

Mesodermal Derivatives And Limb Formation

READING ASSIGNMENT:

Mesoderm:

Review Larsen Chapter 3: Figures 3-2, 3-3, 3-8
Larsen Chapter 3: pp. 60-65
Larsen Chapter 4: 79-85; Figures 4.6-4.9

Limb:

Larsen Chapter 11: pp. 315-328 (that portion of bone development covered in SBPM/histology should just be reviewed); 336-340 (We will only cover the **concepts** of limb patterning as it arises in studying the limb but will not concentrate on the specific molecular events.)

LEARNING OBJECTIVES:

We will focus on formation and differentiation of the paraxial mesoderm and its somite derivatives and on formation of the limbs from somite and lateral plate mesoderm.

1. Review the formation of the germ layers and know the placement (medial to lateral) of axial, paraxial, intermediate and lateral plate mesoderm.
2. Understand where and how the somites form and their role in the segmentation of the body (and nervous system). Recognize the orderly process of their formation.
3. Understand the migratory routes taken by the somite derivatives: sclerotome and dermamyotome.
4. Understand how the vertebrae and segmental muscles arise.
5. Understand the contributions made by somite and lateral plate mesoderm to the limbs. Note that there is also a contribution from intermediate mesoderm in the form of the blood vessel.
6. Understand the role of the apical ectodermal ridge and progress zone in limb elongation and the concept of positional information. Note the laying down of limb elements in a proximal to distal direction.
7. Understand the initial segmental pattern of innervation (Figure 11-9) of the limbs and how it is complicated by limb rotation (see figure 11-10).
8. Understand the concept of diffusible signals that pattern the hand (as well as other parts of the limb).

GLOSSARY:

Mesoderm and its derivatives

Axial mesoderm - This midline mesoderm gives rise to the notochord.

Intermediate mesoderm - The intermediate mesoderm lies between the paraxial mesoderm and lateral plate mesoderm from the cervical to the sacral regions. It forms embryonic and definitive kidneys and part of the male genital system.

Lateral plate mesoderm - This mesodermal sheet is lateral to the intermediate mesoderm. It splits into somatopleuric mesoderm (next to ectoderm) and splanchnopleuric mesoderm (next to endoderm) during the third week. Somatopleuric mesoderm forms the parietal serous lining of the body cavities while splanchnopleuric mesoderm forms the serous membrane ensheathing visceral organs. The cavity formed by the splitting of these two layers becomes the intraembryonic coelom which gives rise to the definitive pleural, pericardial and peritoneal cavities.

Notochordal process - The notochordal process is one of the first mesodermal structures to arise by gastrulation as cells surrounding the primitive pit form a hollow tube that extends cranially in the axial midline. It elongates as cells surrounding the primitive pit are added at its caudal end. The notochordal process condenses into the notochord.

Mesenchyme - an embryonic connective tissue that can be derived from mesoderm or neural crest.

Mesoderm - This "middle" layer of the trilaminar embryo, arises from the epiblast by gastrulation during the third week. It is divided into paraxial, intermediate or lateral plate mesoderm.

Paraxial mesoderm - immediately adjacent to the notochord. Condenses into the epithelial somites.

Prechordal plate mesoderm - This small block of mesoderm forms just cranial to the tip of the notochordal process. It induces cranial midline structures such as the anterior brain.

Somite - The paraxial mesoderm segments into blocks of mesoderm called somites. The most cranial somites appear at about day 20 and subsequent somites are produced at the rate of 3 - 4 pairs per day. 42 to 44 pairs are formed by day 30, including 4 occipital, 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 8 - 10 coccygeal. 5 - 7 coccygeal pairs disappear leaving 37 pairs of somites. Somites caudal to S1 arise from the caudal eminence (see text). Somites split into **sclerotome (future vertebrae)**, **dermatome (dermis)** and **myotomes** (source of **skeletal muscle**, formation of segmental musculature and role in limb).

Somitomere - precursor to somites. The first 7 form the occipital bone and the rest for true somites.

Limb formation (review bone development and adult bone structures from histology)

Apical ectodermal ridge (AER) - This ectodermal thickening at the distal end of the limb bud sequentially induces the underlying mesodermal core to differentiate into appropriate regions of the skeletal elements of the limb. The specific character of the response (type of segment produced) of the mesodermal core depends on its age.

Brachial plexus - This mixture of ventral primary rami of spinal nerves C5 - T1 innervates the upper extremity.

Decision making point - Specific nerve fibers "make a decision" to leave the nerve trunk to innervate specific end organs at a specific decision making point. The divergence of the nerve may occur in response to a chemoattractant or tropic substance (or a chemorepellent) or result from the growth cone's unique capacity to follow structural or molecular cues already present in the substrate.

Limb bud - Somites in the limb regions (C5 - C8; L3 - L5) induce somatopleuric lateral plate mesoderm to proliferate, forming upper and lower limb buds, consisting of an ectodermal cap and a mesodermal core. A specialization of the limb bud ectodermal cap, the AER, then induces regions of the mesodermal core to produce specific limb segments, from the shoulder and hip to the phalanges. The upper limb buds appear at about 24 days, while the lower limb buds appear at about 28 days. Thereafter (until the eighth week), development of the upper limb buds precedes development of the lower buds by a few days.

Permissive pathways - Growth cones of elongating nerves may grow along permissive pathways, most notably devoid of dense mesenchyme or glycosaminoglycans.

Progress Zone - mesoderm under AER where mesenchymal cells proliferate. This is where (it is thought) cells acquire positional information (will they be proximal or distal elements of limb?).

Mesodermal core - The limb buds are first composed of a core of lateral plate mesoderm (the mesodermal core) and a cap of ectoderm.

Sacral plexus - This large plexus of nerves (anterior to the piriformis muscle and the sacrum) is composed of ventral primary rami of the lumbosacral trunk (L4, L5) and S1 - S4. All of the nerves of the sacral plexus exit by way of the greater sciatic foramen.

Zone of polarizing activity (ZPA) - A region of mesoderm on the posterior aspect of the developing limb. The ZPA and the overlying AER secrete interacting substances: the ZPA produces the pattern formation signal while the AER secretes other molecules that initial turn mesoderm into ZPA and then maintain ZPA function.