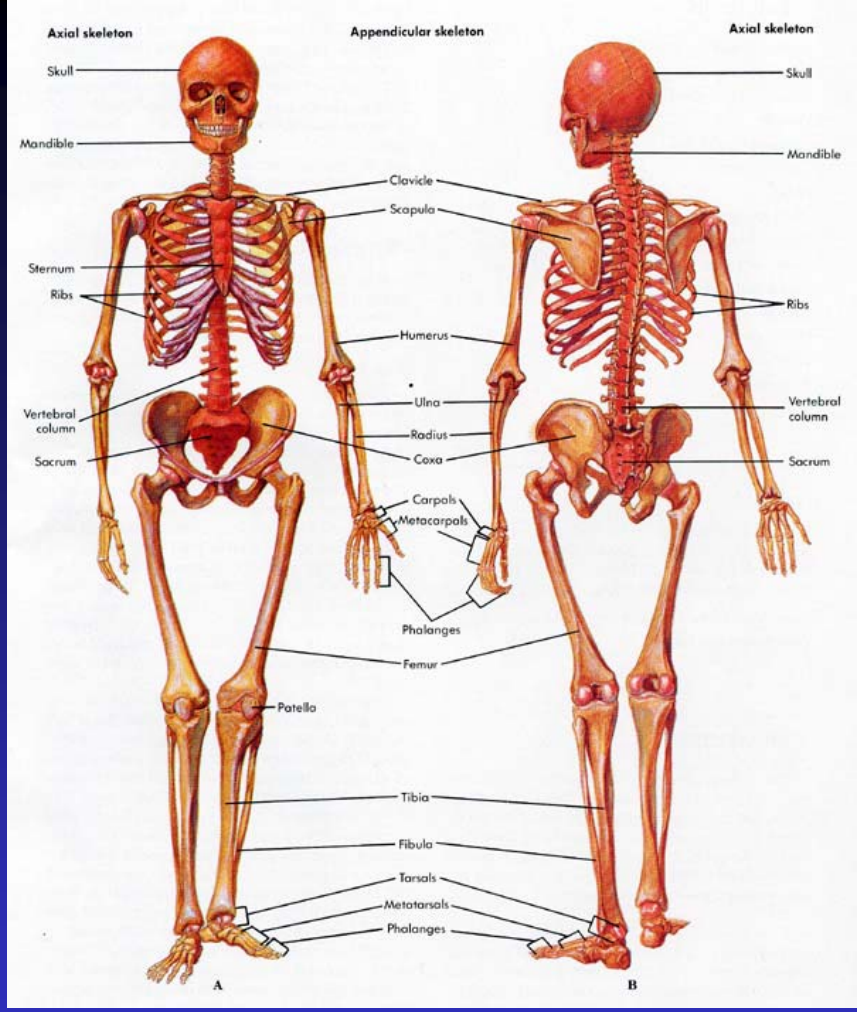
Skeletal Development

Multiple Cellular Origins

1 - **Paraxial Mesoderm**
Somite, Sclerotome
Axial Skeleton (e.g. vertebra)

2 - **Lateral Plate Mesoderm**
Appendicular Skeleton – (e.g. limb)

3 - **Neural Crest**
Head Skeleton



Established as

- 1 - **Hyaline Cartilage** – replaced by **Endochondrial Ossification**
- 2 – **Intramembranous Bone Formation** - direct ossification

Intramembranous Bone

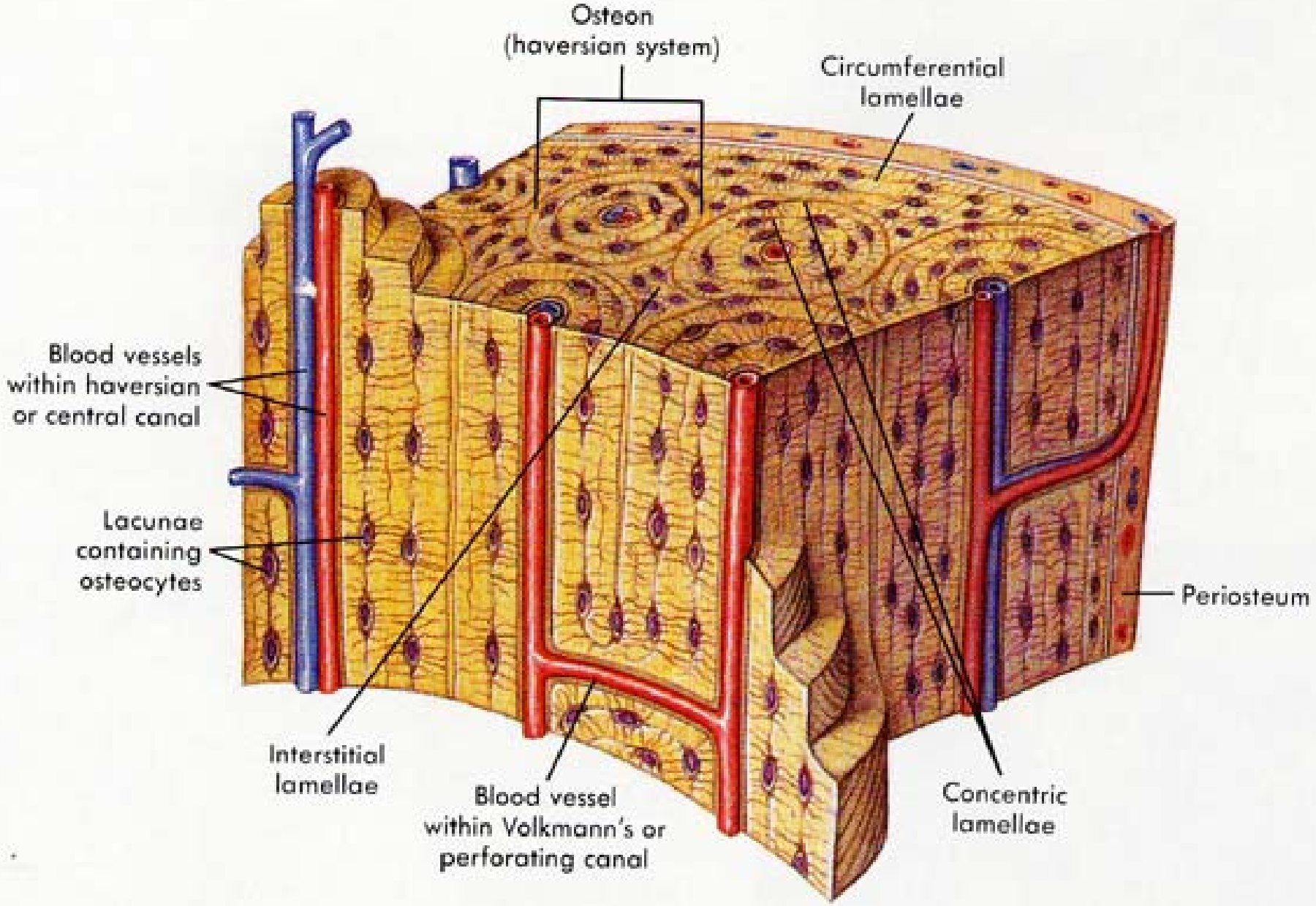
Intramembranous bone = dermal bone (e.g. skull, clavicle)

Mesenchymal condensation, becomes vascularized

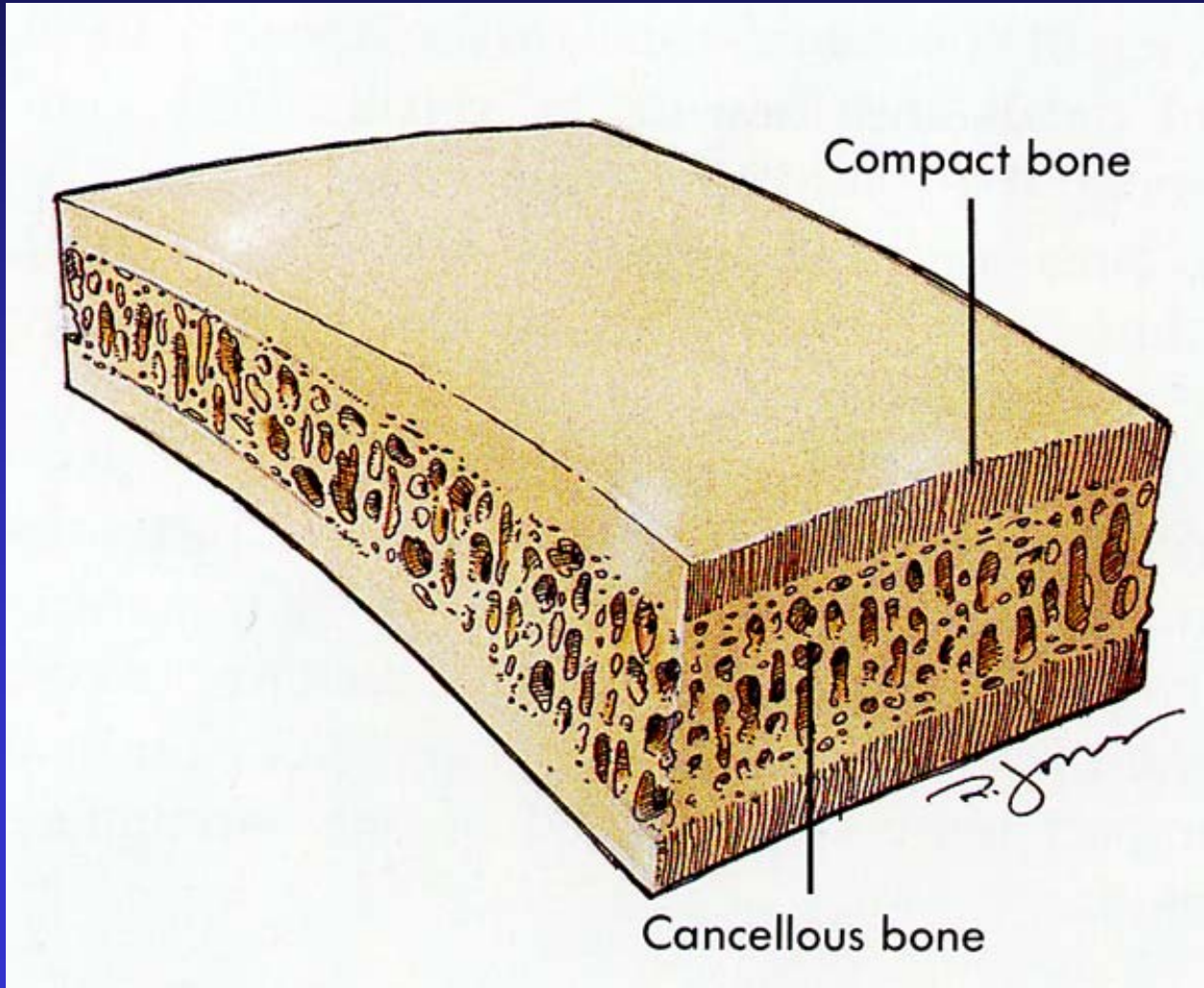
Osteoid Tissue (prebone) - cells differentiate into osteoblasts - matrix deposition - Calcium Phosphate

Osteoblast → Osteocytes - trapped in matrix

Bone Spicules organized around blood vessels - concentric layers = Haversian system.


Osteon
(haversian system)
Circumferential
lamellae
Blood vessels
within haversian
or central canal
Lacunae
containing
osteocytes
Periosteum
Interstitial
lamellae
Blood vessel
within Volkmann's or
perforating canal
Concentric
lamellae

- Compact Bone - Osteoblast in periphery lay down layers of compact bone
- Spongy bone - beneath bony plates - osteoclasts breaks down bone
- Continual bone remodeling via action of osteoblasts and osteoclast
- Bone marrow differentiates from mesenchyme in spongy bone



Endochondrial Bone

Endochondral ossification – Hyaline cartilage template of bone forms

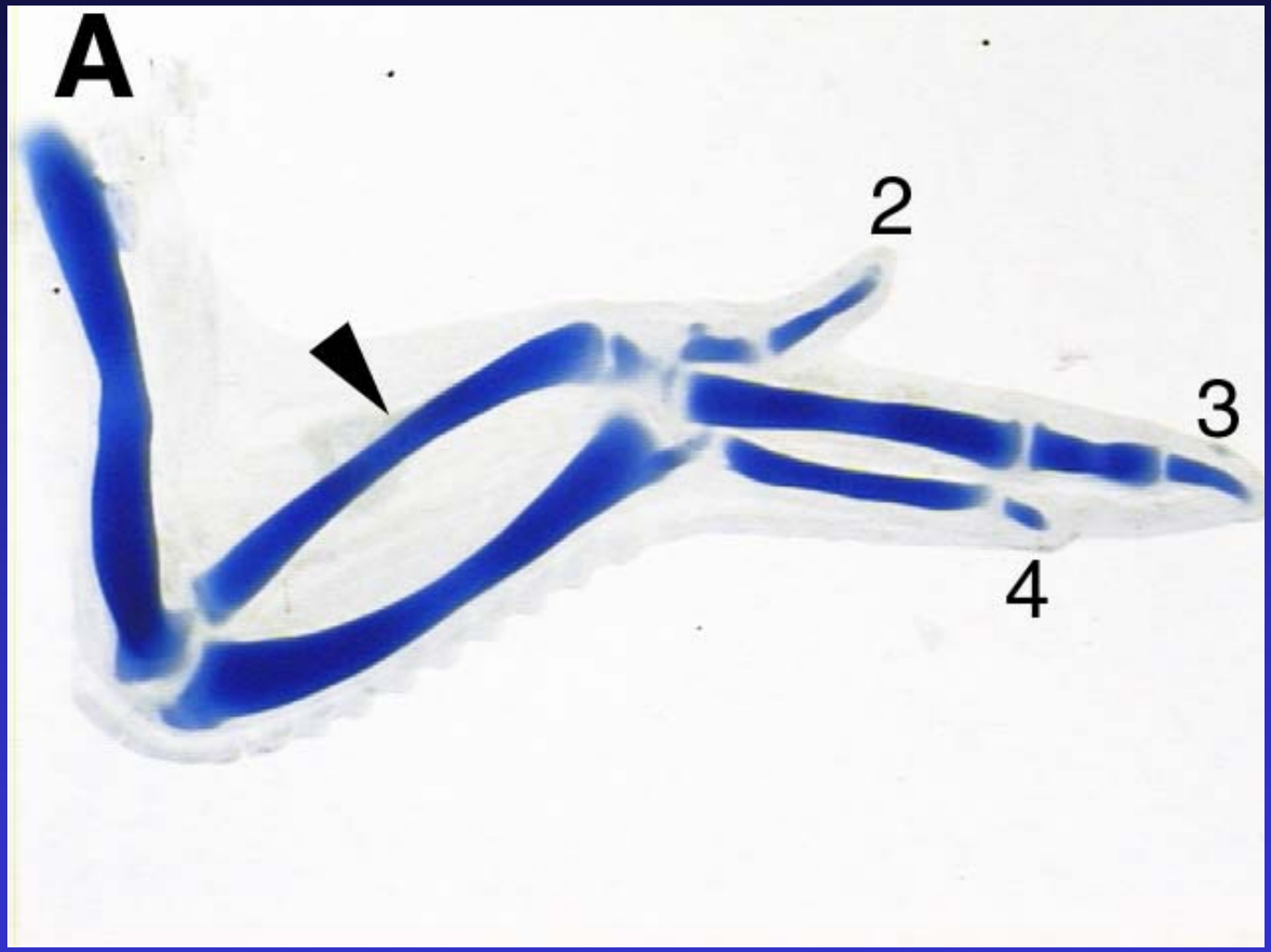
Cartilage - differentiates from mesenchyme cells

Chondroblasts - condenses - become rounded and deposit matrix - collagen fibers or elastic fiber

Three types of cartilage - hyaline (most common), fibrocartilage, elastic cartilage

Perichondrium - outer layer of cells

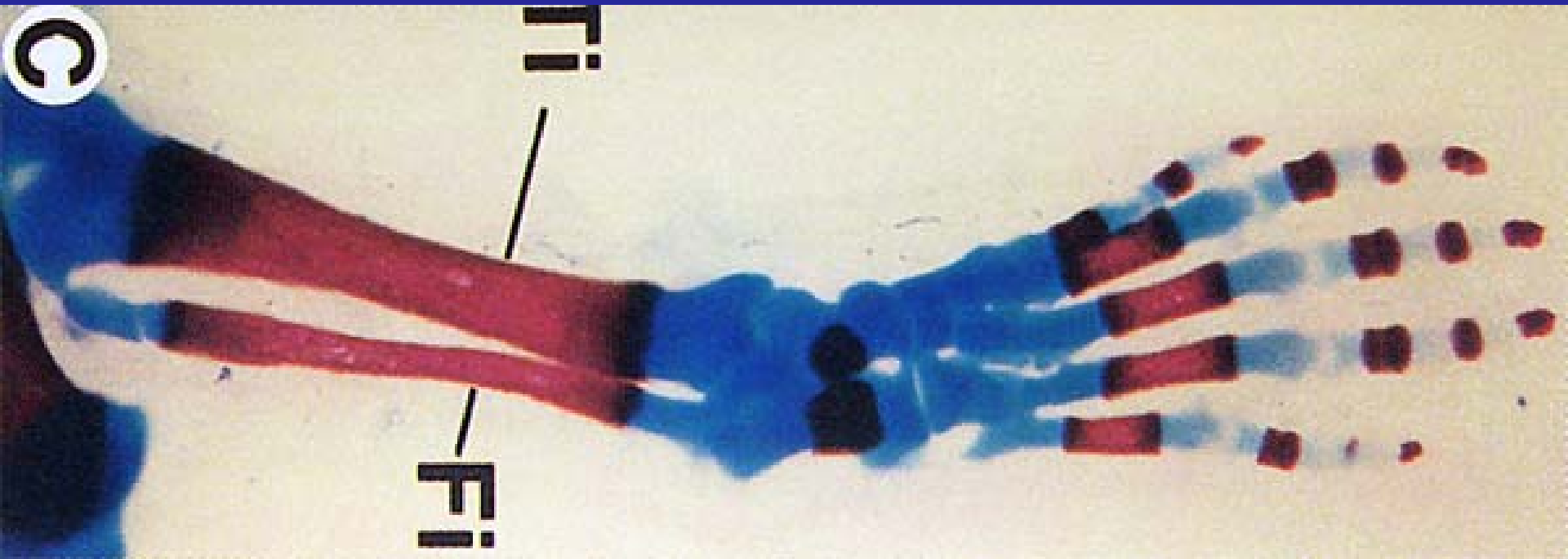
Cartilage template of the limb in the Chick wing



Endochondrial Bone

Primary ossification center - initiation of ossification

Perichondrial cells differentiate into Osteoblasts - deposit matrix as a collar in center of long bone – diaphysis



Endochondrial Bone

Perichondrium becomes Periostium

Ossification spreads towards ends of bone

Osteoclasts differentiate and begin to breakdown bone

Chondrocytes die off – center is invaded by vascular system – the bone marrow.

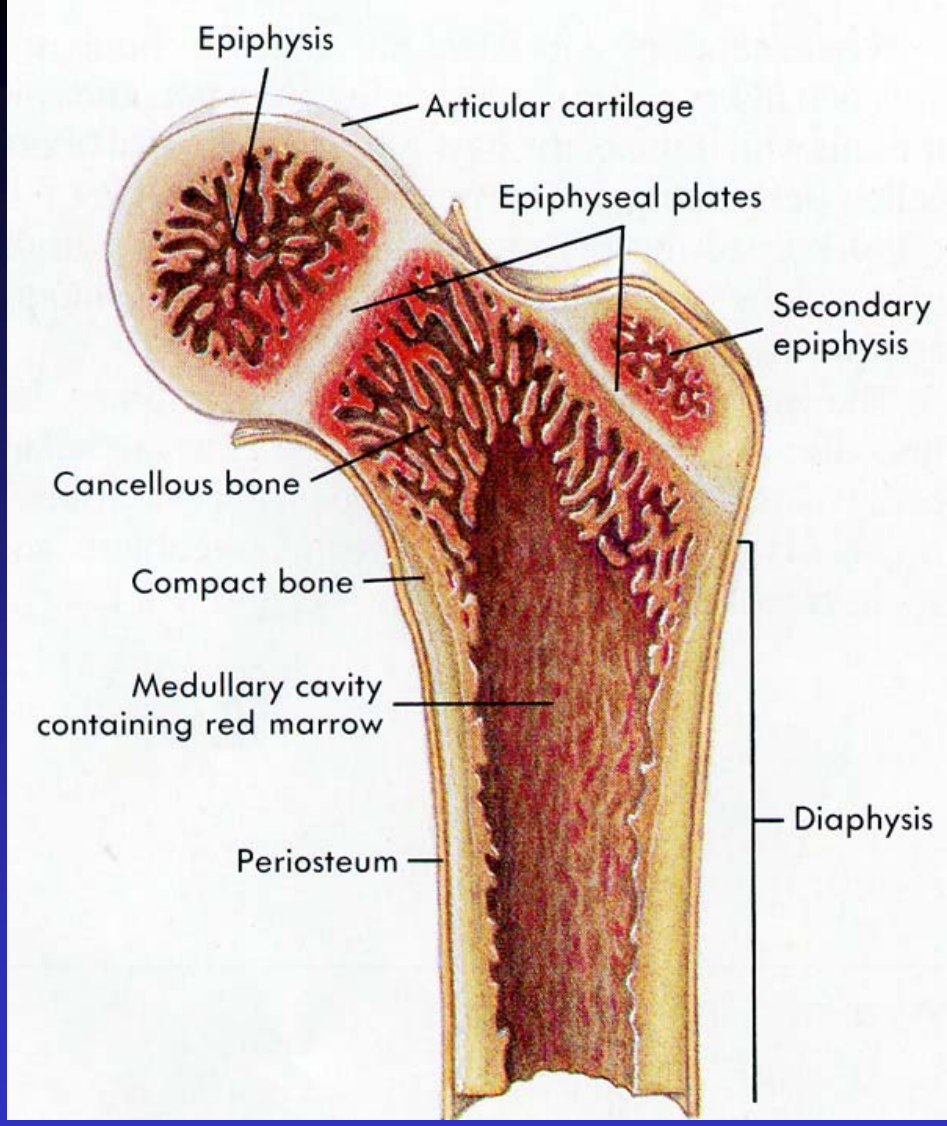
Cells also invade and differentiate into osteoblasts - forming bone spicules that are remodeled by osteoclasts

Bone Growth

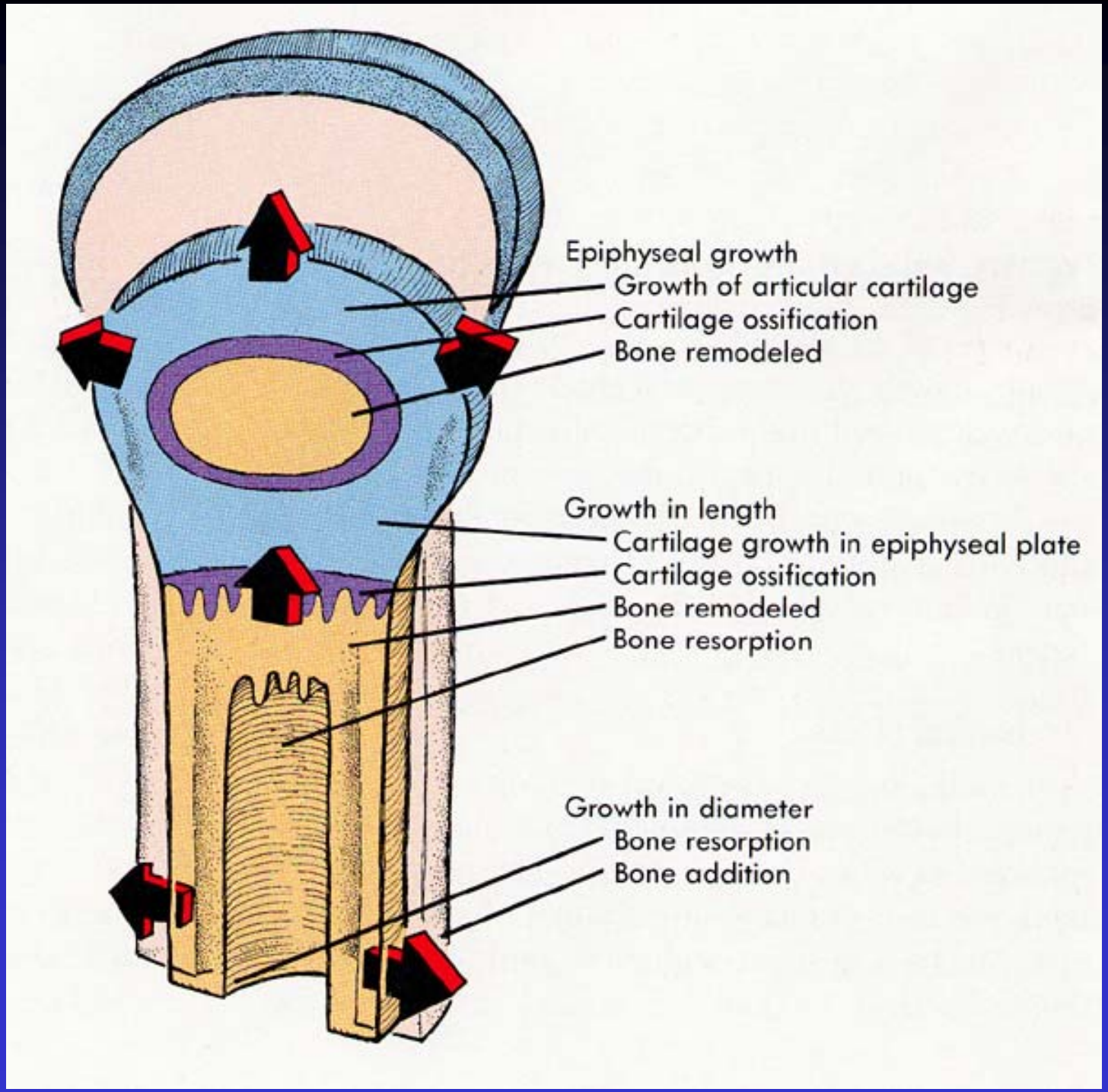
Bone lengthening occurs at diaphyseal-epiphyseal junction - epiphyseal cartilage plate (growth plate)

Epiphysis - chondrogenic

Secondary ossification centers in the epiphysis after birth

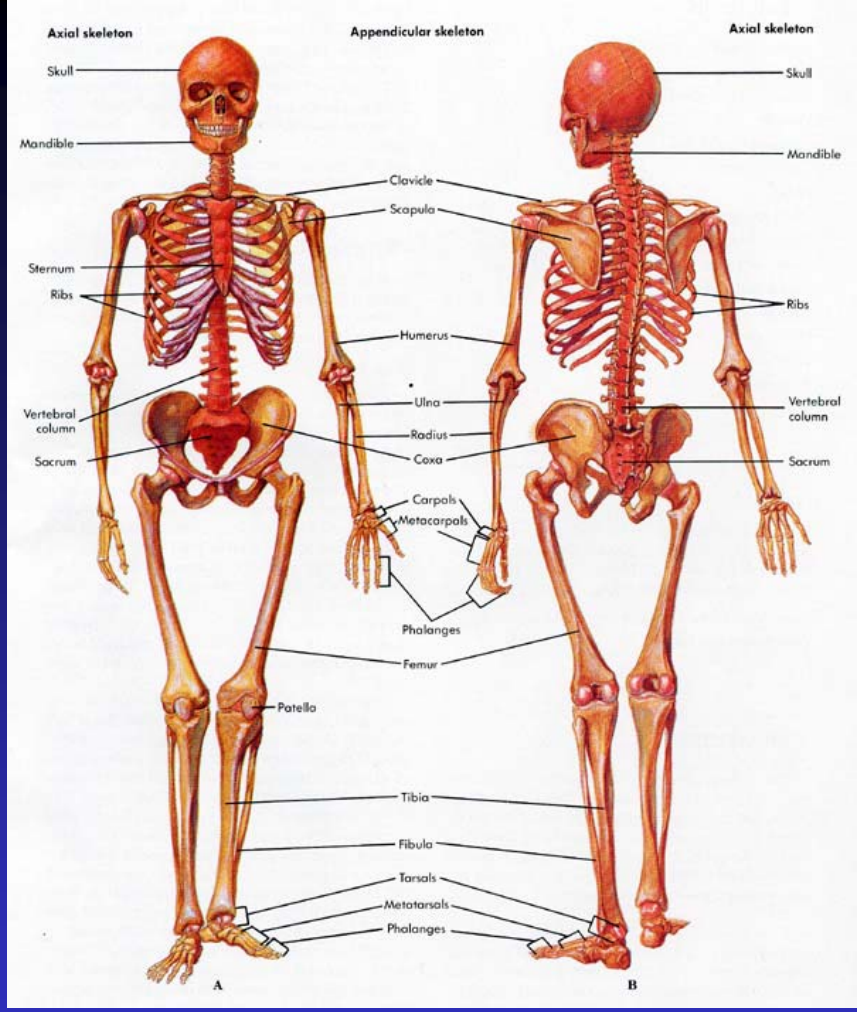


After growth termination the epiphyseal cartilage plate is replaced with spongy bone


Epiphyseal growth
Growth of articular cartilage
Cartilage ossification
Bone remodeled
Growth in length
Cartilage growth in epiphyseal plate
Cartilage ossification
Bone remodeled
Bone resorption
Growth in diameter
Bone resorption
Bone addition

Skeletal Development

Multiple Cellular Origins



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Head Skeleton

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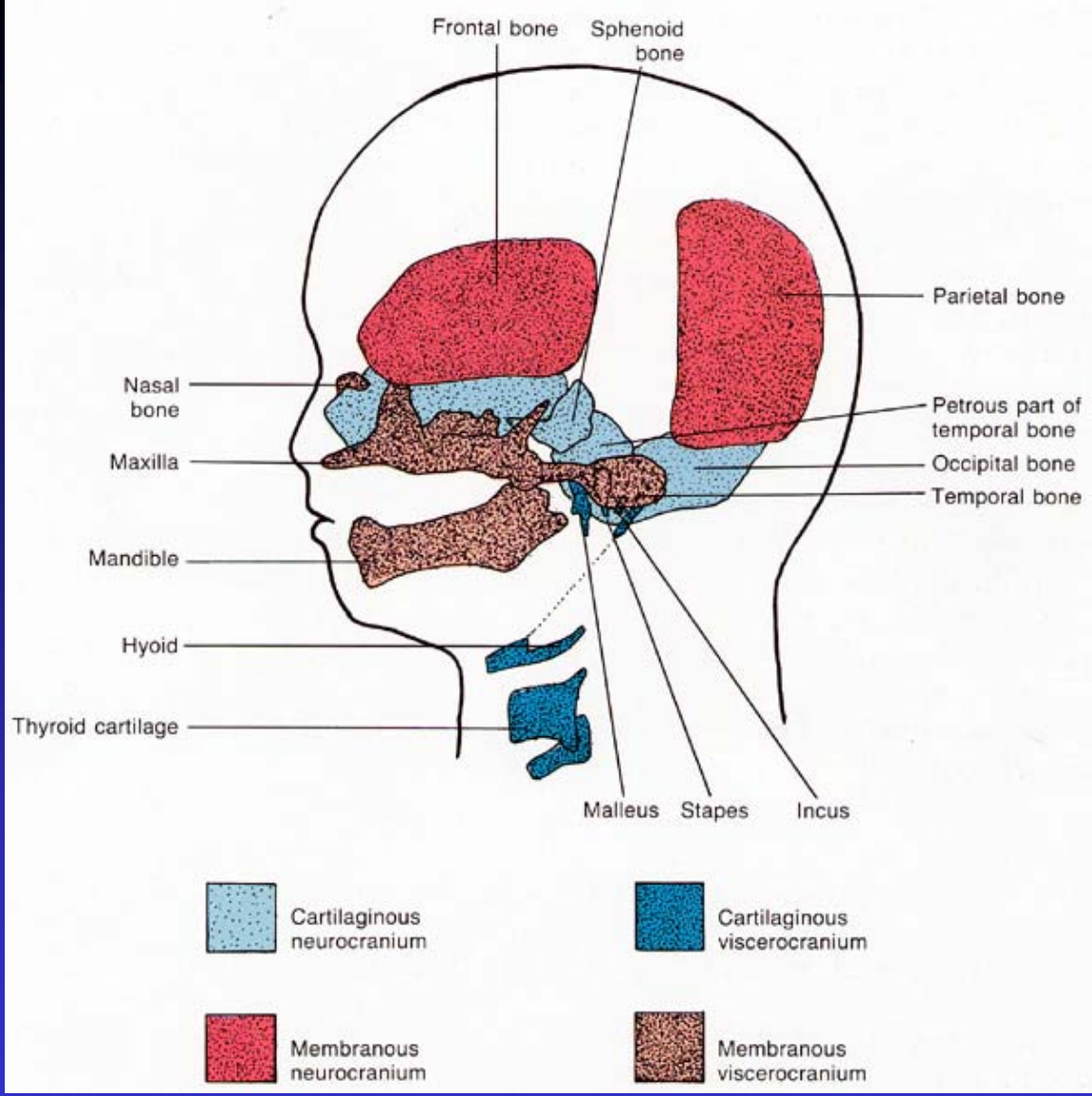
Skull / Head

Neurocranium
skeleton around the brain

Viscerocranium
skeleton of the face

Both consist of two components:
Membranous (Intramembranous ossification)
Cartilaginous (Endochondrial ossification)



Neurocranium

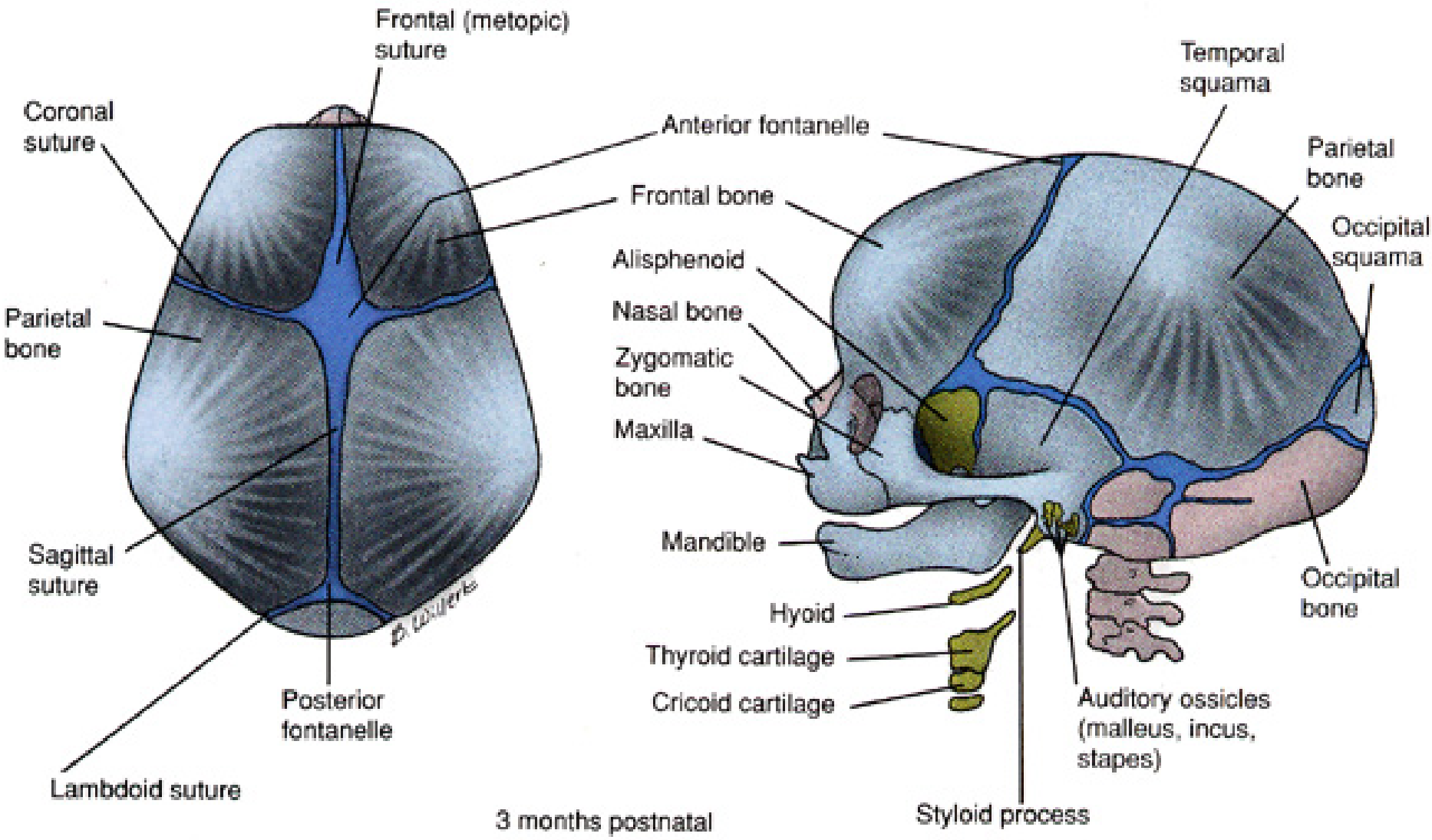
Membranous neurocranium
    cranial vault = calvaria
    flat bones of skull

Sutures - fibrous joints between flat bones

Fontanelles - where several sutures meet

Moldling - bones are soft, sutures are loose – allows for changes during birth

Cartilaginous neurocranium – bones at the base of the skull



3 months postnatal

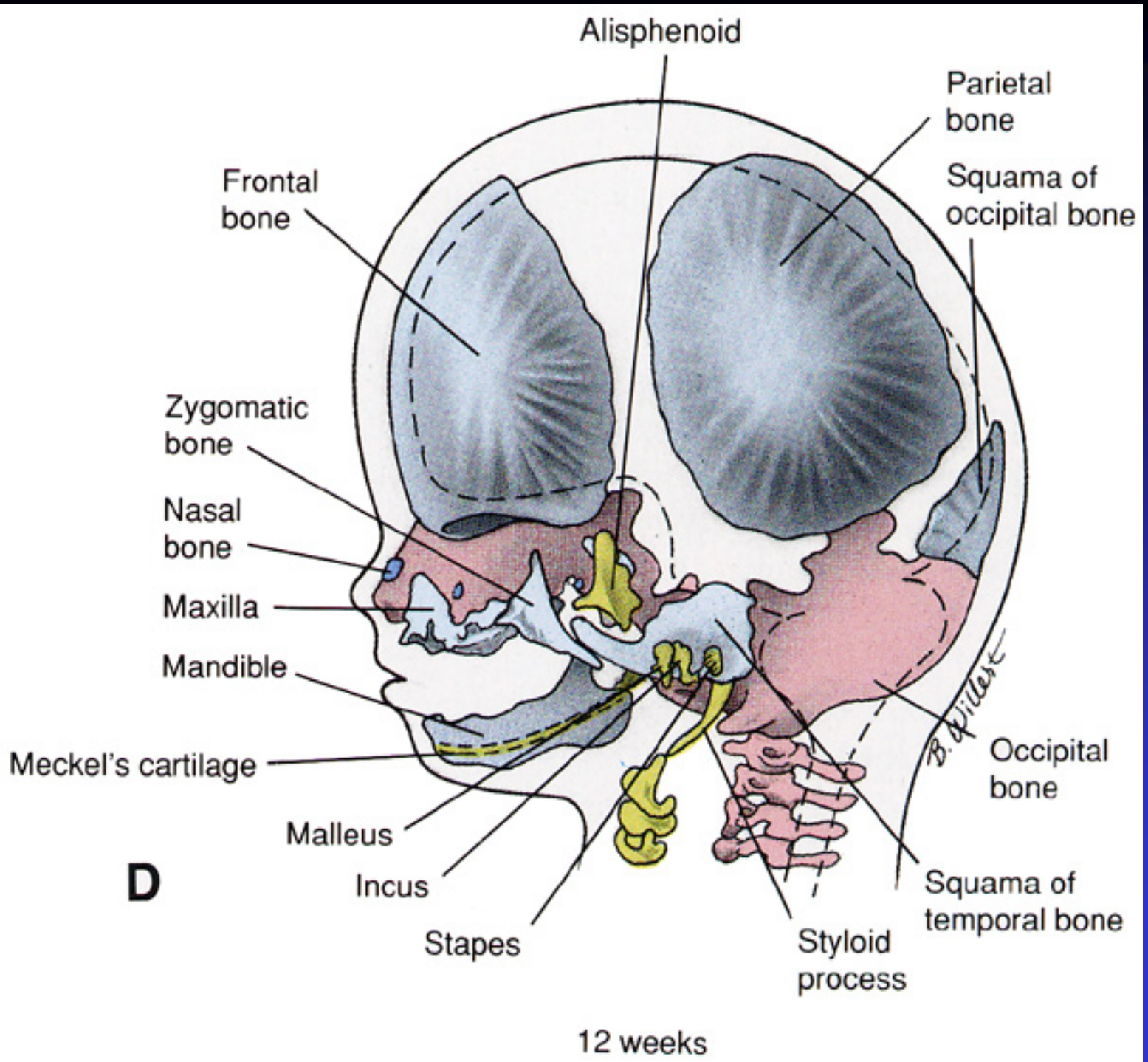
Viscerocranium

Cartilaginous viscerocranium

- middle ear bones - incus, malleus, stapes
- reichert's cartilage
- hyoid bone

Membranous viscerocranium

- Jaw Bones – maxilla, zygomatic, squamous
- temporal bones, mandible


Alisphenoid
Parietal bone
Squama of occipital bone
Frontal bone
Zygomatic bone
Nasal bone
Maxilla
Mandible
Meckel's cartilage
Occipital bone
Malleus
Incus
Stapes
Styloid process
Squama of temporal bone
D
12 weeks

Apert syndrome

Pfeiffer's syndrome

Crouzon's syndrome

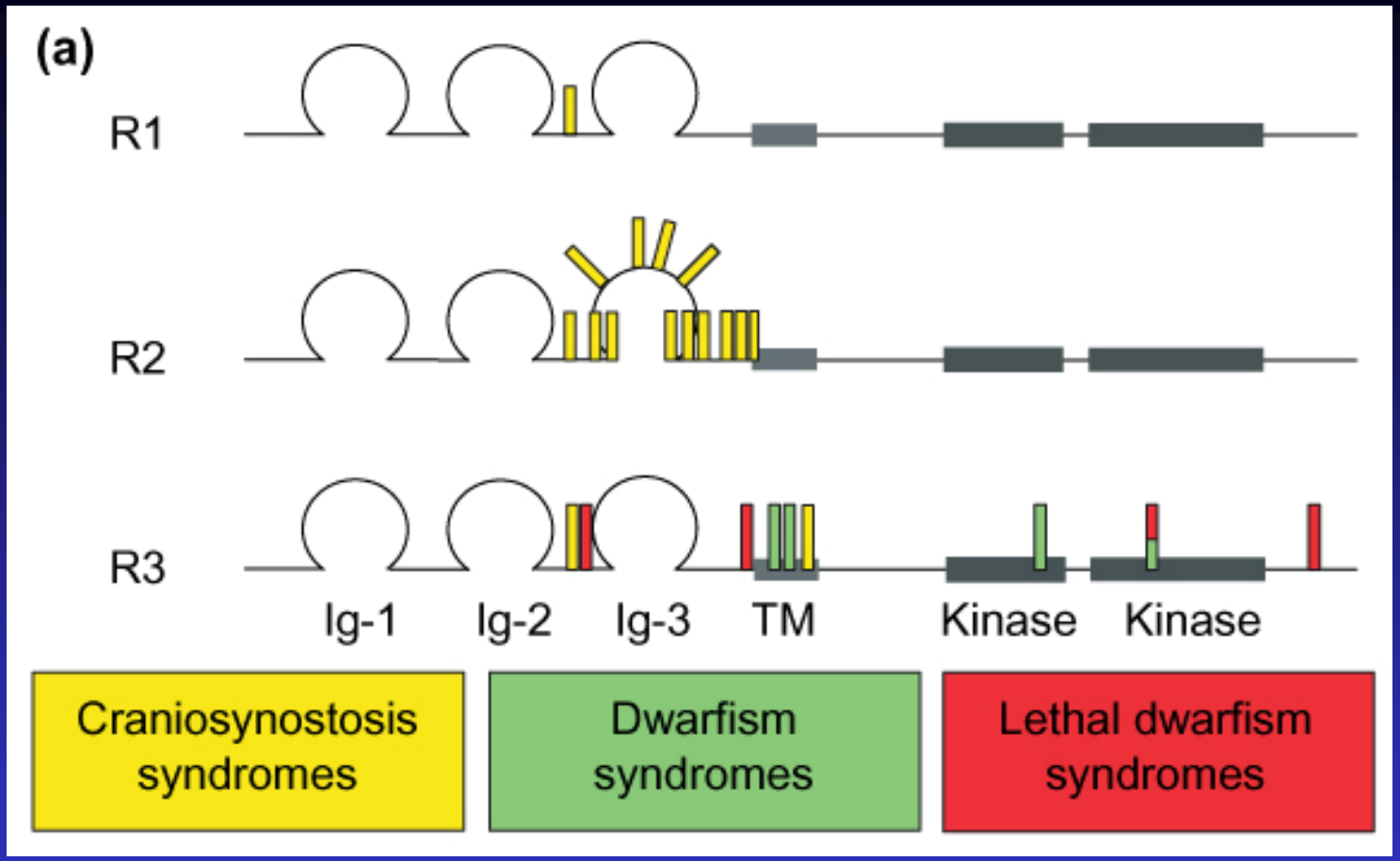
Craniosynostosis

Premature closure of sutures

Abnormal skull shape

Multiple causes:

- FGF signaling
- Msx gene function

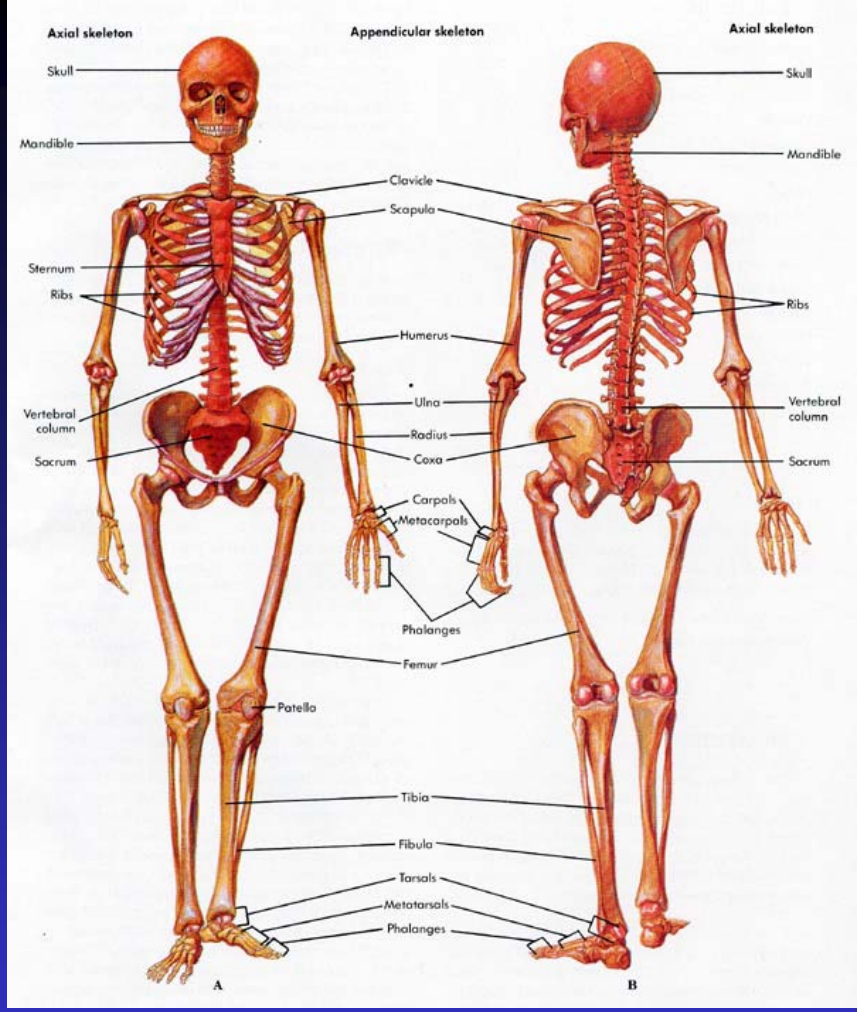


FGF Receptor (FGFR) mutations cause craniosynostosis

Autosomal dominant – abnormal dimer function

Skeletal Development

Multiple Cellular Origins



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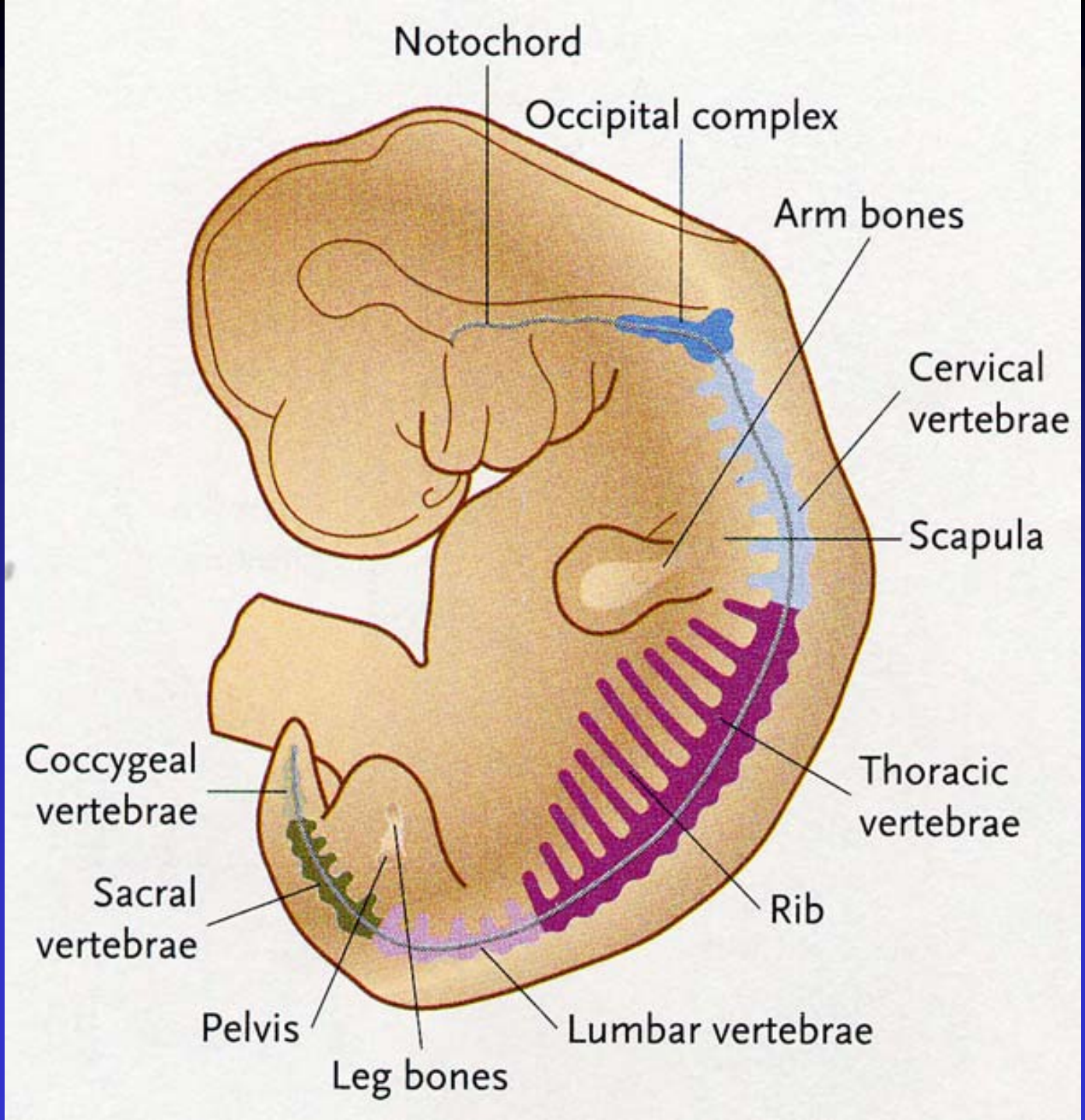
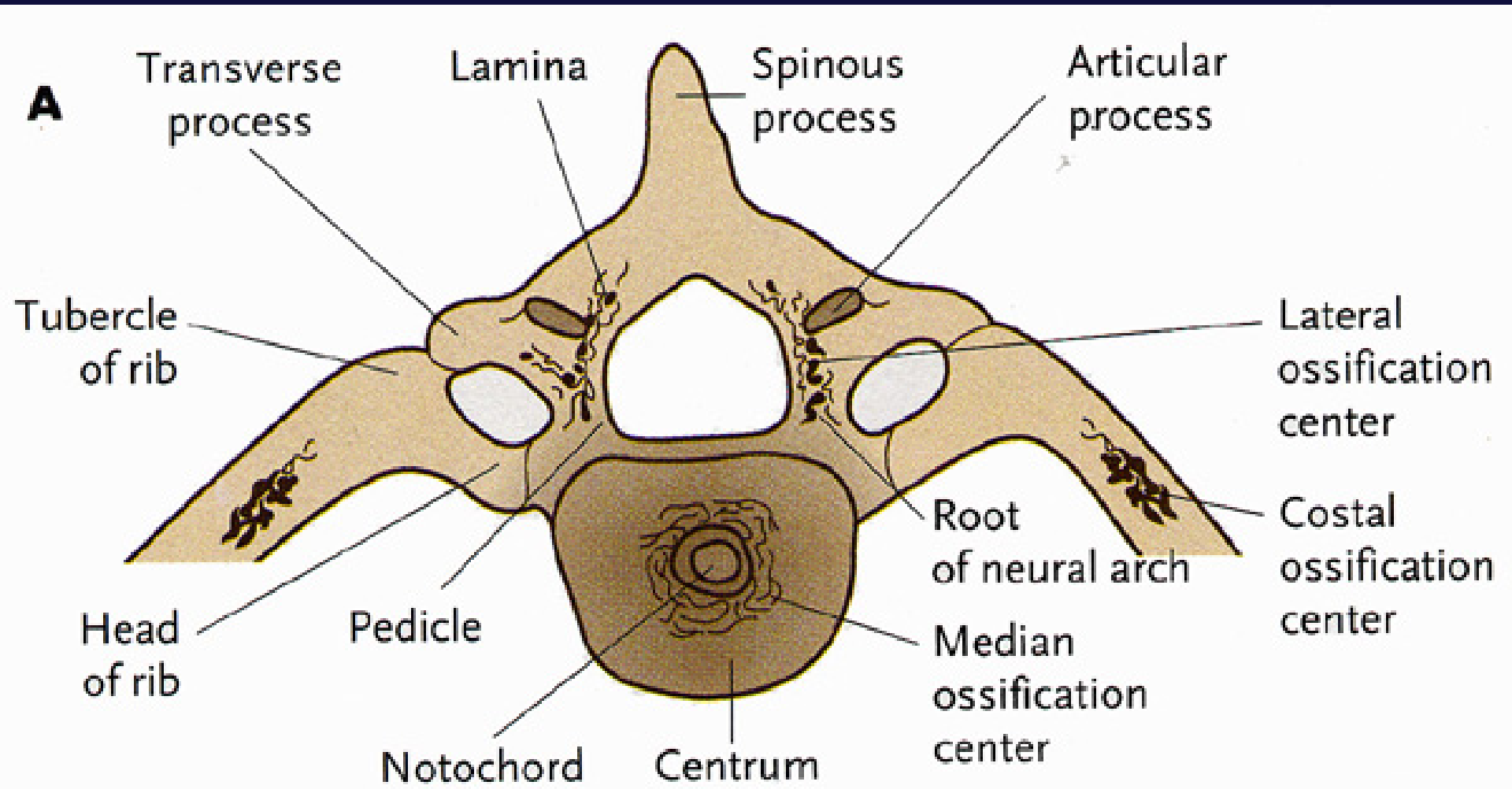
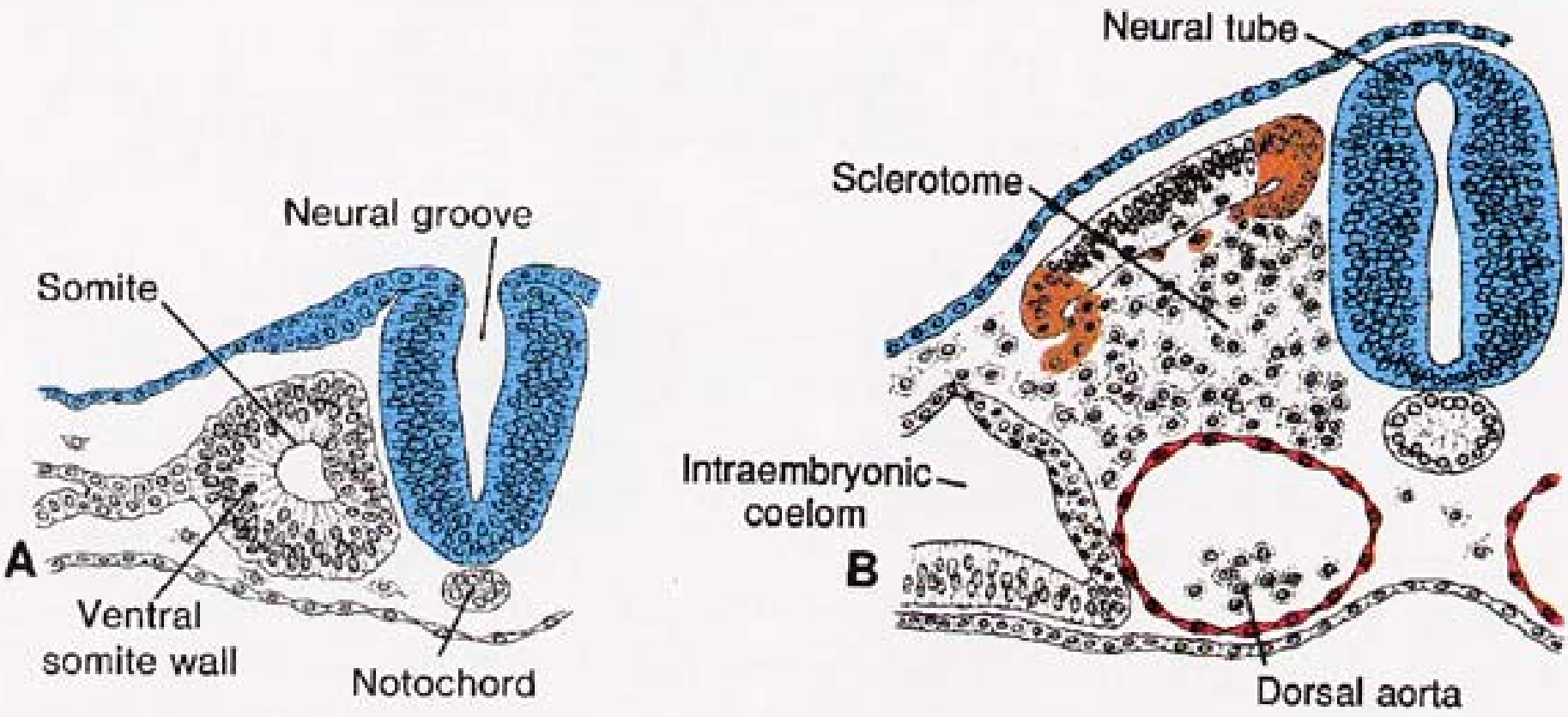

Notochord
Occipital complex
Arm bones
Cervical vertebrae
Scapula
Coccygeal vertebrae
Thoracic vertebrae
Sacral vertebrae
Rib
Pelvis
Lumbar vertebrae
Leg bones

Vertebral Column



Three parts to each vertebra - body, vertebral arch, ribs



Sclerotome cells form a mesenchyme that chondrofies around the notochord to form the centrum

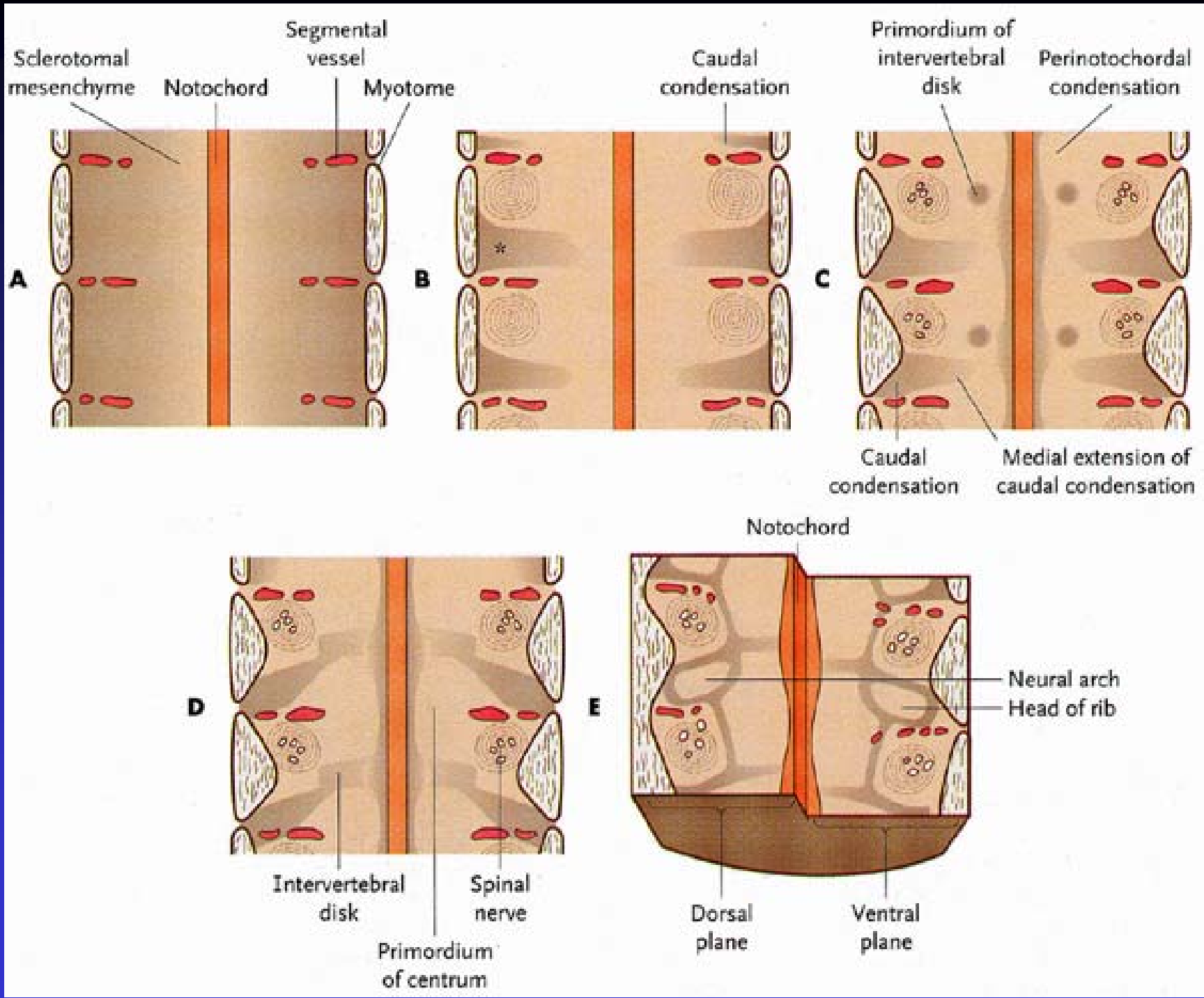
Development of Vertebra

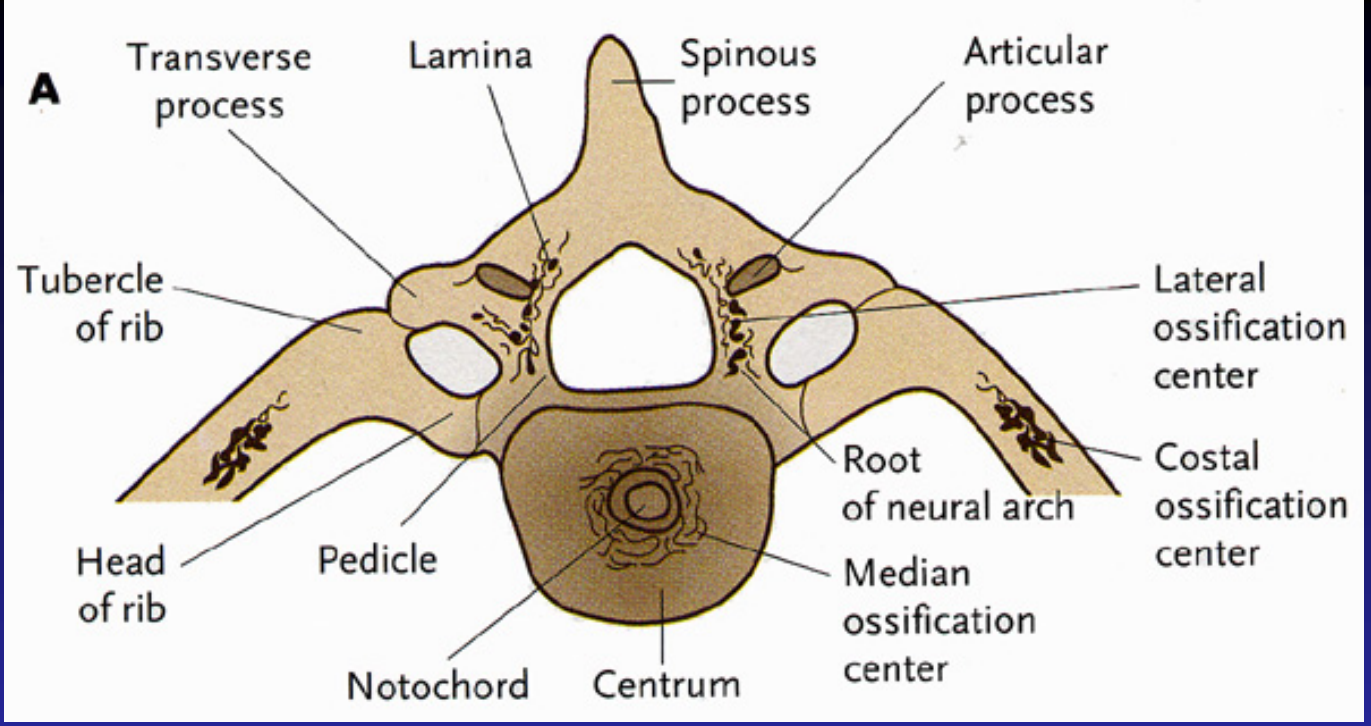
Sclerotome - cells surround notochord on both sides
- cranial - loosely arranged cells
- caudally - densely packed cells

Each vertebra is derived from two sclerotome segments
- Caudal (dense) cells from a cranial sclerotome
- Cranial (loose) cells from the next caudal sclerotome

Intervertebral disc between vertebra

Intervertebral disc forms at the interface between loose and dense cells (center of sclerotome)


Sclerotomal mesenchyme
Notochord
Segmental vessel
Myotome
A
Caudal condensation
B
*
Primordium of intervertebral disk
Perinotochordal condensation
C
Caudal condensation
Medial extension of caudal condensation
D
Intervertebral disk
Spinal nerve
Primordium of centrum
Notochord
E
Neural arch
Head of rib
Dorsal plane
Ventral plane



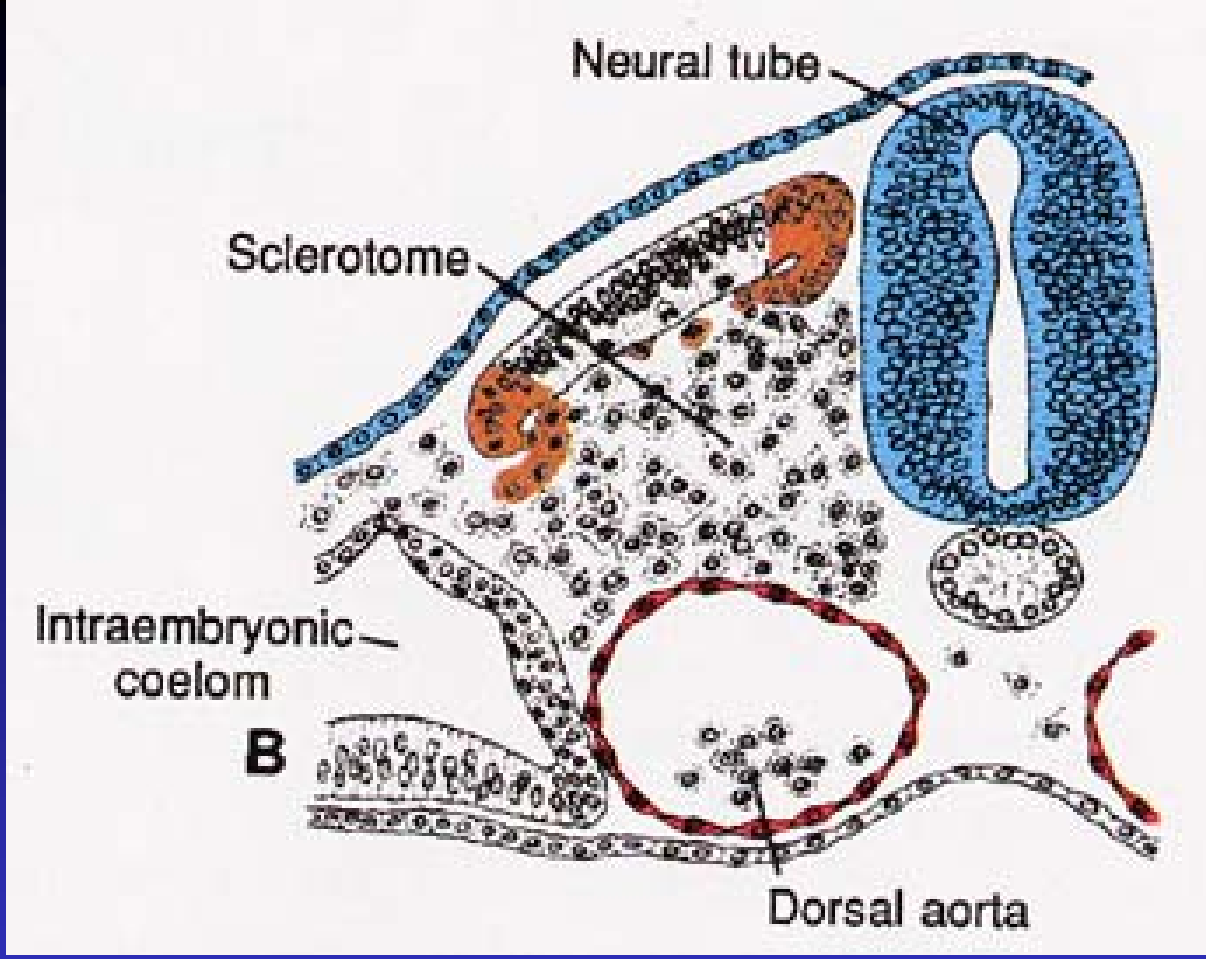
The centrum is the primordium of the body

Notochord degenerates in the center of body

Notochord expands in the intervertebral disc region
forms the nucleus pulposus = gelatinous disc center

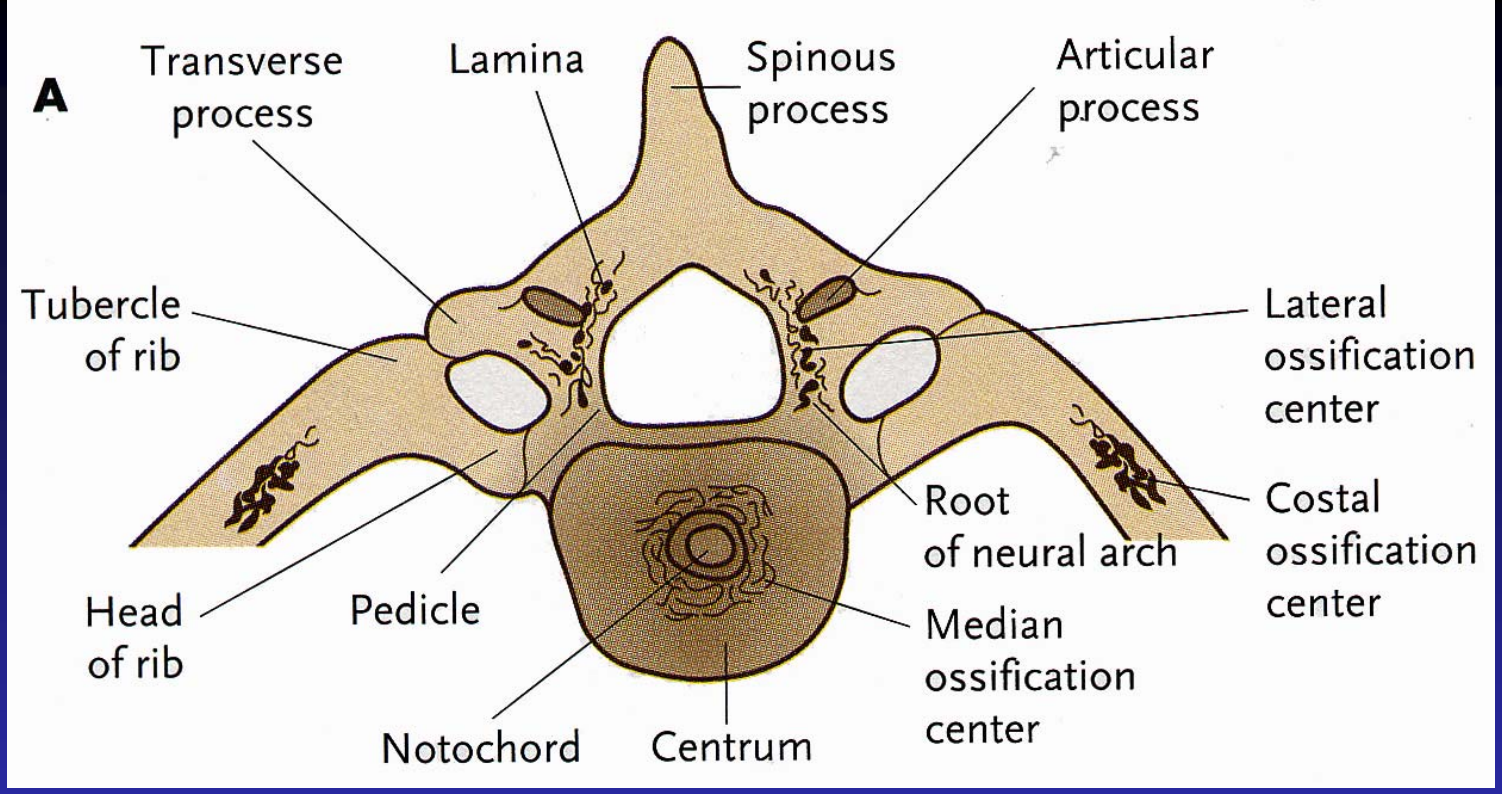
The nucleus pulposus is surrounded by fibrous tissue (concentric) - anulus fibrosus

Development of Vertebra



Sclerotome cells surround the neural tube - forms the vertebral arch - fuses ventrally with the centrum

Sclerotome cells in the body wall form the costal processes, the ribs



Primary ossification centers

1 - Surrounding the notochord in the centrum

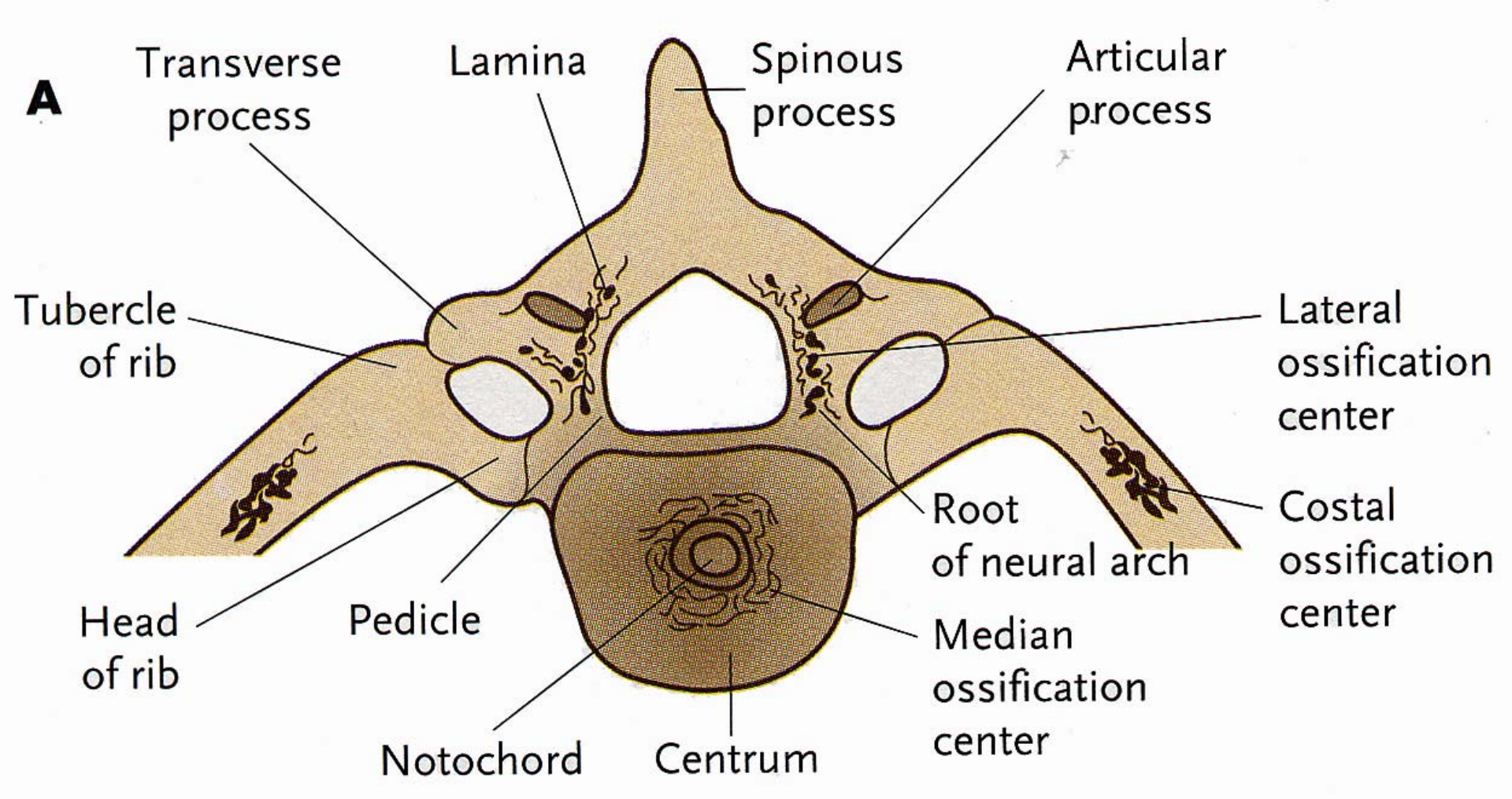
2 - Lateral to the neural tube in the vertebral arch

Secondary ossification centers

1 - anular epiphyses - between body and intervertebral disc)

2 - tip of spinous process

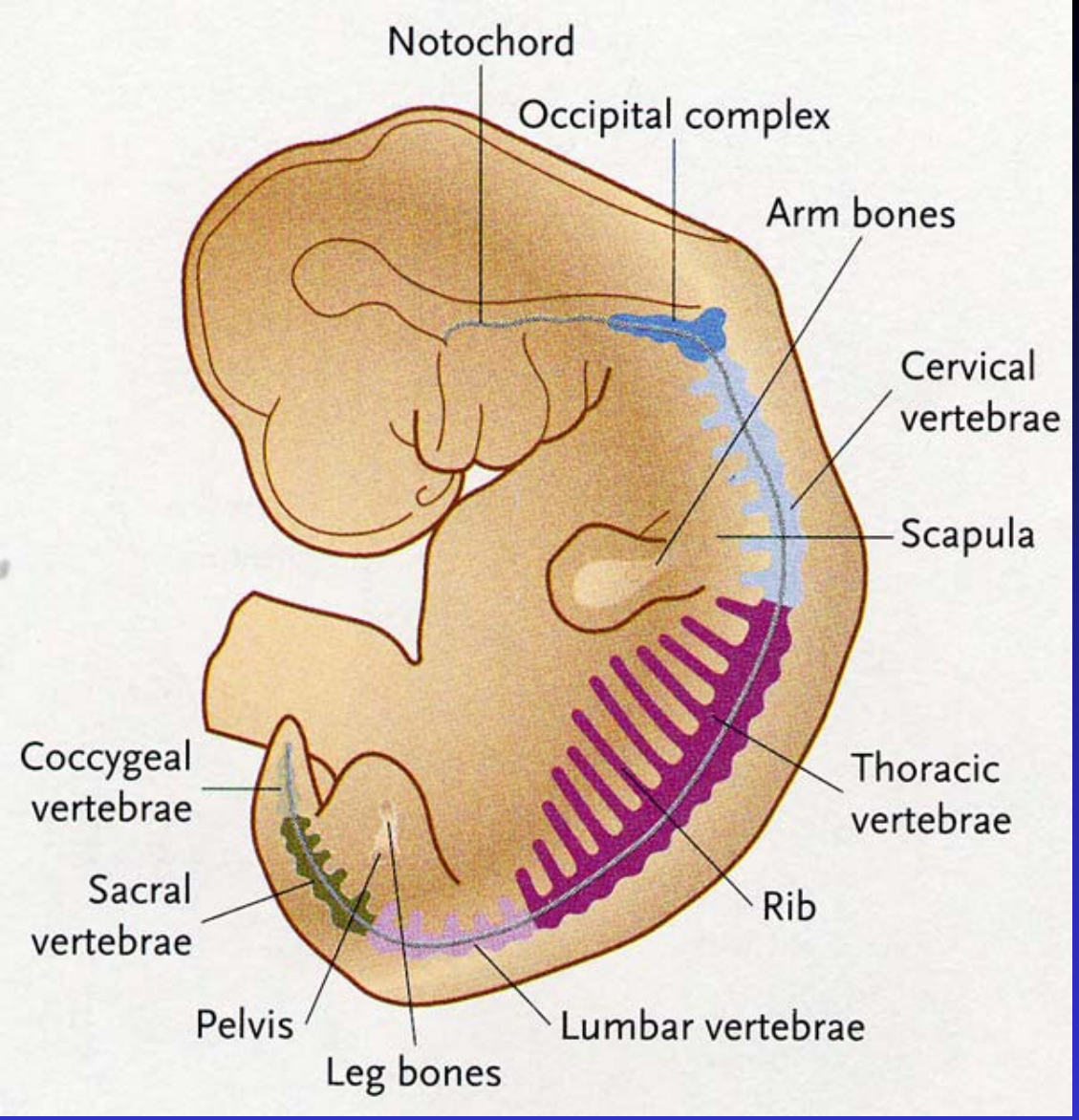
3 – tips of transverse processes

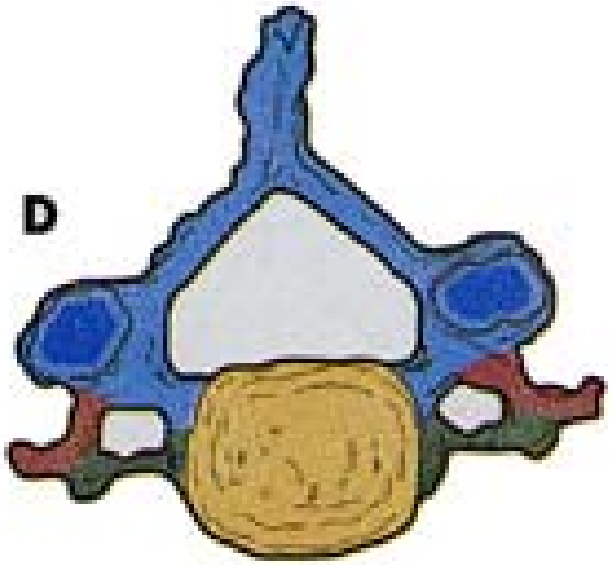


Joints: neurocentral joint - centrum / vertebral arch - allows for growth of the spinal cord until 5 years

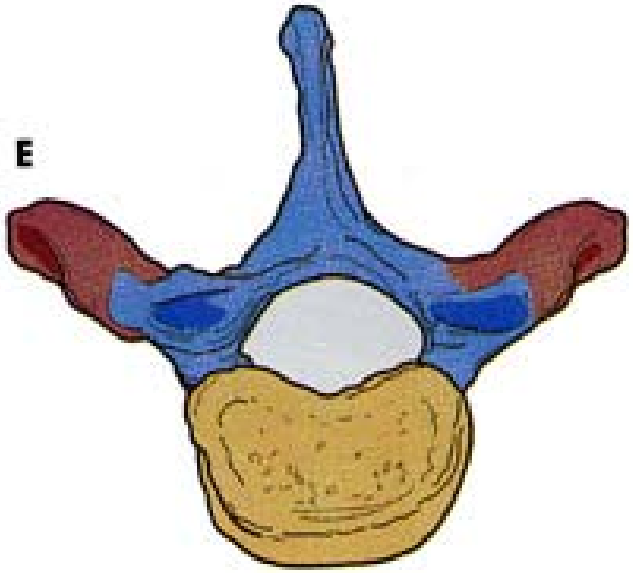
Costovertebral synchondrosis - vertebral arch / ribs

synovial joint

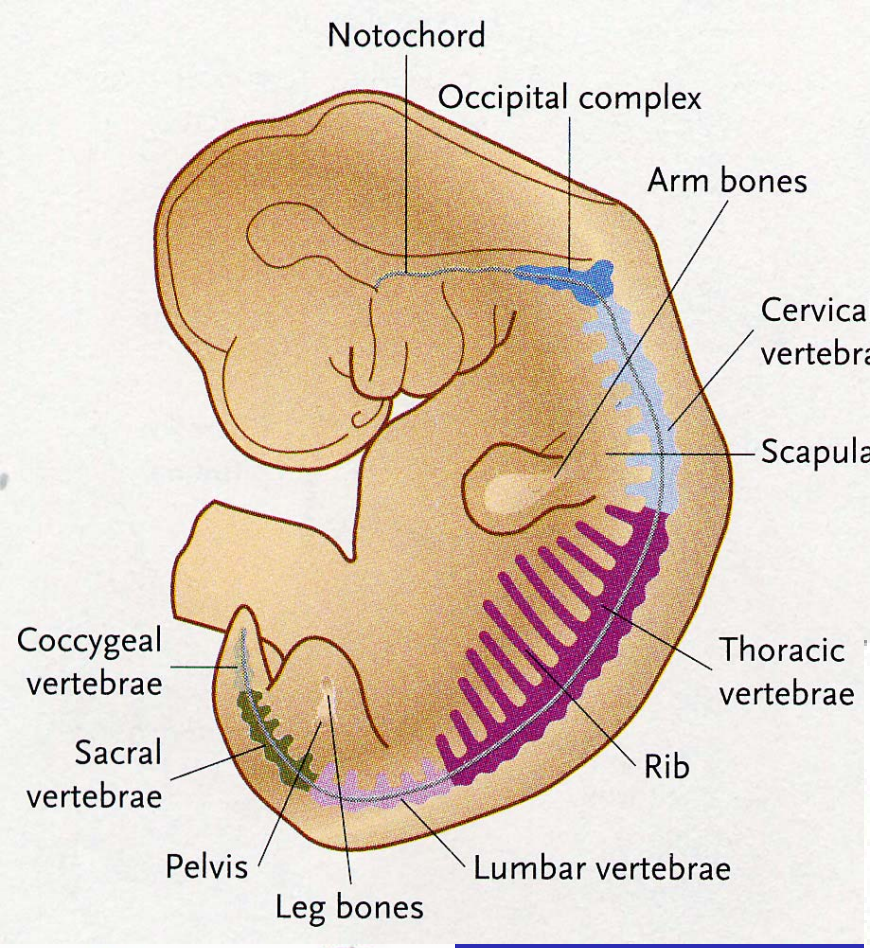




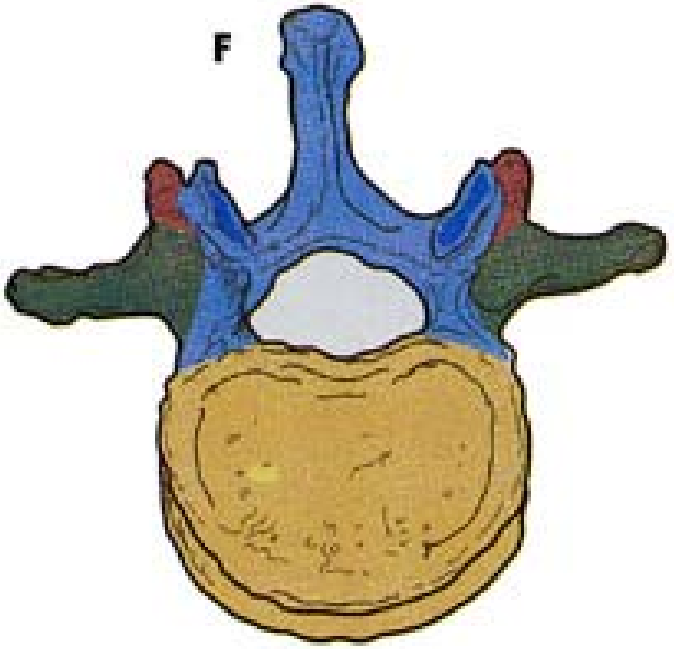
Cervical

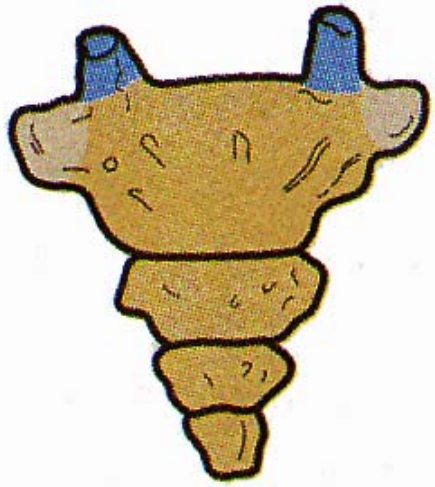


Thoracic



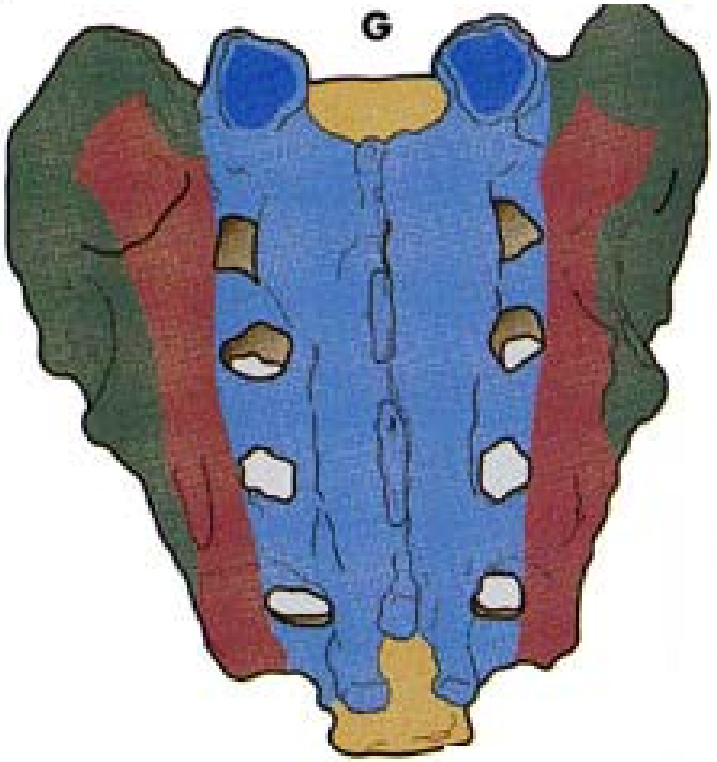
Lumbar





Sacrum

Coccyx

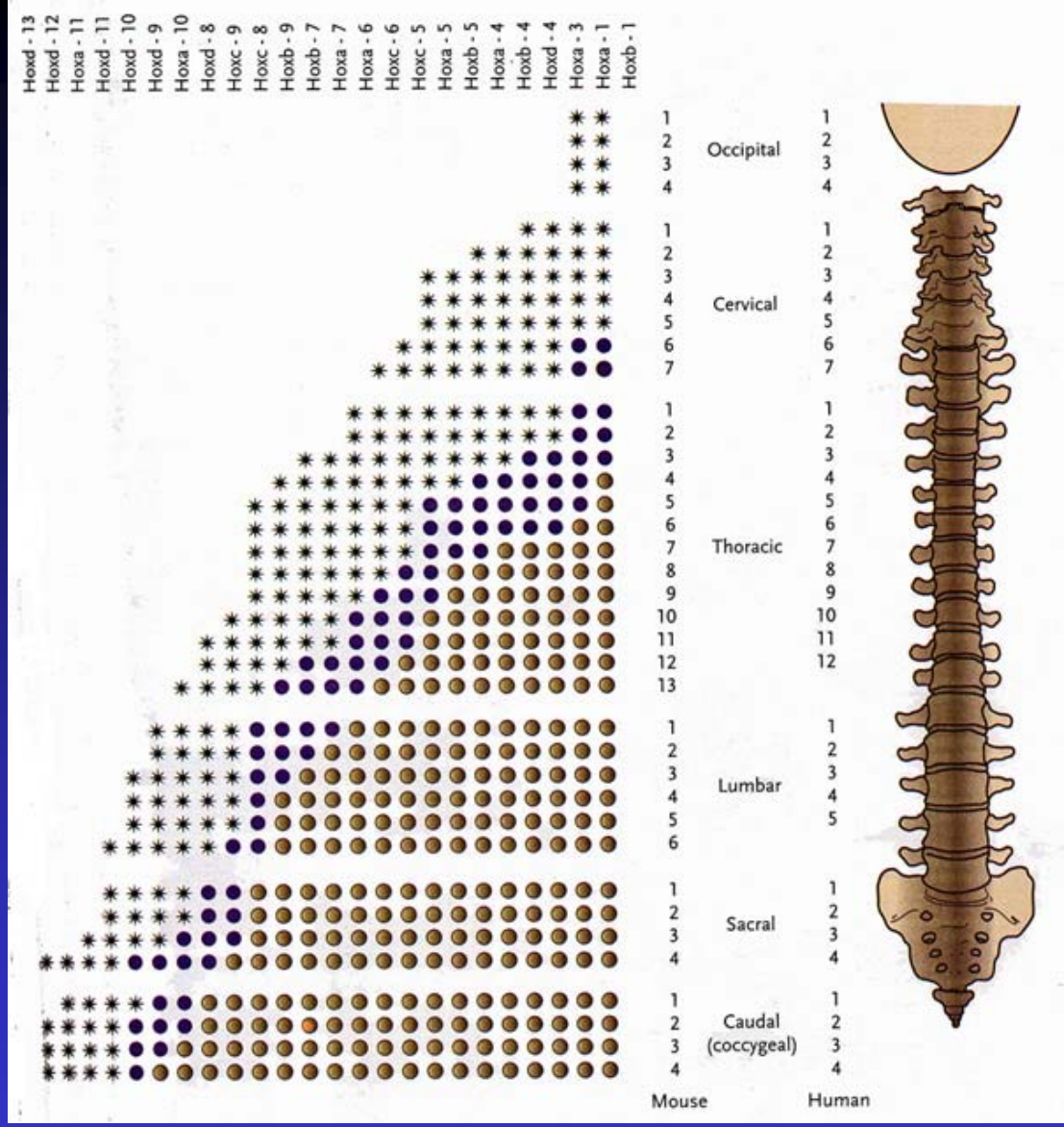


Hox Genes

Regional characteristics of vertebrae are specified by unique combinatorial expression of Hox genes

Homeotic transformations of vertebrae have been described

Retinoic Acid can cause cranial to caudal segment shifts



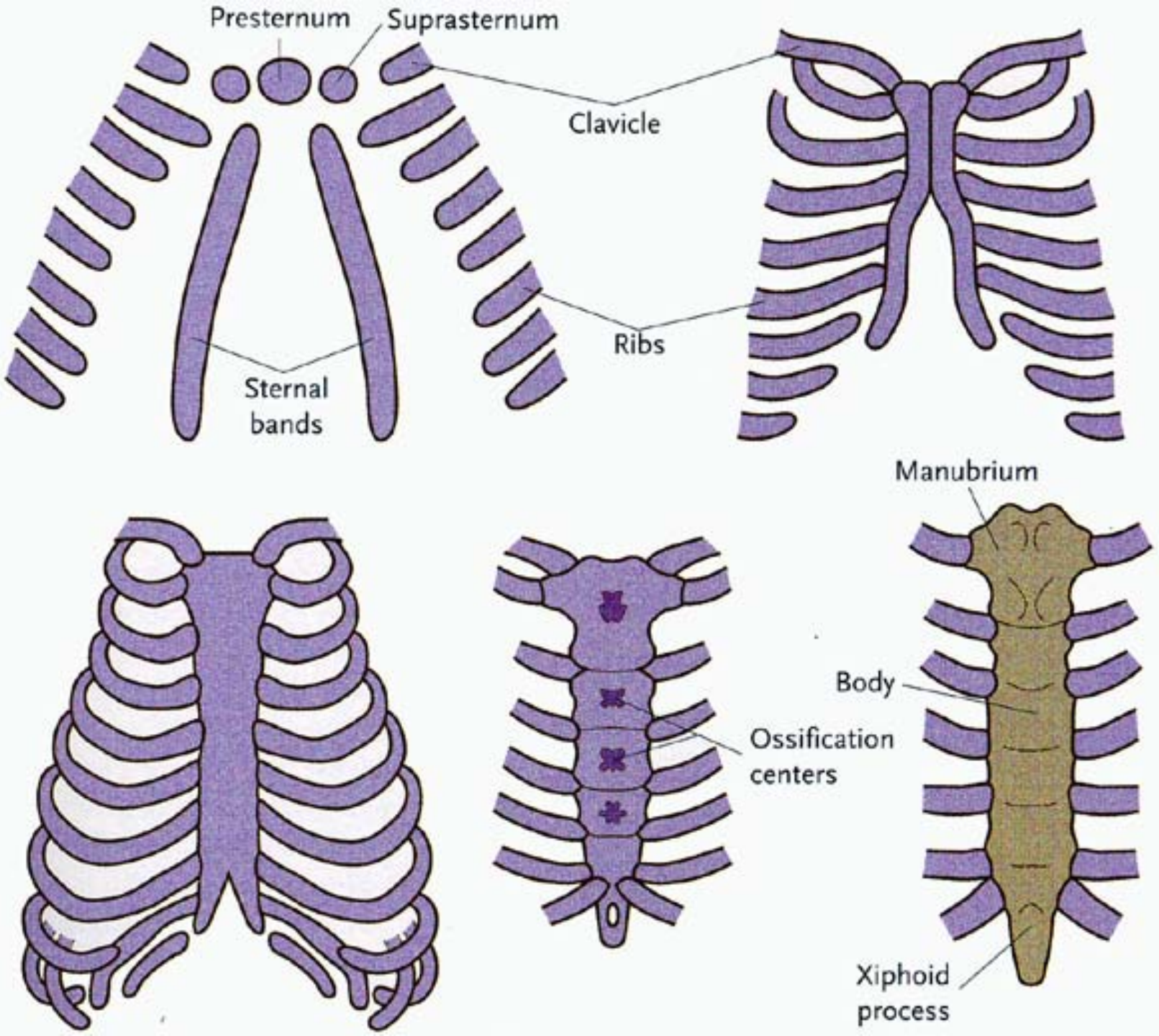
Ribs / Sternum

Sclerotome cells in the body wall form the costal processes that form the ribs

The Sternum forms from a pair of ventral cartilagenous bands that converge at the ventral midline

Converged sternal bands undergo secondary segmentation – similar to joint formation

Sternal segments later fuse


Presternum
Suprasternum
Clavicle
Ribs
Sternal bands
Manubrium
Body
Ossification centers
Xiphoid process

Muscle Development

Muscle types – Skeletal, Cardiac, Smooth

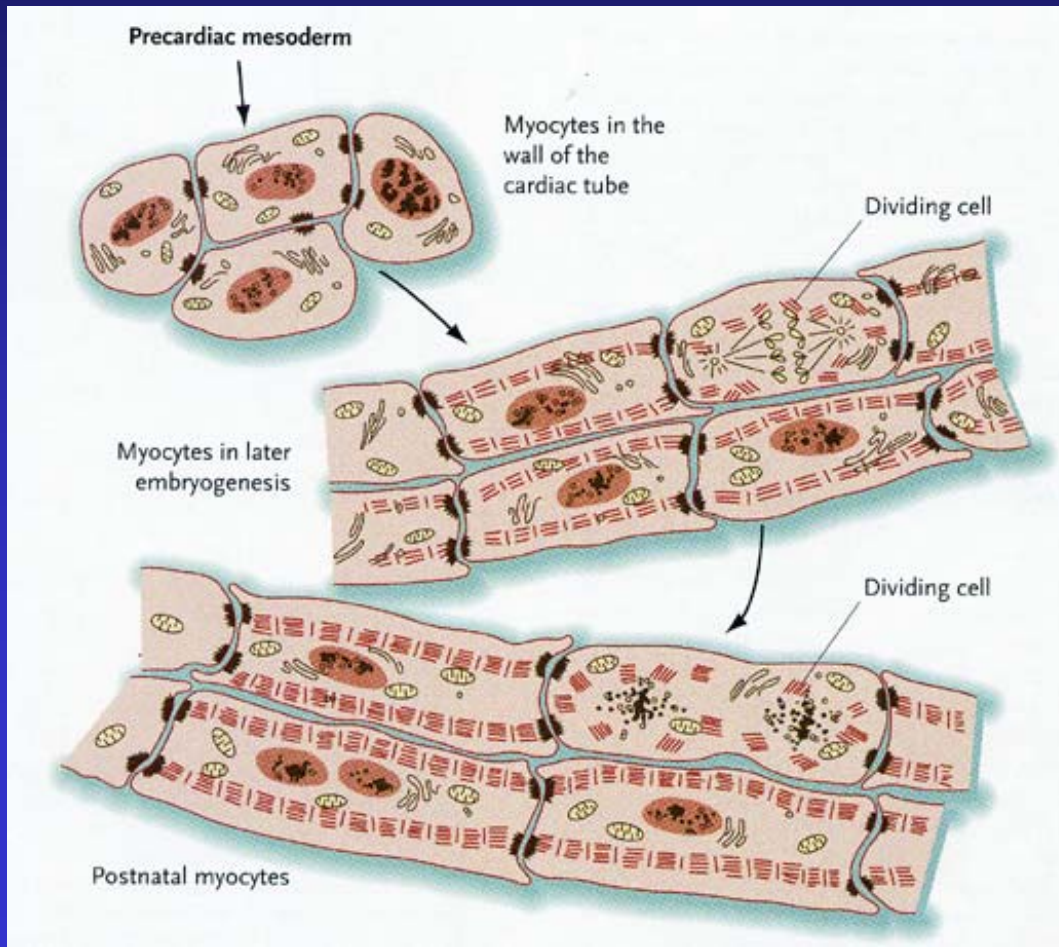
Smooth muscle : Derived from splanchnic mesoderm surrounding gut. Cellular elongation without cell fusion

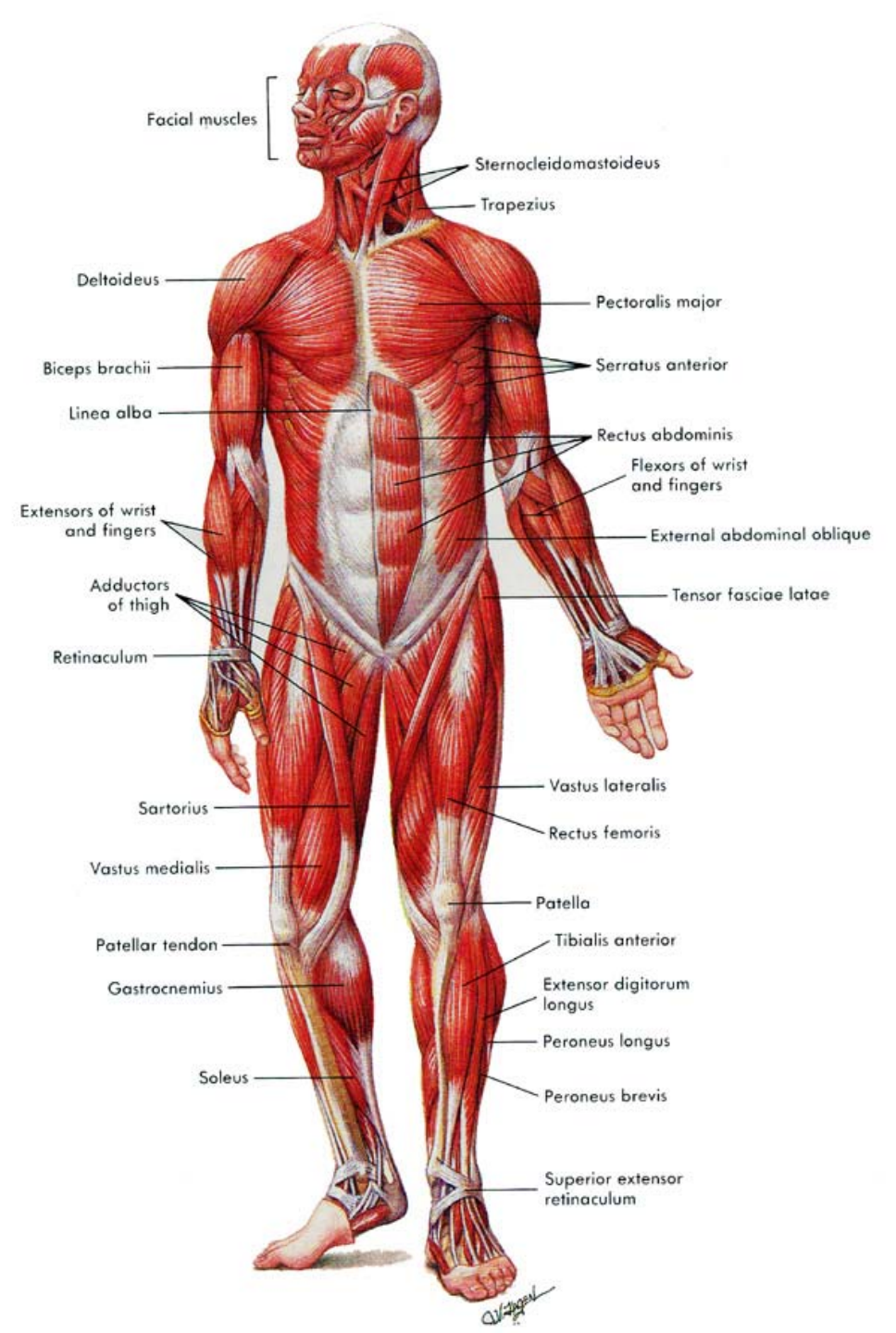
Cardiac muscle

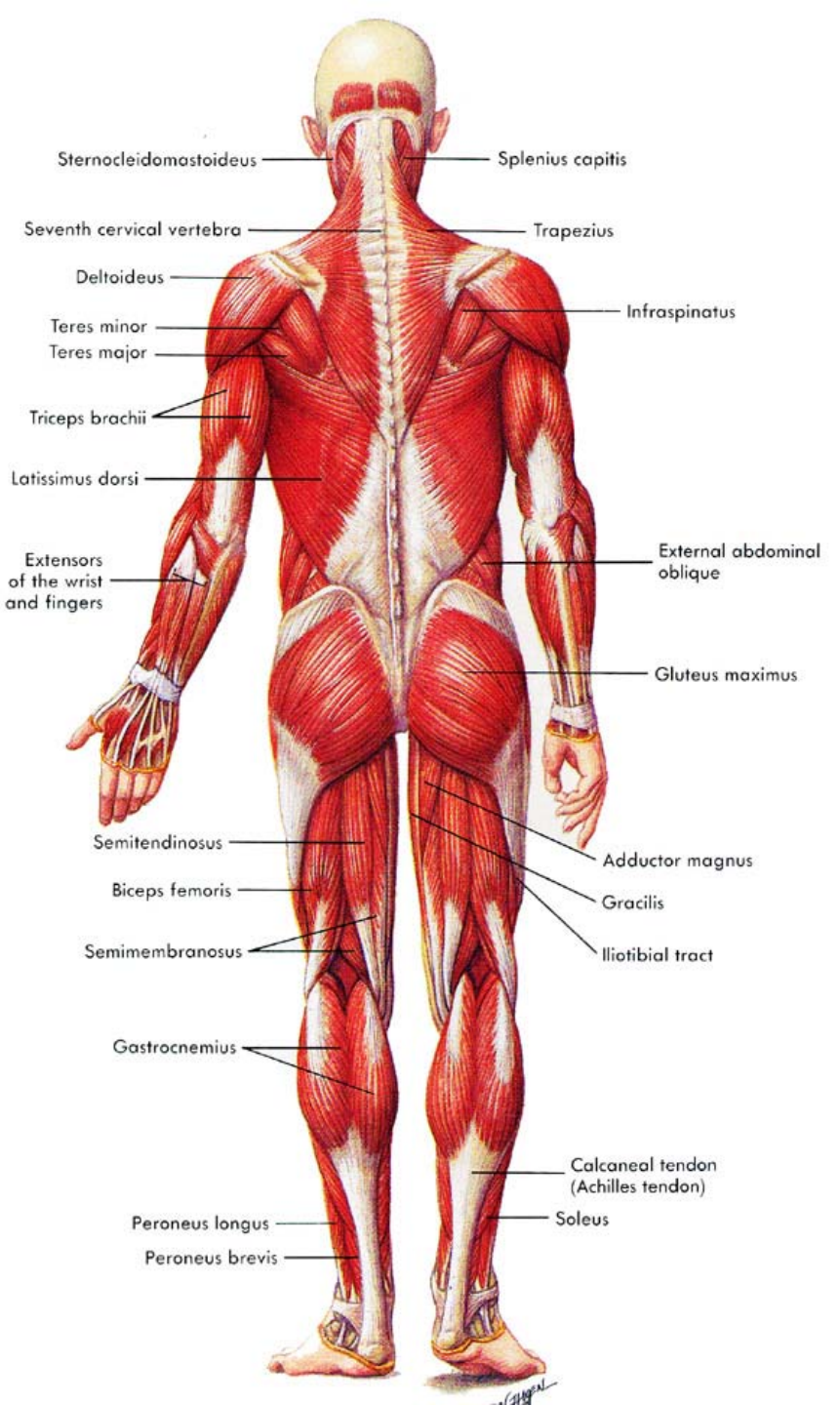
Derived - splanchnic mesoderm

Myoblasts adhere but do not fuse

Form intercalated discs




Facial muscles
Sternocleidomastoideus
Trapezius
Deltoideus
Pectoralis major
Biceps brachii
Serratus anterior
Linea alba
Rectus abdominis
Flexors of wrist and fingers
Extensors of wrist and fingers
External abdominal oblique
Adductors of thigh
Tensor fasciae latae
Retinaculum
Vastus lateralis
Sartorius
Rectus femoris
Vastus medialis
Patella
Patellar tendon
Tibialis anterior
Gastrocnemius
Extensor digitorum longus
Peroneus longus
Soleus
Peroneus brevis
Superior extensor retinaculum


Sternocleidomastoideus
Splenius capitis
Seventh cervical vertebra
Trapezius
Deltoideus
Infraspinatus
Teres minor
Teres major
Triceps brachii
Latissimus dorsi
External abdominal oblique
Extensors of the wrist and fingers
Gluteus maximus
Semitendinosus
Adductor magnus
Biceps femoris
Gracilis
Semimembranosus
Iliotibial tract
Gastrocnemius
Calcaneal tendon (Achilles tendon)
Peroneus longus
Soleus
Peroneus brevis

Skeletal Muscle

Head region skeletal musculature
- Derived from head mesenchyme
- Migration from the cranial somitomeres

Trunk region skeletal musculature
- Myoblasts derived from somites
- Migration - FGF controlled
- Spindle shaped cells - line up and fuse
- Multinucleated syncitium
- Myofibrils with cross-striations - actin-myosin

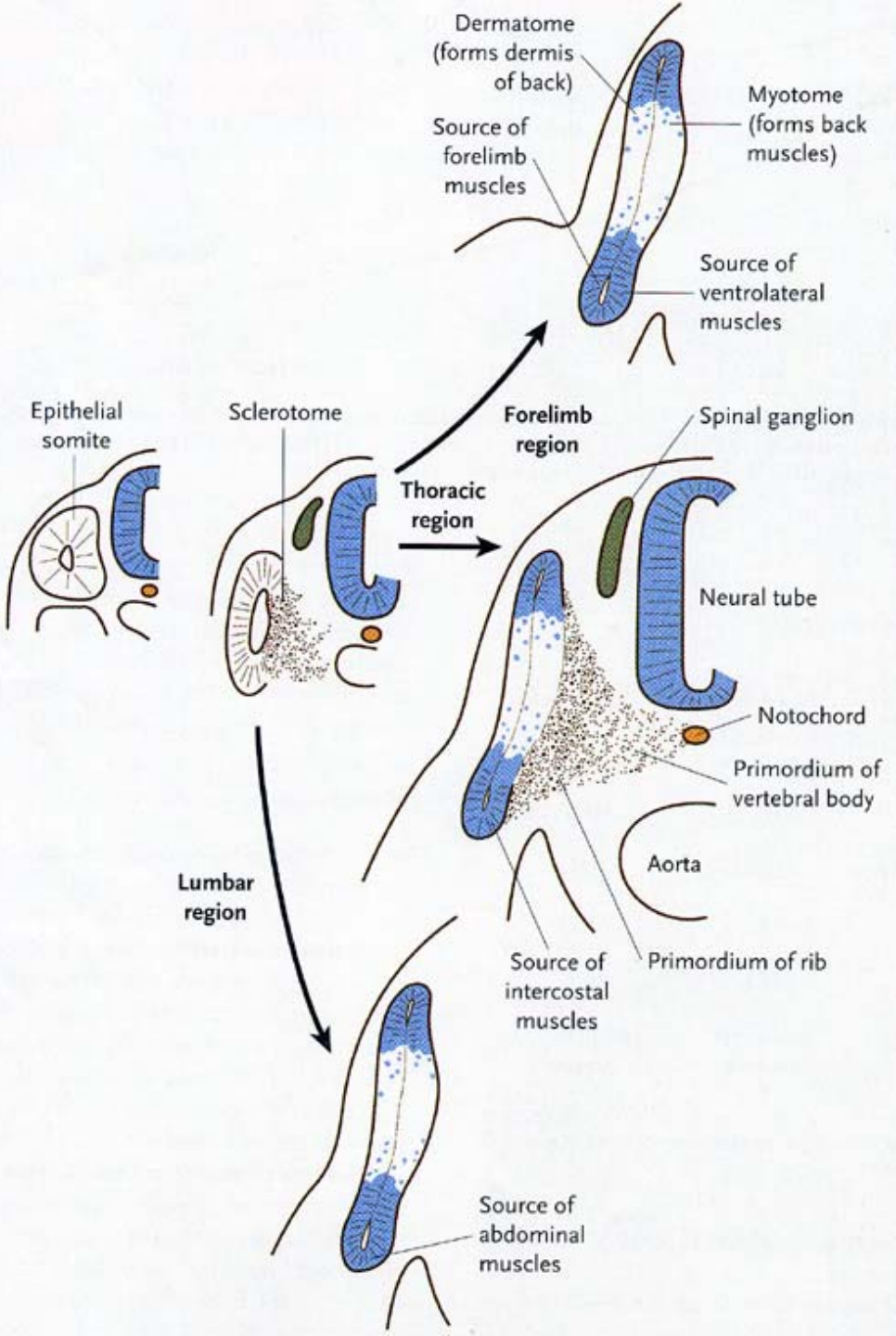
Region-Specific myoblast behavior

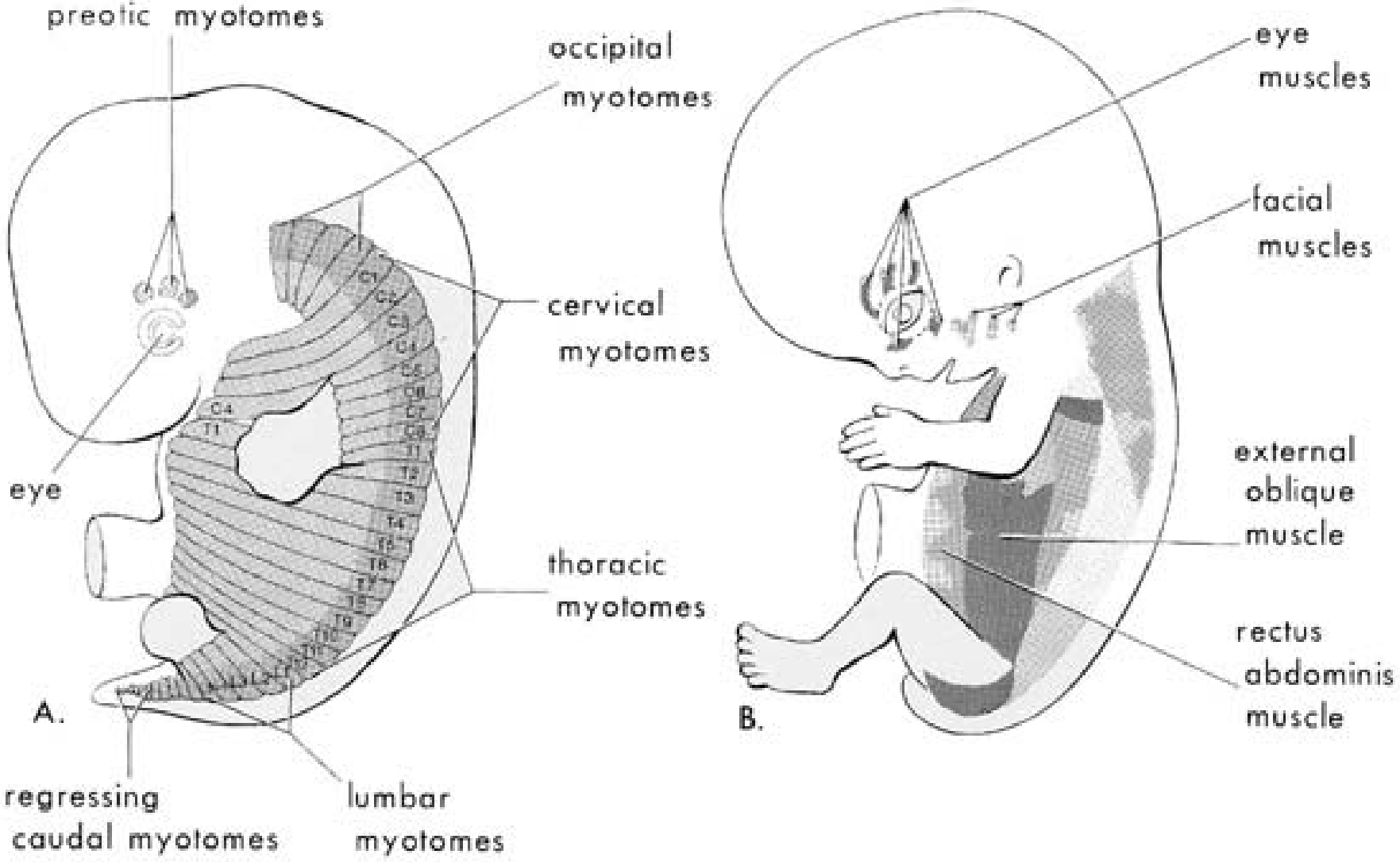
Limb Region – myoblast migration into limb primordia, Differentiation is delayed

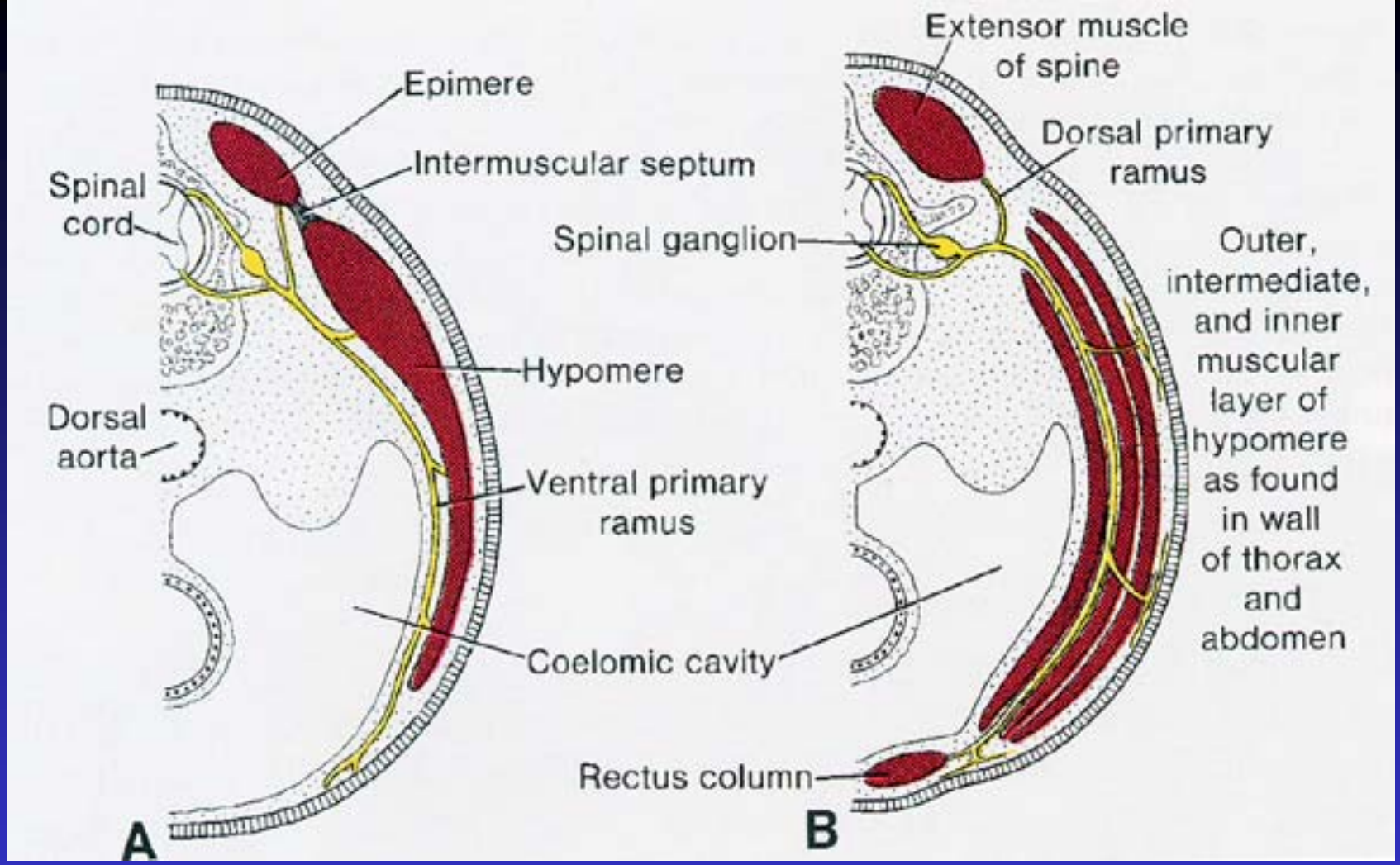
Thoracic Region – myotubes form at the somite – then invade the body wall to form the intercostal muscles

Lumbar Region – myoblast migrate to form the abdominal muscles

Myoblast behavior is controlled by their environment



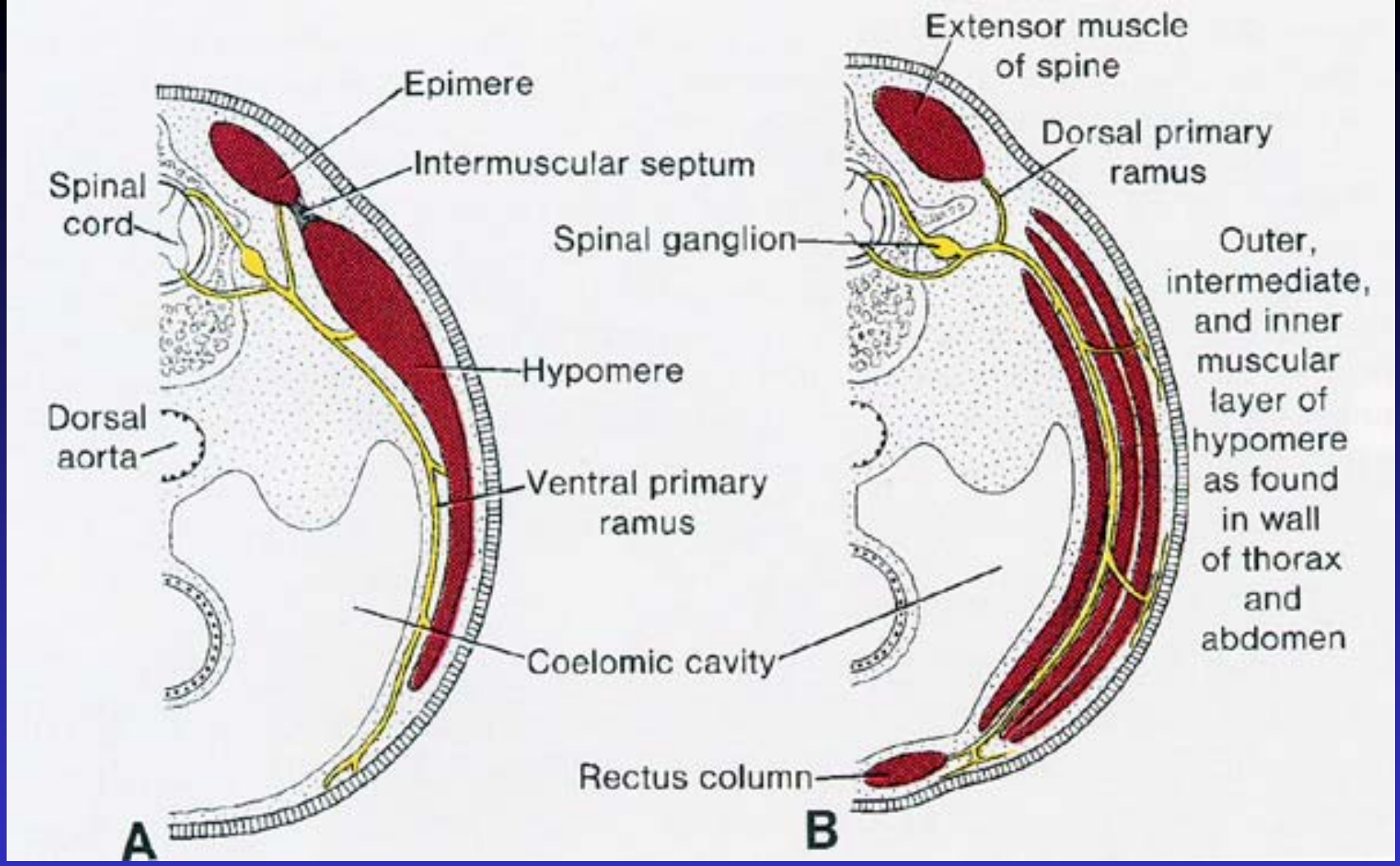

preotic myotomes
occipital myotomes
cervical myotomes
thoracic myotomes
lumbar myotomes
regressing caudal myotomes
eye
A.
eye muscles
facial muscles
external oblique muscle
rectus abdominis muscle
B.



Myotome: two parts

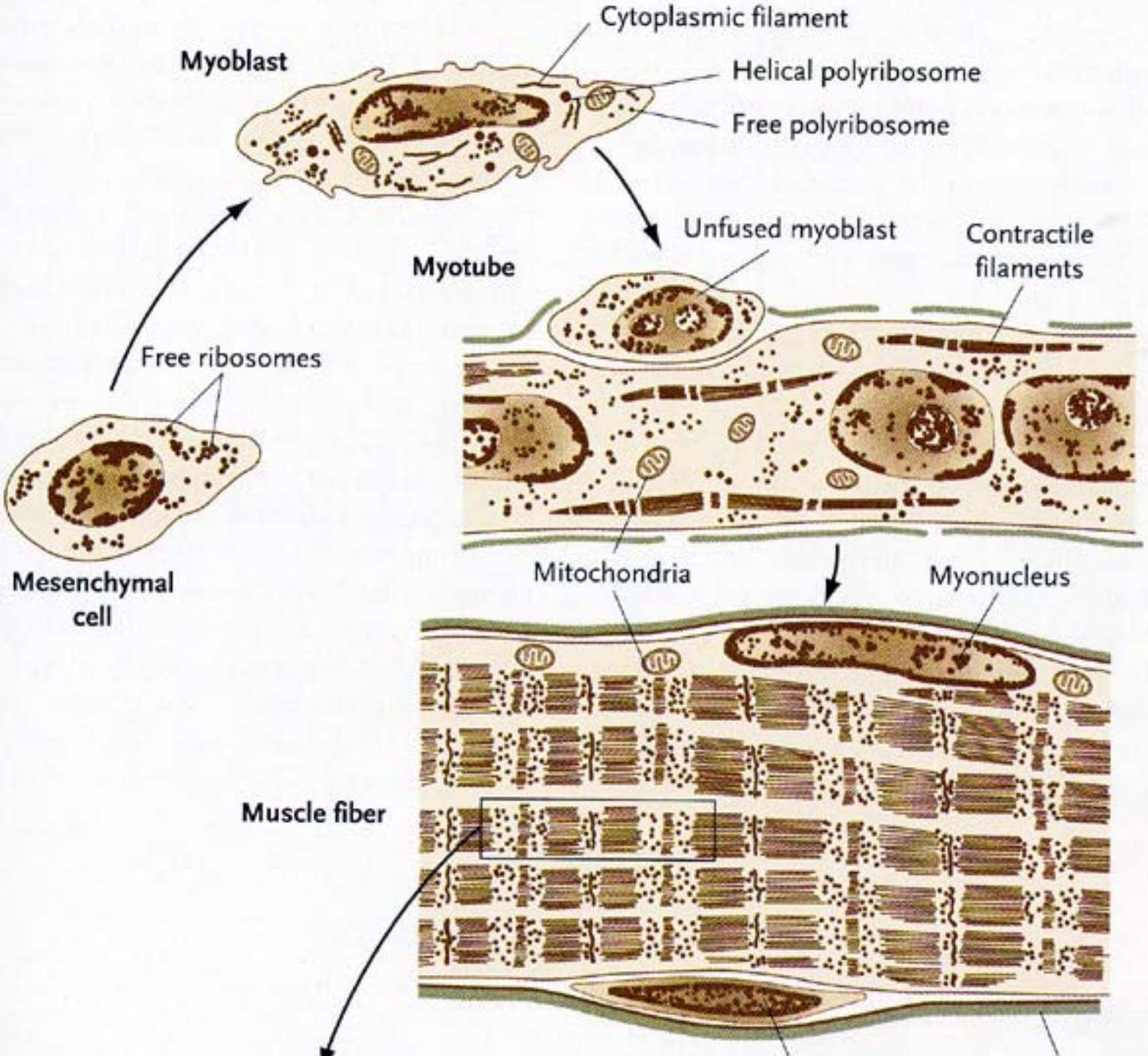
Epimere→Dorsomedial → Extensors of Vertebral column
Hypomere→Ventrolateral → limb/body wall

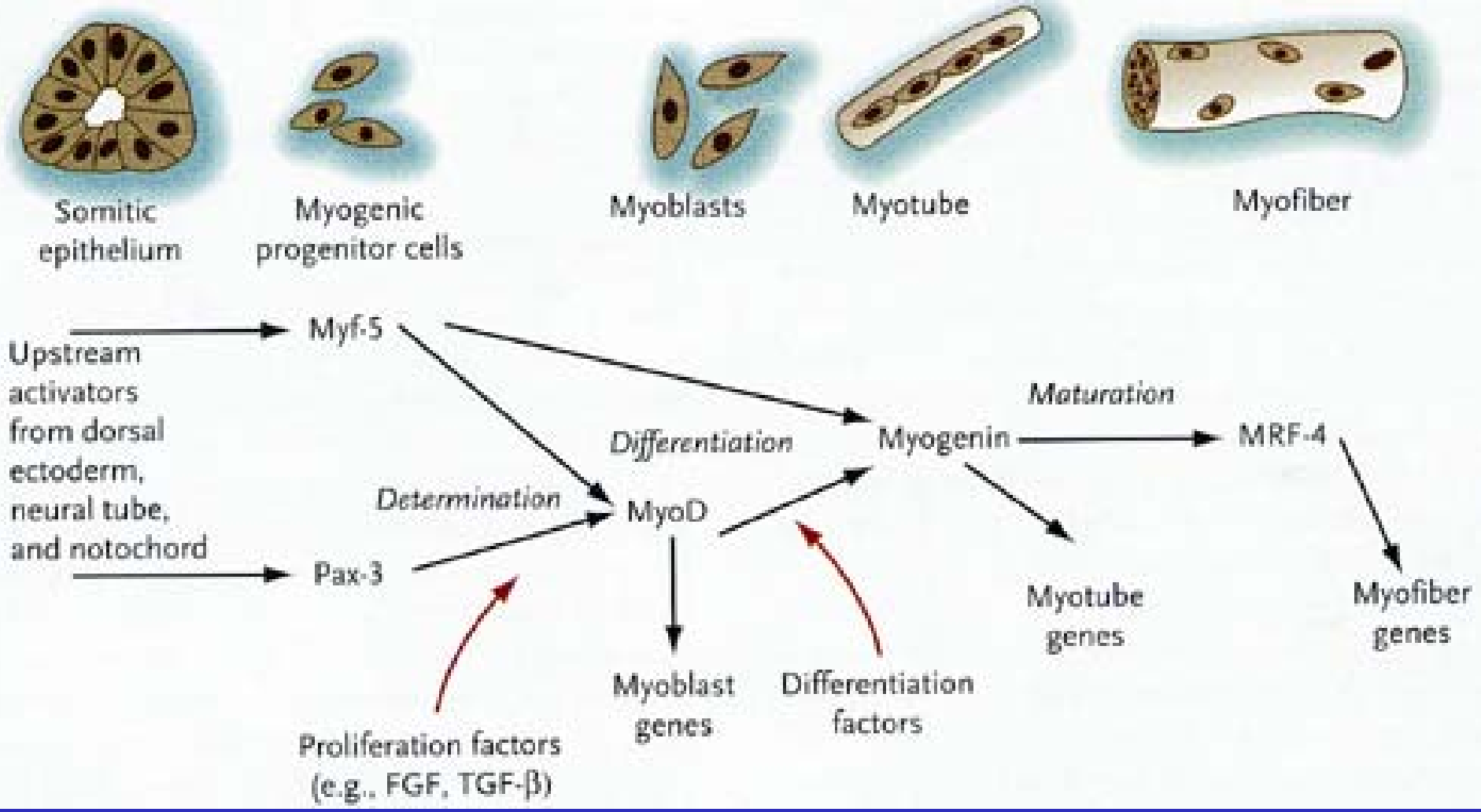
Innervating nerves – Dorsal ramus; Ventral ramus



Thoracic level – 3 myogenic layers – external intercostal, internal intercostal, transversus abdominis muscles

Ribs maintain segmented musculature, elsewhere fusion → large muscle sheets


Cytoplasmic filament
Myoblast
Helical polyribosome
Free polyribosome
Unfused myoblast
Myotube
Contractile filaments
Free ribosomes
Mesenchymal cell
Mitochondria
Myonucleus
Muscle fiber



Determination of myoblast occurs very early

Key regulators – Myf-5, Pax3, MyoD