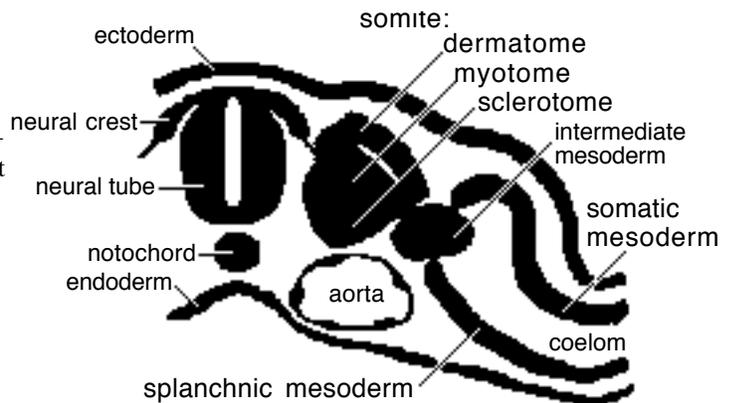


Musculo-Skeletal System (Trunk, Limbs, and Head)

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Bilaterally, paraxial mesoderm become somites and somitomeres. (Somitomeres develop rostral to the notochord in the head. They are like somites, but smaller and less distinctly organized.) The mesoderm comprising each somite differentiates into three regions:

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Mesoderm Regions

Note: Nerves make early connections with adjacent myotomes and dermatomes, establishing a segmental innervation pattern. As myotome/dermatome cells migrate to assume adult positions, the segmental nerve supply must follow along to maintain its connection to the innervation target. (Recurrent laryngeal & phrenic nerves travel long distances because their targets migrated far away.)

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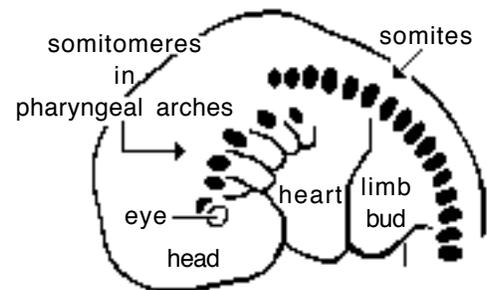
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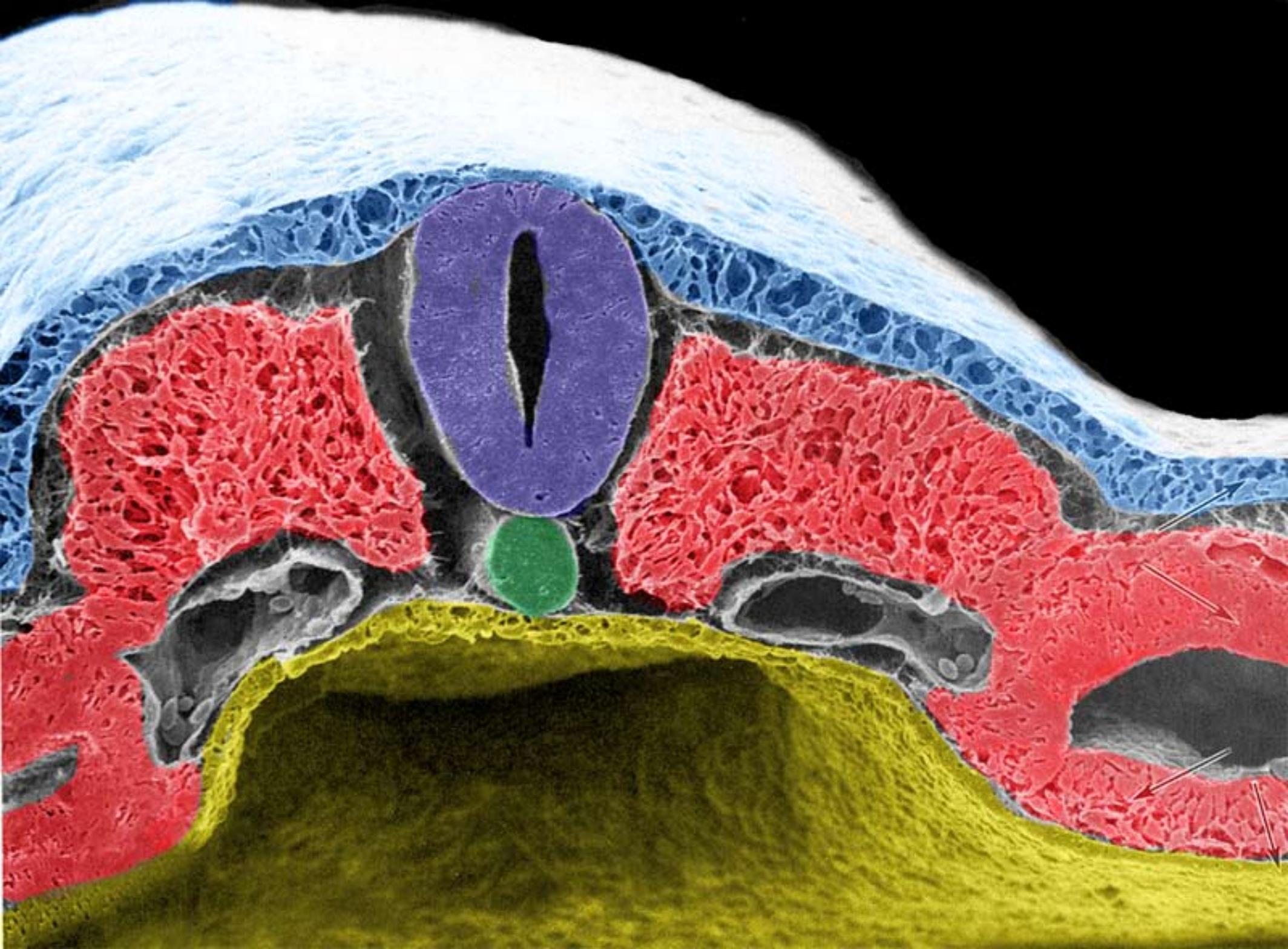
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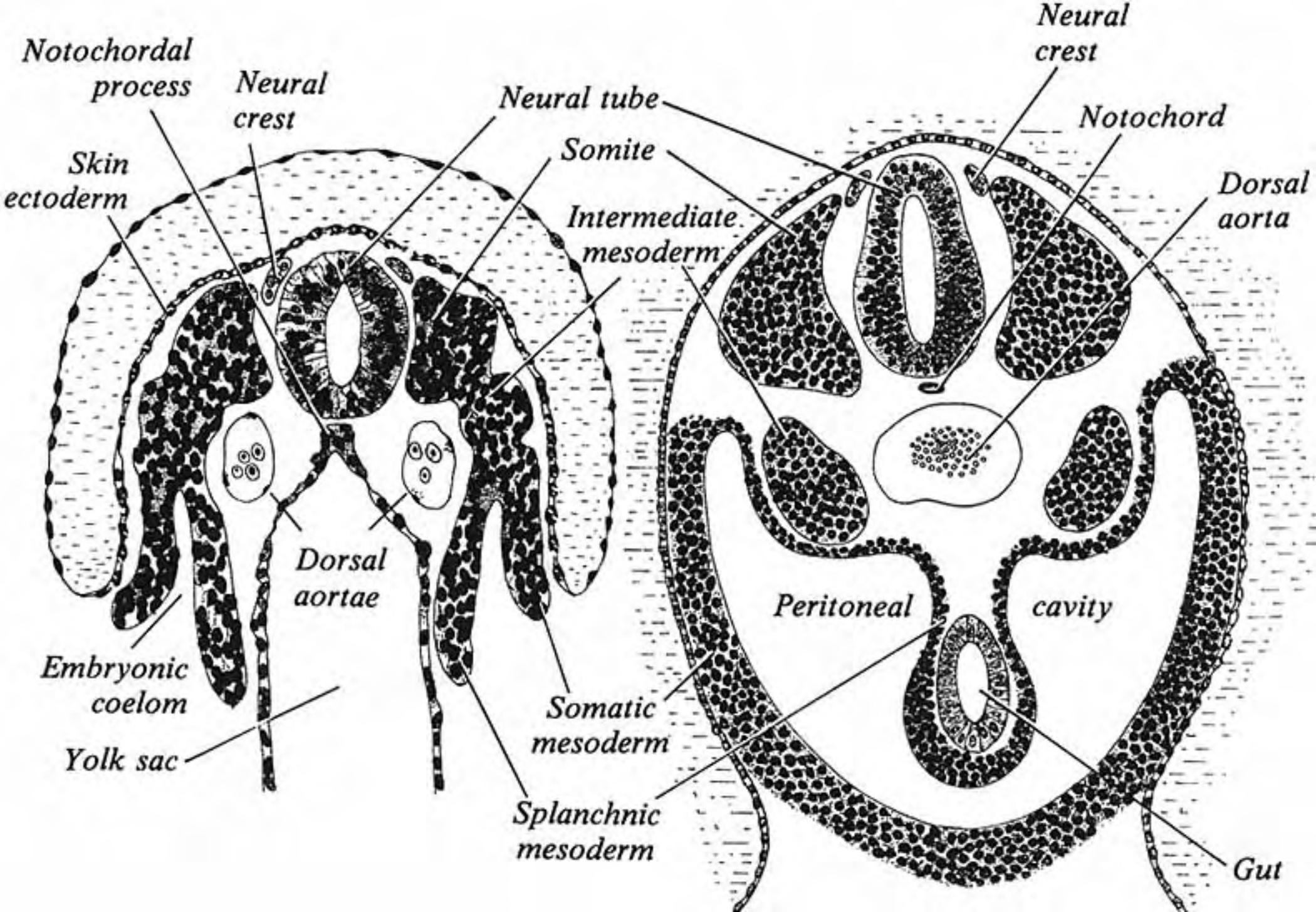
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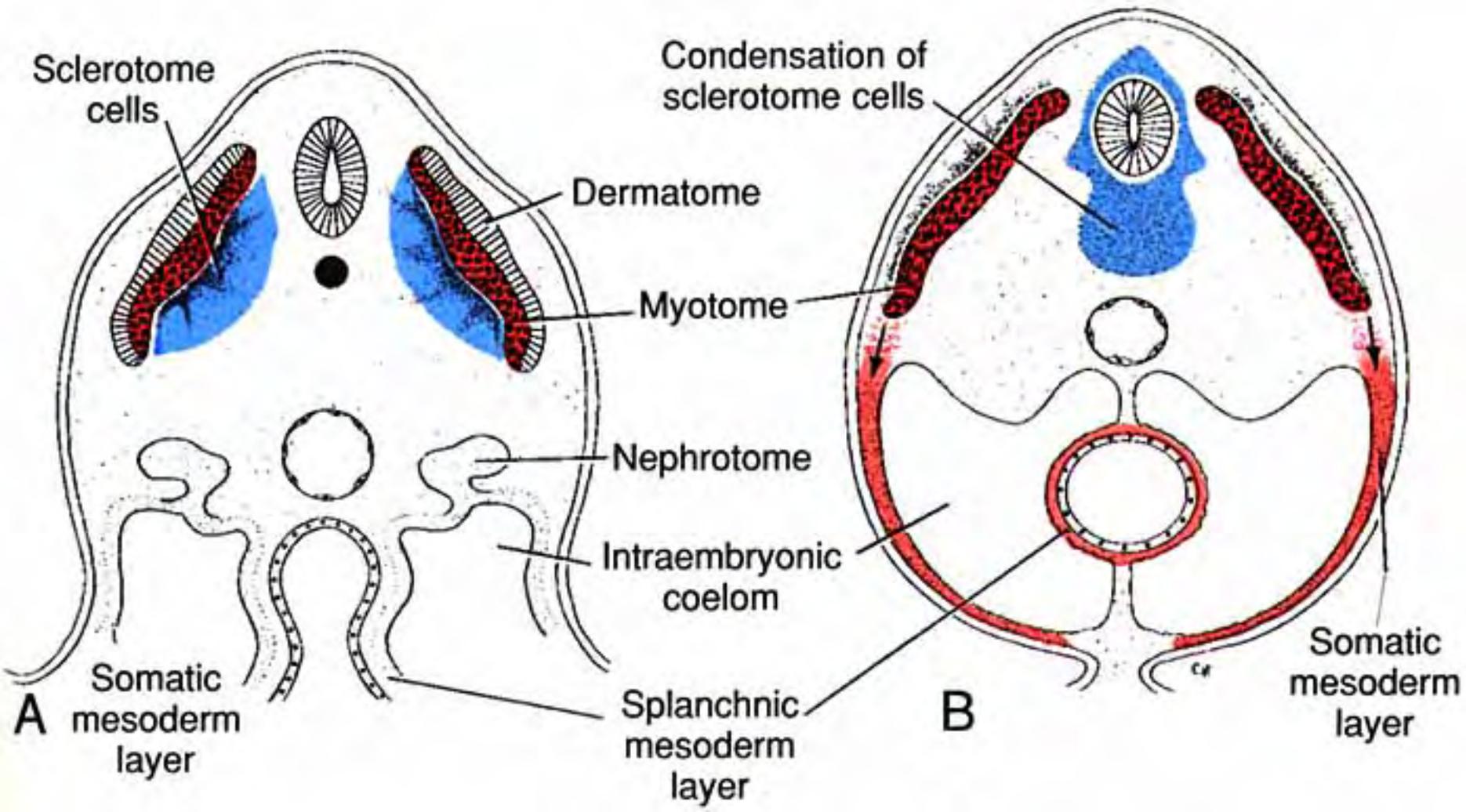


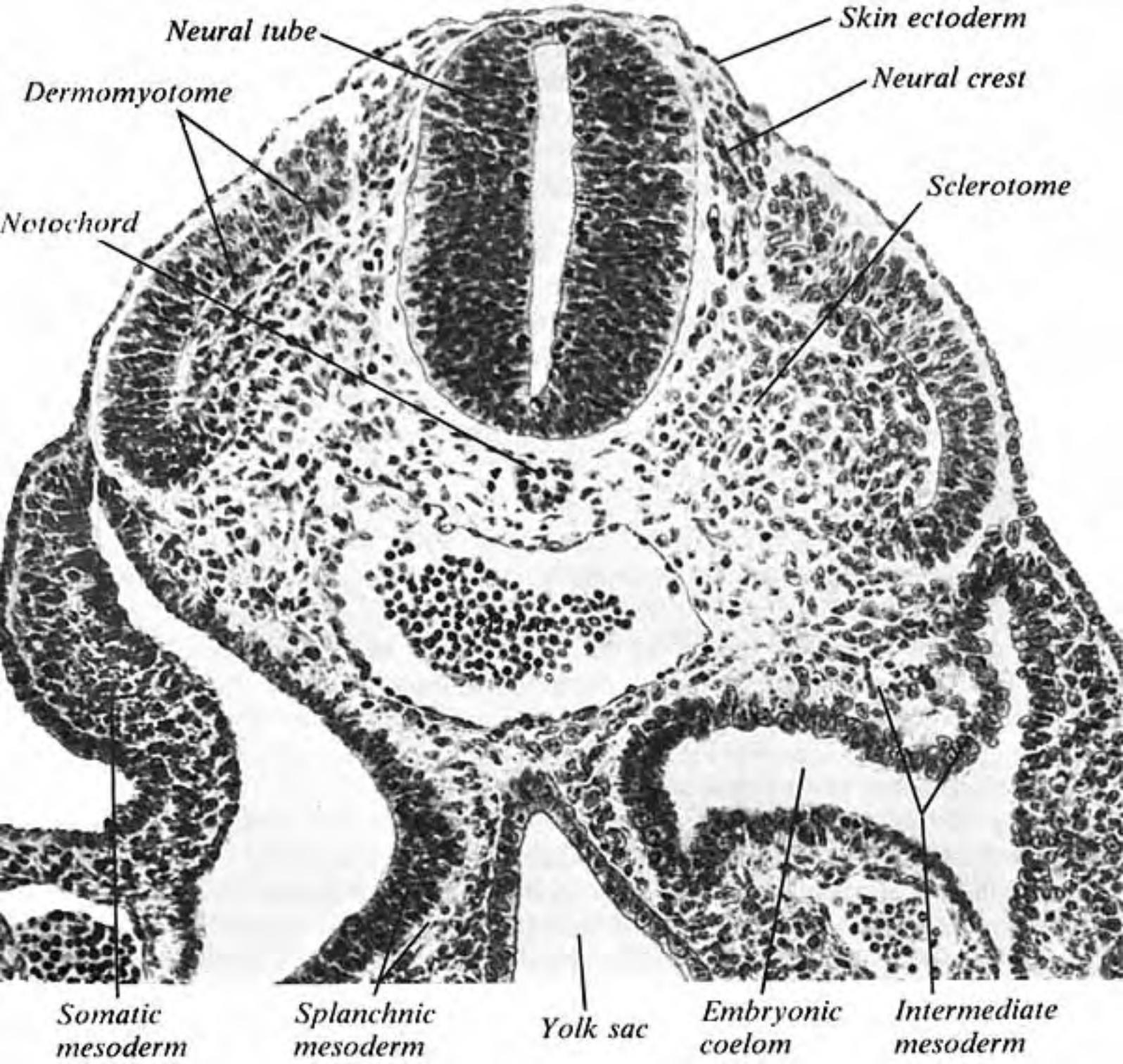
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The INNervation PROBLEM: How to establish connections between nerves and their targets during embryonic development? Would you . . .

- A]** First, have targets migrate to their locations, then have nerves find them.
- B]** First, connect nerves to targets, then have nerves follow targets as they migrate.







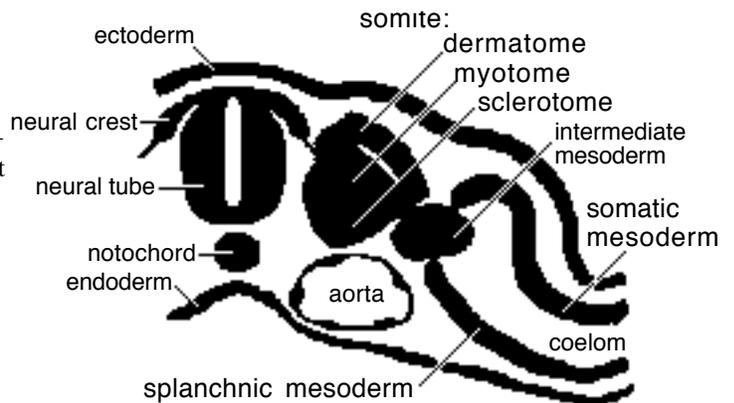


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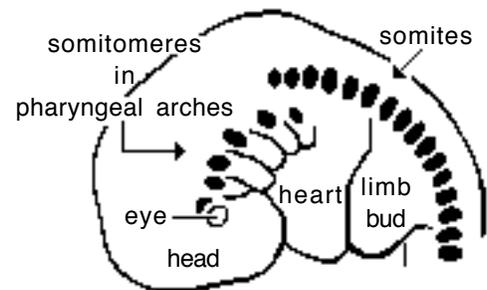
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Free Nerve Endings

Meissner's Corpuscle

Tactile Disks

Sebaceous Gland

End Bulb of Krause

Sweat Gland

Epidermis

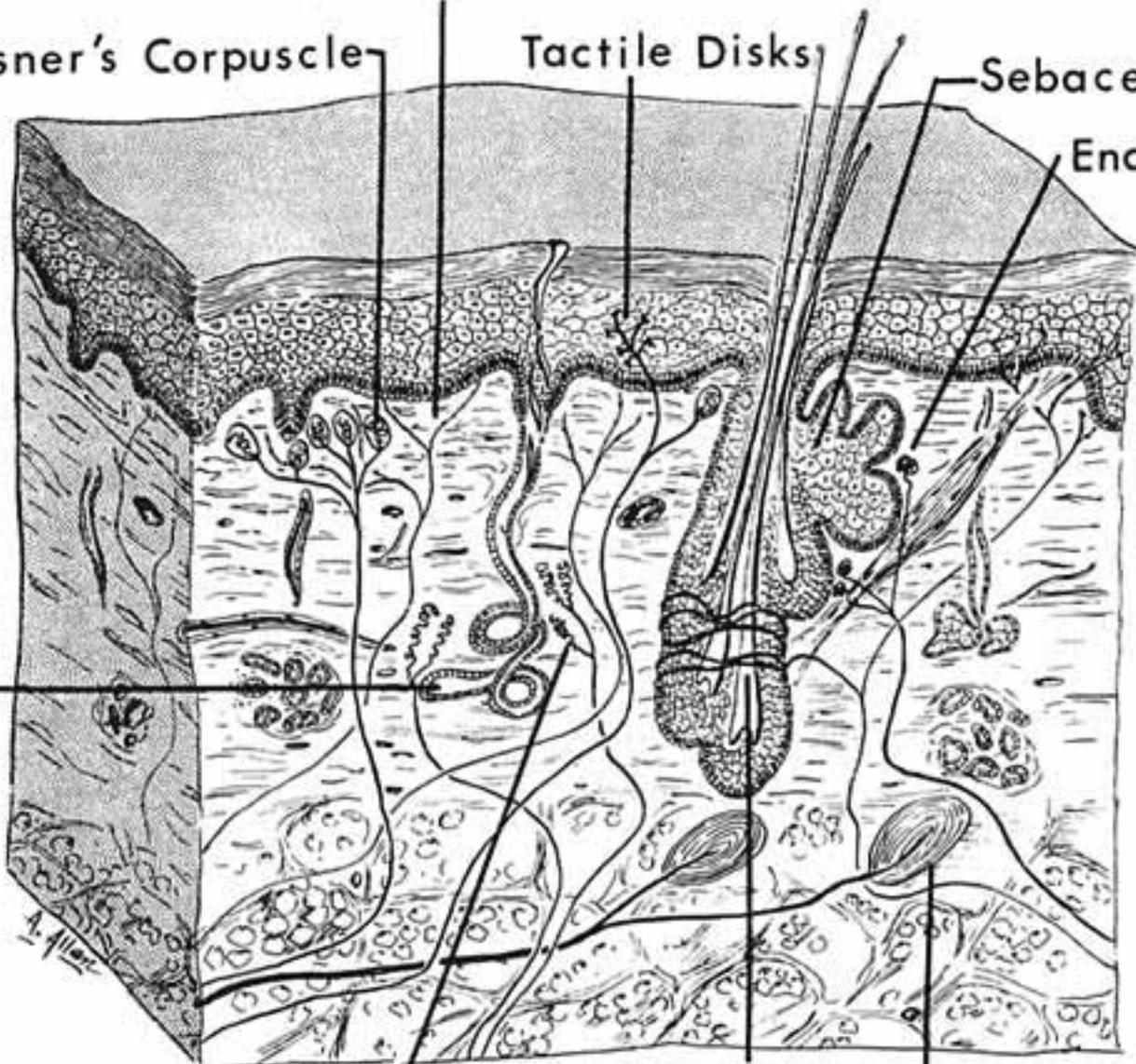
Dermis

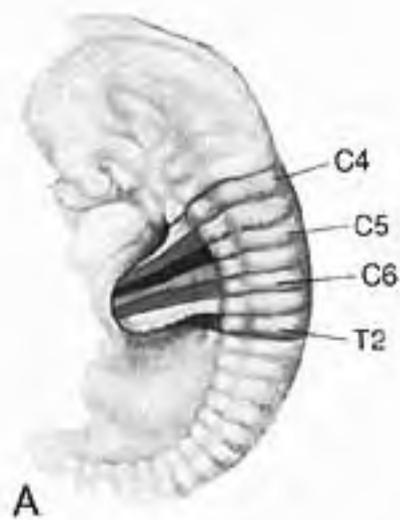
Subcutaneous Fat

Nerve Ending

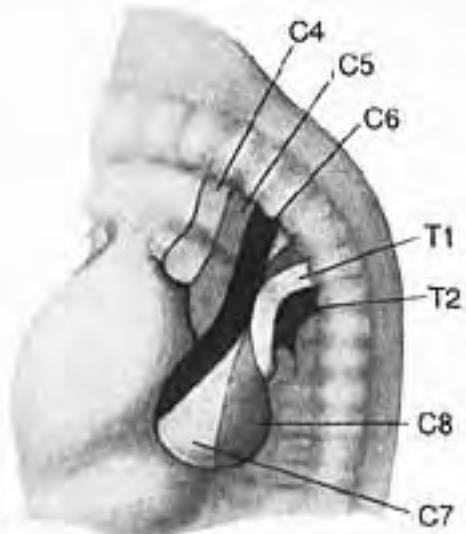
Nerve Ending around Hair Follicle

Pacinian Corpuscle

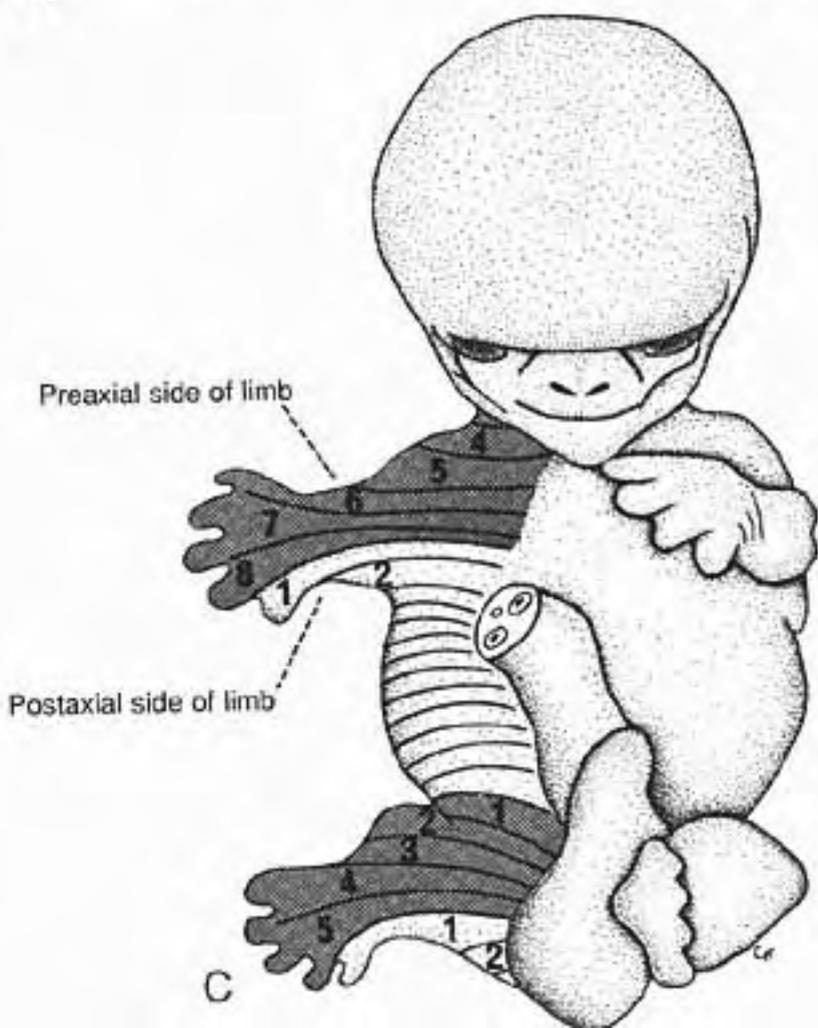




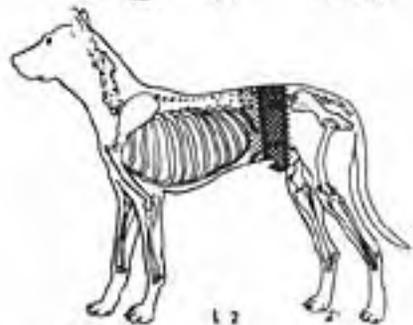
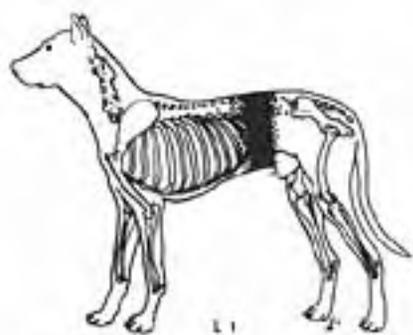
A



B



C

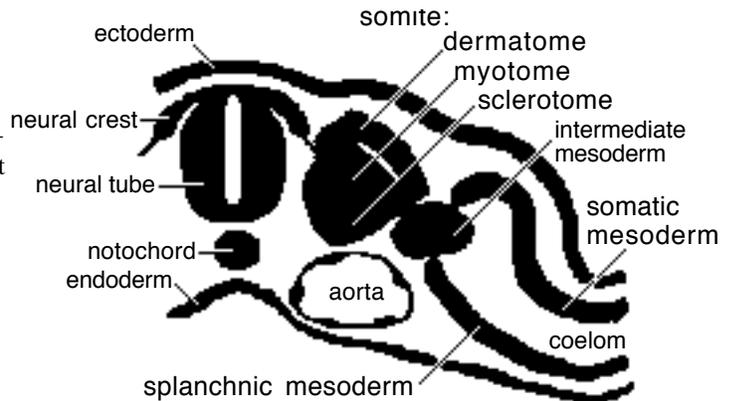


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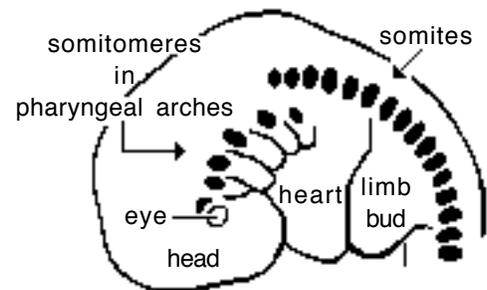
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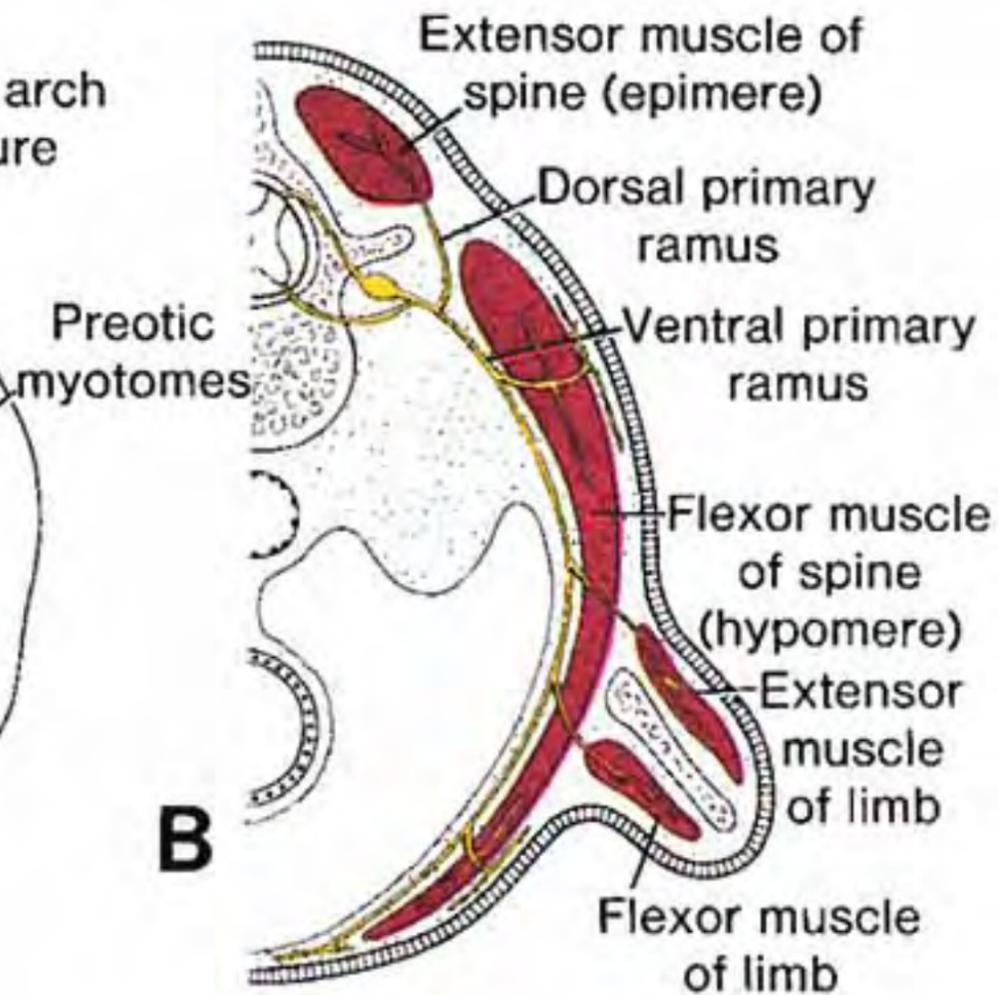
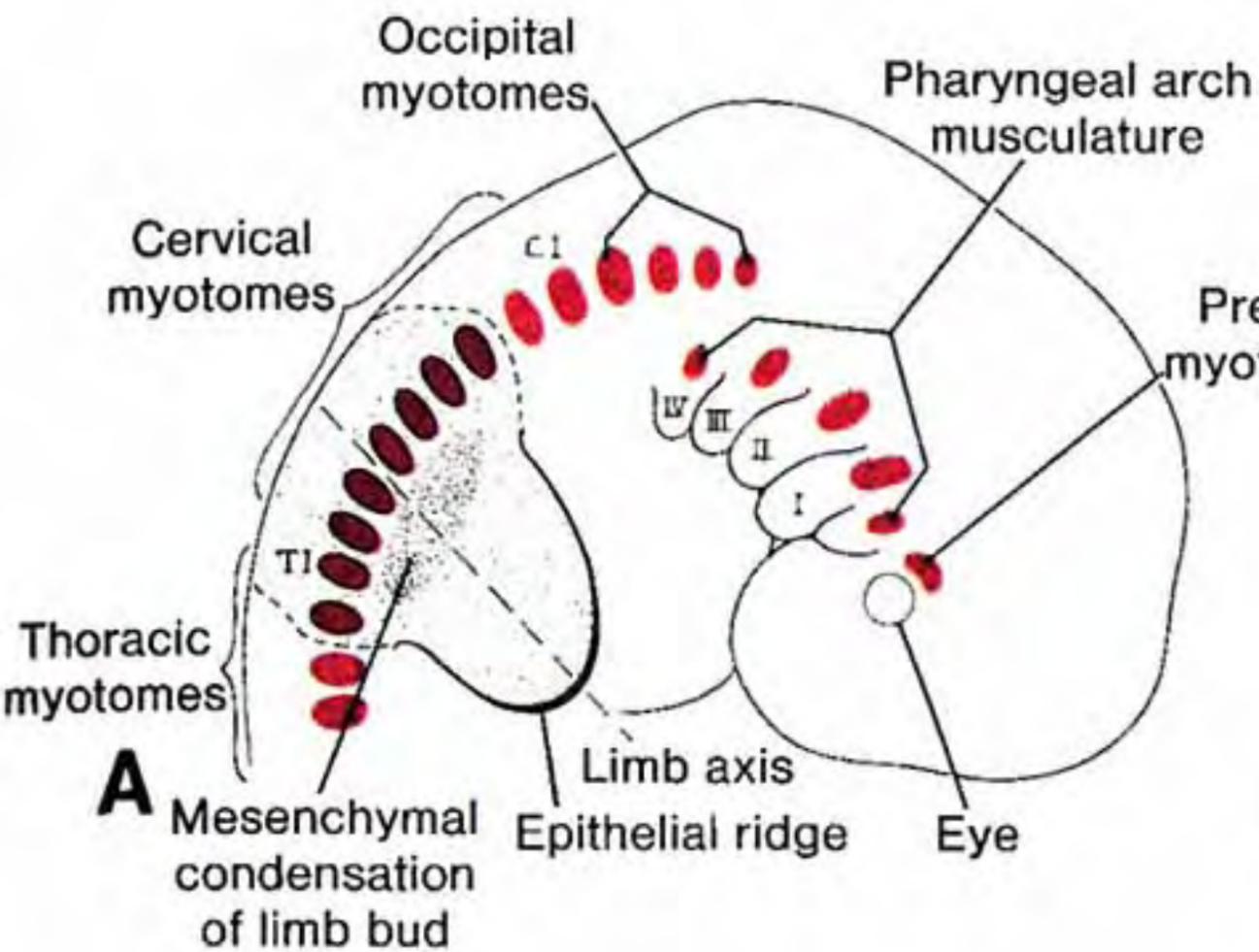
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Thus, most bones are formed endochondrally (ossification of a cartilage model), but bones of the calvaria (top of the skull) and the face are formed intramembranously (ectomesenchyme cells become osteoblasts directly rather than becoming chondroblasts).

Endochondral bone formation:

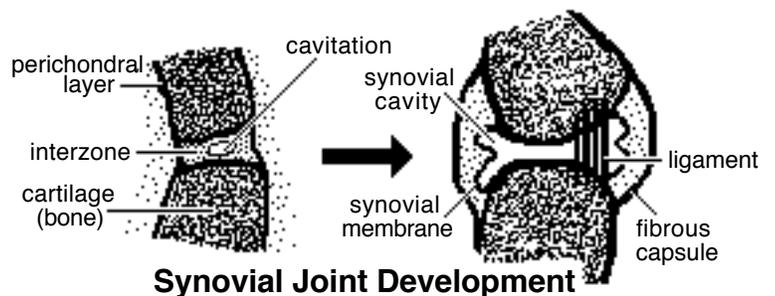
- local mesenchyme undergoes condensation; some cells differentiate into chondroblasts
- chondroblasts secrete matrix to produce a cartilage model of the future bone; the model is surrounded by perichondral fibrous tissue
- the diaphysis of the cartilage model undergoes ossification first; epiphyseal ossification occurs later; physis ossification is postponed until bones stop growing in length.
- overall bone shape is genetically determined; surface irregularities of bone are acquired due to localized tension (stress) produced by ligaments and tendons.

Joints. Condensation of mesenchyme produces an *interzone* region within perichondral tissue connecting adjacent cartilage models of bones. According to the nature of the future joint, the interzone becomes fibrous connective tissue, or fibrocartilage, or a synovial cavity.

Synovial joints form as follows:

- mesenchyme at the center of the interzone undergoes cavitation and the tissue bordering the cavity become *synovial membrane*; uneven expansion of the synovial cavity creates synovial folds (the interzone mesenchyme also forms intra-articular ligaments and tendons where these are present);

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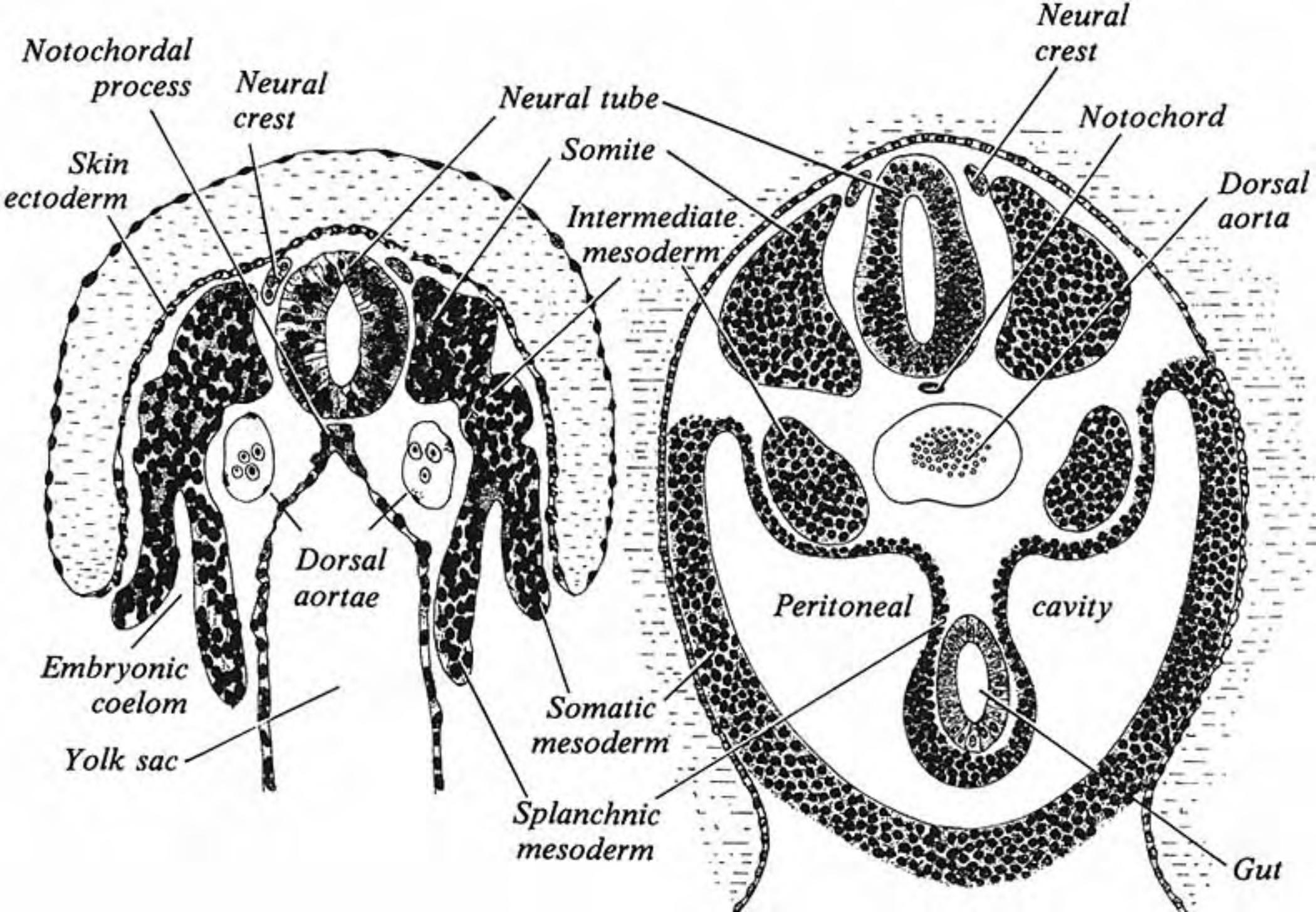
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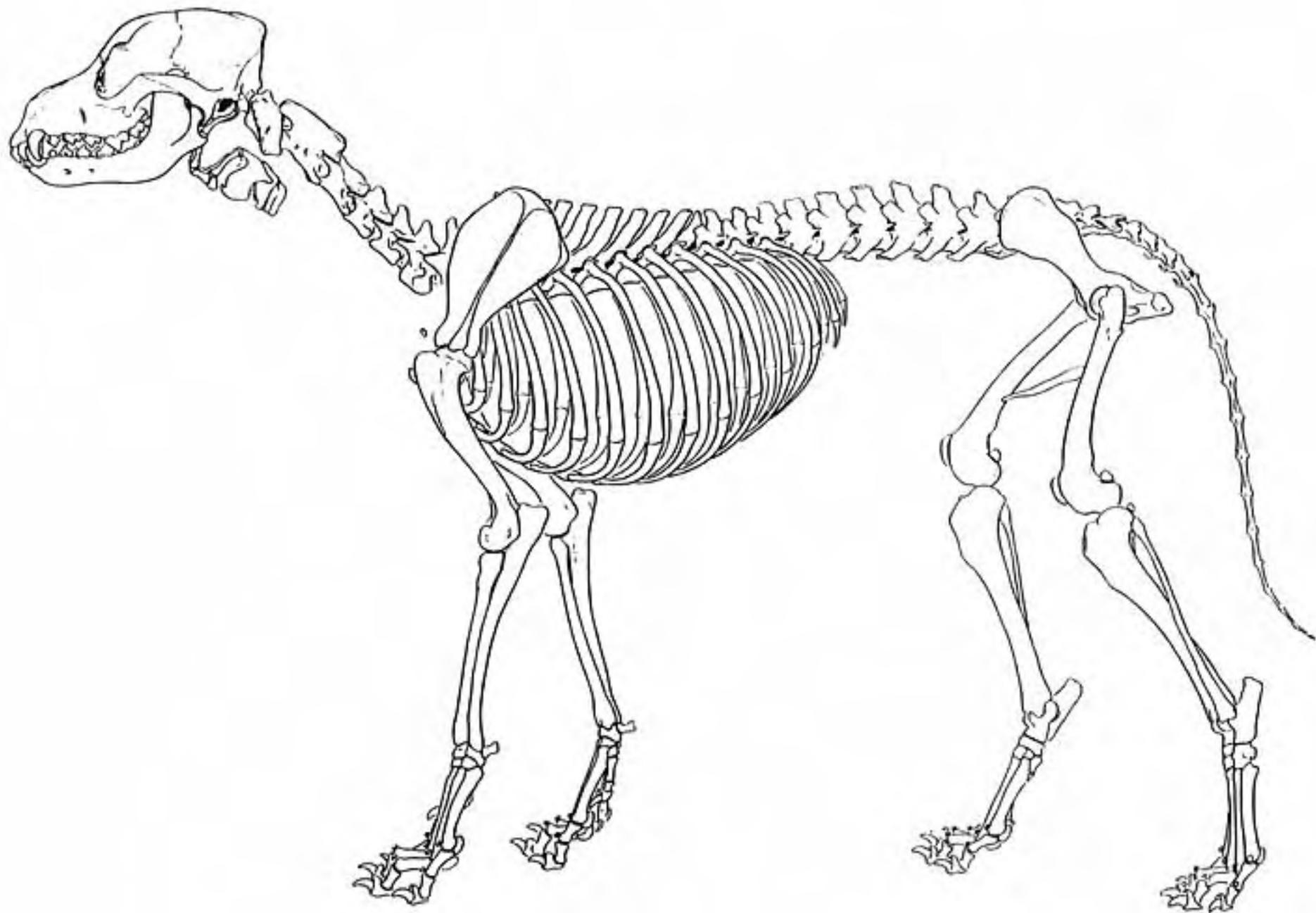
Regional Specifics

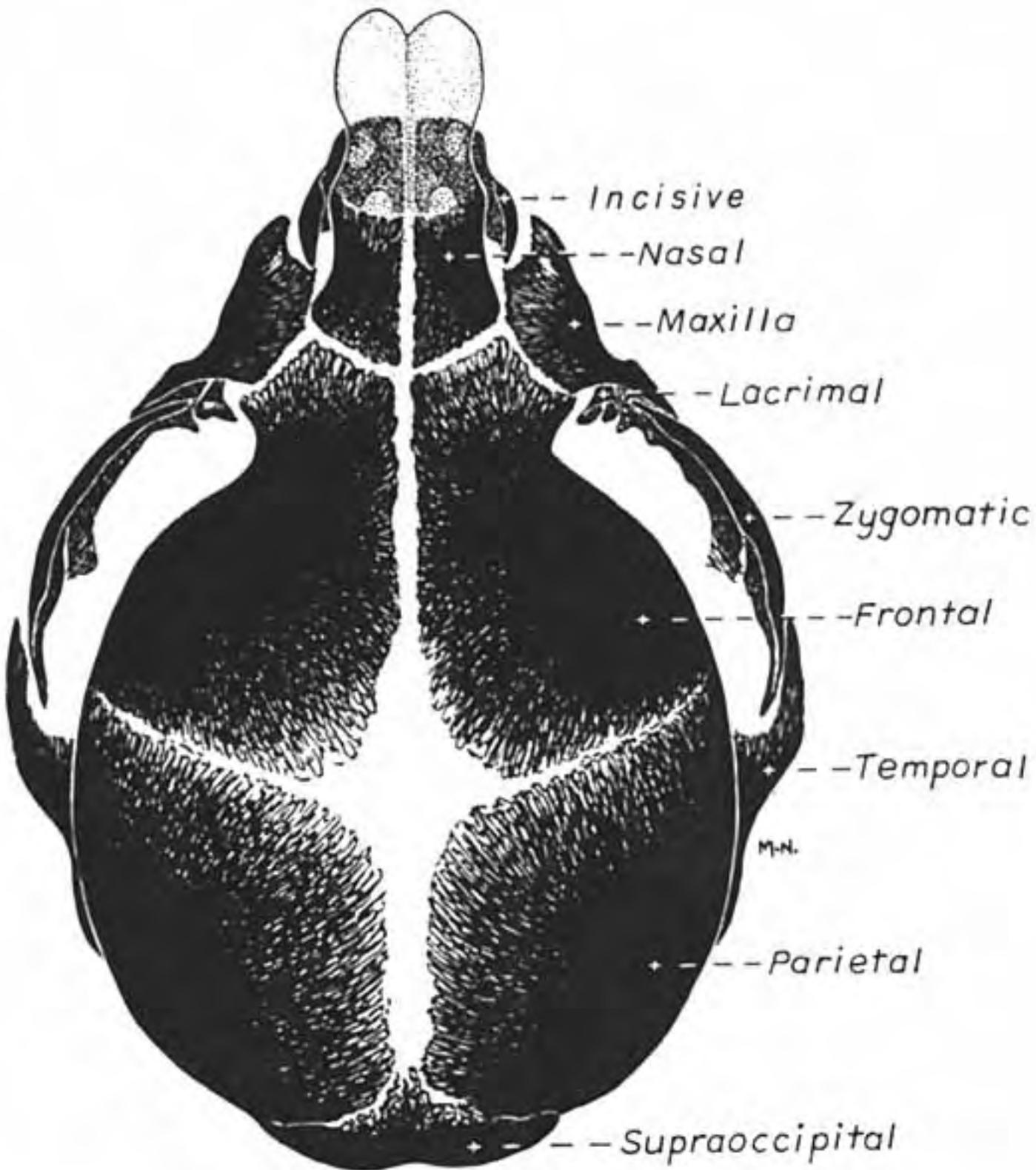
Trunk Region:

Skeletal musculature is formed by somite myotomes which fuse to form broad muscles that are segmentally innervated (each myotome brings its own innervation as it merges with adjacent myotomes). Myotome accumulations segregate into a dorsal mass (epimere) innervated by dorsal branches of spinal nerves and a ventral mass (hypomere) innervated by ventral branches of spinal nerves. The epimere becomes *epaxial muscles* and the hypomere becomes *hypaxial muscles*.

Sclerotomes give rise to vertebrae and ribs. The sternum develops differently, from chondrification/ossification of somatic mesenchyme of the ventral thorax.







-- *Incisive*

-- *Nasal*

-- *Maxilla*

-- *Lacrimal*

-- *Zygomatic*

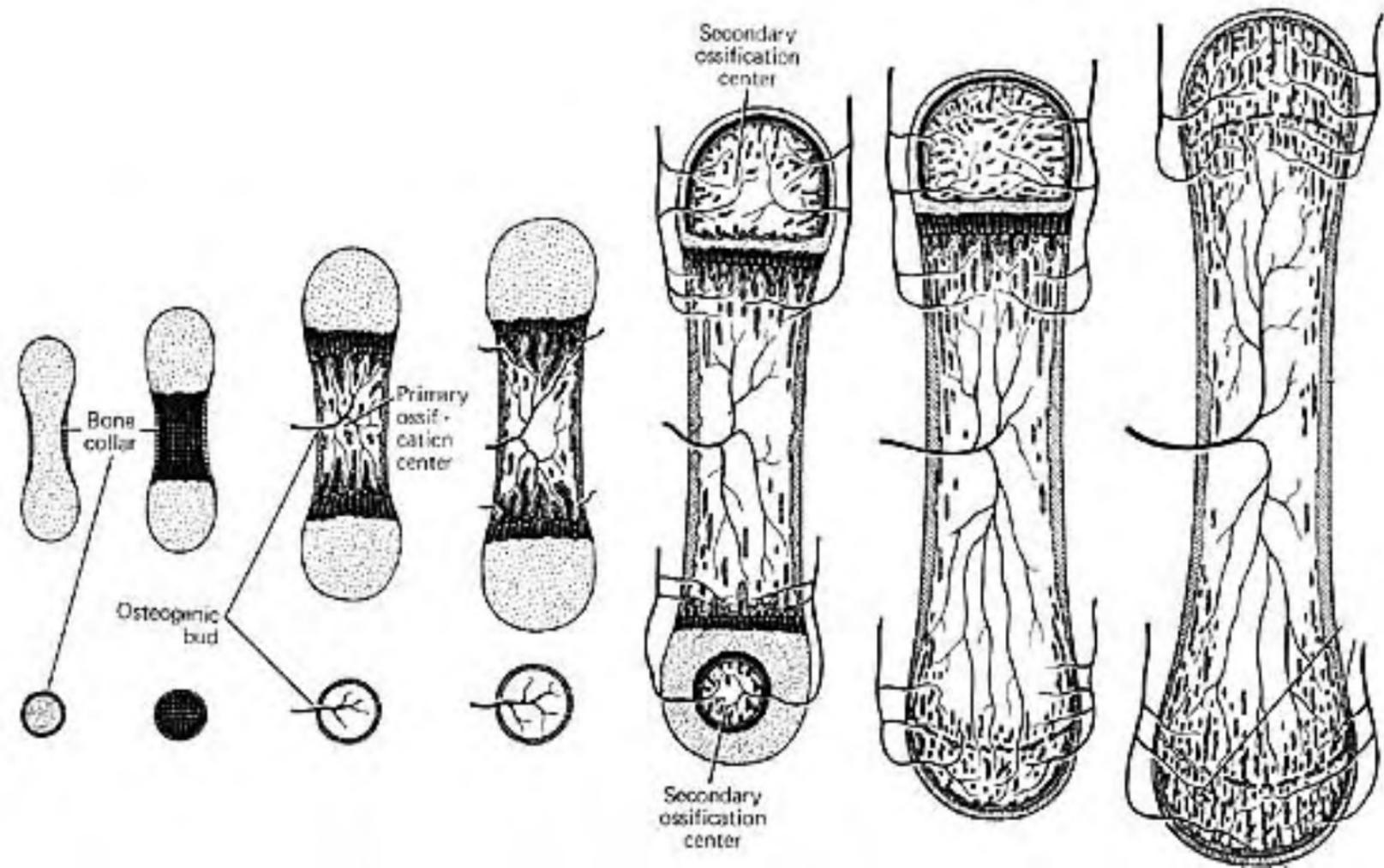
-- *Frontal*

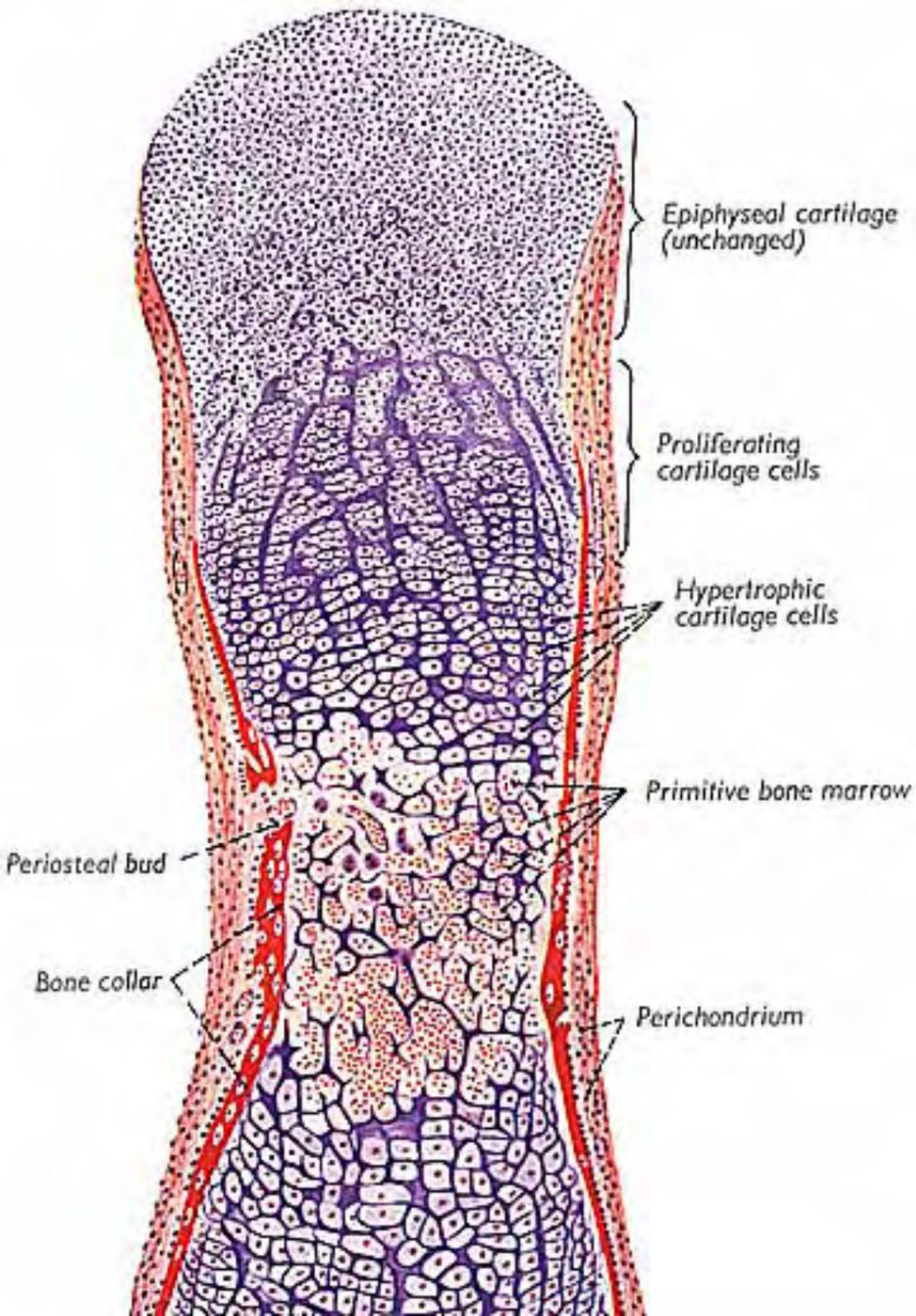
-- *Temporal*

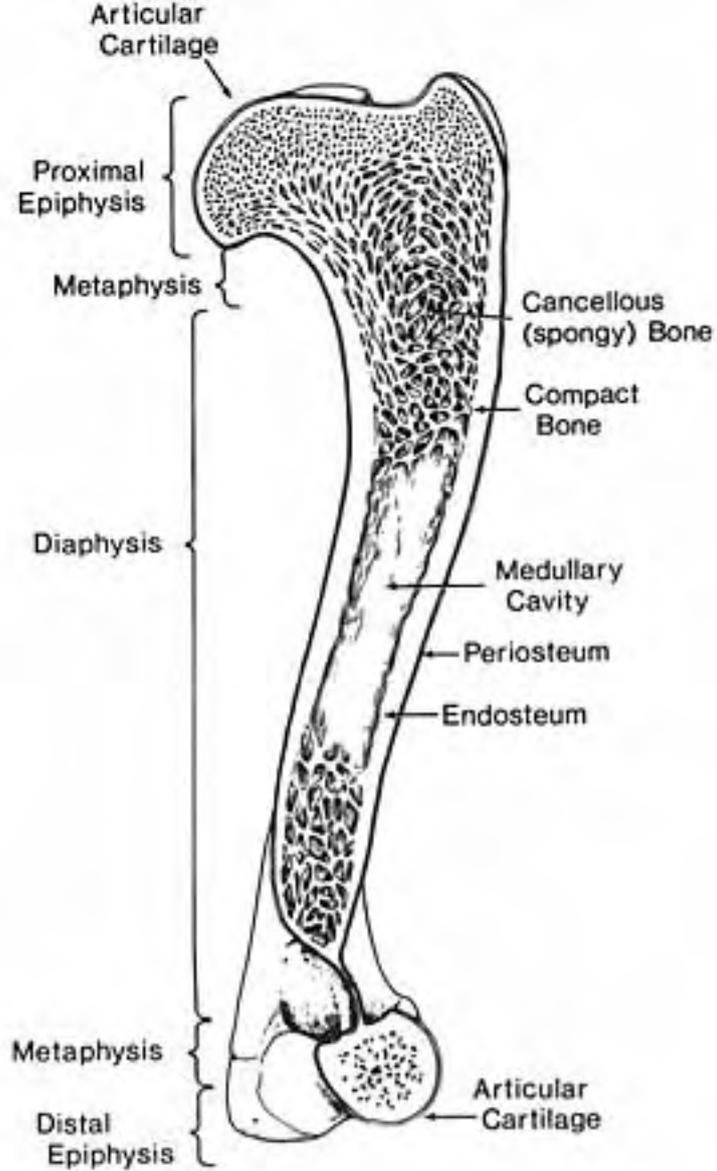
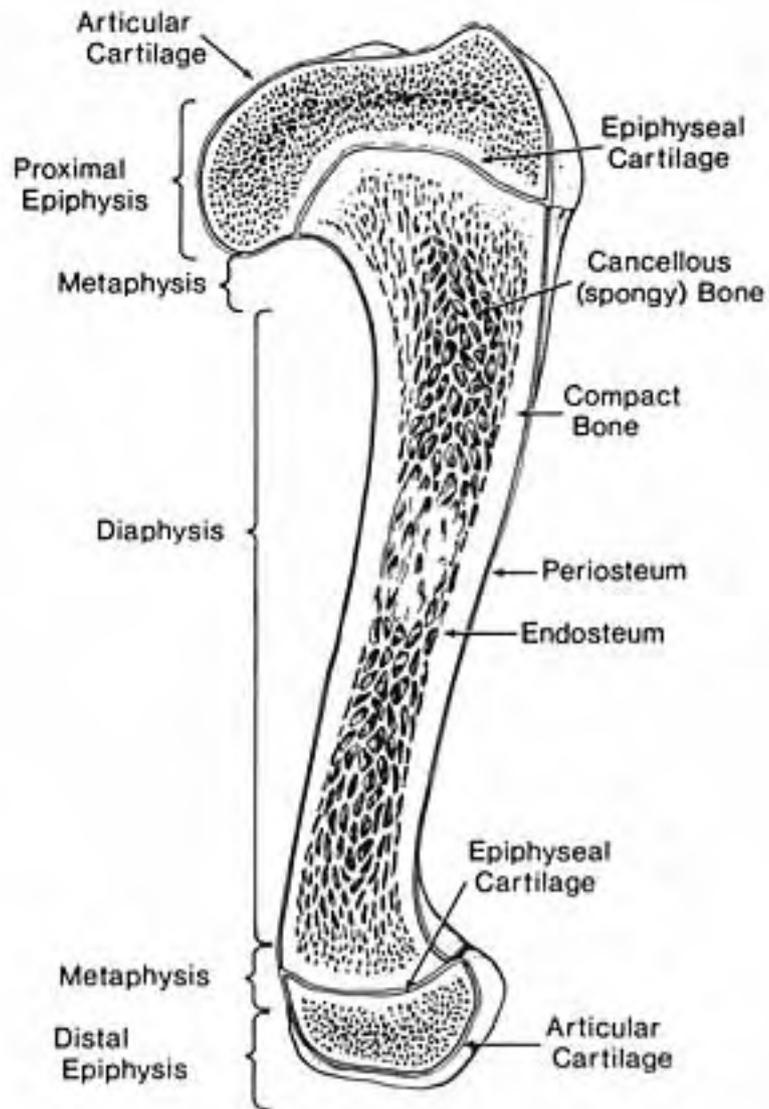
M.N.

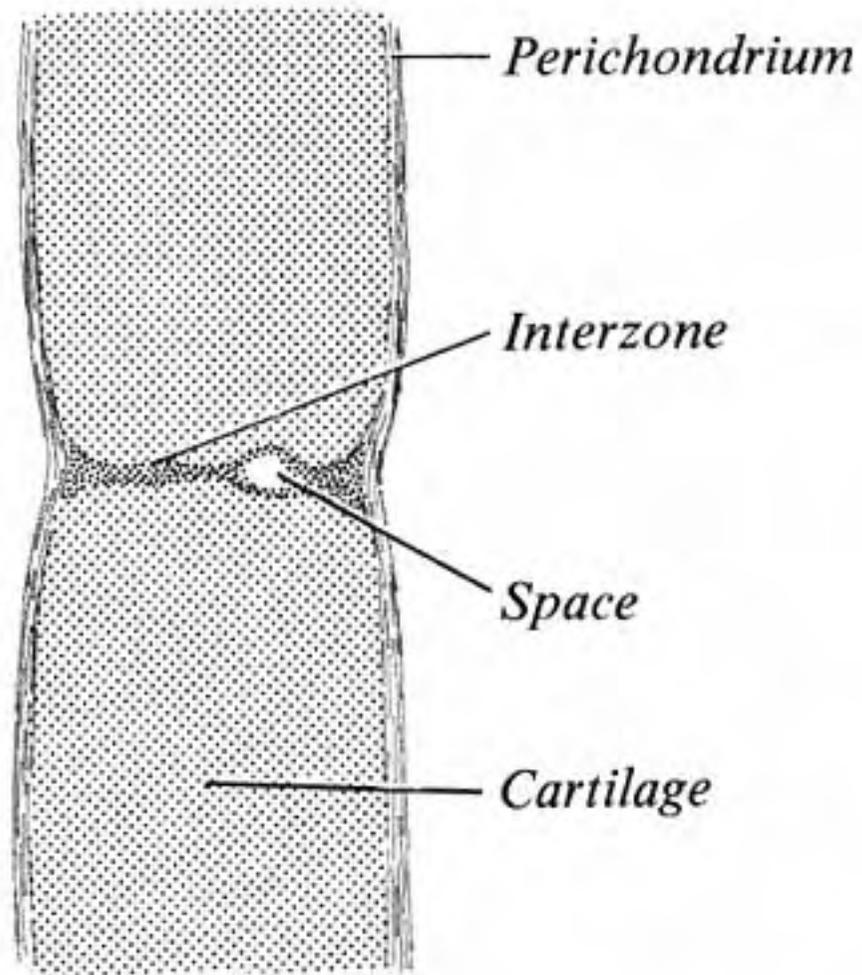
-- *Parietal*

-- *Supraoccipital*

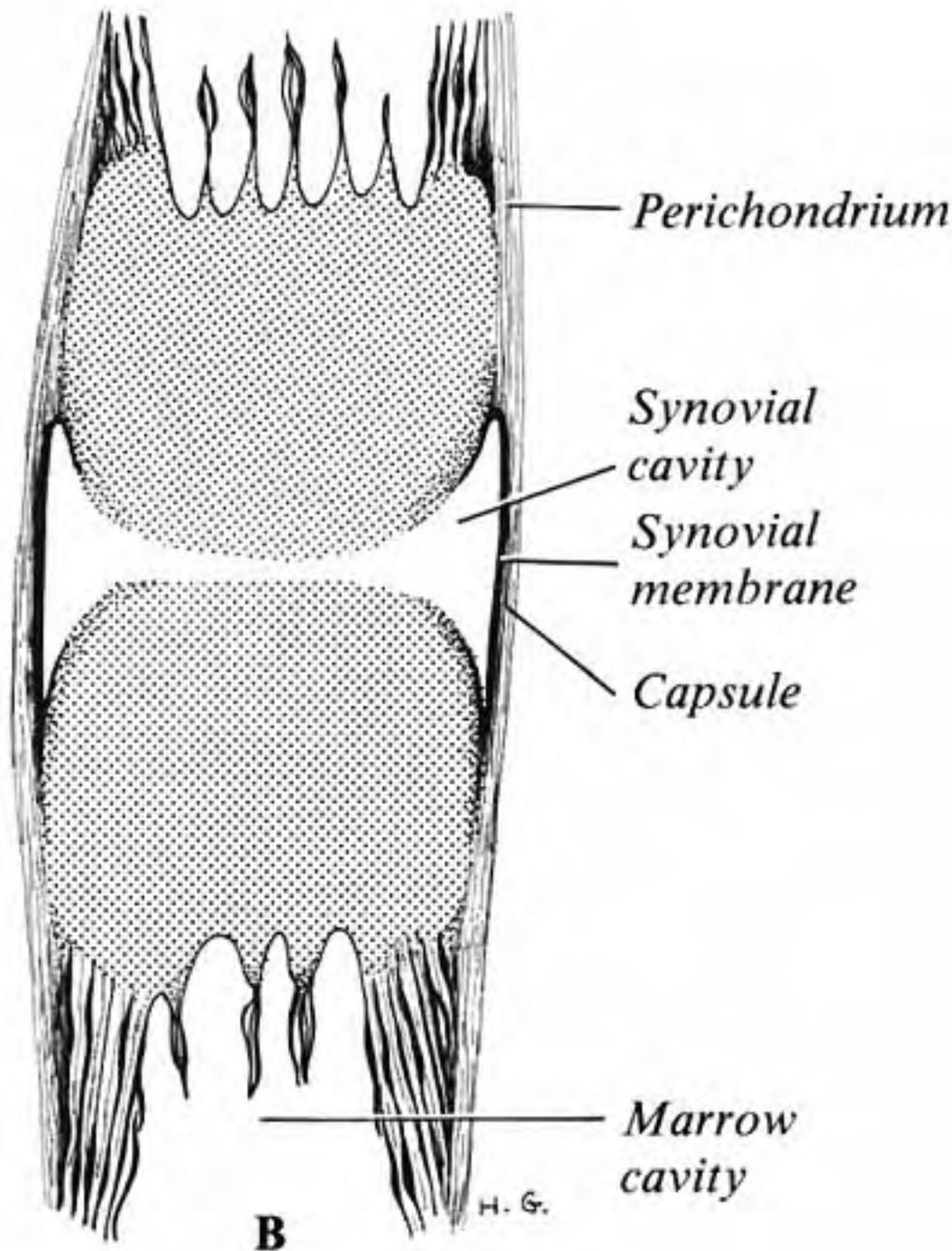






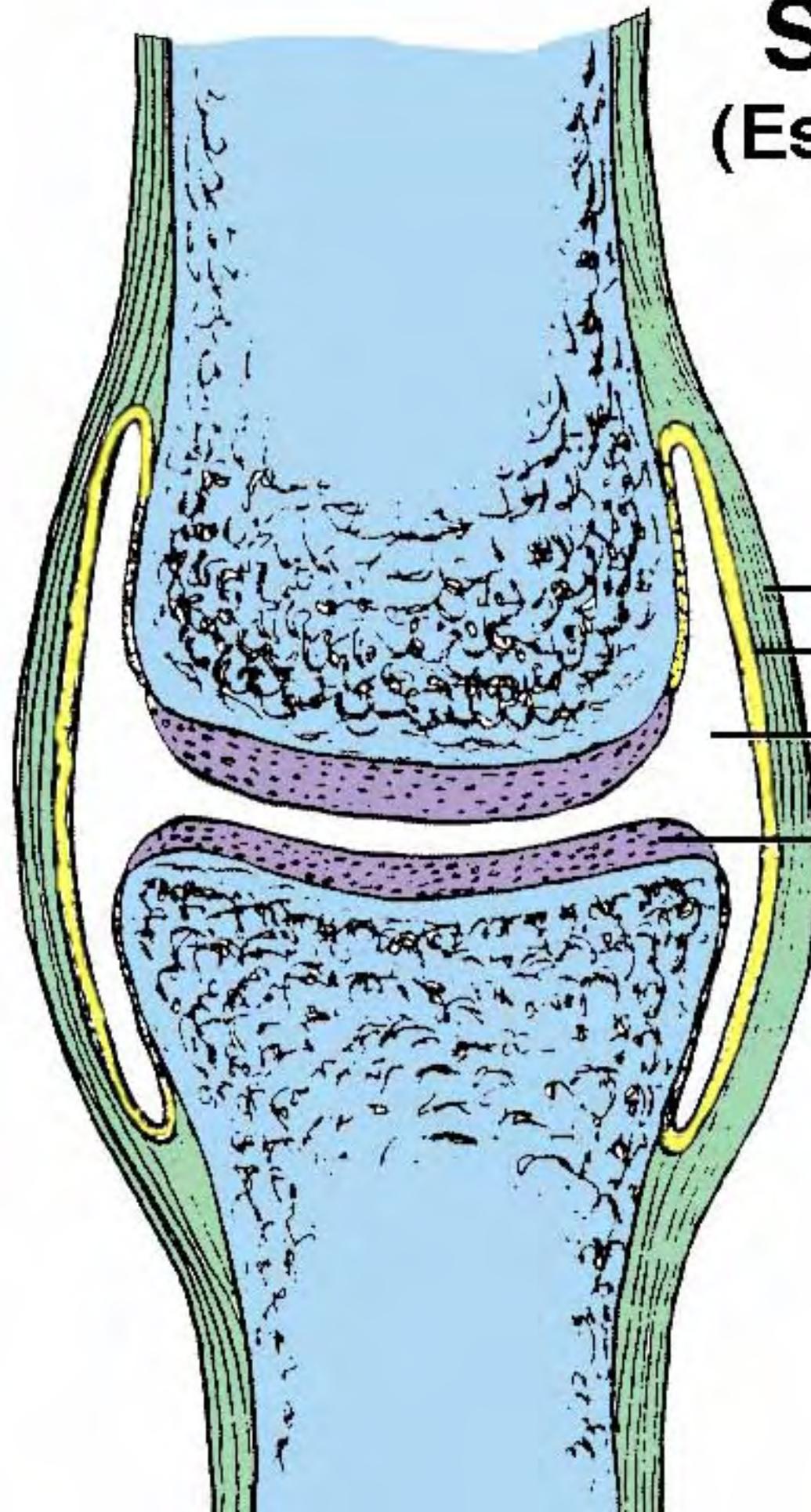


A



B

Synovial Joint (Essential Structures)



Joint capsule:

— fibrous layer

— synovial membrane

— Joint cavity

— Articular cartilage

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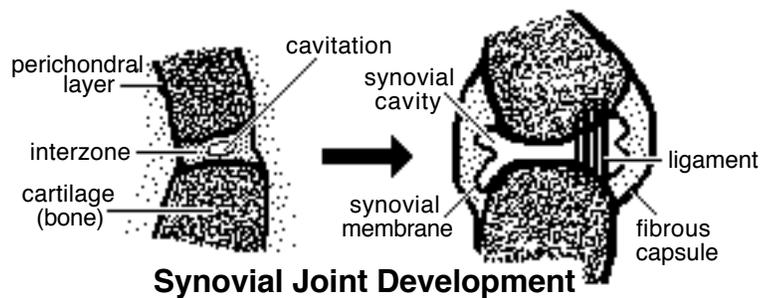
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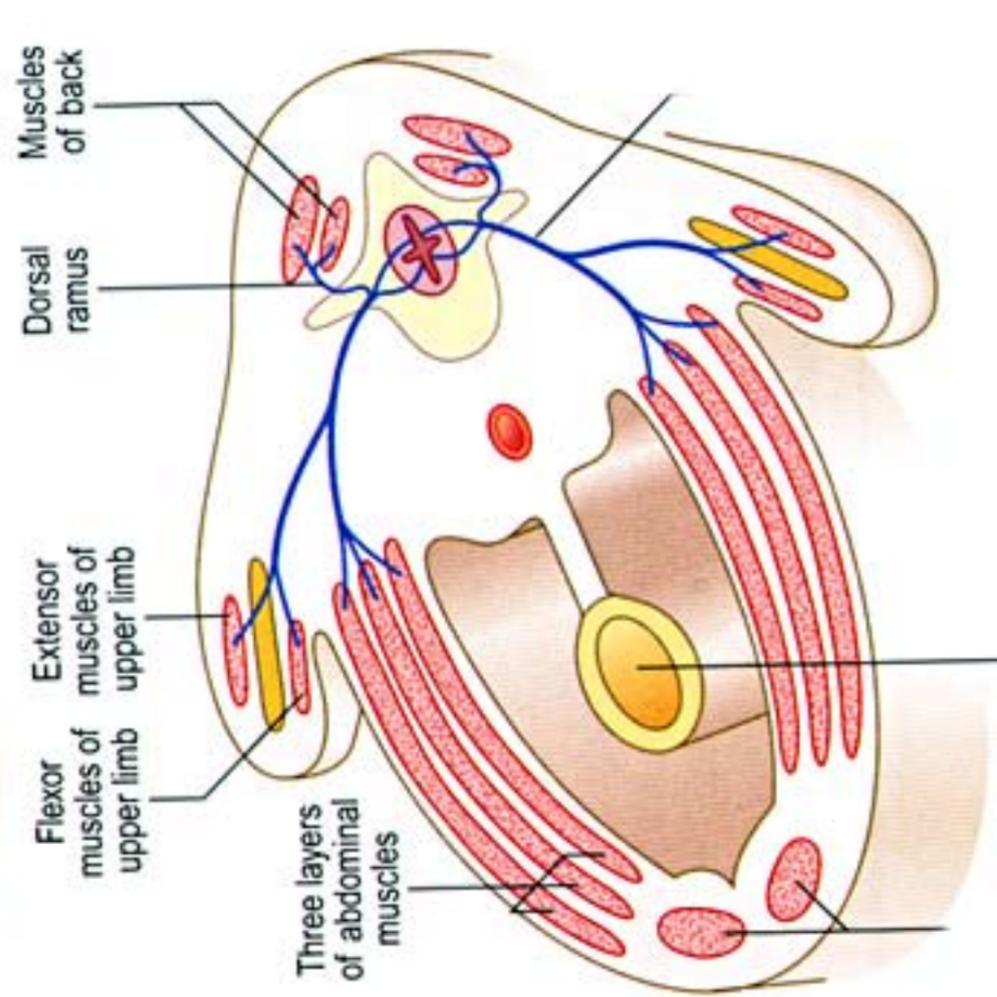
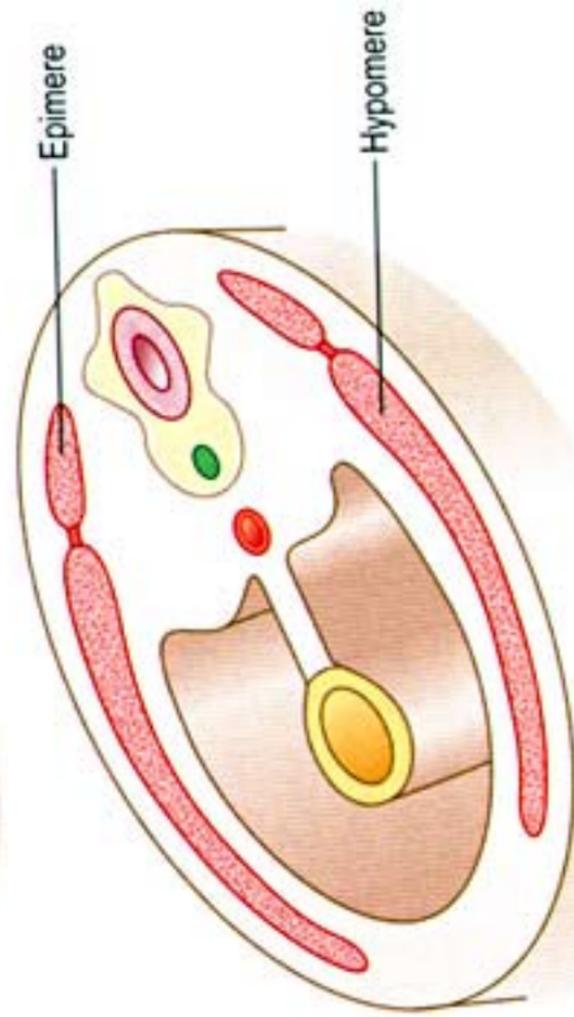
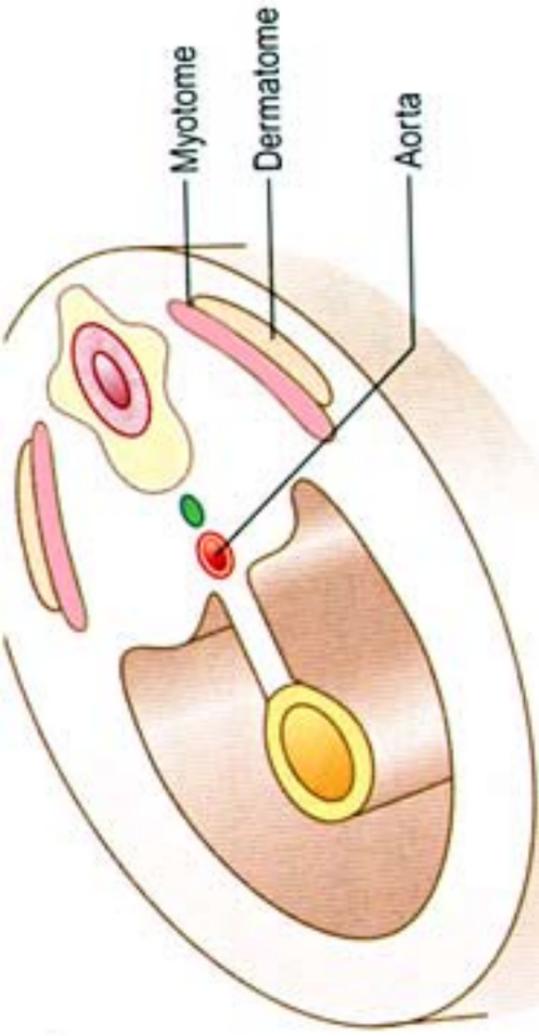
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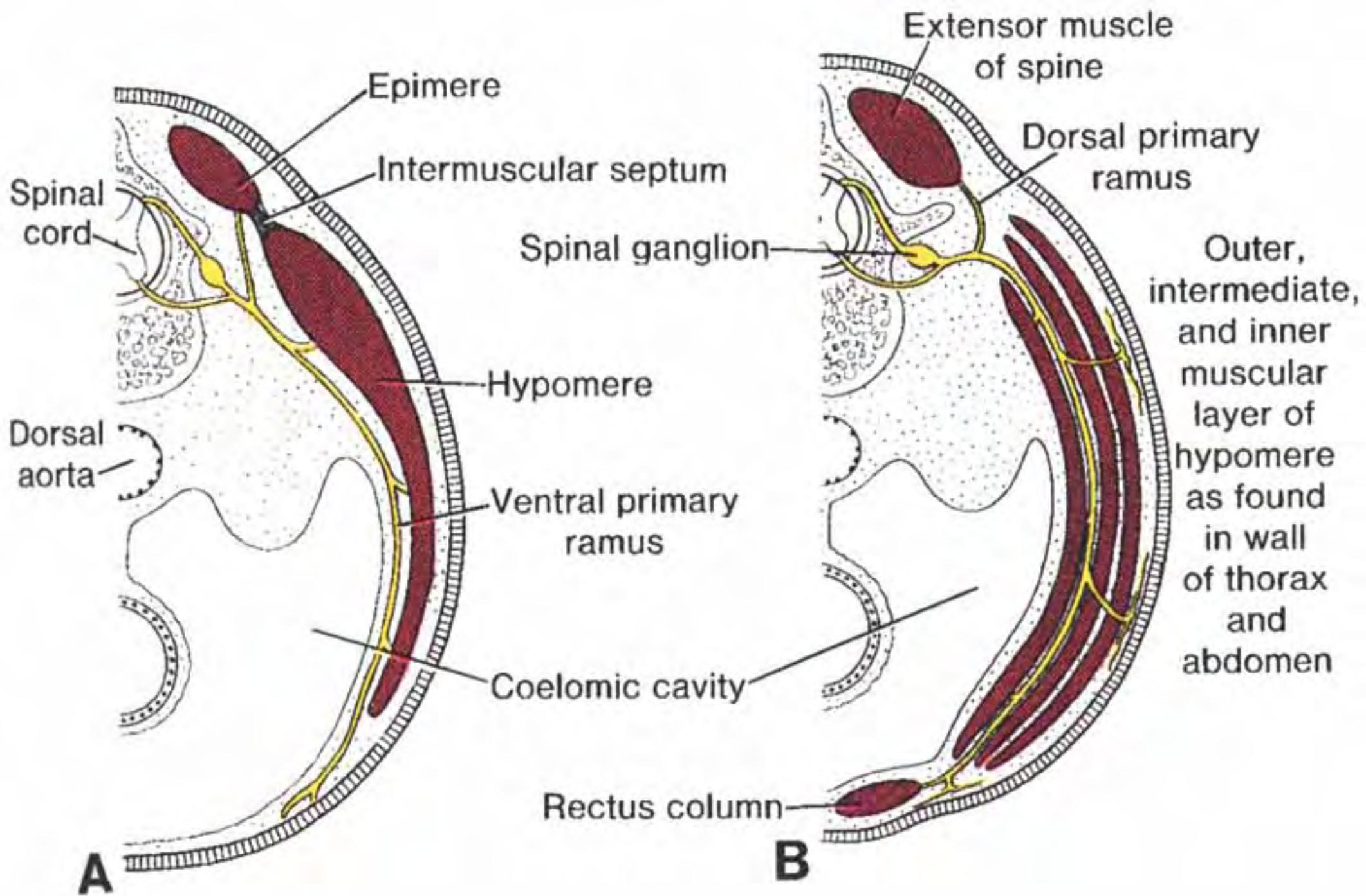
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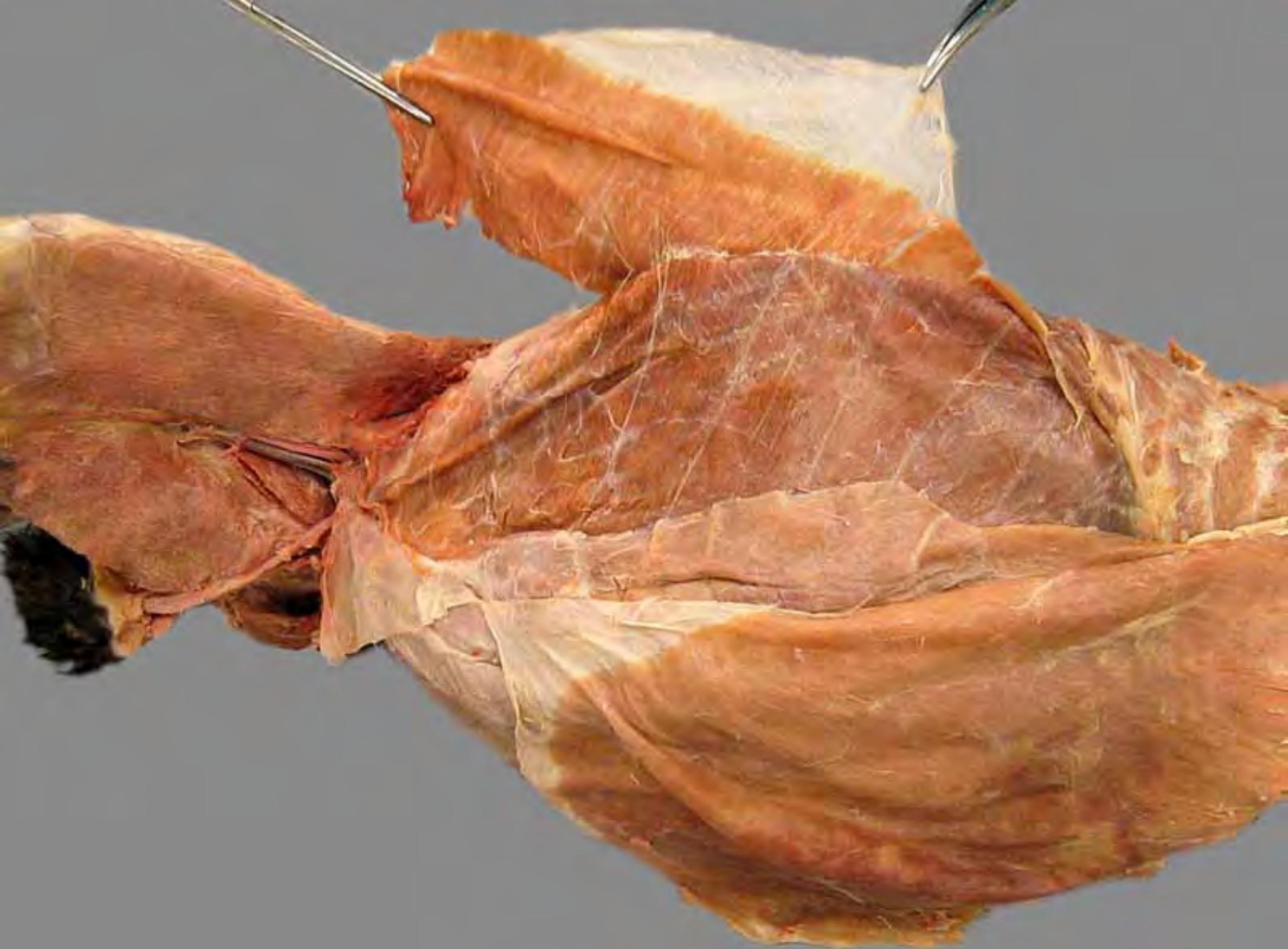
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Formation of Vertebrae and Ribs:

— sclerotome regions of somites migrate & become a continuous mass surrounding the notochord and neural tube. Thus the original somite segmentation is lost

— the continuous mass differentiates into diffuse & dense regions per original sclerotome. The diffuse region from one somite combines with the dense region of an adjacent somite to produce a cartilage model of one vertebra.

— between newly formed vertebrae (intervertebral disc regions) sclerotome mesenchyme forms *annulus fibrous* and notochord forms *nucleus pulposus* (notochord degenerates in the region of the vertebral body)

— ribs develop as processes of thoracic vertebrae.

Note: As a result of the above re-segmentation, vertebrae are shifted relative to other segmental structures (see next page). Consequently, muscles span adjacent vertebrae; spinal nerves traverse intervertebral foramina (located dorsal to intervertebral discs); and embryonic intersegmental arteries become spinal arteries that run along side vertebral bodies.

Vertebral anomalies include: stenosis of the vertebral canal; mal-articulation; hemivertebra; and spinal bifida (absent vertebral arch). The notochord, neural tube, and neural crest all play a role directing somite differentiation and vertebral segmentation (formation).

Note: The dens originates as the body of vertebra C₁ (atlas), but it fuses with vertebra C₂ (axis).

Limbs:

Limbs grow outward from body wall somatopleure as limb buds. Bone, cartilage, and connective tissue of the limb arise from somatic mesoderm of the limb bud. Dermis and skeletal muscle come from dermatome and myotome migrations into the limb.

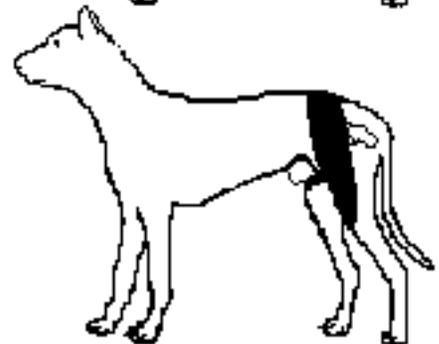
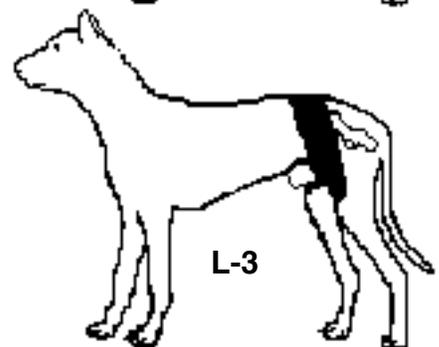
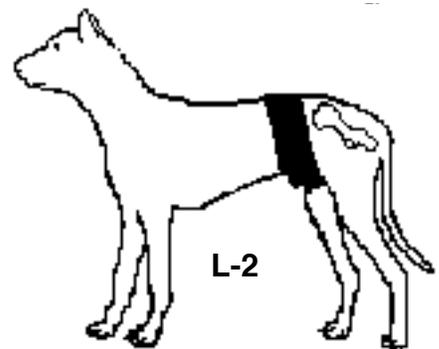
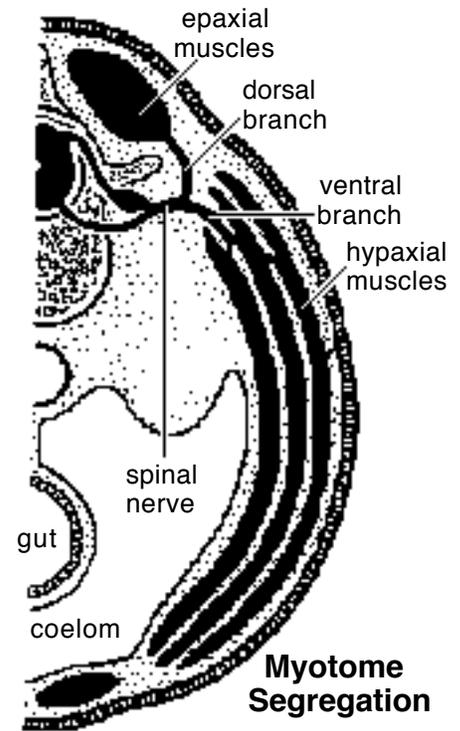
Limb Morphogenesis:

— a limb begins as a limb field (an area of somatopleure committed to forming a limb)

— next, a *limb bud* is produced by localized proliferation & condensation of mesenchyme, covered by ectoderm

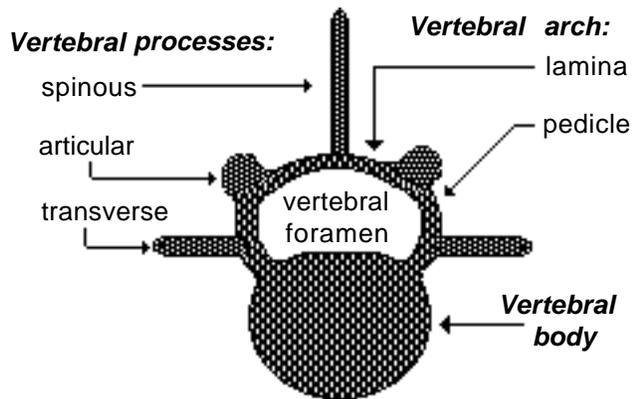
— regions of the limb develop in proximodistal order as the limb bud elongates (the shoulder/hip appears first, the manus/pes is the last to be added)

— the distal end of the limb bud (footplate) is flattened like a paddle and ectoderm along its outer margin thickens to form an *apical ridge* (the ridge is induced to form by underlying mesoderm and it induces the mesoderm to continue growing and differentiating into a limb)

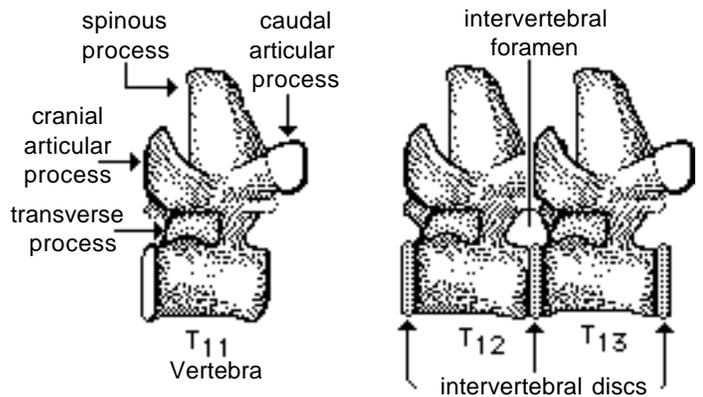


Canine Dermatomes

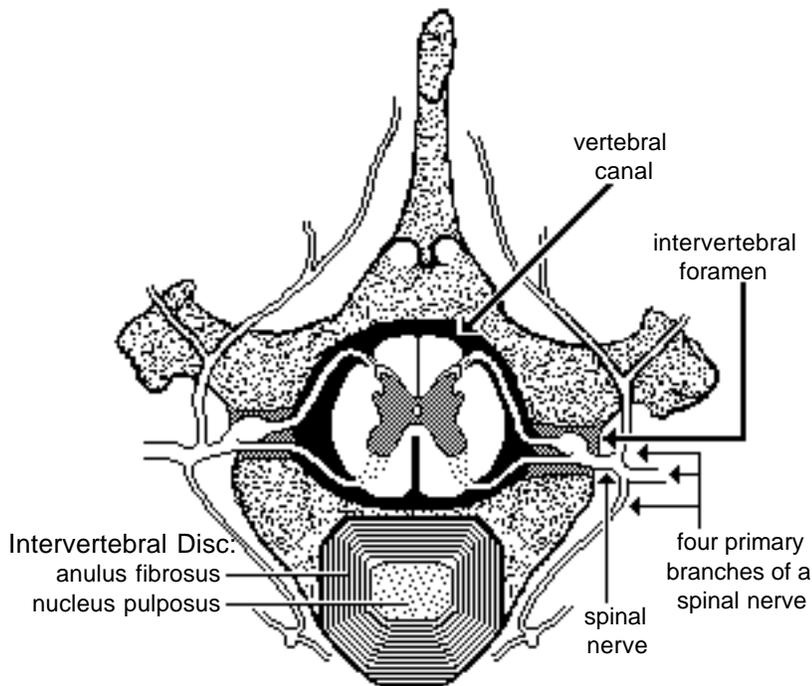
Features of Vertebrae



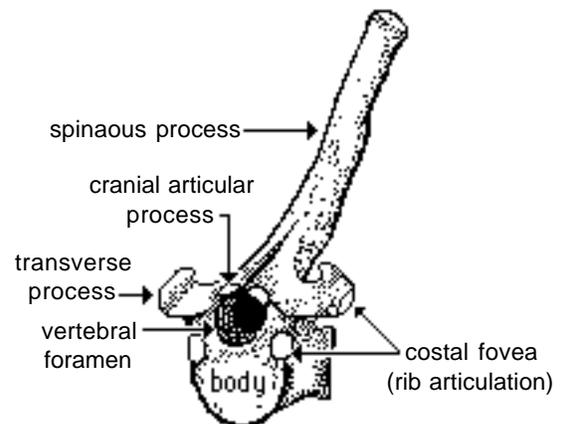
Transverse Section Through A Vertebra



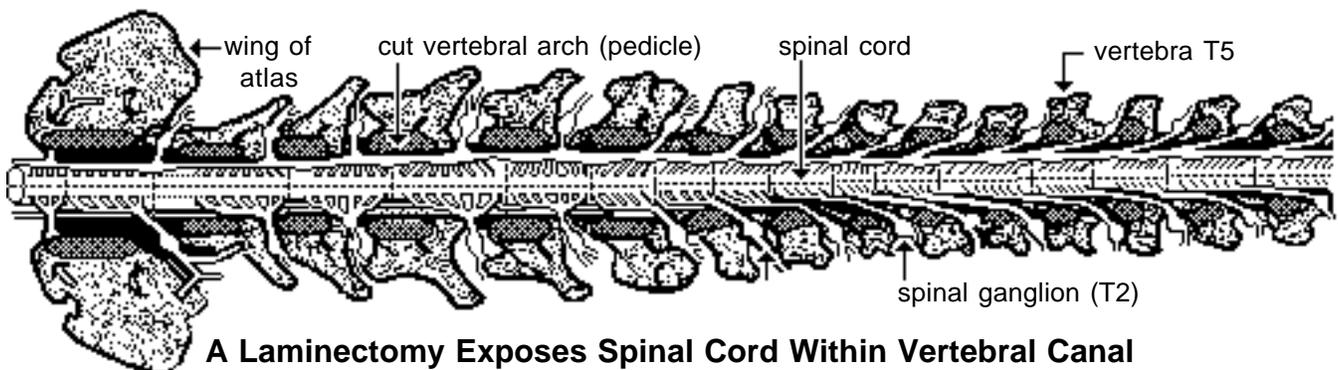
Lateral View of Vertebrae



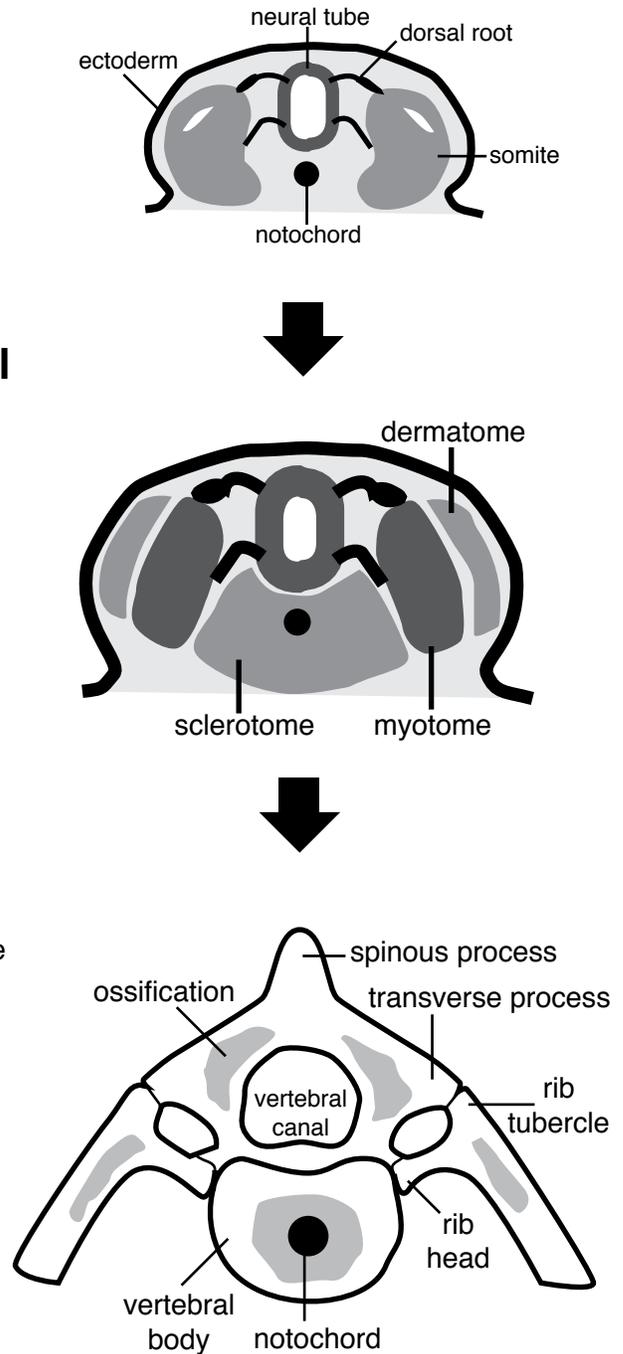
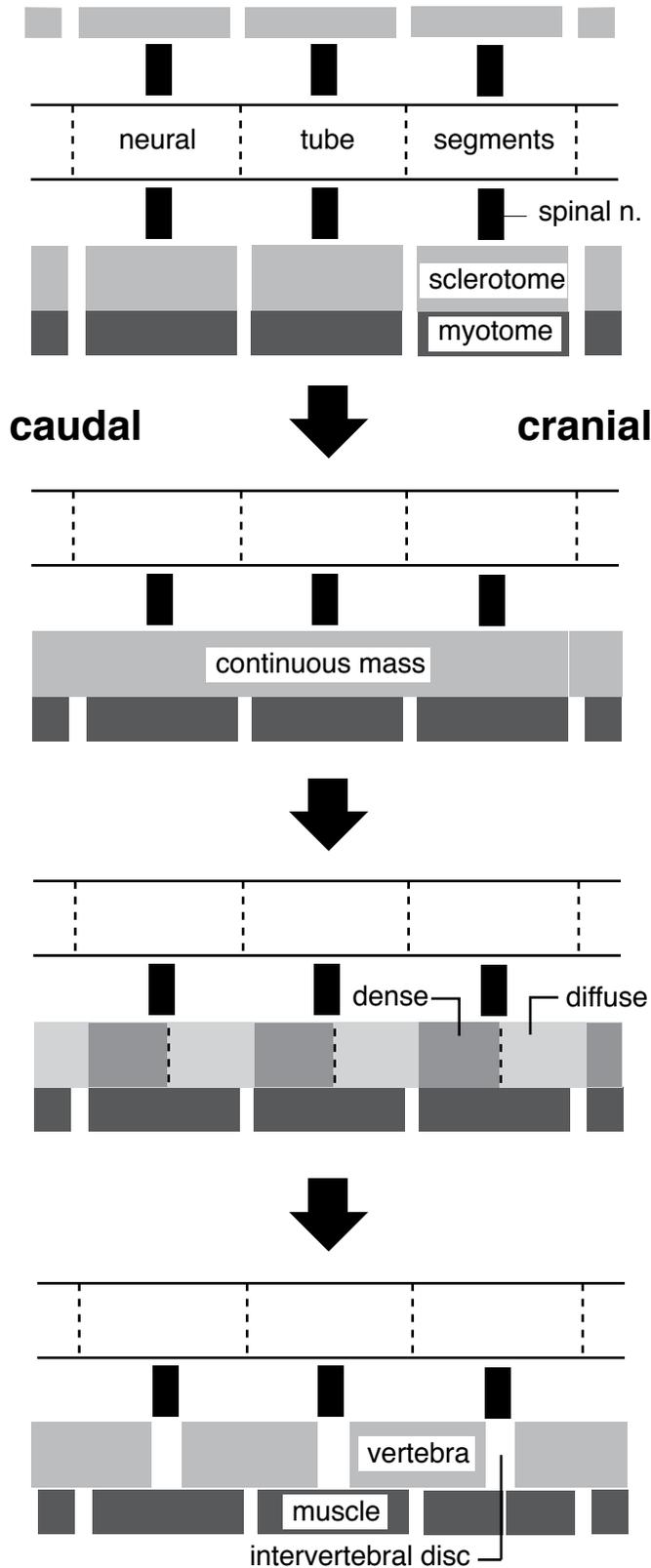
Transverse Section through an Intervertebral Disc

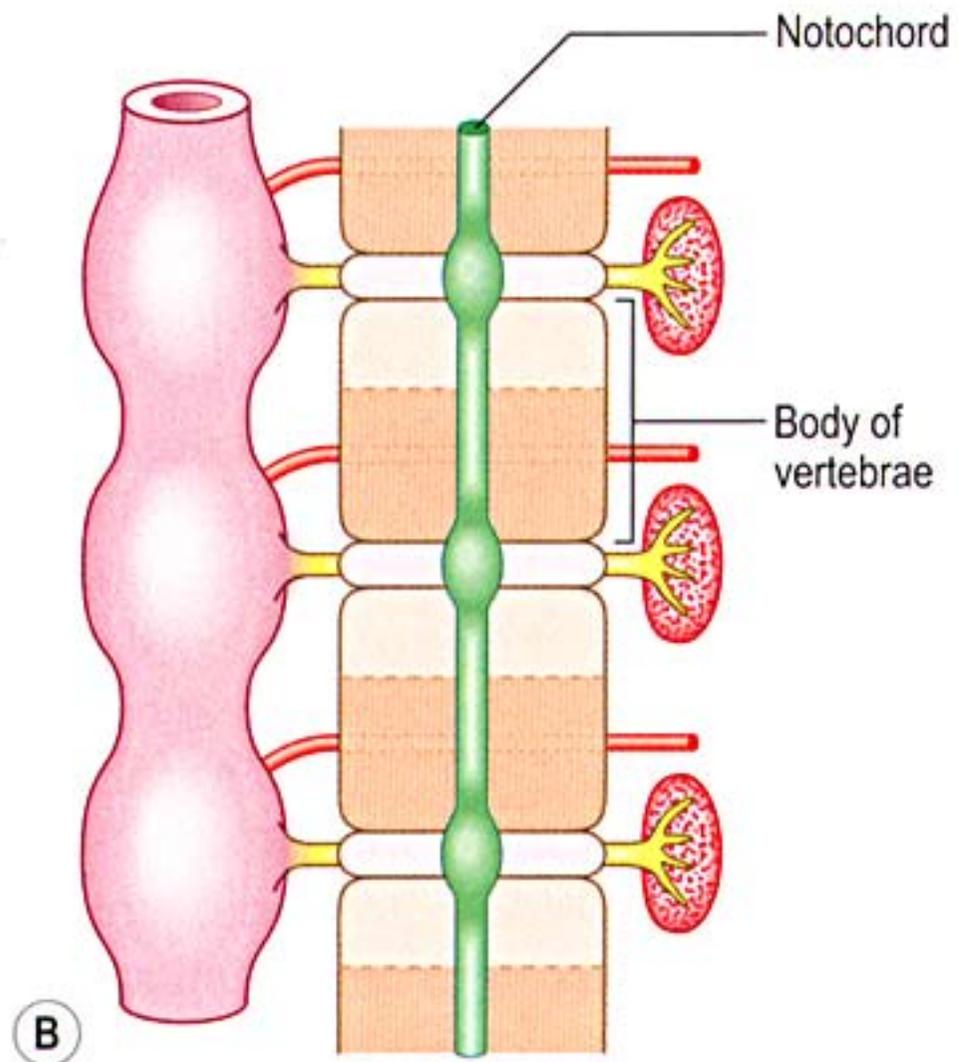
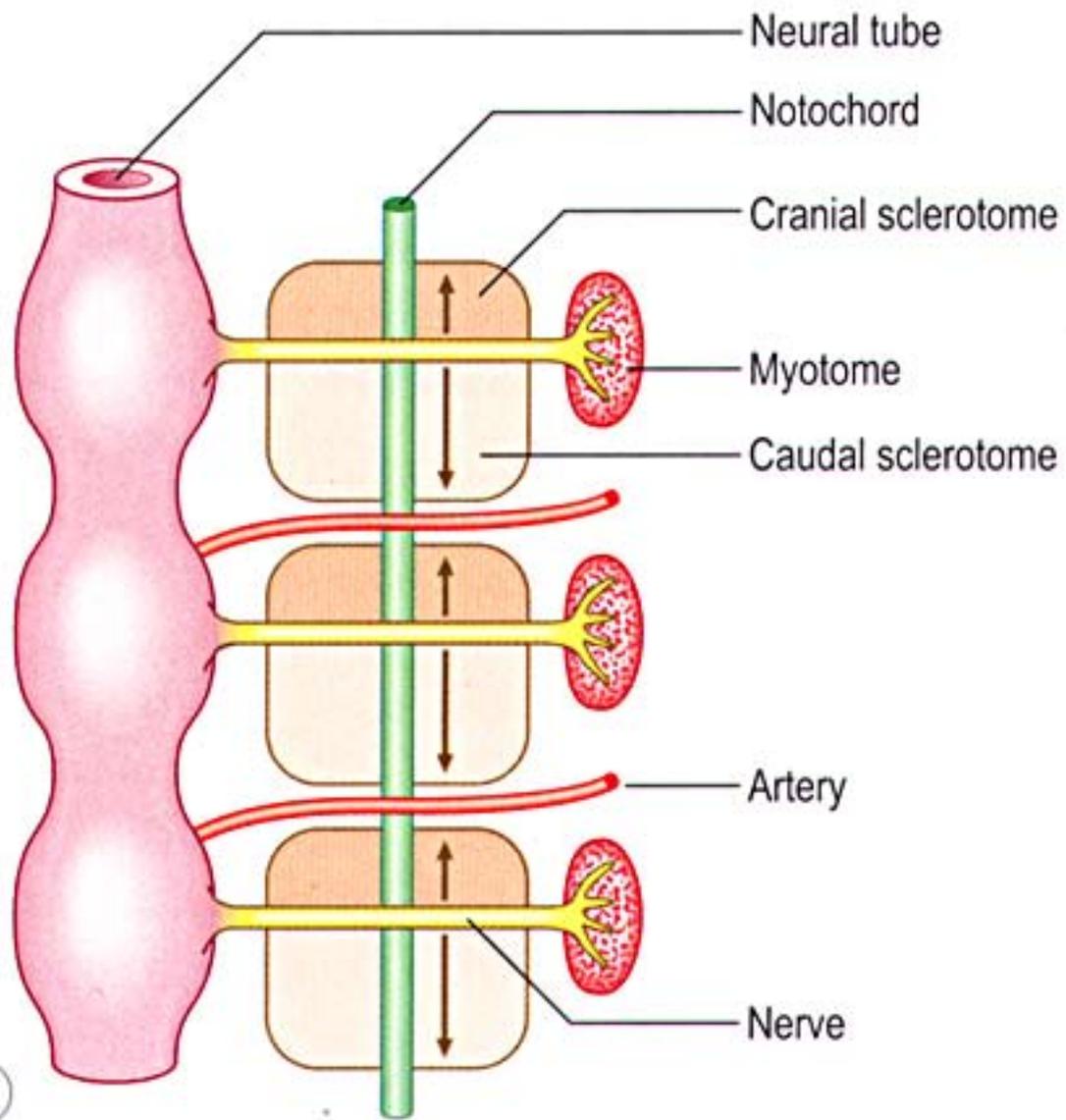


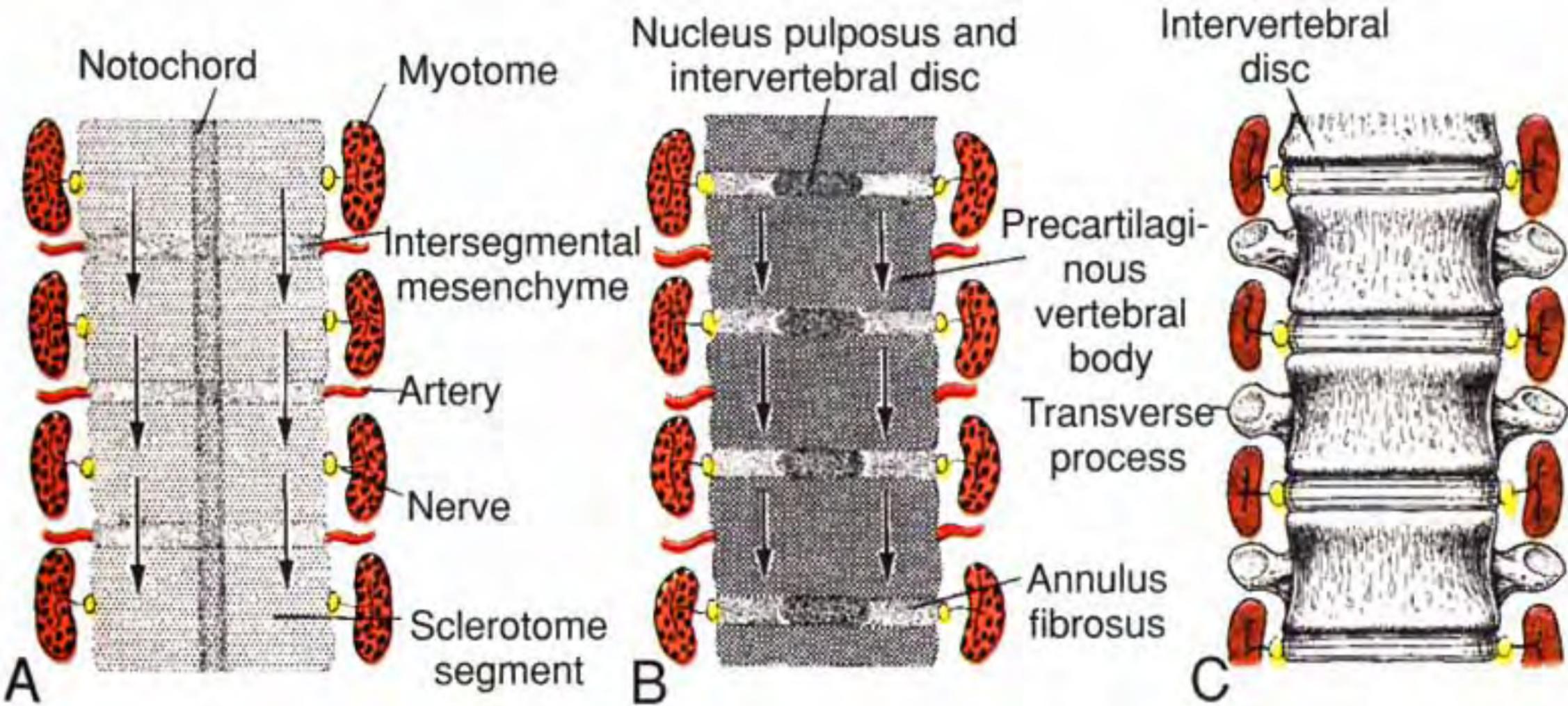
Cranio-lateral View of a Thoracic Vertebra

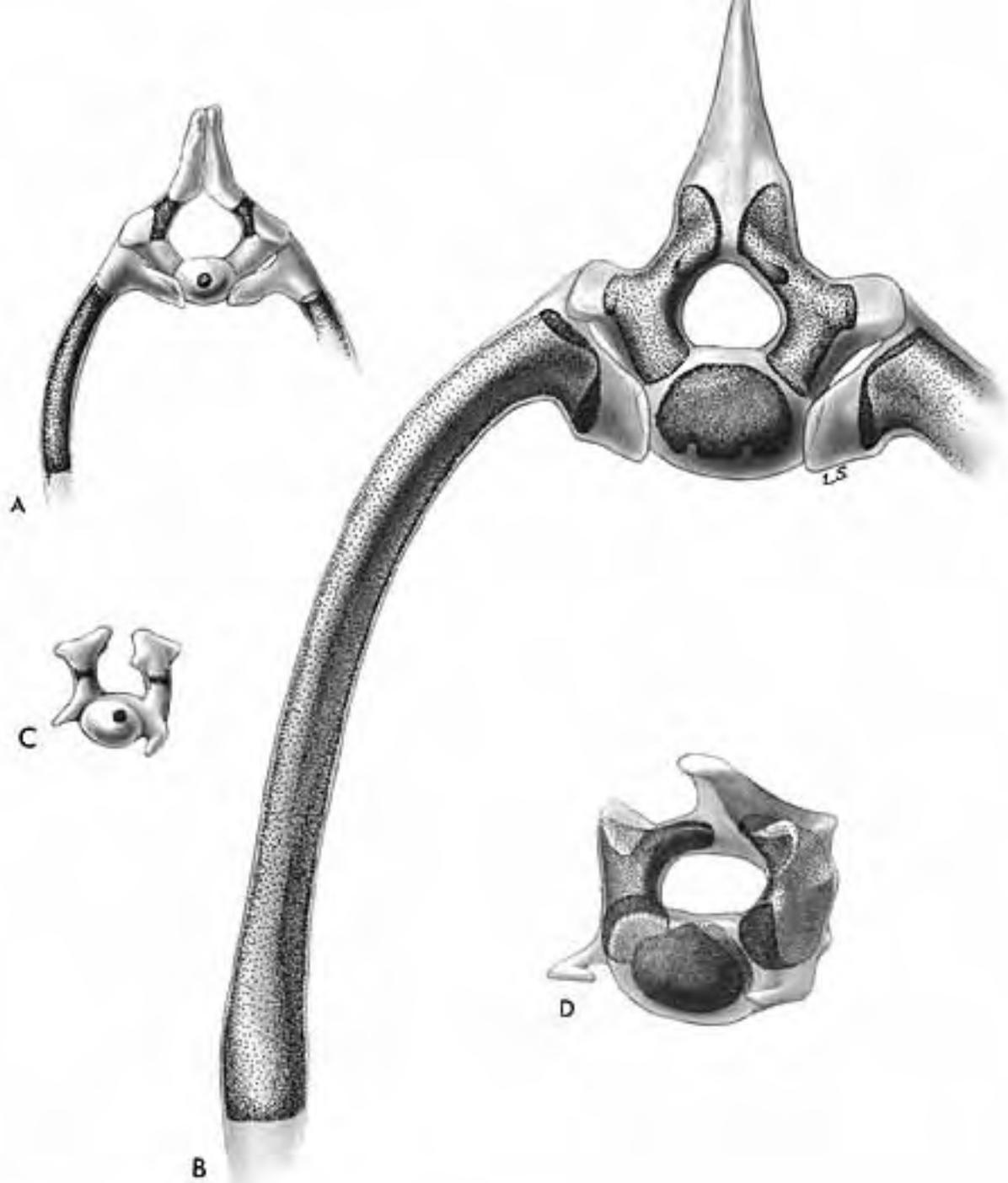


Sclerotomes to Vertebrae











LIMB GROWTH: Limbs arise from the lateral wall of the body. Thus limbs are products mainly of . . .

- A]** paraxial mesoderm
- B]** intermediate mesoderm
- C]** somatic lateral mesoderm
- D]** splanchnic lateral mesoderm

LIMB GROWTH

How do limbs grow?

A] proximal to distal order

B] distal to proximal order

How do digits grow?

A] digits grow outward from manus/pes

B] digits appear by selective degeneration of manus/

Formation of Vertebrae and Ribs:

— sclerotome regions of somites migrate & become a continuous mass surrounding the notochord and neural tube. Thus the original somite segmentation is lost

— the continuous mass differentiates into diffuse & dense regions per original sclerotome. The diffuse region from one somite combines with the dense region of an adjacent somite to produce a cartilage model of one vertebra.

— between newly formed vertebrae (intervertebral disc regions) sclerotome mesenchyme forms *annulus fibrous* and notochord forms *nucleus pulposus* (notochord degenerates in the region of the vertebral body)

— ribs develop as processes of thoracic vertebrae.

Note: As a result of the above re-segmentation, vertebrae are shifted relative to other segmental structures (see next page). Consequently, muscles span adjacent vertebrae; spinal nerves traverse intervertebral foramina (located dorsal to intervertebral discs); and embryonic intersegmental arteries become spinal arteries that run along side vertebral bodies.

Vertebral anomalies include: stenosis of the vertebral canal; mal-articulation; hemivertebra; and spinal bifida (absent vertebral arch). The notochord, neural tube, and neural crest all play a role directing somite differentiation and vertebral segmentation (formation).

Note: The dens originates as the body of vertebra C₁ (atlas), but it fuses with vertebra C₂ (axis).

Limbs:

Limbs grow outward from body wall somatopleure as limb buds. Bone, cartilage, and connective tissue of the limb arise from somatic mesoderm of the limb bud. Dermis and skeletal muscle come from dermatome and myotome migrations into the limb.

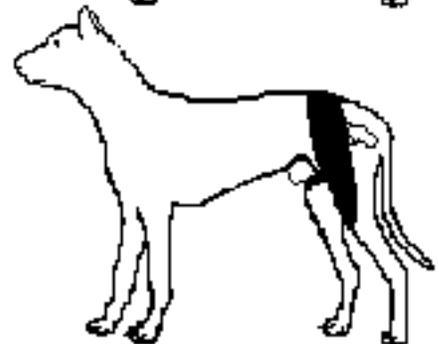
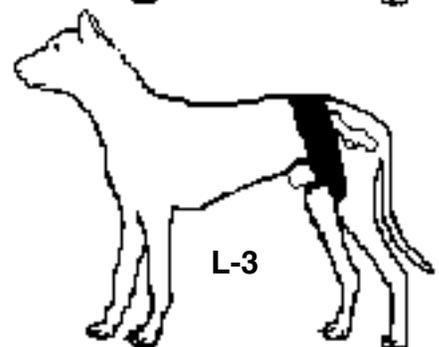
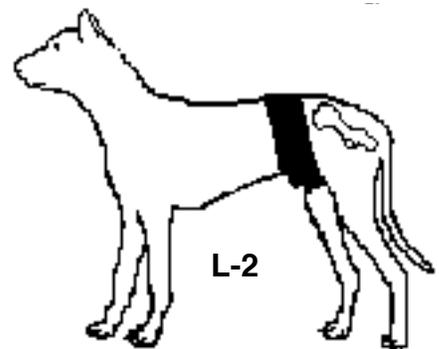
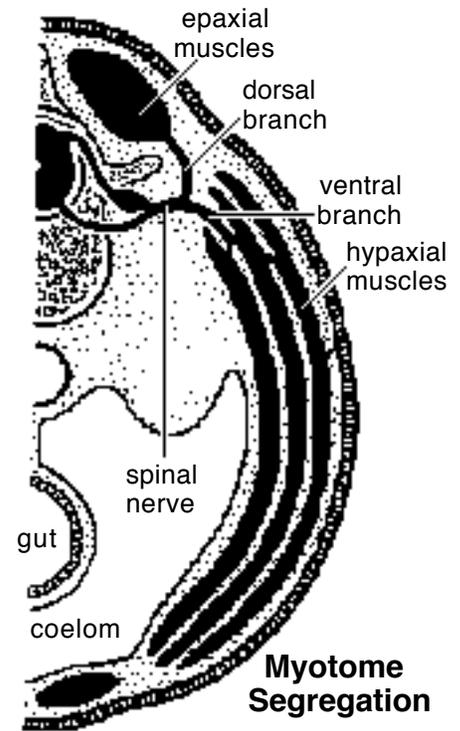
Limb Morphogenesis:

— a limb begins as a limb field (an area of somatopleure committed to forming a limb)

— next, a *limb bud* is produced by localized proliferation & condensation of mesenchyme, covered by ectoderm

— regions of the limb develop in proximodistal order as the limb bud elongates (the shoulder/hip appears first, the manus/pes is the last to be added)

— the distal end of the limb bud (footplate) is flattened like a paddle and ectoderm along its outer margin thickens to form an *apical ridge* (the ridge is induced to form by underlying mesoderm and it induces the mesoderm to continue growing and differentiating into a limb)



Canine Dermatomes

- mechanically, limb growth consists of:
 - elongation of a dorsoventrally flattened limb bud
 - ventroflexion of the distal half of the limb (ventral now faces medially)
 - pronation of the distal half (previous medial surface now becomes caudal)
- separate digits are produced by interdigital necrotic zones (species with fewer digits undergo further degeneration and/or fusion of digits);
- local mesenchyme condenses to form cartilage models of limb bones
- myotome cells migrate into the base of the limb forming extensor & flexor muscle masses that subsequently segregate into the individual muscles of the limb;
- vessels and nerves grow into the limb.

Clinical considerations:

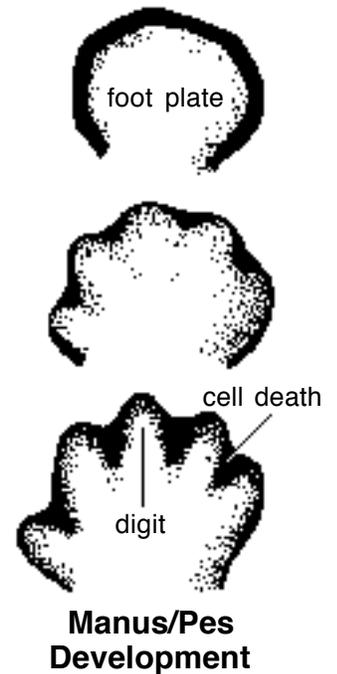
Achondroplasia (dwarfism; Dachshund) — inherited, systemic premature ossification of physes of extremities.

Arthrogryposis [Gr. gryposis = crooked] can result from malformed joints, denervation, abnormal muscle tension, or impaired mobility *in utero*.

Polydactyly (extra digits); syndactyly (fused digits); brachydactyly (stumpy digits Gr. dactylos = digit)

Amelia (no limb); meromelia (absence of part of limb); micromelia (small limb Gr. melos = limb)

Note: phocomelia (seal limb) = absence of proximal segment(s) of limb was a consequence of pregnant women taking thalidomide in the late 1950s.



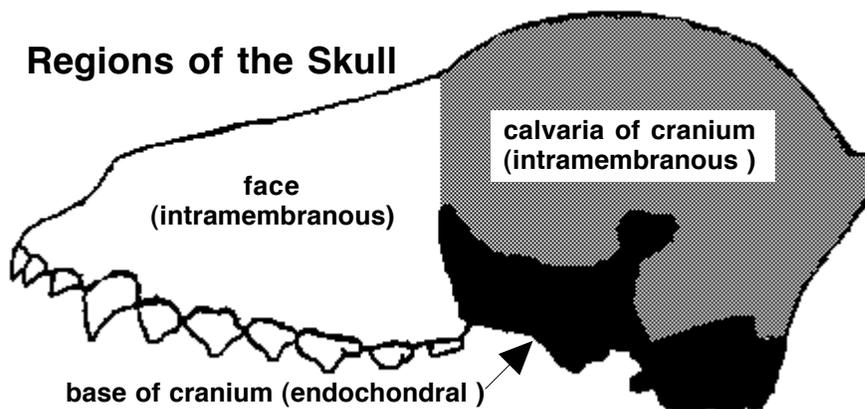
Head Region:

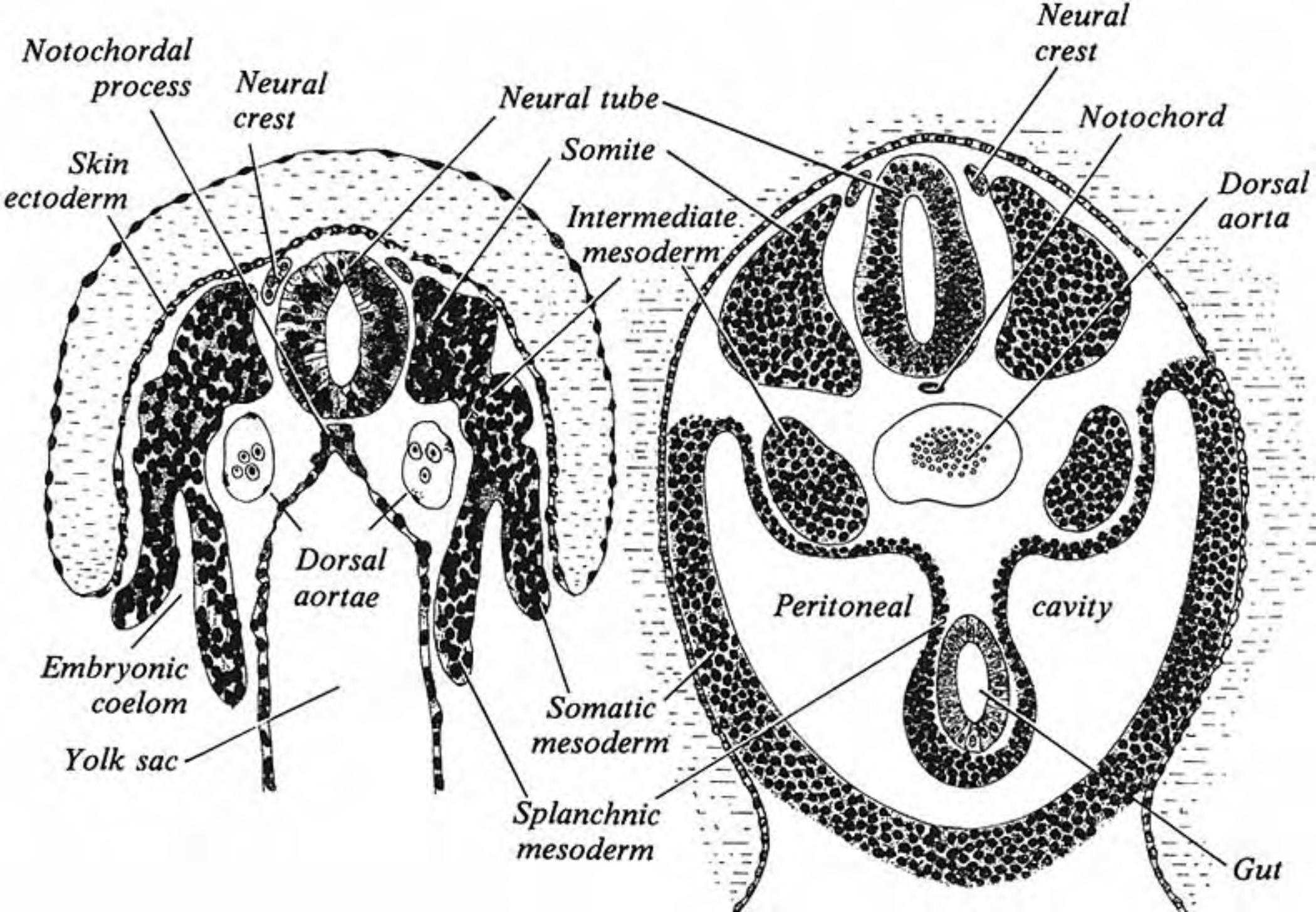
The head consists of a cranium, which contains the brain within a cranial cavity, and a face. The face develops separately from the frontonasal process and first pharyngeal arch. Since the face and cranium have different embryonic origins they can be independently influenced genetically (e.g., in the case of brachycephalic breeds) or by teratogens.

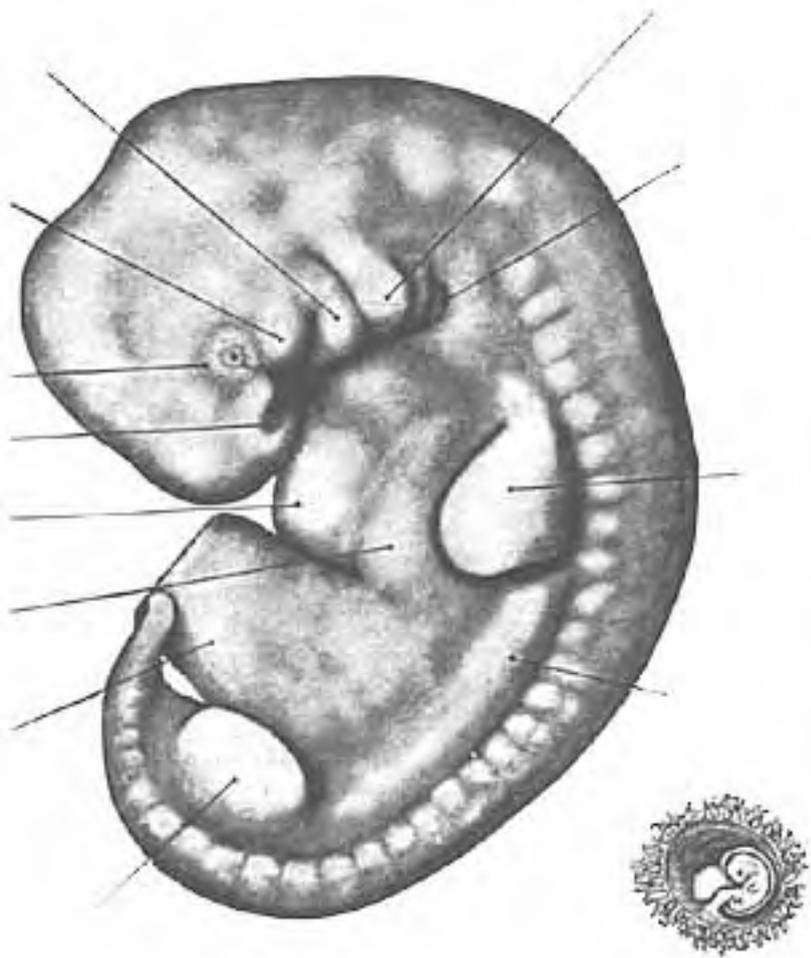
Skull. Bones of the base of the cranium develop endochondrally; the relatively flat bones that comprise the calvaria (roof of the cranium) and the face develop intramembranously. (The mandible has a complex origin involving both endochondral and intramembranous development.)

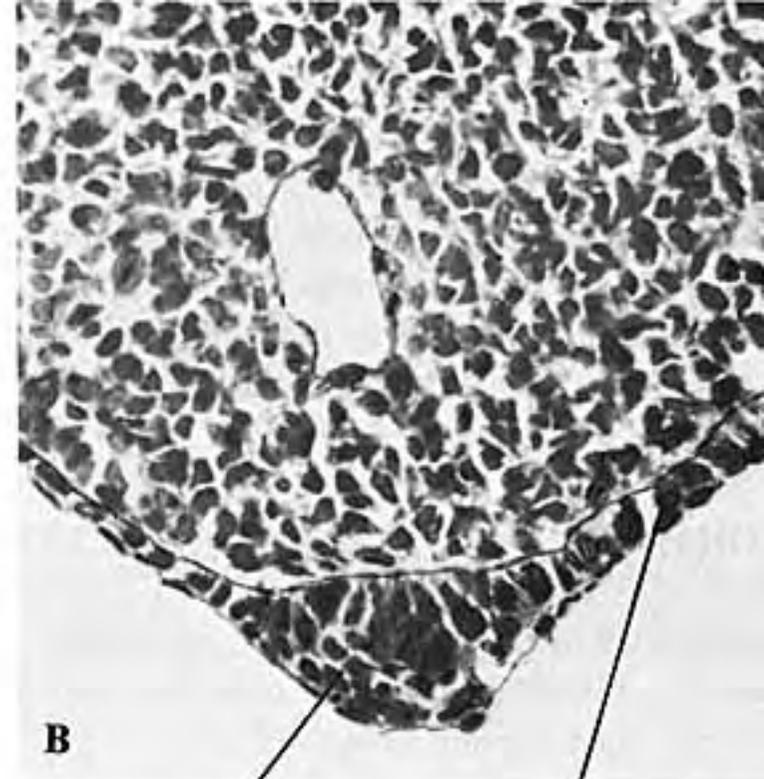
The endochondral bones are formed from sclerotomes of somitomers and sclerotomes of the first four somites (occipital somites).

The intramembranous bones arise from ectomesenchyme (mesenchyme derived from neural crest), which gives rise to cartilage, bone, and connective tissue of the face and dorsal head. Intramembranous bones articulate by means of fibrous joints called sutures. Widened suture areas, at the corners of growing bones, are called fontanelles. Sutures and fontanelles allow bony plates to overlap one another during parturition.









Apical ectodermal ridge

Skin ectoderm

Limb mesenchyme

Marginal vein



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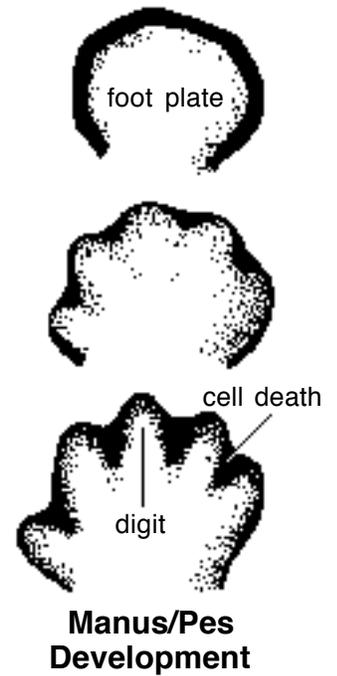
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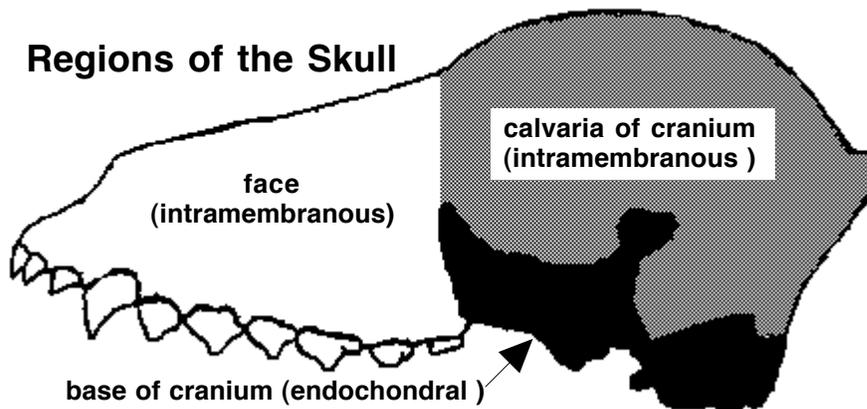
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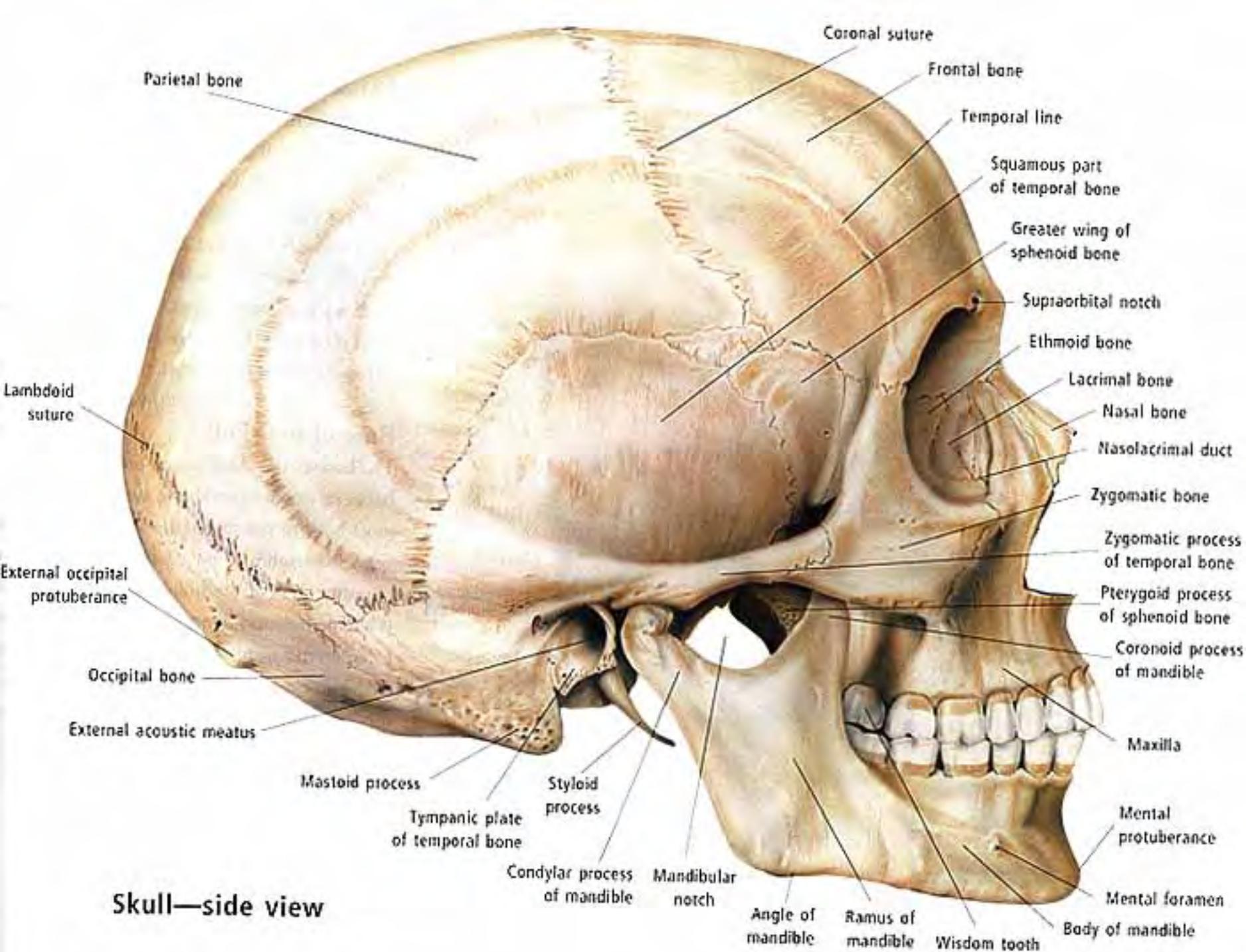
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Note: Auditory ossicles arise endochondrally from pharyngeal arches I (malleus & incus) and II (stapes).

Muscles. Muscles of the head arise from myotomes derived from somitomeres (seven) or somites (four occipital somites:

Somitomere myotomes migrate to the orbit (two giving rise eye muscles) or they migrate to pharyngeal arches (becoming muscles of mastication, facial expression muscles).

Somite myotomes become tongue and neck muscles and they migrate to pharyngeal arches (IV-VI), becoming pharyngeal, laryngeal & esophageal muscles.

Cranial nerves establish early connections with adjacent somitomeres & somites and accompany them to definitive muscle sites. Pharyngeal arches are each innervated by specific cranial nerves (I=trigeminal; II=facial; III=glossopharyngeal; IV-VI=vagus).

Pharyngeal (Branchial) Arch Summary:

Ectomesenchyme migrates to pharyngeal arches to form connective tissue, cartilage and bone. Somitomere/somite myotomes migrate into the arches and give rise to skeletal muscle. Each arch is innervated by a particular cranial nerve.

First arch. (innervated by cranial nerve V)

- jaw bones (mandible & maxilla); also, ossicles of the middle ear (incus & stapes)
- muscles of mastication, plus rostral digastricus, mylohyoid, & tensor tympani mm.

Second arch: (innervated by cranial nerve VII)

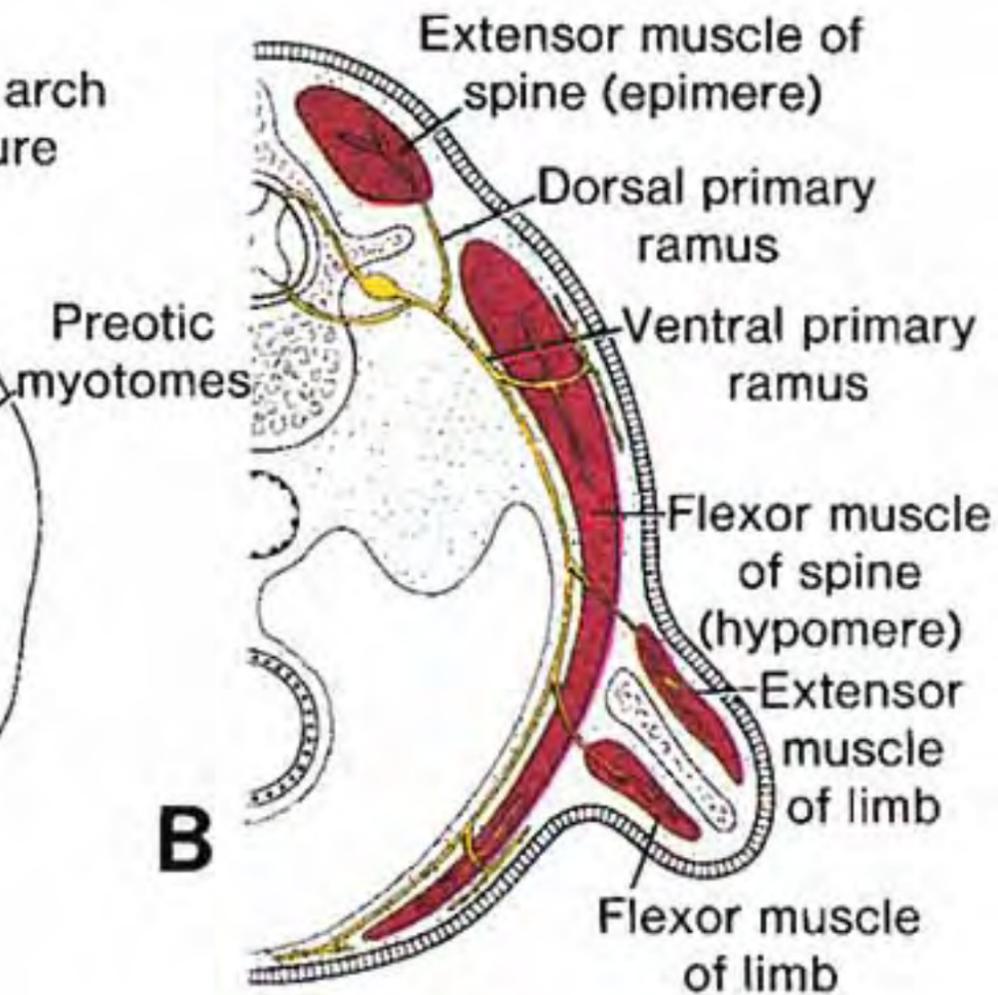
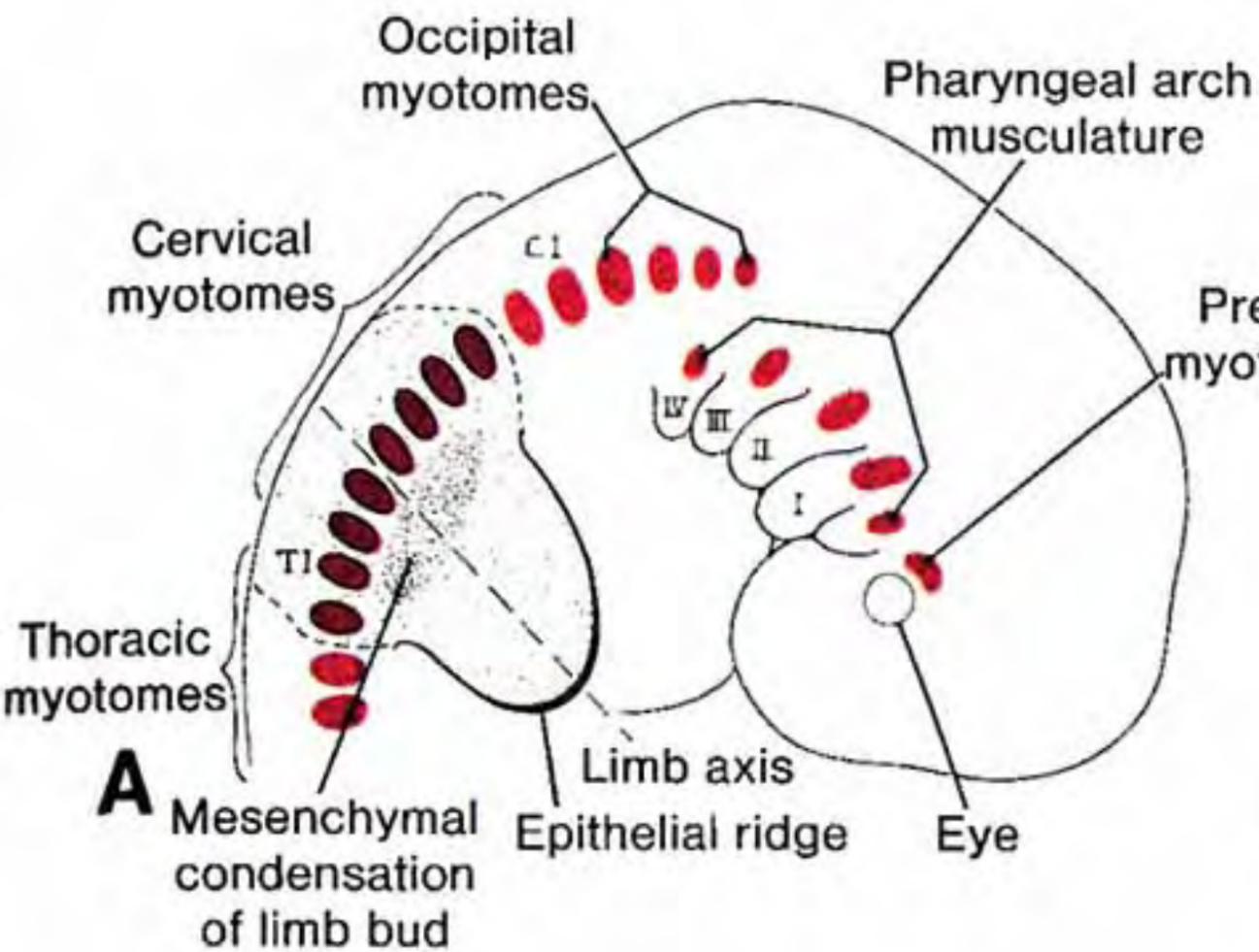
- hyoid bones & stapes (ossicle of the middle ear)
- muscles of facial expression, including caudal digastricus & stapedius mm.

Third arch: (innervated by cranial nerve IX)

- hyoid bones
- one pharyngeal muscle (stylopharyngeus mm.)

Arches IV through VI: (innervated by cranial nerve X)

- laryngeal cartilages
- pharyngeal mm & cricothyroid m — innervated by cranial branch of X
- intrinsic laryngeal mm — innervated by recurrent laryngeal n. of X



Pig Embryo (7.5 mm)

