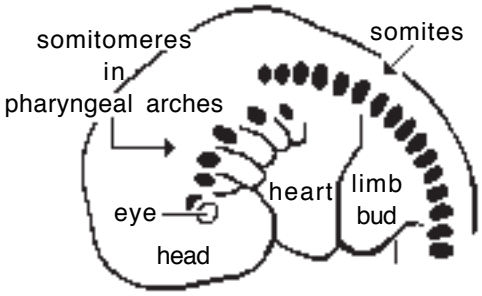
Musculo-Skeletal System
(Trunk, Limbs, and Head)

General Statements:

- Mesoderm gives rise to skeletal muscle, skin dermis, endochondral bones and joints.
- Notochord induces paraxial mesoderm to form somites (somitomeres develop rostral to the notochord in the head).
- Each somite differentiates into three regions:
  - **sclerotome** (medial): forms most of the axial skeleton (vertebrae, ribs, and base of the skull).
  - **dermatome** (lateral): migrates to form dermis of the skin
  - **myotome** (middle): migrates to form skeletal muscles. Individual adult muscles are produced by merger of adjacent myotomes.



Somites & Somitomeres

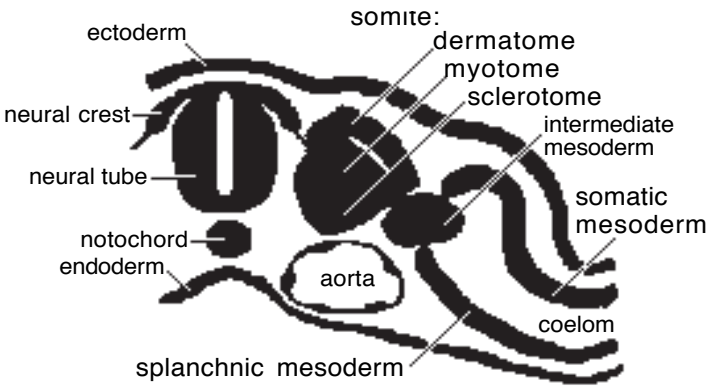
Note: Early in development, nerves make connections with adjacent myotomes and dermatomes, establishing a segmental innervation pattern. As myotome/dermatome cells migrate to assume adult positions, the segmental nerve supply must follow along to maintain its connection to the innervation target. (Recurrent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

Skin.

Consists of dermis and epidermis:

Epidermis, including hair follicles & glands, is derived from ectoderm. Neural crest cells migrate into epidermis and become *melanocytes*. (Other neural crest cells become tactile disc receptors.)

Dermis arises from dermatomes of somites. Adjacent dermatomes overlap; thus, each skin region is innervated by 2 or 3 spinal nerves.



Mesoderm Regions

Muscle.

All *skeletal muscle* is derived from paraxial mesoderm which forms *somites* and, rostrally in the head, *somitomeres*. (The one exception is iris musculature, derived from optic cup ectoderm.)

Cardiac and *smooth muscles* originate from splanchnic mesoderm.

Myotome cells differentiate into myoblasts which fuse to form multinucleate myocytes (muscle fibers). The myocytes synthesize myosin & actin (the myofilaments align producing a striated muscle appearance). Developing muscles and tendons must be under tension (stretched by growing bone) in order to grow to proper lengths.

Muscle development requires innervation. Muscles release trophic molecules that determine muscle cell type (I, IIa, IIb). Also, muscles release trophic molecules that affect nerve growth.

Note:	Each anatomical muscle is genetically allocated a specific number of myoblasts that is determined by the time of birth. Thereafter, muscle cell growth is due solely to cellular hypertrophy. Regeneration (hyperplasia) of adult muscle cells does not occur.

Bone.

- Most bones are formed *endochondrally* (ossification of cartilage precursor)
- Bones of the calvaria (top of the skull) & face are formed *intramembranously* (osteoblasts arise directly from ectomesenchyme cells rather than from chondroblasts)

Embryologically, the skeleton originates from different sources:
— *paraxial mesoderm* forms sclerotomes that give rise endochondrally to axial skeleton
— *somatic mesoderm* forms endochondral appendicular bones per particular regions
— *ectomesenchyme* from neural crest forms intramembranous bones of the calvaria and face.

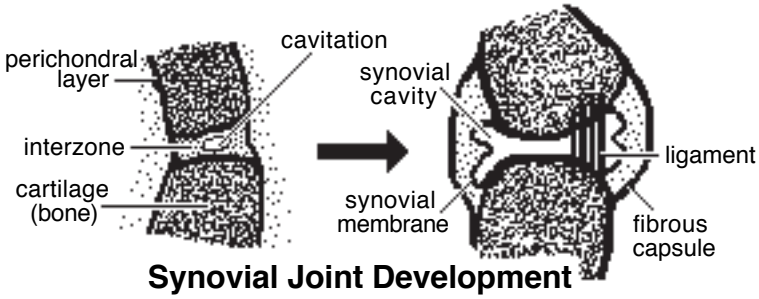
Endochondral bone formation:
— local mesenchyme undergoes condensation and cells differentiate into chondroblasts
— chondroblasts secrete matrix to produce a cartilage model of the future bone; the model is surrounded by perichondral fibrous tissue
— the diaphysis of the cartilage model undergoes ossification first (primary ossification); epiphyseal ossification occurs later (secondary ossification)
— 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.

Ligaments, Tendons & **Fibrous Tissue** originate from local mesenchyme or ectomesenchyme.

Joints.

— condensation of mesenchyme produces an *interzone* region within perichondral tissue connecting adjacent cartilage models of bones

— the interzone becomes fibrous connective tissue or fibrocartilage or a synovial cavity (according to the nature of the future joint)



Synovial Joint Development

Synovial joint formation:
— mesenchyme at the center of the interzone undergoes cavitation
— tissue bordering the cavity become *synovial membrane,* uneven expansion of the cavity creates synovial folds
— interzone mesenchyme also forms intra-articular ligaments where these are present
— perichondral tissue surrounding the interzone becomes *joint capsule* and localized thickenings of the joint capsule forms *ligaments*

Note:

Nerve driven muscle activity is essential for proper synovial joint development after the joint cavity is formed.

Joints must move during *in utero* and postnatal development to prevent ankylosis (fixed/frozen joint).

Also, muscles must be stretched by growing bones *in utero*; otherwise, joints would be restricted by contracted muscles at birth.

Regional Specifics

Trunk Region:

Skeletal Muscles.

— adjacent myotomes merge, forming broad muscles that are segmentally innervated (each myotome brings its own innervation when it overlaps 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.

— epimere and hypomere masses subdivide, the epimere becomes *epaxial muscles* and the hypomere becomes *hypaxial muscles*.

Axial Skeleton.

— sclerotomes give rise to vertebrae and ribs.

— the sternum develops differently, from chondrification/ossification of local somatic mesenchyme of the ventral thorax.

Formation of Vertebrae and Ribs:

— somite sclerotomes 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

— to produce a cartilage model of one vertebra, the diffuse region from one somite combines with the dense region of an adjacent somite

— intervertebral disc regions develop between newly formed vertebrae, sclerotome mesenchyme forms *annulus fibrous* and notochord forms *nucleus pulposus* (elsewhere notochord degenerates)

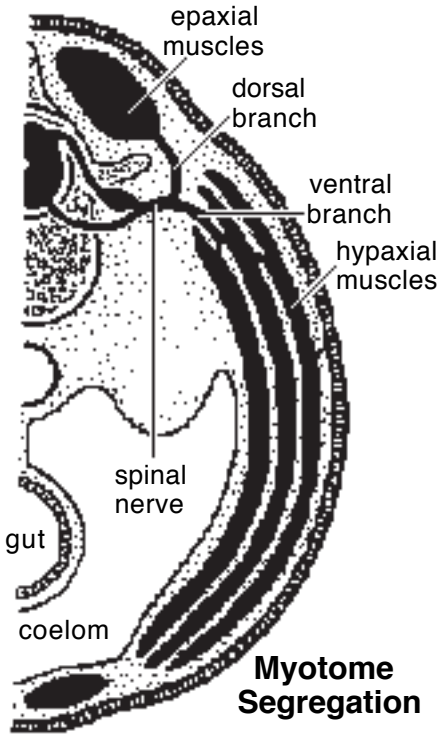
— ribs develop as extensions of thoracic vertebrae processes

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.

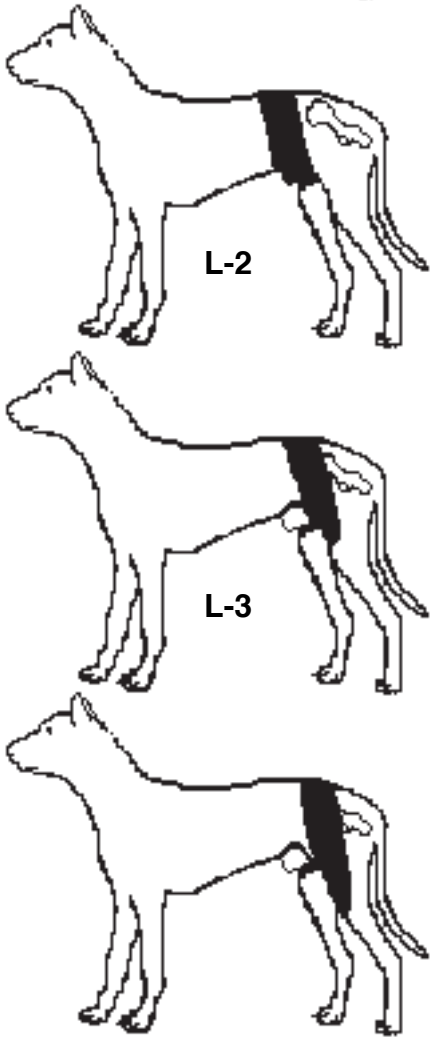
The notochord, neural tube, and neural crest all play a role directing somite differentiation and vertebral segmentation (formation).

Vertebral anomalies include:
stenosis of the vertebral canal;
mal-articulation;
hemivertebra; and
spinal bifida (absent vertebral arch).

Note: The dens originates as the body of vertebra C_1 (atlas), but it fuses with vertebra C_2 (axis).

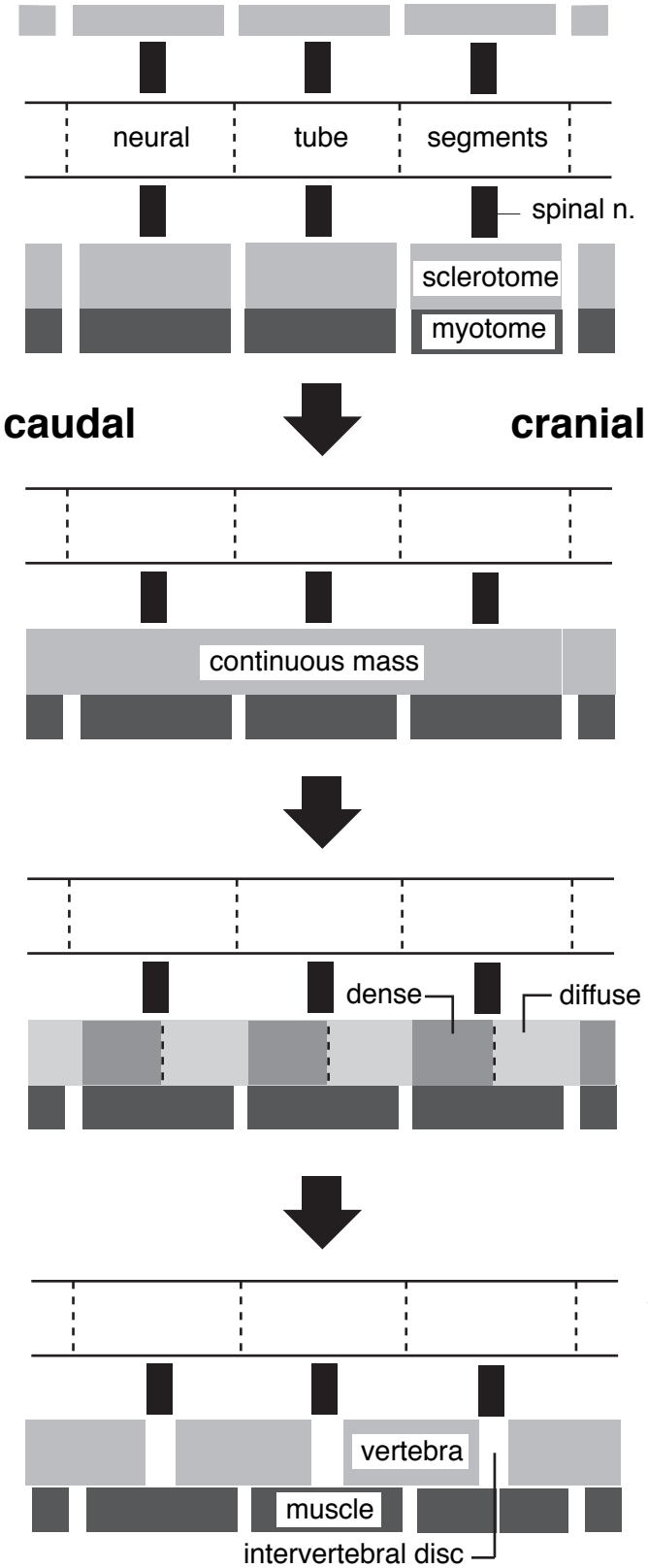


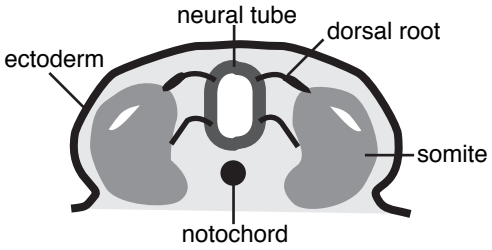
Myotome Segregation

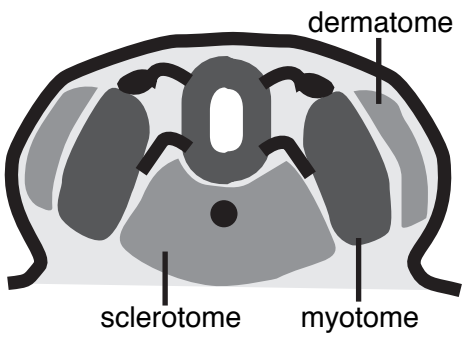


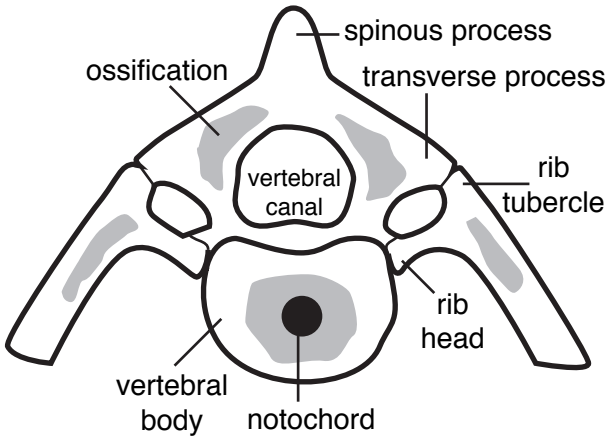
Canine Dermatomes

Sclerotomes to Vertebrae

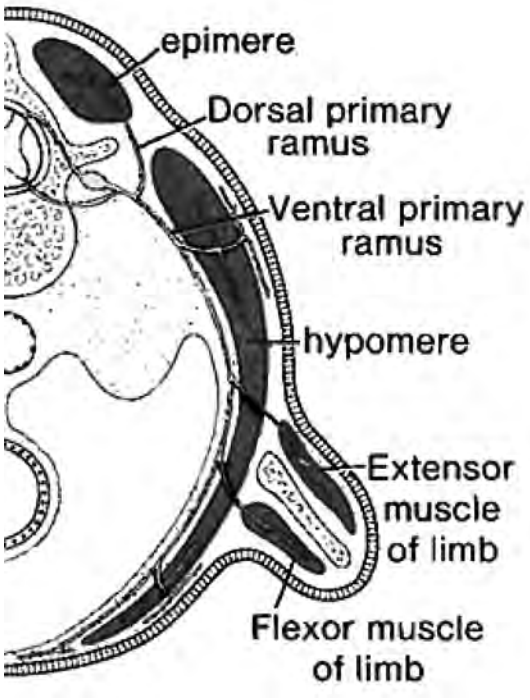








Limbs:



Skeletal Muscles.

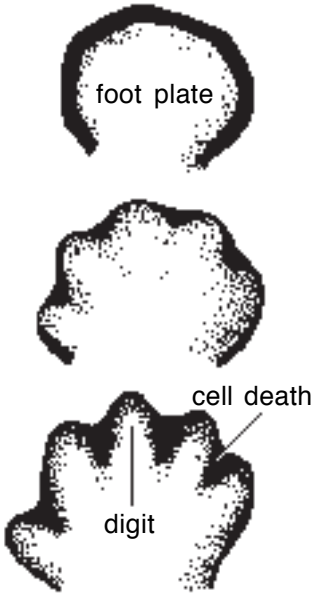
— hypomere myotomes along with their innervation migrate into the developing limb bud.
— myotomes segregate initially into an extensor mass and a flexor mass
— subsequently the two masses subdivide into the individual *extensor muscles* and *flexor muscles*.

Appendicular Skeleton and Skin.

— bone, cartilage, and connective tissue of the limb arise from the local somatic mesoderm of the limb bud.
— local mesenchyme condenses and forms cartilage models of limb bones
— dermis comes from dermatome migrations into the limb bud
— vessels and nerves grow into the limb.

Limb Morphogenesis:

— limbs grow outward from body wall somatopleure as limb buds
— a limb bud begins as a limb field (an area of somatopleure committed to forming a limb)
— a ***limb bud*** is produced by localized proliferation & condensation of mesenchyme, surface covered by ectoderm
— regions of the limb develop in proximal to distal 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 & ectoderm along its outer margin forms a thickened apical ridge
— the ***apical ridge*** is induced to form by underlying mesoderm and, in turn, it induces the mesoderm to continue growing into a limb)
— 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);



Manus/Pes Development

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 cranium is formed during growth of the head process; the face develops from outgrowths of 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.

Skeletal Muscles.

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

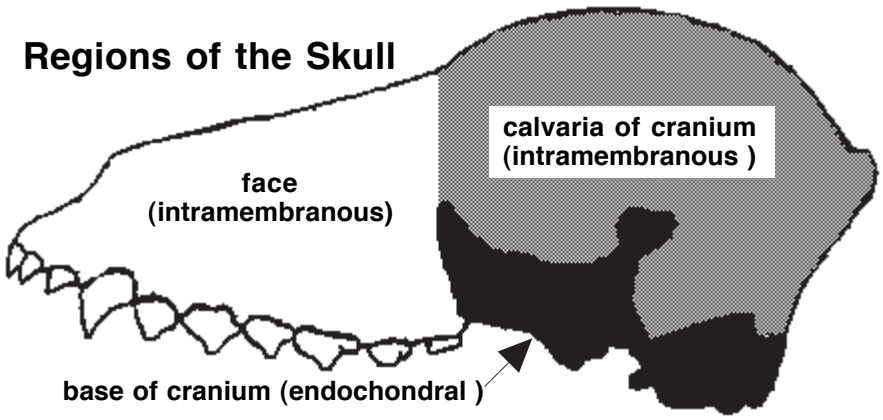
- *Somitomere* myotomes migrate to the orbit (two giving rise eye muscles) or they migrate to pharyngeal arches (becoming muscles of mastication, facial expression muscles).
- *Somite* myotomes become tongue and neck muscles and they migrate to pharyngeal arches (IV-VI), becoming pharyngeal, laryngeal & esophageal muscles.
- Cranial nerves establish early connections with adjacent somitomeres & somites and accompany them to definitive muscle sites. Each pharyngeal arch is innervated by specific cranial nerves (I=trigeminal; II=facial; III=glossopharyngeal; IV-VI=vagus).

Skull.

Bones of the base of the cranium develop endochondrally; but the relatively flat bones that comprise the calvaria (roof of the cranium) and the face develop intramembranously.

- Endochondral bones are formed from the sclerotomes of somitomeres and the first four somites (occipital somites).
- Intramembranous bones arise from ectomesenchyme (derived from neural crest). Intramembranous bones articulate by means of fibrous joints called sutures. Widened suture areas, at the corners of growing bones, are called *fontanels*. Sutures and fontanels allow bony plates to overlap one another during parturition.
- The mandible has a complex origin involving both endochondral and intramembranous development.
- Auditory ossicles arise endochondrally from pharyngeal arches I (malleus & incus) and II (stapes).

Note: Ectomesenchyme (mesenchyme derived from neural crest) gives rise to cartilage, bone, and connective tissue of the face and dorsal head (calvaria).



Pharyngeal Arch Summary:

- Ectomesenchyme fills pharyngeal arches and forms connective tissue, cartilage and bone.
- Somitomere/somite myotomes migrate into pharyngeal arches and give rise to the skeletal muscles that arise from that arch
- . 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 (malleus & incus)
- — 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