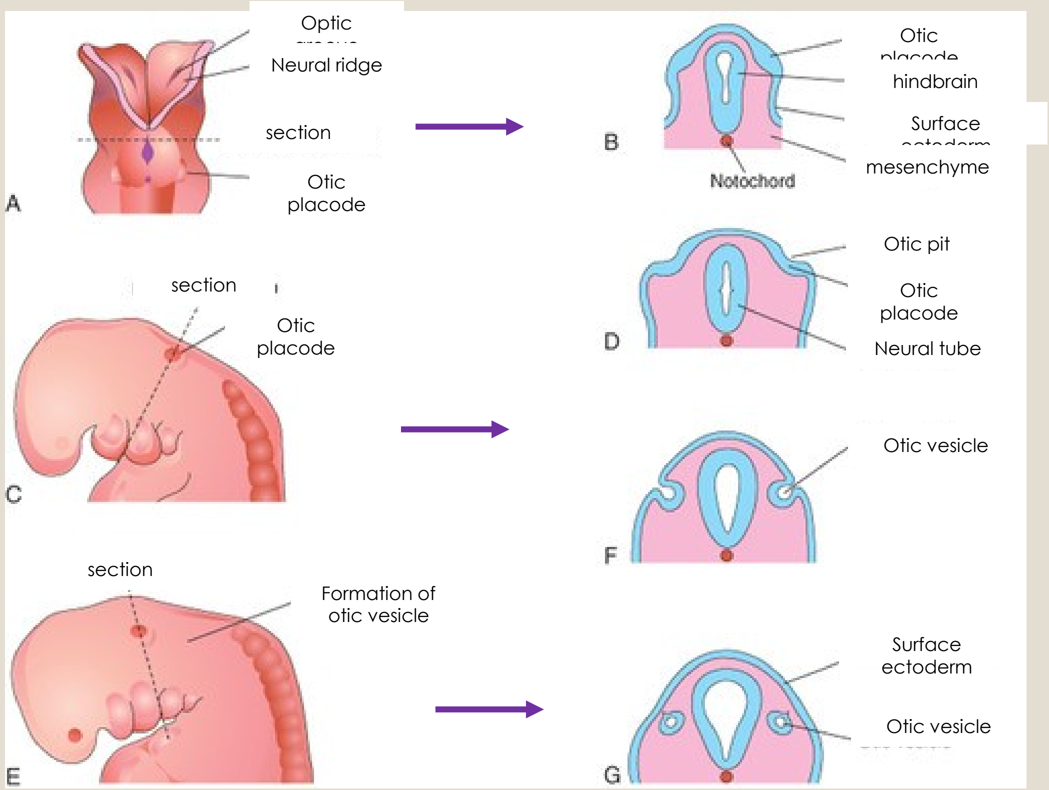
Anthwal and Thompson, 2015. J Anat





Development of inner ear

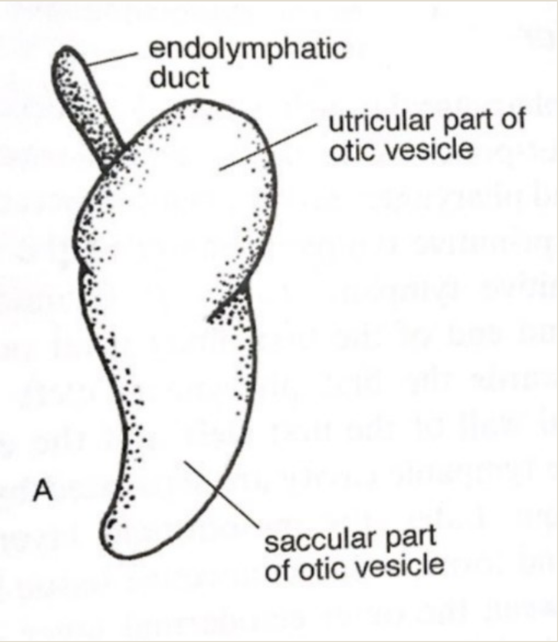
- formation of **ectodermal thickening** in the hindbrain region – **otic placode**
- epithelial **cells** of otic **placode** start to **invaginate** to mesenchyme around hindbrain – formation of **otic pit**
- **Otic pit separates** from surface ectoderm – formation of **hollow structure** lined by cylindrical epithelium – **otic vesicle**, cavity filled with endolymph
- **Otic vesicle** localized in region between surface ectoderm **covered** by **mesenchymal** cells – **ear capsule**
- **some epithelial** cells – leave vesicle and **form** sensory **ganglia** of **VIII. cranial nerve** (vestibulocochlear)

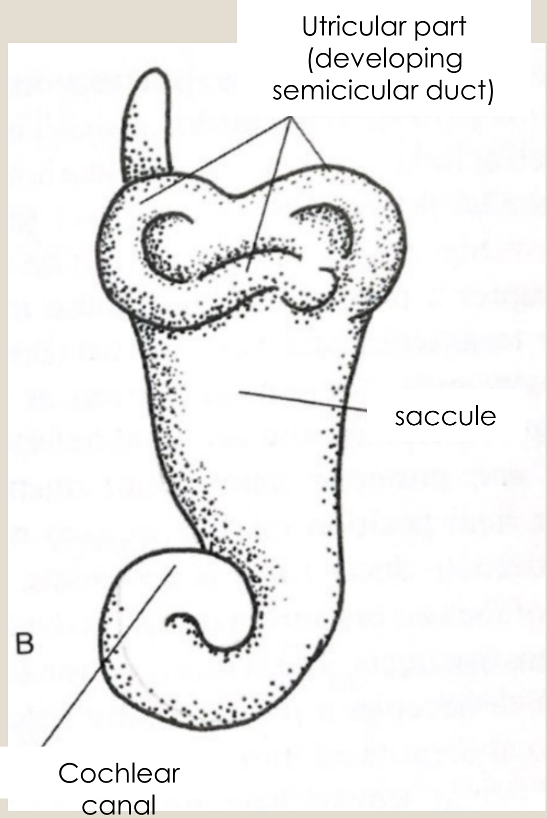


Moore and Persaud. The developing Human 8e

Differentiation of otic vesicle

- from **otic vesicle** – formation of membranous **labyrinth** lined with epithelium
- epithelium **differentiation** – regions with different thickness of epithelium
- Otic vesicle divides into 2 parts:
  - **dorsal** – **utricular** (vestibular basis – vestibular/balancing system)
  - **ventral** – **saccular** (inner ear basis – hearing)
- **dorsomedial** – evagination leads to formation of **endolymphatic duct**, with terminal extension – **endolymphatic vesicle** (regulation of volume and pressure of endolymph)





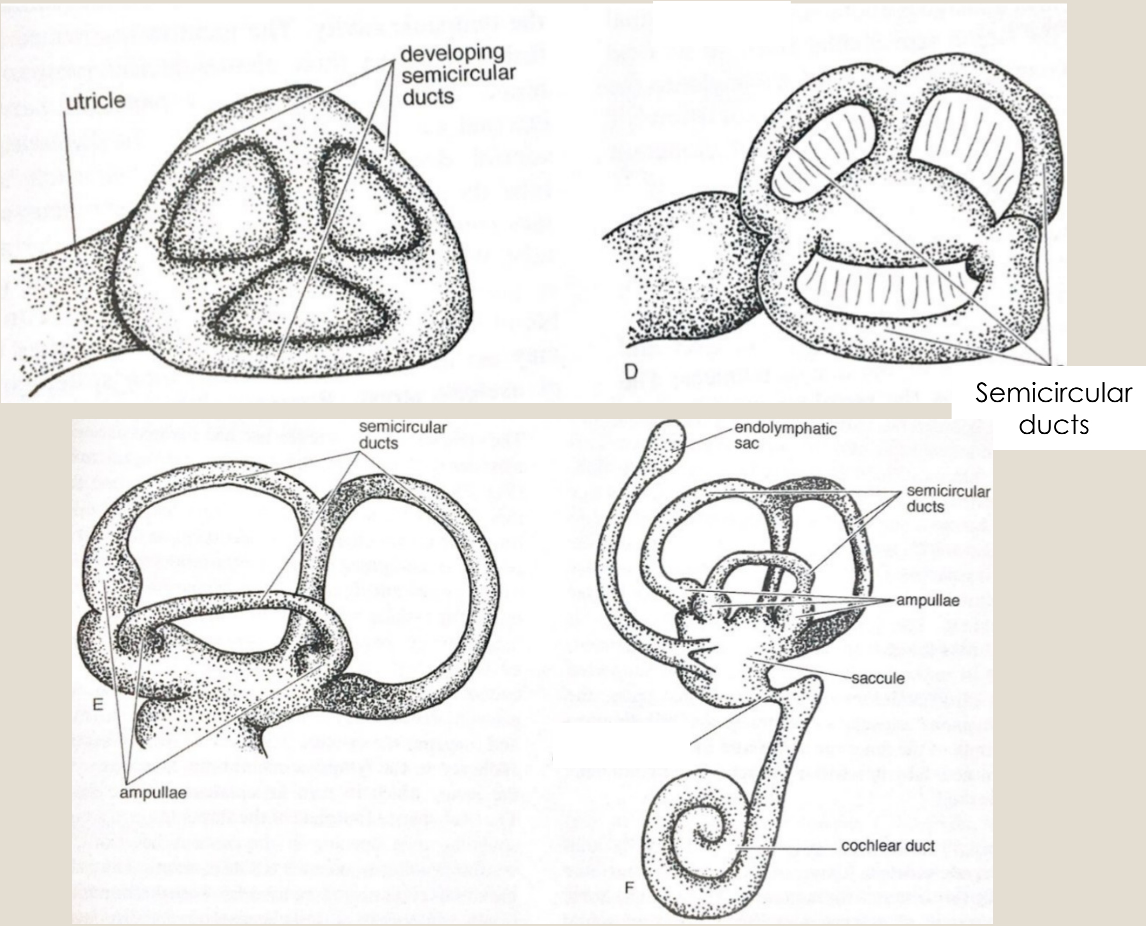
Edited: McGeady et al. Veterinary Embryology. 2009

Development of vestibular system

- from dorsal **utricle** - **semicircular ducts**

- Formation of 3 **semicircular ducts:**
  - **2 vertically** oriented
  - **1** oriented under **90 °** angle to **vertical** ducts

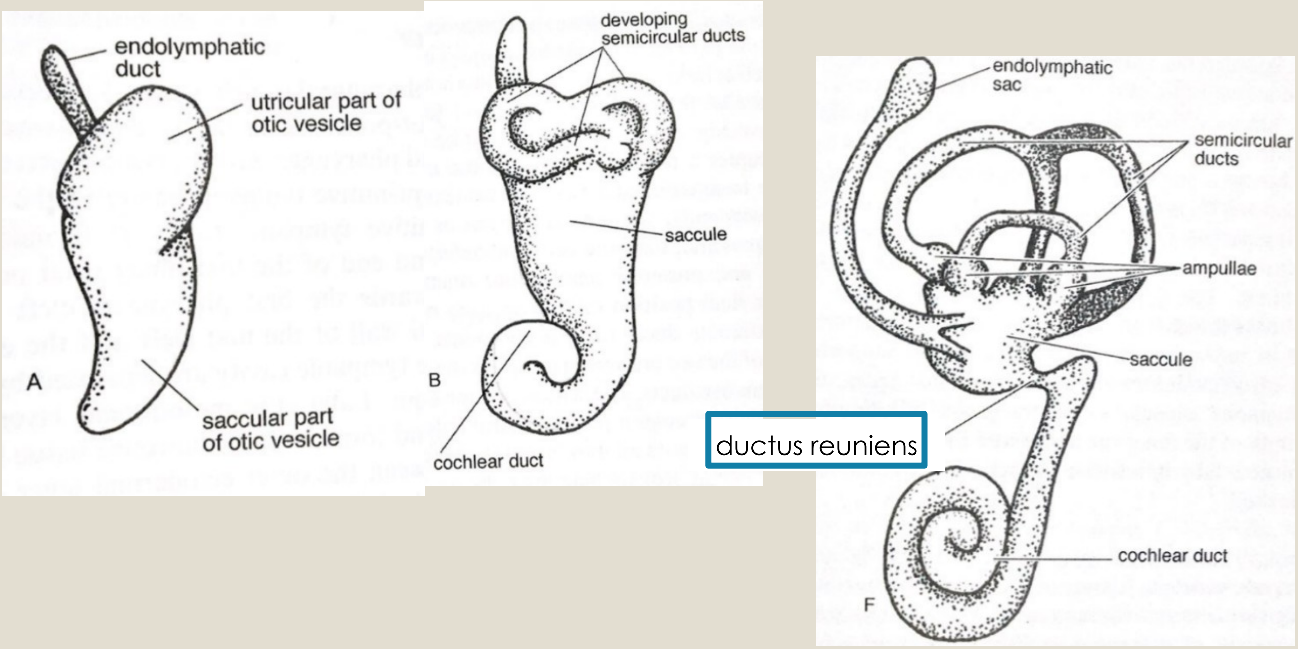
- at the end of each canal - **extension** called **ampullae** containing sensory organs



Edited: McGeady et al. Veterinary Embryology. 2009

Development of cochlear system

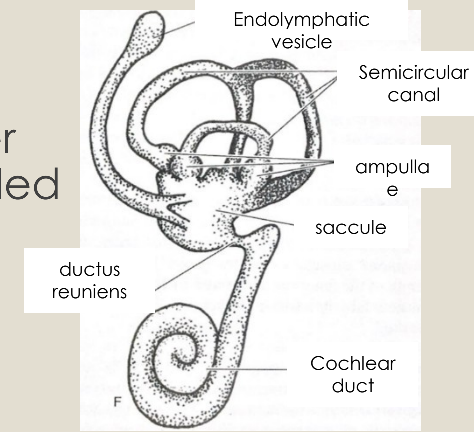
- from ventraly oriented **saccule** formation of **evagination** – **cochlear duct**
- **duct** first **prolongates** and **narrows** and later **convolutes**
- narrow duct connecting **saccule** and **cochlear** duct – **ductus reuniens**
- adjacent **mesenchyme** – **differentiation** to **auditory cartilage**

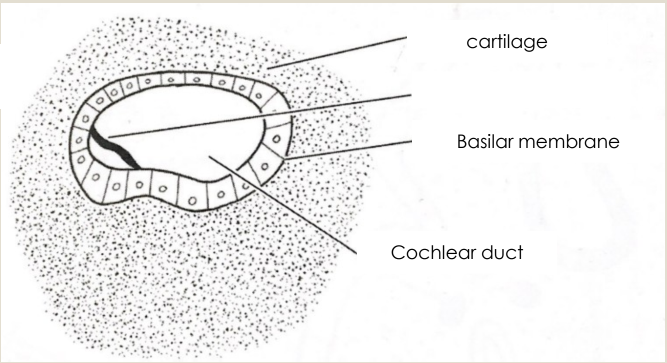


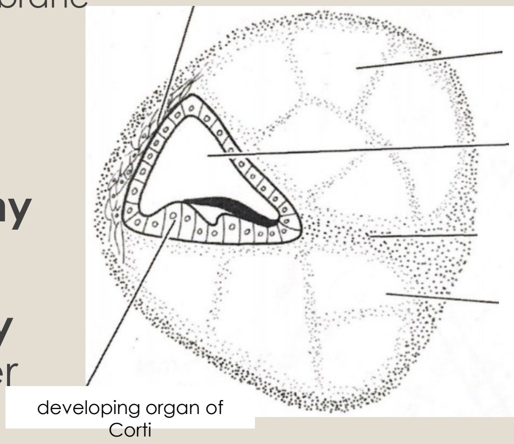
Edited: McGeady et al. Veterinary Embryology. 2009

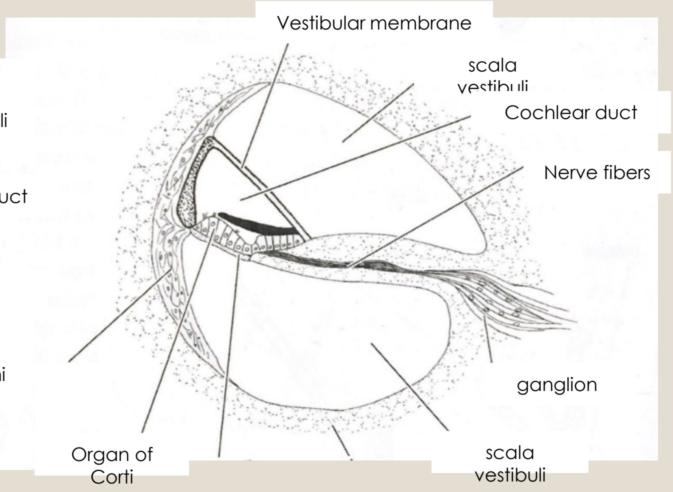
Development of cochlear system

- **part** of **cartilage** adjacent to basillary membrane is **vacuolated**
- formation of **cavity between** outer **cartilaginous** layer and membranous **labyrinth** – **perilymphatic space** filled with perilymph
- Perilymphatic space divided to:
  - **Scala vestibuli** – cochlear duct separated by vestibular membrane
  - **Scala tympani** – cochlear duct separated by basilar membrane
- differentiation of basal cells in cochlear duct – formation of organ of **Corti**
- **cartilaginous** labyrinth **ossify** – formation of **bony labyrinth**
- **migration** of cells from **medial sac wall medialy** – formation of **statoacoustic ganglion** (together with neural crest cells)









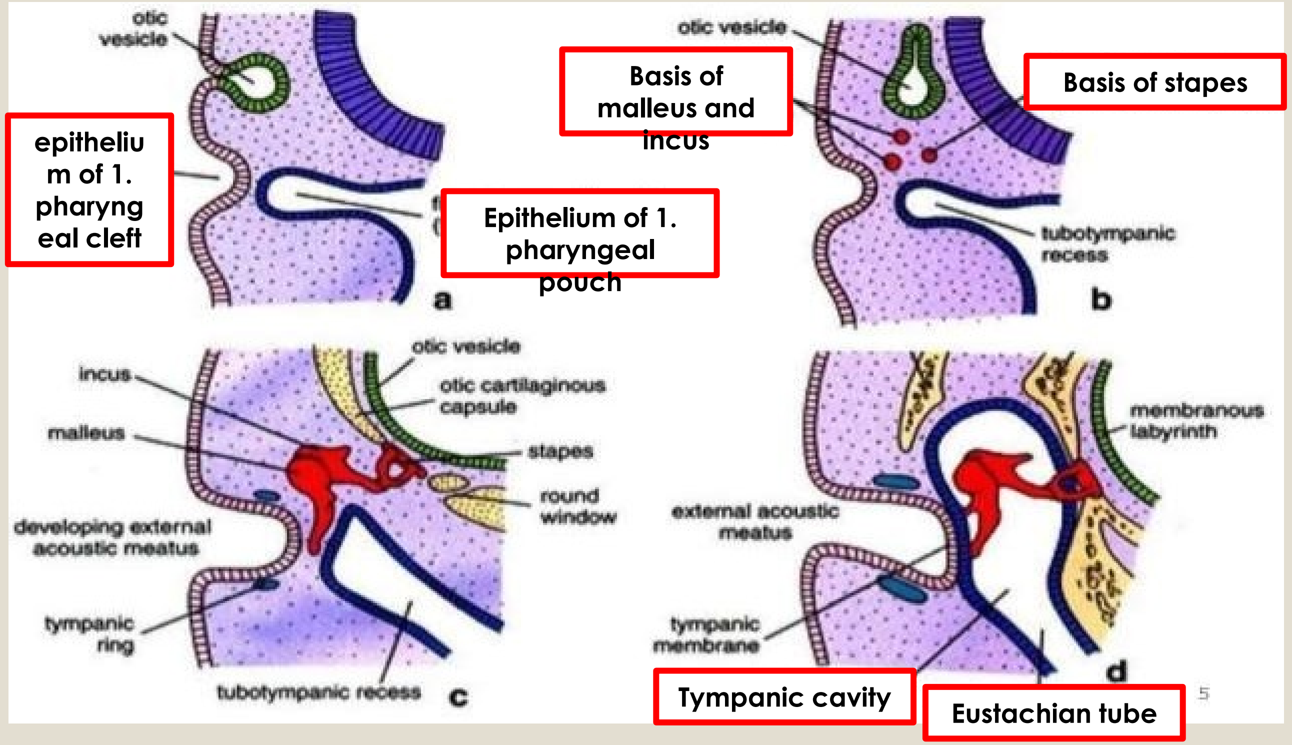
Edited: McGeady et al. Veterinary Embryology. 2009

Development of middle ear

- Tympanic cavity, Eustachian tube, bones and muscles

- **Epithelium of 1. pharyngeal arch pouch (endoderm)**
  - **Tympanic cavity**
  - **Eustachian tube**

- **middle ear ossicles – mesenchyme** of pharyngeal arches

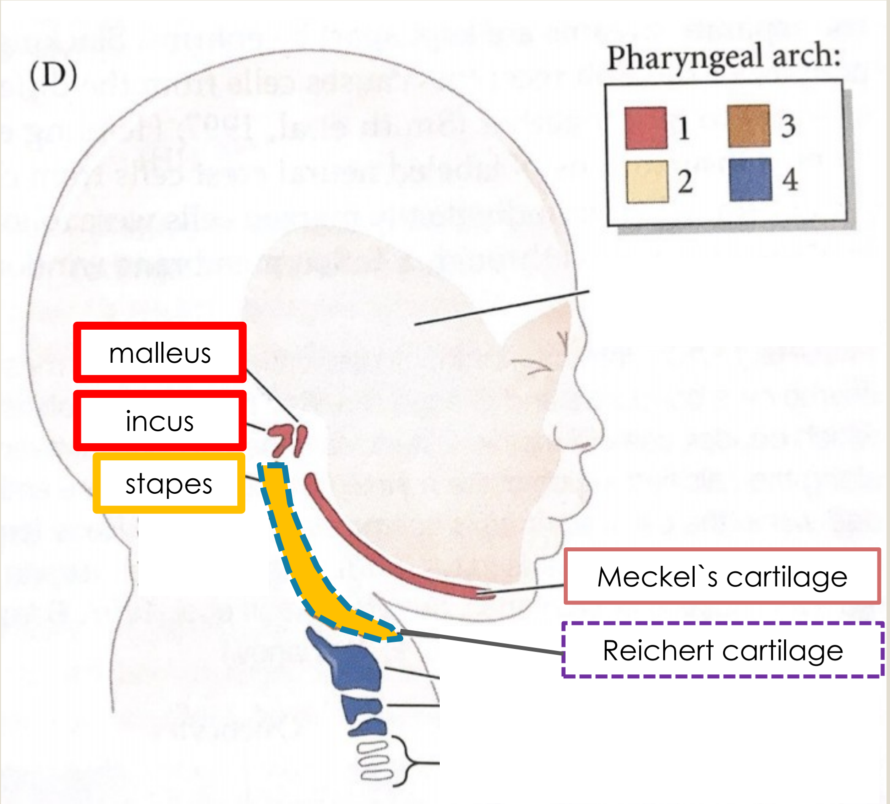


Development of middle ear ossicles

- Malleus, incus and stapes develop from 1. and 2. pharyngeal arches

- **1. pharyngeal arch** – endochondral ossification of Meckel`s cartilage:
  - **Malleus**
  - **incus**

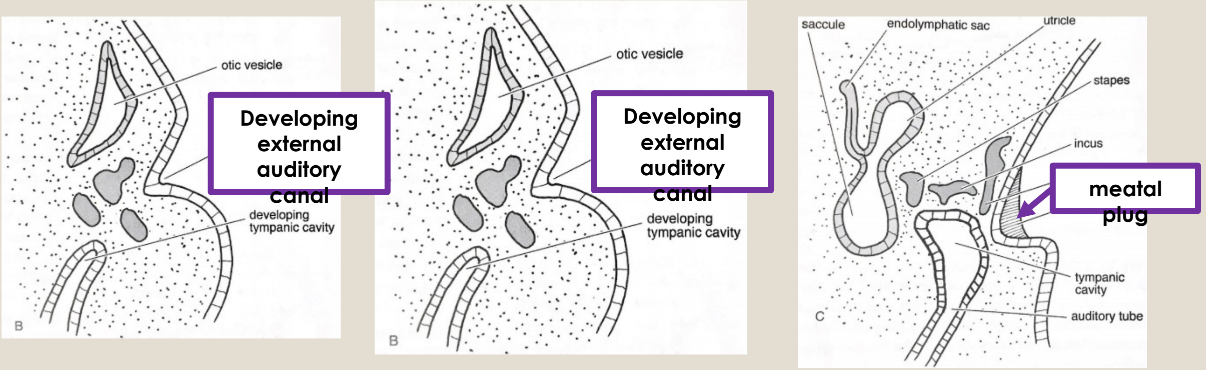
- **2. pharyngeal arch** – endochondral ossification of Reichert cartilage:
  - **stapes**

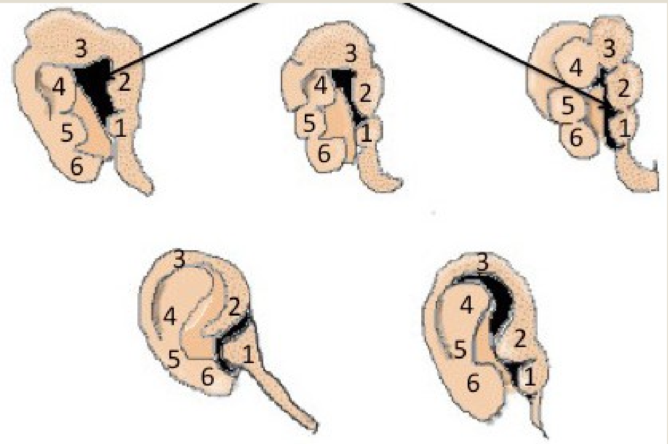


Scott Gilbert. Developmental Biology 10th edition

Development of external ear

- external canal, auricle, tympanic membrane
- epithelium of **1. pharyngeal arch cleft** (**ectoderm**)
  - **External auditory canal**
  - **partly tympanic membrane** and **auricle**
- **proliferation** of pharyngeal cleft **cells –** formation of **transitional epithelial plug** of ear canal - **meatal plug**
- **ectodermal** wall get to **contact** with **endodermal** wall, **separated** by thin **mesenchymal** layer – basis for formation of **tympanic membrane**
- in human – **external ear** (**auricle**) develops from **mesenchyme of 1. and 2. pharyngeal arch** covered by **ectoderm** – basis for 6 **auricular swellings**



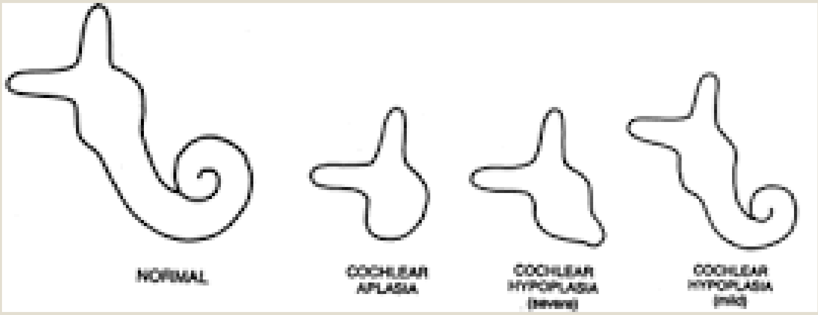


Edited: McGeady et al. Veterinary Embryology. 2009

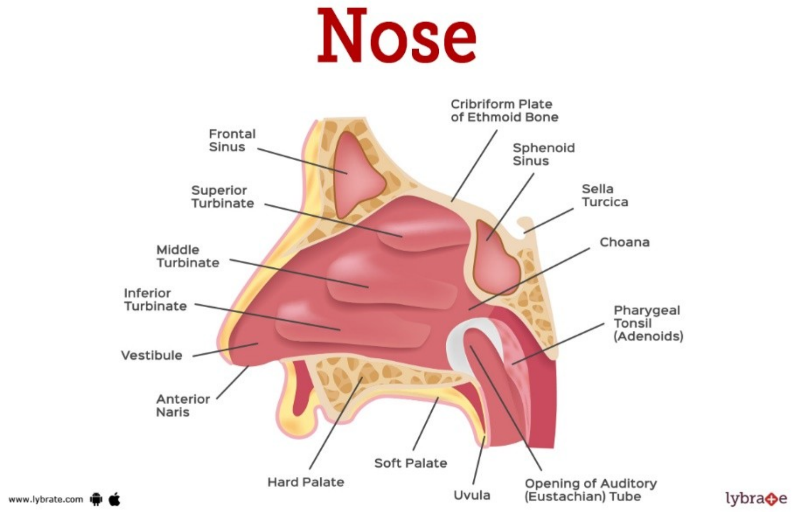
Developmental defects of ear

- **Anotia/microtia**
  - Insufficient development of auricle and external auditory canal
  - Anotia – complete missing of external ear (rare)
  - Microtia – small insufficiently developed ear

- **Cochlear aplasia/hypoplasia**
  - Altered development of middle ear labyrinth and adjacent structures
  - Aplasia – complete absence of cochlear and vestibular apparatus
  - Hypoplasia – smaller cochlear and vestibular apparatus

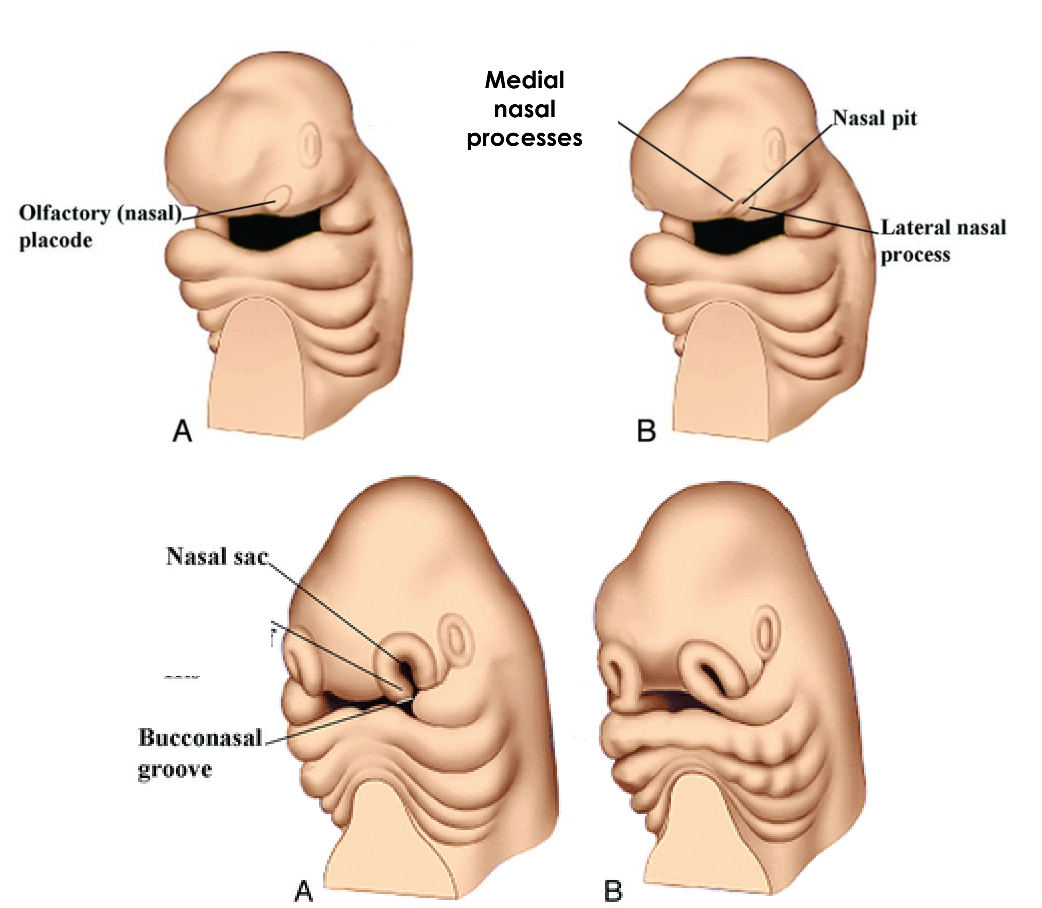


NOSE


Nose
Cribriform Plate of Ethmoid Bone
Frontal Sinus
Sphenoid Sinus
Superior Turbinate
Sella Turcica
Choana
Middle Turbinate
Inferior Turbinate
Pharygeal Tonsil (Adenoids)
Vestibule
Anterior Naris
Soft Palate
Hard Palate
Uvula
Opening of Auditory (Eustachian) Tube
www.lybrate.com
lybrate

Development of nasal cavity

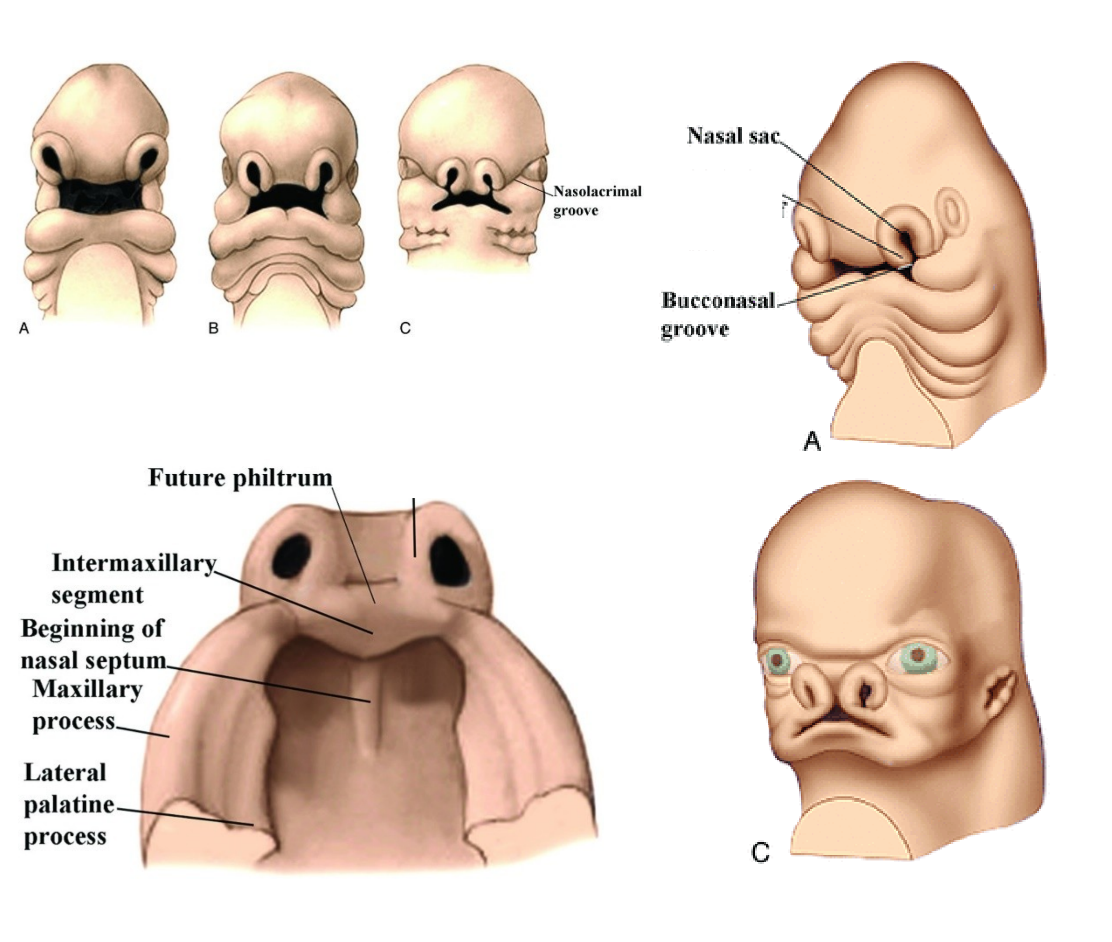
- formation of **nasal placodes** – **ectodermal thickening**, epithelium growth and mesenchymal proliferation around placodes
- Placode **deepening** – formation of **nasal pit**, **lateral nasal processes** on sides, **medial nasal processes** are formed **later**
- deepening and extension of nasal pit – **nasal groove**
- deepening of nasal groove, approaching stomodeum – formation of **nasal sac**



Som and Naidich, 2013. Am J Neurorad

Separation of primitive nasal and oral cavities

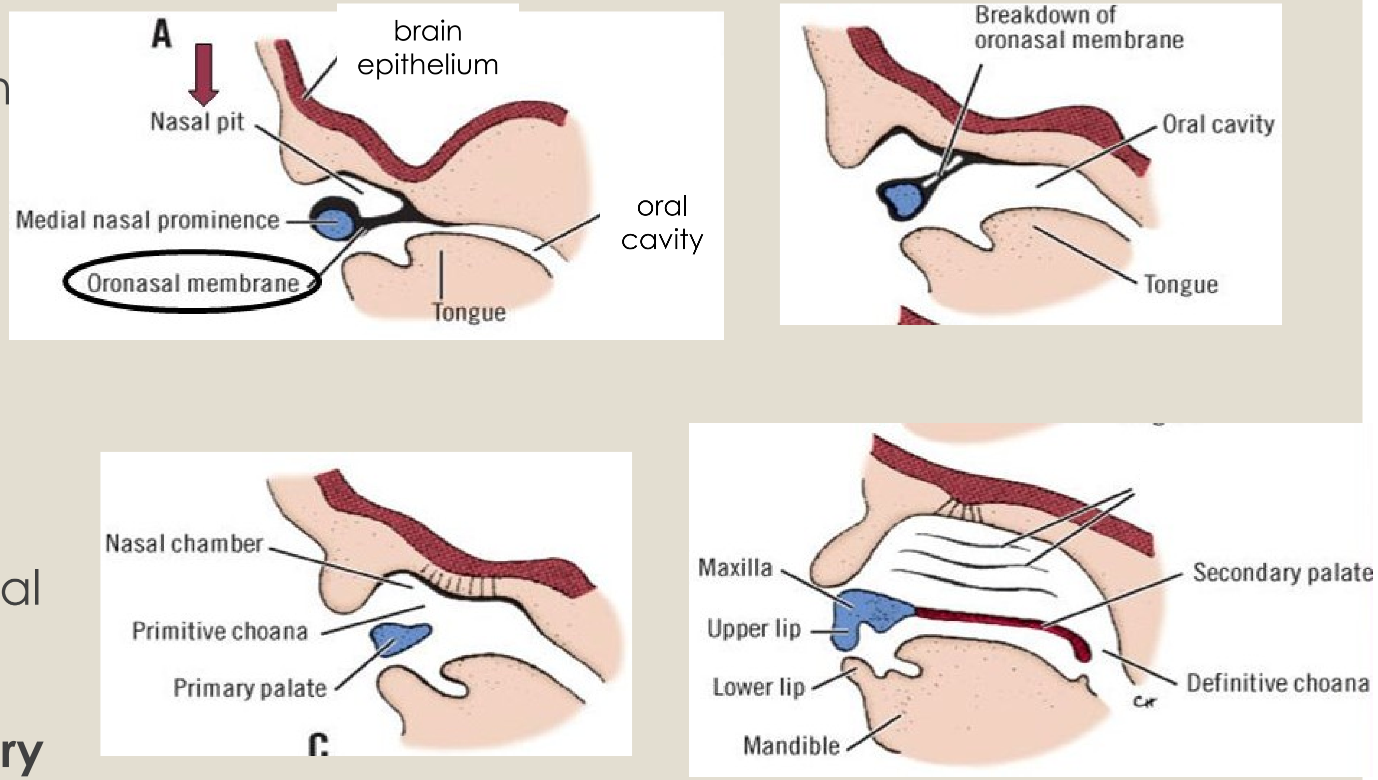
- **maxillary** prominences grow **medially** – nasal **sacs** are pushed **medially**
- medial nasal prominence form **intermaxillary segment**
- **closing** space between **maxillary** and **medial nasal prominences** – **buconasal groove** disappears → **closing** of the **nasal sac** lower part
- primitive nasal and oral cavities **separated**



Som and Naidich, 2013. Am J Neurorad

Formation of nasal and oral cavities

- primitive nasal cavity epithelium **grows to** underlying **mesenchyme** – formation of **oronasal membrane** (connection of primitive nasal and oral epithelium)
- **differentiation** of the **olfactory epithelium** dorsally
- **oronasal membrane breakdown**
- **communication** between oral and nasal cavitites through **primitive choana**
- **secondary palate** formed from **maxillary prominences**, **definitive choana** formed caudally



McGraw-Hill, 2006

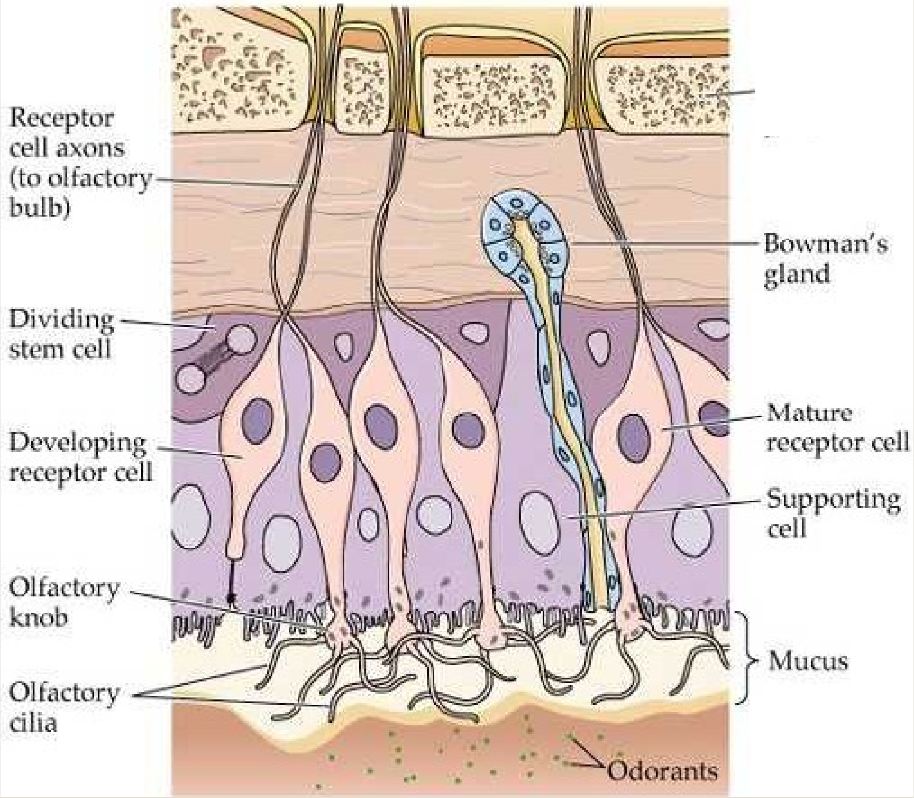
Differentiation of olfactory epithelium

- **dorsal** part of **nasal cavity** – differentiation of **olfactory epithelium**
- 2 sources:
  - **ectoderm** – sensory bipolar neurons, basal epithelial cells
  - **neural crest** – ensheathing supporting cells

- **Sensory bipolar** neurons:
  - **1. outgrowth** – nasal cavity
  - **2. outgrowth** – axon leading to olfactory lobe in brain

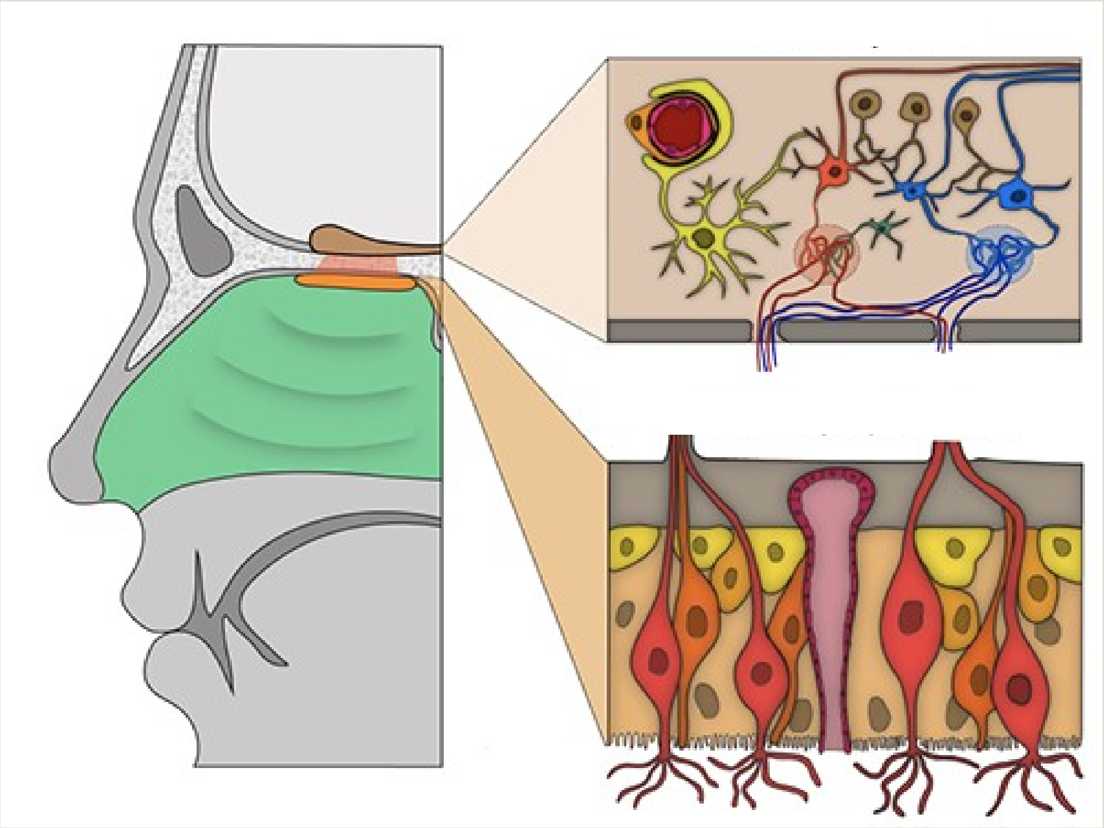
- **basal** epithelial cells – **stem cells** of **sensory olfactory neurons** (basis for recovery of sensory neurons)

- **Supporting cells** – **glial** cells of sensory olfactory neurons

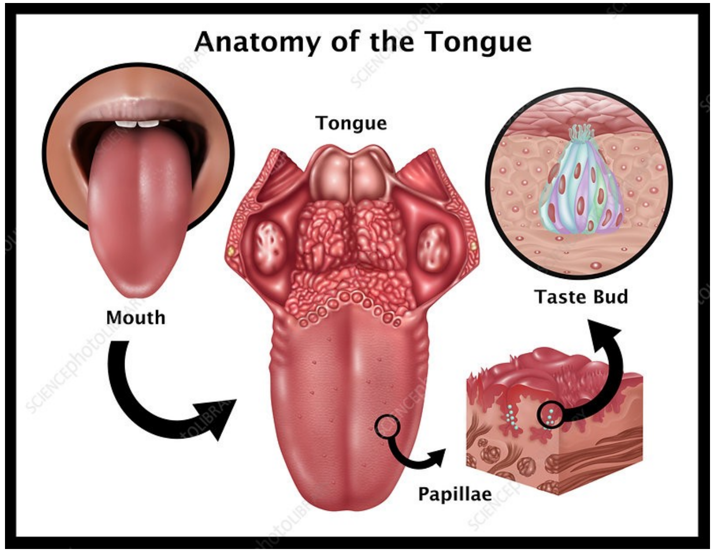


Developmental defects of olfactory epithelium

- **Anosmia/hyposmia**
  - Altered development of olfactory epithelium
  - Mostly no differentiation of olfactory epithelium
  - Defective communication between epithelium and brain
  - Can be also caused by infections – ability to regenerate
  - Anosmia – complete absence of olfactory epithelium
  - Hyposmia – partial defect in olfactory epithelium differentiation

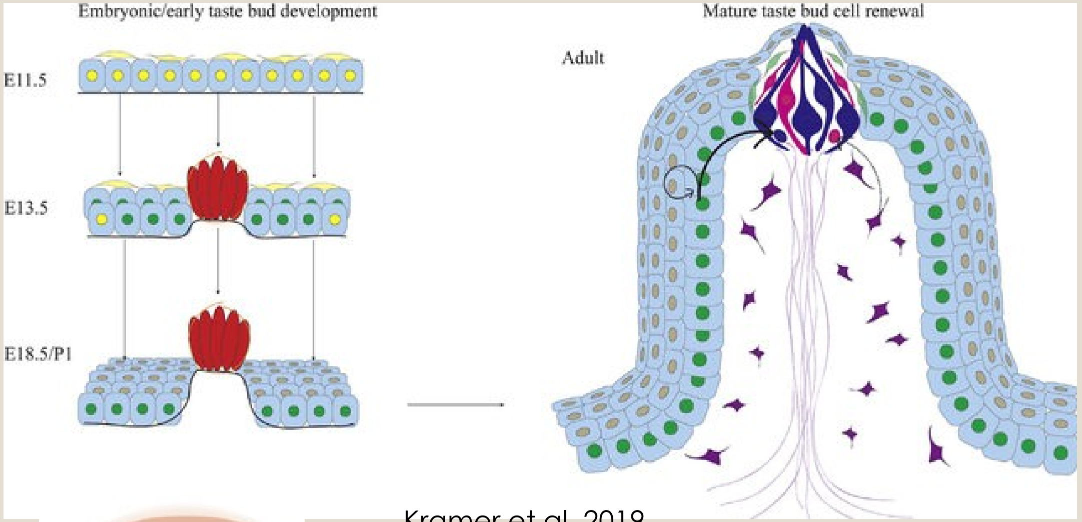


TASTE

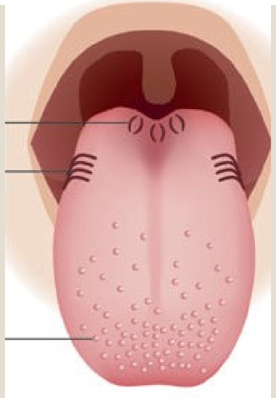


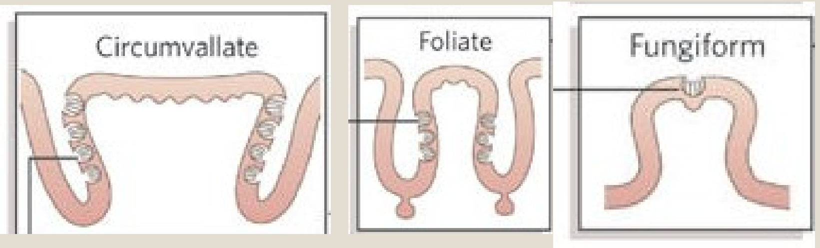
Development of taste system

- formation of **taste placodes** – **cylindrical cells** in cubic tongue epithelium – **invagination** to underlying mesenchyme – **taste papilla**
- **taste papilla** – mesenchymal basis covered by epithelium
- cells in placode and adjacent epithelial cells undergo morphogenesis which give rise to morphologically diverse taste papilla:
  - **circumvallate** – posterior tongue
  - **foliate** – lateral tongue
  - **fungiform** – anterior tongue
- epithelial placodal cells in papilla **differentiate** to **sensory** cells and form **taste buds**



Kramer et al. 2019

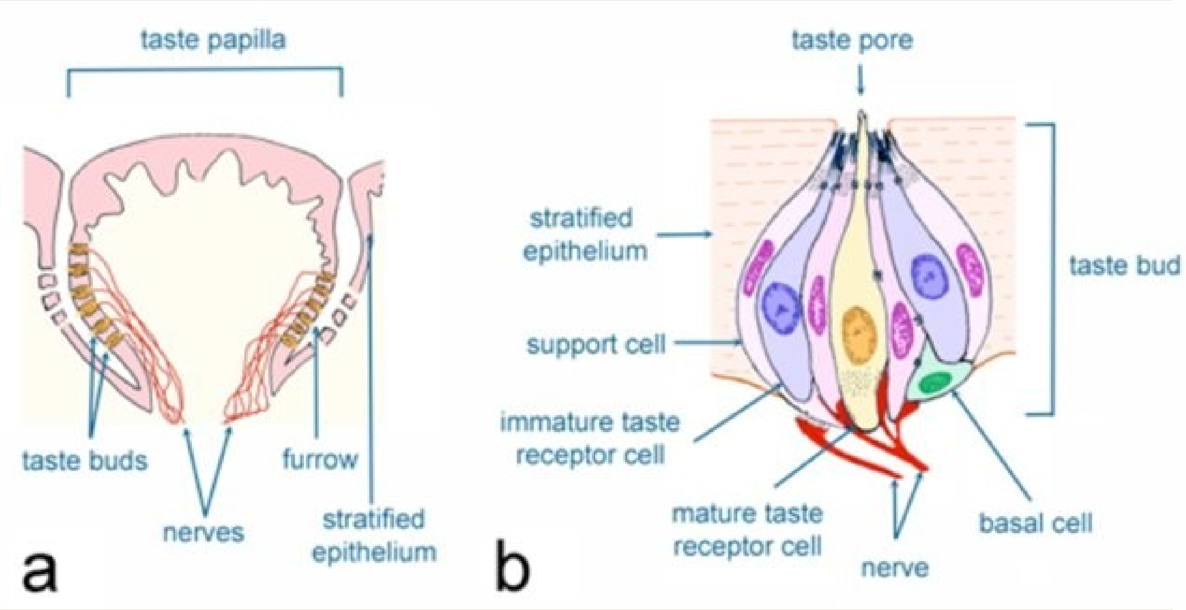




Chandrashekar et al. 2016.
Nature

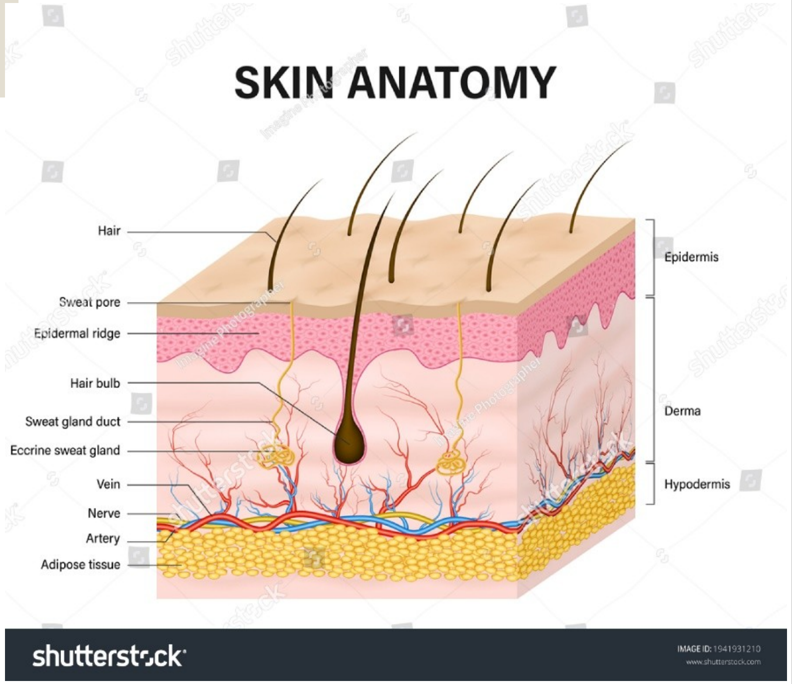
Cells forming taste bud

- taste buds localized in multilayered epithelium, taste bud **connected** with oral cavity through **taste pore**
- **Receptor** cells – individual types of receptor taste cells, connected to afferent sensory nerve fibers, differentiate from ectoderm
- **Support** cells – glia-like cells covering receptor cells
  - most numerous
  - develops from precursors originating in neural crest
- **Basal** cells – stem cells of taste buds – ability to recover taste cells



Pagella et al. 2014. Cell Mol Life Sci

INTEGUMENT



SKIN ANATOMY
Hair
Sweat pore
Epidermal ridge
Hair bulb
Sweat gland duct
Eccrine sweat gland
Vein
Nerve
Artery
Adipose tissue
Epidermis
Derma
Hypodermis
shutterstock

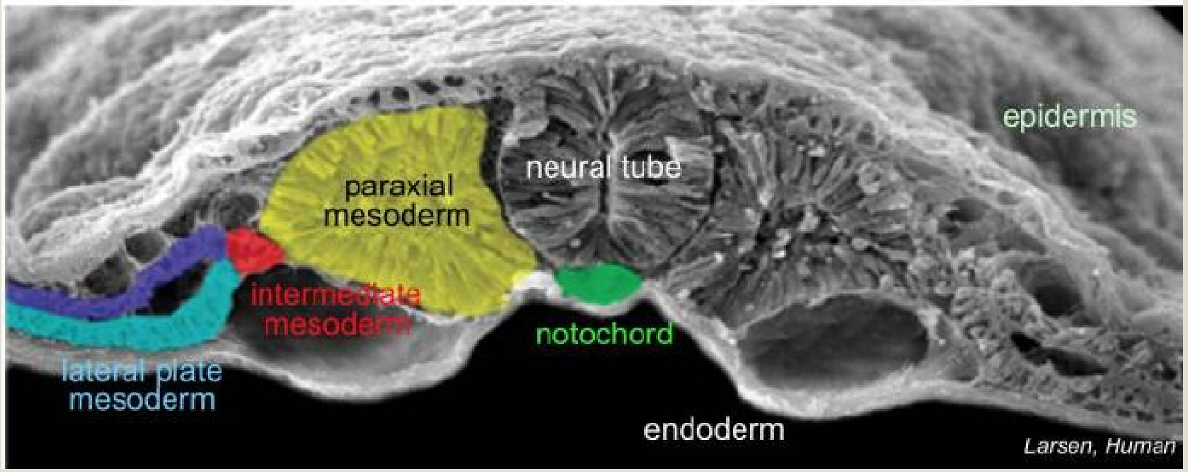
Functions of skin

- formation of outer layer of individuals body and other structures (hair, fingernails, feathers)

- Formation of protective layer with multiple functions:
  - barrier against physical, chemical, mechanical and biological factors
  - termoregulation
  - secretion
  - immune response
  - pigmentation

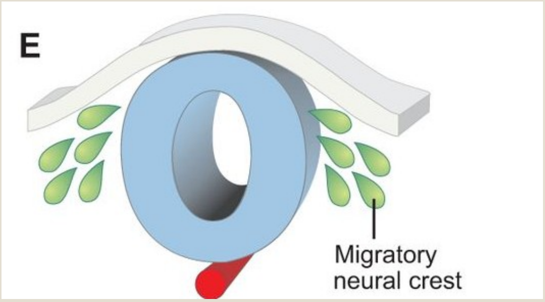
Origin and development of skin and its derivatives

- main source for development of external surface:
  - epidermis - **ectoderm**



Introduction to Anatomy and Development, University College London

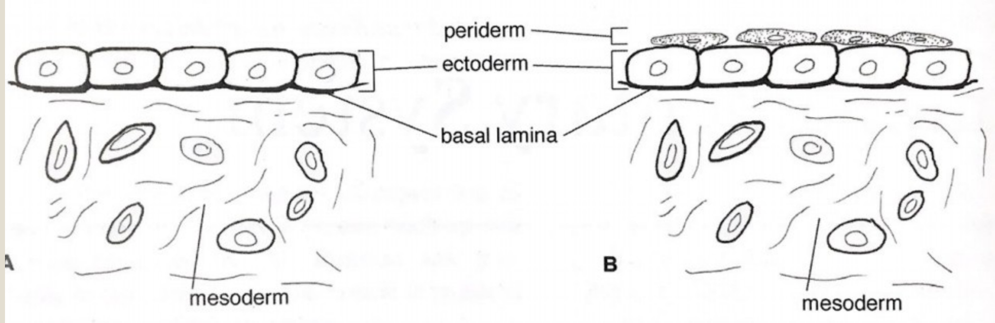
- **dermis**
  - **paraxial mesoderm** – trunk
  - **somatic** part of **lateral plate mesoderm** – trunk, limbs
  - **cranial neural crest** - head

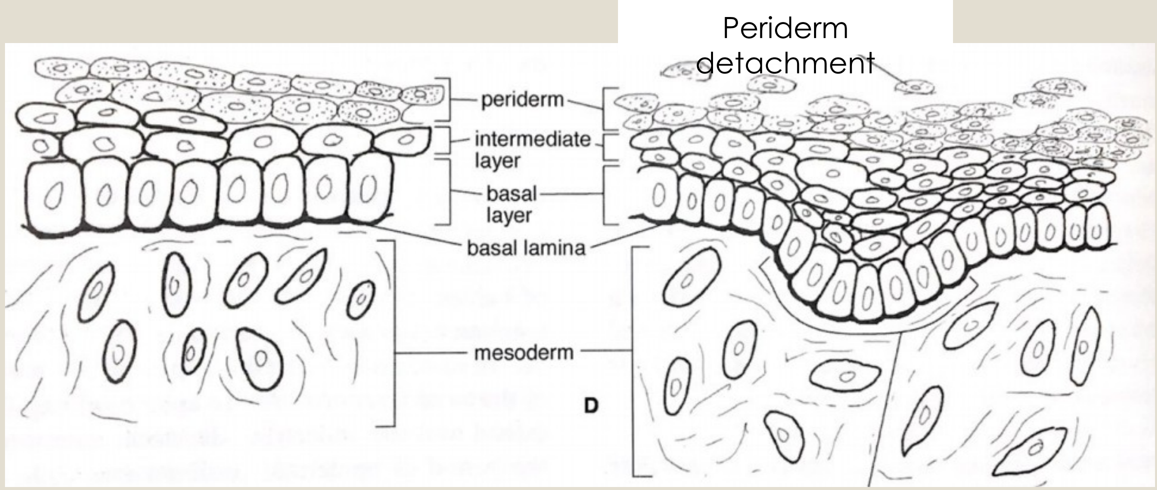


Green et al. 2015. Nature

Epidermis development

- epidermis – **outer** layer of skin
- cuboidal epithelium, basal membrane in **contact** with mesenchyme
- after neurulation – 2 layers:
  - **Basal layer** – cuboidal epithelium, mitotically active
  - **periderm** – flat cells on surface, first **differentiation** of basal cells, cover developing body
- **Basal** cells **proliferate** – formation of **intermediate** layer – onset of **multilayered** epidermis formation
- Basal layer cells **differentiate** into cells specific for individual **layers**
- during differentiation – **peridermal** cells **detach** from **epidermis surface**

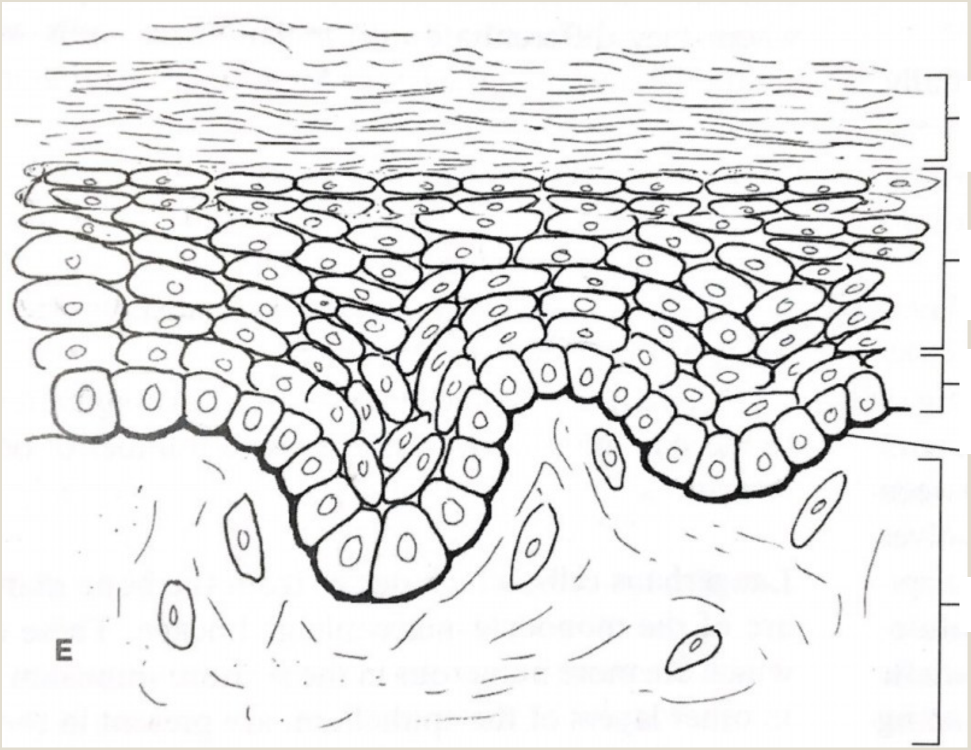




Edited: McGeady et al. Veterinary Embryology. 2009

Epidermis development

- **differentiation** of **basal** cell layer below the periderm – formation of epidermis **layers**:
  - stratum **basale**
  - stratum **spinosum**
  - stratum **granulosum**
  - stratum **corneum**
- **differentiation** of **basal** cells **induced** by **factors produced** in underlying **mesenchyme** (mesoderm) – formation of **keratinocytes** in epidermis (keratin production)
- formation of **keratinizing multilayered squamous** epithelium
- **melanoblasts migration** (neural crest) to forming epidermis – formation of **melanocytes** (**pigment** production), or migration of **Schwann cell precursors** (also formation of **melanocytes**)



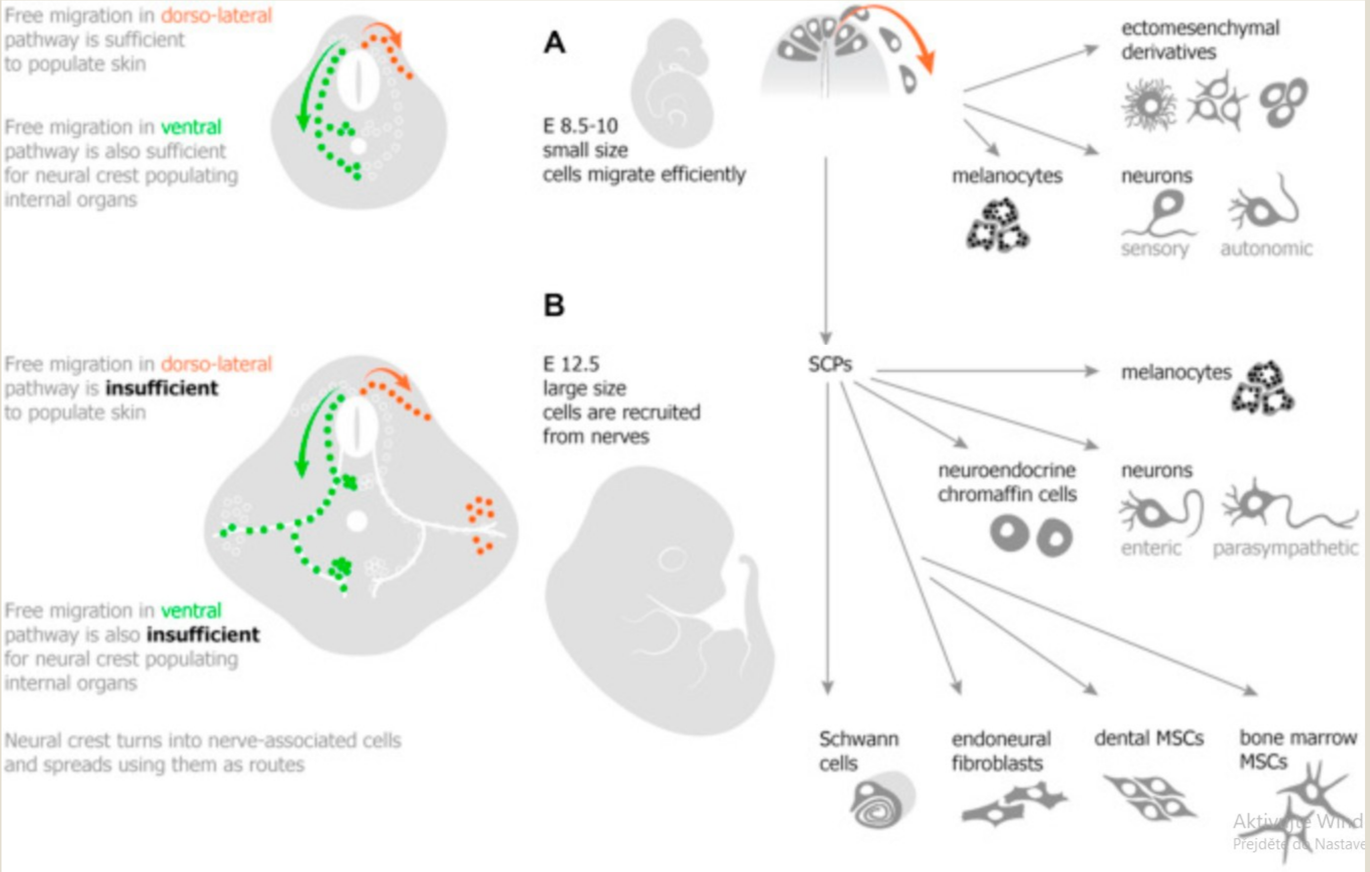
Edited: McGeady et al. Veterinary Embryology. 2009

Migration – important mechanism for development of diverse tissues and organs

free migration – **small** body size (earlier then E12 stage), cells migrate **efficiently**

perineural migration – **large** body size (later then E12 stage), cells do **not** migrate **efficiently** – participation of **nerves**

Schwan cell precursors (SCPs) – migrating precursors for different cell types



Furlan and Adameyko, 2018

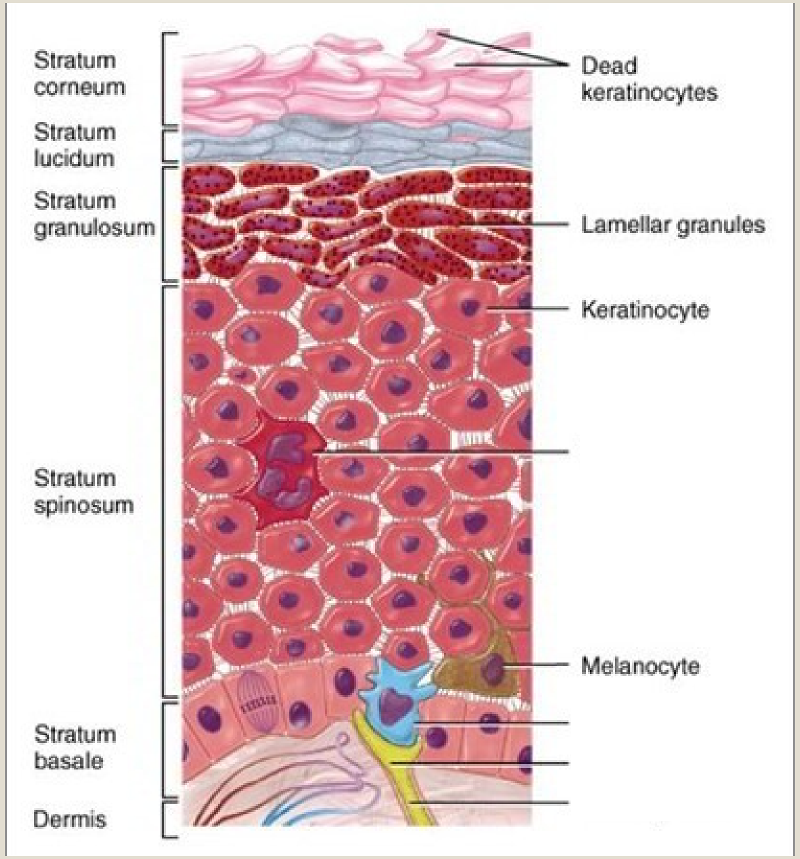
Epidermal layers

- **Stratum basale** – cuboidal to cylindrical cells, stem cells and keratinocytes, melanocytes, proliferating cell layer - regeneration of epidermis

- **Stratum spinosum** – the thickest layer formed of kerytinocytes, in deeper layers proliferating cells, cells produce keratin fibers and flatten
- **Stratum granulosum** – multiple layers of flat keratinocytes, contain keratohylian granules

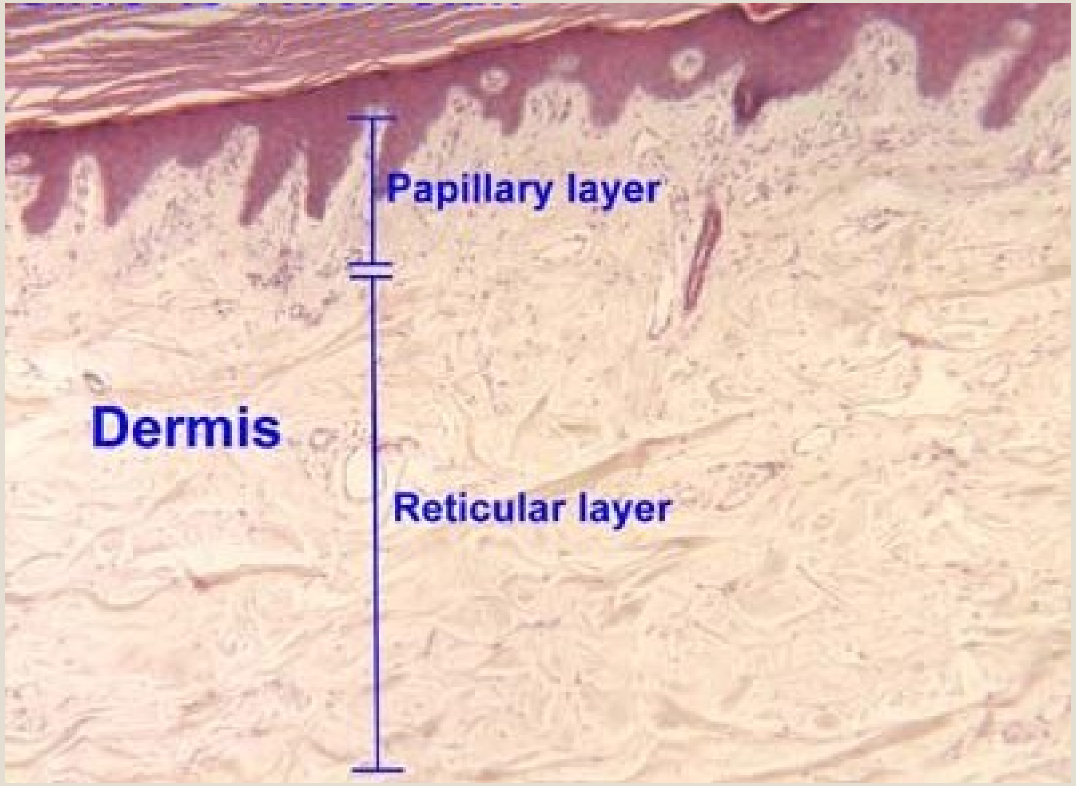
- **Stratum lucidum** – tightly connected keratinocytes without nuclei and organeles

- **Stratum corneum** – multiple layers of dead keratinizing cells, formation of durable and strong surface



Dermis development

- dermis – layer underlying the epidermis
- Formed from different sources:
  - **paraxial mesoderm** – basis for **dermis** formation in **trunk** region
  - **somatic lateral plate mesoderm** – basis for **dermis** development in **trunk** and **limbs**
  - **Cranial neural crest** – basis for **dermis** in **head** region
- **mesenchymal cells** of dermis **differentiate** to **fibroblasts** (connective tissue cells)
- fibroblasts produce **collagen** and **elastic fibers**
- surface **papillary** layer – **loose** connective tissue
- underlying **reticular** layer – **dense** connective tissue, large amount of collagen and elastic fibers
- localization of **nerves**, **vessels**, **glands** and hair **follicles**



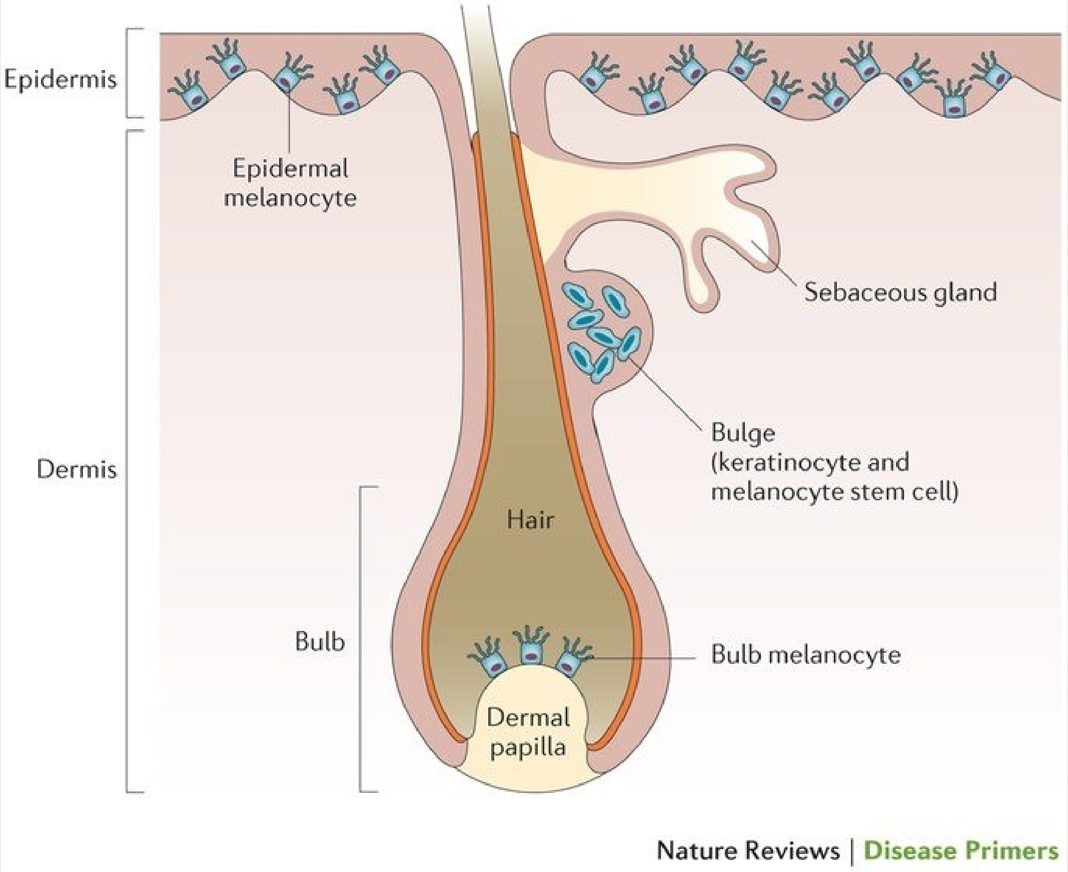
Developmental defects of skin

- **Congenital skin aplasia** (aplasia cutis congenita)
  - congenitally missing skin
  - local or the whole surface
  - The most often - missing skin on head
  - patogenesis not clear – caused by drug use and other substances during pregnancy
  - insufficient closure of surface ectoderm
- **Cephalocele**
  - permeation of intracranial structures through opening in the skull
  - caused by insufficient separation of neuroectoderm from surface ectoderm
  - formation of sac filled with neural tissue covered by skin

Origin and development of hair follicle

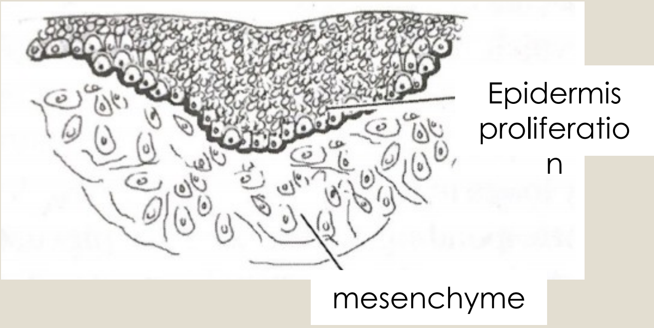
- Origin of hair follicle:
  - **basal** layer of **epidermis** (ectoderm) **grows through** the underlying **mesenchyme** (dermis - mesoderm or neural crest)
  - formation of hair **follicle**

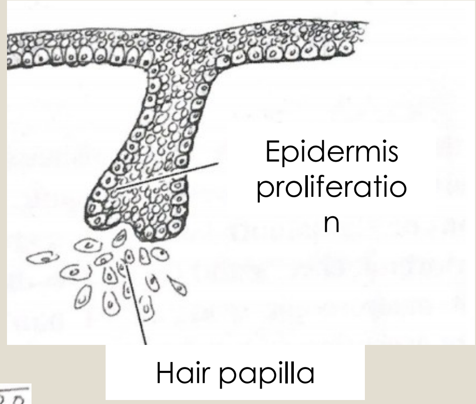
- **stages**:
  - epidermal placode
  - hair bud
  - hair bulb
  - hair cone
  - hair

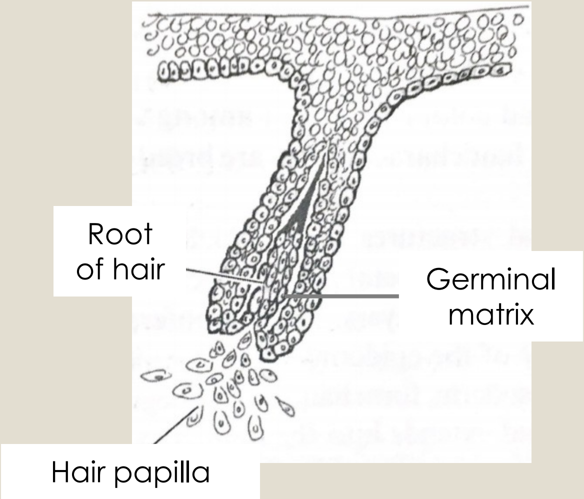


Developmental stages of hair

- formation of **epidermal thickening** - **placode** in epidermis
- epidermal placode cells rearrange, proliferate and **invaginate** to underlying mesenchyme – formation of **hair bud**
- mesenchymal cells **condensate** around the **bud** region – bud prolongation, mesenchymal cells surrounded by epithelial (**hair papilla**) – formation of **hair bulb**
- **Hair papilla – germ** cells, **matrix** cells, **melanocytes**
- **Hair papila induces** formation of **inner epidermal** cells – formation of **germinal matrix**:
  - Hair **fiber**
  - **epithelial root sheet**
- formation of **cavity** in hair **bulb** – **connection** of germinal matrix and surface



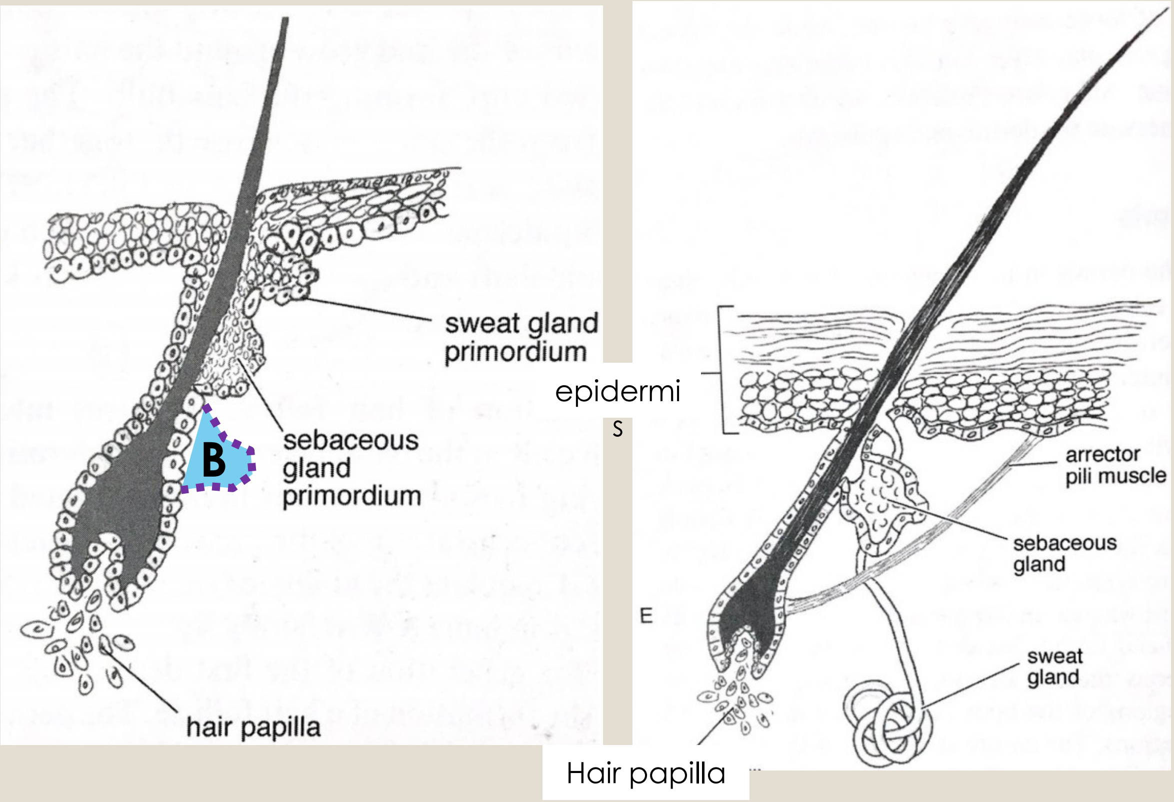




Edited: McGeady et al. Veterinary Embryology. 2009

Developmental stages of hair

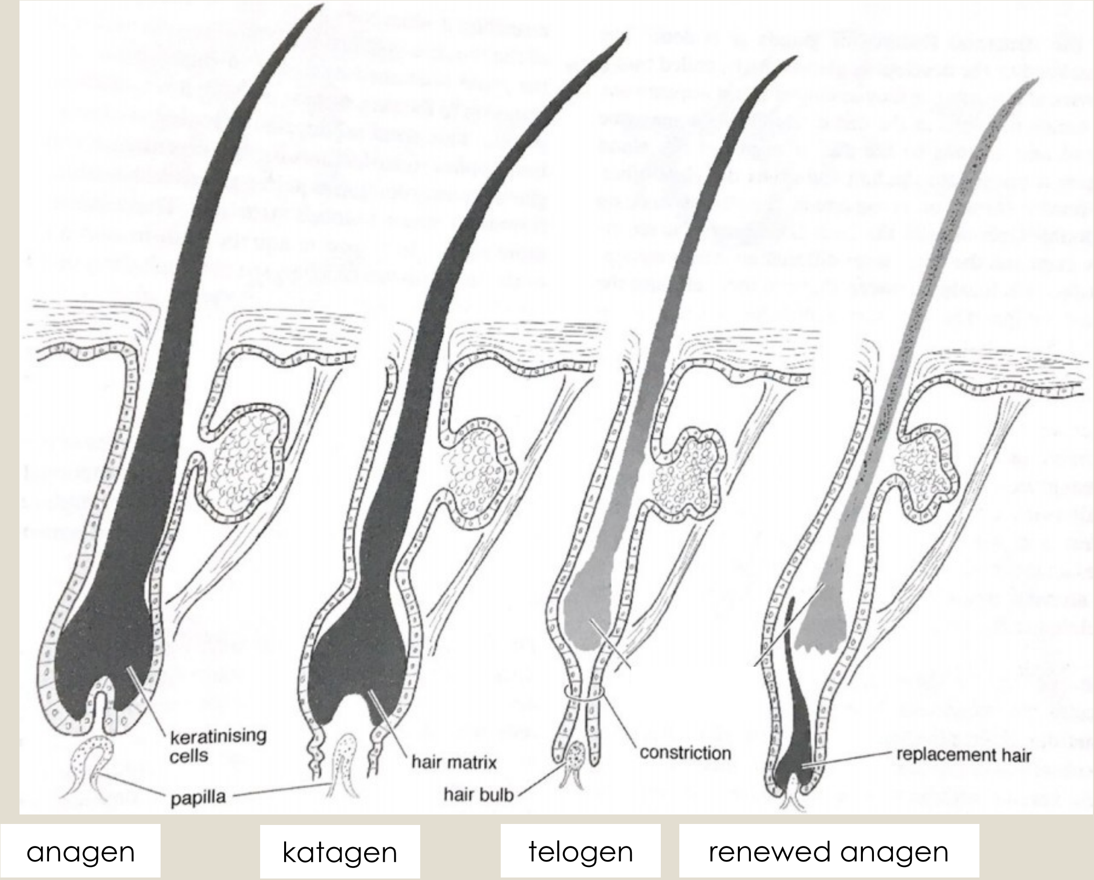
- **outer epidermal** cells line the cavity – **outer hair** sheet, localization of Bulge – hair follicle stem cells
- **germinal matrix** cells – proliferate and transfer to cavity in outer hair sheet – **keratinization** of cells and formation of **hair fiber**
- continuous **proliferation** of **basal cells** in matrix cause **pushing** of the **hair fiber** towards the **surface**
- surrounding **mesenchyme**:
  - connective tissue
  - smooth muscles – **arrector hair fiber** muscle
- **invagination** of **basal epidermal** layer in **hair** region:
  - **sebaceous** glands
  - **sweat** glands



Edited: McGeady et al. Veterinary Embryology. 2009

Hair life cycle

- postnatal – changing proliferation and resting phases:
- **anagen**
  - Active growth
  - Proliferation of papillary cells
- **katagen**
  - regression stage (recess)
  - proliferation in papilla is **inhibited**
  - hair root changed – club-shape
- **telogen**
  - outer epidermal cells **constriction** in **hair root** region
  - hair follicle **attached** by strands of epithelial cells to recessing **papilla**
- **renewed anagen**
  - formation of replacement hair
  - epithelial strands – formation of renewed hair bulb surrounding new hair papilla
  - old hair pushed out by replacement hair



Edited: McGeady et al. Veterinary Embryology. 2009

Developmental defects of hair

- **Congenital hypotrichosis**
  - hair absence during fetal period – often during whole life
  - isolated defect, no other skin defects
  - caused by mutations in genes important for growth, proliferation and differentiation of hair bulb cells

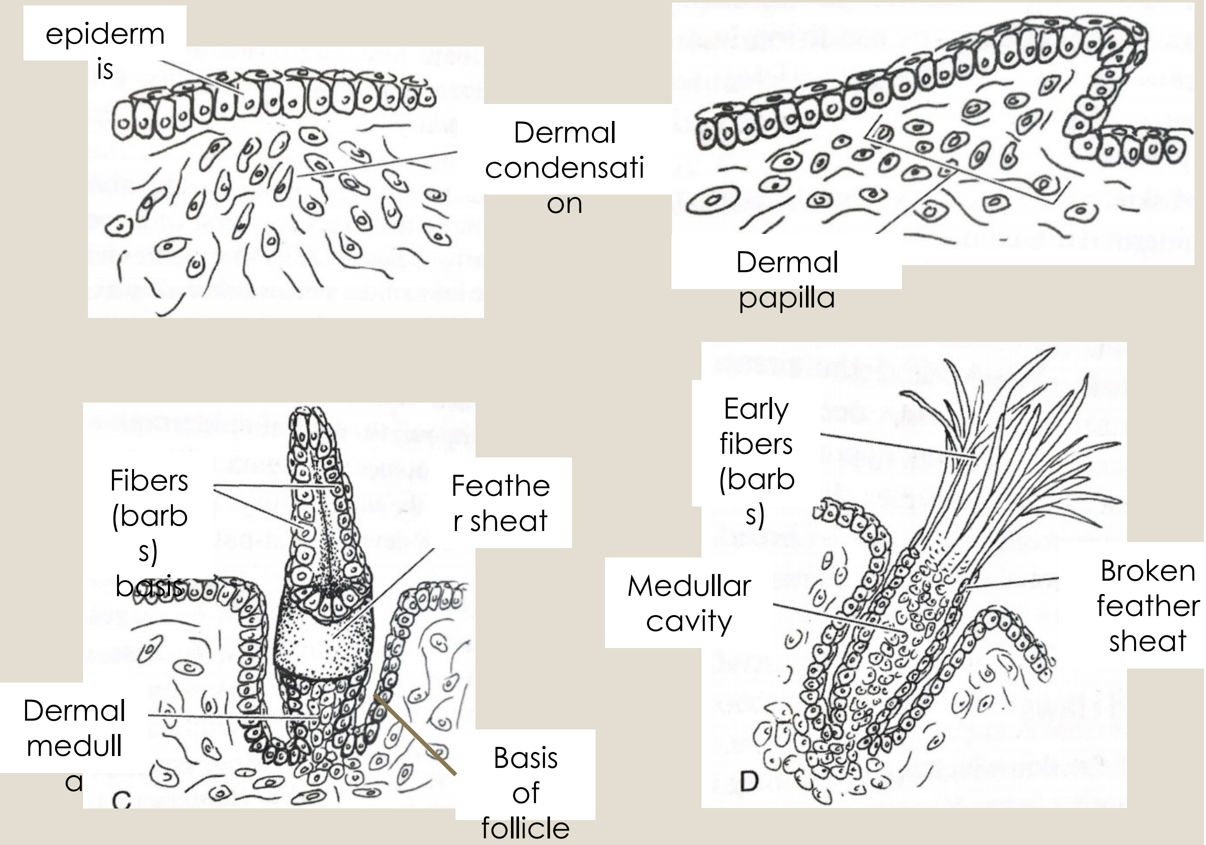
- **Congenital hypertrichosis**
  - also called **Werewolf** syndrome
  - overproduction of hair due to formation of more hair follicles
  - often fetal hair preserved
  - caused by mutation in genes responsible for formation and growth of hair follicles
  - mutations often caused by drug use during pregnancy (antibiotics, anti-inflammatory drugs, immunosuppressive drugs)

Romero and Grimalt, 2014.

Shah et al. 2018. Ind J Dermatol Vener Leprol

Origin and development of feathers

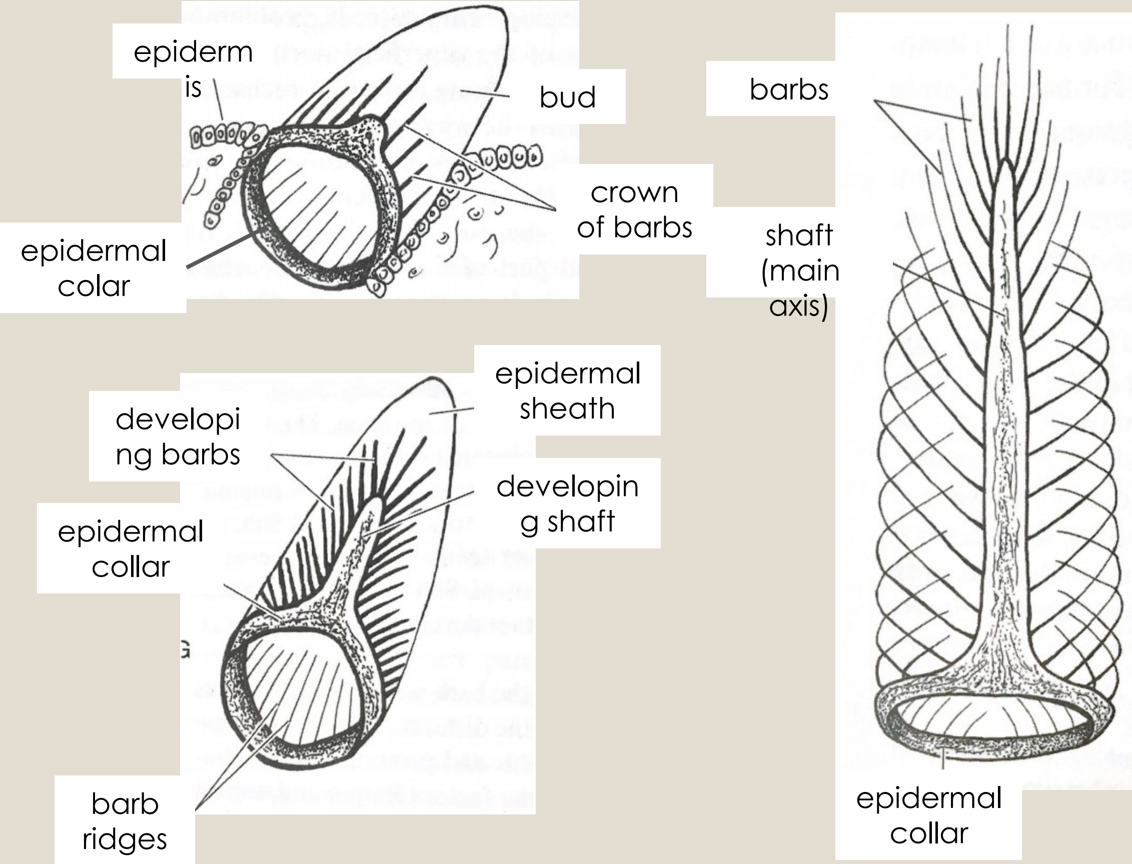
- interaction of **epithelial thickening** (**epidermis** – ectoderm) with condensing **dermal cells** (mesoderm, neural crest)
- formation of conical **papilla** – **epidermal** surface, underlying **dermal papilla**
- **dermal papilla** continuously **push out** covering epidermis – formation of basic **feather bud**
- **invagination** of **epidermal** cells at the **base** of **feather bud** into **dermis** – formation of **follicles** covered with **epidermis** (ectoderm)
- **follicle prolongation** – feather bud tips start to form **protrusions** of follicles (fibers/barbs basis)
- **Down feathers** – basal cells in papilla proliferate – formation of epithelial **colar**, formation of cellular protrusions to medullary cavity
- **separation** of **protrusions** and **keratinization** – formation of individual fibers



Edited: McGeady et al. Veterinary Embryology. 2009

Origin and development of feathers

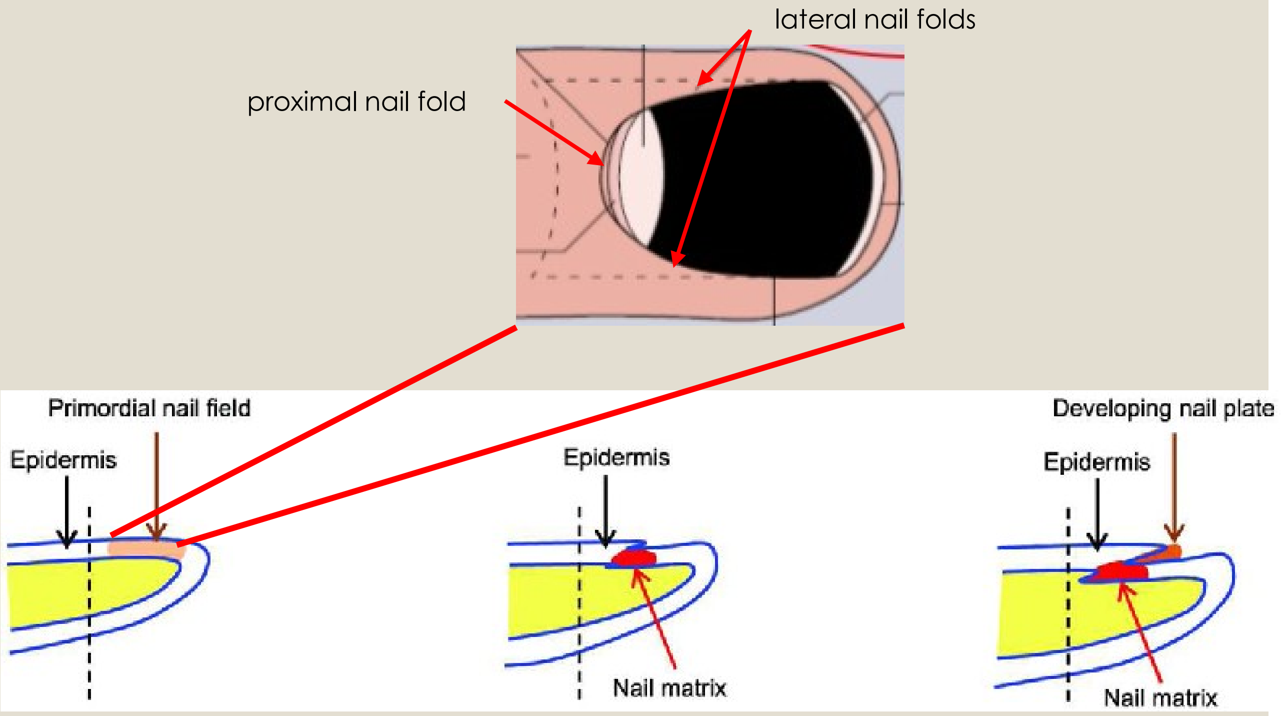
- **contour feathers** – early development **identical** with down
- formation of **epidermal collar** at the base of developing bud
- **proliferation** in the **surface collar** region – formation of basis for **shaft** (axis) of feather – **prolongation** towards **distal** part of bud
- smaller **barbs** outgrow from main **shaft** on both sides – basis for **vane**



Edited: McGeady et al. Veterinary Embryology. 2009

Development of fingernail

- formation of thickened epidermal region (ectoderm) in dorsal region of last (distal) phalanx – **nail field**
- both sides from the nail field – **lateral nail folds** – **overgrow** nail field, connected to **proximal nail fold**
- under the proximal nail fold – formation of **nail matrix** – production of nail-forming **material**
- nail matrix cells are **keratinizing** – formation of **nail plate**
- nail plate grows **distally** over the nail bed towards the end of finger



Cui et al. 2013. J Investig Derm

Developmental defects of fingernail

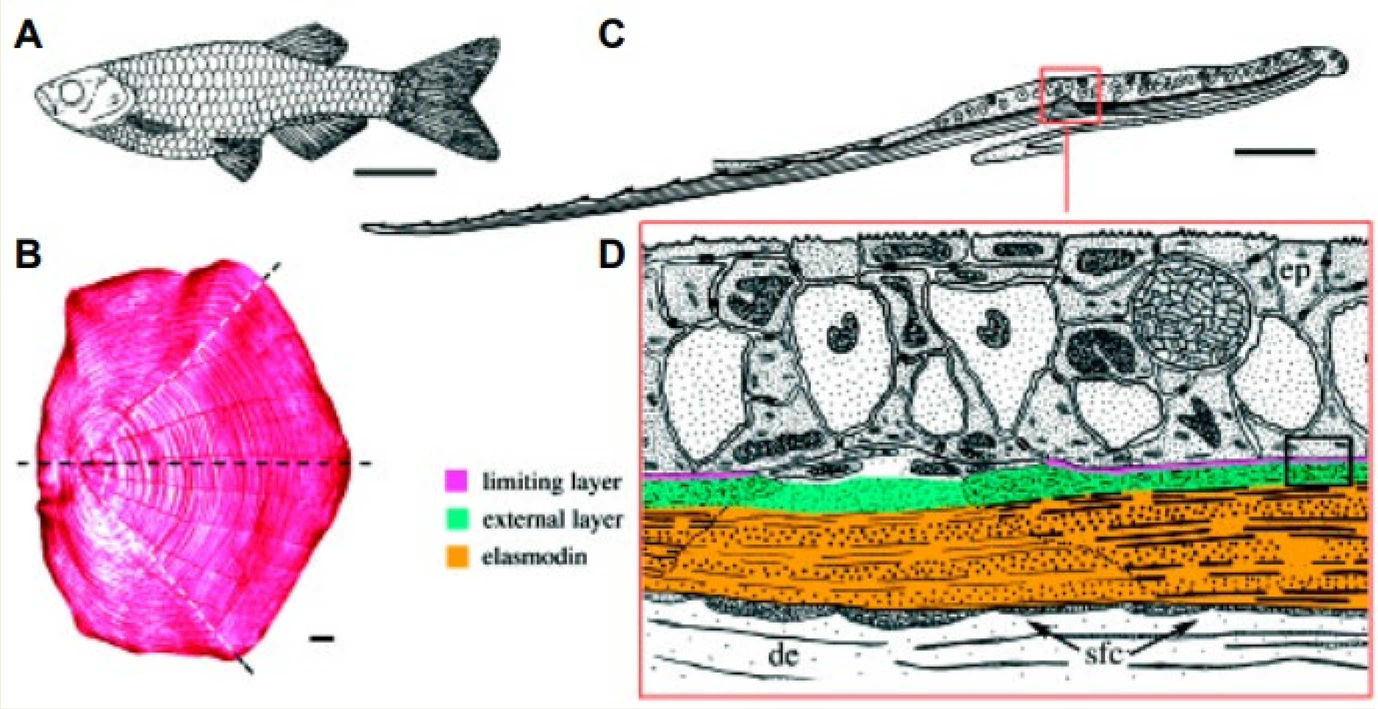
- **Congenital anonychia**
  - partial or total absence of fingernails on feet and/or hands
  - caused by defects in nail matrix formation or inability to produce material for nail formation

Khan et al. 2015. Br J Dermatol

Etensel et al. 2002. Eur J Plast Surg

Origin and development of scales in bony fish

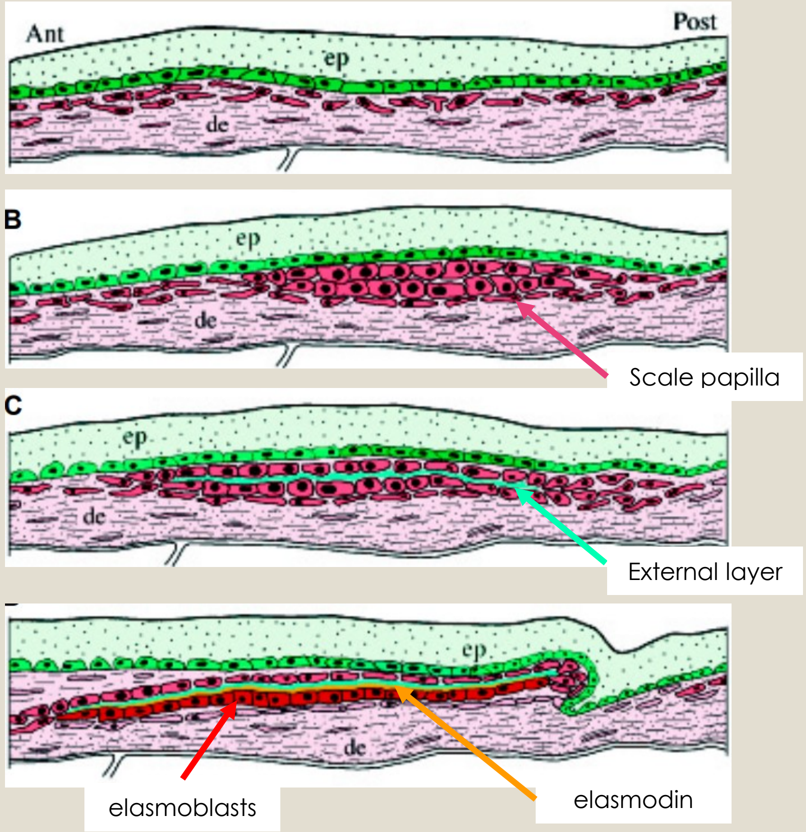
- zebrafish (*Danio rerio*) – formation of leptoid scales – the most often scale type
- **leptoid/elasmoid scales** – concentrically shaped scales formed of 4 layers:
- **elasmodin** – deepest layer, not completely mineralized, formed of collagen fibers in layers (plywood look)
- **External layer** – thin well mineralized layer formed of collagen fibers
- **Limiting layer** – highly mineralized layer with no collagen fibers
- surface layer – formed of **epidermis,** almost the whole surface



Sire and Akimenko, 2004. In J Dev Biol

Origin and development of scales in bony fish

- Interaction of epithelial **epidermal** cells (**ectoderm**) with mesenchymal **dermal** cells (**paraxial mesoderm**) – accumulation of **mesenchymal cells** under the **basal** epidermal layer (**early morphogenesis**)
- **late morphogenesis** – accumulation (condensation) of **mesenchymal cells** in **scale papilla**
- **early differentiation** – upper layers of papilla differentiate to scale-forming cells, accumulation of first scale parts between papilla-forming cells – **external layer**
- **late differentiation** – deeper layers of papilla under the external layer differentiate to **elasmoblasts** – production and accumulation of **elasmodin**
- **bending** and **invagination** – epidermis **bends** around posterior part of developing scale – formation of **overlay** over the **next** scale, in **anterior** part **invagination** of scale to dermis



Sire and Akimenko, 2004. In J Dev Biol

Fun facts

- How quick is the transfer of infos in the brain?
- How many watts can brain generate?
- If eye would be a camera, what woudl be its resolution?
- When ear lobe stop growing?