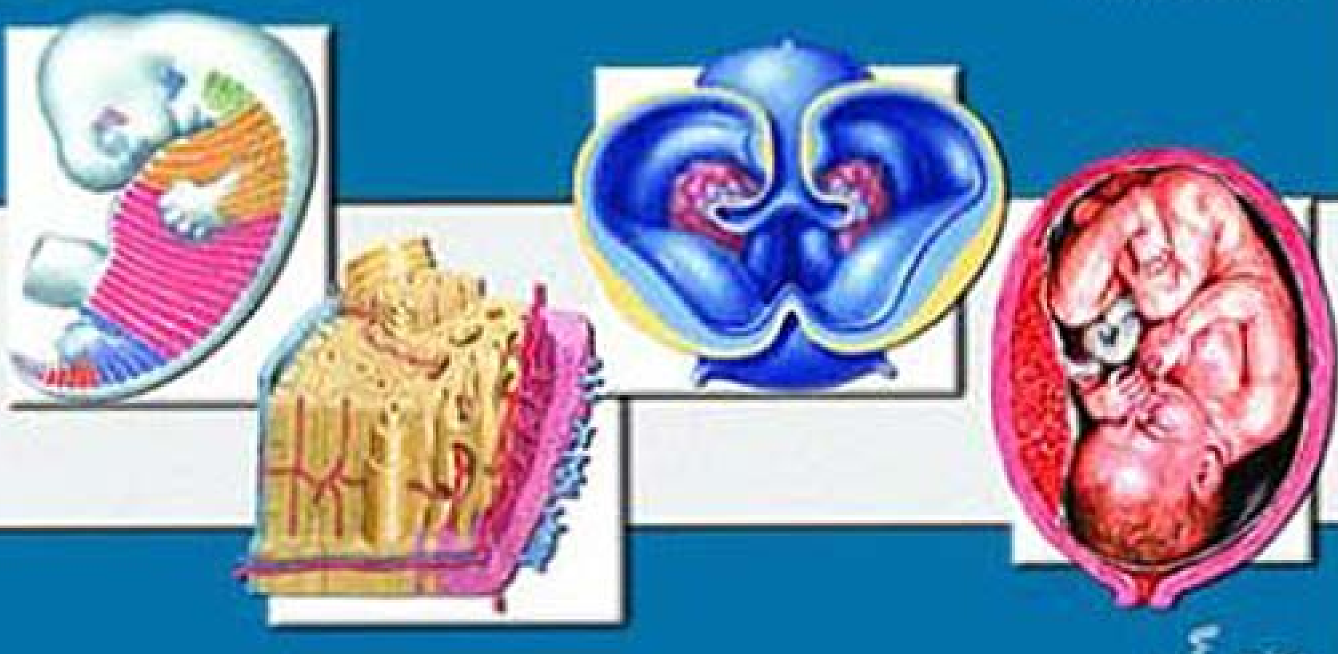
Netter's Atlas of Human Embryology

Larry Cochard



AN OVERVIEW OF DEVELOPMENTAL EVENTS, PROCESSES, AND ABNORMALITIES: TIMELINE

Prenatal Time Scale (Months)

First 2 weeks

Blastocyst

This is a period of cell proliferation from the zygote to the morula, blastocyst, and formation of the bilaminar embryonic disc. Birth defects do not originate in this period because body systems and structures have not yet developed. Teratogens usually cause the loss of the entire conceptus.

Main Embryonic Period

Weeks 3 to 8 is the dynamic period of gastrulation, folding of the embryo, and the formation of all the organ systems. Because this is the most active period of development and differentiation, the embryo in weeks 3 to 8 is most vulnerable to major birth defects.

1

Embryo

2

3

4

Fetal Period

5

Fetus

6

Months 3 to 9 (full term) are mainly characterized by the growth of all the major structures that have already appeared. Birth defects in this period are usually not as severe or obvious and include small size, mental retardation, and defects in the eyes, ears, teeth, and external genitalia.

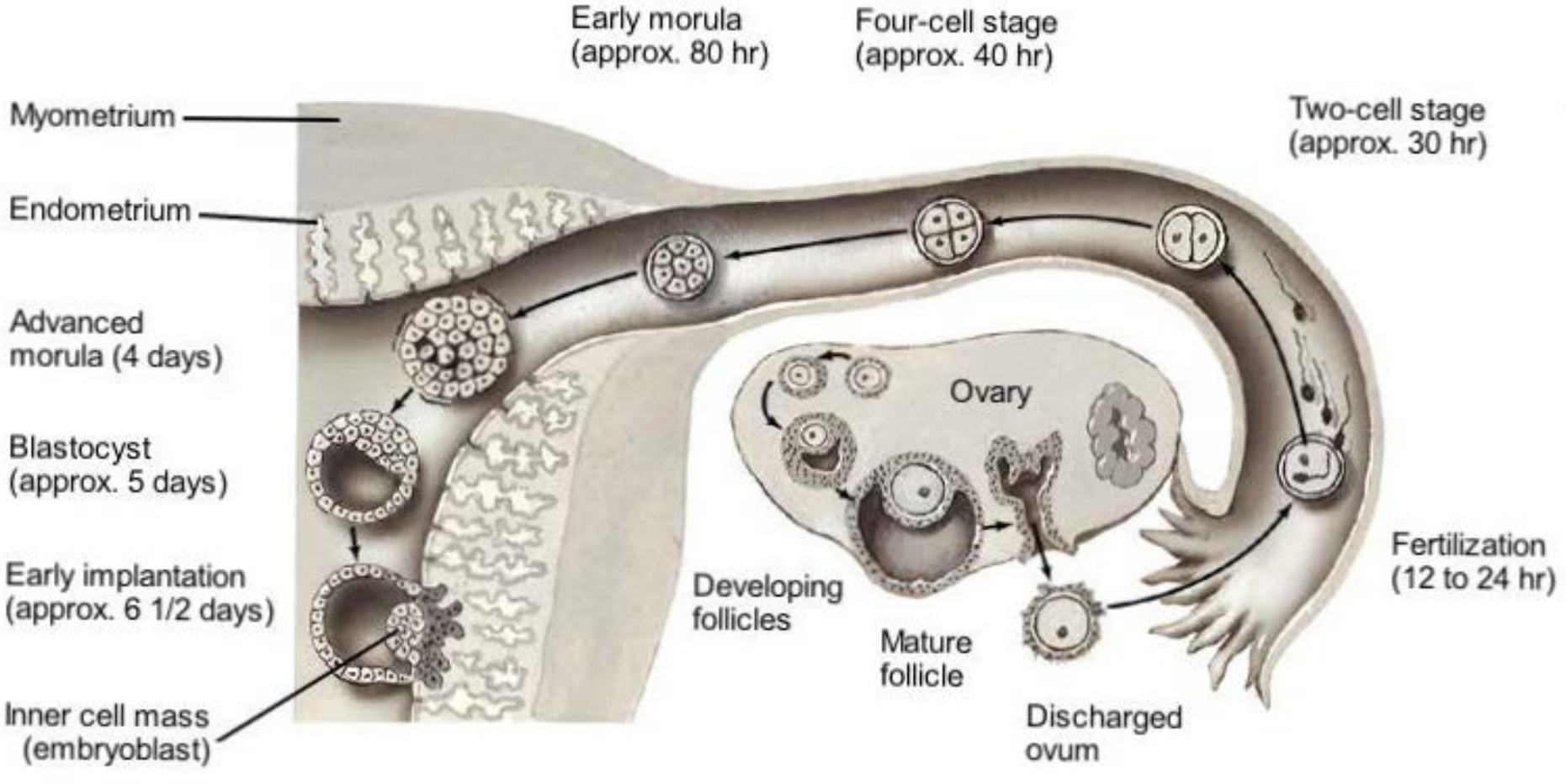
7

8

9

Birth

The First Week



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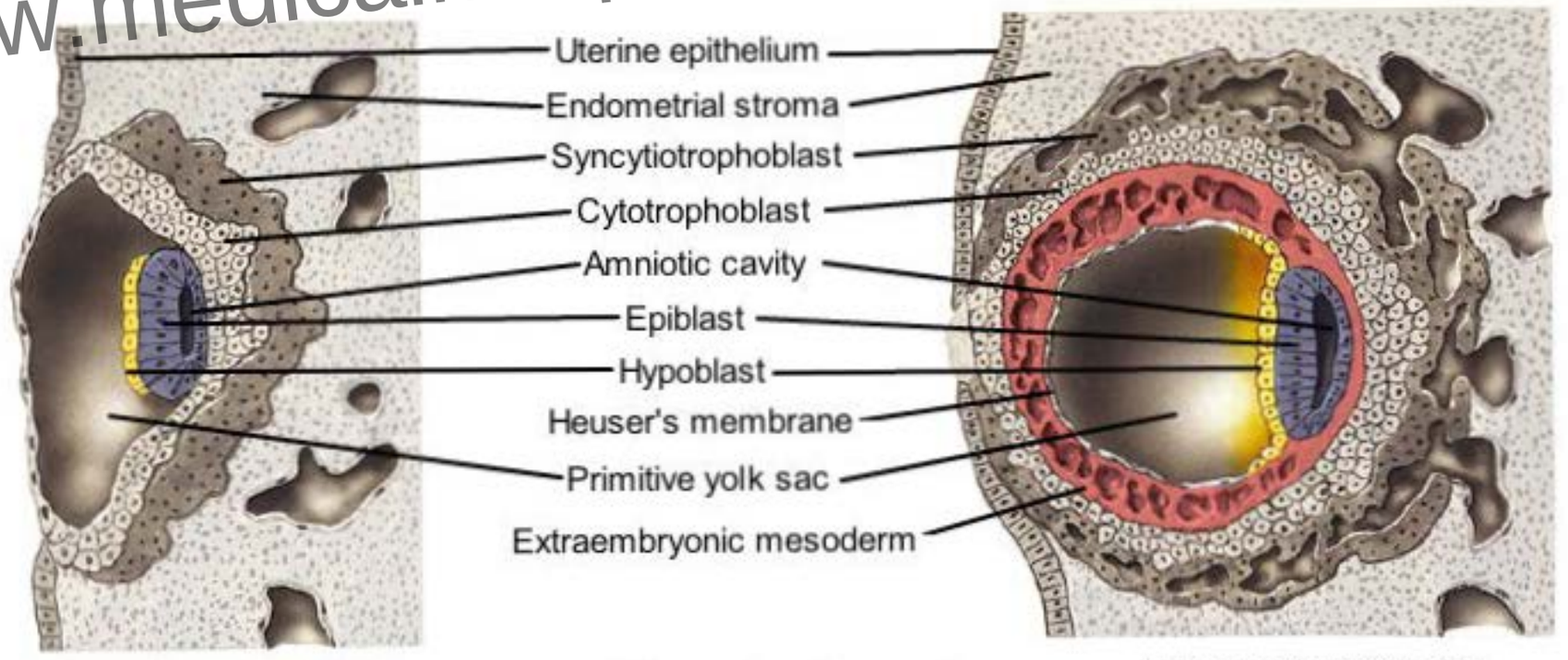
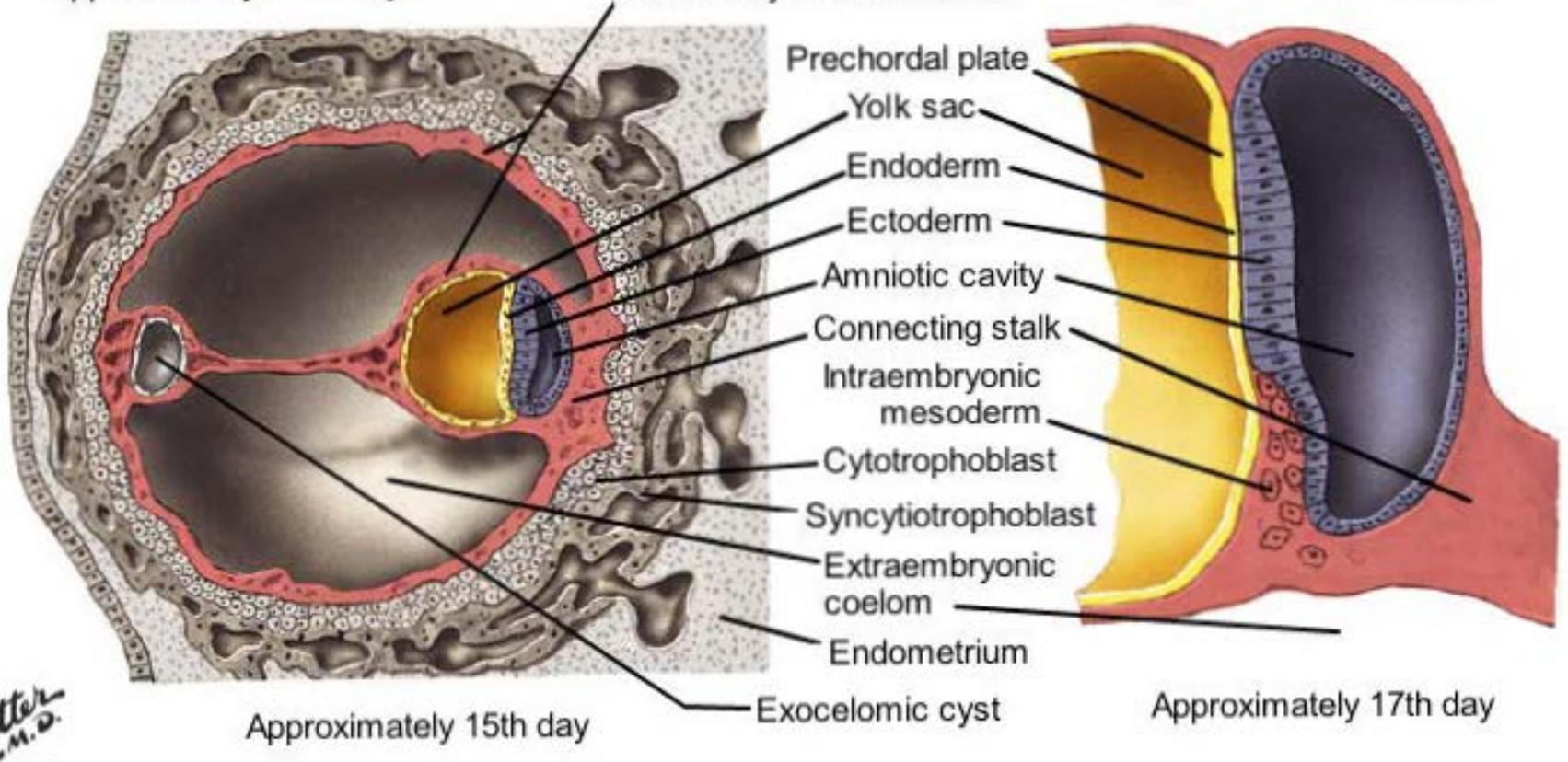
The Second Week



Approximately 7 1/2 days

Approximately 12th day



Approximately 15th day

Approximately 17th day

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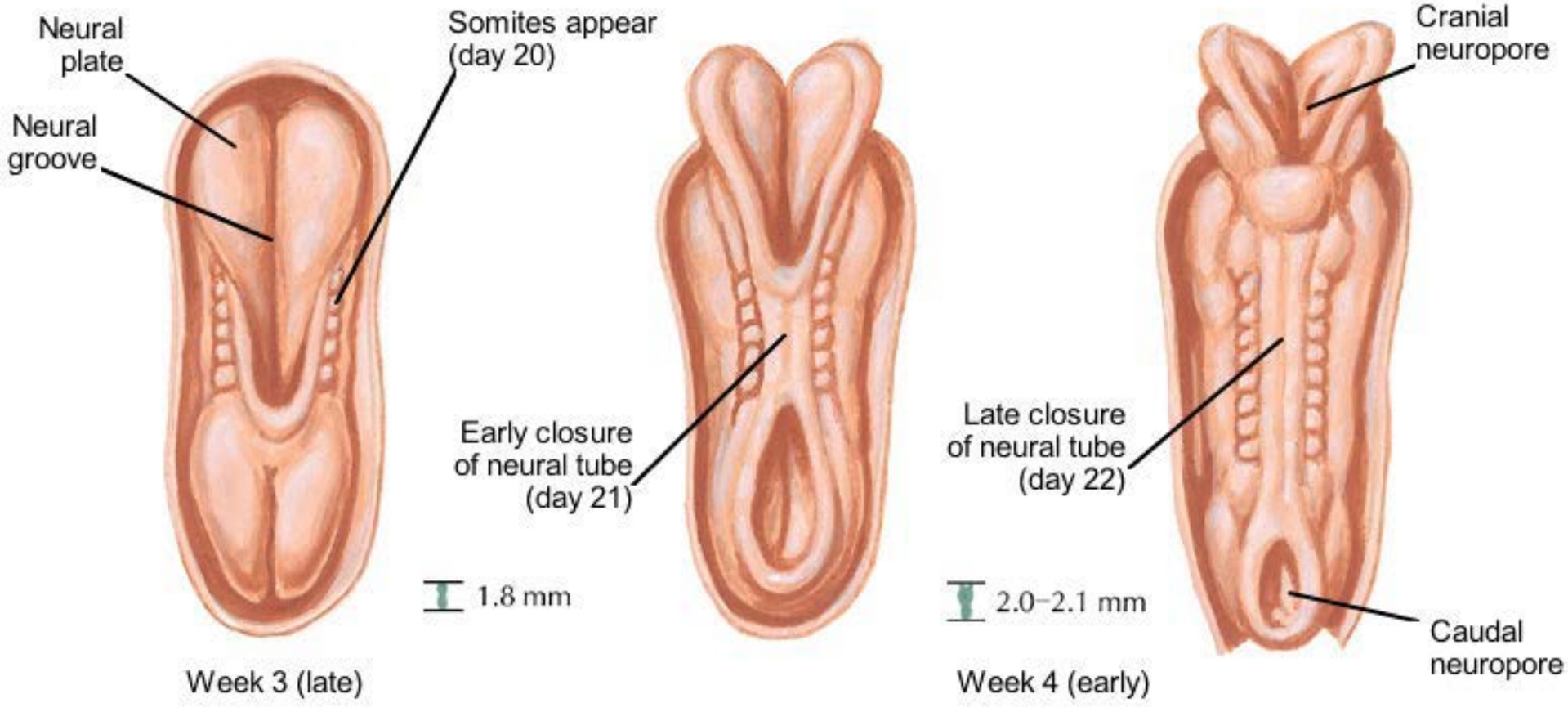
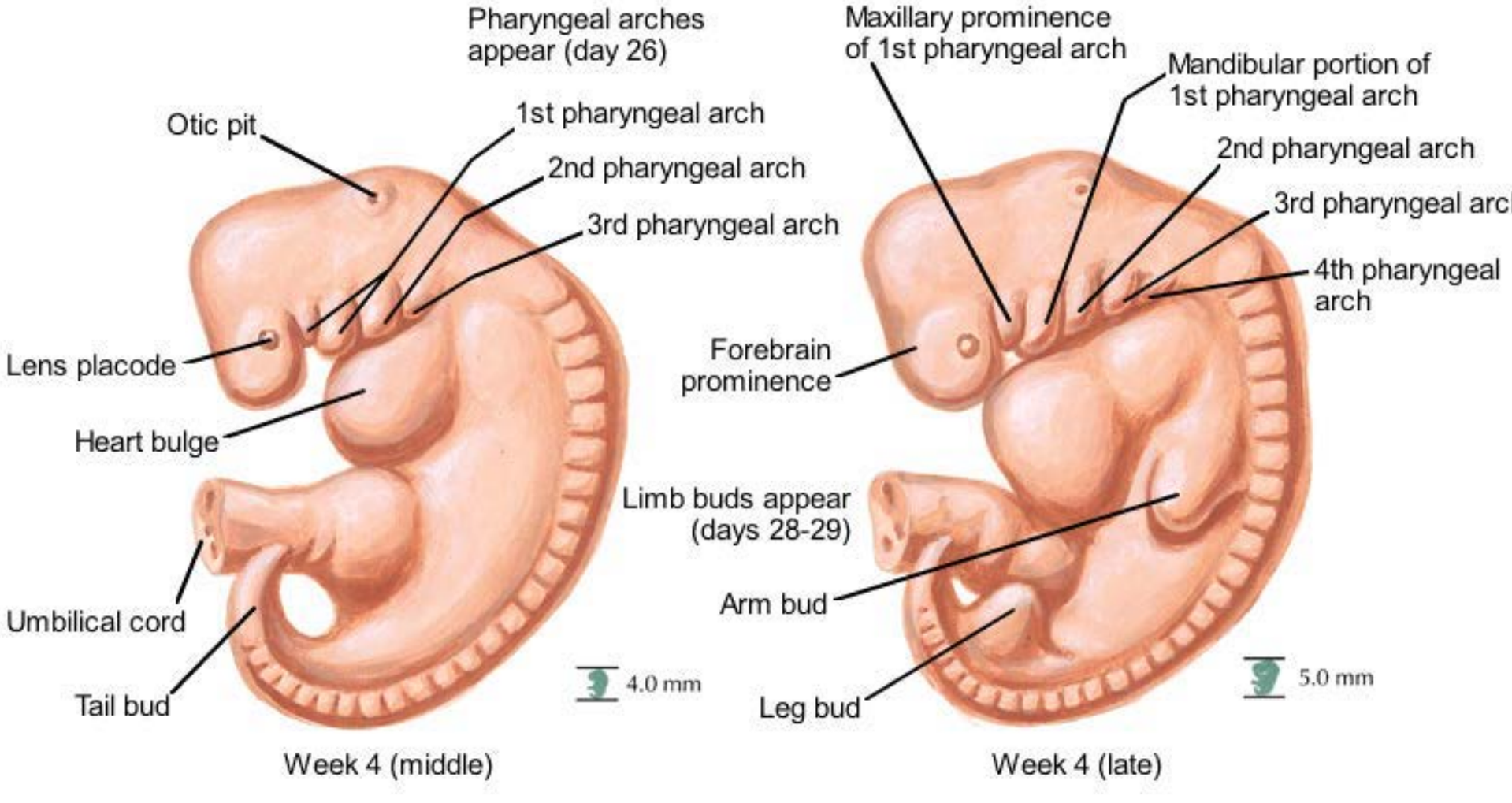
The Embryonic Period

Dorsal Views

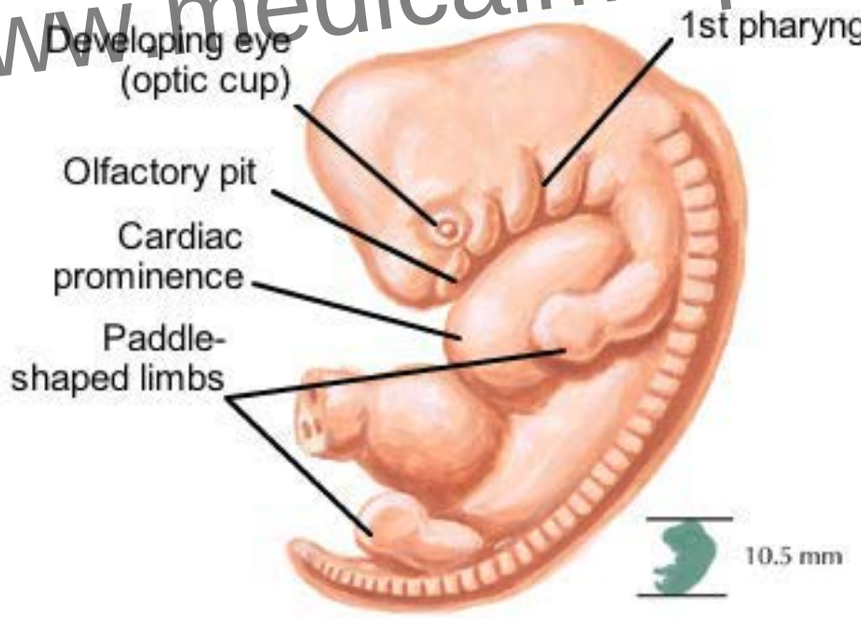


The Embryonic Period

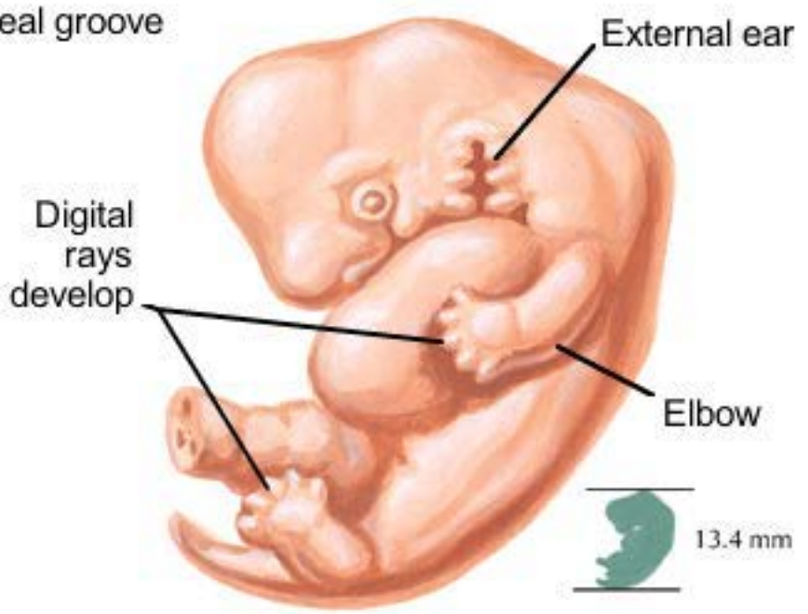
Sagittal Views



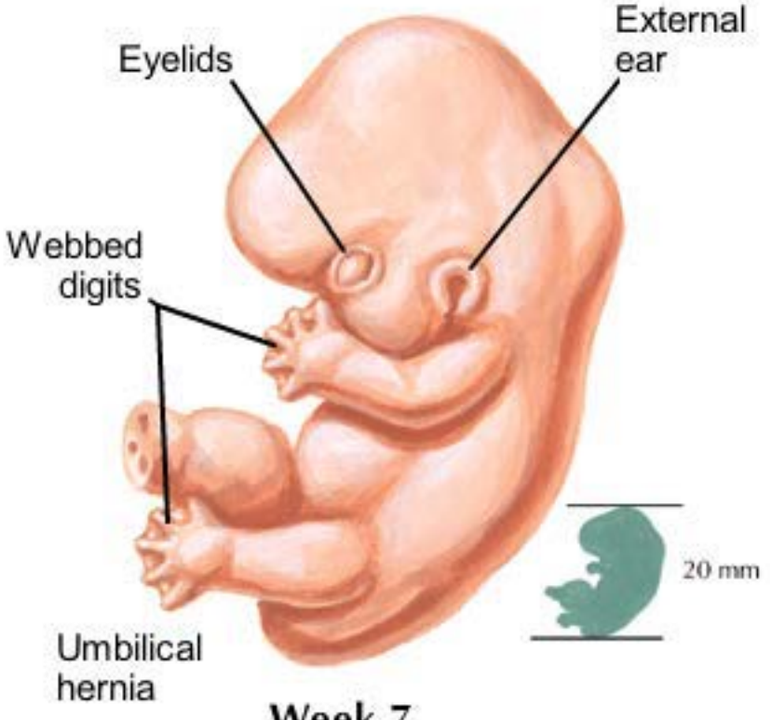
The Embryonic Period



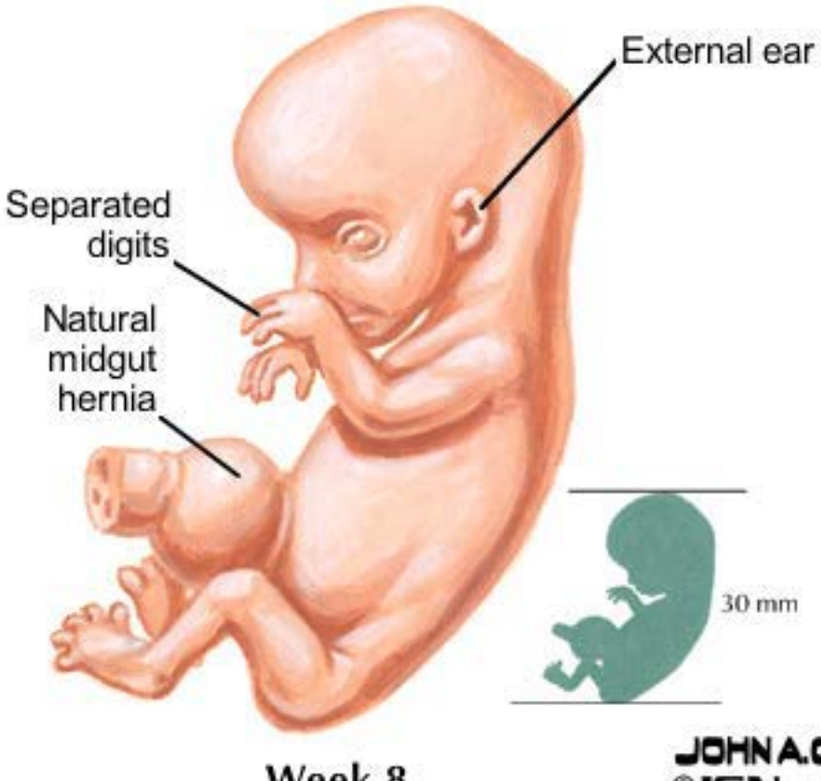
Week 5 (late)



Week 6 (early)

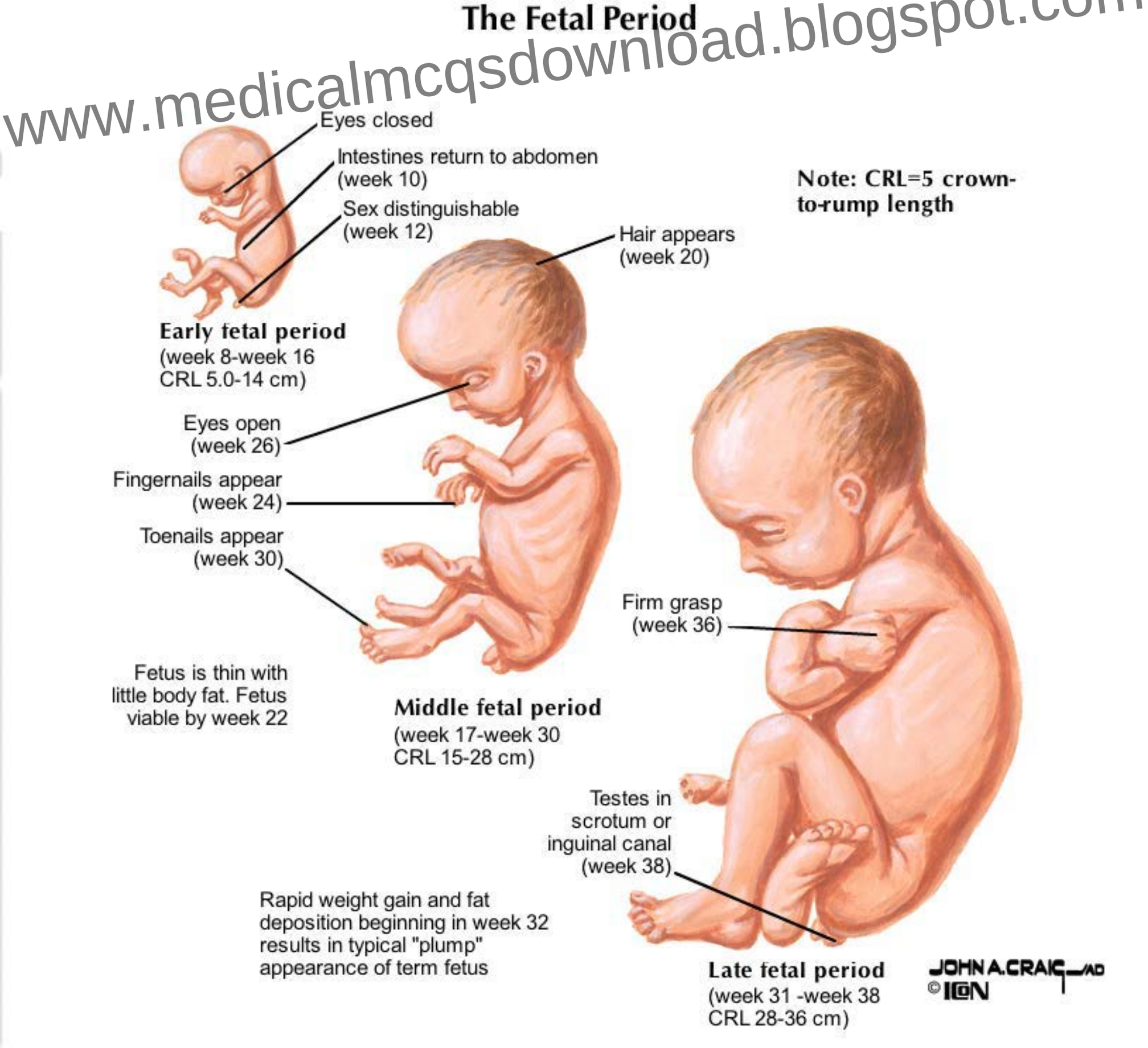


Week 7



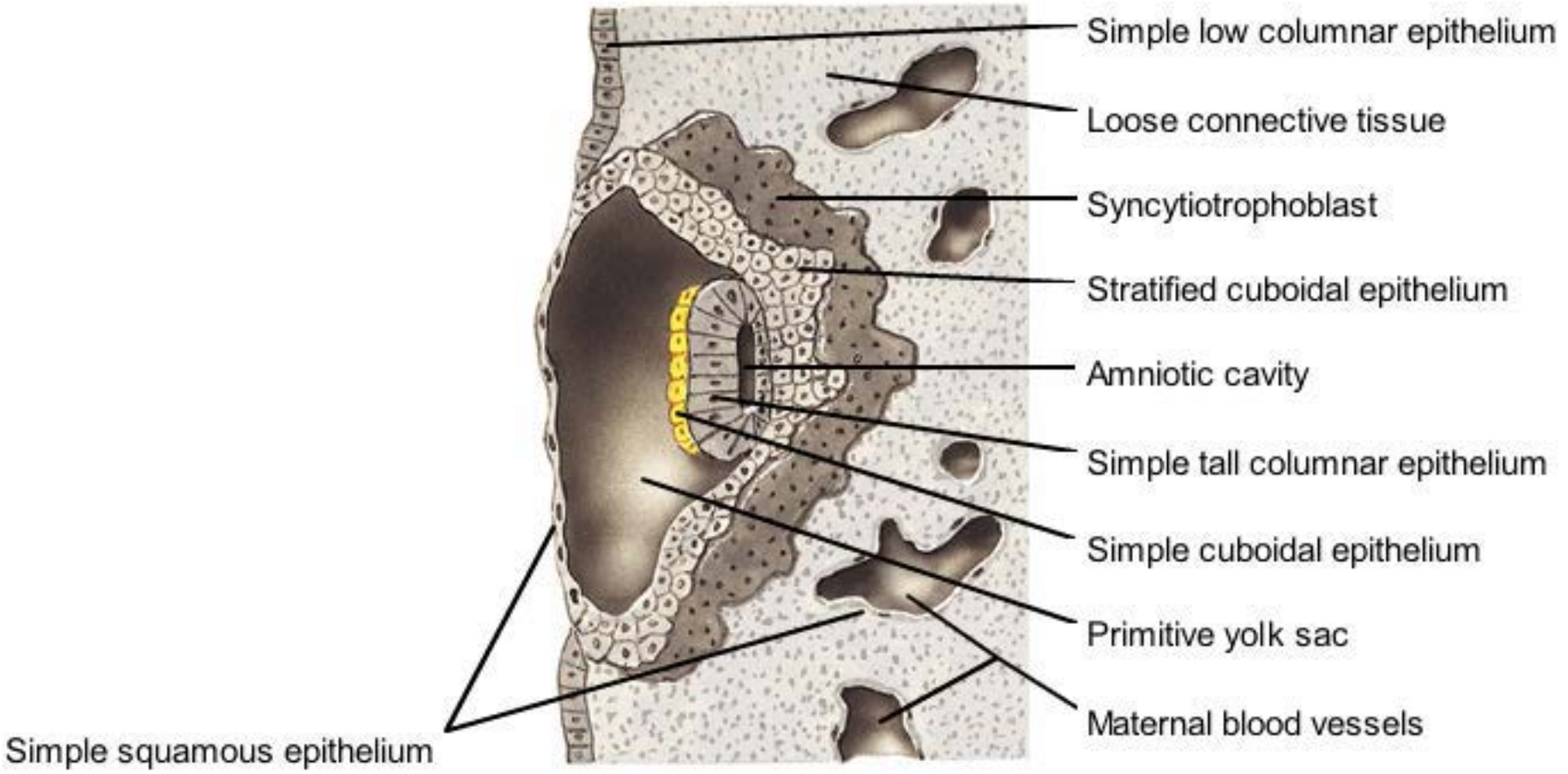
Week 8

The Fetal Period



Histological Concepts

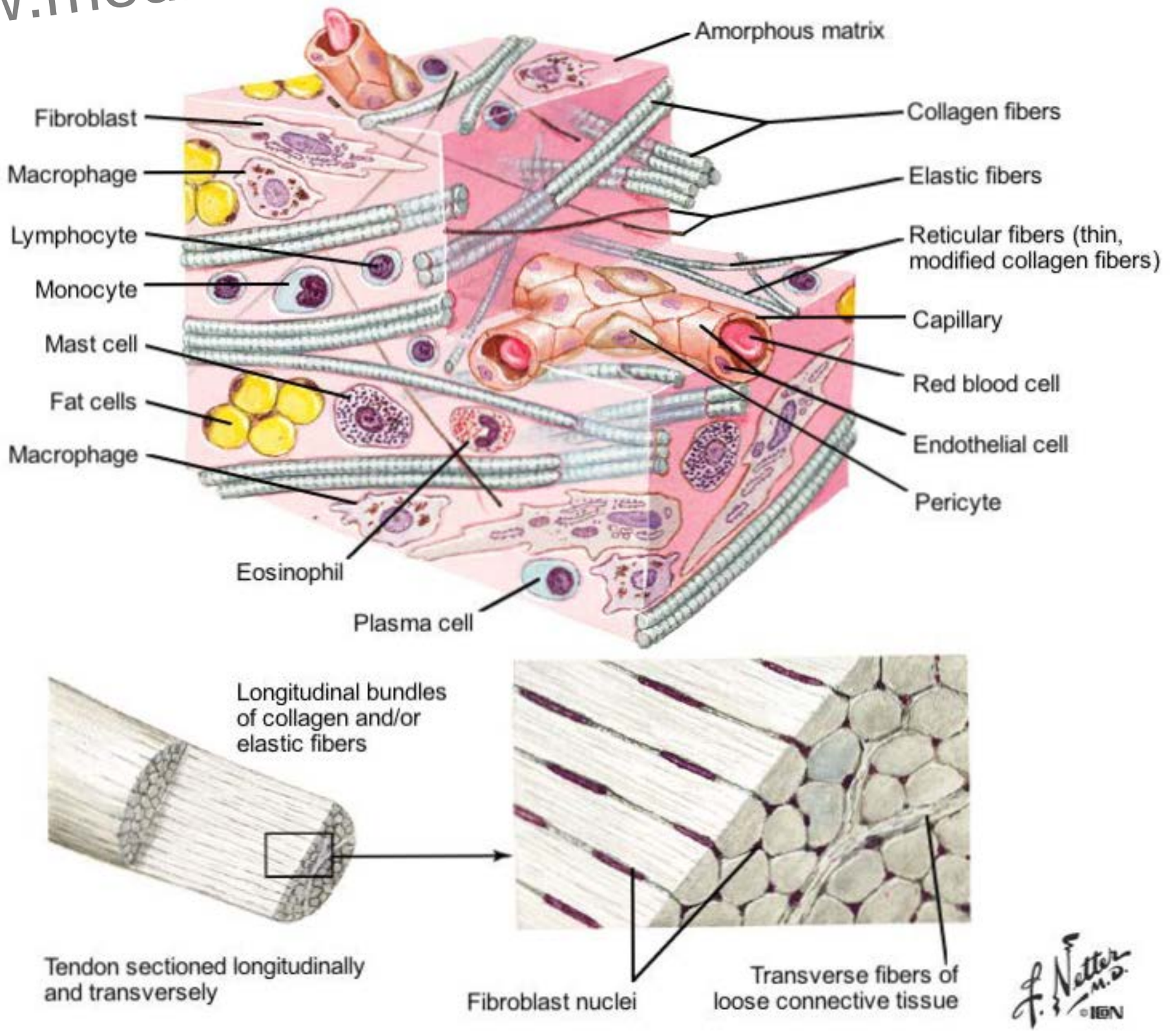
Blastocyst with embryo within the uterine mucosa



Approximately 7 1/2 days

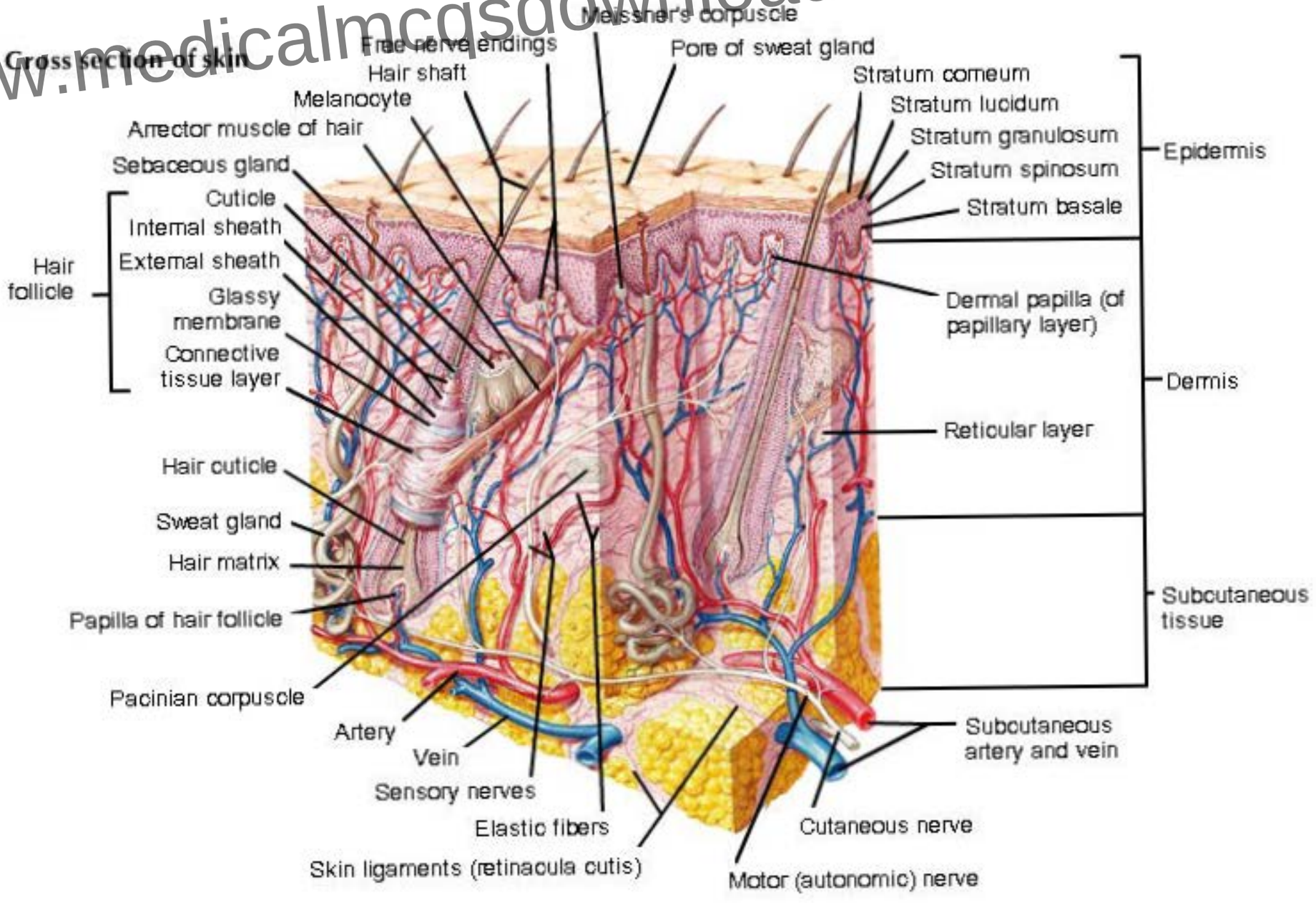
Histological Concepts

Loose and dense connective tissue

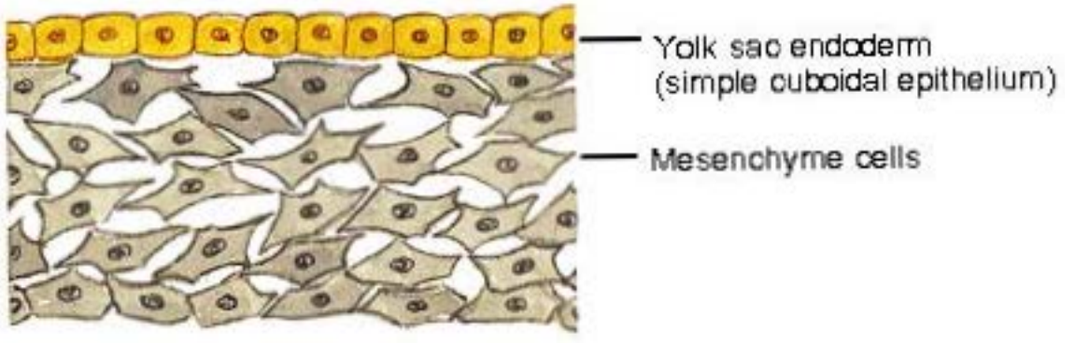


Histological Concepts

Gross section of skin



Wall of the yolk sac



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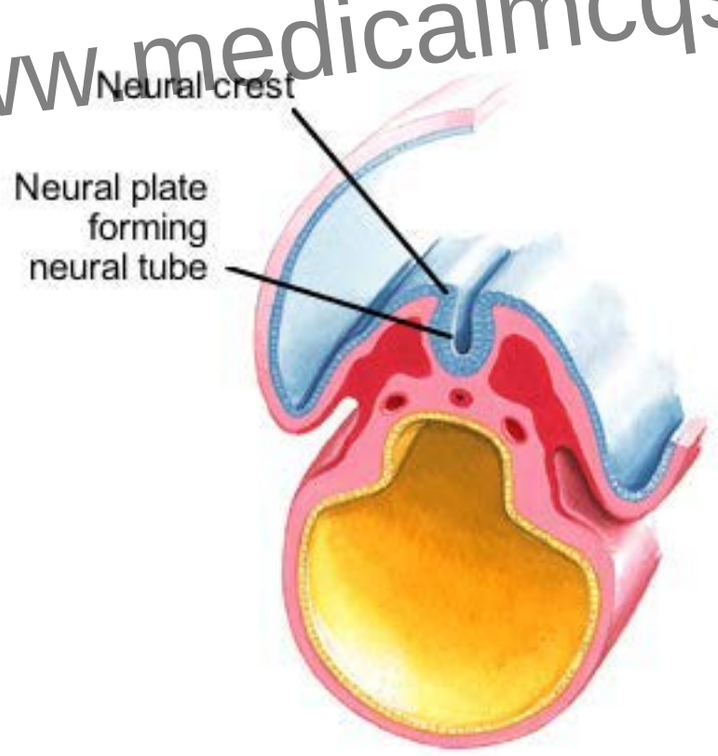
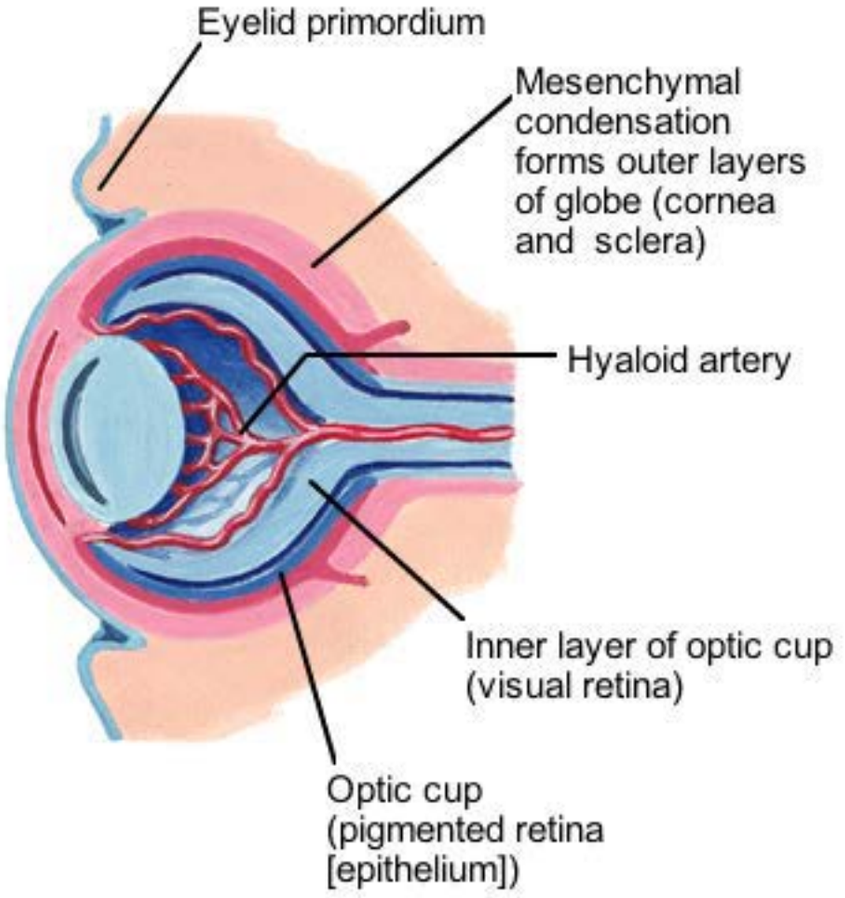
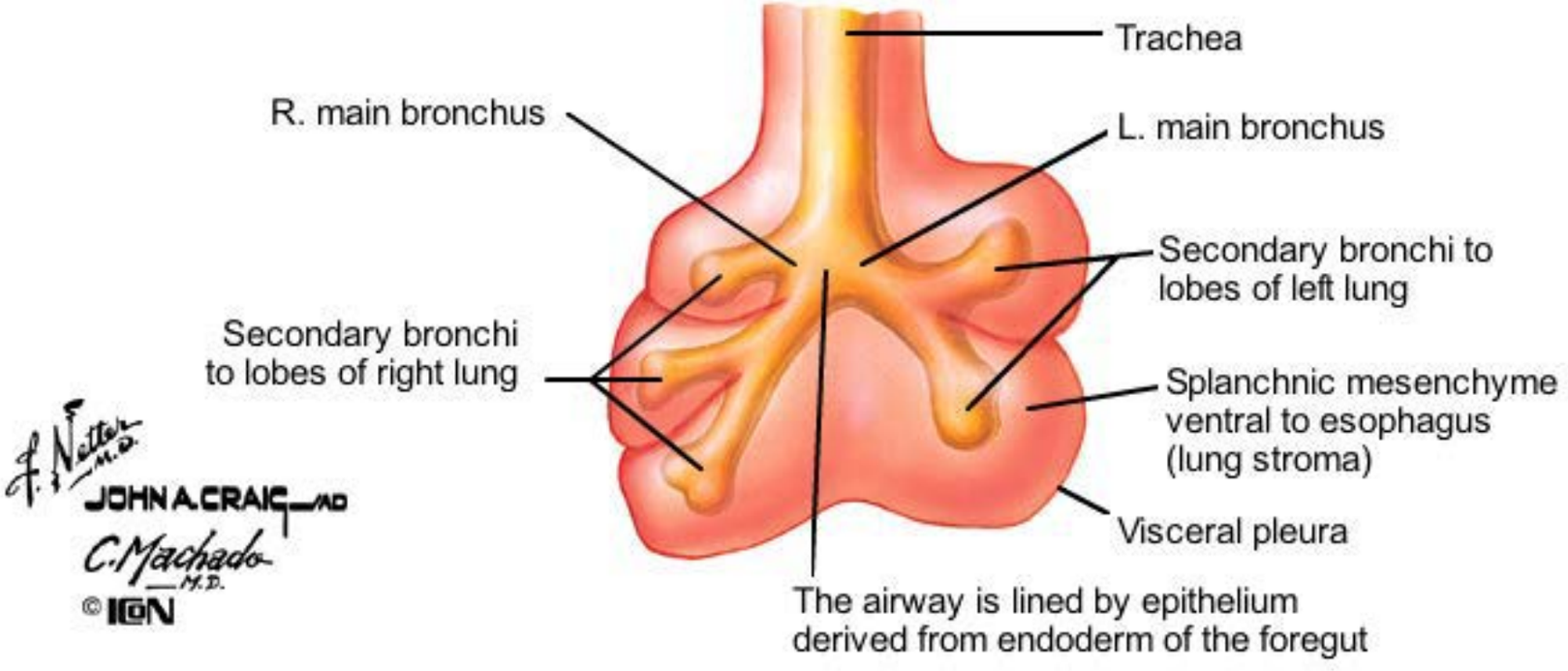
Induction



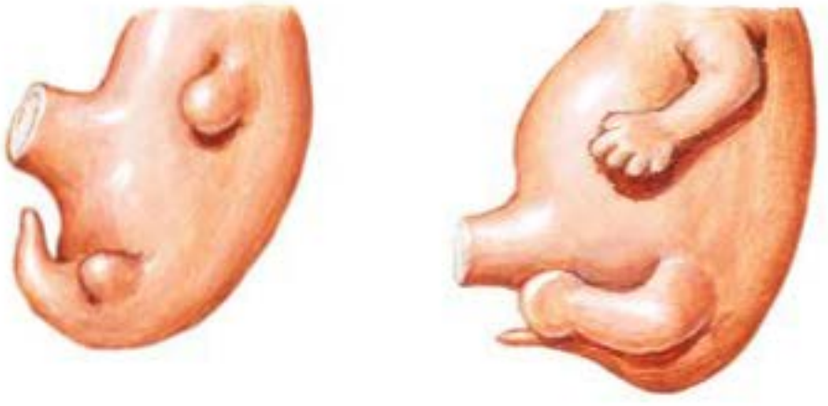


Bronchi and lungs at 5 to 6 weeks

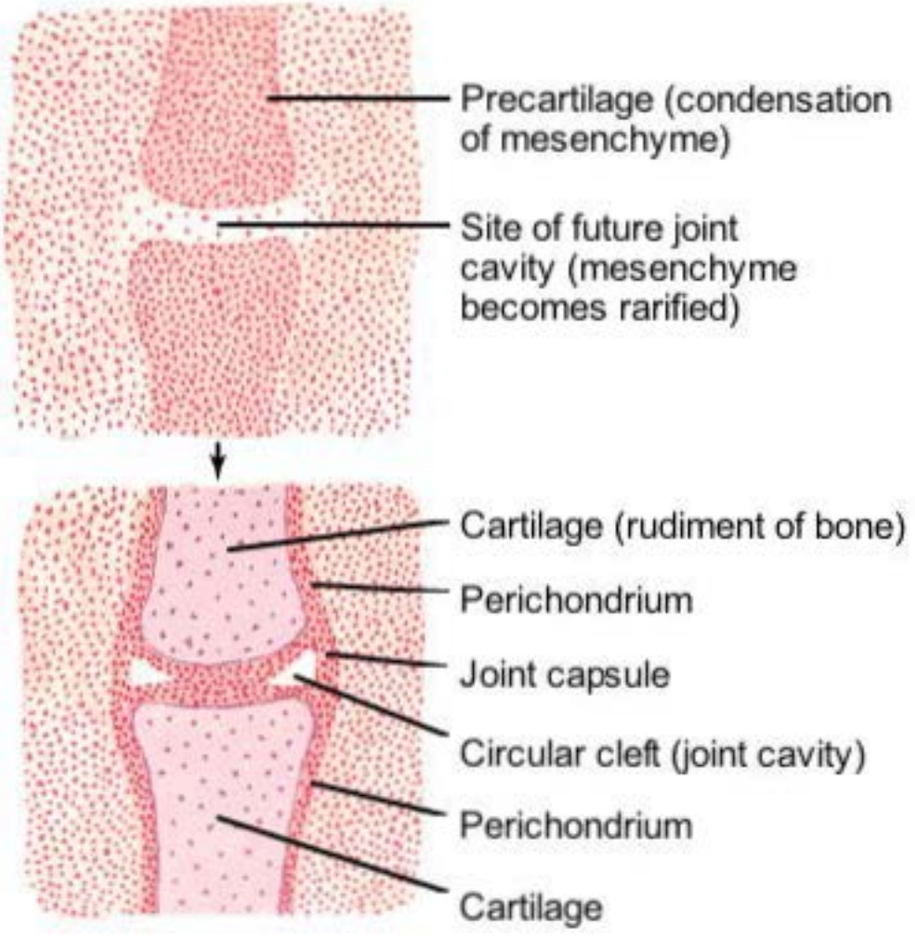


Apoptosis

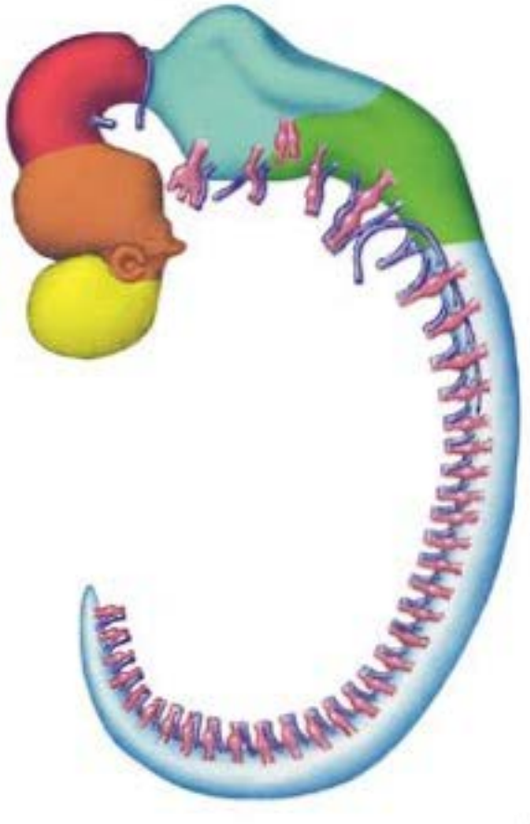
Upper and lower limb buds at 5 and 6 weeks



Formation of a joint cavity between two developing bones



Cranial and spinal nerves at 36 days



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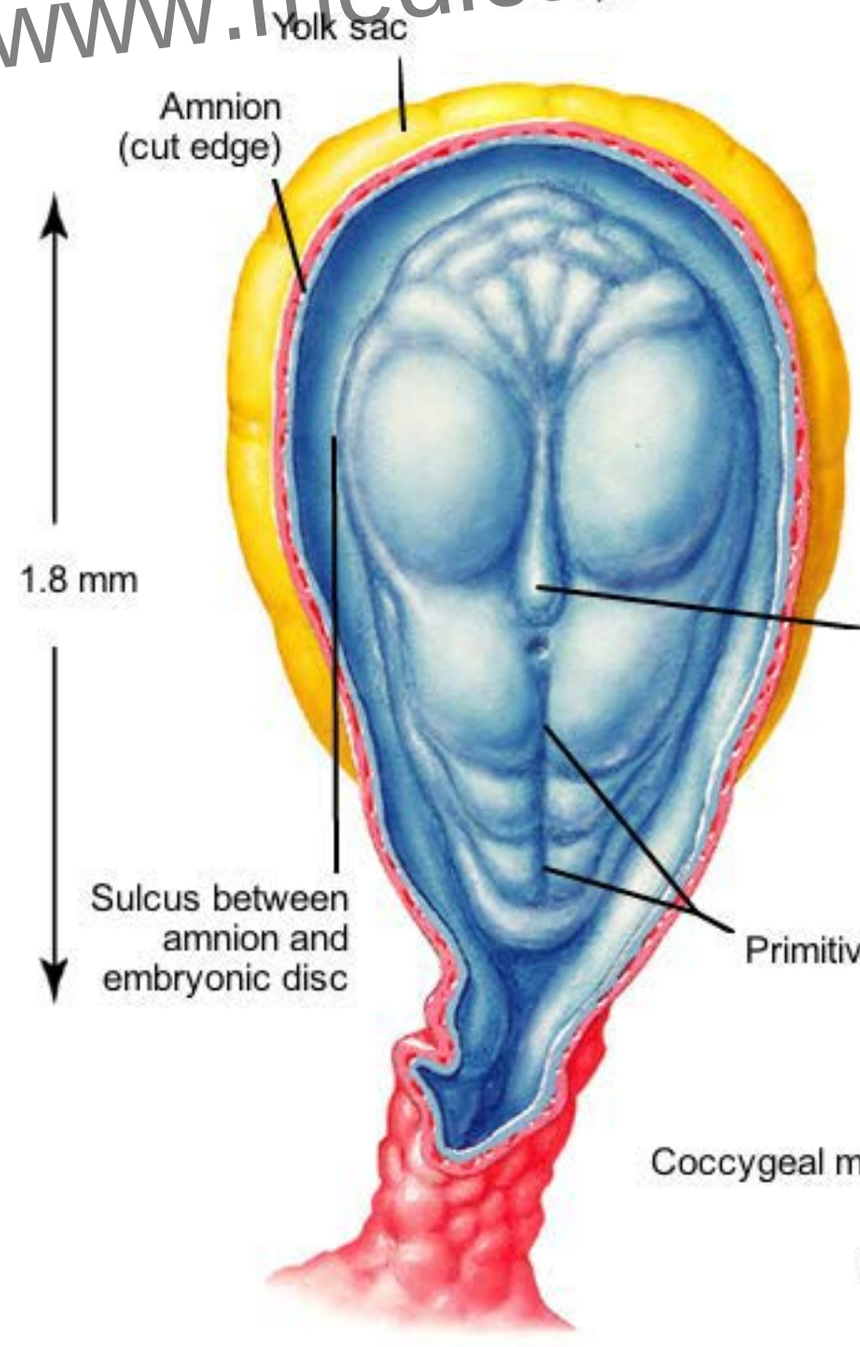
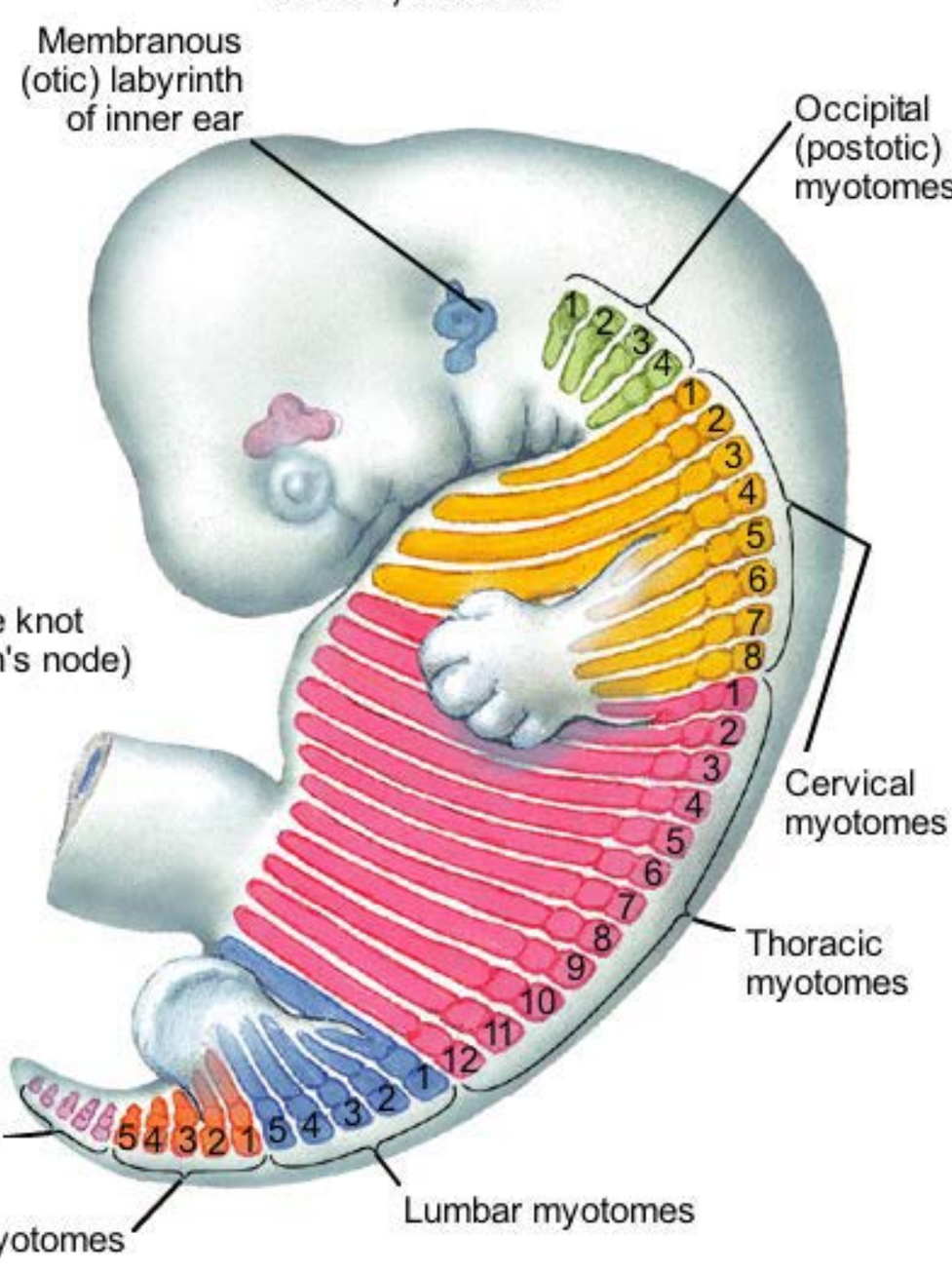
Segmentation and Early Pattern Formation

Dorsal view of the embryonic disc at 18 days



Segmental distribution of dermatomes and myotomes



Region of each trunk myotome also represents territory of dermatome into which motor and sensory fibers of segmental spinal nerve extend

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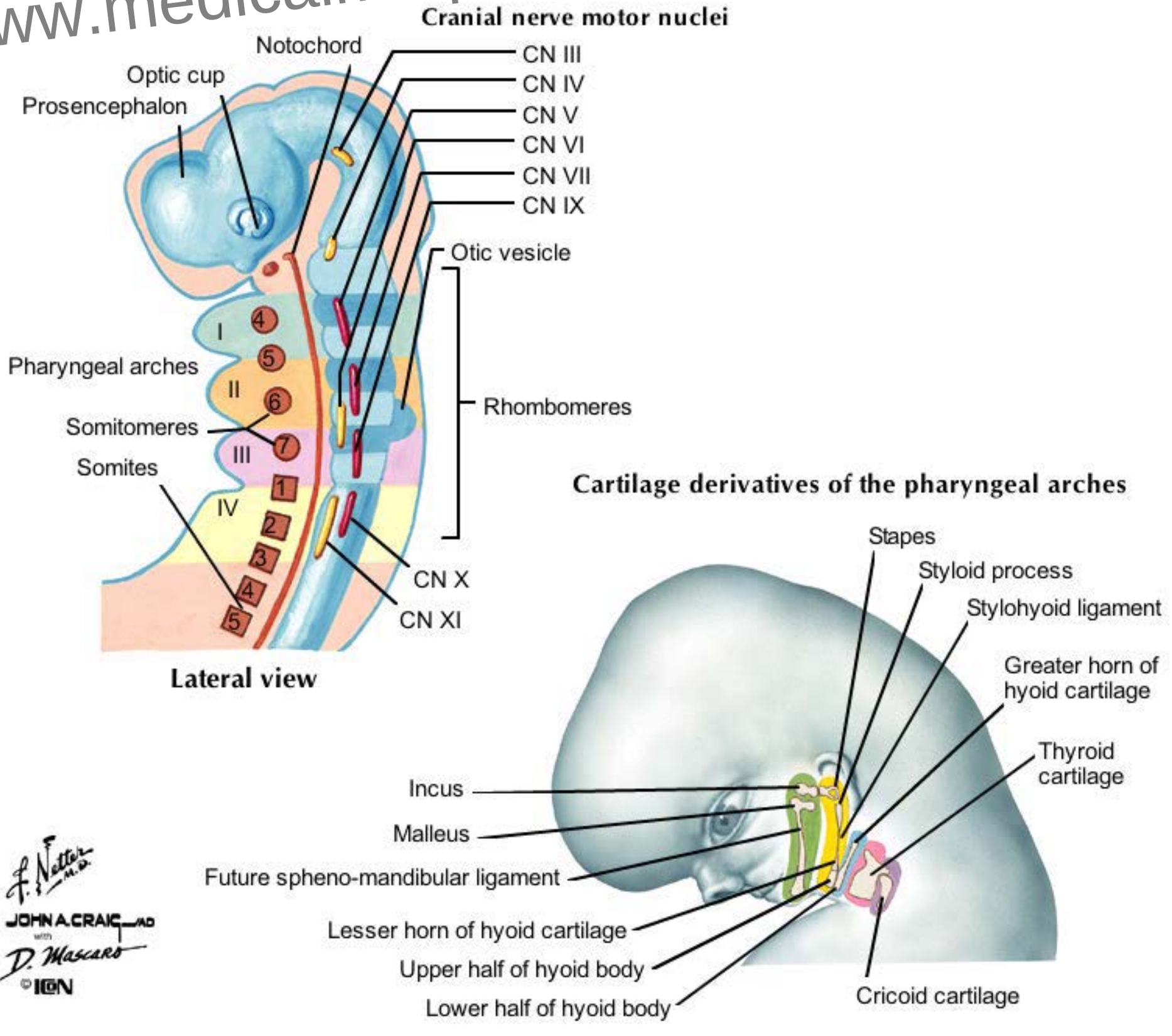
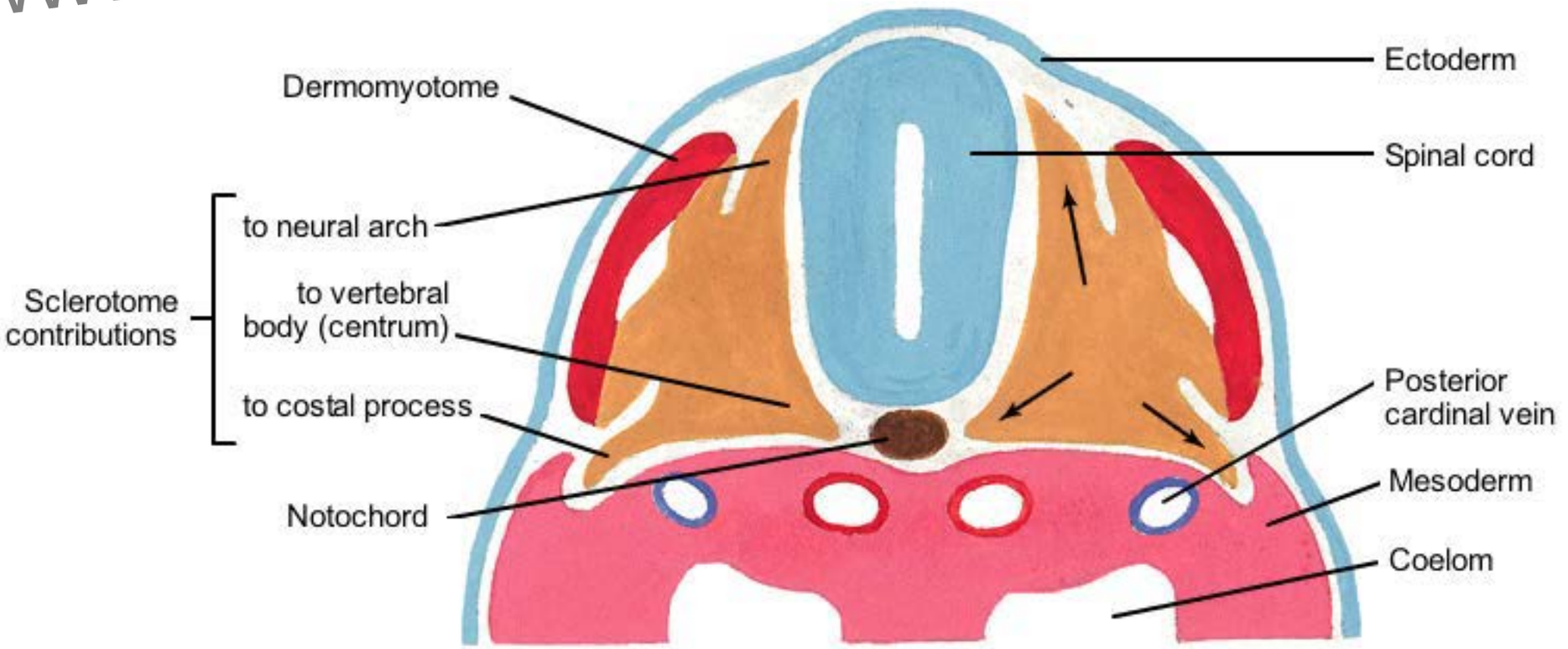
Segmentation and Early Pattern Formation

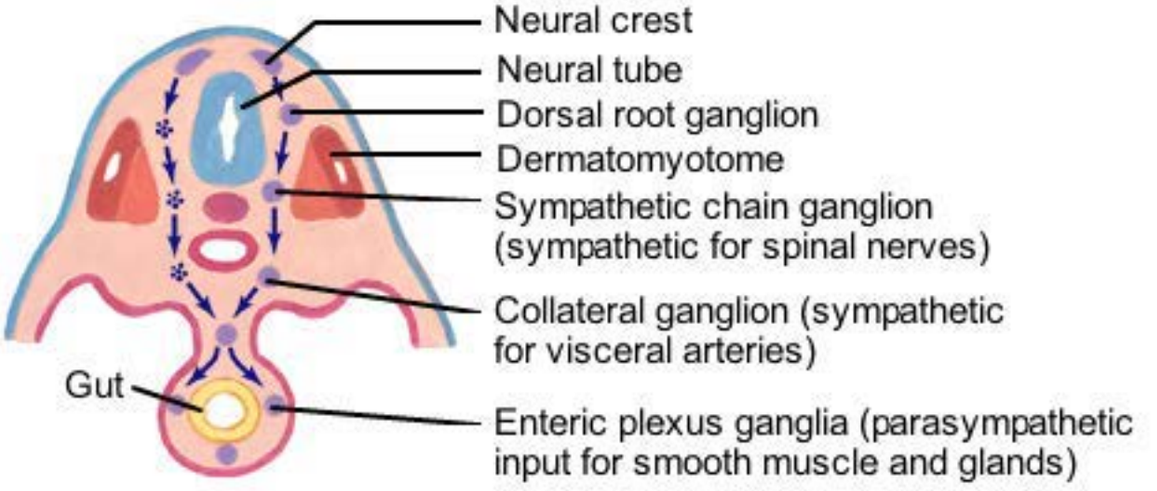


Cell Adhesion and Cell Migration

Somite sclerotome cells dispersing to surround the neural tube in the formation of the vertebral column



The migration of neural crest cells to form autonomic ganglia



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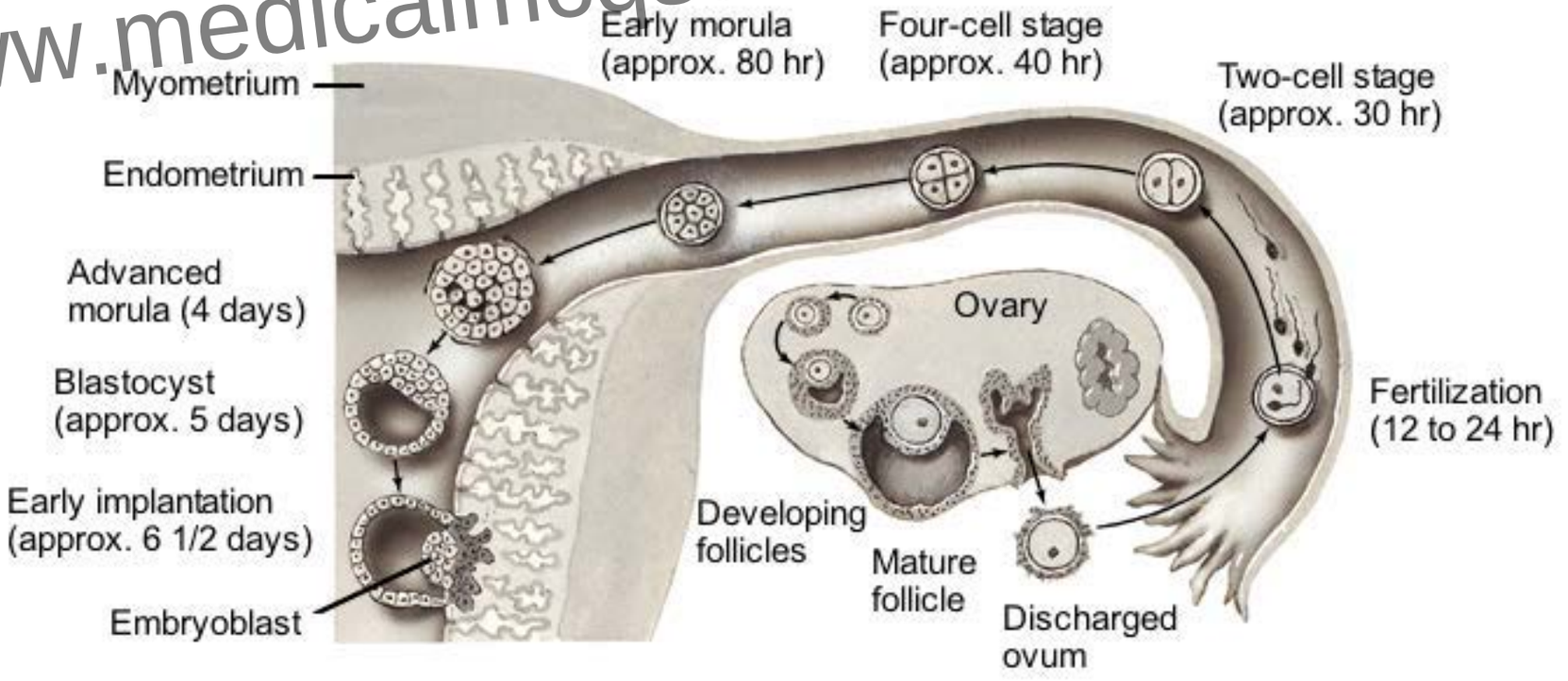
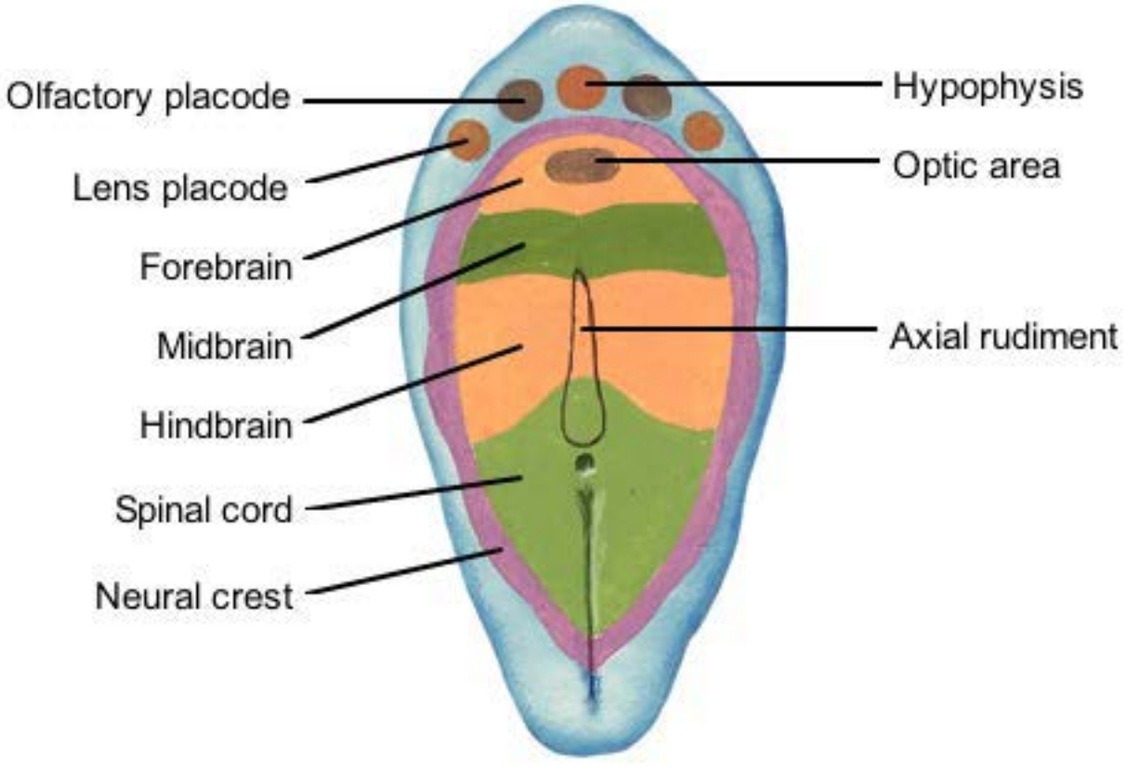
Migration of neural crest cells form peripheral ganglia of autonomic nervous system

Cell Differentiation and Cell Fates

The first week of development



Cellular fate map of the embryonic disc showing ectodermal contributions to the future nervous system



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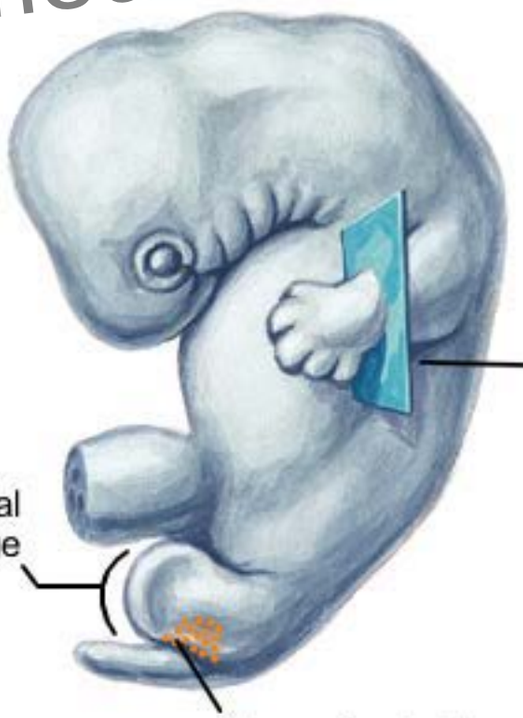
Growth Factors

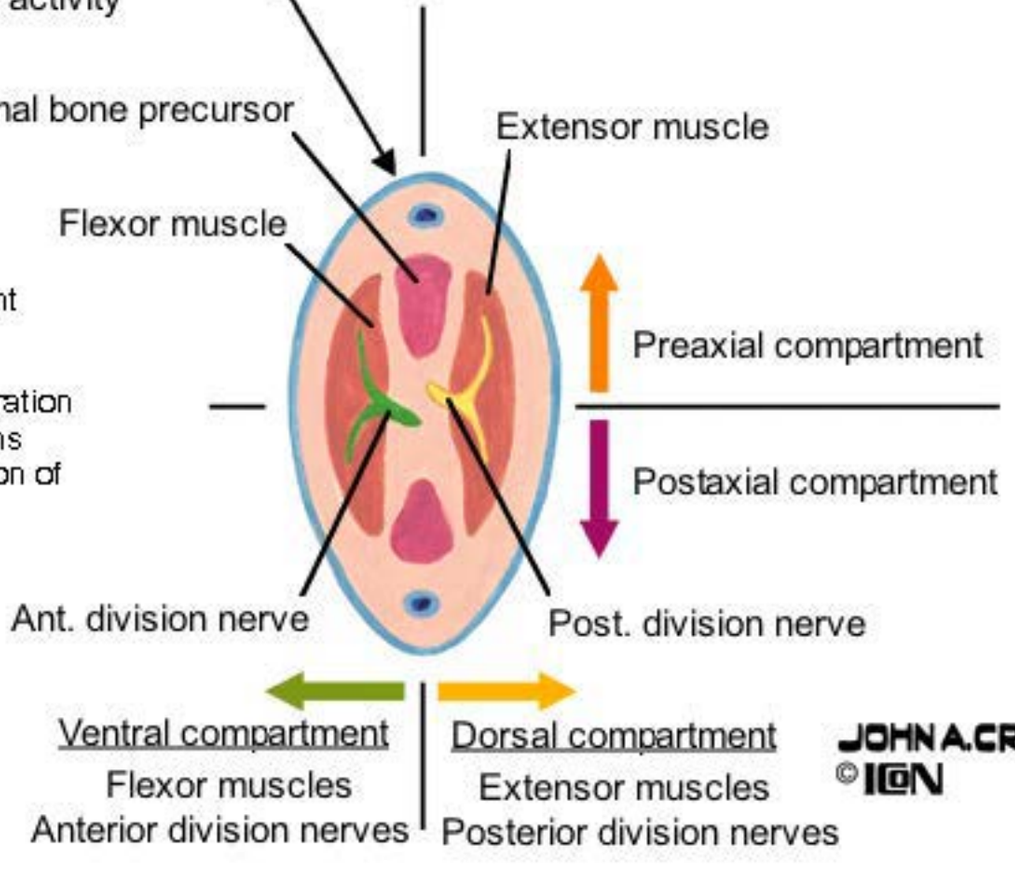


Growth factors that influence limb morphology:

Fibroblast growth factor-8 (FGF-8)-limb bud initiation
Retinoic acid-limb bud initiation
FGF-2, 4, and 8-outgrowth of the limbs
Bone morphogenetic proteins-apoptosis of cells between digits
Sonic hedgehog-establishment of craniocaudal limb axes
Wnt-7a-dorsal patterning of the limbs
En-1-ventral patterning of the limbs

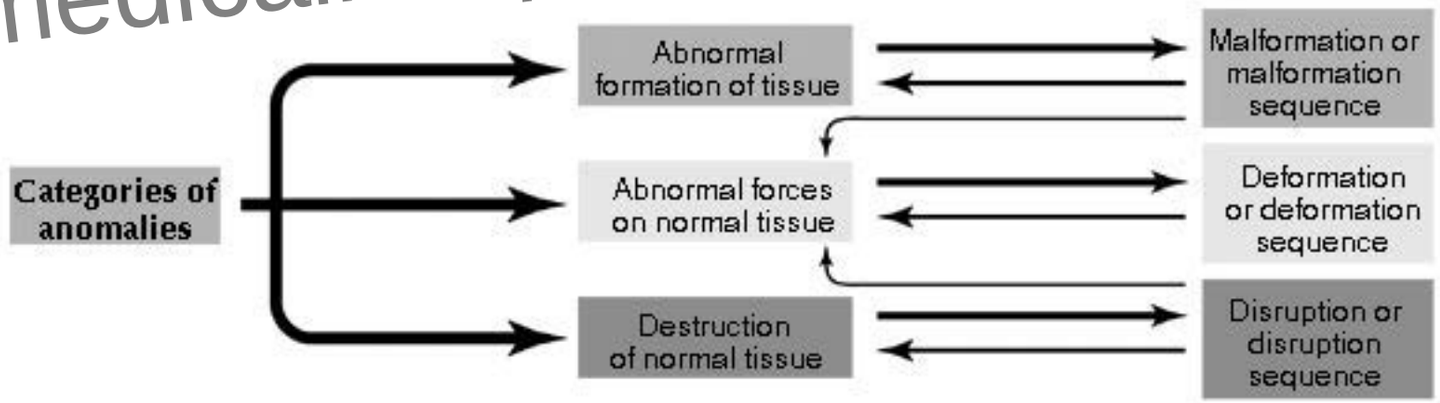
Growth factors that promote tissue development:

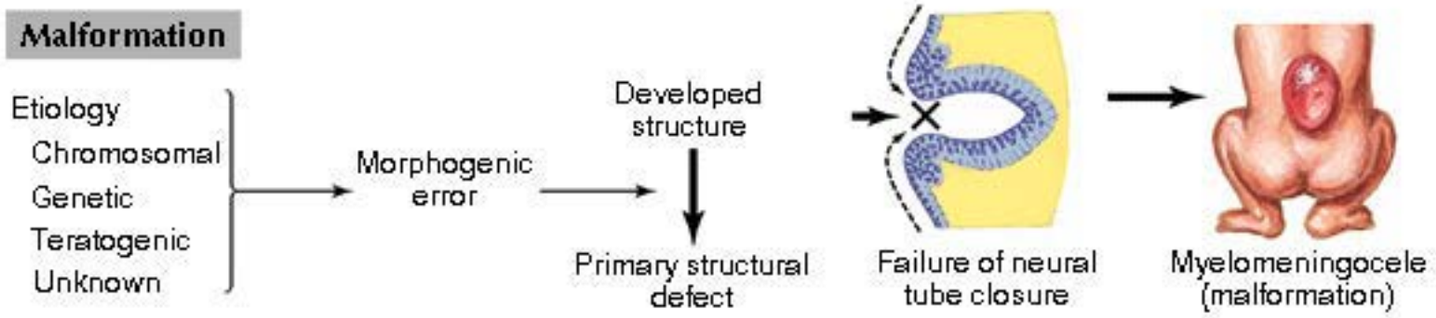
Bone morphogenetic protein family-bone development
Indian hedgehog-bone development
Growth/differentiation factor 5-joint formation
Transforming growth factor-β family-myoblast proliferation
Nerve growth factor-sensory and sympathetic neurons
Insulin-like growth factor-1 (IGF-1)-general proliferation of limb mesoderm
Scatter factor (hepatic growth factor)-myotome cell migration in the limbs



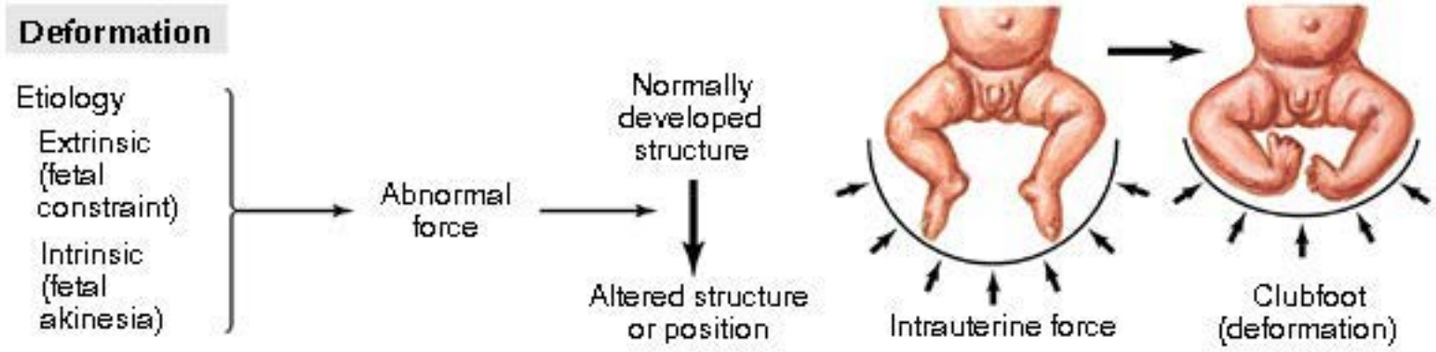
Classification of Abnormal Processes

The Classification of Errors of Morphogenesis

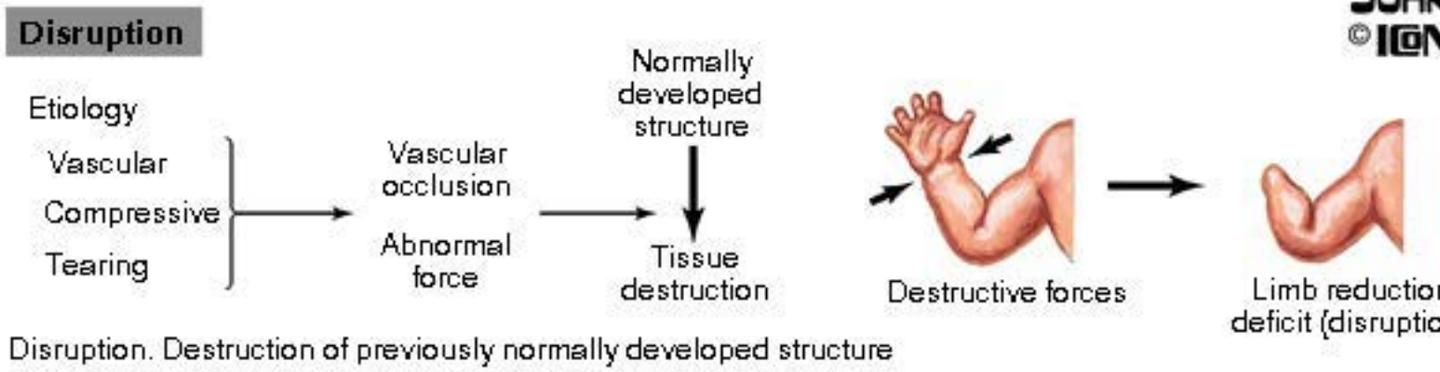




Malformation. Primary structural defect resulting from error in tissue formation



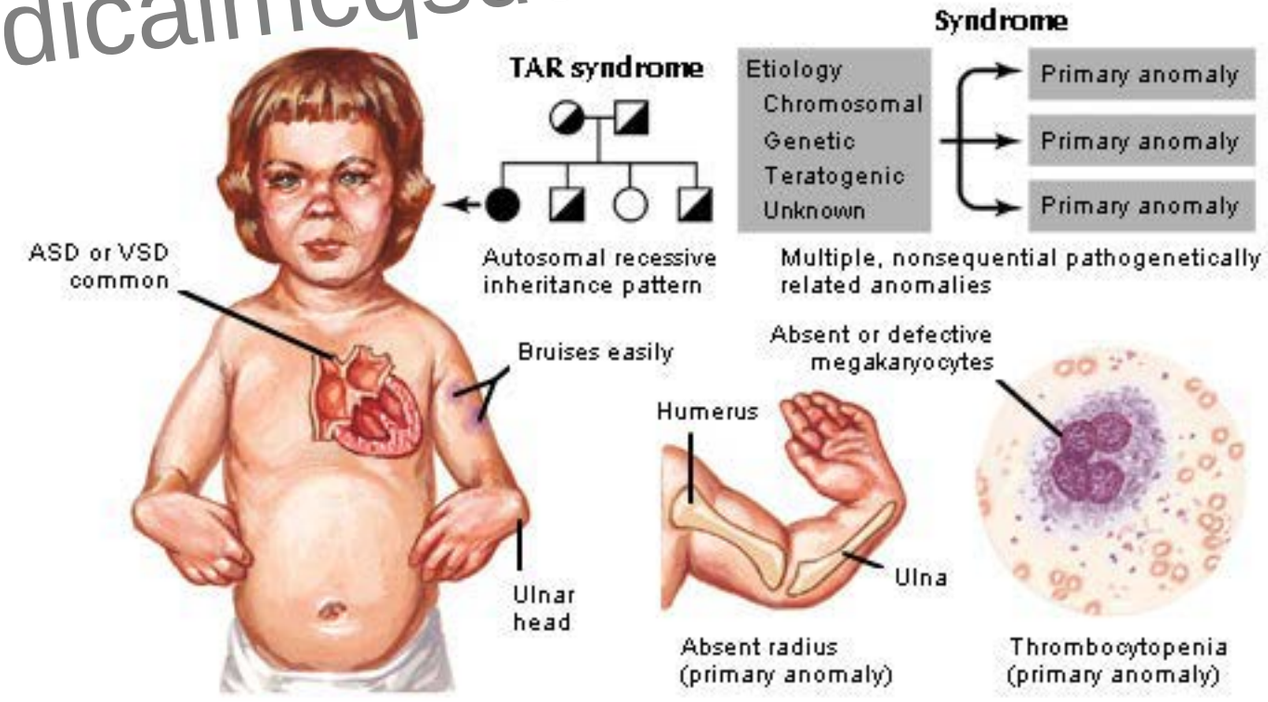
Deformation. Alteration in shape or position of normally developed structure



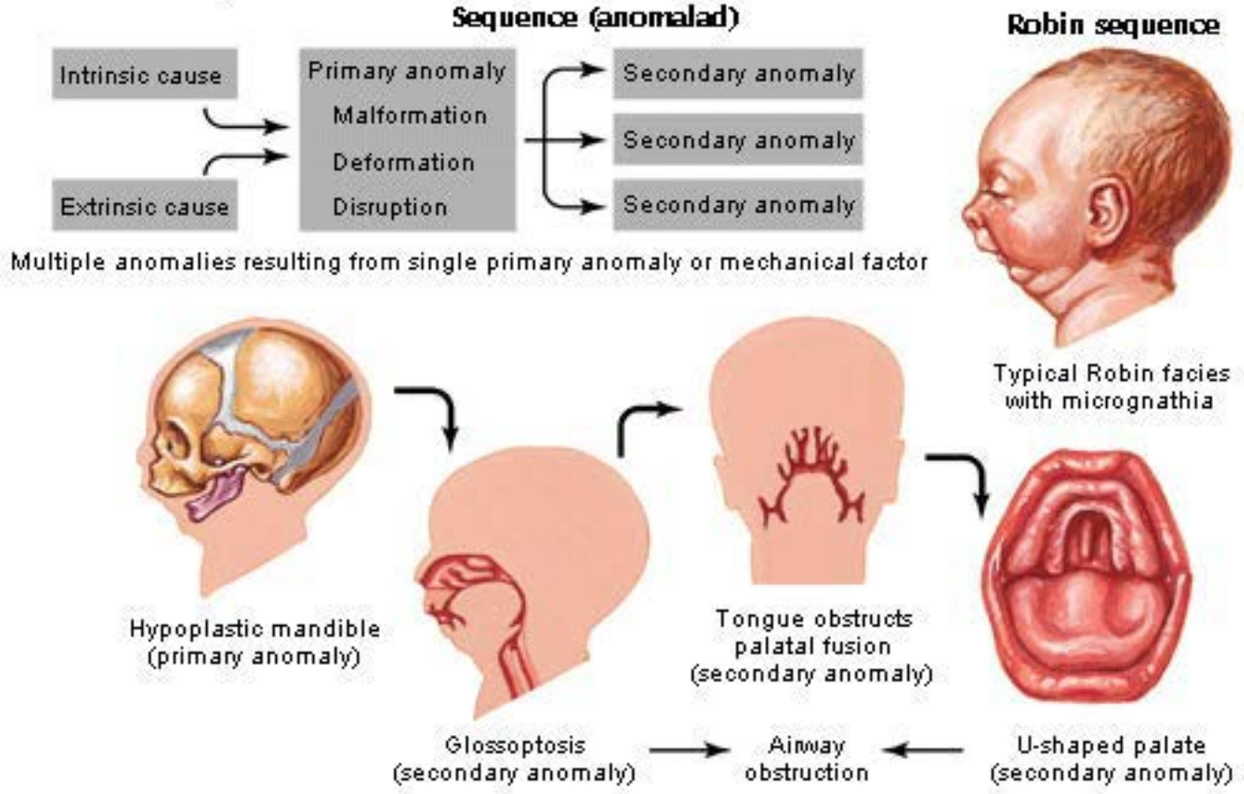
Disruption. Destruction of previously normally developed structure

Classification of Multiple Anomalies

Patterns of Multiple Anomalies: Syndrome Versus Sequence



TAR syndrome. Includes two anomalies: thrombocytopenia (T) and absent radius (AR). May be associated with congenital heart anomalies; autosomal recessive transmission

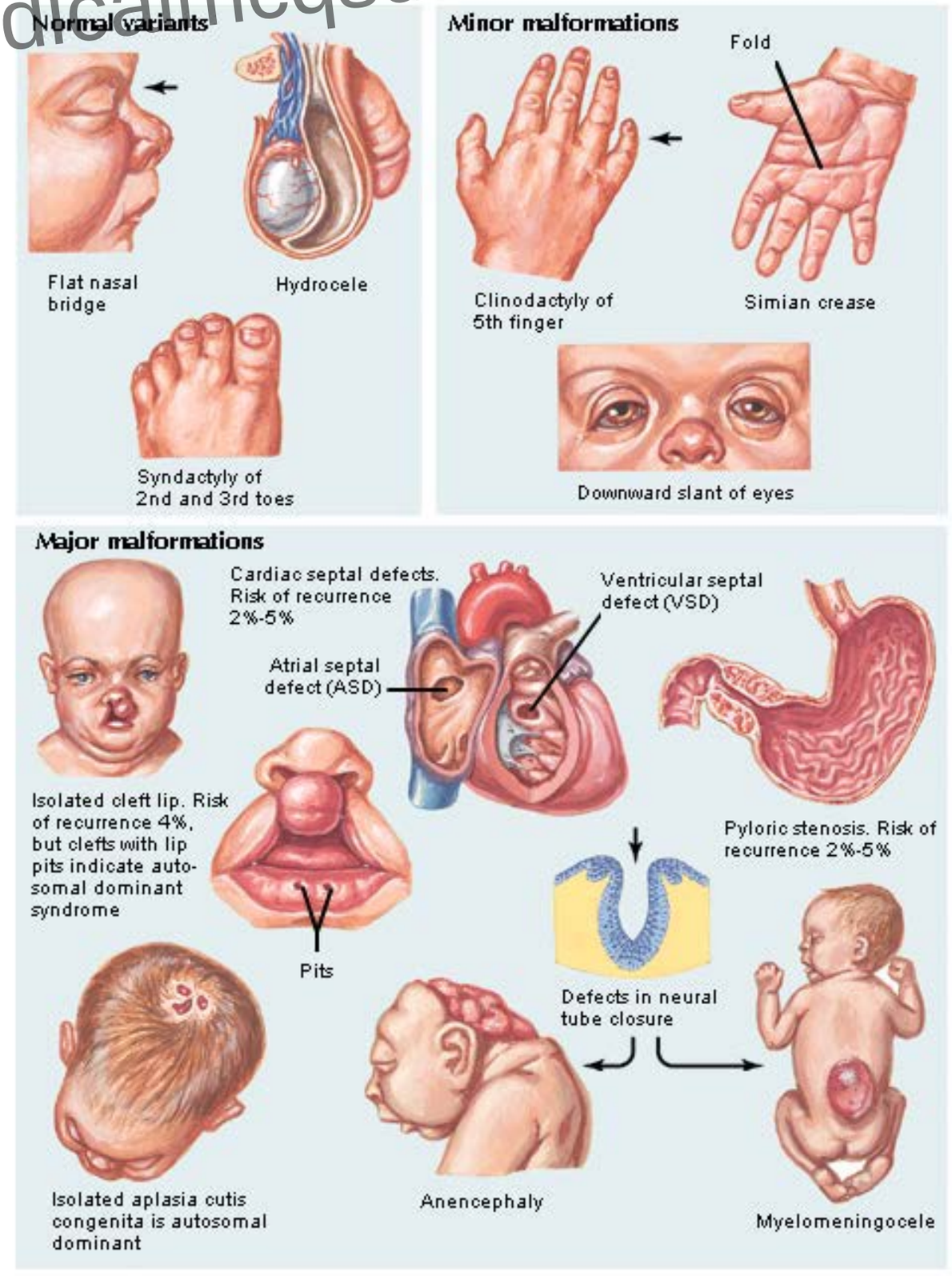


Multiple anomalies resulting from single primary anomaly or mechanical factor

Sequence of anomalies initiated by hypoplastic mandible that causes glossoptosis. Resulting palatal defect with glossoptosis may obstruct airway

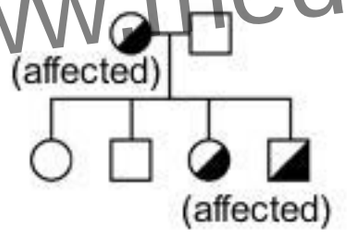
Normal Versus Major Versus Minor Malformations

The Classification of Malformations

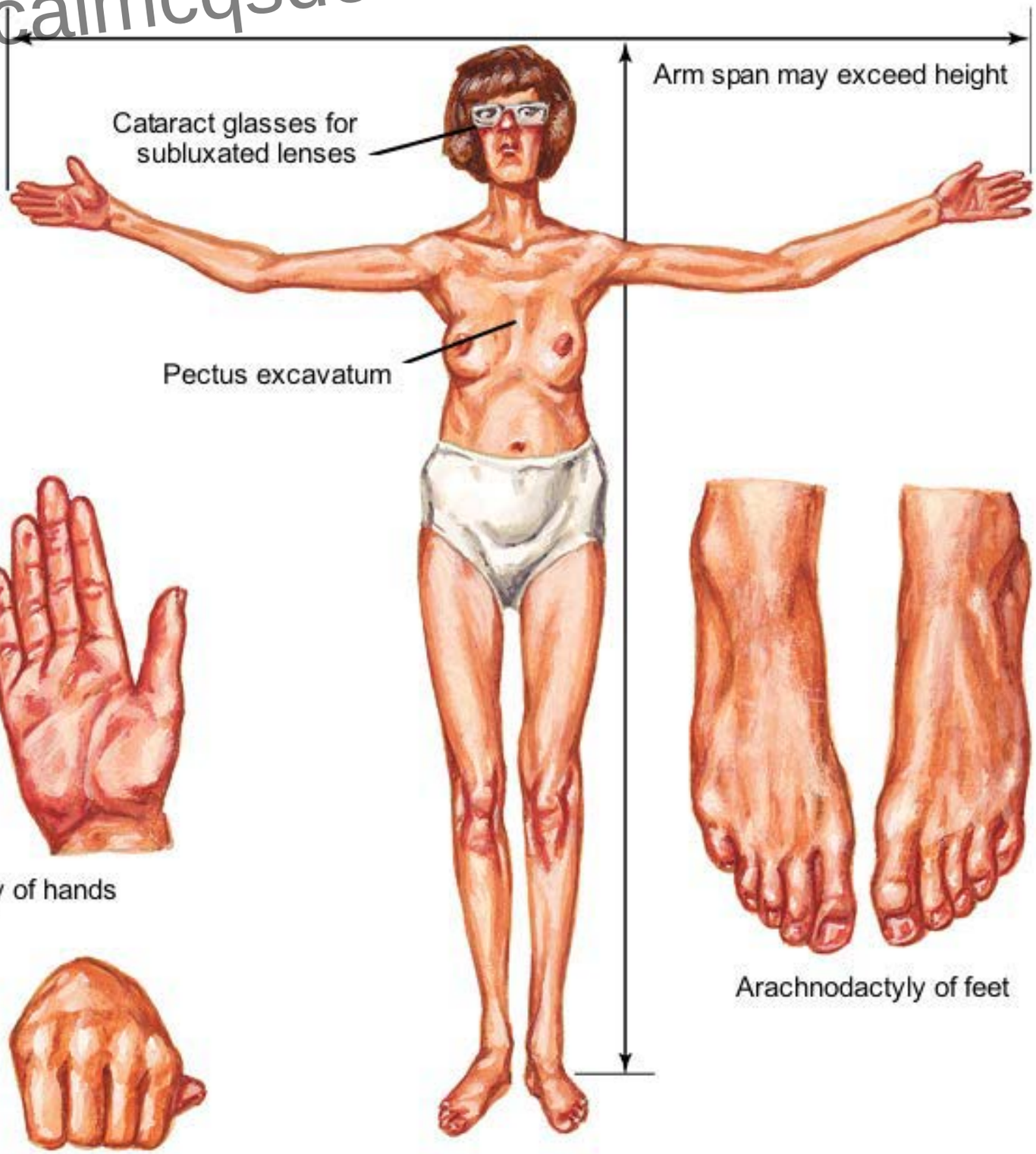


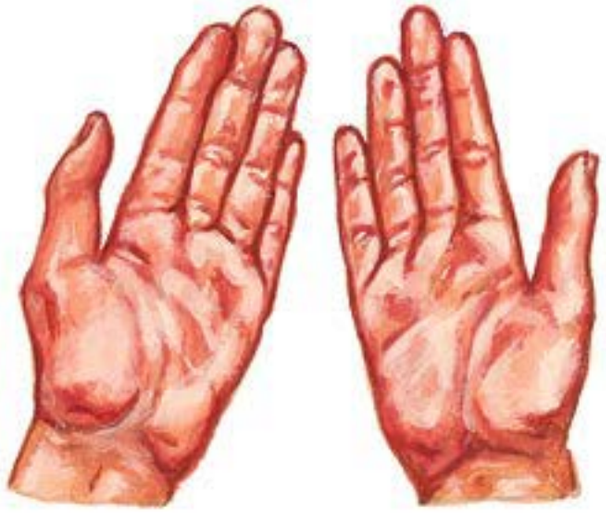
Major and minor malformations may occur as isolated entities or as components of multiple malformation syndrome. Risk of recurrence depends on the cause of the defect

Marfan Syndrome



Autosomal dominant inheritance pattern





Arachnodactyly of hands

Arachnodactyly of feet

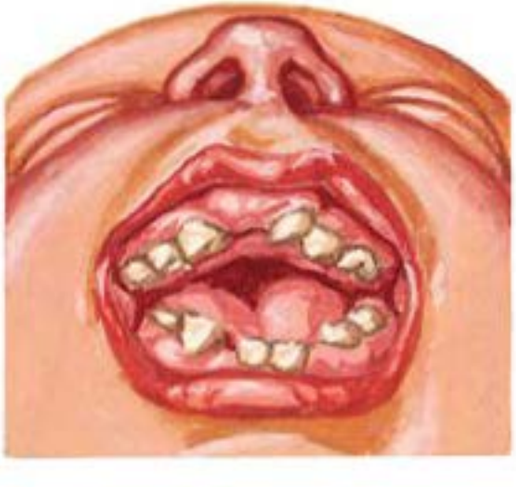
Steinberg sign. Tip of thumb protrudes when thumb folded inside fist. Thumb and index finger overlap when encircling opposite wrist

Apert Syndrome

Typical facies with acrocephaly, hypertelorism, and downward slant of the eyes

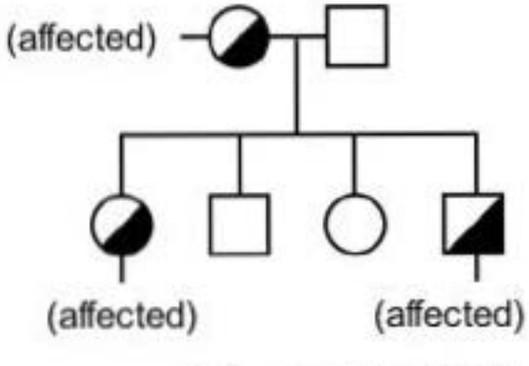
Palmar "spoon" deformity

Dorsal "mitten" deformity



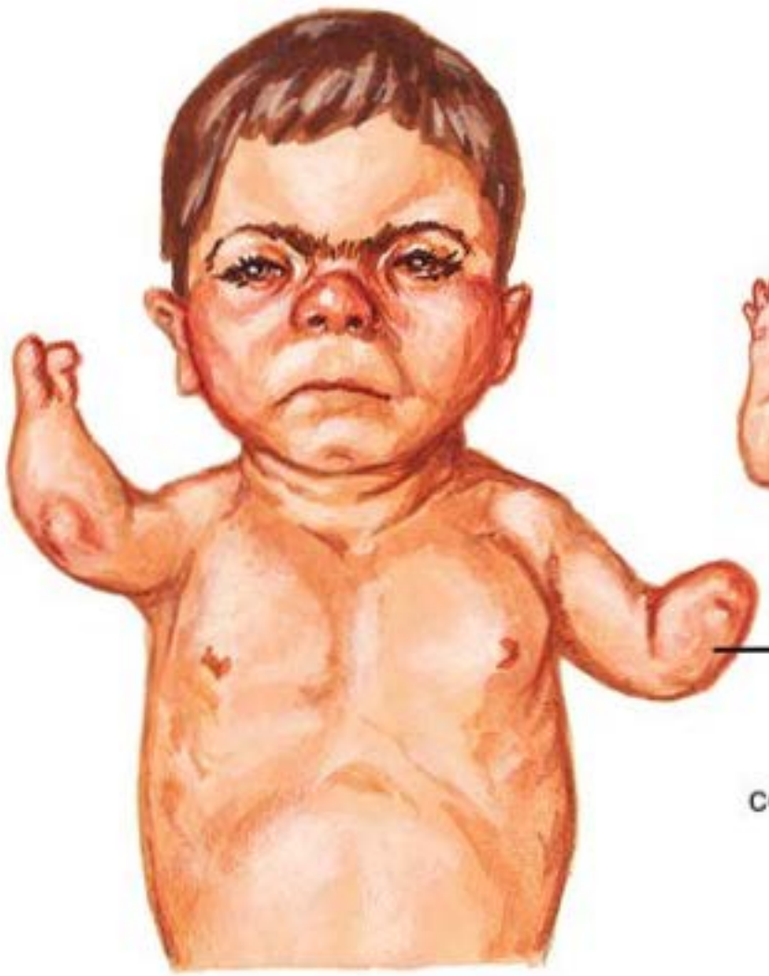
High-arched palate and dental anomalies

Acrocephaly with flattened midface

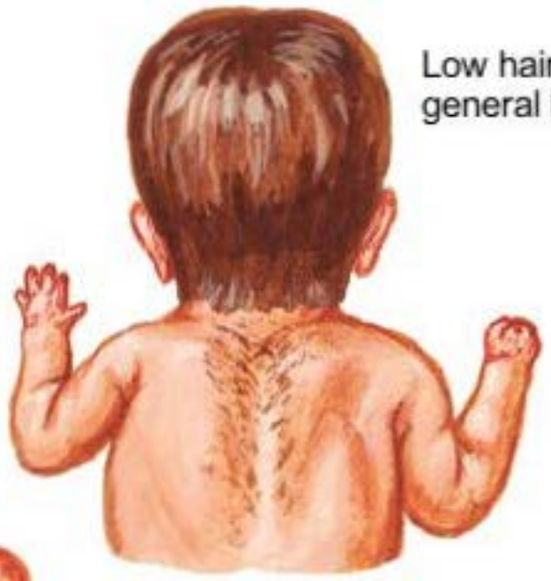


Autosomal dominant inheritance pattern

De Lange Syndrome



Infant facies with thick, conjoined eyebrows (synophrys) and thin lips

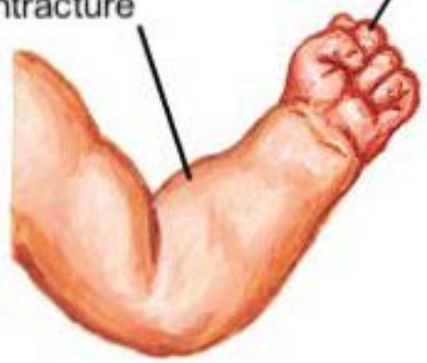


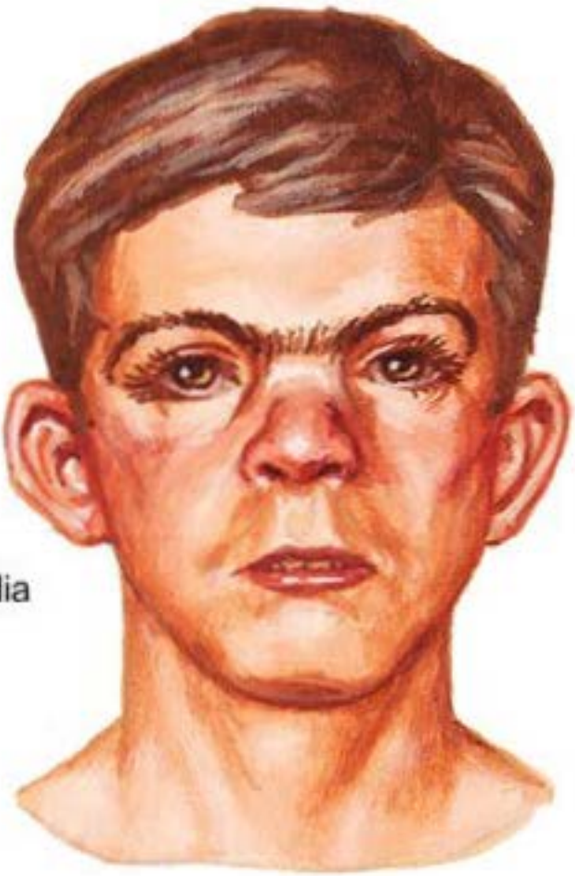
Low hairline and general hirsutism

Phocomelia

Flexion contracture

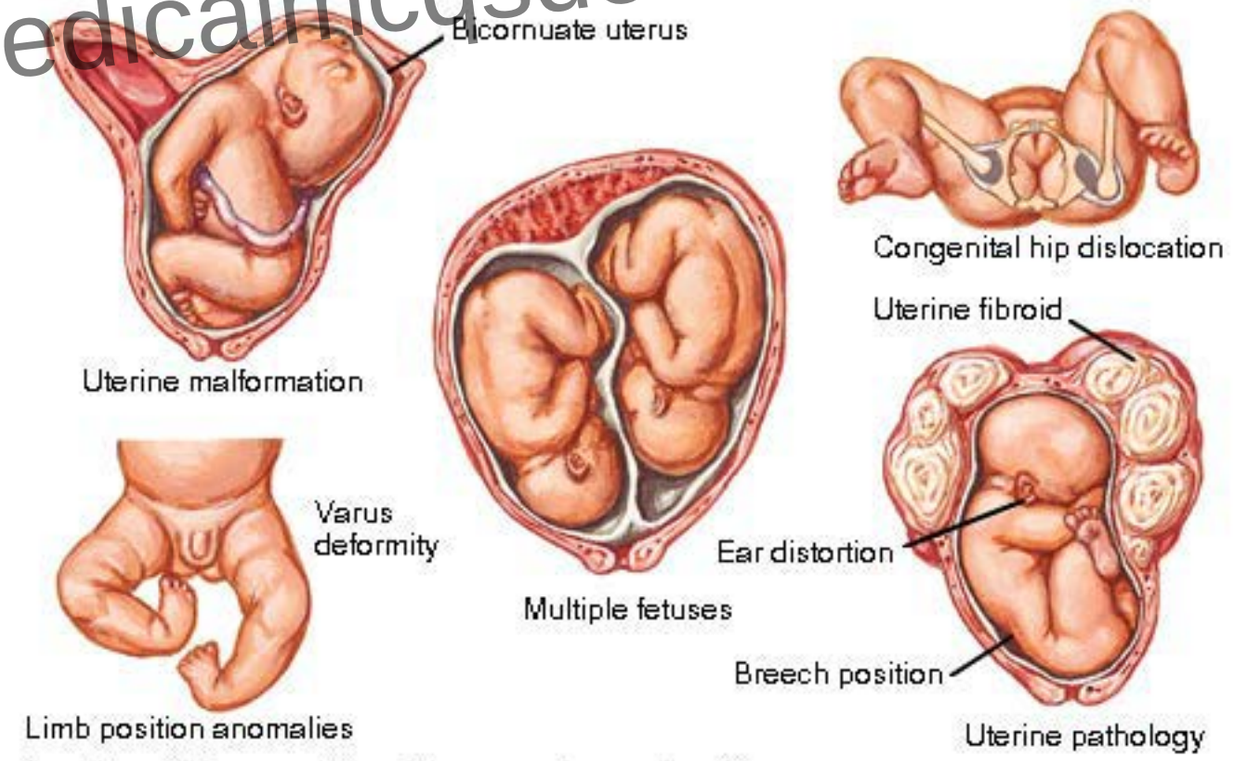
Micromelia



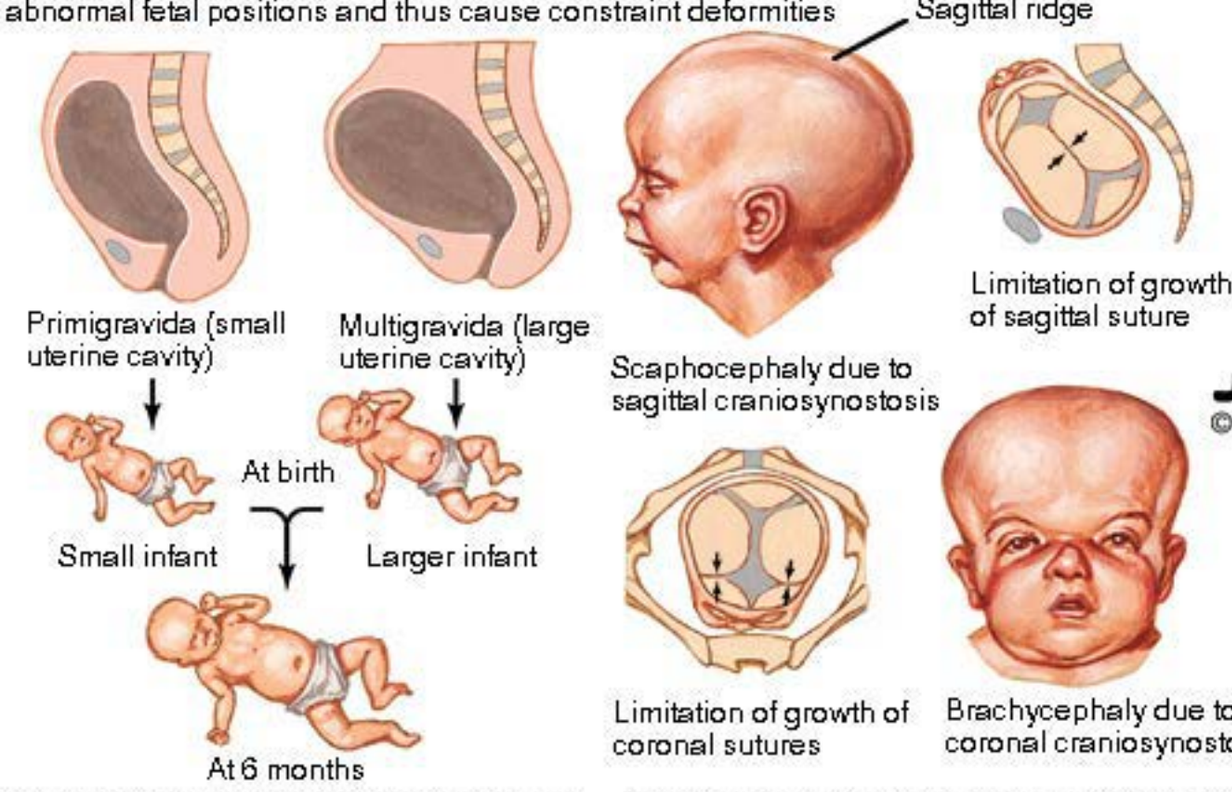


Adult facies with synophrys and long eyelashes

Examples of Deformations



Conditions that cause intrauterine crowding can lead to abnormal fetal positions and thus cause constraint deformities

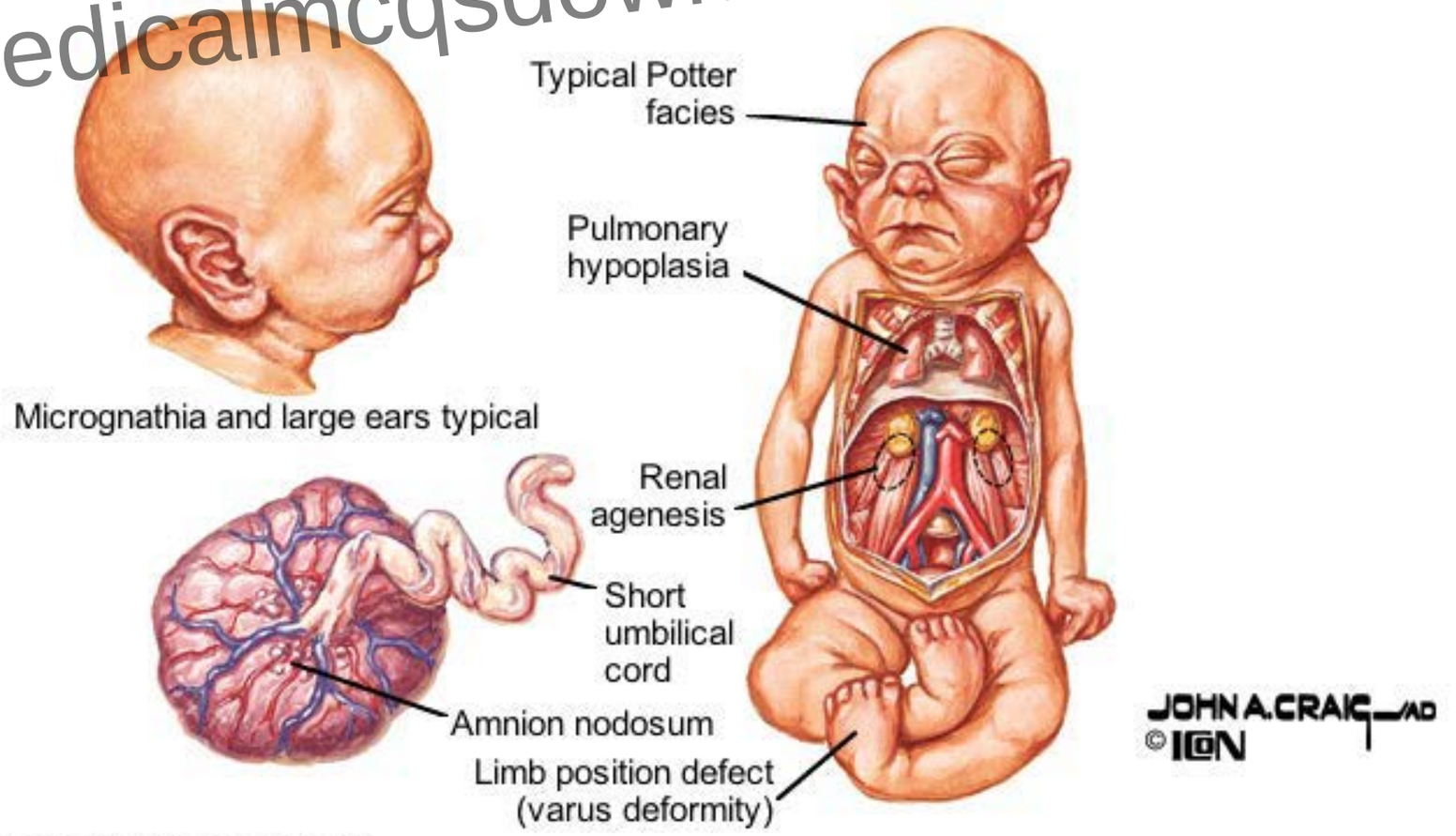


Constraint-related growth deficiency is transient. Given room, small infants catch up rapidly

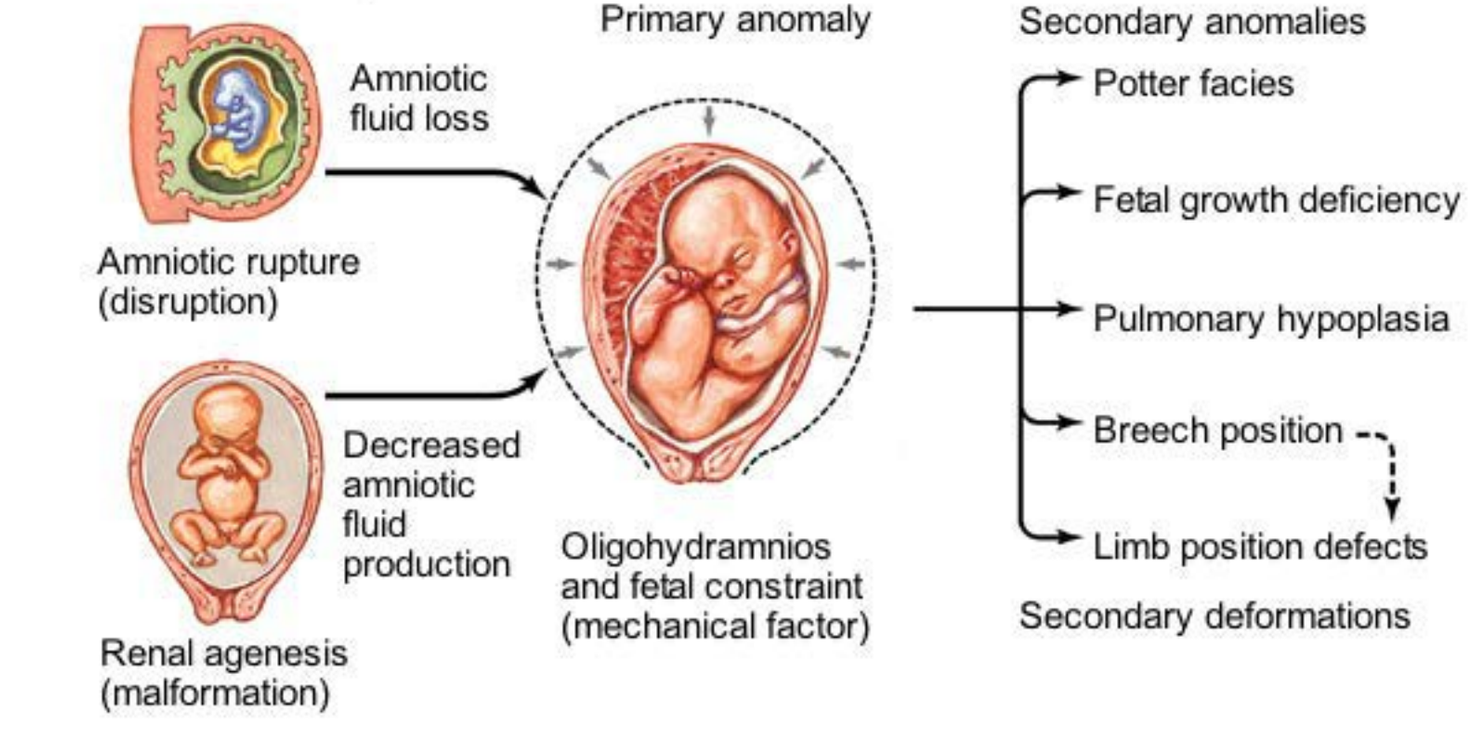
Early engagement of fetal head may limit sutural growth and result in craniosynostotic skull deformities

Example of a Deformation Sequence

Potter Sequence

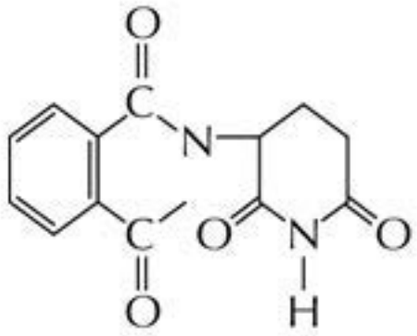


Events in Potter sequence



Drug-Induced Embryopathies

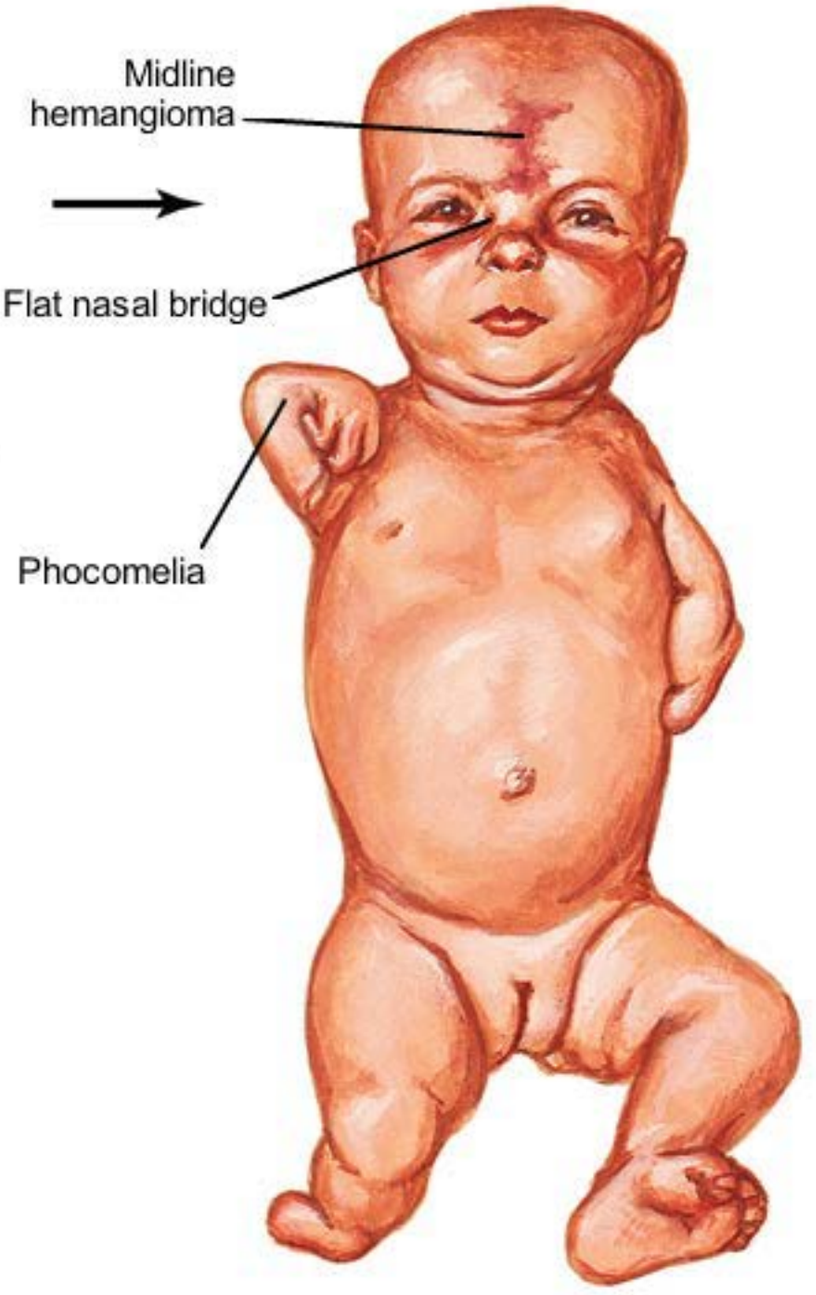
Thalidomide



(α[*N*-phthalimido]glutarimide)

27- to 33-day embryo

Limb defects. From hypoplasia to complete absence of radius, ulna, and humerus; fibula and tibia less commonly involved

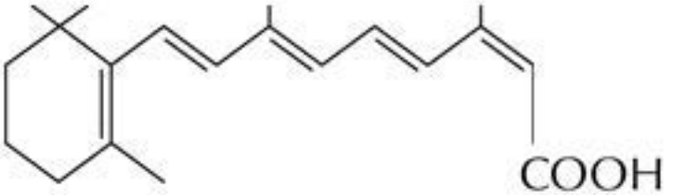


Clinical features of thalidomide embryopathy

Drug-Induced Embryopathies

Retinoic acid

Facial features. Ocular hypertelorism with down-slanting palpebral fissures, micrognathia, and U-shaped palate



(13-*cis*-retinoic acid)

Hydrocephalus may occur

EARLY EMBRYONIC DEVELOPMENT AND THE PLACENTA

TIMELINE

Prenatal Time Scale (Months)

1 week

Ovulation, fertilization, and formation of the morula and blastocyst. Implantation begins.

Blastocyst

2 weeks

Implantation completed. The amnion, chorion, and yolk sac form. The placenta begins to develop.

3 weeks

Gastrulation occurs.

Embryo

1

4 weeks

Folding of the embryo occurs, and the vertebrate body plan is established.

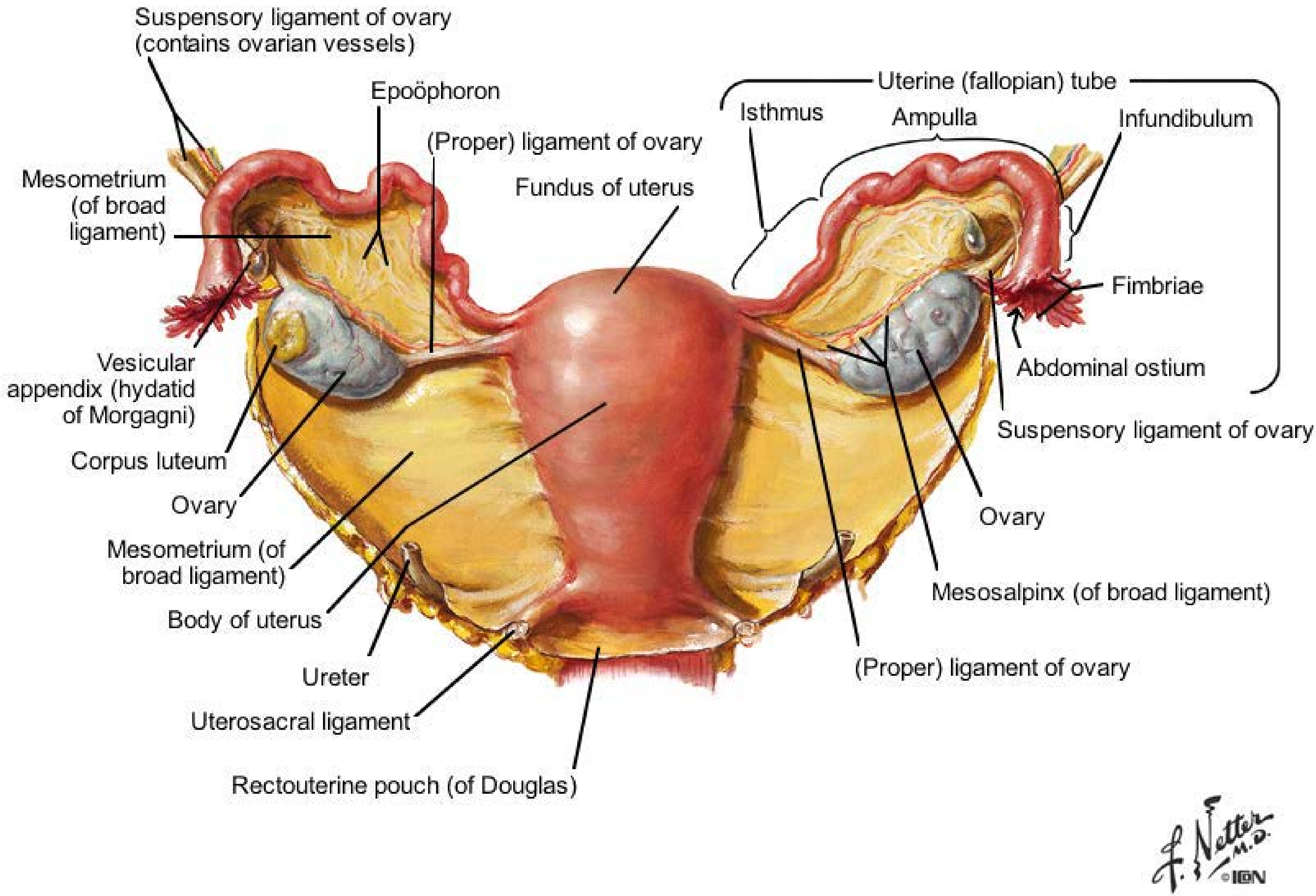
Fetus

9

Birth

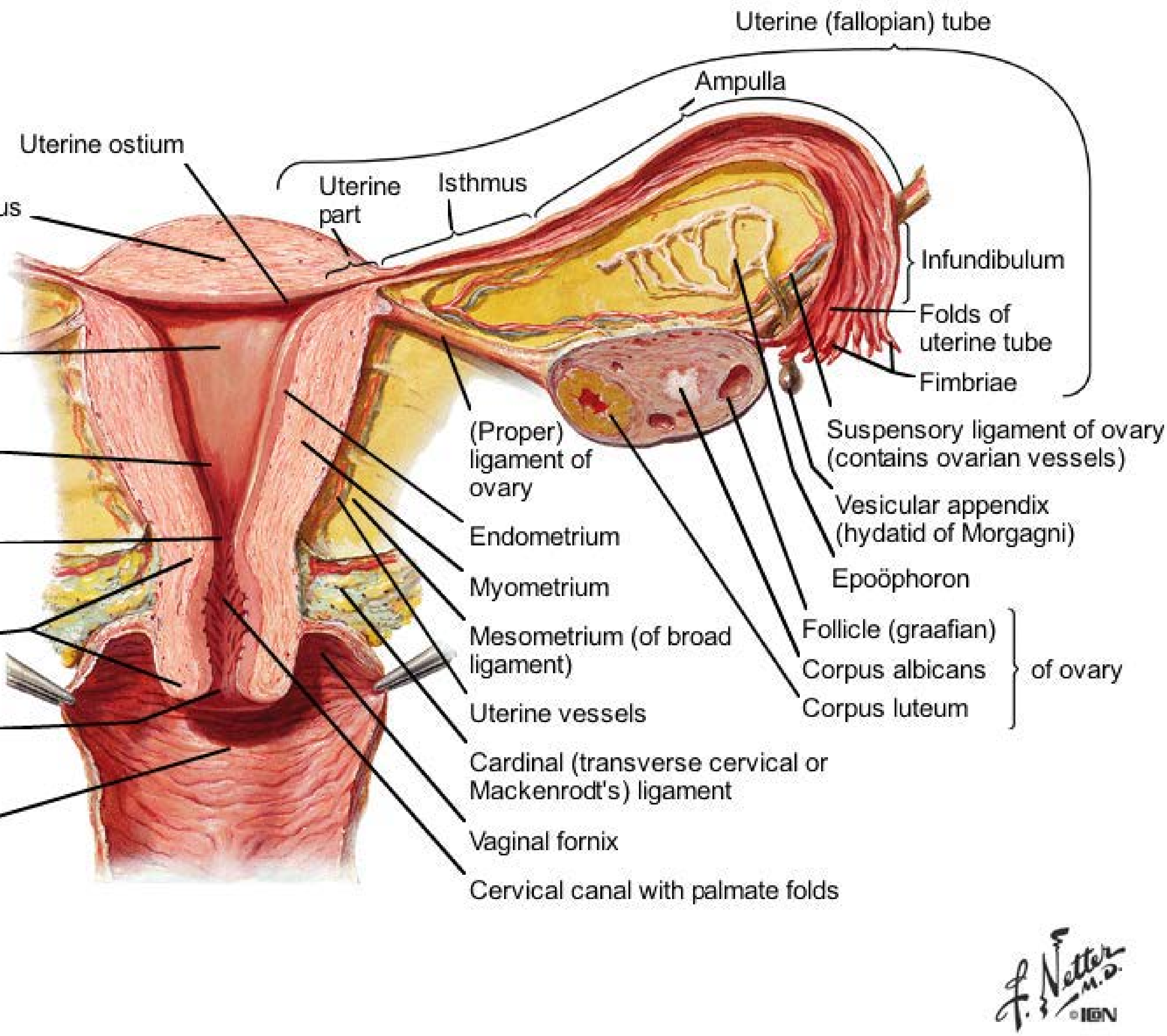
Adult Uterus, Ovaries, and Uterine Tubes

Posterior view

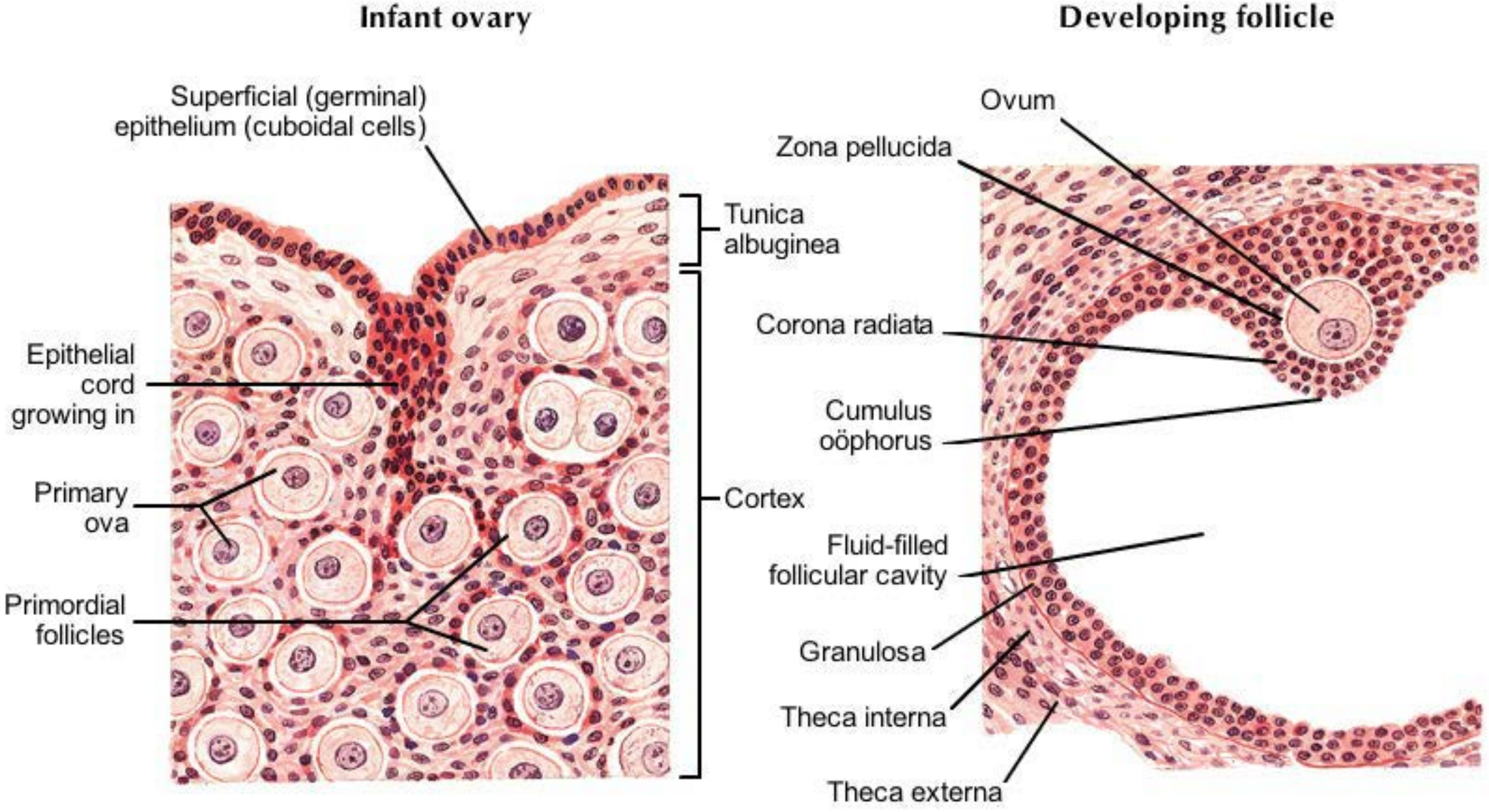


Adult Uterus, Ovaries, and Uterine Tubes

Frontal section



Ovary, Ova, and Follicle Development



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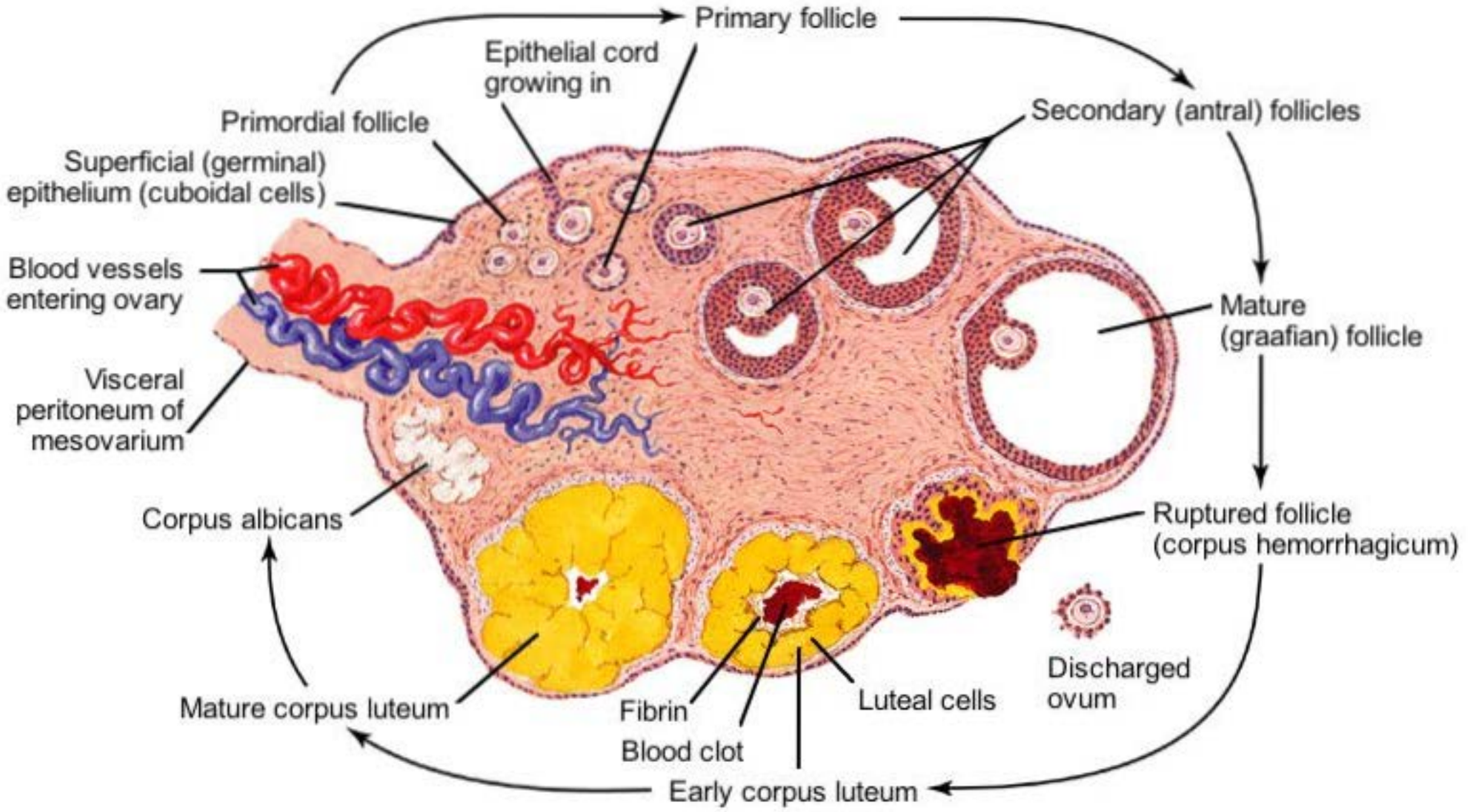
Ovary, Ova, and Follicle Development

Stages of ovum and follicle



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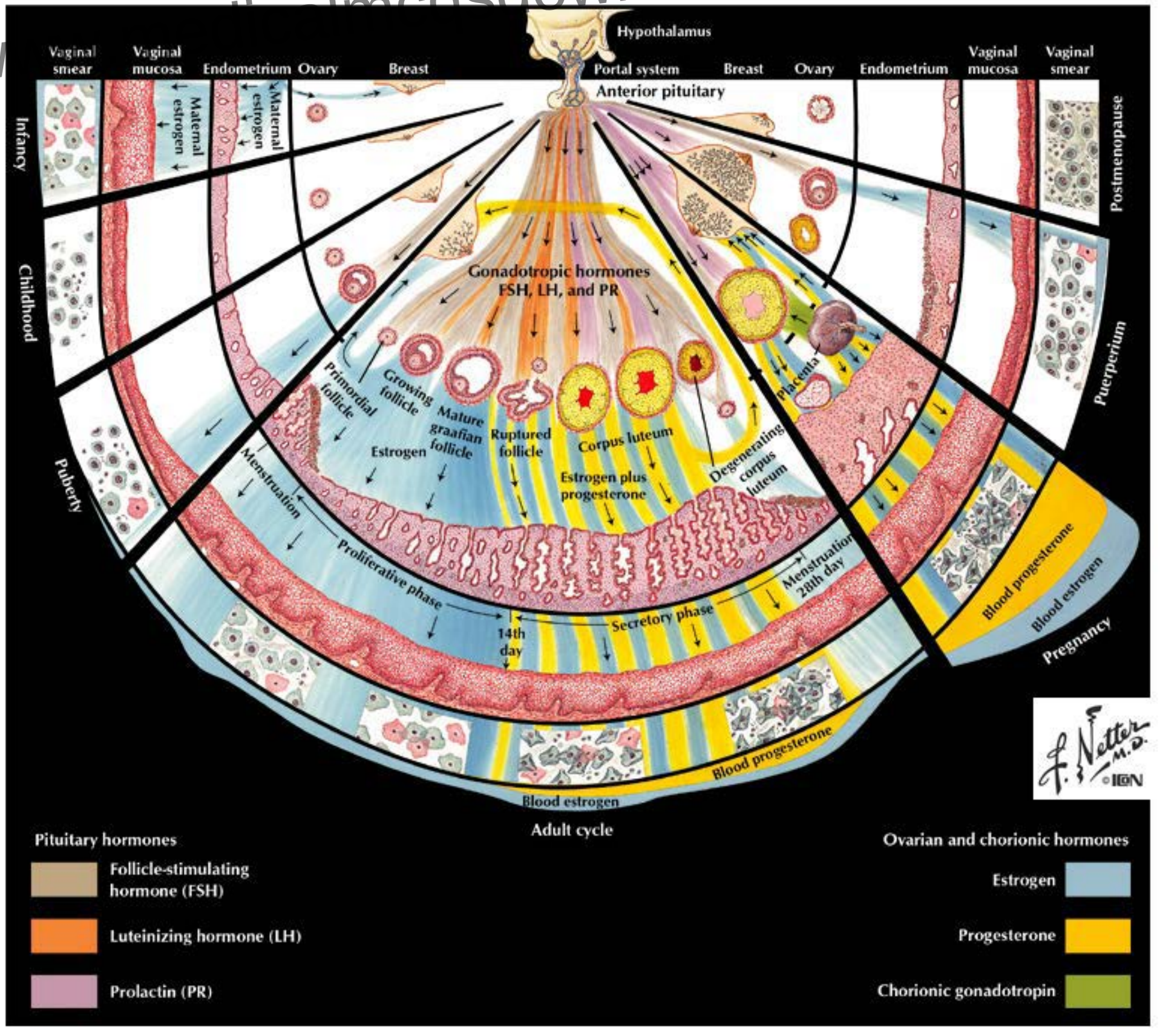
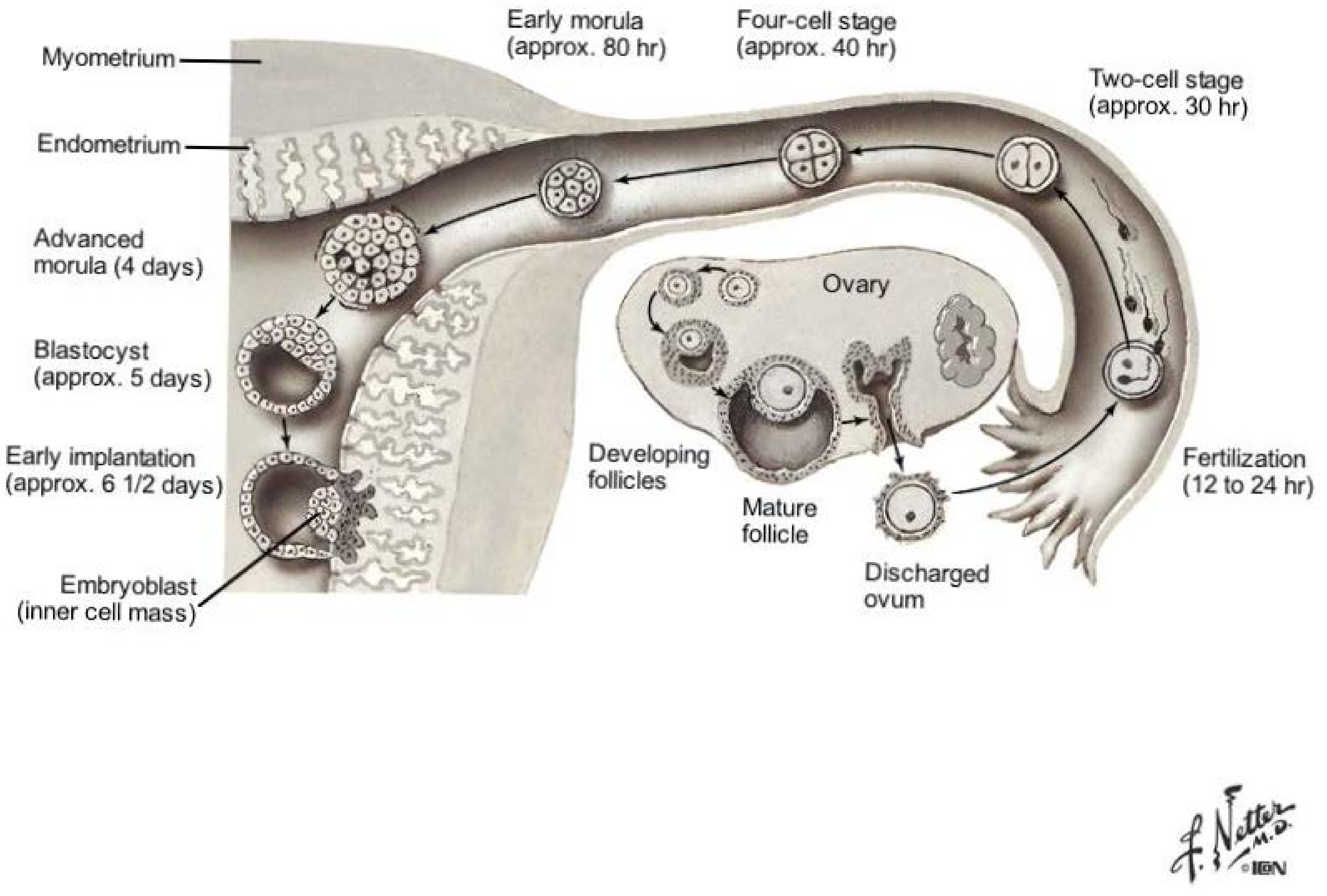
The Menstrual Cylce and Pregnancy

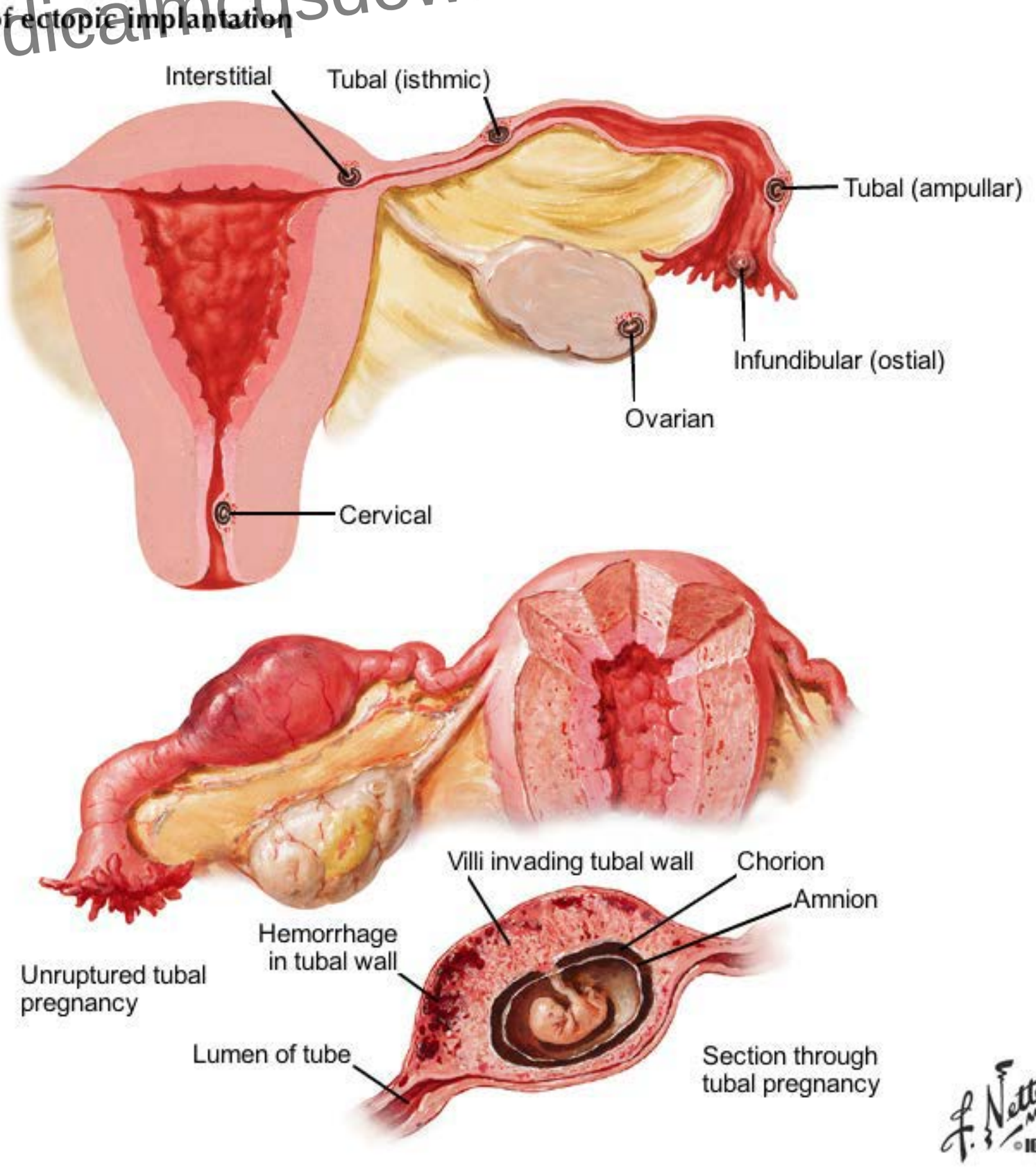
Regulation of follicle and endometrial development and pregnancy



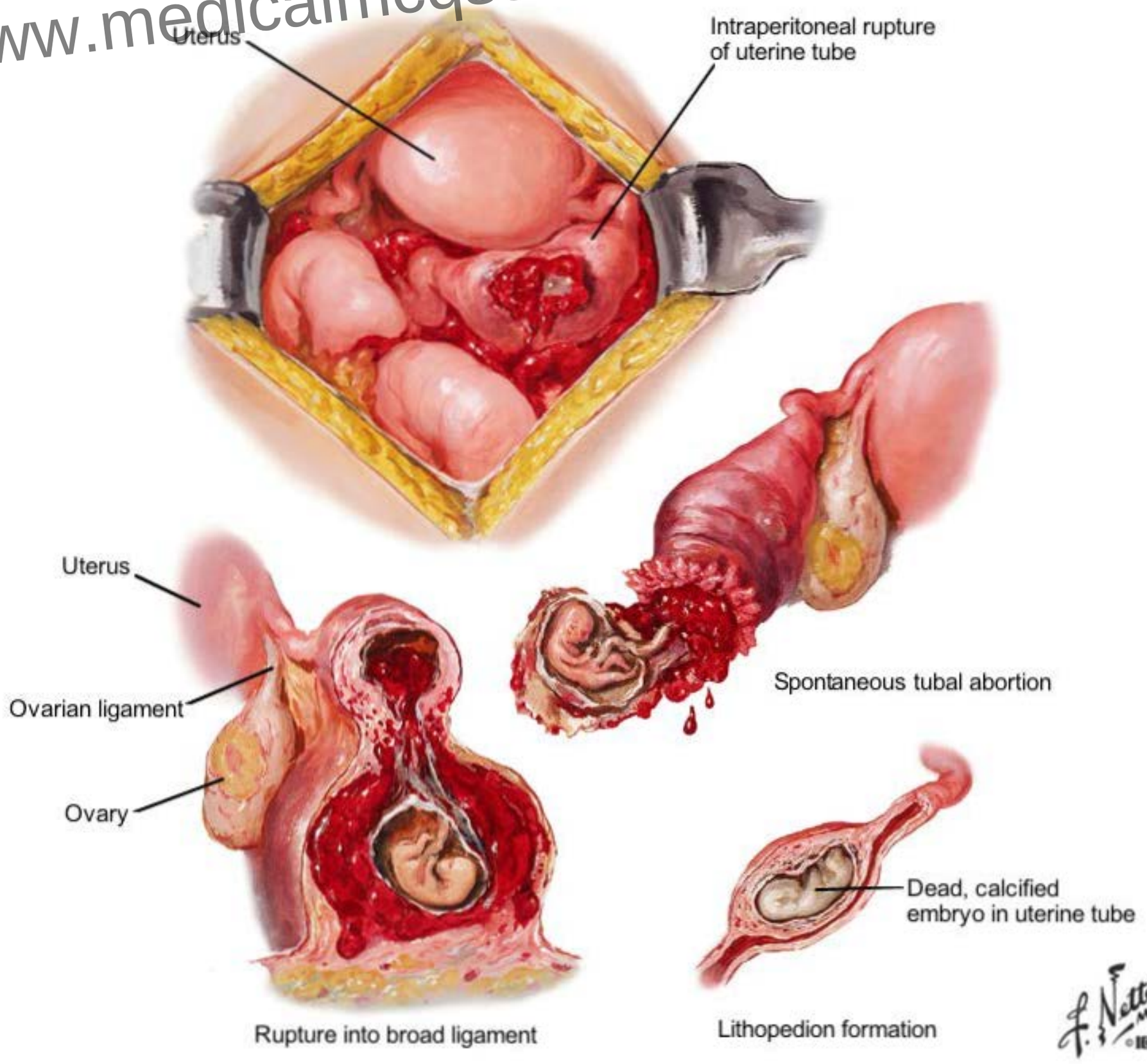
The First Week



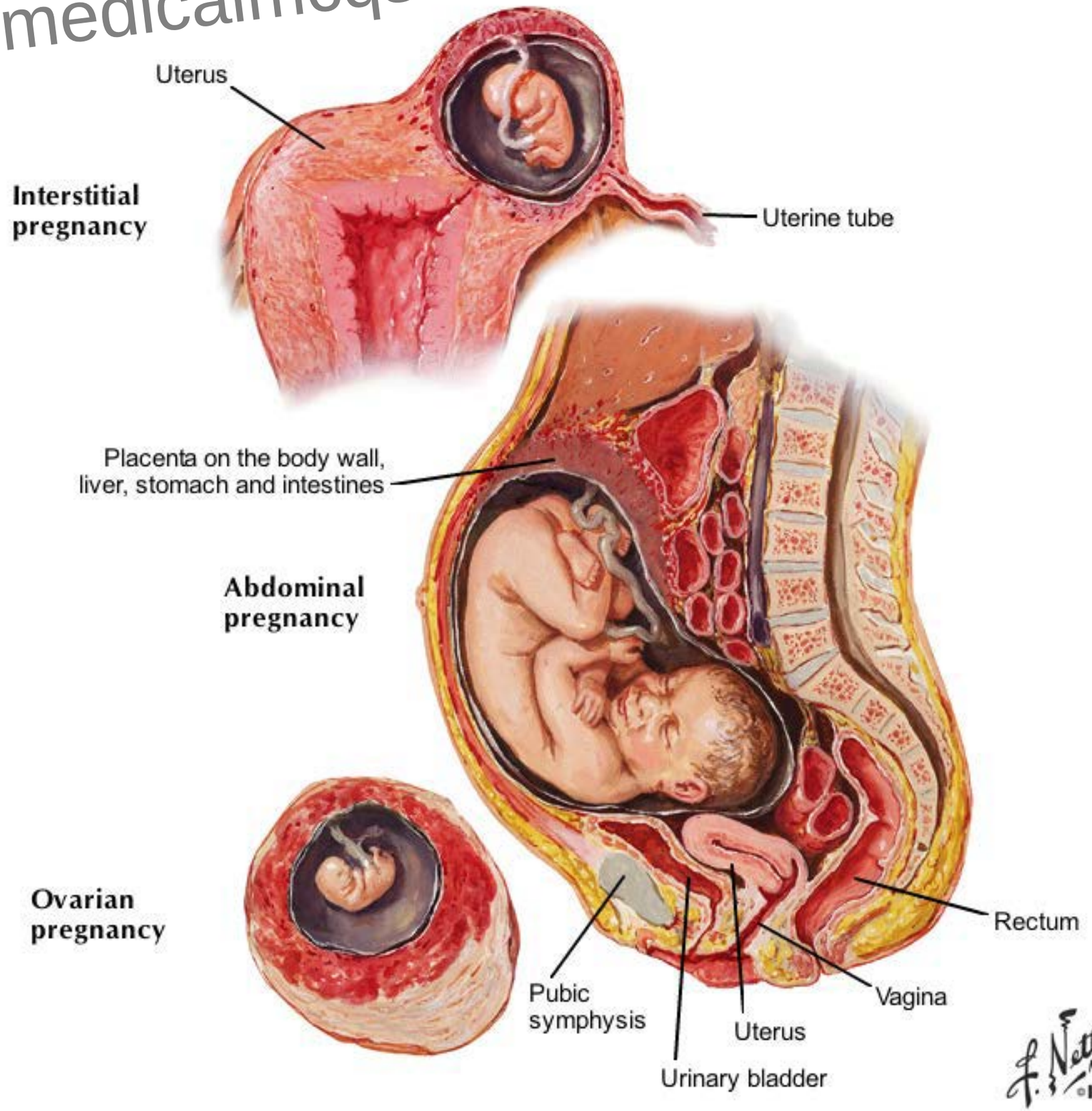
Ectopic Pregnancy



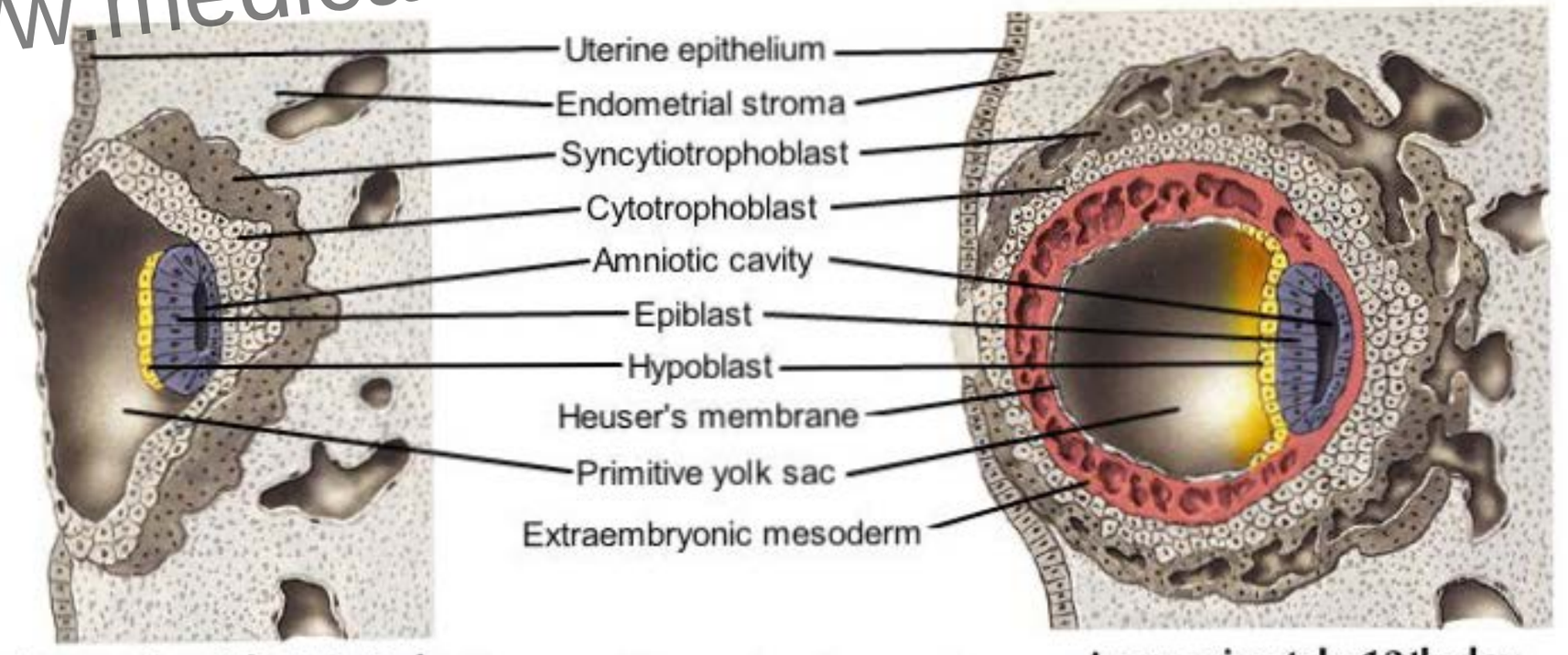
Tubal Prenancy



Interstitial, Abdominal, and Ovarian Pregnancy

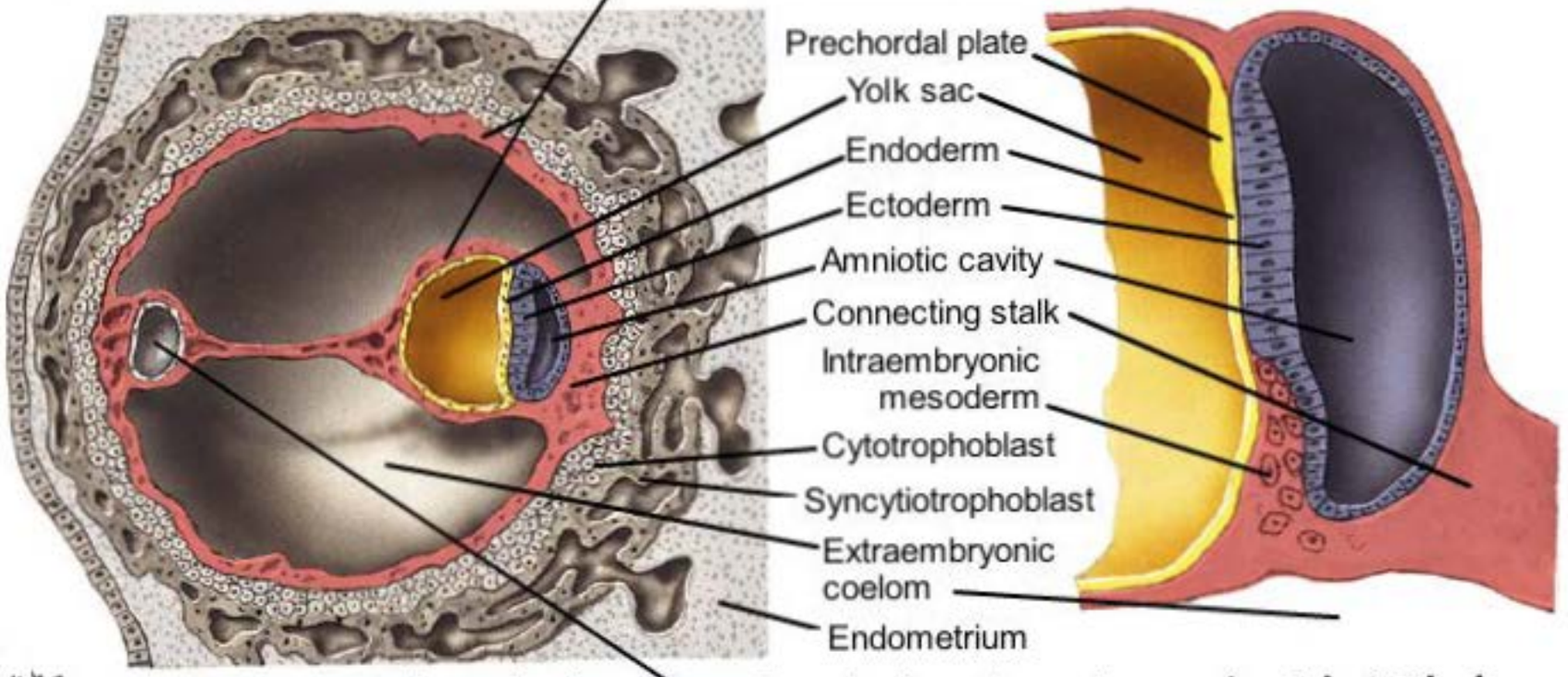


The Second Week



Approximately 7 1/2 days

Approximately 12th day



Approximately 15th day

Approximately 17th day

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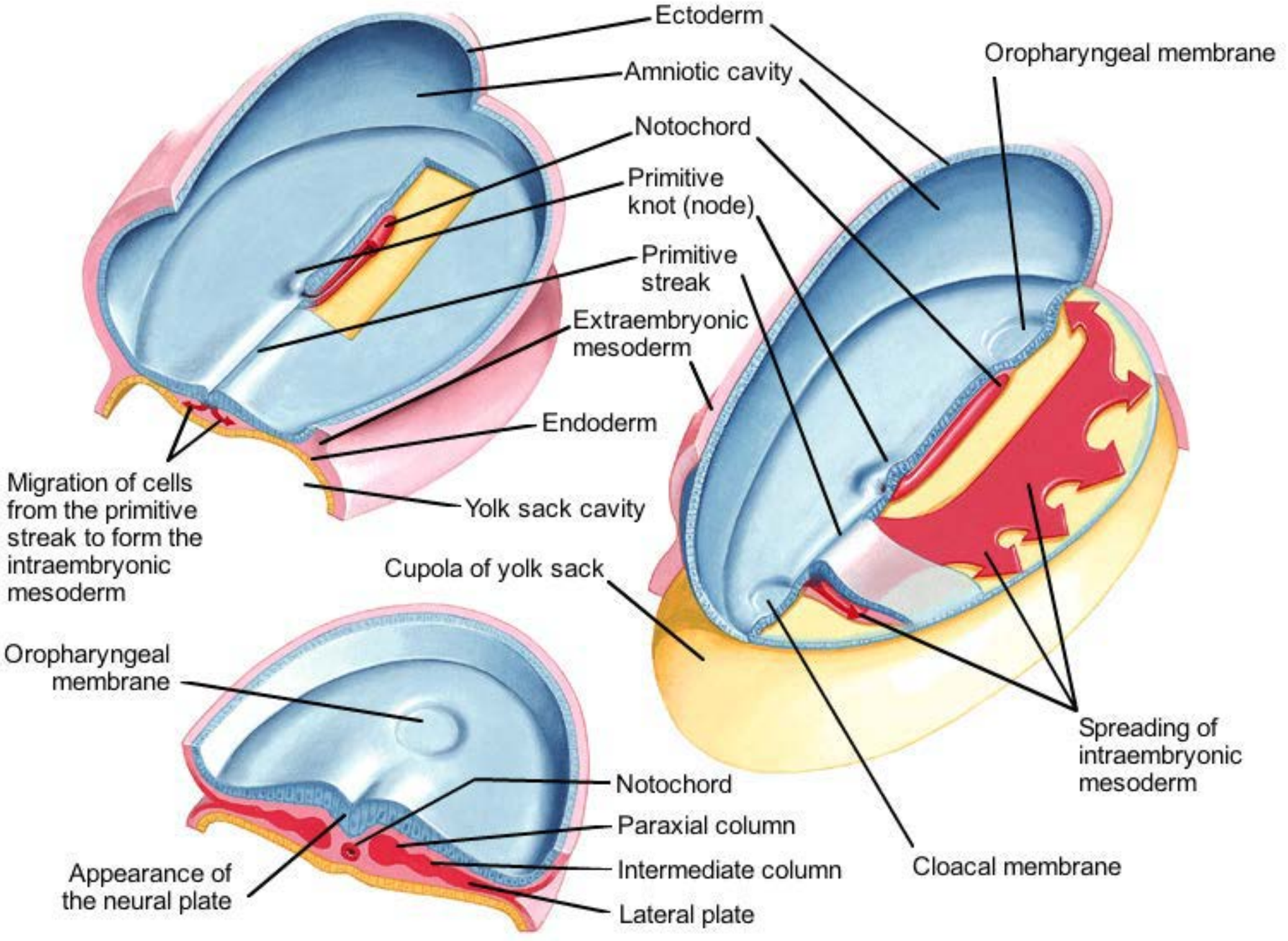
The Third Week

Formation of Intraembryonic Mesoderm from the Primitive Streak and Node (Knot)



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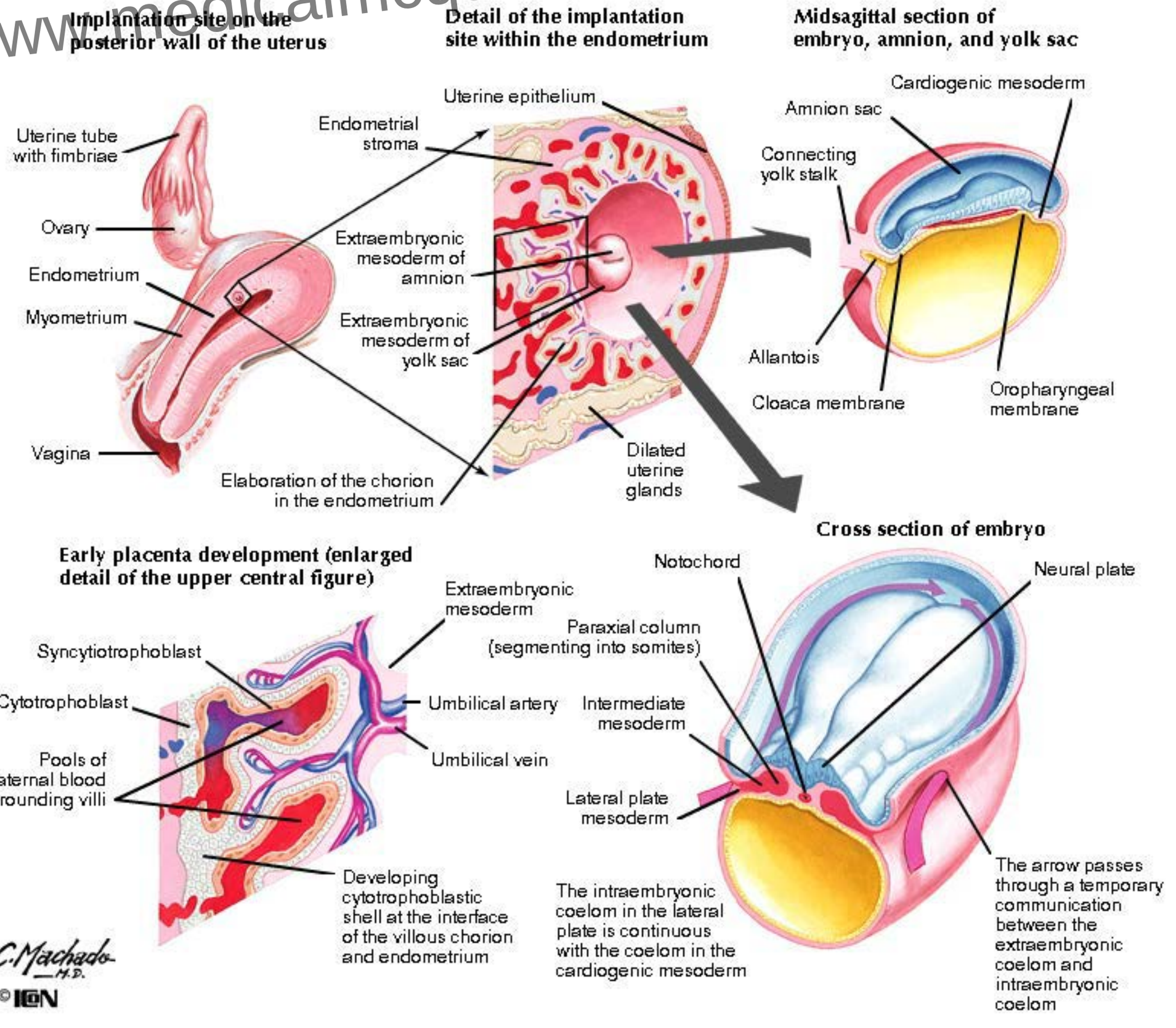
Events Related to Gastrulation



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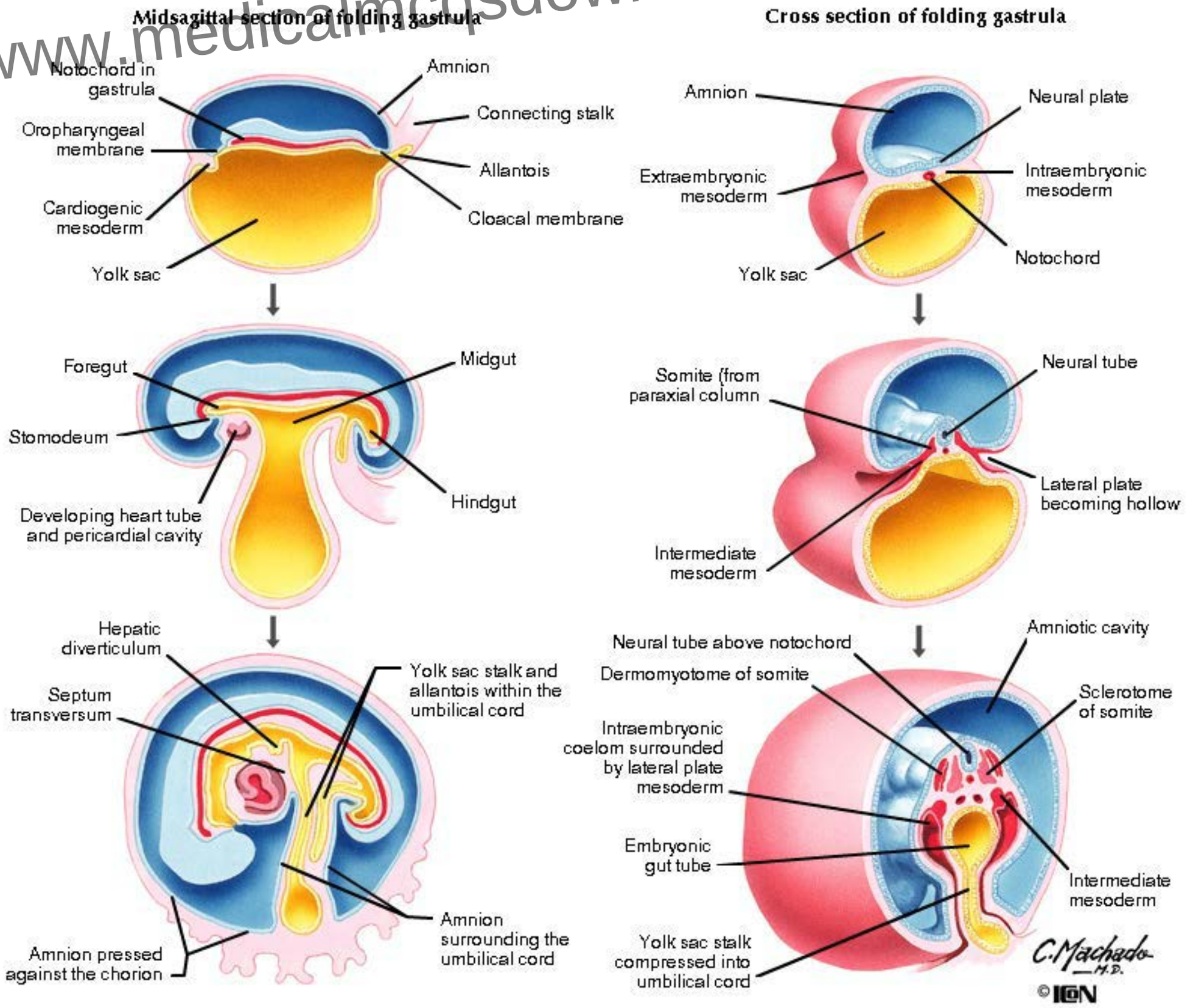
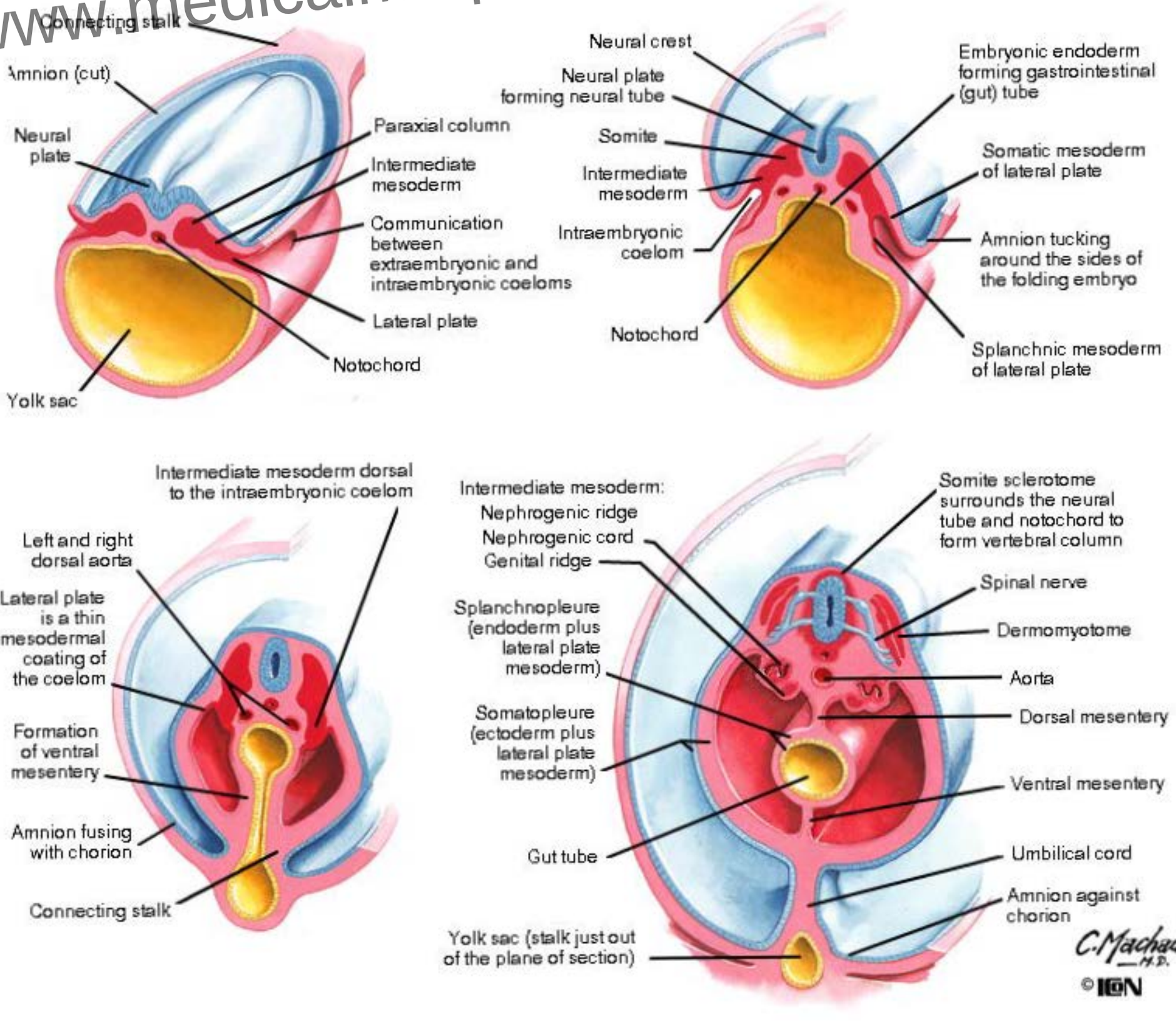
Folding of the Embryo in Week 4

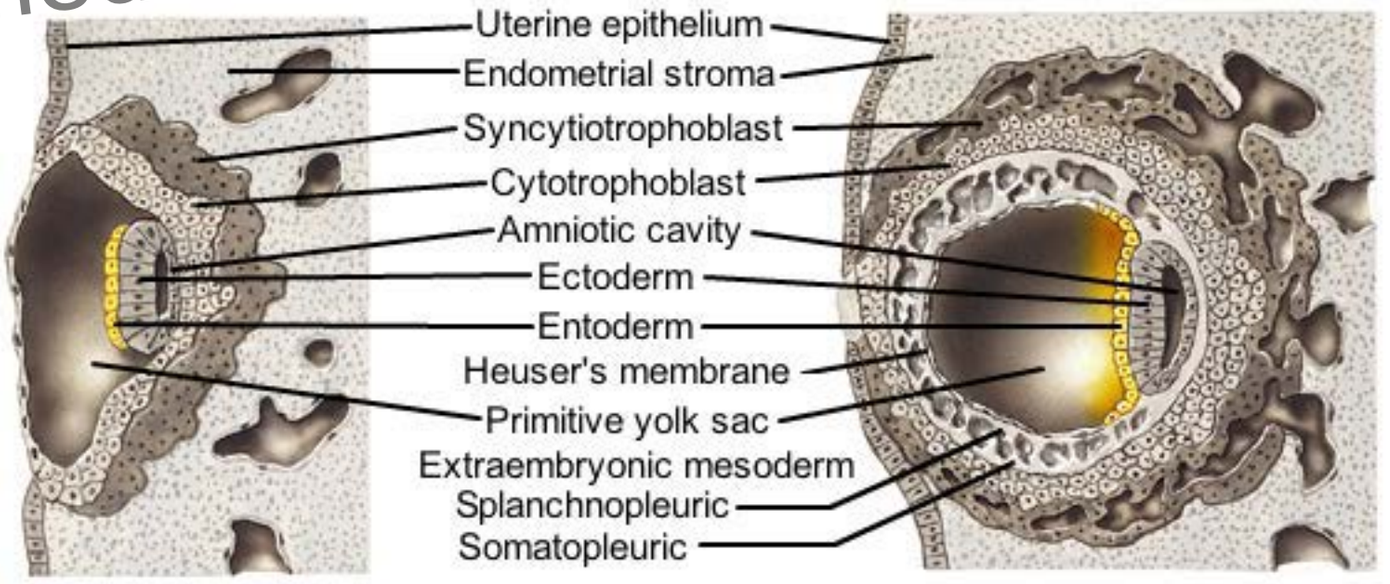


The Vertebrate Body Plan

Vertebrate Body Plan after 4 Weeks



Formation of the Placenta



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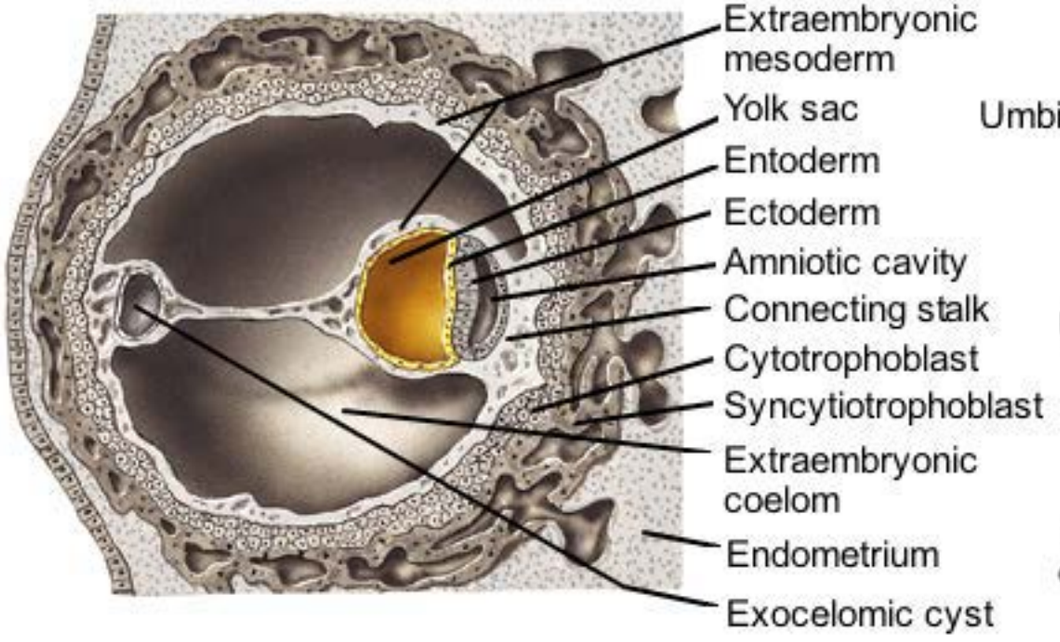
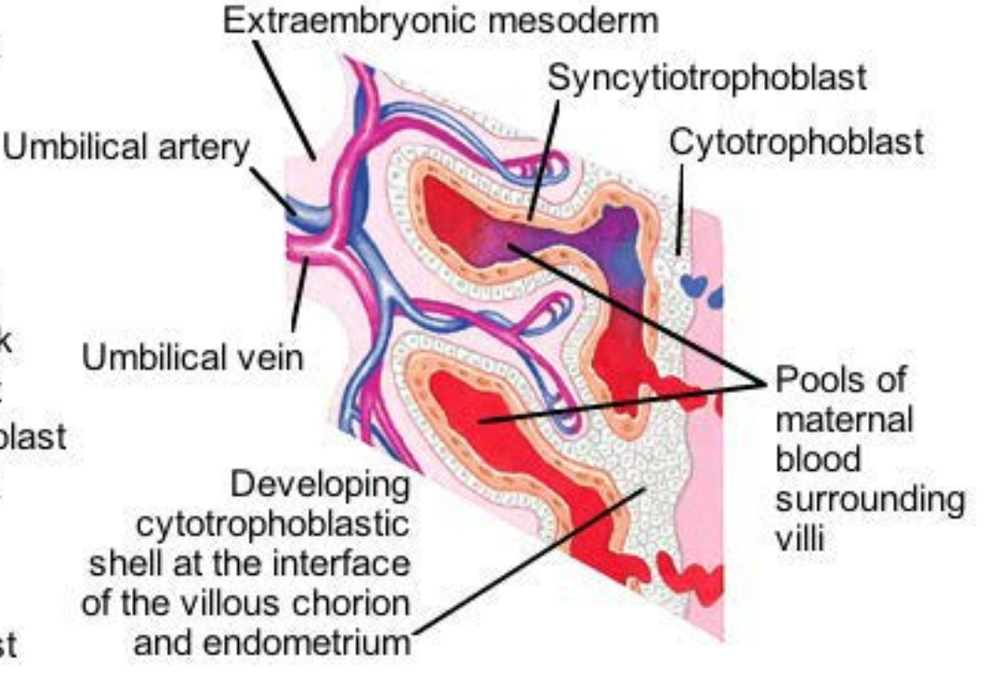
Approximately 7 1/2 days

Approximately 12th day



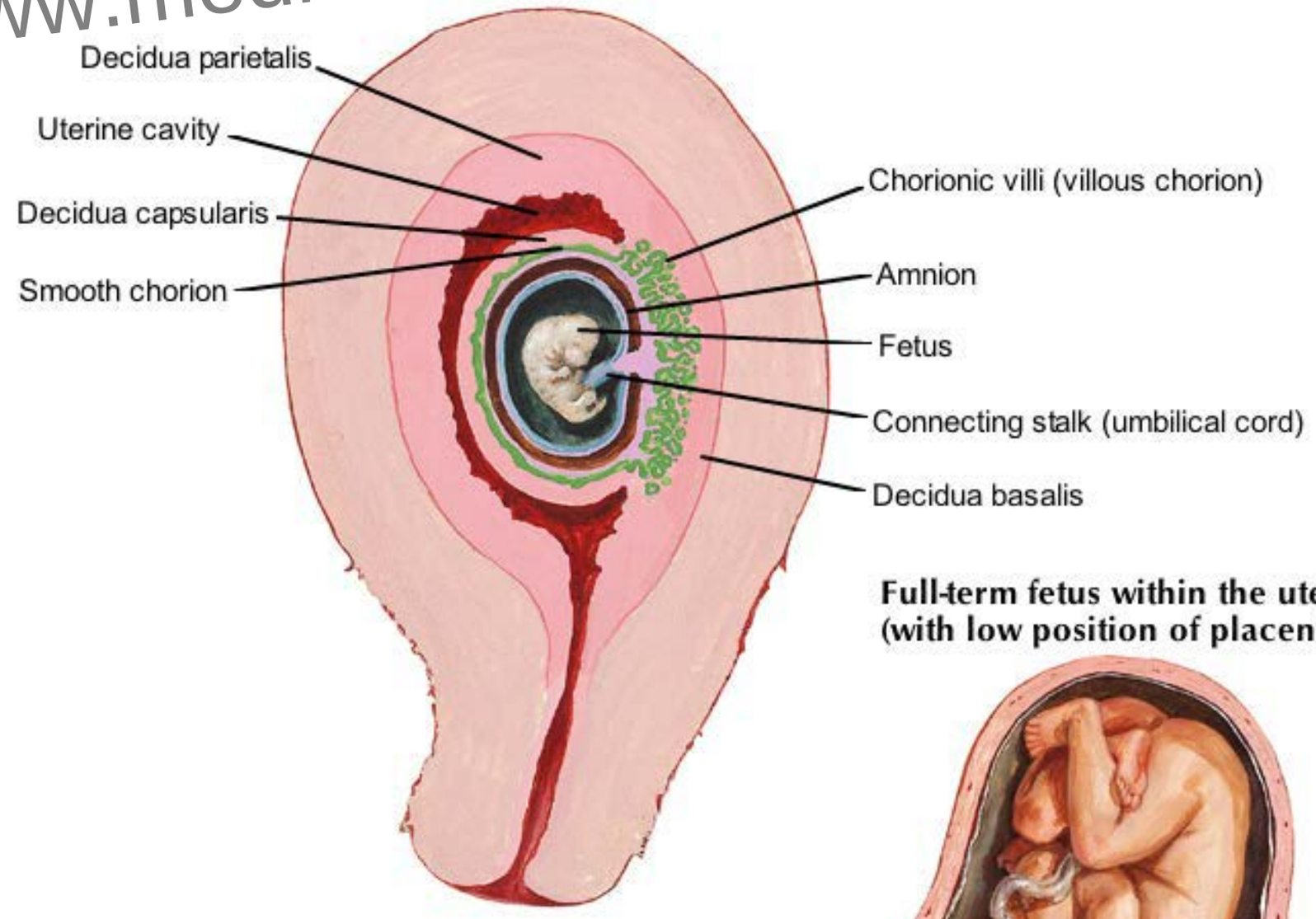
Approximately 15th day



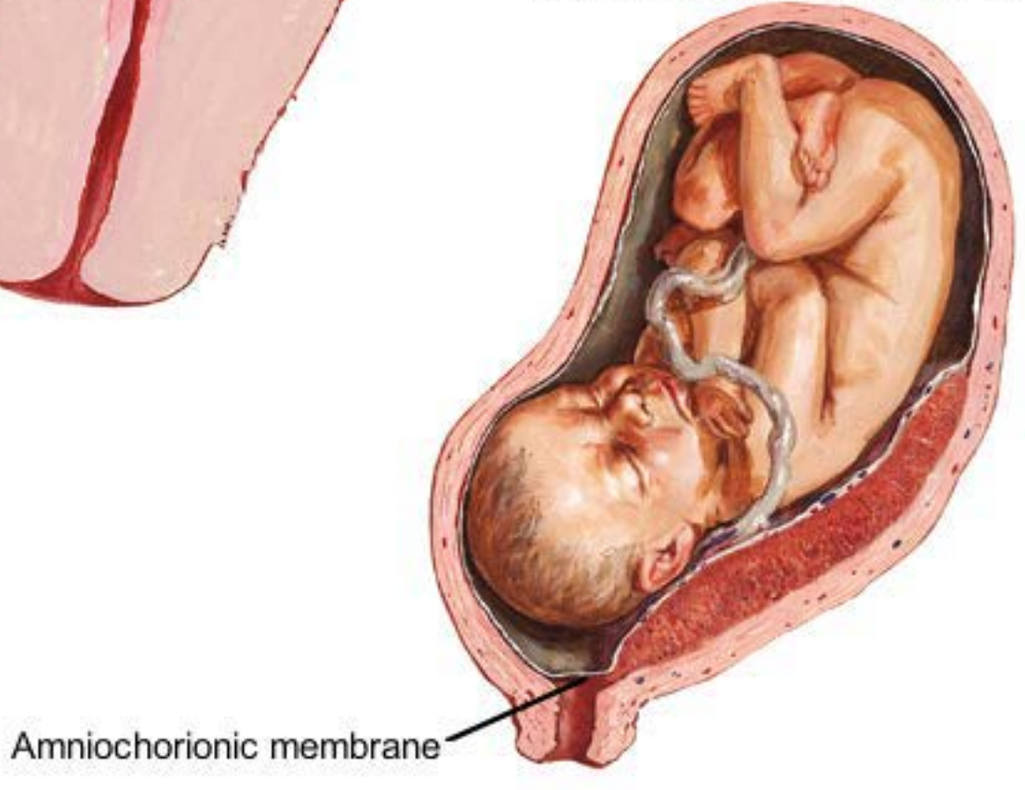
Approximately 25th day and the establishment of placental circulation

The Endometrium and Fetal Membranes

Early fetal development and membrane formation in relation to the uterus as a whole (schematic)



Full-term fetus within the uterus (with low position of placenta)



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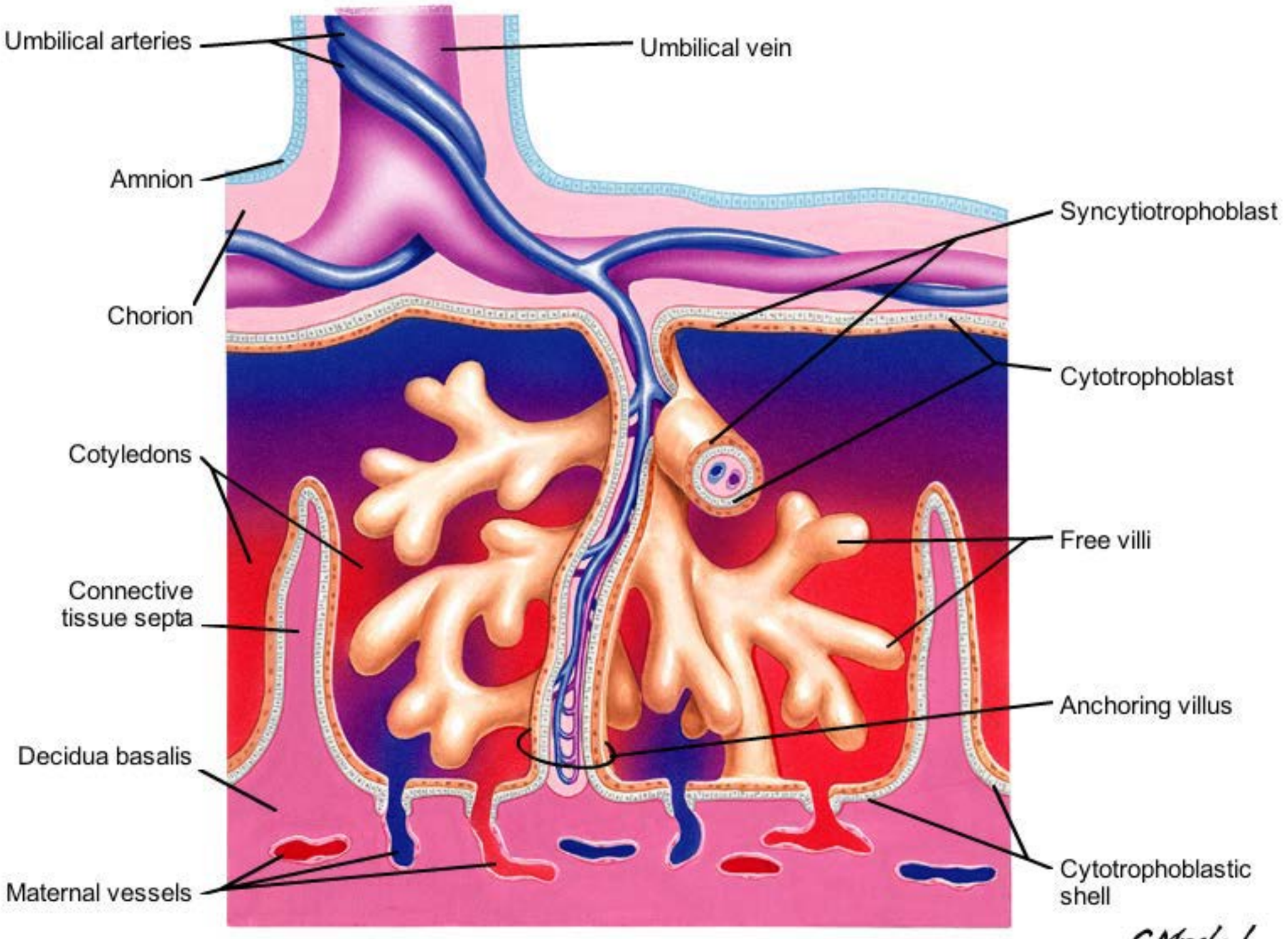
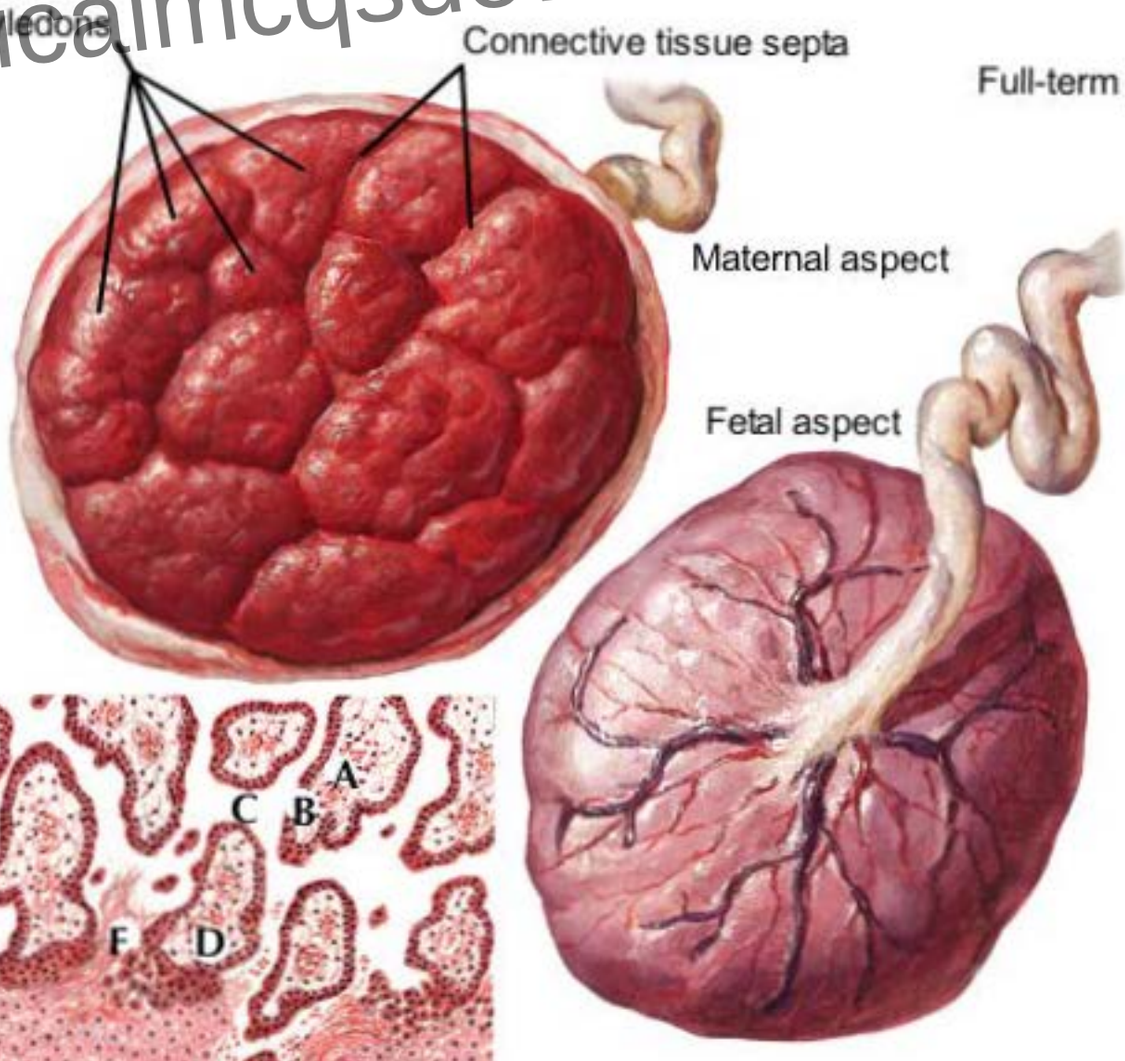
Placental Structure

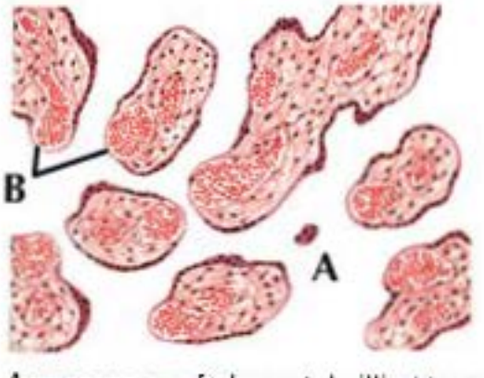
Development of the placenta: chorionic villi



Placental Structure



Section through deep portion of placenta-early gestation
(A) Villus, (B) trophoblast, (C) intervillous space, (D) anchoring villus, (E) villus invading blood vessel, (F) fibrinoid degeneration, (G) decidua basalis, (H) gland



Appearance of placental villi at term
(A) Syncytial cell mass becoming trophoblastic embolus, (B) fetal blood vessel endothelium against a thinned syncytiotrophoblast, where they share a basal lamina. The cytotrophoblast has disappeared

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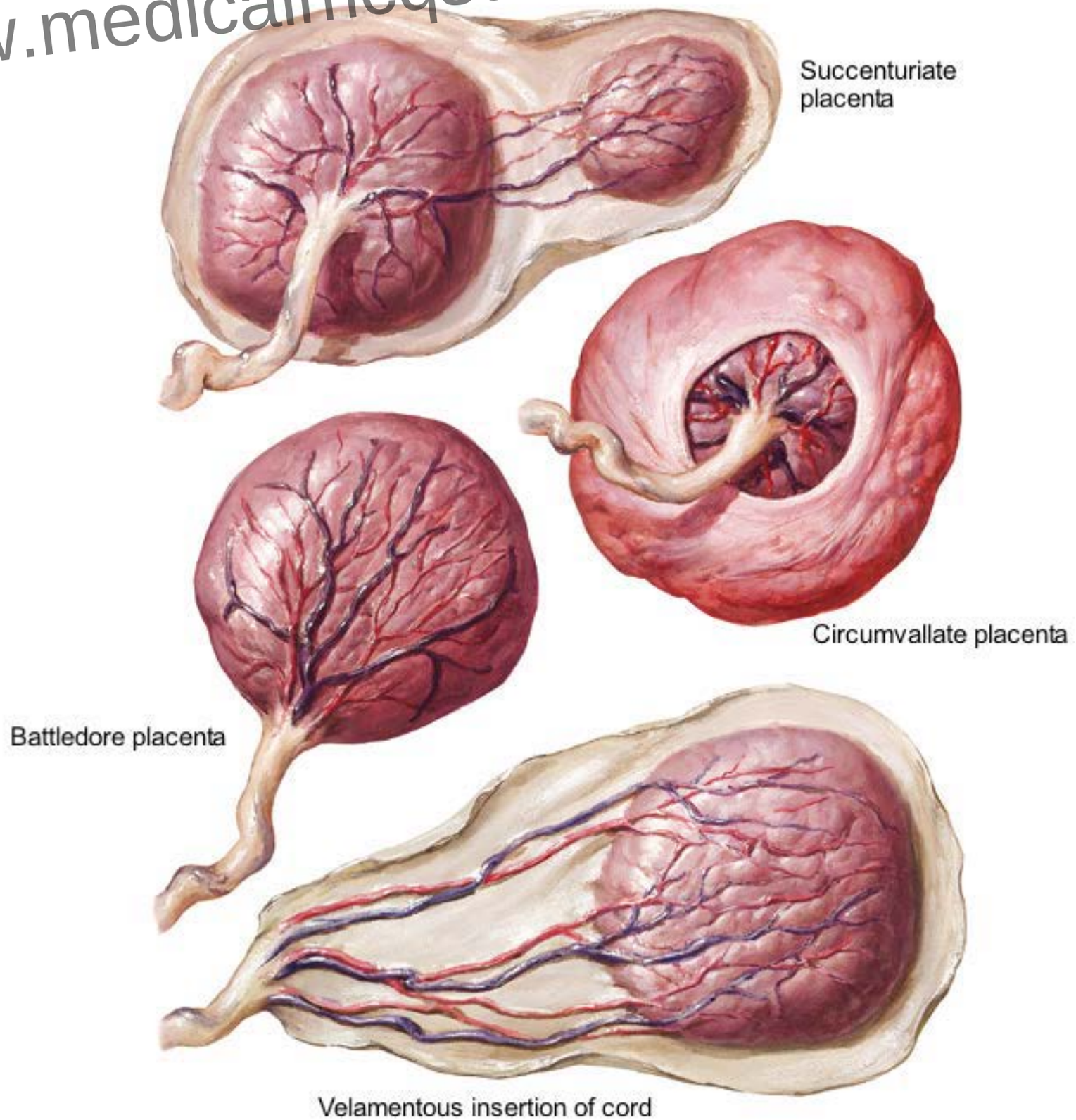
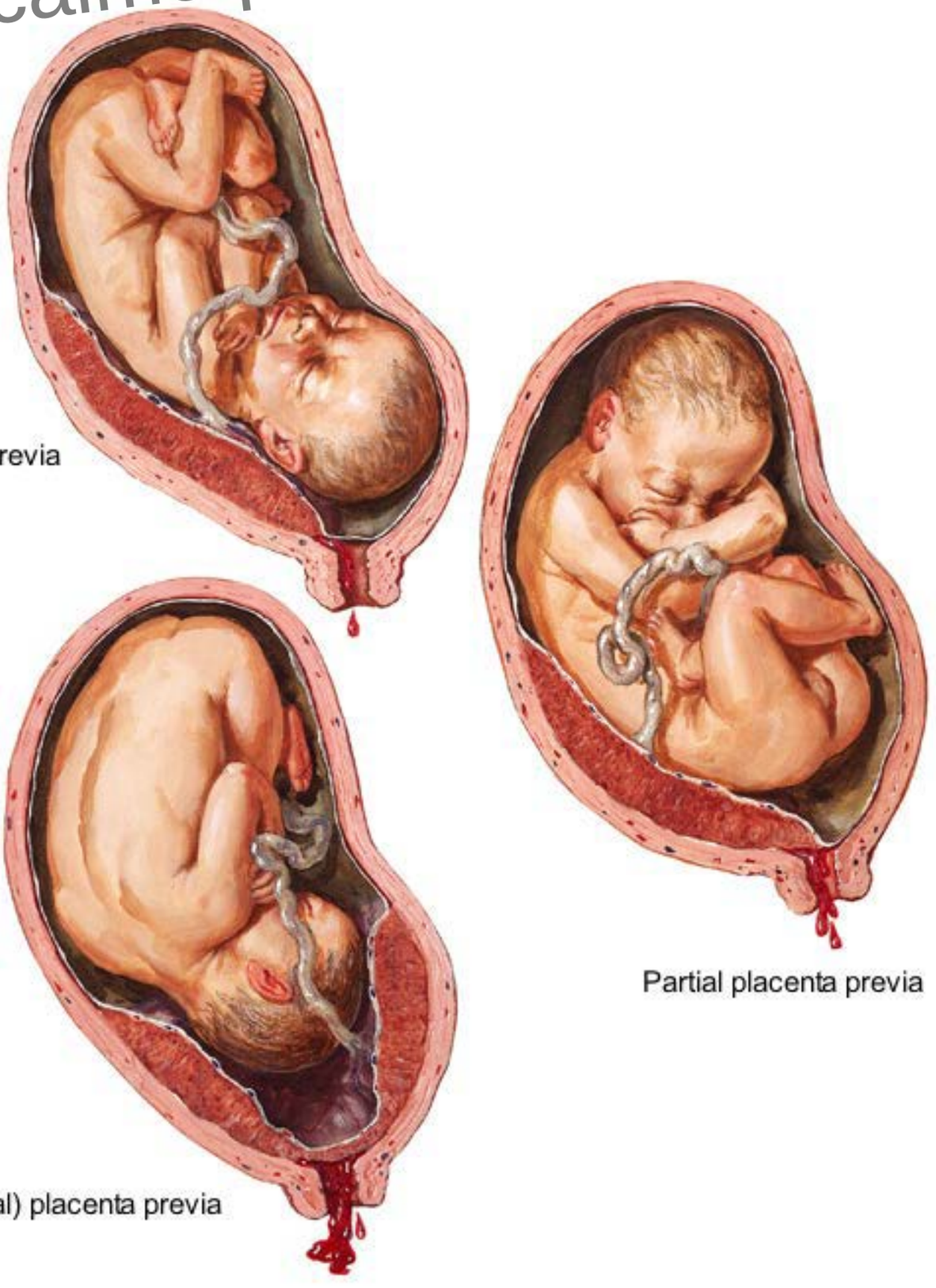
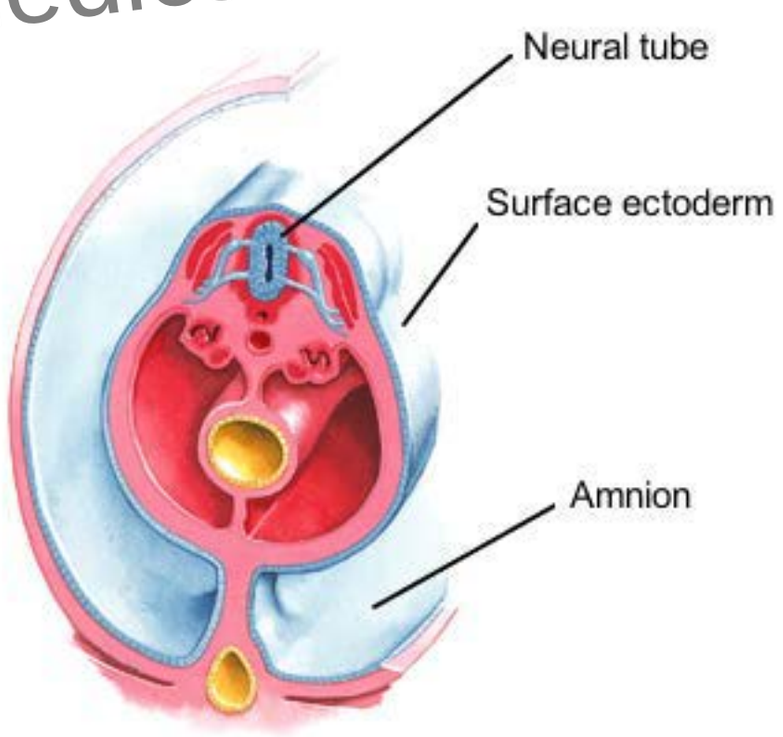
Placental Variations

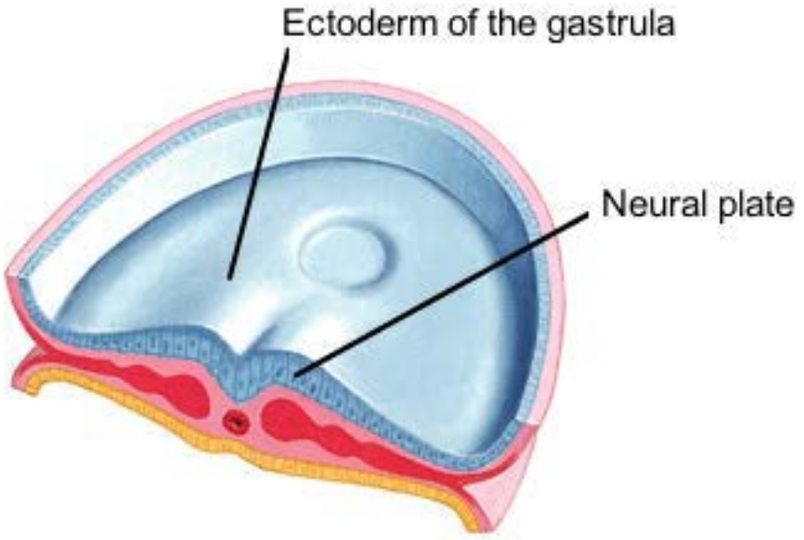


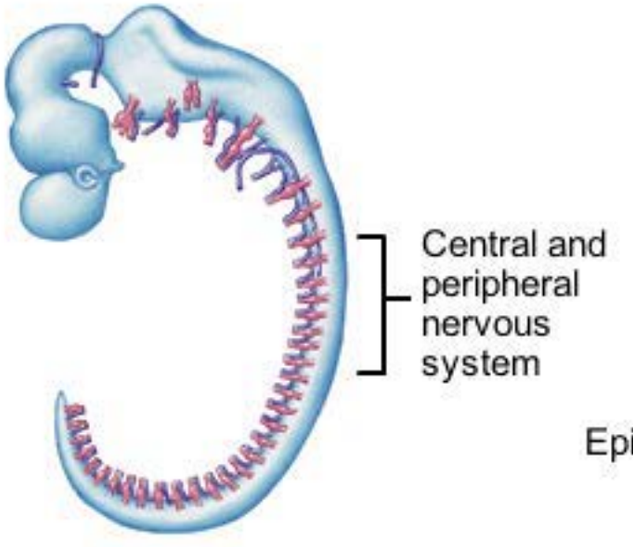
Placenta Previa



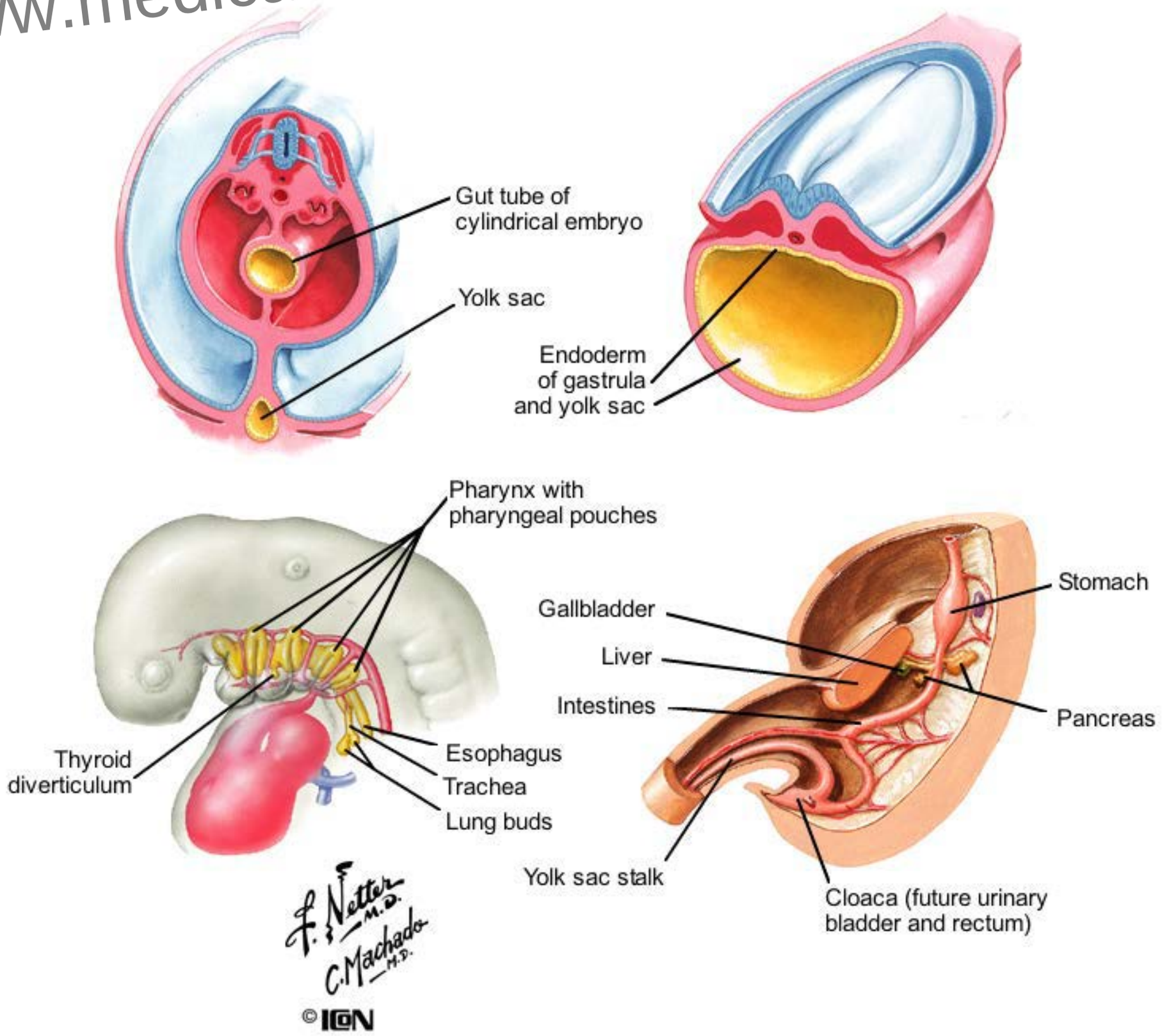
Summary of Ectodermal Derivatives



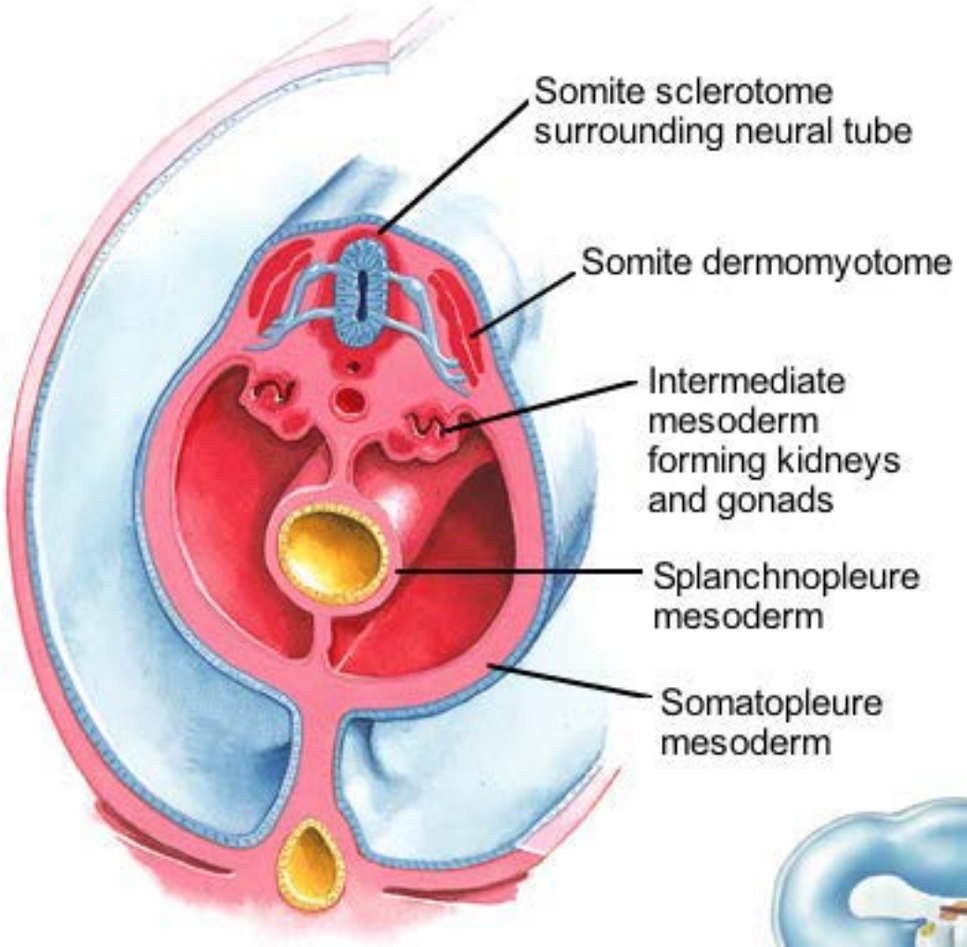


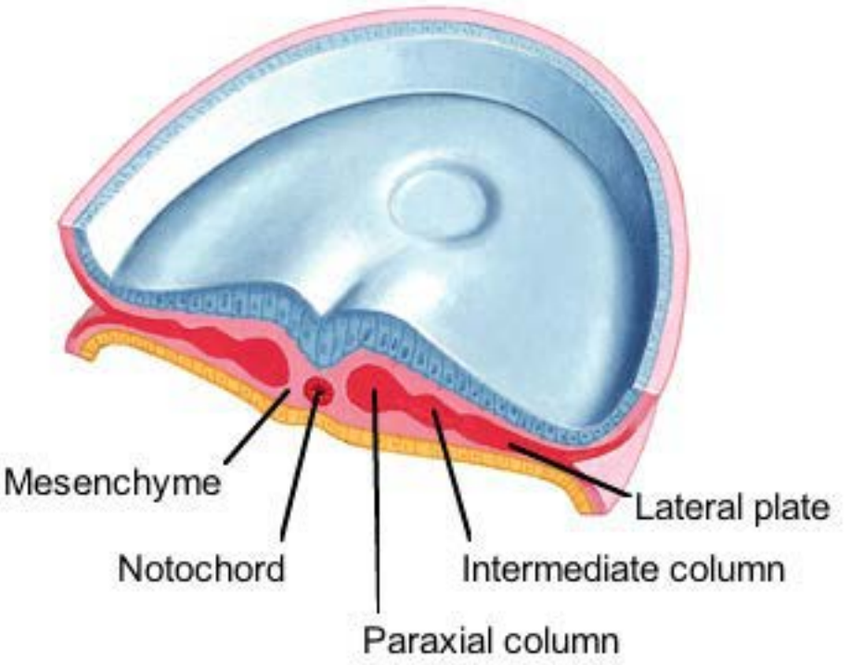


Summary of Endodermal Derivatives



Summary of Mesodermal Derivatives





Axial and appendicular skeleton, 5 weeks

Developing skeletal muscles, 8 weeks

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C. Machado M.D.

Chart 2.1 Ectodermal Derivatives

Primordia	Derivatives or Fate
Surface ectoderm	Epidermis of the skin
	Sweat, sebaceous, and mammary glands
	Nails and hair
	Tooth enamel
	Lacrimal glands
	Conjunctiva
	External auditory meatus
(Stomodeum and nasal placodes)	Oral and nasal epithelium
	Anterior pituitary
(Otic placodes)	Inner ear
(Lens placodes)	Lens of eye
Neural tube	Central nervous system
	Somatomotor neurons
	Branchiomotor neurons
	Presynaptic autonomic neurons
	Retina/optic nerves
	Posterior pituitary
Neural crest	Peripheral sensory neurons
	Postsynaptic autonomic neurons
	All ganglia
	Adrenal medulla cells
	Melanocytes
	Bone, muscle, and connective tissue in the head and neck
Amnion	Protective bag (with chorion) around fetus

Chart 2.2 Endodermal Derivatives

CHART 2.2 ENDODERMAL DERIVATIVES

Primordia	Epithelial Derivatives or Fate
Gut tube endoderm	GI tract (enterocytes) Mucosal glands of GI tract Parenchyma of GI organs (liver, pancreas) Airway lining (larynx, trachea, bronchial tree) Thyroid gland Tonsils
Cloaca (part of hindgut)	Rectum and anal canal Bladder, urethra, and related glands Vestibule Lower vagina
Pharyngeal pouches (part of foregut)	Auditory tube and middle ear epithelium Palatine tonsil crypts Thymus gland Parathyroid glands C cells of the thyroid gland
Yolk sac	Embryonic blood cell production (mesoderm) Pressed into umbilical cord, then disappears
Allantois (from yolk sac, then cloaca)	Embryonic blood cell production (mesoderm) Vestigial, fibrous urachus Umbilical cord part disappears

GI, Gastrointestinal.

Chart 2.3 Mesodermal Derivatives

CHART 2.3 MESODERMAL DERIVATIVES

Primordia	Derivatives or Fate
Notochord	Nucleus pulposus of an intervertebral disc Induces neurulation
Paraxial columns (somites)	Skeletal muscle Bone Connective tissue (e.g., dorsal dermis, meninges)
Intermediate mesoderm	Gonads Kidneys and ureters Uterus and uterine tubes Upper vagina Ductus deferens, epididymis, and related tubules Seminal vesicles and ejaculatory ducts
Lateral plate mesoderm	Dermis (ventral) Superficial fascia and related tissues (ventral) Bones and connective tissues of limbs Pleura and peritoneum GI tract connective tissue stroma
Cardiogenic mesoderm	Heart Pericardium

GI, Gastrointestinal.

THE NERVOUS SYSTEM
TIMELINE

Prenatal Time Scale (Months)

Blastocyst

Embryo

1

2

3

4

Fetus

5

6

9

Birth

3rd week

Neurulation.

End of 4th week

Flexures and swellings distinguish the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon).

5th week

Spinal nerves grow into the body wall; autonomic nerves grow into the viscera within the body cavities.

End of 5th week

Forebrain divides into the diencephalon and telencephalon (future cerebral cortex).

3 Months

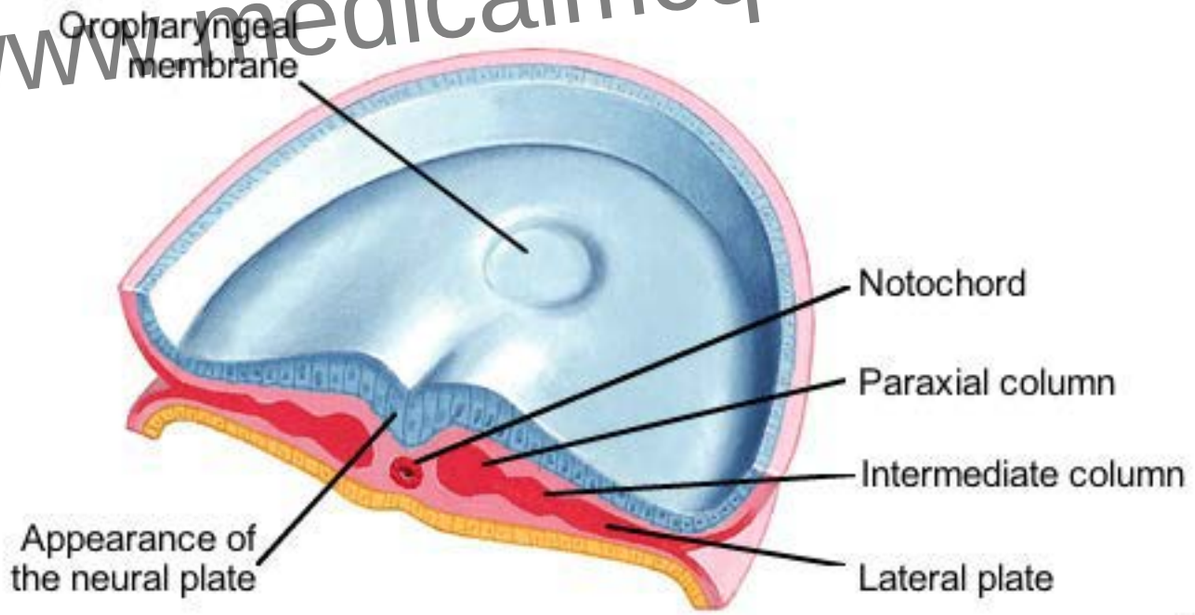
Cerebral cortex (telencephalon) overgrows the midbrain.

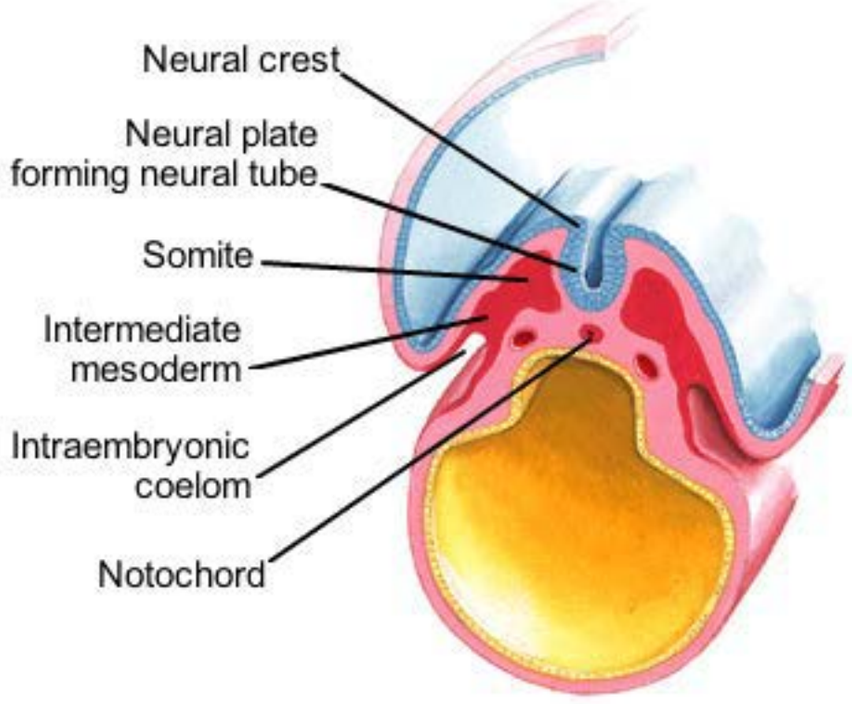
6 months

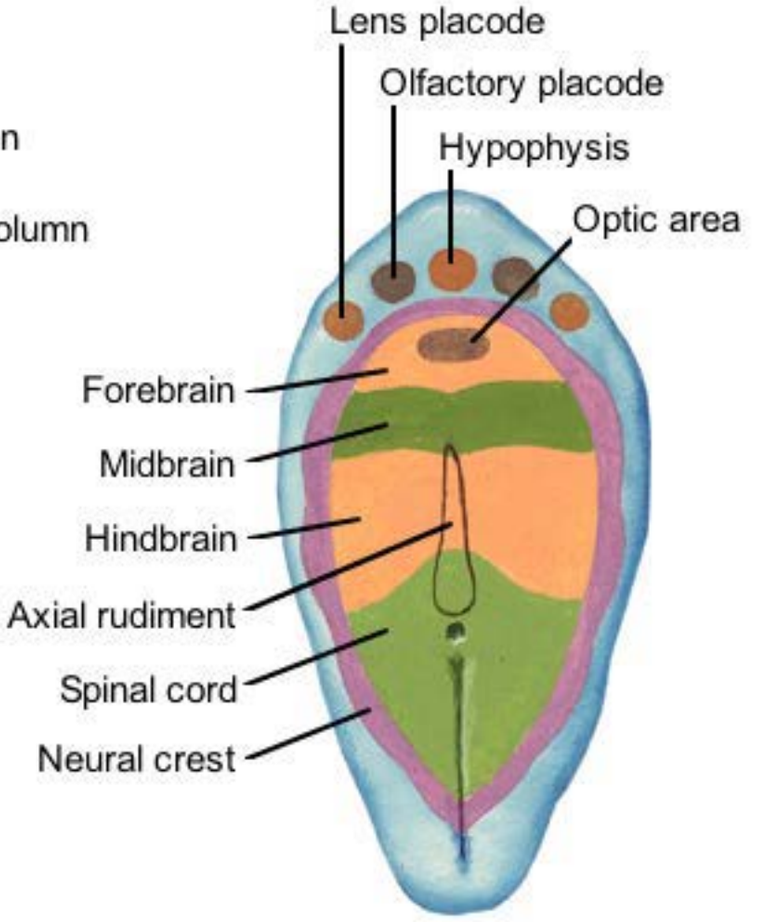
Primary gyri begin to appear.

Secondary gyri are present; brain is 25% of its adult size.

Formation of the Neural Plate







Developmental fates of local regions of ectoderm of embryonic disc at 18 days

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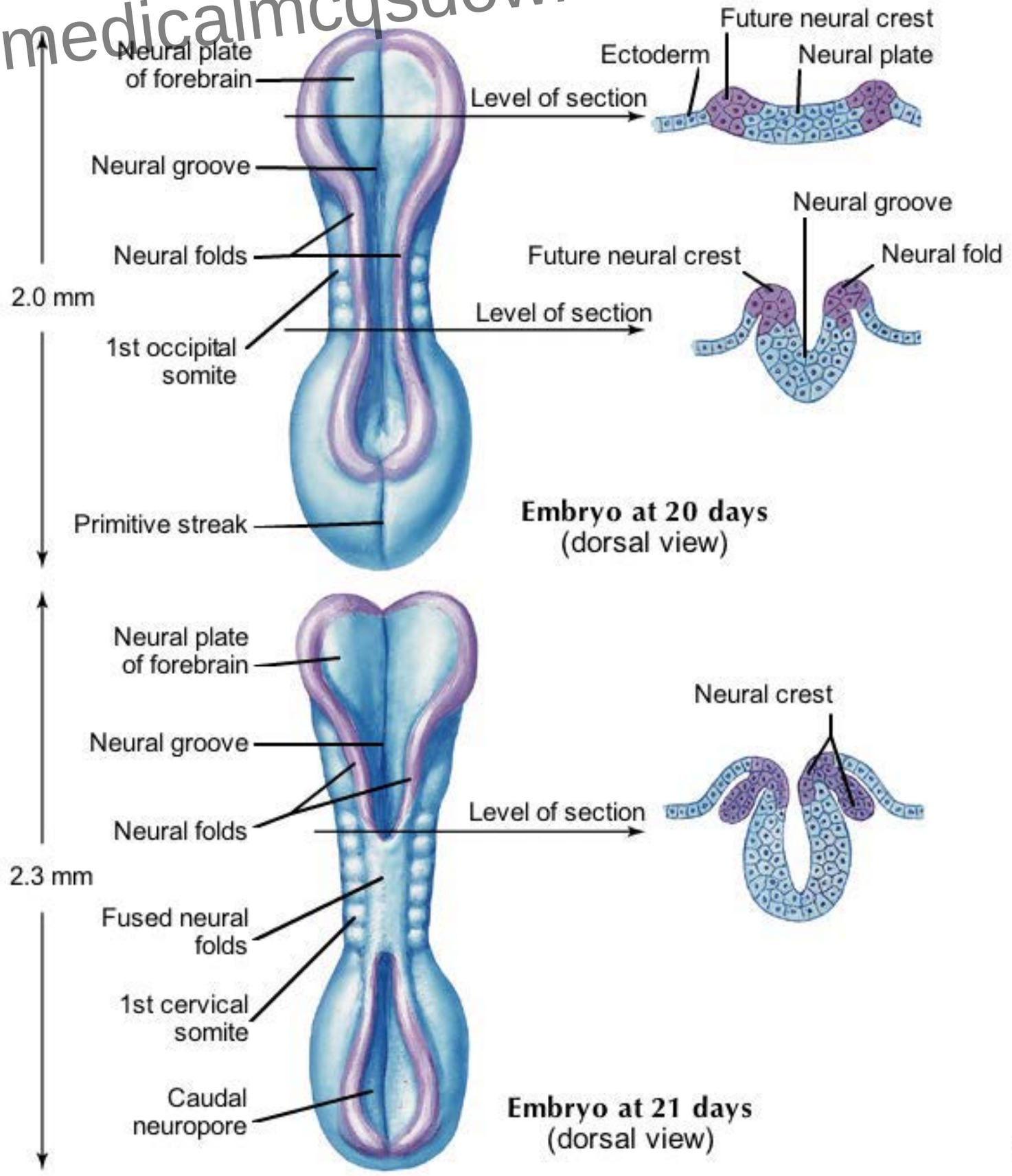
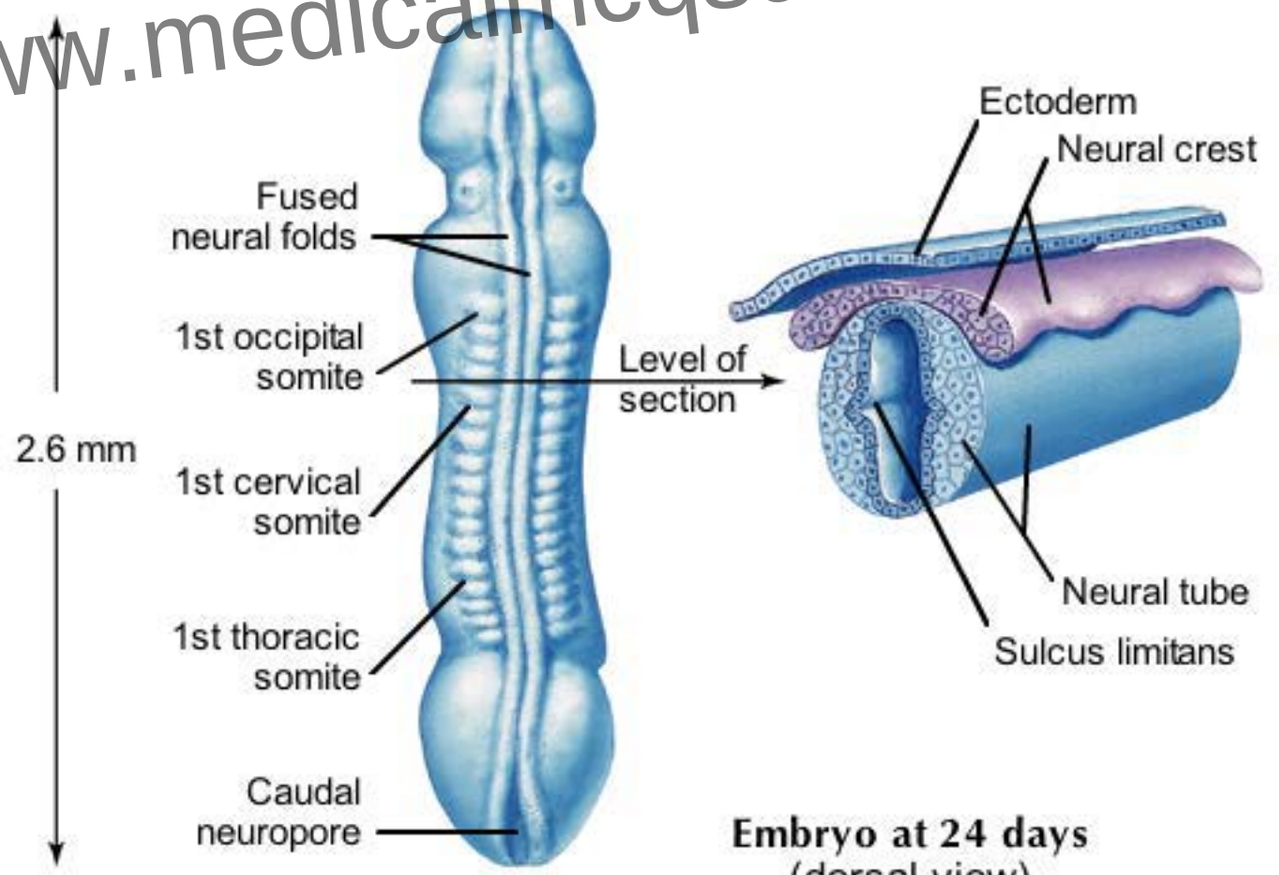
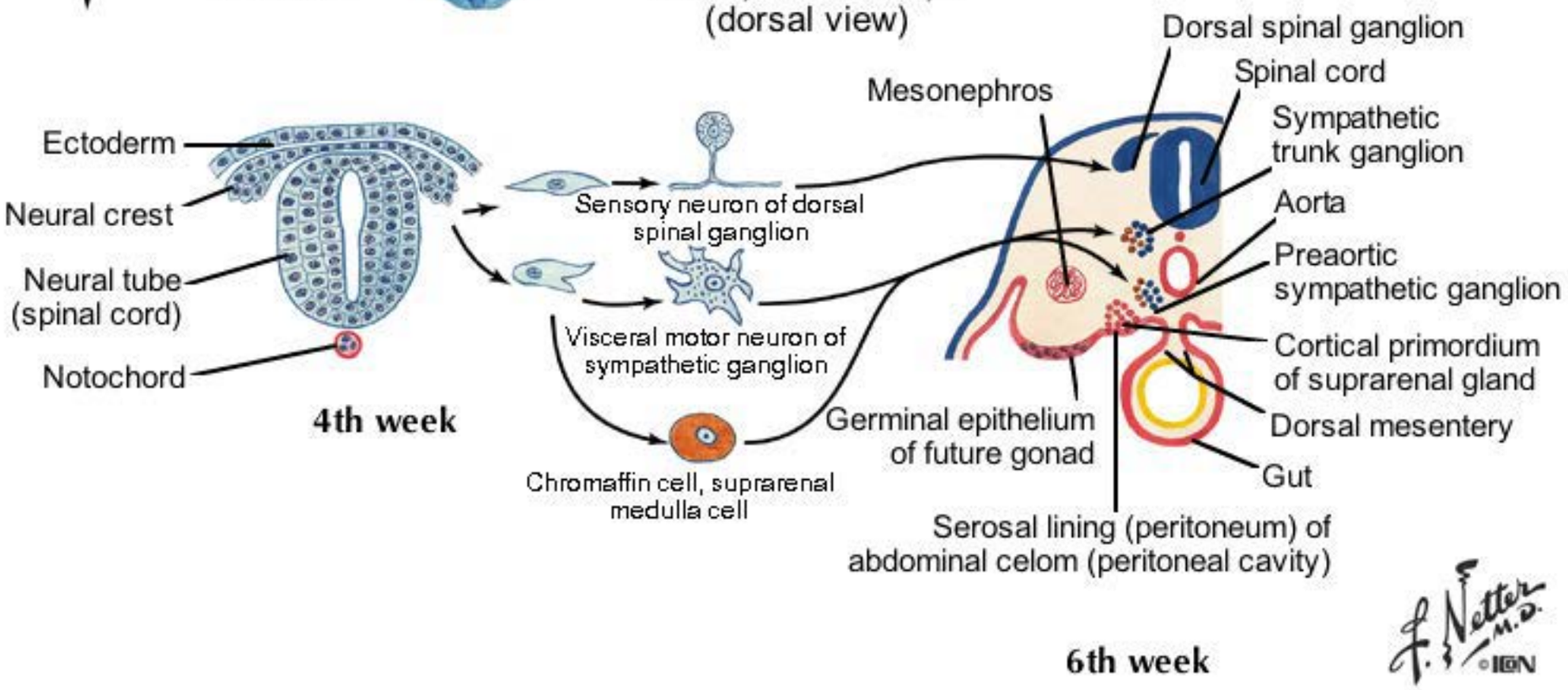
Neurulation



Neural Tube and Neural Crest

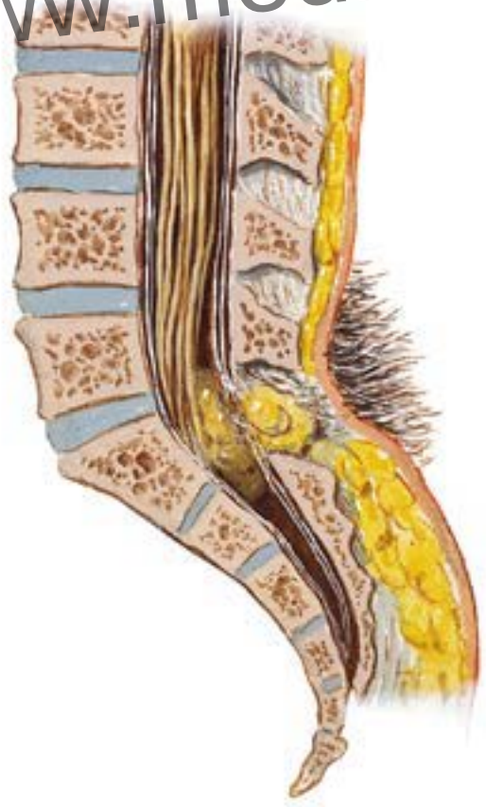


Embryo at 24 days
(dorsal view)

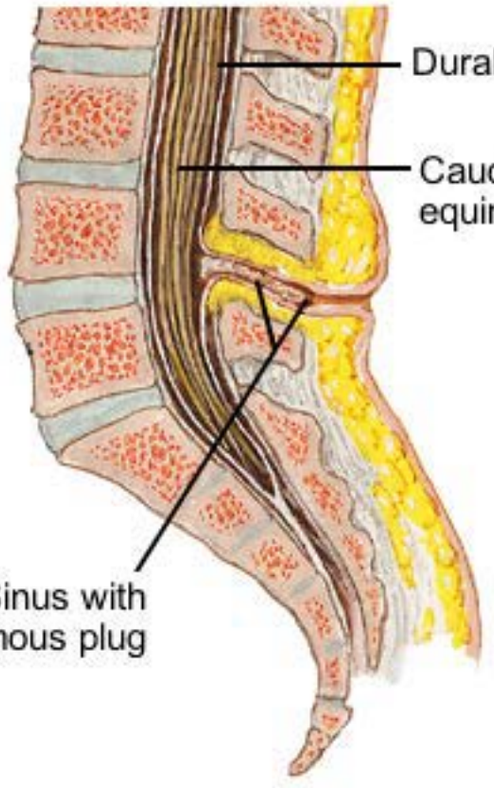


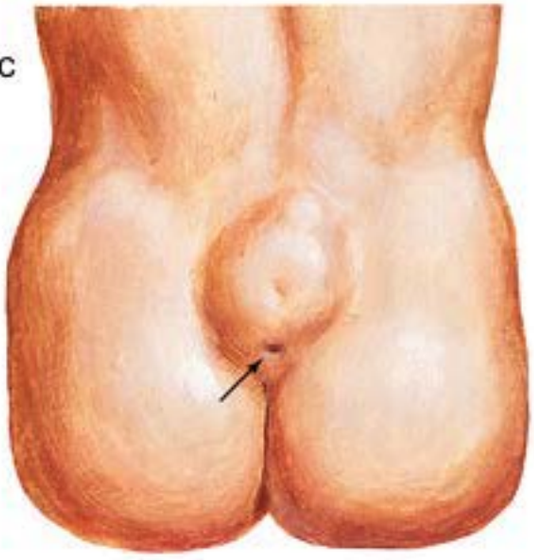
Neural Tube Defects

Spinal bifida occulta



Dermal sinus





Fat pad overlying spina bifida occulta. Tuft of hair or only skin dimple may be present, or there may be no external manifestation. Dermal sinus also present in this case (arrow)

Types of spina bifida aperta with protrusion of spinal contents

Meningocele

Meningomyelocele

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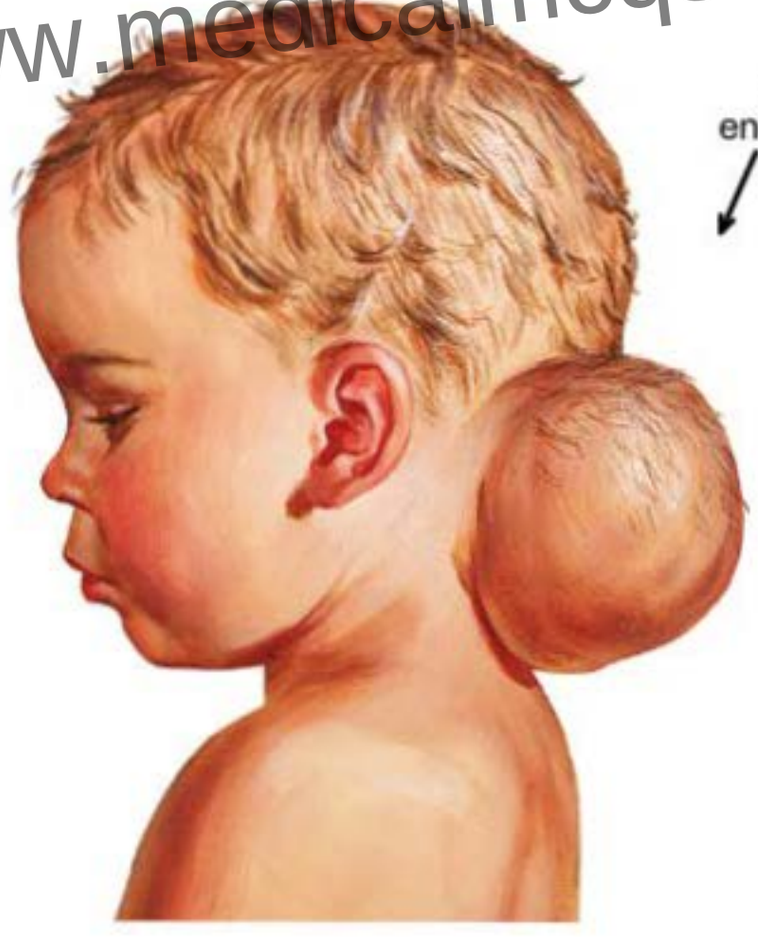
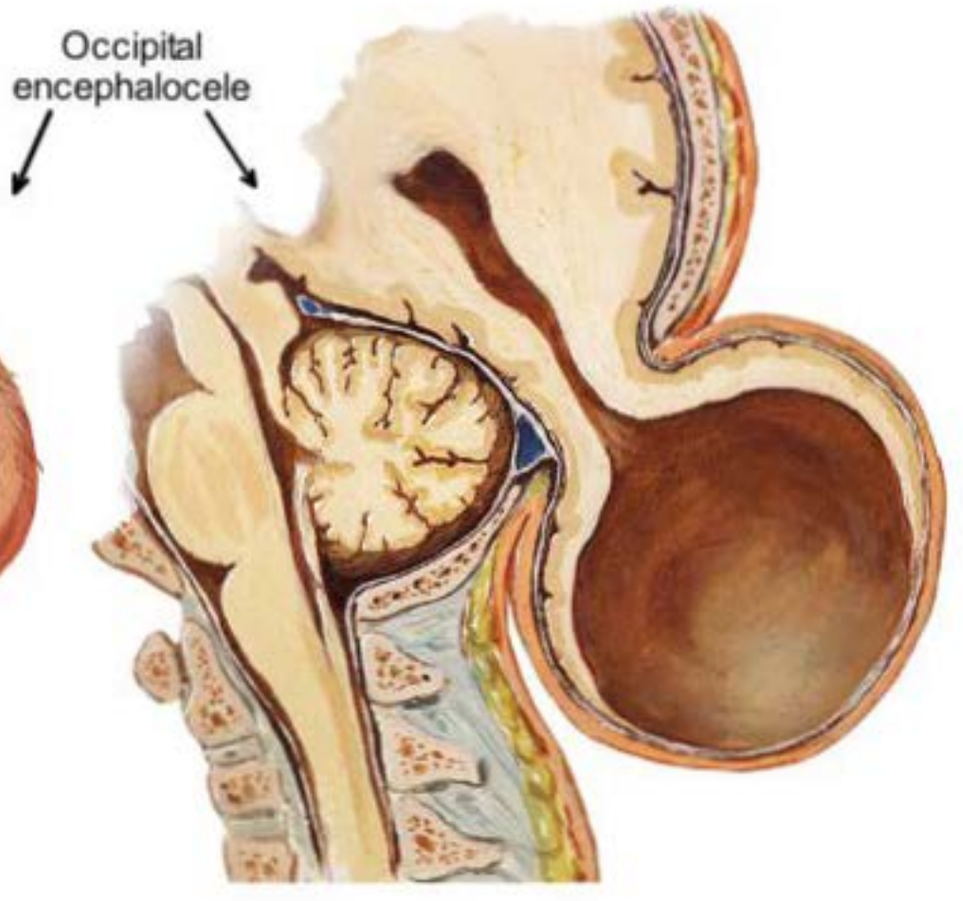
Neural Tube Defects



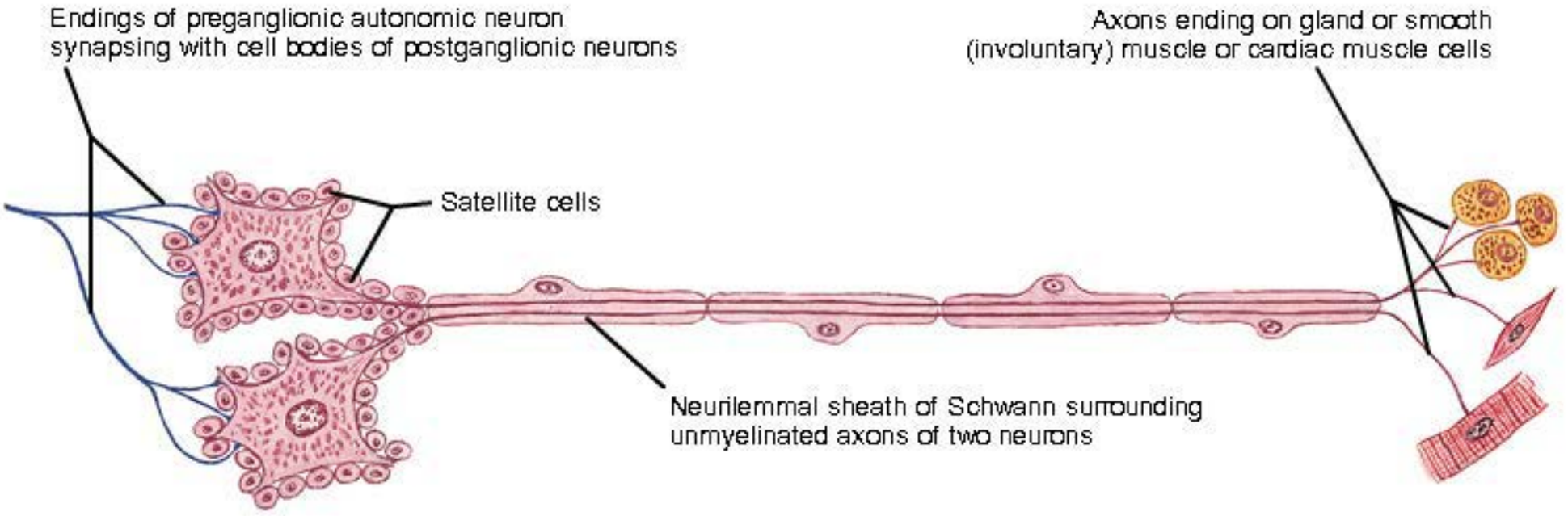


Frontal encephalocele

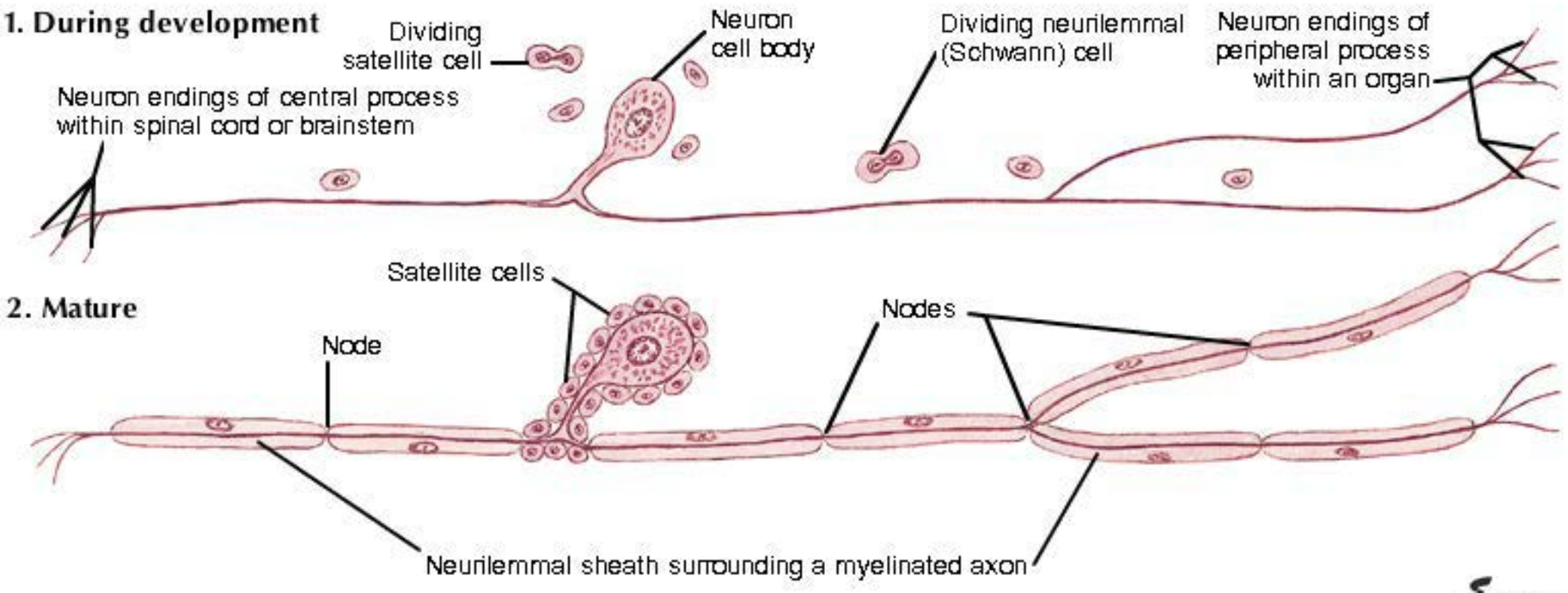
Anencephaly

Neuron Development

Two postganglionic autonomic neurons of a sympathetic or parasympathetic ganglion



Somatic or visceral sensory neuron of a spinal ganglion or sensory ganglion of cranial nerves V, VII, IX, or X

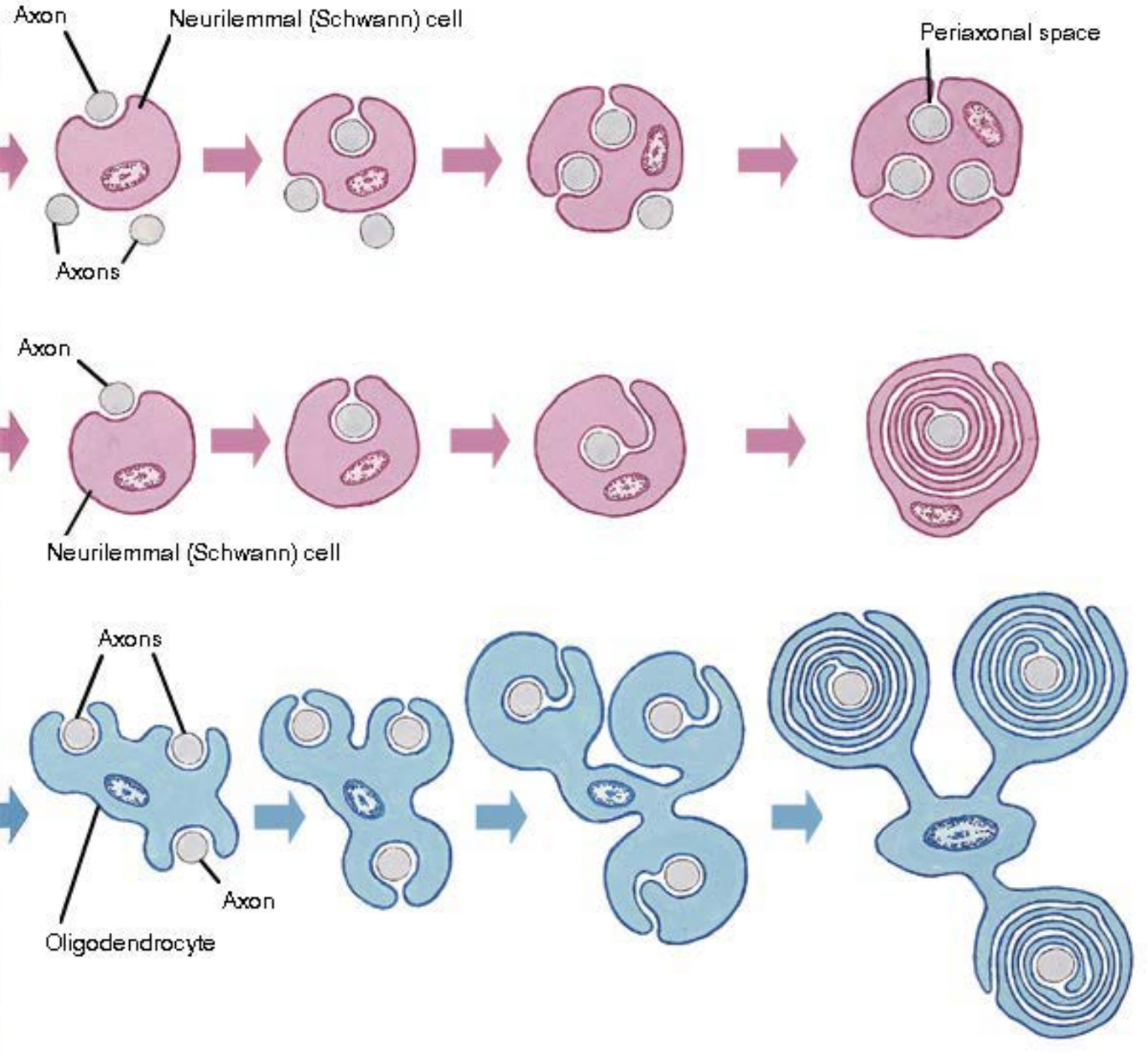


Development of the Cellular Sheath of Axons

Unmyelinated axons of peripheral neurons (sensory, somatic motor, or visceral motor) being surrounded by cytoplasm of a neurilemmal (Schwann) cell

Myelinated axon of peripheral neuron (sensory, somatic motor, or visceral motor) being surrounded by a wrapping of cell membrane of a neurilemmal (Schwann) cell

Myelinated axon of CNS neurons being surrounded by a wrapping of cell membrane of an oligodendrocyte.
Unmyelinated axons of CNS neurons surrounded by cytoplasm of an oligodendrocyte in manner shown for neurilemmal cell in A



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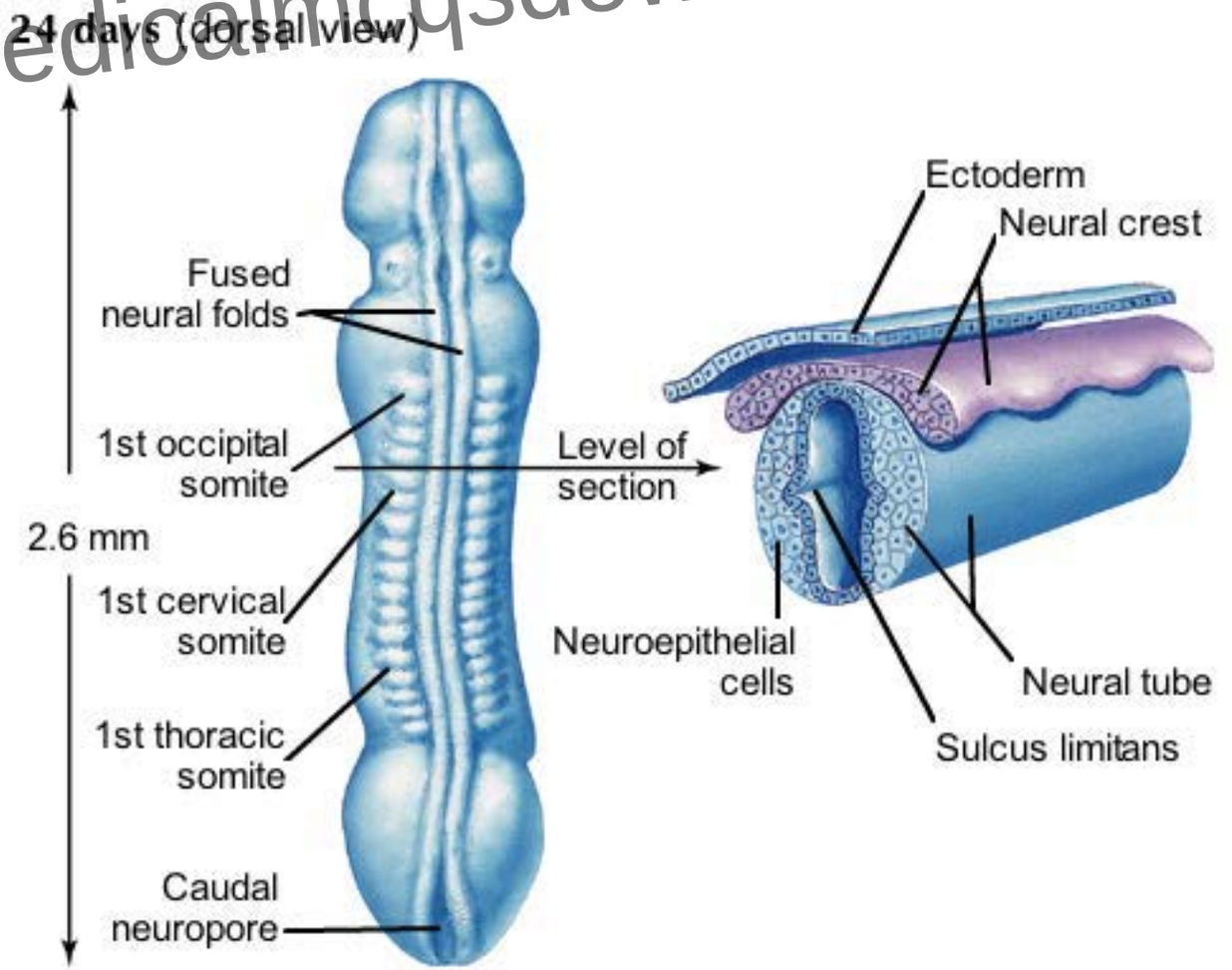
Development of the Spinal Cord Layers



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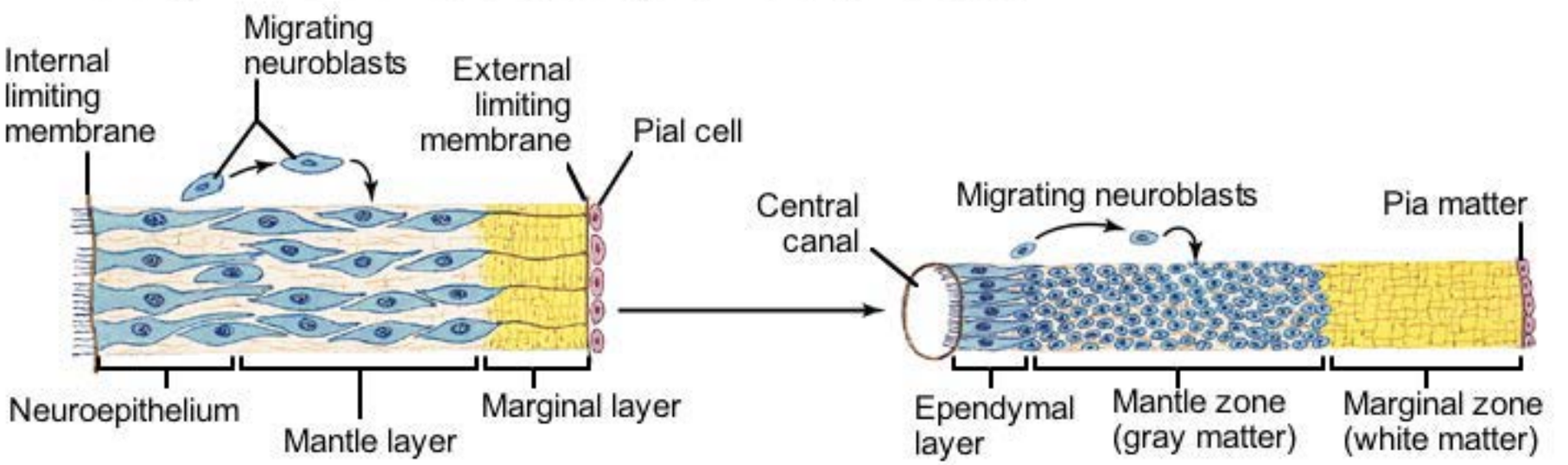
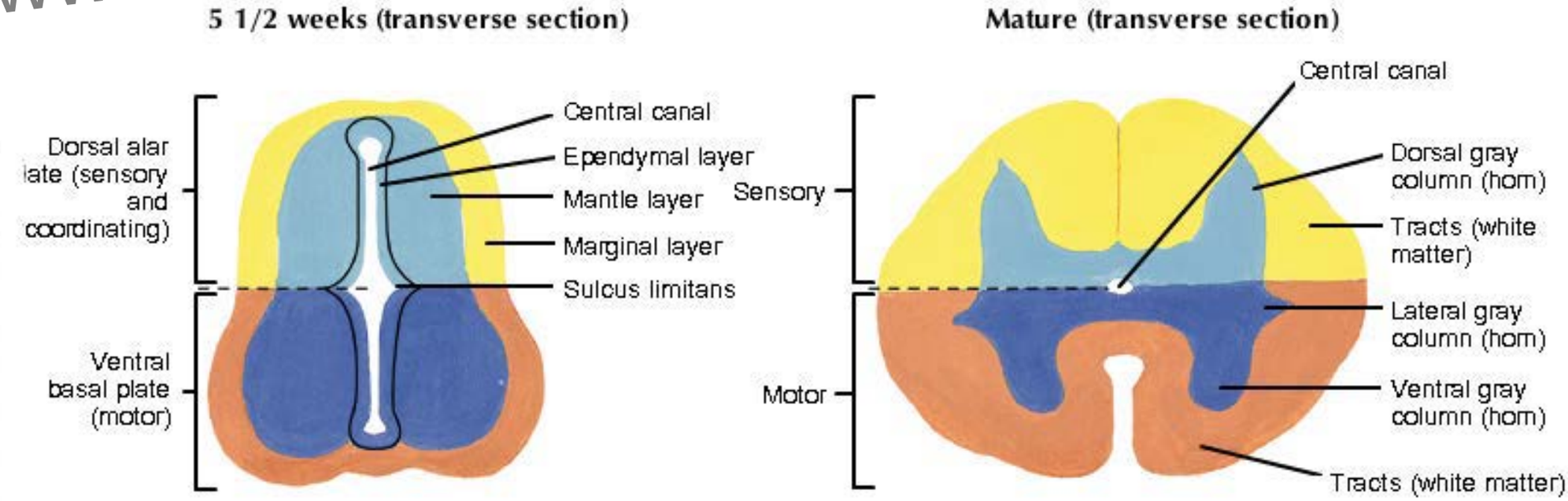
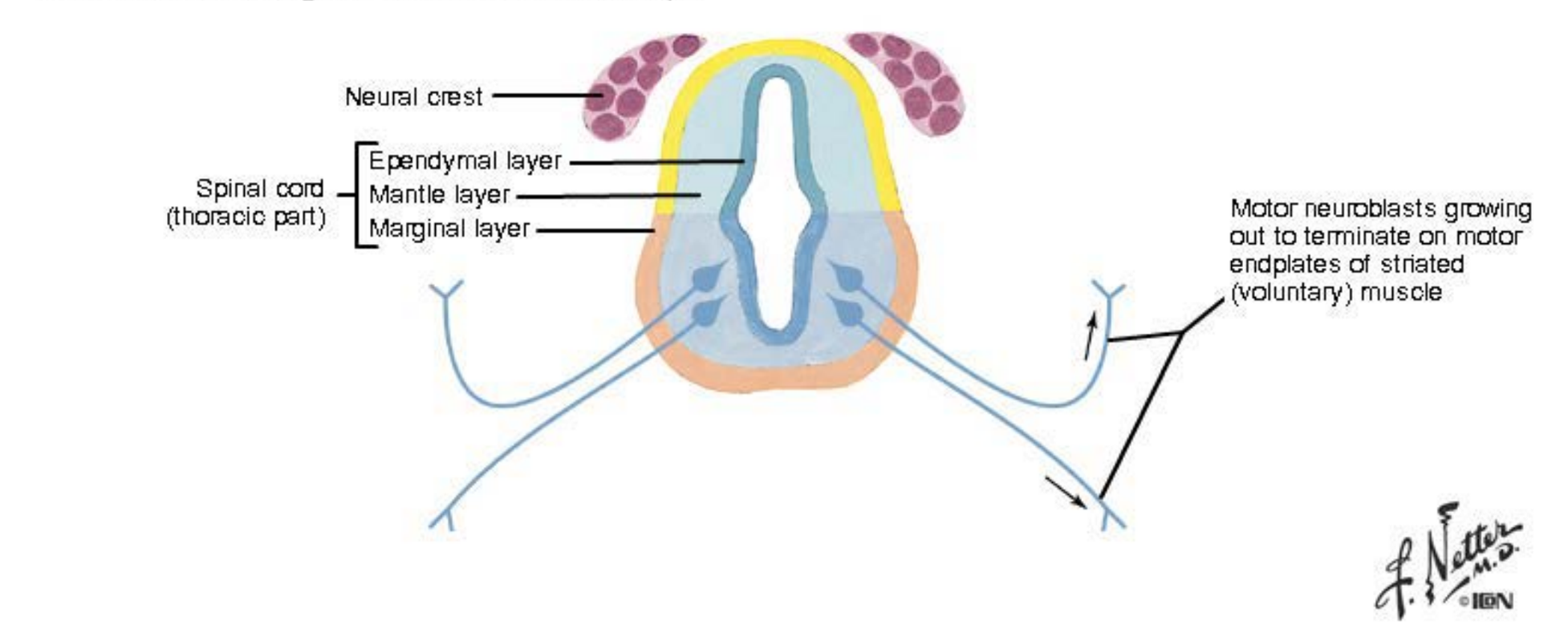
Development of the neural tube layers in the spinal cord



Neural tube at 5 weeks **Spinal cord at 3 months**

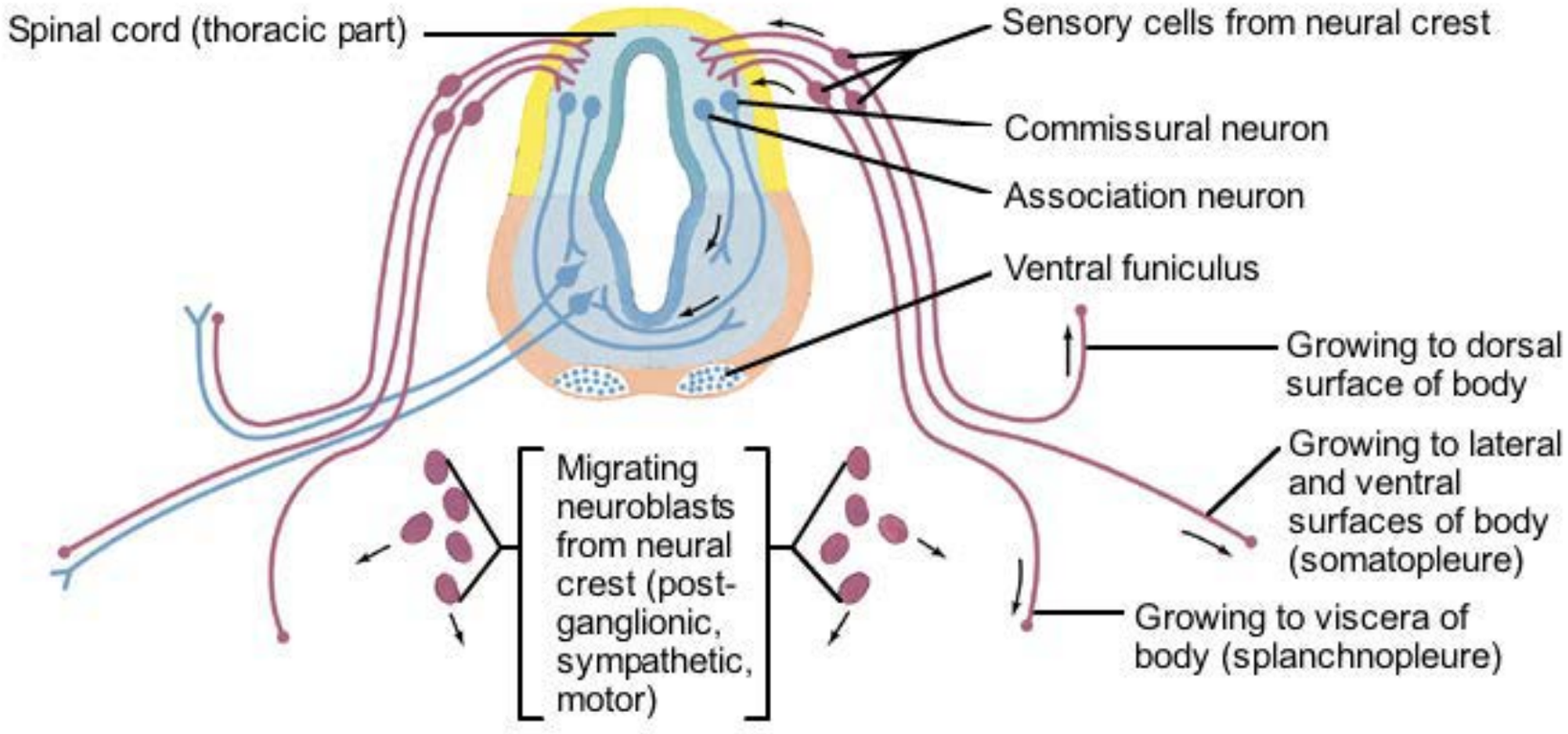
Development of the Spinal Cord





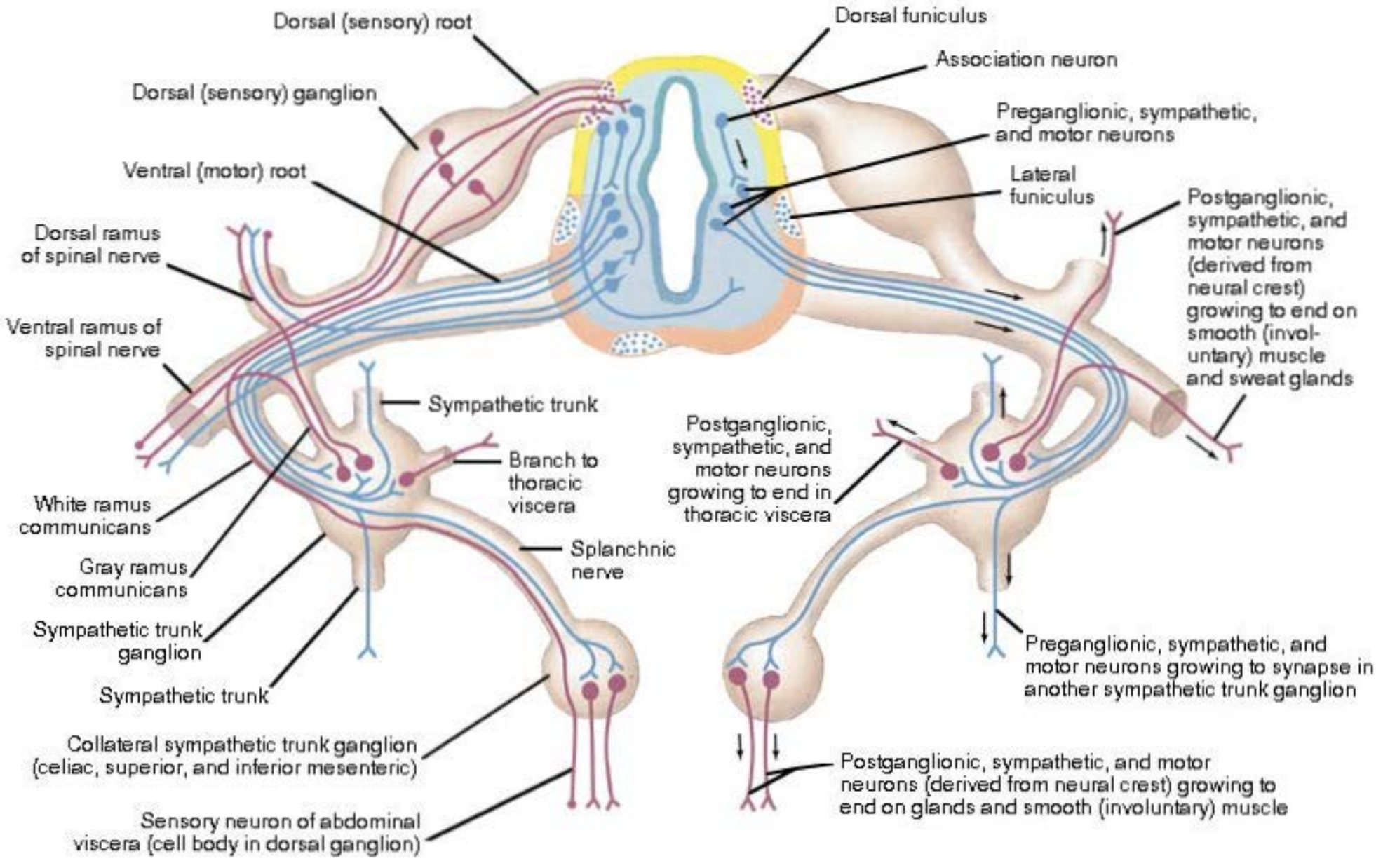
Peripheral Nervous System

Differentiation and growth of neurons at 28 days
(right side of diagram shows newly acquired neurons only)



Peripheral Nervous System

Differentiation and growth of neurons at 5 to 7 weeks
(right side of diagram shows neurons acquired since 28th day only)



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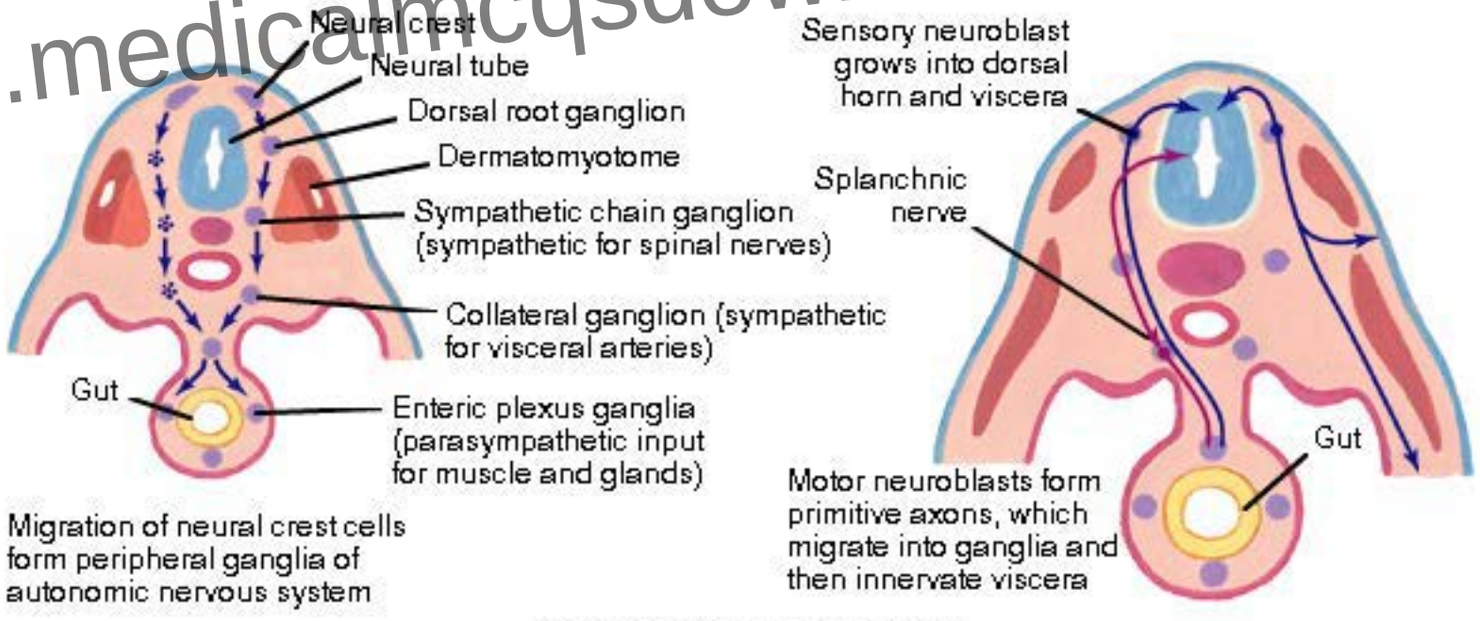
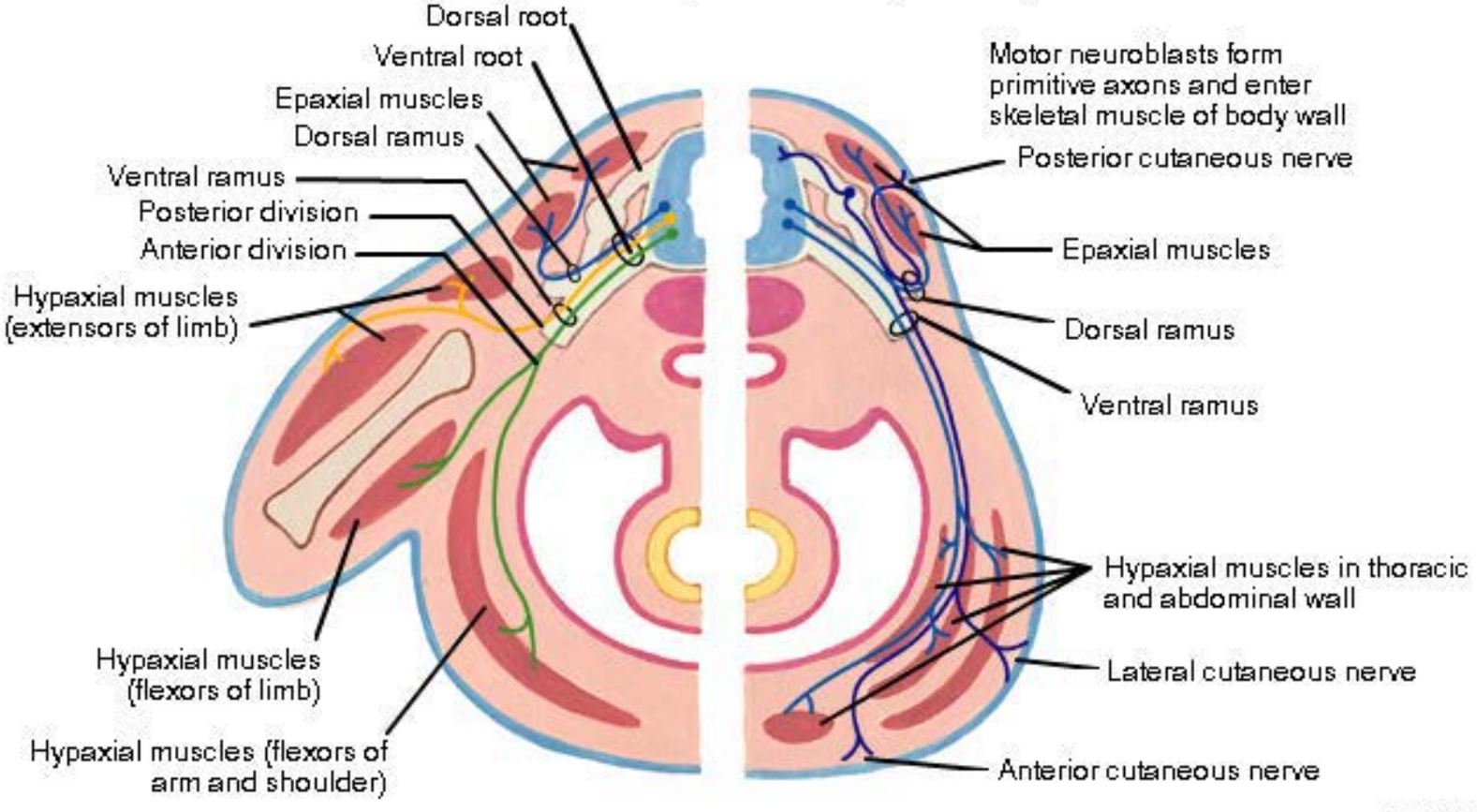
Peripheral Nervous System



Autonomic Development

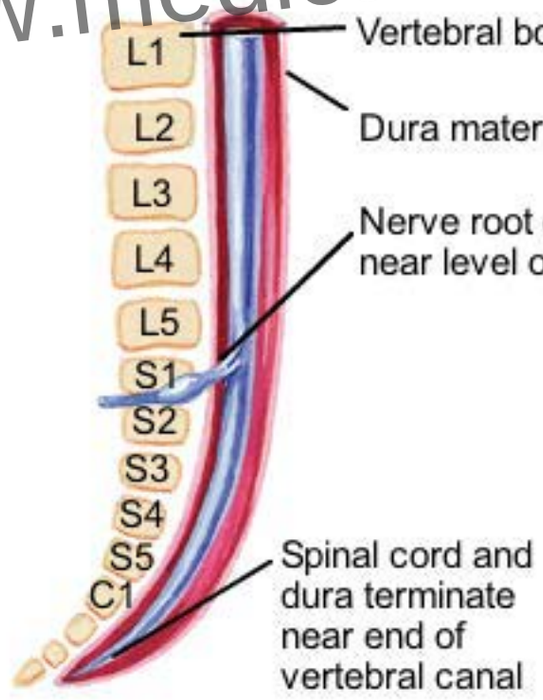
Autonomic nervous system mostly innervates splanchnopleure (viscera)



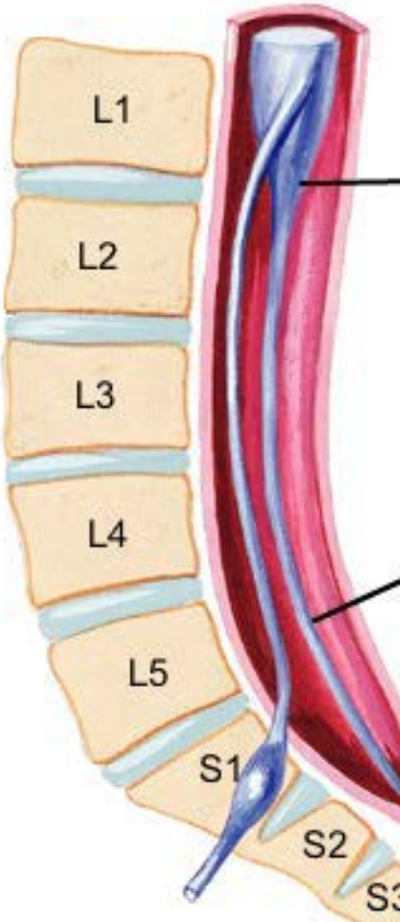
Somatic Development

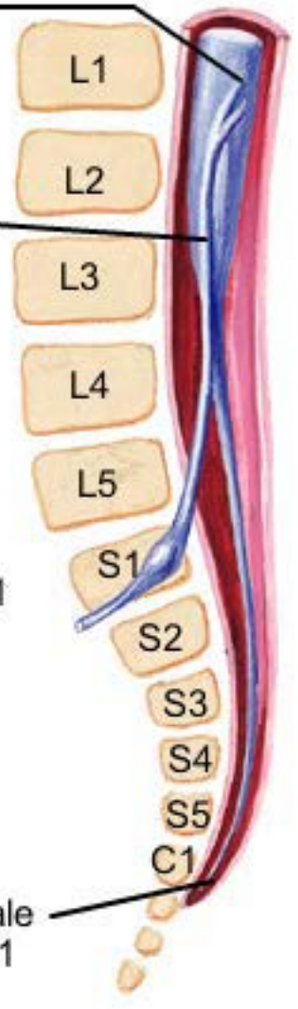
Somatic nervous system innervates somatopleure (body wall)

Growth of the Spinal Cord and Vertebral Column



Relationships in fetus at 2—3 months





Relationships at birth

Nerve root of spinal nerve S1 must travel from level of L1 vertebral body to exit at S1 vertebral level

Relationships in adult

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D. Mascaro
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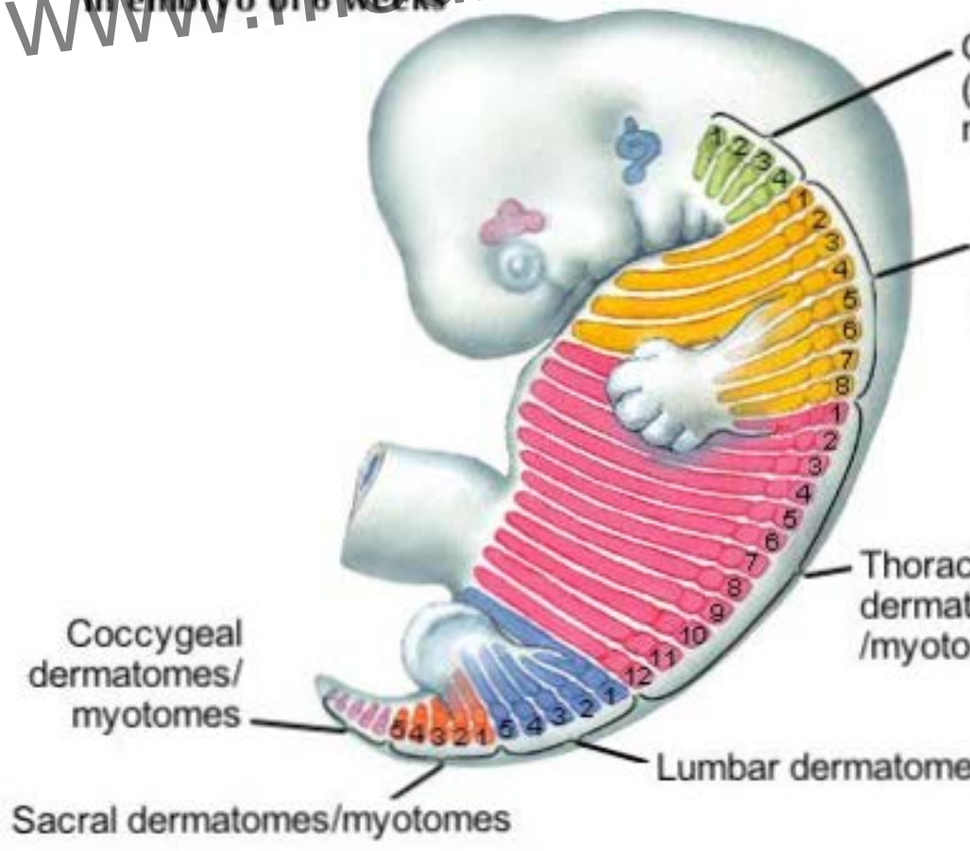
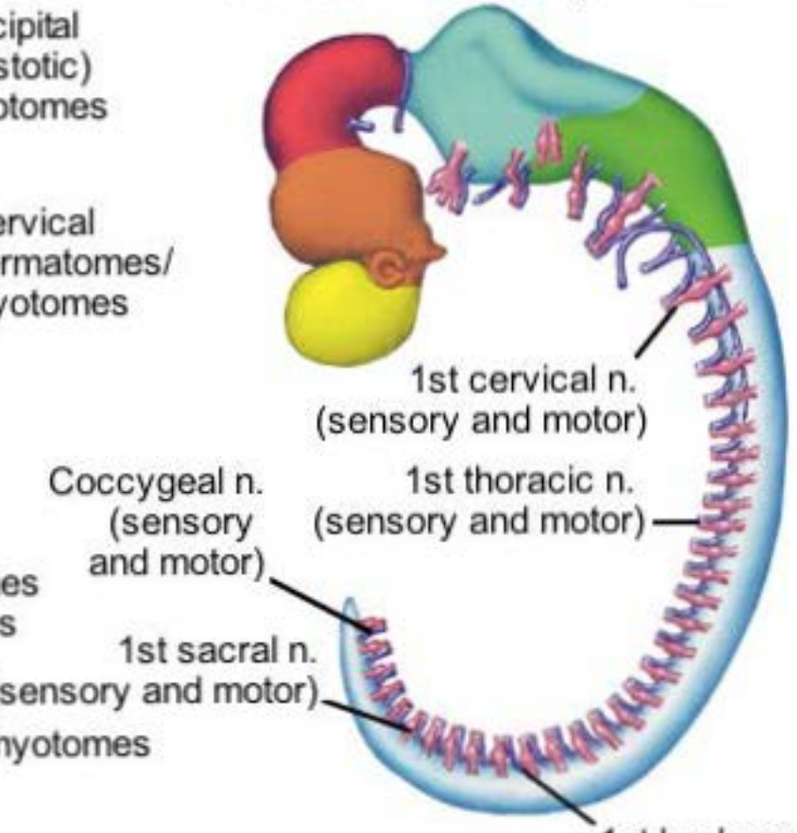
Embryonic Dermatomes

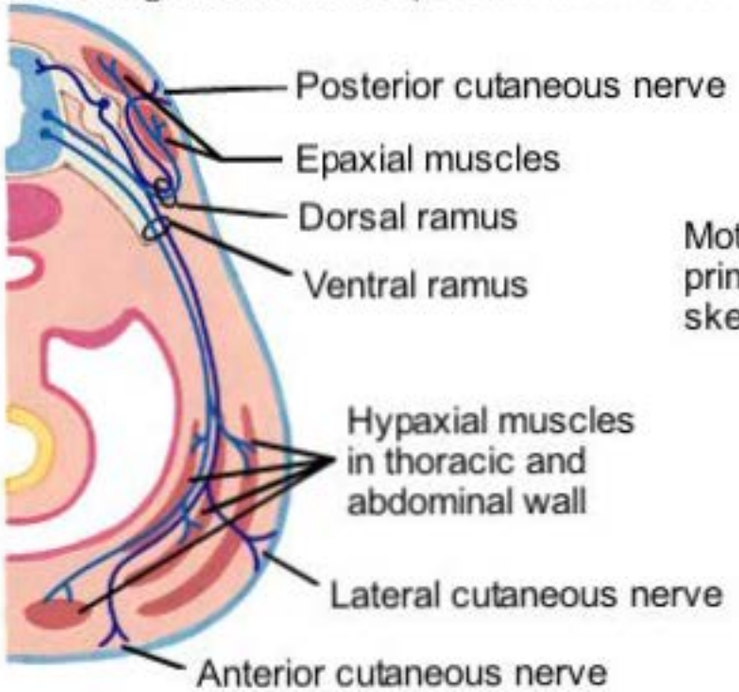
Segmental distribution of dermatomes/myotomes in embryo of 6 weeks



One pair of spinal nerves relates to each of the dermatomes/myotomes



Cross section of the dorsal and ventral ramus of a spinal nerve innervating dermatome/myotome derivatives



Motor neuroblasts form primitive axons and enter skeletal muscle of body wall

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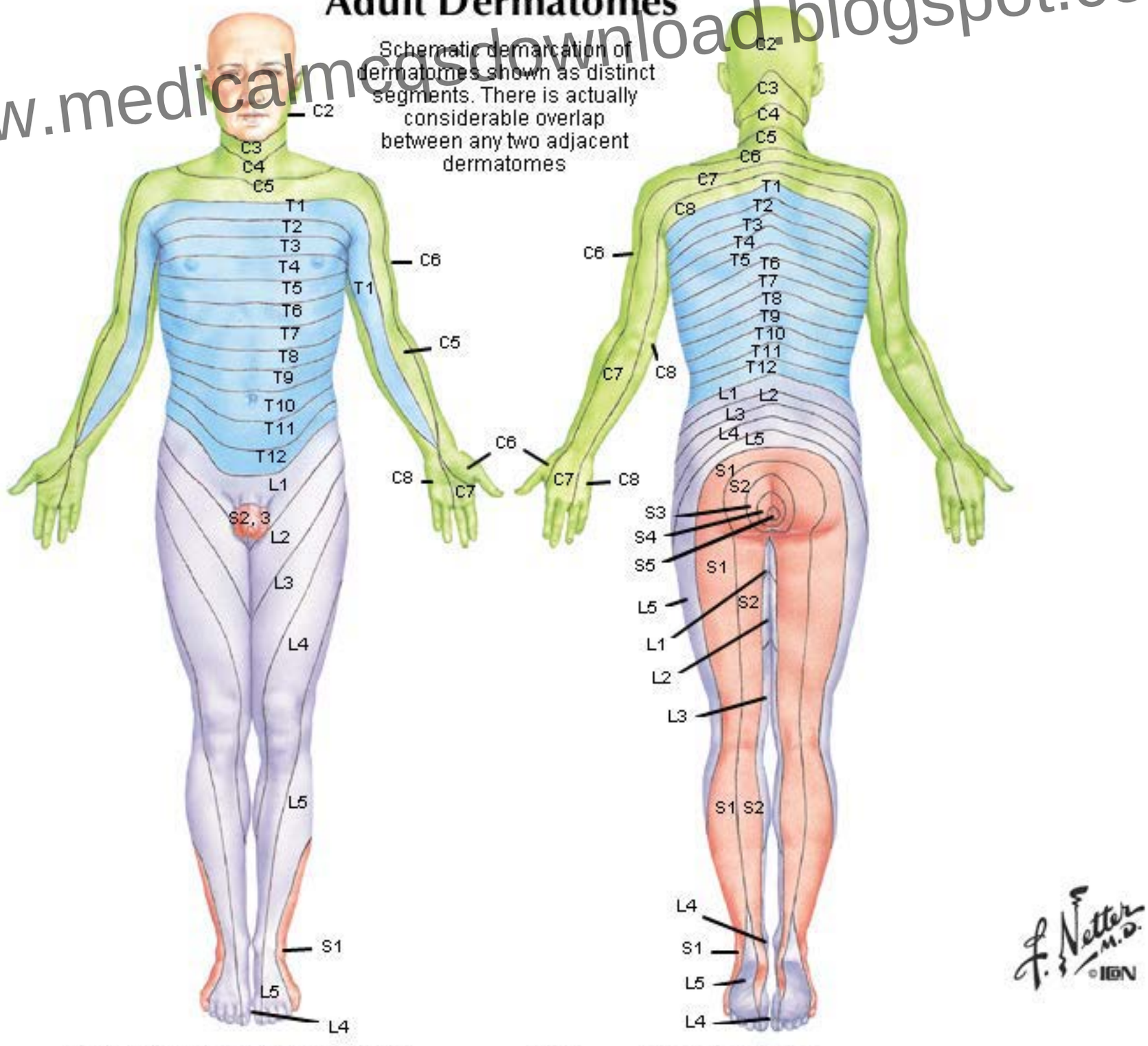
Adult Dermatomes

Schematic demarcation of dermatomes shown as distinct segments. There is actually considerable overlap between any two adjacent dermatomes



Levels of principal dermatomes

C5	Clavicles
C5, 6, 7	Lateral parts of upper limbs
C8, T1	Medial sides of upper limbs
C6	Thumb
C6, 7, 8	Hand
C8	Ring and little fingers
T4	Level of nipples
T10	Level of umbilicus
T12	Inguinal or groin regions
L1, 2, 3, 4	Anterior and inner surfaces of lower limbs
L4, 5, S1	Foot
L4	Medial side of great toe
S1, 2, L5	Posterior and outer surfaces of lower limbs
S1	Lateral margin of foot and little toe
S2, 3, 4	Perineum

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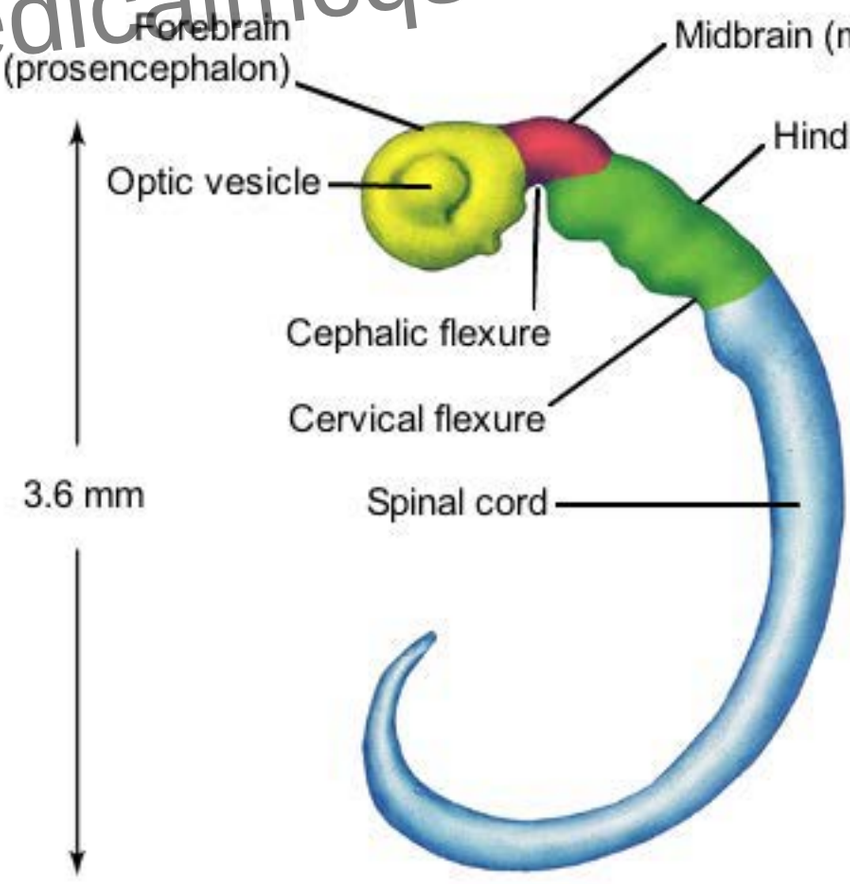
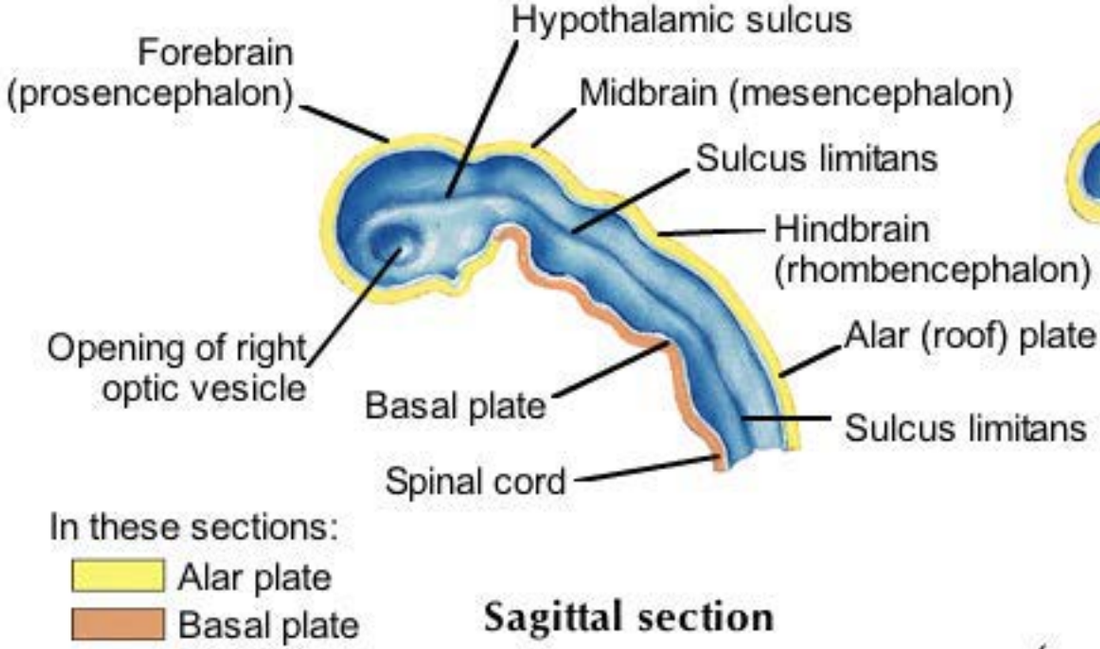
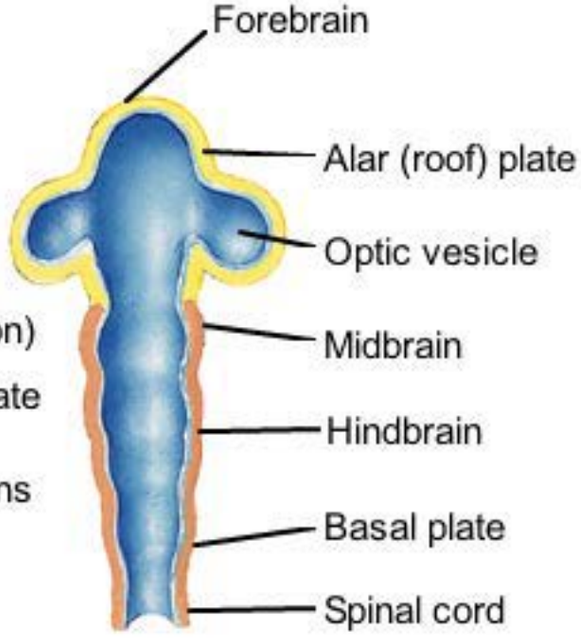
Development of the Brain

Central nervous system at 28 days



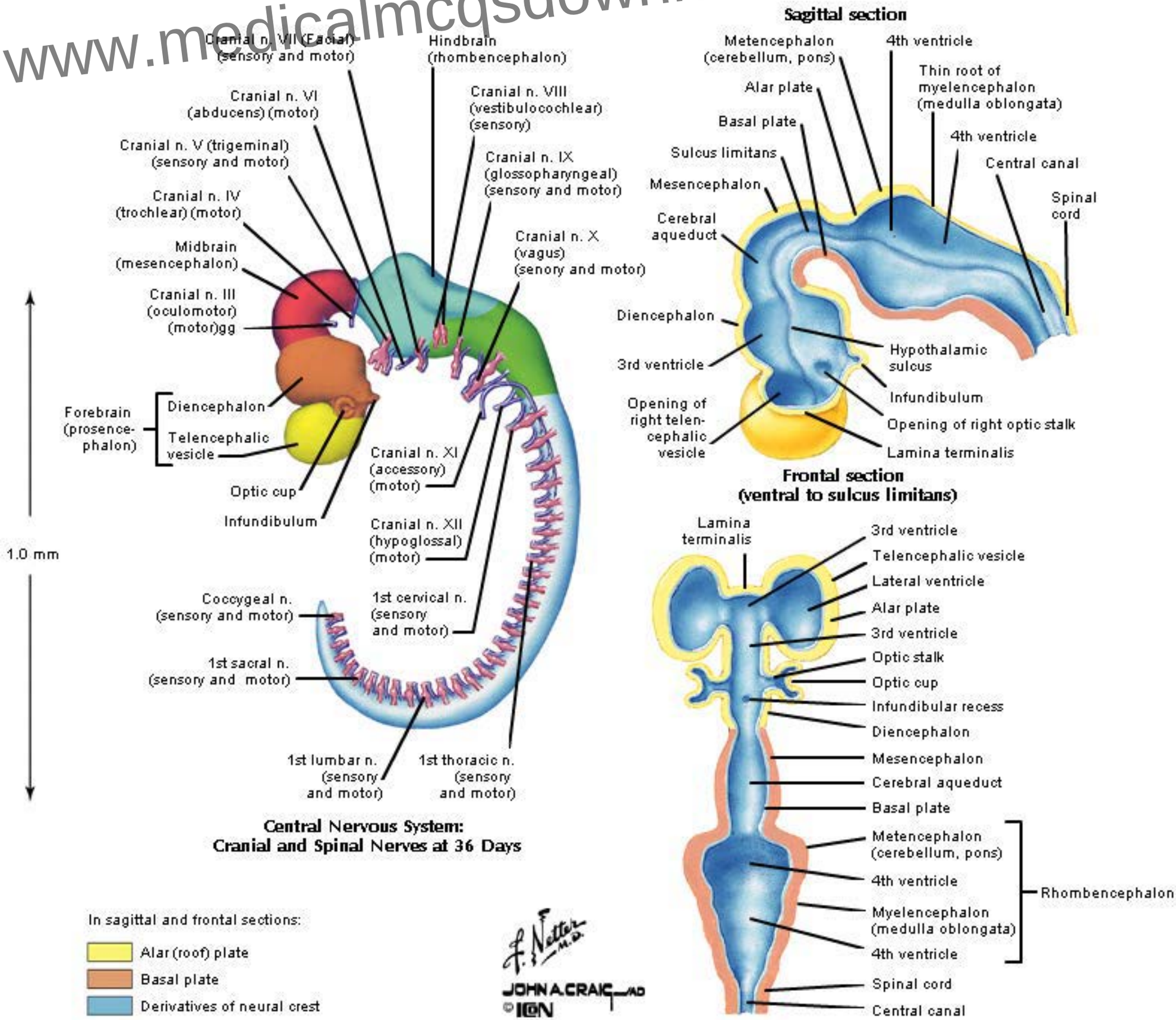


Sagittal section



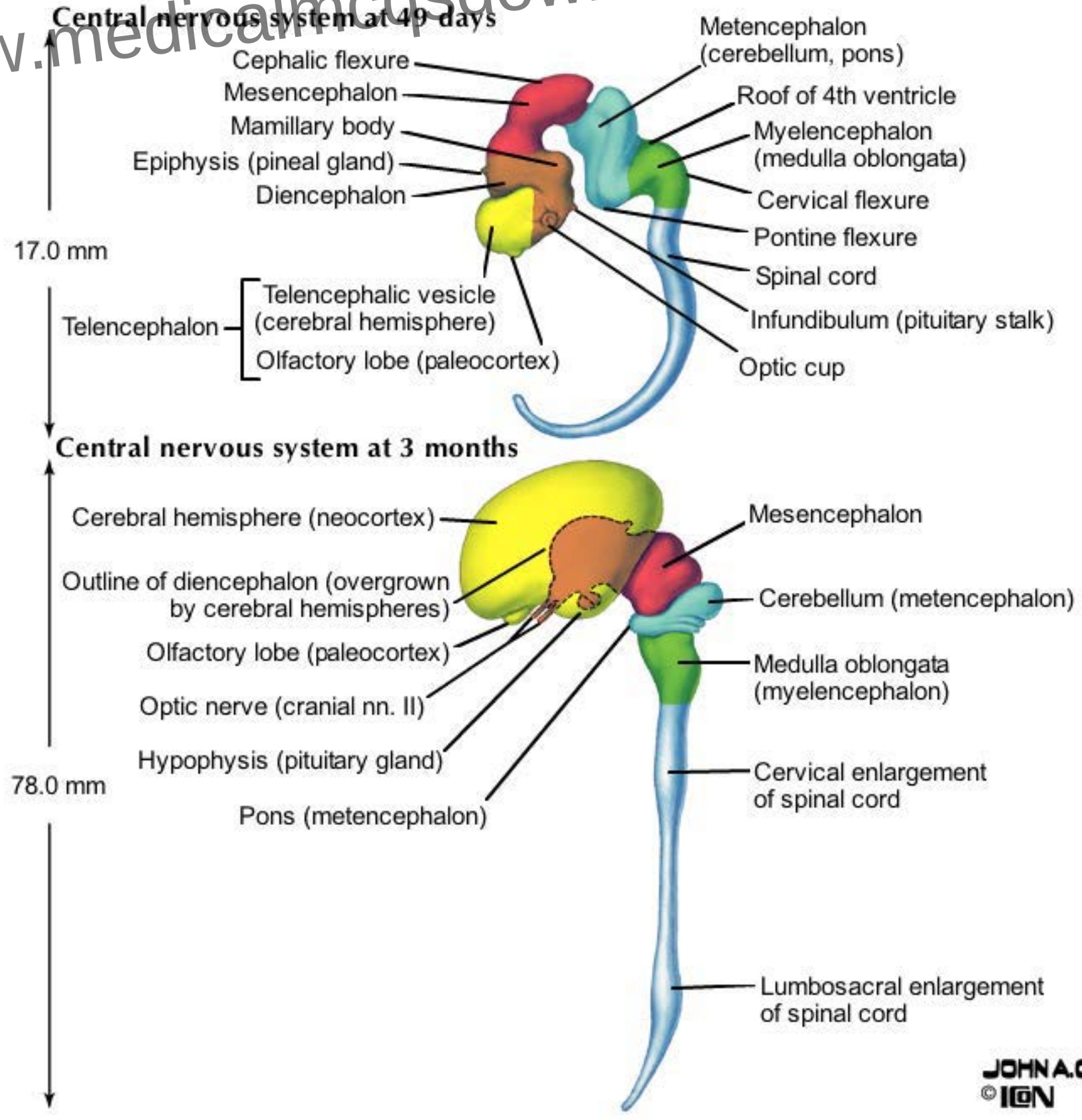
Frontal section (ventral to sulcus limitans)

Development of the Brain



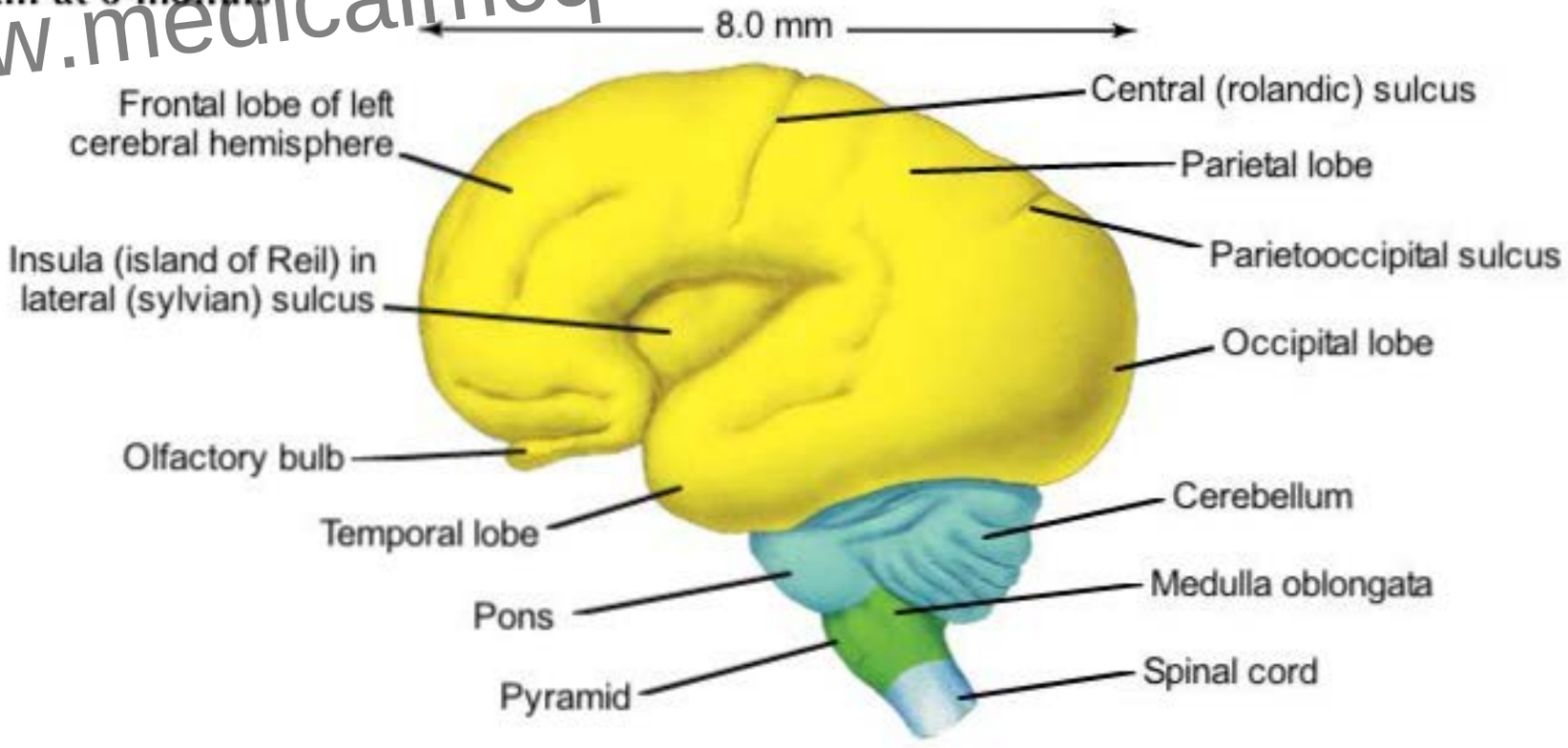
Central Nervous System: Cranial and Spinal Nerves at 36 Days

Development of the Brain

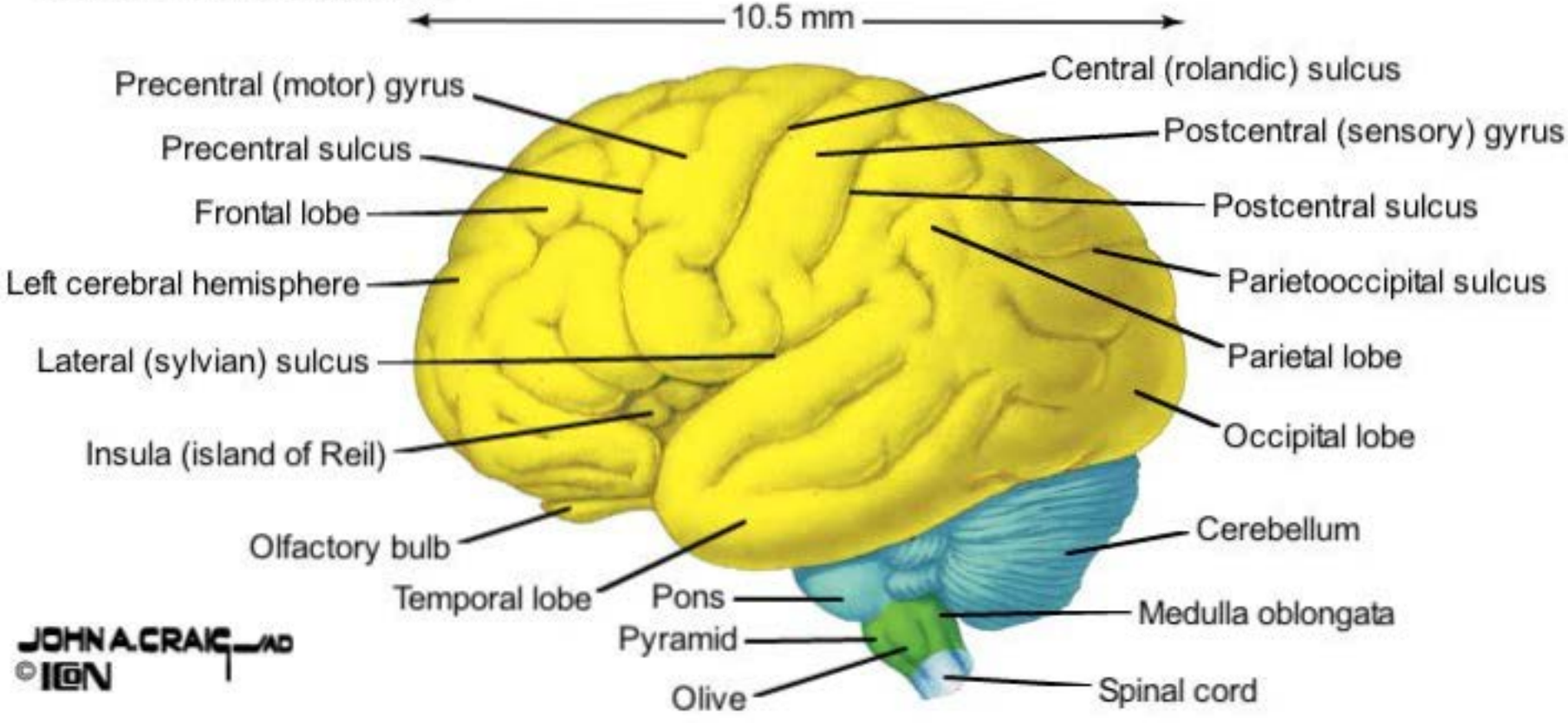


Growth of the Cerebral Hemispheres

Brain at 6 months



Brain at 9 months (birth)



Derivatives of the Forebrain, Midbrain, and Hindbrain

Adult derivatives of brain primordia

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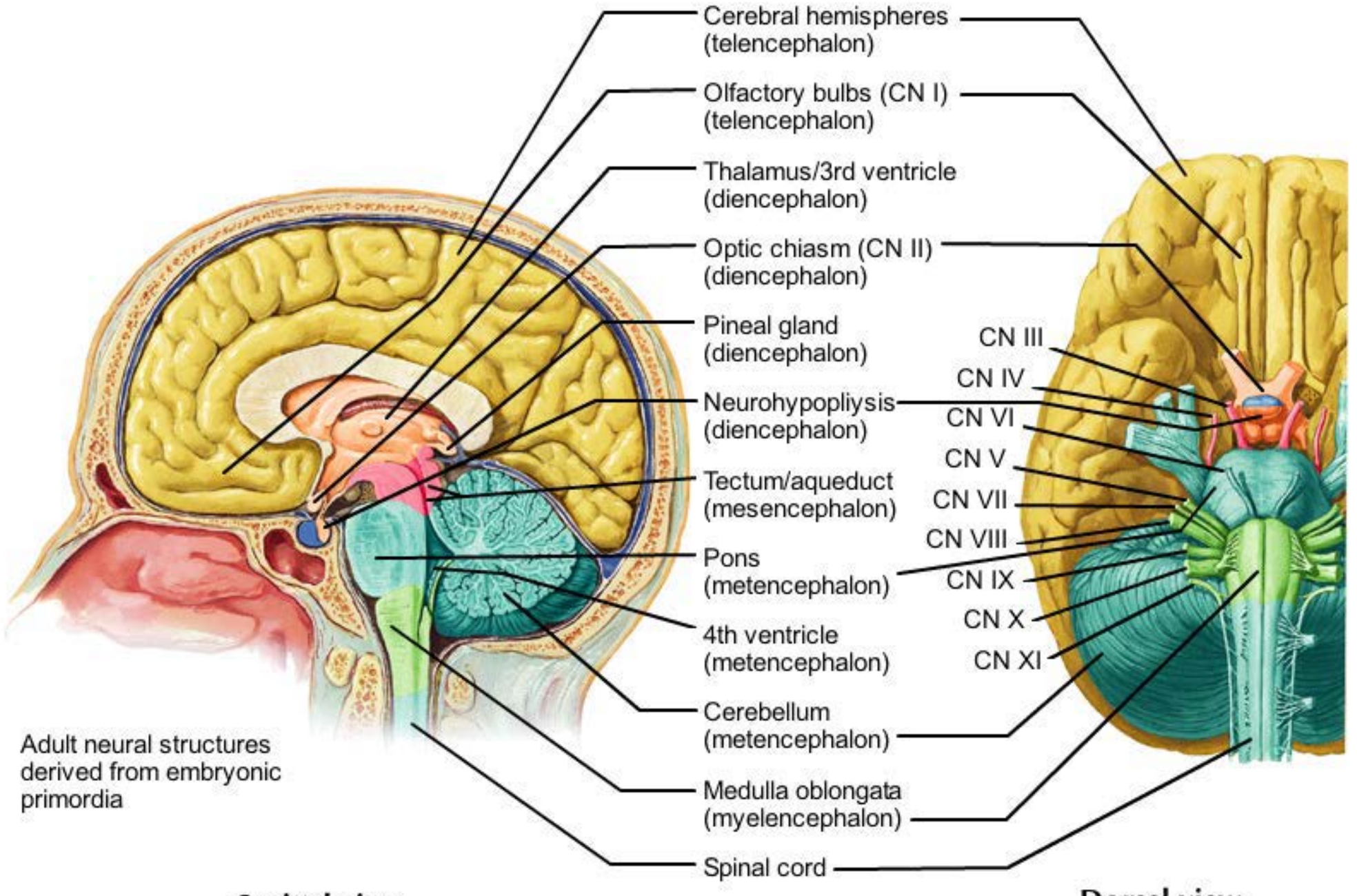
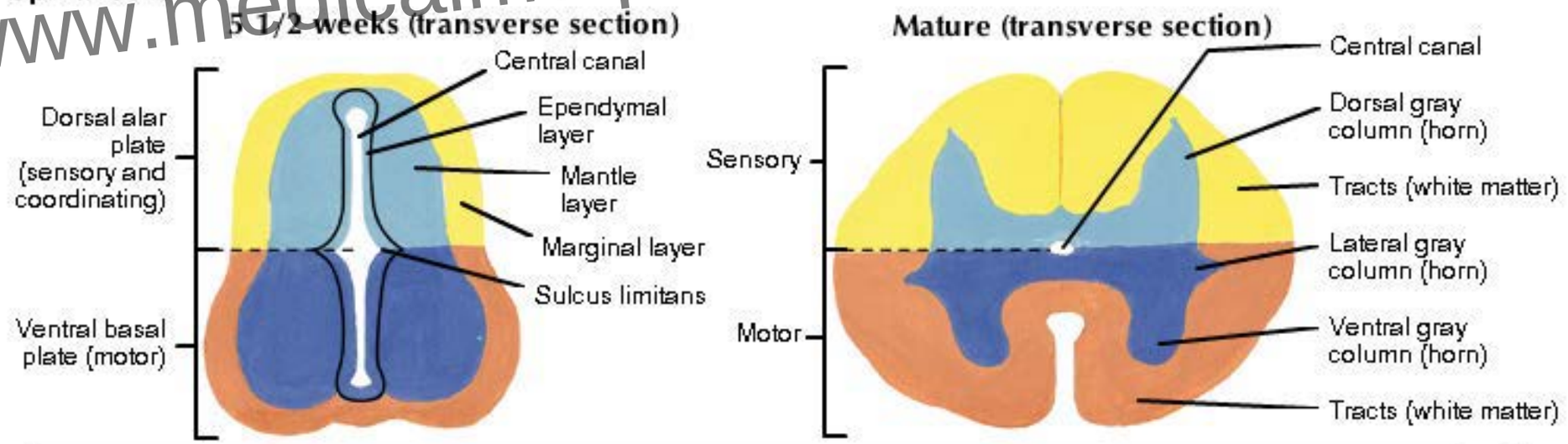
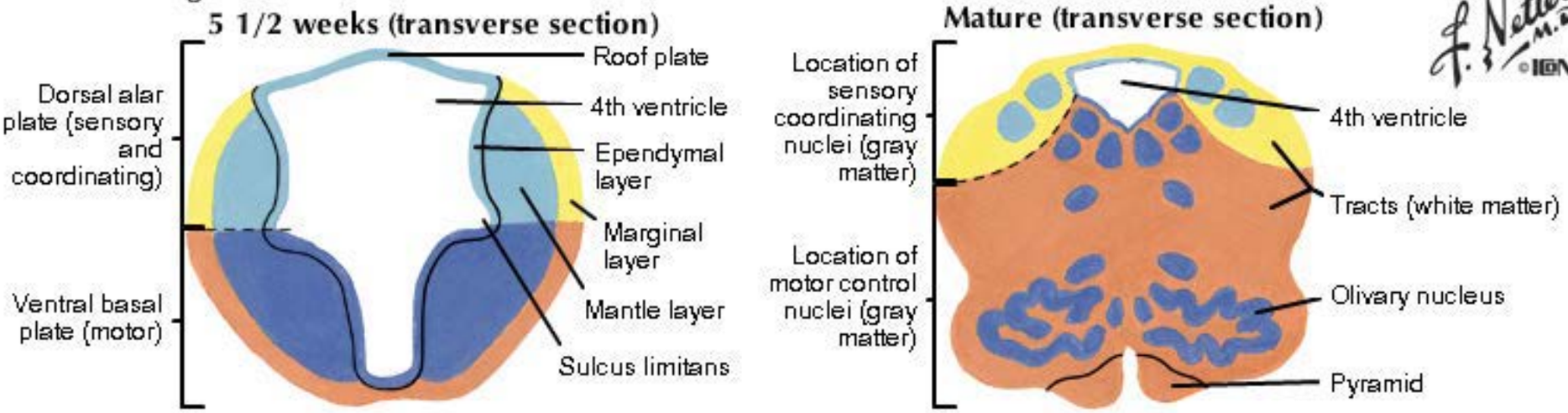


Cross Sections of the Midbrain and Hindbrain

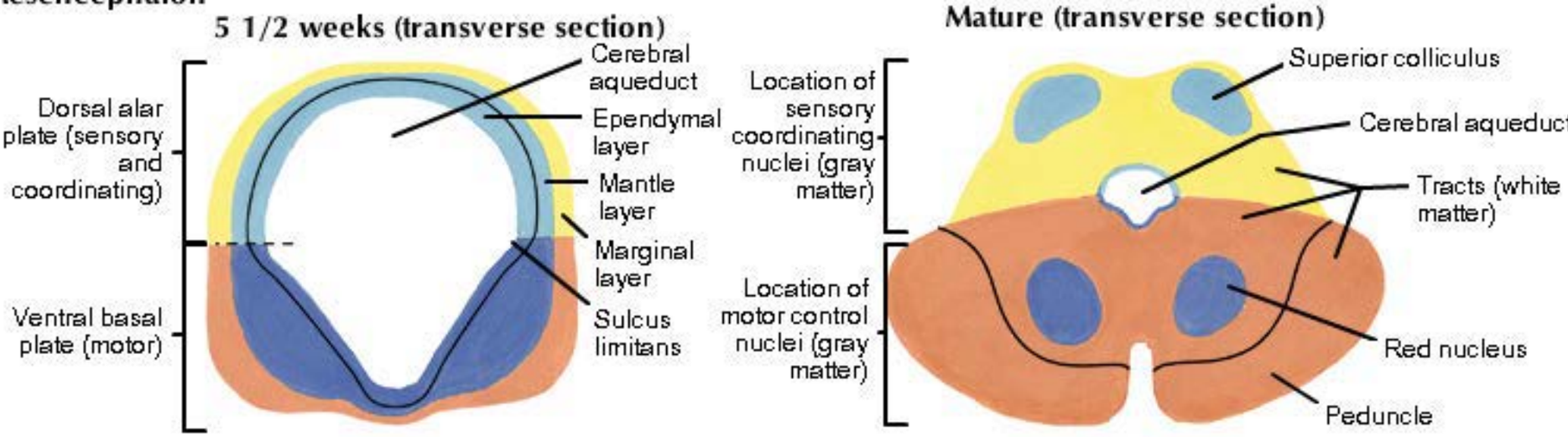
Spinal cord



Medulla oblongata

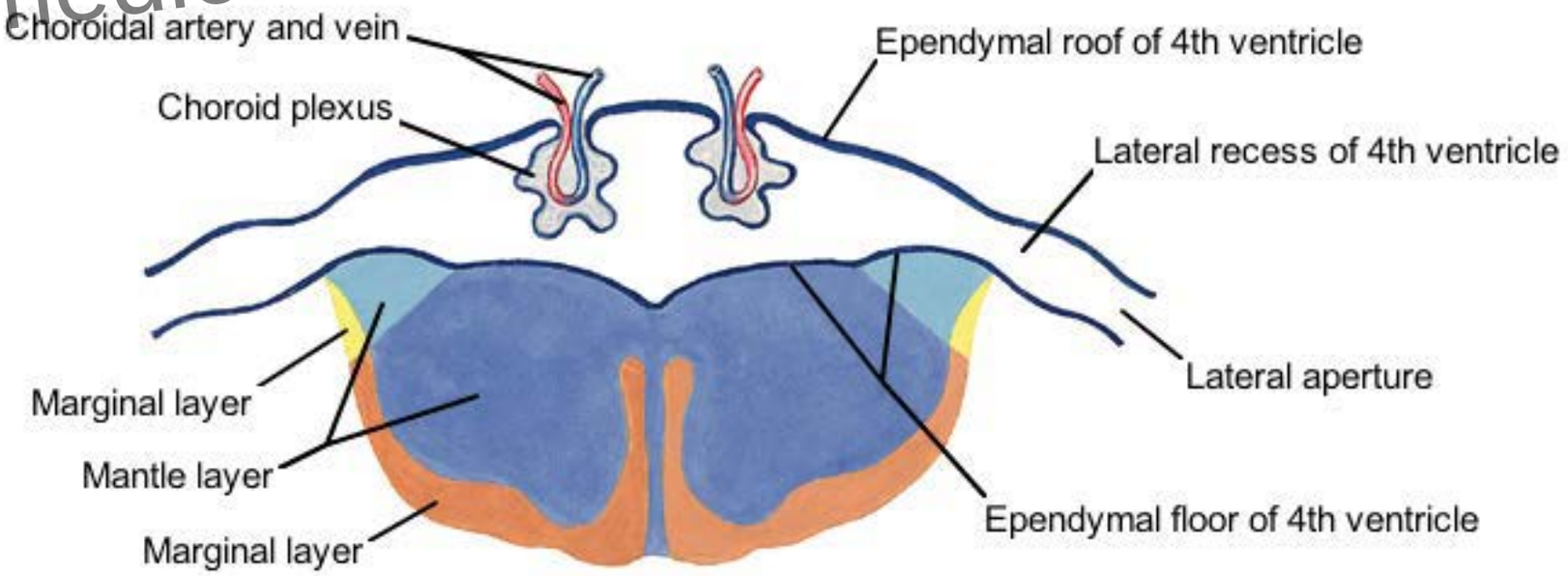


Mesencephalon

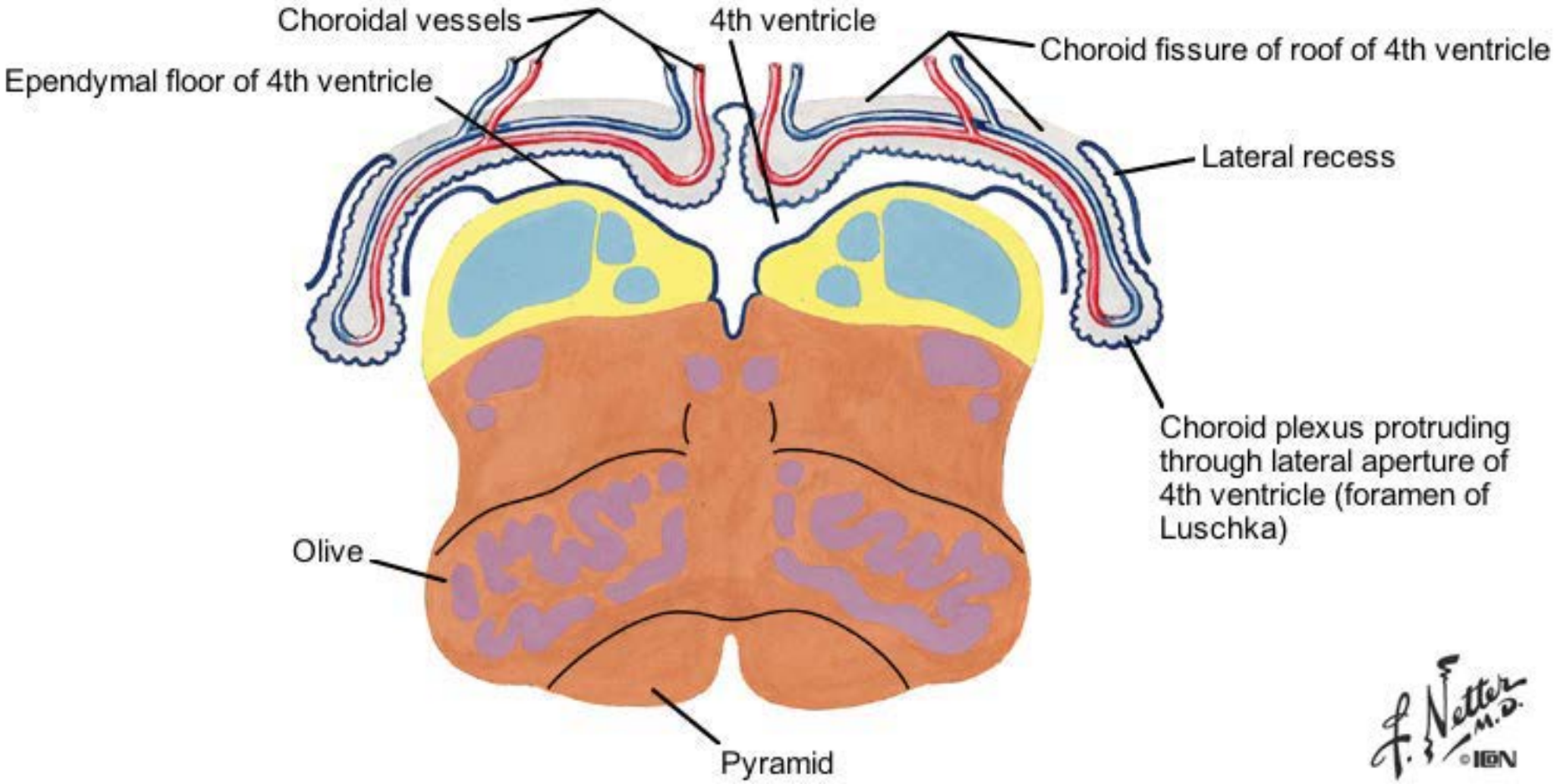


Production of Cerebrospinal Fluid

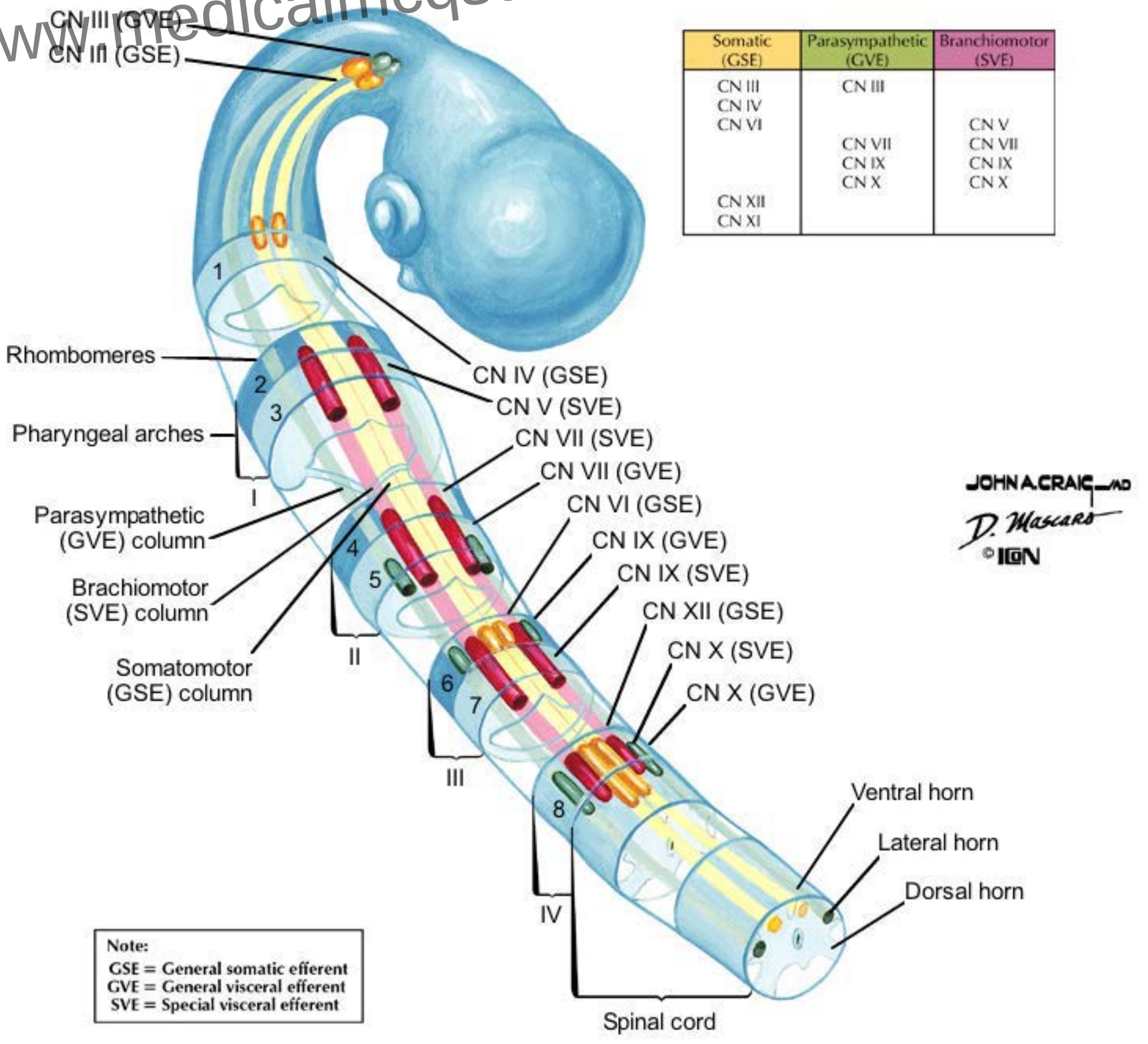
Medulla oblongata at 3 1/2 months (transverse section)



Medulla oblongata, mature (transverse section)



Development of Motor Nuclei in the Brainstem



Somatic (GSE)	Parasympathetic (GVE)	Branchiomotor (SVE)
CN III	CN III	
CN IV		
CN VI		CN V
	CN VII	CN VII
	CN IX	CN IX
	CN X	CN X
CN XII		
CN XI		

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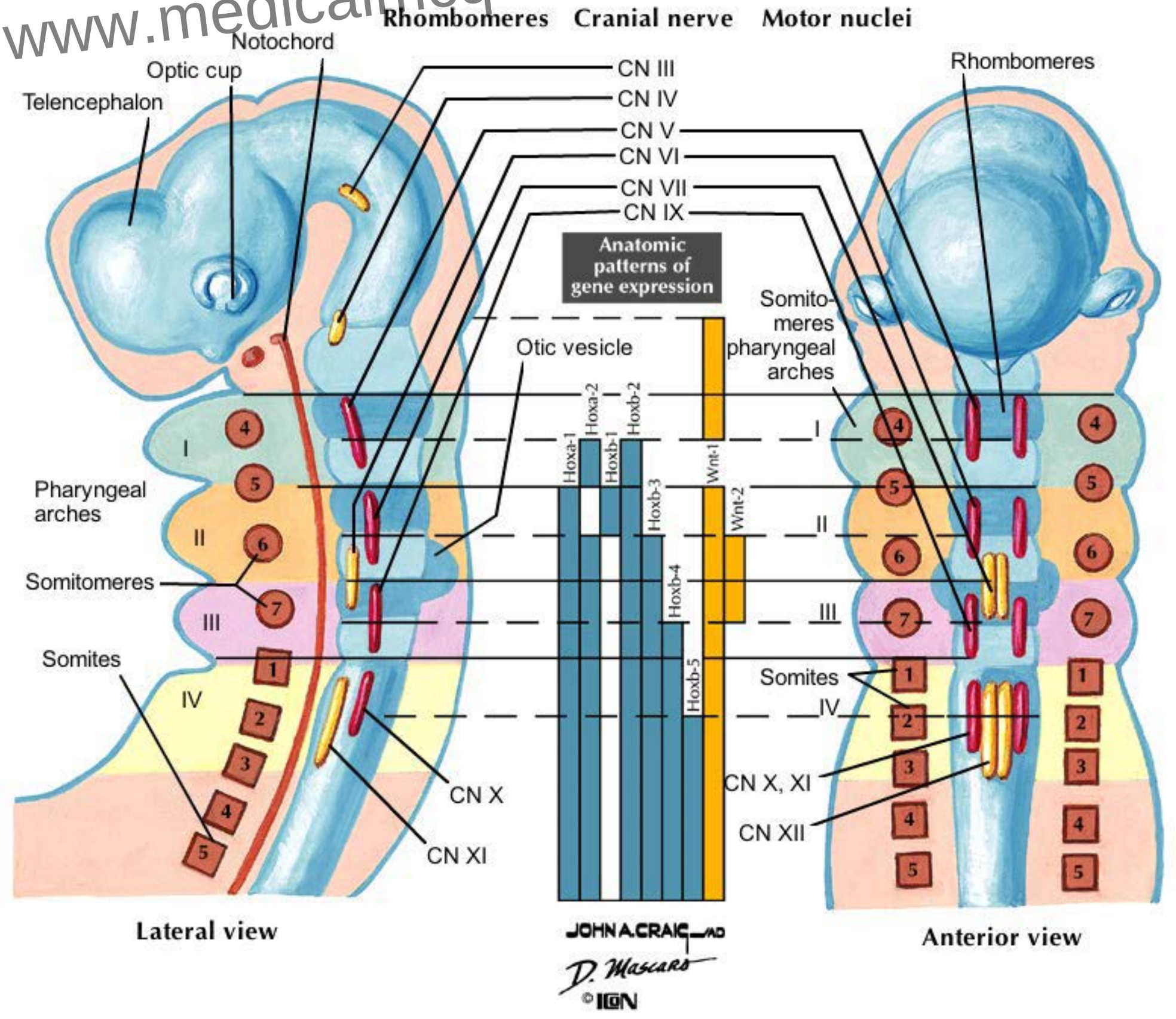
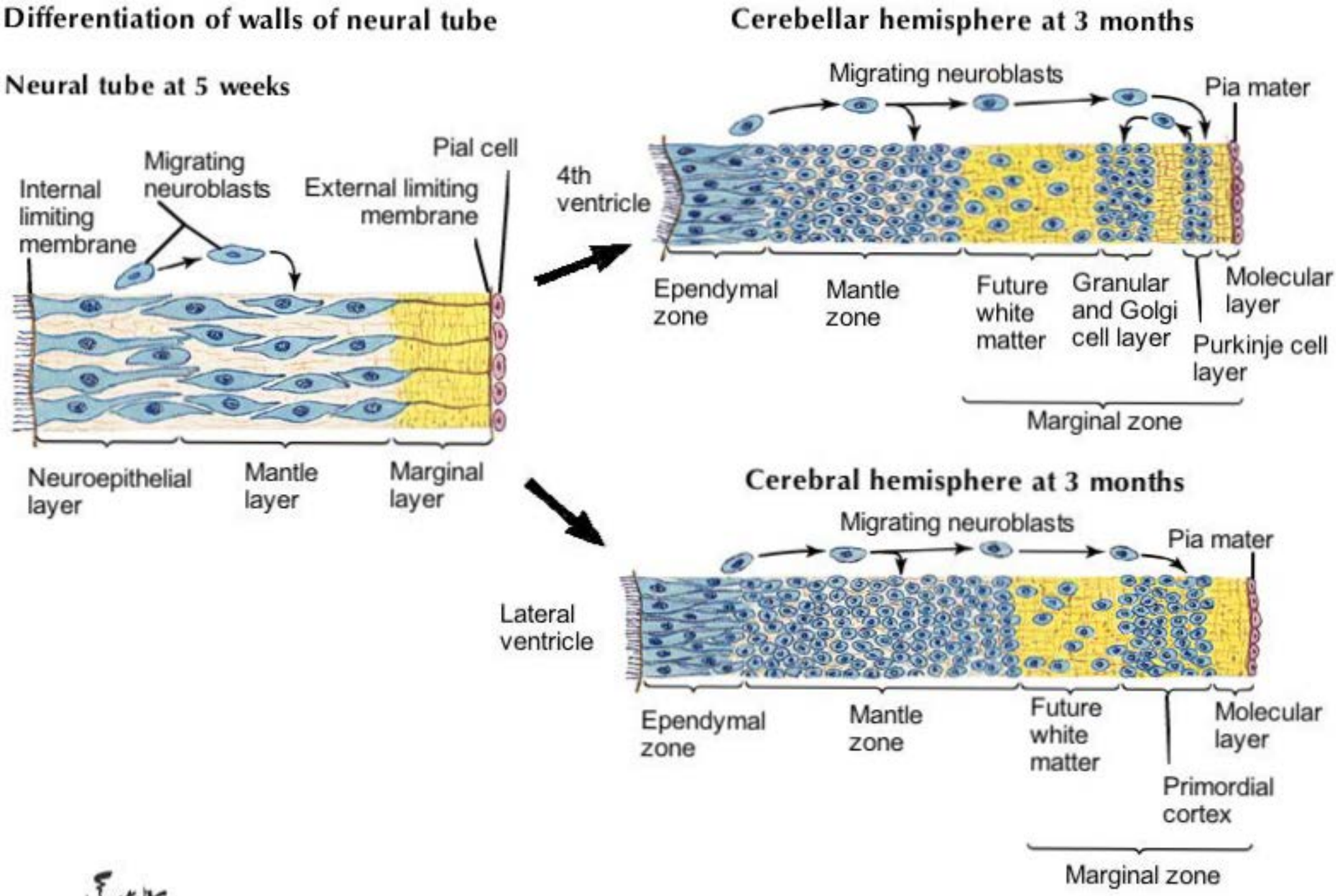
Note:
GSE = General somatic efferent
GVE = General visceral efferent
SVE = Special visceral efferent

Segmentation of the Hindbrain

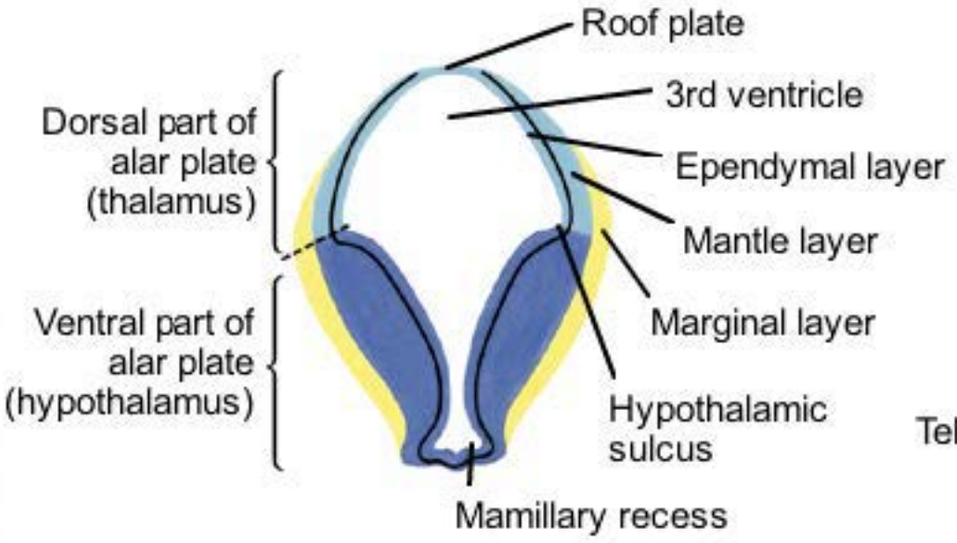


Development of the Forebrain

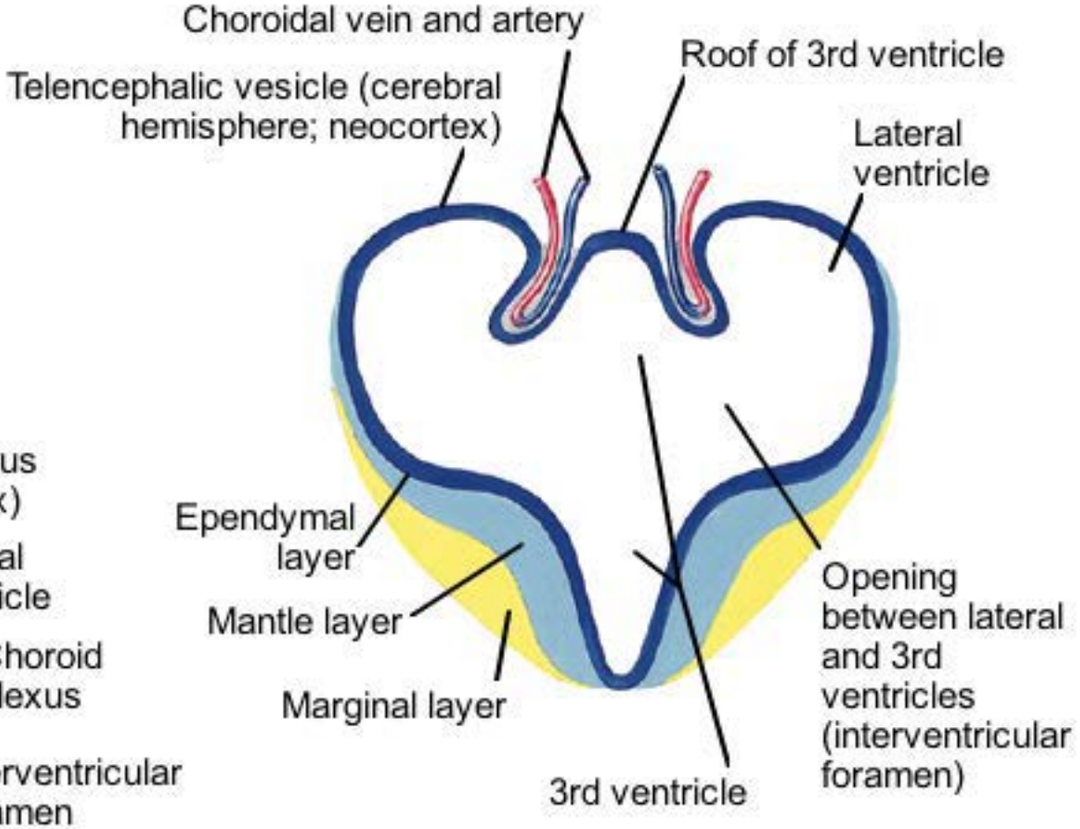


Development of the Forebrain

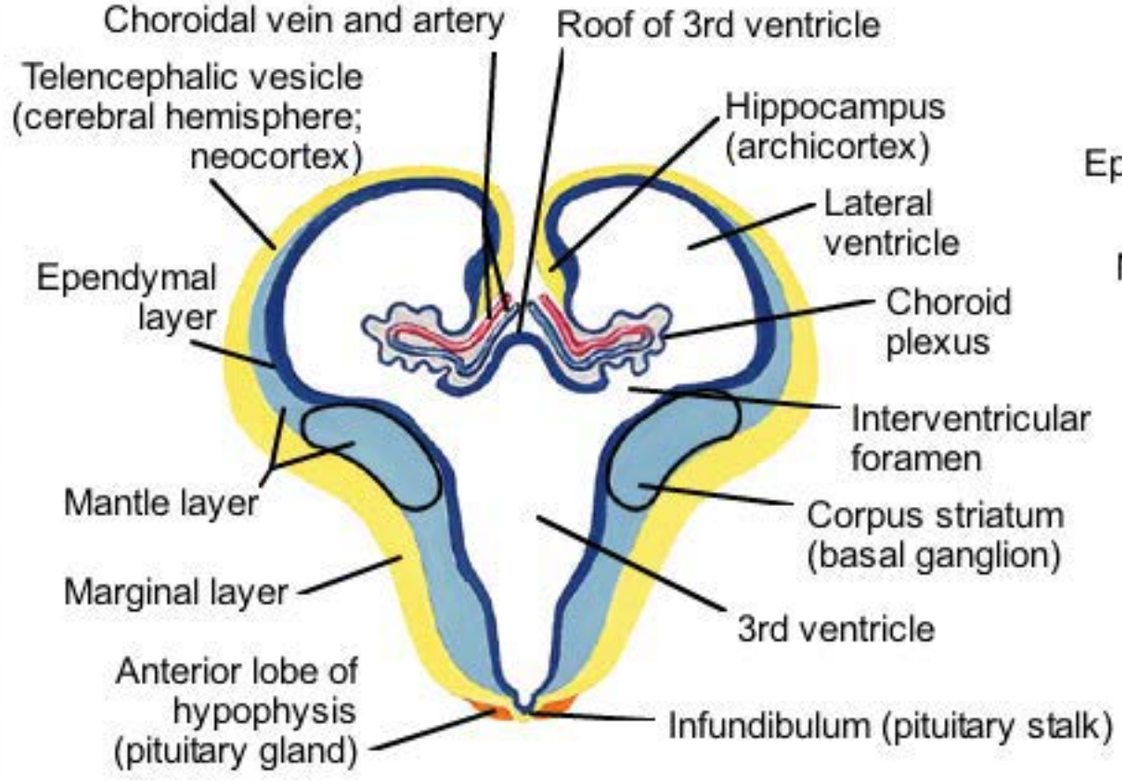
Diencephalon 5 1/2 weeks (transverse section)



Forebrain at 7 weeks (transverse section)



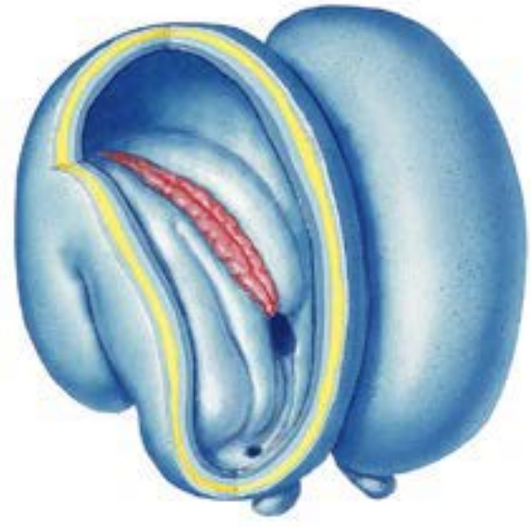
Telencephalon at 7 1/2 weeks (transverse section)



Develoment of the Forebrain

Forebrain at 2 Months
(coronal section; anterior view)

Telencephalon at 2 1/2 months
(right anterior view)



Right cerebral hemisphere at 3 months
(medial aspect)

Cerebral hemispheres at 3 months
(coronal section)

Diencephalon and telencephalon
Mature (coronal section)

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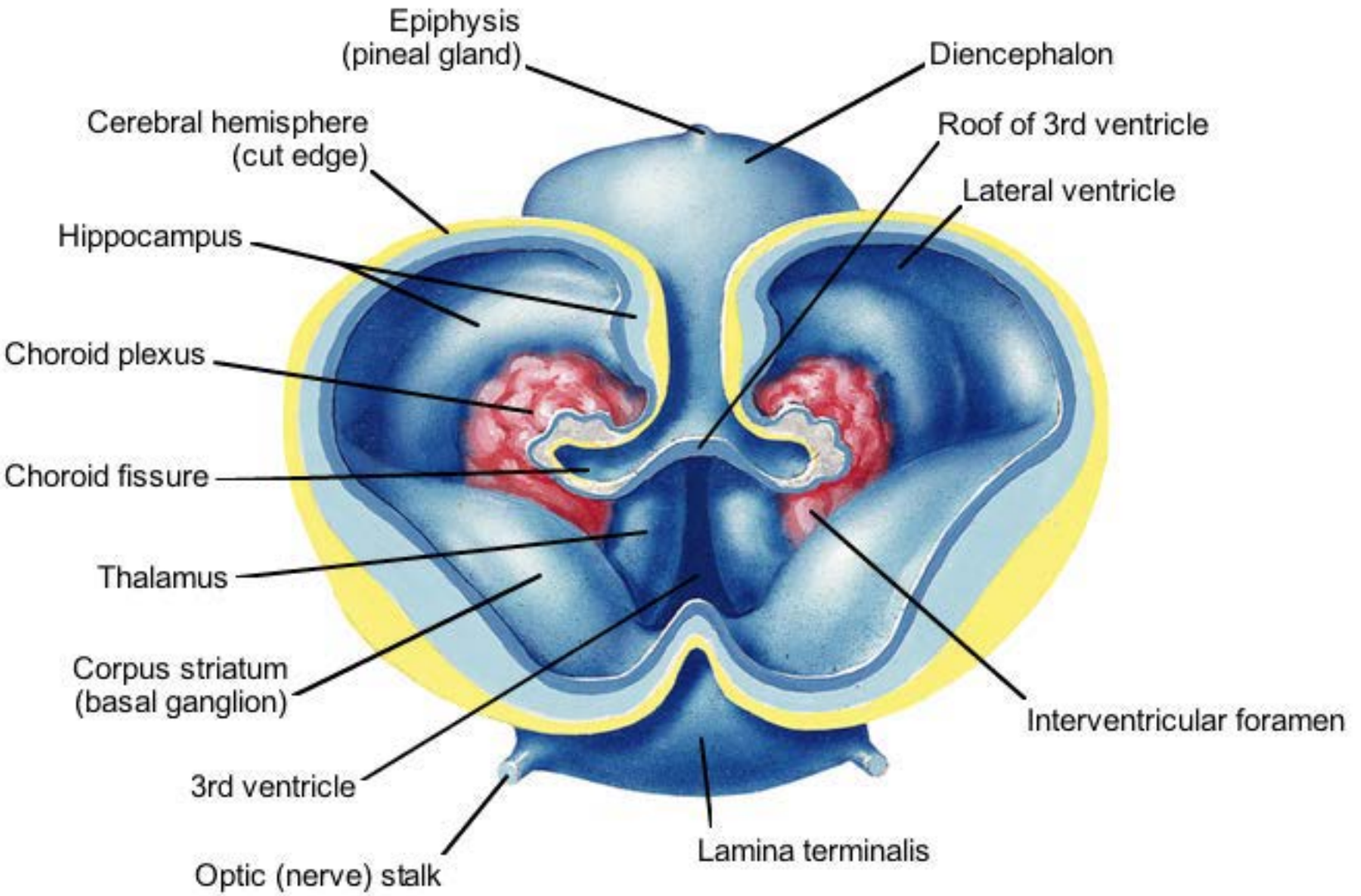
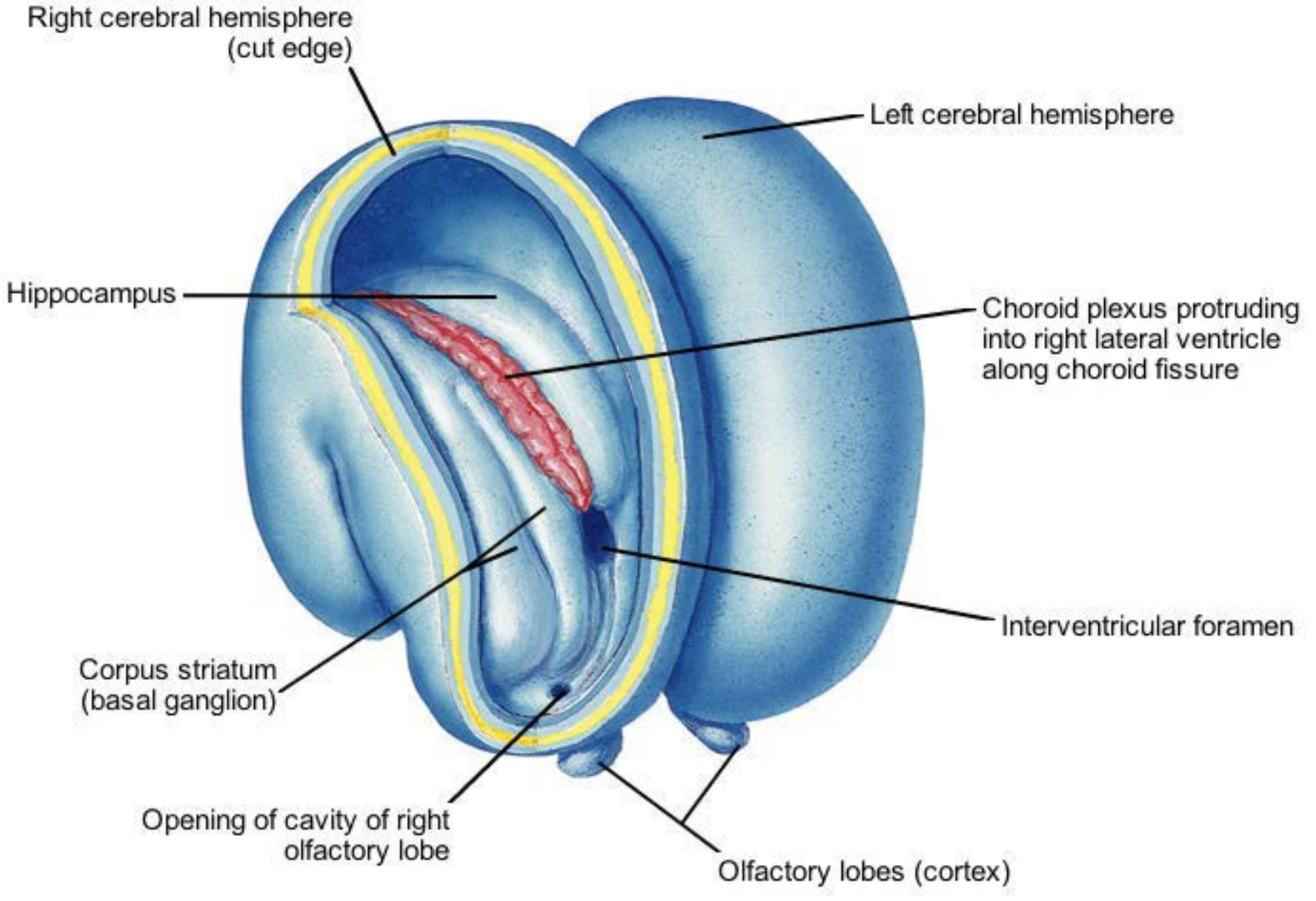
Development of the Forebrain

Forebrain at 2 Months (coronal section; anterior view)



Development of the Forebrain

Telencephalon at 2 1/2 months (right anterior view)



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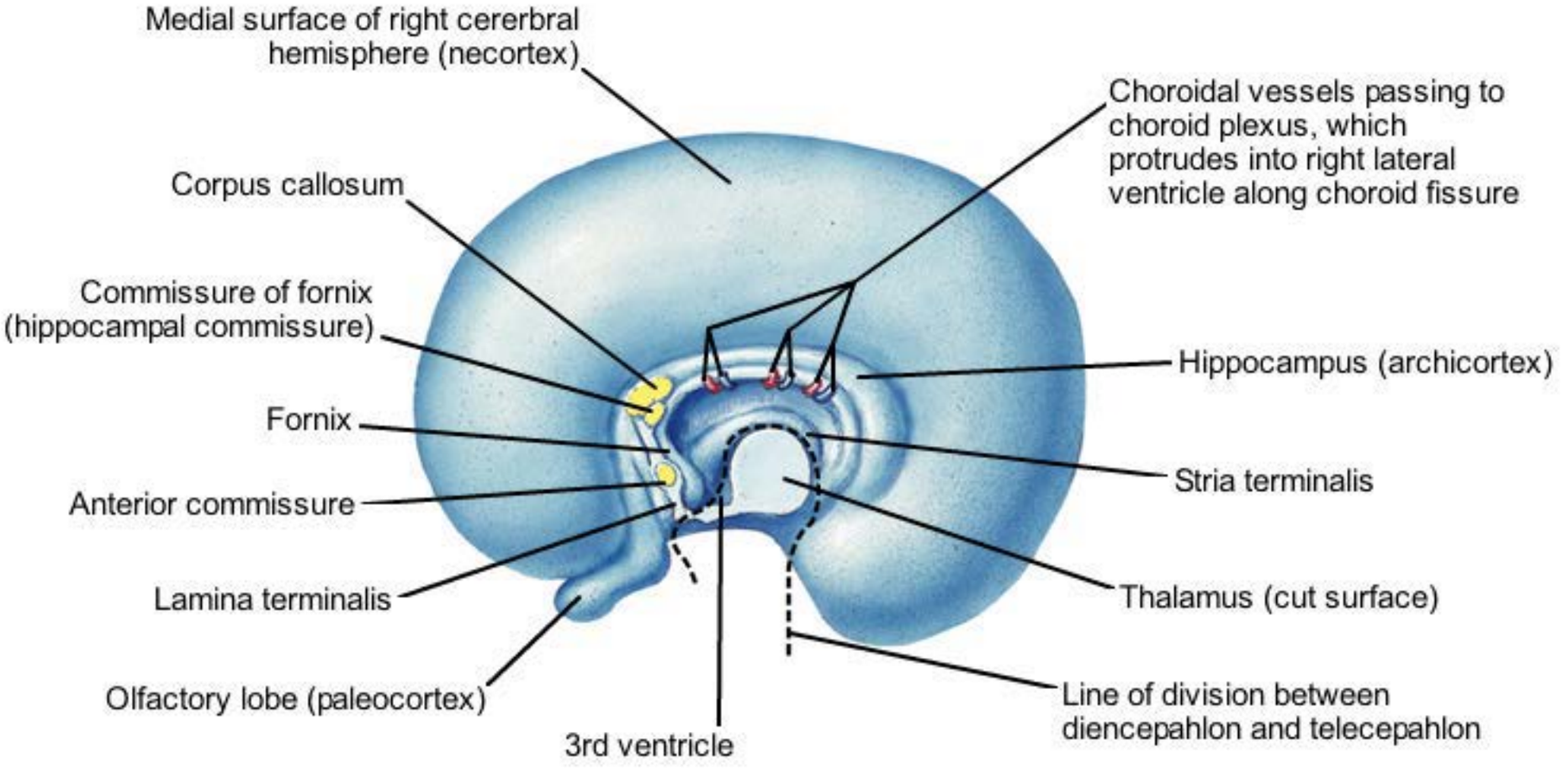
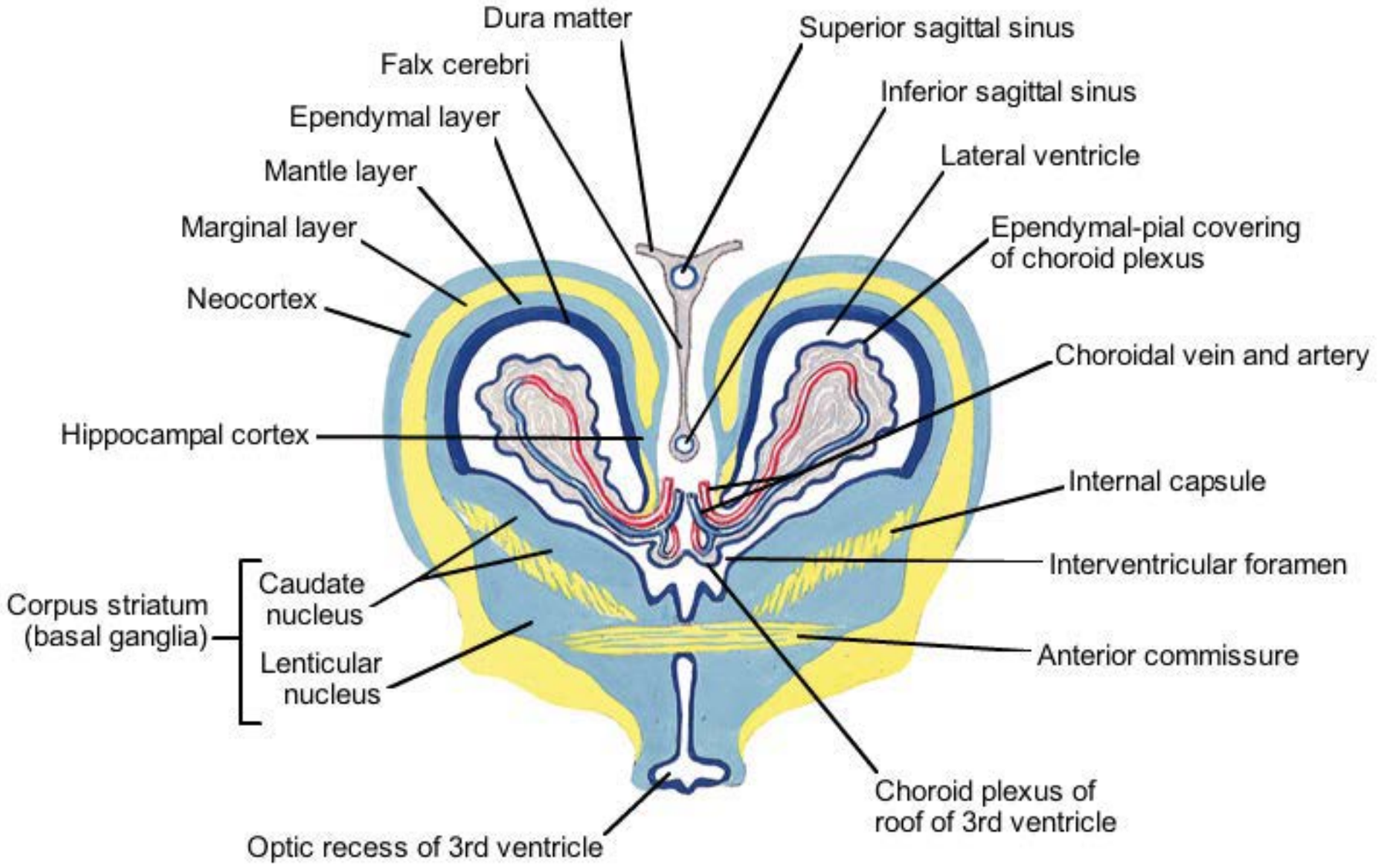
Development of the Forebrain

Right cerebral hemisphere at 3 months (medial aspect)



Development of the Forebrain

Cerebral hemispheres at 3 months (coronal section)



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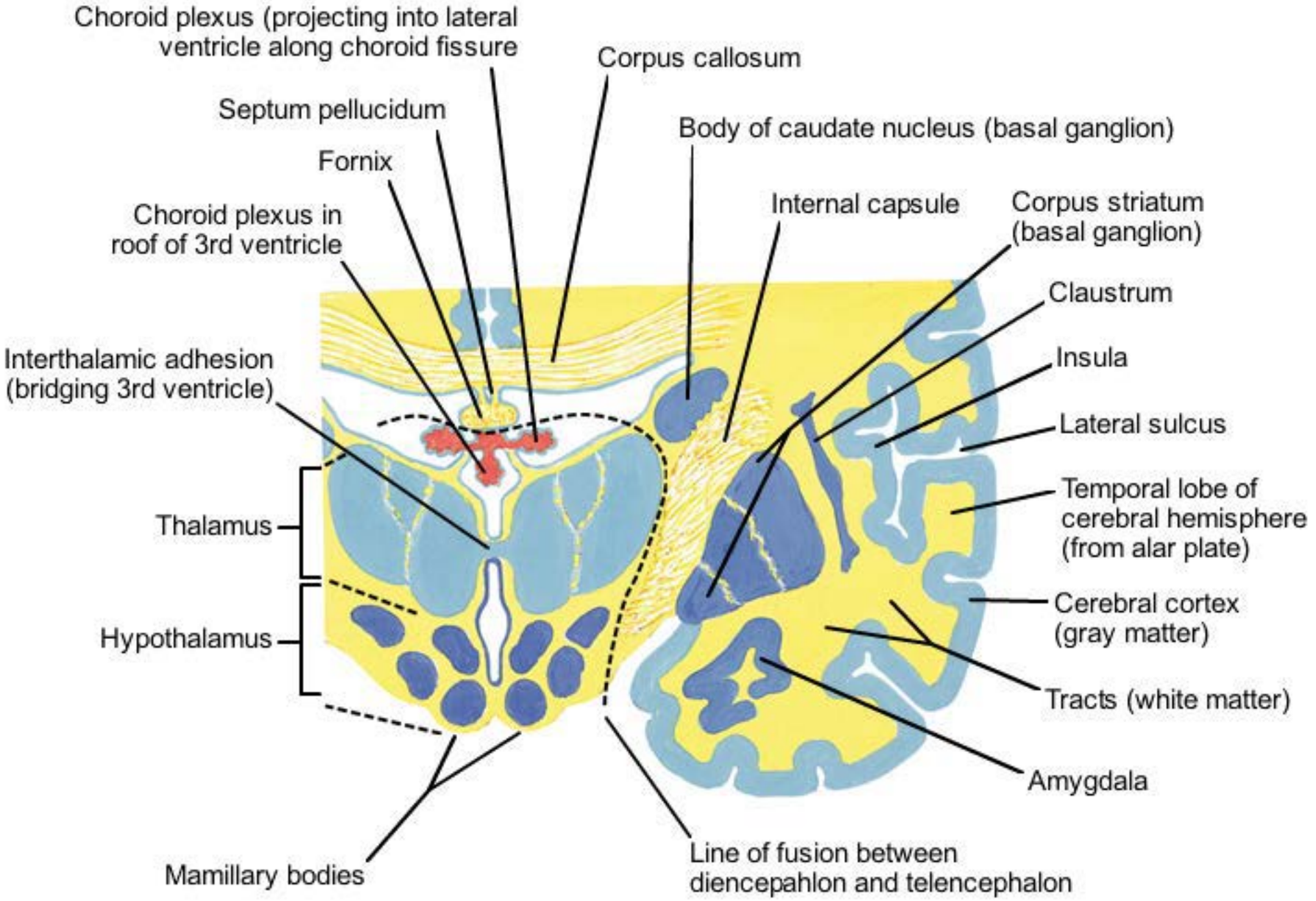
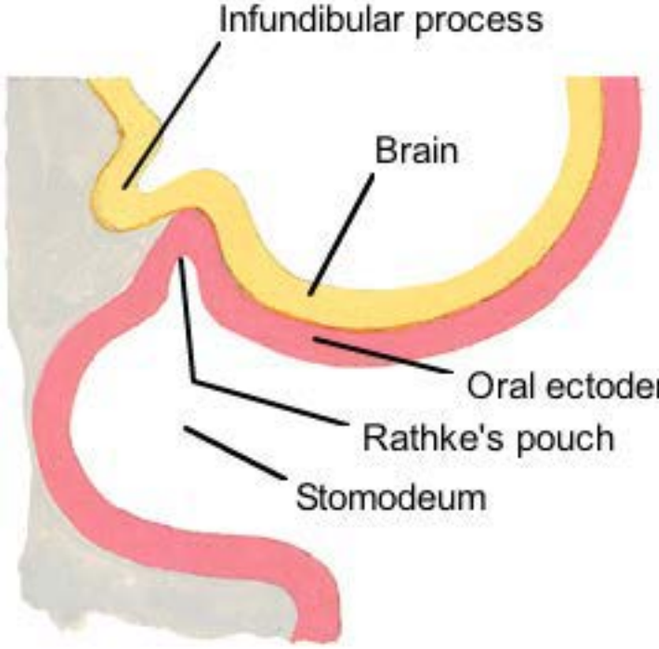
Development of the Forebrain

Diencephalon and telencephalon

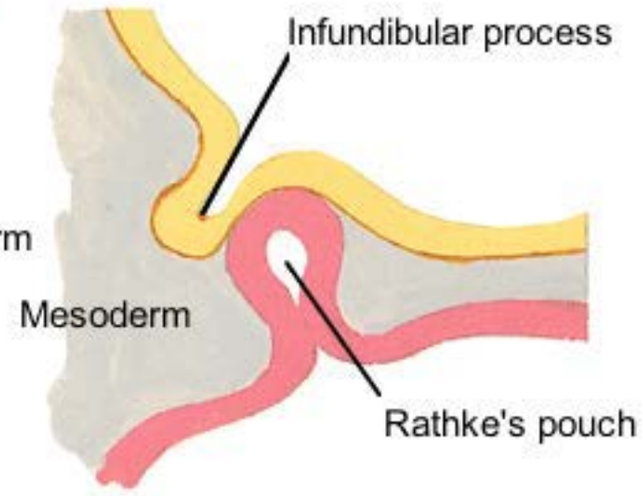
Mature (coronal section)



Development of the Pituitary Gland

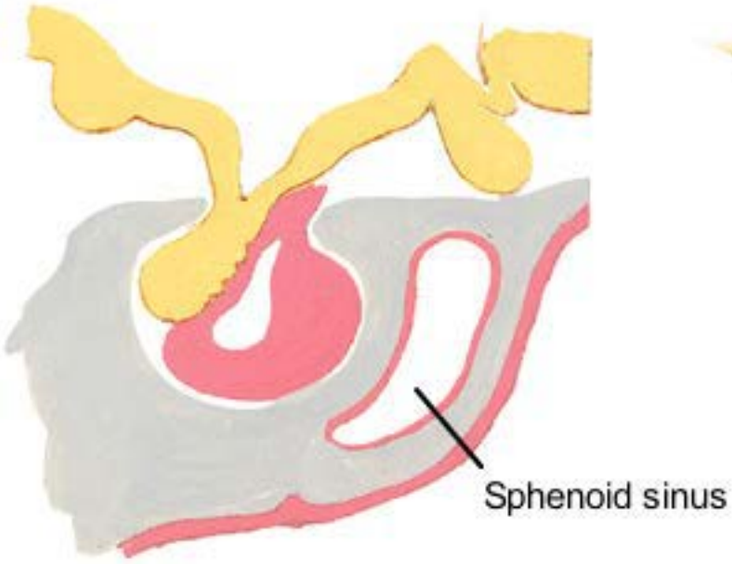


1. Beginning formation of Rathke's pouch and infundibular process

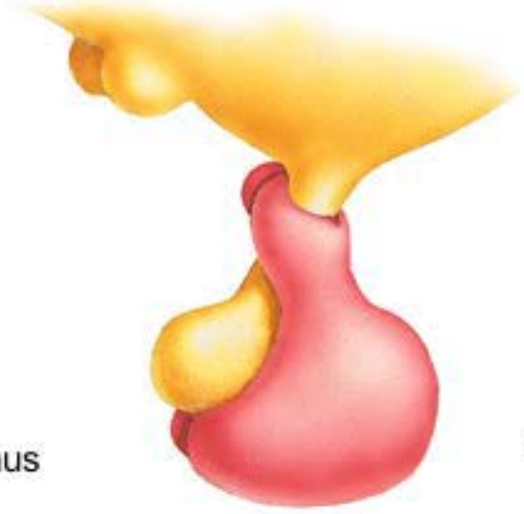


2. Neck of Rathke's pouch constricted by growth of mesoderm

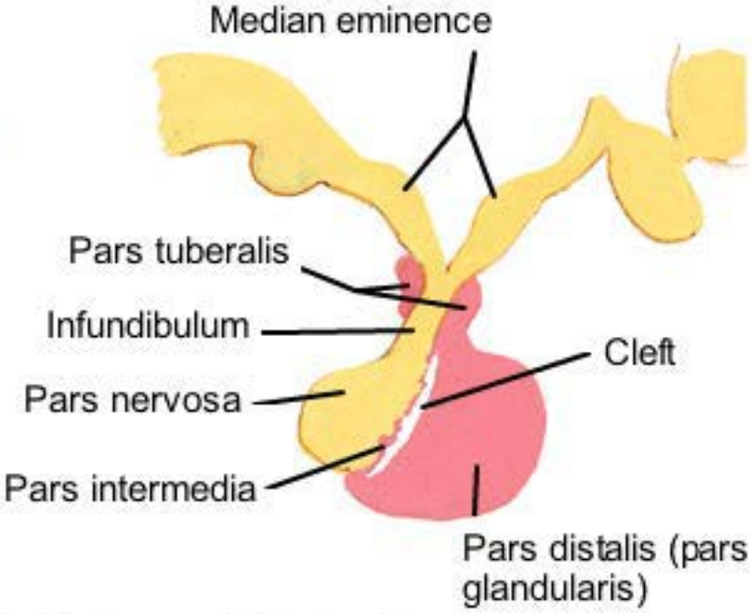
3. Rathke's pouch "pinched off"



4. "Pinched off" segment conforms to neural process, forming pars distalis, pars intermedia and pars tuberalis



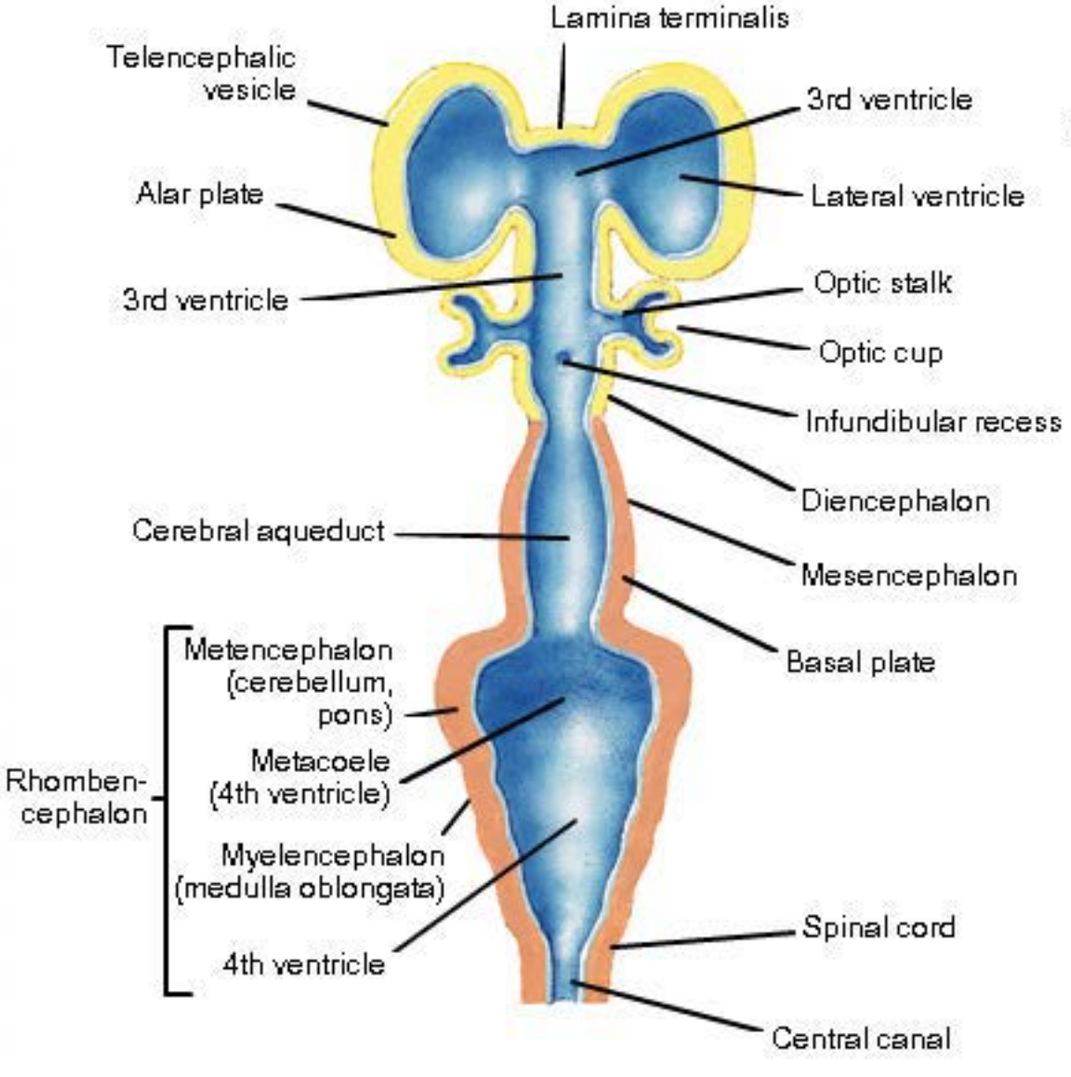
5. Pars tuberalis encircles infundibular stalk (lateral surface view)



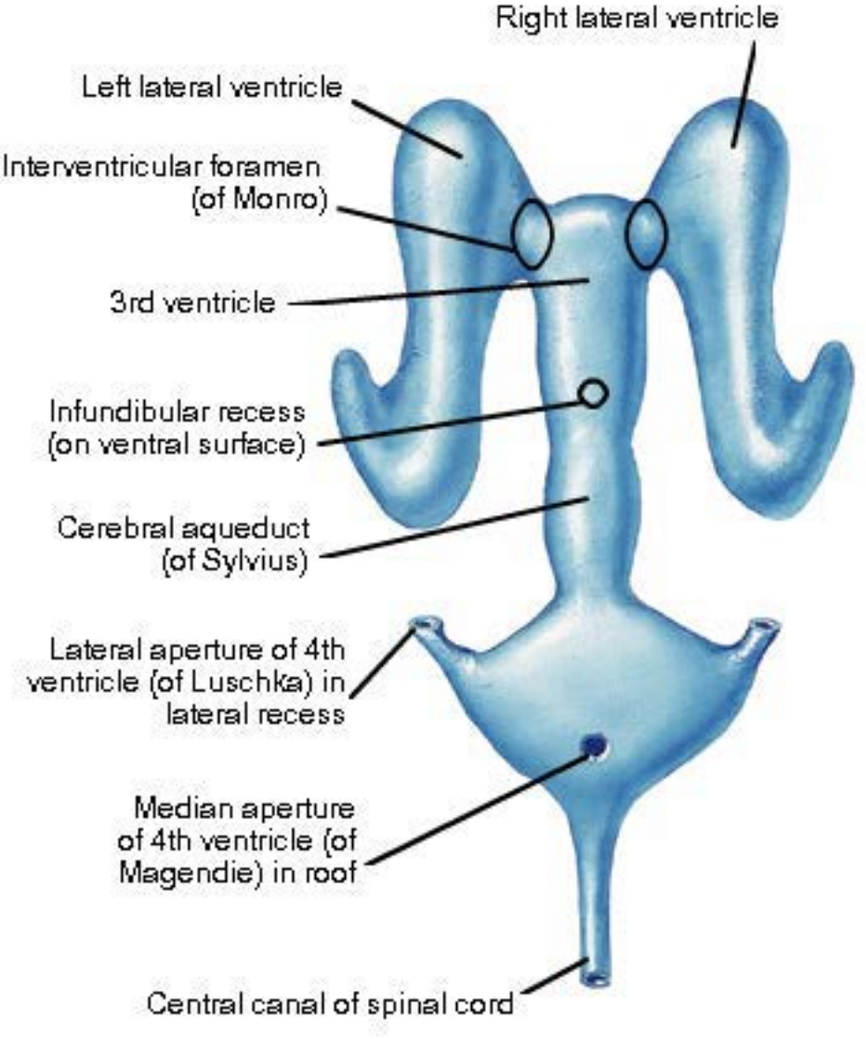
6. Mature form

Development of the Ventricles

Frontal section (ventral to sulcus limitans) at 36 days



Ependymal lining of cavities of brain at 3 months



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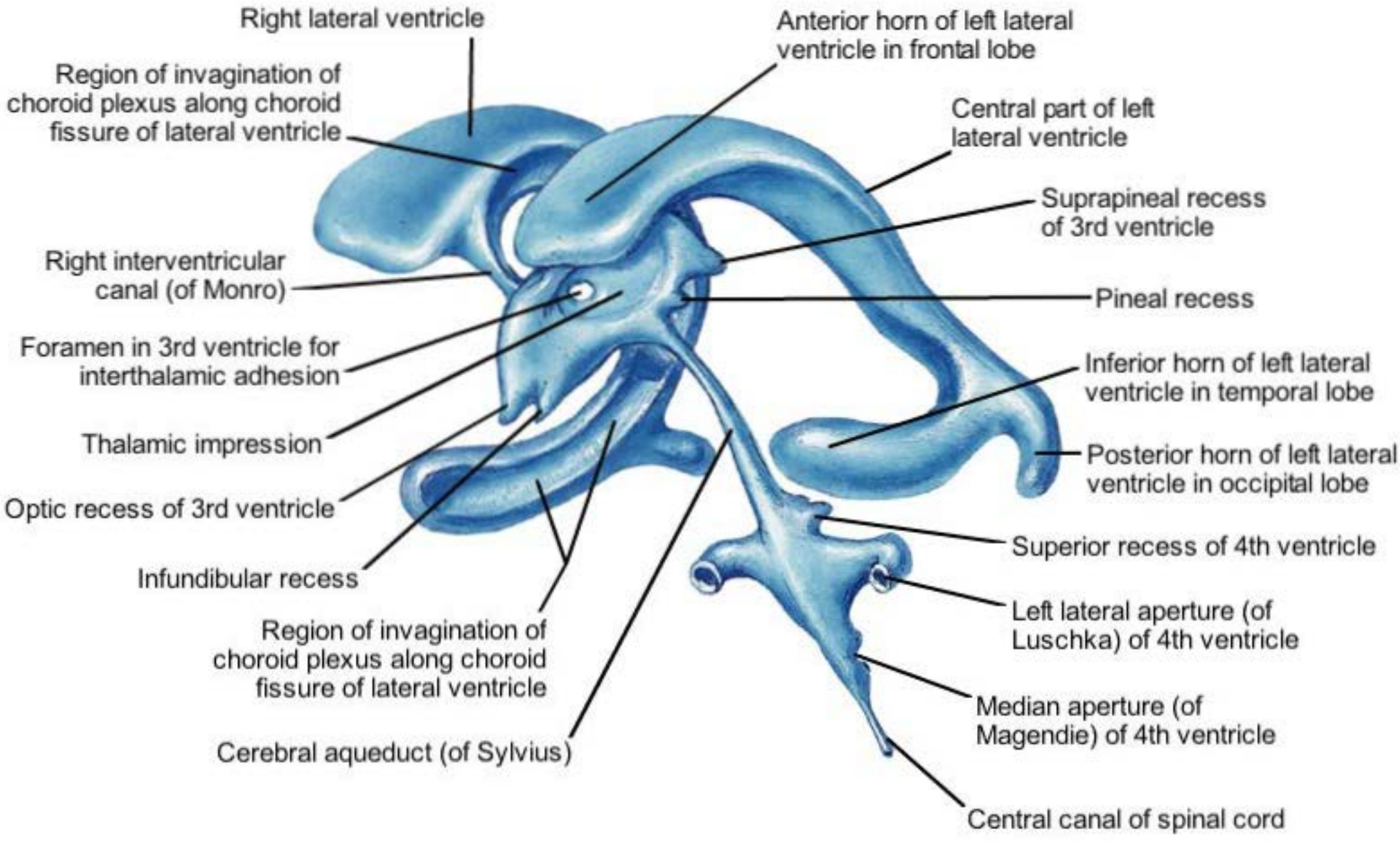
Development of the Ventricles

Ependymal lining of cavities of brain at 9 months (birth)



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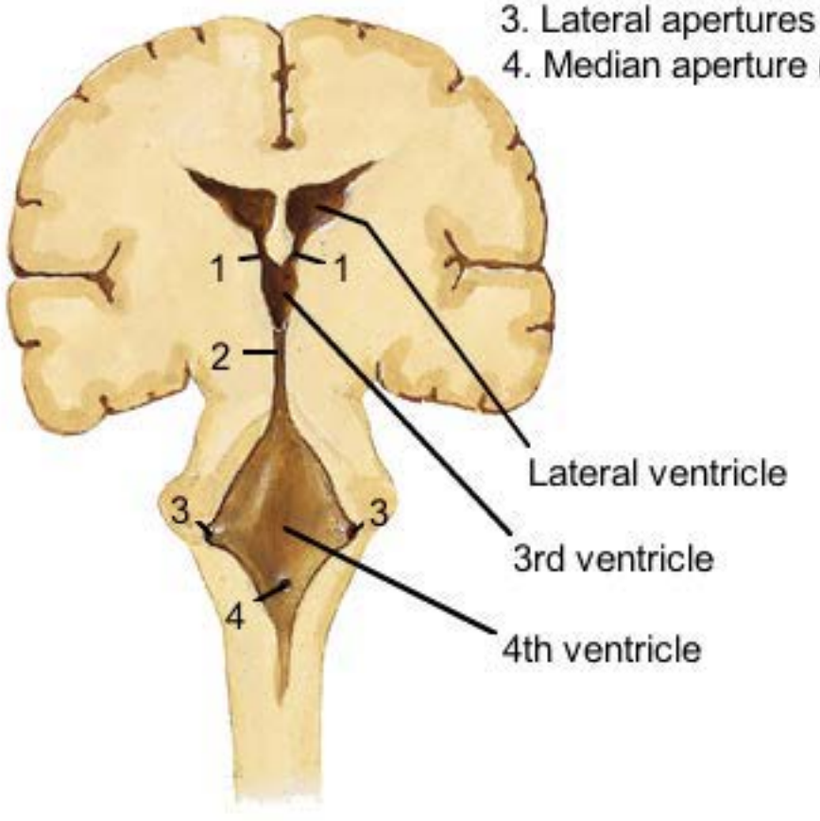
Congenital Ventricular Defects

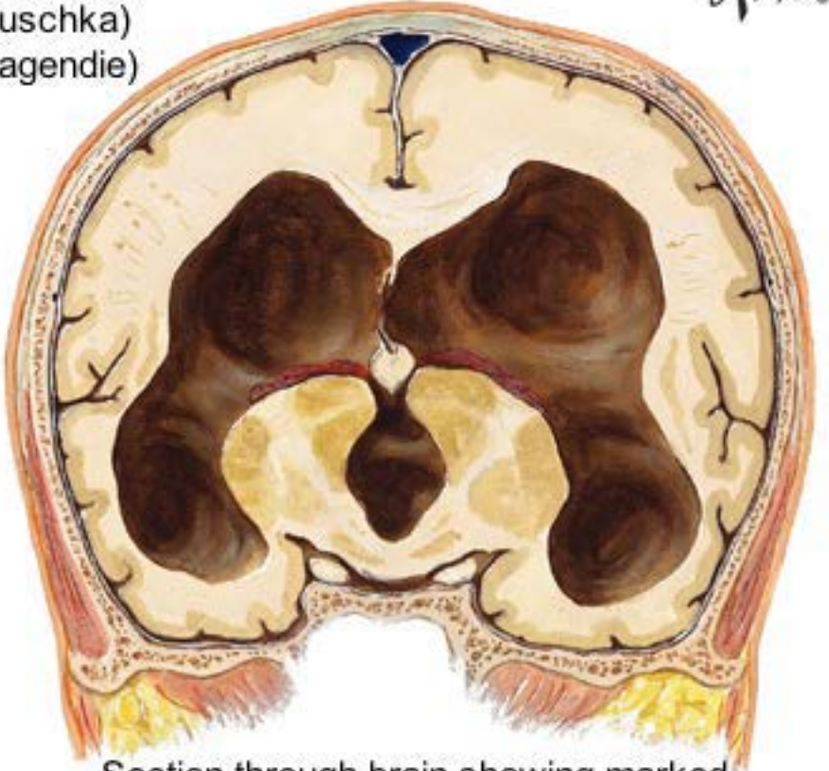
Hydrocephalus

Clinical appearance in advanced hydrocephalus

Potential lesion sites in obstructive hydrocephalus

1. Interventricular foramina (of Monro)
2. Cerebral aqueduct (of Sylvius)
3. Lateral apertures (of Luschka)
4. Median aperture (of Magendie)





Section through brain showing marked dilation of lateral and 3rd ventricles

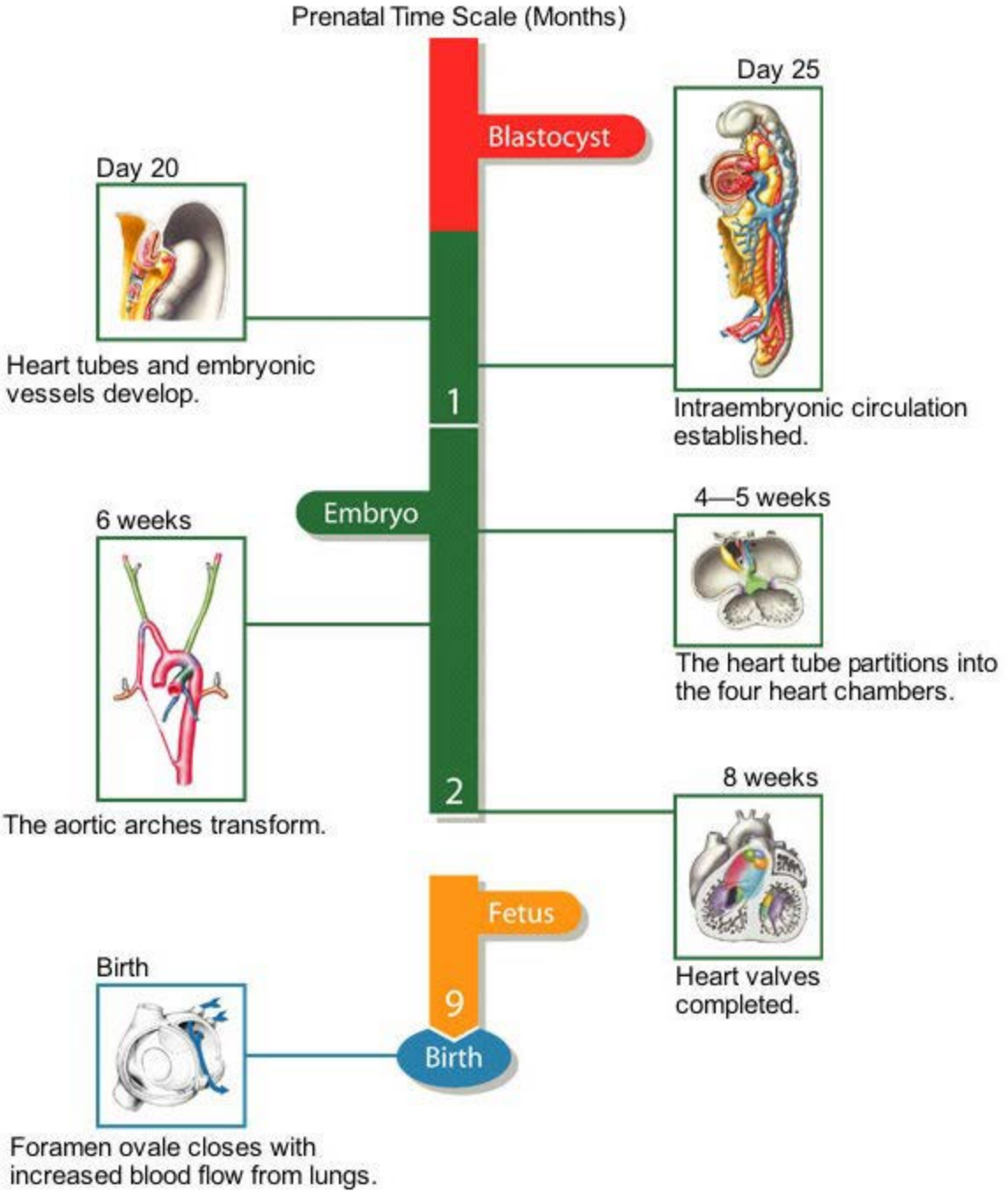
Adult Derivatives of the Forebrain, MidBrain, and Hindbrain

Forebrain	Telencephalon	Cerebral hemispheres (neocortex) Olfactory cortex (paleocortex) Hippocampus (archicortex) Basal ganglia/corpus striatum Lateral and 3rd ventricles	Nerves: Olfactory (I)
	Diencephalon	Optic cup/nerves Thalamus Hypothalamus Mammillary bodies Part of 3rd ventricle	Optic (II)
Midbrain	Mesencephalon	Tectum (superior, inferior colliculi) Cerebral aqueduct Red nucleus Substantia nigra Crus cerebelli	Oculomotor (III) Trochlear (IV)
Hindbrain	Metencephalon	Pons Cerebellum	Trigeminal (V) Abducens(VI) Facial (VII) Acoustic (VIII) Glossopharyngeal (IX) Vagus (X) Hypoglossal (XI)
	Myelencephalon	Medulla oblongata	

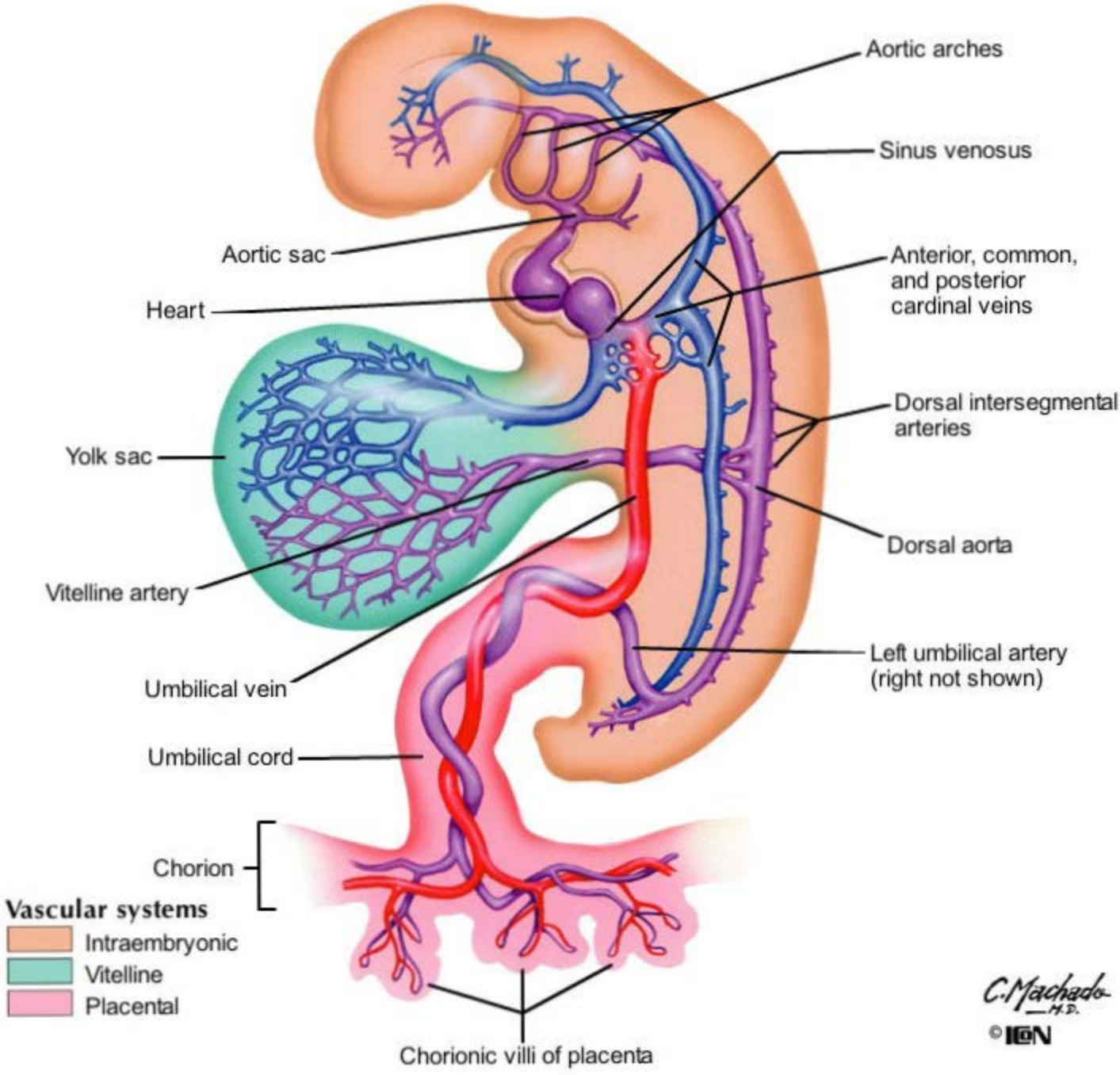
Pituitary Hormones

From the Anterior Lobe (Pars Distalis)		From the Posterior Lobe (Pars Nervosa)
Follicle-stimulating hormone (FSH)	Thyroid-stimulating hormone (TSH)	Vasopressin
Luteinizing hormone (LH)	Adrenocorticotropic hormone (ACTH)	Oxytocin
Prolactin	Growth hormone (GH)	

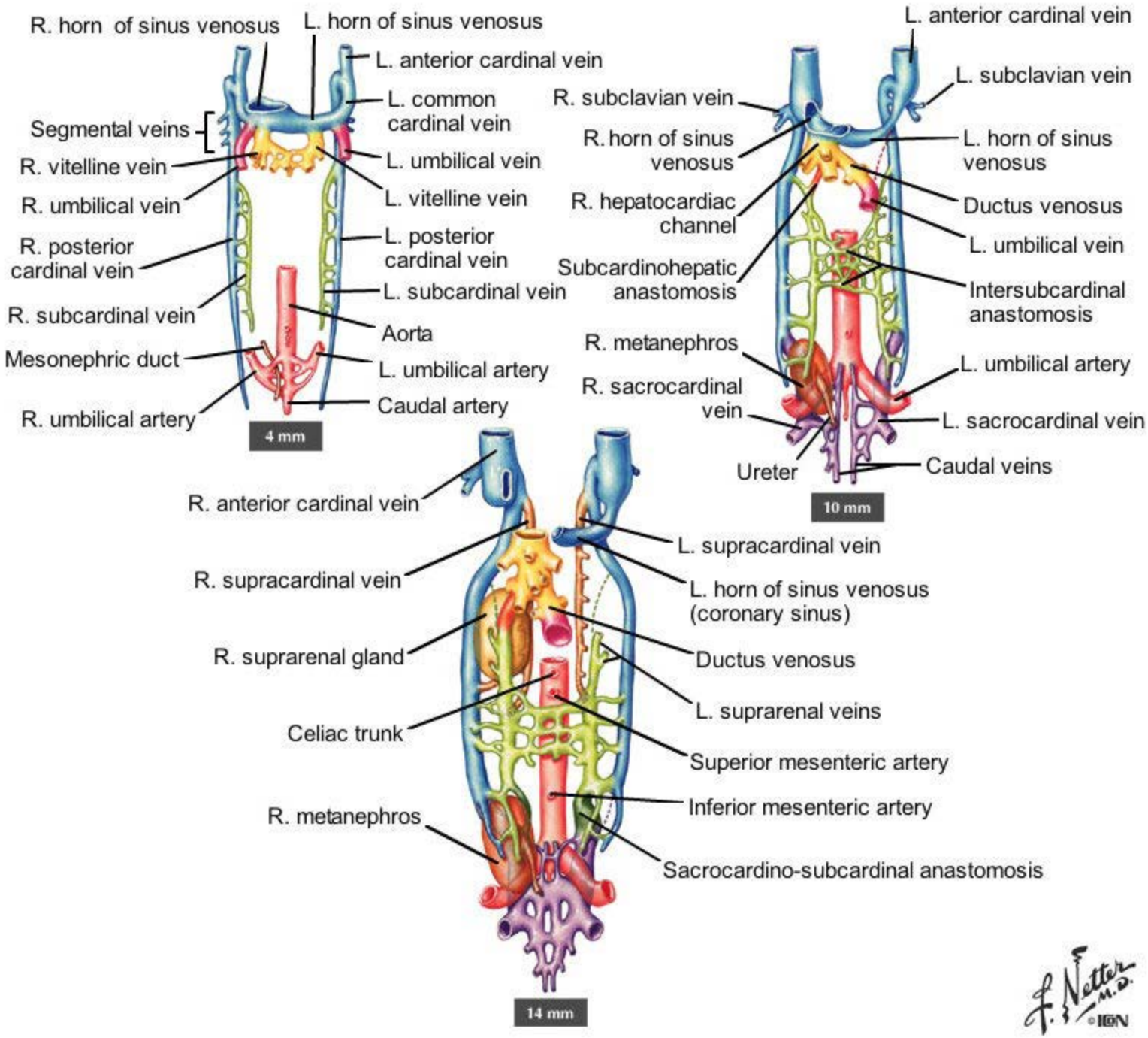
THE CARDIOVASCULAR SYSTEM
TIMELINE



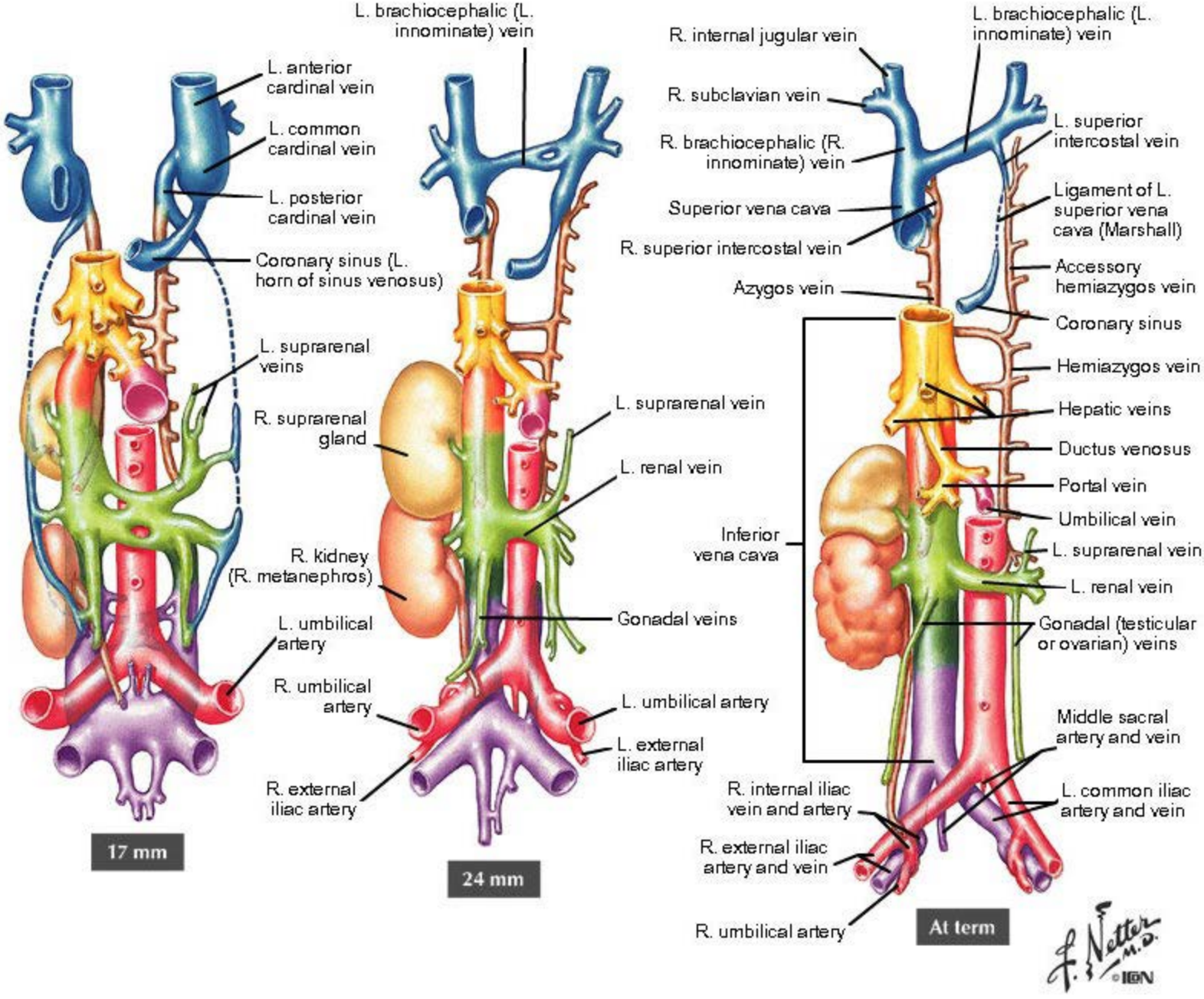
Early Vascular Systems



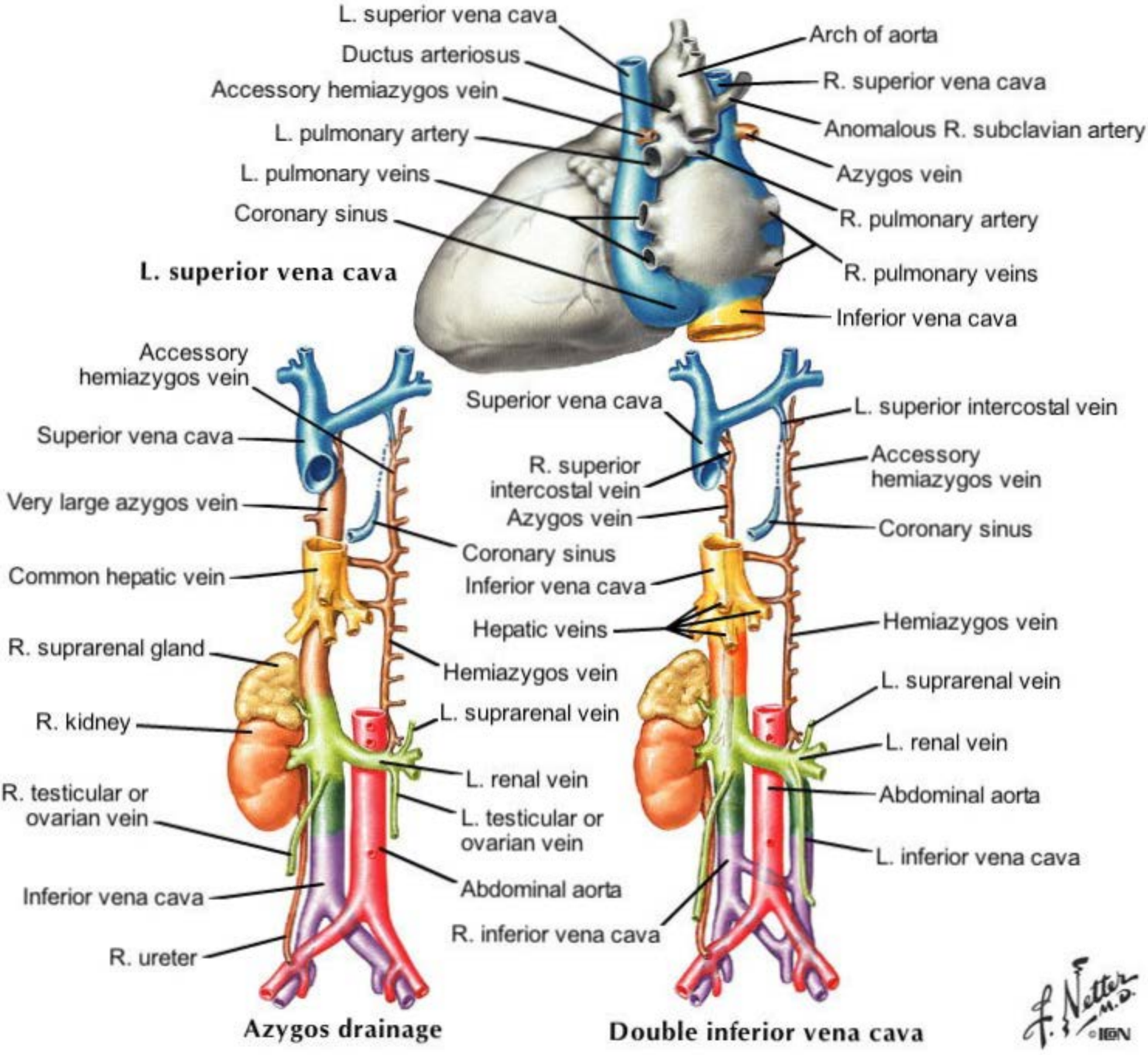
Vein Development



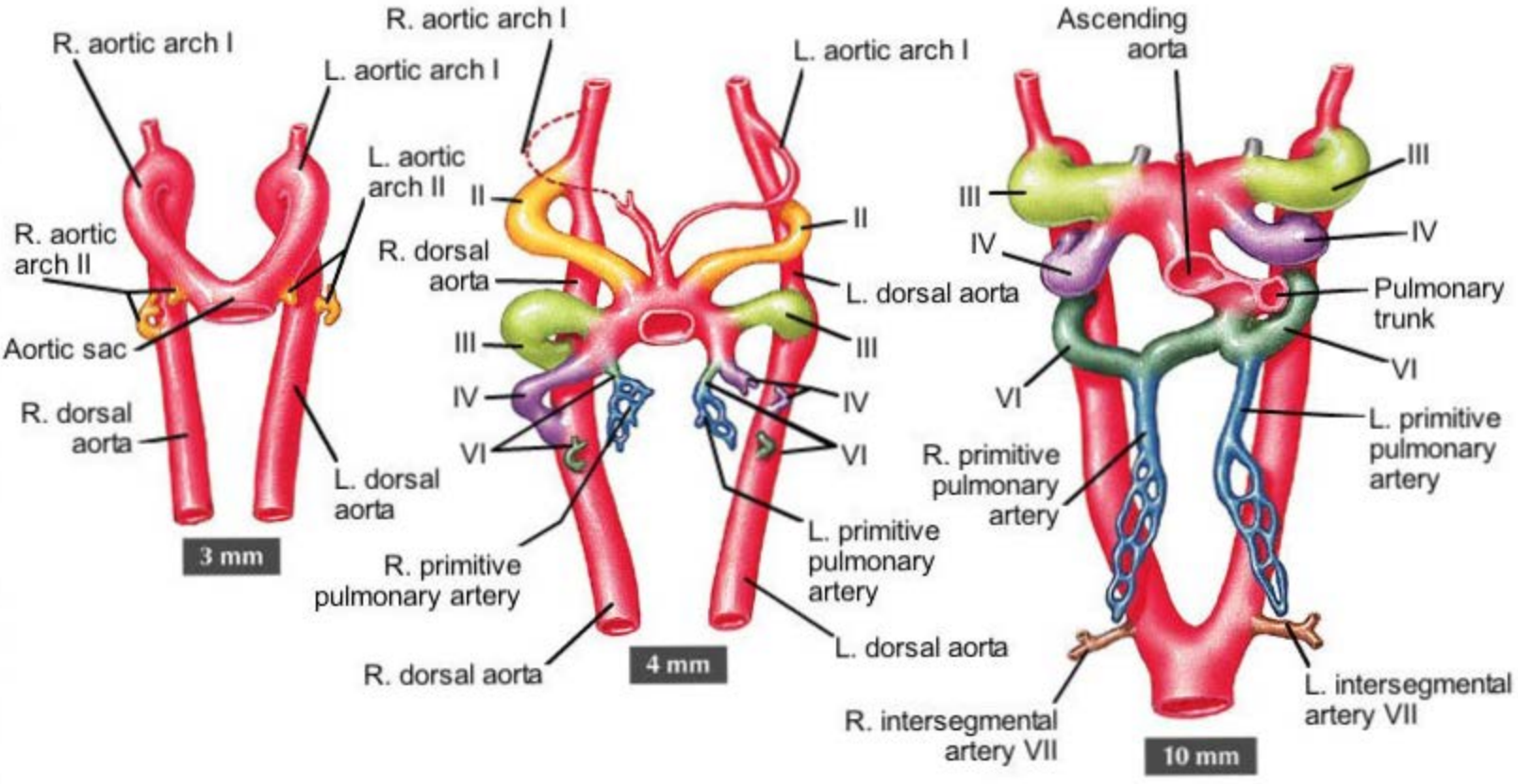
Vein Development



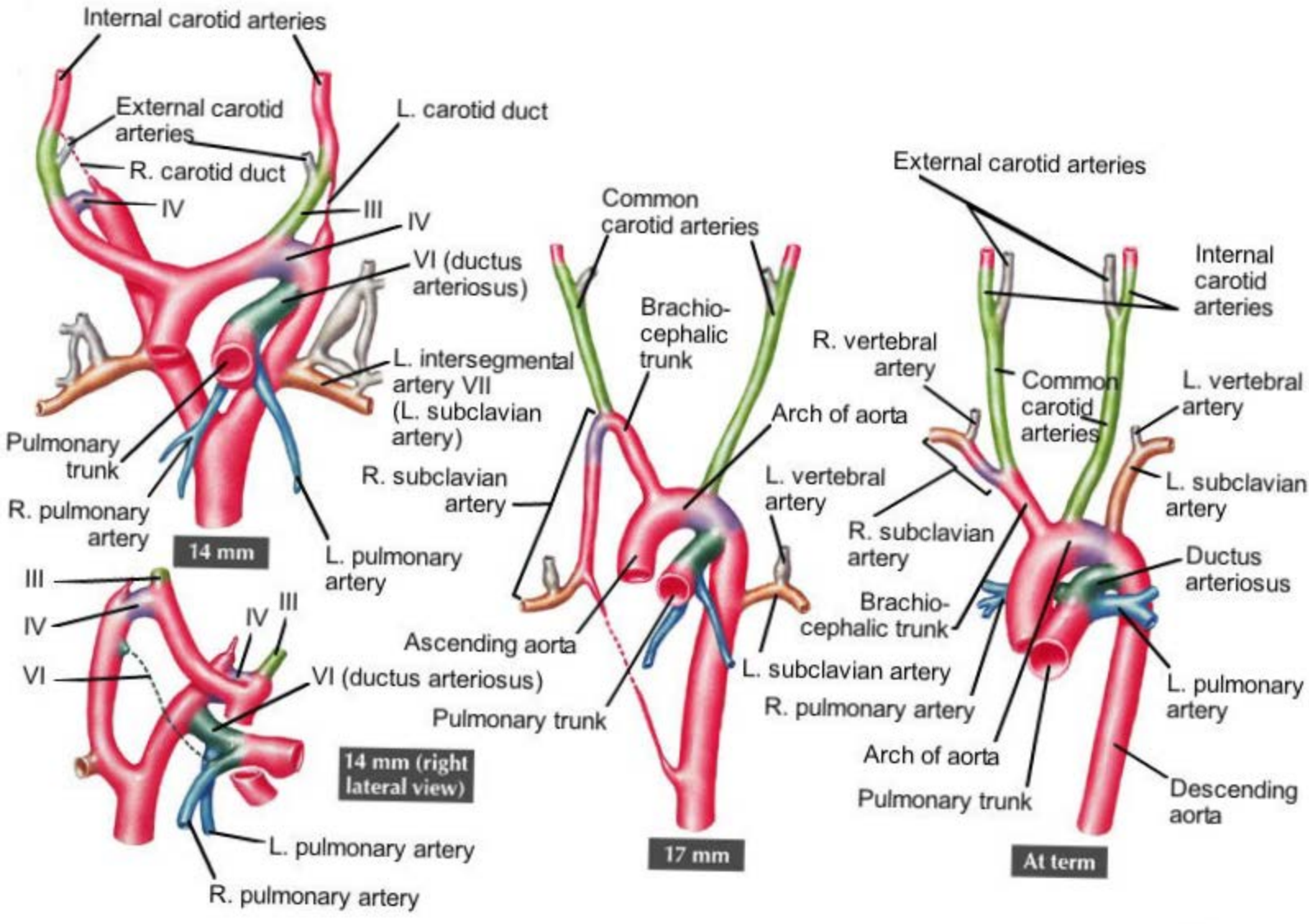
Vein Anomalies



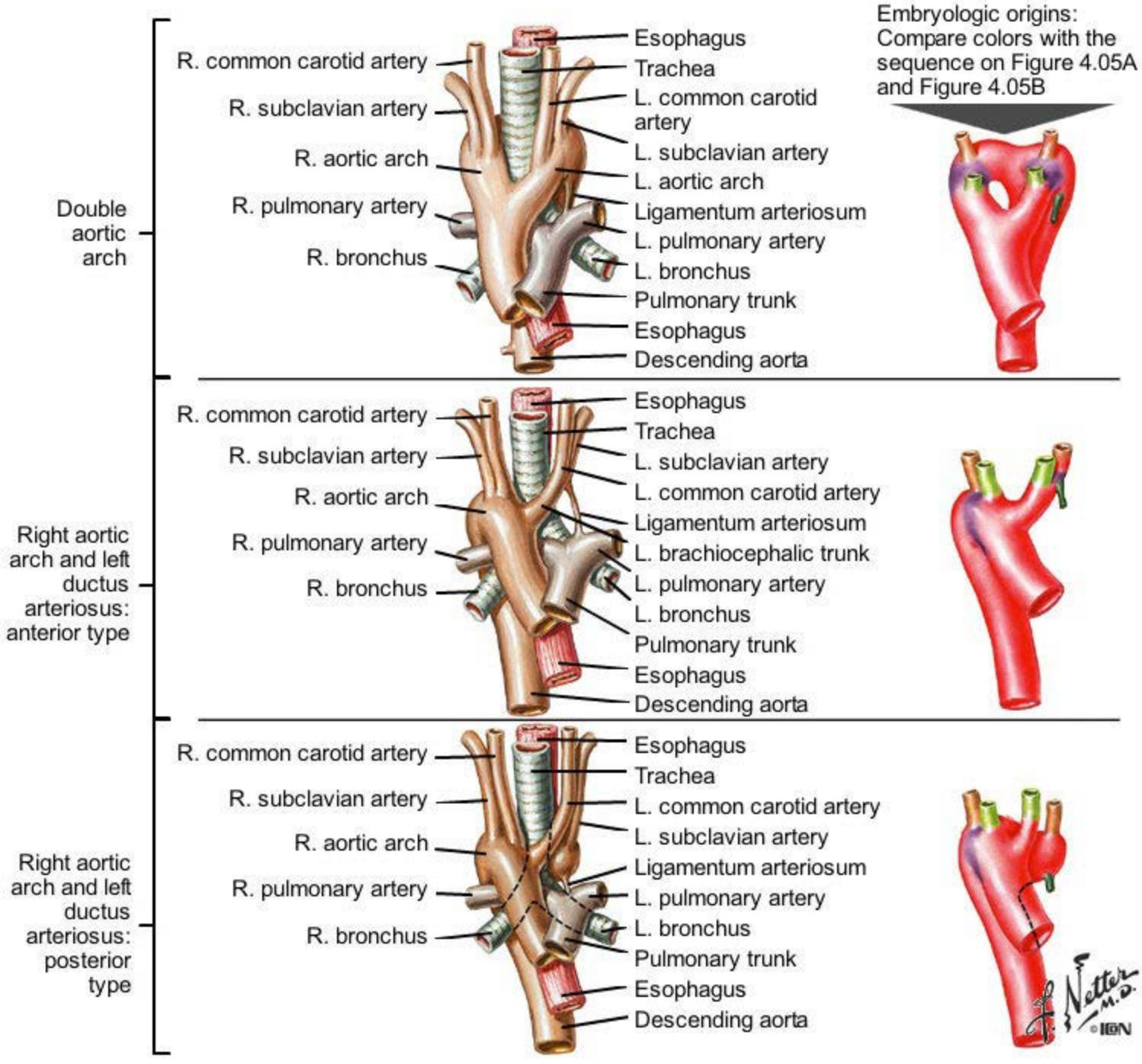
Aortic Arch Arteries



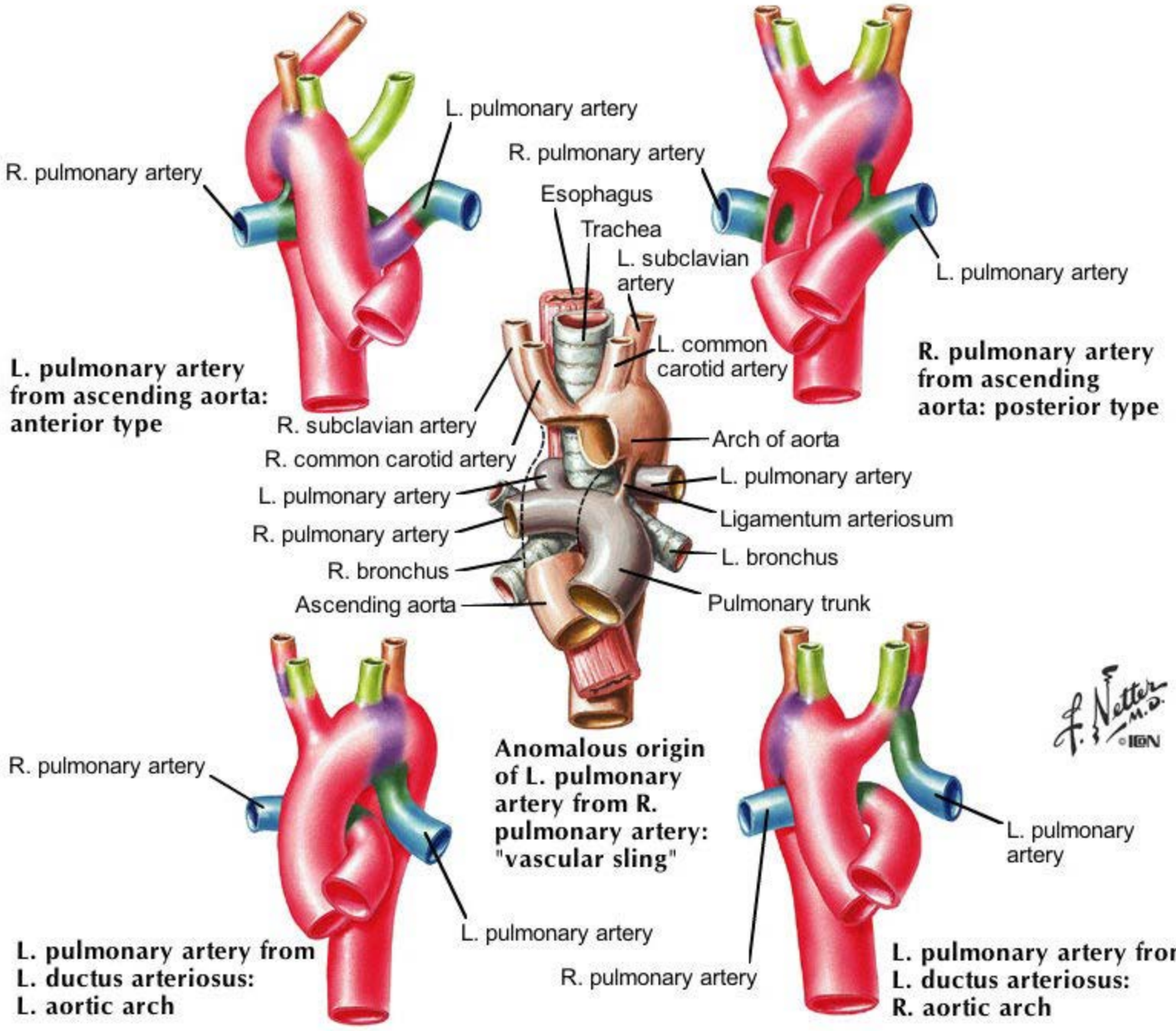
Aortic Arch Arteries



Artery Anomalies

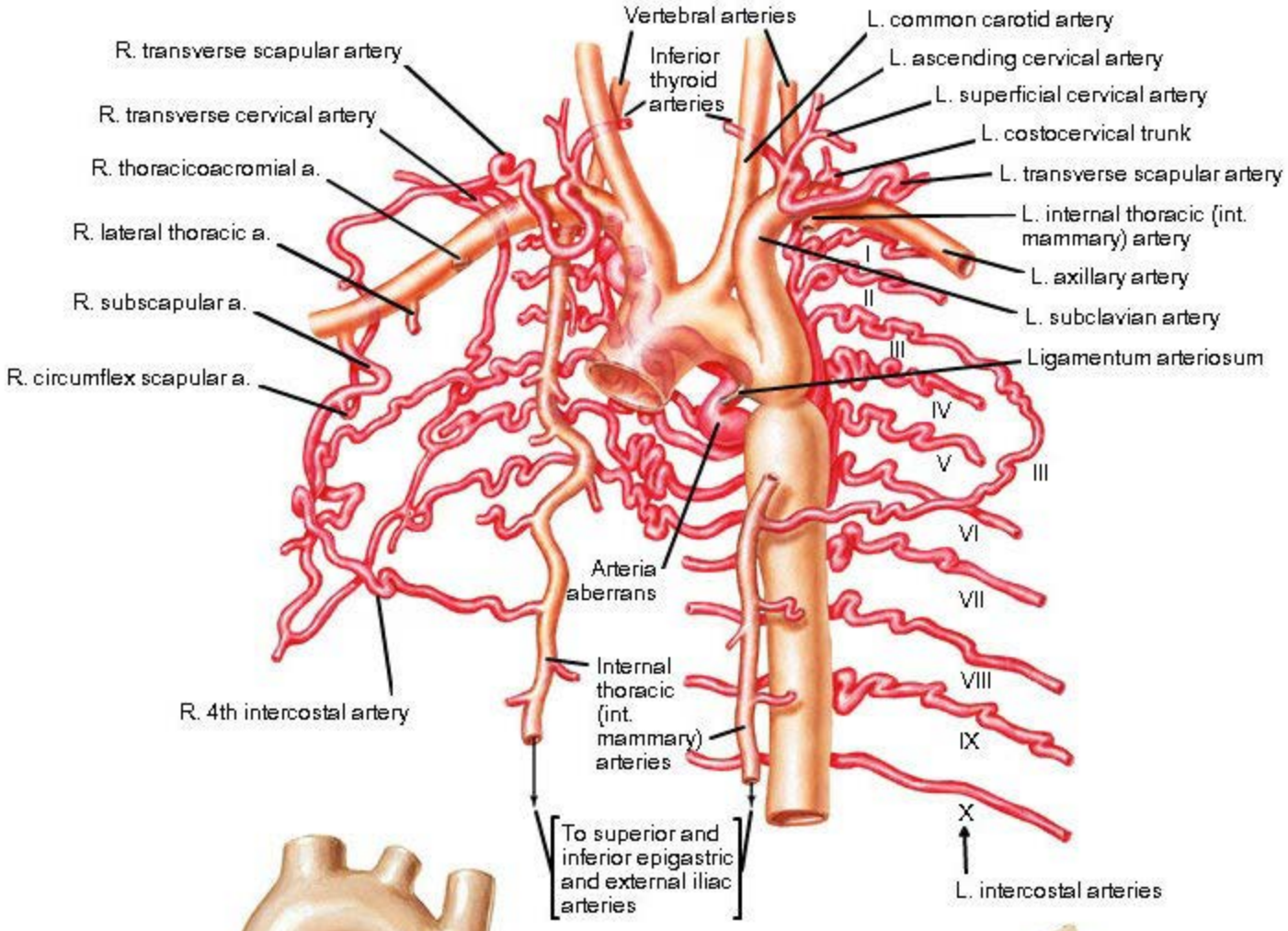


Artery Anomalies

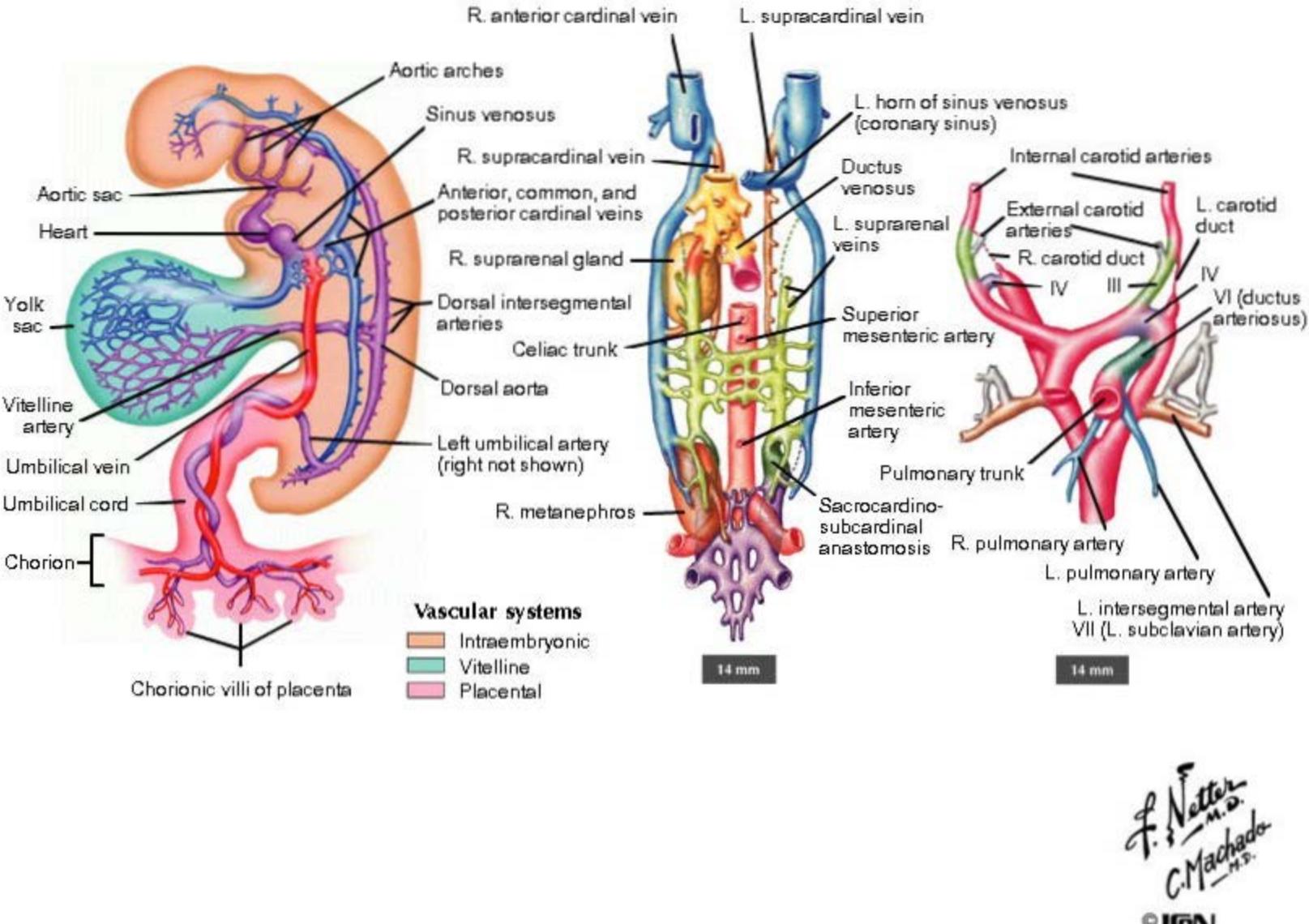


Intersegmental Arteries and Coarctation of the Aorta

Coarctation of the aorta



Summary of Embryonic Blood Vesel Derivatives



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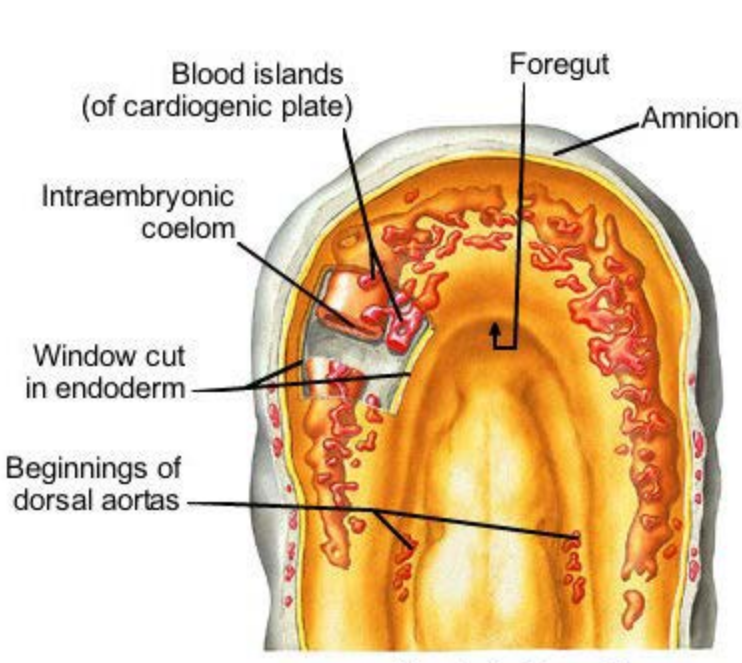
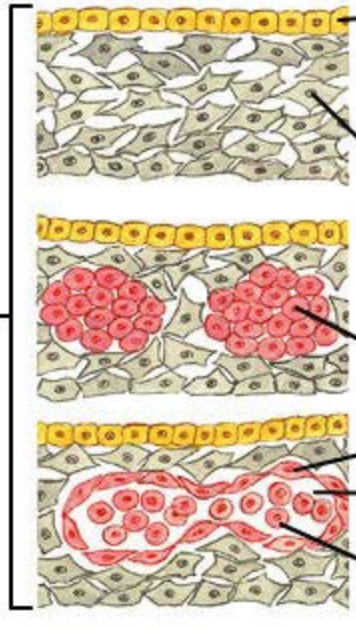
C. Machado M.D.

Formation of Blood Vessels

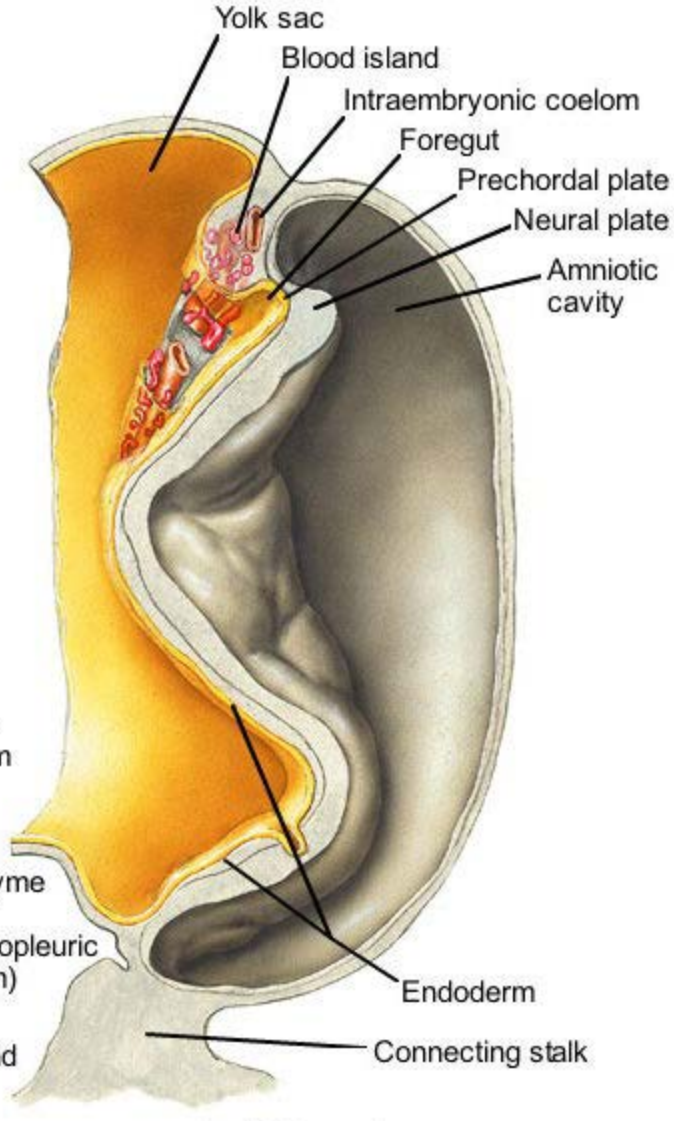
Presomite stage (1.5-mm embryo) at approximately 20 days



Ventral dissection



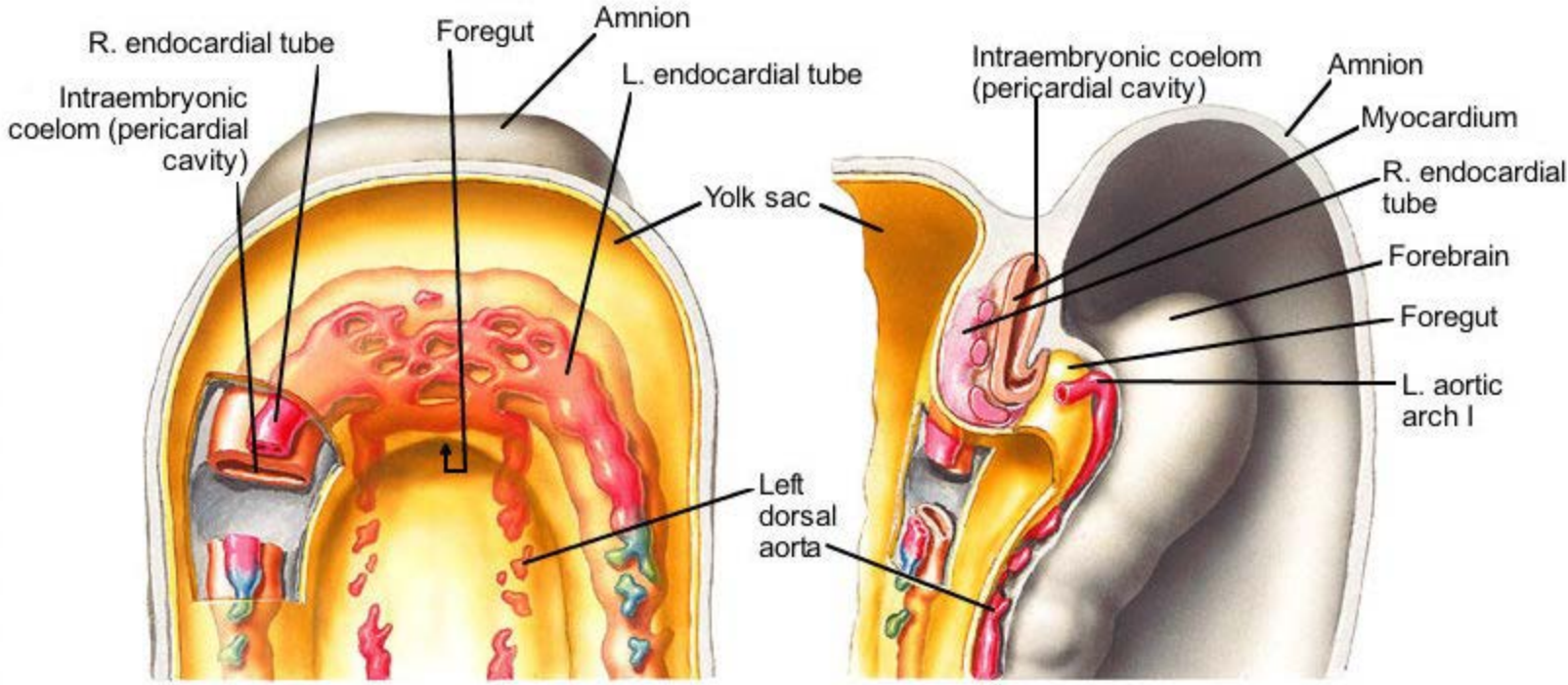
Progressive stages in blood vessel formation



Sagittal dissection (paramedian)

Formation of the Heart Tube

One-somite stage (1.5 mm) at approximately 20 days

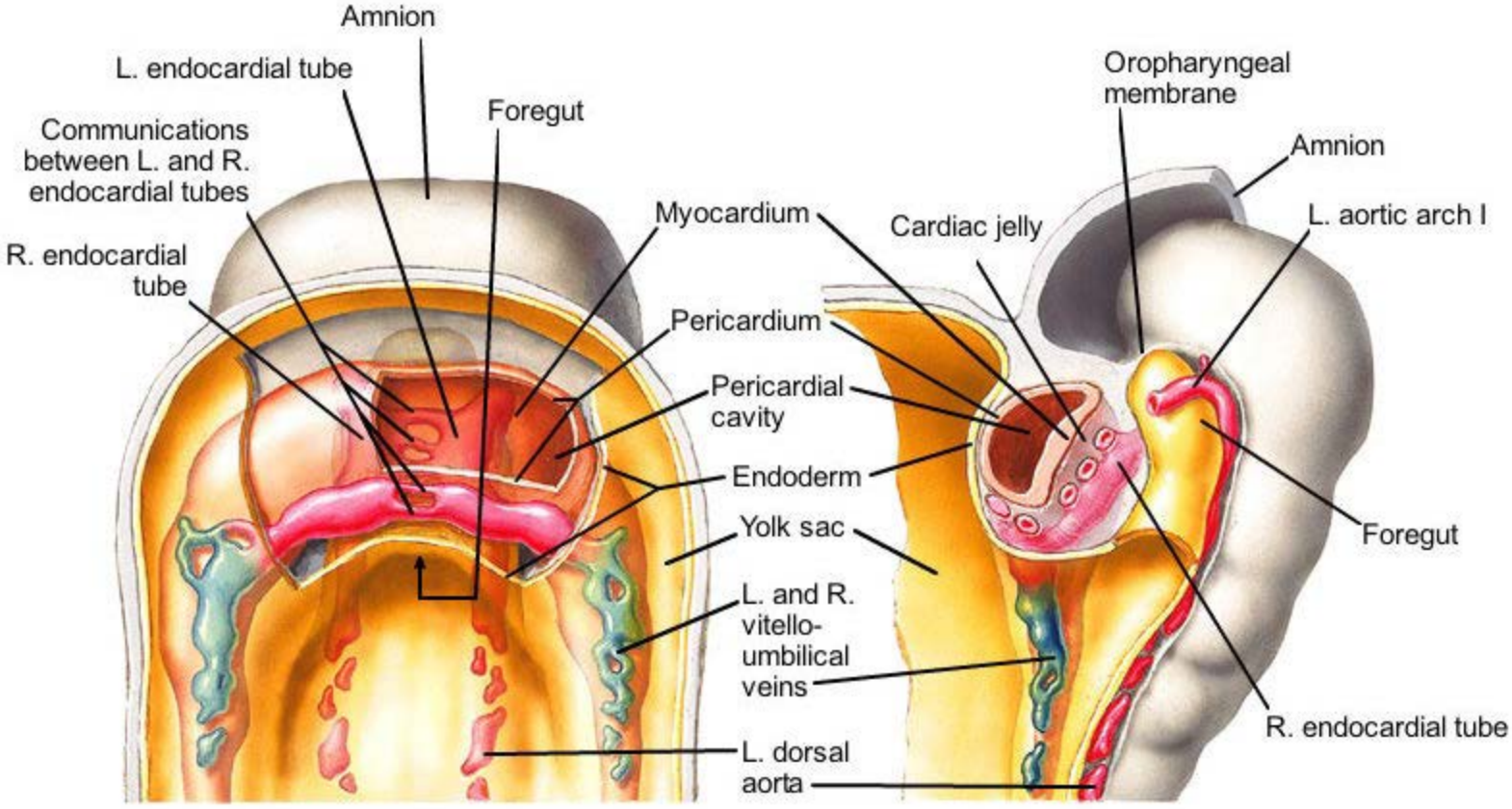


Ventral dissection

Sagittal dissection

Formation of the Heart Tube

Two-somite stage (1.8 mm) at approximately 21 days



Ventral dissection **Sagittal dissection**

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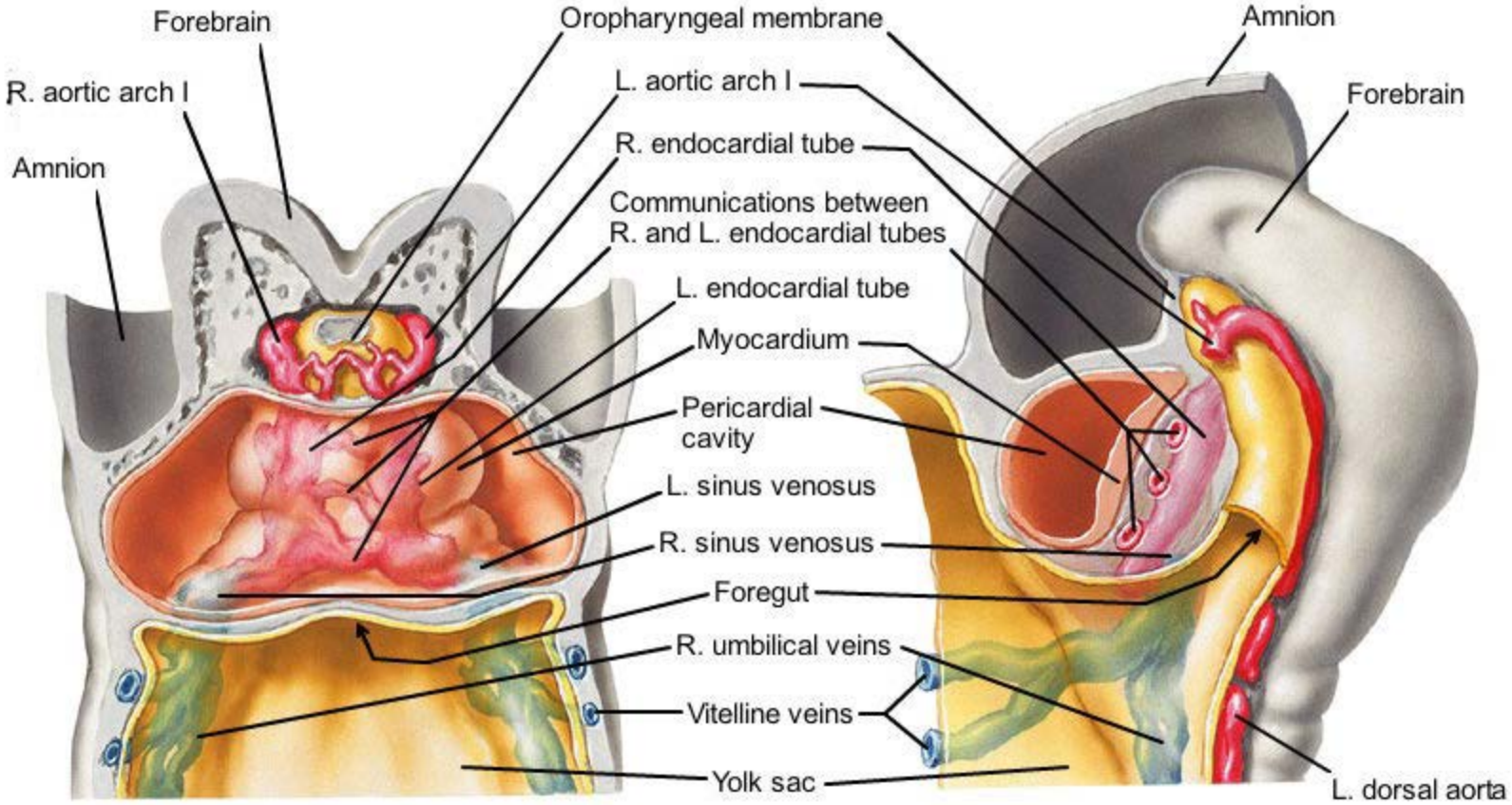
Formation of the Heart Tube

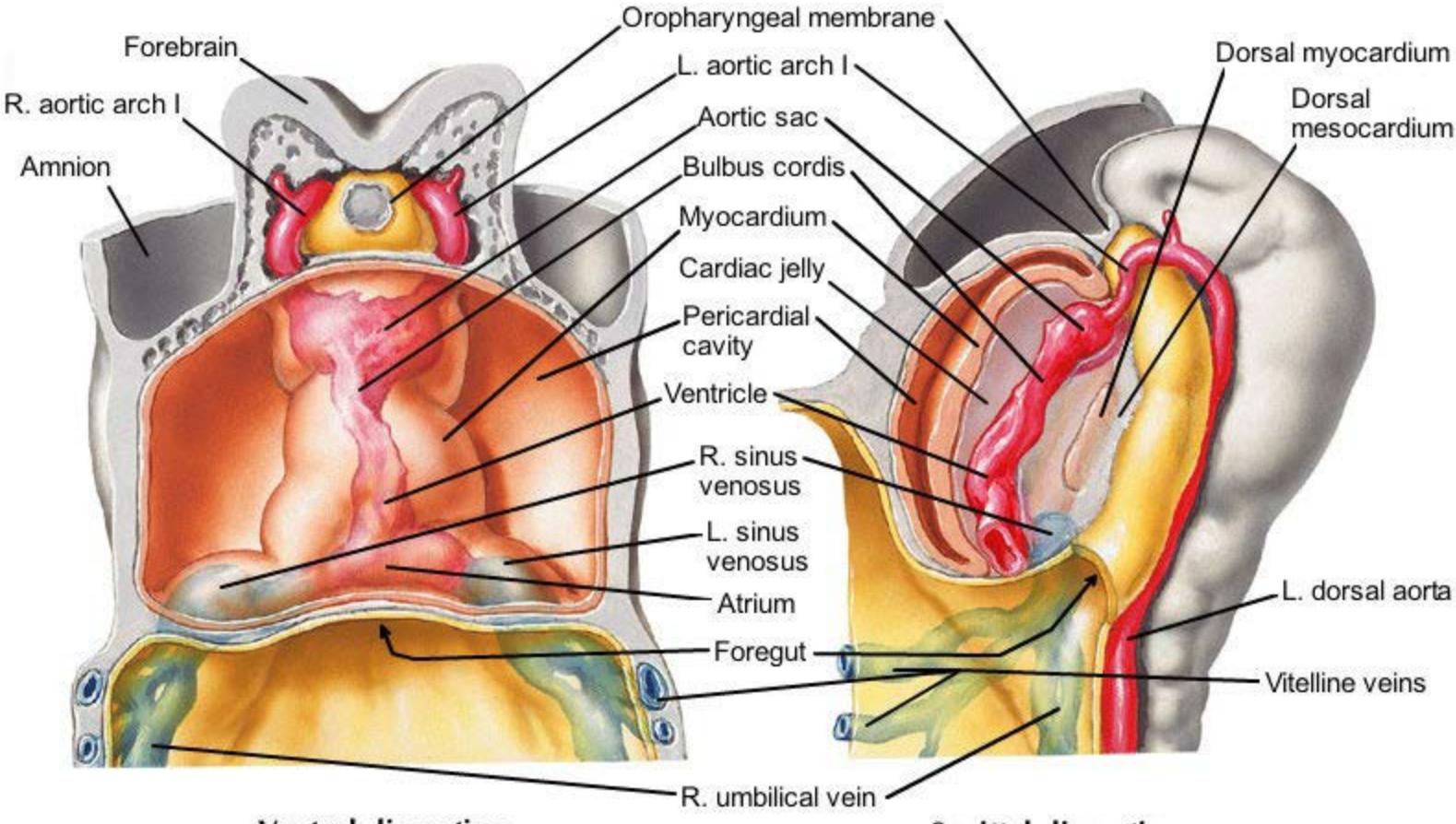
Four-somite stage (2.0 mm) at approximately 22 days



Ventral dissection **Sagittal dissection**

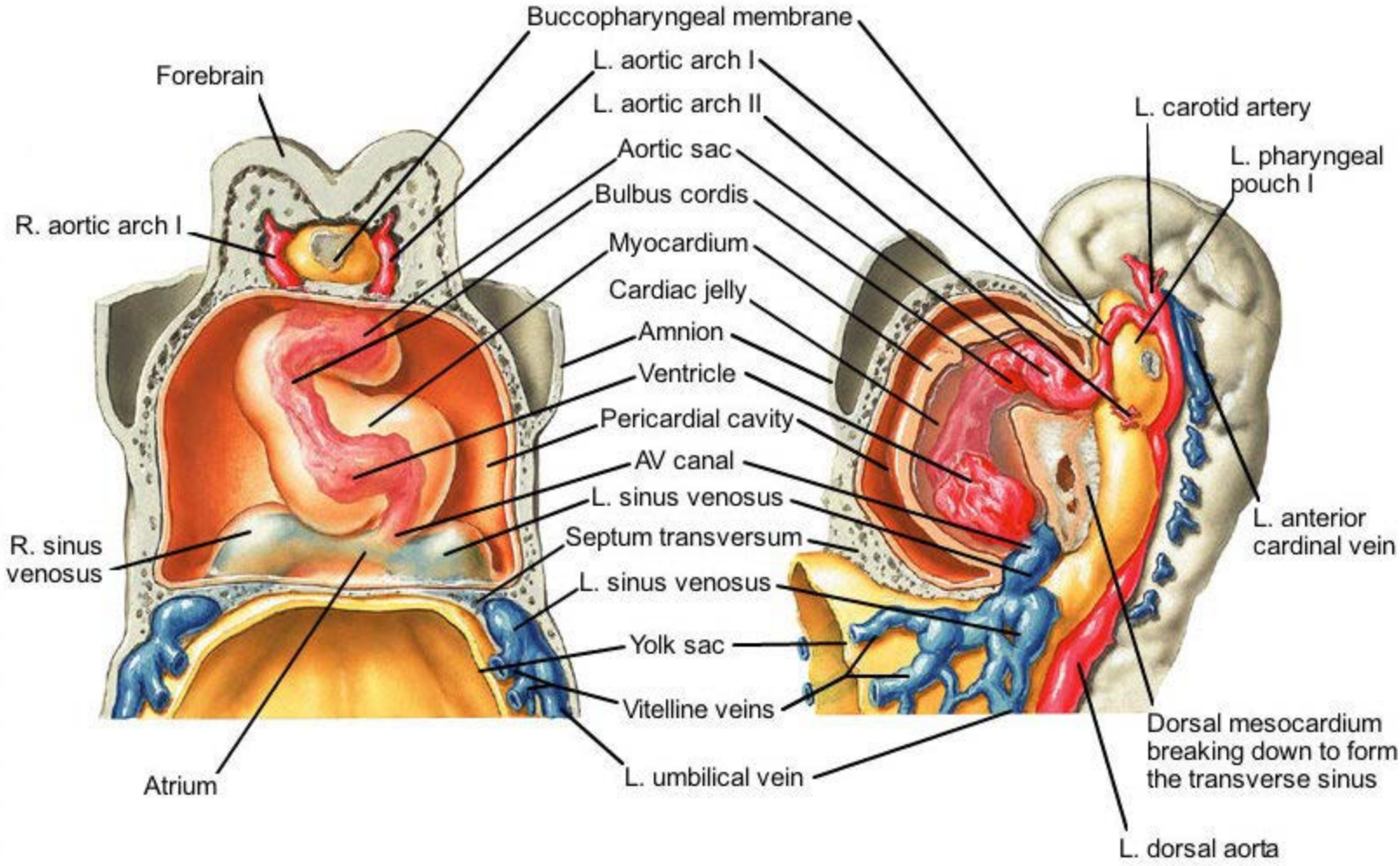
Formation of the Heart Tube

Seven-somite stage (2.2 mm) at approximately 23 days



Chambers of the Heart Tube

Ten-somite stage (2.5 mm) at approximately 23 days



Ventral dissection

Sagittal dissection

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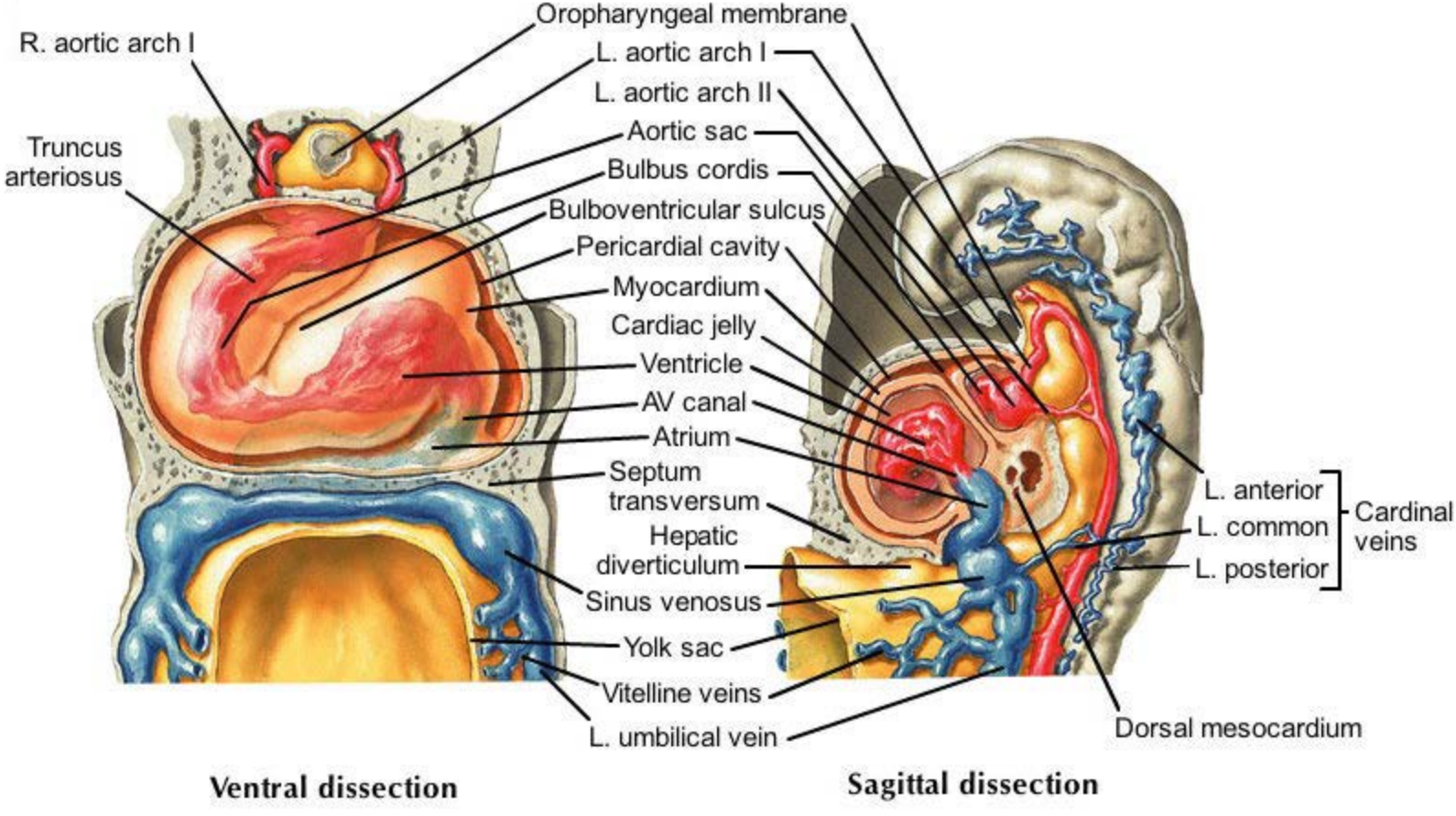
Chambers of the Heart Tube

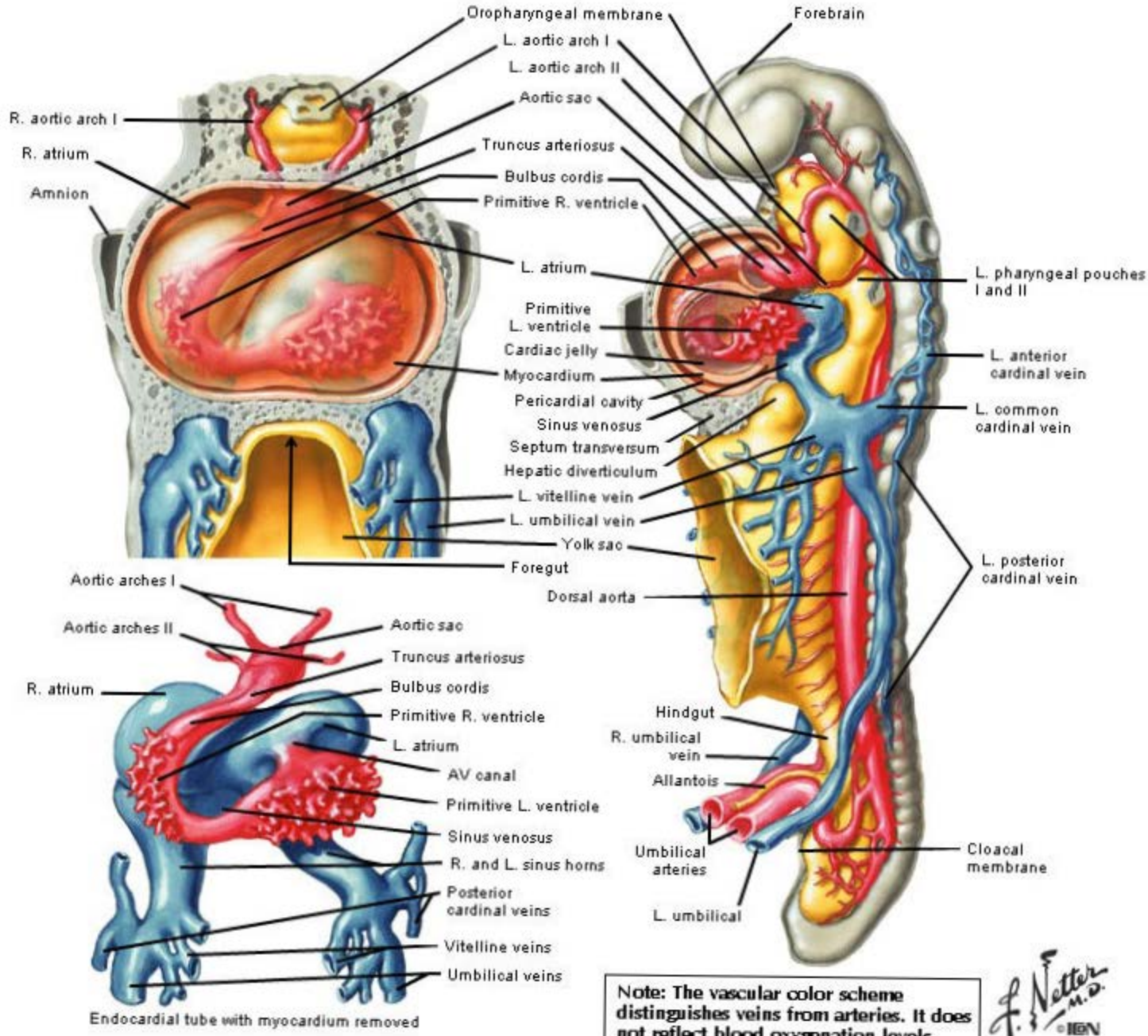
Fourteen-somite stage (3.0 mm) at approximately 24 days



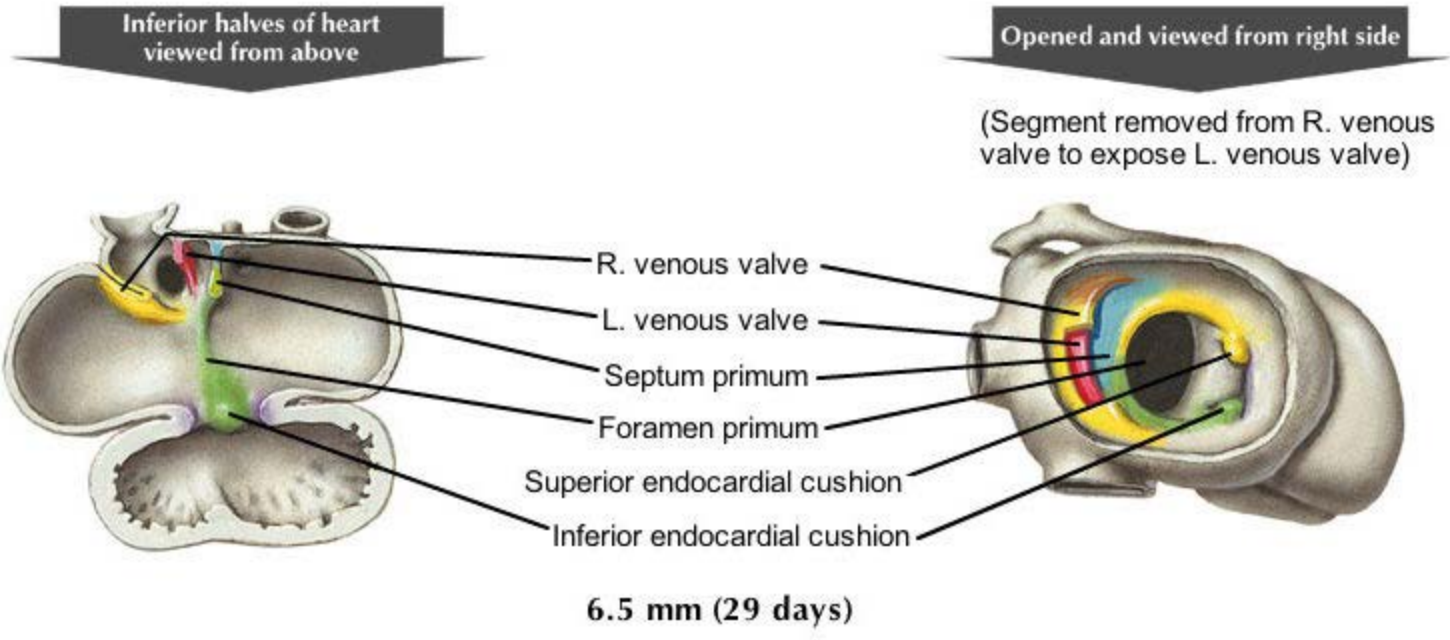
Ventral dissection **Sagittal dissection**

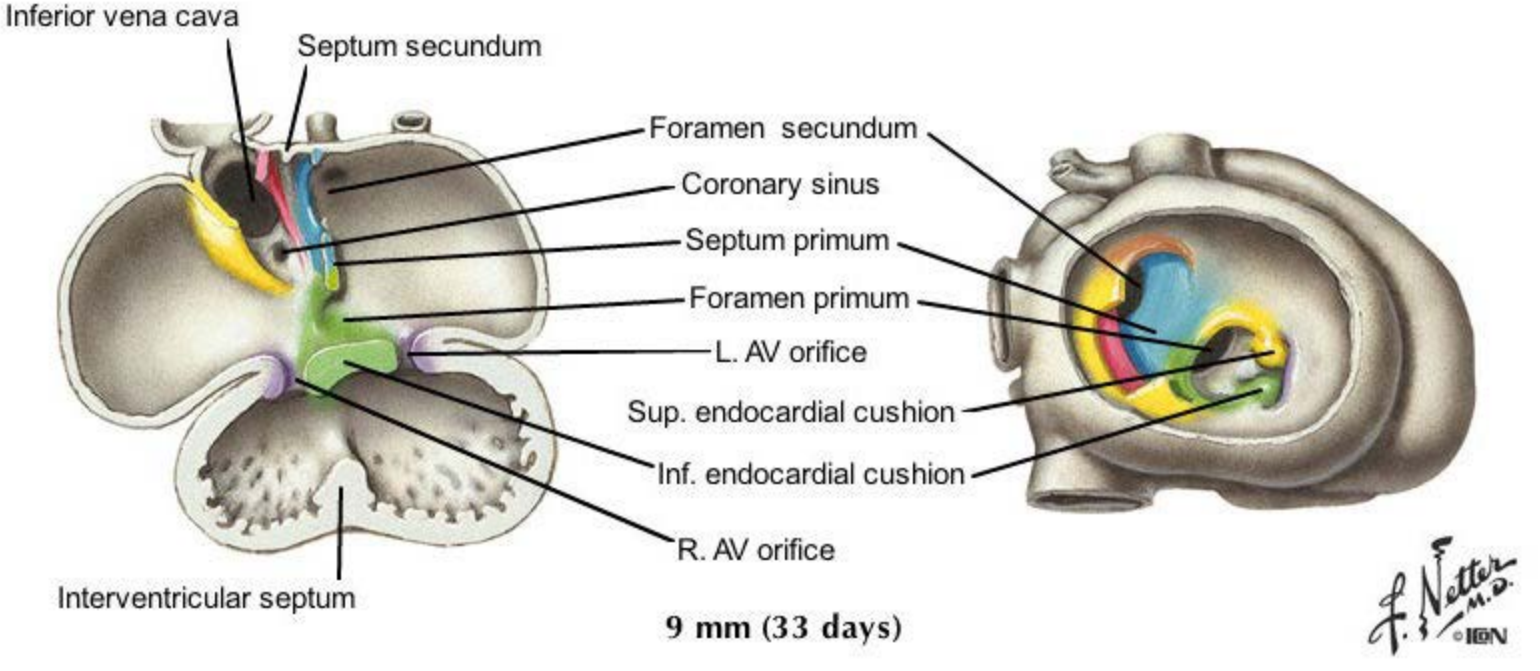
Bending of the Heart Tube

Twenty-somite stage (3.2 mm) at approximately 25 days

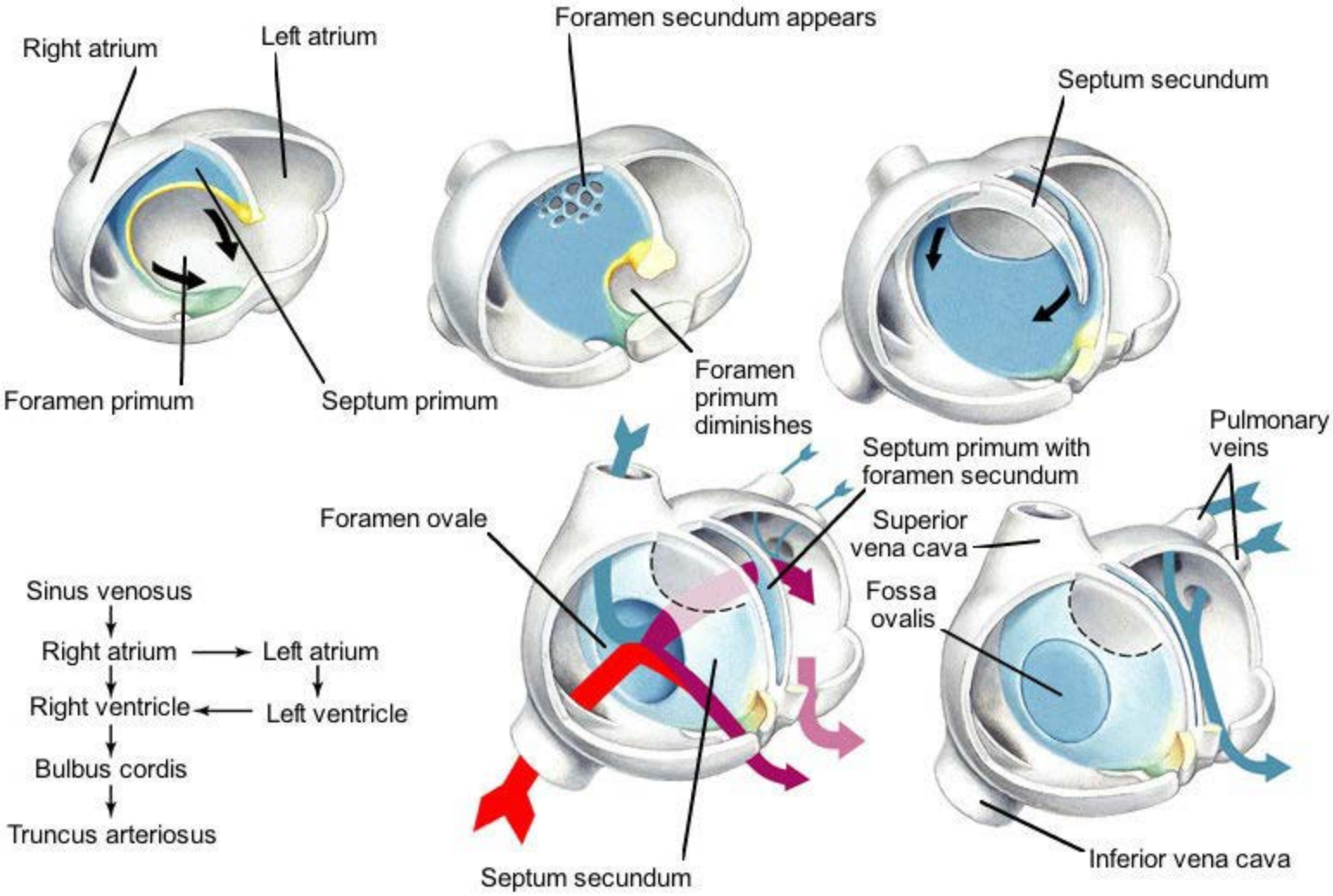


Partitioning the Heart Tube

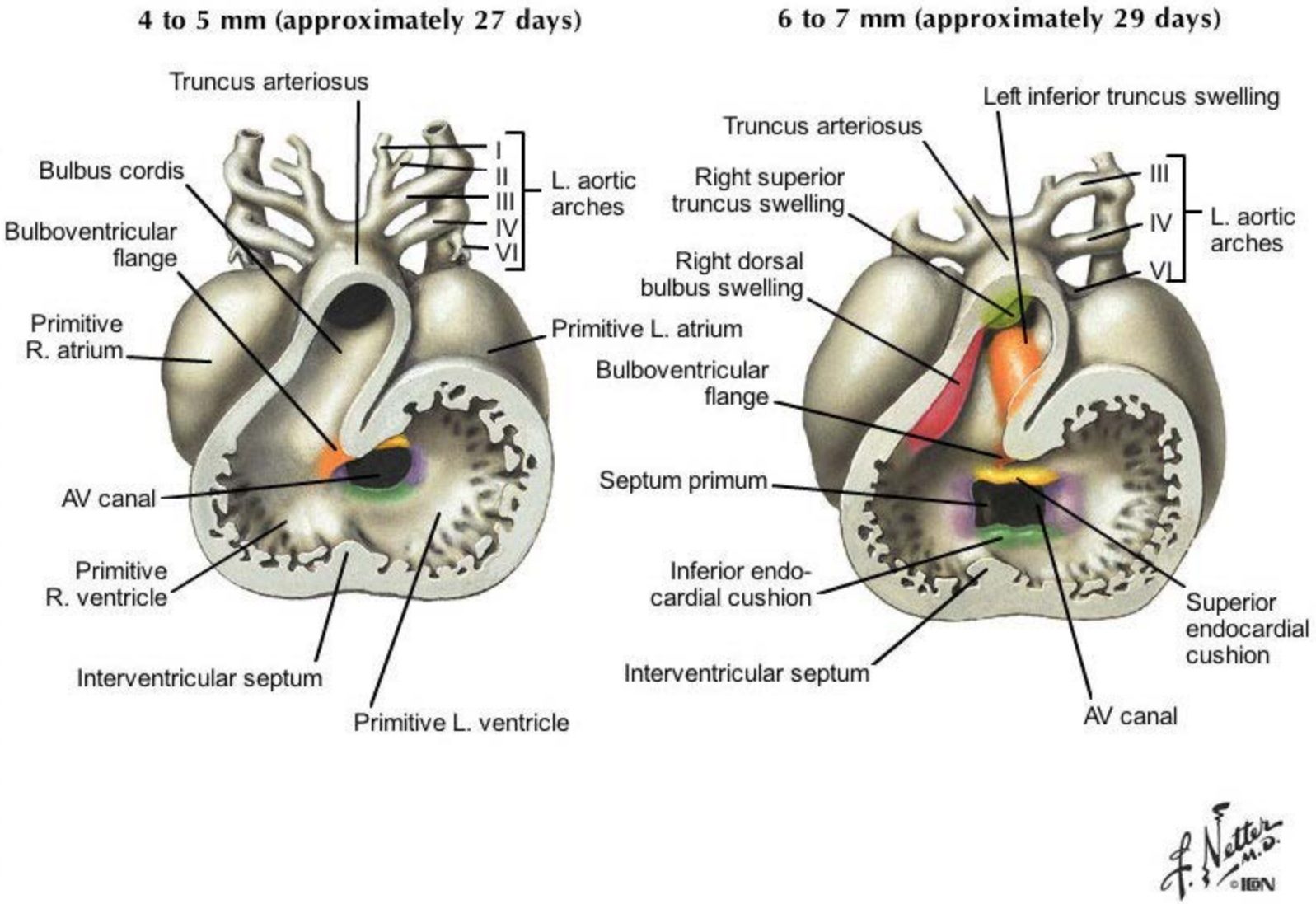




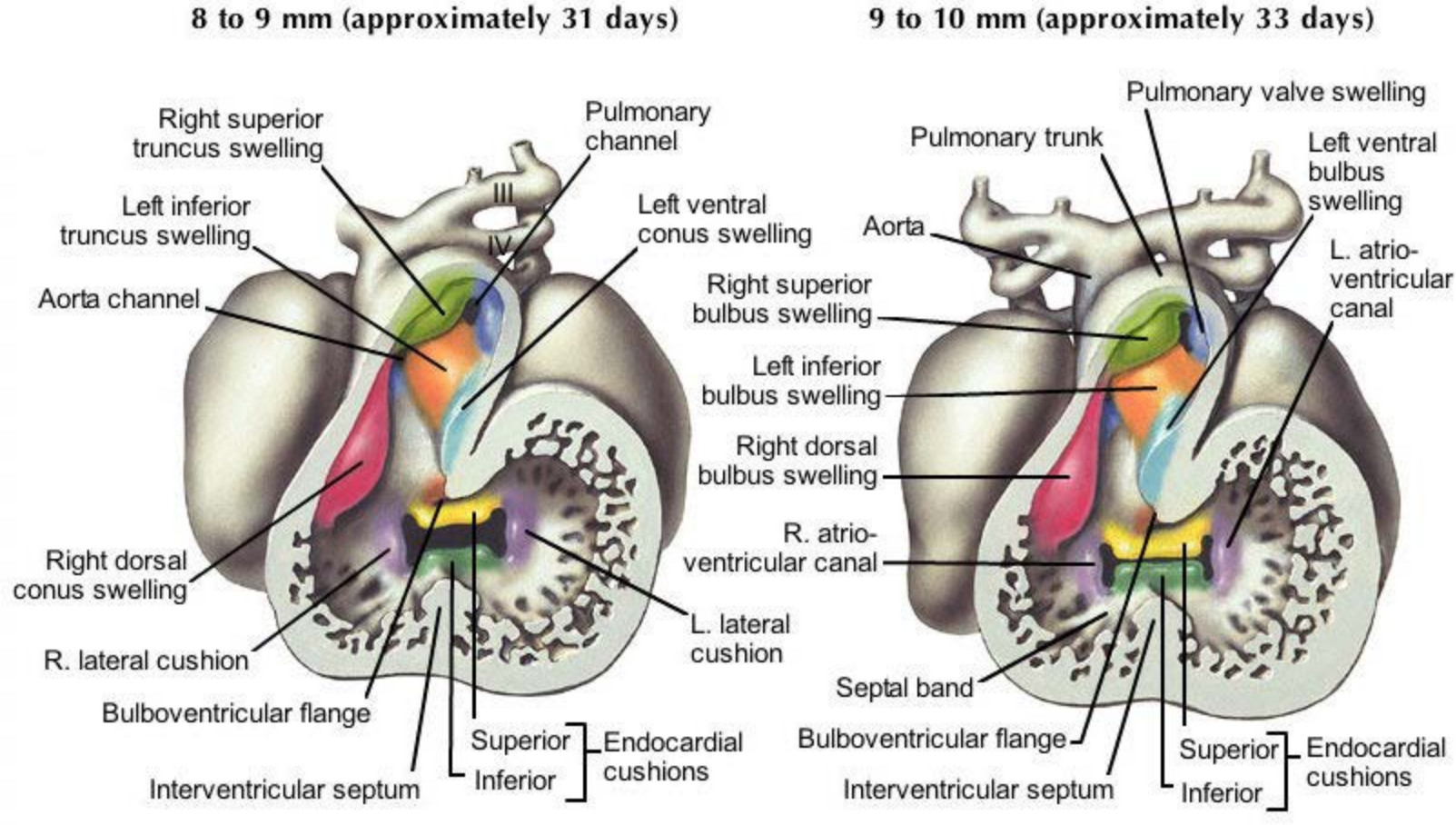
Atrial Separation



Spiral (Aorticopulmonary) Septum

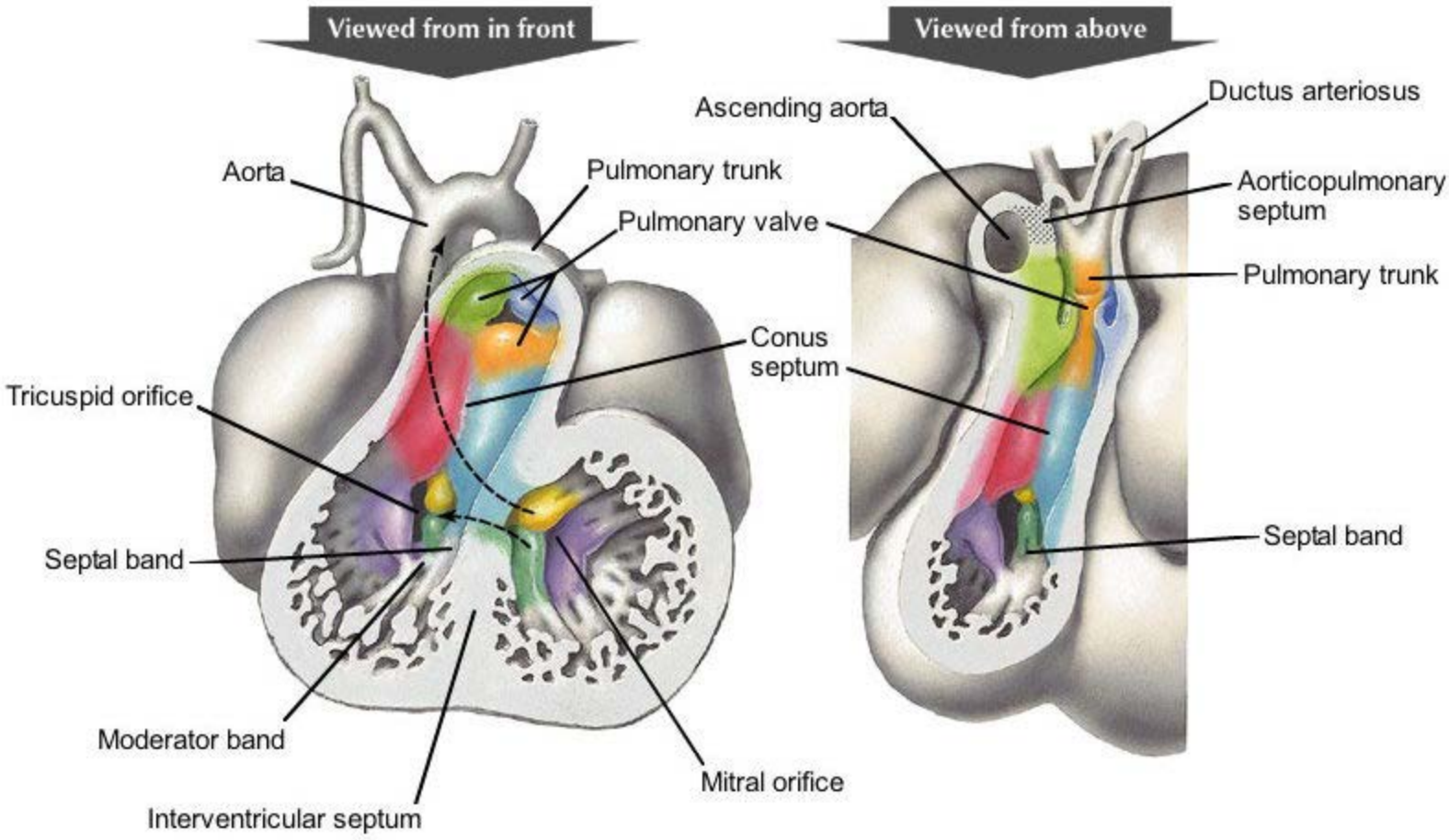


Spiral (Aorticopulmonary) Septum



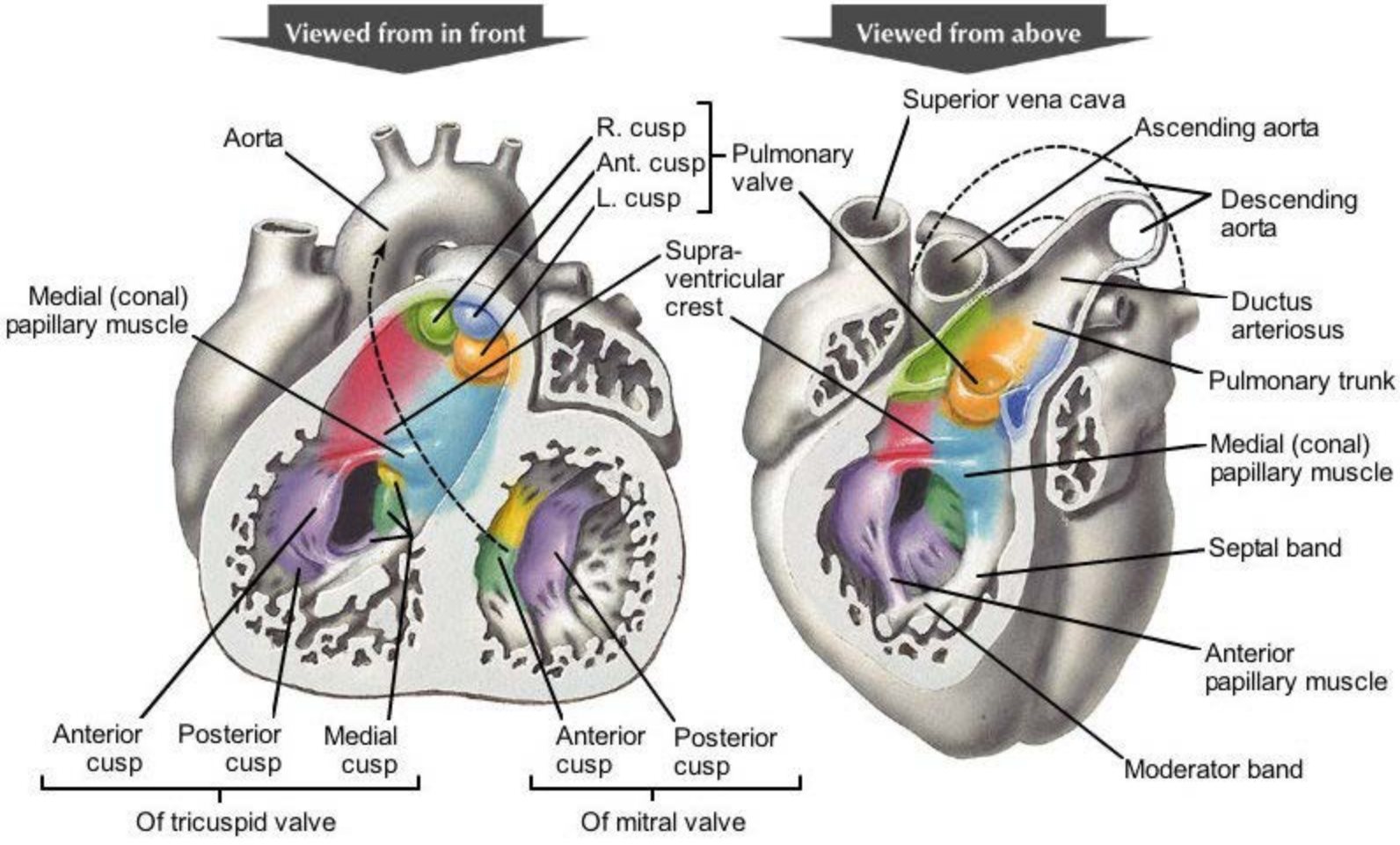
Completion of the Spiral (Aorticopulmonary) Septum

16 mm (approximately 37 days)

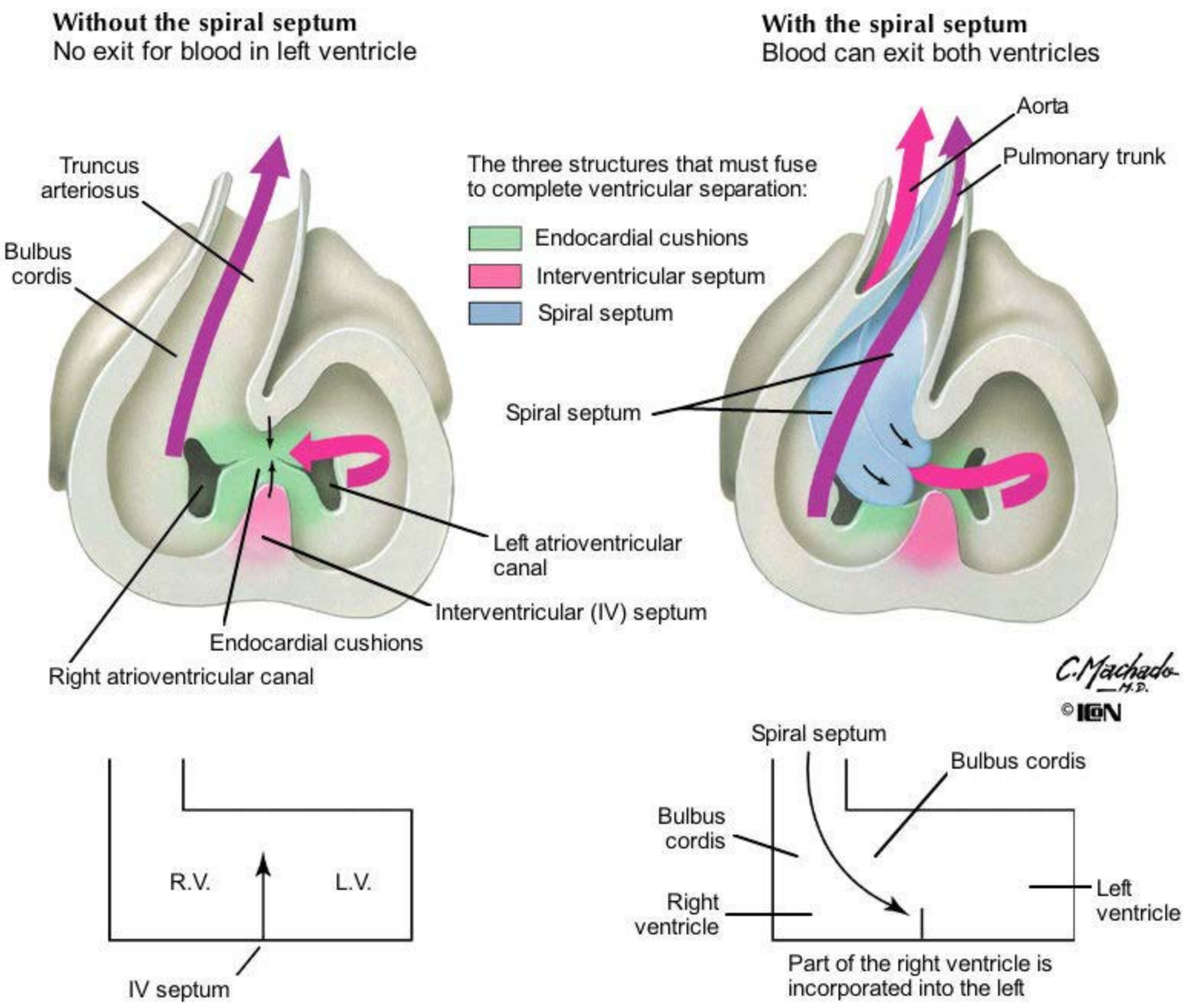


Completion of the Spiral (Aorticopulmonary) Septum

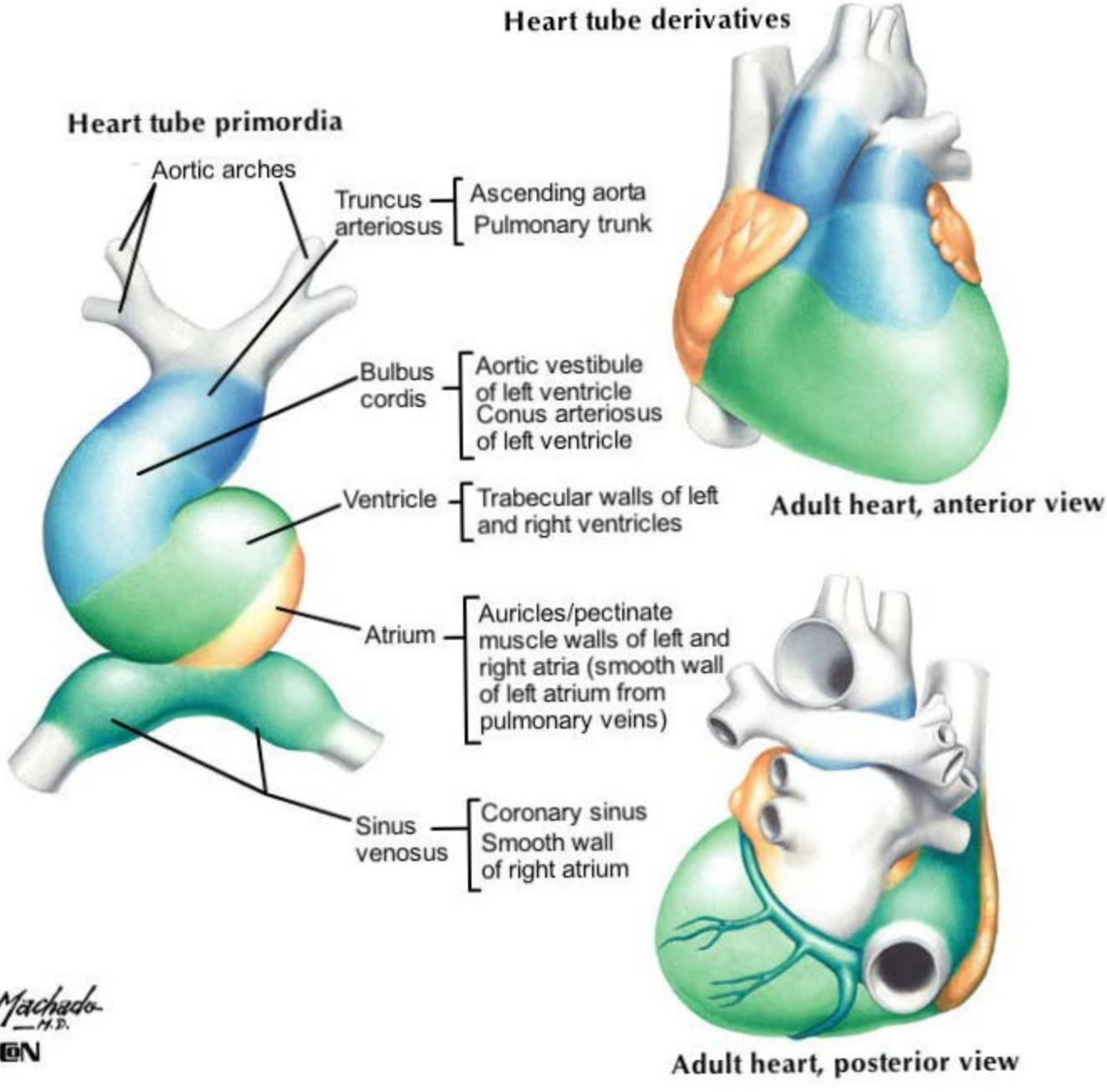
40 mm (approximately 55 days)



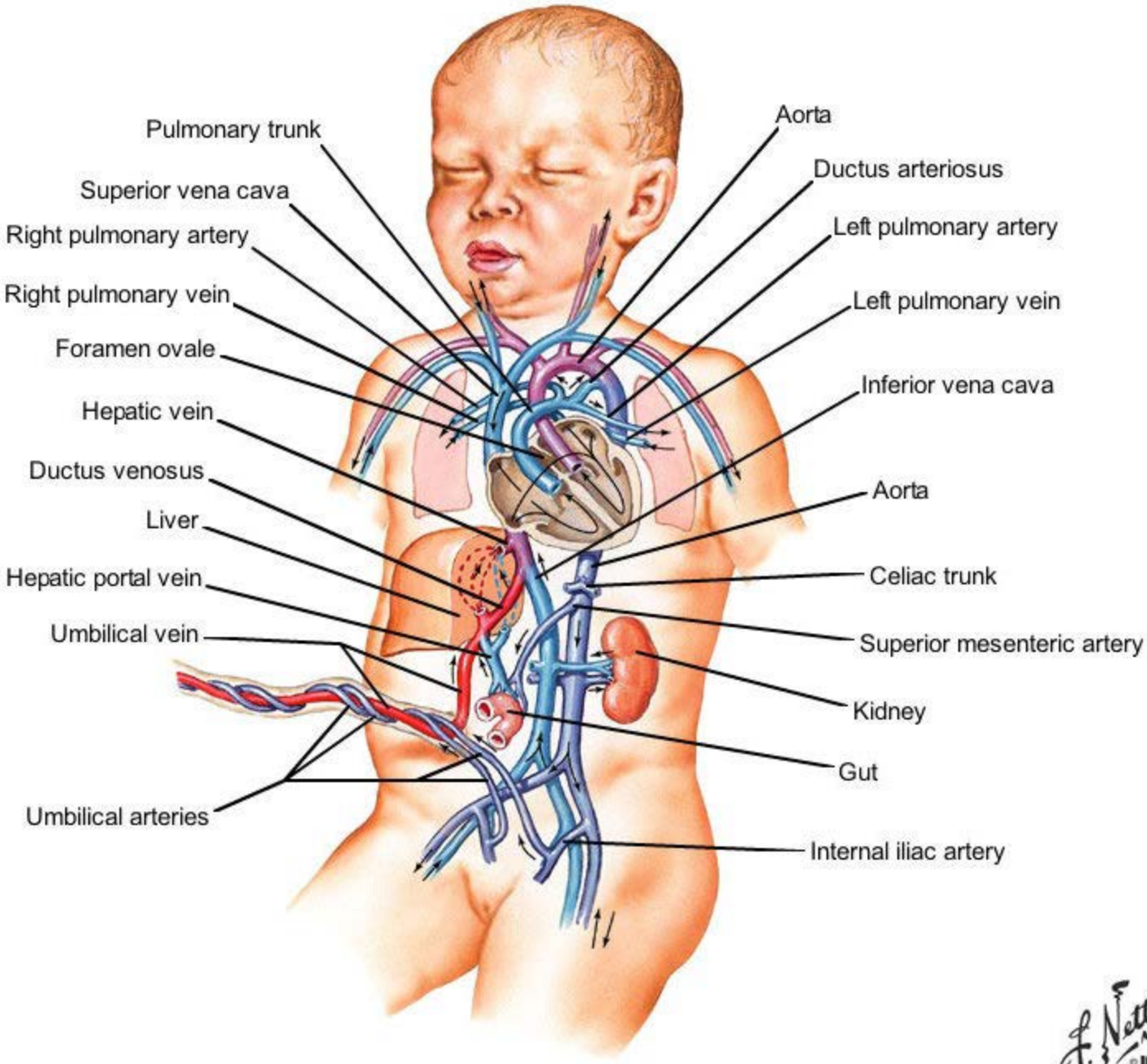
Ventricular Separtion and Bulbus Cordis



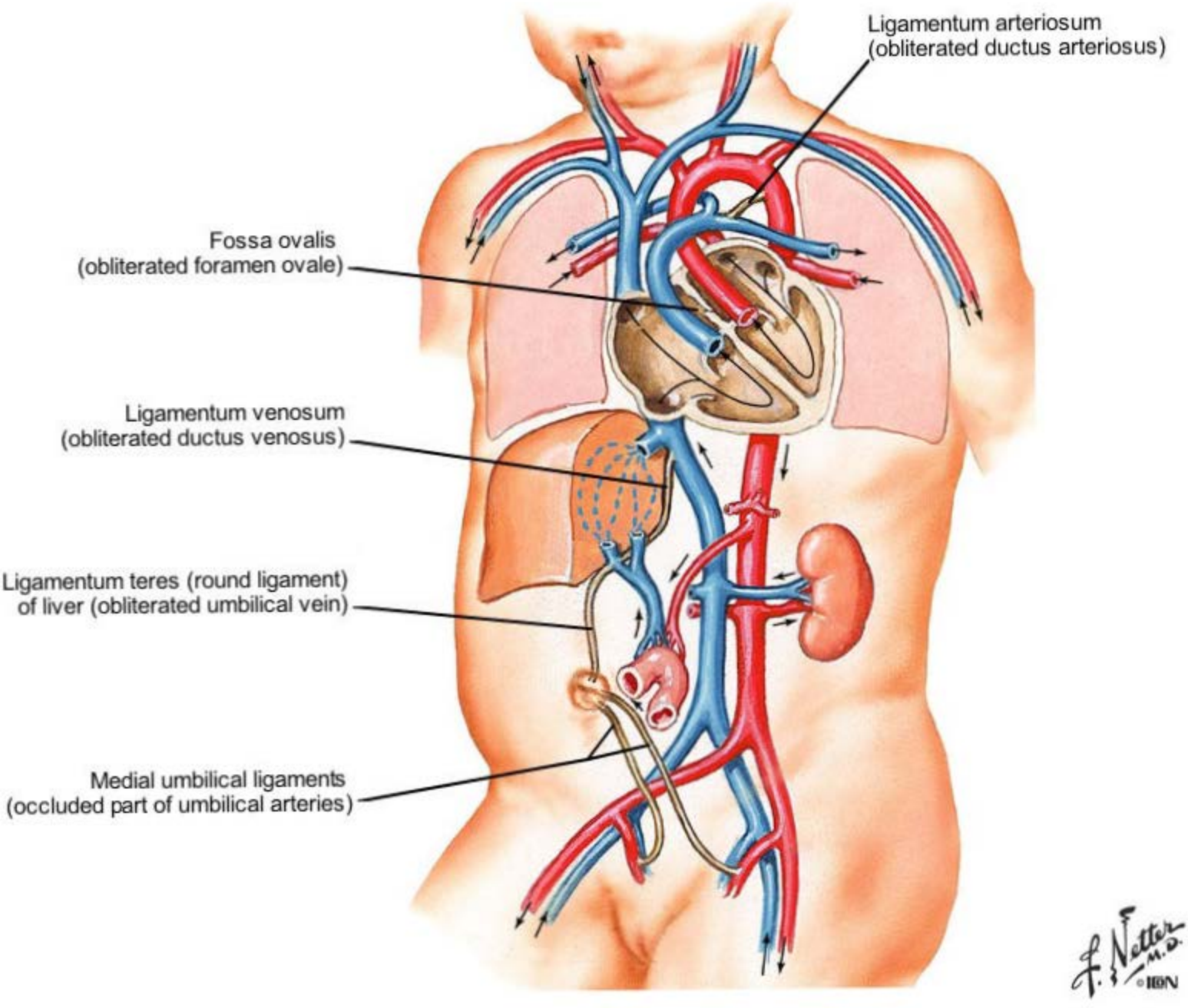
Adult Derivatives of the Heart Tube Chambers



Fetal Circulation



Transition to Postnatal Circulation



Congenital Heart Defect Concepts

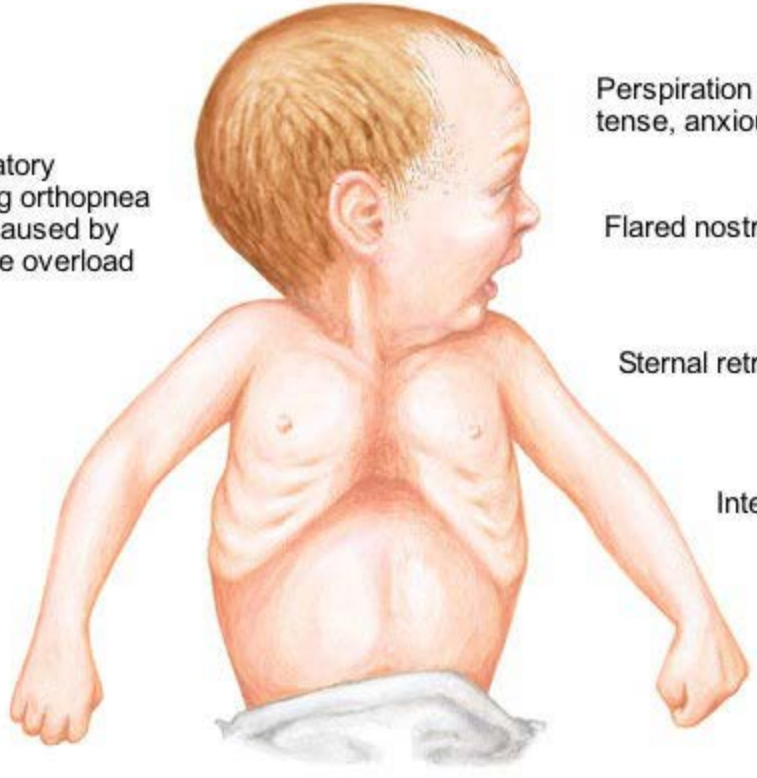
Clinical characteristics of too little pulmonary flow

Cyanosis

Clubbing of fingers

Clinical characteristics of too much pulmonary flow (pulmonary volume overload)

Infant with respiratory distress (including orthopnea and tachypnea) caused by pulmonary volume overload



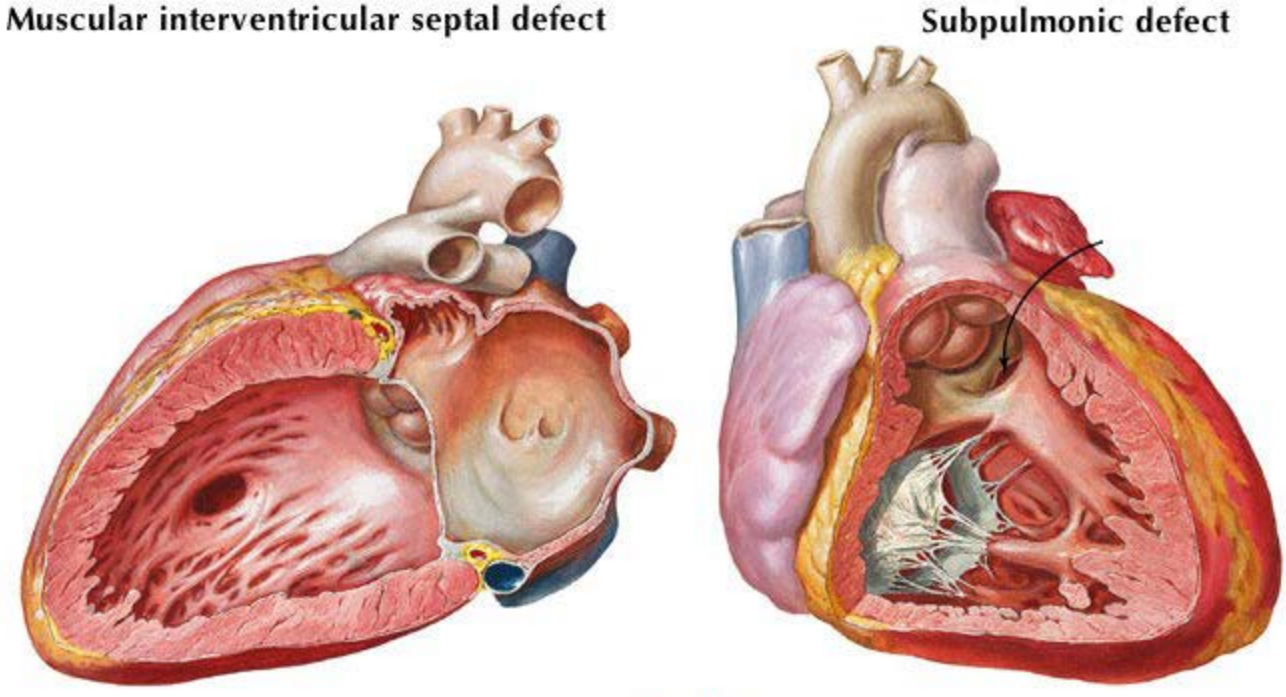
Perspiration and tense, anxious facies

Flared nostrils

Sternal retraction

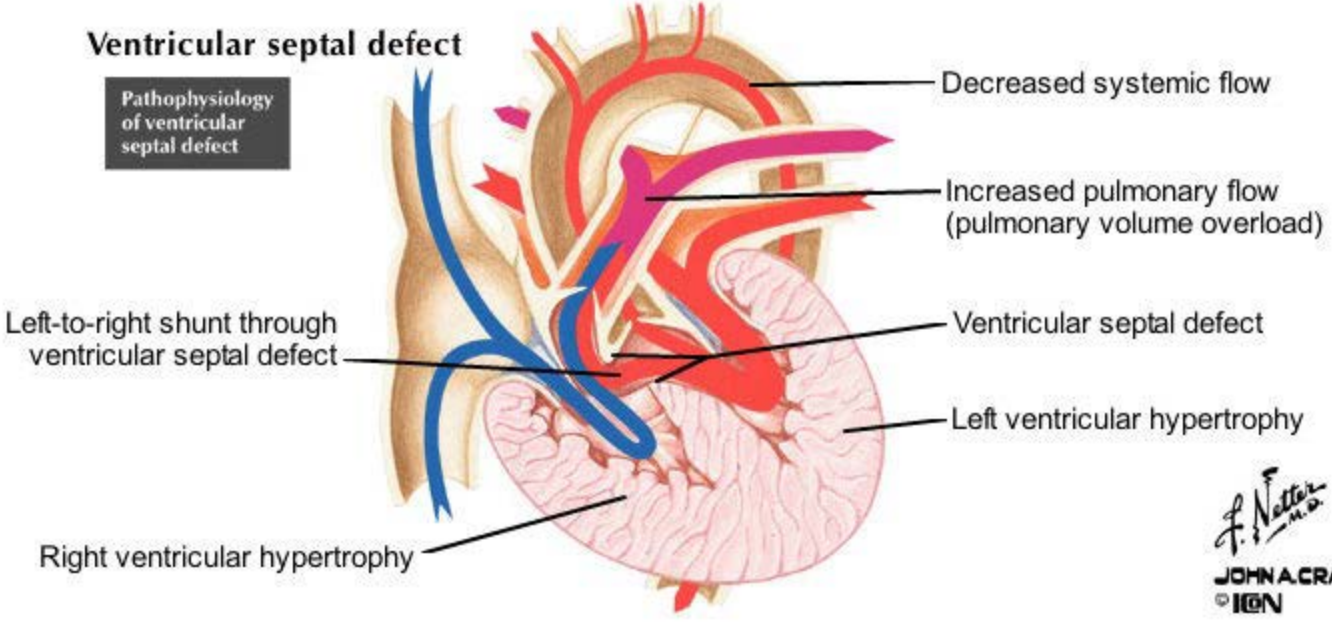
Intercostal retractions

Ventricular Septal Defects



Ventricular septal defect

Pathophysiology of ventricular septal defect



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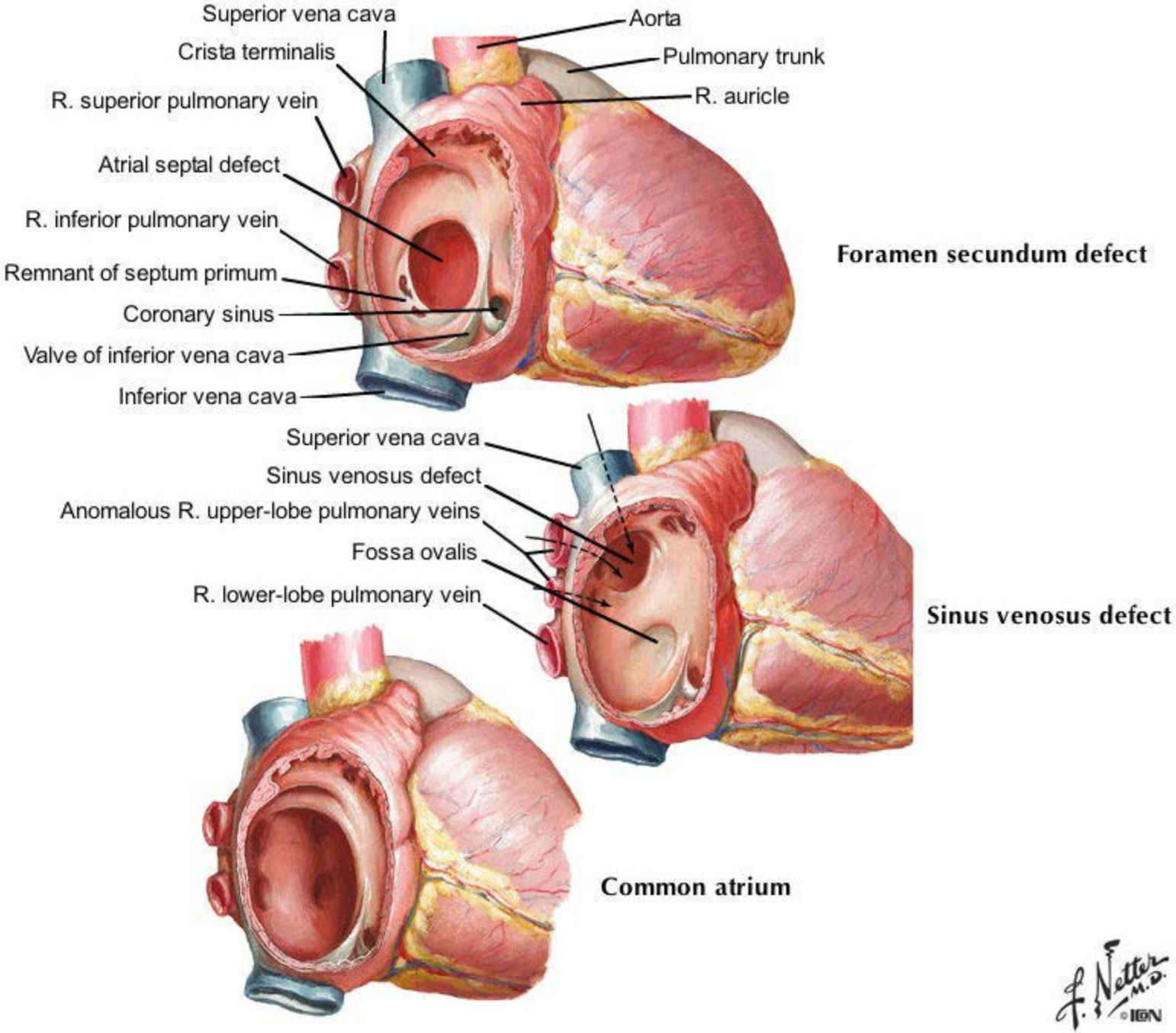
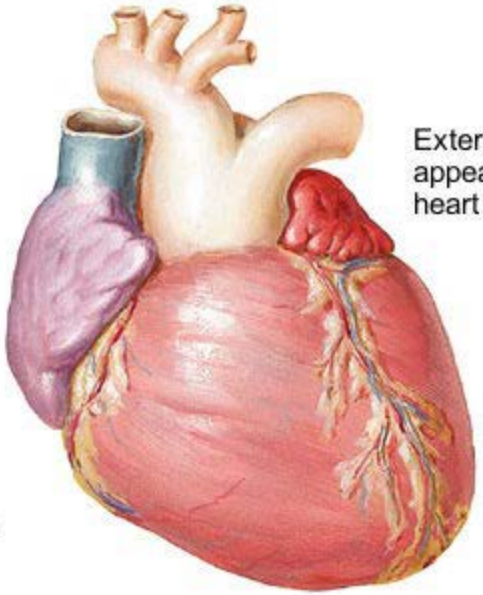
Atrial Septal Defects



Spiral Septum Defects

Persistent truncus arteriosus



External appearance of heart

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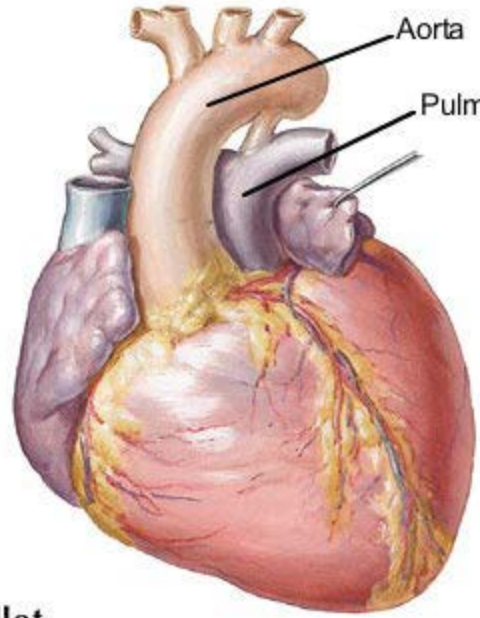
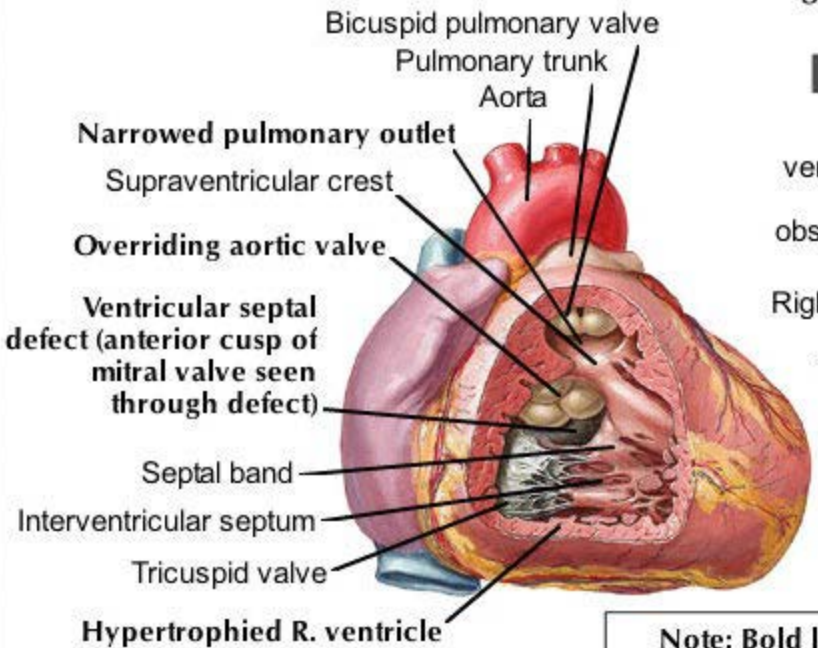
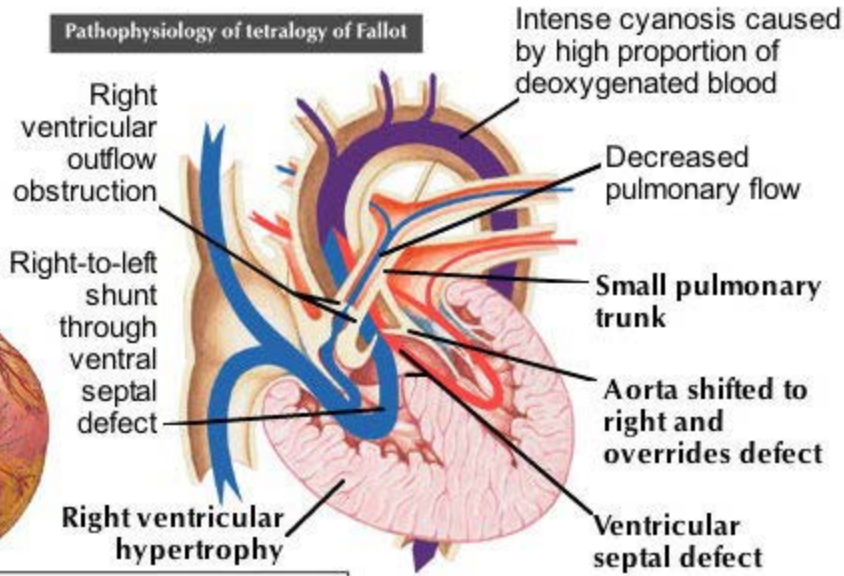
Transposition of great vessels



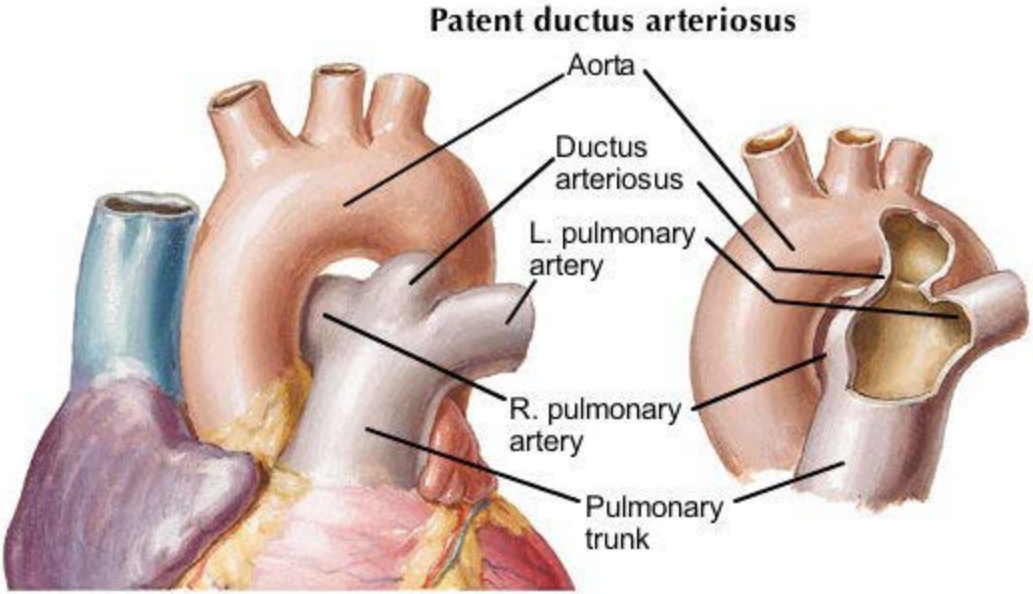
Tetralogy of Fallot





Note: Bold labels indicate the four primary defects

Patent Ductus Arteriosus



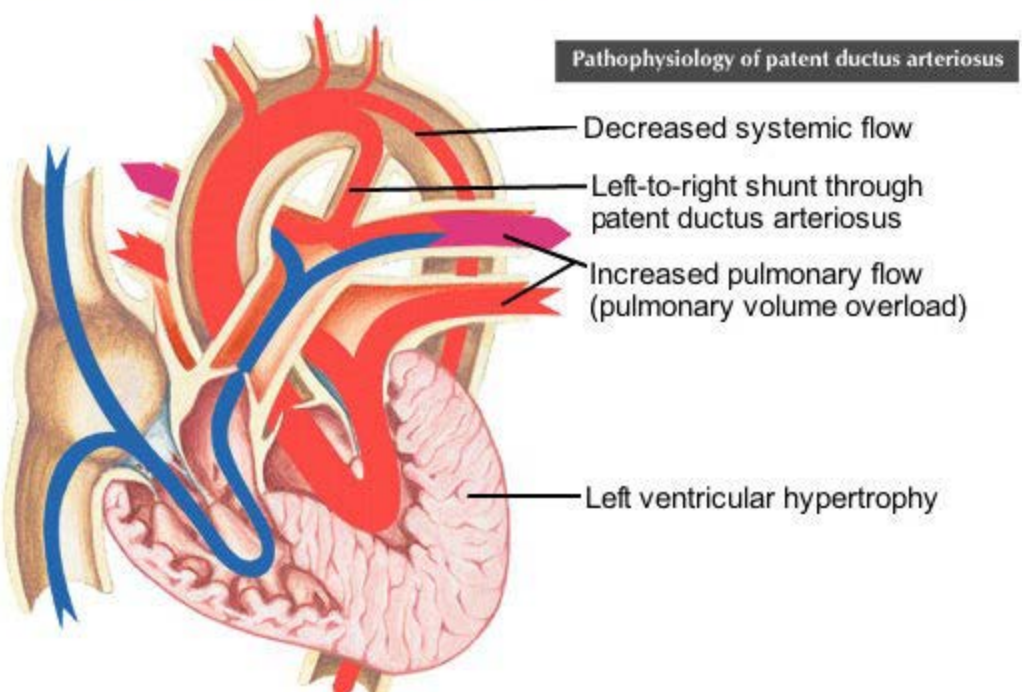


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Chart 4.1 Embryonic Blood Vessel Derivatives

CHART 4.1 EMBRYONIC BLOOD VESSEL DERIVATIVES

Embryonic Vessels	Major Derivatives
Aortic arch artery 1	Part of maxillary arteries
Aortic arch artery 3	Common and internal carotid arteries
Aortic arch artery 4	Right subclavian artery; part of aortic arch
Aortic arch artery 6	Ductus arteriosus; proximal pulmonary arteries
Intersegmental arteries	Intercostal arteries Lumbar arteries Common iliac arteries Parts of vertebral, subclavian, and lateral sacral arteries
Umbilical arteries	Medial umbilical ligaments on the internal aspect of the abdominal wall
Umbilical vein	Round ligament of the liver (ligamentum teres)
Vitelline arteries	Celiac trunk Superior mesenteric artery Inferior mesenteric artery
Vitelline veins	Hepatic portal system Hepatic veins Intrahepatic segment of the inferior vena cava
Anterior cardinal veins	Superior vena cava Brachiocephalic (innominate) veins Internal jugular veins
Subcardinal veins (and anastomoses between the systems)	Lower inferior vena cava Renal and suprarenal veins Gonadal veins
Supracardinal veins	Azygous system of veins Segment of the inferior vena cava between the kidneys and liver

THE RESPIRATORY SYSTEM
TIMELINE

Prenatal Time Scale (Months)

Blastocyst

Embryo

1

4—5 weeks

Laryngotracheal diverticulum off the foregut divides into left and right bronchial/lung buds.

5—6 weeks

Cervical somite myotomes migrate into the septum transversum to form the diaphragm. The nasal placode invaginates to form the nasal sac, the anterior part of the primitive nasal cavity.

2

6—7 weeks

Tertiary (segmental) bronchi have formed.

7—8 weeks

Primary palate fuses to secondary palate.

3

8—10 weeks

Nasal septum fuses to completed secondary palate.

4

Fetus

5 months

Epithelium in distal part of the airway in the lungs is cuboidal. No gas exchange is possible in a premature infant.

5

6 months

Alveolar epithelium thins out against capillaries. Breathing is possible in a premature infant with artificial surfactant.

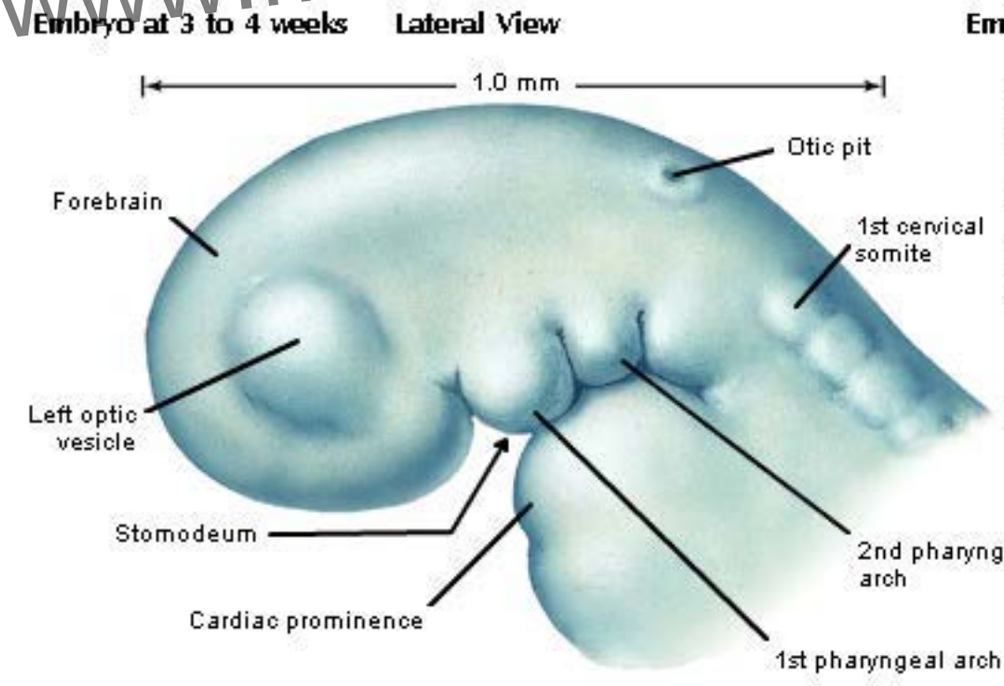
6

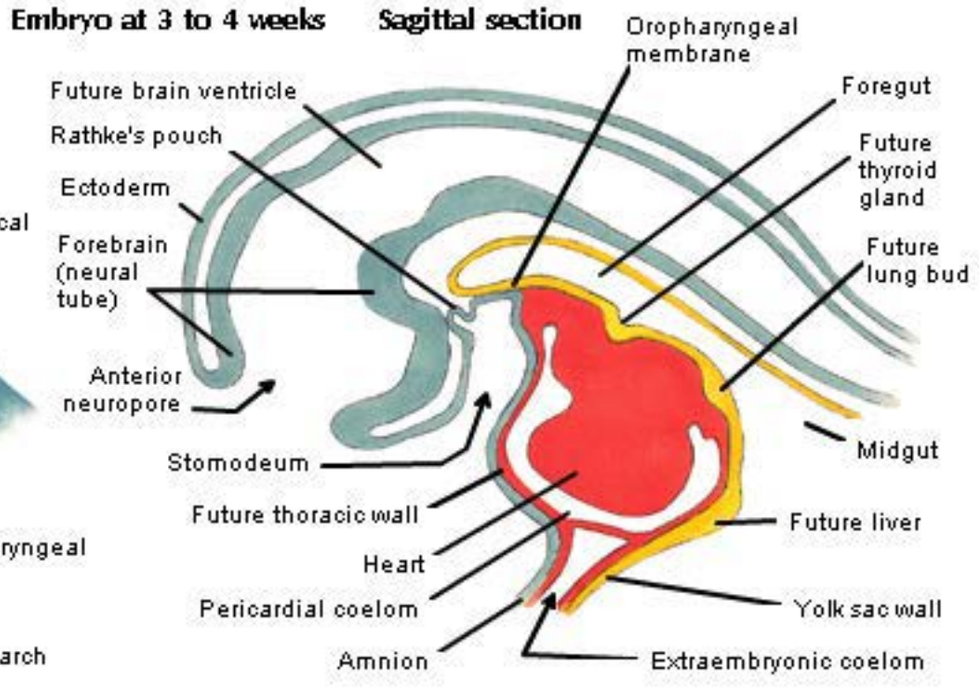
9

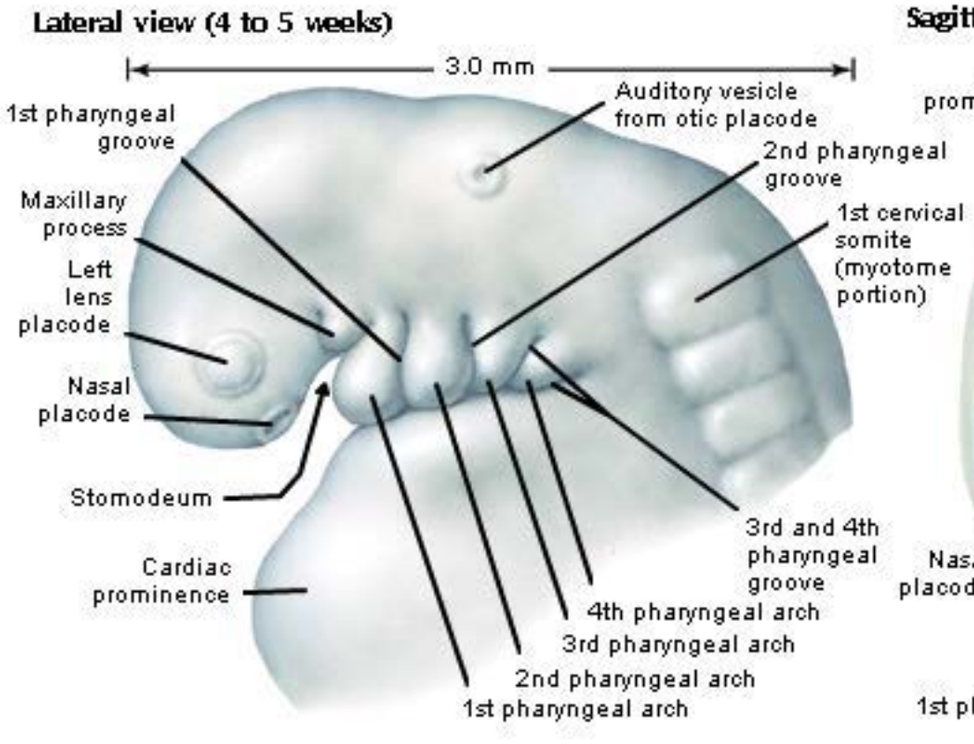
Birth

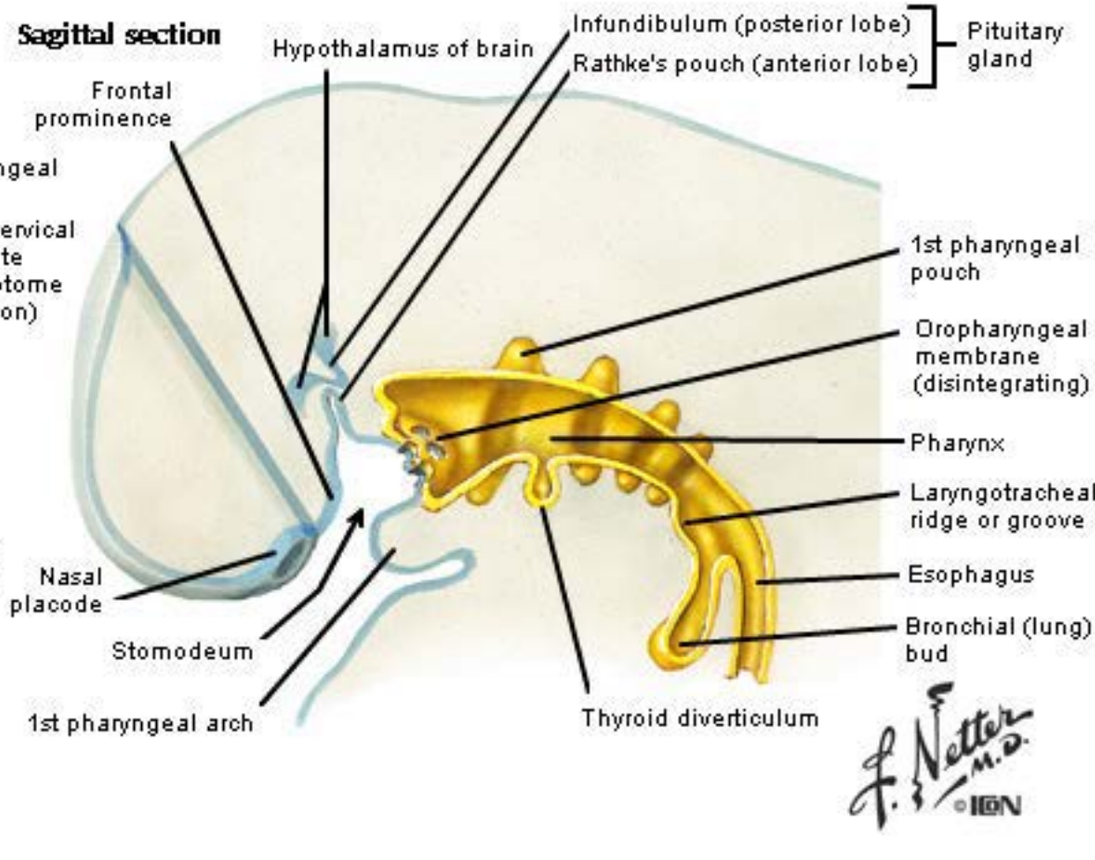
Soft palate and epiglottis overlap in a short pharynx to help separate air and gastrointestinal passages during breastfeeding.

Early Primordia



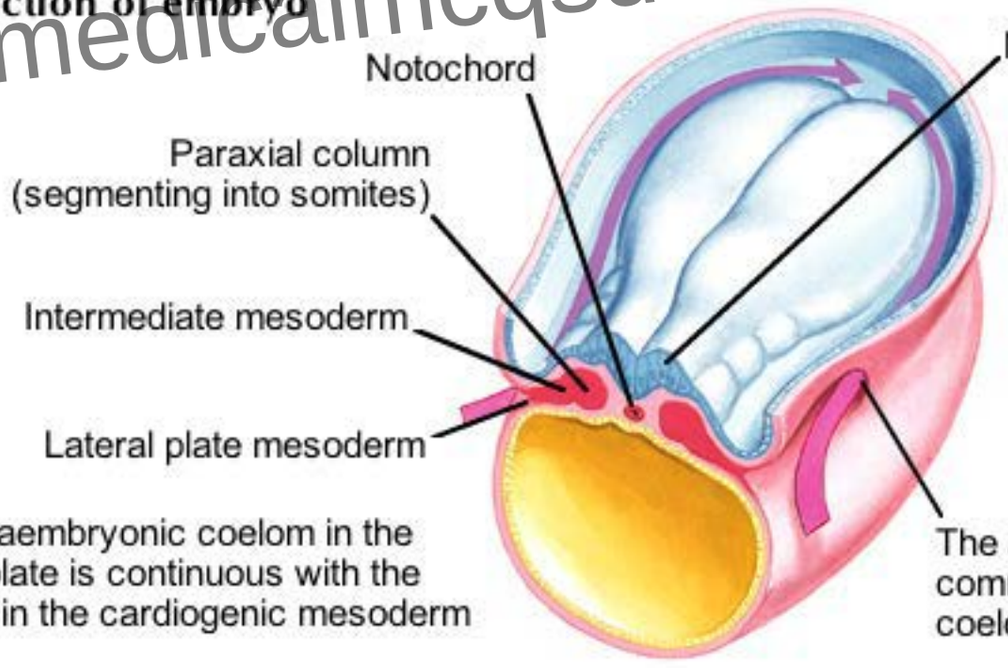




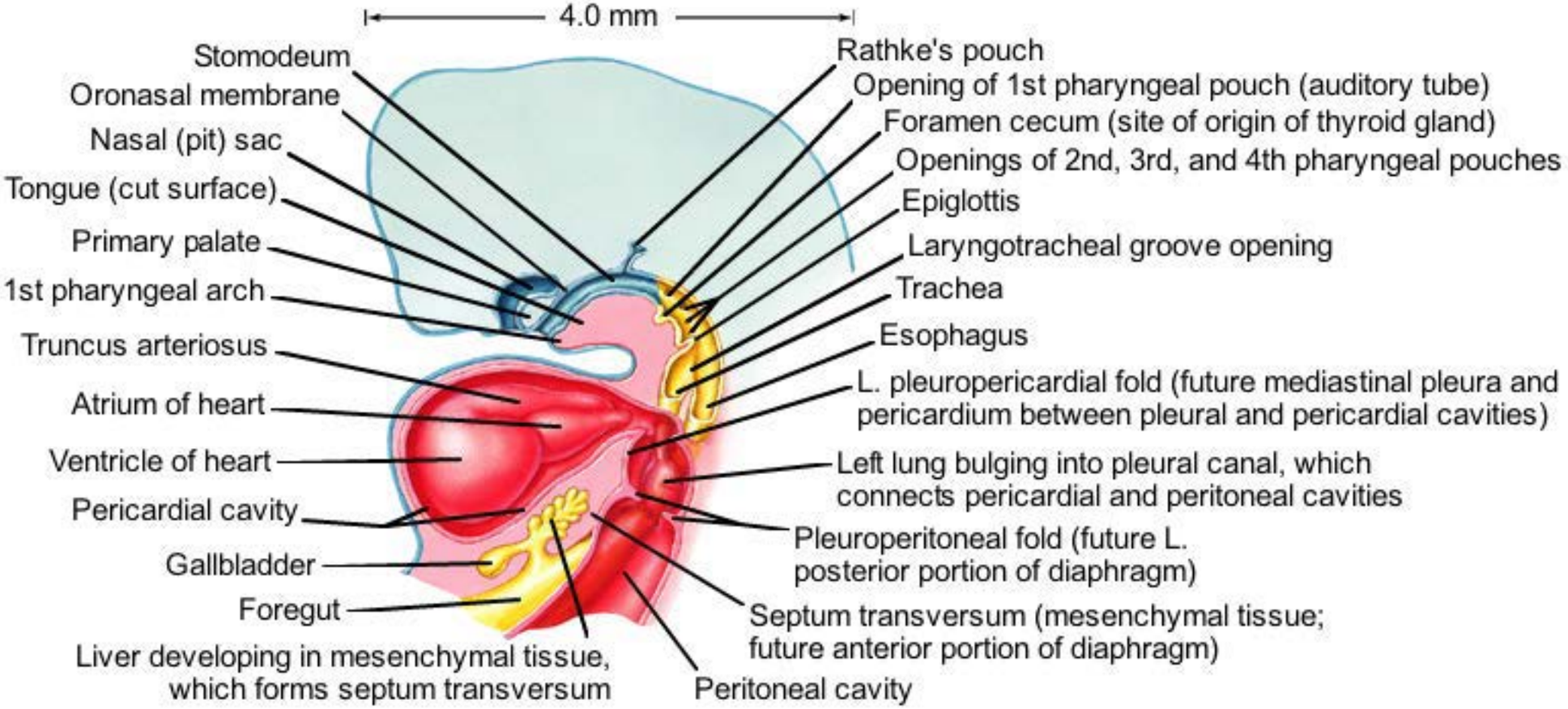


Formation of the Pleural Cavities

A. Cross section of embryo

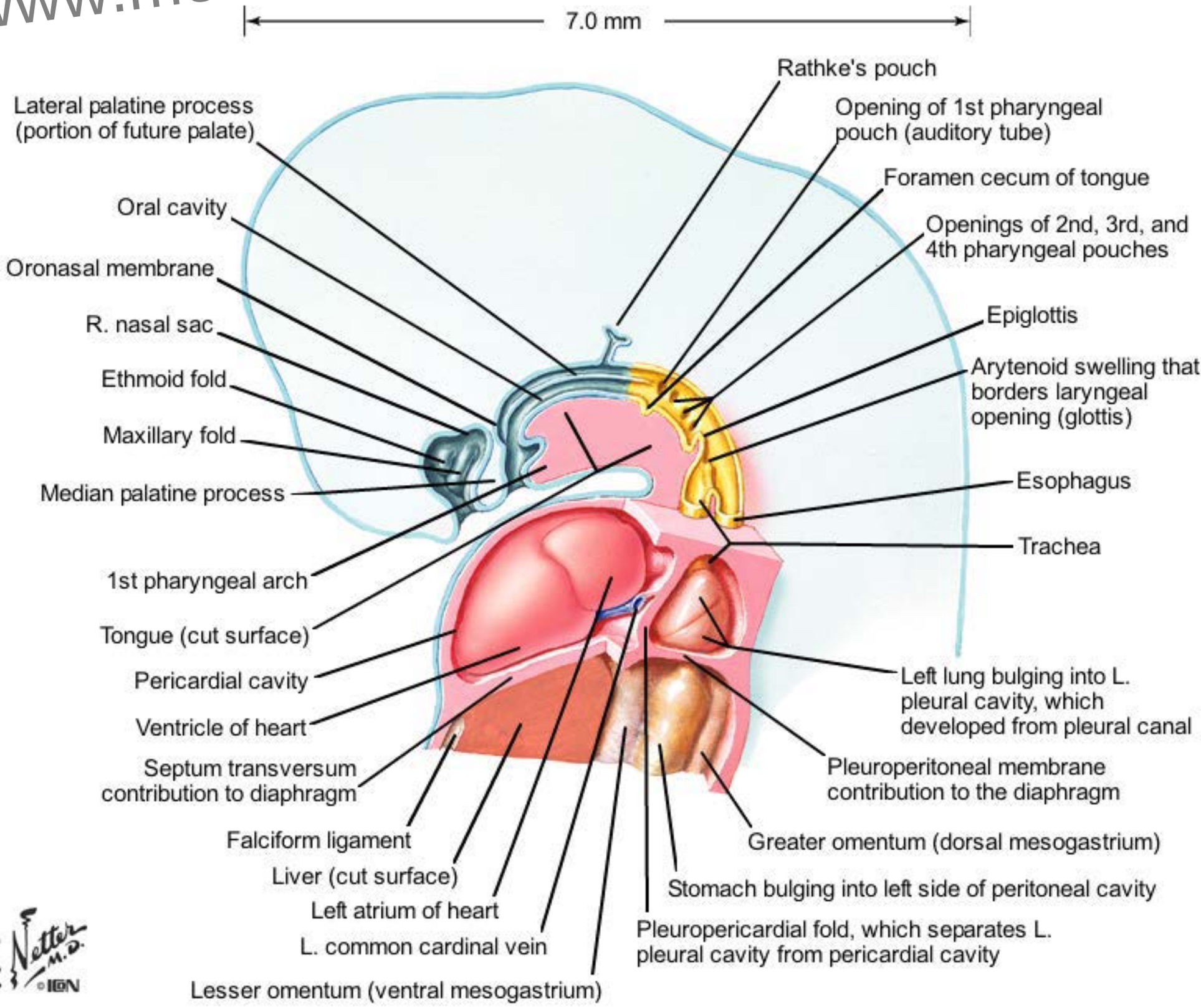


B. Sagittal section at 5 to 6 weeks



The Relationship Between Lungs and Pleural Cavities

Sagittal section at 6 to 7 weeks



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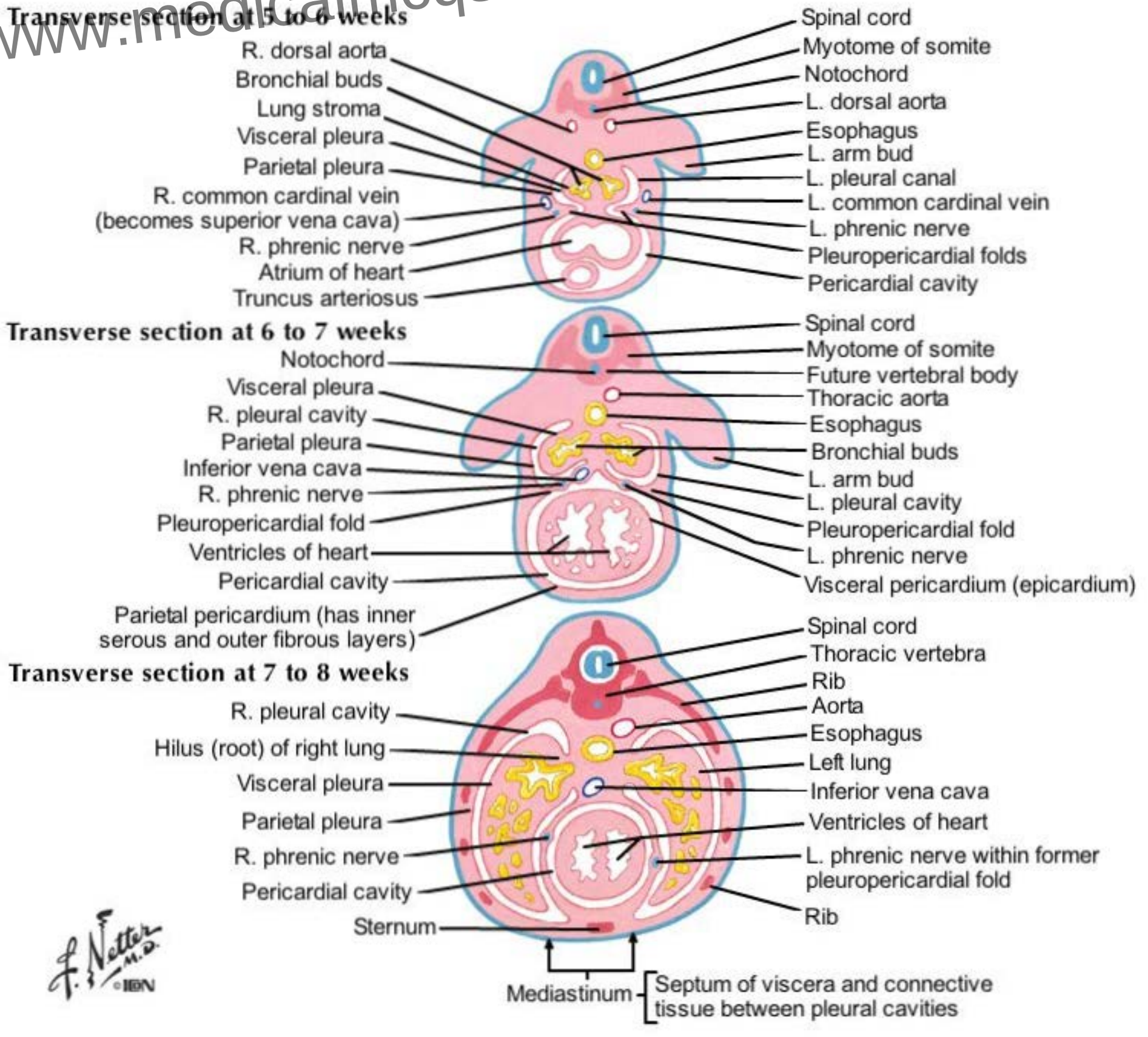
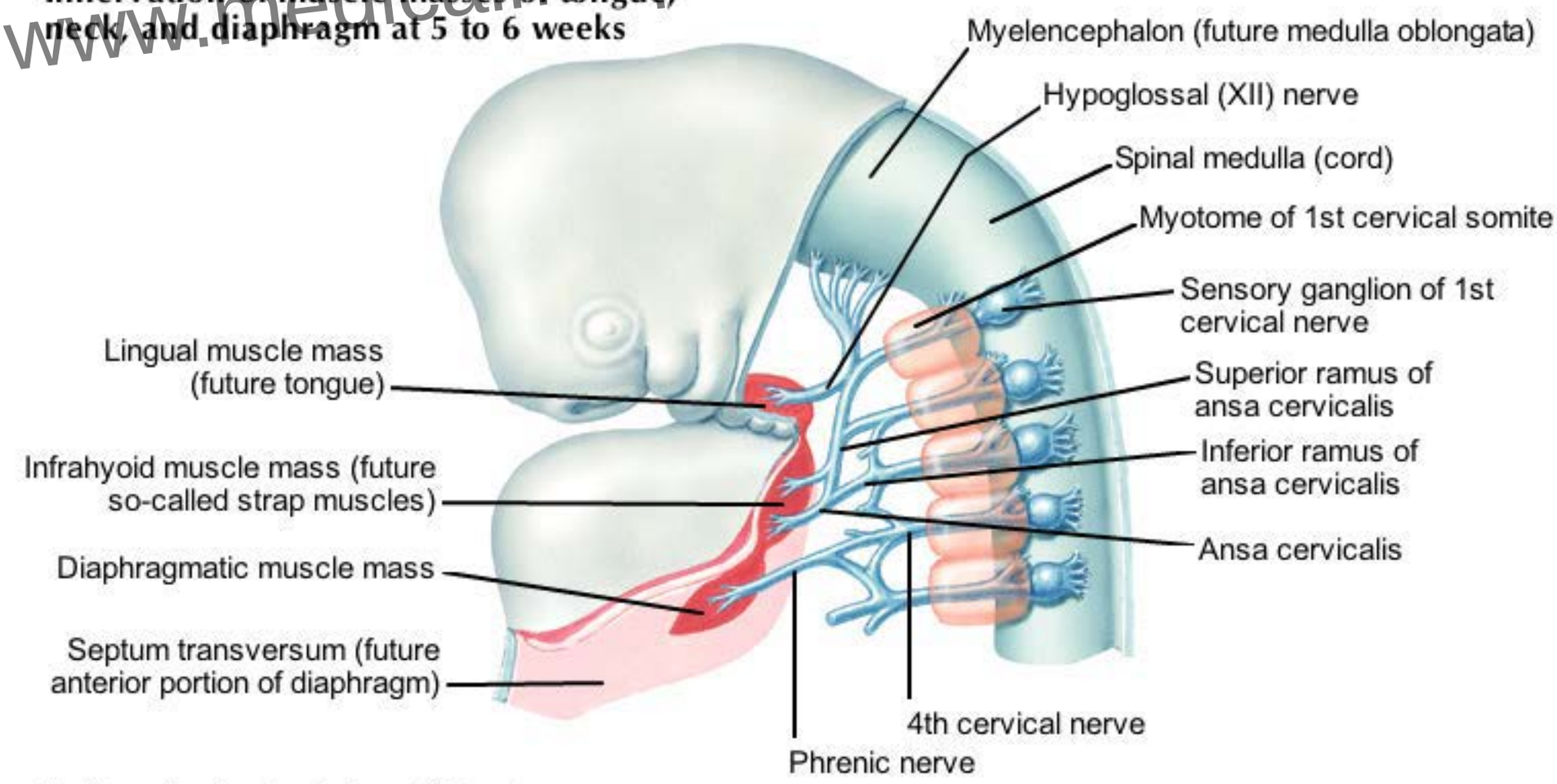
Visceral and Parietal Pleura

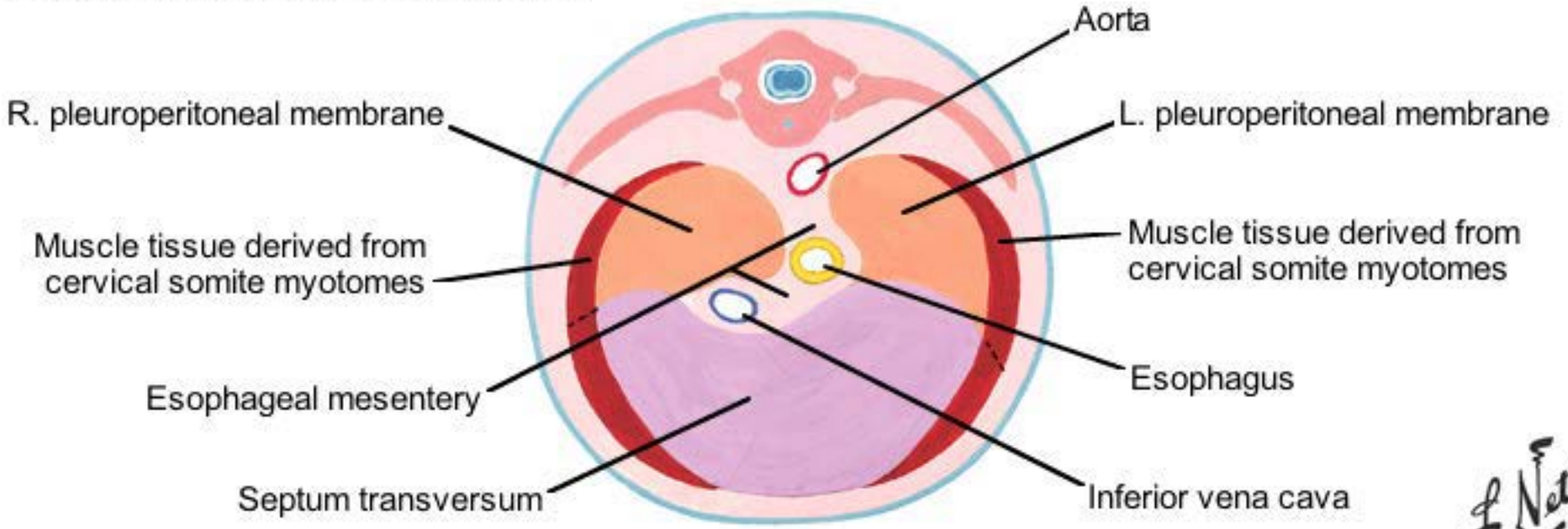


Development of the Diaphragm

Innervation of muscle masses of tongue, neck, and diaphragm at 5 to 6 weeks



Embryological origins of diaphragm



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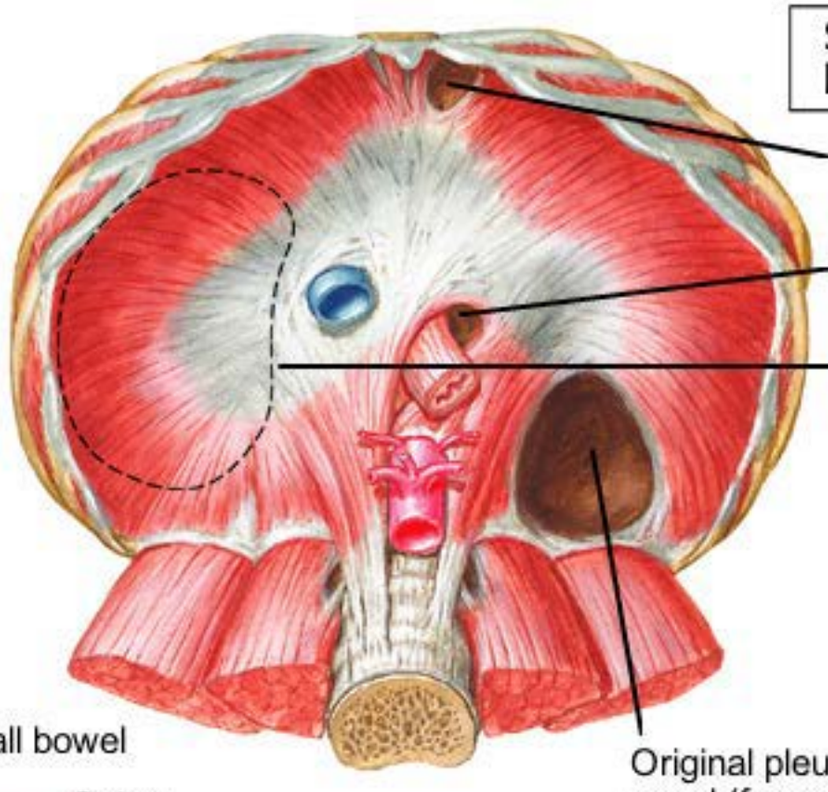
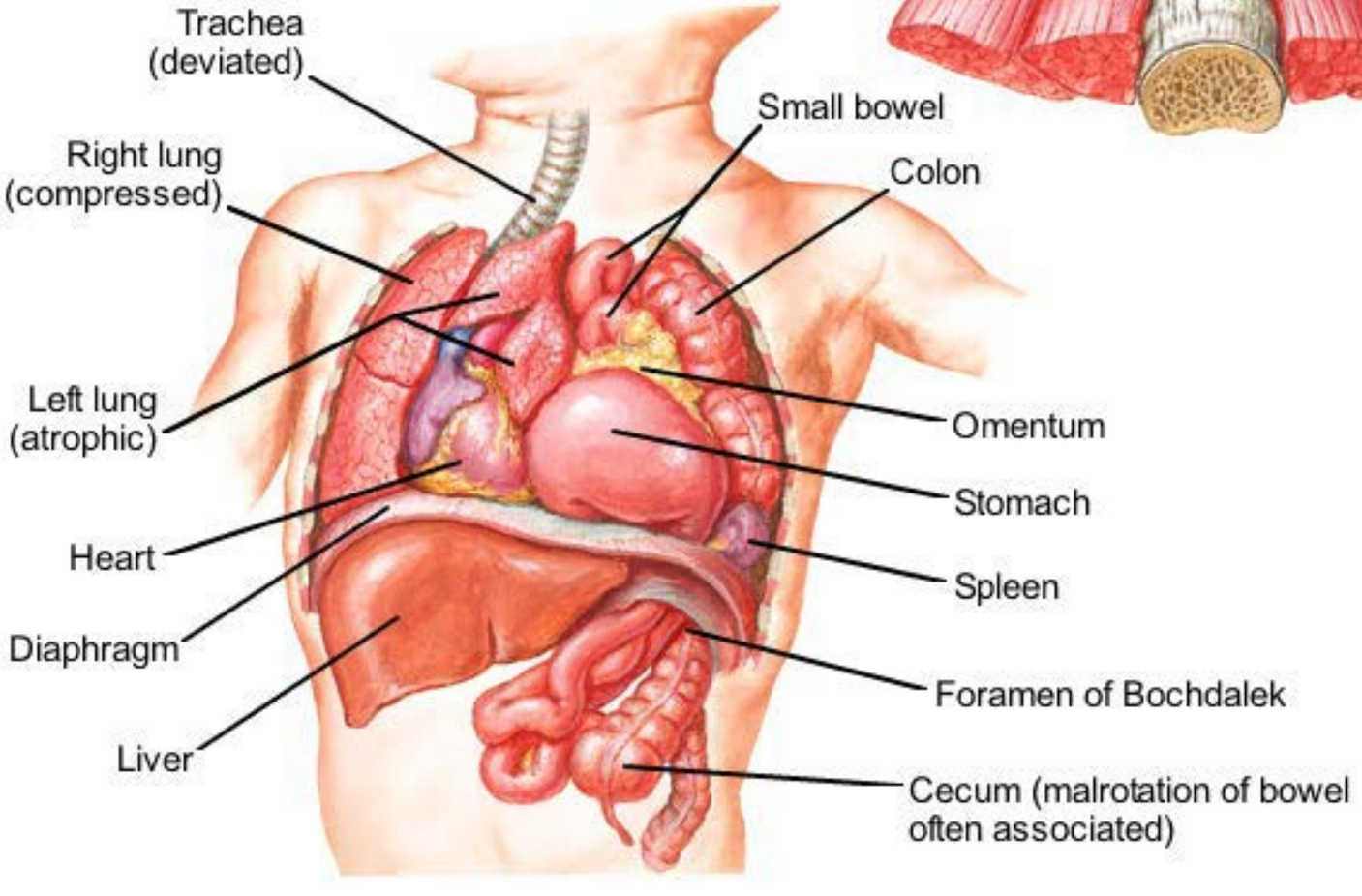
Congenital Diaphragmatic Hernia





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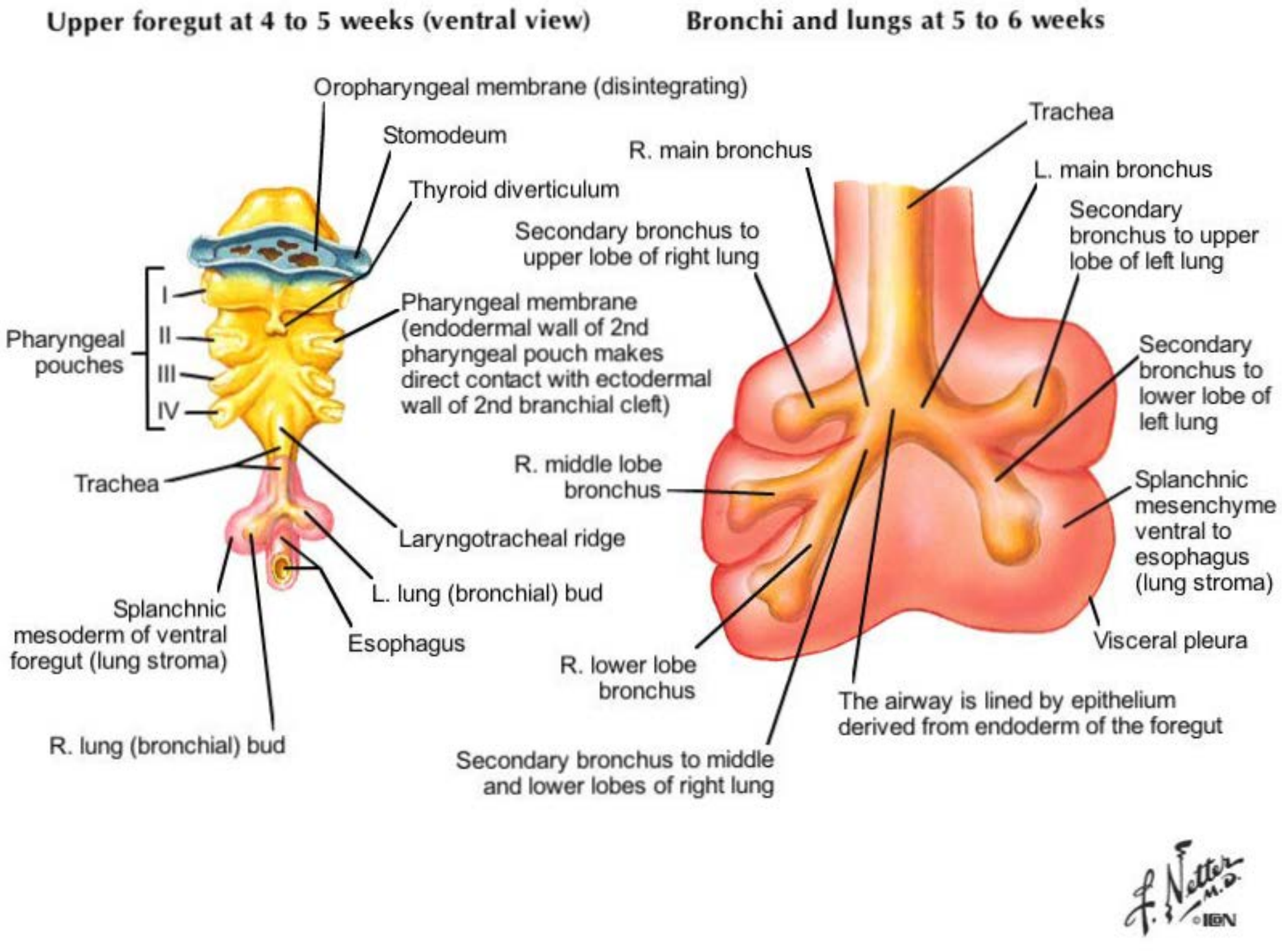
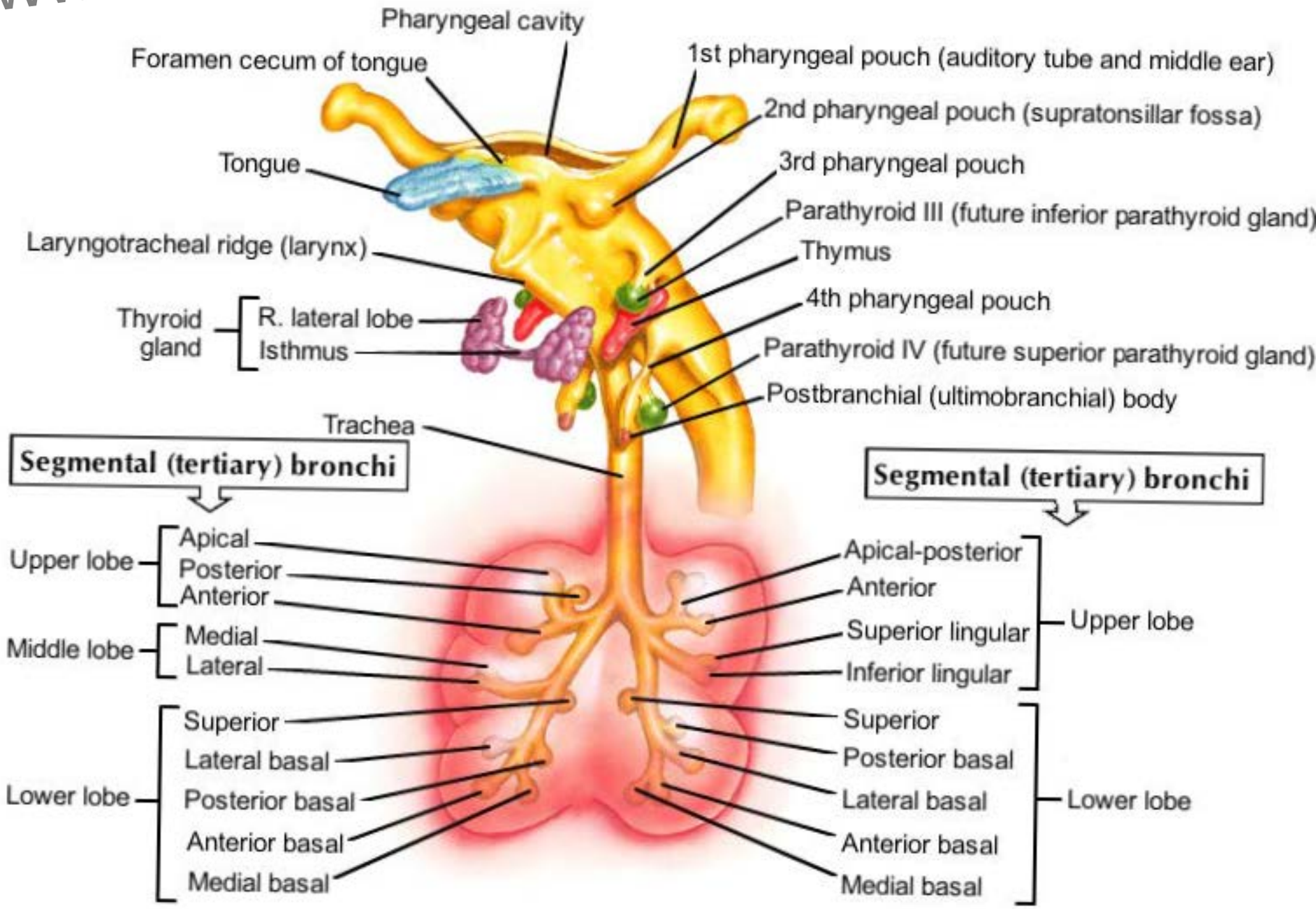
Airway Branching



Airway Branching

Respiratory system at 6 to 7 weeks



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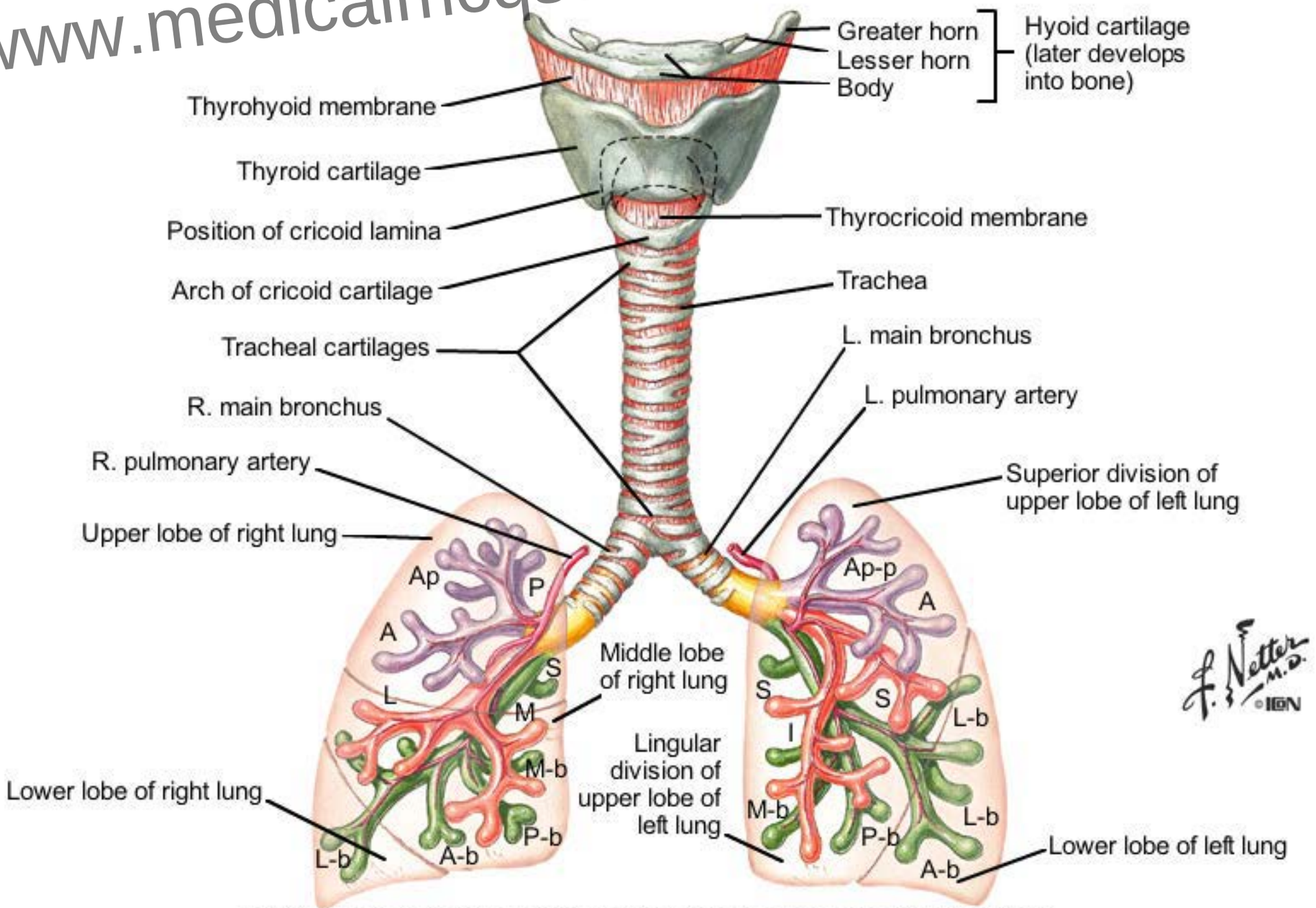
Airway Branching

Larynx, Tracheobronchial Tree, and Lungs at 7 to 10 Weeks



Tertiary branches of bronchi to bronchopulmonary segments

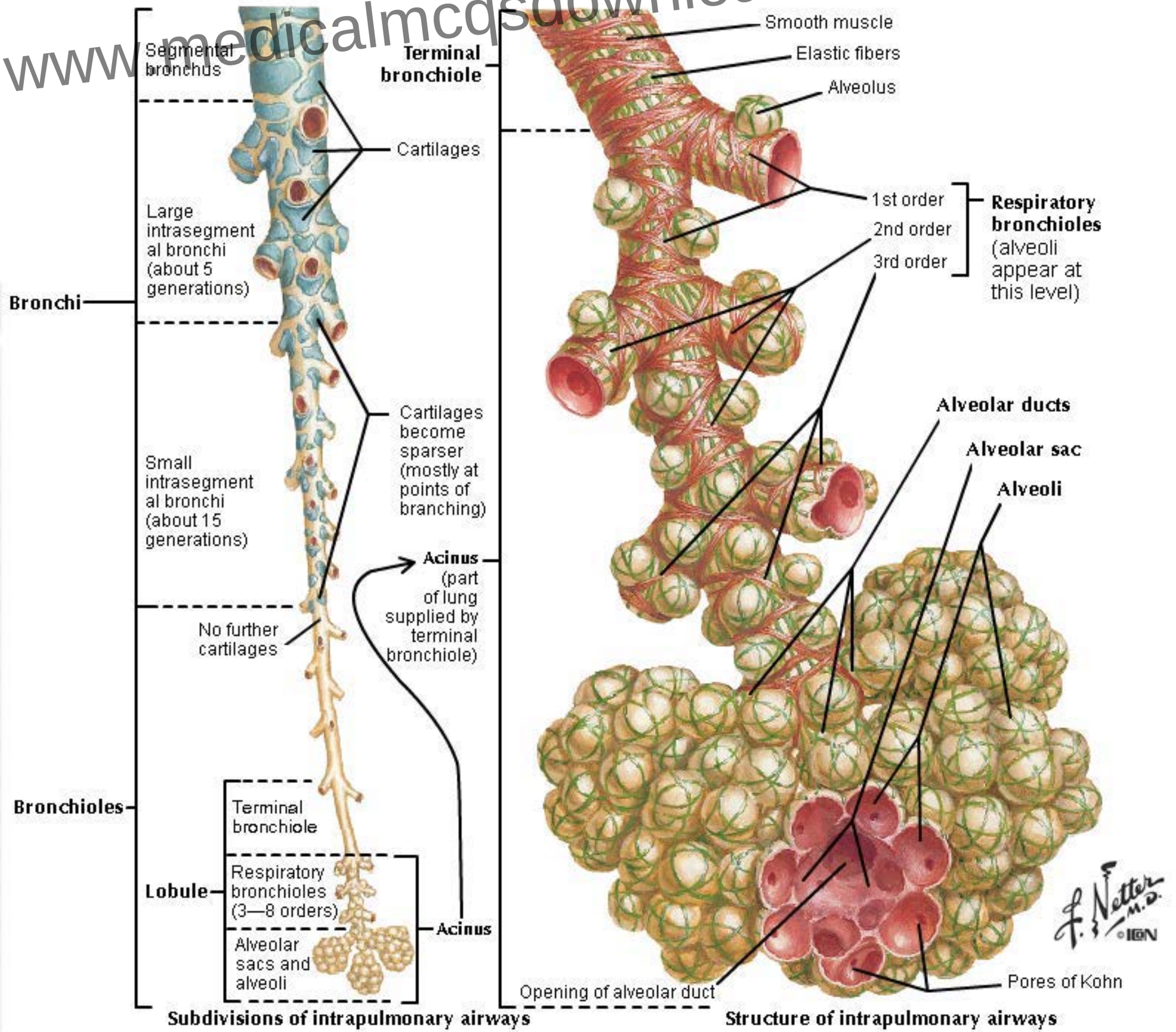
Right lung

Upper lobe	Apical (Ap), posterior (P), anterior (A)	
Middle lobe	Medial (M), lateral (L)	
Lower lobe	Superior (S), anterior basal (A-b), posterior basal (P-b), medial basal (M-b), lateral basal (L-b)	

Left lung

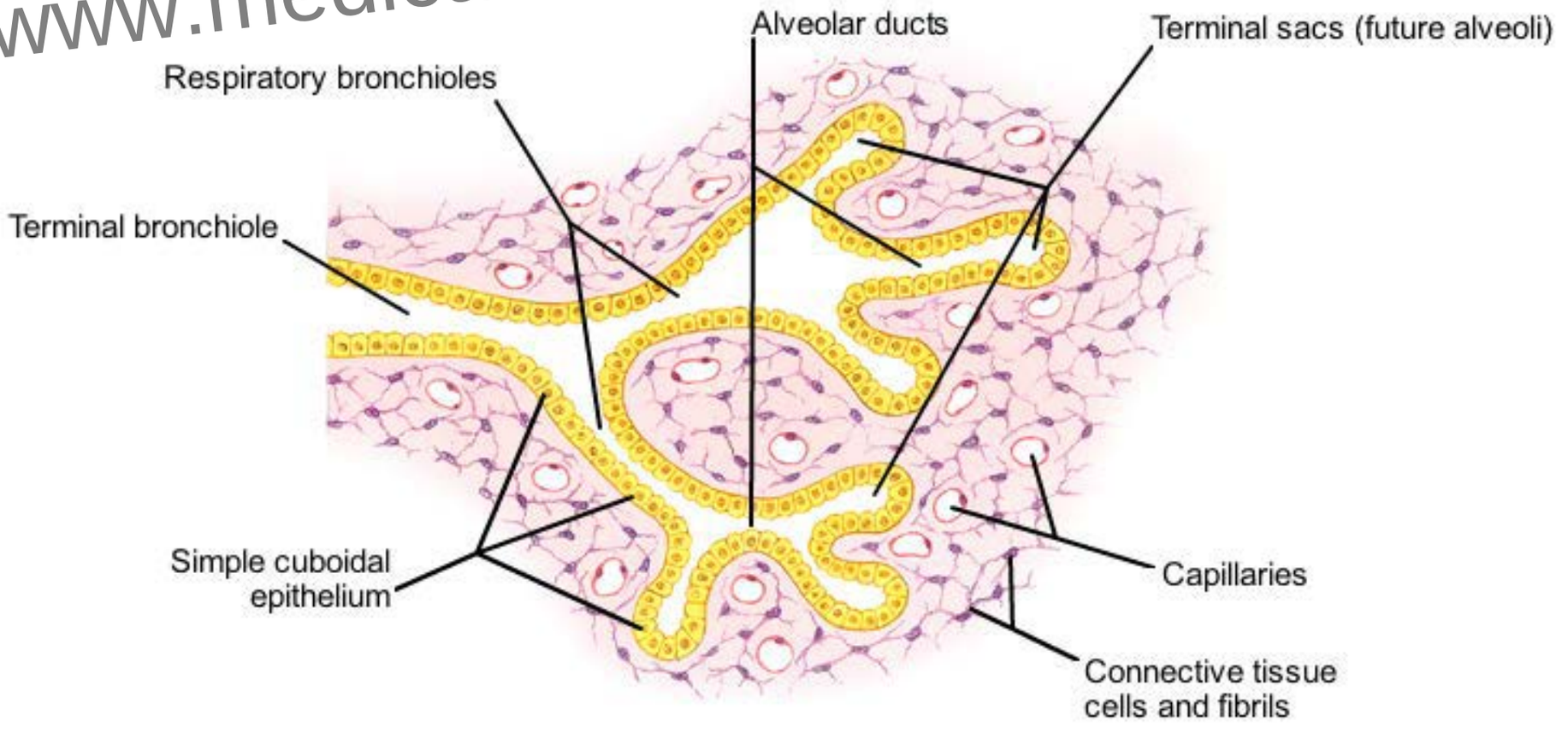
Upper lobe	Superior division	Apical-posterior (Ap-p), Anterior (A)
	Lingular division	Superior (S), inferior (I)
Lower lobe	Superior (S), anterior basal (A-b), medial basal (M-b), posterior basal (P-b), lateral basal (L-b)	

Airway Branching

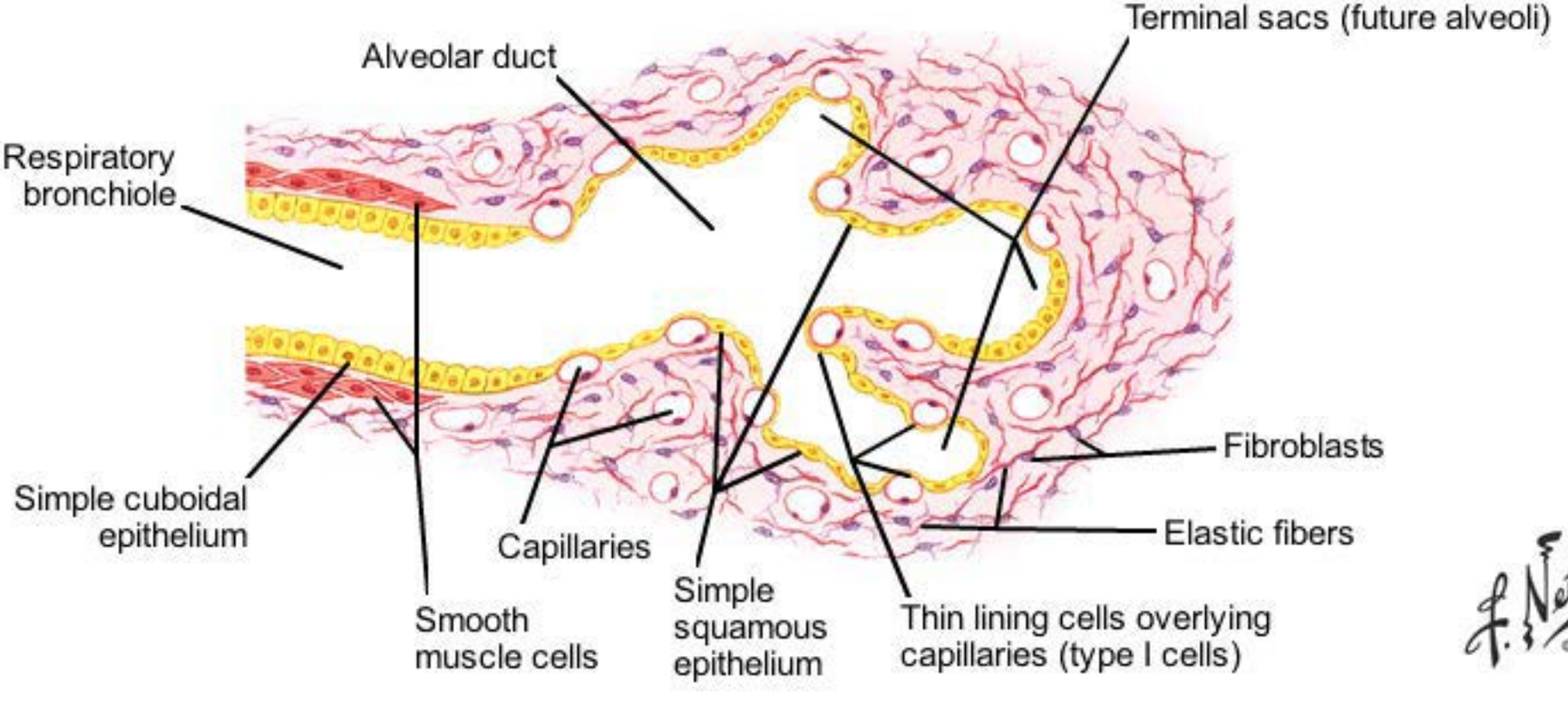


Bronchial Epithelium Maturation

Terminal air tube at 20 weeks



Terminal air tube at 24 weeks



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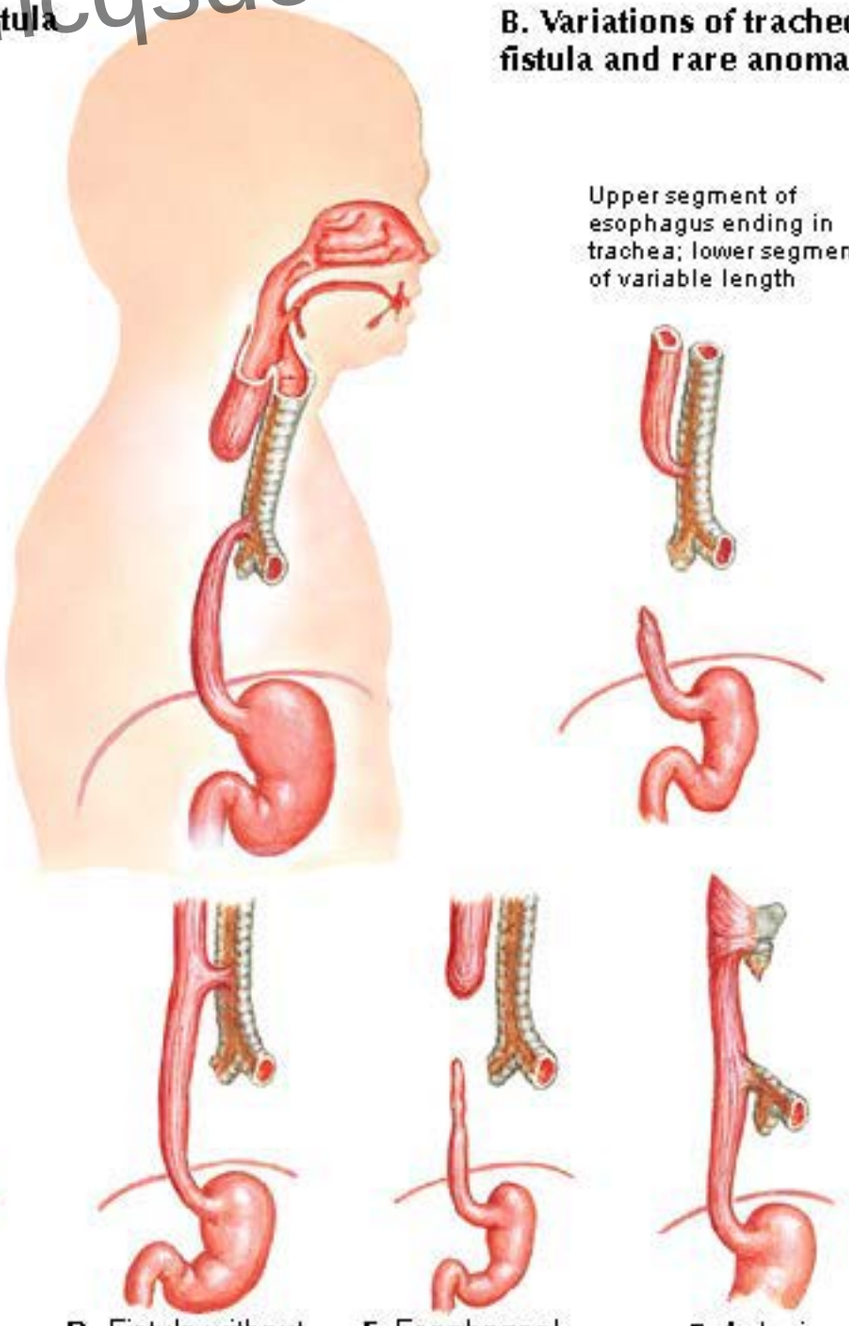
Congenital Anomalies of the Lower Airway

A. Tracheoesophageal fistula

Most common form (90% to 95%) of tracheoesophageal fistula. Upper segment of esophagus ending in blind pouch; lower segment originating from trachea just above bifurcation. The two segments may be connected by a solid cord

B. Variations of tracheoesophageal fistula and rare anomalies of trachea

Upper segment of esophagus ending in trachea; lower segment of variable length

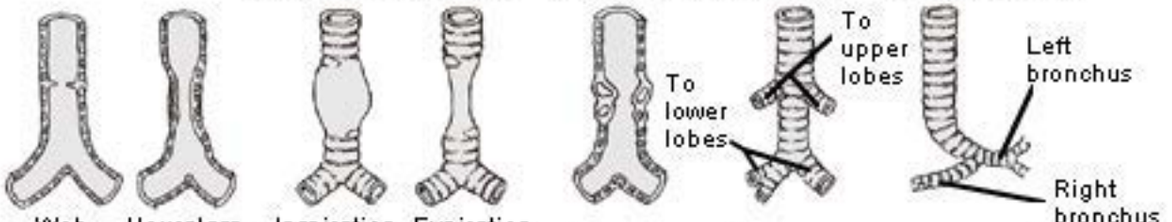


C. Double fistula

D. Fistula without esophageal atresia

E. Esophageal atresia without fistula

F. Aplasia of trachea (lethal)



G. Stricture of trachea **H.** Absence of cartilage **I.** Deformity of cartilage **J.** Abnormalities of bifurcation

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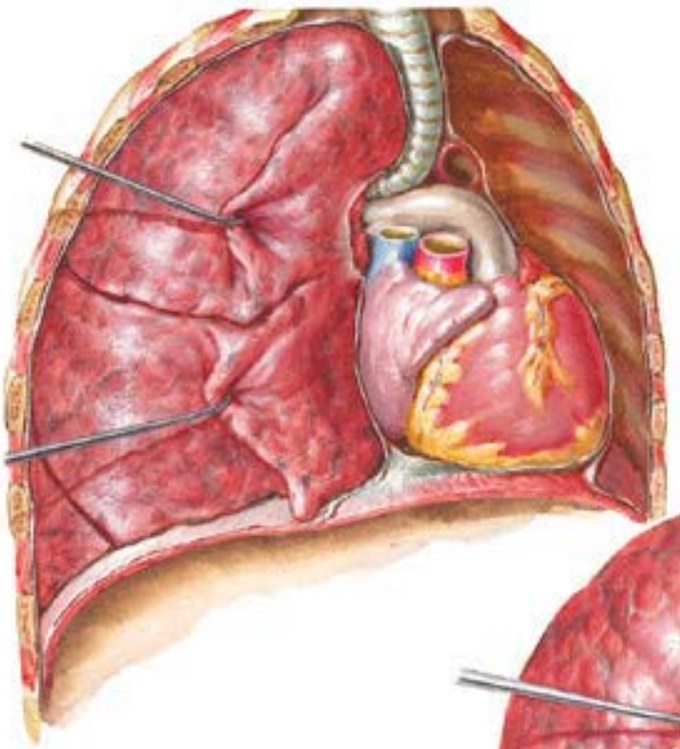
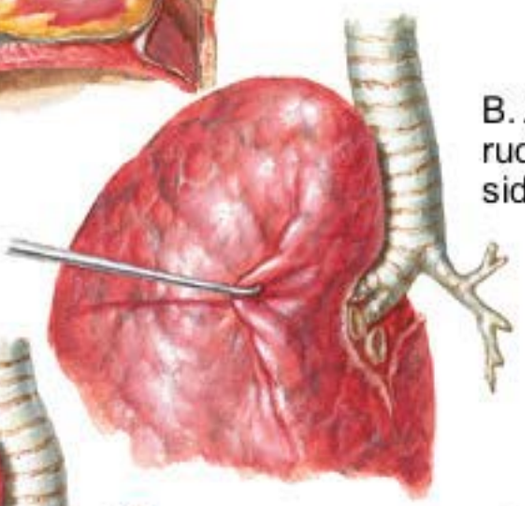
Airway Branching Anomalies

Pulmonary agenesis, aplasia, and hypoplasia

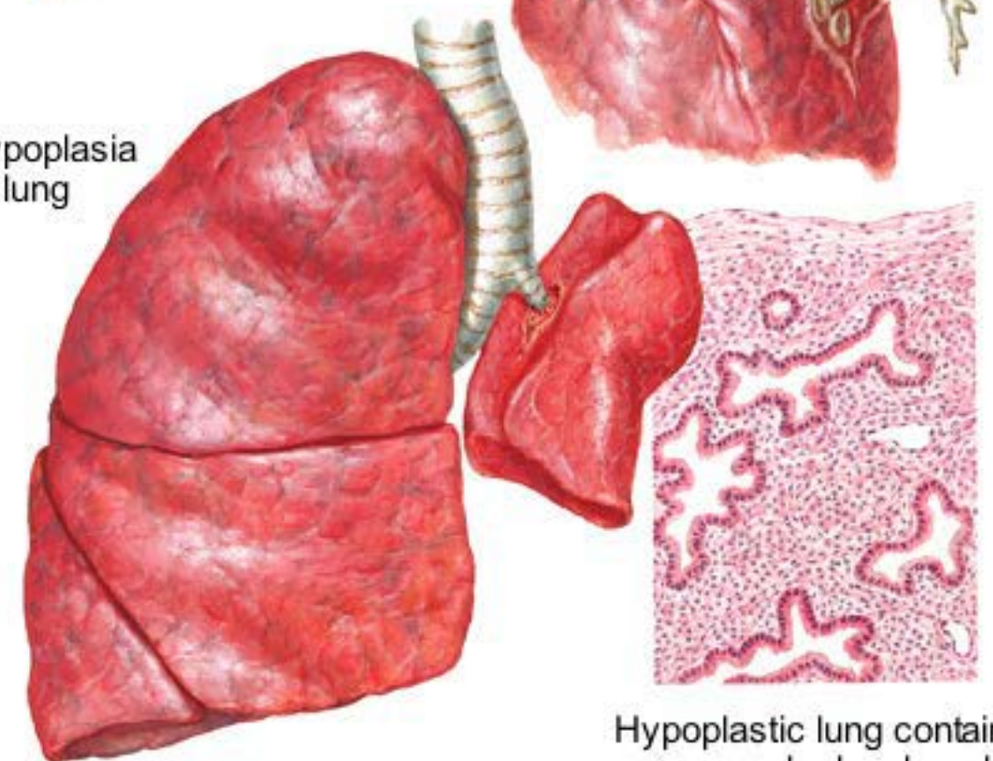


A. Complete unilateral agenesis. Left lung and bronchial tree are absent. Right lung is greatly enlarged with resultant shift of mediastinum to left, elevation of left diaphragm, and approximation of ribs on that side



B. Aplasia of left lung. Only rudimentary bronchi on left side, which end blindly

C. Hypoplasia of left lung



Hypoplastic lung contains some poorly developed bronchi but no alveolar tissue

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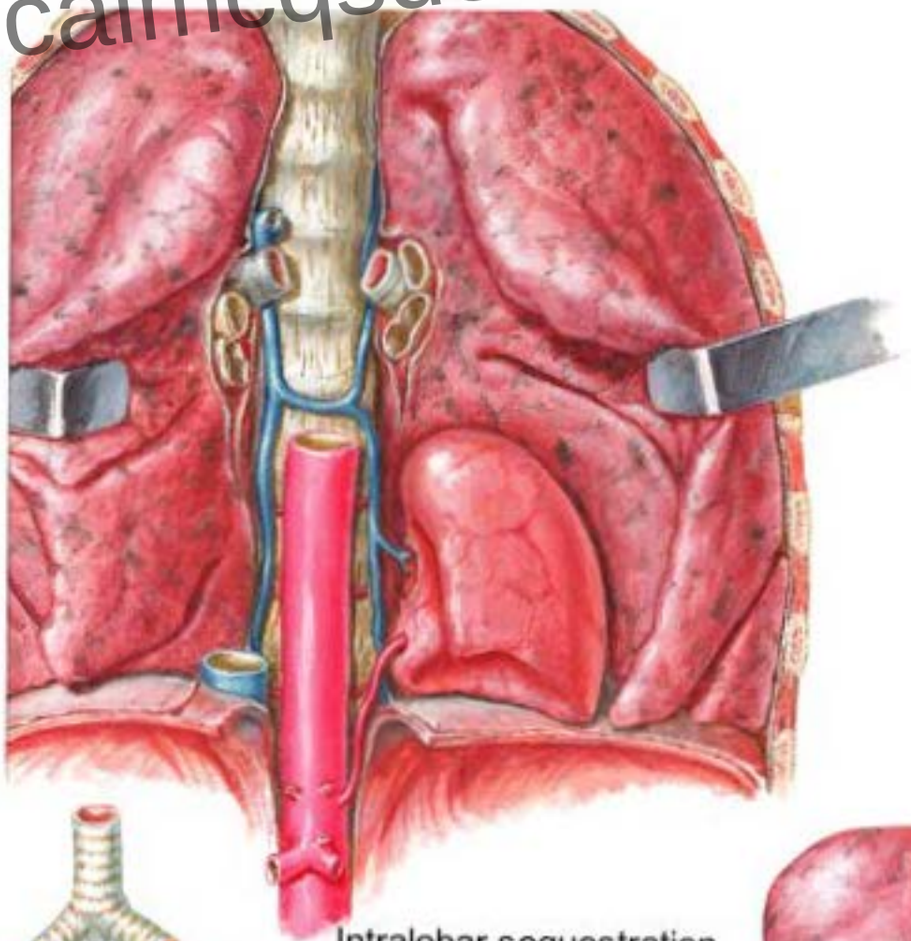
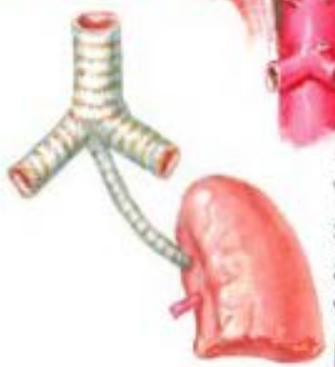
Bronchopulmonary Sequestration

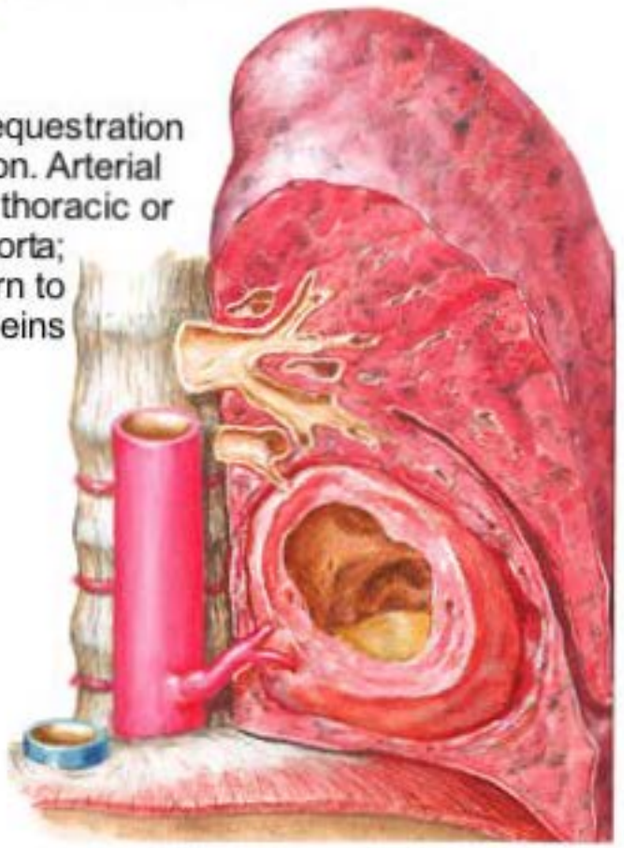


Extralobar sequestered lobe of left lung. Arterial supply from thoracic or abdominal aorta, venous return to hemiazygos vein



Extralobar sequestered lobe supplied by accessory bronchus

Intralobar sequestration with cavitation. Arterial supply from thoracic or abdominal aorta; venous return to pulmonary veins



Extralobar sequestered lobe with communication from esophagus (communication with cardia of stomach has also been observed)

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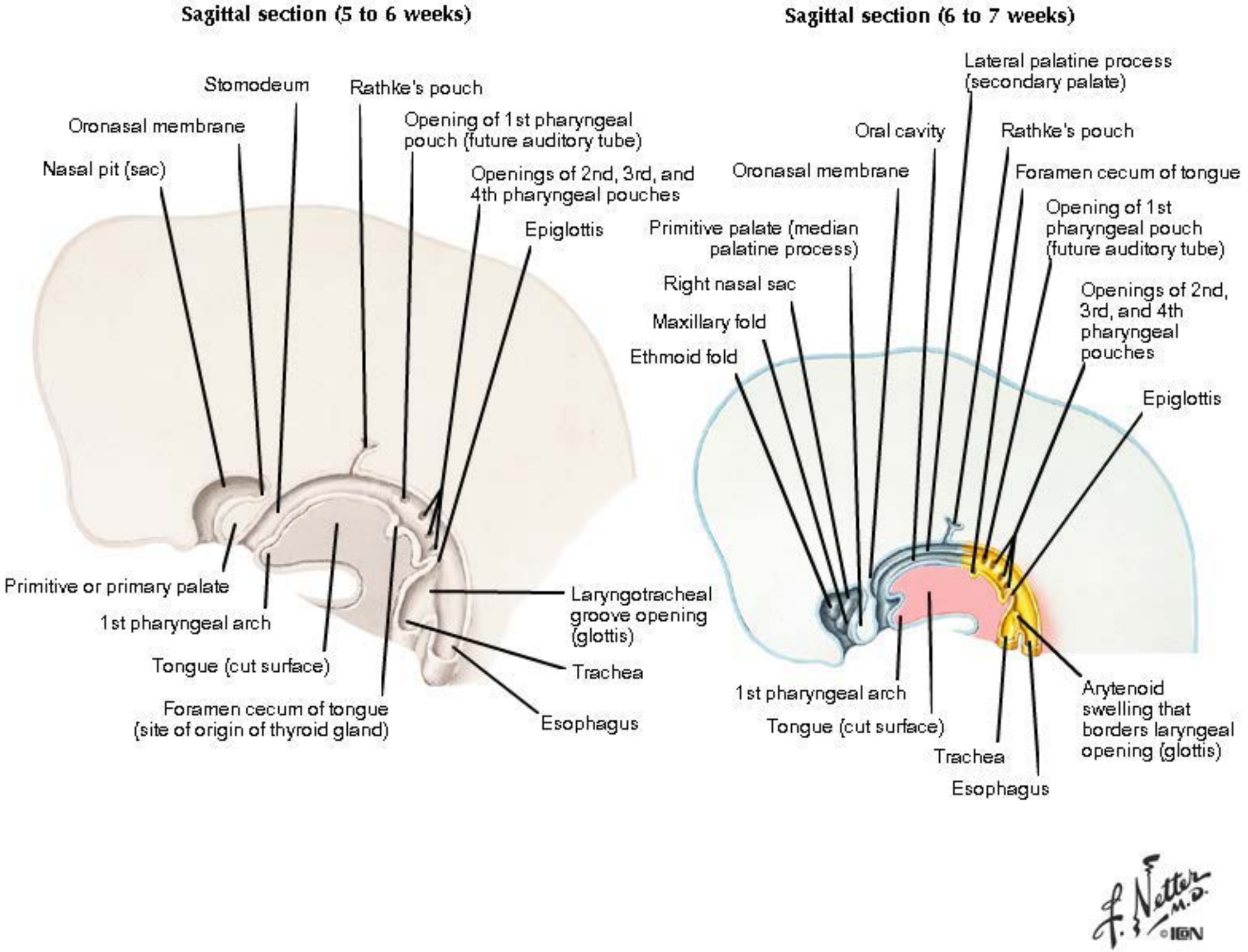
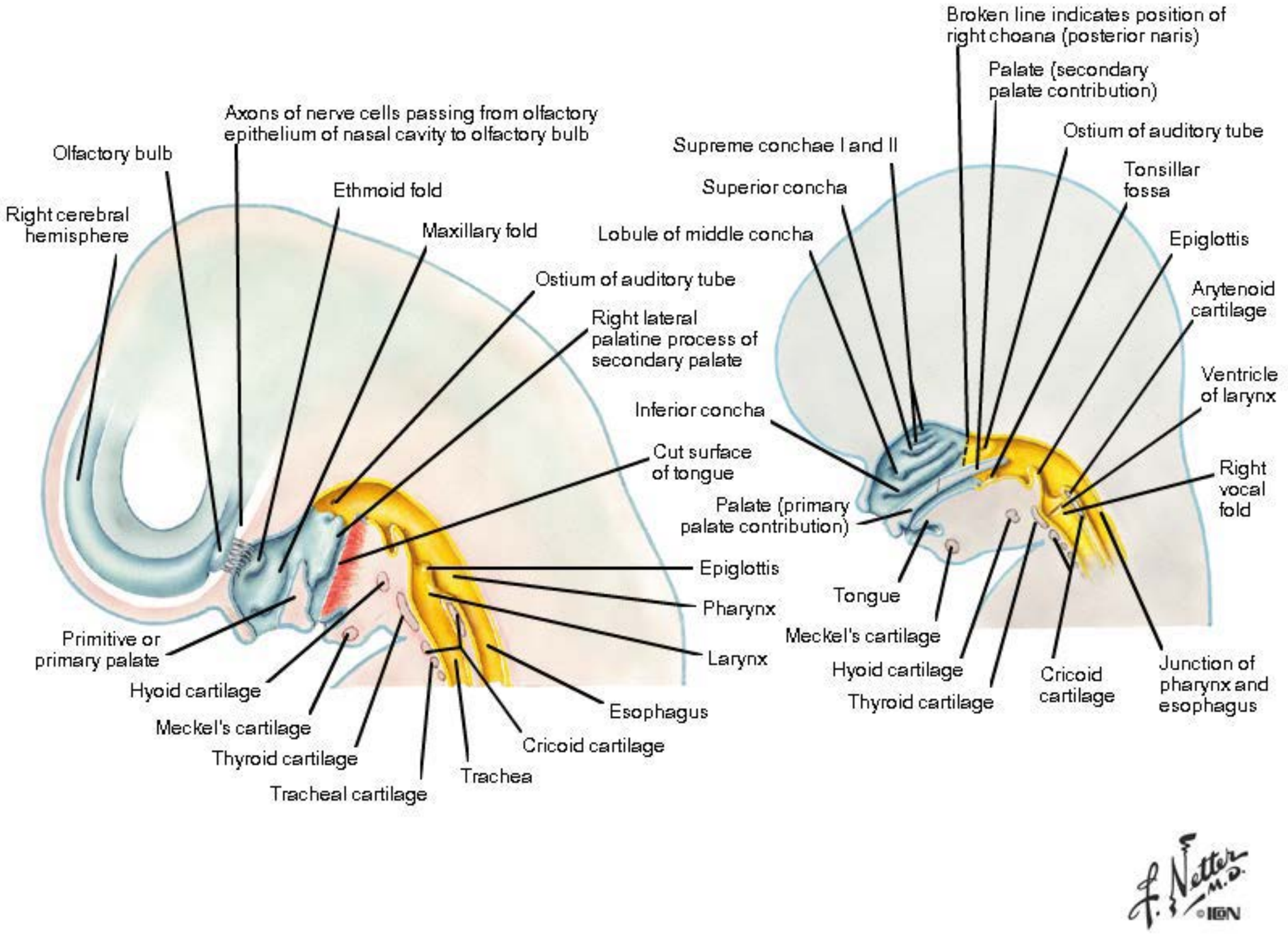
Palate Formation in the Upper Airway



Palate Formation in the Upper Airway



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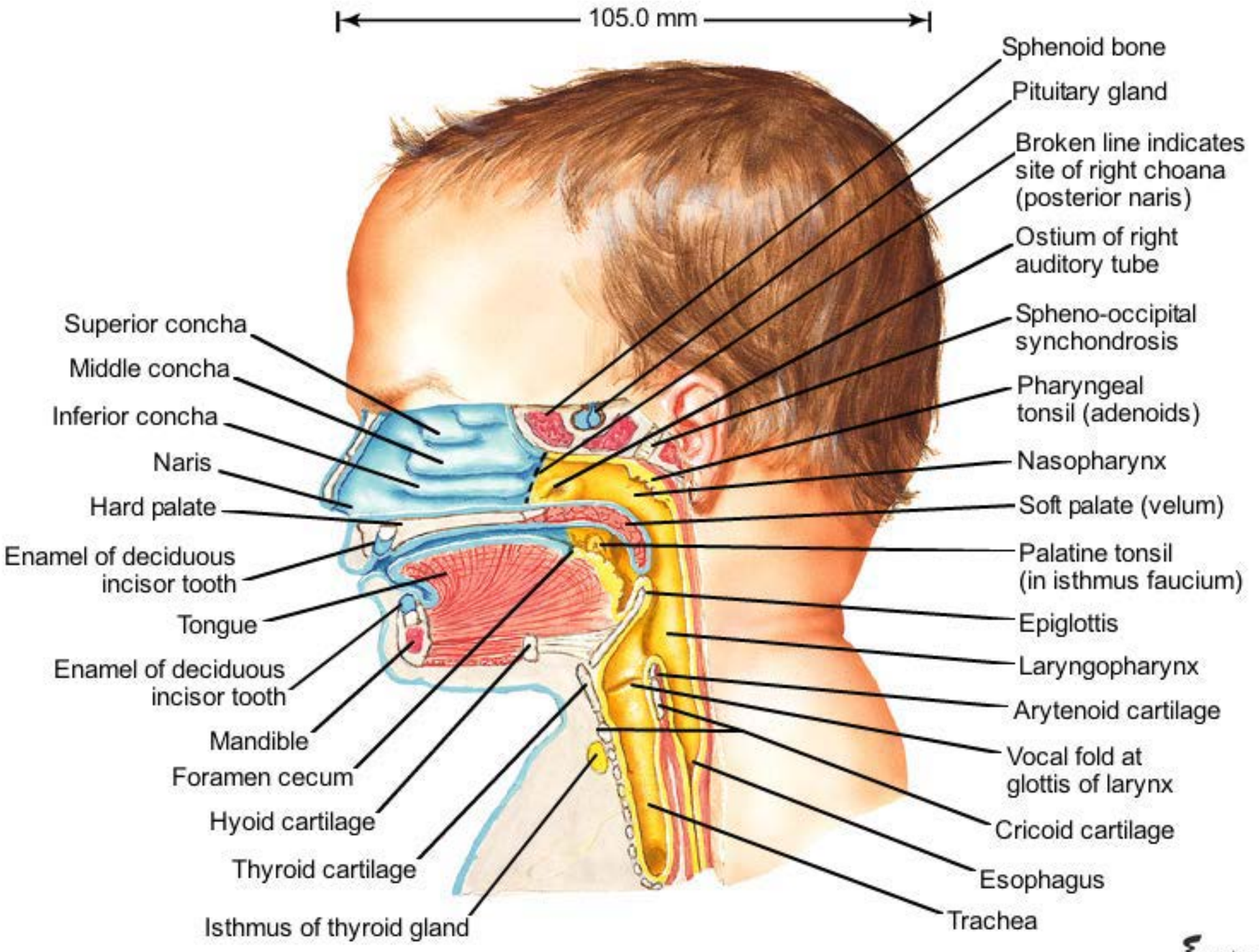
The Newborn Upper Airway

During quiet respiration with mouth closed (partial midsagittal section with nasal septum removed)

Newborn (36 weeks)



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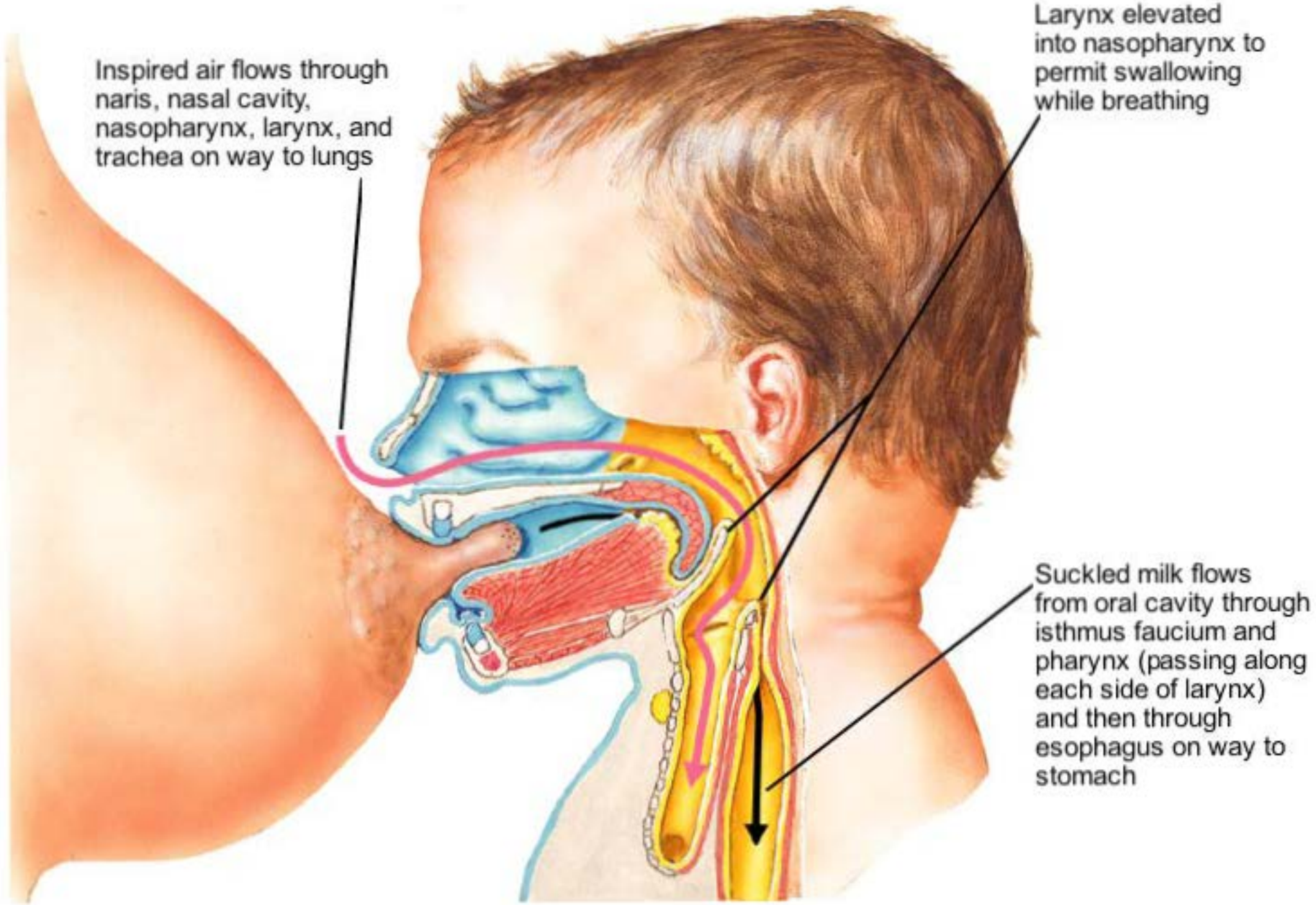
The Newborn Upper Airway
During nursing

Newborn (36 weeks)



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THE GASTROINTESTINAL SYSTEM AND ABDOMINAL WALL

TIMELINE

Prenatal Time Scale (Months)

Blastocyst

Embryo

Fetus

1

2

3

4

5

6

7

8

9

Birth

1 month

Thyroid, lung, liver, and pancreas buds from the foregut appear. The ventral mesentery of the midgut and hindgut breaks down. The yolk sac begins to get compressed into the umbilical cord.

2—3 weeks

The gastrula folds to form the gut tube.

5 weeks

The yolk sac is now a stalk in the umbilical cord with the urachus. The peritoneal cavity separates from the thoracic cavities. The three primary gut arteries develop.

6 weeks

Midgut loop extends into the umbilical cord. The lesser peritoneal sac begins to develop from the dorsal mesogastrium.

10 weeks

Midgut returns to abdominal cavity.

2 months

Midgut begins to grow in the umbilical cord and rotate 270 degrees around the superior mesenteric artery.

4—5 months

Pancreas, duodenum, and ascending and descending colon fuse to the posterior abdominal wall.

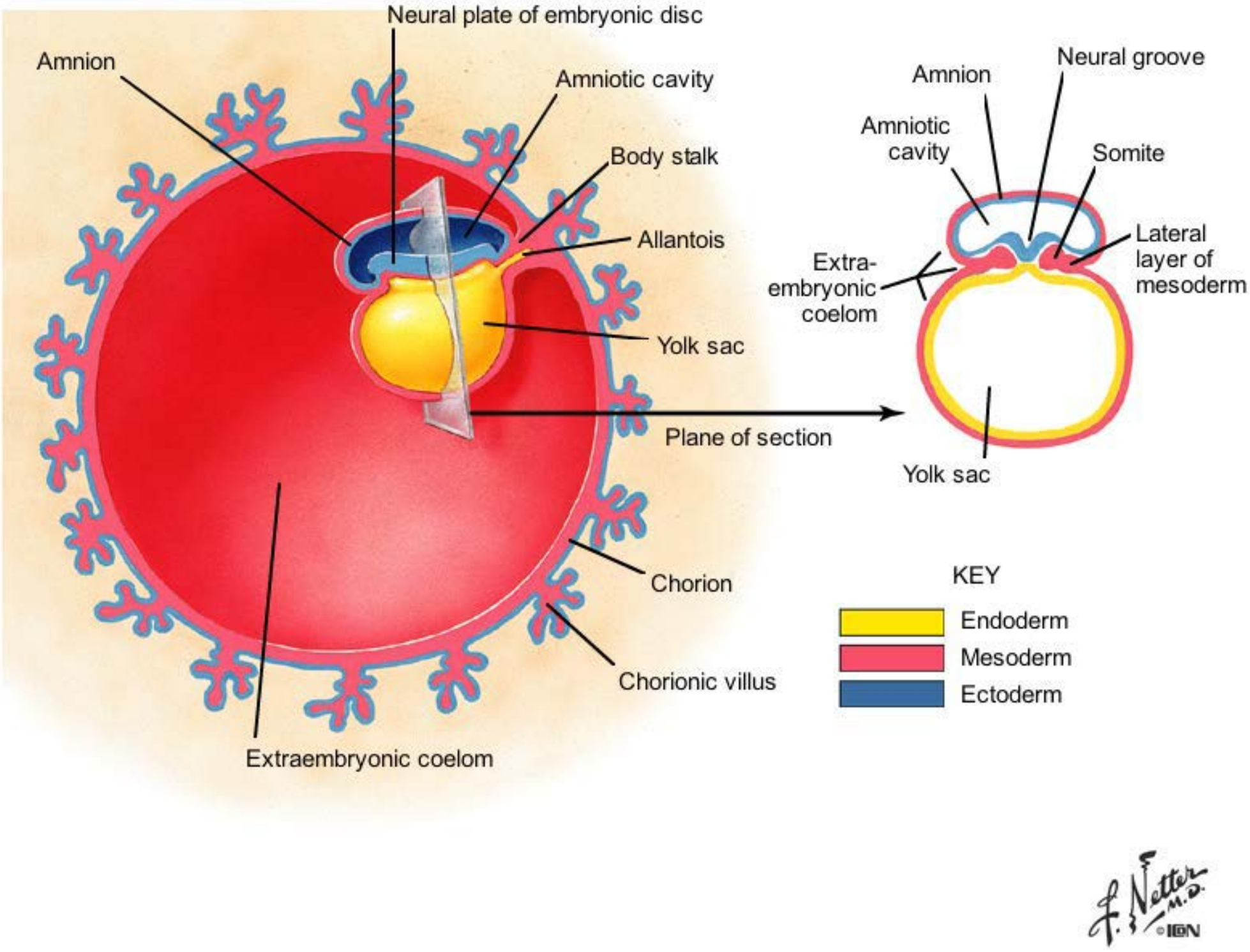
8 months

Abdominal wall: testes pass through the inguinal canal.

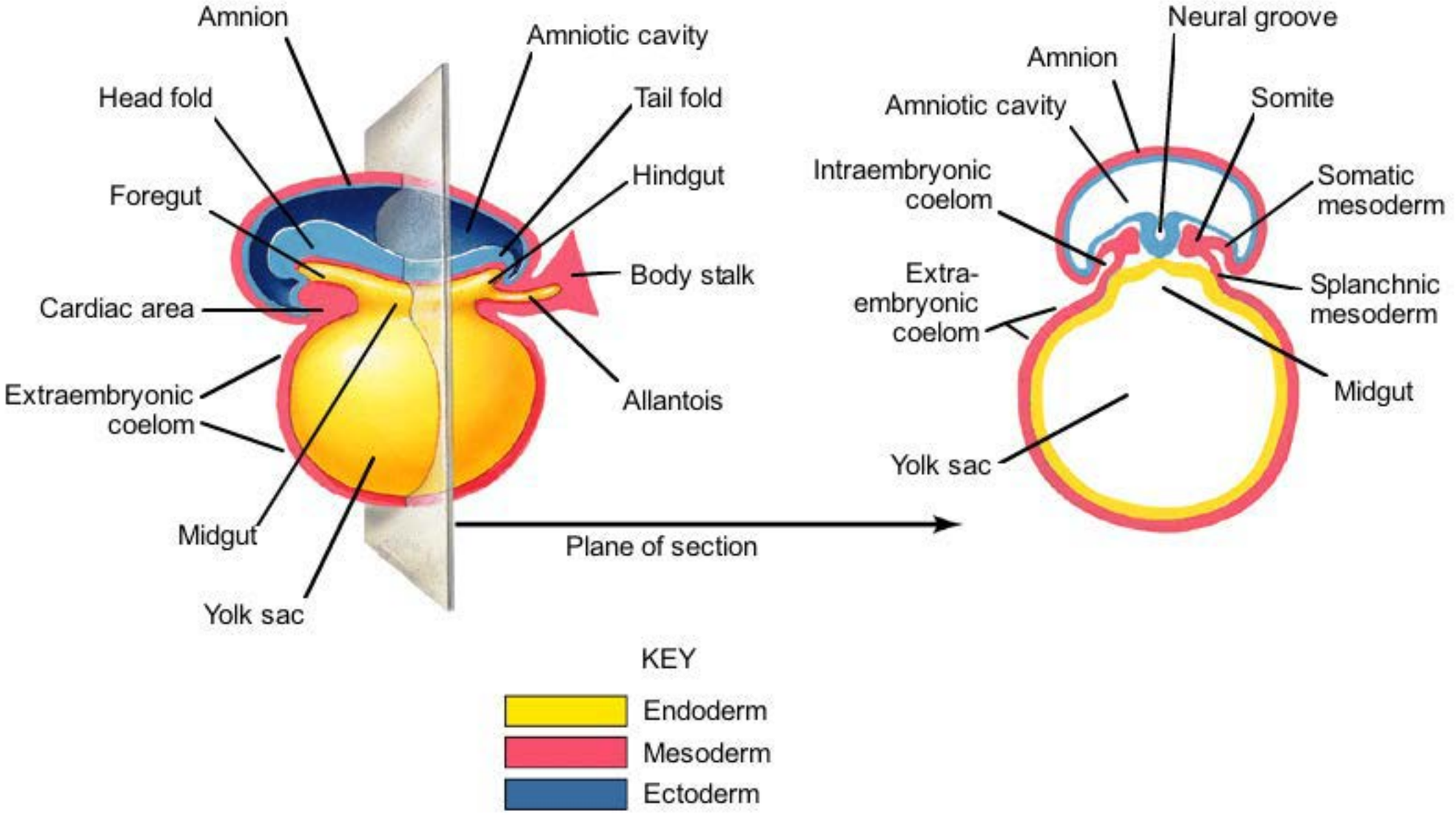
9 months

Testes enter the scrotum.

Early Primordia
14 days

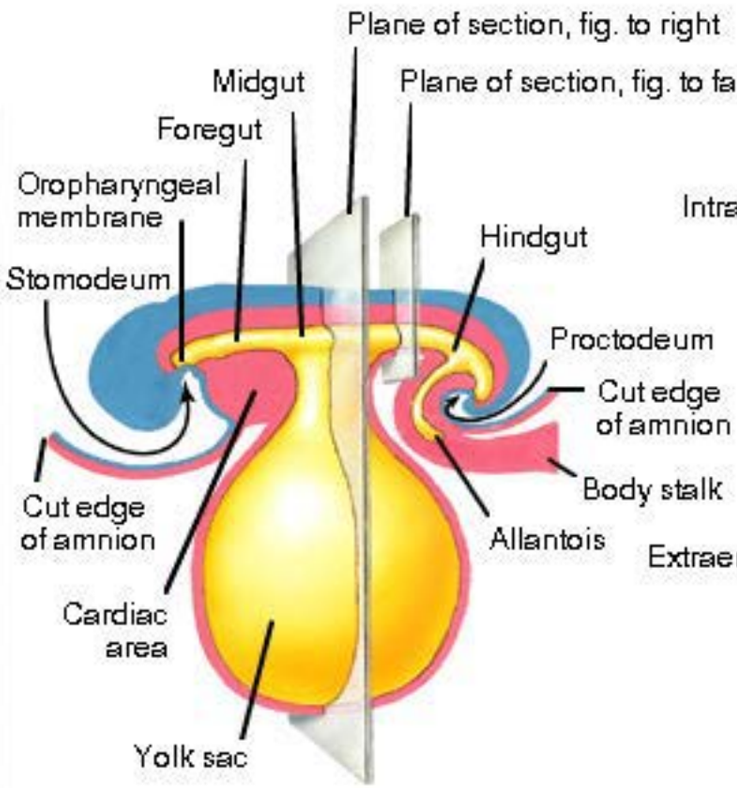


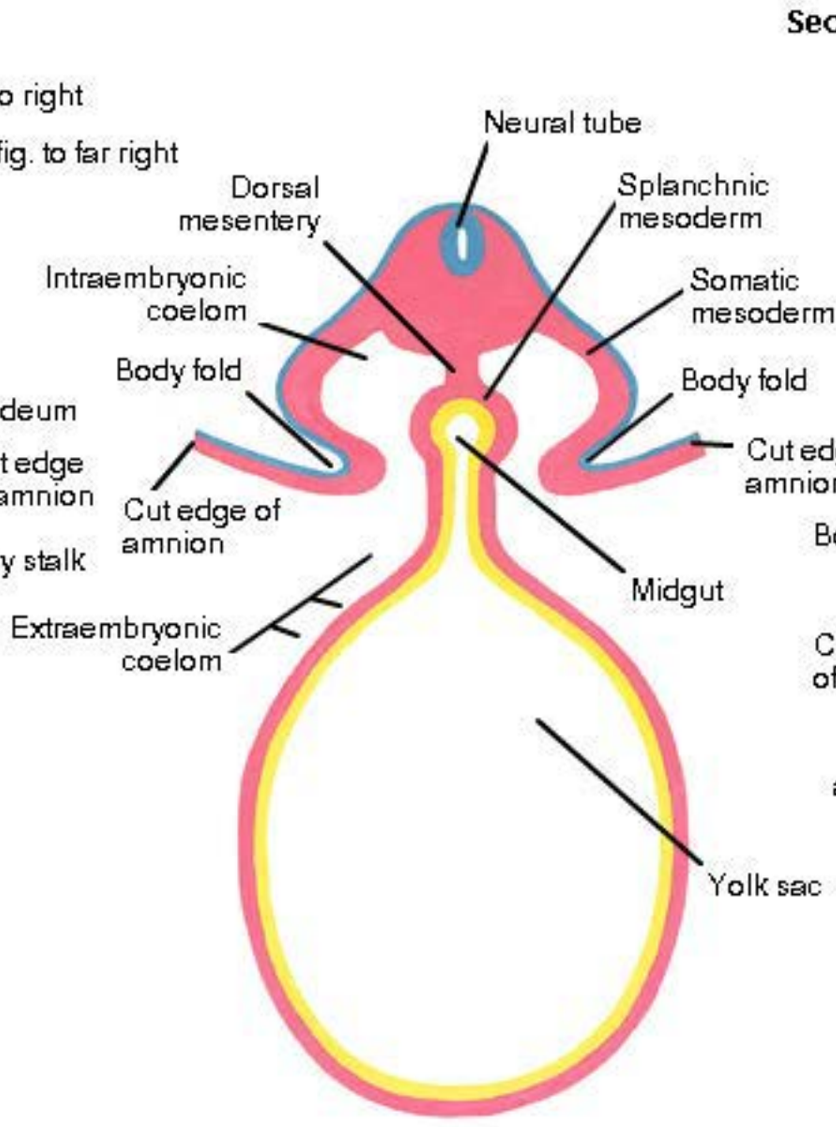
Early Primordia
16 days



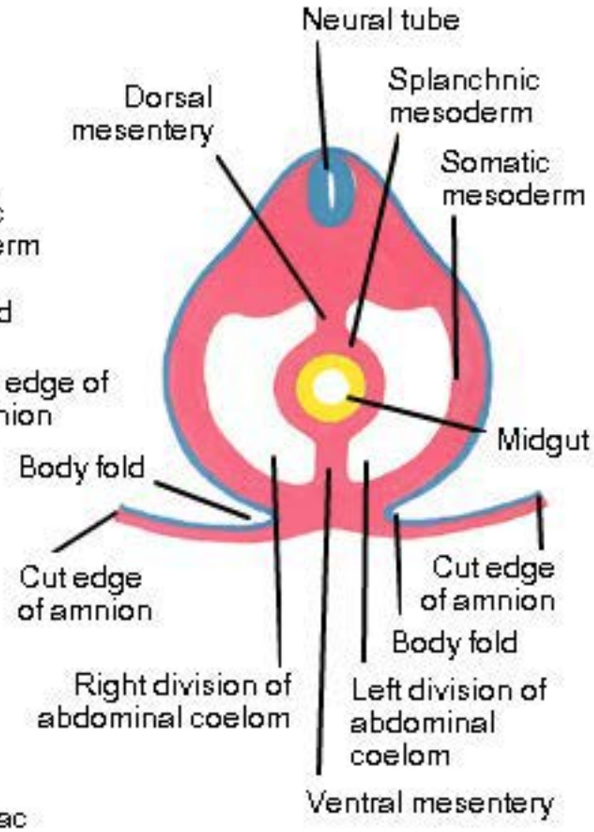
Formation of the Gut Tube and Mesenteries

18 days



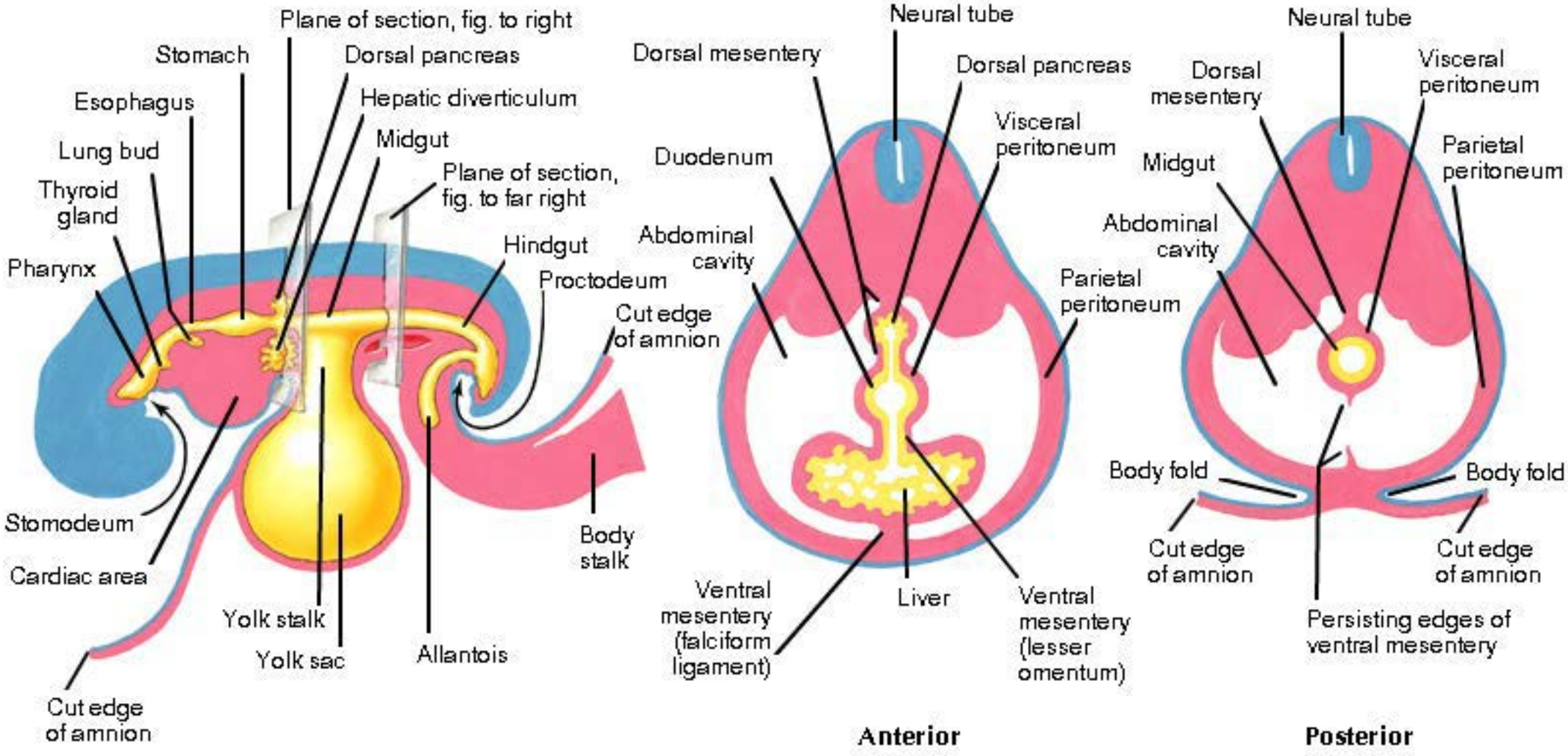


Sections



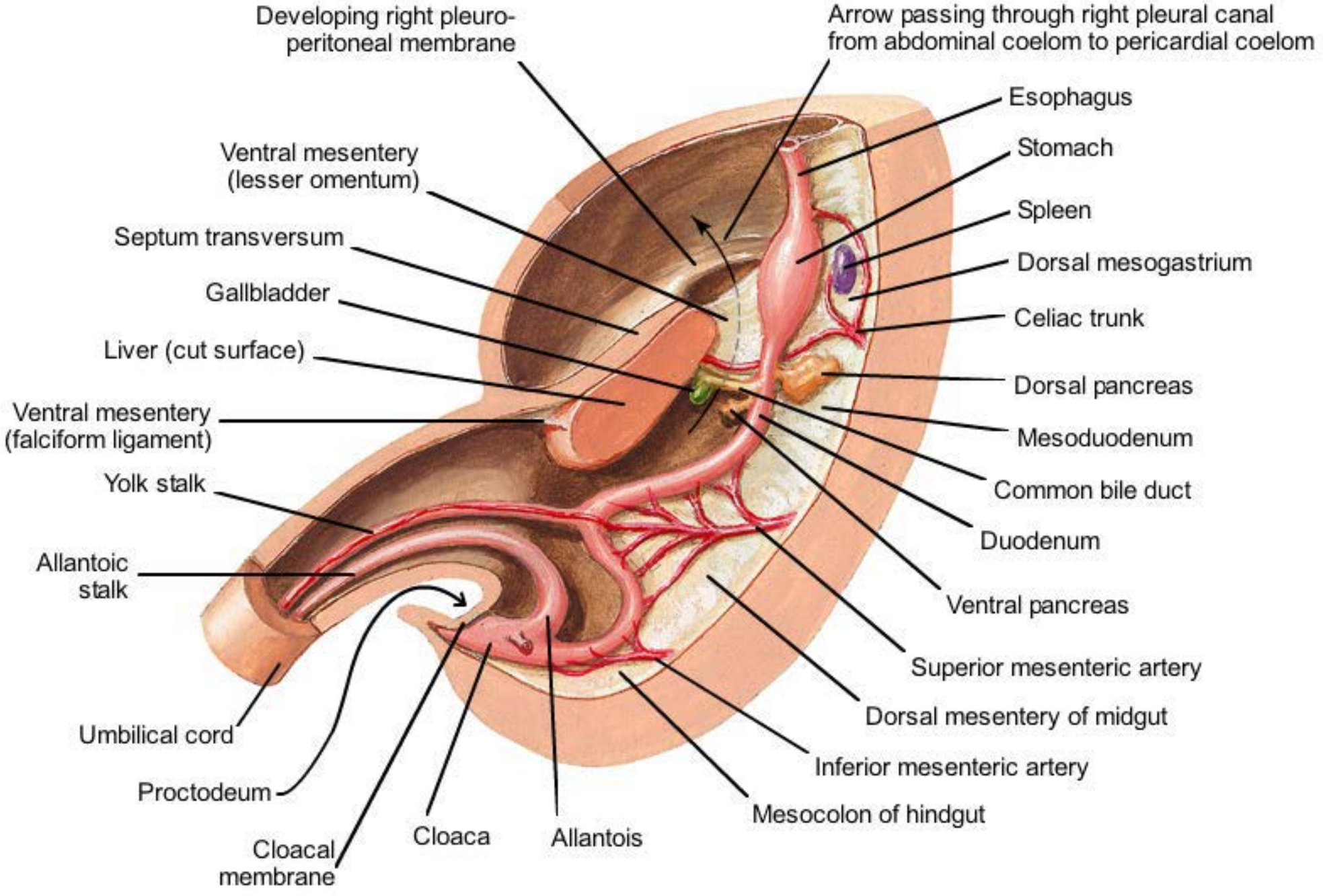
Formation of the Gut Tube and Mesenteries

1 month



Foregut, Midgut, and Hindgut

5 weeks



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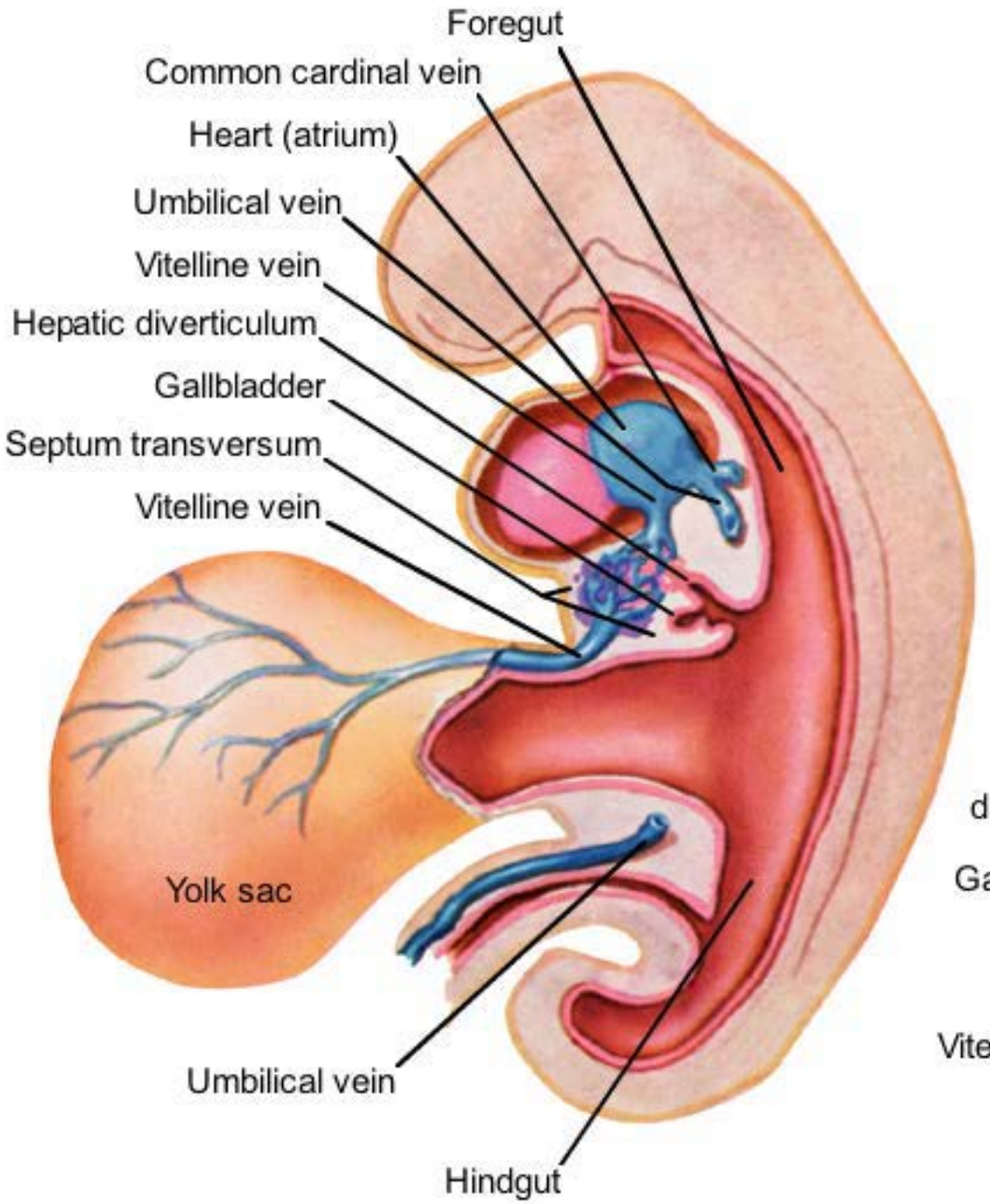
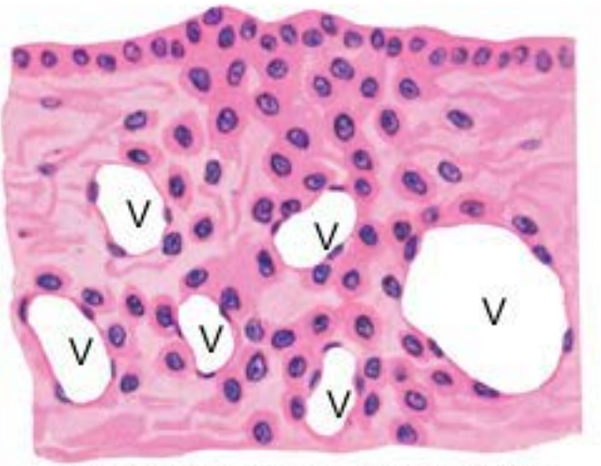
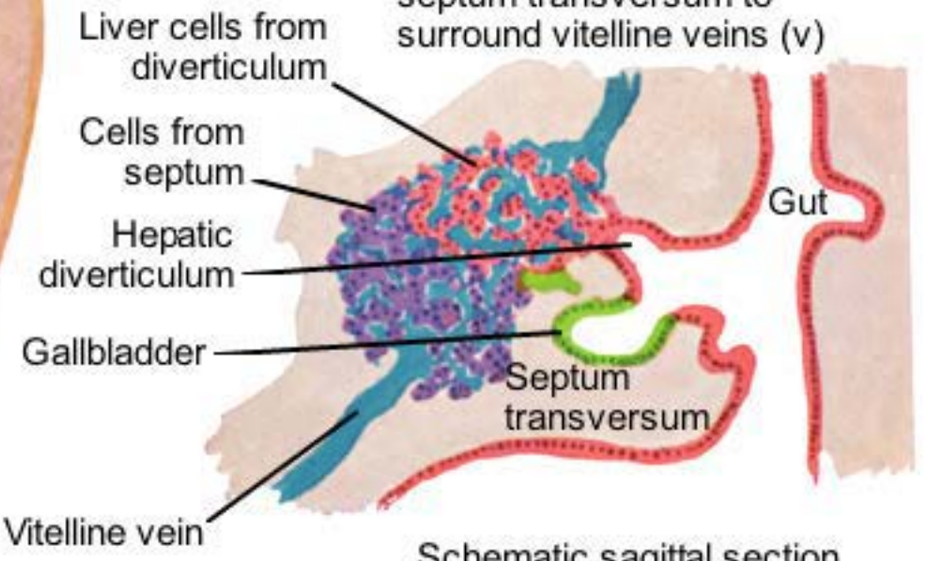
Abdominal Veins

Hepatic diverticulum in embryo of about 4-mm





Endodermal cells penetrating septum transversum to surround vitelline veins (v)



Schematic sagittal section of septum in 5-mm embryo

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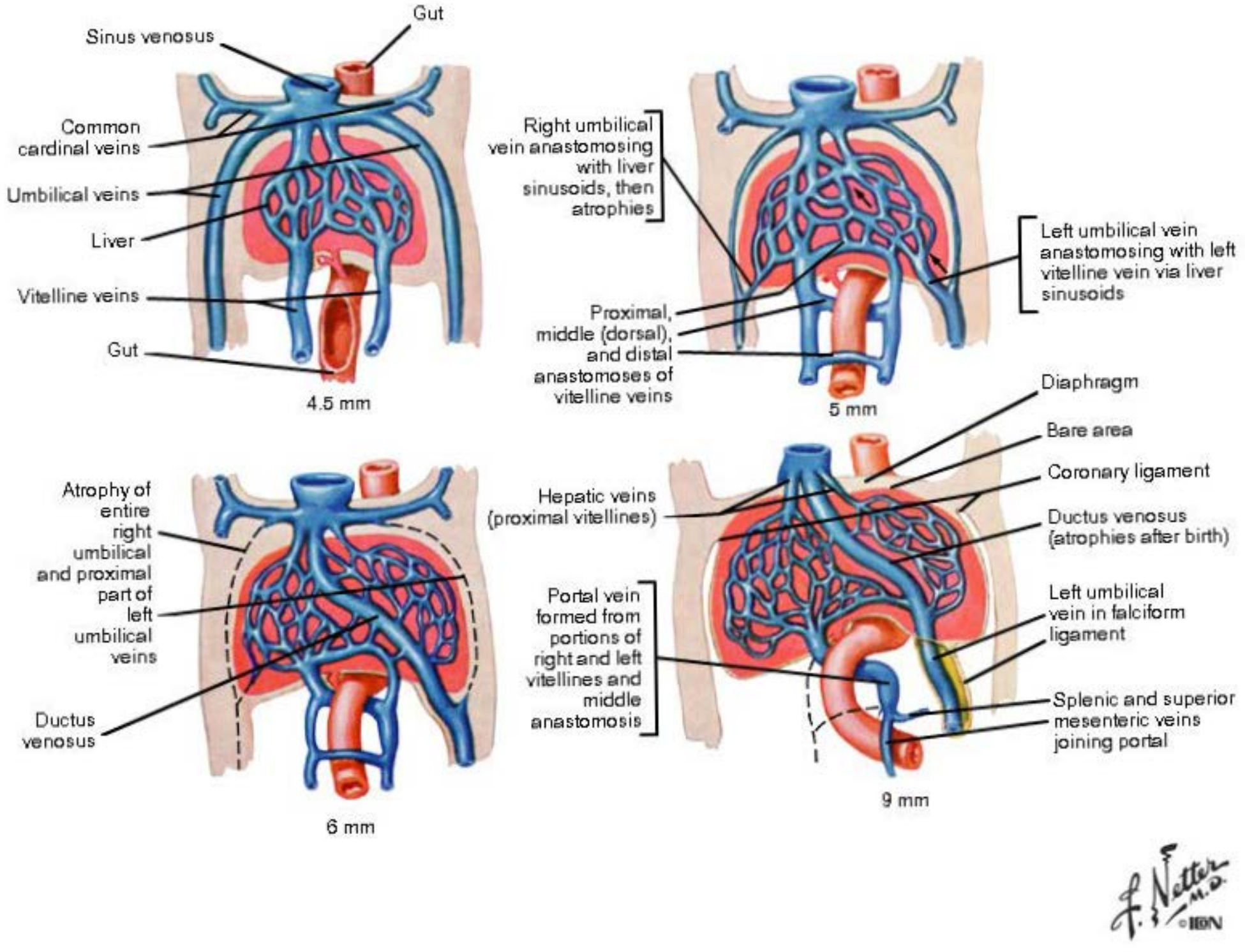
Abdominal Veins

Development of liver veins



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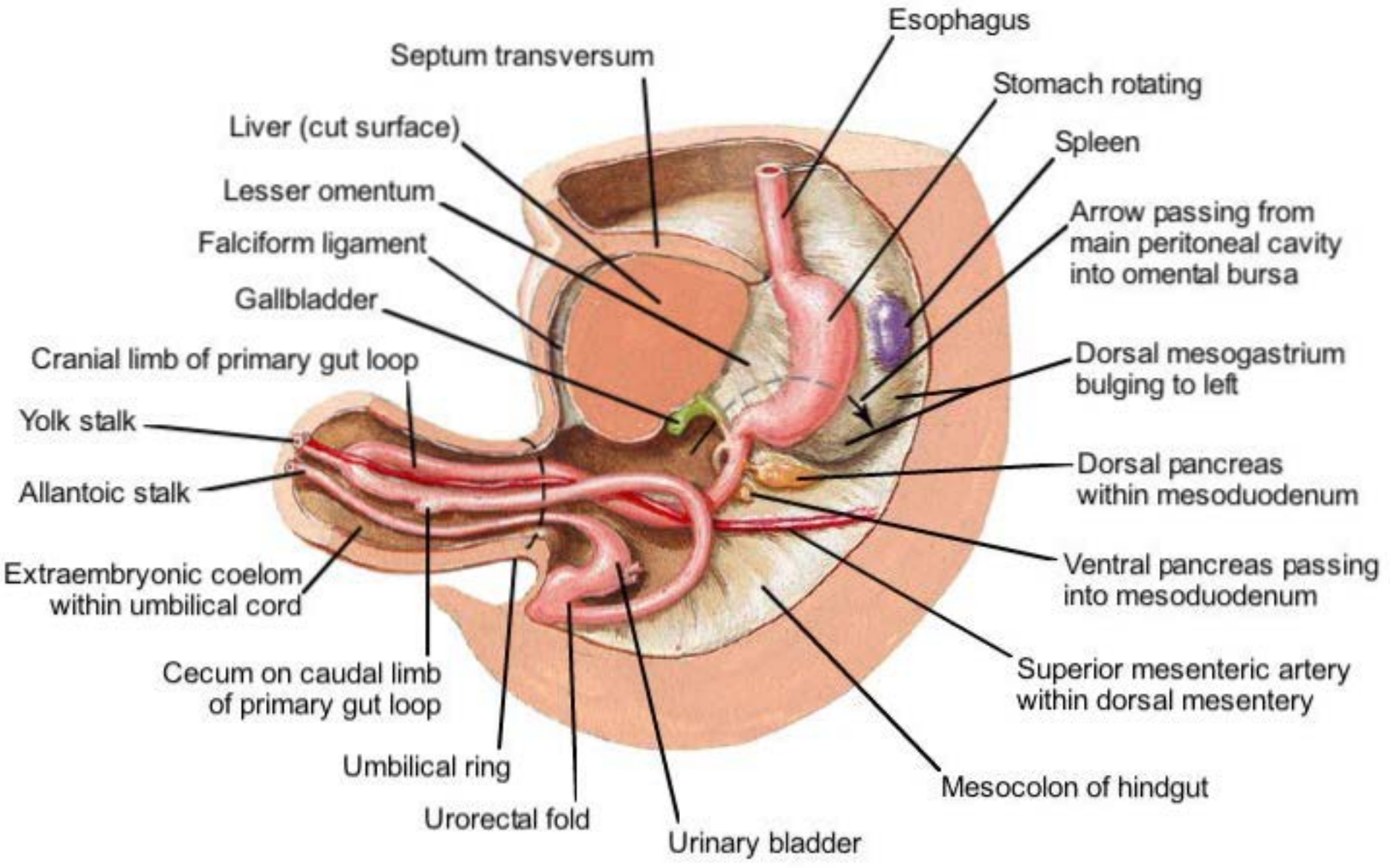
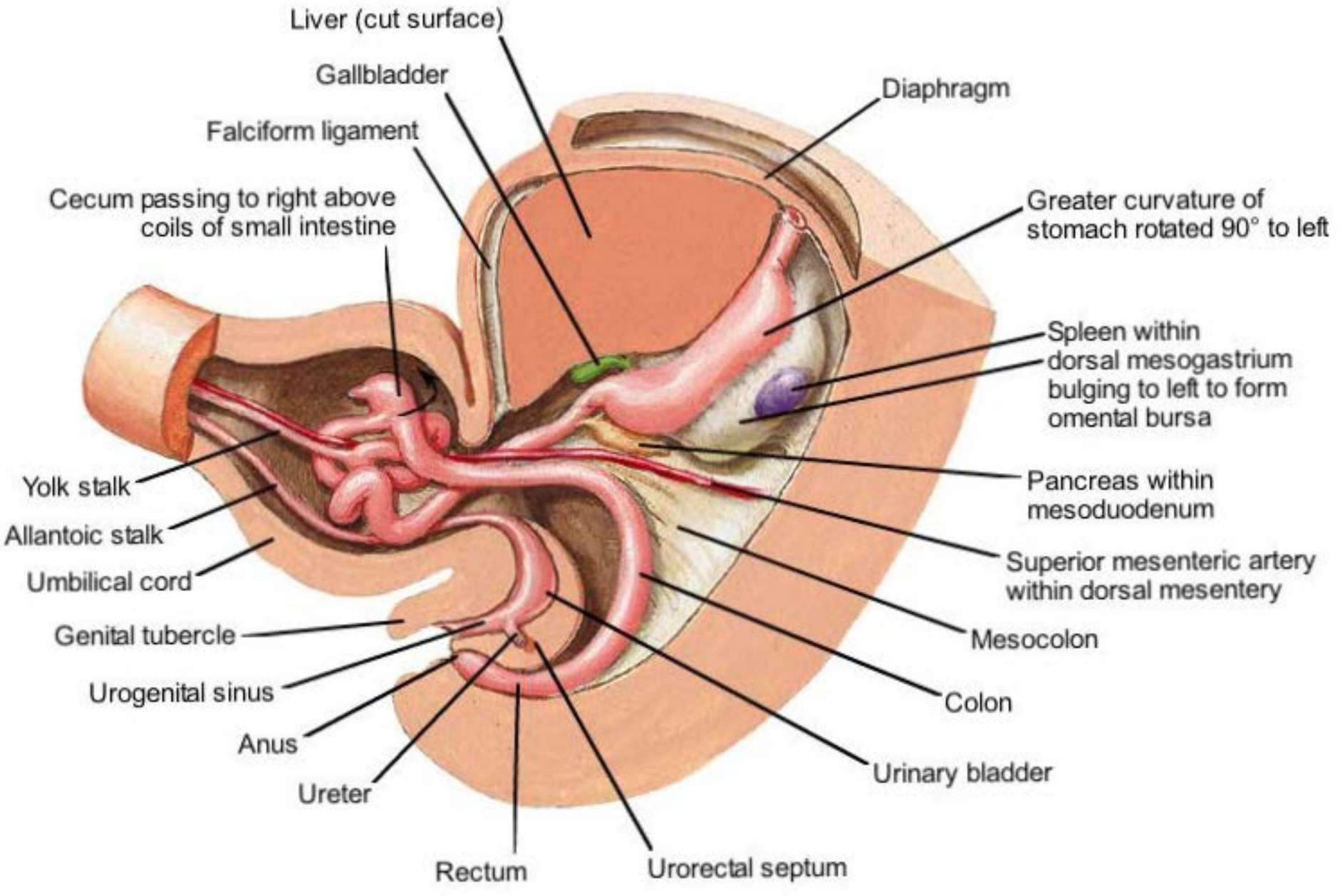
Foregut and Midgut Rotations

6 weeks



Foregut and Midgut Rotations

8 weeks



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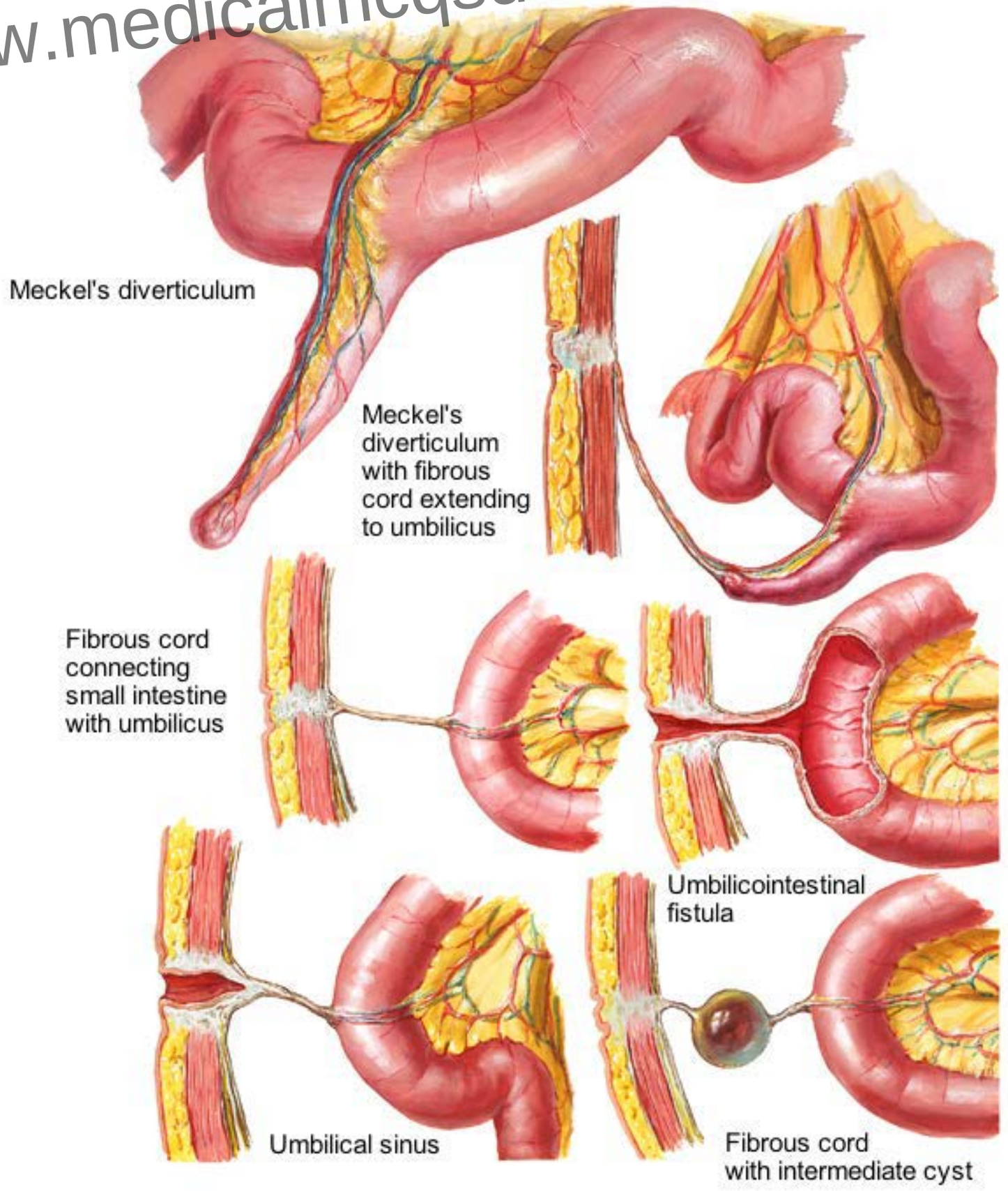
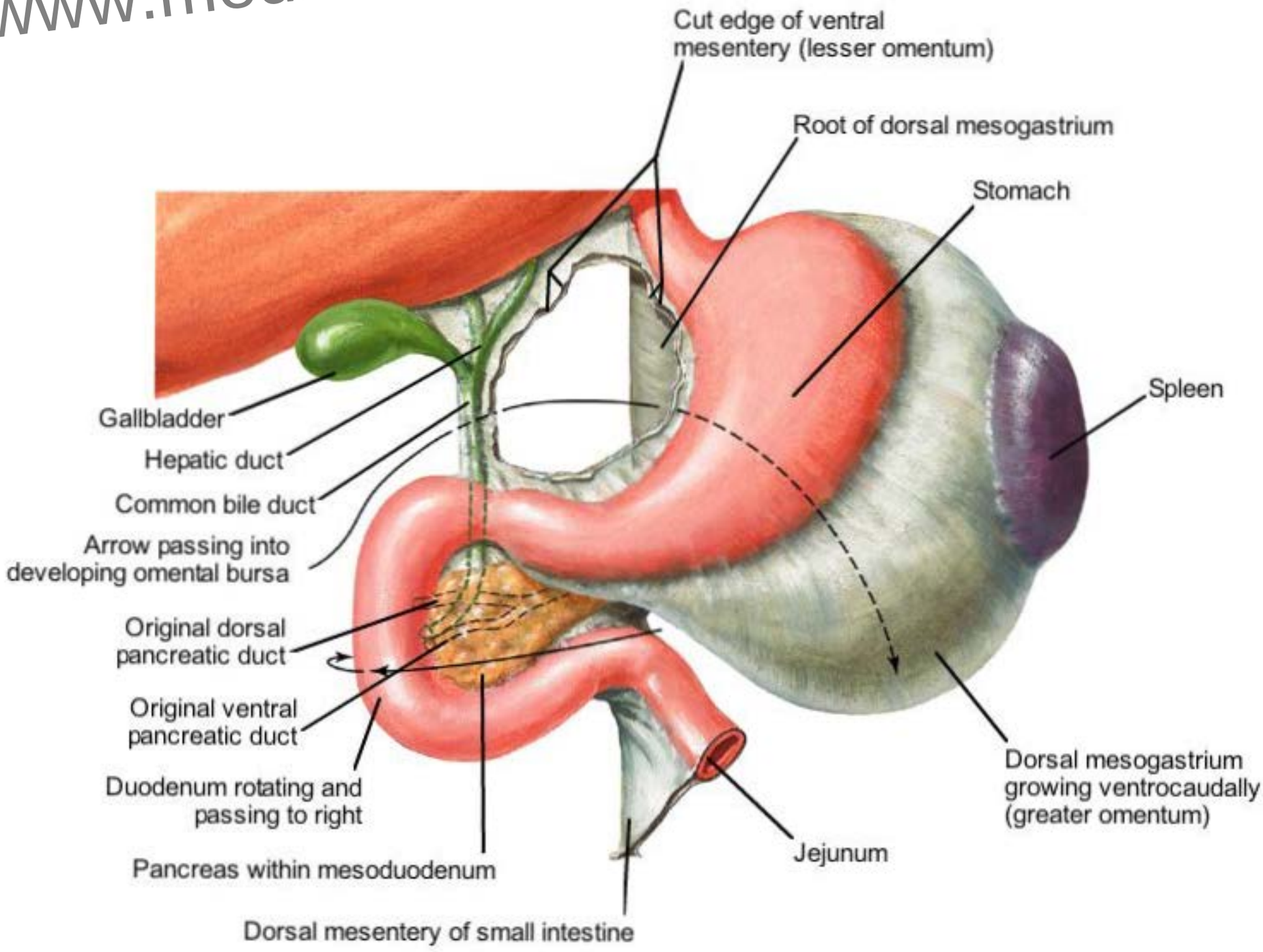
Merkel's Diverticulum



Lesser Peritoneal Sac

2 months



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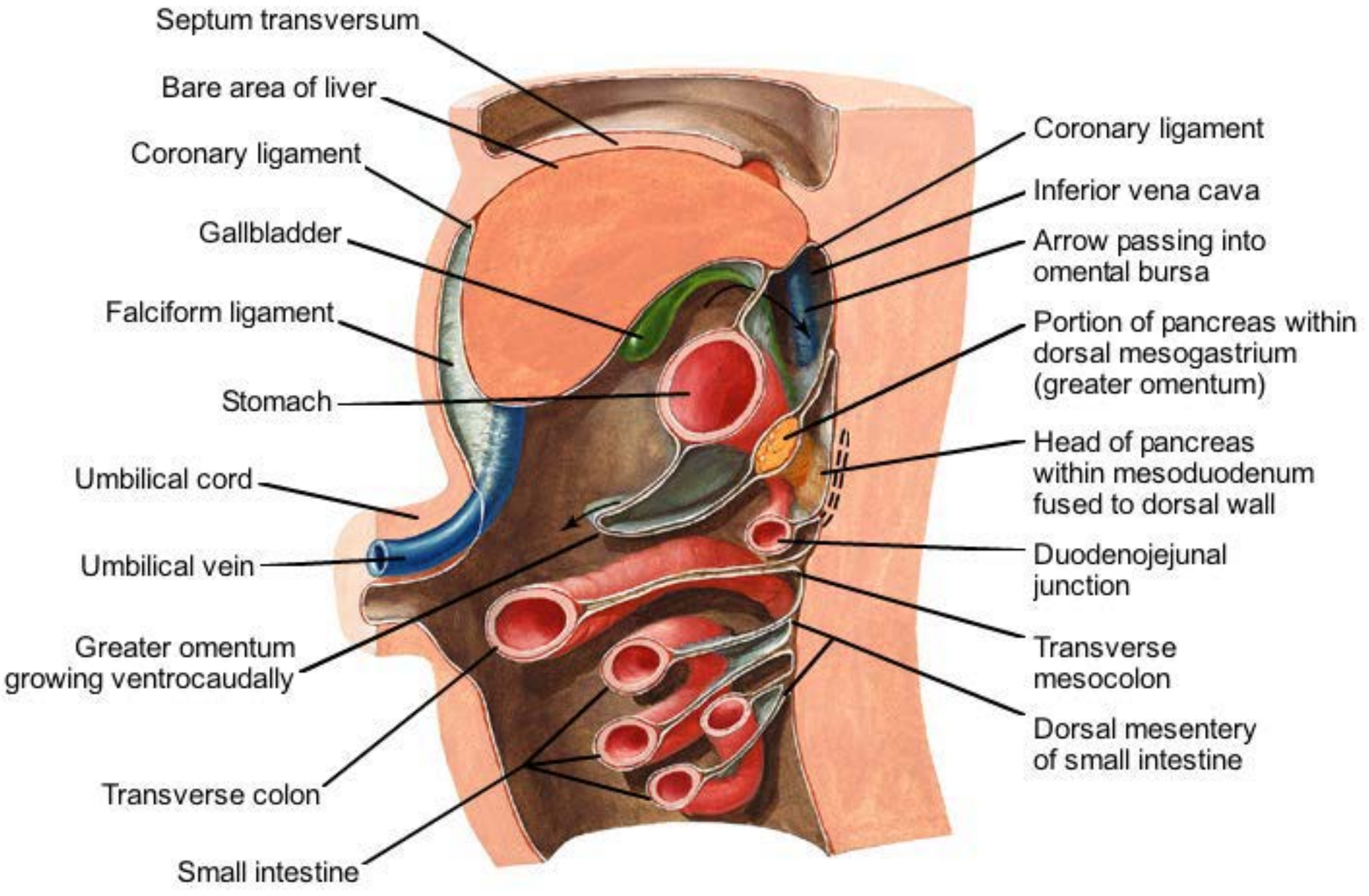
Lesser Peritoneal Sac

2 to 3 months



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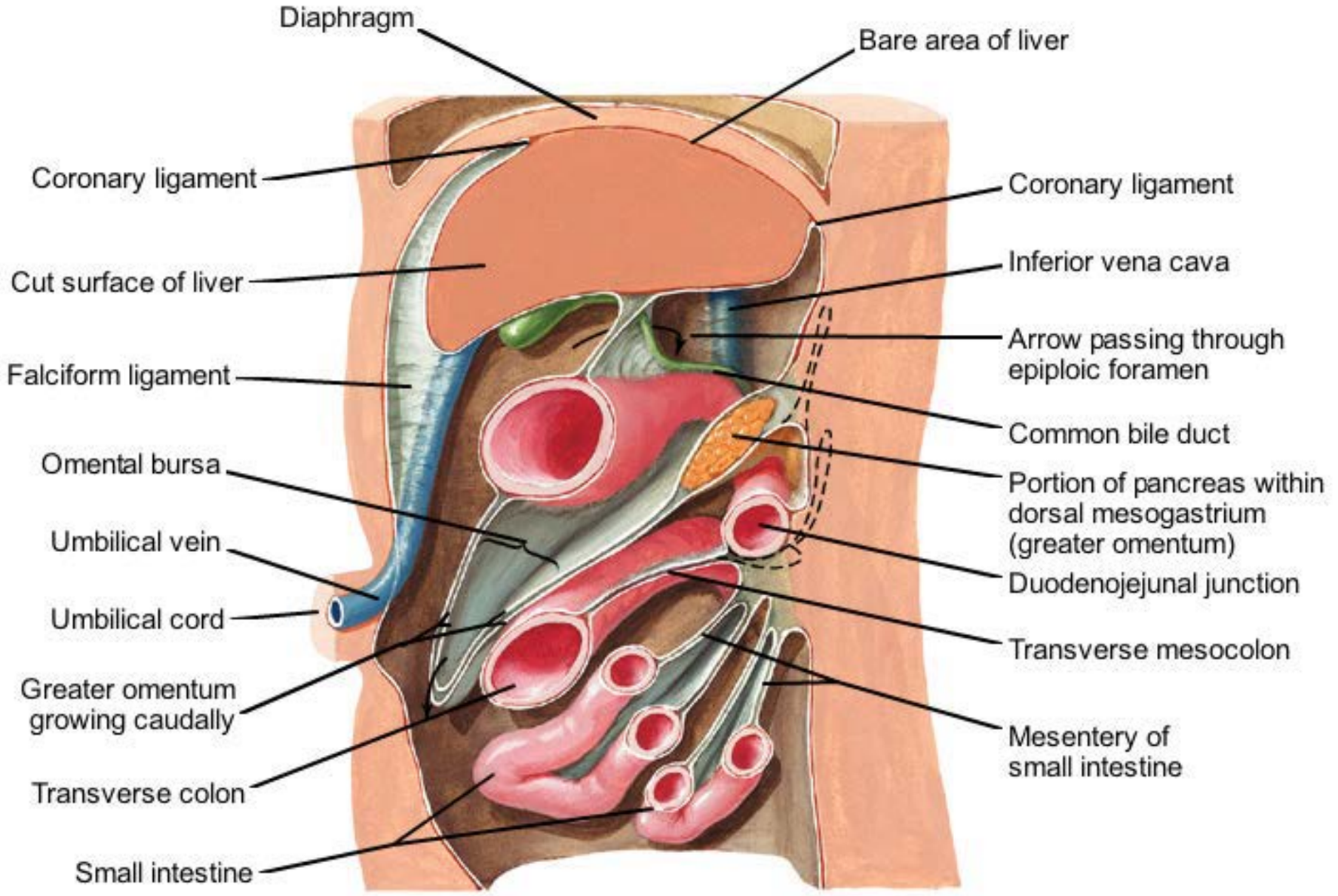
Introduction to the Retroperitoneal Concept

3 to 4 months



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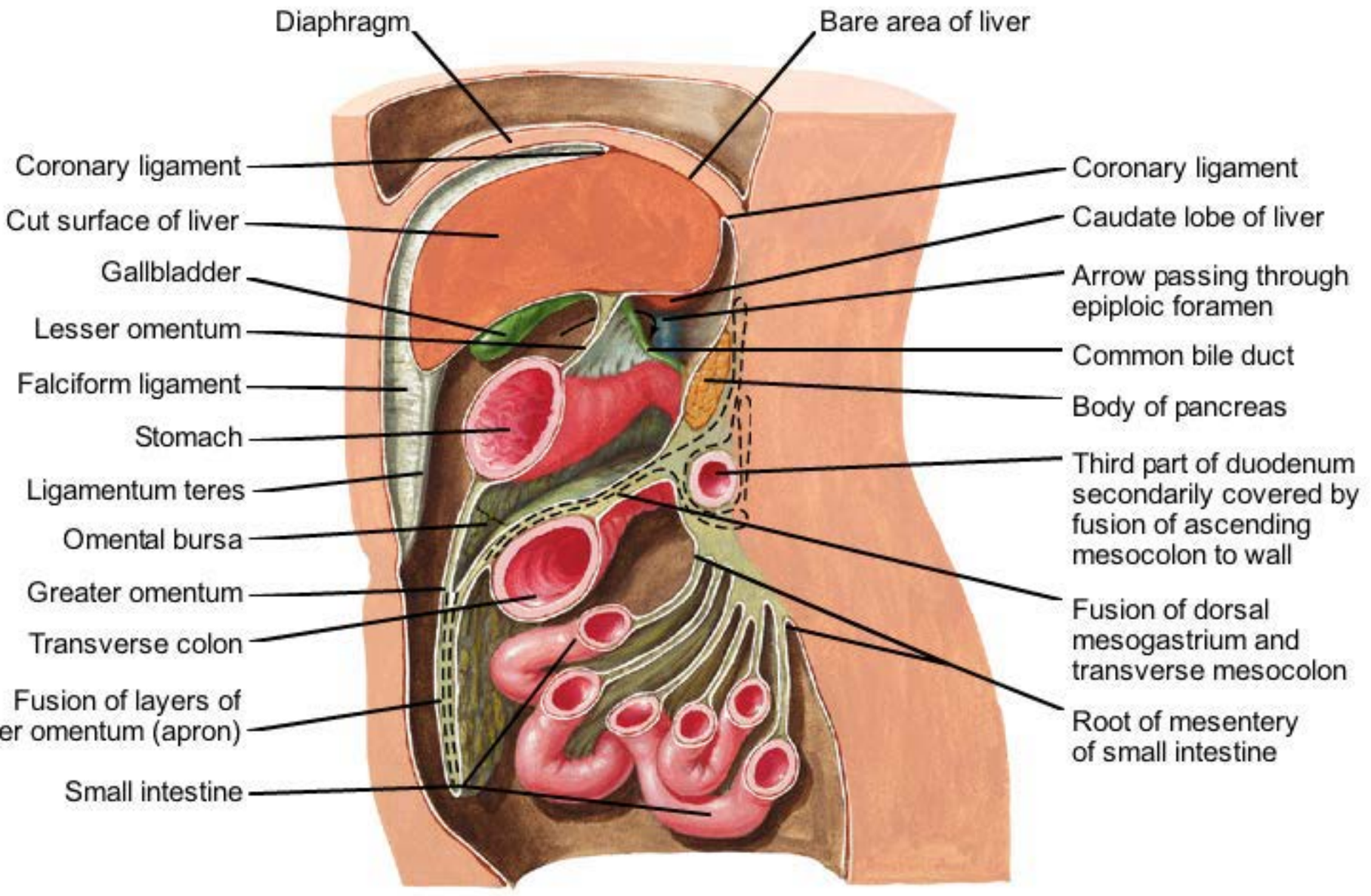
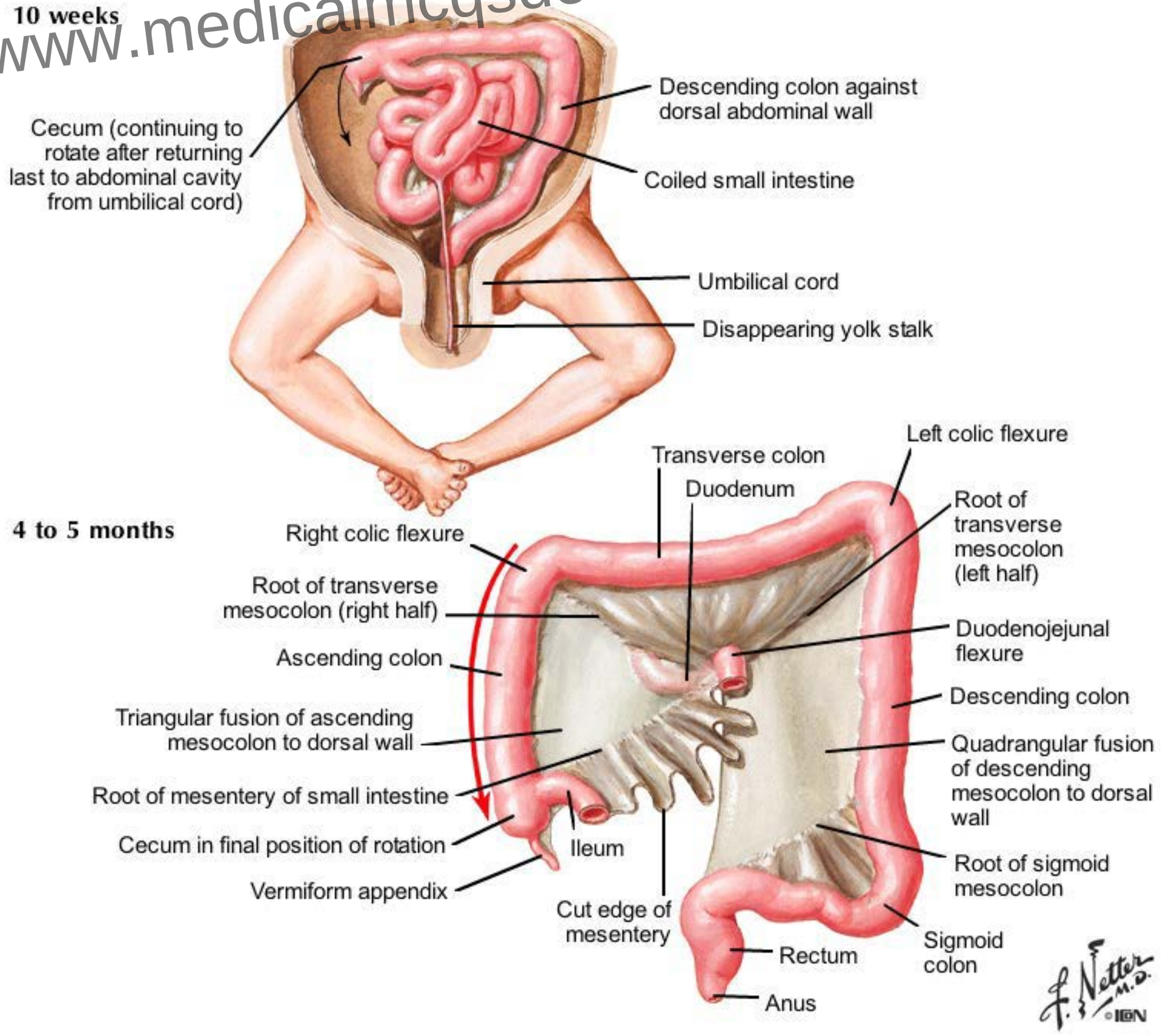
Introduction to the Retroperitoneal Concept

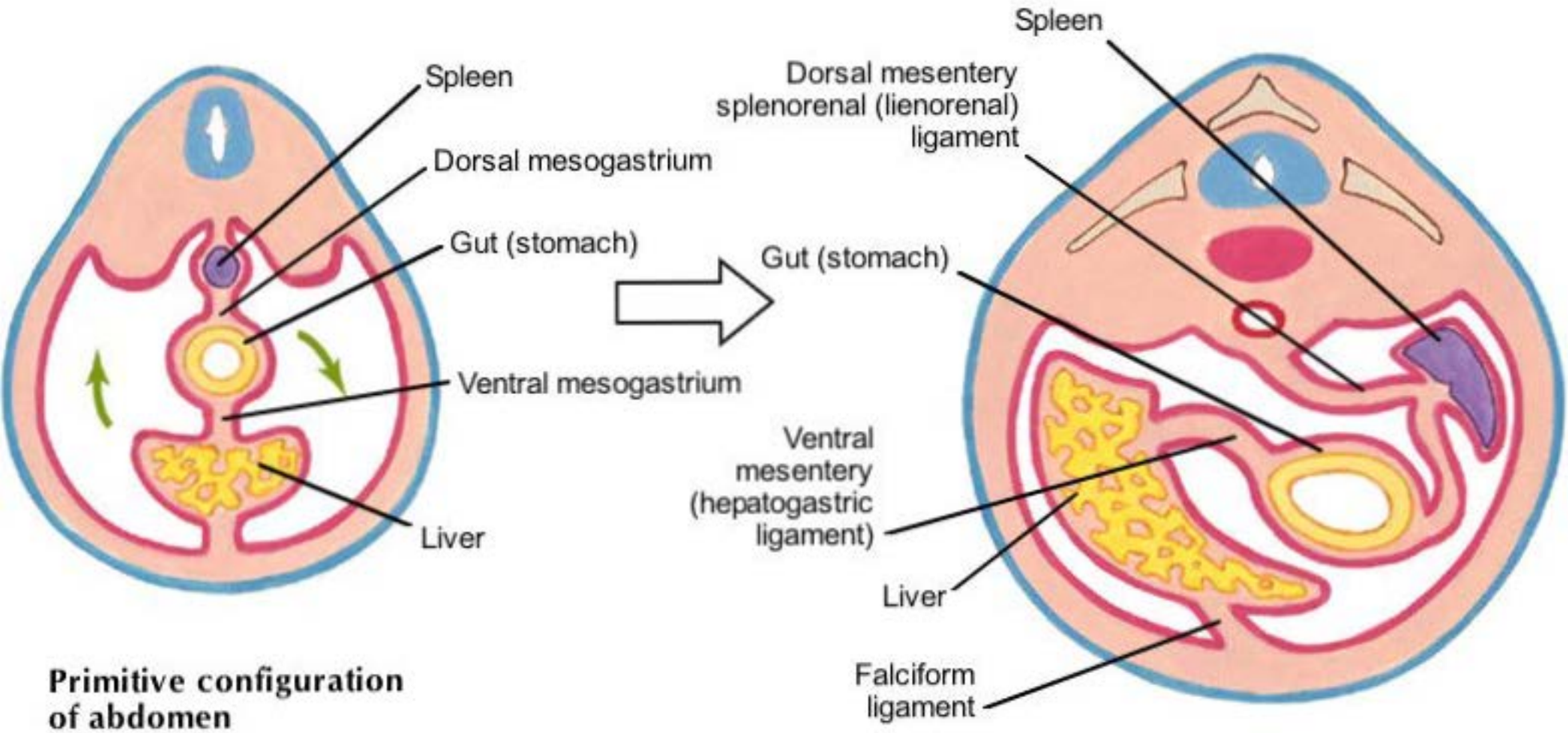
Adult relationships



Midgut Loop



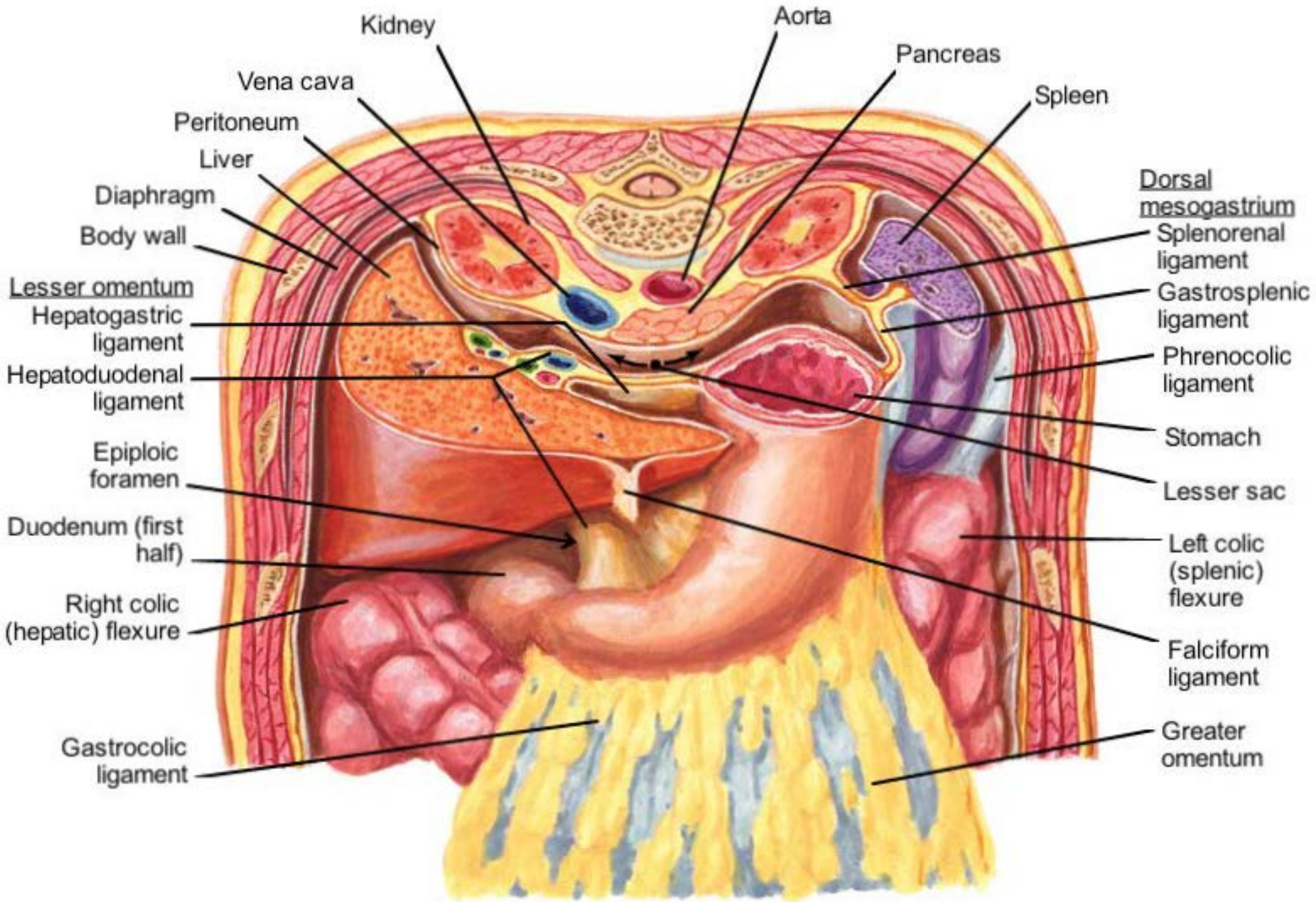
Abdominal Ligaments



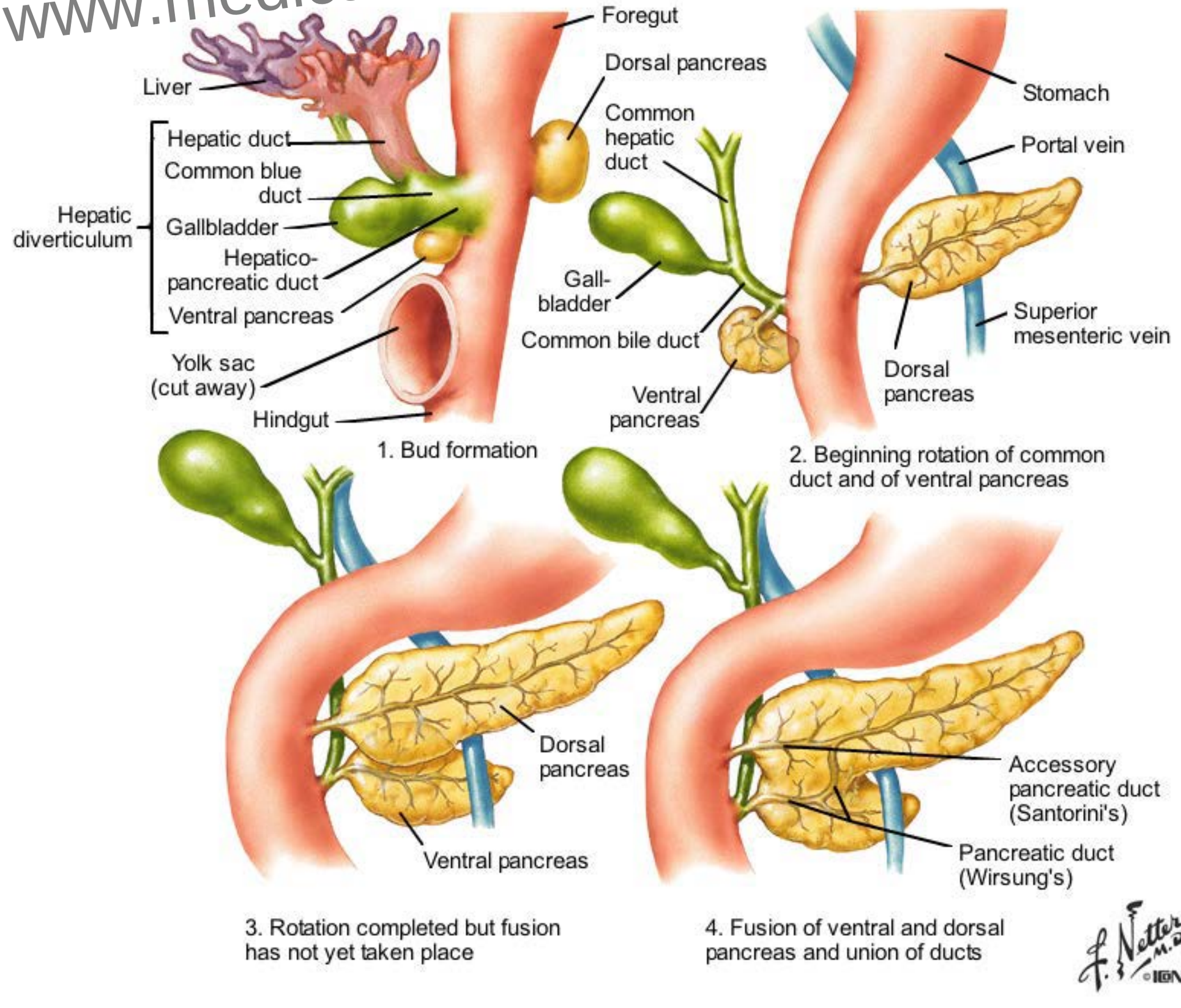
Primitive configuration of abdomen

Configuration of abdominal organs and mesenteries after gut rotation

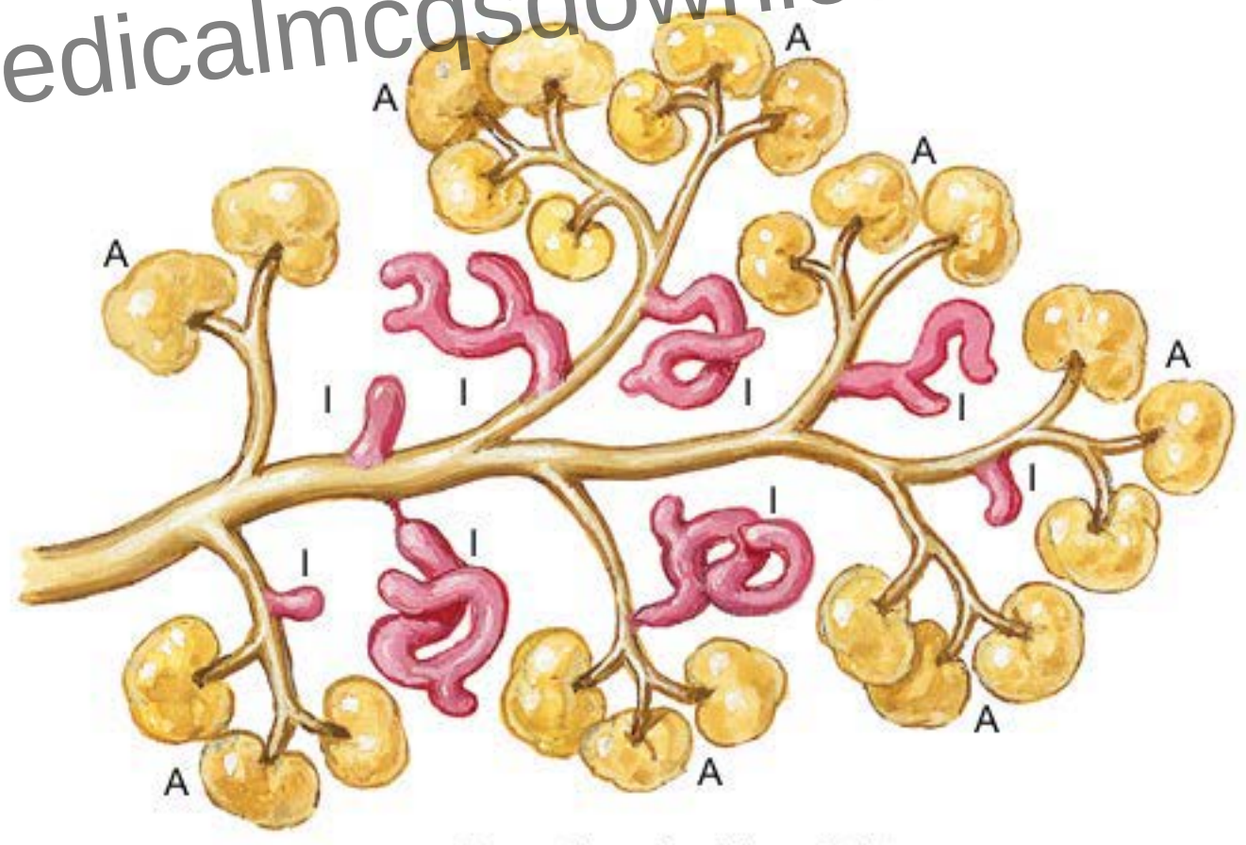
Abdominal Ligaments



Abdominal Foregut Organ Development



Development of Pancreatic Acini and Islets



Formation of acini and islets from ducts. **A**-acini; **I**-islets in various stages of development

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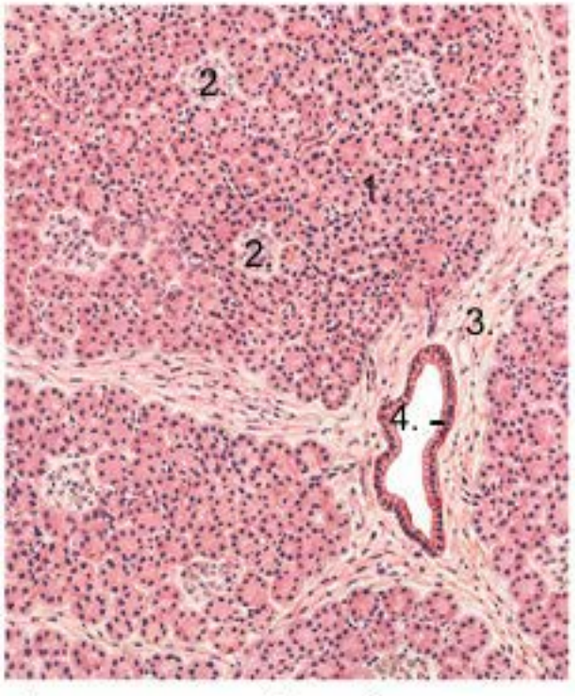
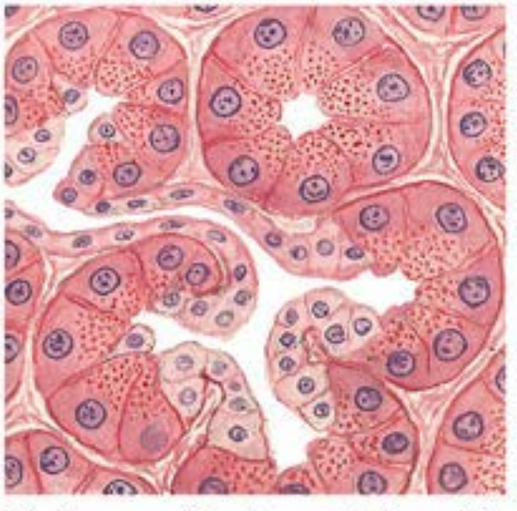
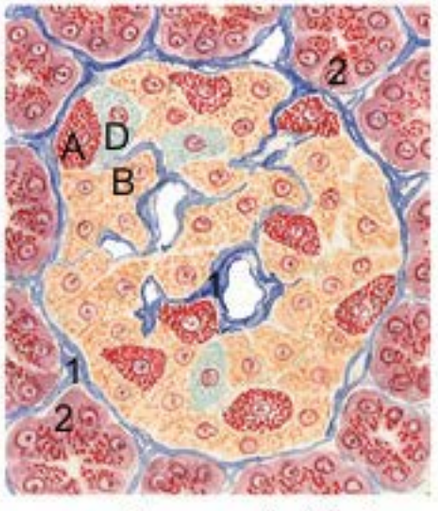


Low-power section of pancreas
1. Acini, **2**. islet, **3**. interlobular septum, **4**. interlobular duct

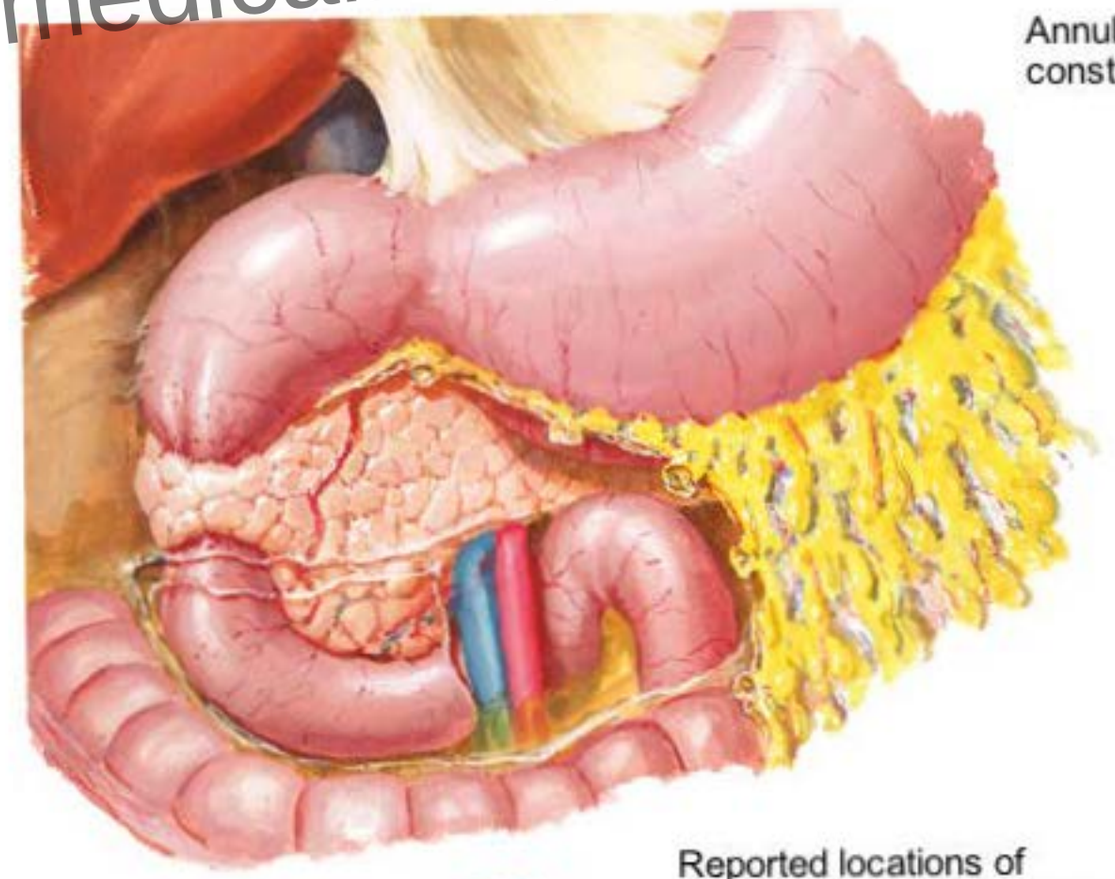


High magnification: relationship of intercalated duct and centroacinar cells to acini

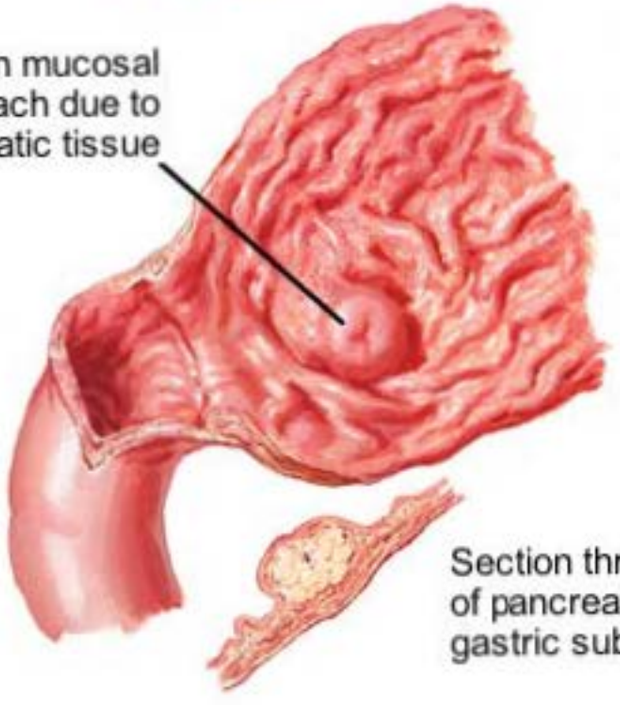


Pancreatic islet
A (=α-), **B** (=ß-) and **D**-cells.
1. reticulum, 2. acini

Congenital Pancreatic Anomalies



Annular pancreas constricting duodenum

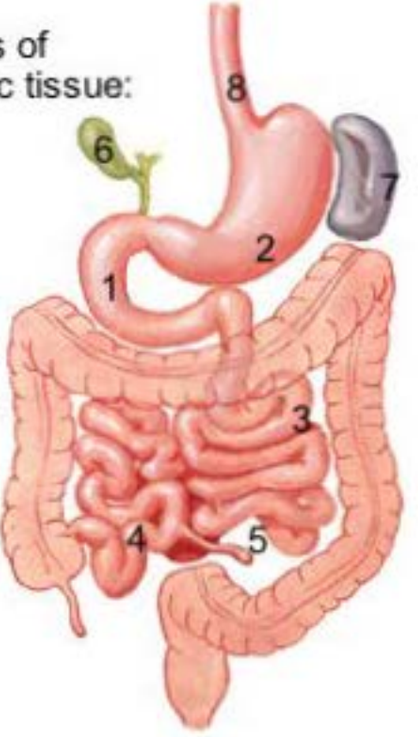


Nodule on mucosal aspect of stomach due to aberrant pancreatic tissue

Section through nodule of pancreatic tissue in gastric submucosa

Reported locations of aberrant pancreatic tissue:

1. Duodenum
2. Stomach
3. Jejunum
4. Ileum
5. Meckel's diverticulum
6. Gallbladder
7. Splenic capsule
8. Esophagus



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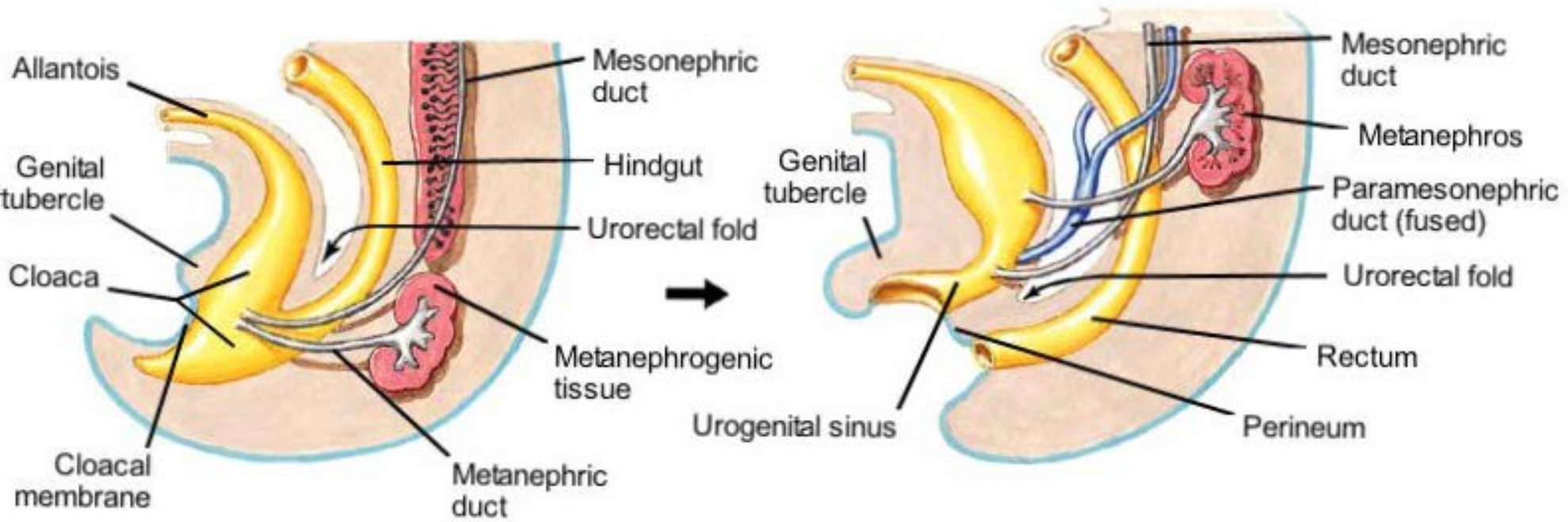
Development of the Hindgut



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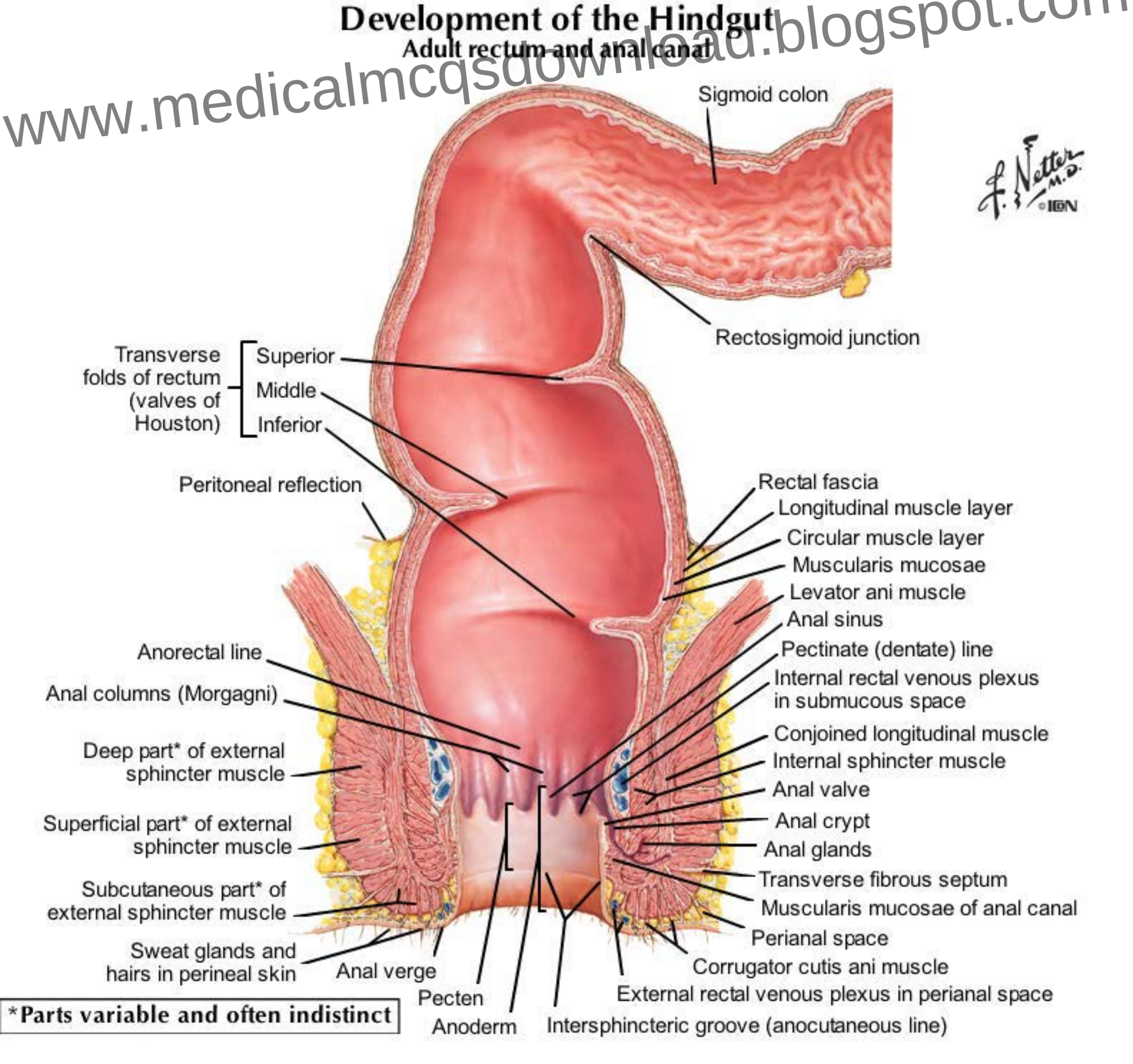
Development of the Hindgut

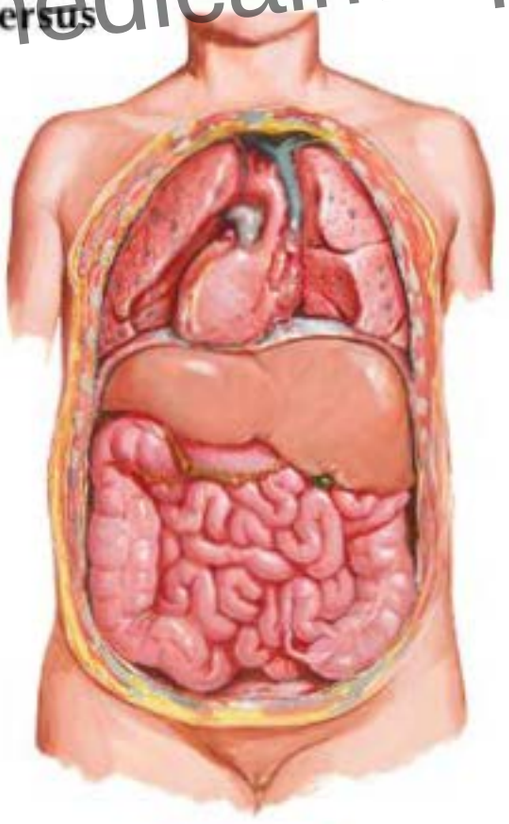
Adult rectum and anal canal



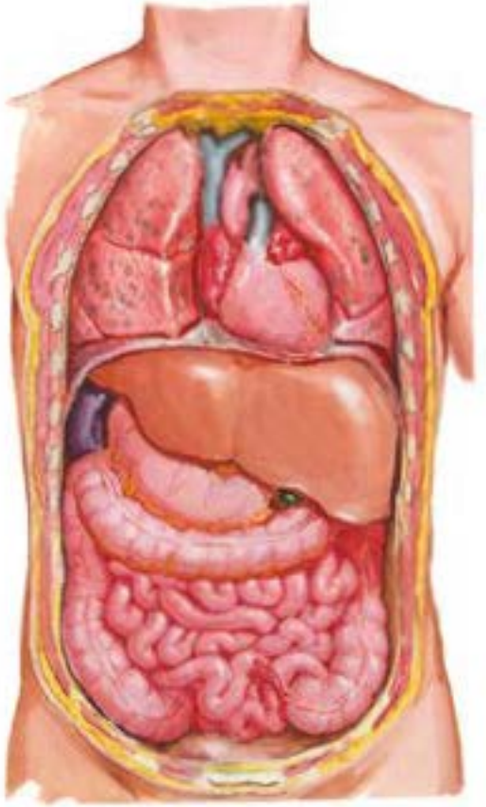
*Parts variable and often indistinct

Congenital Anomalies

Situs inversus



Complete situs inversus



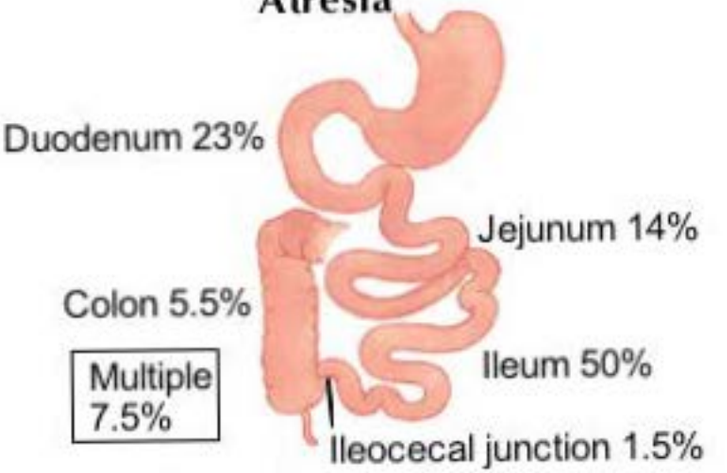
Partial situs inversus

Duplications

Locations of alimentary tract duplications (*indicates most common sites)

- Base of tongue
- Esophagus* extending into thorax from duodenum or jejunum
- Stomach
- Duodenum
- Transverse colon (mesenterialized)
- Jejunum
- Cecum or ascending colon
- Ileocecal region*
- Ileum*
- Sigmoid colon
- Rectum

Atresia



Approximate regional incidence (gross)

Ends connected by cordlike structure

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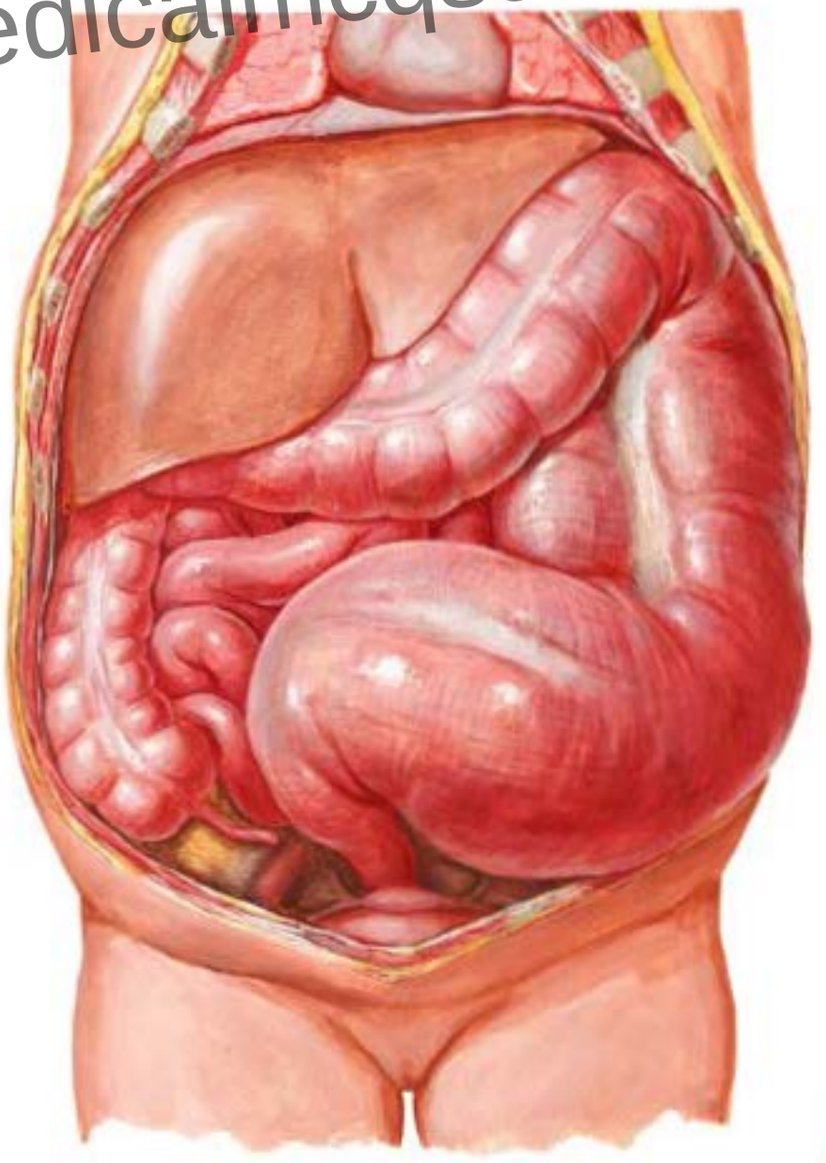
Congenital Anomalies

Megacolon (Hirschsprung's Disease)



Tremendous distention and hypertrophy of sigmoid and descending colon; moderate involvement of transverse colon; distal constricted segment

Typical abdominal distention

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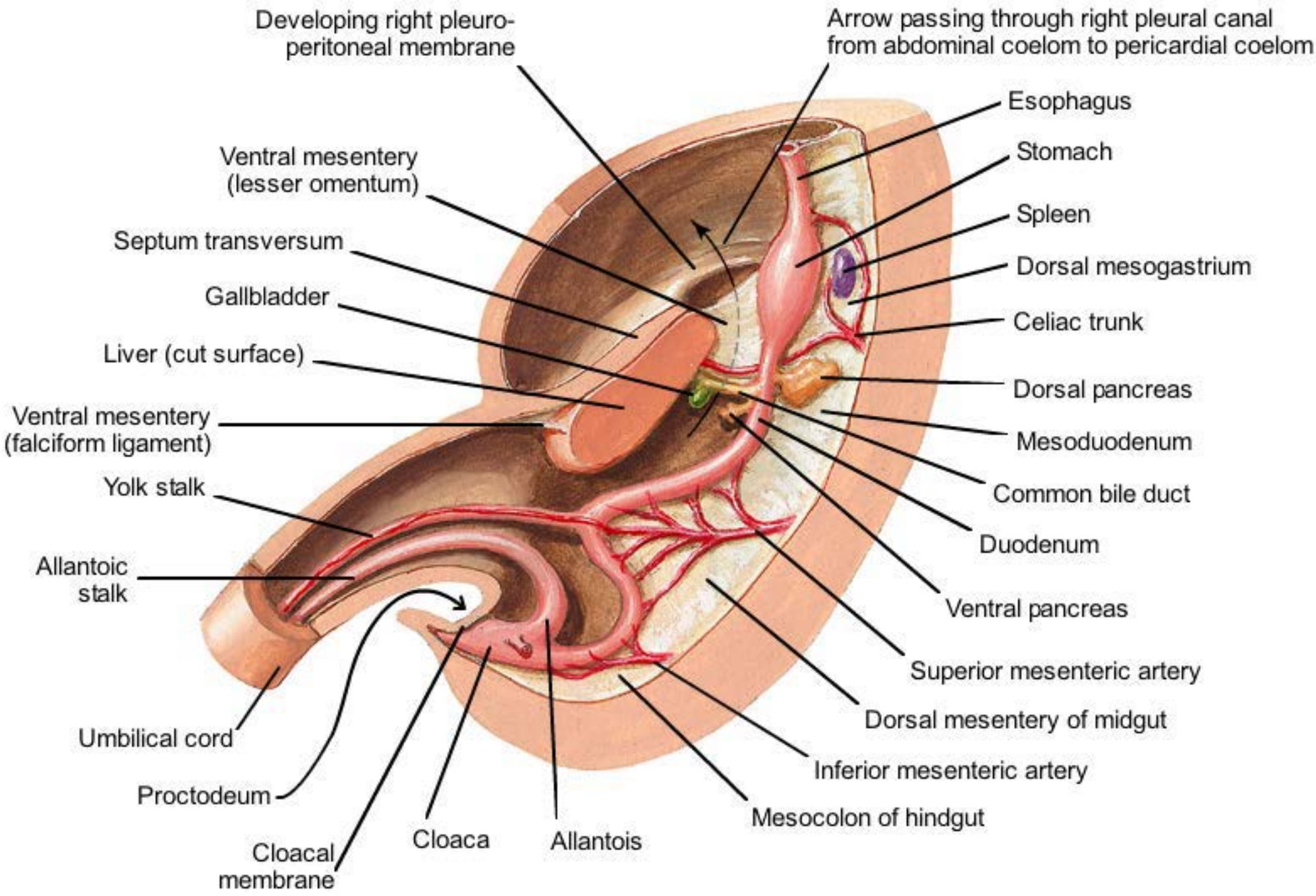
Summary of Gut Organization

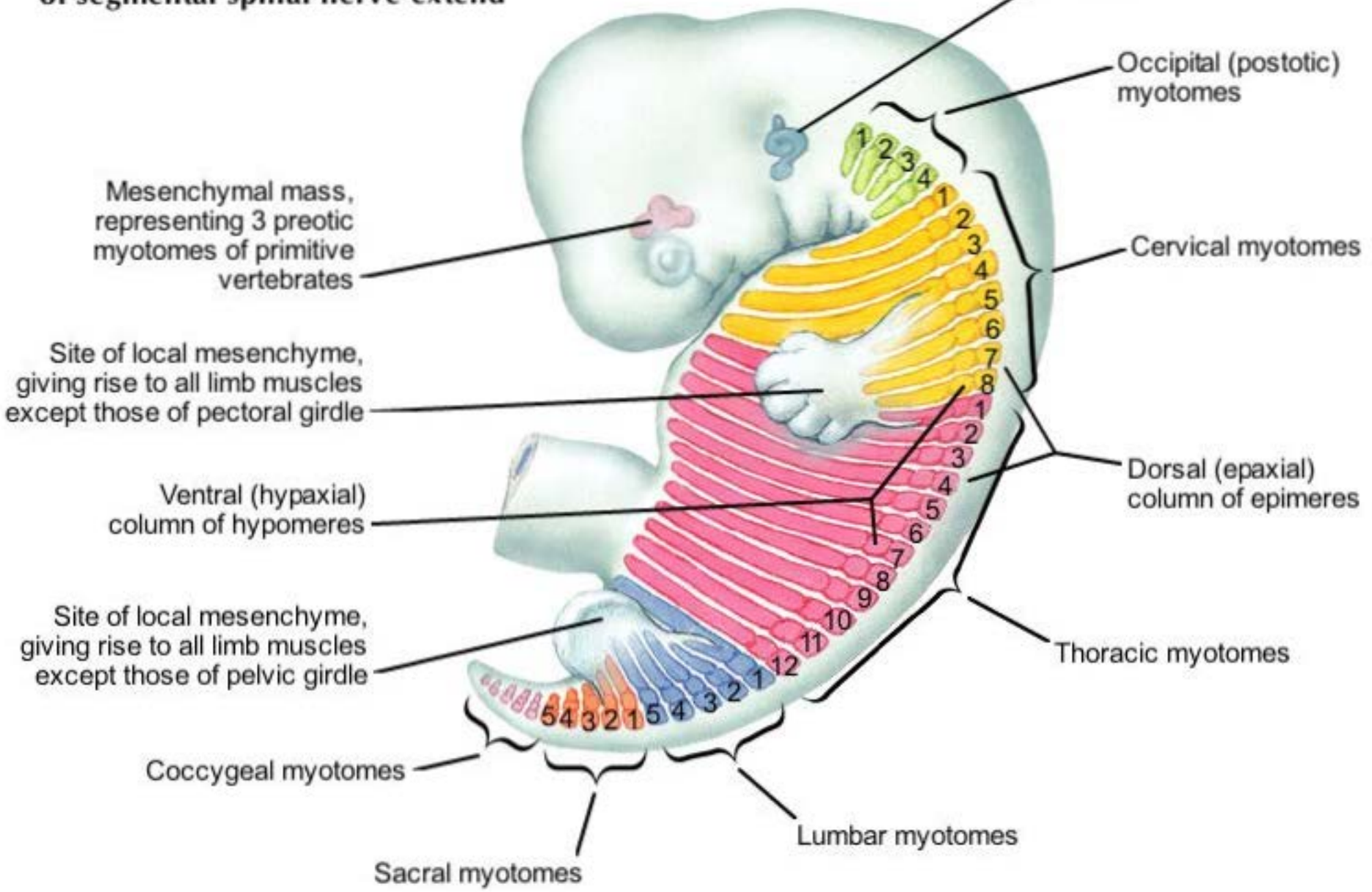
5 weeks



Development of the Abdominal Wall

Segmental distribution of myotomes in fetus of 6 weeks

Region of each trunk myotome also represents territory of dermatome into which motor and sensory fibers of segmental spinal nerve extend



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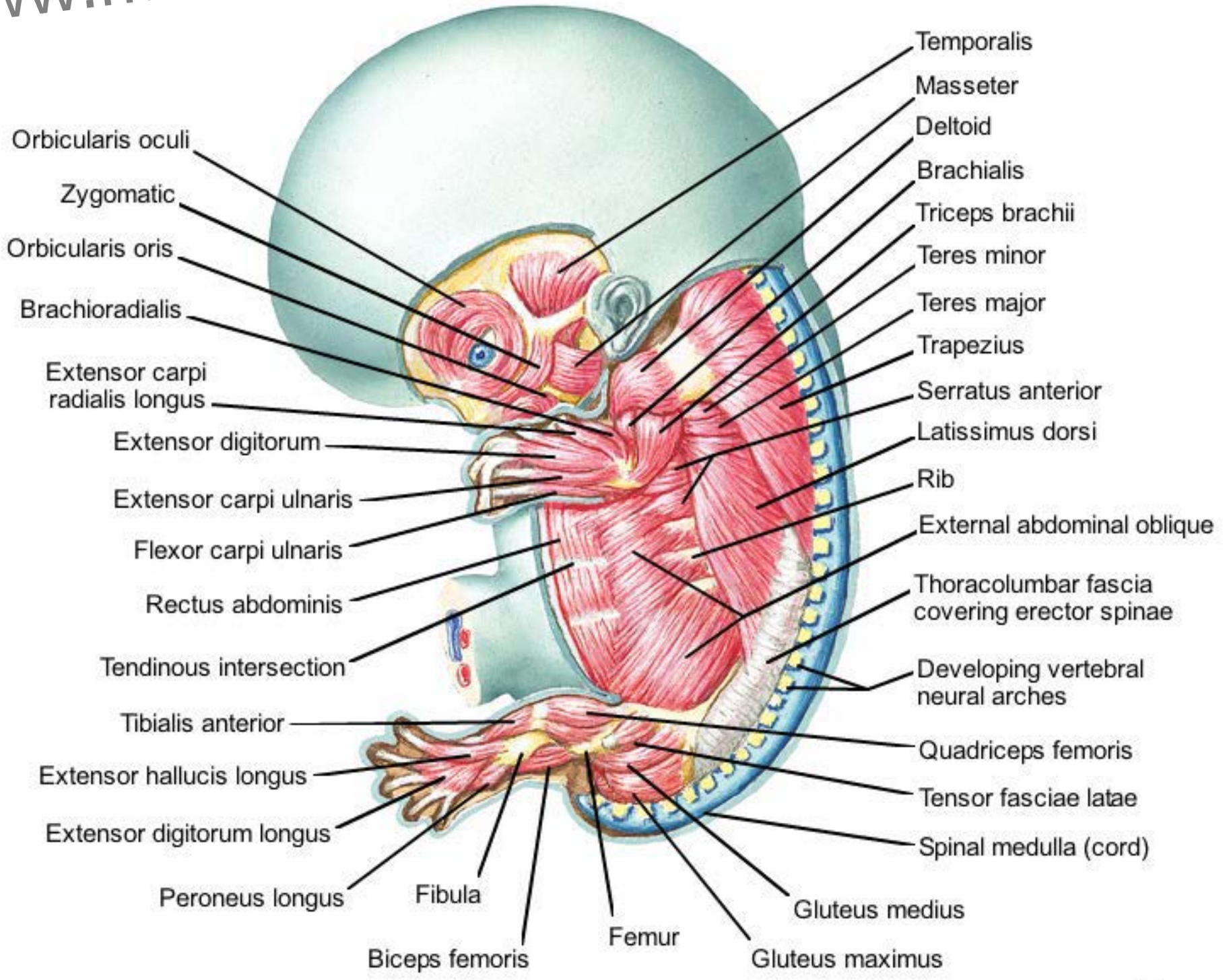
Development of the Abdominal Wall

Developing skeletal muscles at 8 weeks (superficial dissection)



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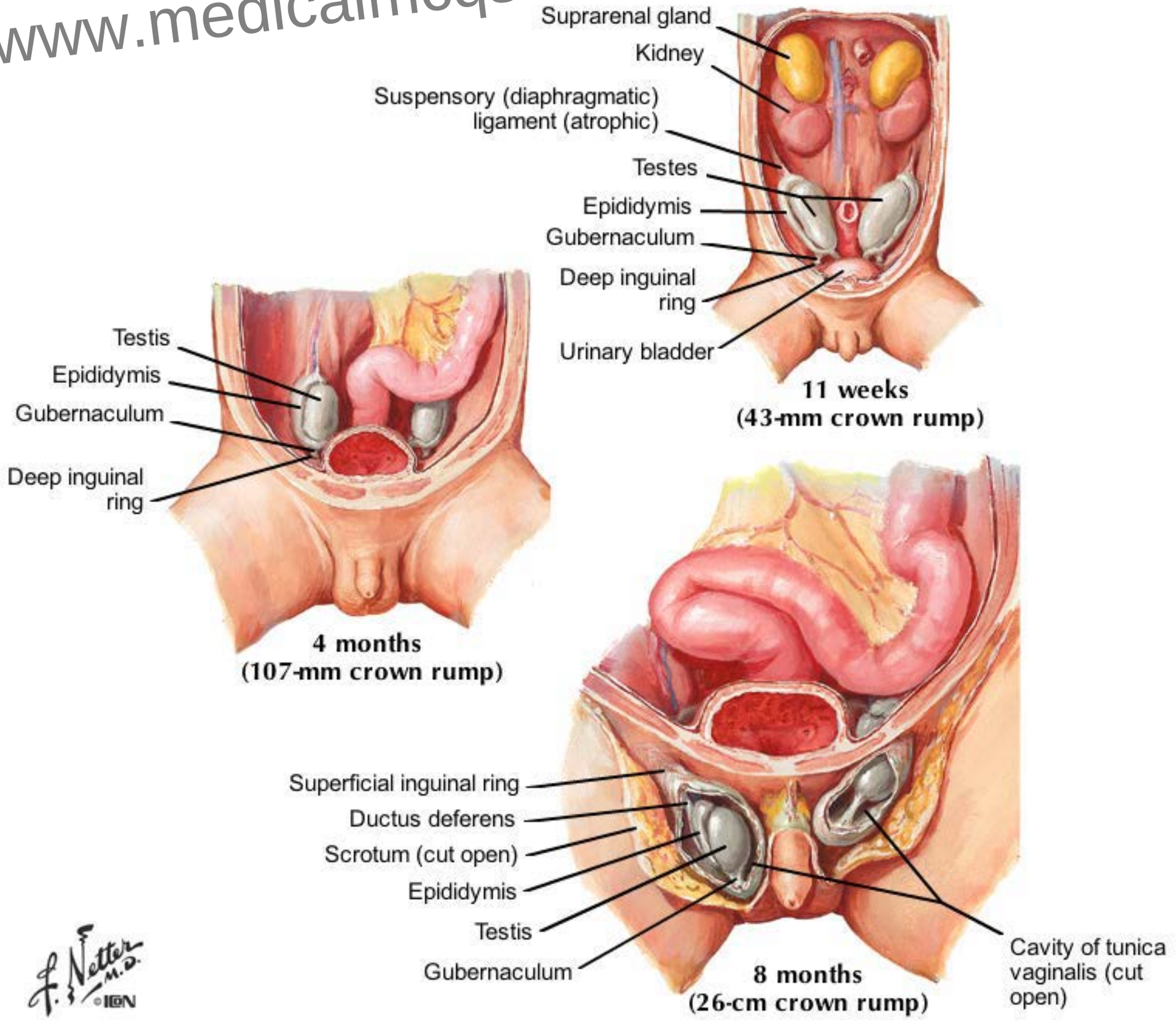
The Inguinal Region



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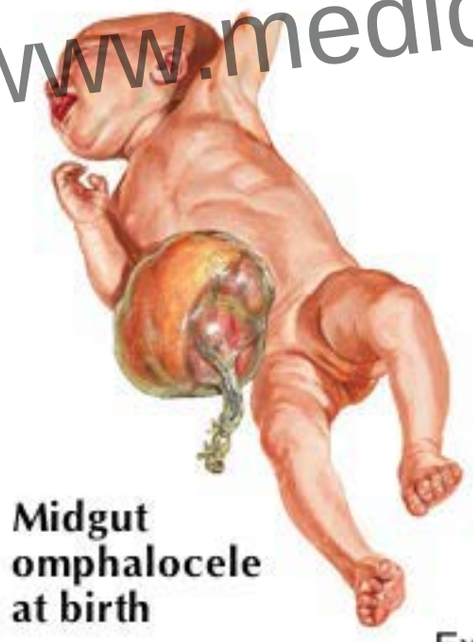
Umblical Hernia



Midgut omphalocele at birth

Midgut at 6 weeks in the umbilical cord

Septum transversum
Esophagus
Lesser omentum
Stomach rotating
Liver (cut surface)
Spleen
Falciform ligament
Arrow passing from main peritoneal cavity into omental bursa
Gallbladder
Cranial limb of primary gut loop
Yolk stalk
Pancreas within mesoduodenum
Allantoic stalk
Extraembryonic coelom within umbilical cord
Ventral pancreas passing into mesoduodenum
Cecum on caudal limb of primary gut loop
Superior mesenteric artery
Umbilical ring
Urorectal fold
Urinary bladder
Mesocolon of hindgut

Liver (cut surface)
Gallbladder
Falciform ligament
Cecum passing to right above coils of small intestine
Diaphragm
Greater curvature of stomach rotated 90° to left
Spleen
Yolk stalk
Pancreas within mesoduodenum
Allantoic stalk
Superior mesenteric artery
Umbilical cord
Mesocolon
Genital tubercle
Colon
Urogenital sinus
Urinary bladder
Anus
Ureter
Rectum
Urorectal septum

Midgut at 2 months in the umbilical cord

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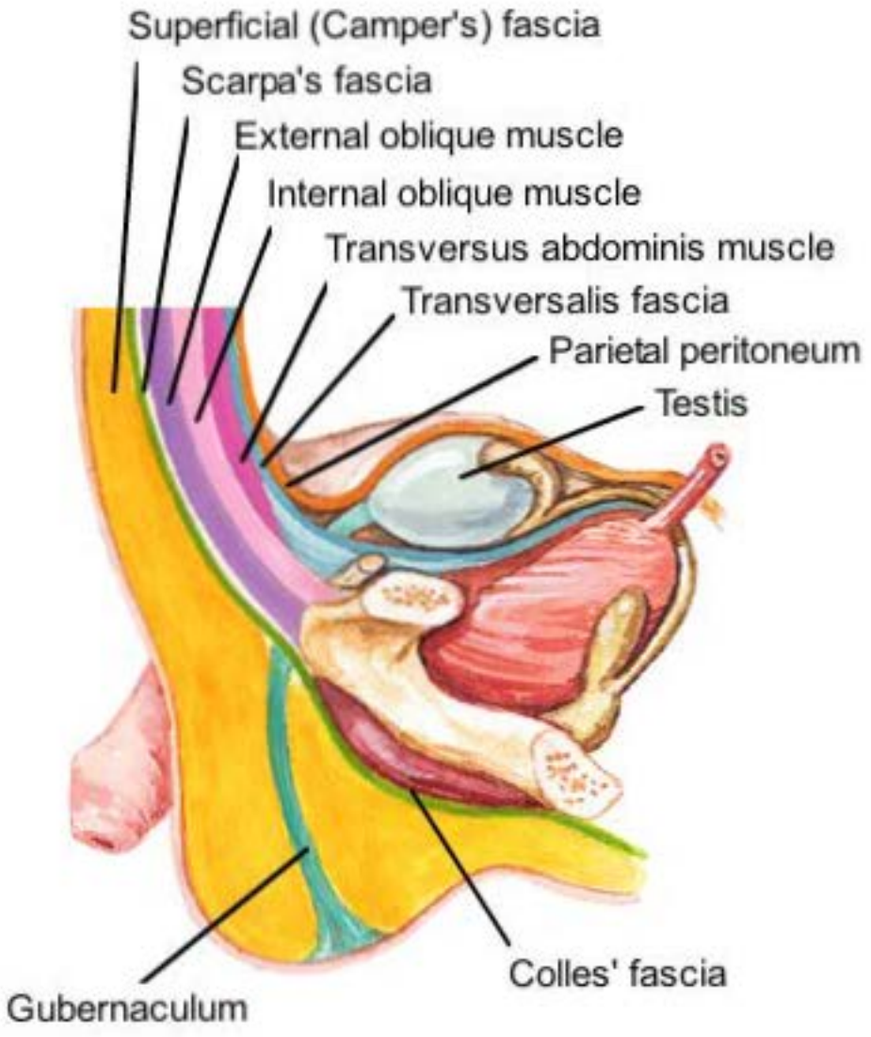
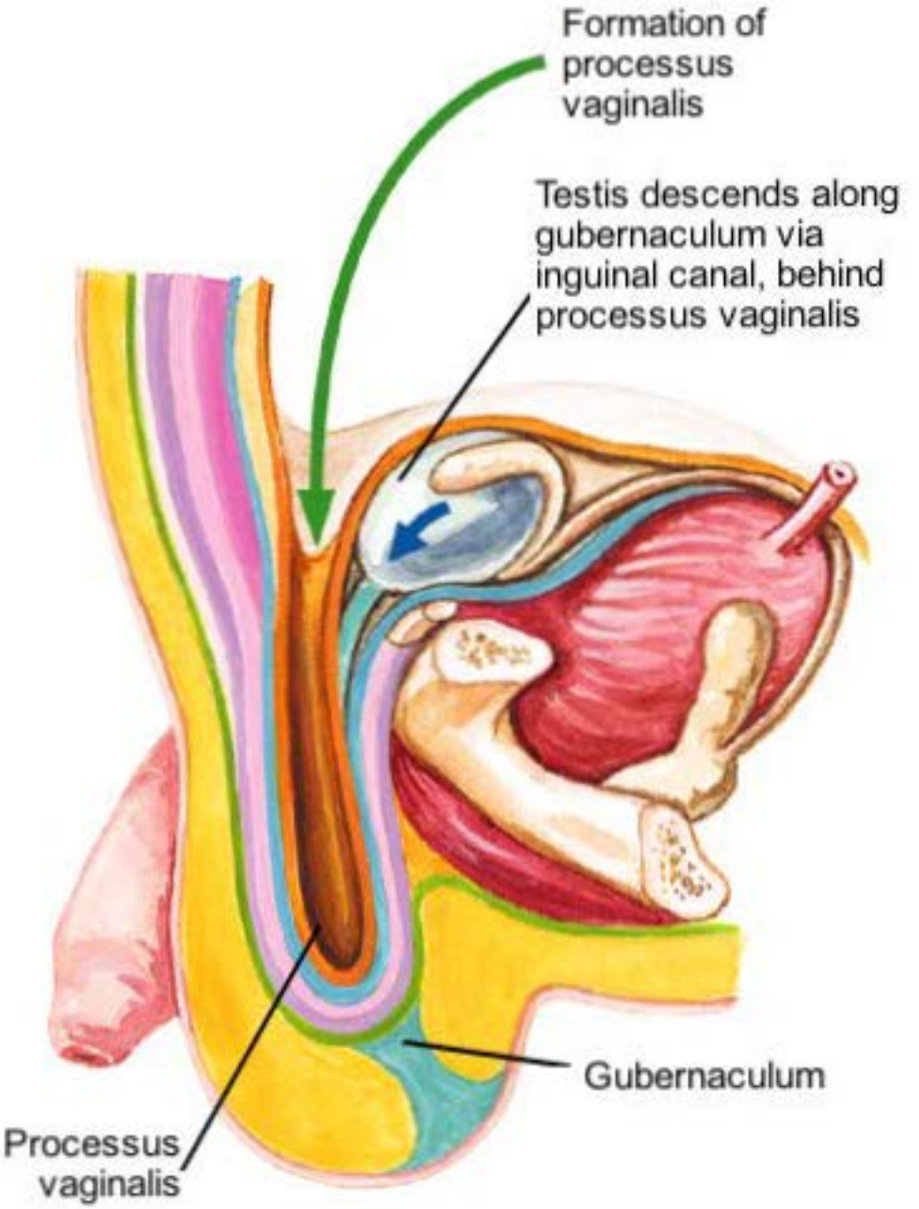
Anterior Testis Decent

Testicular descent

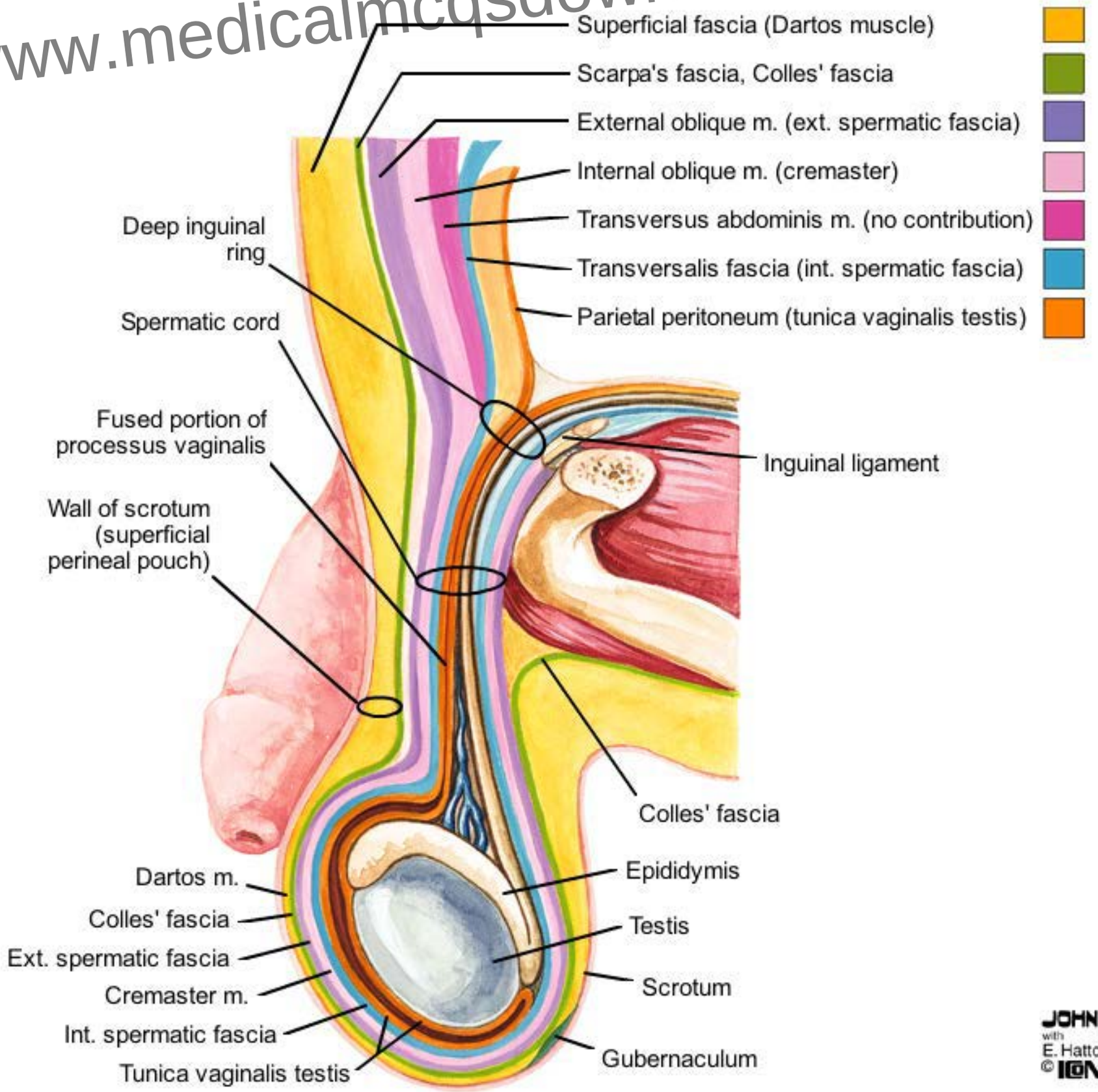


Abdominal position of testis (between parietal peritoneum and transversalis fascia)



Anterior Testis Descent

Adult configuration



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with
E. Hatton
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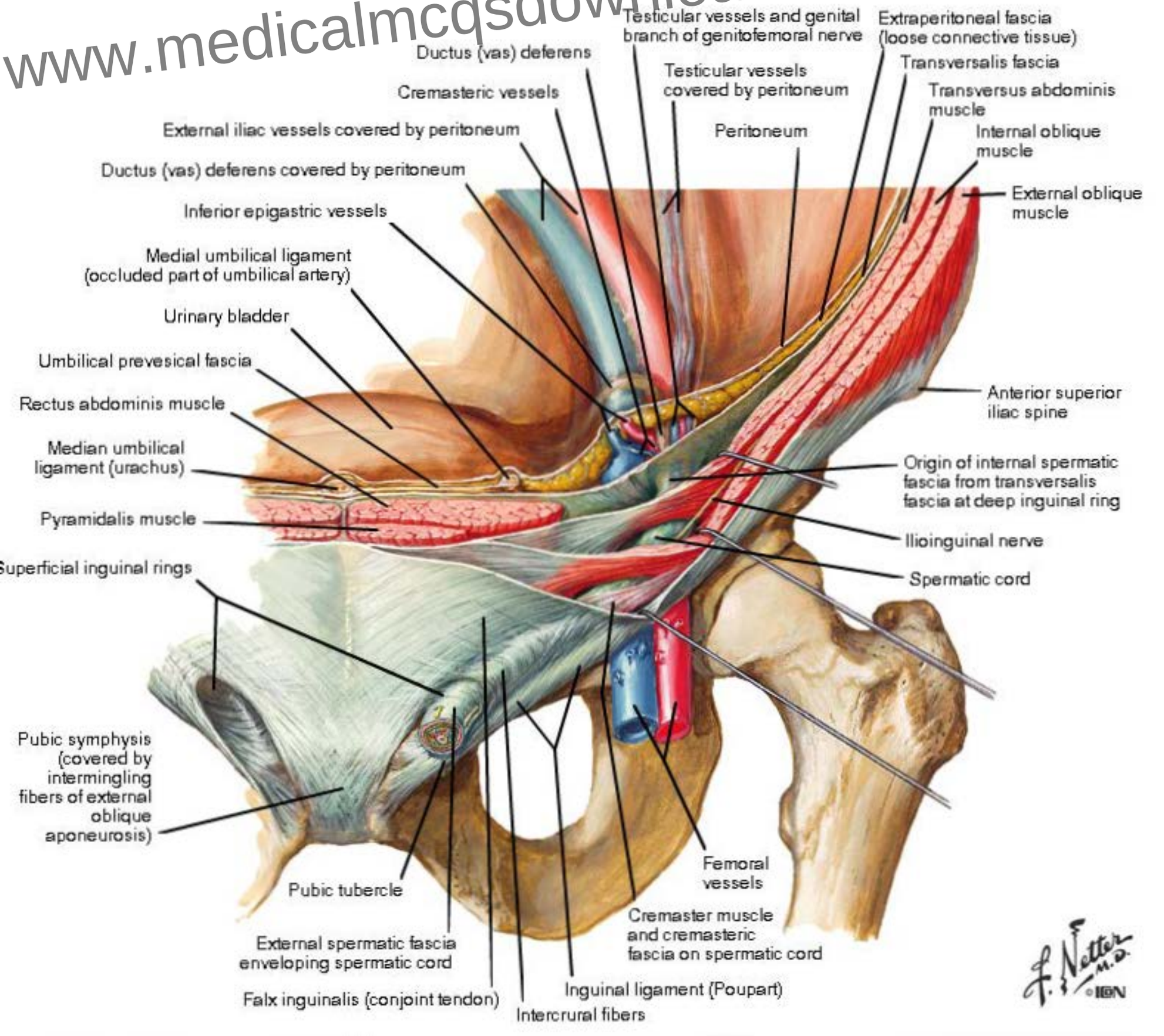
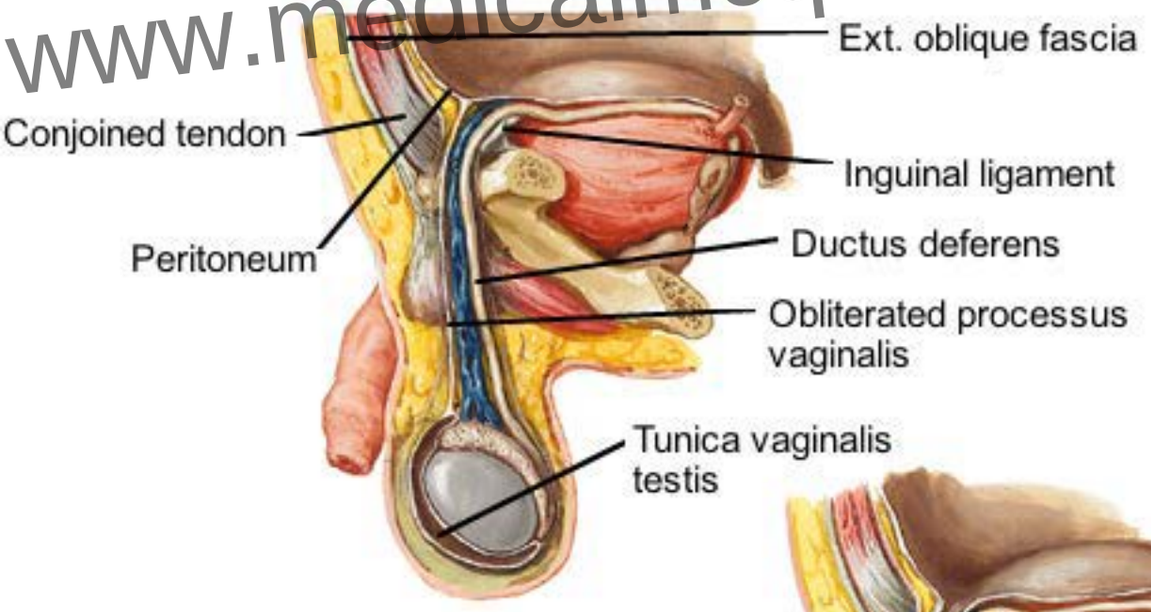
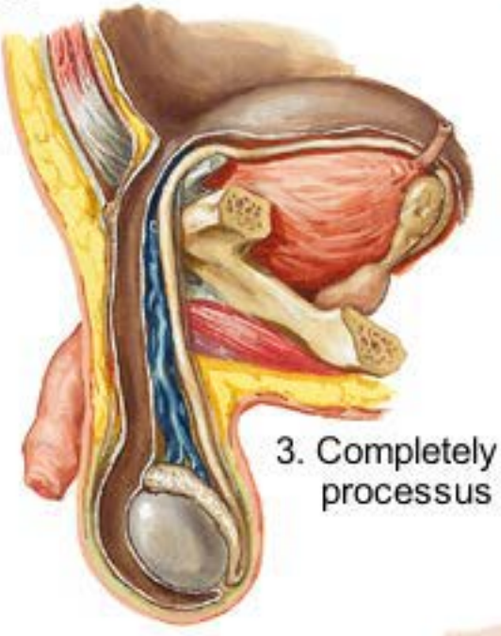
The Adult Inguinal Region



Anomalies of the Processus Vaginalis



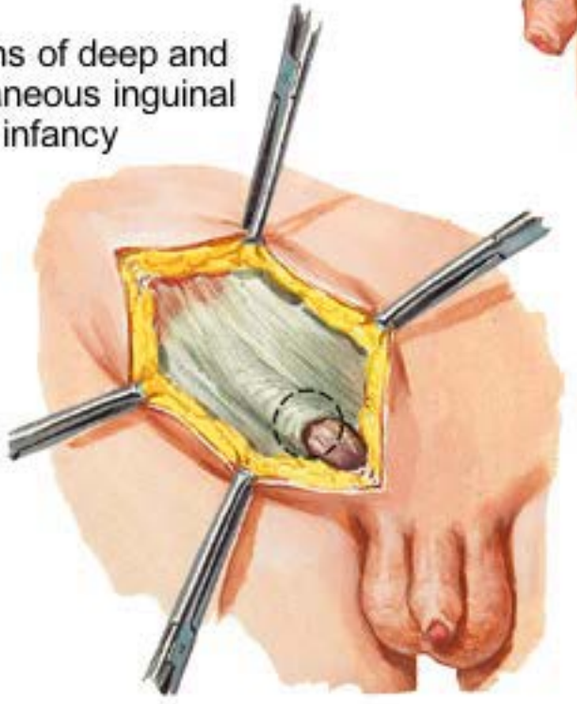
1. Normally obliterated processus vaginalis



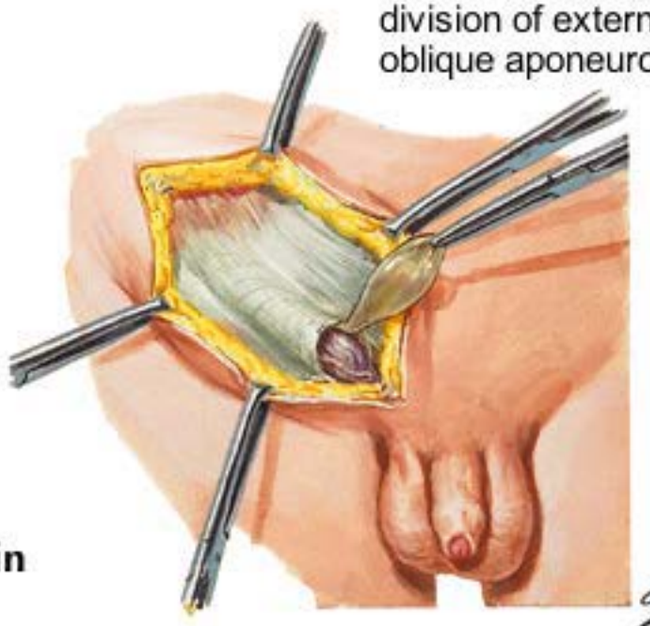
3. Completely patent processus vaginalis

2. Partially patent processus vaginalis (small congenital hernia)

Relations of deep and subcutaneous inguinal rings in infancy



Sac liberated without division of external oblique aponeurosis



Hernia in infancy

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Organization of the Abdominal GI Tract

ORGANIZATION OF THE ABDOMINAL GI TRACT

	Foregut	Midgut	Hindgut
Organs	Stomach Liver Gallbladder Pancreas Spleen 1st half of duodenum	2nd half of duodenum Jejunum and ileum Cecum Ascending colon 2/3 of transverse colon	Left 1/3 of transverse colon Descending colon Sigmoid colon Rectum
Arteries	Celiac trunk: Splenic artery Left gastric Common hepatic	Superior mesenteric: Ileocolic Right colic Middle colic	Inferior mesenteric: Left colic Sigmoid branches Superior rectal
Ventral mesentery	Lesser omentum Falciform ligament Coronary/triangular ligaments	None	None
Dorsal mesentery	Gastrosplenic ligament Splenorenal ligament Gastrocolic ligament Greater omentum	Mesointestine Mesoappendix Transverse mesocolon	Sigmoid mesocolon
Motor nerve supply	Vagus	Vagus	Pelvic splanchnic nerves

THE UROGENITAL SYSTEM

TIMELINE

Prenatal Time Scale (Months)

Blastocyst

1

Embryo

5 weeks

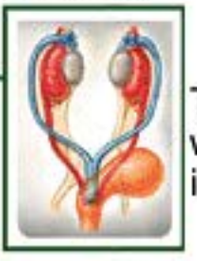
Urogenital ridges form from the intermediate mesoderm, and germ cells migrate from the gut wall. Ureteric buds have entered the metanephric mesoderm.

6—7 weeks

Major and minor calices develop. Kidneys begin to ascend. Nephrons begin to form; they will connect to collecting tubules and function by 10 weeks.

2

2 months



The "indifferent" stage with identical primordia in both sexes.

10—12 weeks

In males, primary sex cords form seminiferous tubules. In females, secondary sex cords form ovarian follicles.

3

3 months

External genitalia develop.

Fetus

7

8—9 months

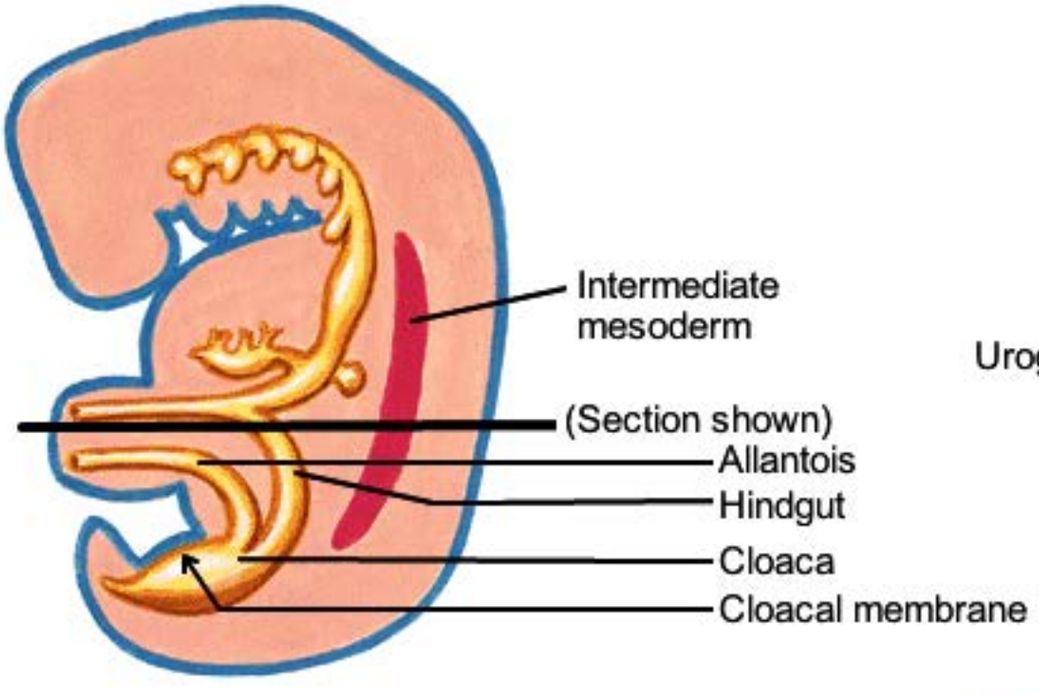
Testes pass through the inguinal canal and into the scrotum.

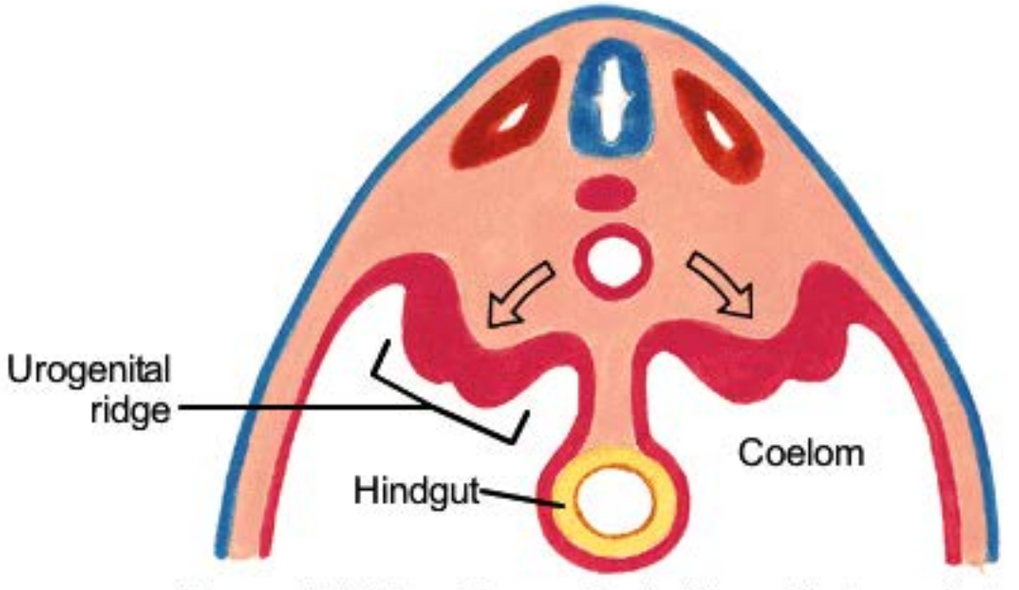
8

9

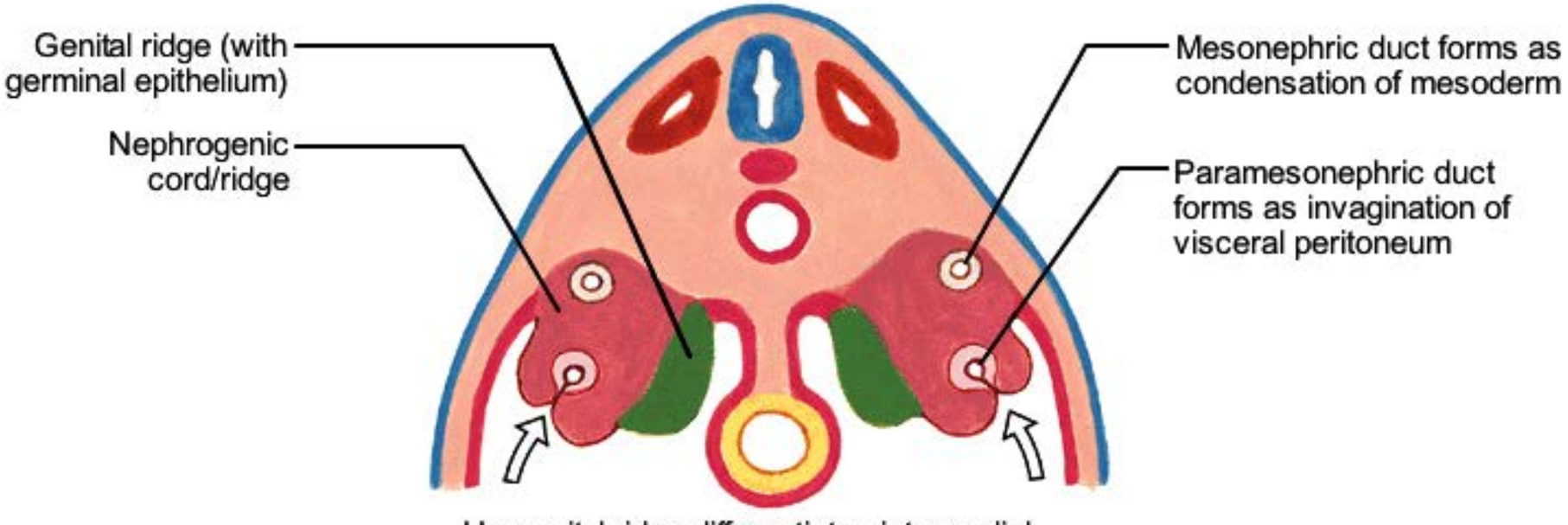
Birth

Early Primordia



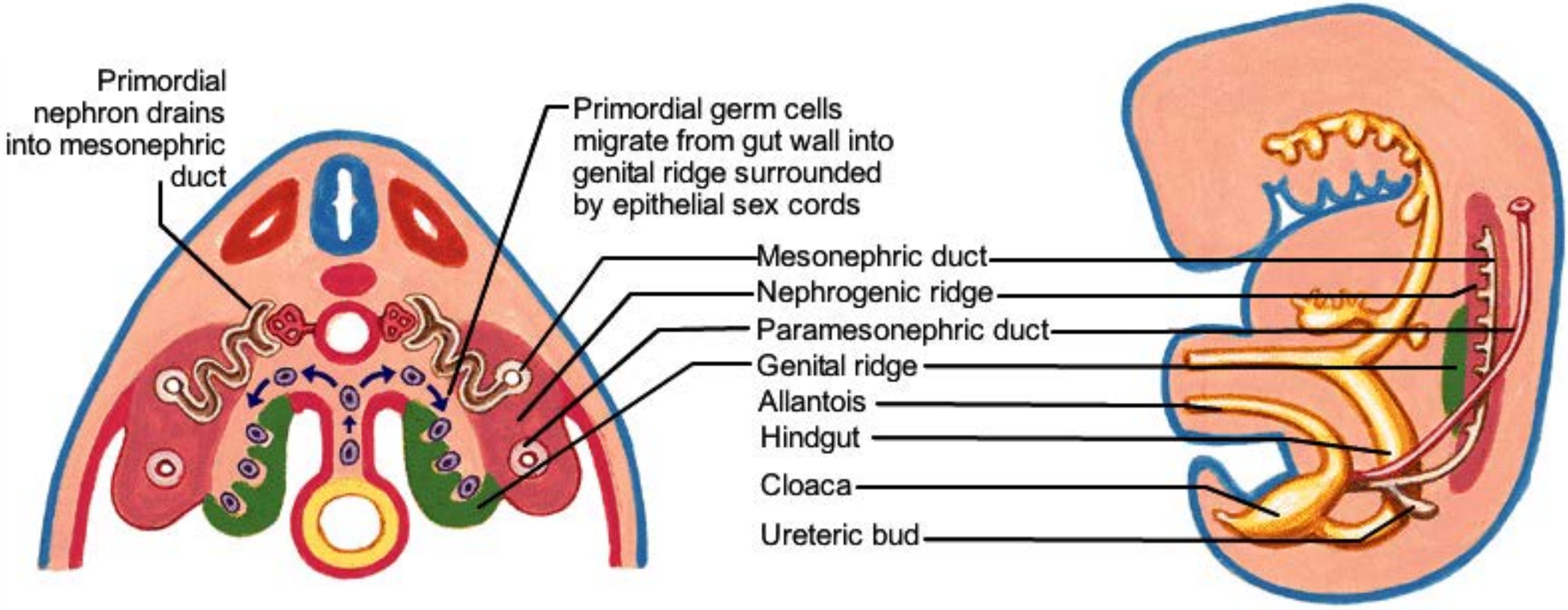


Urogenital ridges formed by bulging of intermediate mesoderm into coelomic cavity



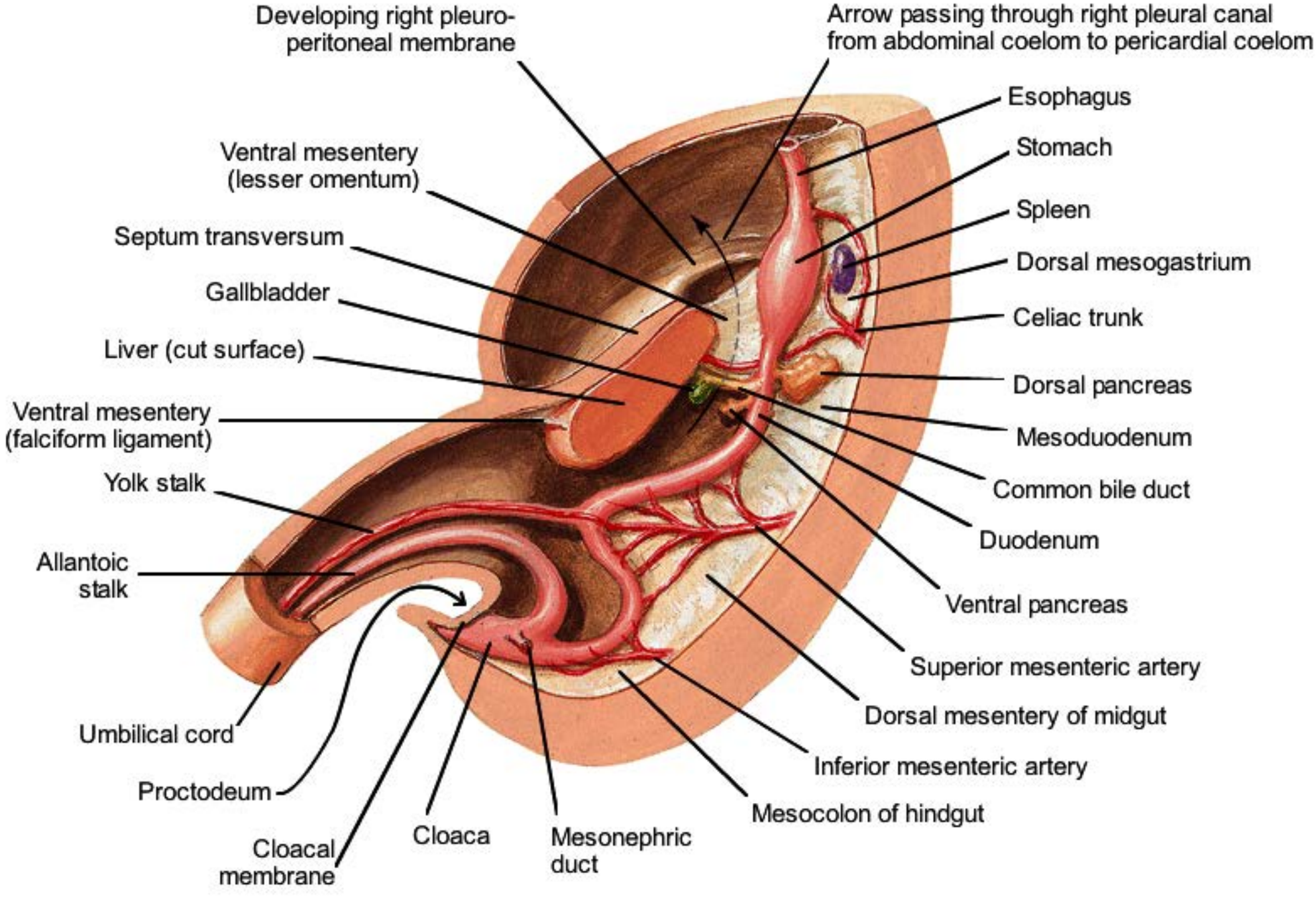
Urogenital ridge differentiates into medial genital ridge and a lateral nephrogenic ridge

Early Primordia

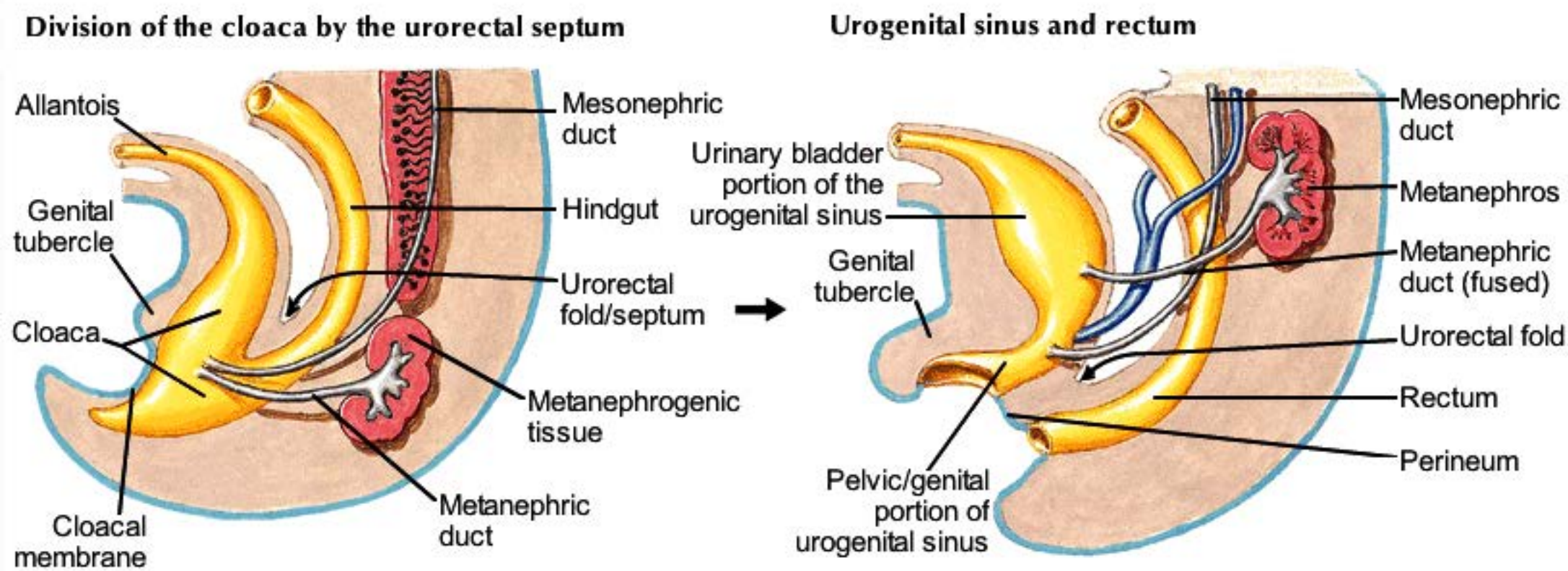


Division of the Cloaca

Abdominal foregut, midgut, and hindgut at 5 weeks

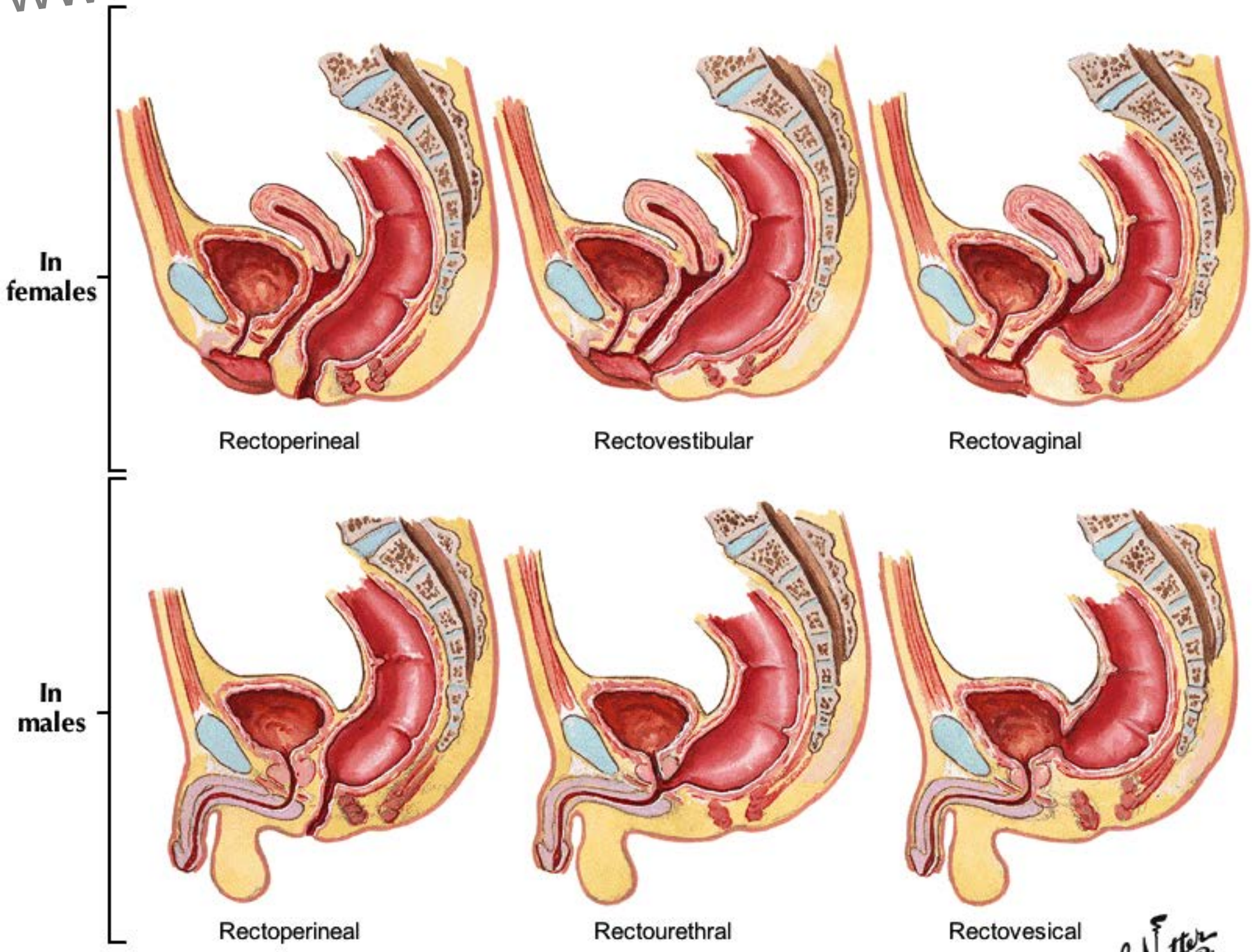


Division of the Cloaca



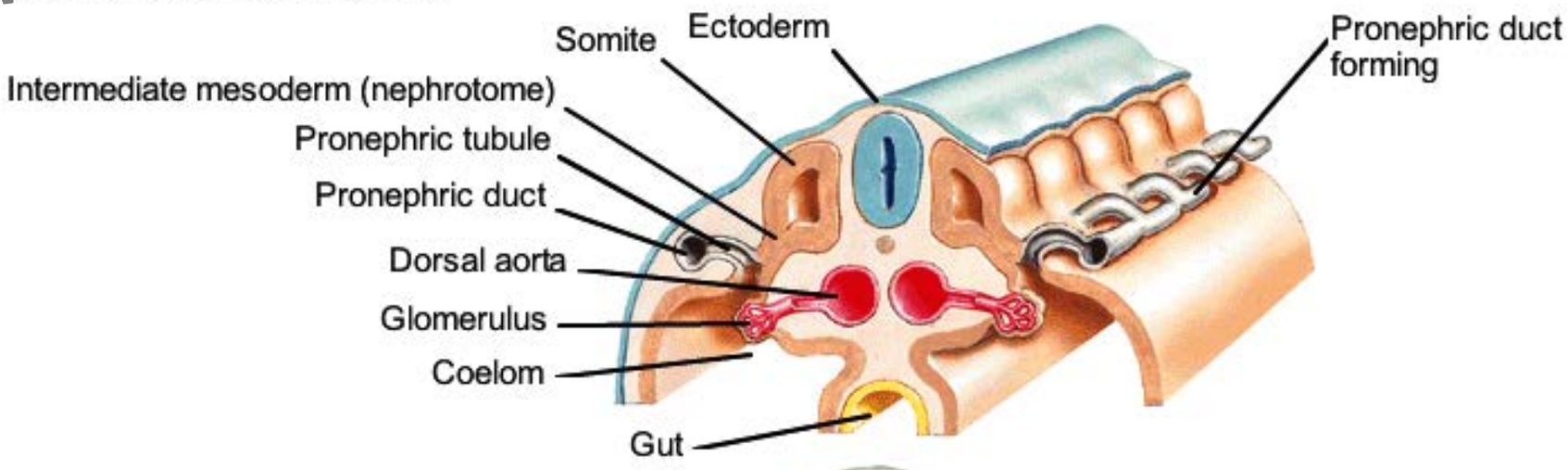
Congenital Cloacal Anomalies

Fistulas resulting from the incomplete division of the cloaca

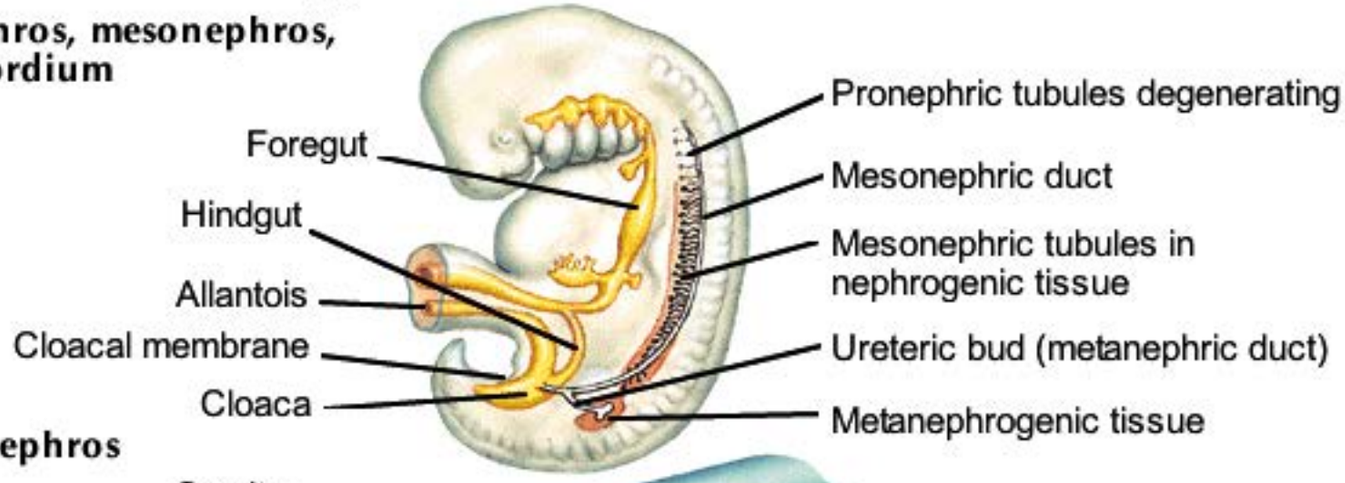


Pronephros, Mesonephros, and Metanephros

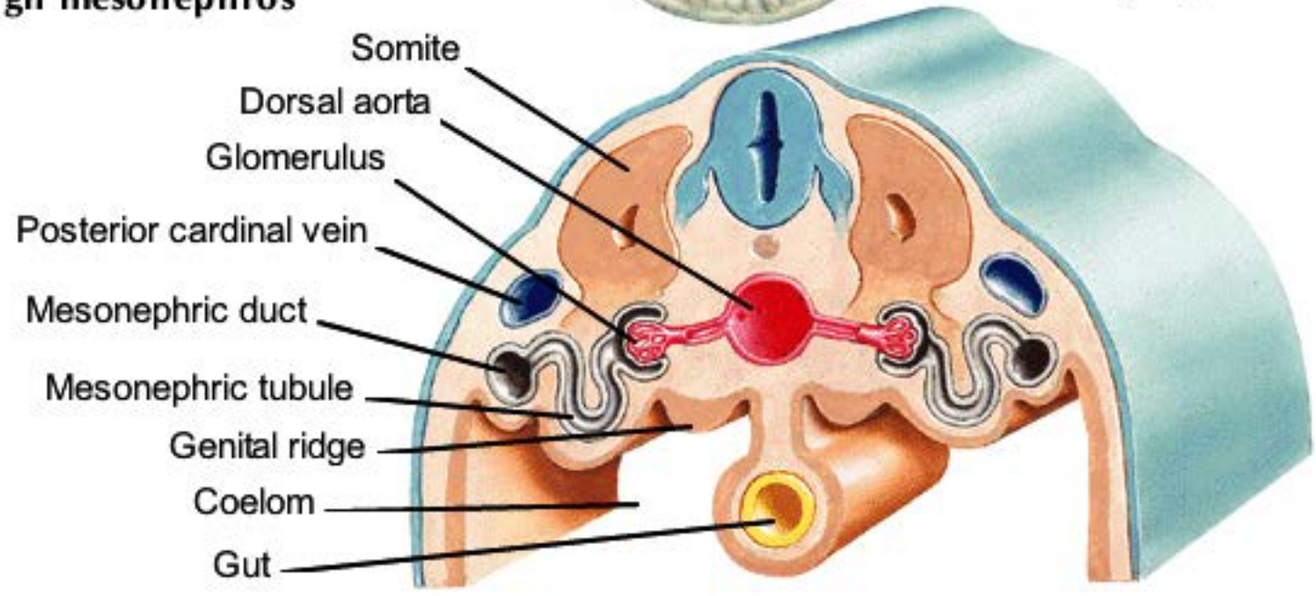
Section through pronephros



Topography of pronephros, mesonephros, and metanephric primordium



Section through mesonephros



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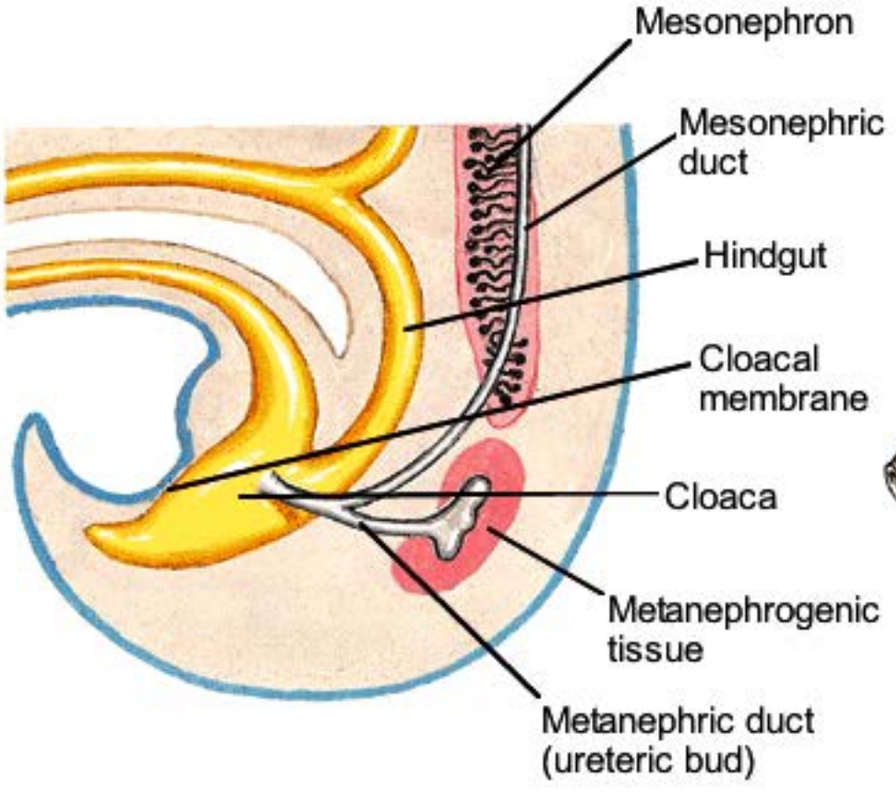
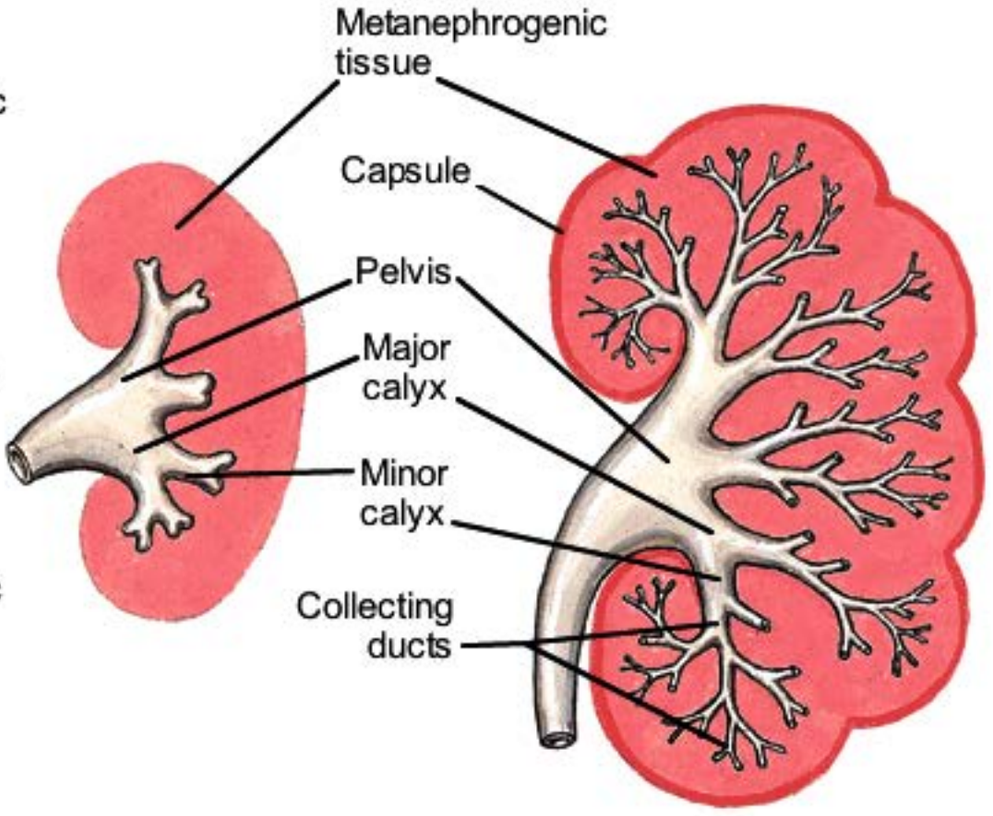
Development of the Metanephros



A. The metanephric duct (ureteric bud) has grown out from the mesonephric duct, close to termination of latter in cloaca, and has invaded the metanephrogenic mesoderm.



B. Within the metanephrogenic tissue, the ureteric bud expands to form a pelvis, which branches into calyces, and these, in turn, bud into successive generations of collecting ducts.

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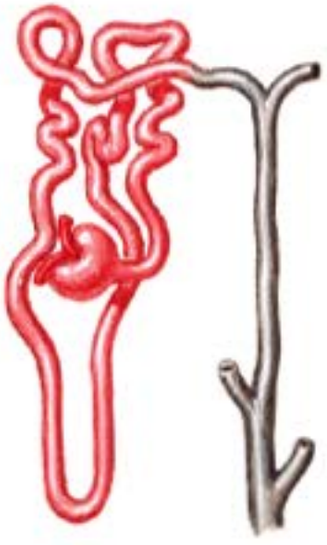
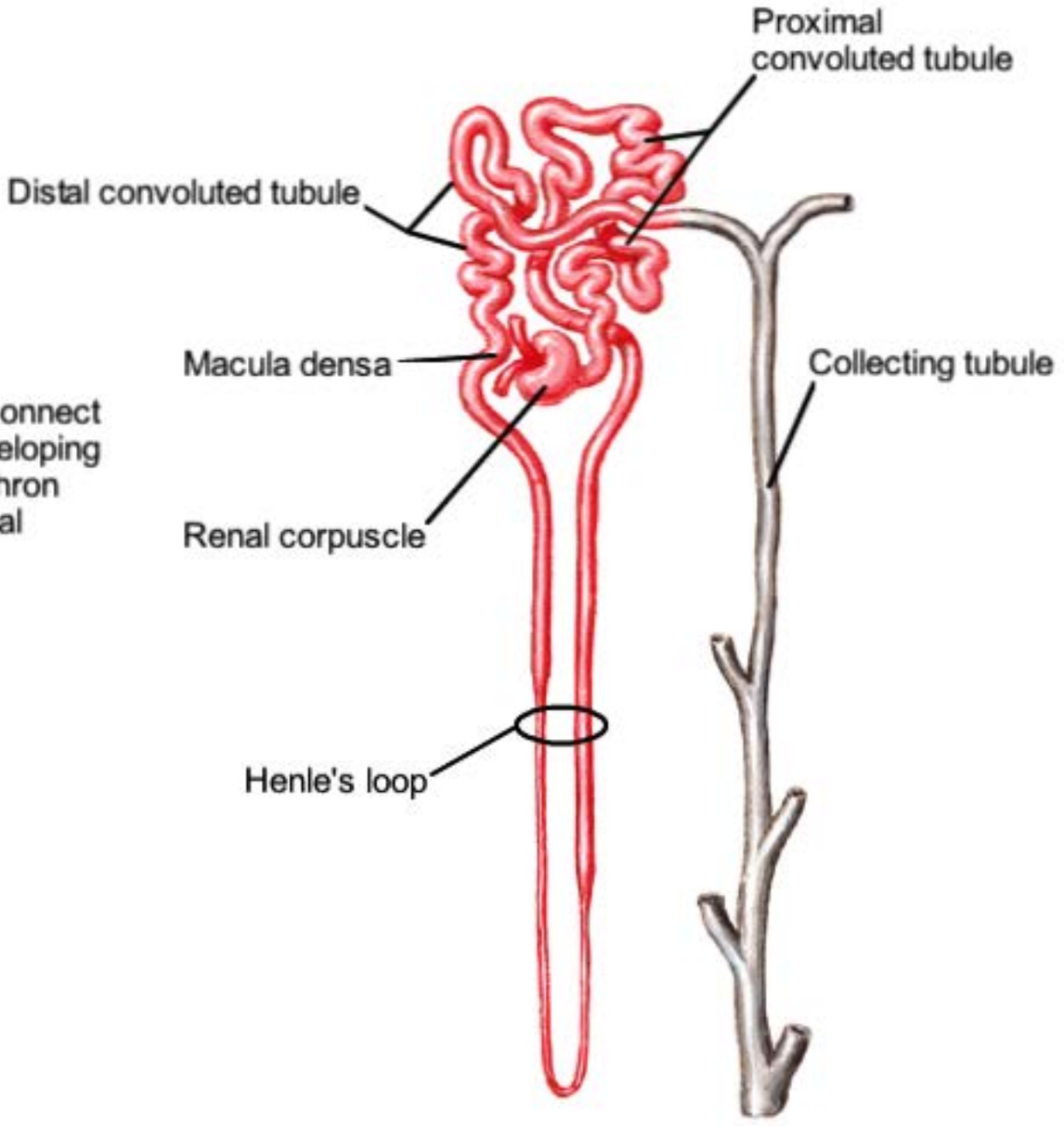
Development of the Metanephros

C. The distal ends of the collecting ducts connect with the tubule system of the nephron developing from the metanephric mesoderm. The nephron extends from the collecting duct to the renal corpuscle.



D. The tubule lengthens, coils, and begins to dip down toward the renal pelvis, as Henle's loop; one area of the tubule remains close to the glomerular mouth, as the future macula densa.



E. The loop elongates; renal corpuscle, proximal tubule, Henle's loop, distal tubule, and macula densa of mature nephron are thus derived from metanephrogenic mesoderm and collecting tubules from the metanephric duct.

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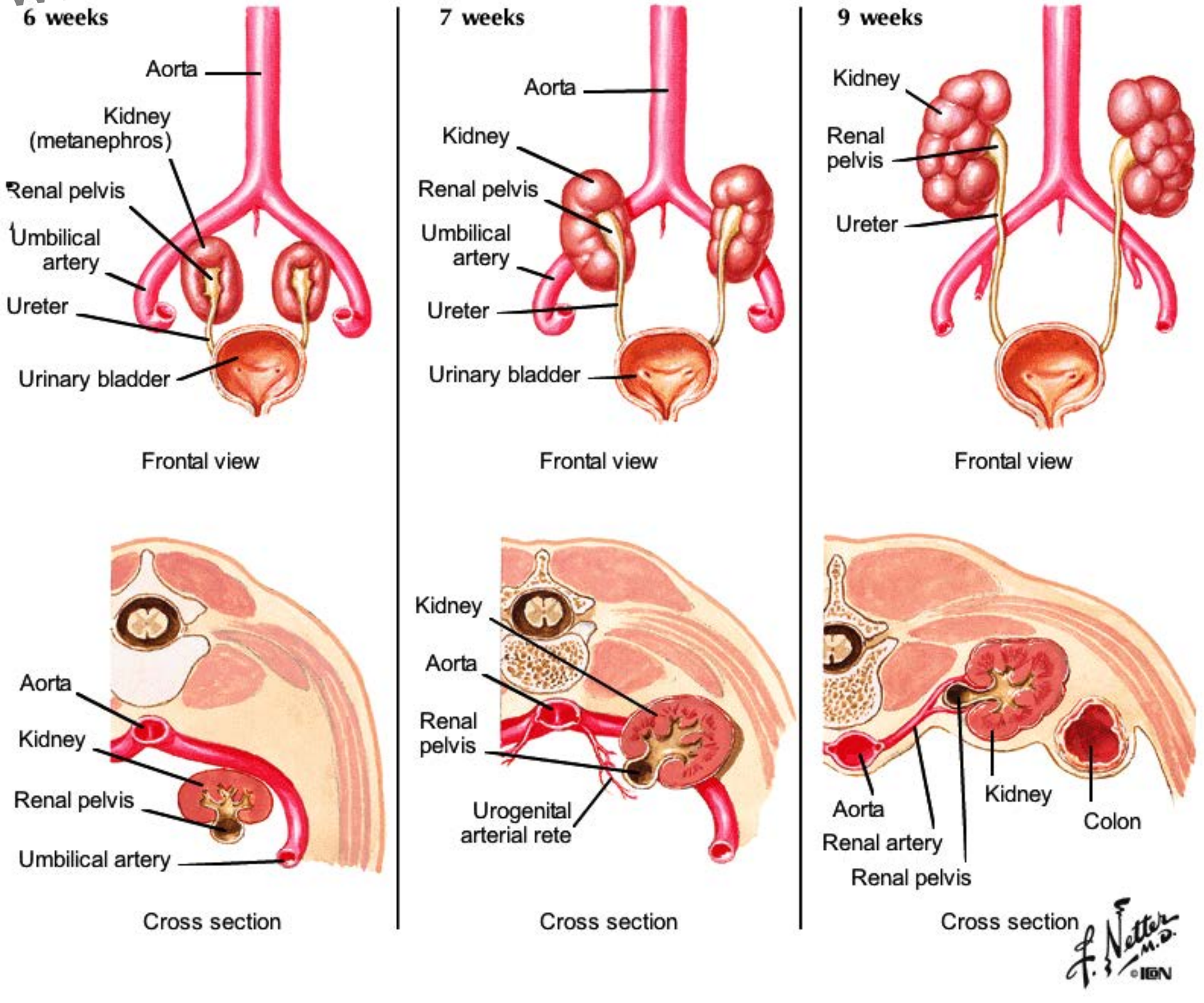
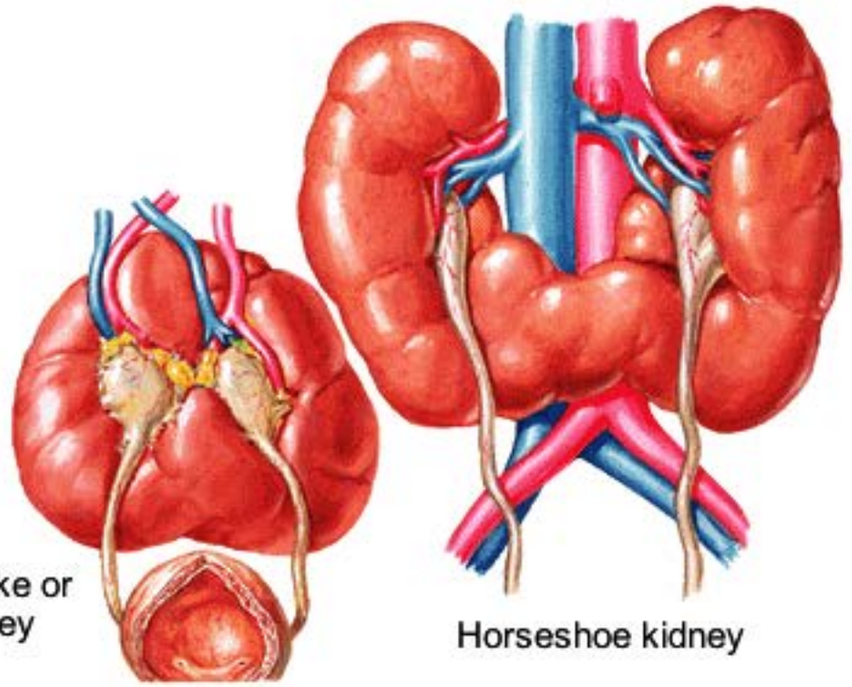
Ascent and Rotation of the Metanephric Kidneys

Apparent "ascent and rotation" of the kidneys in embryological development

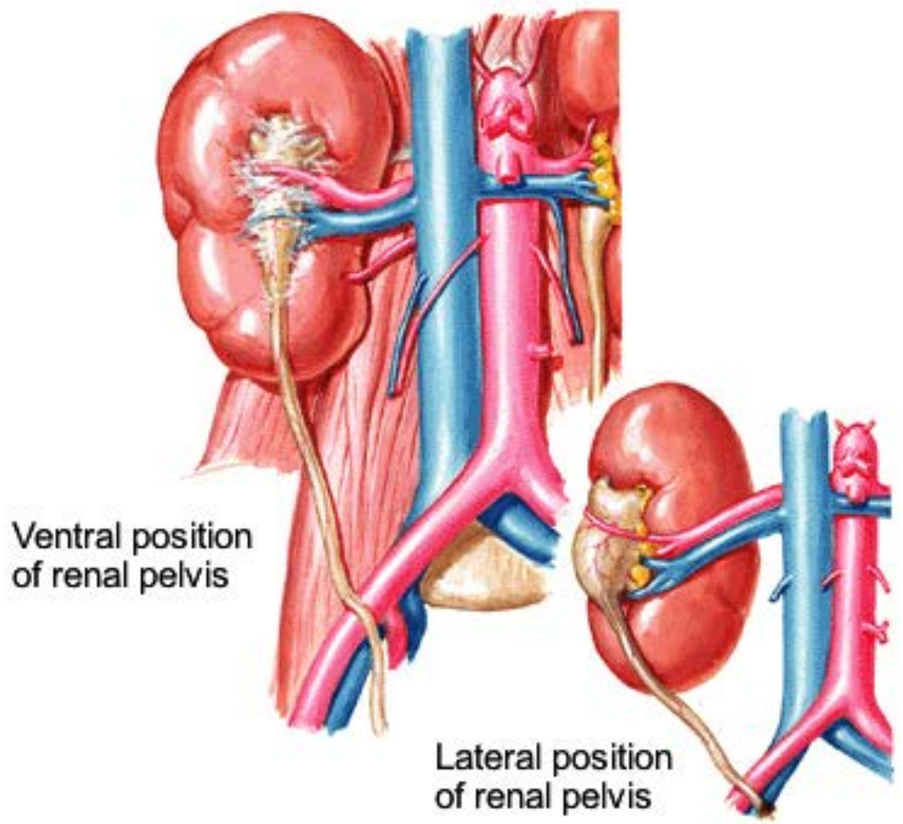


Kidney Rotation and Migration Anomalies

Renal fusion



Anomalies of renal rotation



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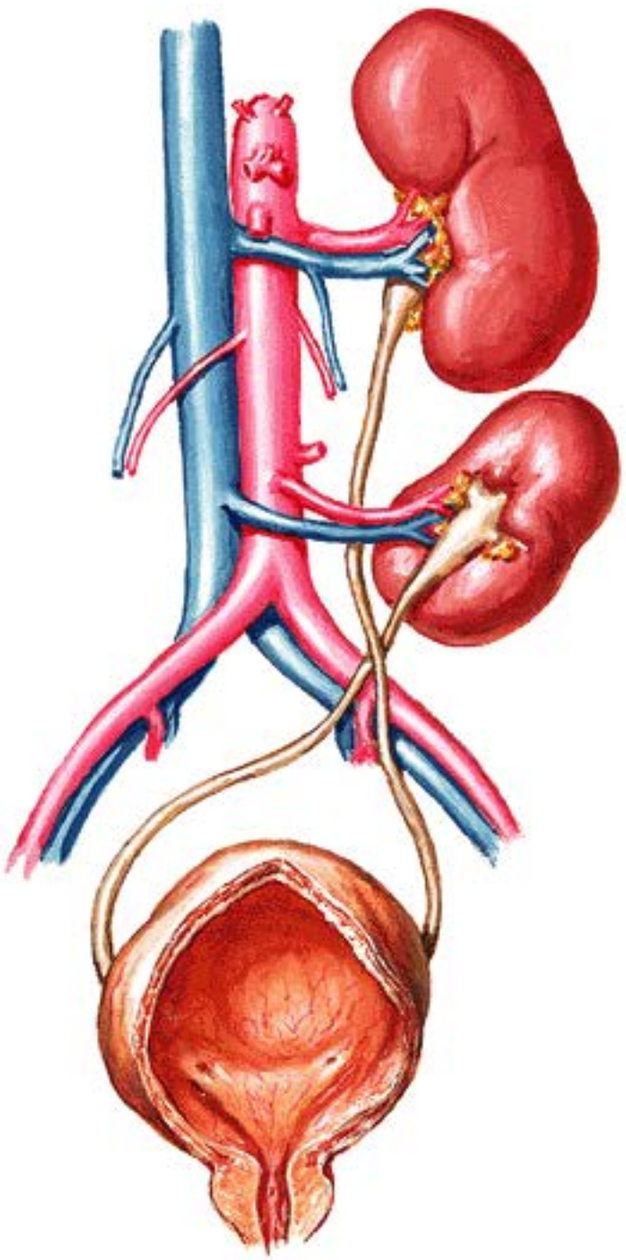
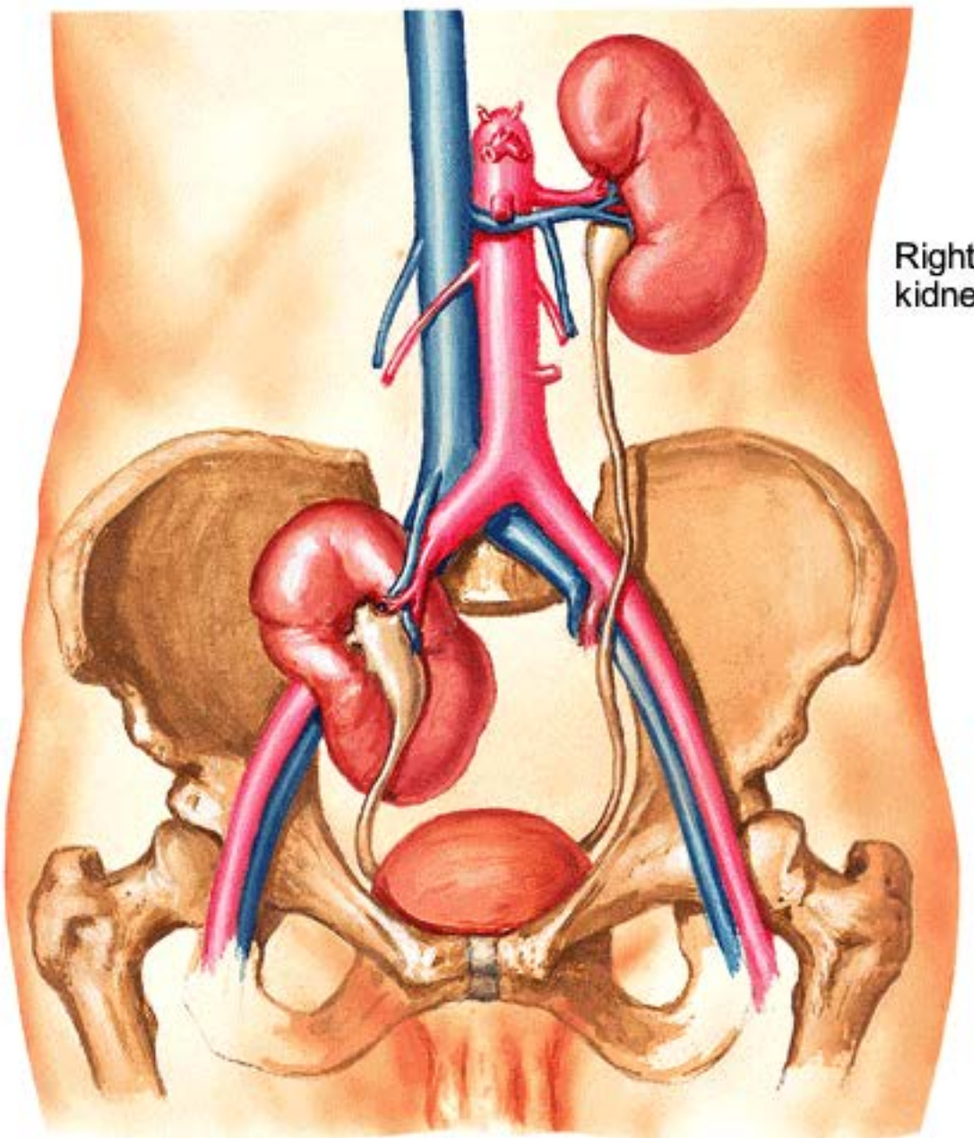
Kidney Rotation and Migration Anomalies

Ectopia of the kidney



Crossed ectopia of the right kidney



Right pelvic kidney

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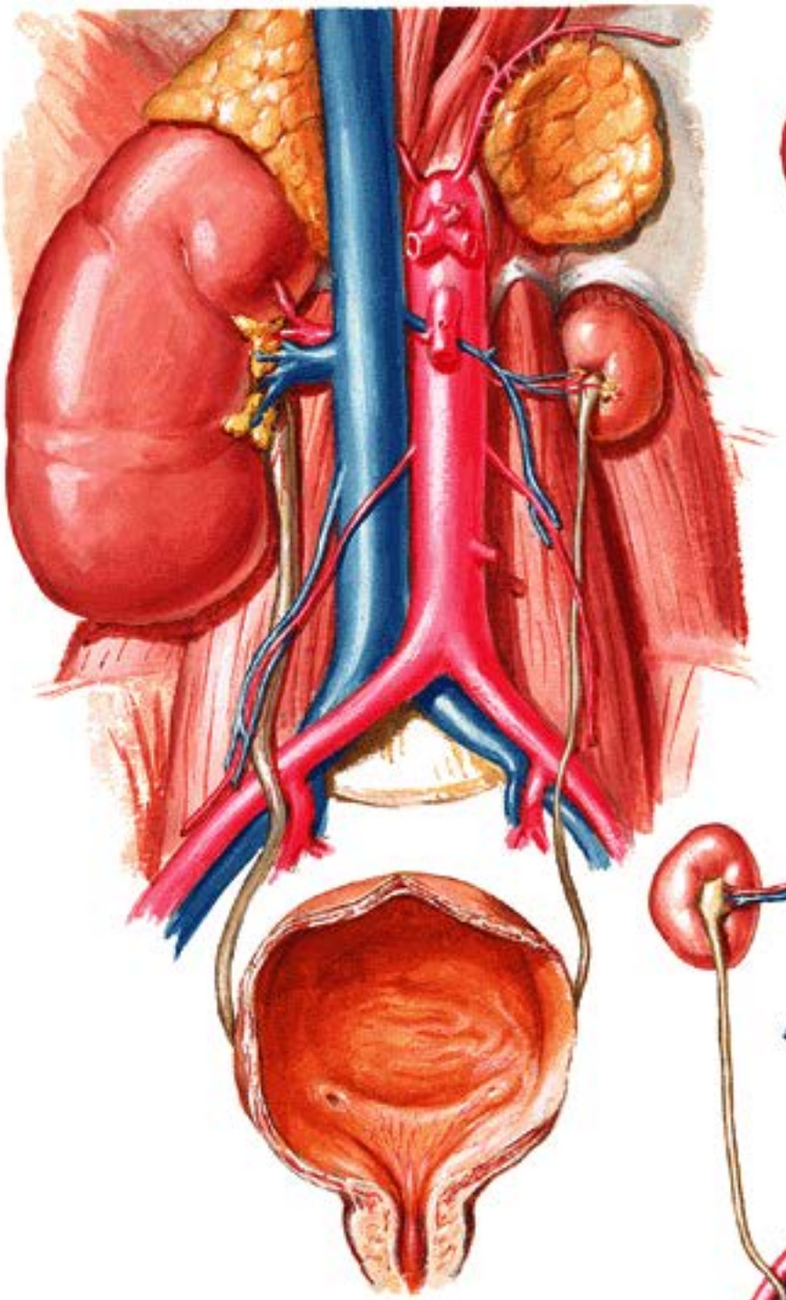
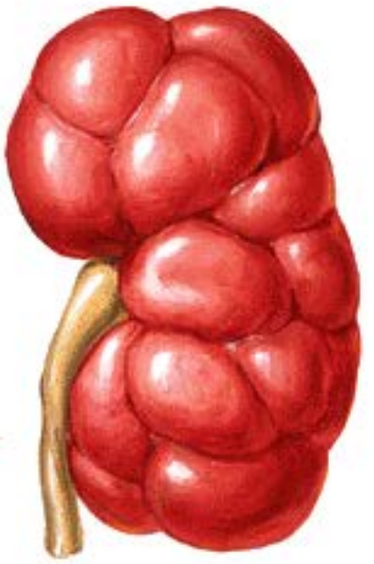
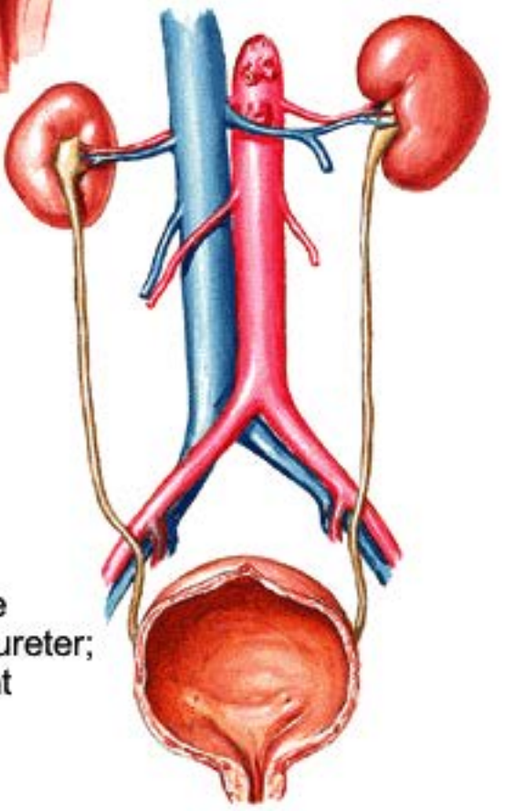
Hypoplasia



Left unilateral hypoplasia of the kidney with narrow but patent ureter; both suprarenal glands present



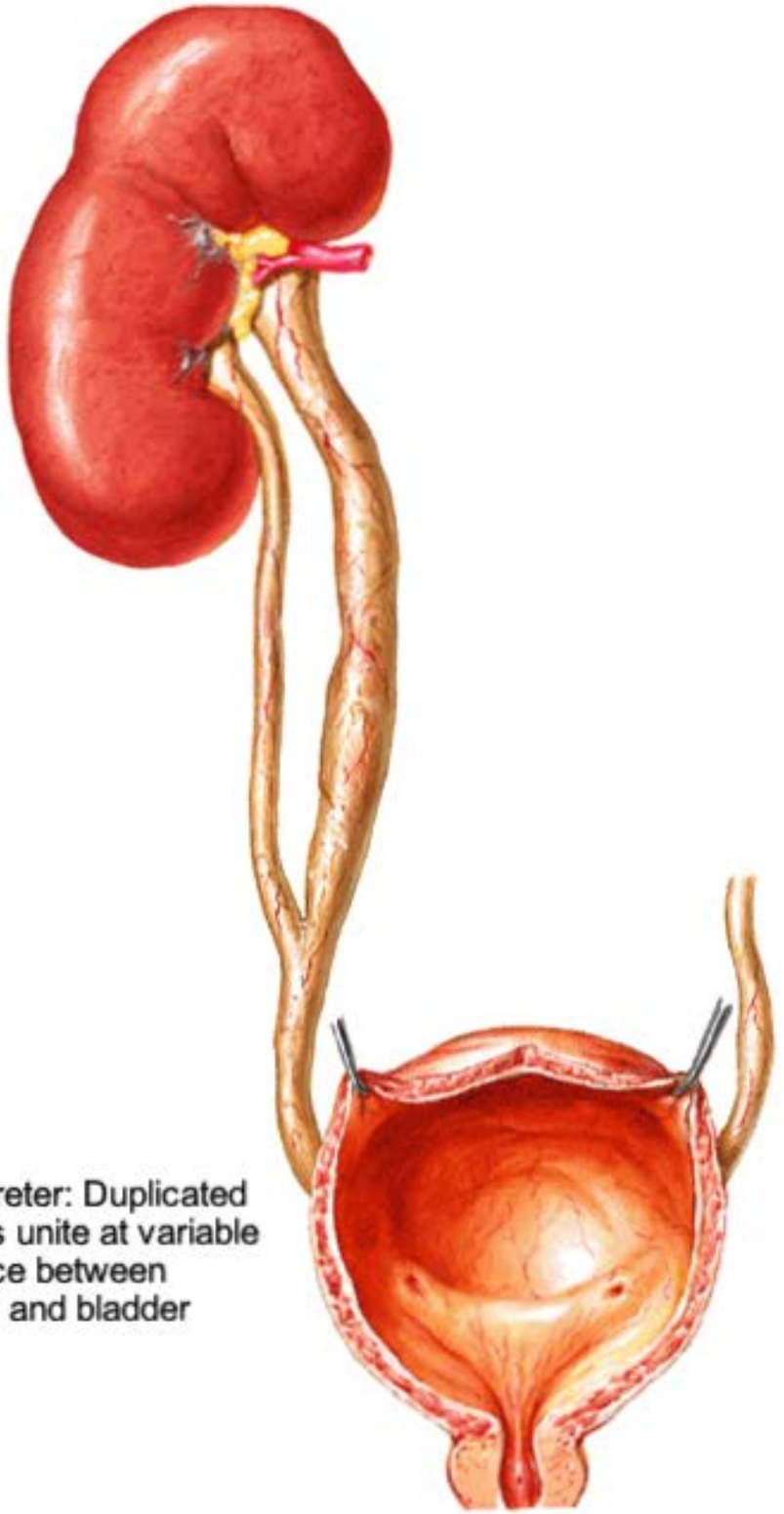
Persistent fetal lobulation



Bilateral renal hypoplasia

Ureteric Bud Duplication

Incomplete duplication of ureter

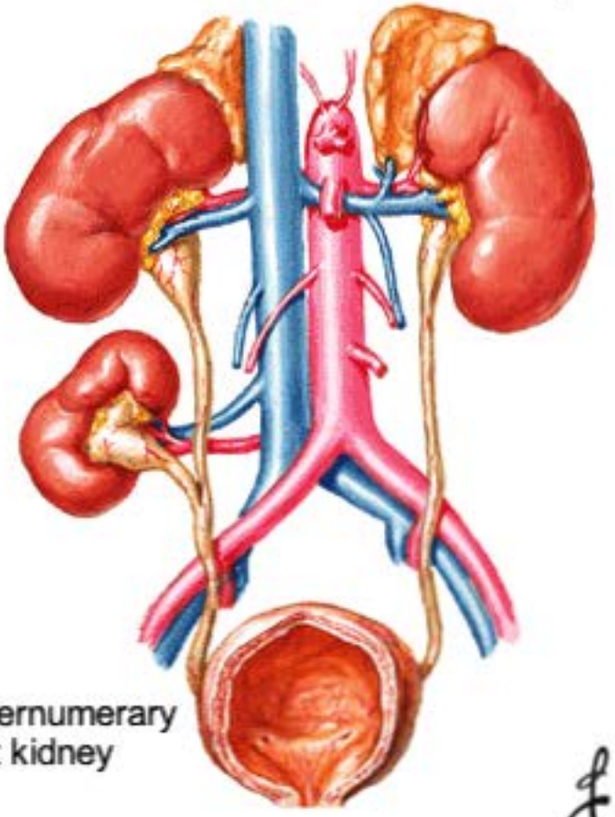


Bifid ureter: Duplicated ureters unite at variable distance between kidney and bladder

Anomalies of renal pelvis and calyces

Duplicated renal pelvis

Anomalies in number of kidneys



Supernumerary right kidney

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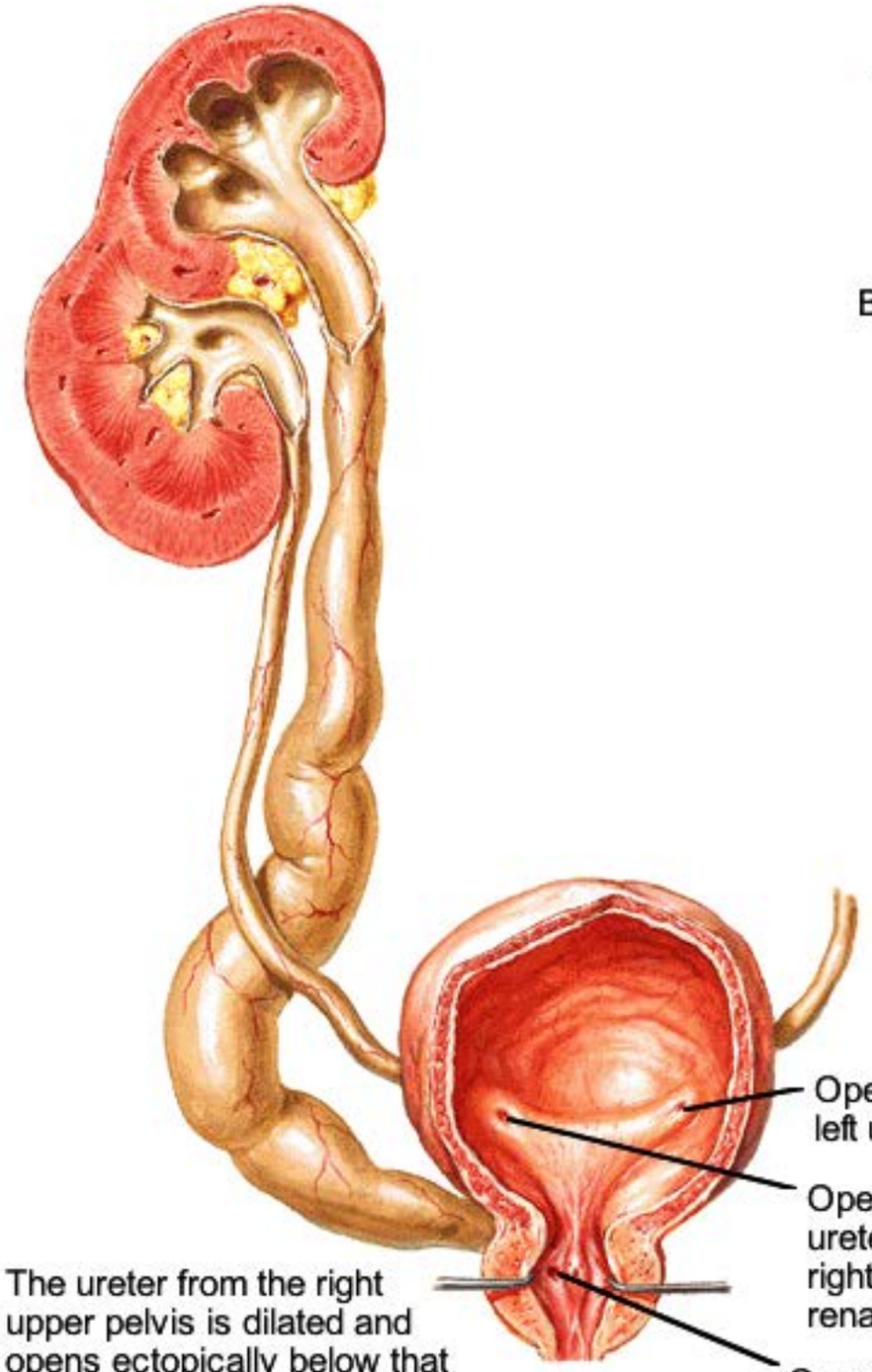
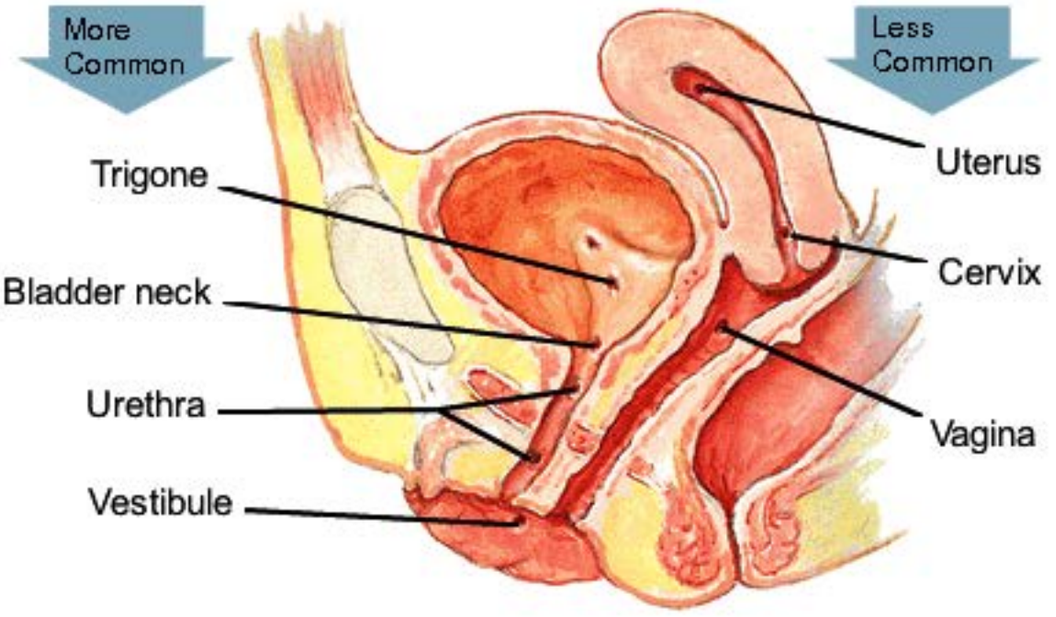
Ectopic Ureters

Complete duplication of the ureter

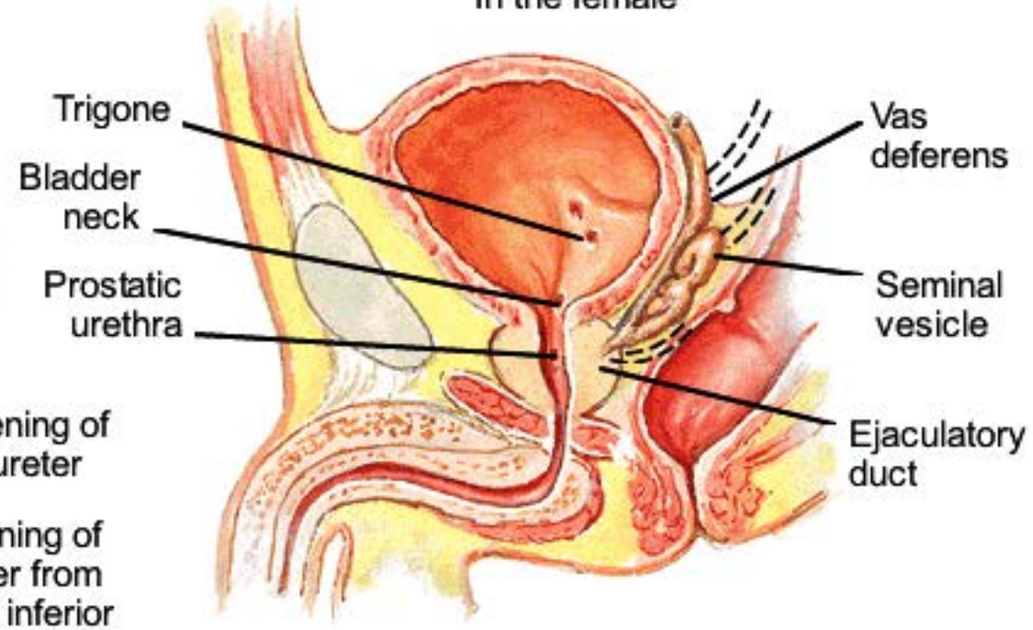


The ureter from the right upper pelvis is dilated and opens ectopically below that from the lower pelvis (in the prostatic urethra) according to the Weigert-Meyer law

Observed sites of ectopic ureteral orifices



In the female



In the male

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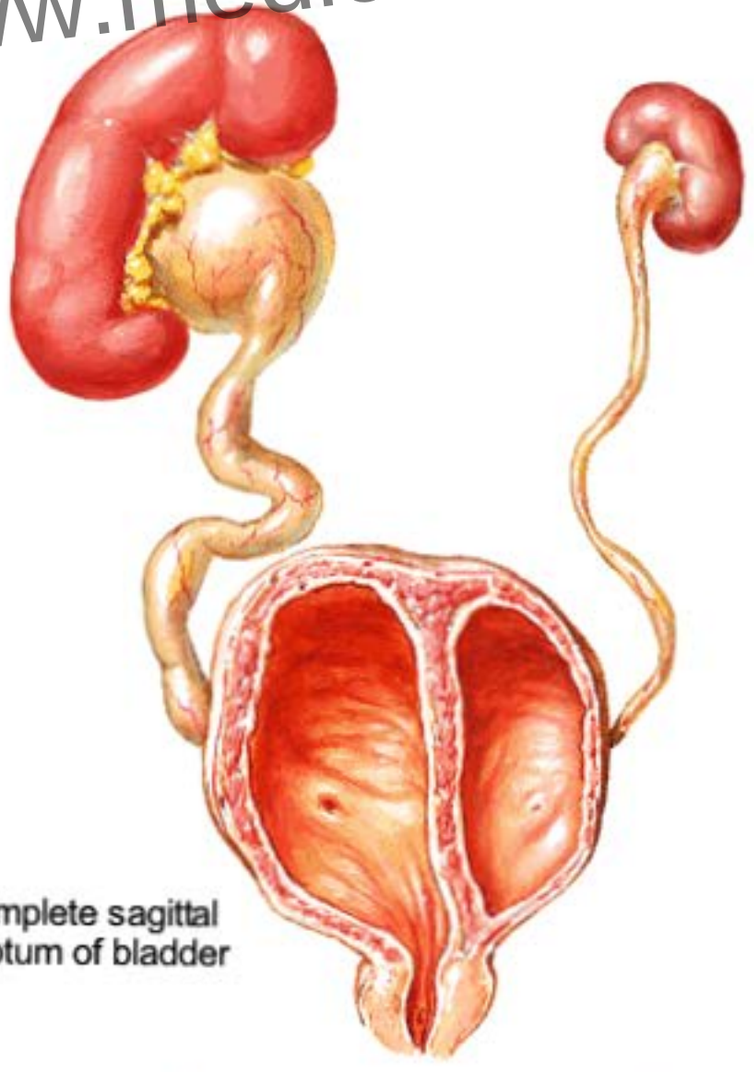
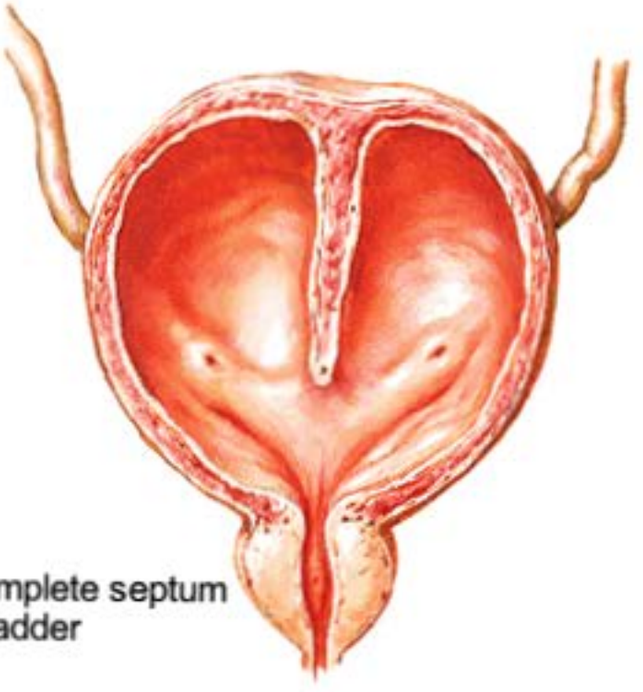
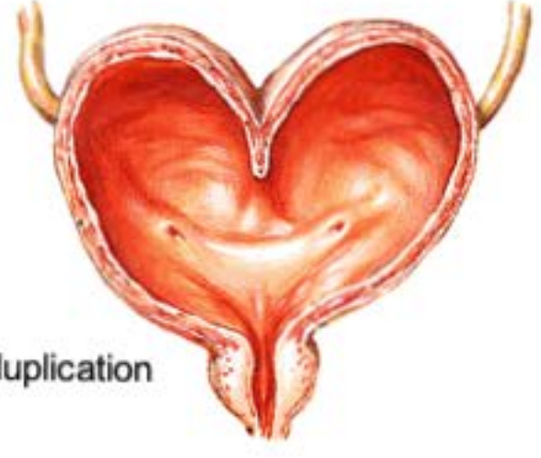
Bladder Anomalies



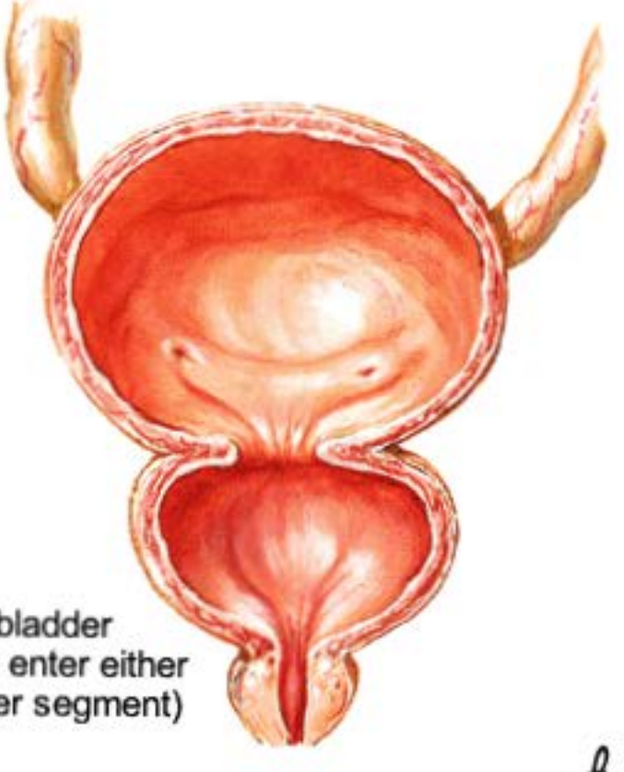
Complete sagittal septum of bladder



Incomplete septum of bladder



Incomplete duplication of bladder



"Hourglass" bladder (ureters may enter either upper or lower segment)

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Allantois/Urachus Anomalies

Completely patent urachus

Partially patent urachus; opening externally, blind internally

Partially patent urachus; opening internally, blind externally

Cyst of urachus

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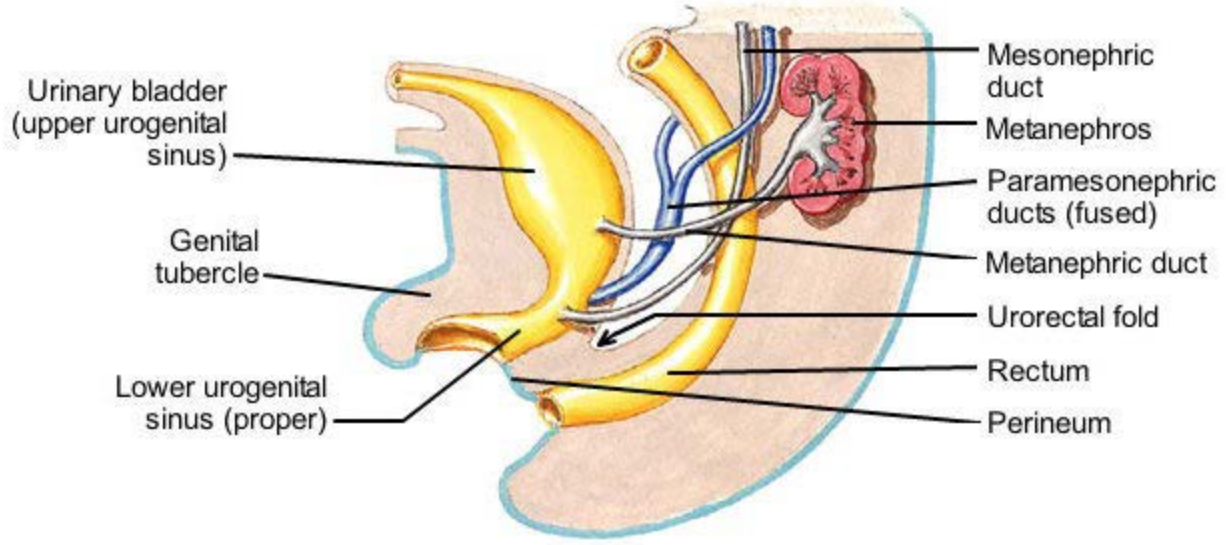
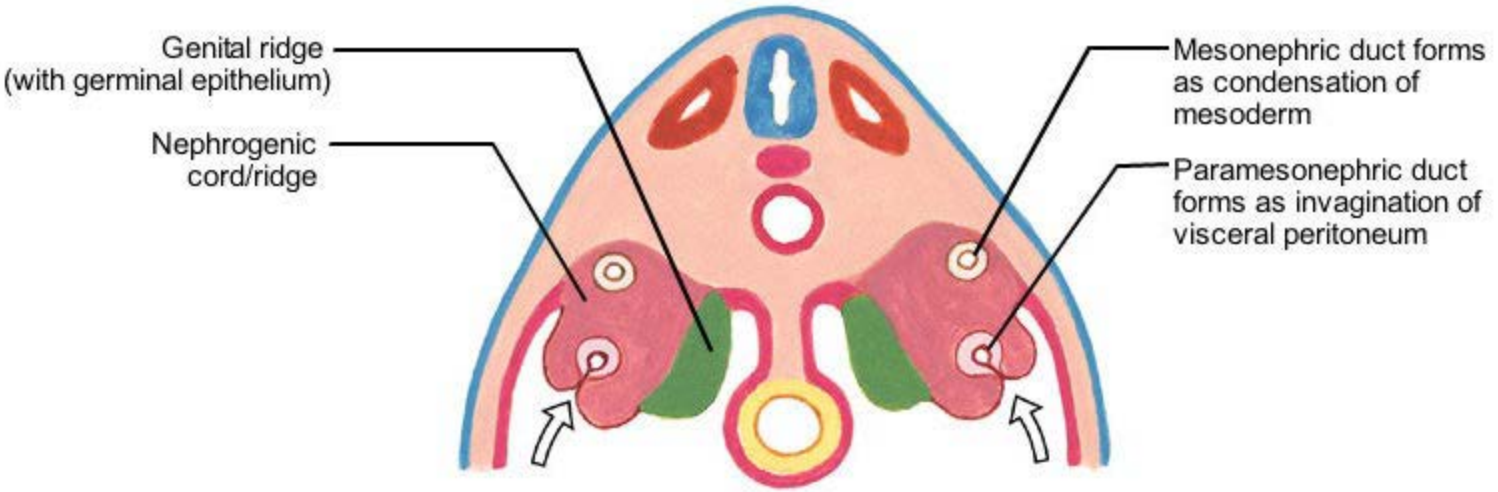
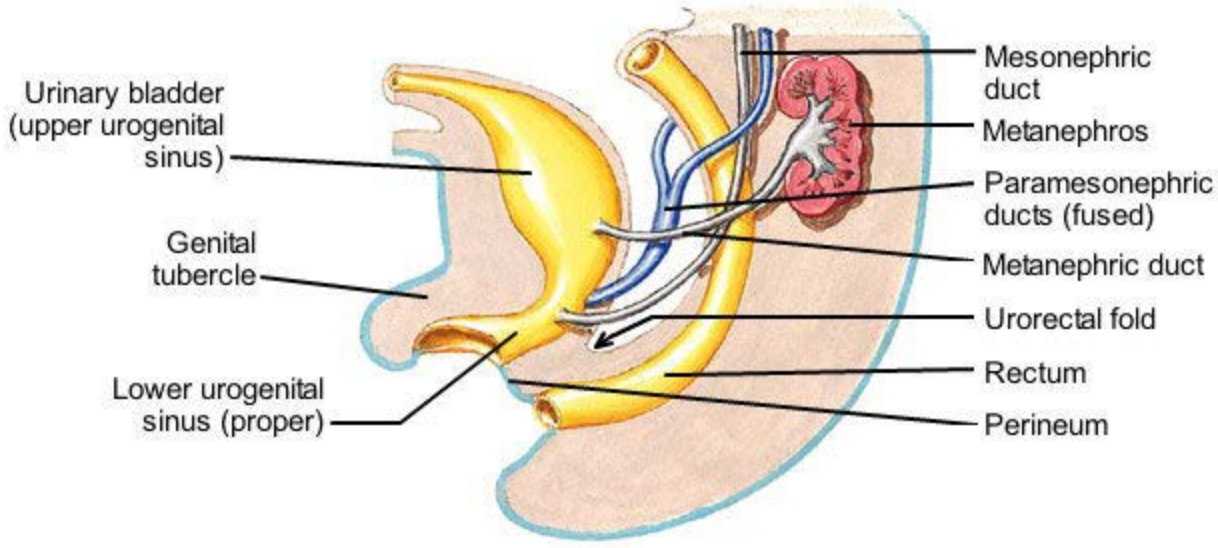
Primordia of the Genital System

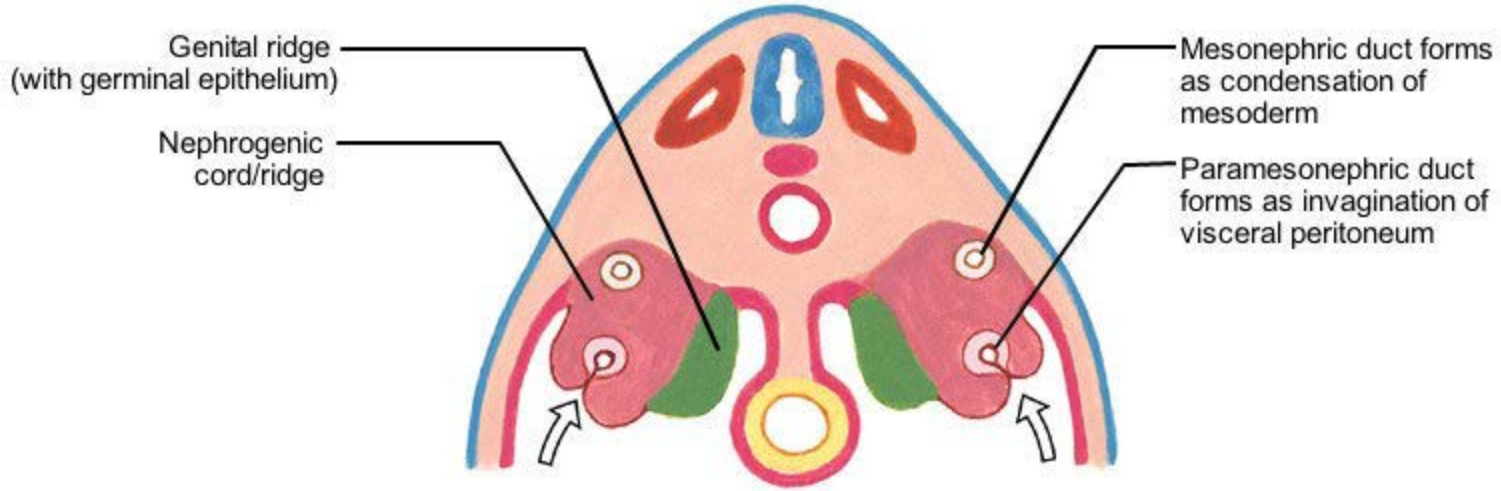




Urogenital ridge differentiates into medial genital ridge and a lateral nephrogenic ridge

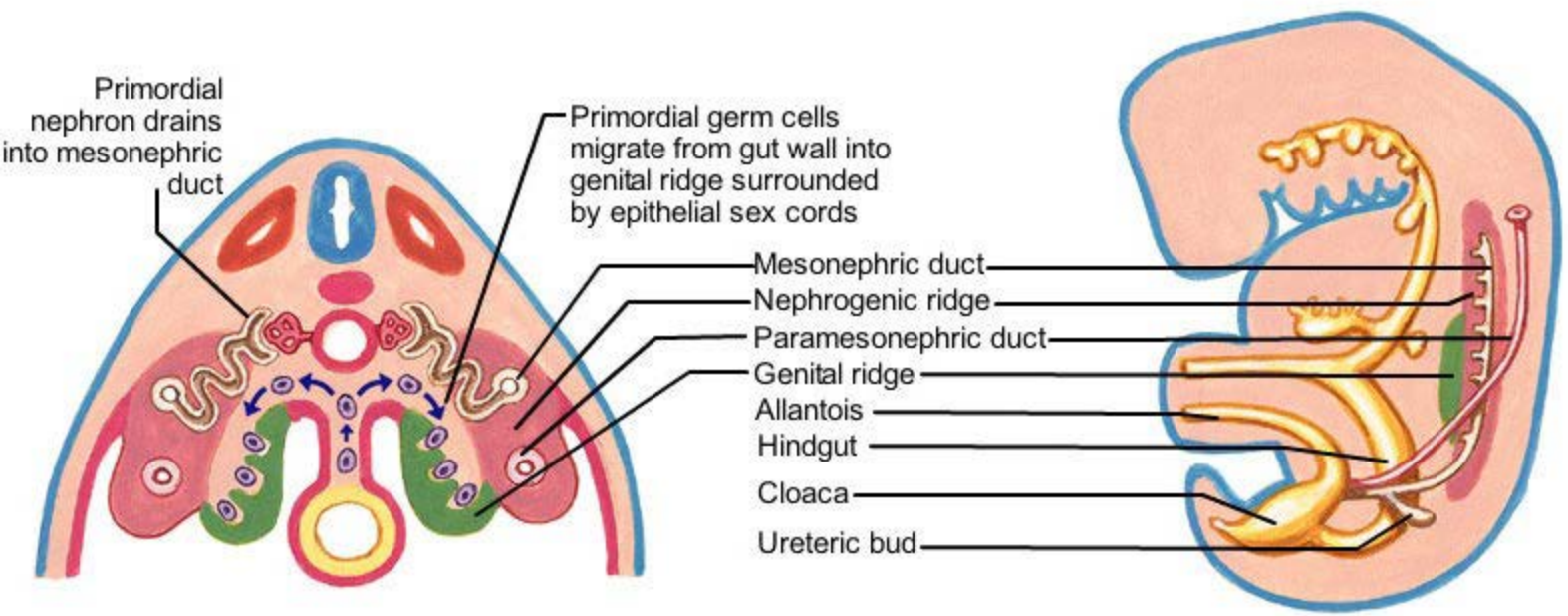
Primordia of the Genital System





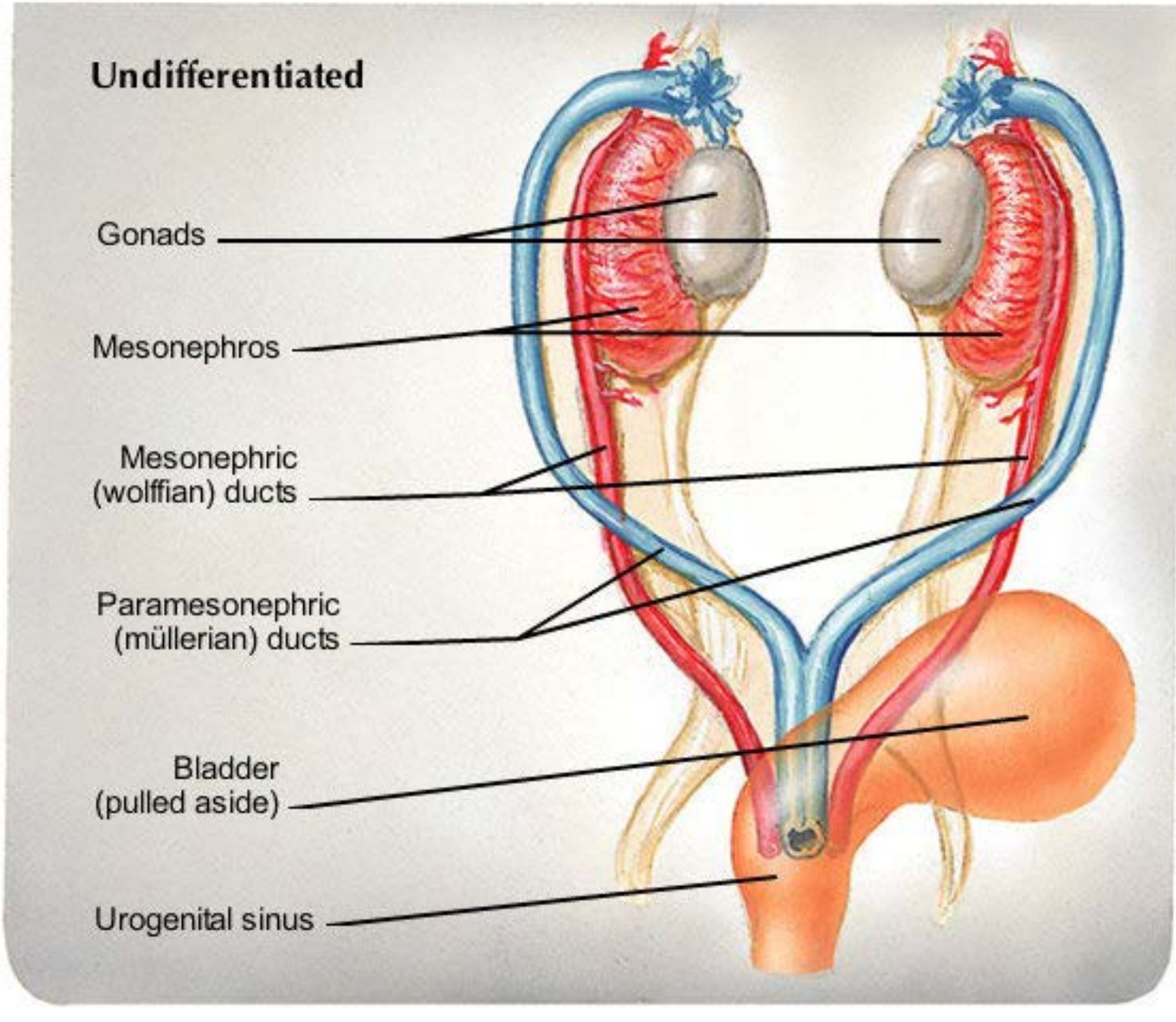
Urogenital ridge differentiates into medial genital ridge and a lateral nephrogenic ridge

Early Primordia



8-Week Undifferentialed (Indifferent) Stage

Anterior view (mesonephros will disappear in both sexes)



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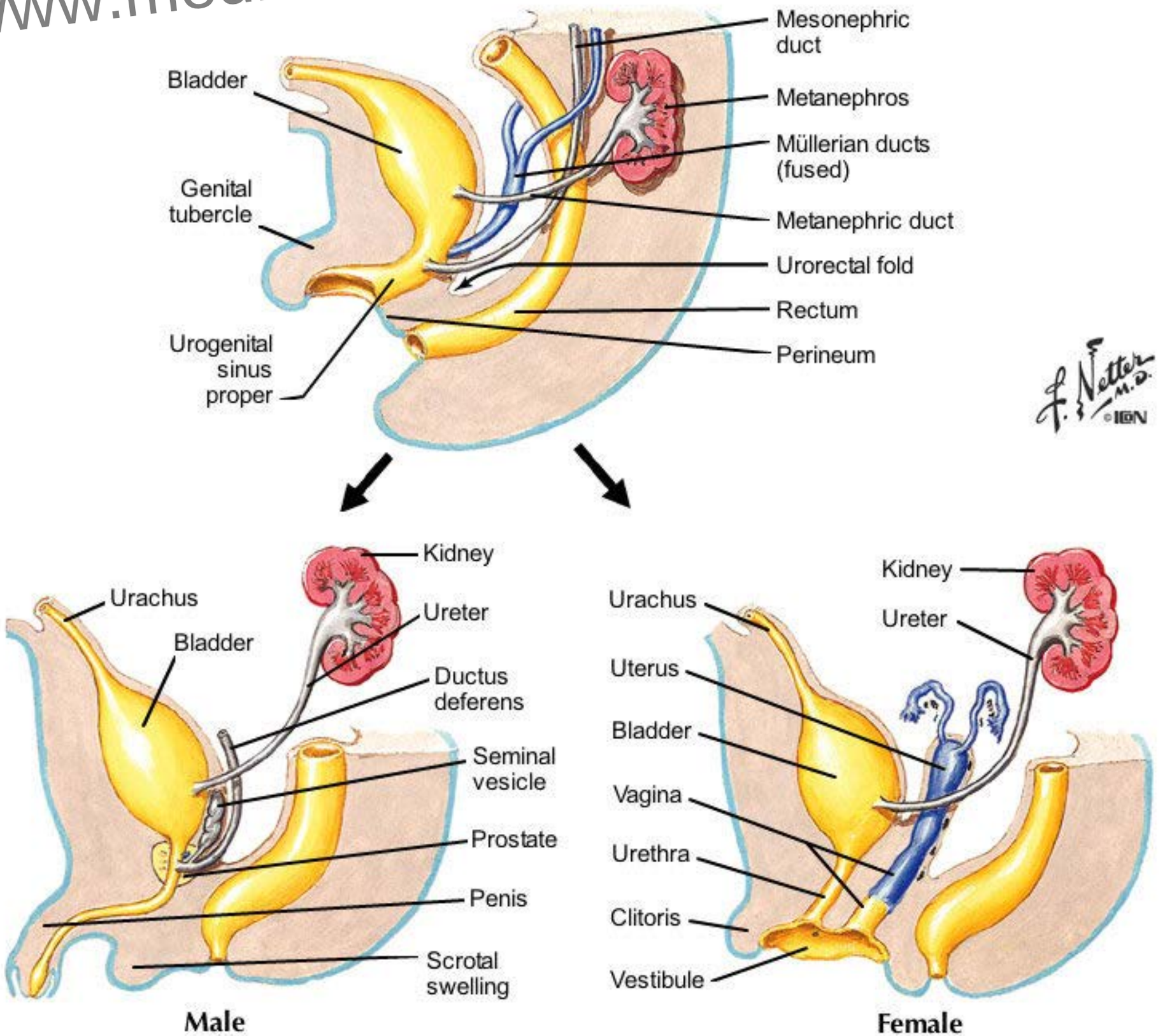
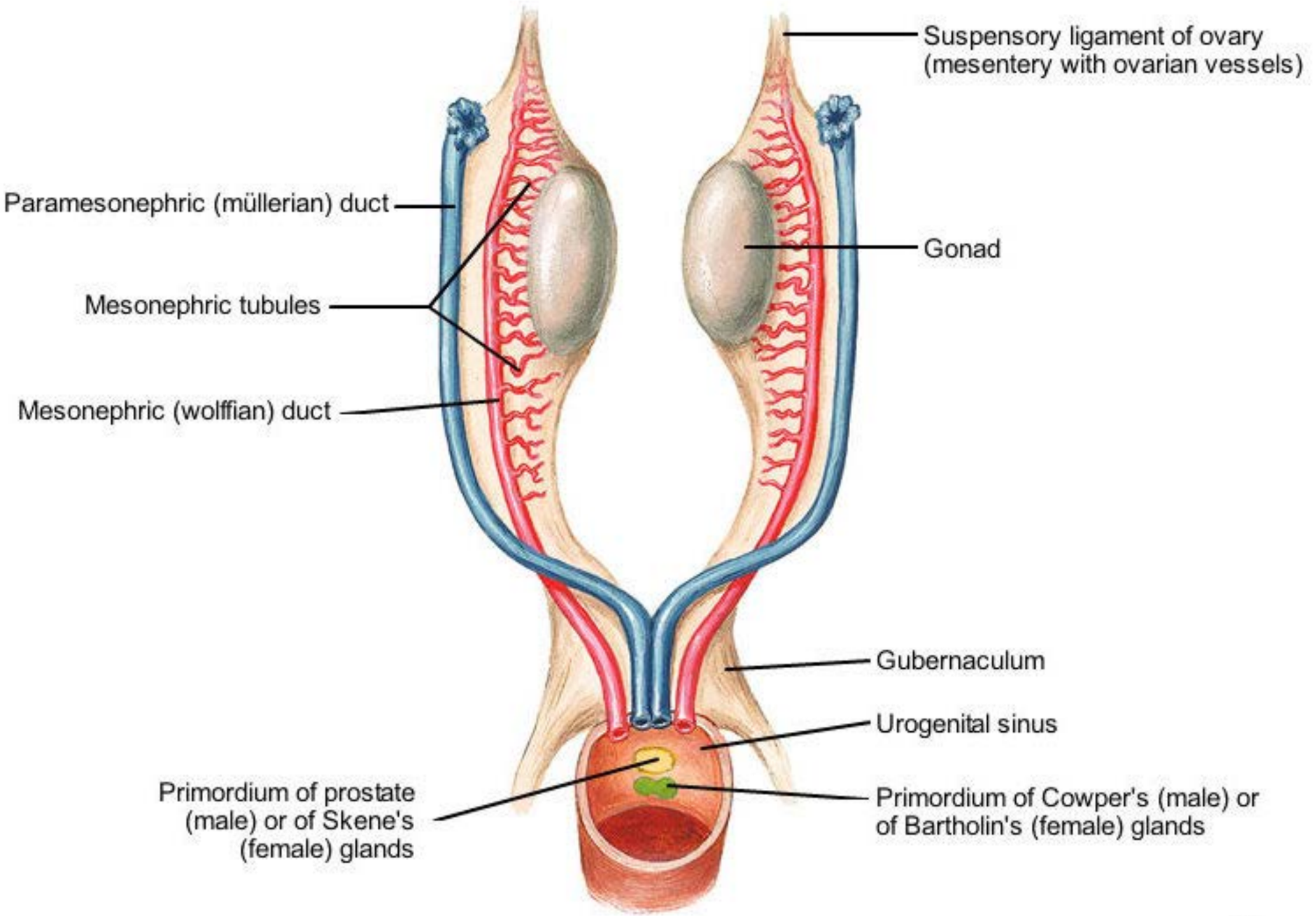
8-Week Undifferentialed (Indifferent) Stage

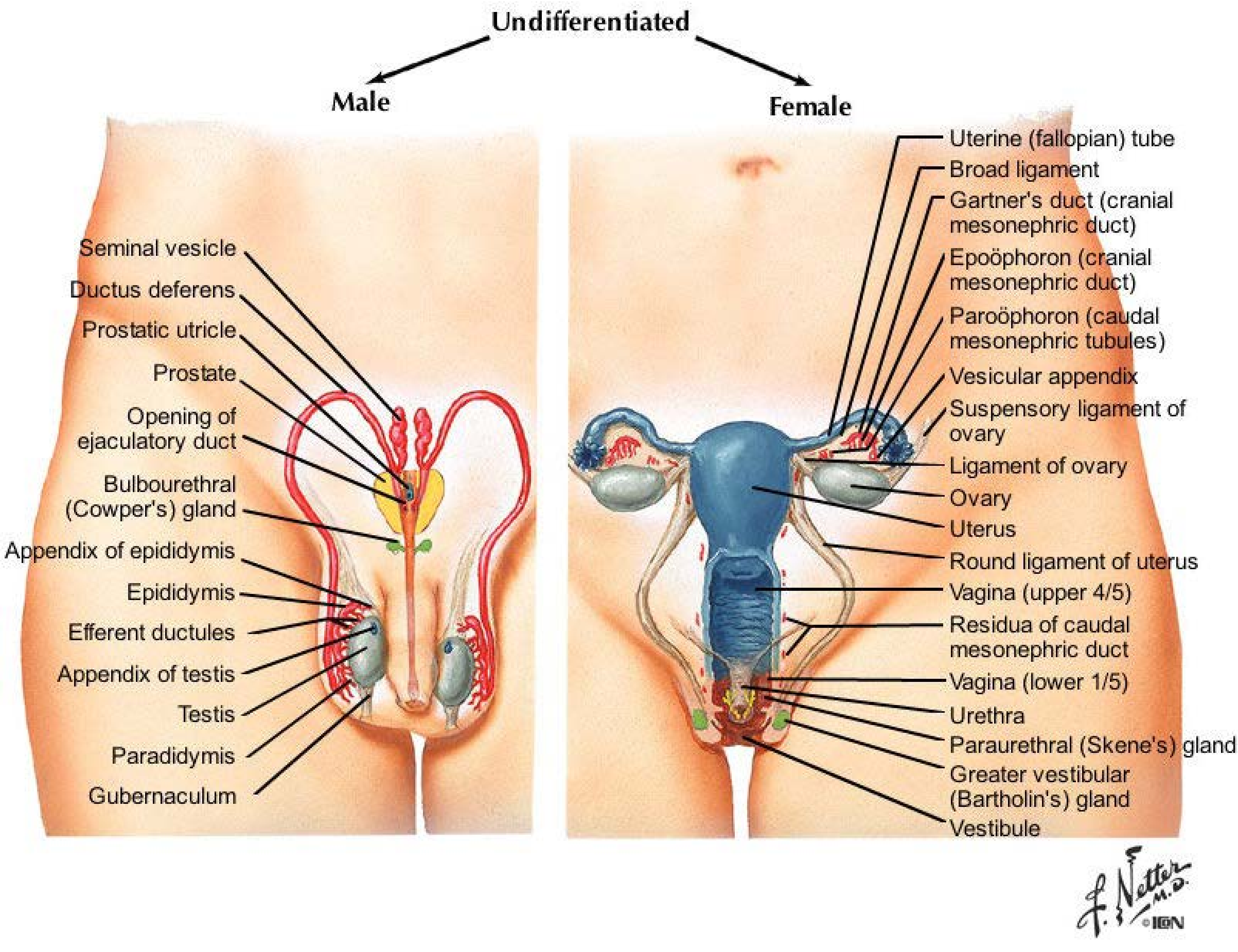
Lateral view (both sexes have identical primordia)



Anterior View of the Derivatives



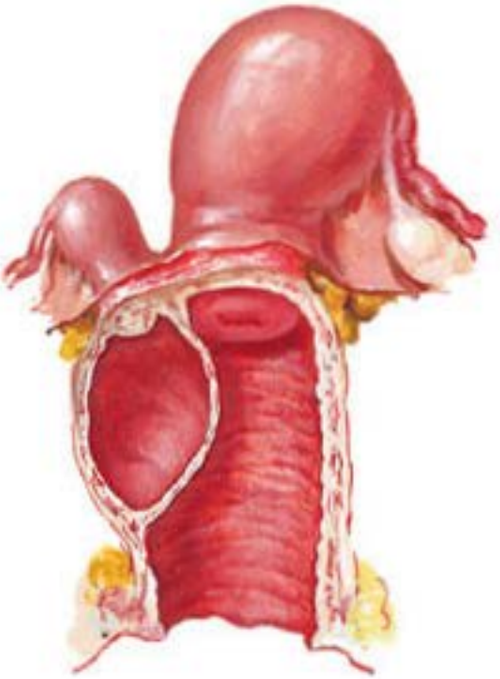
Anterior View of the Derivatives



Paramesonephric Duct Anomalies

Complete septum with double uterus and double vagina

Partial septum



Rudimentary second vagina without external opening, forming cyst

Bicornuate uterus with complete septum (double cervix)

Bicornuate uterus

Double uterus

Septate uterus

Partial septum

Unicornuate uterus

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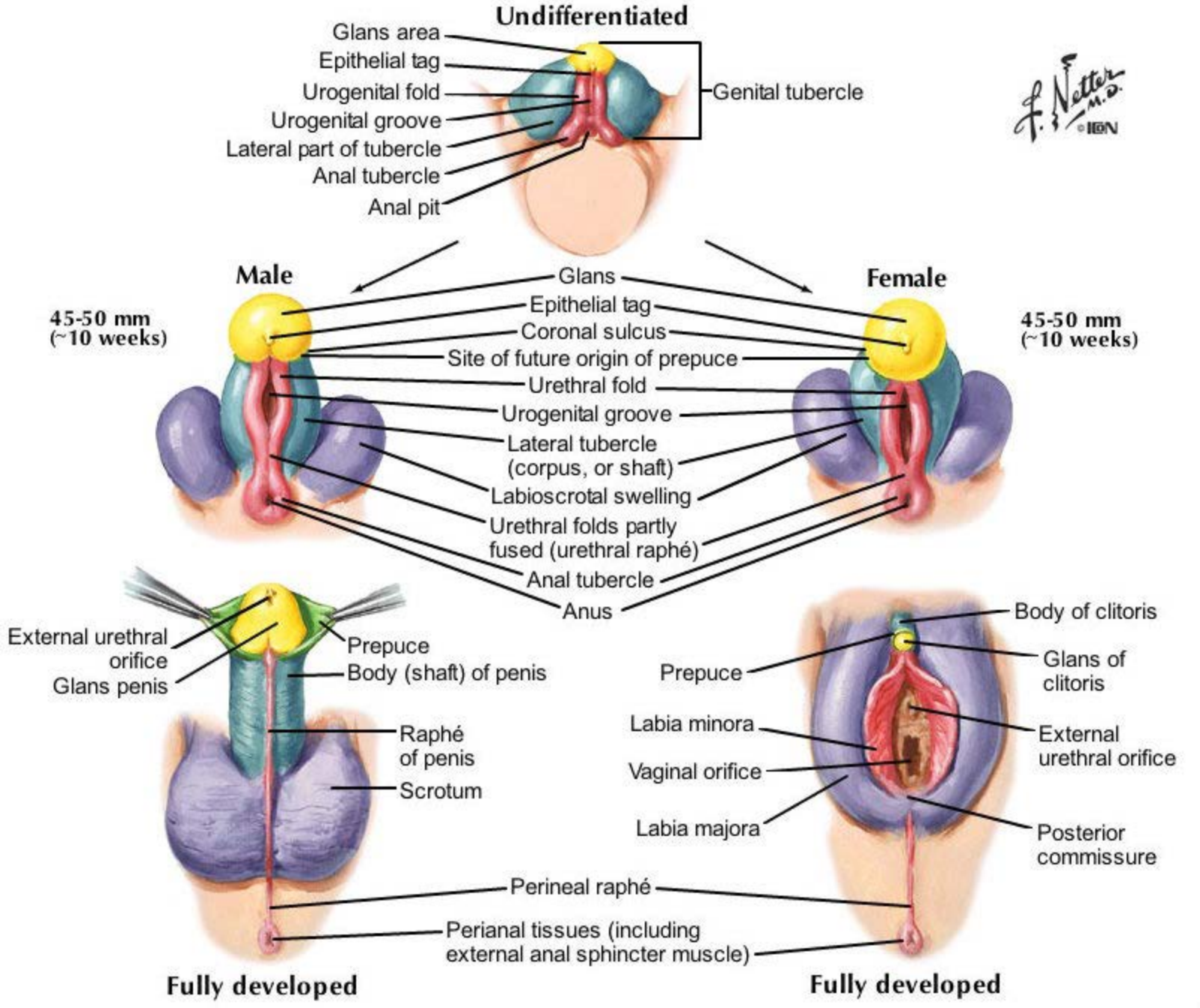
Homologues of the External Genital Organs

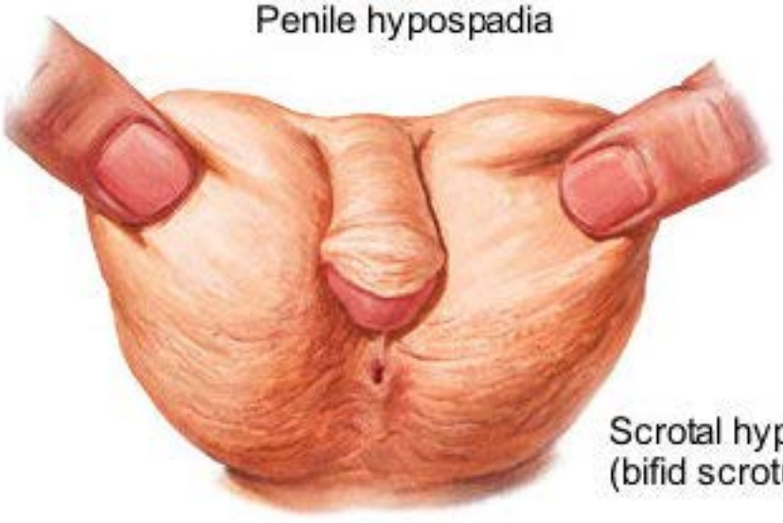


Hypospadia and Epispadias

Glanular hypospadia

Penile hypospadia

Penoscrotal hypospadia
(with chordee)



Scrotal hypospadia
(bifid scrotum, chordee)

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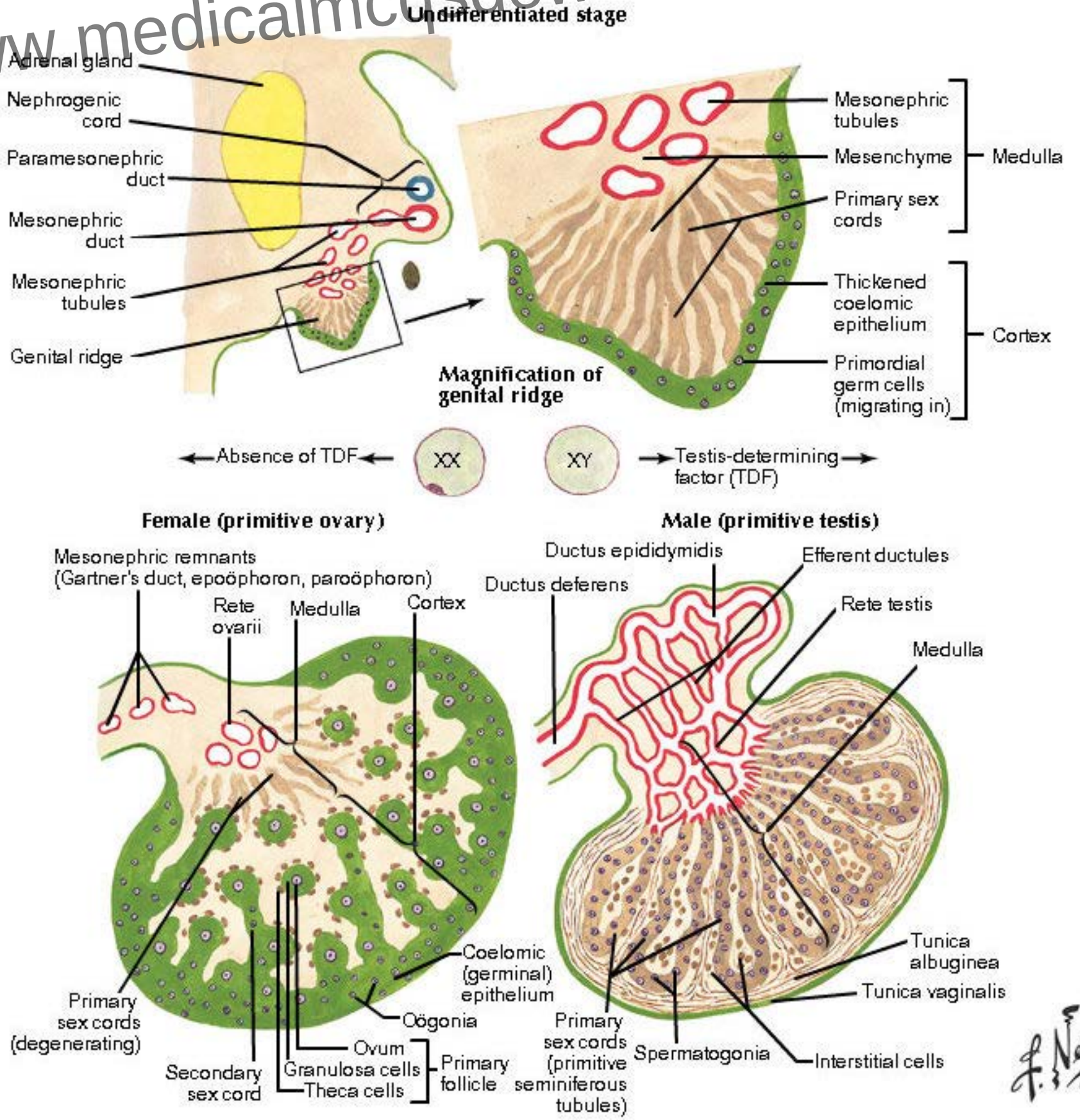
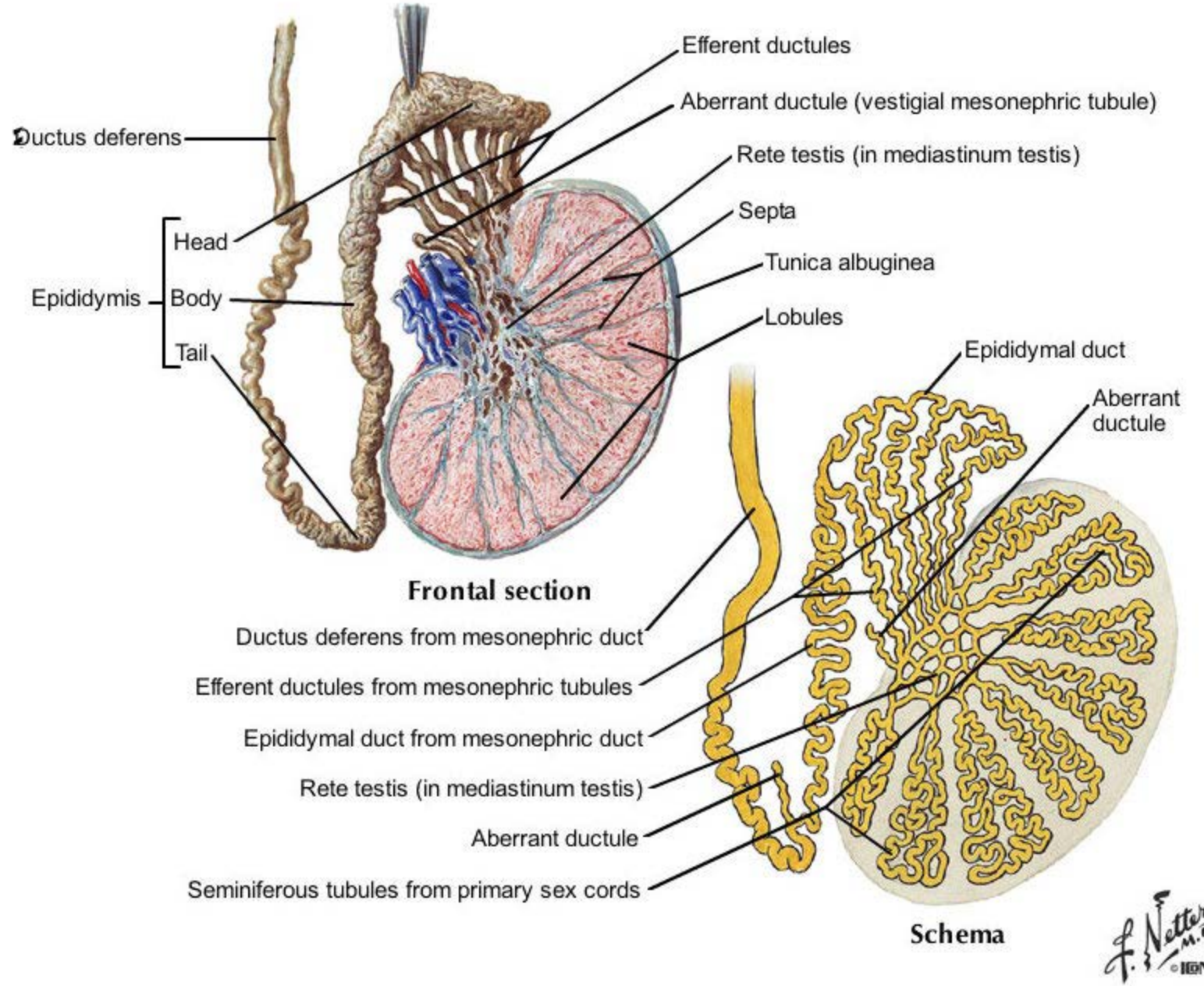
Penile epispadia

Complete epispadia

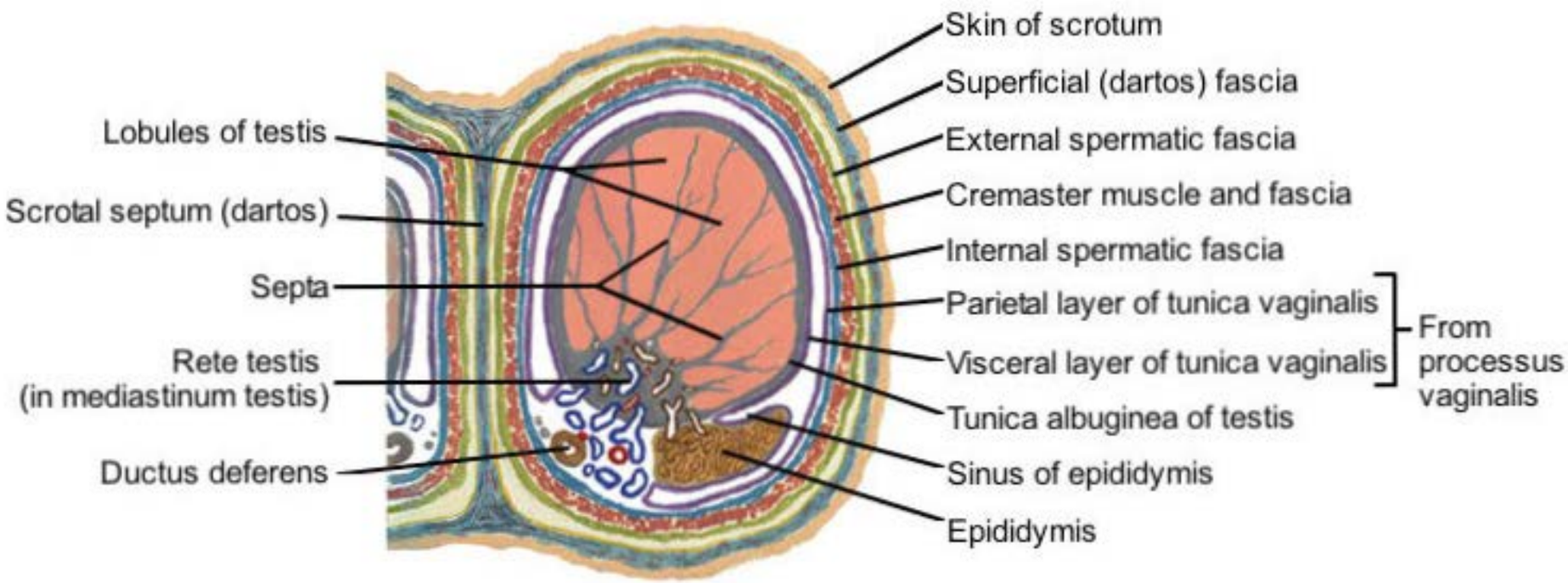
Gonadal Differentiation



Testis, Epididymis, and Ductus Deferens

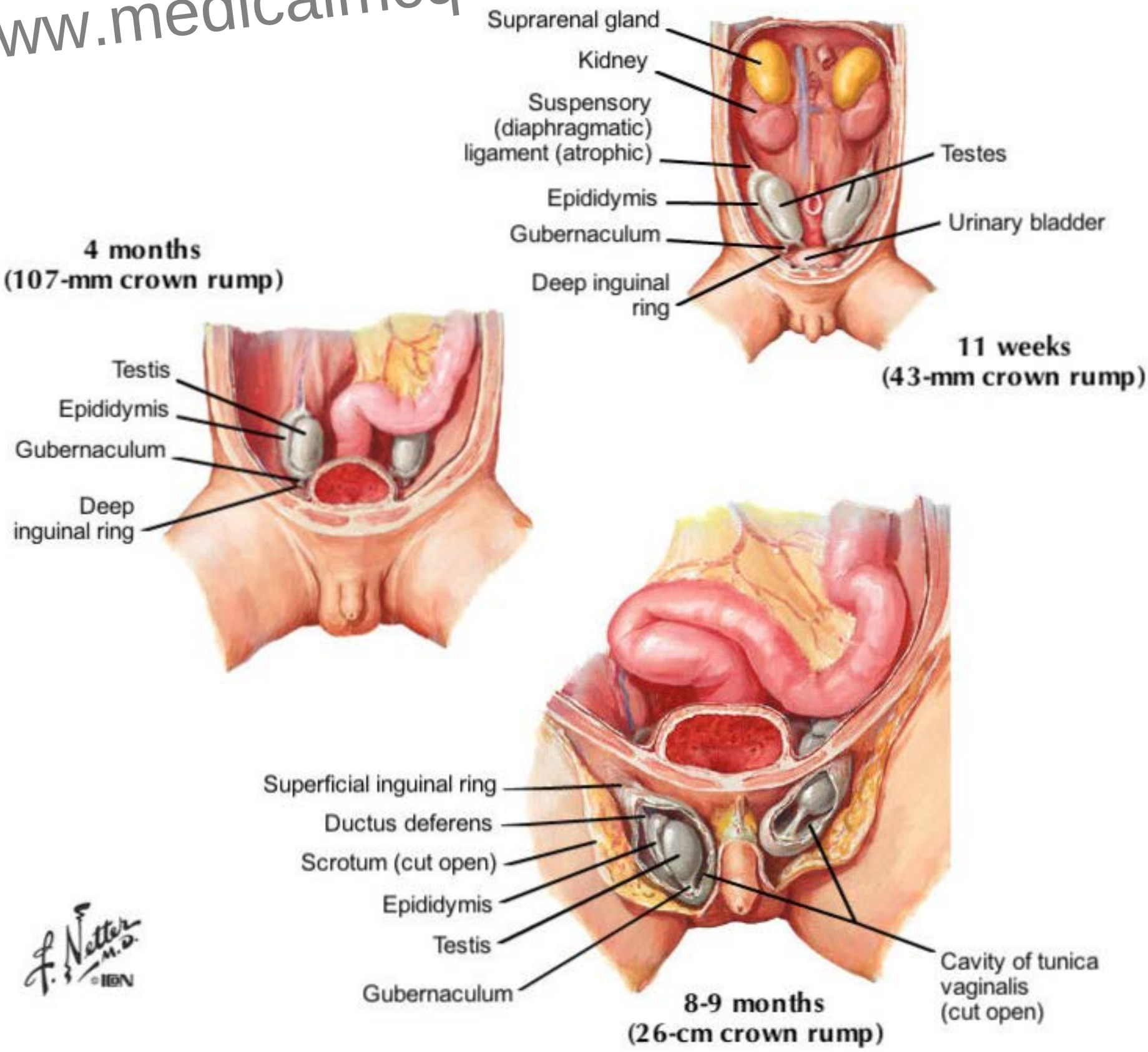


Testis, Epididymis, and Ductus Deferens

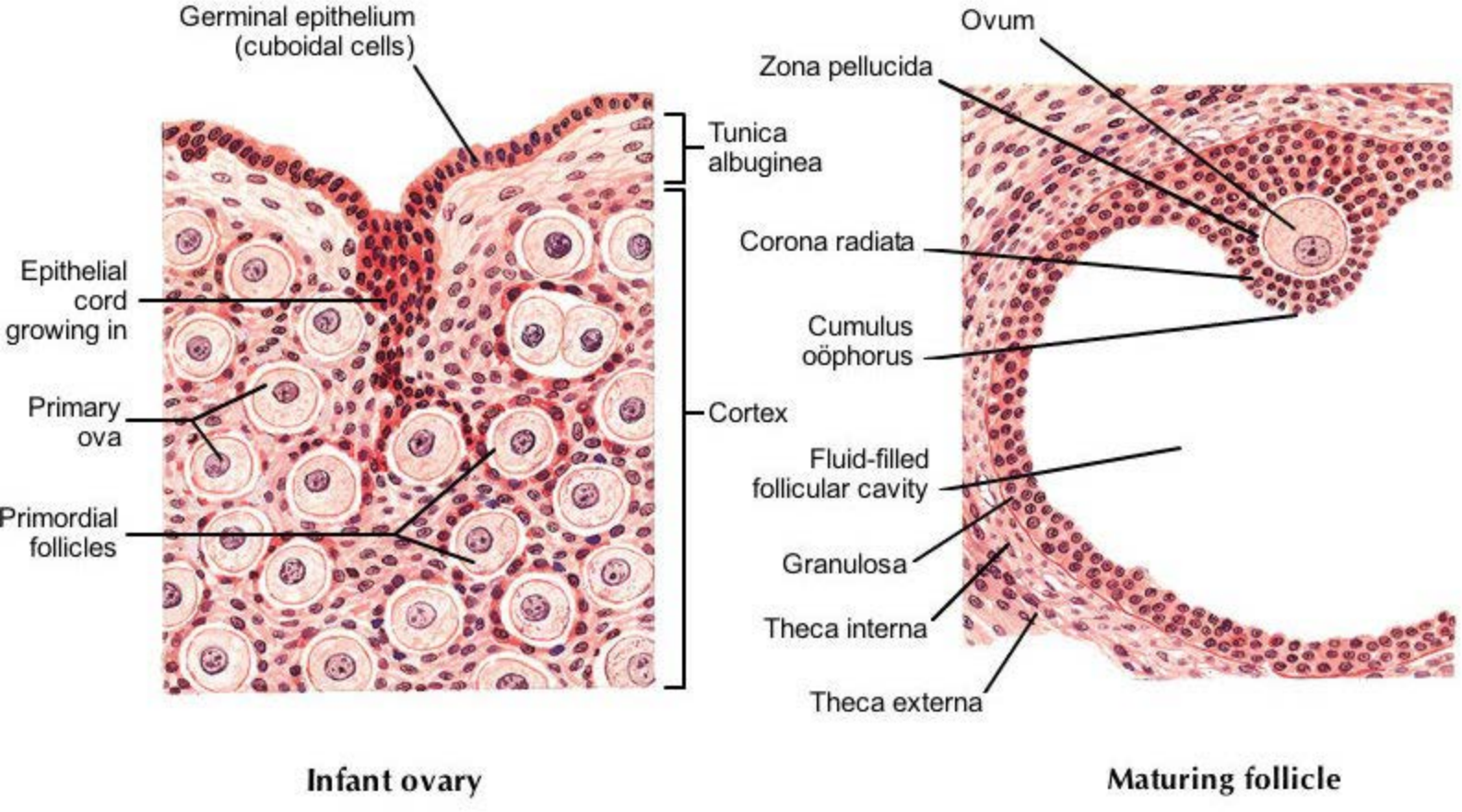


Cross section through scrotum and testis

Descent of Testis



Ova and Follicles

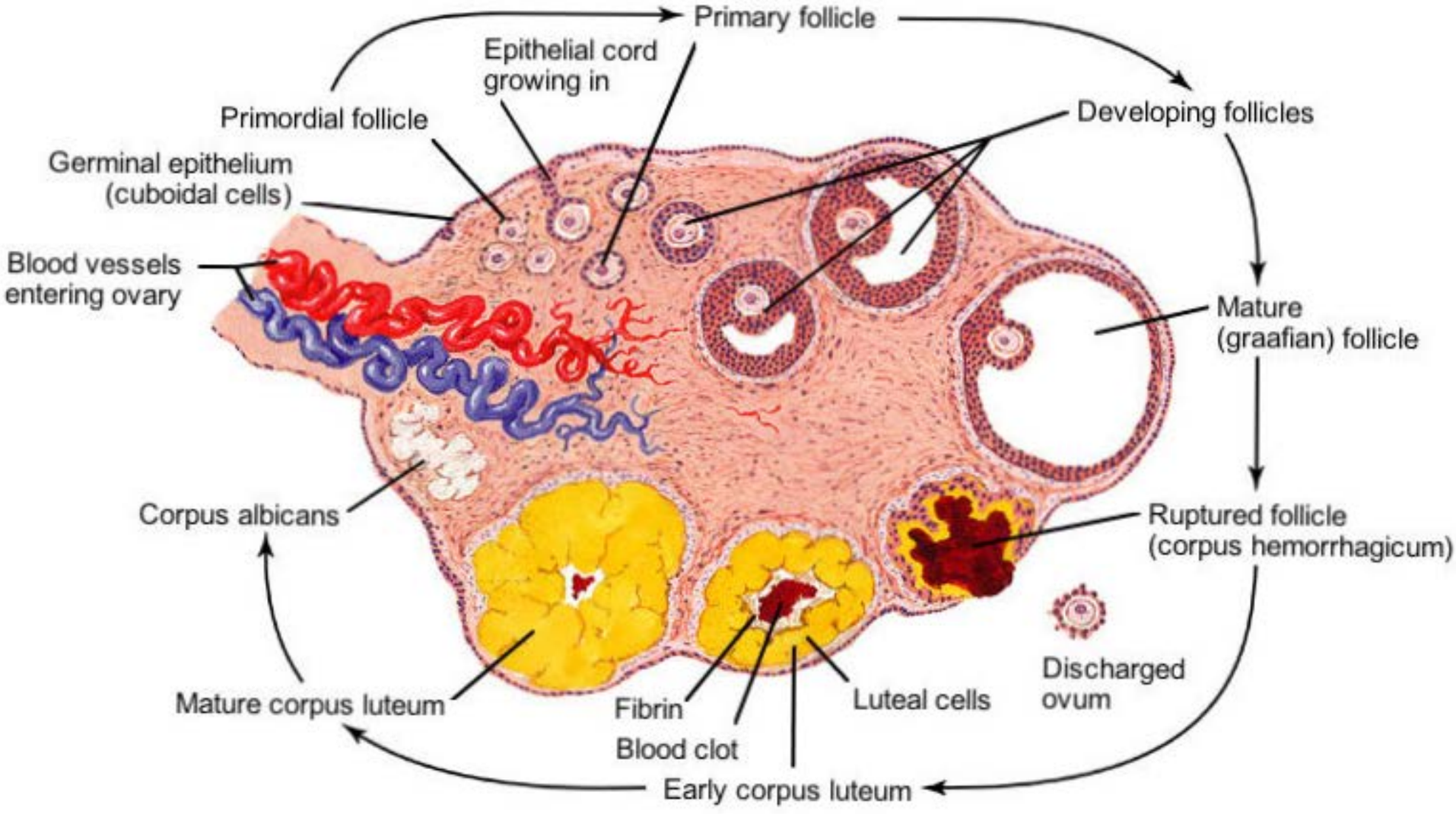


Infant ovary

Maturing follicle

Ova and Follicles

Stages of ovum and follicle



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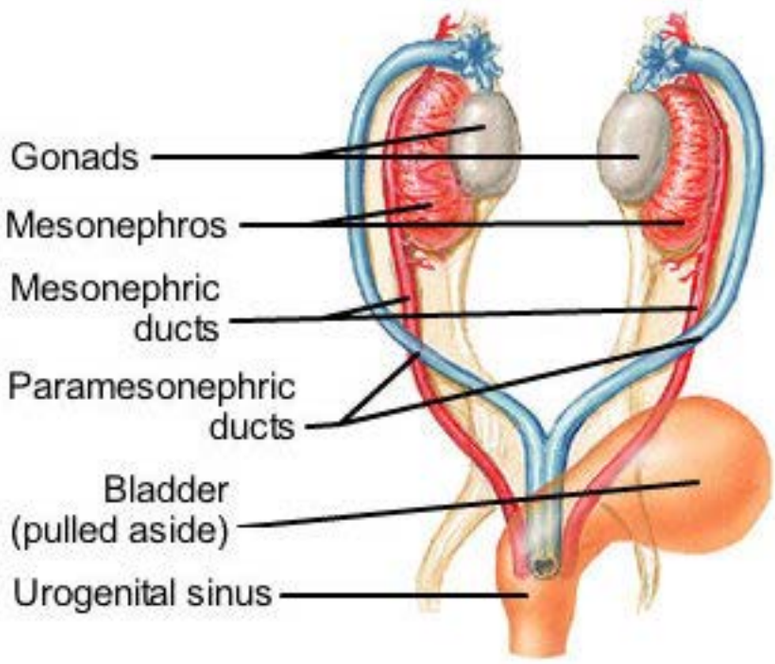
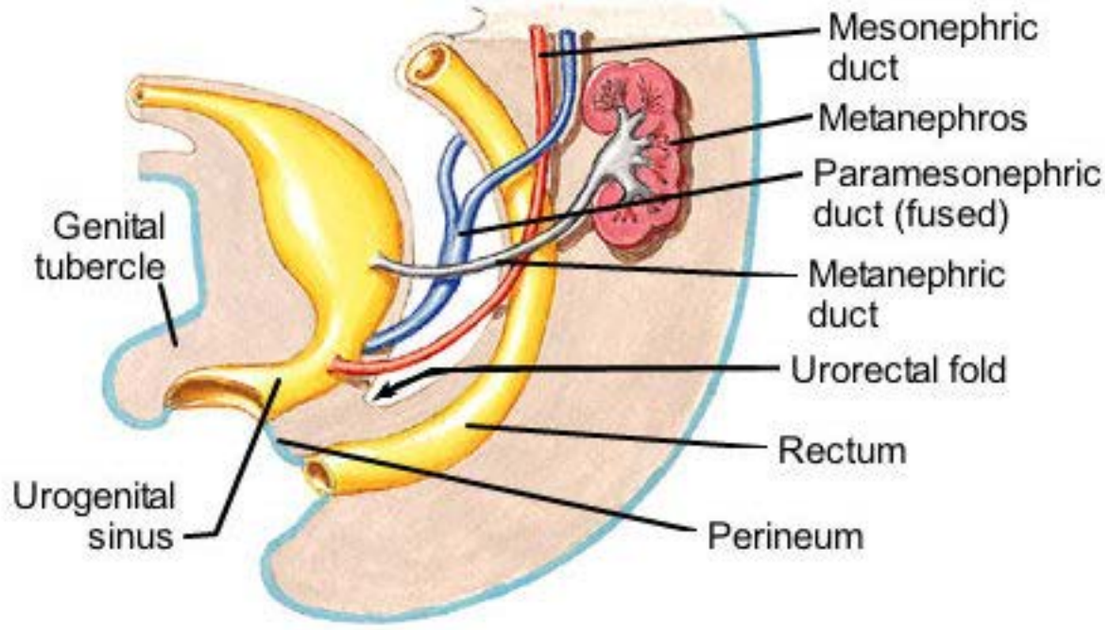
Summary of Urogenital Primordia and Derivatives

Undifferentiated

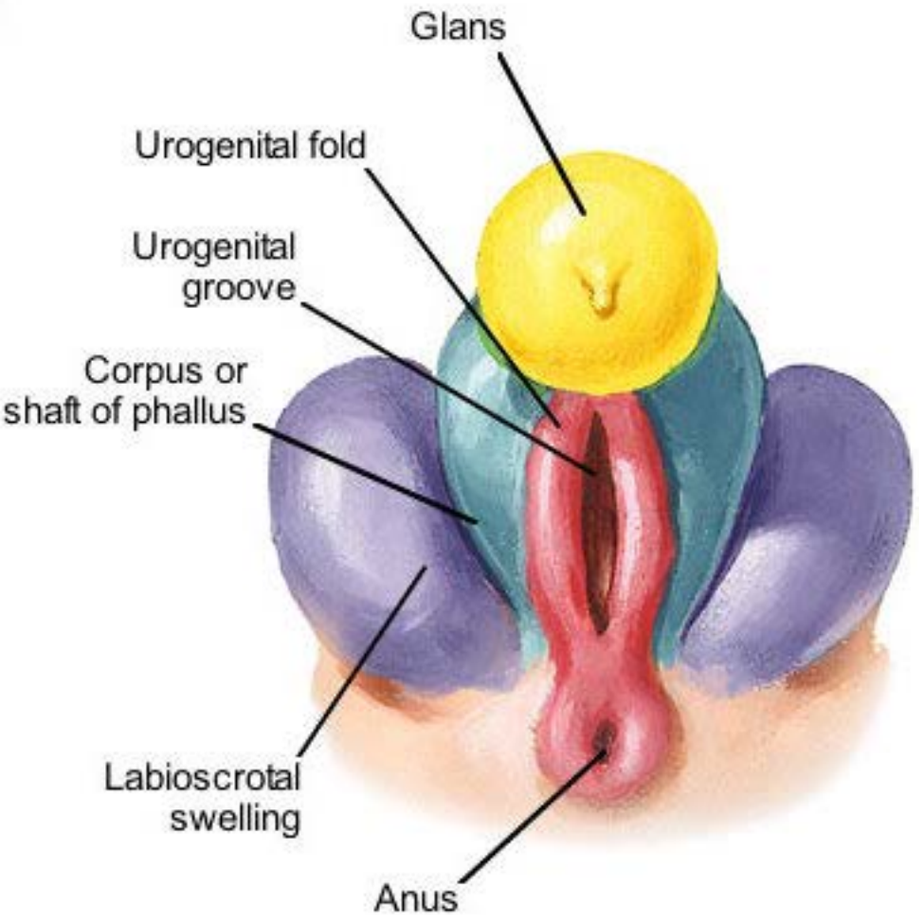


8-week indifferent stage, anterior view

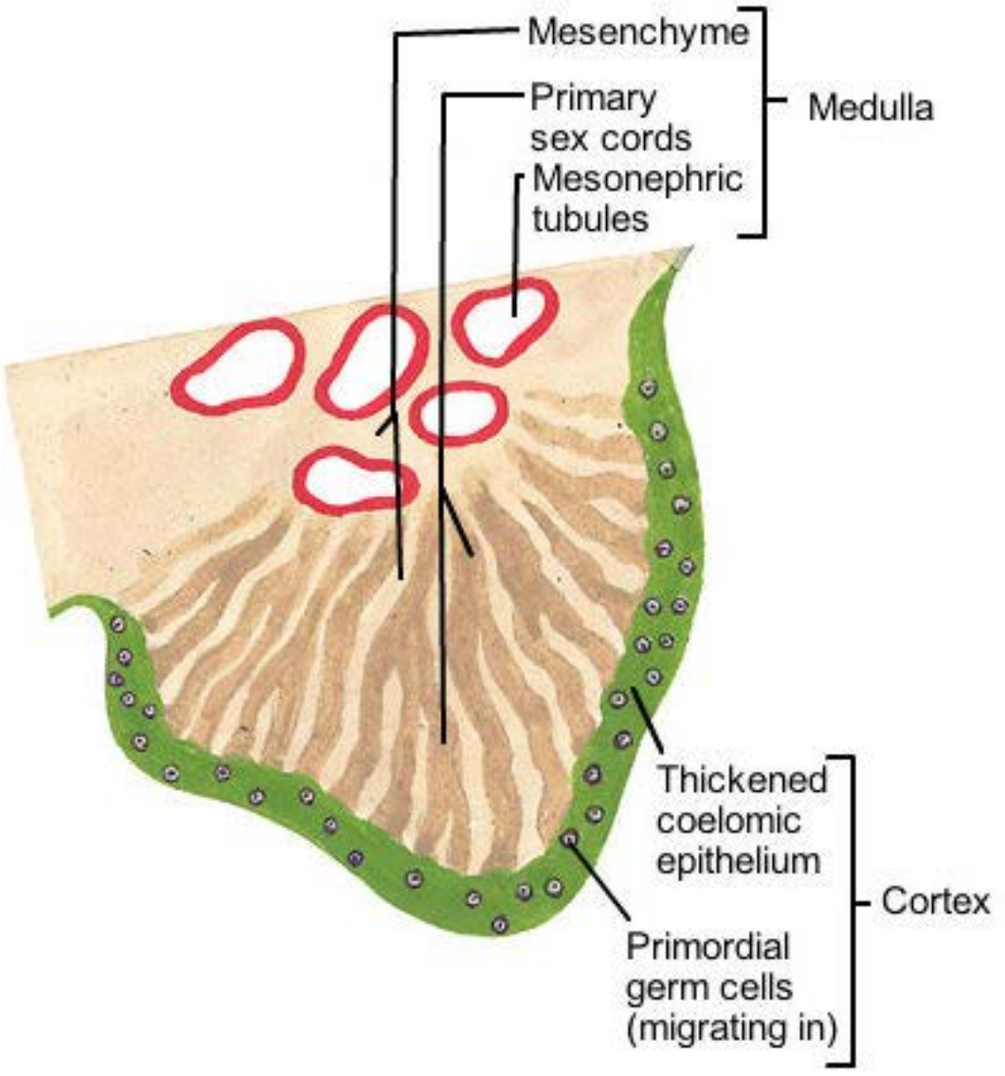


8-week indifferent stage, lateral view (gonad not shown)

Summary of Genital Primordia and Derivatives



10-week external genitalia primordia



Indifferent gonad developing from genital ridge

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Urogenital Primordia and Derivatives

Female	Male
From the Urogenital Sinus	
Urinary bladder Urethra Lower vagina (and vaginal epithelium) Vestibule Greater vestibular/urethral glands	Urinary bladder Urethra (except navicular fossa) Prostate gland Bulbourethral glands
	Vestigial: prostatic utricle
From the Mesonephric Duct and Tubules	
Ureteric bud from mesonephric duct forms: Ureter Renal pelvis Major and minor calices Collecting tubules	Efferent ductules Duct of epididymis Ductus deferens Ejaculatory duct Seminal vesicles Ureter, renal pelvis, calices, and collecting tubules
Vestigial: epoophoron, paoophoron, appendix vesiculosa, Gartner's duct	Vestigial: appendix of testis
From the Paramesonephric Duct	
Uterine tubes, uterus, upper vagina	Vestigial: appendix of testis
Vestigial: hydatid	

Genital Primordia and Derivatives

GENITAL PRIMORDIA AND DERIVATIVES

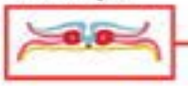
Female	Male
From the Genital Tubercle/Phallus	
Clitoris: Glans clitoridis Corpora cavernosa clitoridis Bulb of the vestibule	Penis: Glans penis (and navicular fossa) Corpora cavernosum penis Corpus spongiosum penis
From the Urogenital Folds	
Labia minora Perineal raphé Perianal tissue (and external anal sphincter)	Ventral aspect of penis Most of the penile urethra Perineal raphé Perianal tissue (and external sphincter)
From the Labioscrotal Folds	
Labia majora	Scrotum
From the Indifferent Gonad	
Ovary: follicles from secondary sex cords in cortex	Testis: seminiferous tubules from primary sex cords Rete testis in medulla
Vestigial: rete ovarii in medulla	
From the Gubernaculum	
Ovarian ligament Round ligament of the uterus	Gubernaculum testis

THE MUSCULOSKELETAL SYSTEM

TIMELINE

Prenatal Time Scale (Months)

19 days



Somites in mature gastrula.

Blastocyst

1 month

Somite sclerotome cells migrate around the neural tube.

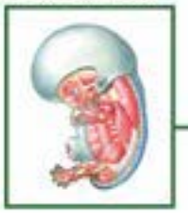
1

6 weeks

Mesenchymal condensation for appendicular skeleton bones.

Embryo

2 months



Individual muscles develop.

2

10 weeks

Primary centers of ossification expand in diaphyses.

Fetus

Newborn

Diaphyses ossified; secondary centers of ossification begin to appear.

3

9

Birth

5 weeks

Mesenchymal precartilage condensations appear for the axial skeleton.

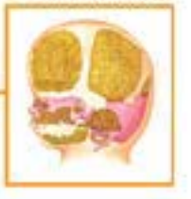
6 weeks

Segmental elaboration of somite myotomes.

7 weeks

The limbs rotate to their adult orientations.

3 months



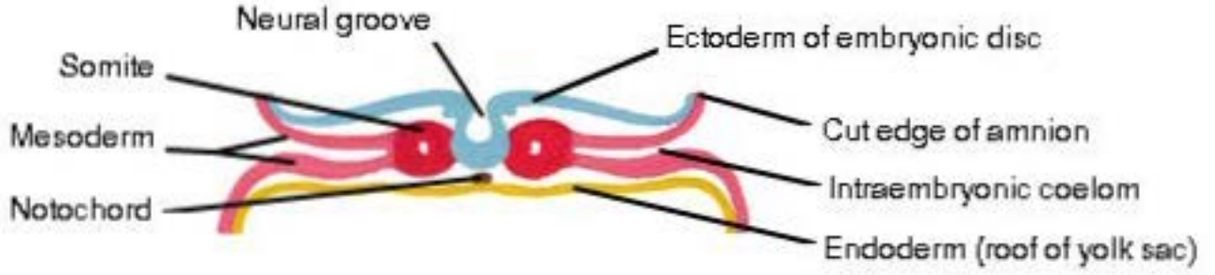
Cartilage and membrane bones of the skull develop.

Muscular System: Primordia

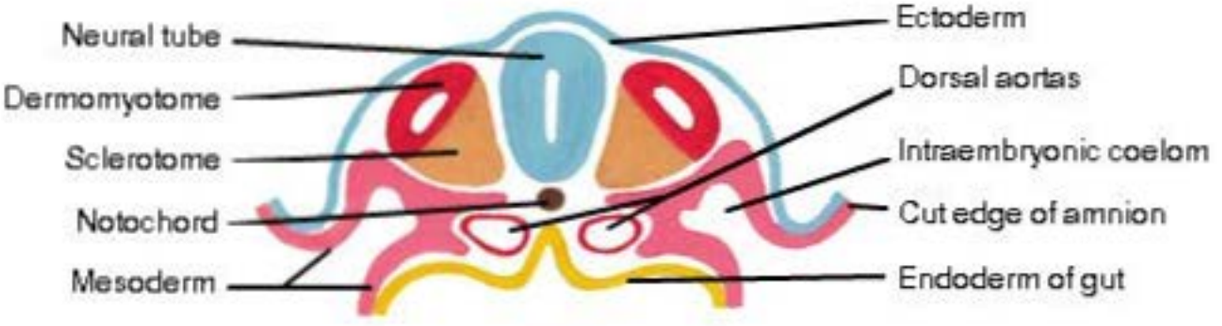
Differentiation of somites into myotomes, sclerotomes, and dermatomes

Cross section of human embryos

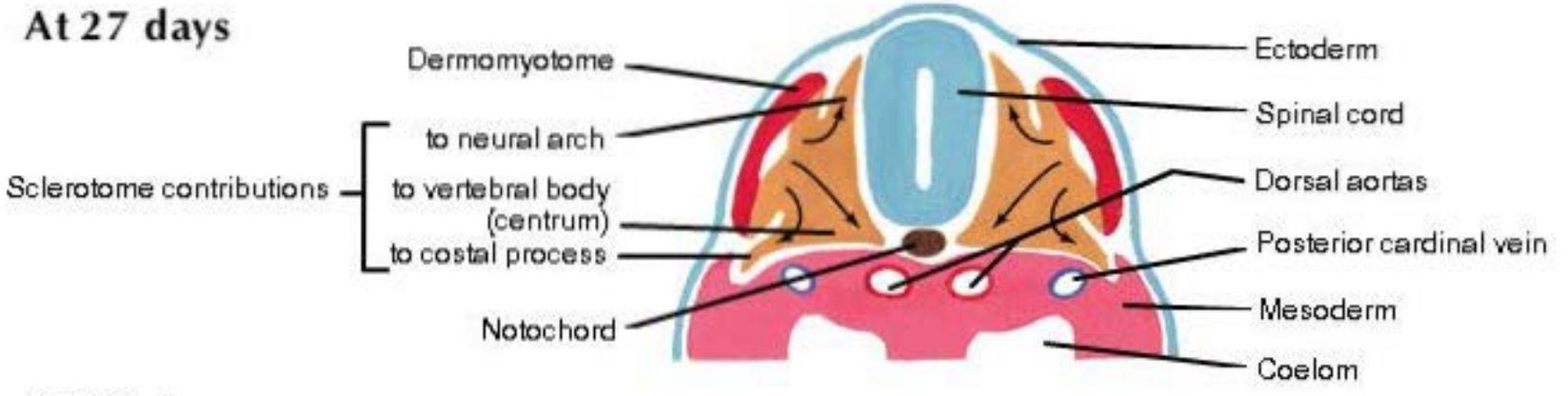
At 19 days



At 22 days



At 27 days

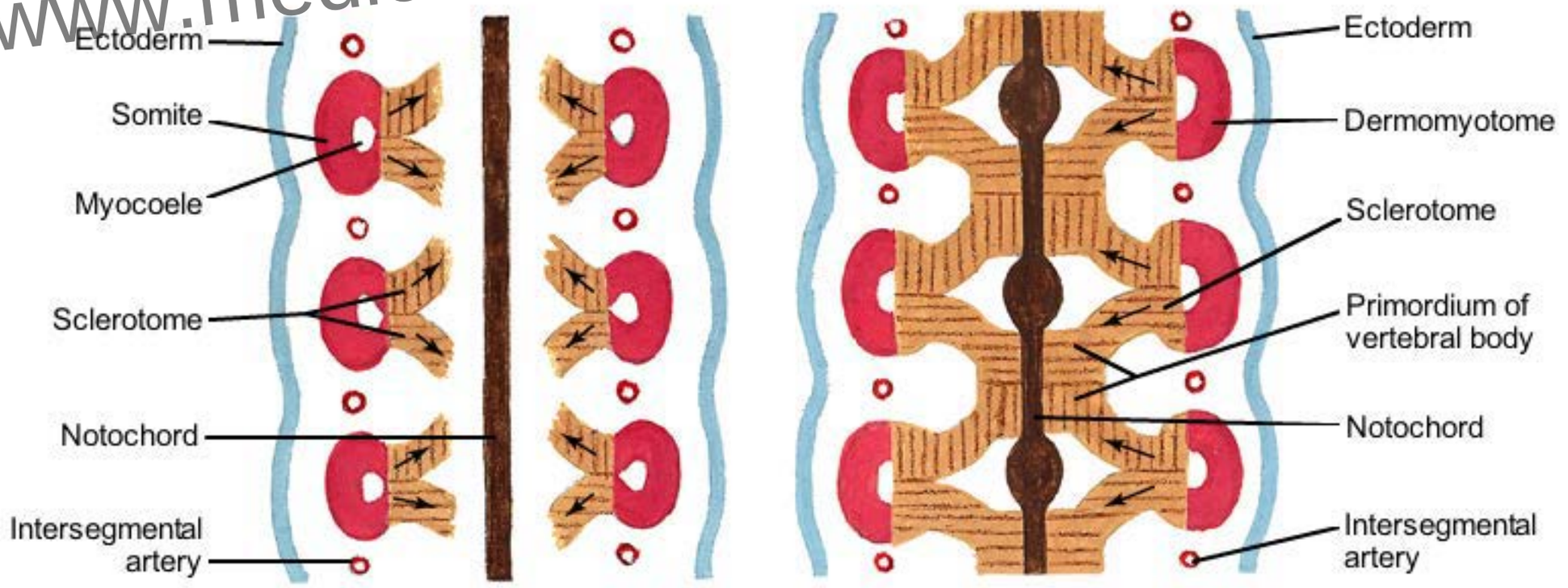


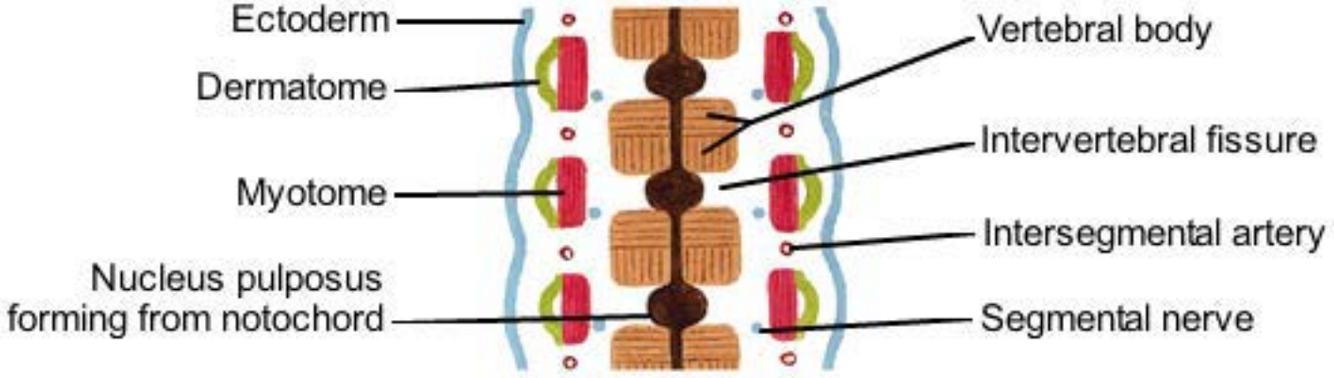
At 30 days

Note: Sections A, B, and C are at level of future vertebral body, but section D is at level between developing bodies

Muscle and Vertebral Column Segmentation

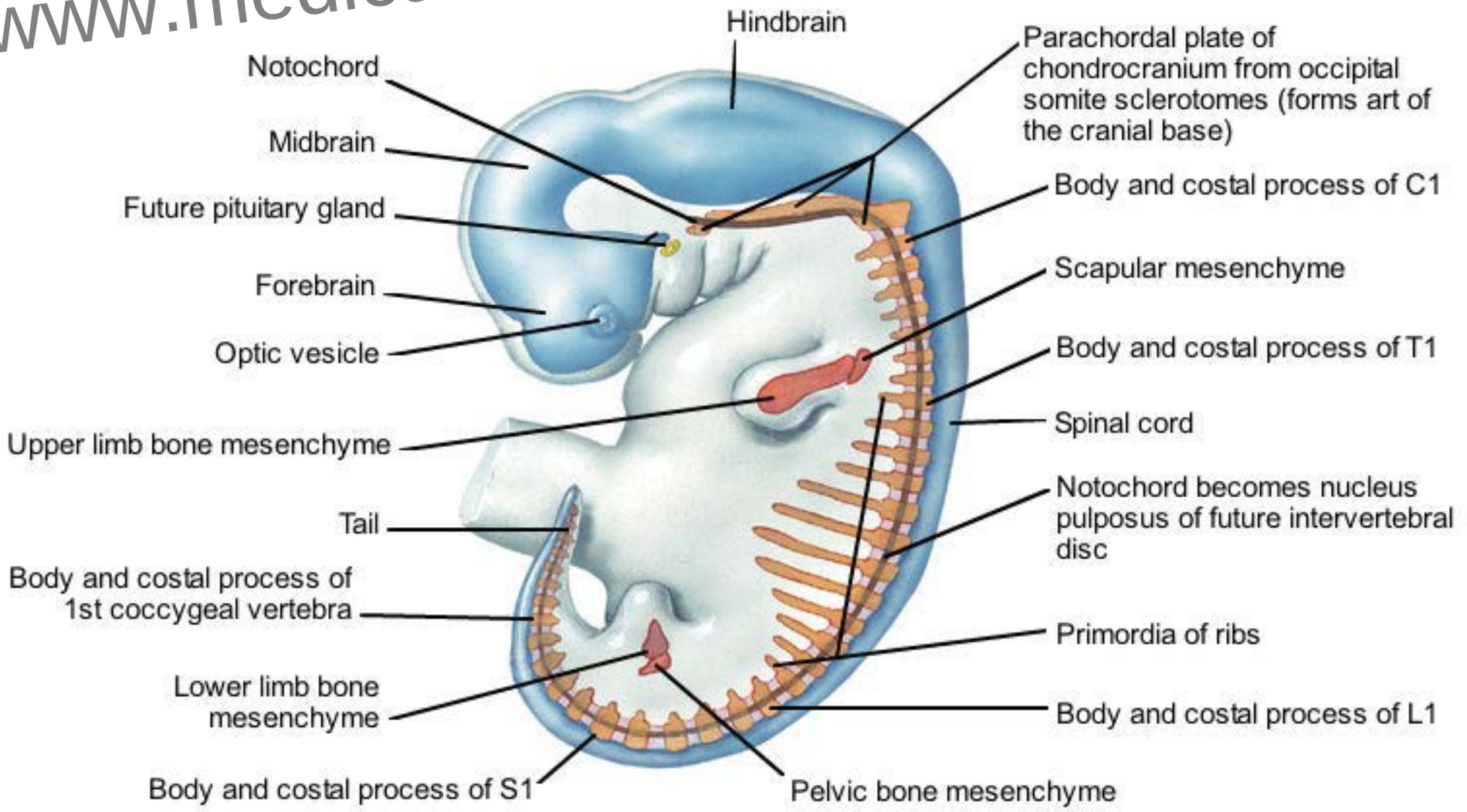
Progressive stages in formation of vertebral column, dermatomes, and myotomes



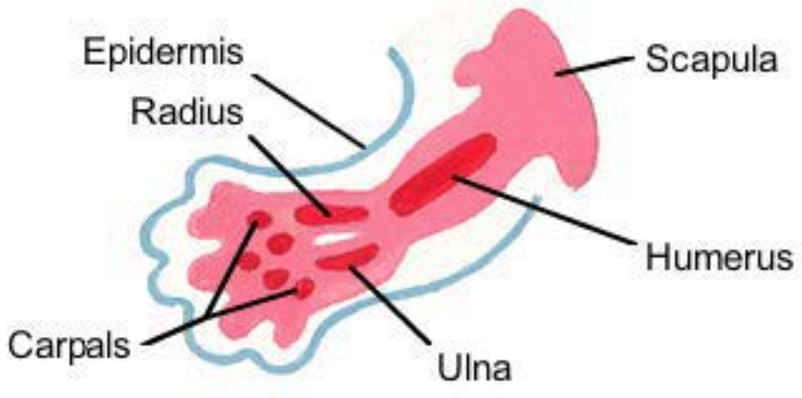


Mesenchymal Primordia and 5 and 6 Weeks

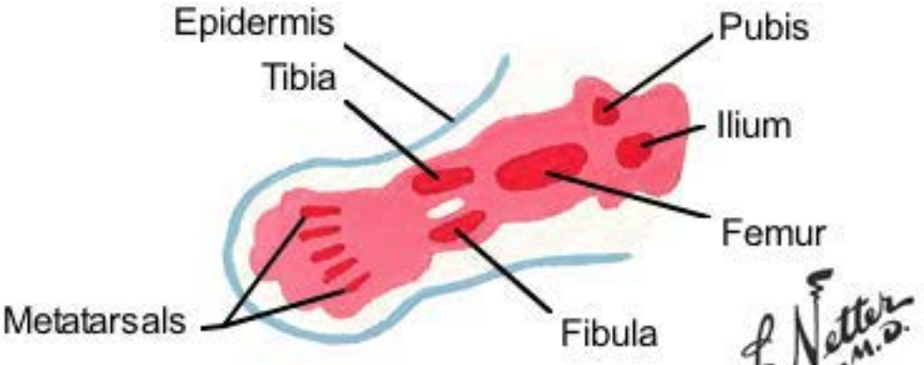
Mesenchymal precartilage primordia of axial and appendicular skeletons at 5 weeks



Precartilage mesenchymal cell condensations of appendicular skeleton at 6th week



Upper limb



Lower limb

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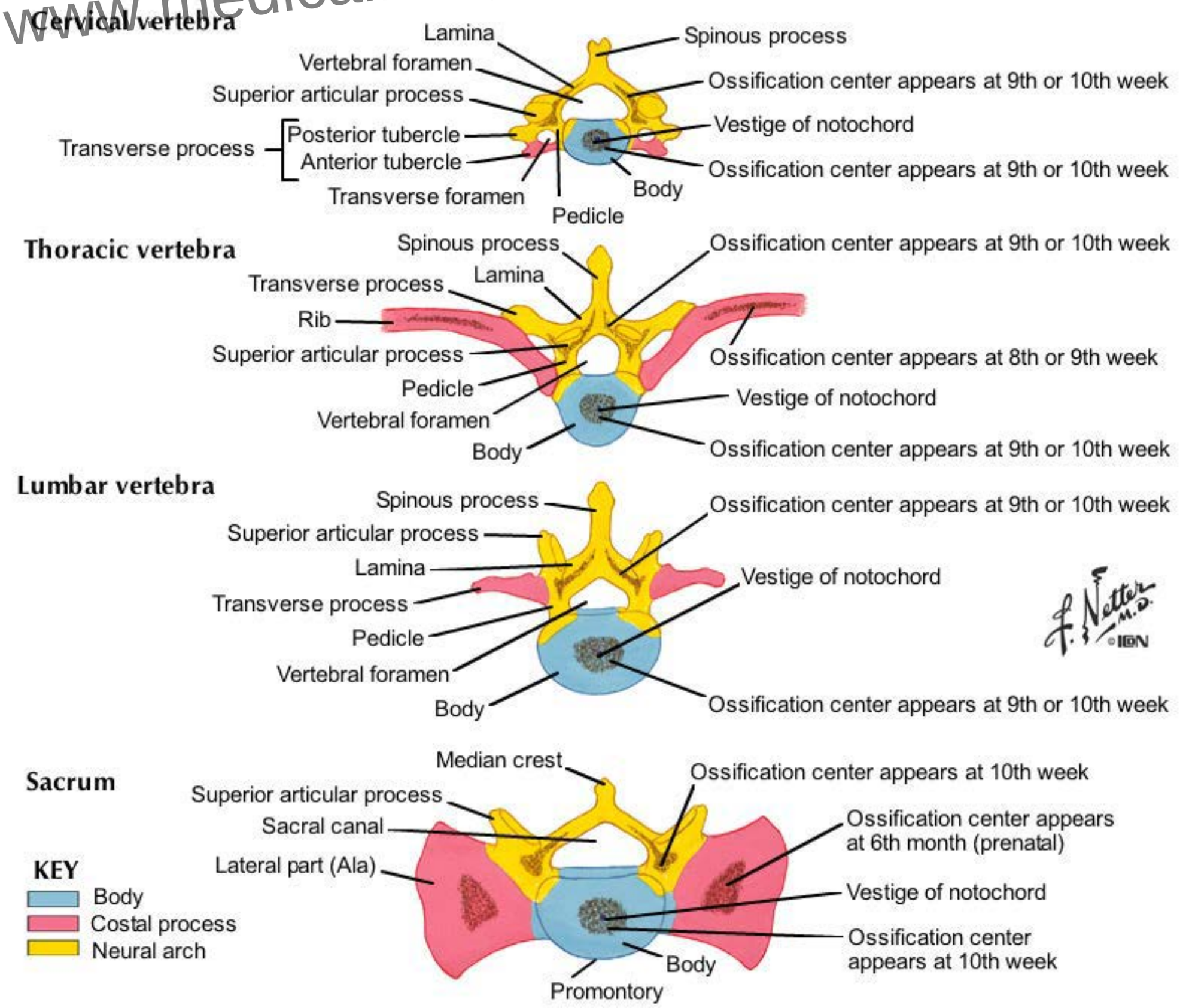
Ossification of the Vertebral Column

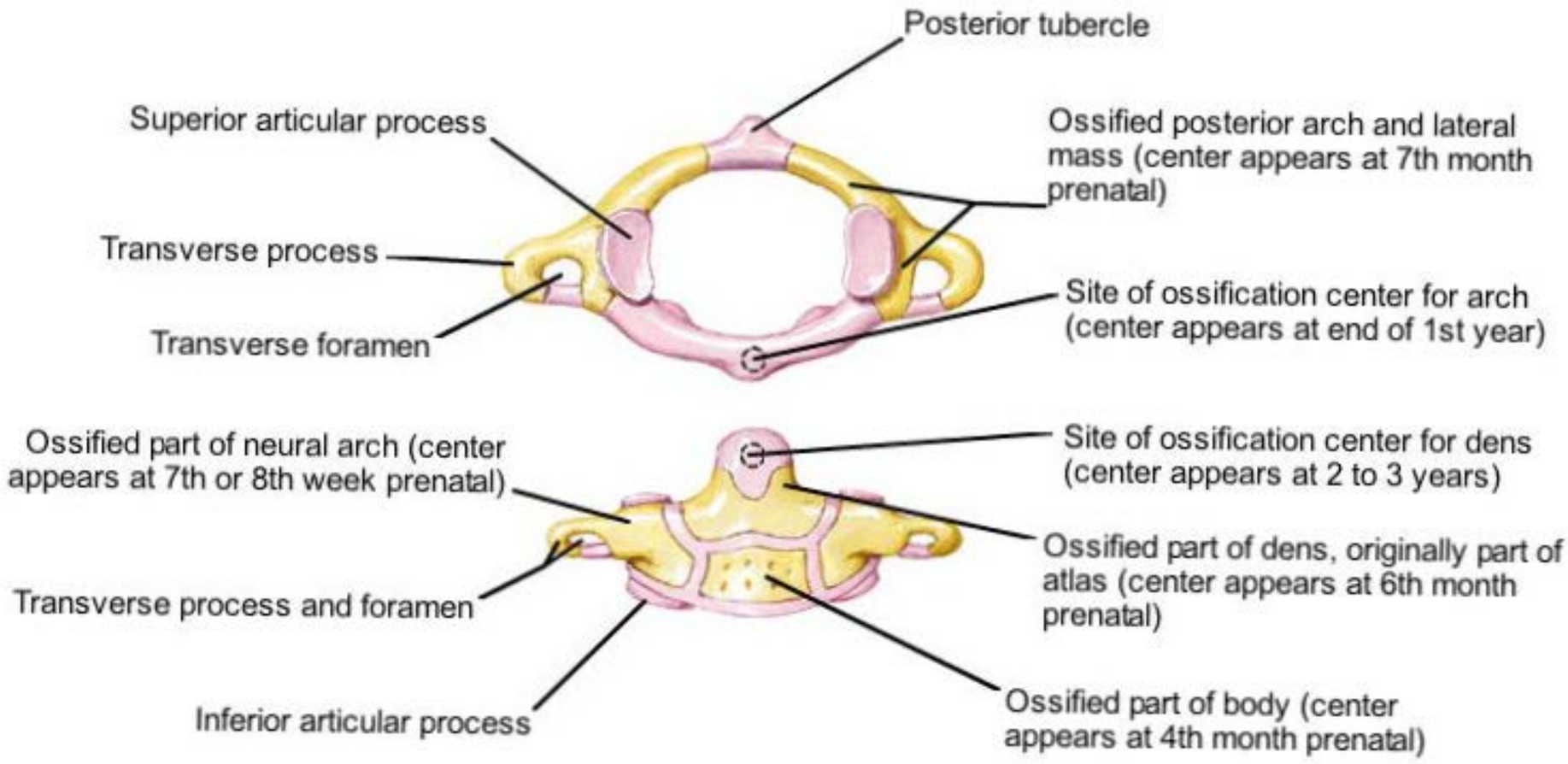
Fate of body, costal process, and neural arch components of vertebral column, with sites and time of appearance of ossification centers



Development of the Atlas, Axis, Ribs, and Sternum

First and second cervical vertebrae at birth

A. 1st cervical vertebra (atlas) (superior view)



B. 2nd cervical vertebra (axis) (anterior view)

KEY

- Cartilage
- Bone

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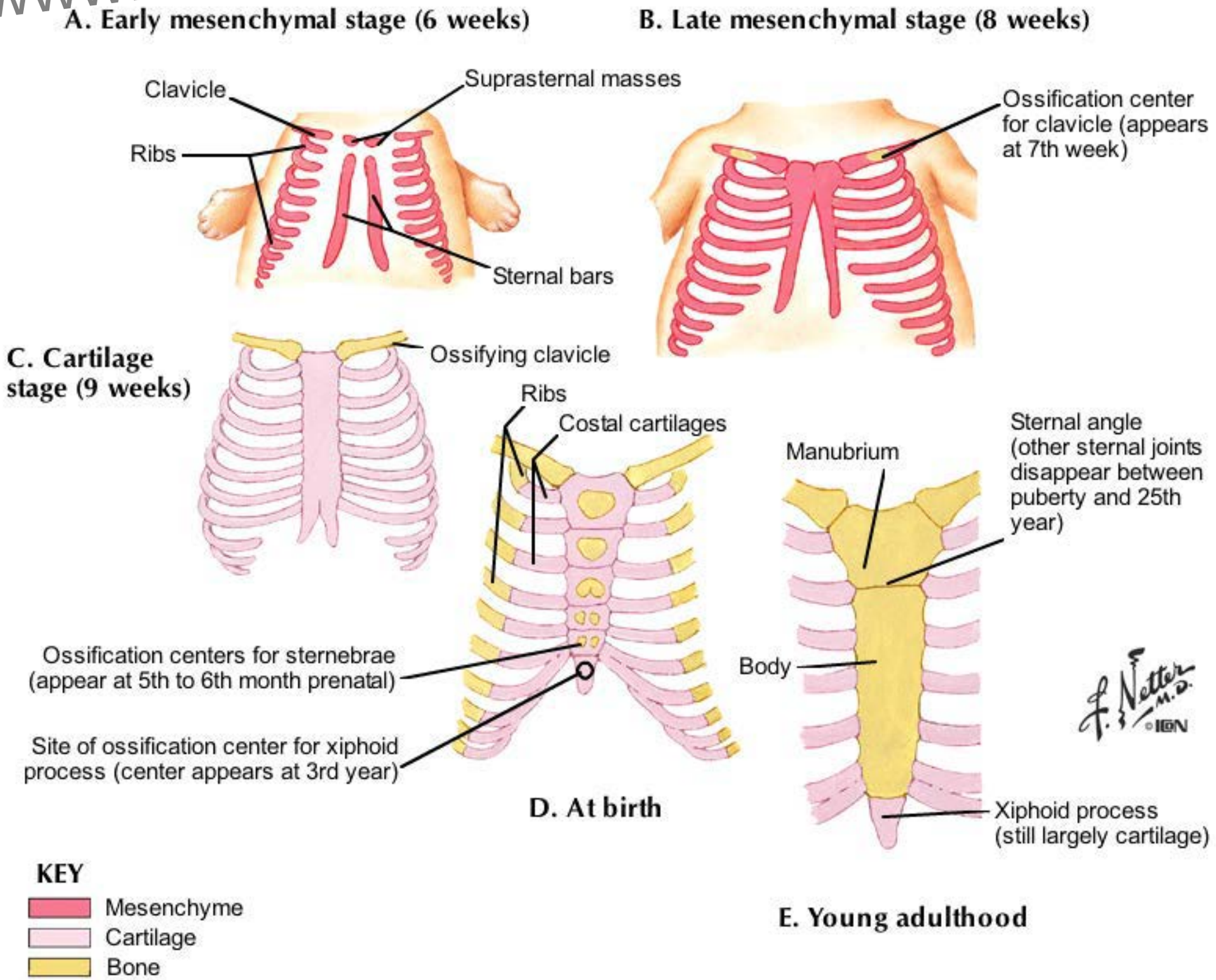
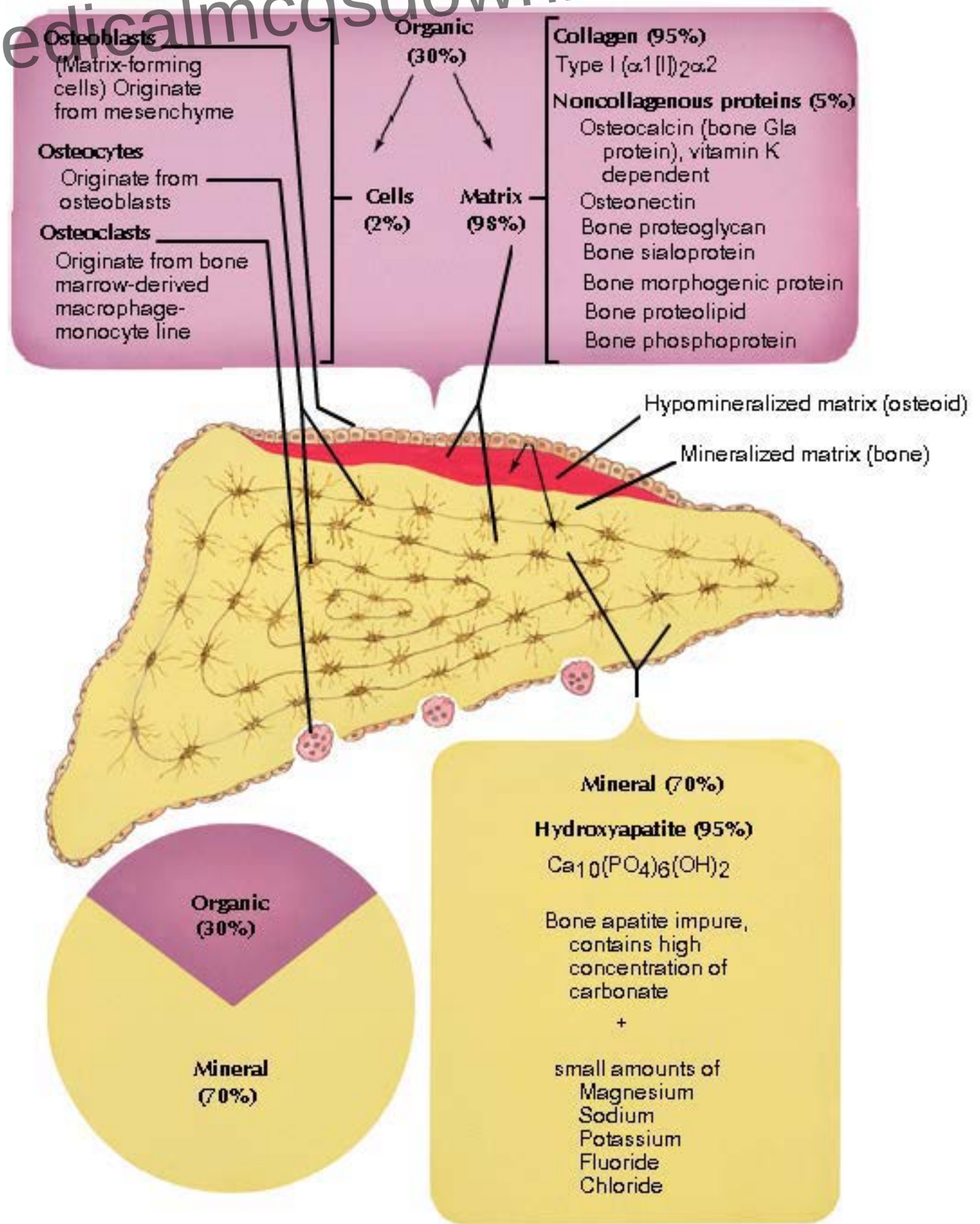
Development of the Atlas, Axis, Ribs, and Sternum

Development of sternum



Bone Cells and Bone Deposition

Composition of bone



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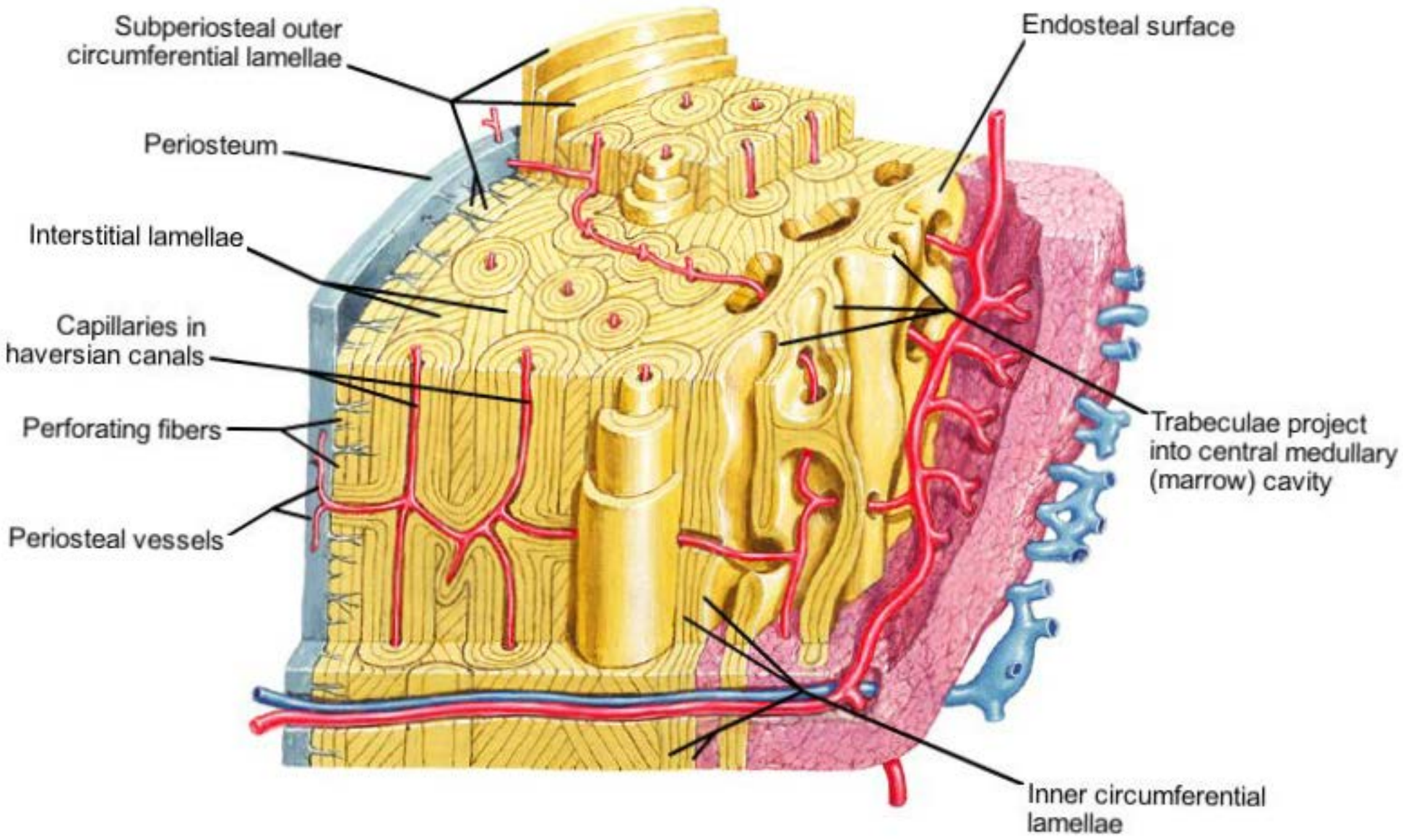
Histology of Bone

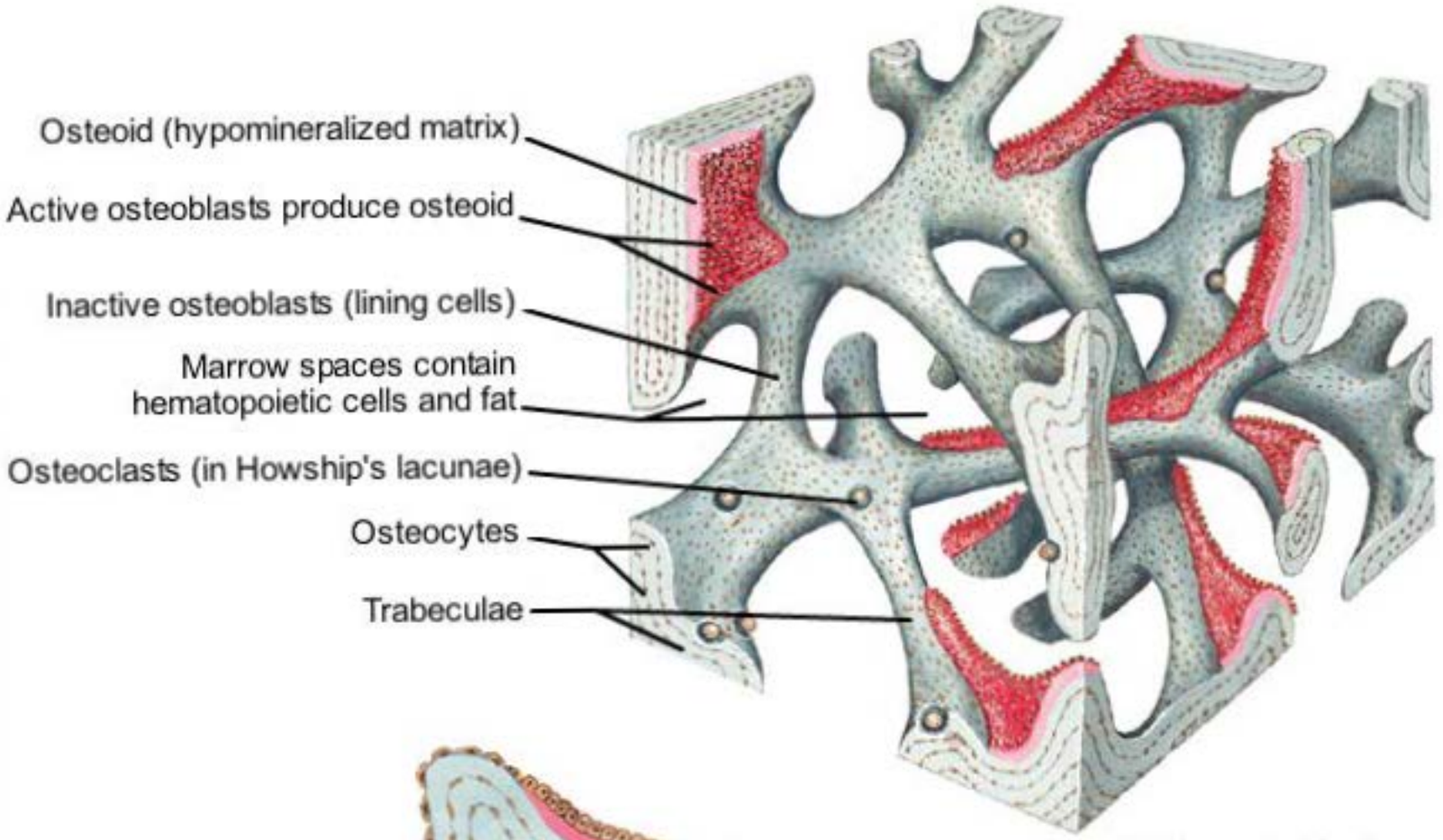
Cortical (compact) bone

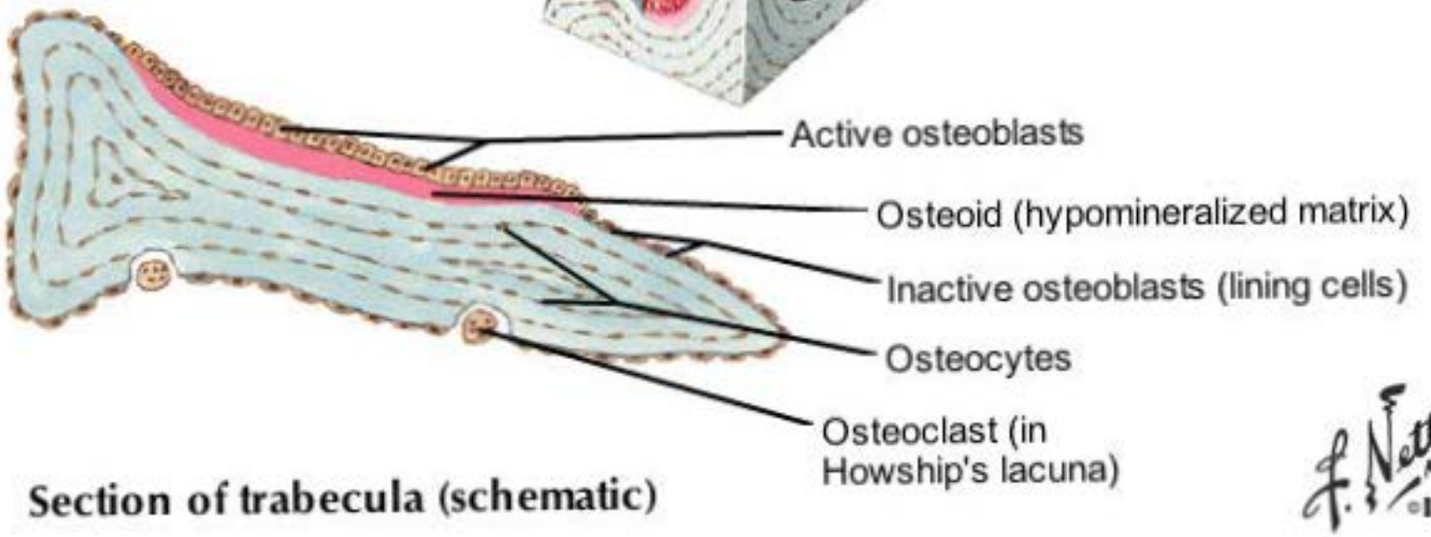


Histology of Bone

Trabecular bone (schematic)

On cut surfaces (as in sections), trabeculae may appear as discontinuous spicules





Section of trabecula (schematic)

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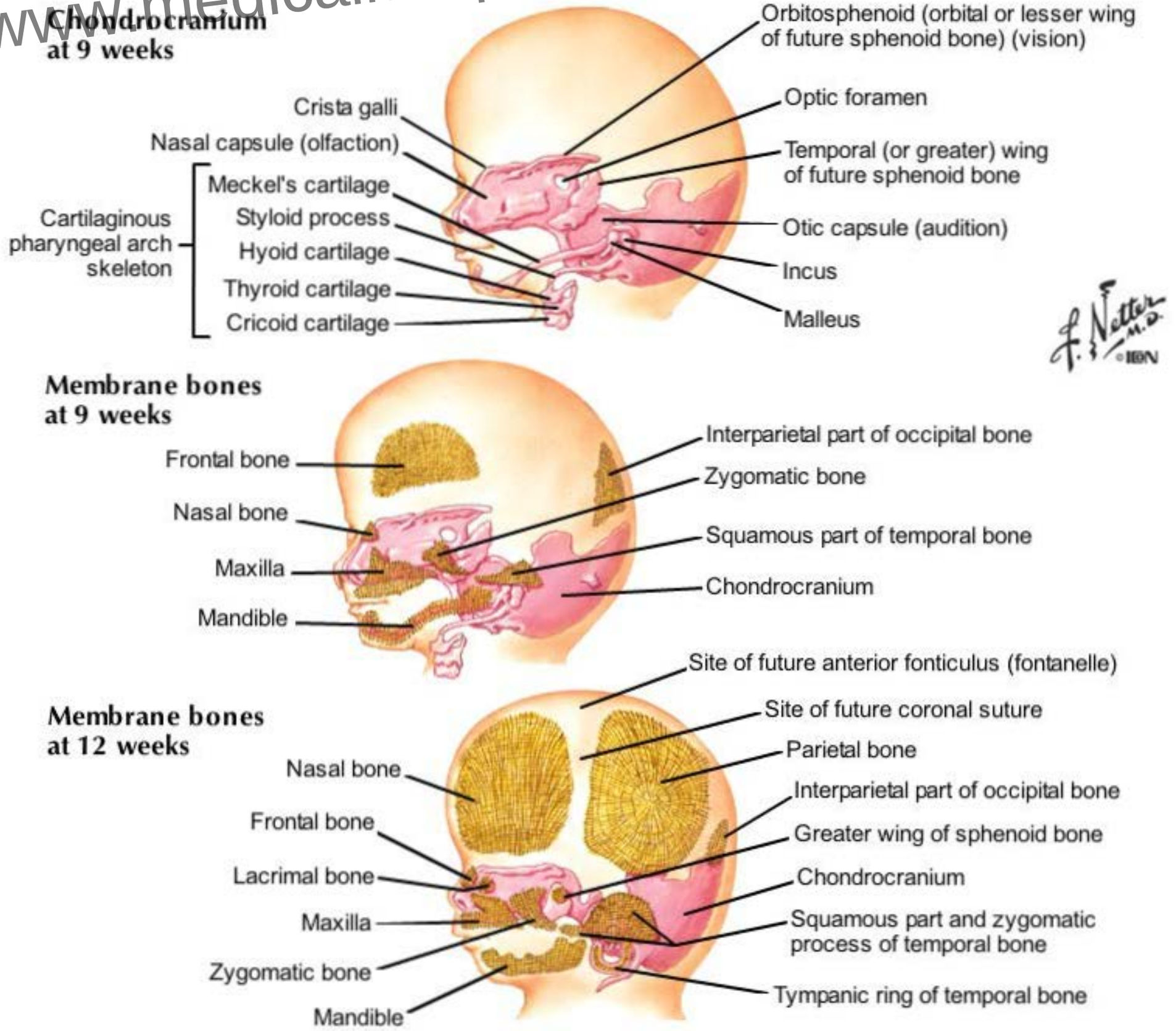
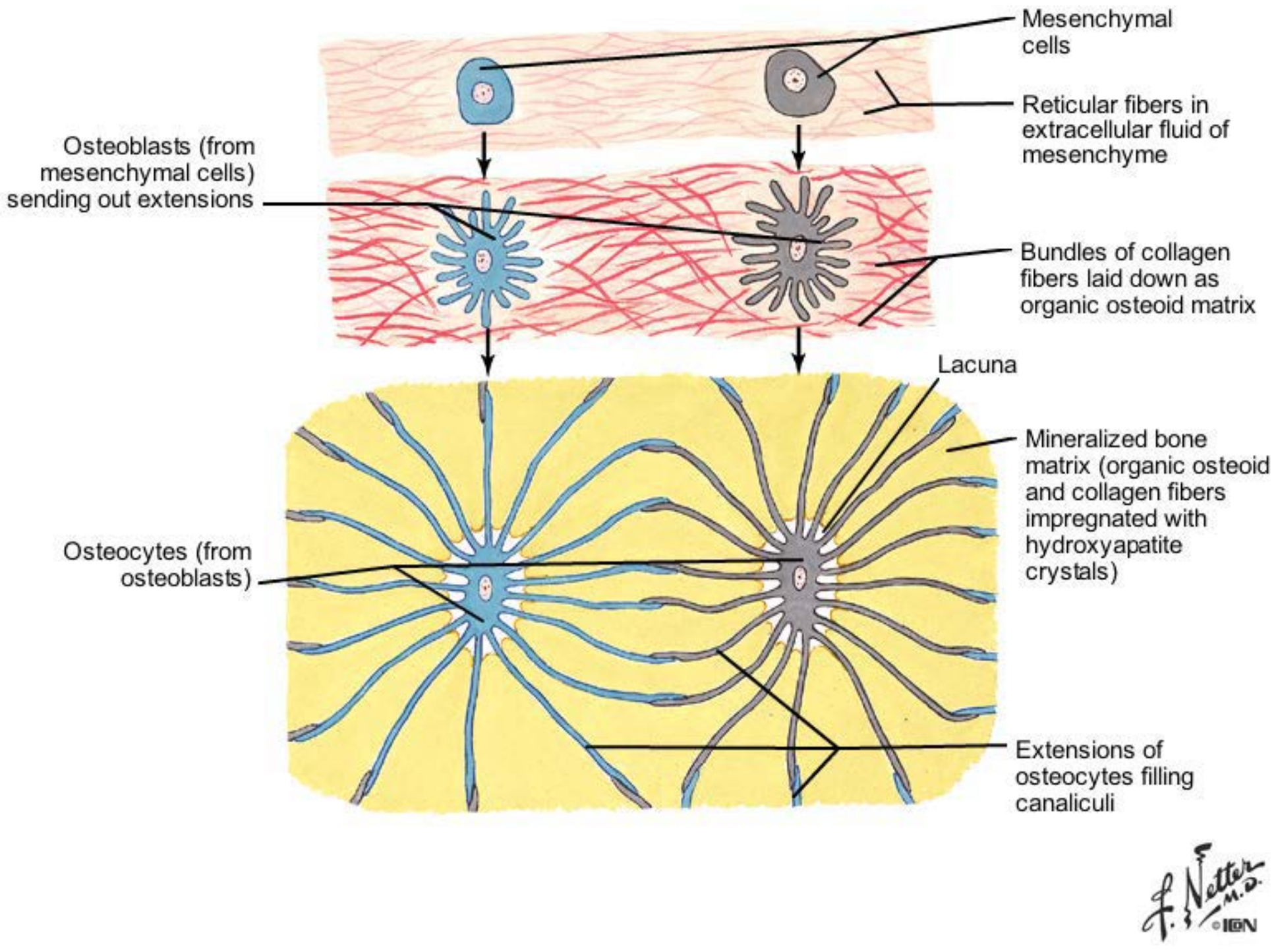
Membrane Bone and Skull Development

Early development of skull



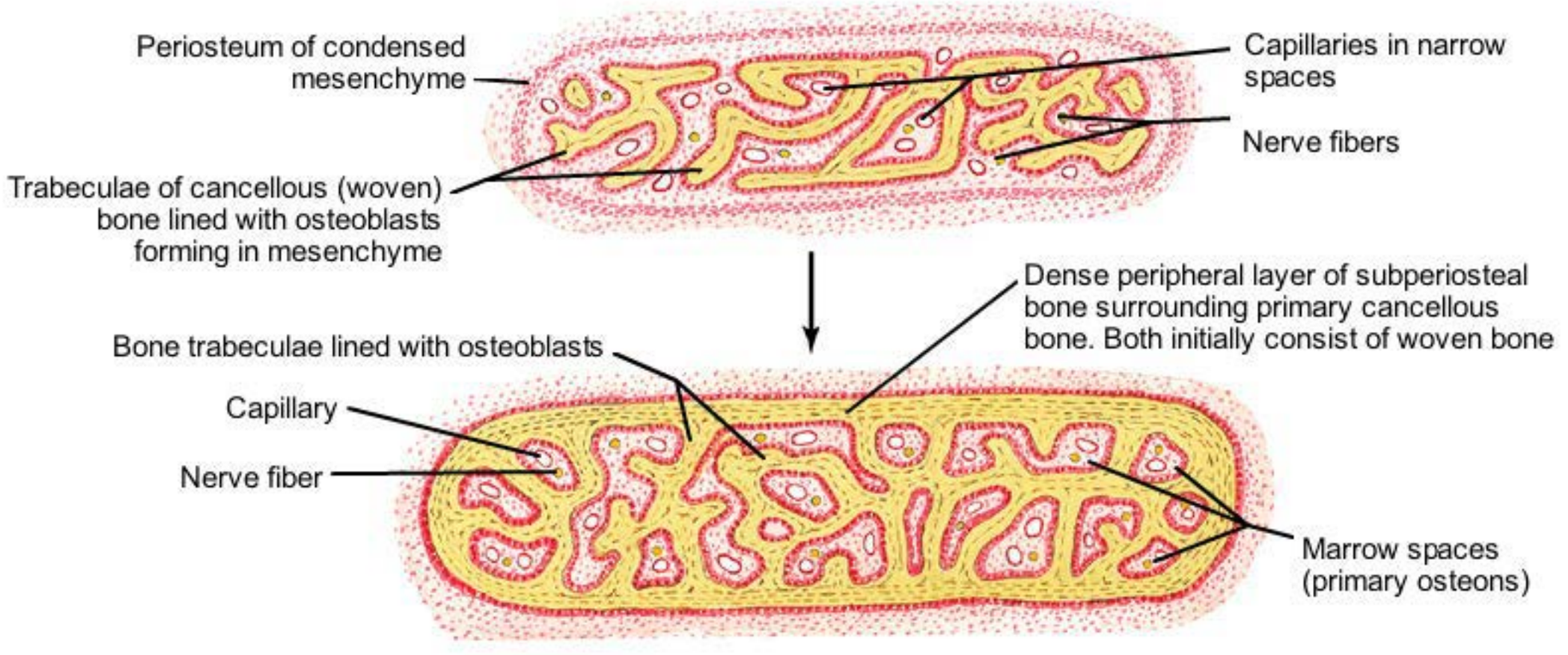
Bone Development in Mesenchyme

Initial bone formation in mesenchyme



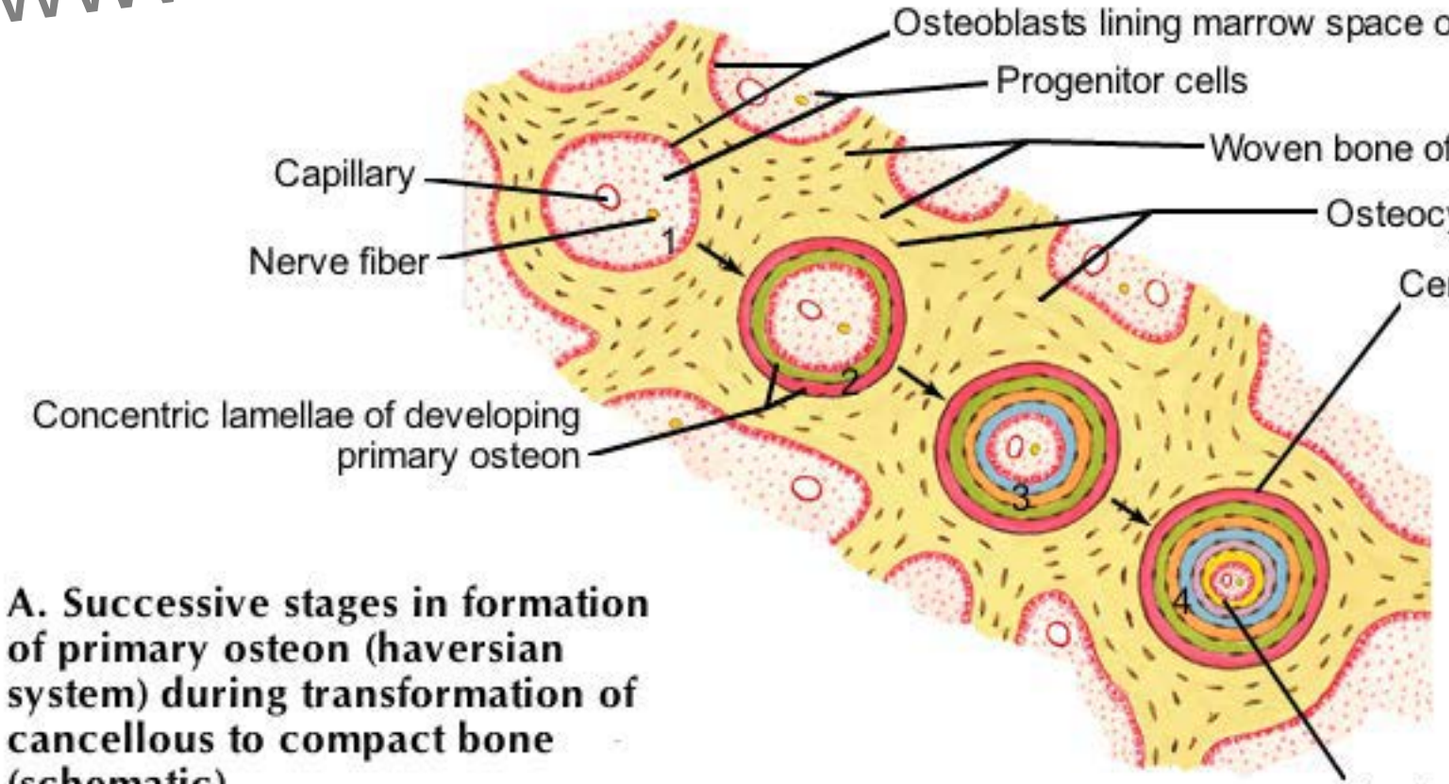
Bone Development in Mesenchyme

Early stages of flat (membrane or dermal) bone formation

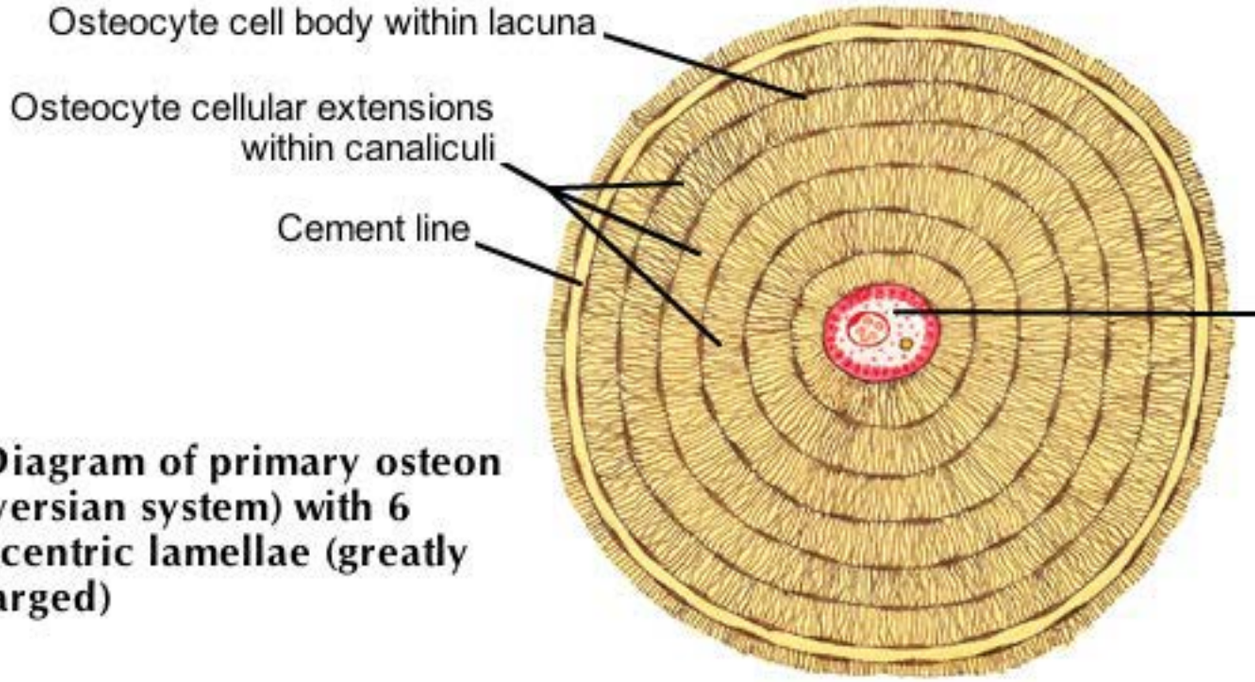


Osteon Formation

Primary osteon formation in mesenchymal bone development



A. Successive stages in formation of primary osteon (haversian system) during transformation of cancellous to compact bone (schematic)



B. Diagram of primary osteon (haversian system) with 6 concentric lamellae (greatly enlarged)

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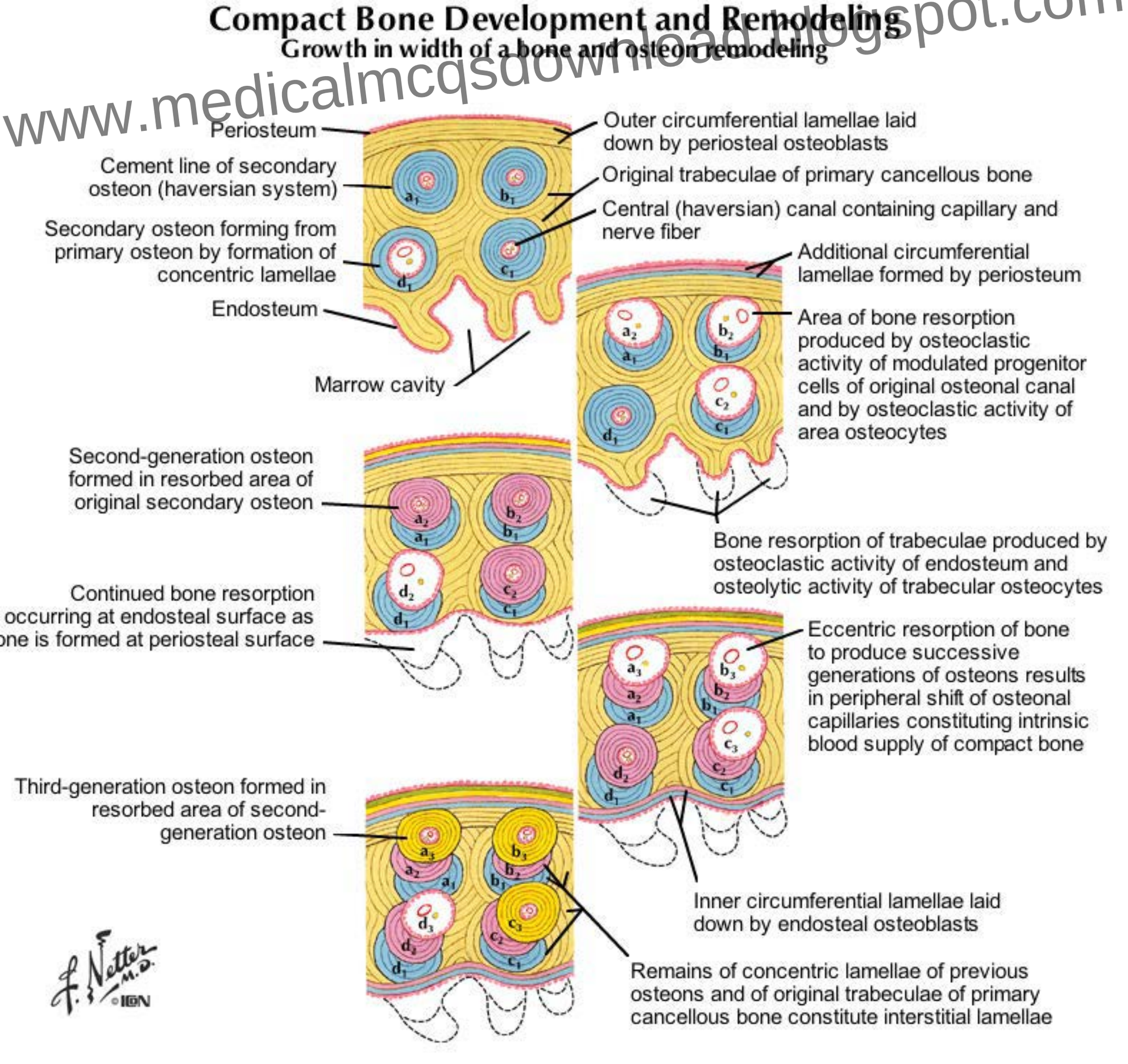
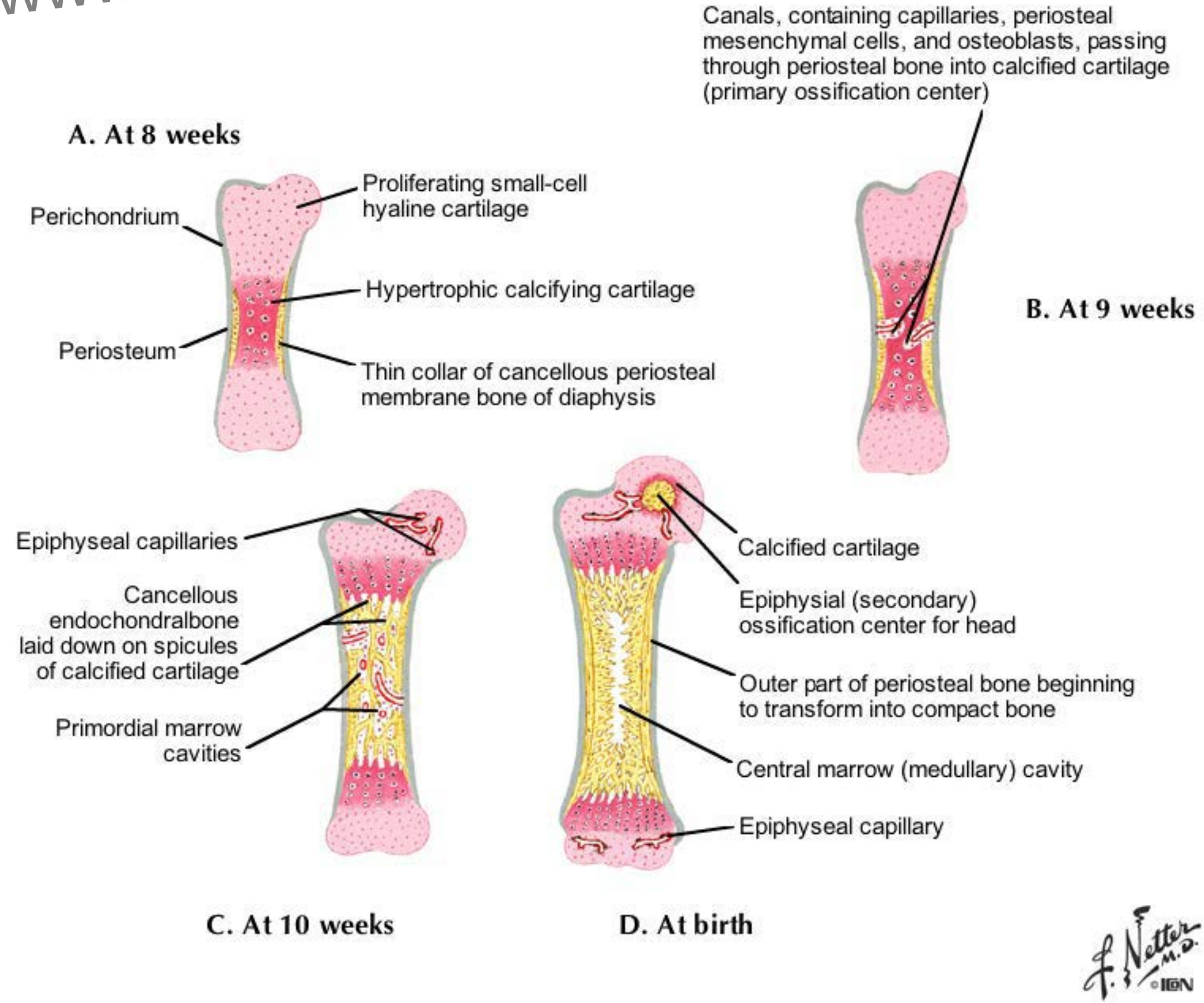
Compact Bone Development and Remodeling

Growth in width of a bone and osteon remodeling



Endochondral Ossification in a Long Bone

Growth and ossification of long bones (humerus, midfrontal sections)



Endochondral Ossification in a Long Bone

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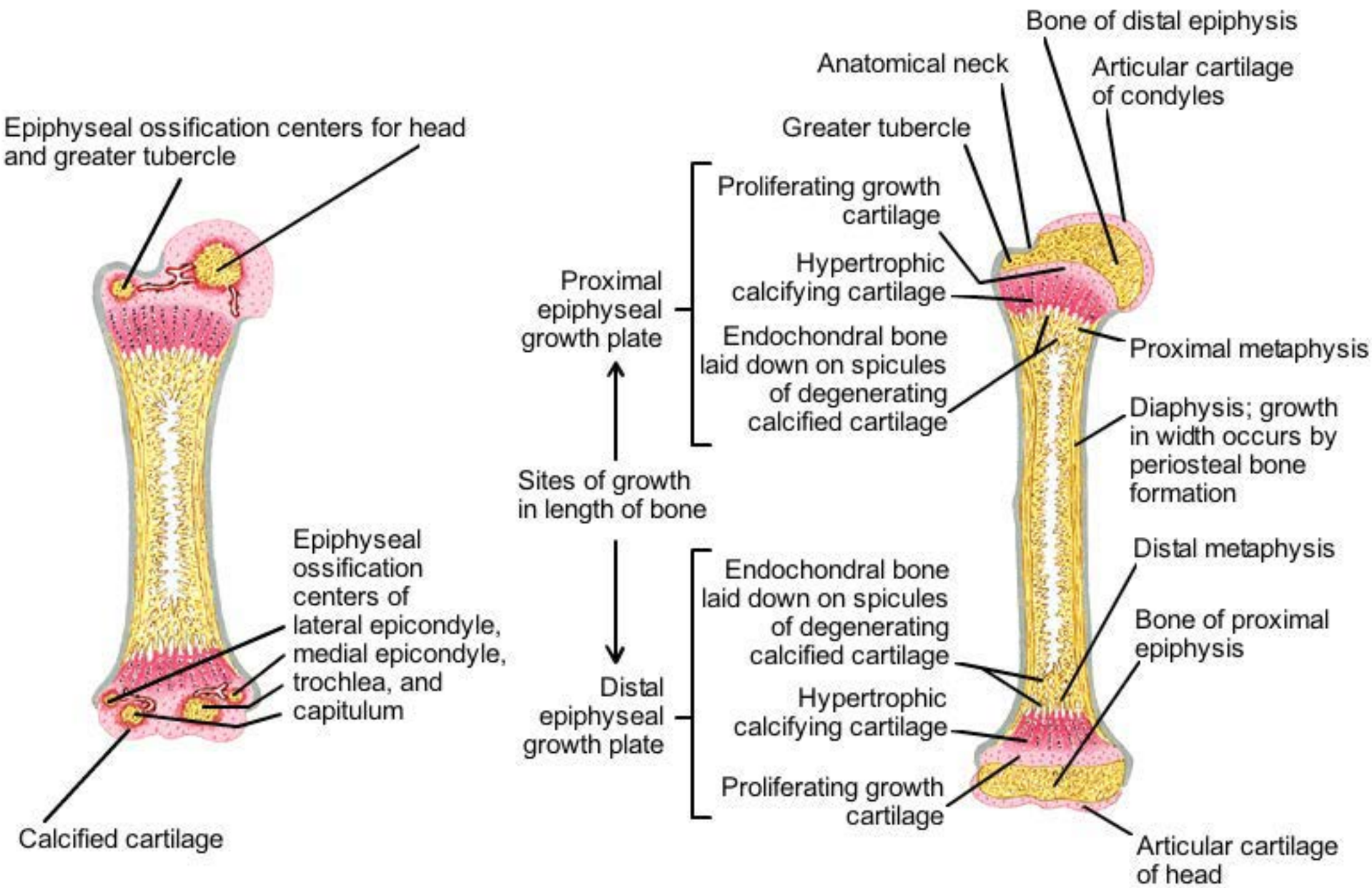

E. At 5 years

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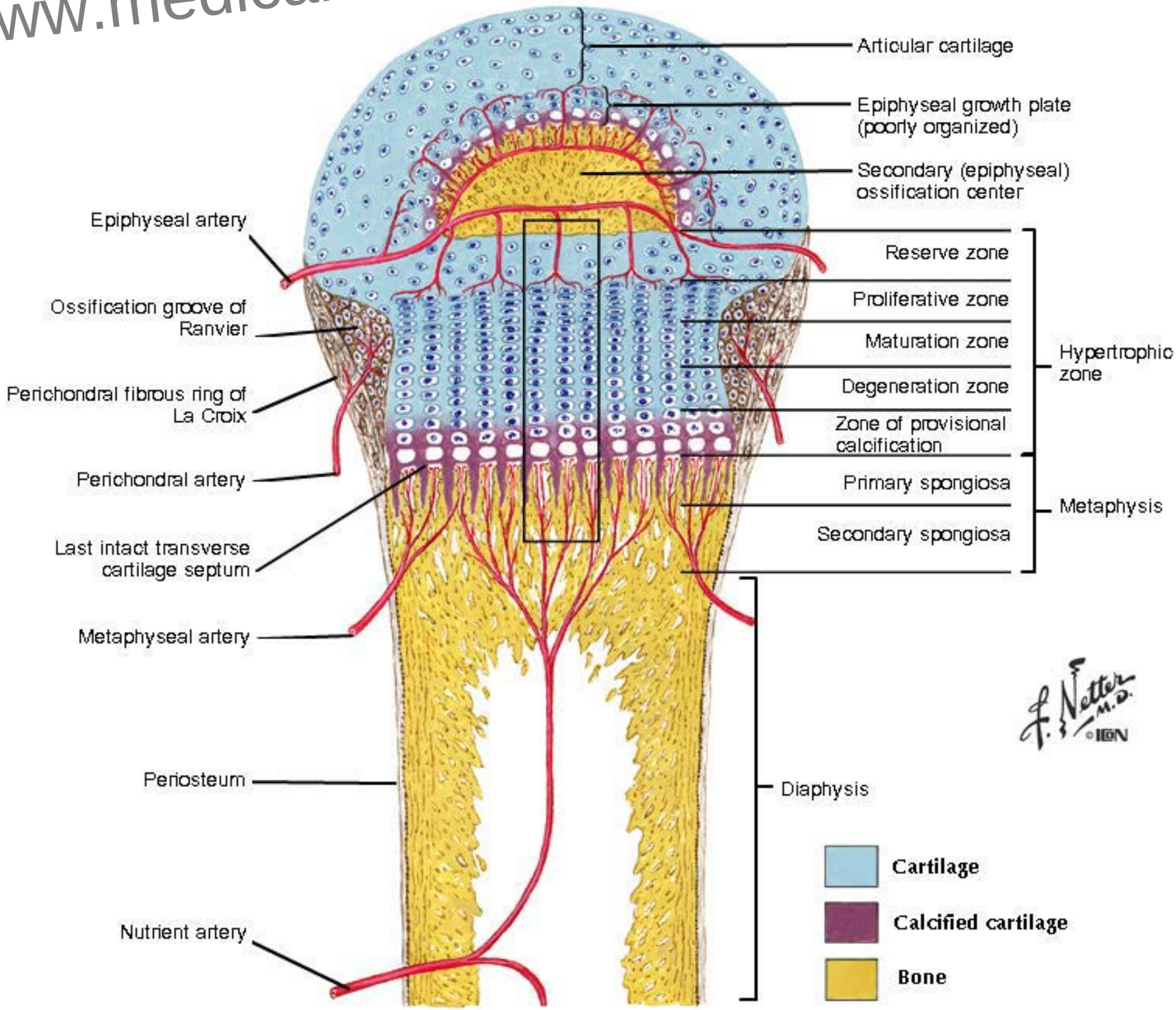
F. At 10 years

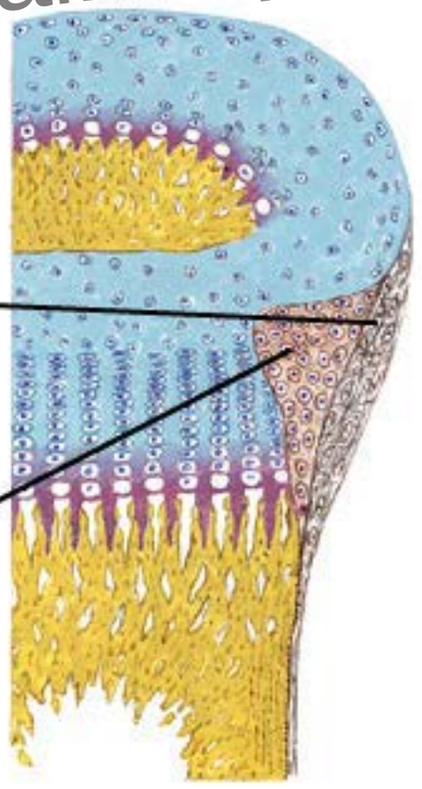
Epiphyseal Growth Plate

Close-up view of developing epiphysis and epiphyseal growth plate

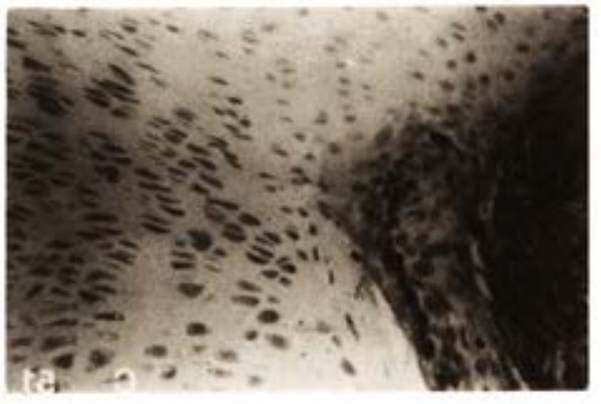


Peripheral Cartilage Function in the Epiphysis

Peripheral fibrocartilaginous element of growth plate



Microscopic section (H&E) corresponds generally to illustration at left



High-power section shows cells of ossification groove of Ranvier apparently "flowing" into cartilage at level of reserve zone, thus contributing to growth in width of growth plate. Note presence of arterioles (cut-in section)

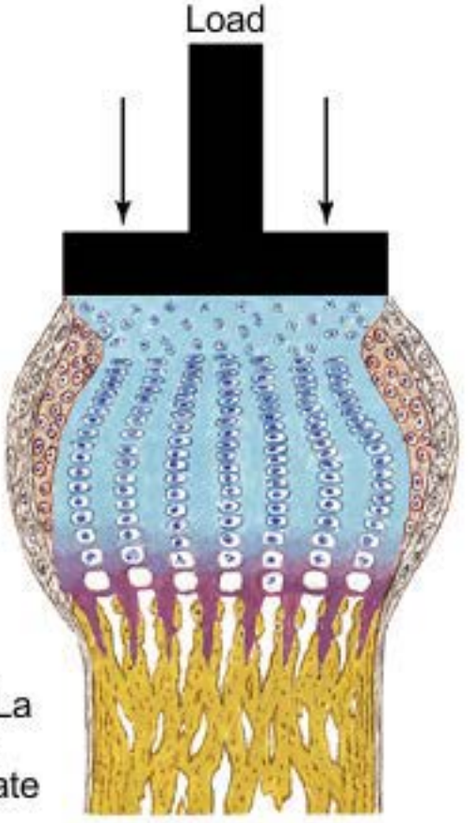


Illustration of how perichondral fibrous ring of La Croix acts as limiting membrane and provides mechanical support to cartilaginous growth plate

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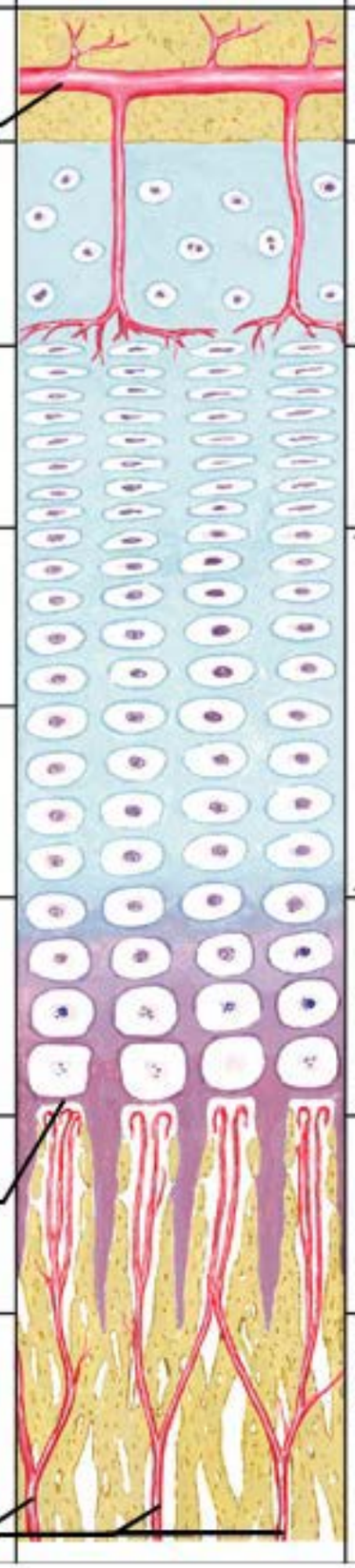
Epiphyseal Growth Plate



Zones Structures	Histology	Functions	Blood supply	PO_2
Secondary bony epiphysis Epiphyseal artery				
Reserve zone		Matrix production Storage	Vessels pass through, do not supply this zone	Poor (low)
Proliferative zone		Matrix production Cellular proliferation (longitudinal growth)	Excellent	Excellent Fair
Hypertrophic zone — **Maturation zone**		Preparation of matrix for calcification	*Progressive decrease*	Poor (low)
Hypertrophic zone — **Degenerative zone**				*Progressive decrease*
Hypertrophic zone — Zone of provisional calcification		Calcification of matrix	Nil	Poor (very low)
Metaphysis — Last intact transverse septum **Primary spongiosa**		Vascular invasion and resorption of transverse septa Bone formation	Closed capillary loops Good	Poor Good
Metaphysis — **Secondary spongiosa** Branches of metaphyseal and nutrient arteries		Remodeling Internal: removal of cartilage bars, replacement of fiber bone with lamellar bone External: funnelization	Excellent	Excellent

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Epiphyseal Growth Plate

Zones / Structures	Histology	Cell (chondrocyte) health	Cell respiration	Cell glycogen
Secondary bony epiphysis				
Epiphyseal artery				
Reserve zone		Good, active. Much endoplasmic reticulum, vacuoles, mitochondria	Anaerobic	High concentration
Proliferative zone		Excellent. Much endoplasmic reticulum, ribosomes, mitochondria. Intact cell membrane	Aerobic	High concentration (less than in above)
Hypertrophic zone — **Maturation zone**		Still good	*Progressive change to anaerobic*	*Glycogen consumed until depleted*
Degenerative zone		Progressive deterioration	Anaerobic glycolysis	
Zone of provisional calcification		Cell death	Anaerobic glycolysis	Nil
Metaphysis — Last intact transverse septum			*Progressive reversion to aerobic*	?
Primary spongiosa				
Secondary spongiosa			Aerobic	?
Branches of metaphyseal and nutrient arteries				

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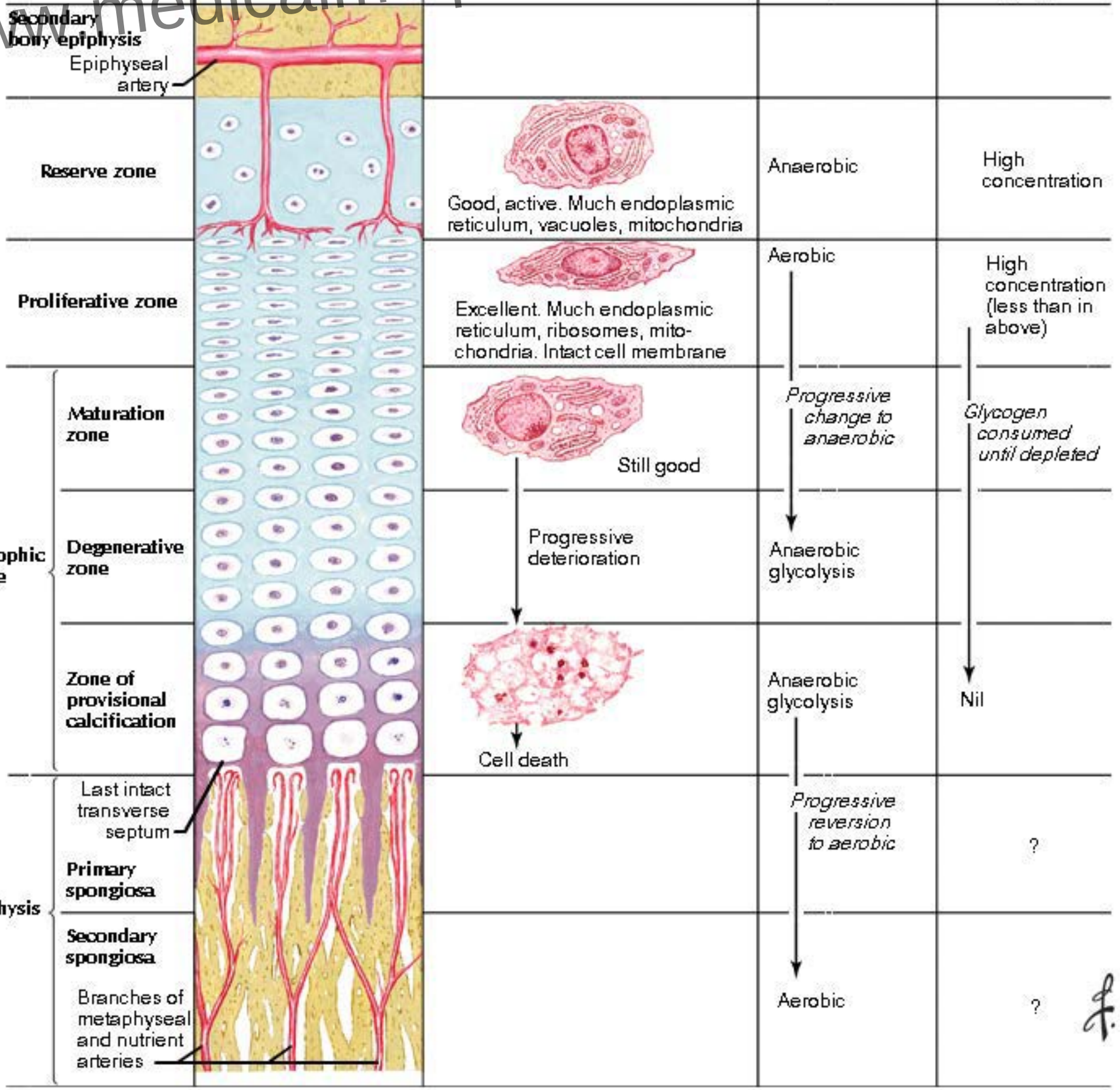
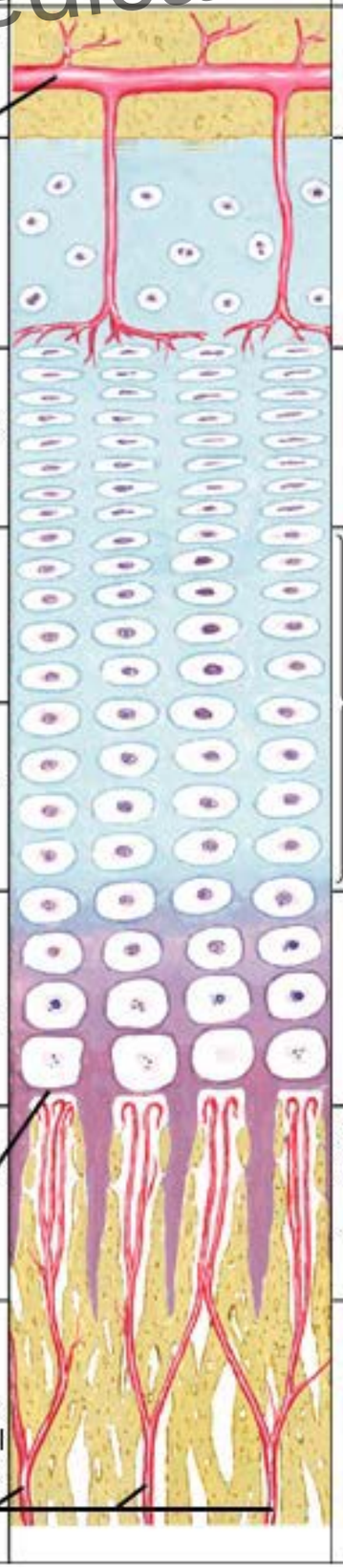
Epiphyseal Growth Plate



Eqiphyseal Growth Plate

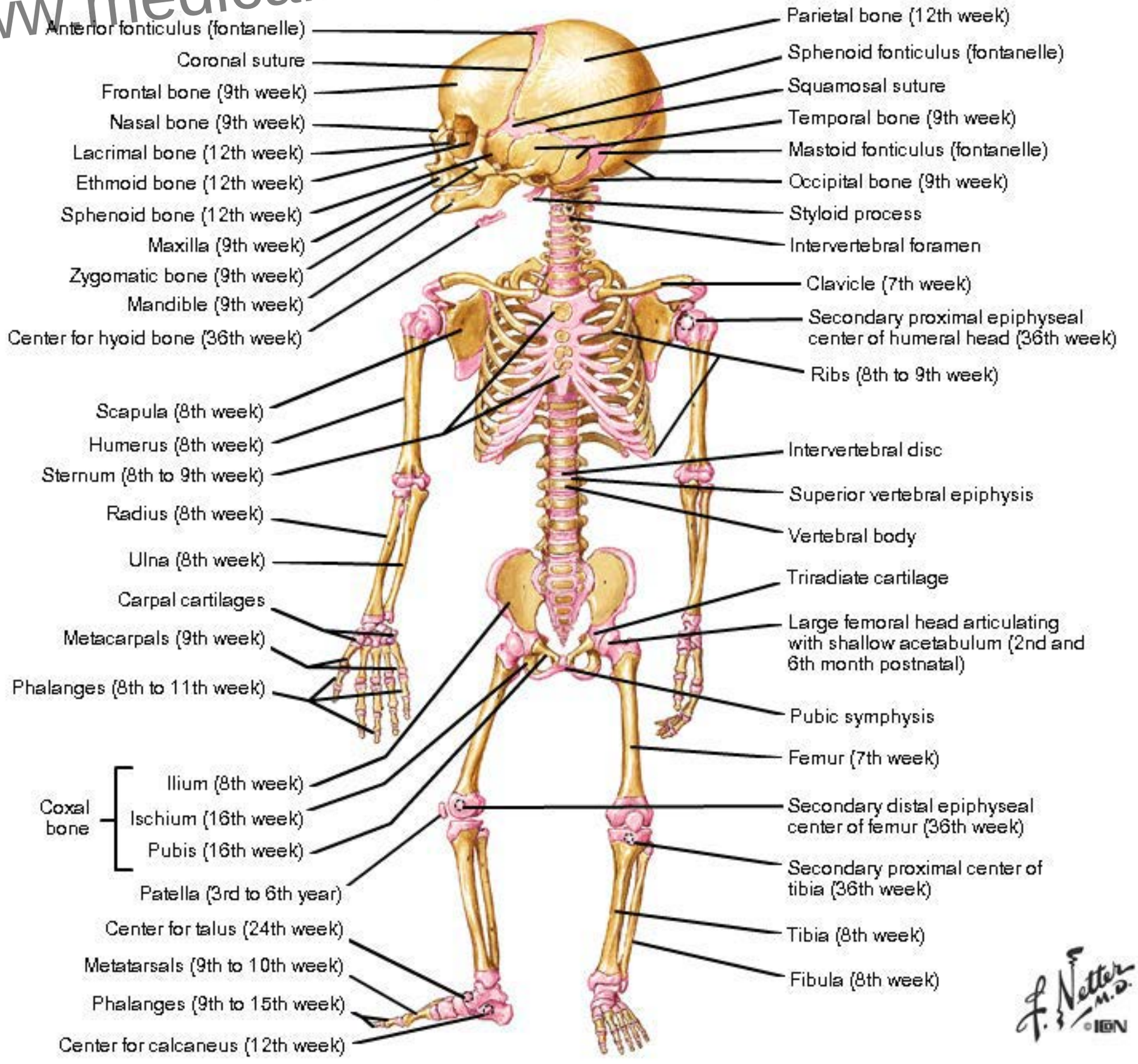


Zones / Structures	Histology	Exemplary diseases	Defect (if known)
Secondary bony epiphysis			
Epiphyseal artery			
Reserve zone		Diastrophic dwarfism (also, defects in other zones)	Defective type II collagen synthesis
		Pseudoachondroplasia (also, defects in other zones)	Defective processing and transport of proteoglycans
		Kniest syndrome (also, defects in other zones)	Defective processing of proteoglycans
Proliferative zone		Gigantism	Increased cell proliferation (growth hormone increased)
		Achondroplasia	Deficiency of cell proliferation
		Hypochondroplasia	Less severe deficiency of cell proliferation
		Malnutrition, irradiation injury, glucocorticoid excess	Decreased cell proliferation and/or matrix synthesis
Hypertrophic zone: Maturation zone		Mucopolysaccharidosis (Morquio's syndrome, Hurler's syndrome)	Deficiencies of specific lysosomal acid hydrolases, with lysosomal storage of mucopolysaccharides
Hypertrophic zone: Degenerative zone			
Hypertrophic zone: Zone of provisional calcification		Rickets, osteomalacia (also, defects in metaphysis)	Insufficiency of Ca^{2+} and/or P_i for normal calcification of matrix
Last intact tranverse septum		Metaphyseal chondrodysplasia (Jansen and Schmid types)	Extension of hypertrophic cells into metaphysis
Metaphysis: Primary spongiosa		Acute hematogenous osteomyelitis	Flourishing of bacteria due to sluggish circulation, low P_{O_2}, reticuloendothelial deficiency
Metaphysis: Secondary spongiosa		Osteopetrosis	Abnormality of osteoclasts (internal remodeling)
		Osteogenesis imperfecta	Abnormality of osteoblasts and collagen synthesis
		Scurvy	Inadequate collagen formation
Branches of metaphyseal and nutrient arteries		Metaphyseal dysplasia (Pyle disease)	Abnormality of funnelization (external remodeling)

Ossification in the Newborn Skeleton

Skeleton of full-term newborn

Time of appearance of ossification centers (primary unless otherwise indicated)



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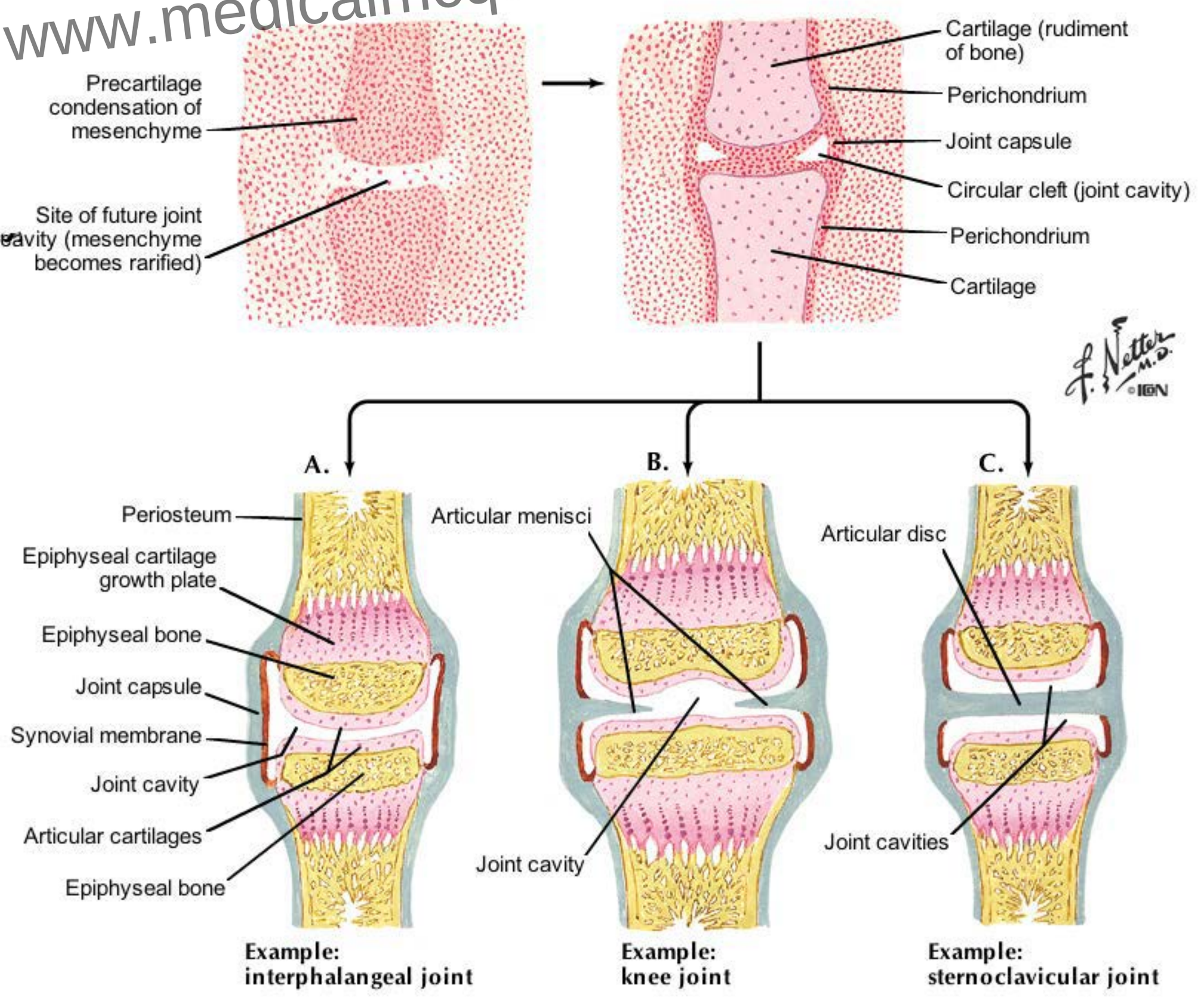
Joint Development

Development of three types of synovial joints

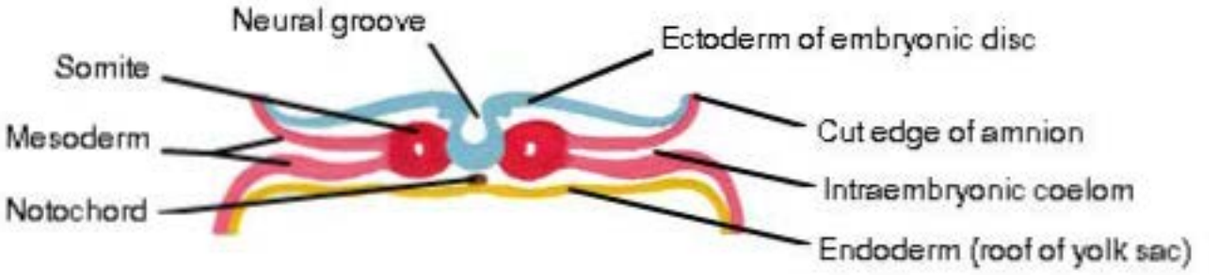


Muscular System: Primordia

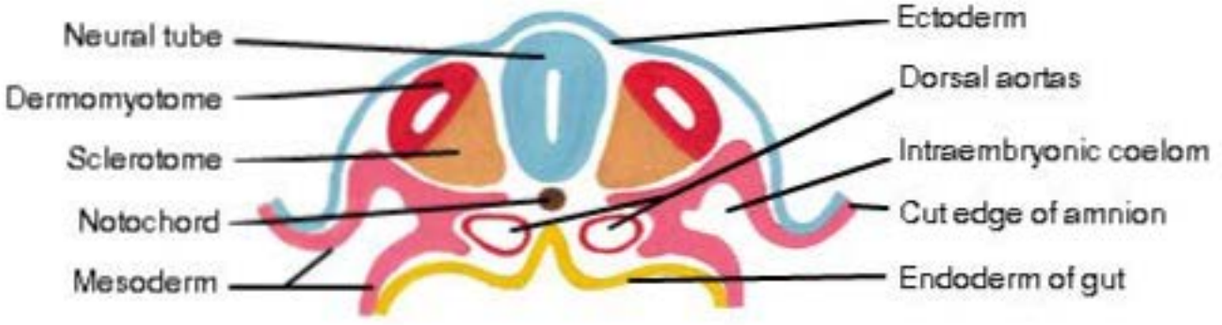
Differentiation of somites into myotomes, sclerotomes, and dermatomes

Cross section of human embryos

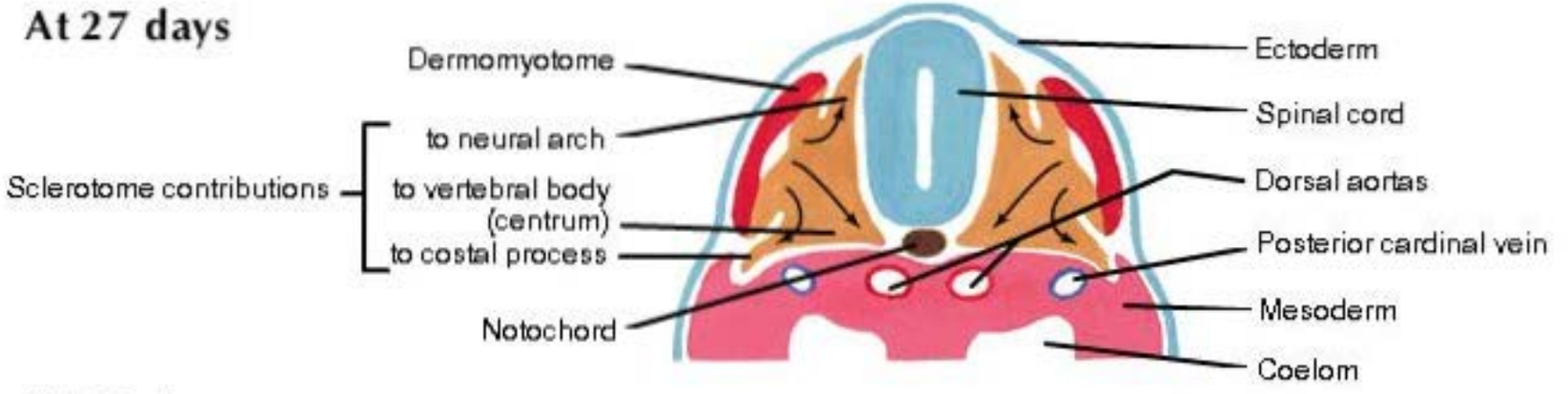
At 19 days



At 22 days



At 27 days



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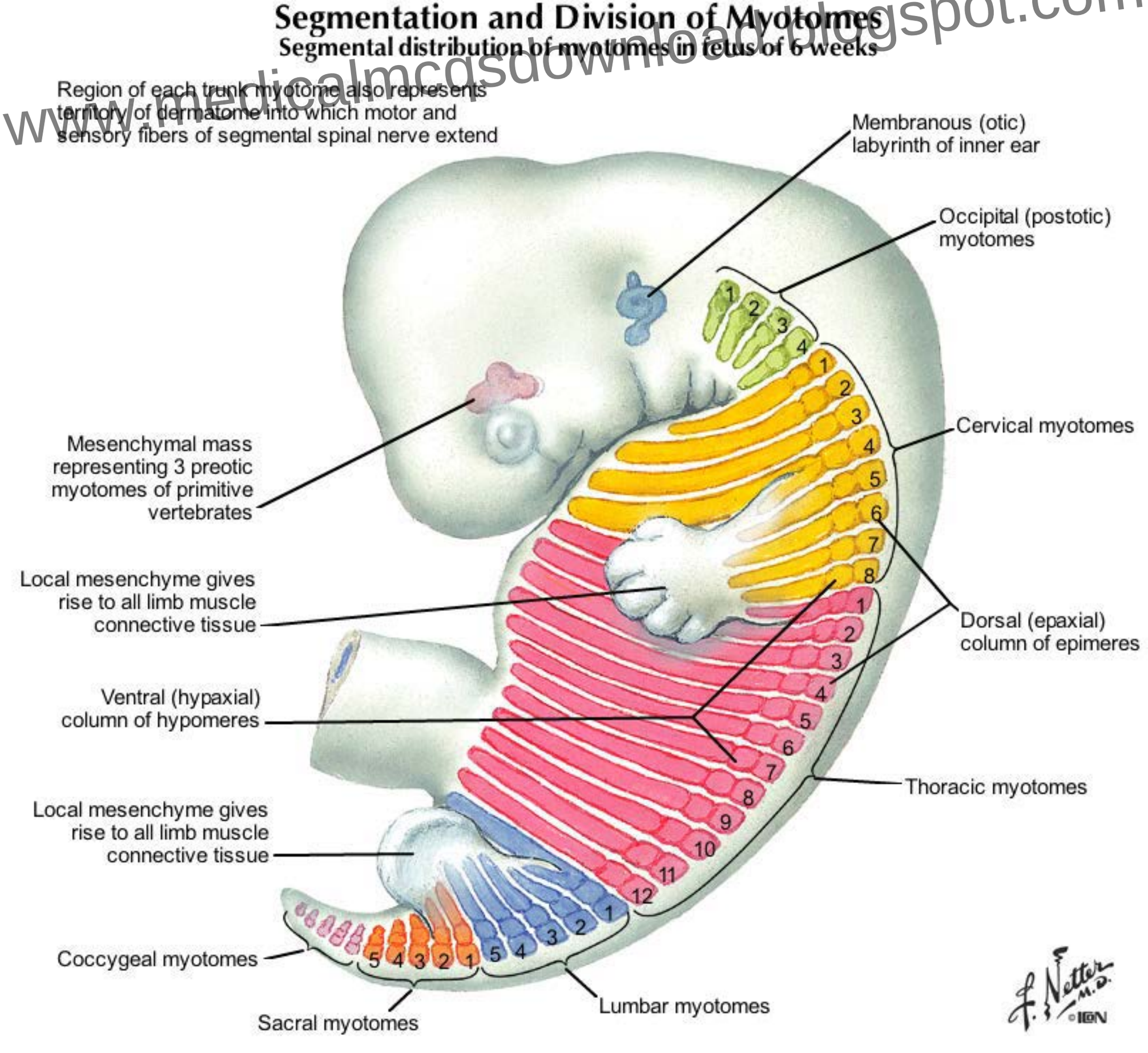
At 30 days

Note: Sections A, B, and C are at level of future vertebral body, but section D is at level between developing bodies

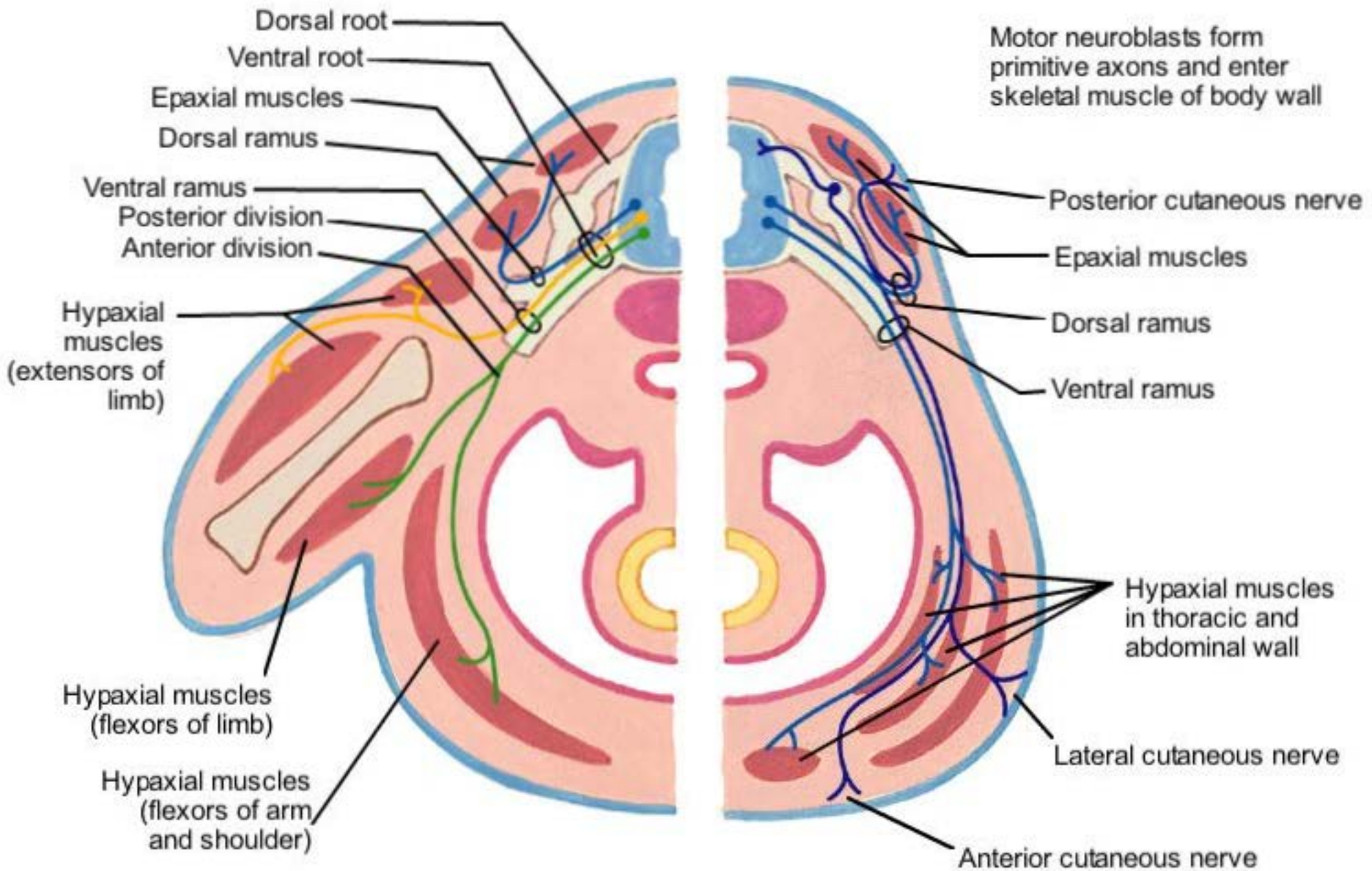
Segmentation and Division of Myotomes

Segmental distribution of myotomes in fetus of 6 weeks



Epimere, Hypomere, and Muscle Groups

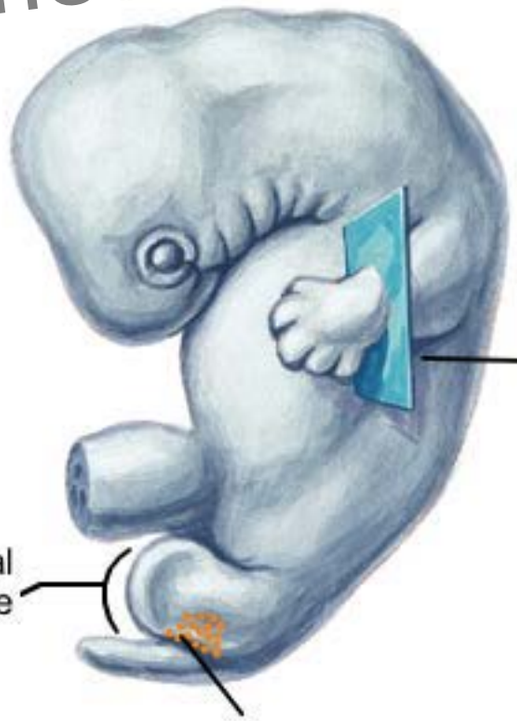
Somatic development



Somatic nervous system innervates somatopleure (body wall)

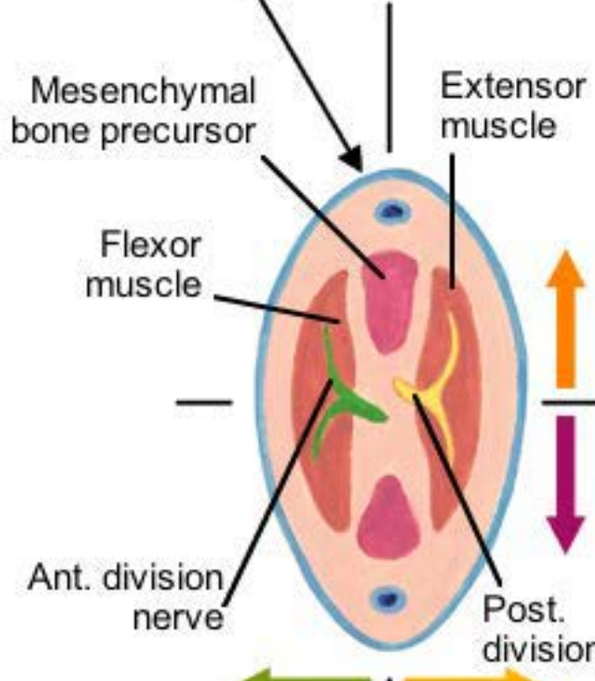
Development and Organization of Limb Buds

Limb buds in 6-week embryo



In the classic model of proximodistal morphological determination, the apical ectodermal ridge interacts with the underlying mesoderm of the progress zone to establish a time sequence of differentiation as the limb elongates. More recent evidence indicates that the morphological information may be programmed early on in the mesenchyme with no particular role for the ectoderm.

Early craniocaudal morphological differentiation is determined by a gradient of sonic hedgehog produced by the zone of polarizing activity (ZPA), a signaling center at the caudal end of each limb bud. The ZPA also stimulates the formation of the apical ectodermal ridge.



Preaxial compartment

In upper extremity:	In lower extremity:
Cephalic vein	Greater saphenous vein
Pollex (thumb)	Hallux (big toe)
Radius	Tibia

Postaxial compartment

In upper extremity:	In lower extremity:
Basilic vein	Lesser saphenous vein
Ulna	Fibula

Ventral compartment

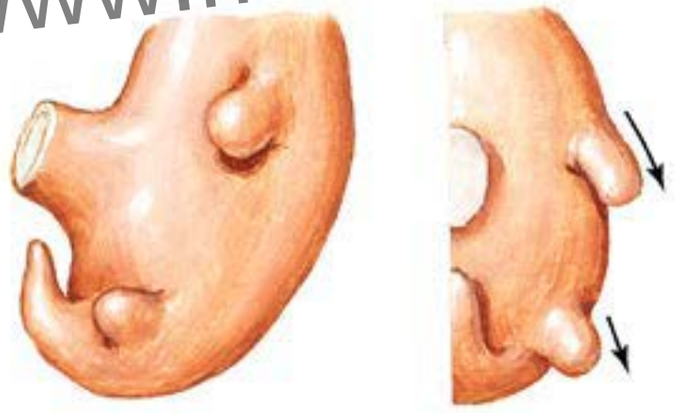
Flexor muscles
Anterior division nerves

Dorsal compartment

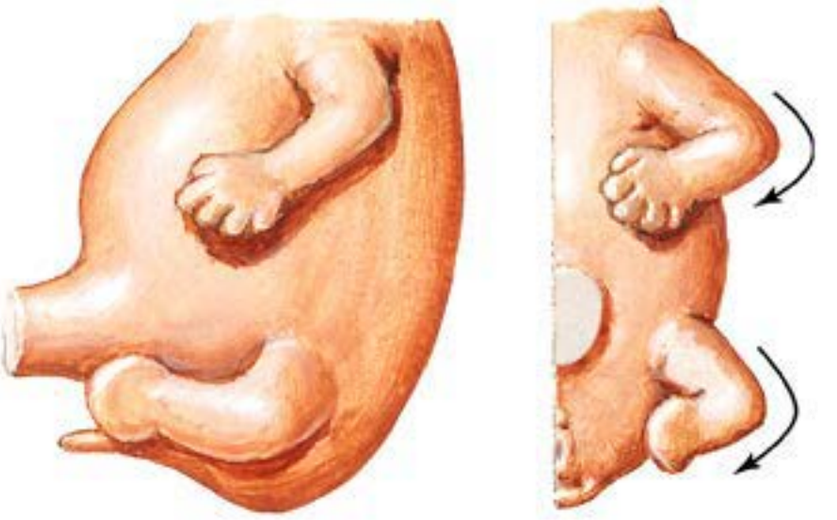
Extensor muscles
Posterior division nerves

Rotation of the Limbs

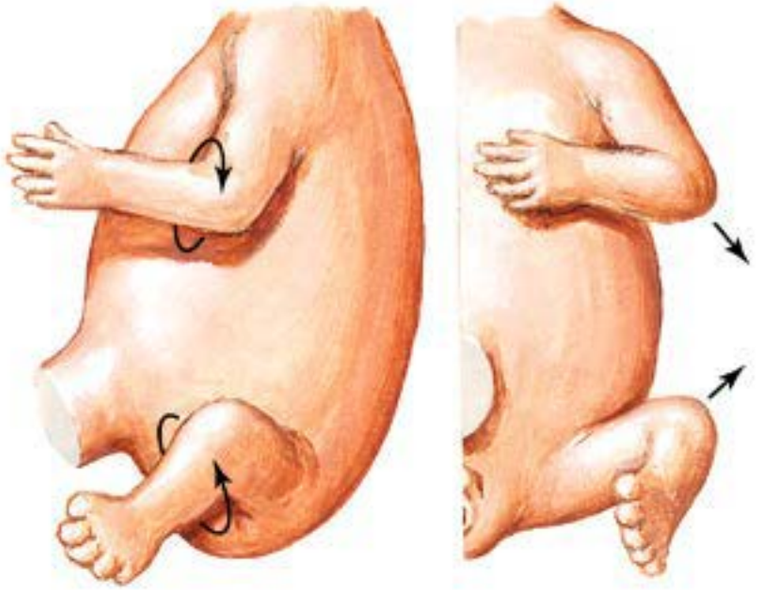
Changes in position of limbs before birth



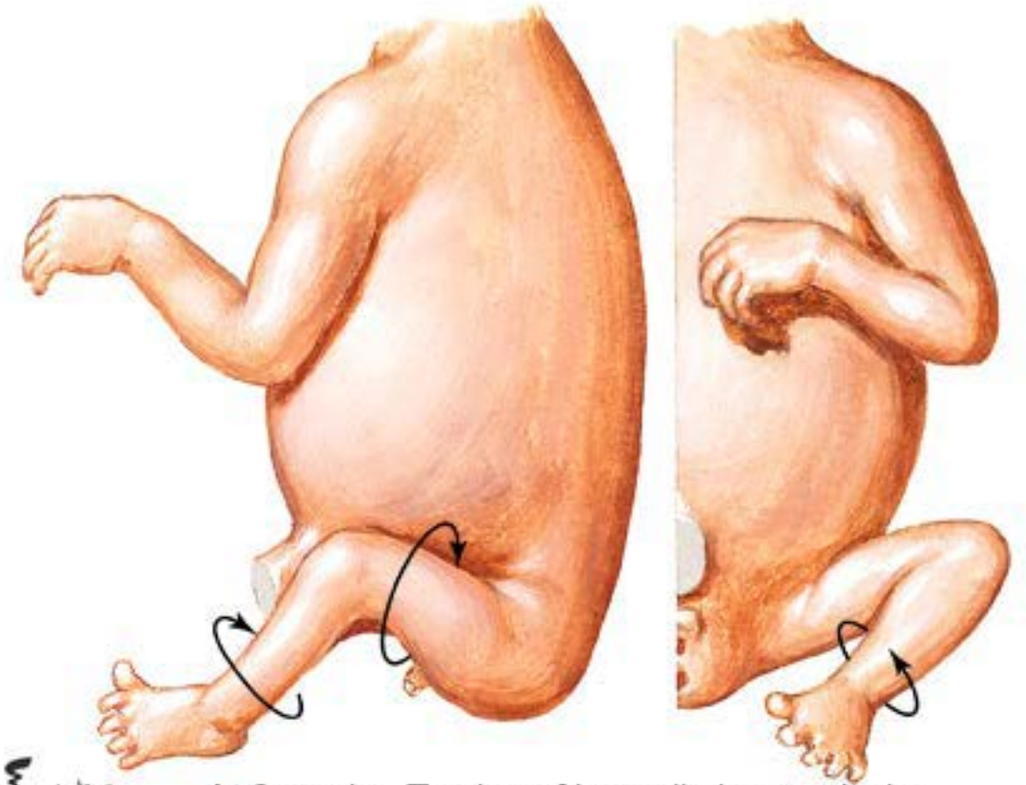
At 5 weeks. Upper and lower limbs have formed as finlike appendages pointing laterally and caudally



At 6 weeks. Limbs bend anteriorly, so elbows and knees point laterally, palms and soles face trunk



At 7 weeks. Upper and lower limbs have undergone 90-degree torsion about their long axes, but in opposite directions, so elbows point caudally and knees cranially



At 8 weeks. Torsion of lower limbs results in twisted or "barber pole" arrangement of their cutaneous innervation

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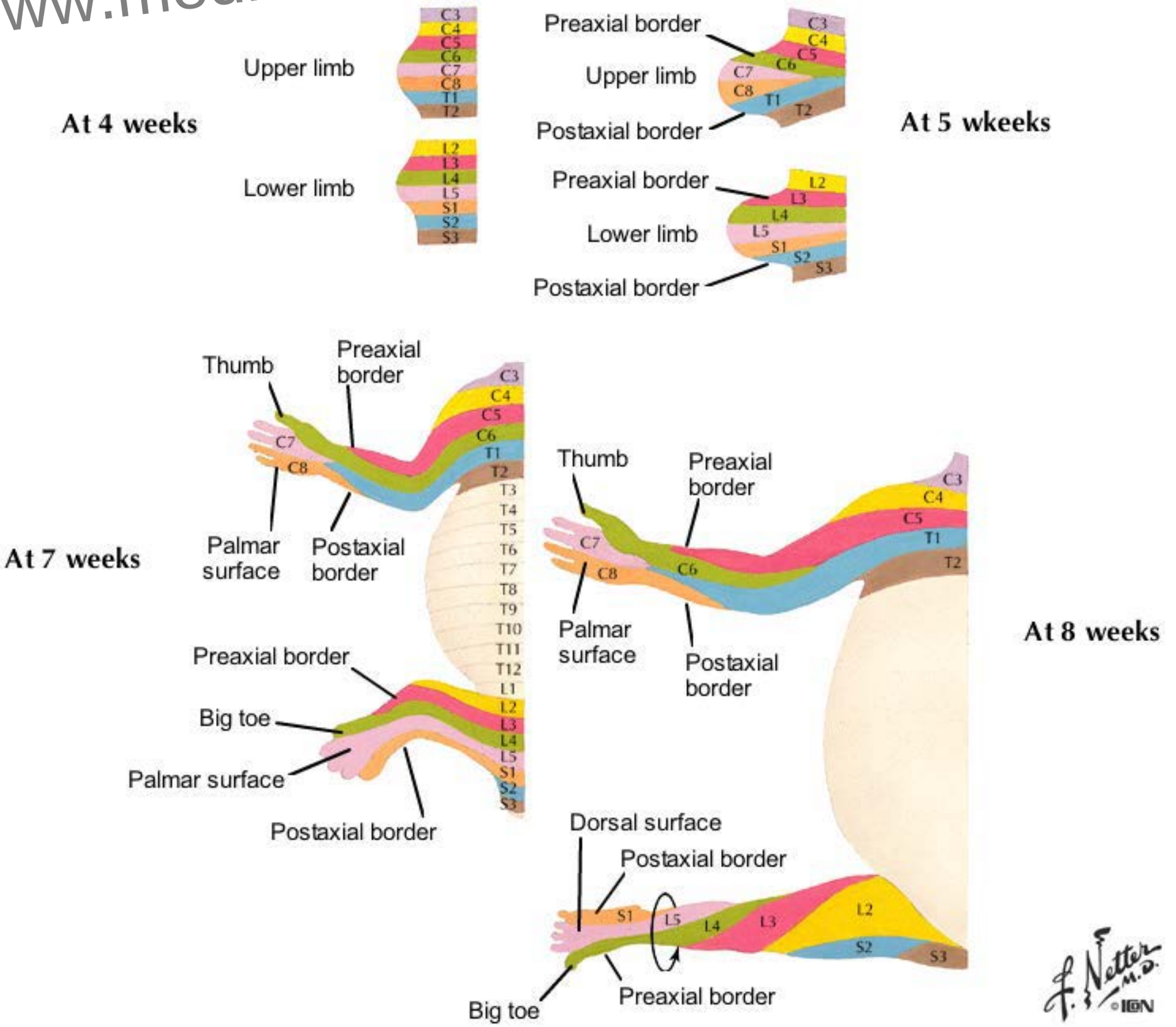
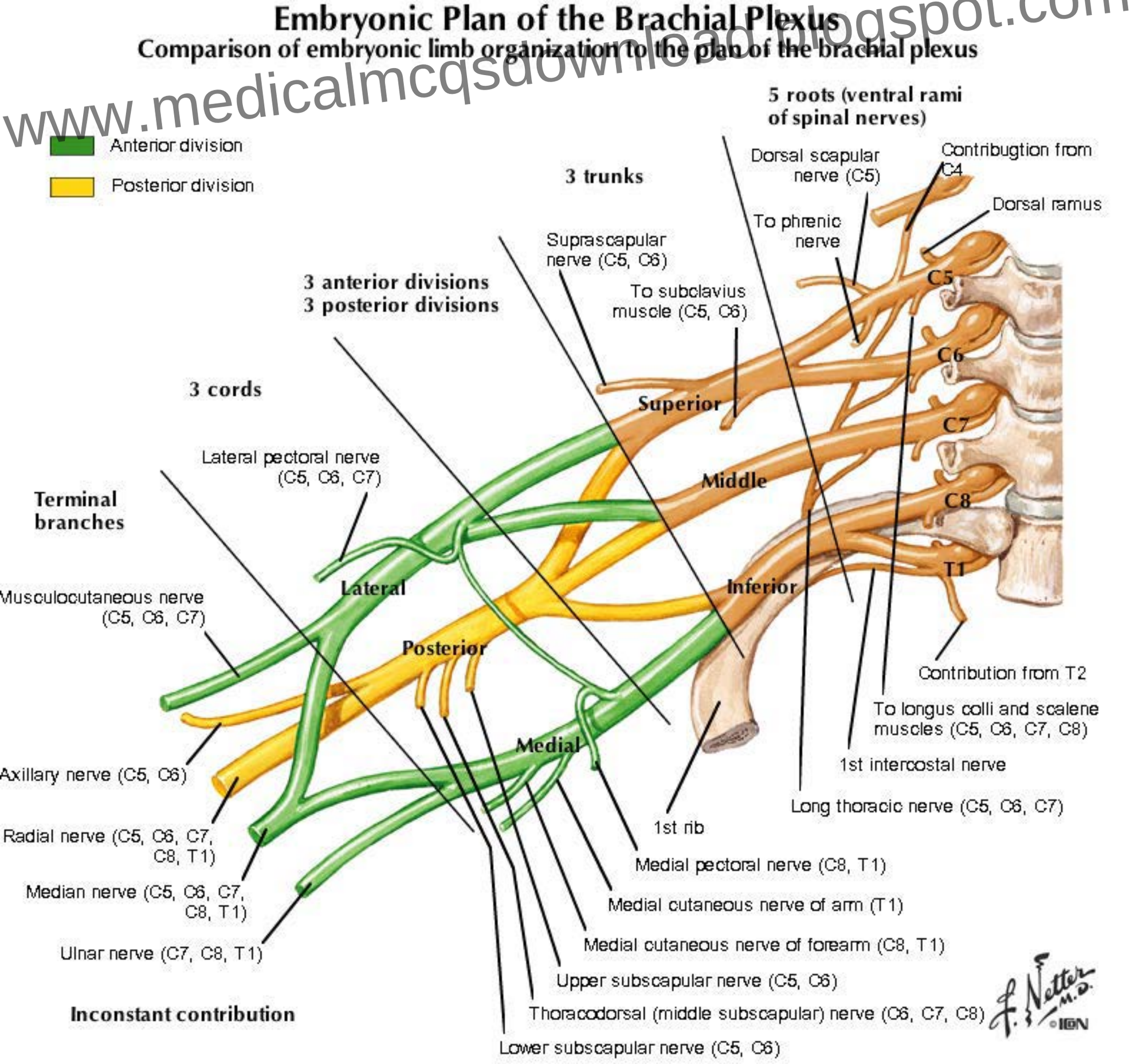
Limb Rotation and Dermatomes

Changes in ventral dermatome pattern (cutaneous sensory nerve distribution) during limb development

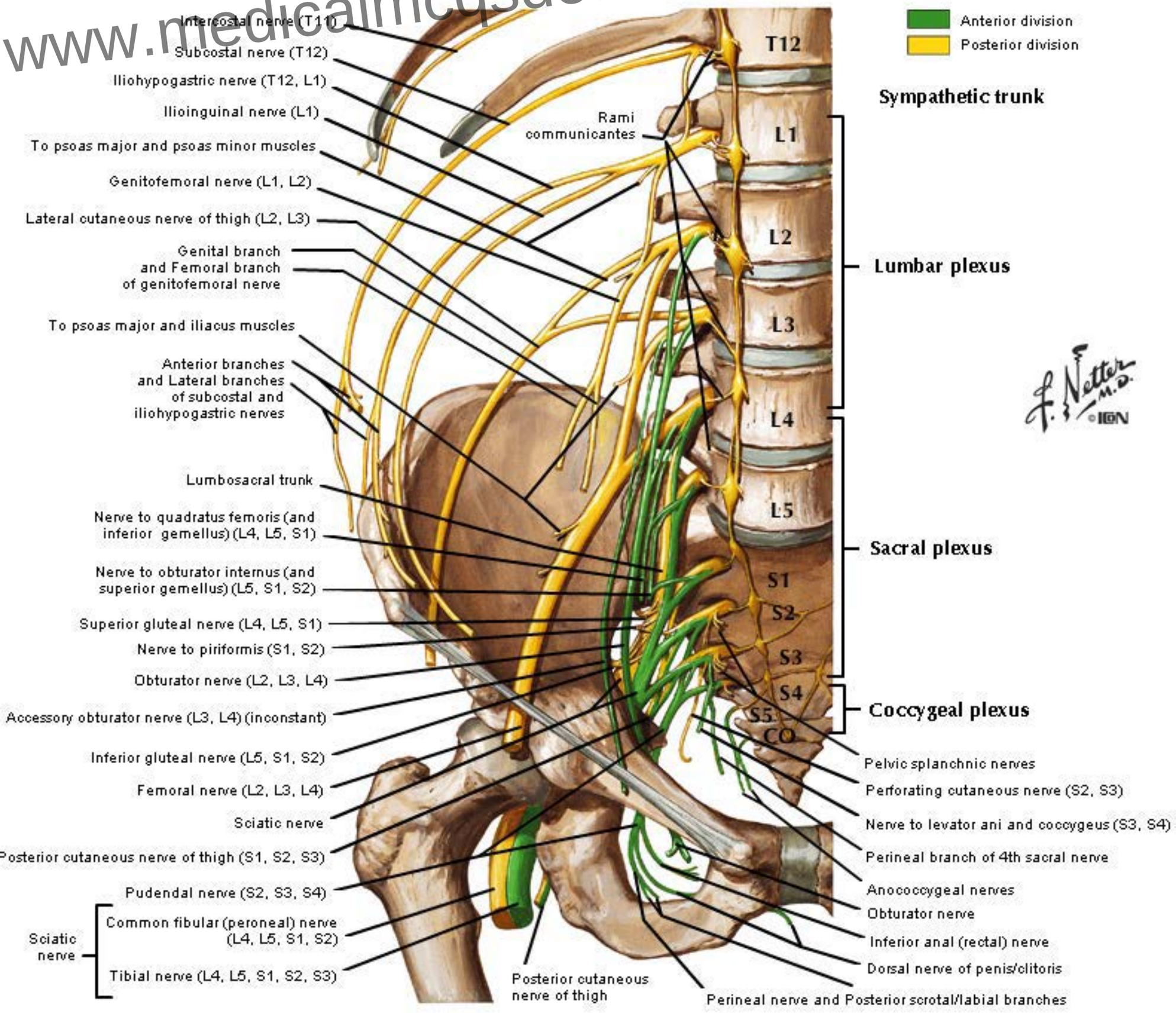


Embryonic Plan of the Brachial Plexus

Comparison of embryonic limb organization to the plan of the brachial plexus

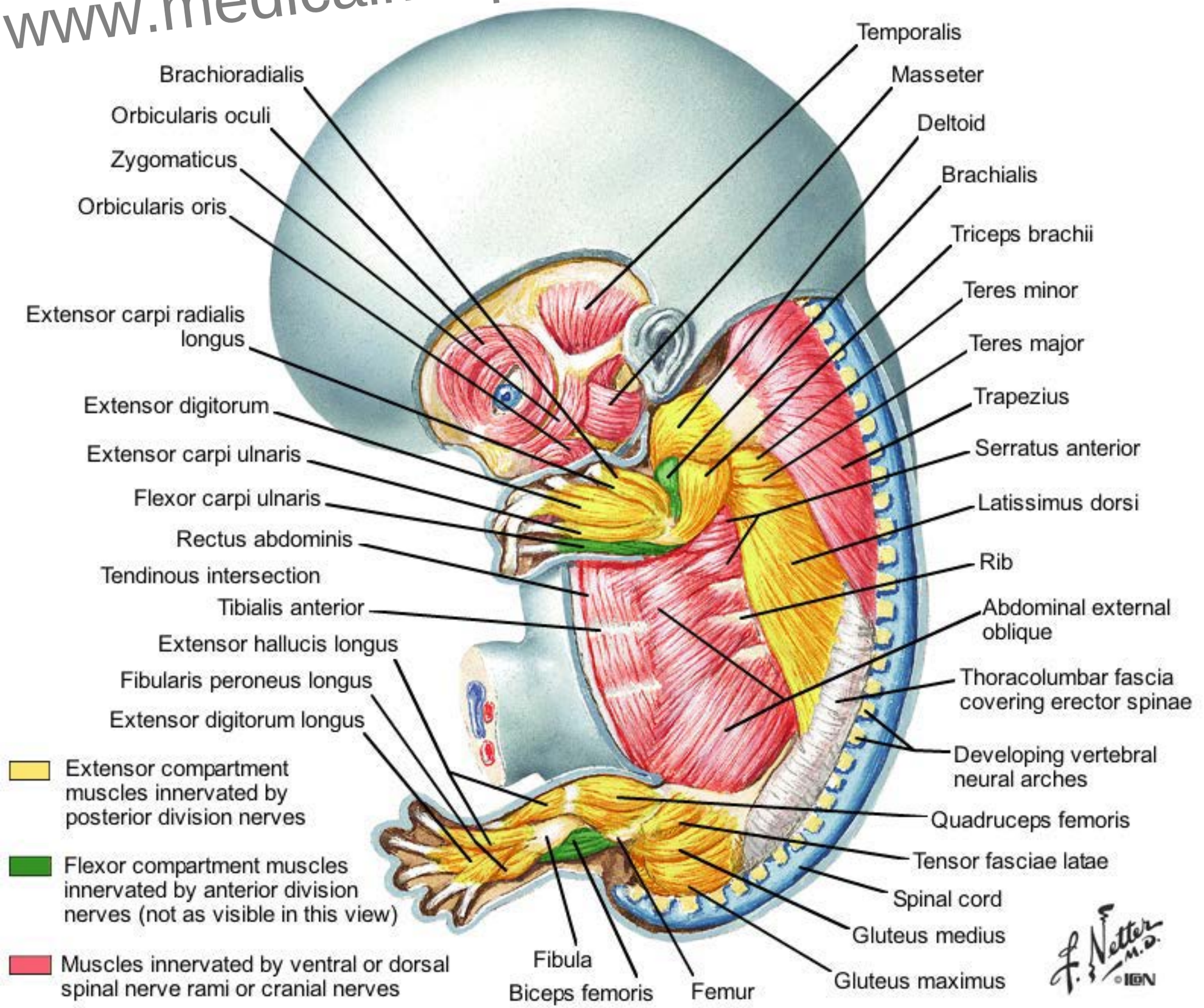


Divisions of the Lumbosacral Plexus



Developing Skeletal Muscles

Developing skeletal muscles at 8 weeks (superficial exposure)



HEAD AND NECK TIMELINE

Prenatal Time Scale (Months)

Blastocyst

Embryo

1

2

Fetus

3

9

Birth

3—4 weeks

The pharyngeal arches are appearing.

4—5 weeks

Lens, nasal, and otic placodes are beginning to invaginate. Pharyngeal arches are approaching full development. Oropharyngeal membrane is disintegrating.

6—7 weeks

Pharyngeal arch tissues migrate and differentiate. Nasal sacs (primitive nasal cavity) are about to communicate with the stomodeum.

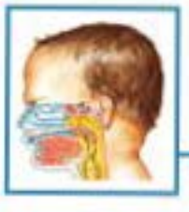
7—8 weeks

Auricle is present. Primary palate is fused, but the secondary palate is not yet completed. Most nerves, muscles, glands, and mesenchymal skeletal elements are in place.

8—10 weeks

Secondary palate is complete and fused to the nasal septum. Eyelids are temporarily fused. Ossification is occurring throughout the skull. Enamel organs of deciduous teeth are forming.

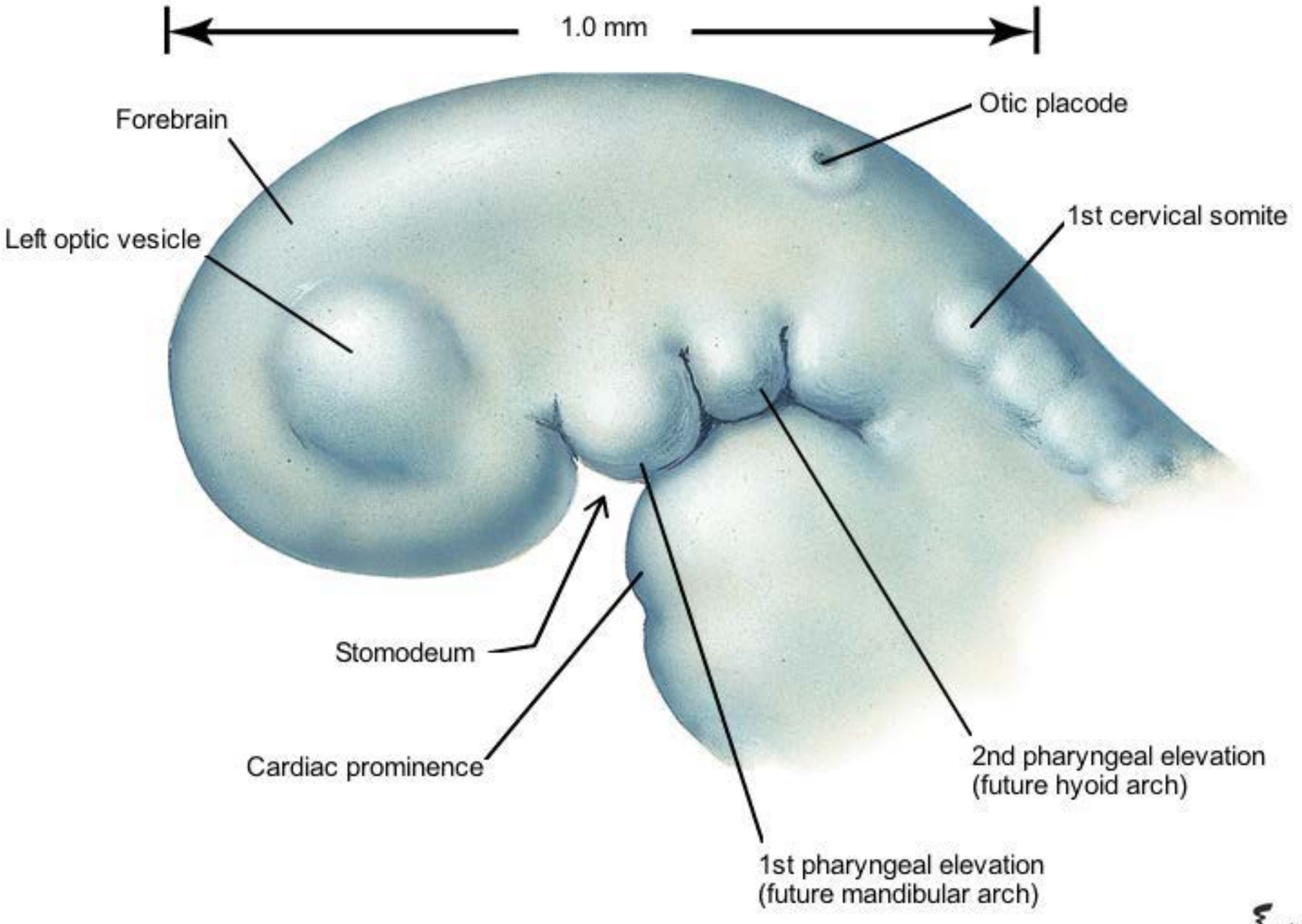
Newborn



Viscerocranium/face is small compared with neurocranium/brain. Bony sinuses are very small. Auditory tube and pharynx are short. Soft palate and epiglottis overlap when soft palate is pulled down against the tongue.

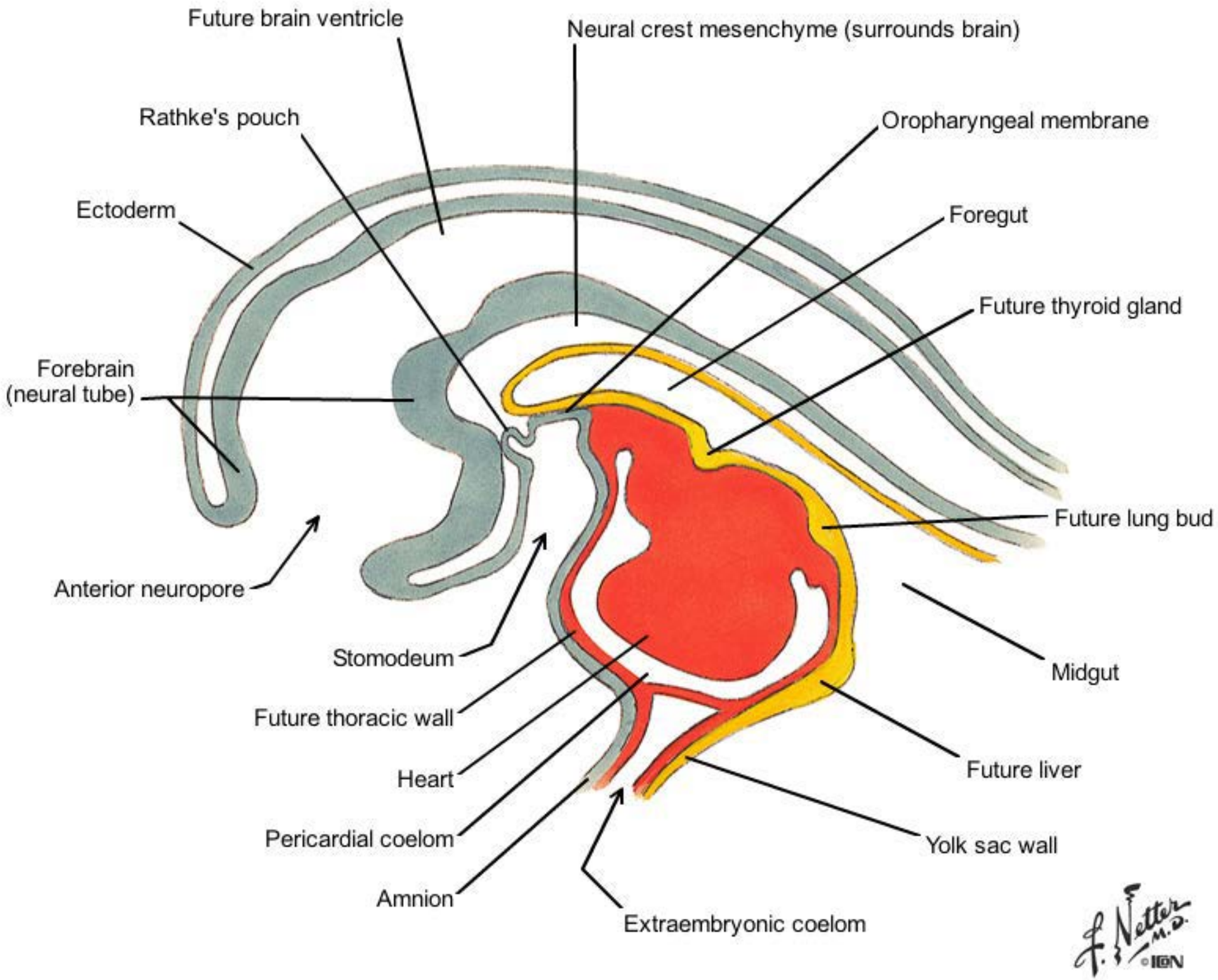
Ectoderm, Endoderm, and Mesoderm

Lateral view (3 to 4 weeks)



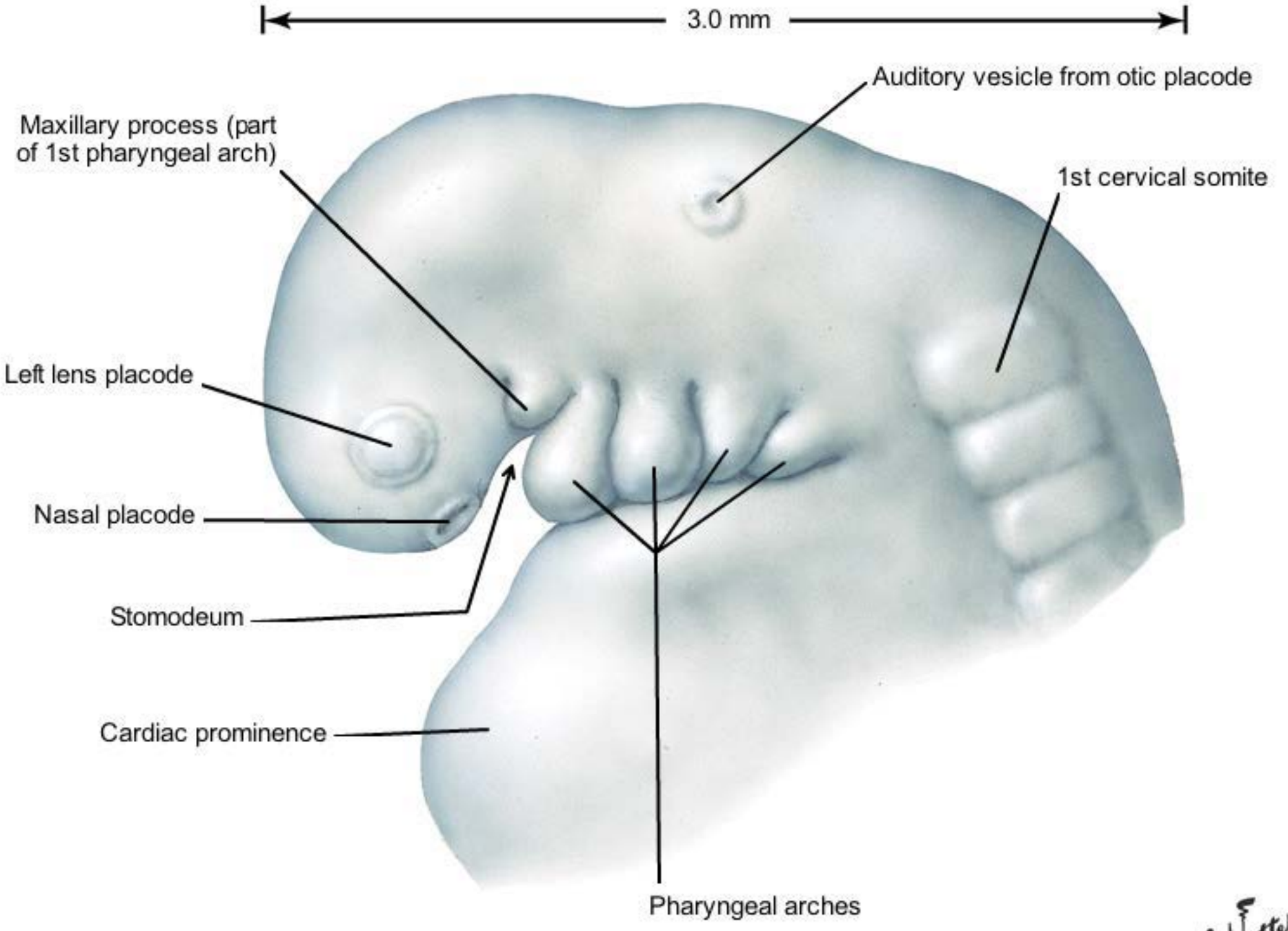
Ectoderm, Endoderm, and Mesoderm

Sagittal section (3 to 4 weeks)



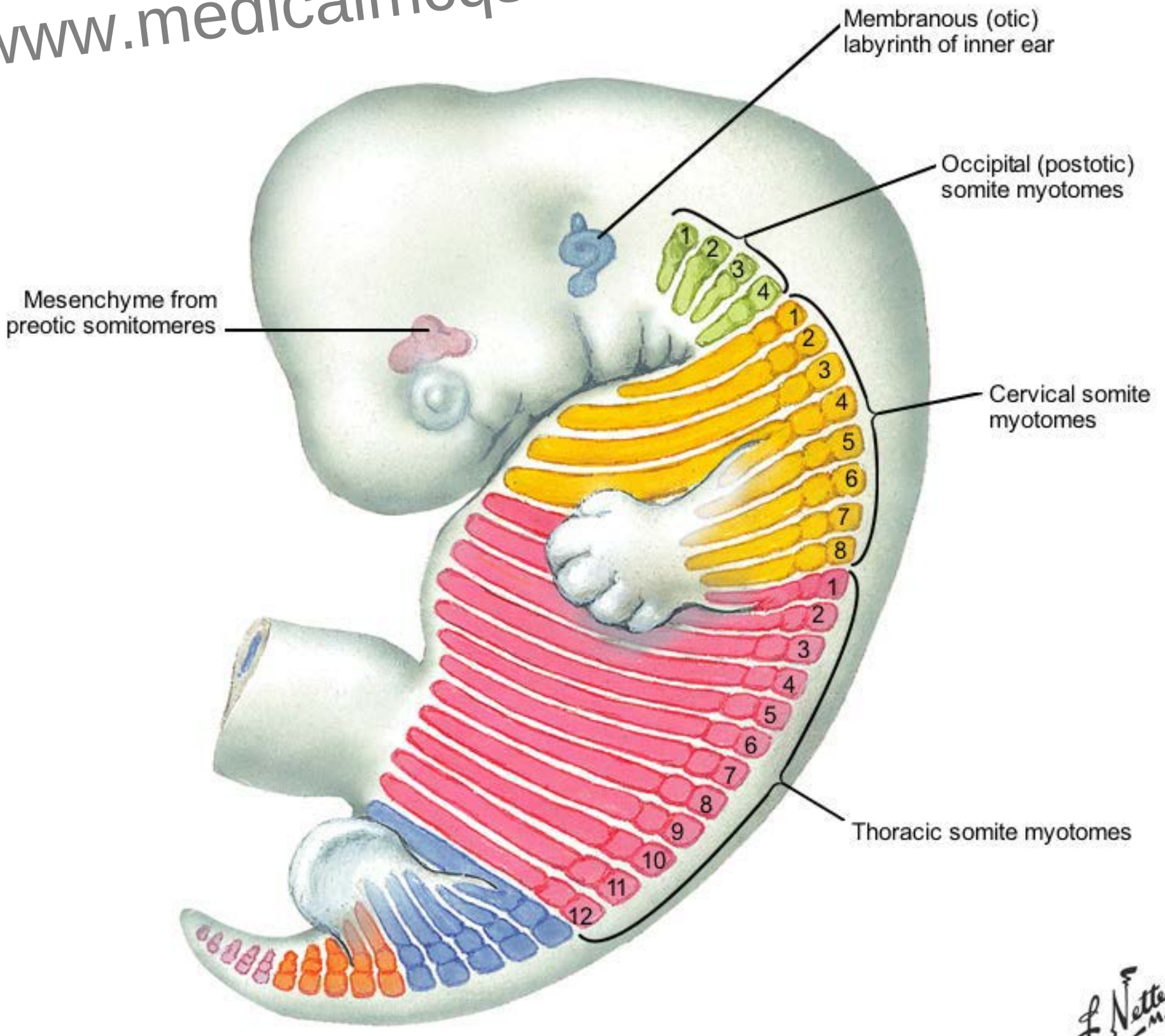
Ectoderm, Endoderm, and Mesoderm

Lateral view (4 to 5 weeks)



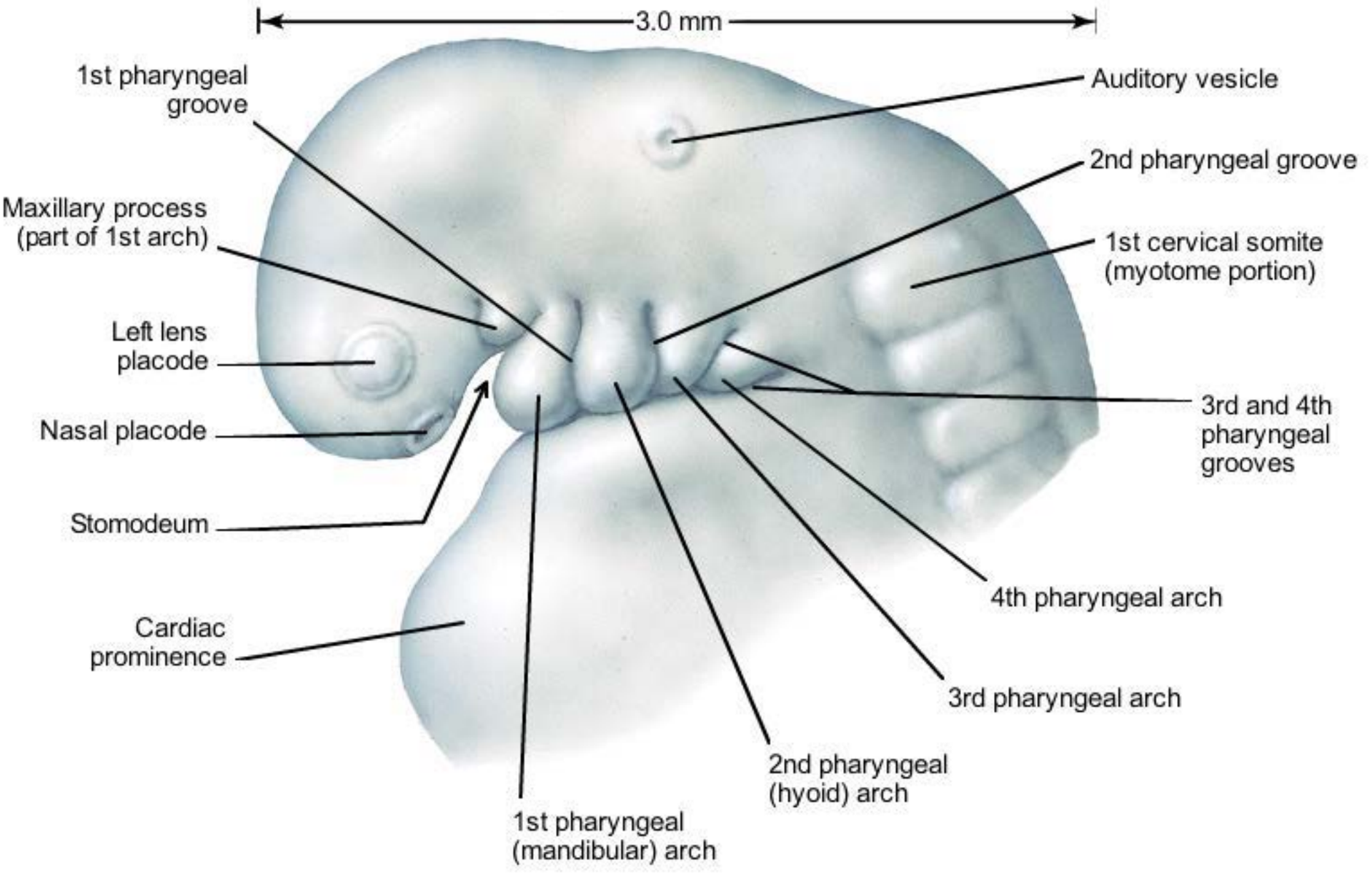
Ectoderm, Endoderm, and Mesoderm

Somites and somitomeres (6 weeks)



Pharyngeal (Branchial) Arches

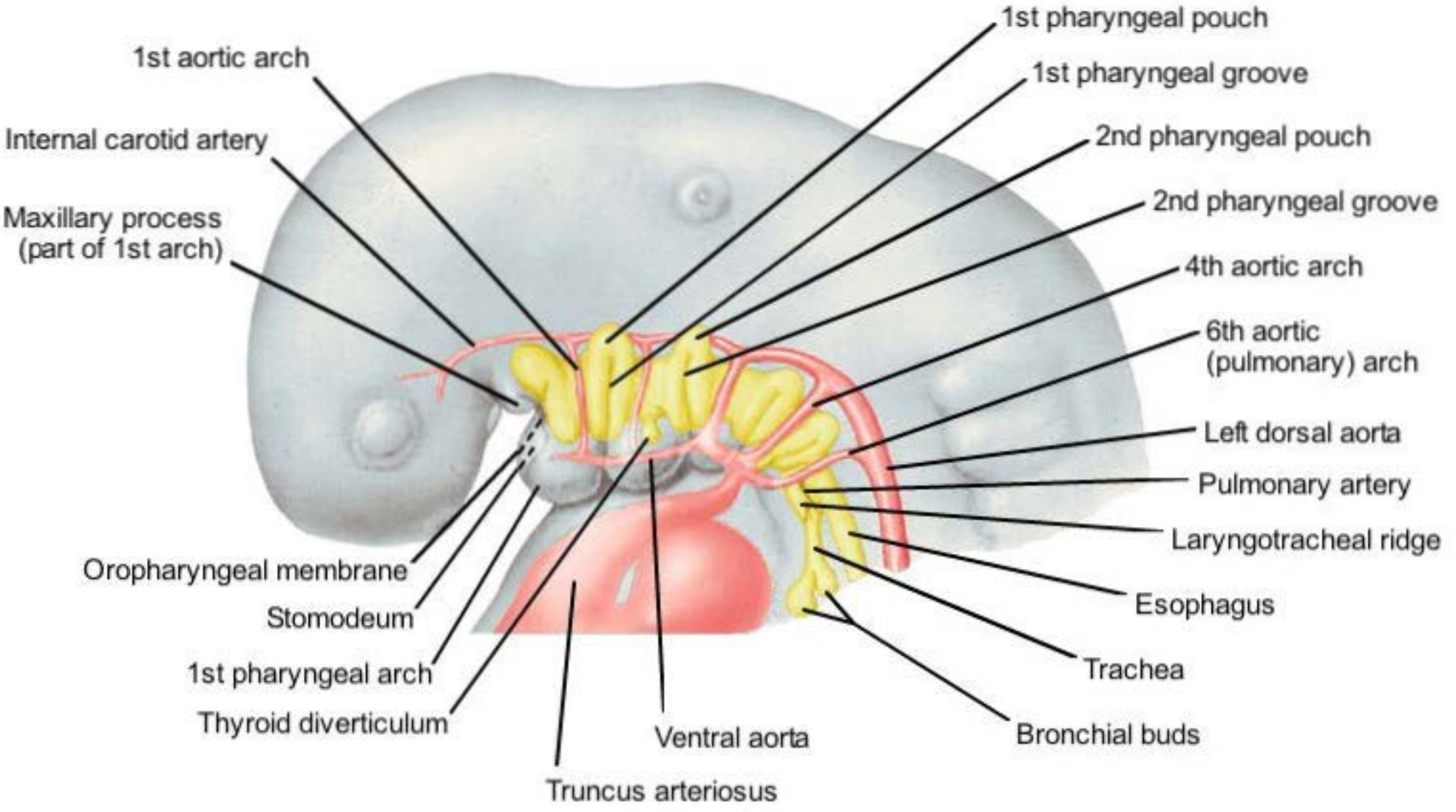
Embryo at 4 to 5 Weeks
Lateral View



Pharyngeal (Branchial) Arches

Pharyngeal pouches and aortic arch arteries

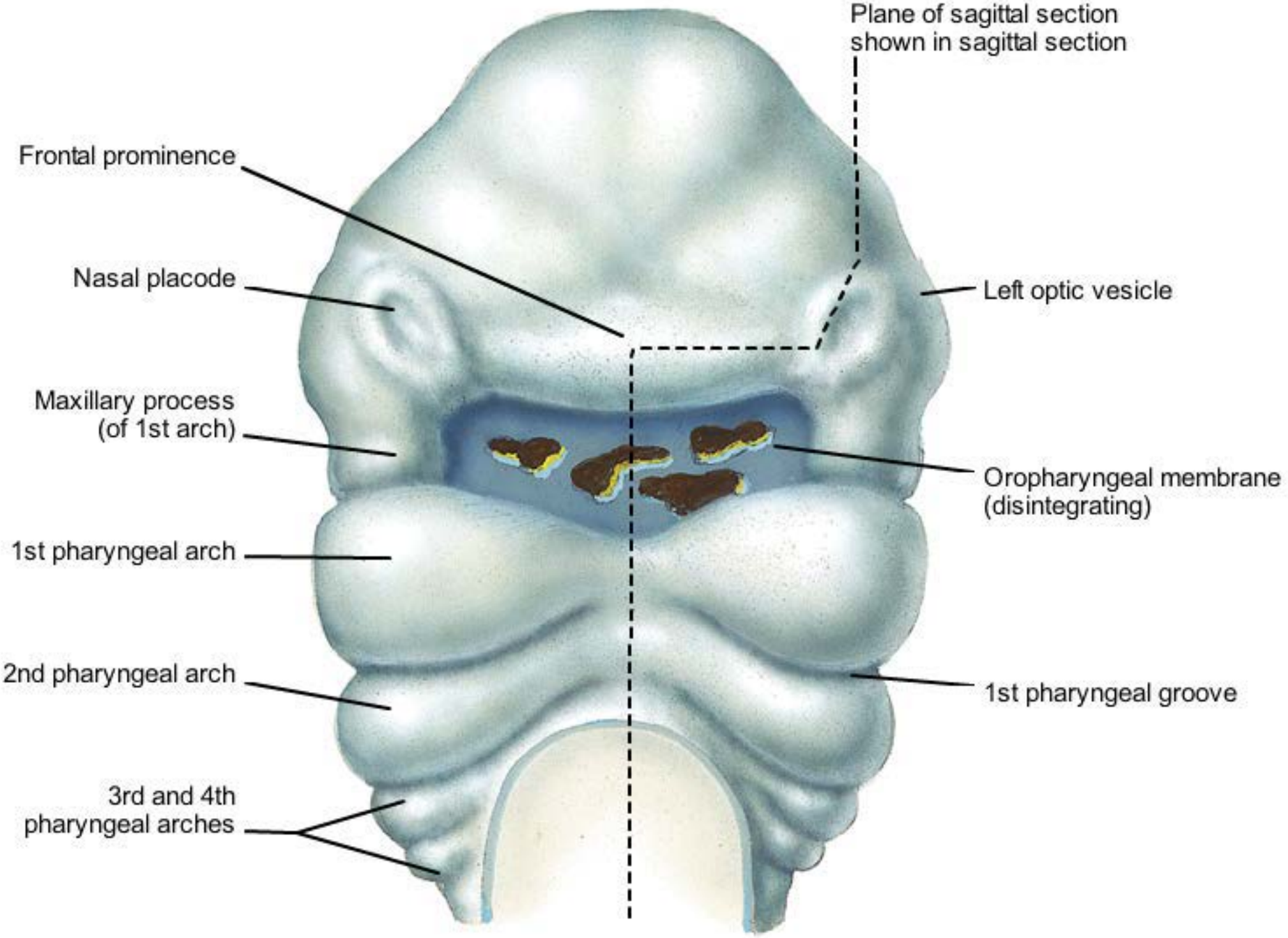
Lateral View



Ventral and Midsagittal Views

Embryo at 4 to 5 weeks

Ventral view



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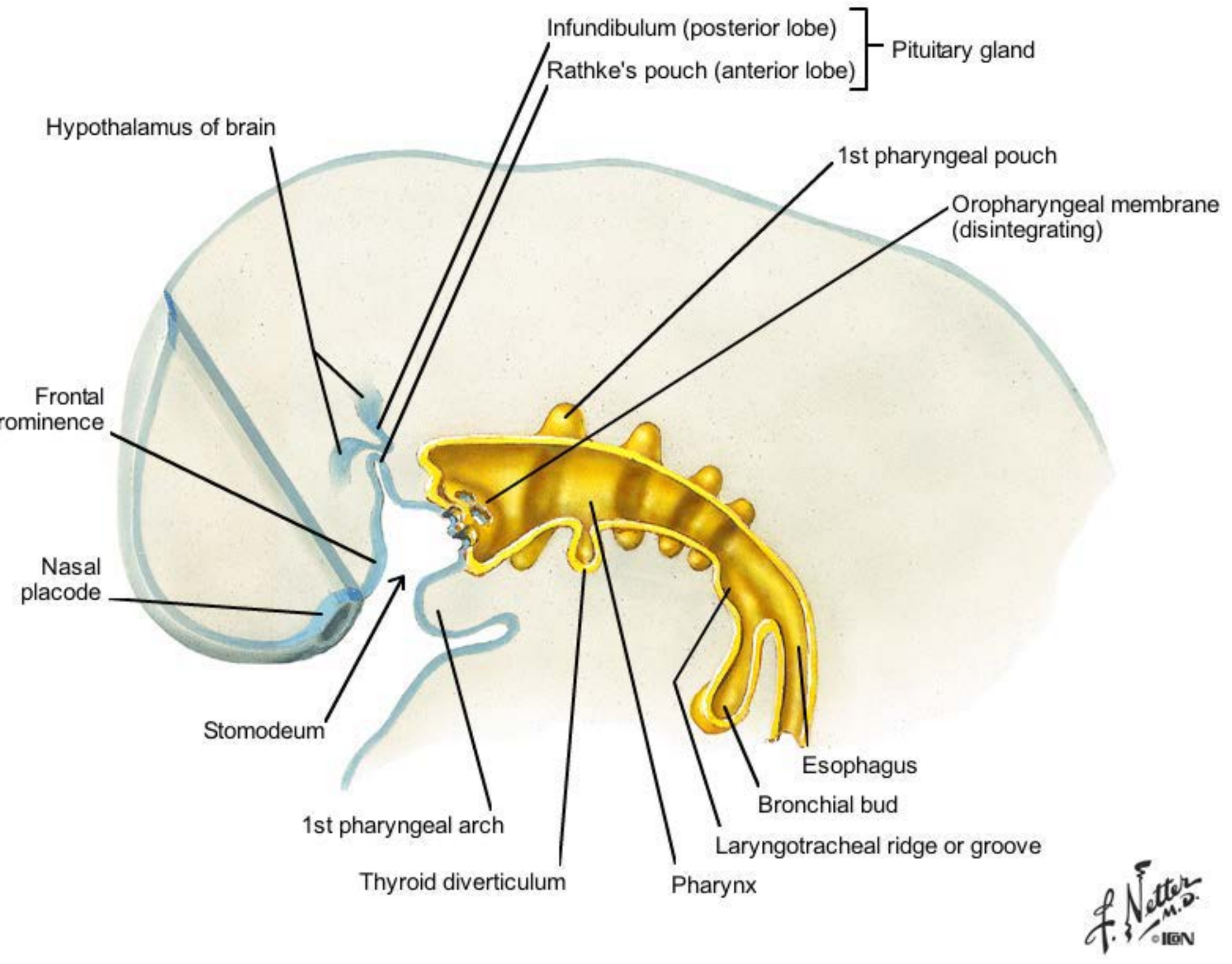
Ventral and Midsagittal Views

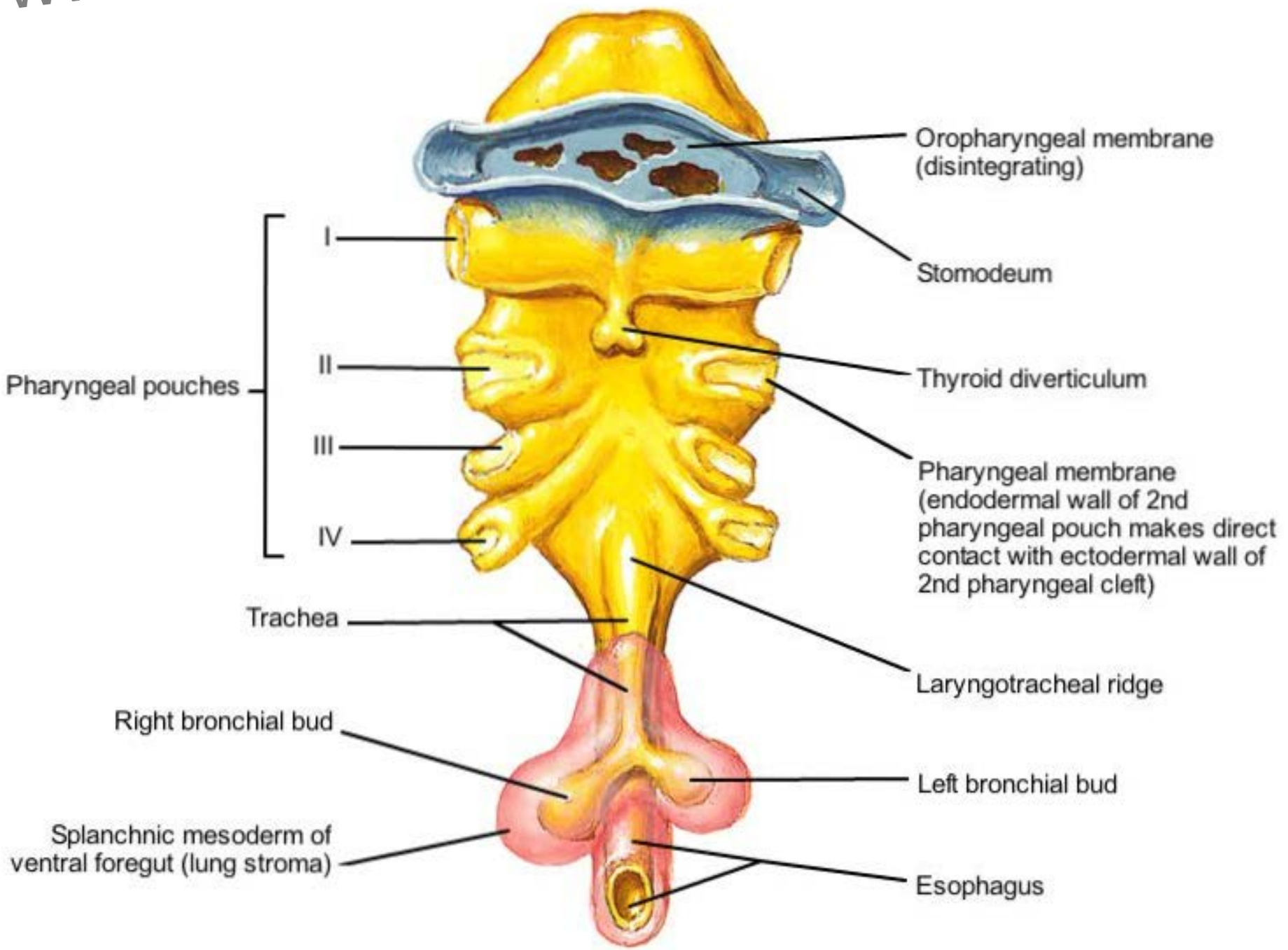
Embryo at 4 to 5 weeks

Sagittal section



Fate of the Pharyngeal Pouches

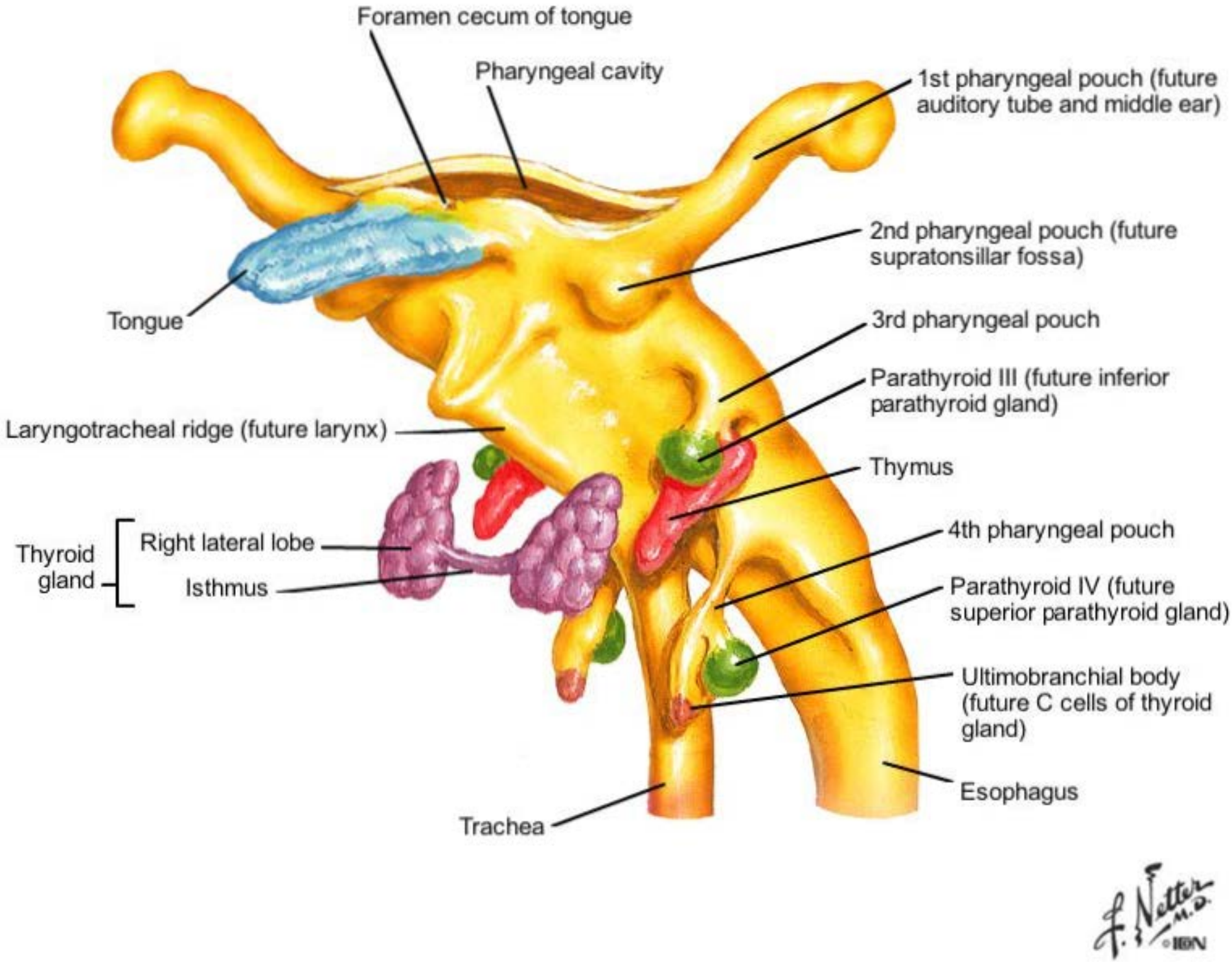
Embryo at 4 to 5 weeks
Pharynx (ventral view)



Fate of the Pharyngeal Pouches

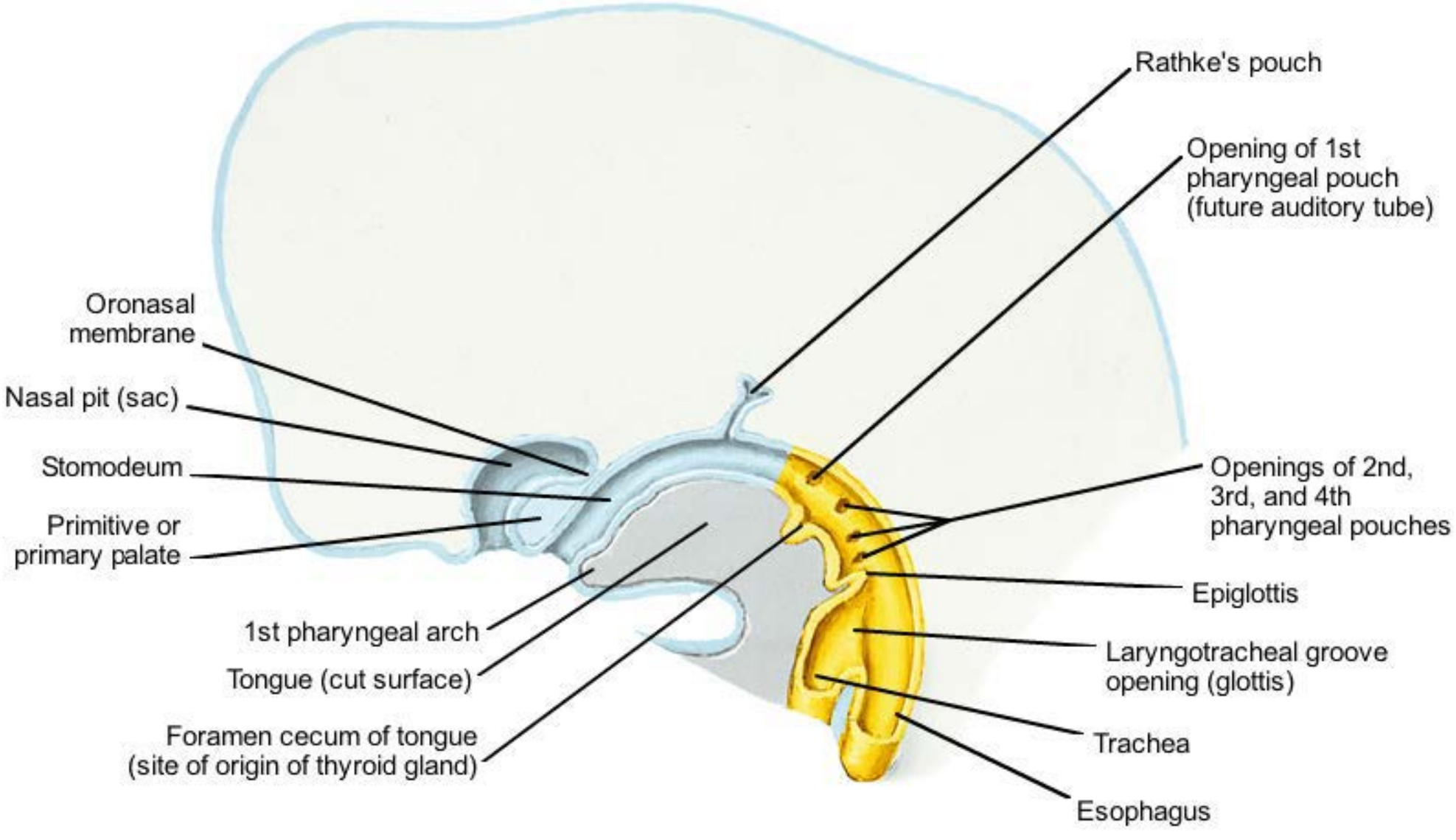
Embryo at 4 to 5 Weeks

Pharynx (anterior view of left side)



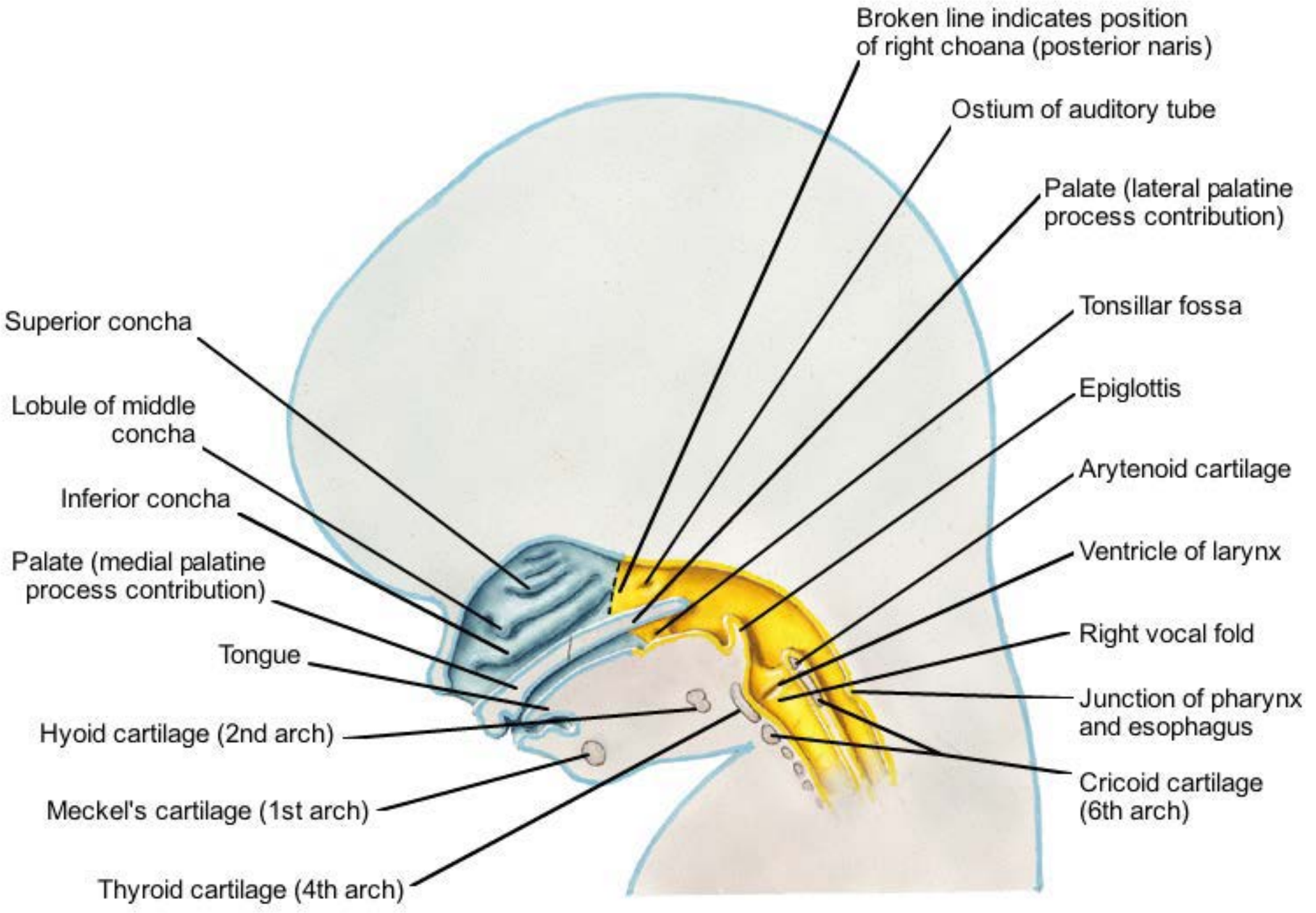
Midsagittal View of the Pharynx

Sagittal section at 5 to 6 weeks



Midsagittal View of the Pharynx

Sagittal section at 8 to 10 weeks



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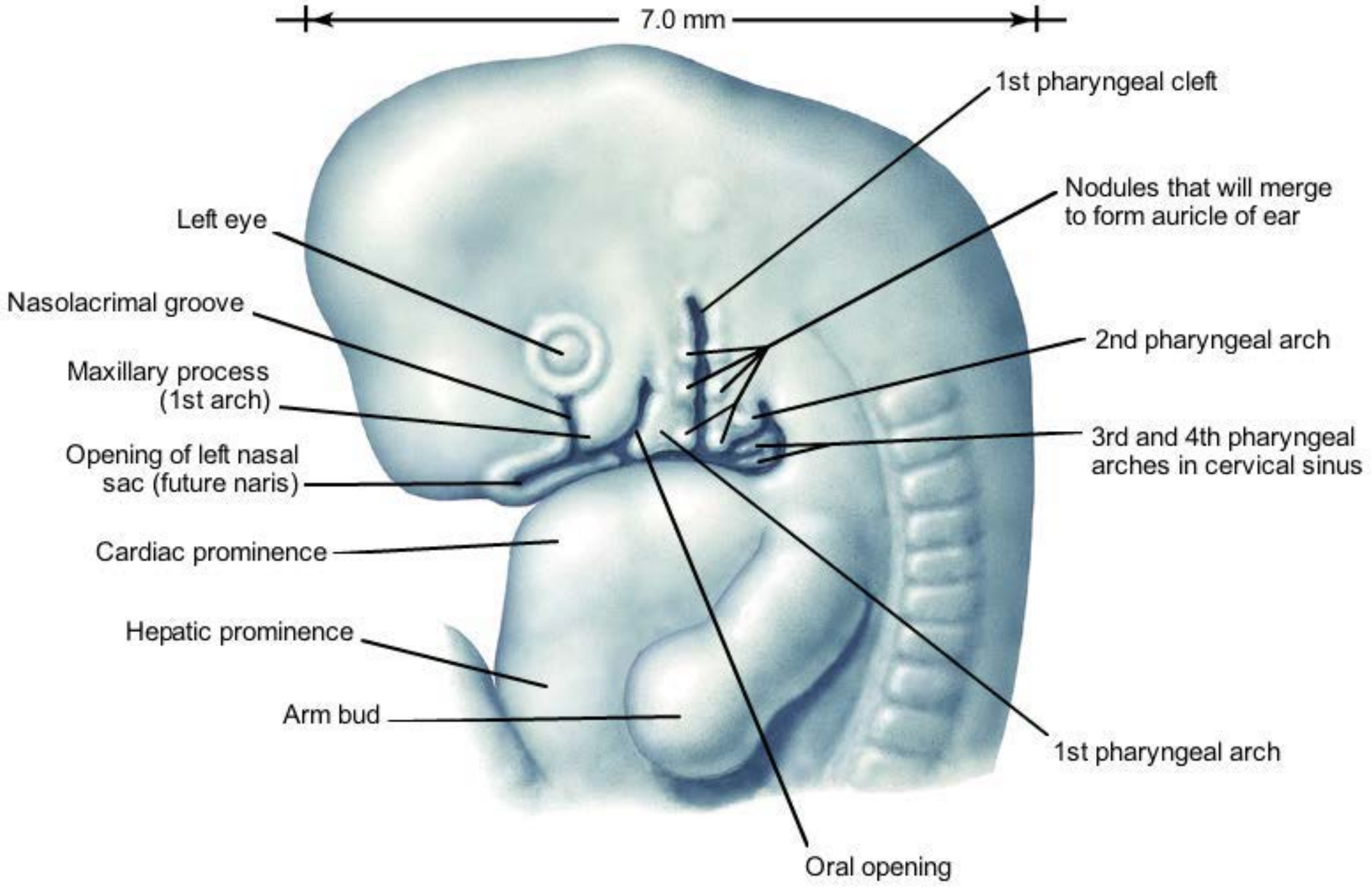
Fate of the Pharyngeal Grooves

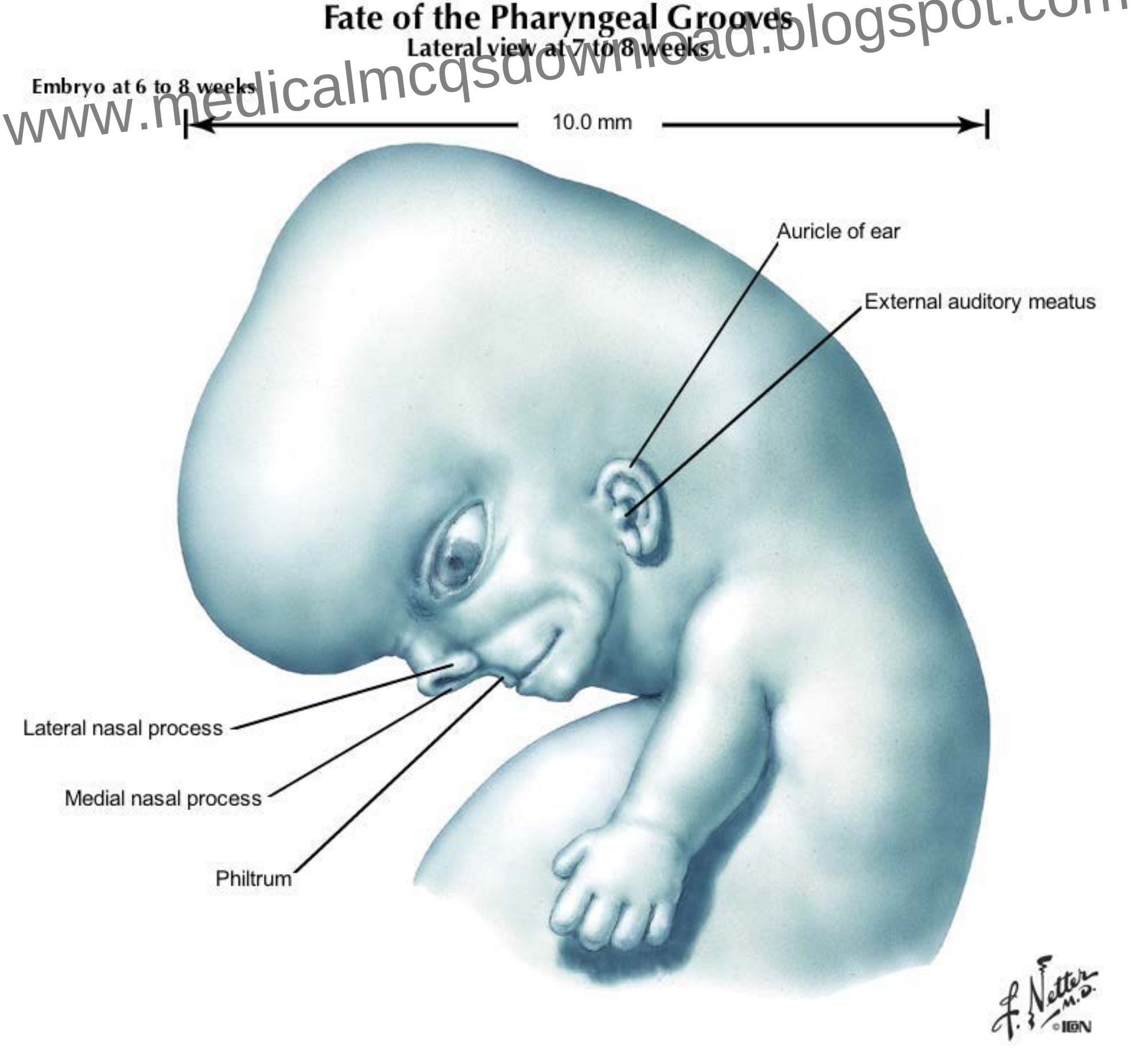
Lateral view at 6 to 7 weeks

Embryo at 6 to 8 weeks



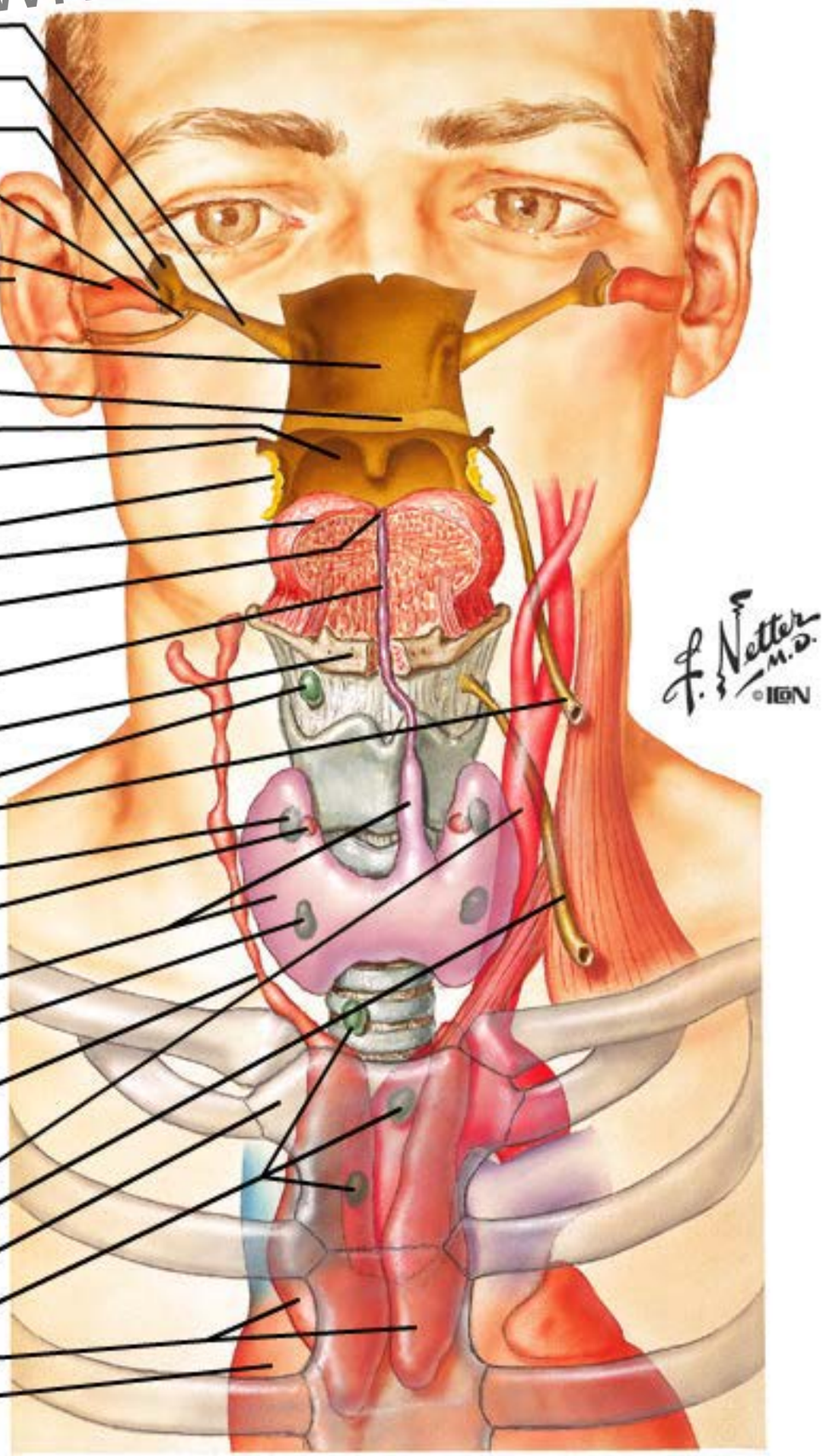
Fate of the Pharyngeal Grooves

Lateral view at 7 to 8 weeks

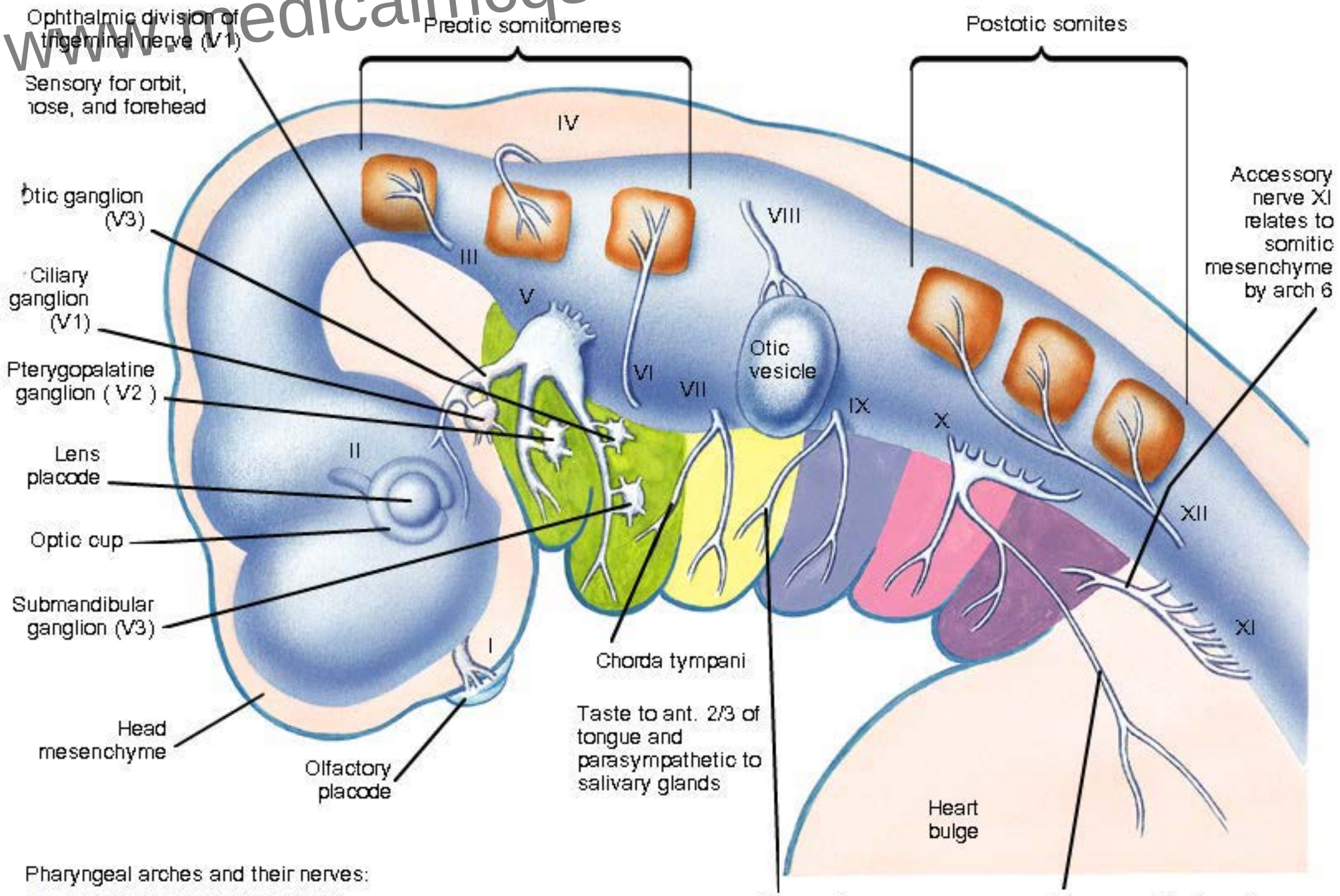


Pharyngeal Groove and Pouch Anomalies

Source	
1st pharyngeal pouch	Auditory tube
	Tympanic cavity
	Eardrum
	Pharyngeal fistula
1st pharyngeal groove	External acoustic meatus
1st and 2nd pharyngeal arches	Auricle
	Nasopharynx
	Soft palate (velum)
	Oropharynx
2nd pharyngeal pouch	Supratonsillar fossa
	Epithelium of palatine tonsil
	Tongue (cut)
Ventral pharyngeal wall	Foramen cecum
	Persistent thyroglossal duct
	Hyoid bone (cut)
3rd pharyngeal pouch	Aberrant parathyroid gland III
2nd pharyngeal pouch	Pharyngeal fistula
4th pharyngeal pouch	Parathyroid gland IV
	Ultimobranchial body
Ventral pharyngeal wall	Pyramidal and lateral lobes of thyroid gland
3rd pharyngeal pouch	Parathyroid gland III
	Persistent cord of thymus
	Common carotid artery
3rd pharyngeal pouch	Pharyngeal fistula
	Manubrium of sternum
3rd pharyngeal pouch	Aberrant parathyroid gland III
	Thymus gland
	Heart



Pharyngeal Arch Nerves



Pharyngeal arches and their nerves:

- Arch 1-trigeminal nerve (V)
  Maxillary part of arch 1-maxillary nerve (trigeminal, V2)
  Mandibular part of arch 1-mandibular nerve (trigeminal, V3)
- Arch 2-facial nerve (VII)
- Arch 3-glossopharyngeal nerve (IX)
- Arch 4-vagus n. (X)
- Arch 6-vagus n. (X)

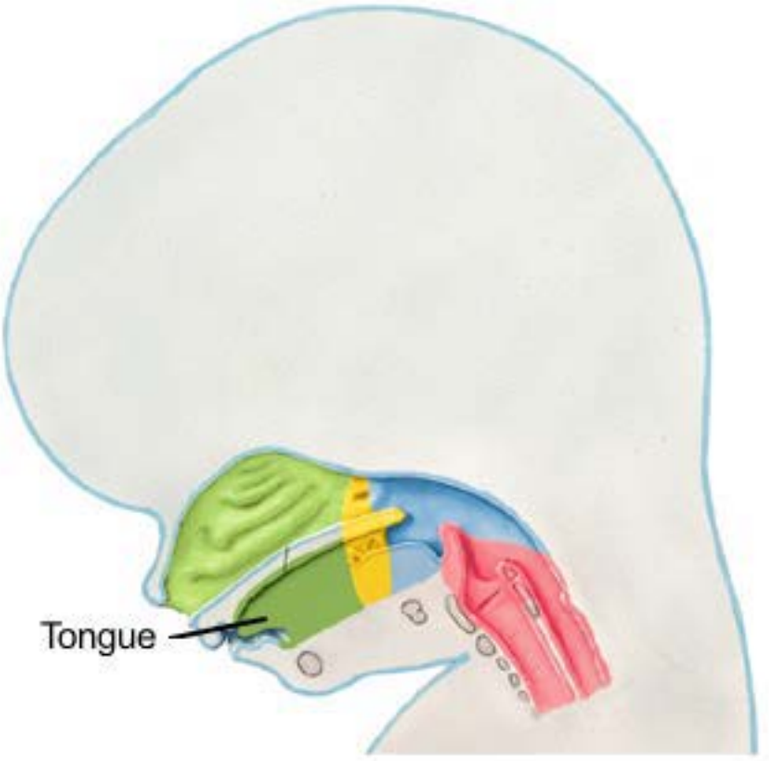
Sensory Innervation Territories

What the sensory nerve territories would be if the embryonic pattern of the pharyngeal arches were retained

Lateral view at 8 to 10 weeks

24.0 mm

Sagittal section at 8 to 10 weeks



Cranial nerves:

- Trigeminal (V1)- Arch 1 (maxillary)
- Trigeminal (V2)-Arch 1 (mandibular)
- Facial (VII)-Arch 2
- Glossopharyngeal-Arch 3
- Vagus (X)-Arches 4 and 6

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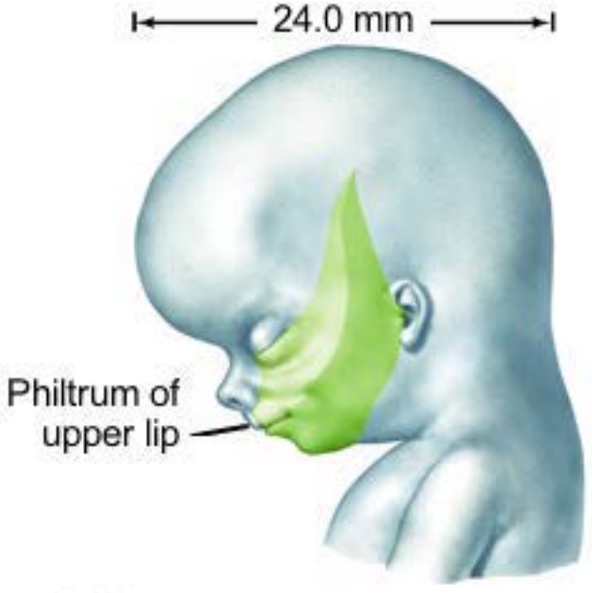
Sensory Innervation Territories

What the sensory territories actually are



Cranial nerves:

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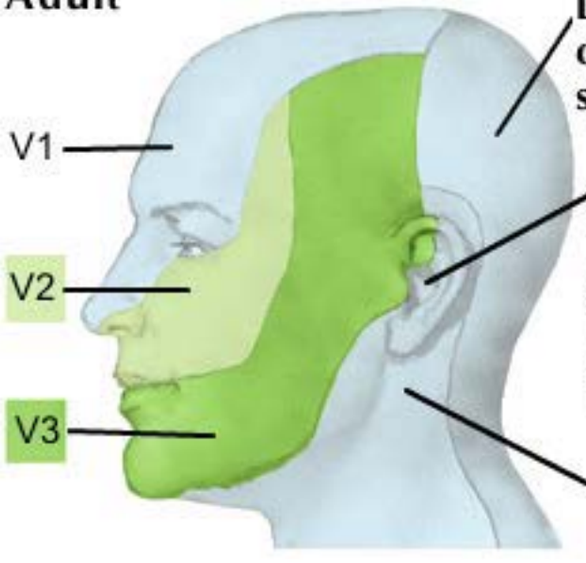
- Facial (VII)-Arch 2
- Glossopharyngeal-Arch 3
- Vagus (X)-Arches 4 and 6

Adult

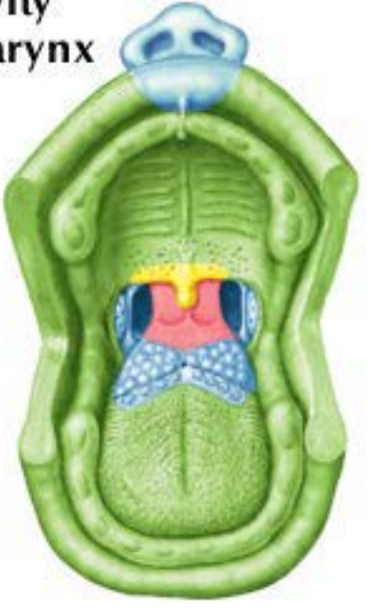


Dorsal rami of cervical spinal nerves

Auricular branch of vagus to external meatus and small area on posteromedial surface of auricle

Branches from cervical plexus

Oral cavity and pharynx



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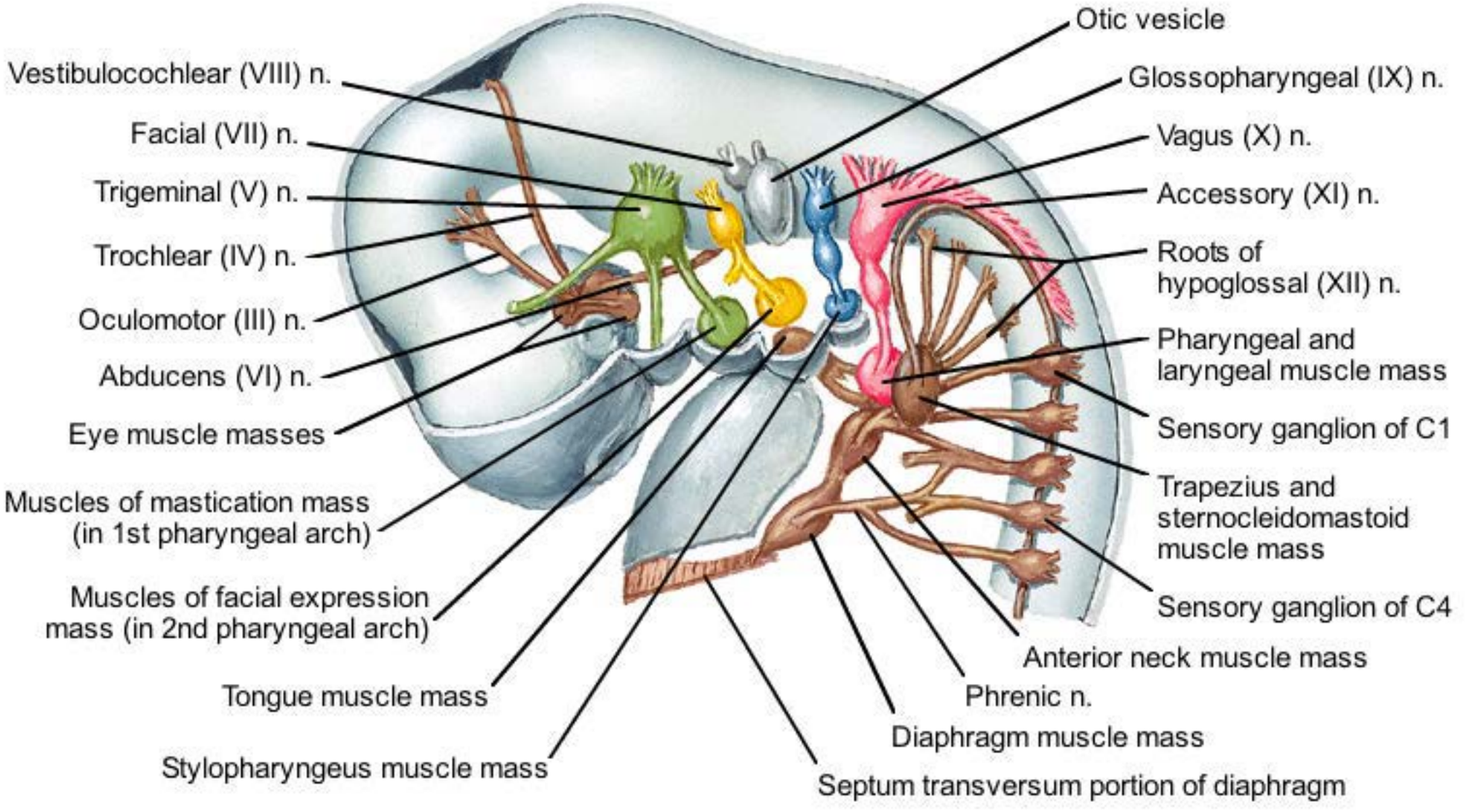
Early Development of Pharyngeal Arch Muscle

Origins and innervations of pharyngeal arch and somite myotome muscles at 5 weeks



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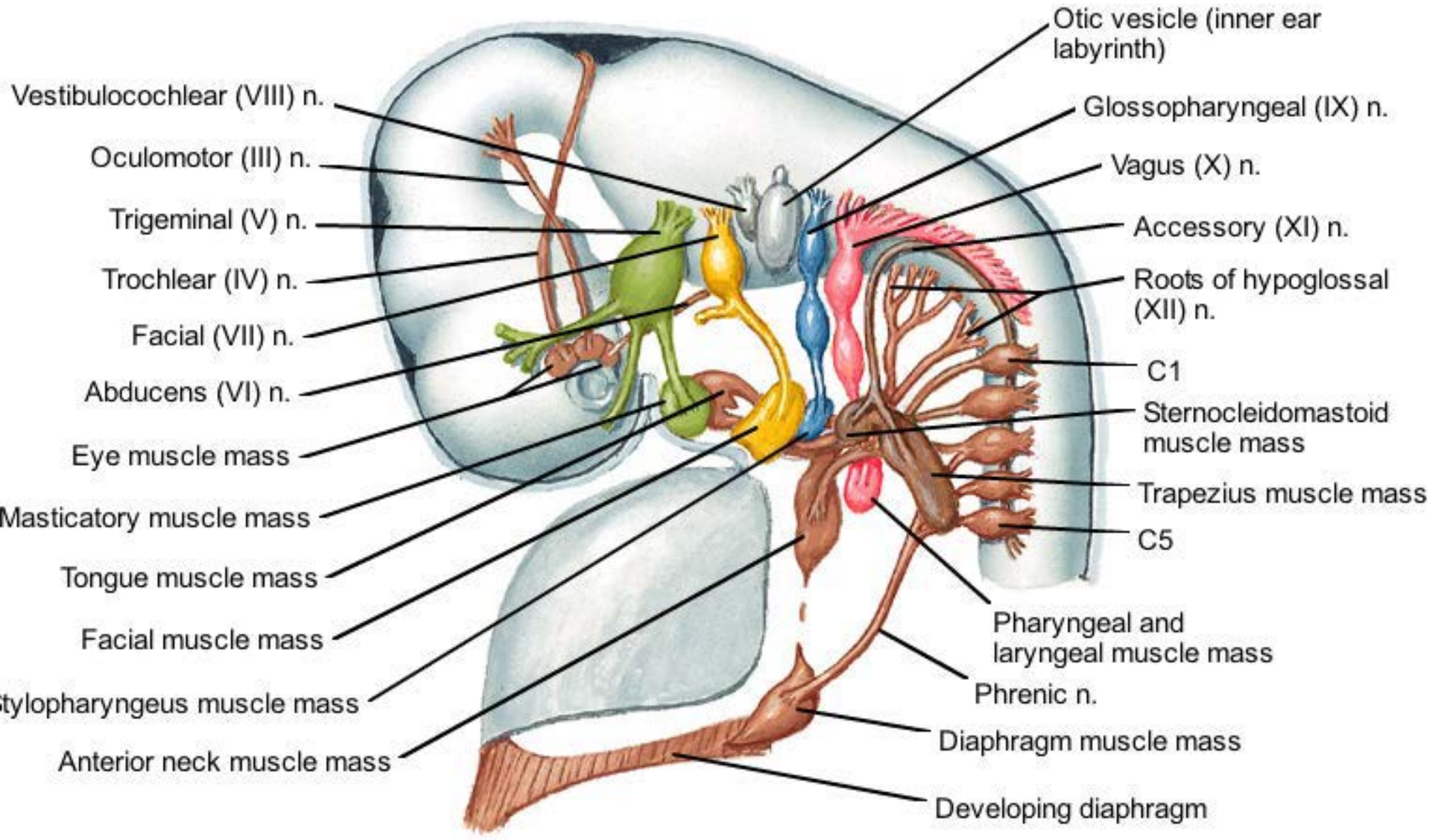
Early Development of Pharyngeal Arch Muscle

Origins and innervations of pharyngeal arch and somite myotome muscles at 6 weeks



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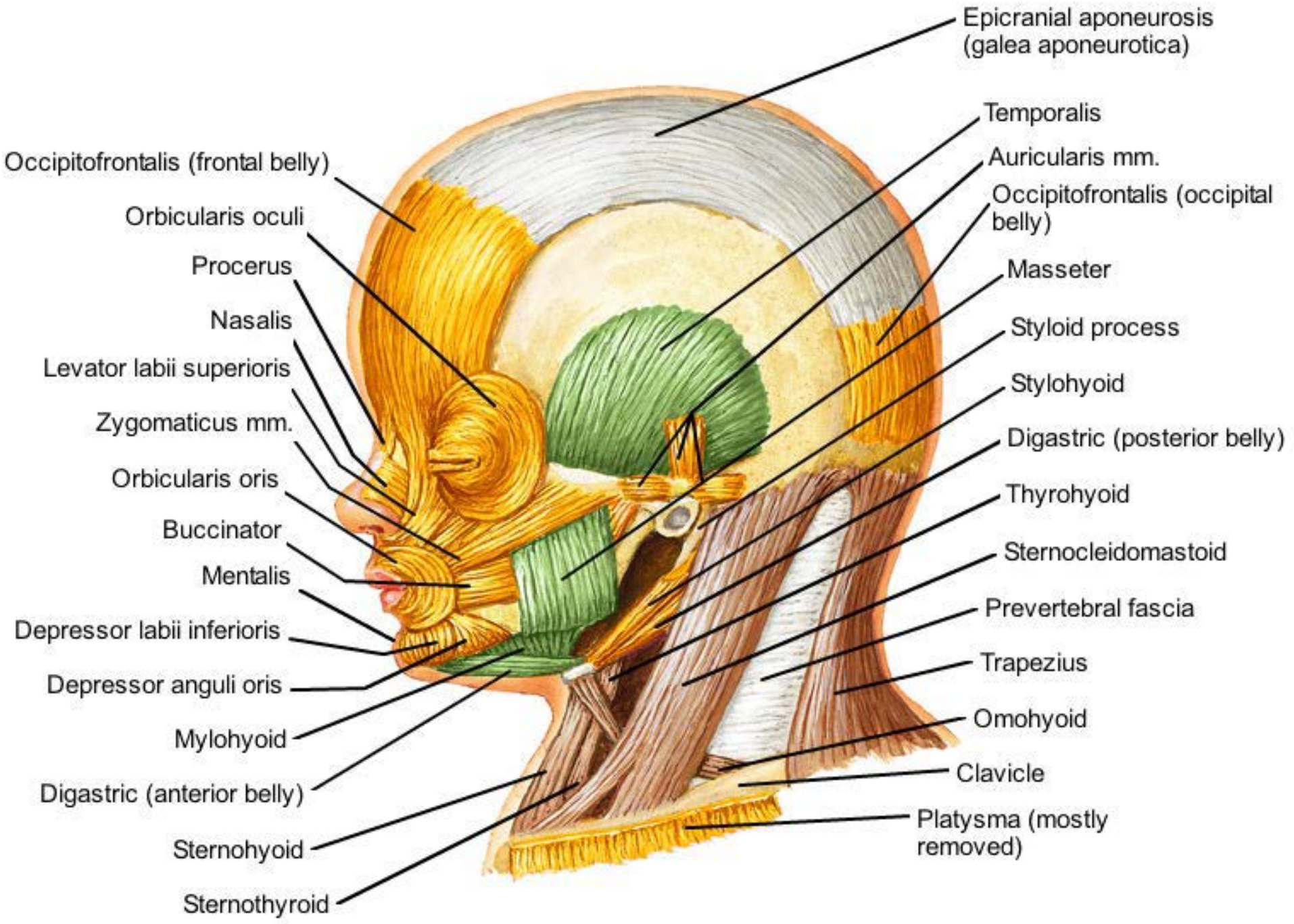
Later Development of Pharyngeal Arch Muscles

Superficial muscles



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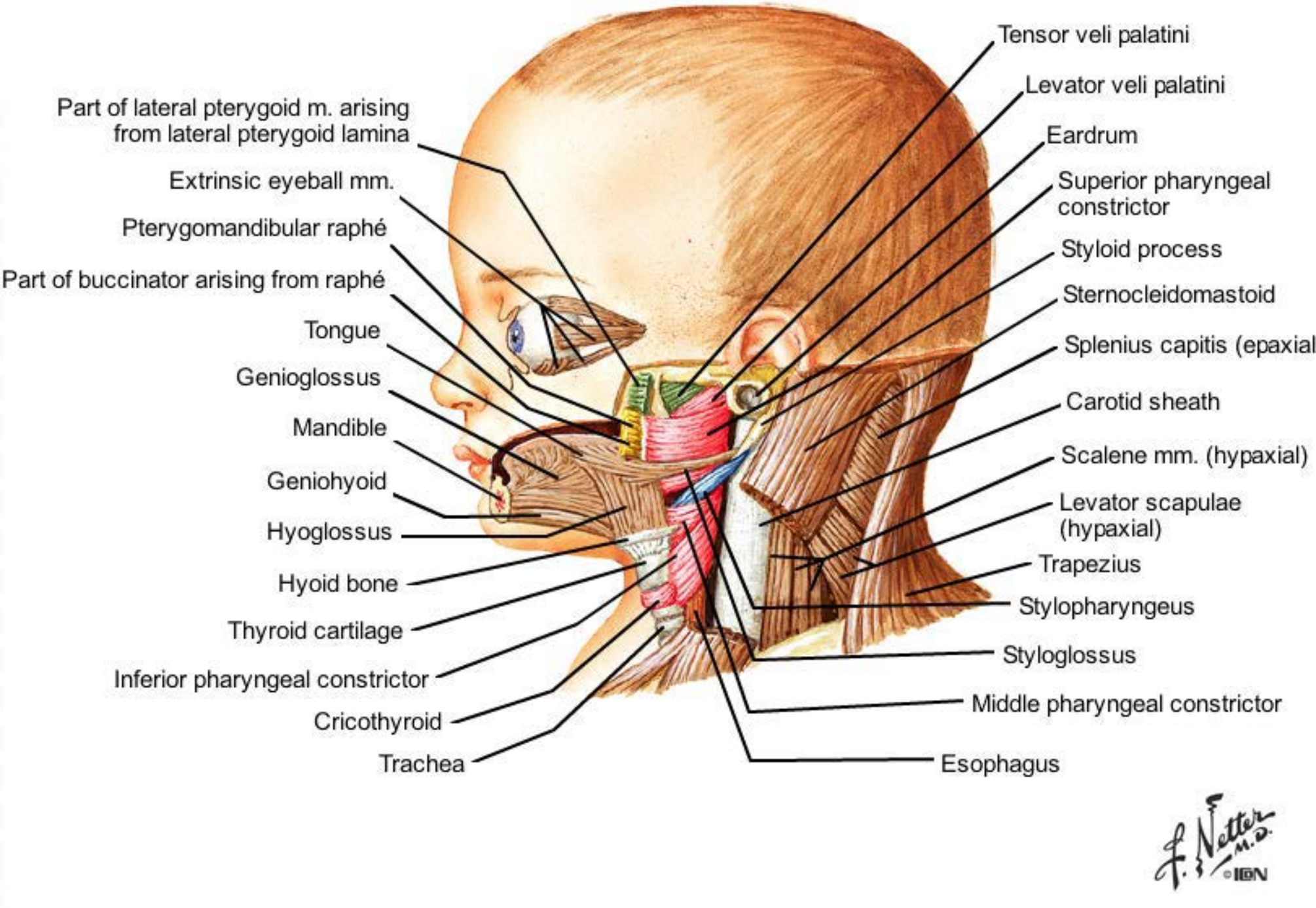
Later Development of Pharyngeal Arch Muscles

Deep muscles



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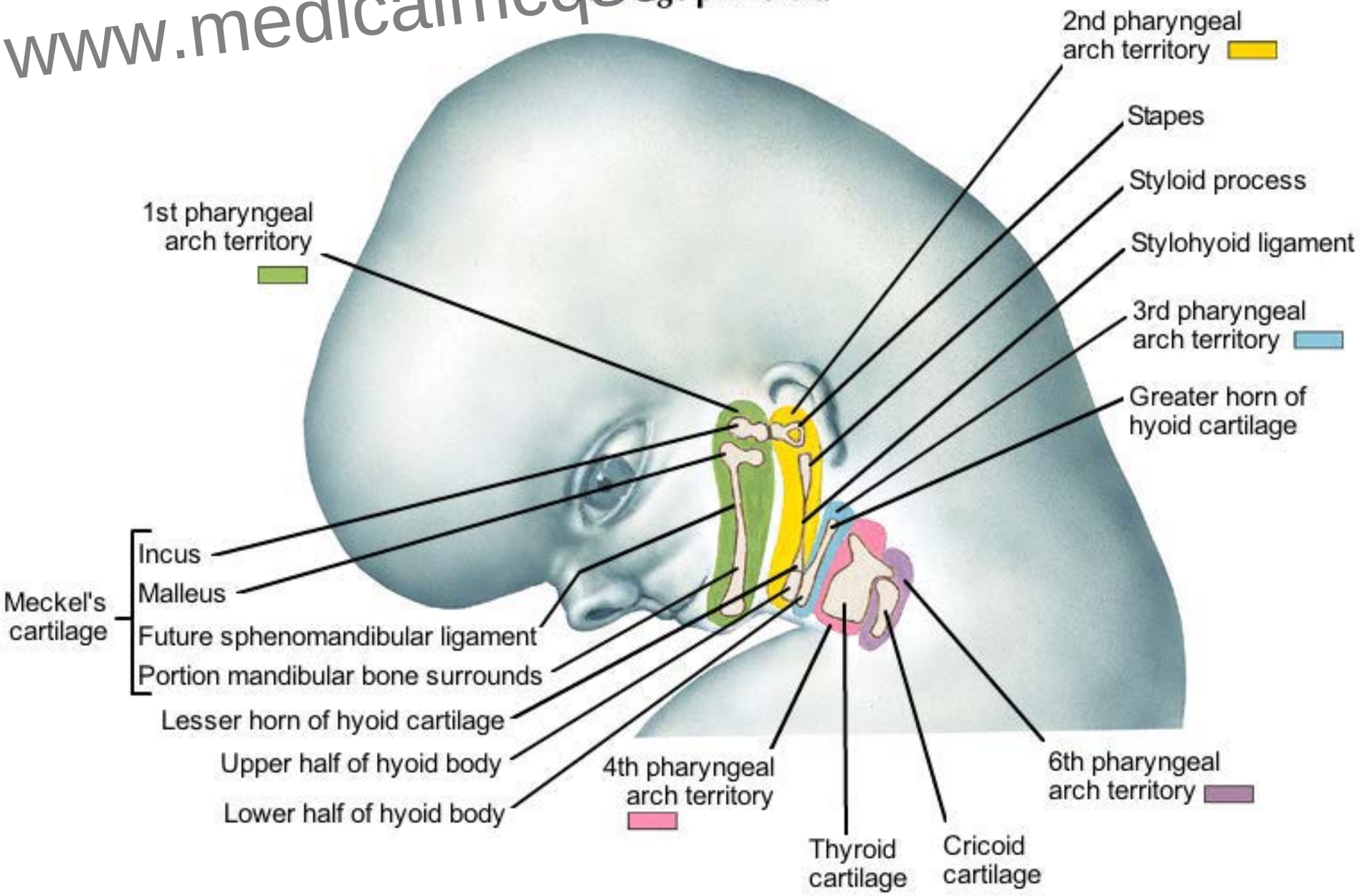
Pharyngeal Arch Cartilages

Embryo at 7 to 8 Weeks

Cartilage primordia



PHARYNGEAL ARCH BONES AND CARTILAGE

Arch #	Derivatives of Arch Cartilages
1	Malleus, incus, sphenomandibular ligament
2	Stapes, styloid process, stylohyoid ligament, upper half of hyoid
3	Lower half and greater horns of hyoid
4	Thyroid and epiglottic cartilages of larynx
6	Cricoid, arytenoid, and corniculate cartilages of larynx

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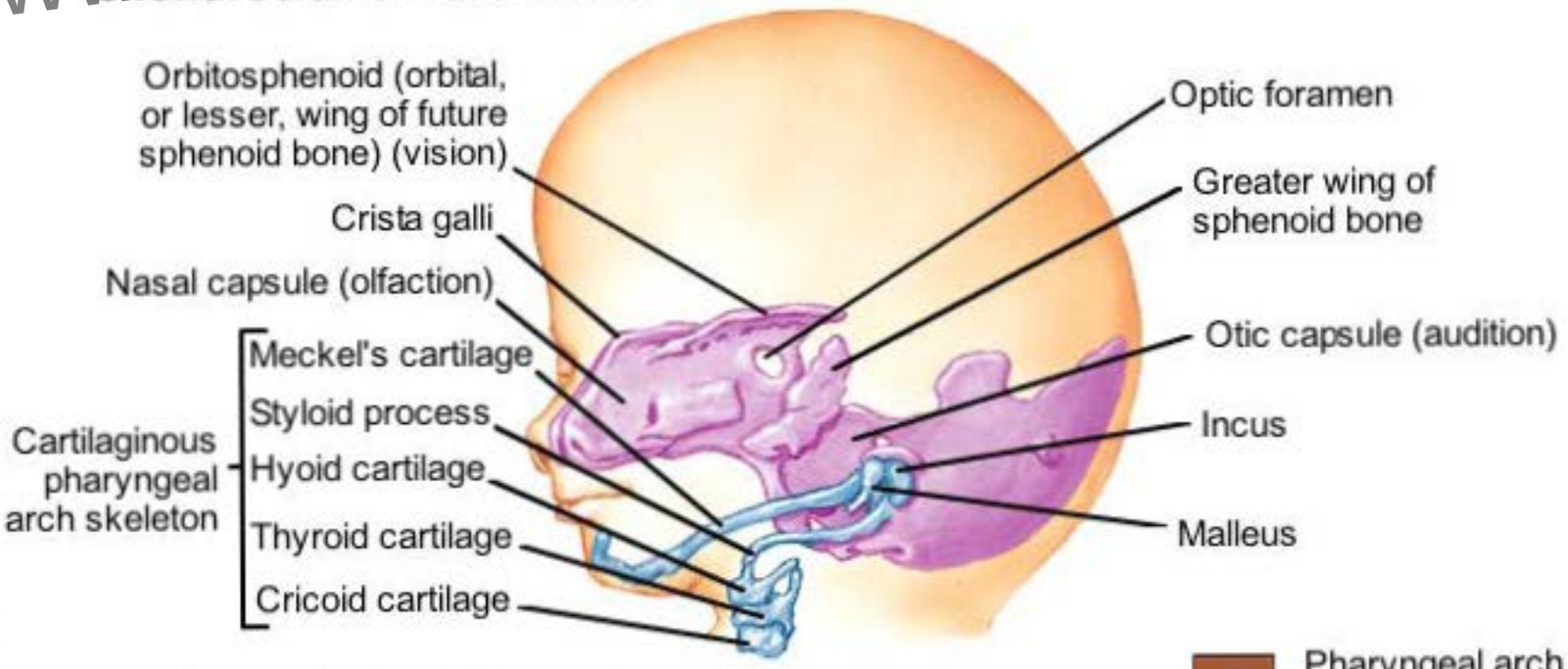
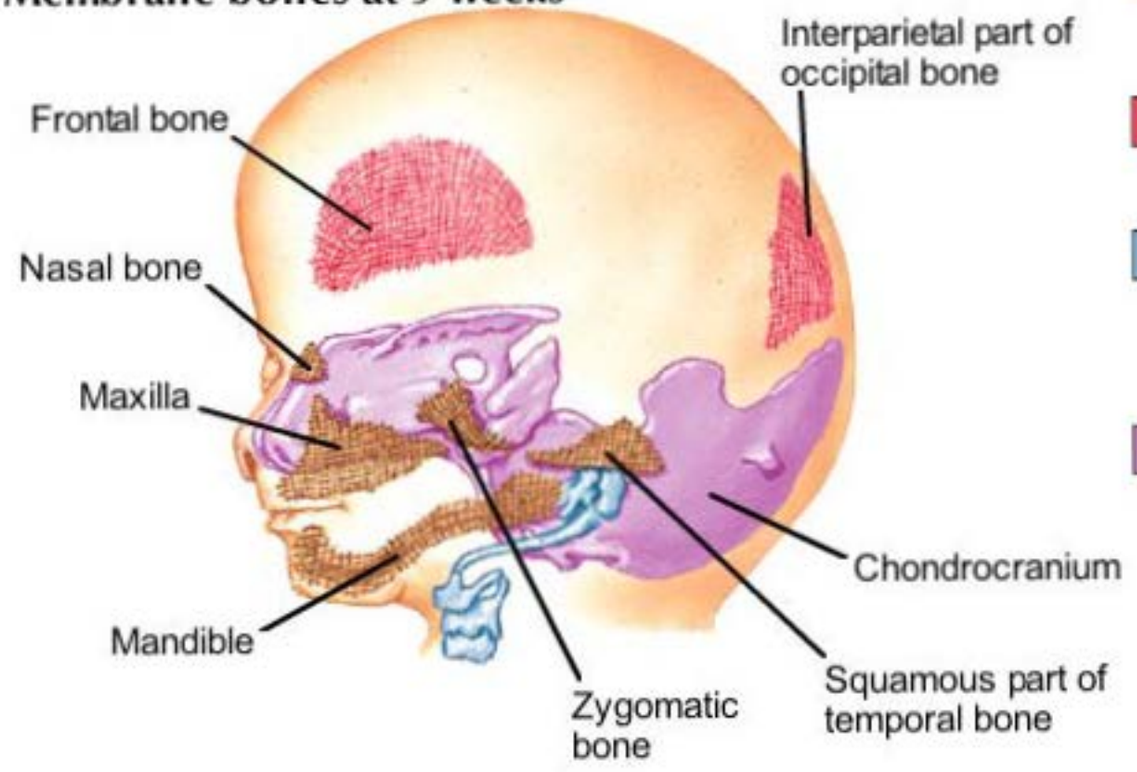
Ossification of the Skull

Chondrocranium at 9 weeks



Membrane bones at 9 weeks



Pharyngeal arch mesenchyme for viscerocranium

Head mesenchyme for neurocranium

Intramembranous ossification (both from neural crest)

Cartilage from pharyngeal arches for viscerocranium and neck cartilages

Cartilage from somite sclerotomes and neural crest anteriorly for base of neurocranium

Endochondral ossification

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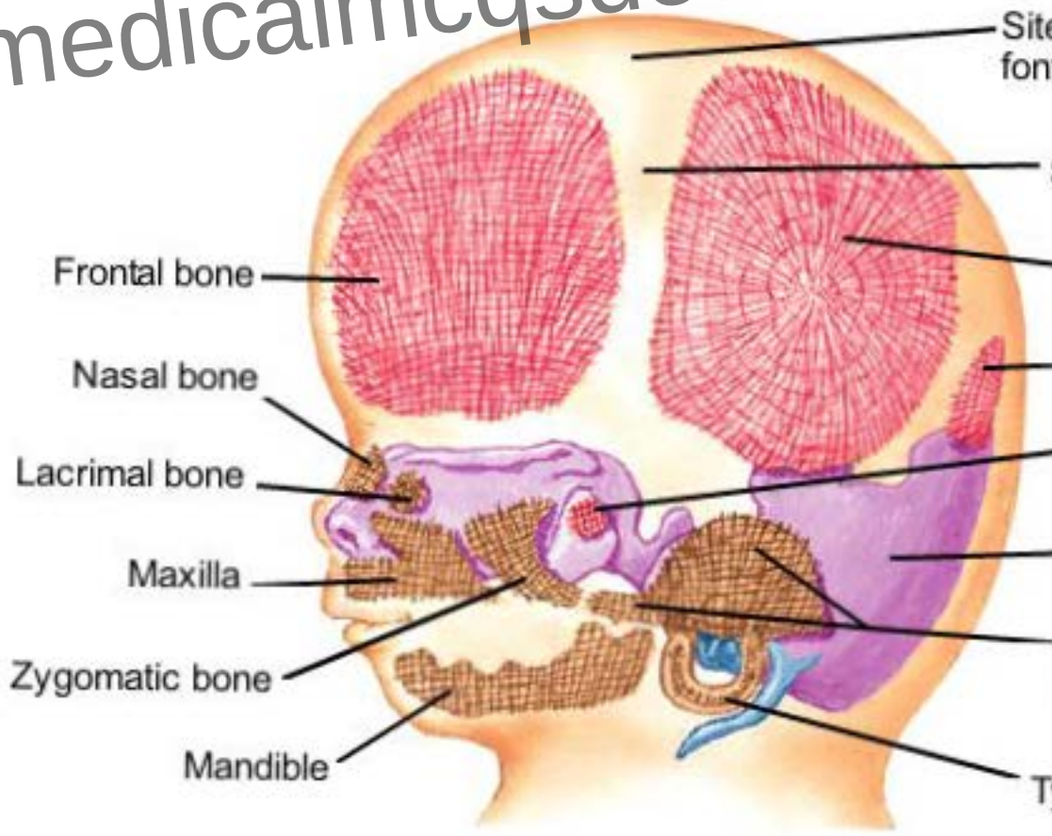
Ossification of the Skull

Membrane bones at 12 weeks



Pharyngeal arch mesenchyme for viscerocranium

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Cartilage from somite sclerotomes and neural crest anteriorly for base of neurocranium

Endochondral ossification

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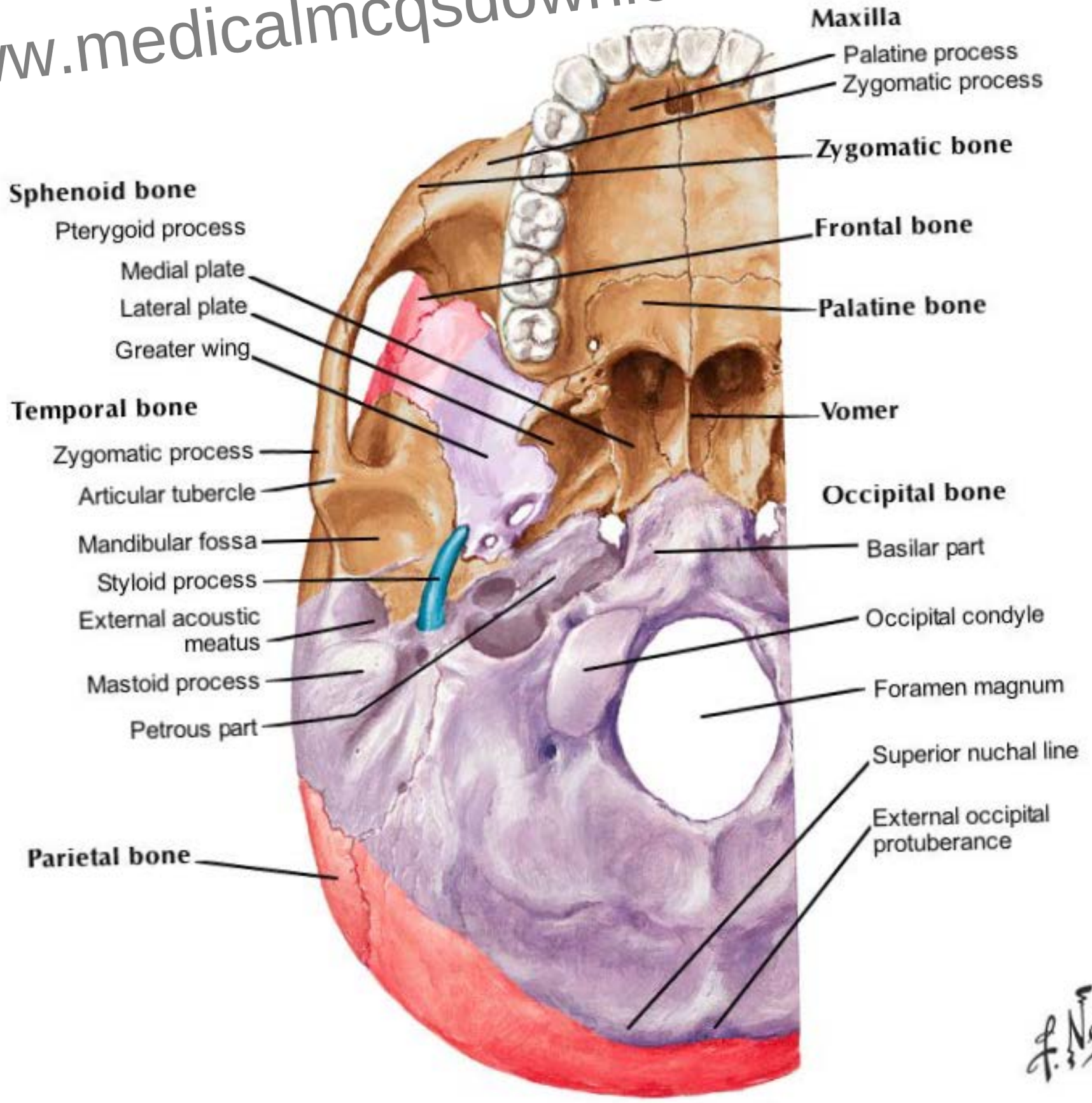
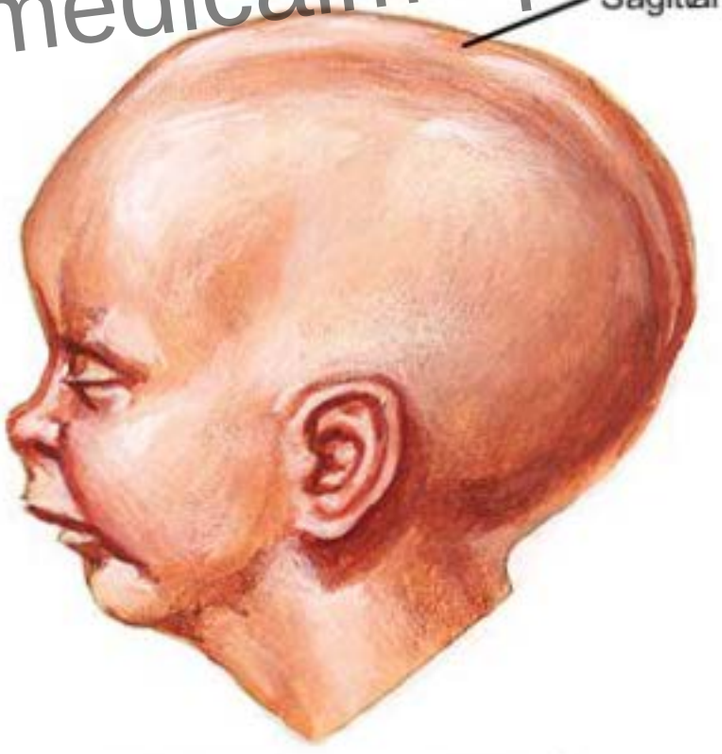
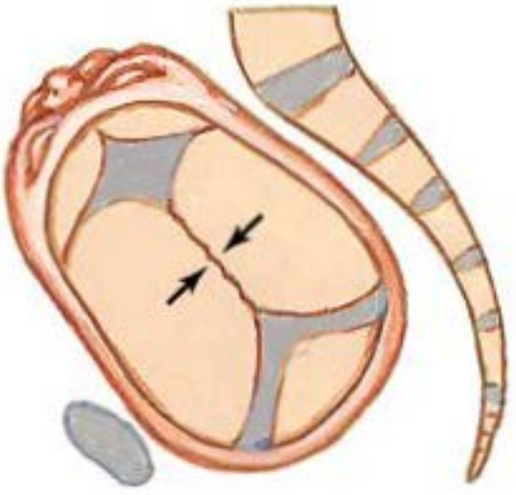
Ossification of the Scull



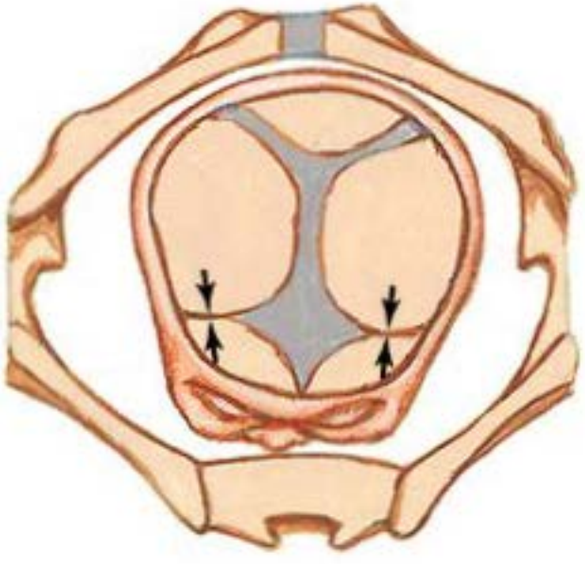
Premature Suture Closure



Scaphocephaly due to sagittal craniosynostosis



Limitation of growth of sagittal suture



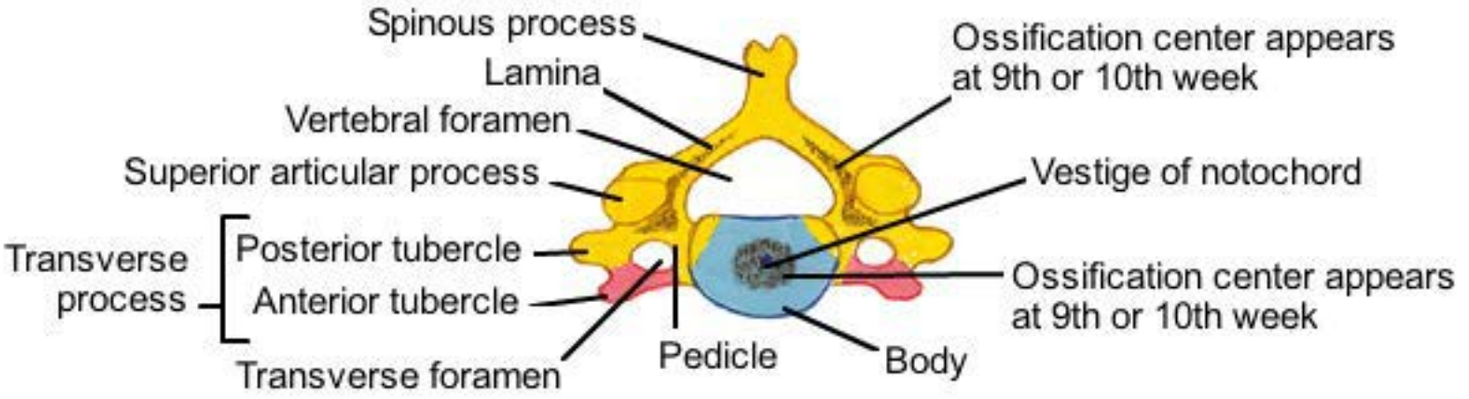
Limitation of growth of coronal sutures

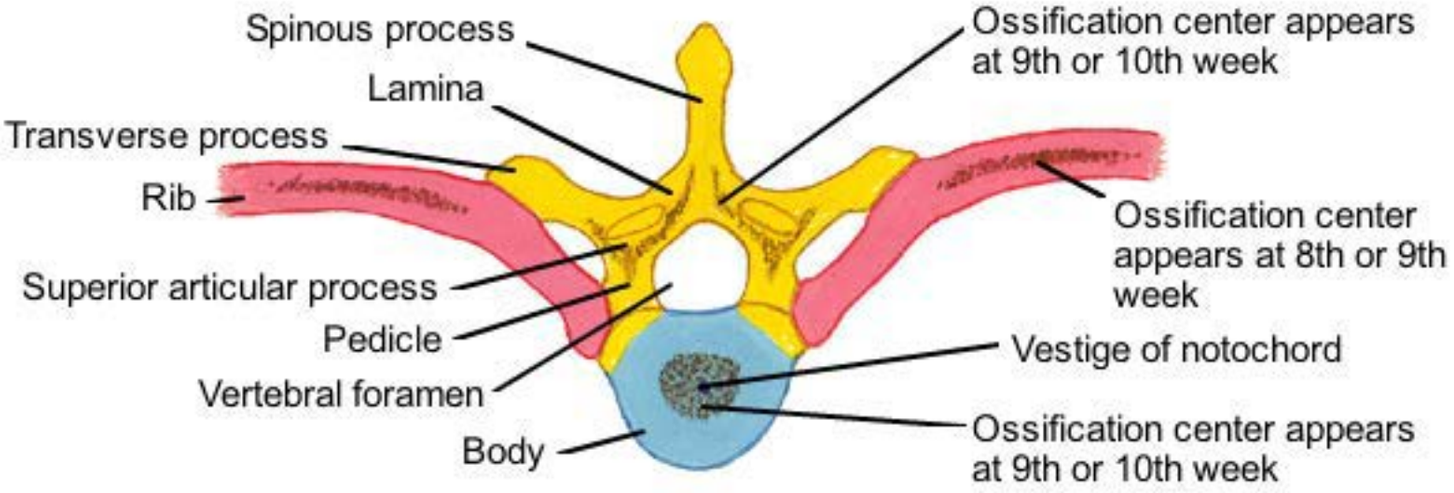
Brachycephaly due to coronal craniosynostosis

Cervical Ossification

Fate of body, costal process, and neural arch components of cervical and thoracic vertebra, with sites and time of appearance of ossification centers

Cervical vertebra





KEY

- Body
- Costal process
- Neural arch

Thoracic vertebra

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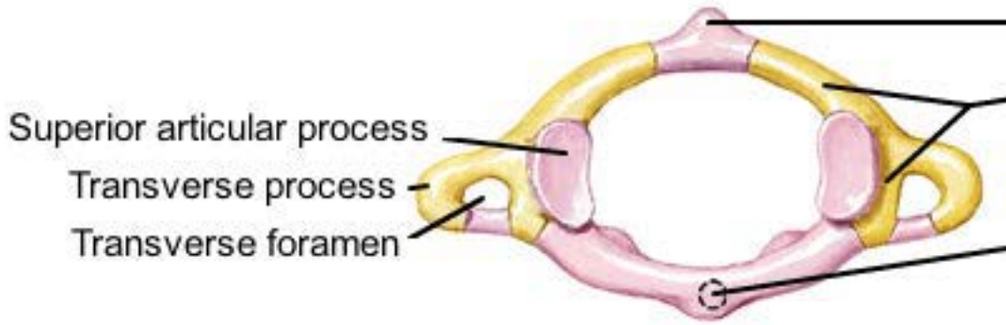
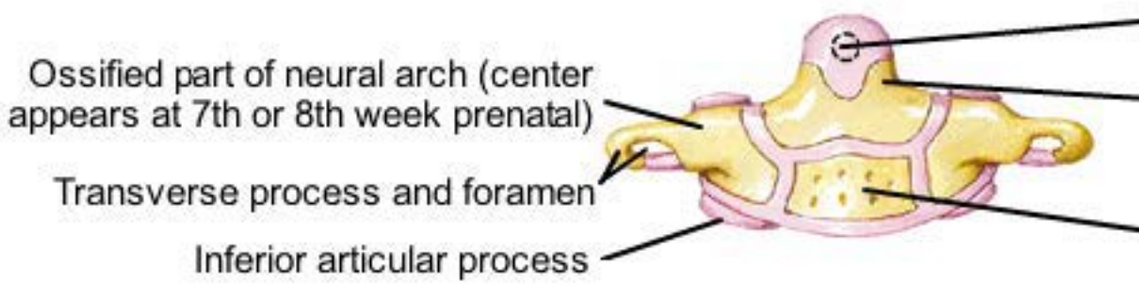
Cervical Ossification

First and second cervical vertebrae at birth

1st cervical vertebra (atlas) (superior view)



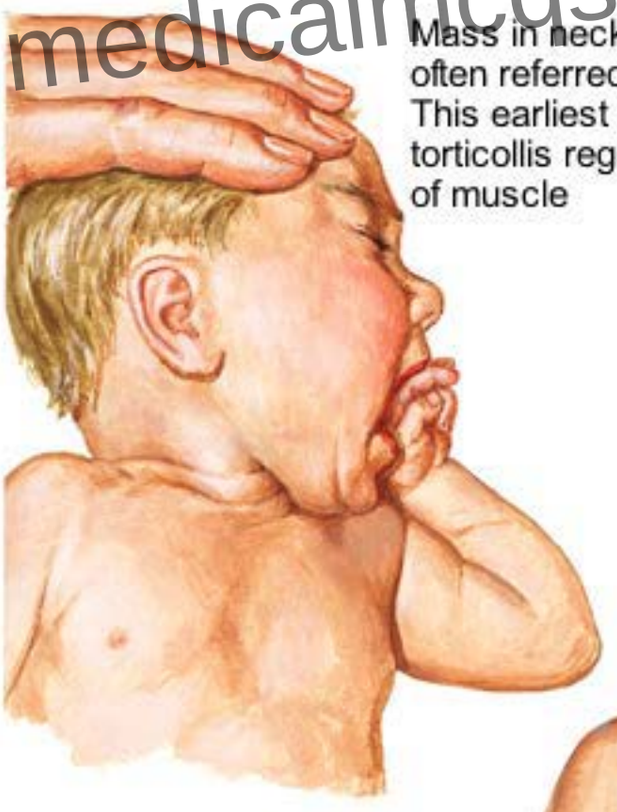


2nd cervical vertebra (axis) (anterior view)

Key

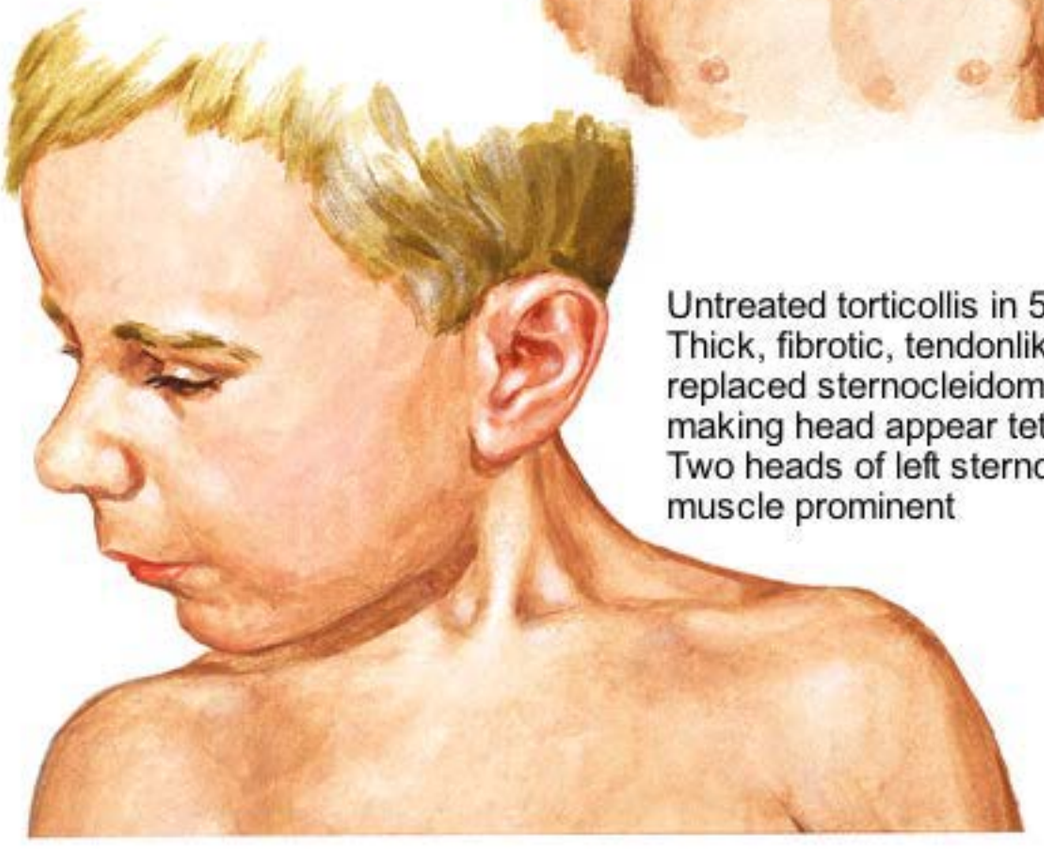
- Cartilage
- Bone

Torticollis



Mass in neck within sternocleidomastoid muscle often referred to as sternocleidomastoid tumor. This earliest manifestation of congenital muscular torticollis regresses, to be followed by contracture of muscle

Child with muscular torticollis. Head tilted to left with chin turned slightly to right because of contracture of left sternocleidomastoid muscle. Note facial symmetry (flattening of left side of face)



Untreated torticollis in 5-year-old boy. Thick, fibrotic, tendonlike bands have replaced sternocleidomastoid muscle, making head appear tethered to clavicle. Two heads of left sternocleidomastoid muscle prominent

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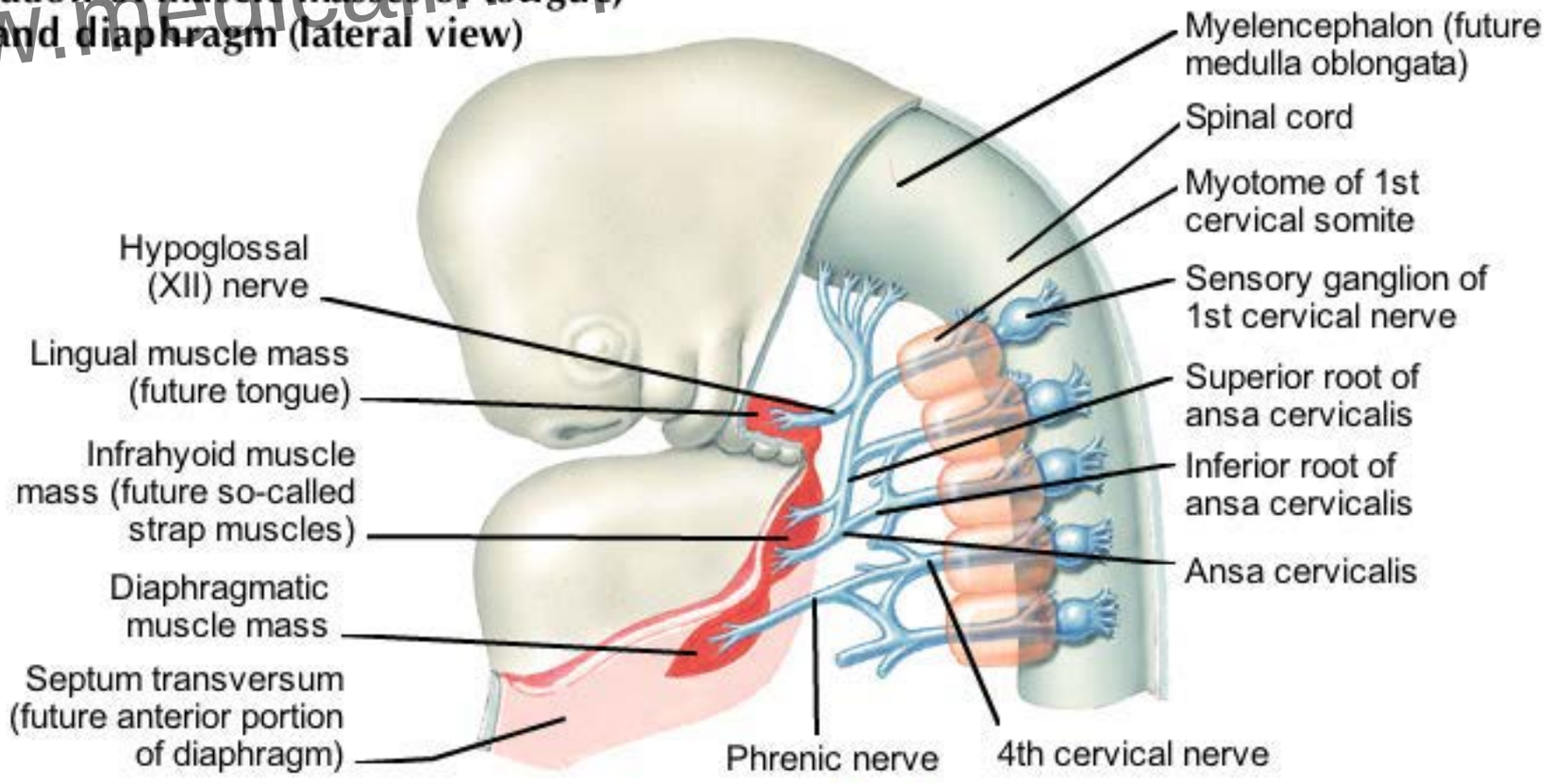
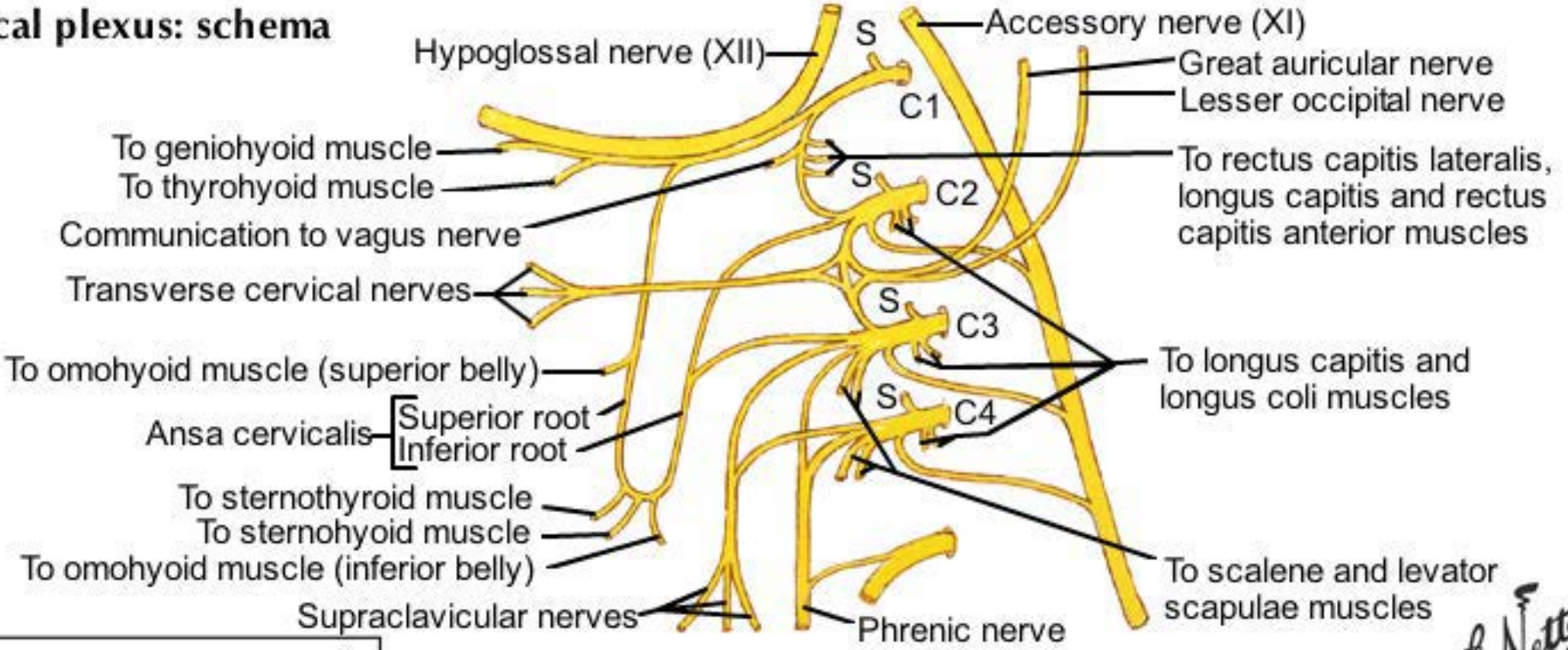
Cervical Plexus

The cervical plexus and hypoglossal nerve in a 5- to 6-week embryo

Innervation of muscle masses of tongue, neck, and diaphragm (lateral view)



Cervical plexus: schema



Note:
S = 5 Gray ramus from superior cervical sympathetic ganglion

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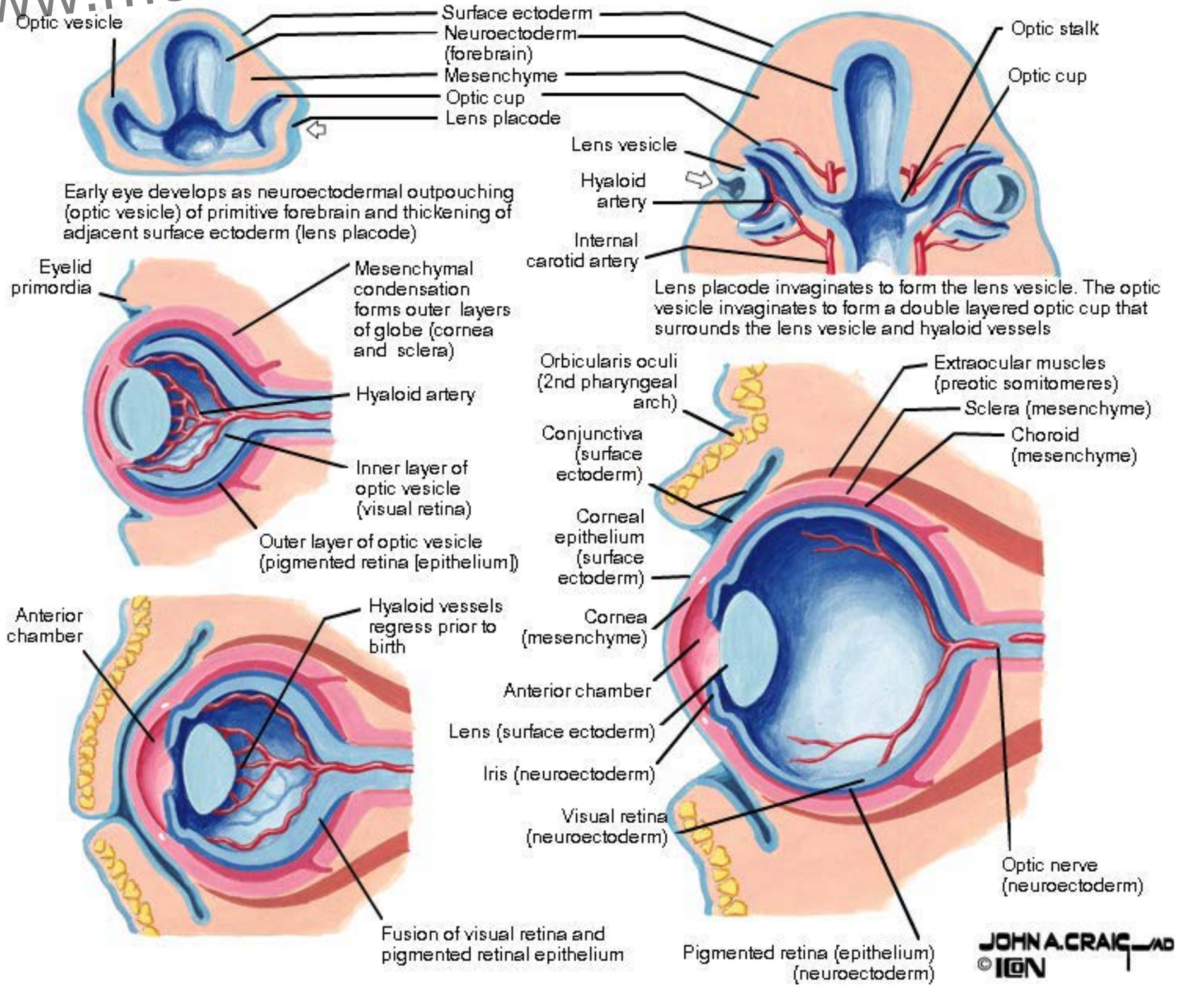
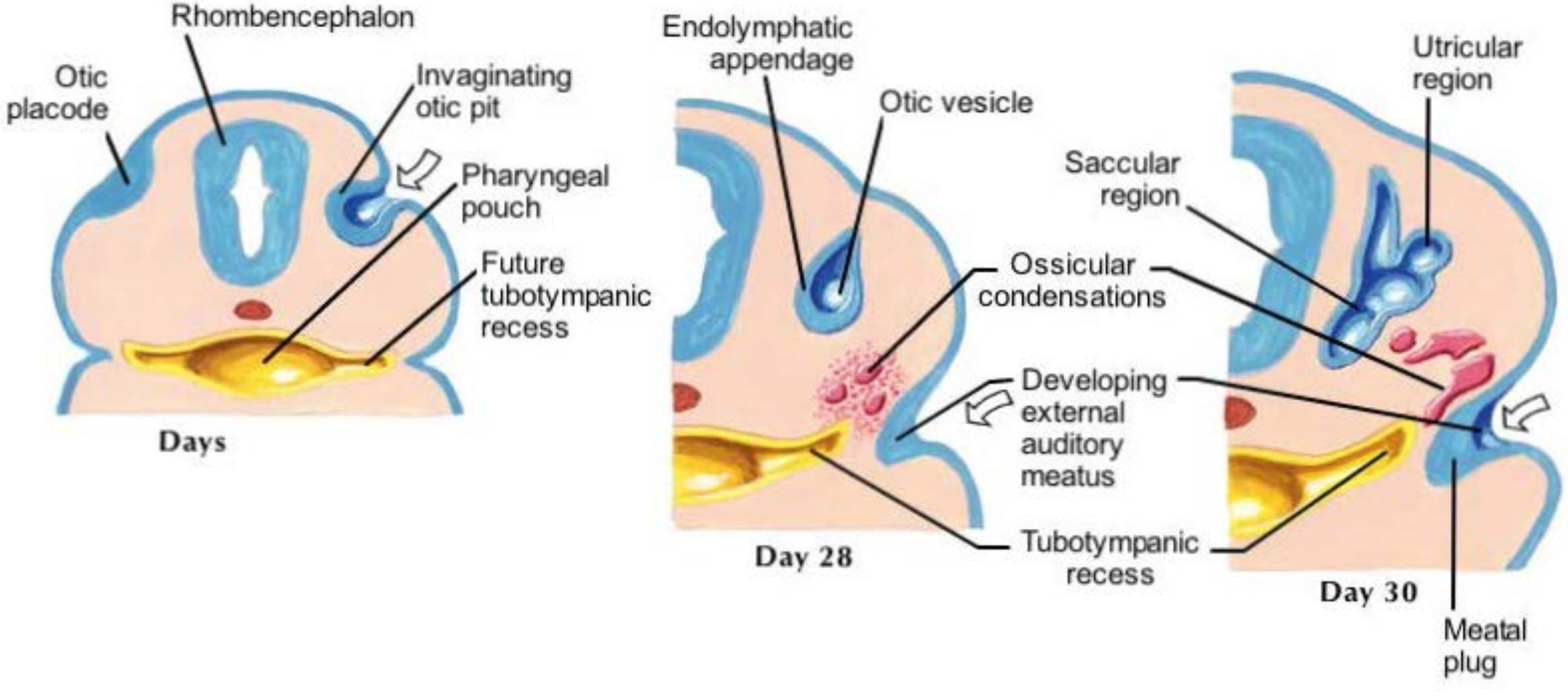
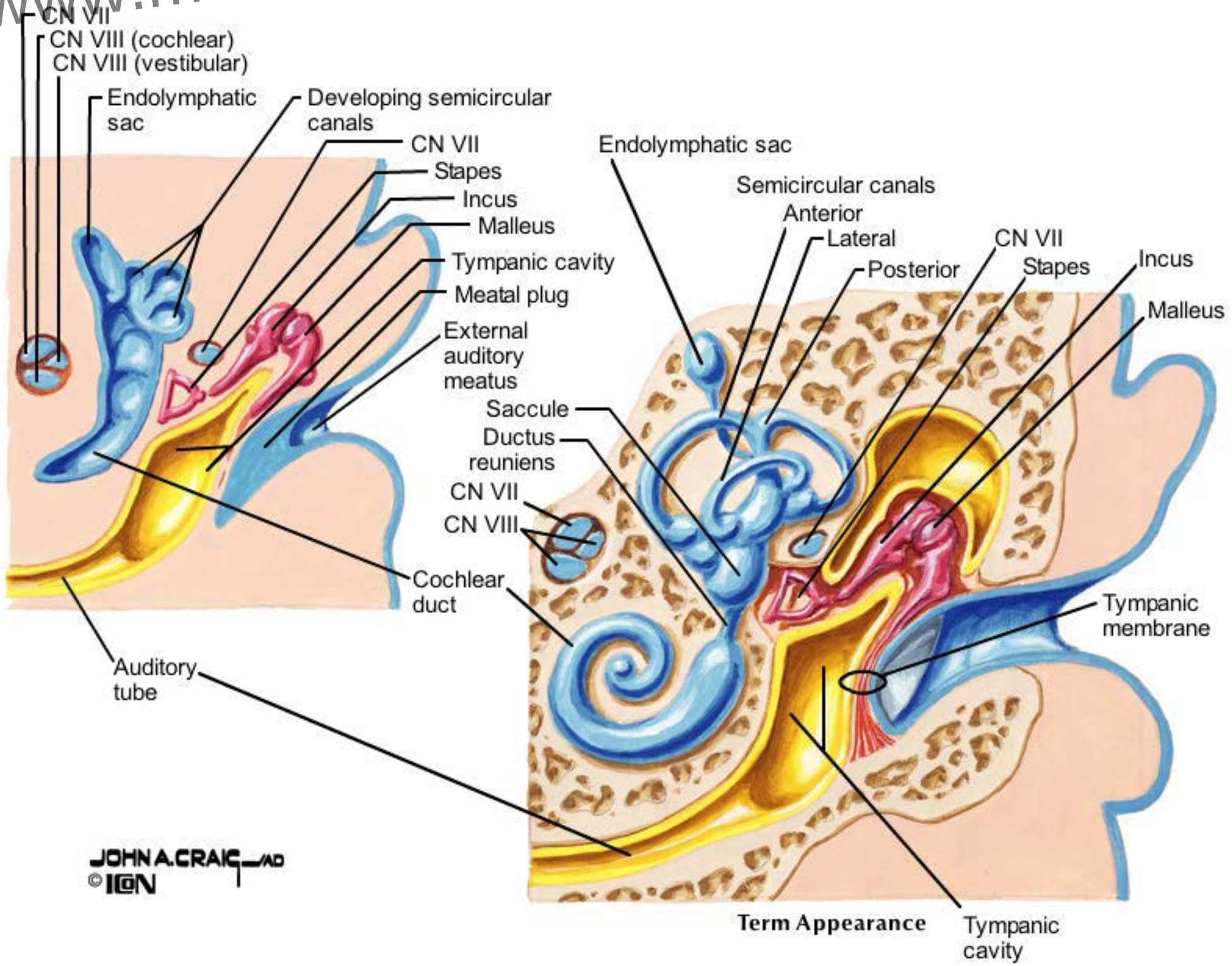
Orbit



Ear Development

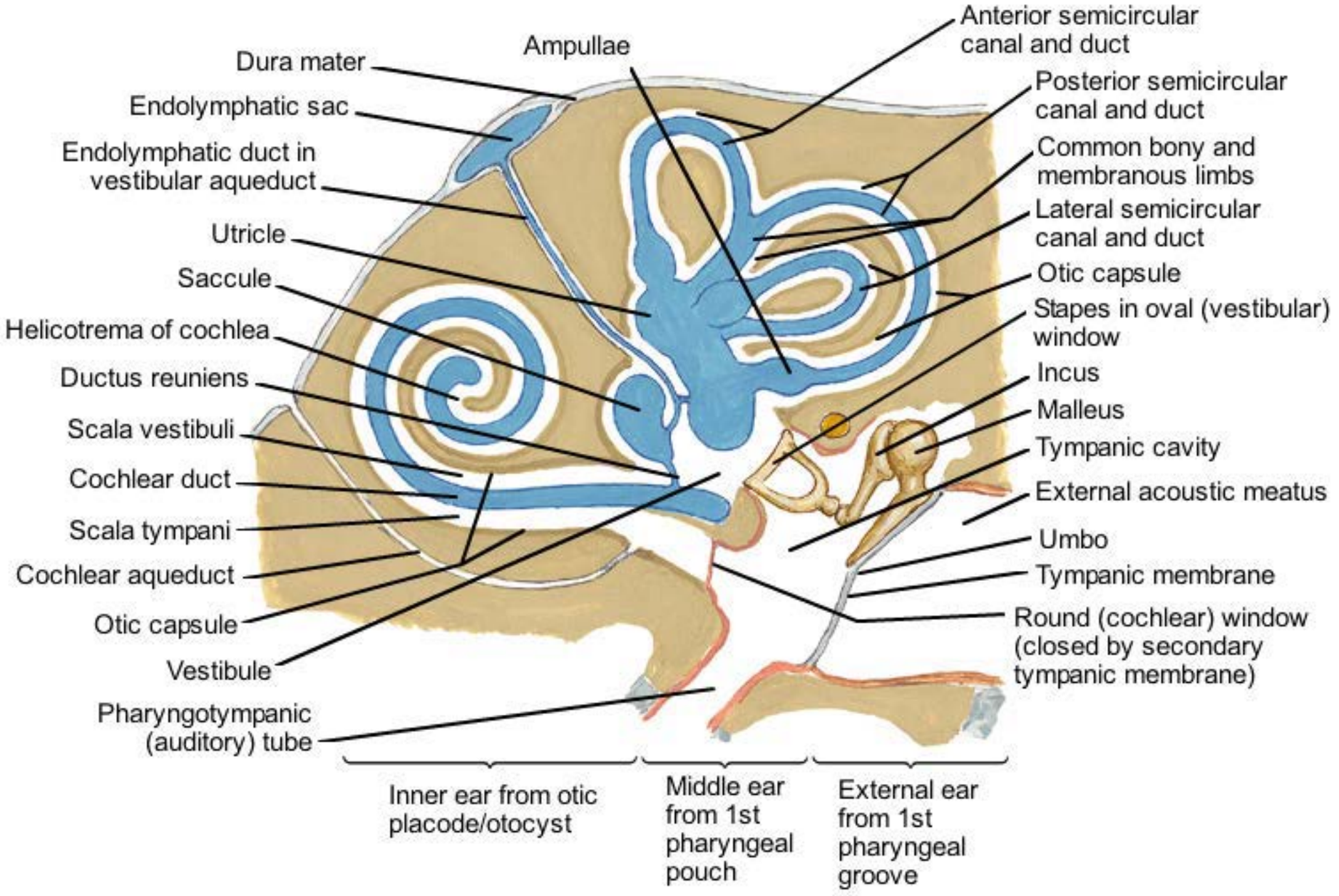


Ear Development



Adult Ear Organization

Bony and membranous labyrinths: schema



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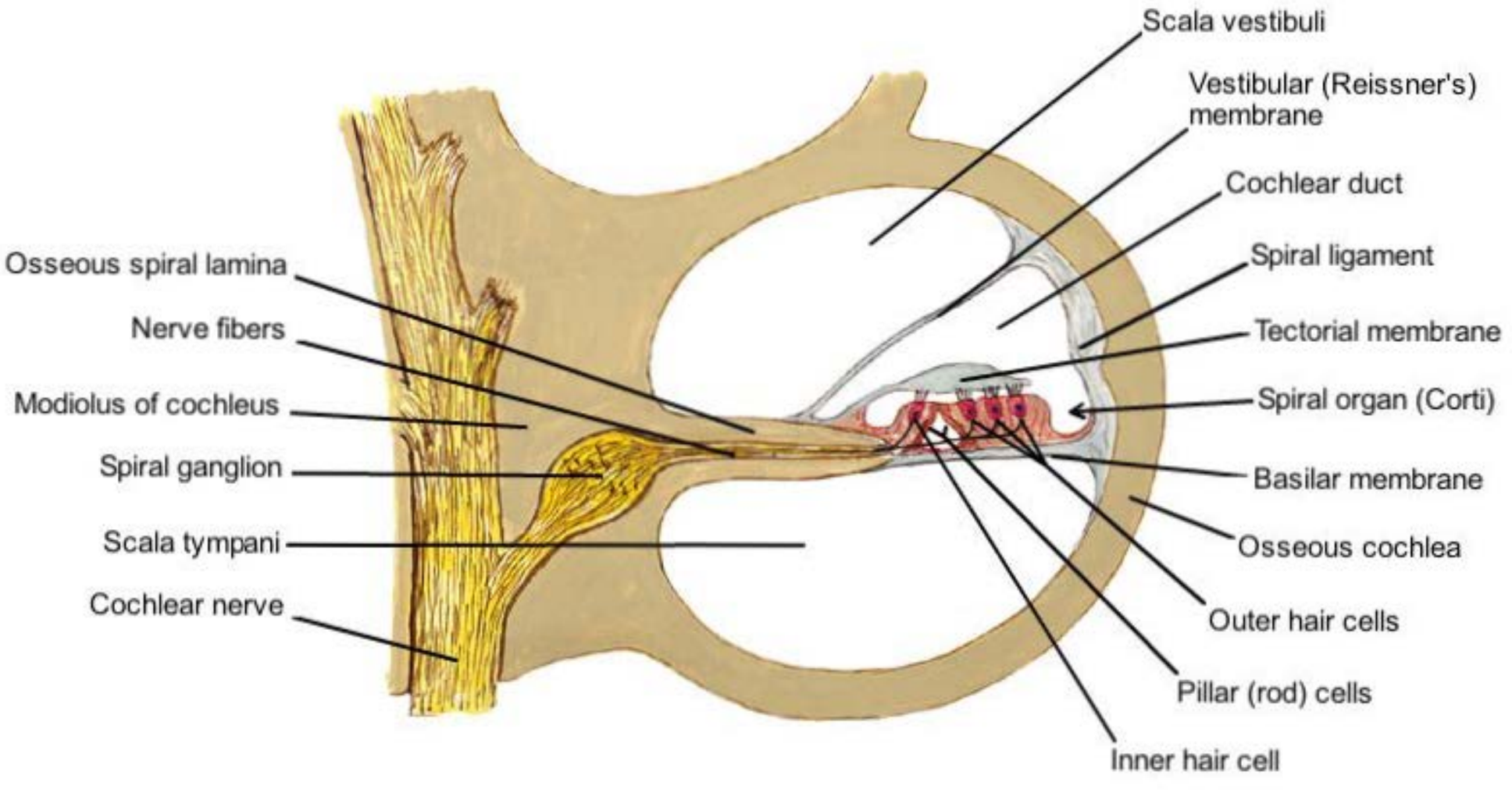
Adult Ear Organization

Section through turn of cochlea



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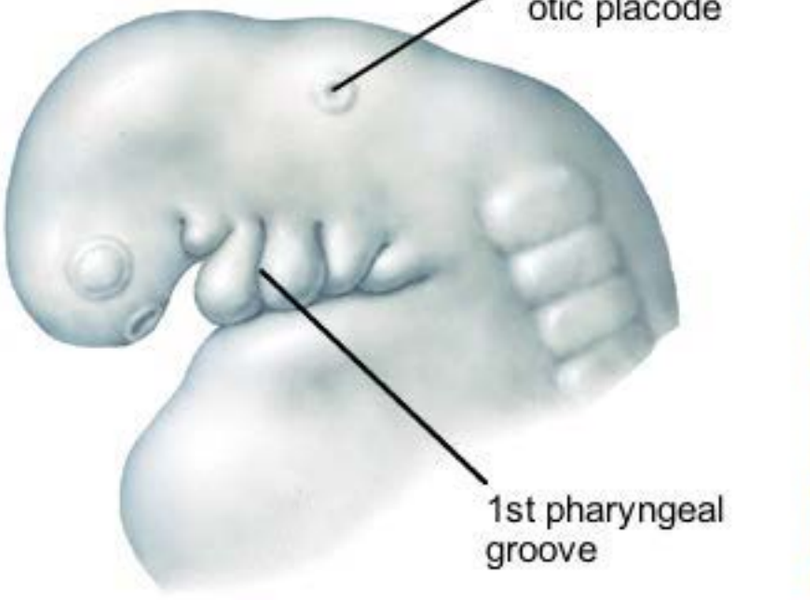
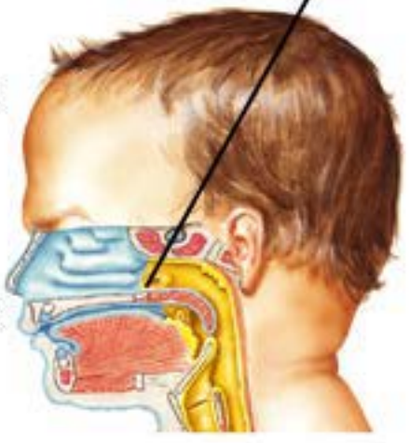
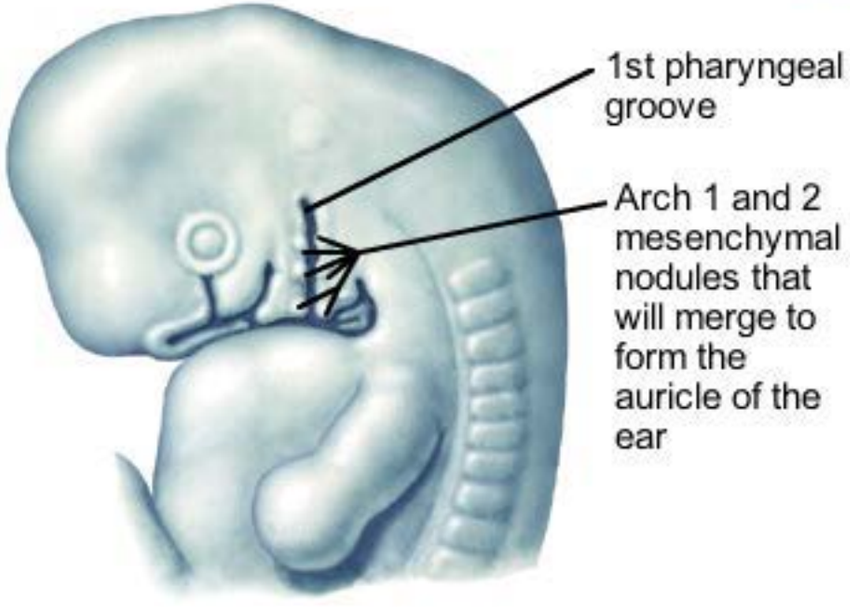
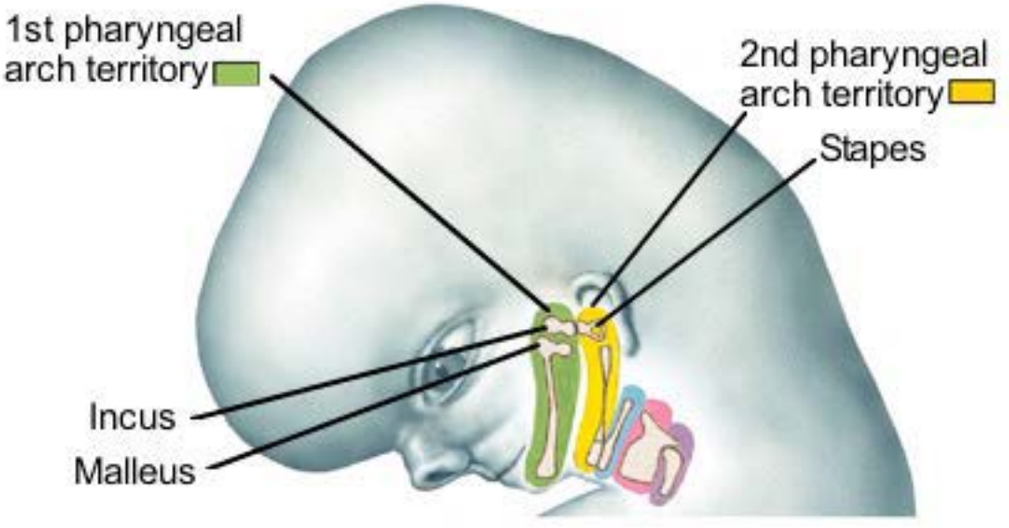
Summary of Ear Development

Primordia of the outer, middle, and inner ear









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Cranial Nerve Primordia

Pharyngeal arches and their nerves:

- Arch 1-trigeminal nerve (V)
  - Maxillary part of arch 1-maxillary nerve (trigeminal, V2)
  - Mandibular part of arch 1-mandibular nerve (trigeminal, V3)
  - Pretrematic branch-ophthalmic nerve (trigeminal, V1)
- Arch 2-facial nerve (VII)
  - Pretrematic branch-chorda tympani
- Arch 3-glossopharyngeal nerve (IX)
  - Pretrematic branch-tympanic nerve
- Arch 4-vagus n. (X)
- Arch 6-vagus n. (X)

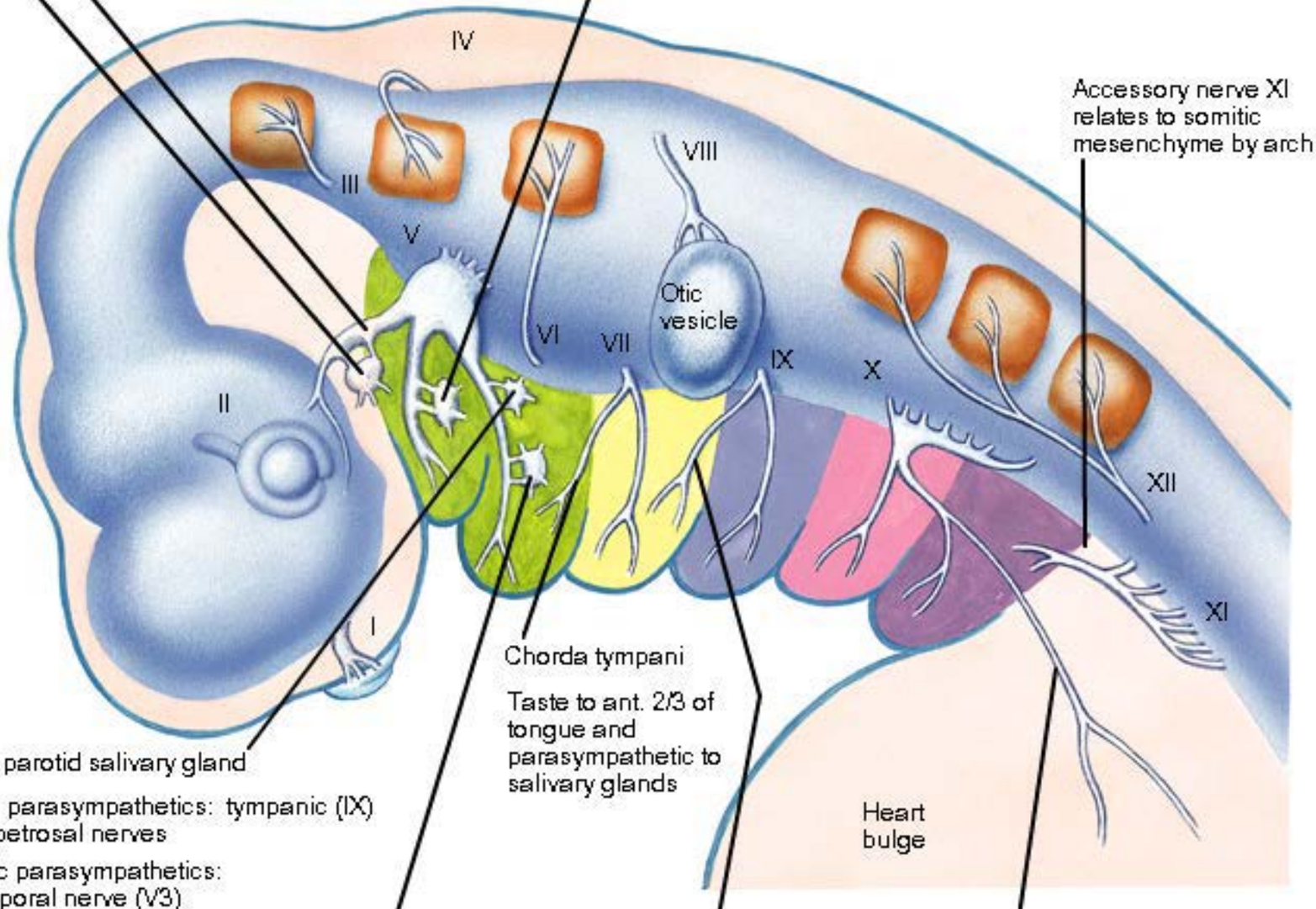
Somite primordia and their nerves:

Preotic somitomeres-oculomotor nerve (III), trochlear nerve (IV), abducens nerve (VI)
Postotic somites-hypoglossal nerve (XII)
Somitic mesenchyme-accessory nerve (XI)

Ectodermal structures and their nerves:

Olfactory placode-olfactory nerve (I)
Optic cup-optic nerve (II)
Otic placode-vestibulocochlear nerve (VIII)

Parasympathetic Innervation and Unique Nerves



Ciliary ganglion for pupil constrictor and ciliary muscle (for visual accommodation)

Presynaptic parasympathetics: oculomotor nerve (III)

Postsynaptic parasympathetics: short ciliary nerves (V1)

Ophthalmic division of trigeminal nerve (V1)

Sensory for orbit, nose, and forehead

Pterygopalatine ganglion for lacrimal gland and mucosa of nasal cavity and palate

Presynaptic parasympathetics: greater petrosal nerve (VII) and nerve of the pterygoid canal

Postsynaptic parasympathetics: zygomatic, greater and lesser palatine, posterior lateral nasal, and nasopalatine branches of V2

Otic ganglion for parotid salivary gland

Presynaptic parasympathetics: tympanic (IX) and lesser petrosal nerves

Postsynaptic parasympathetics: auriculotemporal nerve (V3)

Submandibular ganglion for submandibular and sublingual salivary glands

Presynaptic parasympathetics: chorda tympani (VII)

Postsynaptic parasympathetics: lingual nerve branches (V3)

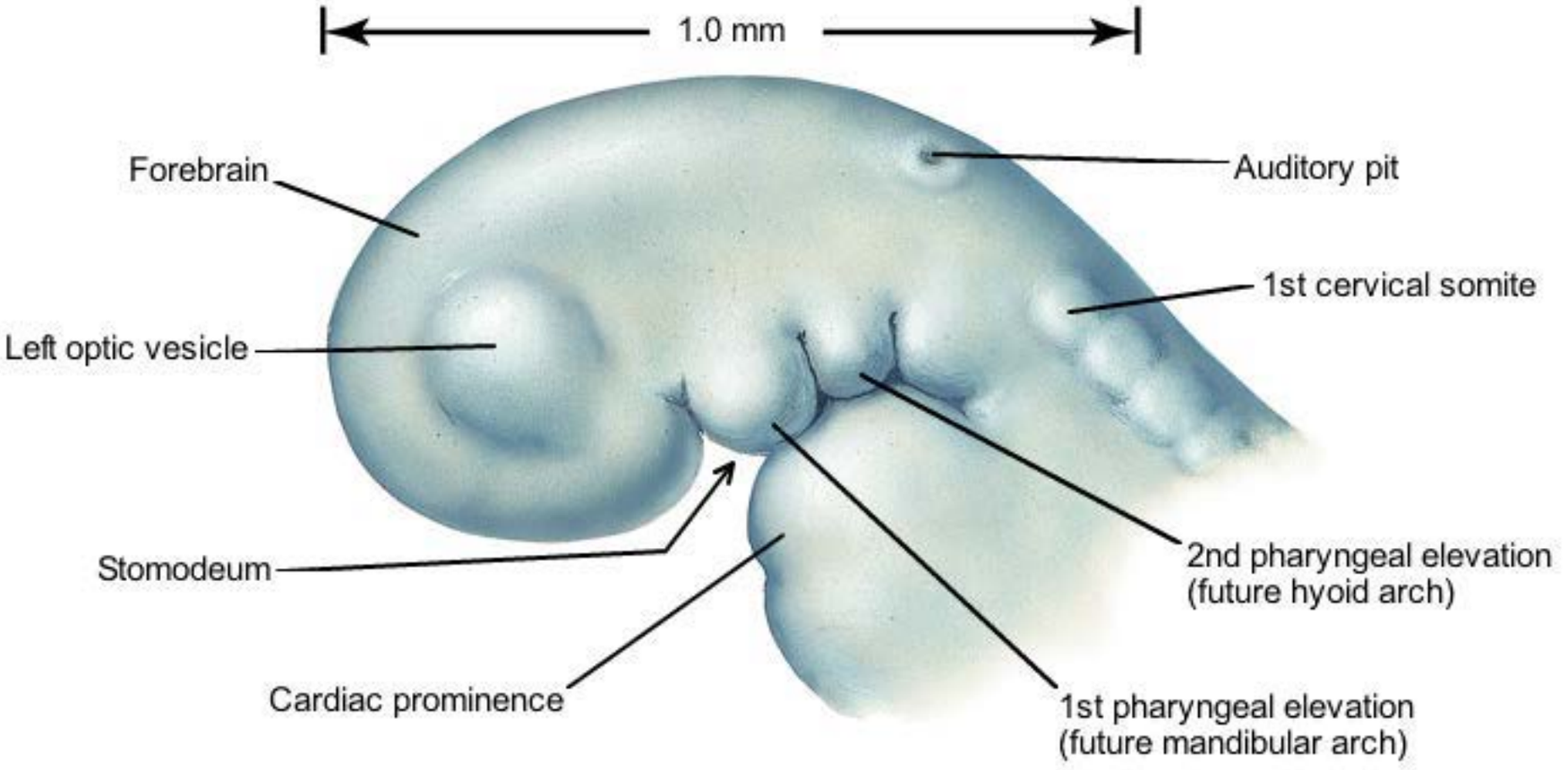
Tympanic nerve

Visceral sensory for middle ear and parasympathetic for parotid gland

Parasympathetic and viseral sensory branch from X for foregut and midgut

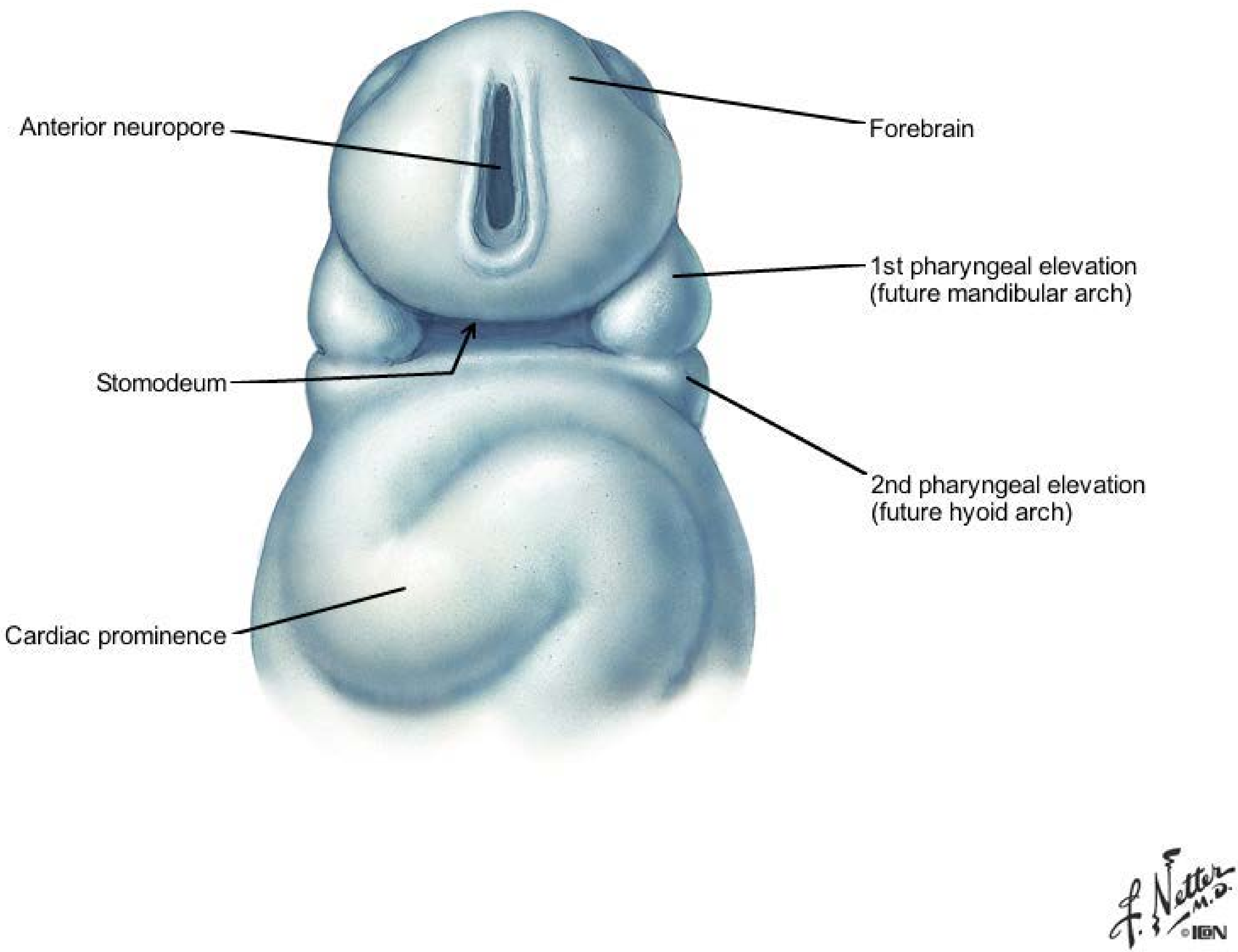
Development of the Face: 3 to 4 Weeks

Lateral view



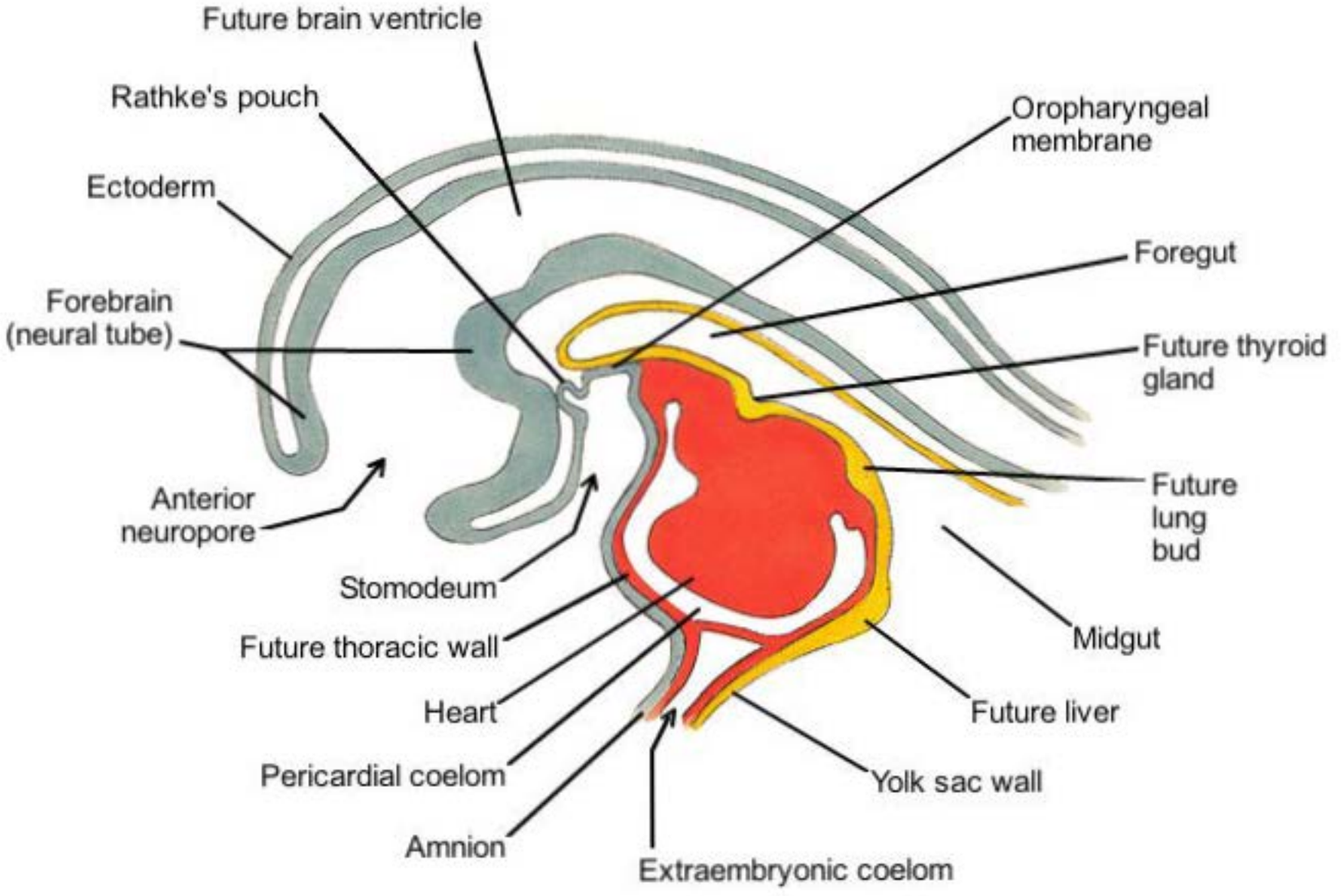
Development of the Face: 3 to 4 Weeks

Lateral view

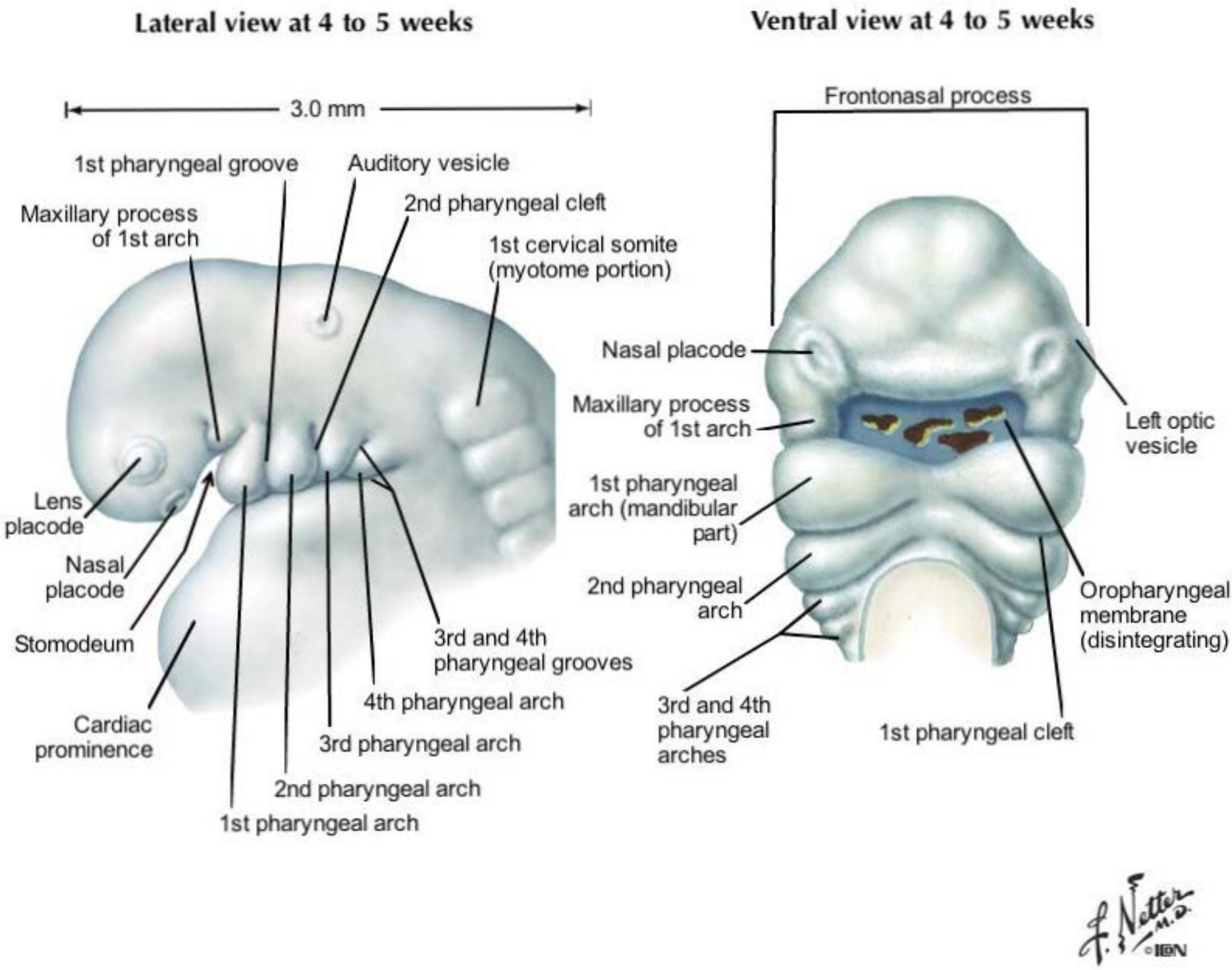


Development of the Face: 3 to 4 Weeks

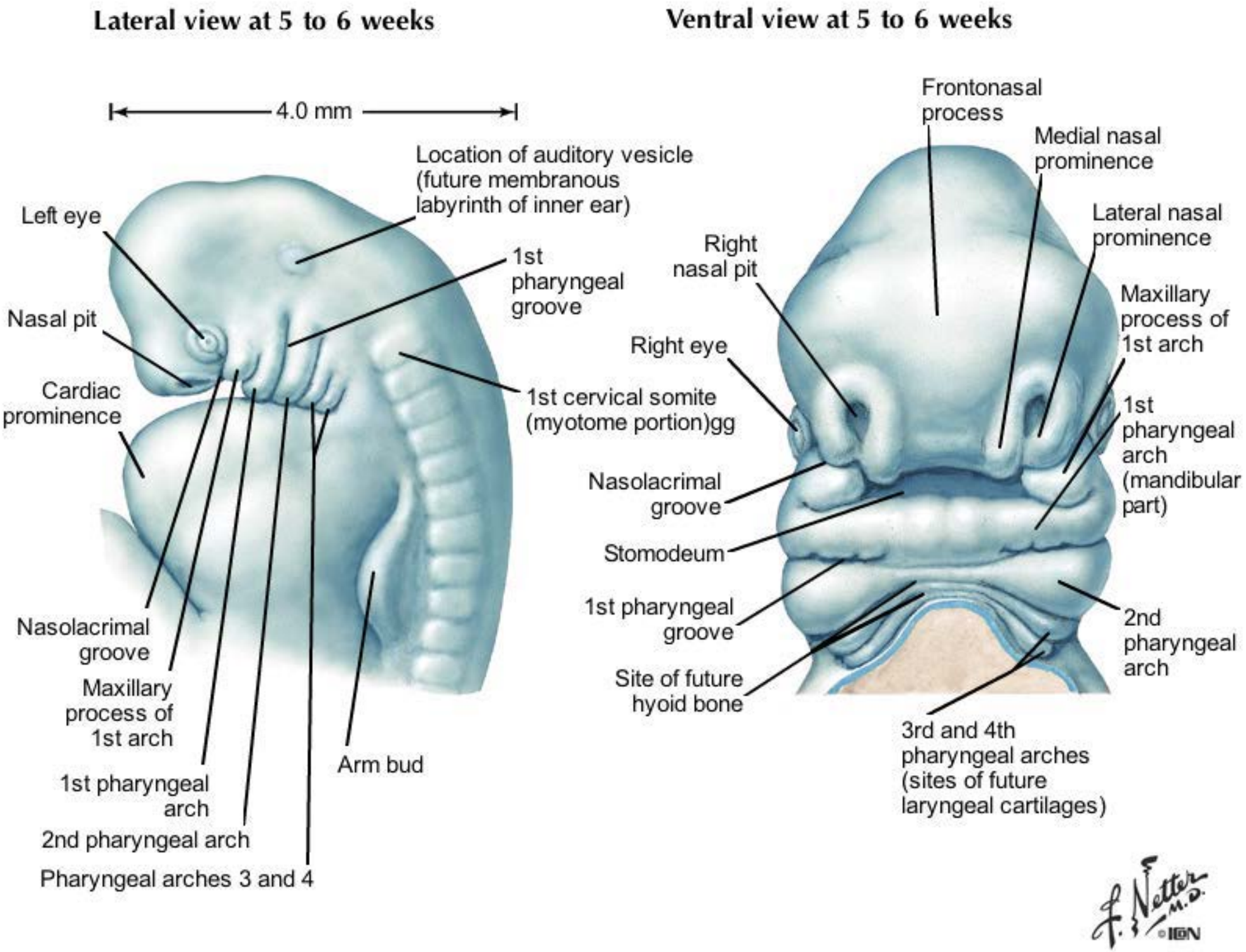
Sagittal section



Early Development of the Face: 4 to 6 Weeks

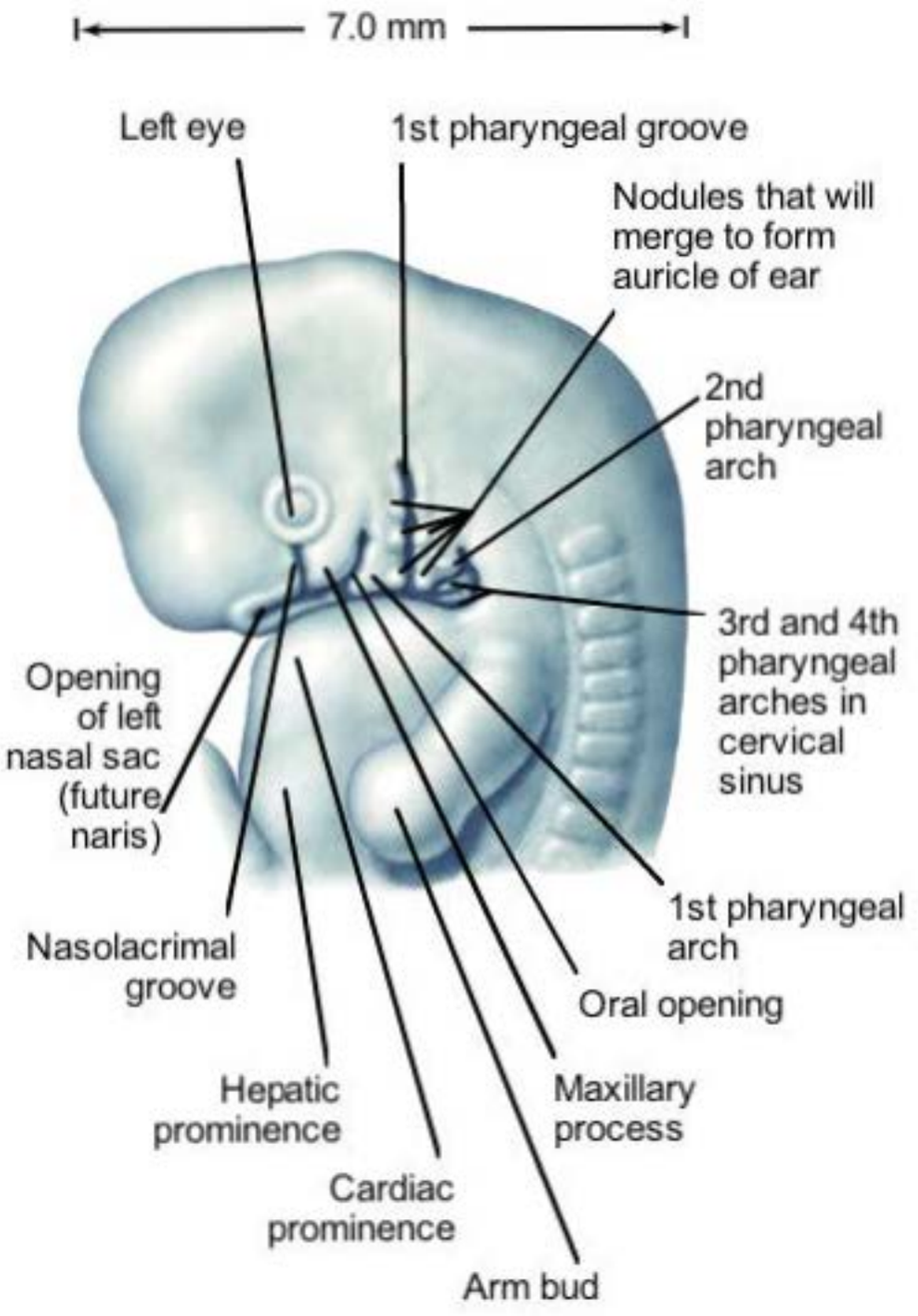


Early Development of the Face: 4 to 6 Weeks

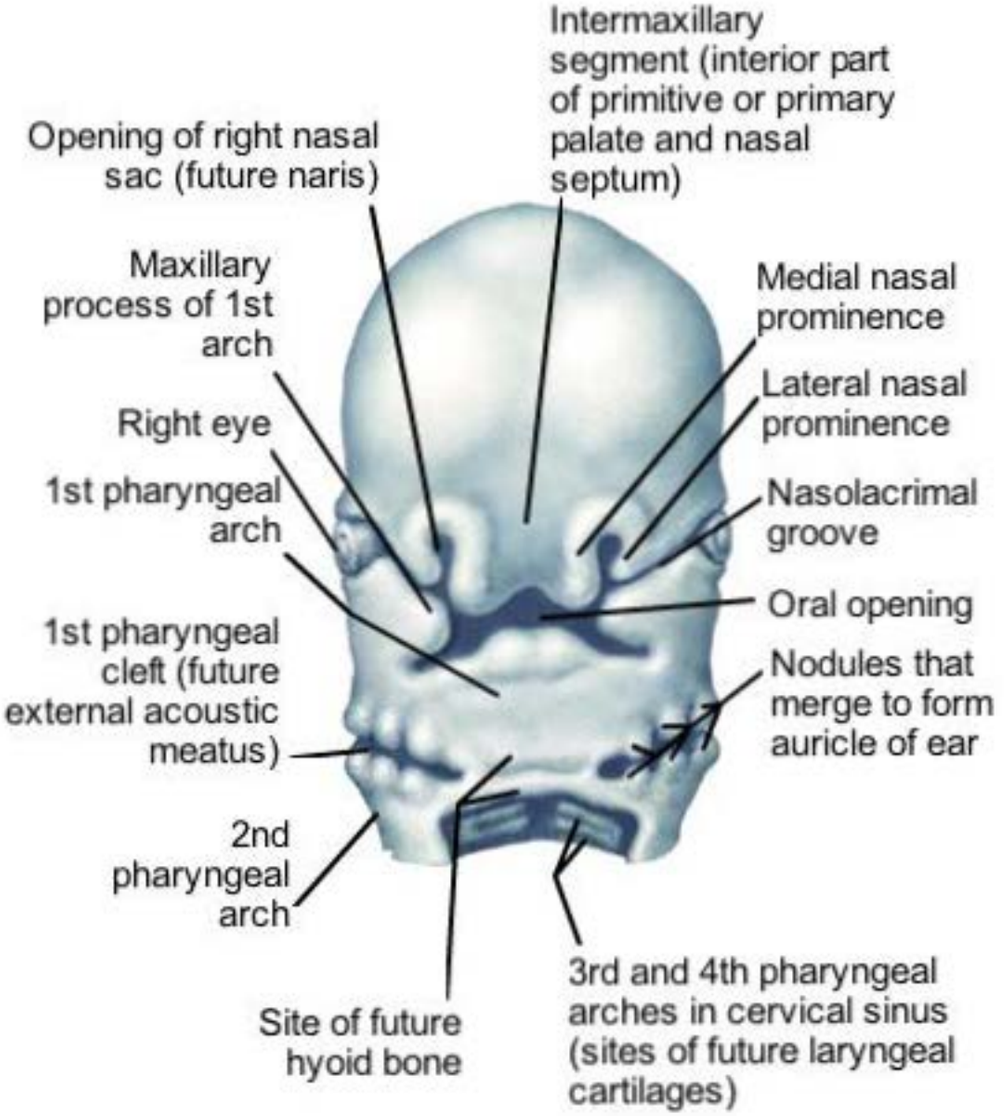


Later Development of the Face

Lateral view at 6 to 7 weeks



Ventral view at 6 to 7 weeks



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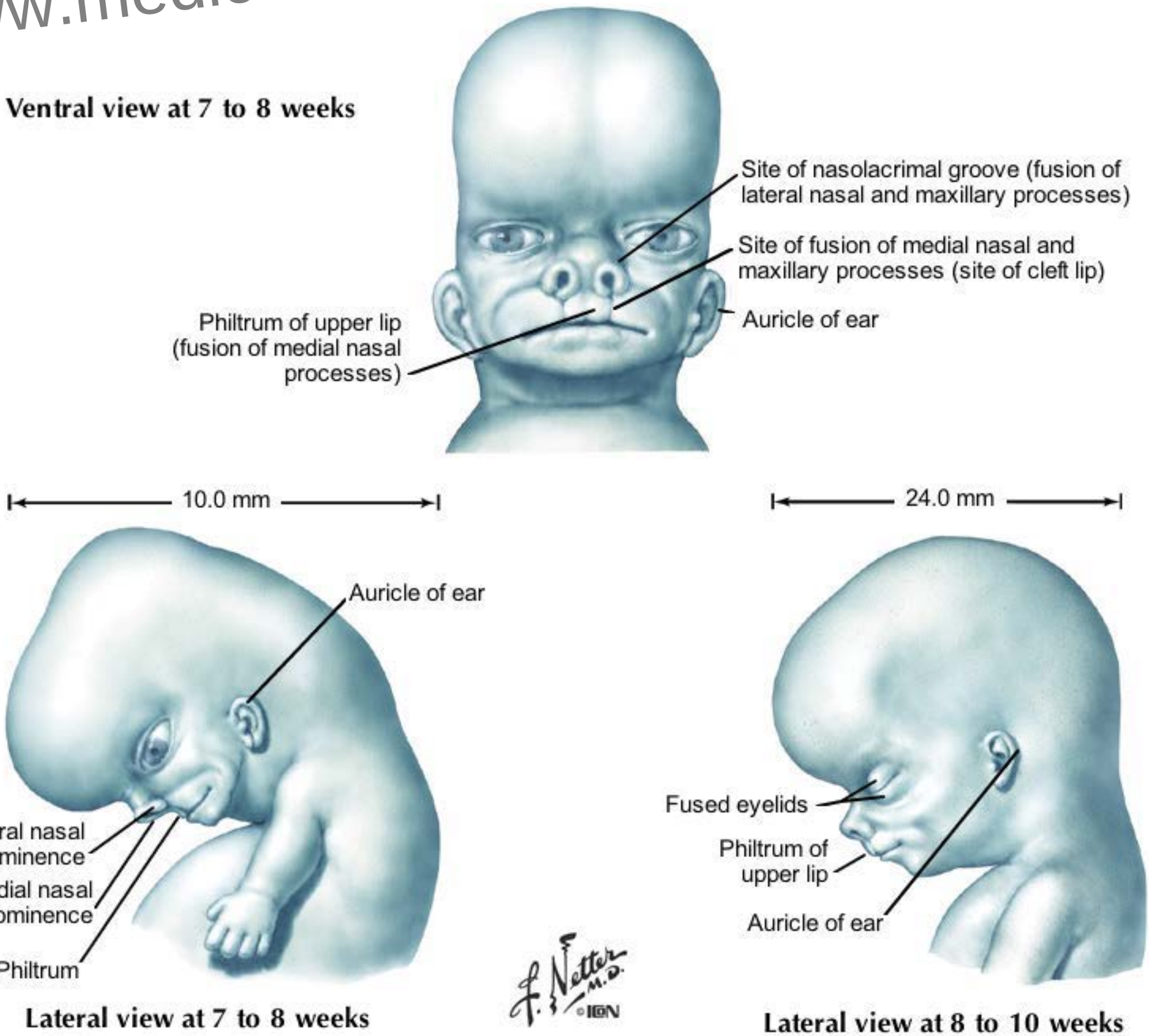
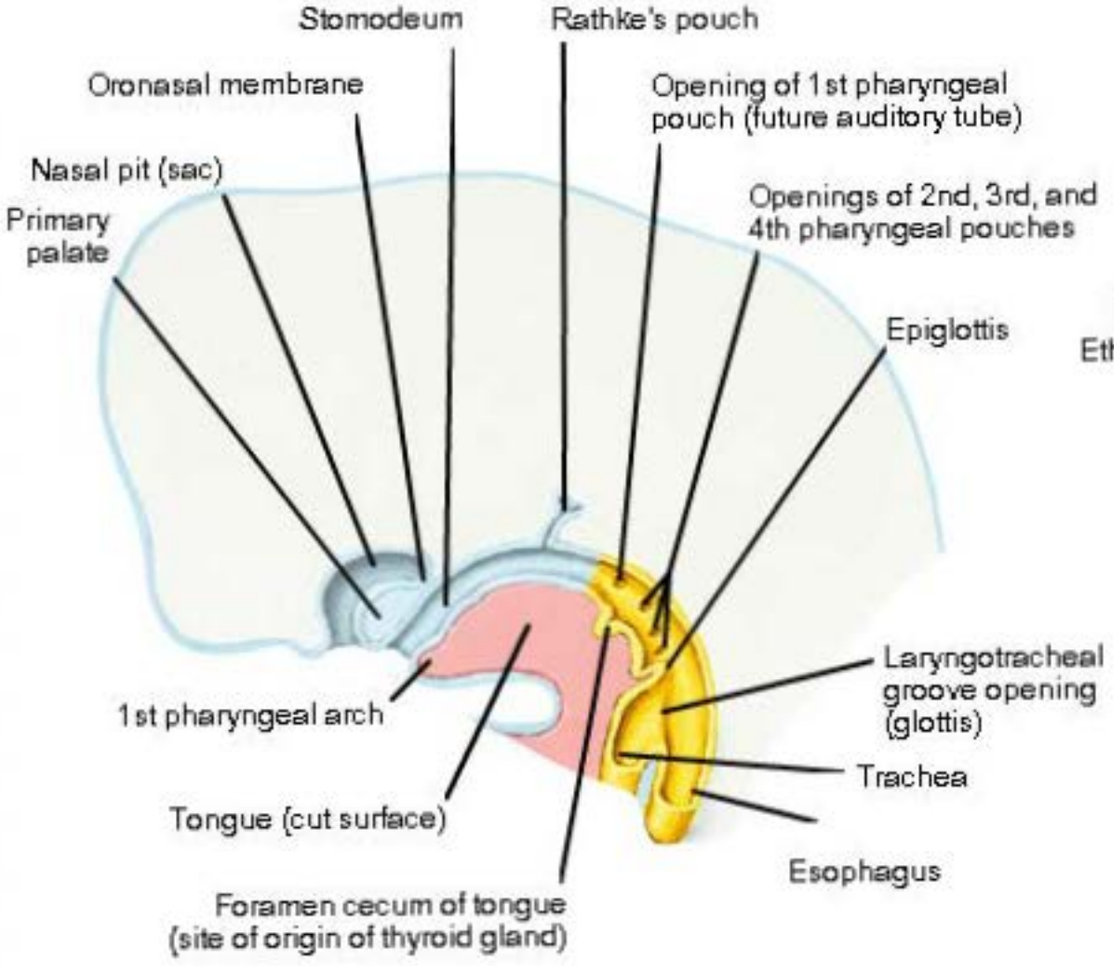
Later Development of the Face

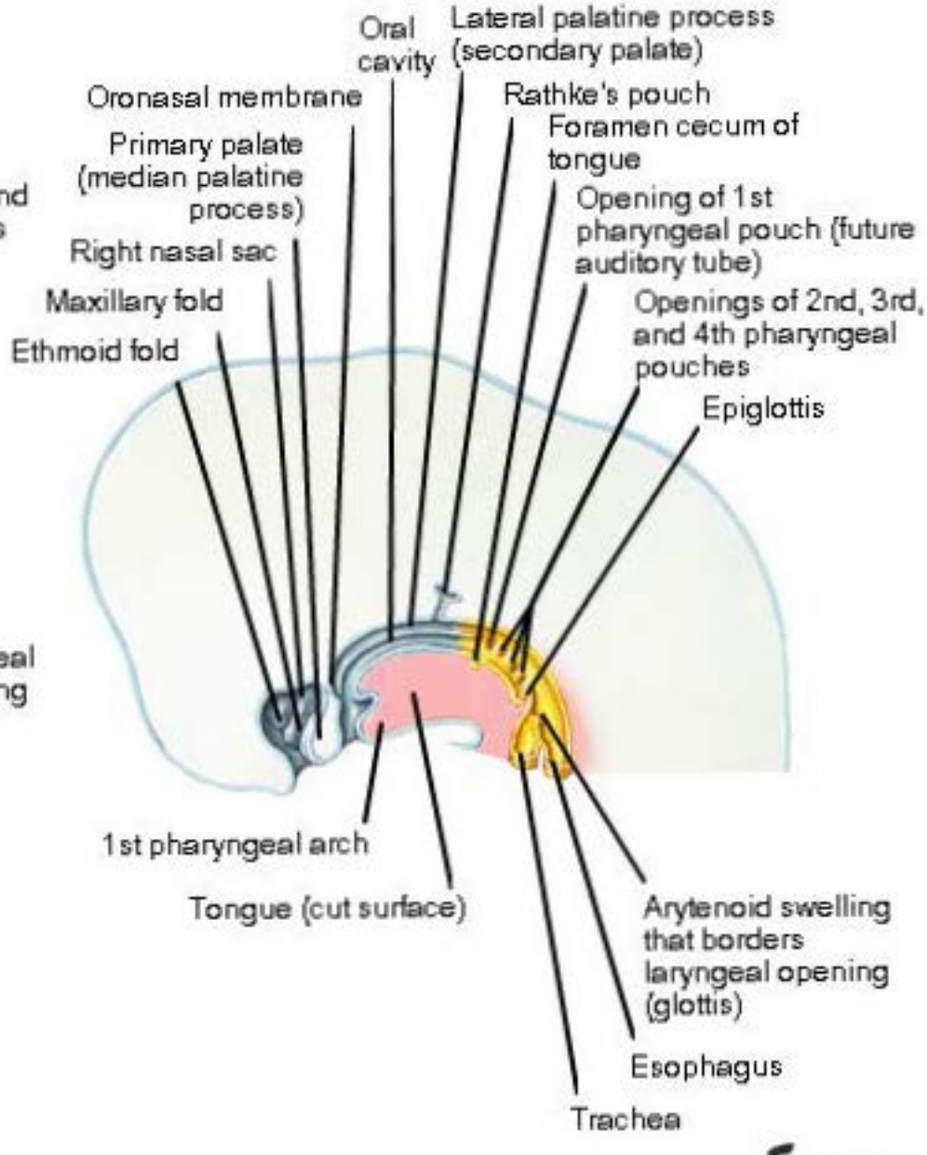


Palate Formation

Sagittal section at 5 to 6 weeks



Sagittal section at 6 to 7 weeks



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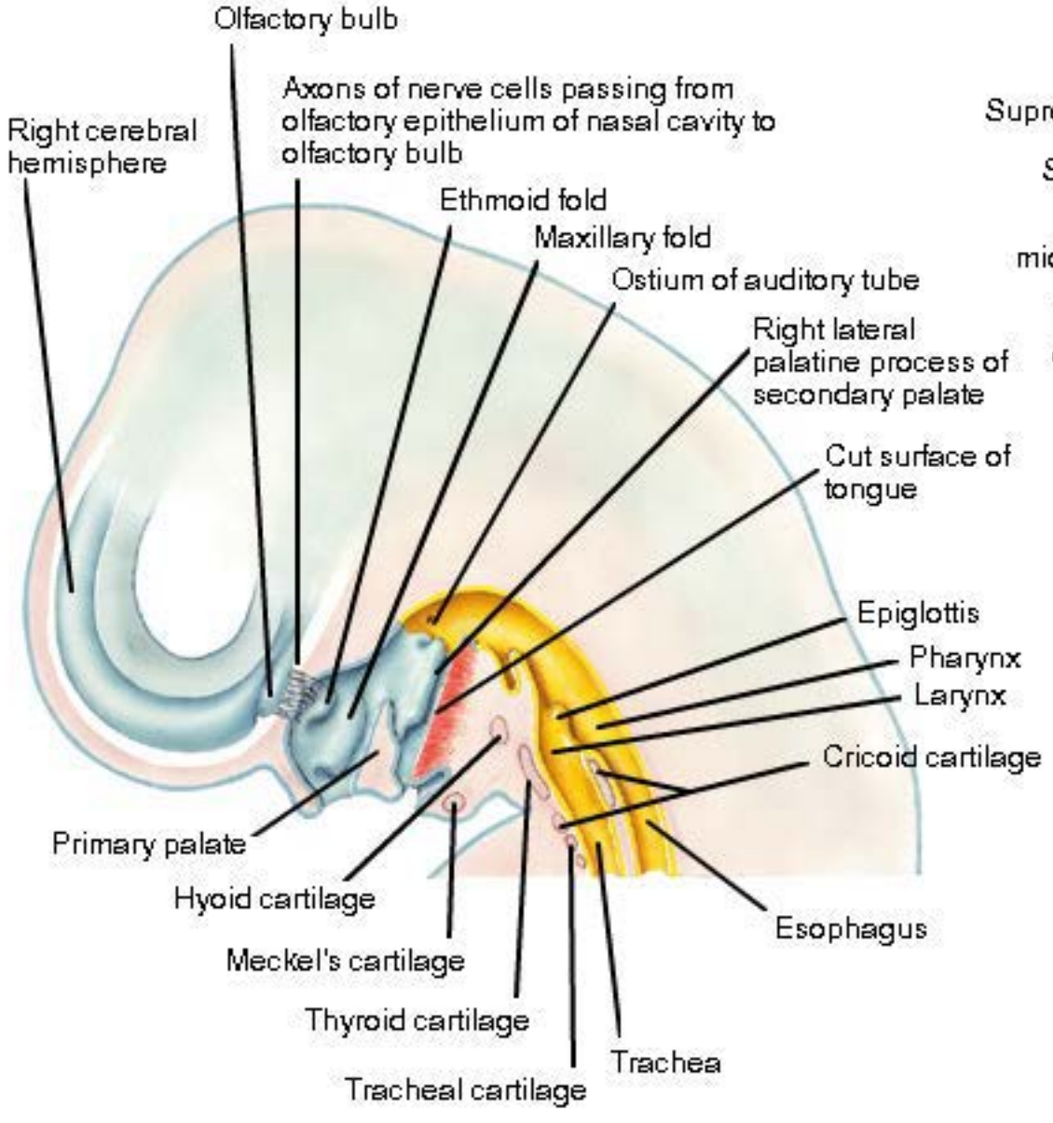
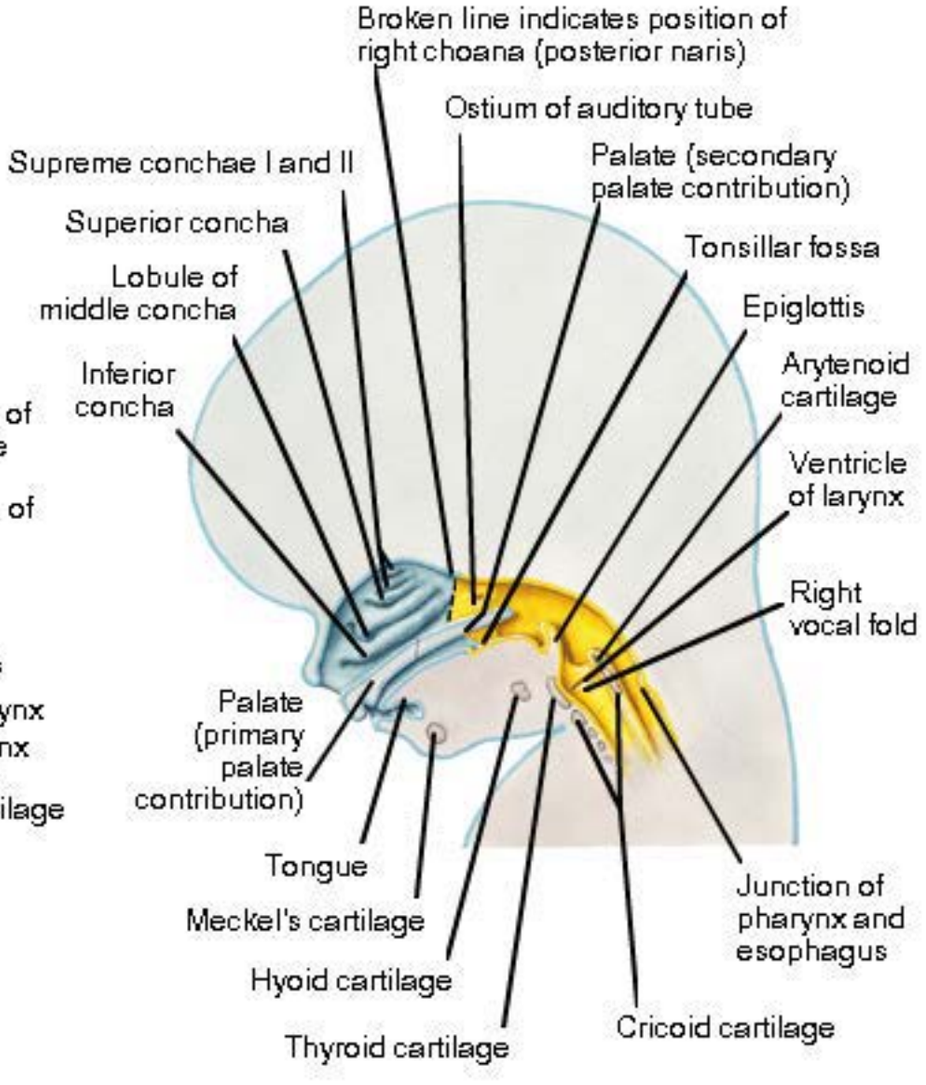
Palate Formation

Sagittal section at 7 to 8 weeks



Sagittal section at 8 to 10 weeks



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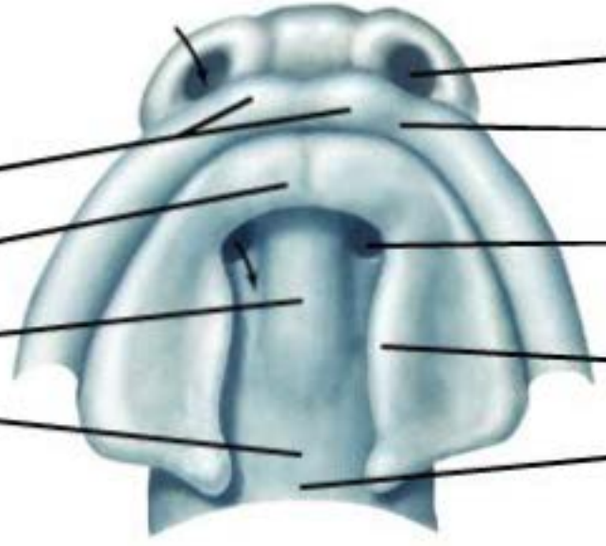
Interior View of Palate Formation

Roof of stomodeum (inferior view; 6 to 7 weeks)

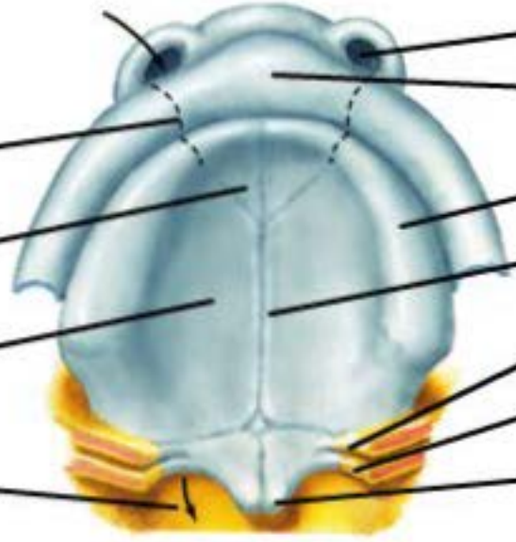
- Opening of right nasal sac
- Right eye
- Primitive or primary palate (median palatine process)
- Oronasal membrane (primitive posterior naris or choana)
- Roof of stomodeum (base of skull)
- Frontal area
- Medial nasal process
- Lateral nasal process
- Nasolacrimal groove
- Definitive nasal septum
- Maxillary process of 1st arch
- Lateral palatine process (secondary palate)
- Opening of Rathke's pouch

Palate formation (inferior view; 7 to 8 weeks)



- Philtrum of upper lip (fusion of medial nasal processes)
- Primary palate (median palatine process)
- Definitive nasal septum
- Mucosa covering base of skull
- Left naris
- Site of fusion of medial nasal and maxillary processes (cleft lip site)
- Primitive posterior naris or choana (former site of oronasal membrane)
- Left lateral palatine process
- Site of evagination of Rathke's pouch

Roof of oral cavity (inferior view; 8 to 10 weeks)



- Broken lines border area formed from nasomedial processes and primitive or primary palate
- Medial palatine process (primary palate contribution to definitive palate)
- Lateral palatine process (secondary palate contribution to definitive palate)
- Arrow emerging from choana (posterior naris of right nasal cavity)
- Left naris
- Upper lip
- Gingiva (gum)
- Palatine raphé (cleft palate site)
- Palatoglossal arch
- Palatopharyngeal arch
- Uvula

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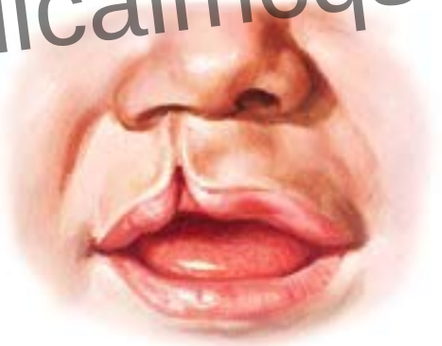
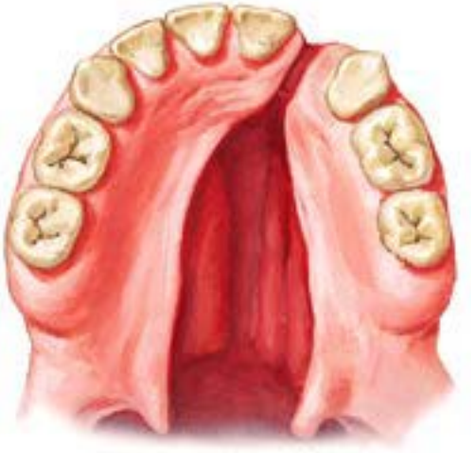
Congenital Anomalies of the Oral Cavity

Unilateral cleft lip-partial



Partial cleft of palate

Unilateral cleft of primary palate-complete, involving lip and alveolar ridge



Complete cleft of secondary palate and unilateral cleft of primary palate

Bilateral cleft lip

Ankyloglossia-restricted tongue movement from a short lingual frenulum

Torus palatinus-bone deposition on palate

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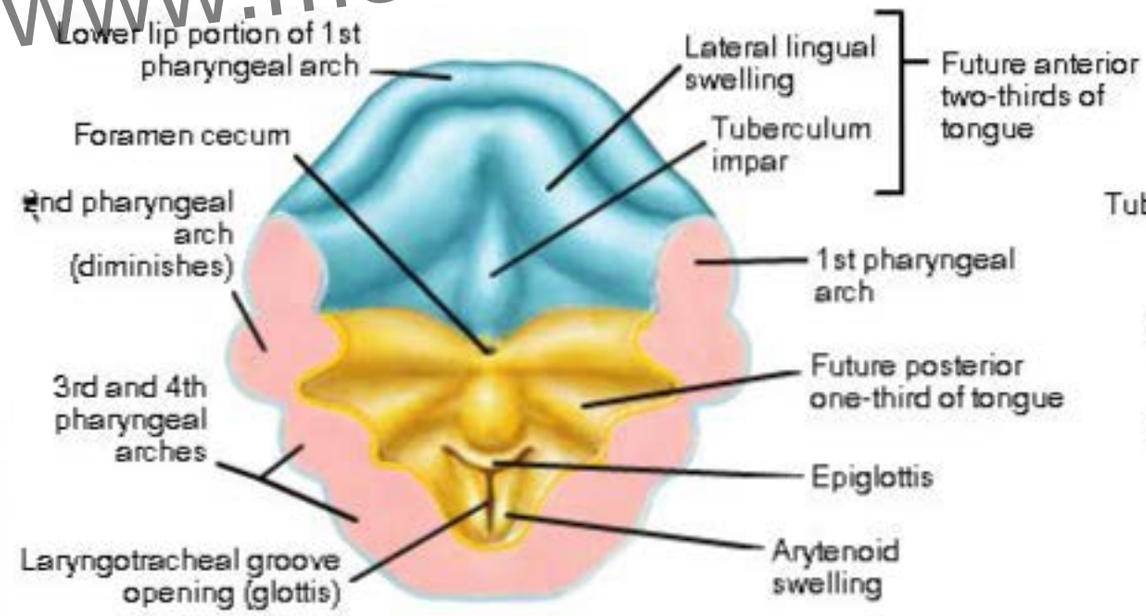
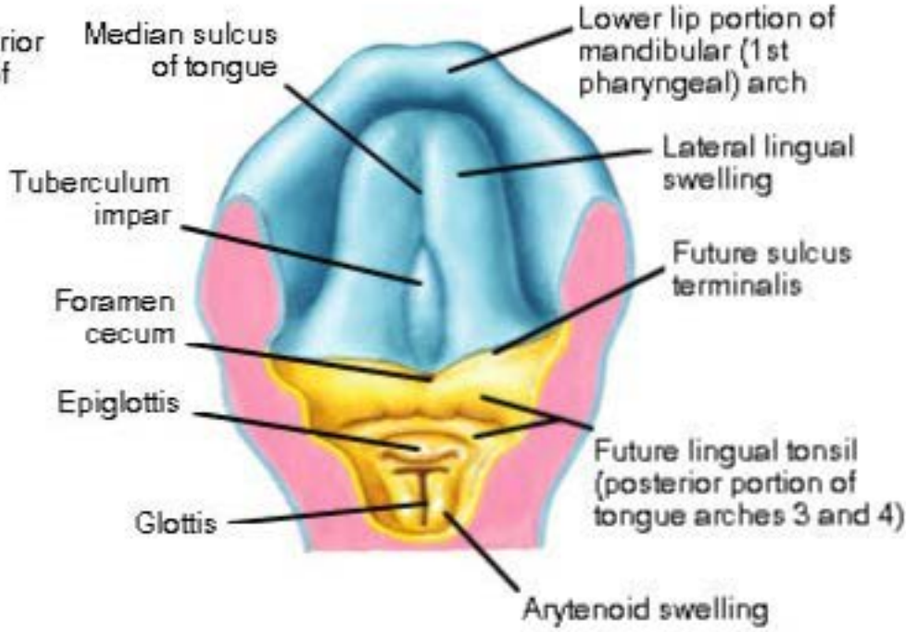
Floor of the Oral Cavity

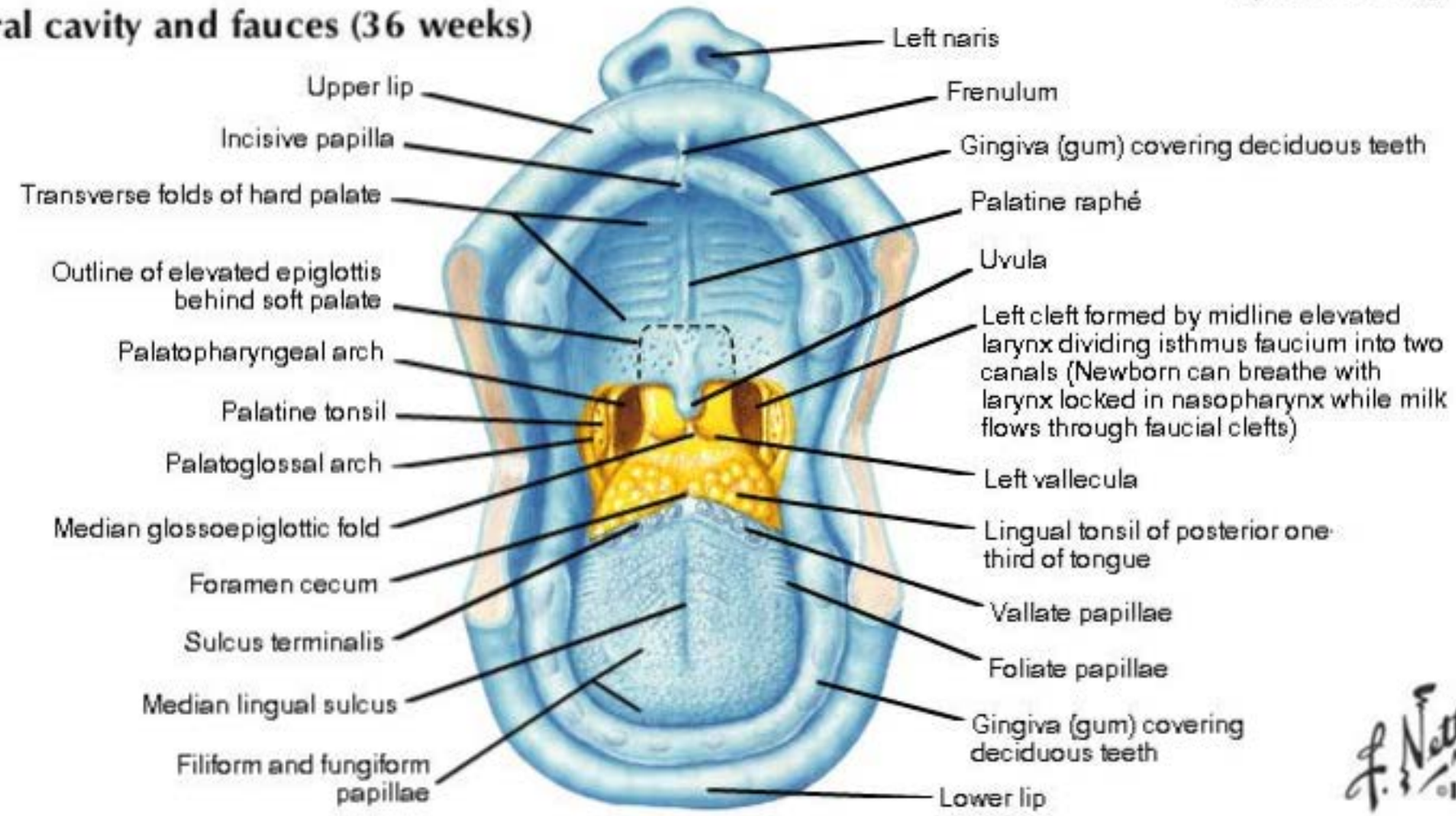
Floor of oral cavity and pharynx (superior view; 5 to 6 weeks)



Floor of oral cavity and pharynx (superior view; 6 to 7 weeks)



Oral cavity and fauces (36 weeks)



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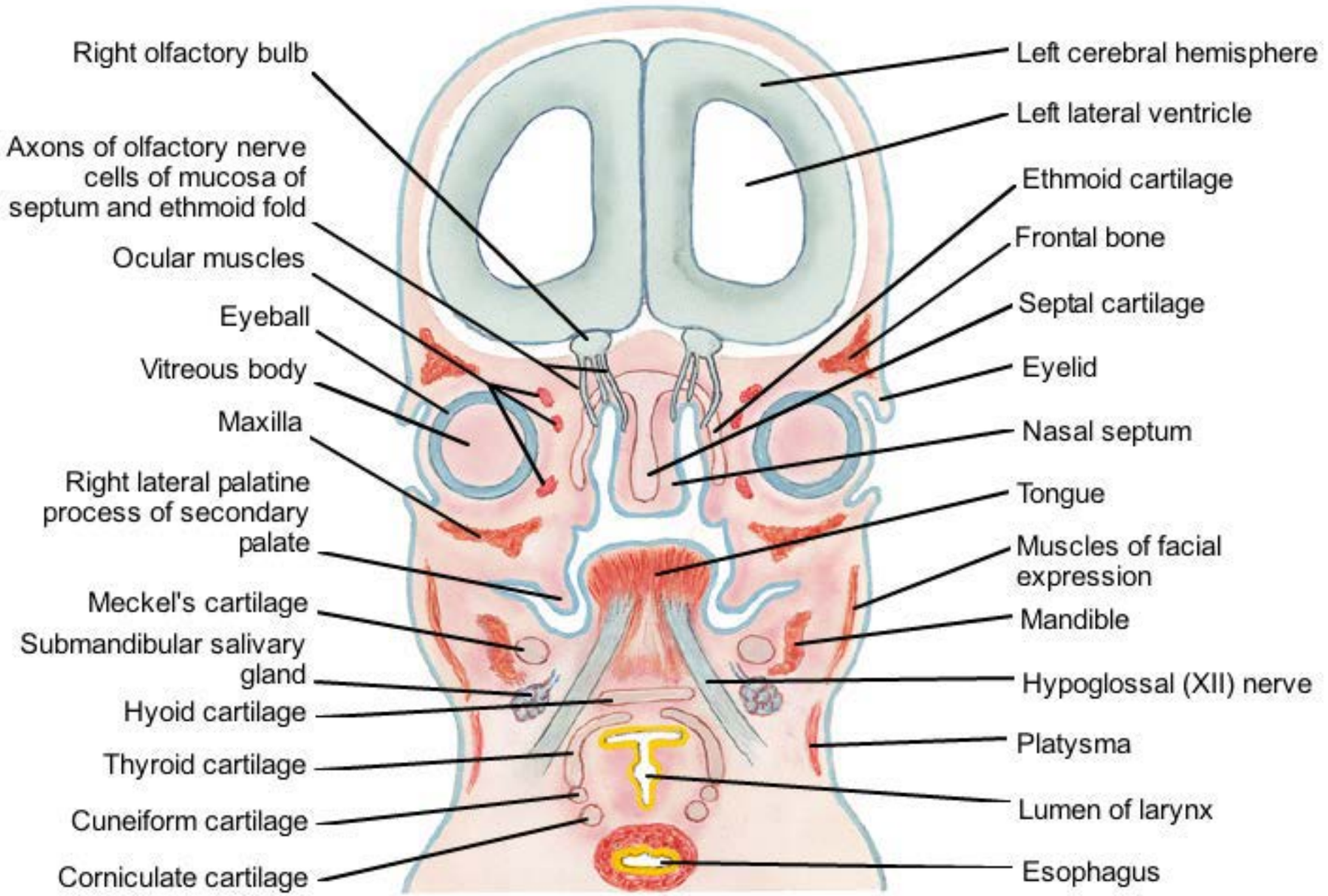
Developmental Cross Sections

Frontal (coronal) section at 7 to 8 weeks



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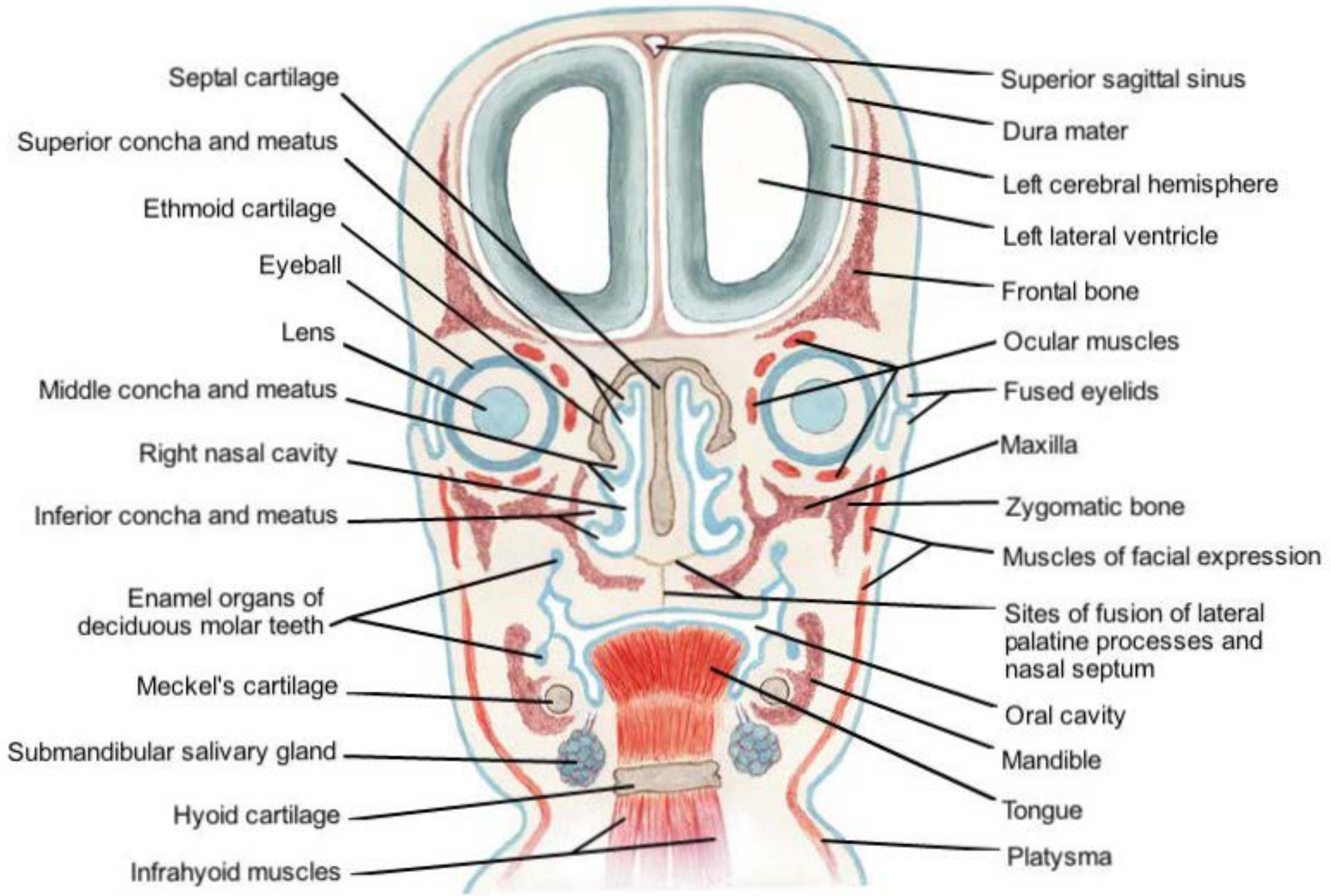
Developmental Cross Sections

Frontal (coronal) section at 8 to 10 weeks



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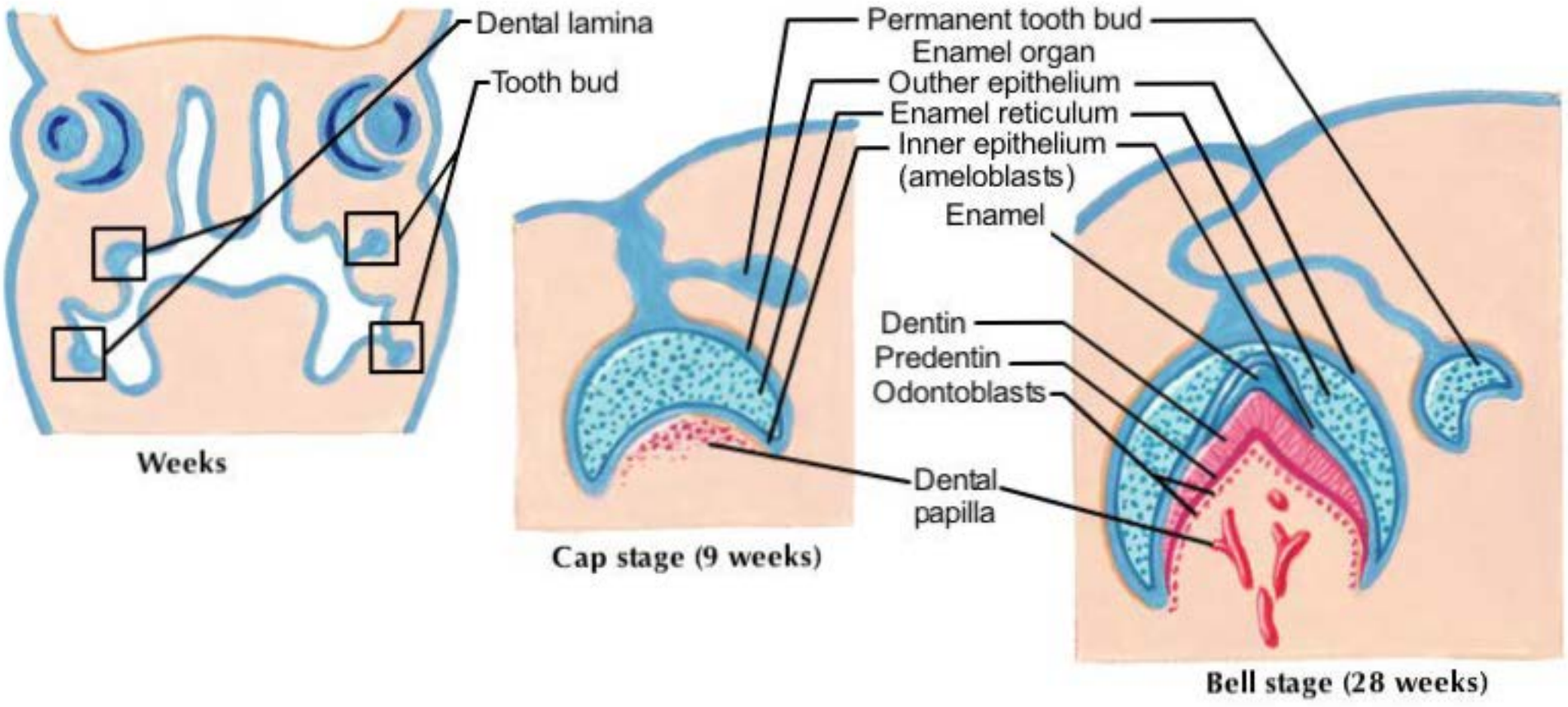
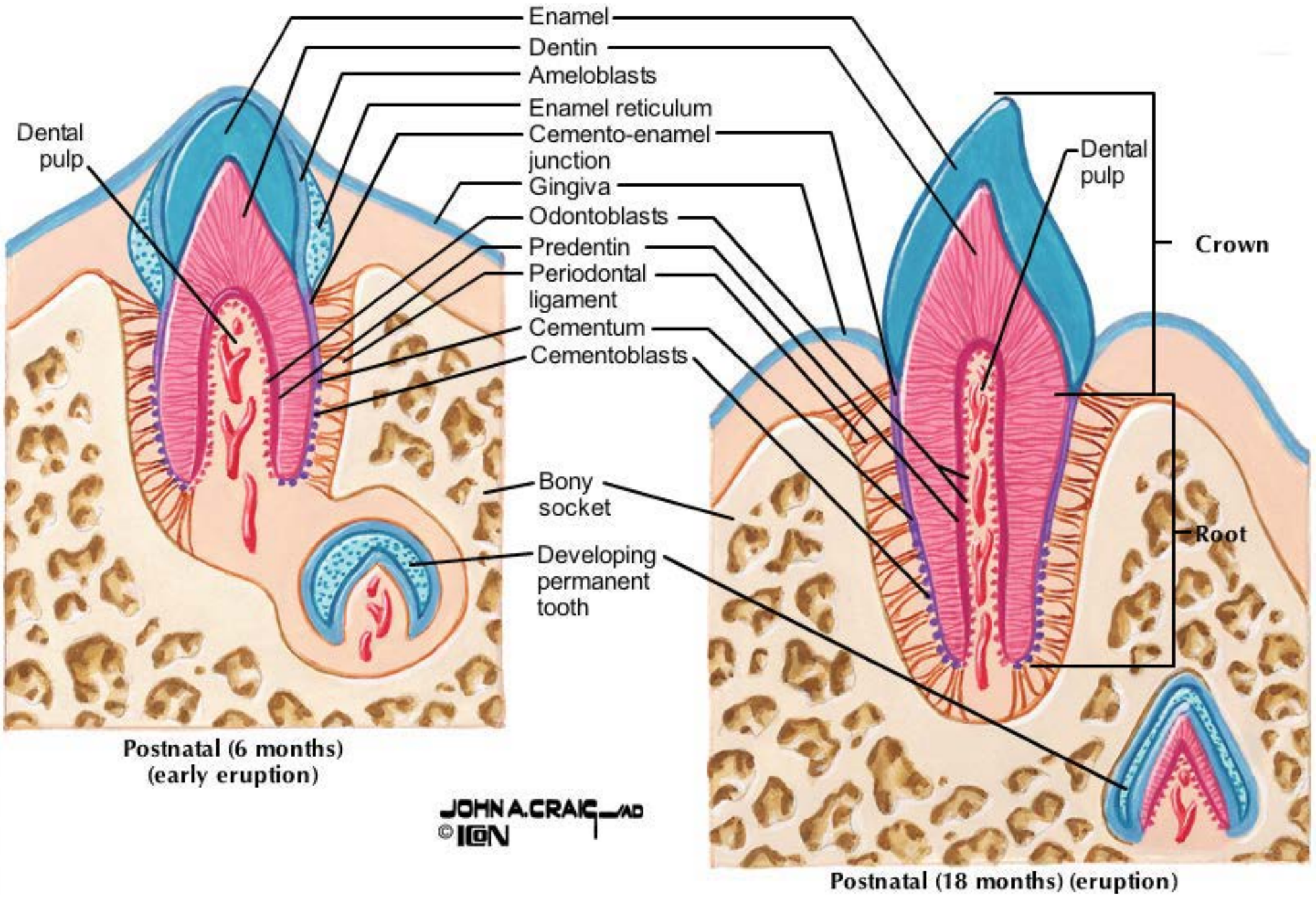
Tooth Development



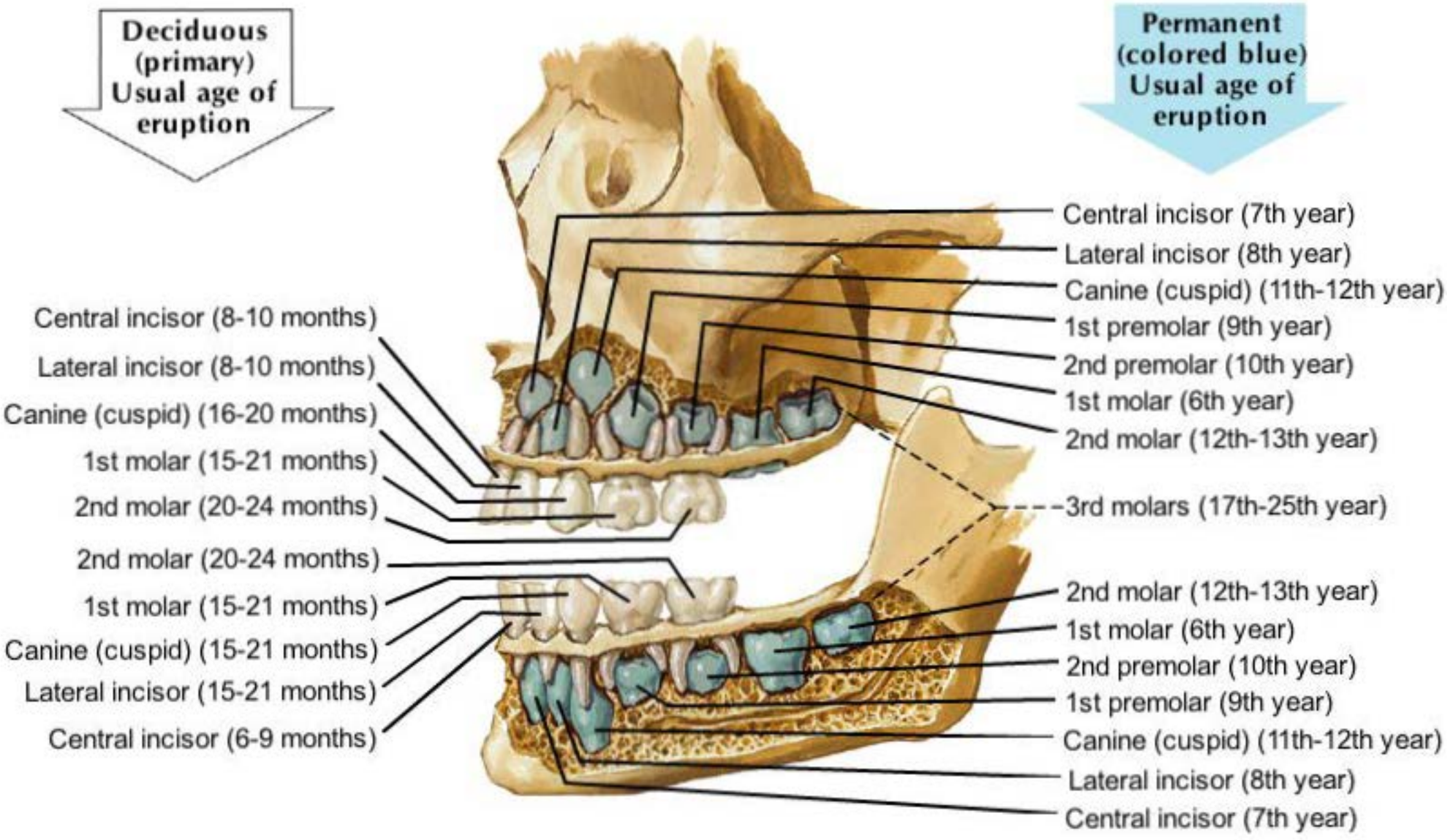
Tooth Development



Postnatal (6 months) (early eruption)

Postnatal (18 months) (eruption)

Dental Eruption



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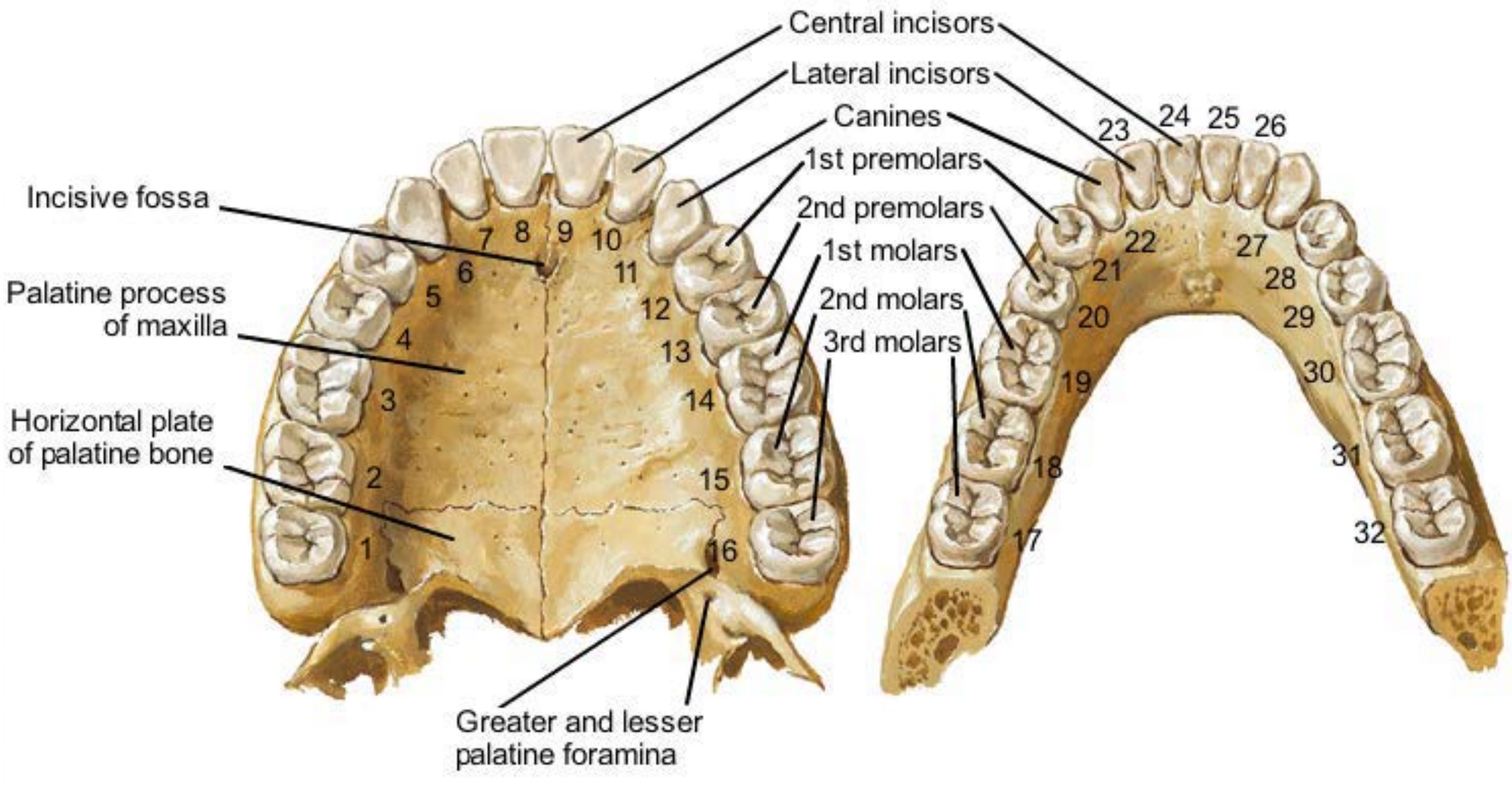
Dental Eruption



Upper permanent teeth **Lower permanent teeth**

Note: Numbers refer to a common scheme dentists use to identify teeth.
(Letters are used for the deciduous definition.)

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Pharyngeal Pouch and Groove Derivatives

No.	From Pouches	From Grooves
1	Auditory tube, middle ear cavity, mastoid air cells	External auditory meatus
2	Palatine tonsil crypts	Cervical sinus (disappears)
3	Inferior parathyroids, thymus	Cervical sinus (disappears)
4	Superior parathyroids, parafollicular cells (C cells) of thyroid	Cervical sinus (disappears)

Ear Structures and Their Primordia

Structures	Primordia
Auricle	Mesenchyme of the 1st and 2nd pharyngeal arches
External auditory meatus	1st pharyngeal groove (ectoderm)
Middle ear cavity; auditory tube, mastoid air cells	1st pharyngeal pouch (endoderm)
Cochlea and semicircular canals	Otic placode/otocyst (ectoderm)
Tympanic membrane	1st pharyngeal membrane (ectoderm/endoderm) with intervening mesenchyme
Ear ossicles	1st pharyngeal arch cartilage (incus and malleus) 2nd pharyngeal arch cartilage (stapes)
Temporal bone	Occipital sclerotomes (mastoid and petrous parts) 2nd pharyngeal arch cartilage (styloid process) 1st pharyngeal arch mesenchyme (squamous and tympanic parts)

Special sensory and Somatomotor Cranial Nerve Components

Nerve	Primordium Innervated	Neuron Components
Olfactory (I)	Olfactory placode	Special sensory (olfaction)
Optic (II)	Optic cup	Special sensory (vision)
Vestibulocochlear (VIII)	Otic placode	Special sensory (hearing and balance)
Oculomotor (III)	Preotic somitomere	Somatomotor to extraocular eye muscles Parasympathetics to ciliary ganglion (for pupil constrictor and ciliary muscle)
Trochlear (IV)	Preotic somitomere	Somatomotor to superior oblique muscle
Abducens (VI)	Preotic somitomere	Somatomotor to lateral rectus muscle
Hypoglossal (XII)	Postotic somites	Somatomotor to tongue muscles
Accessory (XI)	Somitic mesenchyme by arch 6	Somatomotor to sternocleidomastoid and trapezius

Pharyngeal Arch Cranial Nerve Components

Nerve	Arch	Neuron Components
Trigeminal (V)	1	General sensory (face, orbit, nasal and oral cavities) Branchiomotor (muscles of mastication; tensor tympani; tensor veli palatini)
Facial (VII)	2	Branchiomotor (muscles of facial expression; stylohyoid; posterior digastric; stapedius) Special sensory (taste to anterior two-thirds of tongue) Parasympathetic to pterygopalatine and submandibular ganglia (for lacrimal gland, nasal mucosa, and salivary glands)
Glossopharyngeal (IX)	3	Visceral sensory to pharynx Branchiomotor to stylopharyngeus Parasympathetic to otic ganglion (for the parotid gland) Special sensory (taste to posterior tongue; carotid body and sinus)
Vagus (X)	4 and 6	Branchiomotor (pharynx and larynx) Visceral sensory (larynx; foregut below pharynx and midgut) General sensory to external acoustic meatus Parasympathetics (enteric ganglia of foregut and midgut) Special sensory (taste in laryngopharynx; carotid body and sinus)

Innervation of the Tongue

INNERVATION OF THE TONGUE

Anterior two-thirds (oral cavity)	General sensory (GSA)—lingual branch of V3 Taste (SVA)—facial nerve (VII)
Posterior one-third (oropharynx)	Visceral sensory (GVA)—glossopharyngeal nerve (IX) Taste (SVA)—glossopharyngeal nerve (IX)
Root (laryngopharynx)	Visceral sensory (GVA)—vagus nerve (X) Taste (SVA)—vagus nerve (X)
Tongue muscles	Somatomotor—hypoglossal nerve (XII)

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