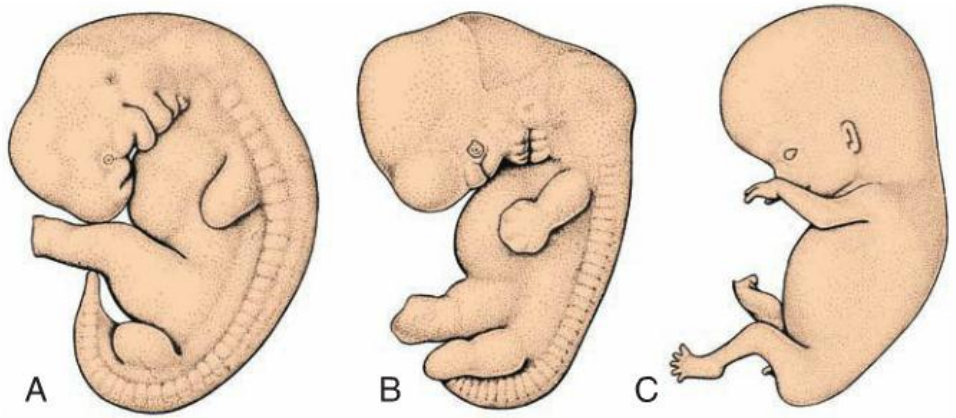
Chapter 12
Limbs

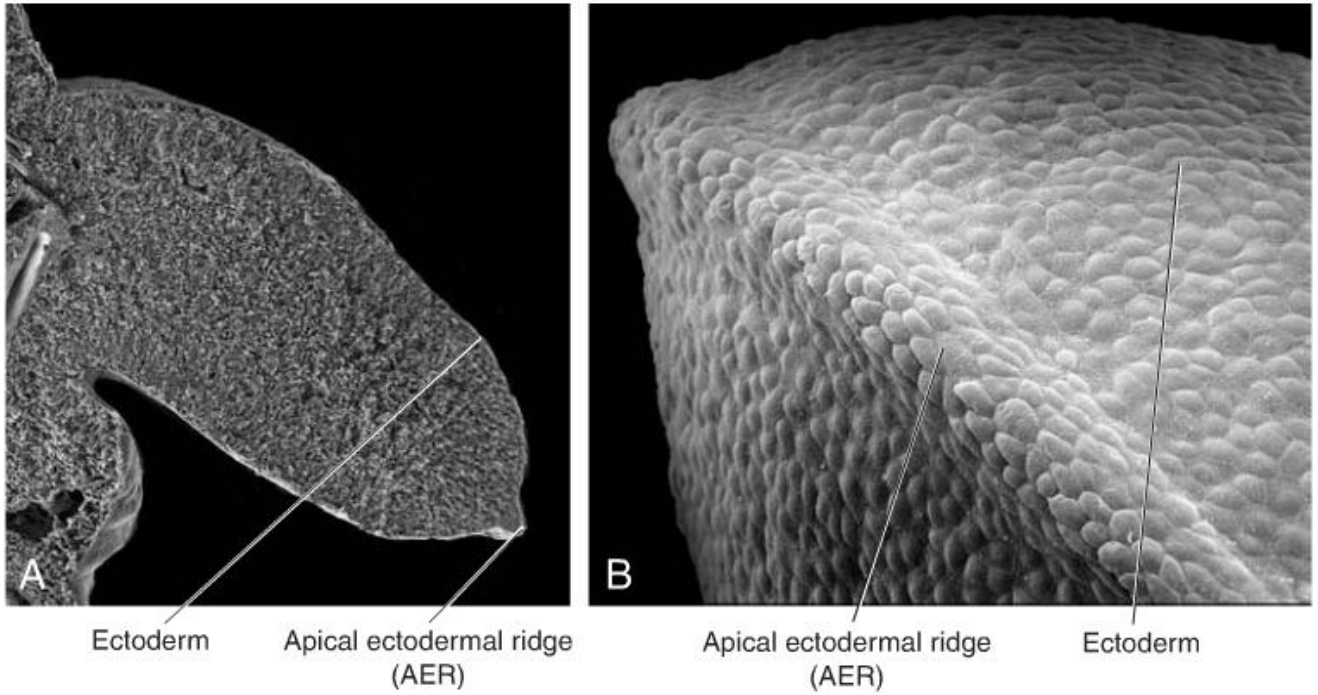
The appendicular skeleton includes:

1. Limbs
2. Shoulder girdle
3. Pelvic girdle

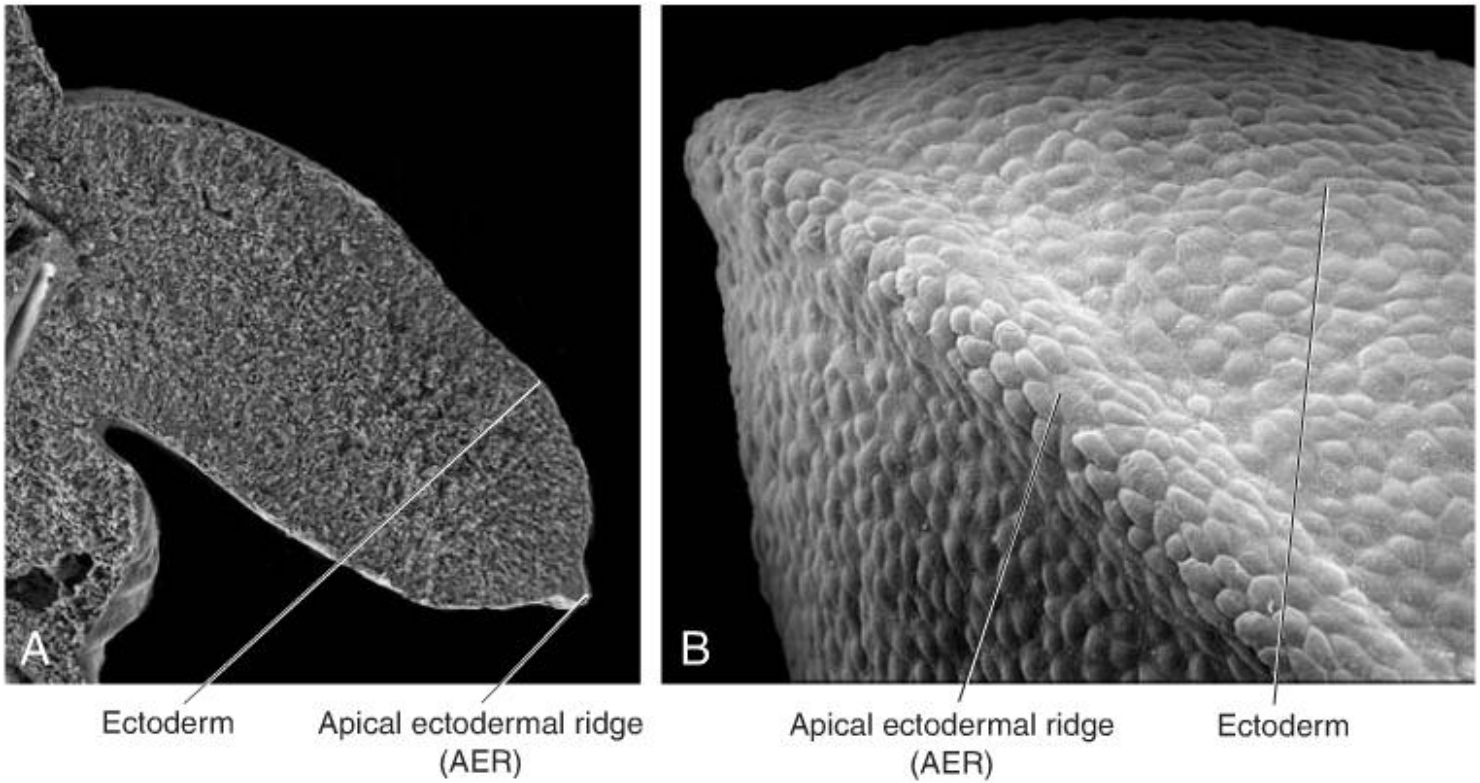
- At **the end of the fourth week** of development, limb buds become visible as outpocketings from the ventrolateral body wall.
- The forelimb appears first followed by the hind limb 1 to 2 days later.



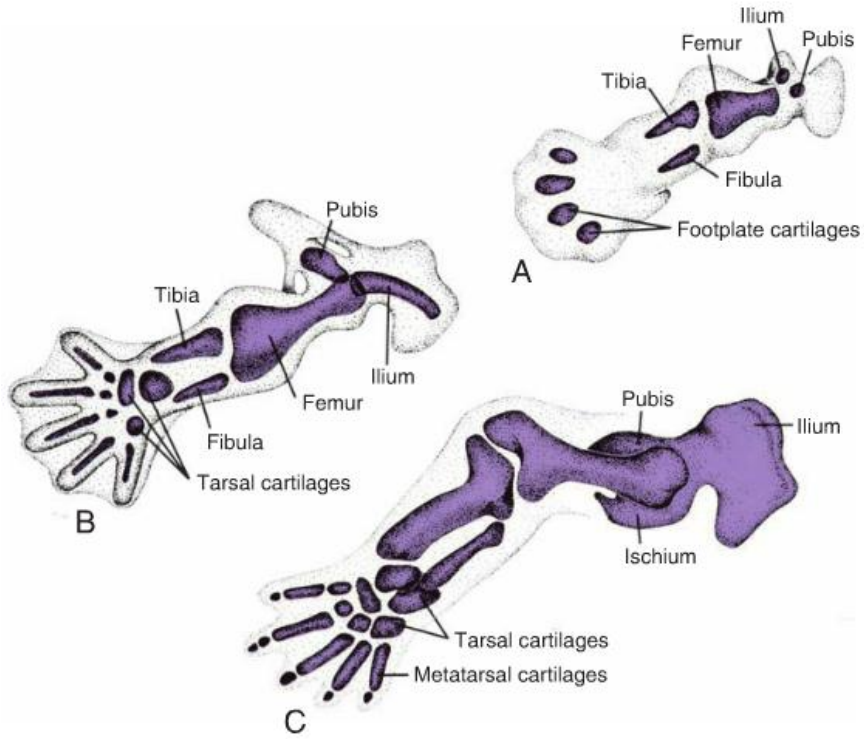
- Initially, the limb buds consist of a mesenchymal core derived from the **parietal (somatic) layer of lateral plate mesoderm** that will form the bones and connective tissues of the limb, covered by a layer of cuboidal ectoderm.

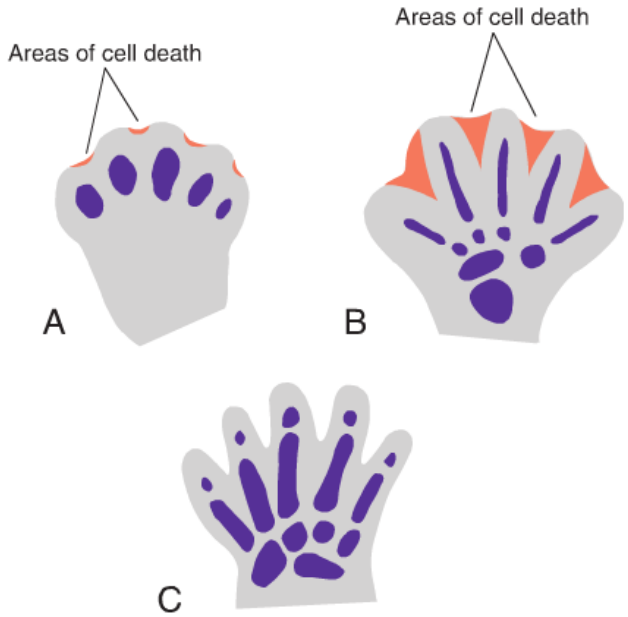


- Ectoderm at the distal border of the limb thickens and forms the **apical ectodermal ridge(AER).**
- This ridge exerts an inductive influence on adjacent mesenchyme, causing it to remain as a population of undifferentiated, rapidly proliferating cells, the **progress zone.**
- As the limb grows, cells farther from the influence of the AER begin to differentiate into cartilage and muscle. In this manner, development of the limb proceeds proximo-distally.



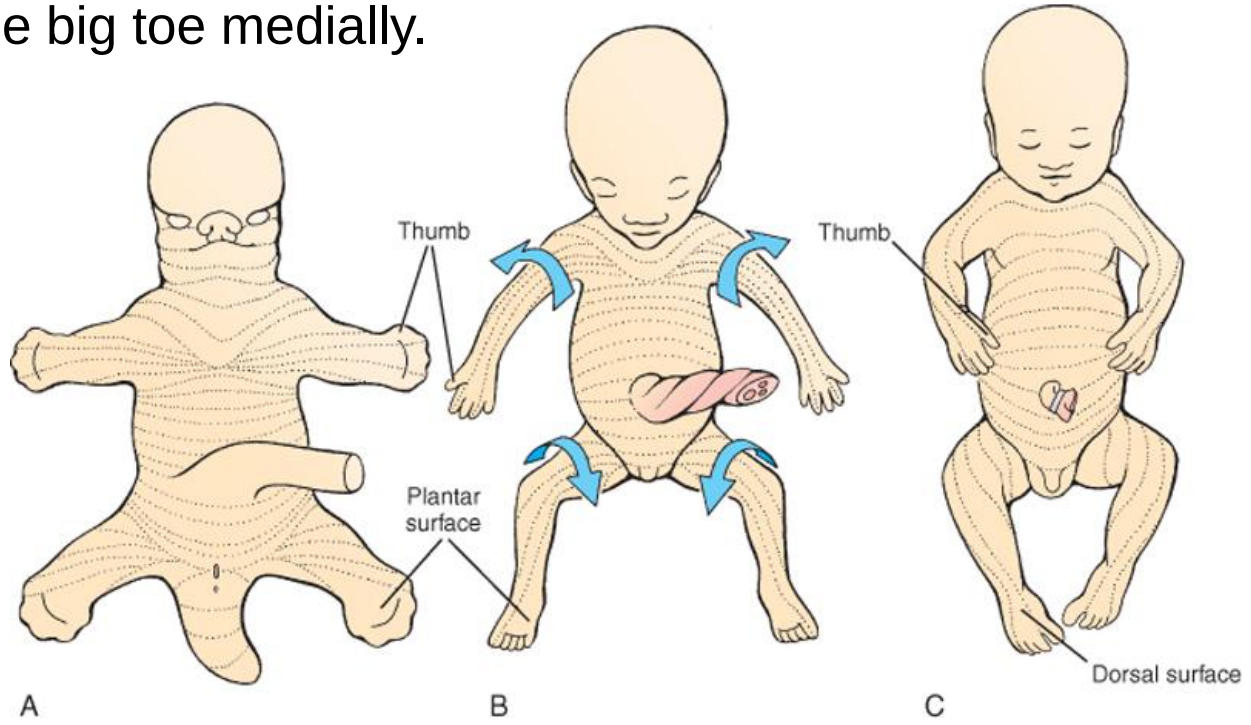
- In **6-week-old** embryos, the terminal portion of the limb buds becomes flattened to form the **hand** and **foot plates** and is separated from the proximal segment by a circular constriction.
- Later, a second constriction divides the proximal portion into two segments, and the main parts of the extremities can be recognized.
- **Fingers and toes** are formed when **cell death in the AER** separates this ridge into five parts.





During **the seventh week** of gestation, the **limbs rotate in opposite directions**.

The upper limb rotates 90°laterally, so that the extensor muscles lie on the lateral and posterior surface, and the thumbs lie laterally, whereas the lower limb rotates approximately 90°medially, placing the extensor muscles on the anterior surface and the big toe medially.



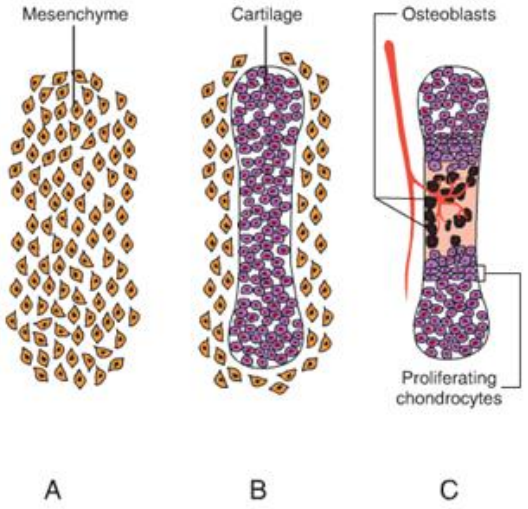
- While the external shape is being established, mesenchyme in the buds begins to condense, and these cells differentiate into chondrocytes.
- By the **sixth week** of development, **the first hyaline cartilage models**, foreshadowing the bones of the extremities, are formed by these chondrocytes .

Ossification: Primary ossification centers

Ossification of the bones of the extremities, **endochondral ossification**, **begins** by the **end of the embryonic period.**

Primary ossification centers are present **in all long bones** of the limbs by the **12th week** of development.

From the primary center in the shaft or diaphysis of the bone, endochondral ossification gradually progresses toward the ends of the cartilaginous model.

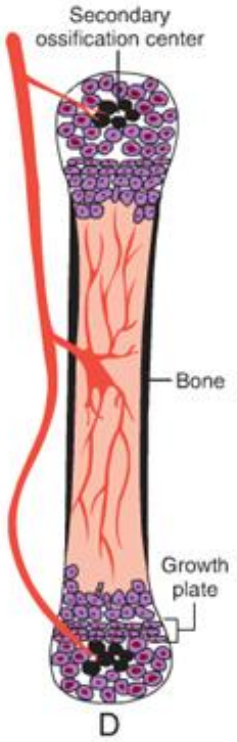


Ossification: secondary ossification centers

At birth, the **diaphysis** of the bone is usually **completely ossified**, but the two ends, the **epiphyses**, are still **cartilaginous**.

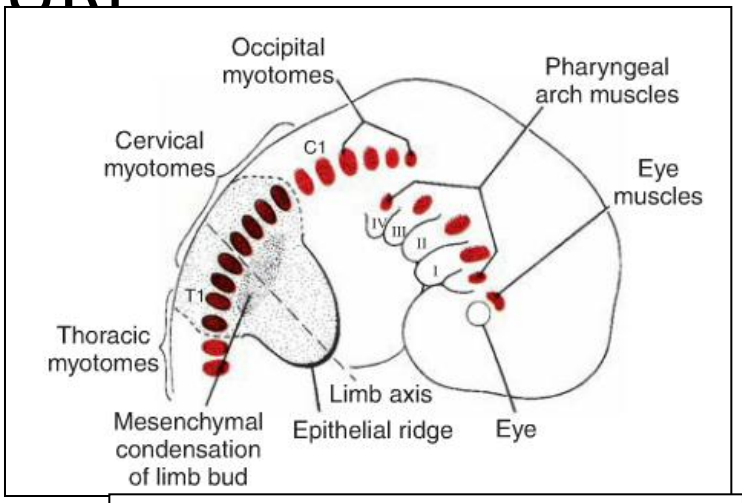
Shortly thereafter ossification centers arise in the epiphyses (**secondary ossification centers**).

Temporarily, a cartilage plate remains between the diaphyseal and epiphyseal ossification centers. This plate, the **epiphyseal plate**, plays an important role in growth in the length of the bones. Endochondral ossification proceeds on both sides of the plate.



LIMB MUSCULATURE

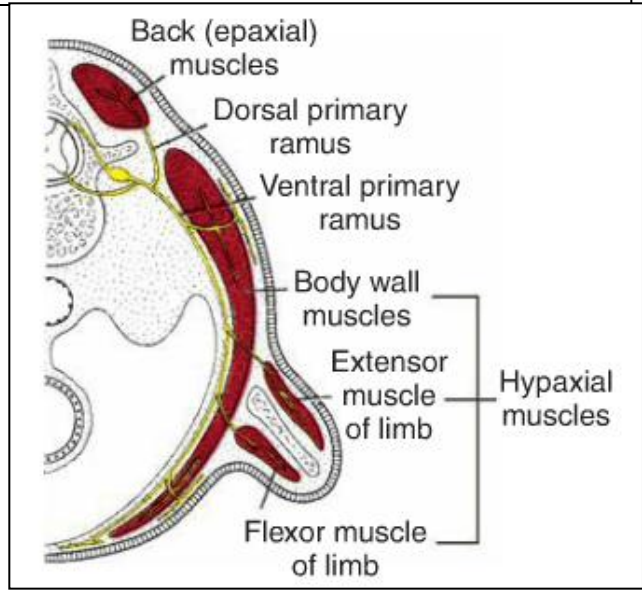
- Limb musculature is derived from muscle precursor cells of the somites that migrate into the limb to form muscles.
- Initially these muscle components are segmented according to the somite from which they are derived.



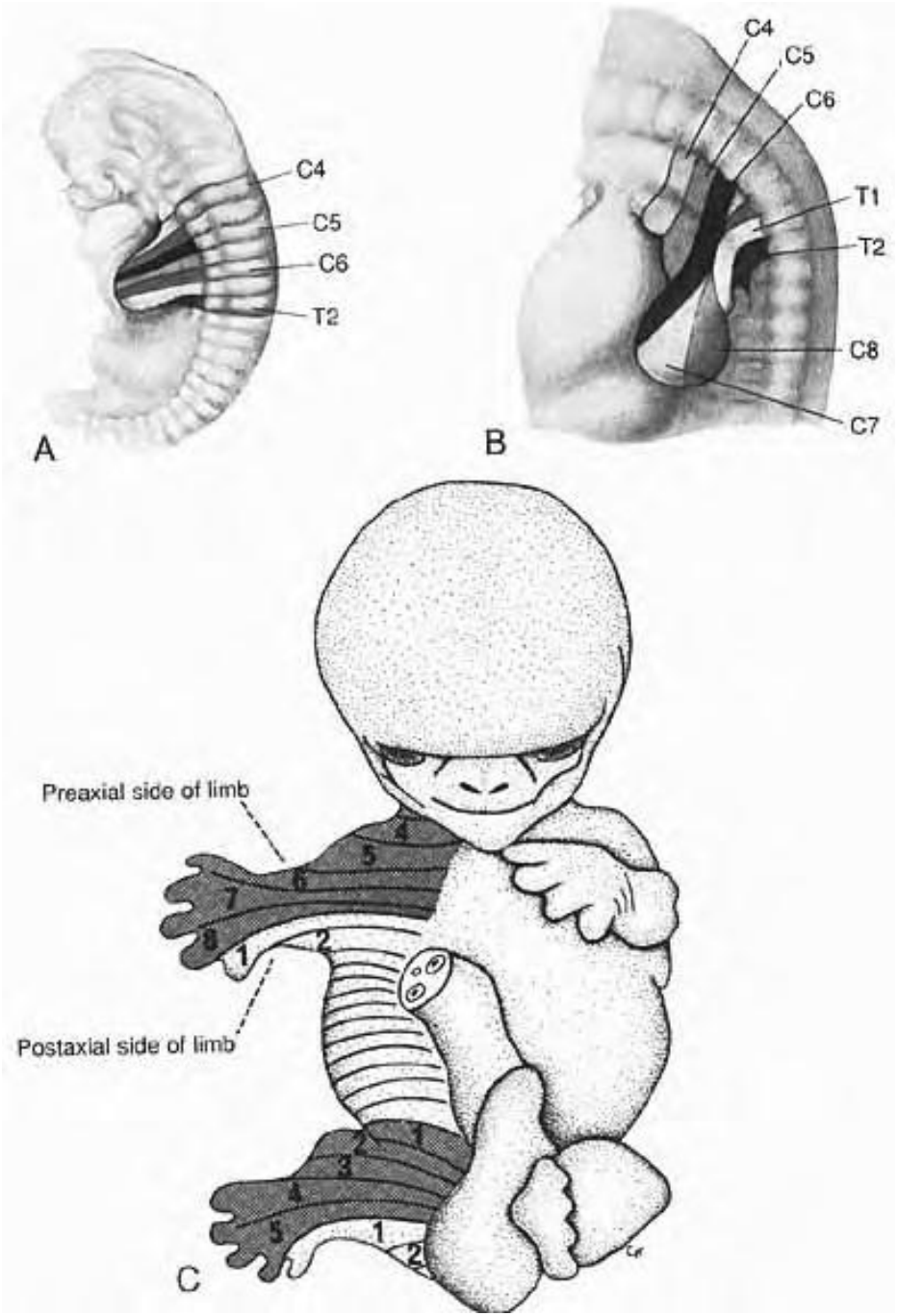
•With elongation of the limb buds, the muscle tissue **splits** into **flexor** and **extensor** components

•Additional **splitting and fusion** occur such that a **single muscle** may be formed from **more than one original segment.**

•The resultant complex **pattern of muscles** is determined by **connective tissue derived from lateral plate mesoderm.**



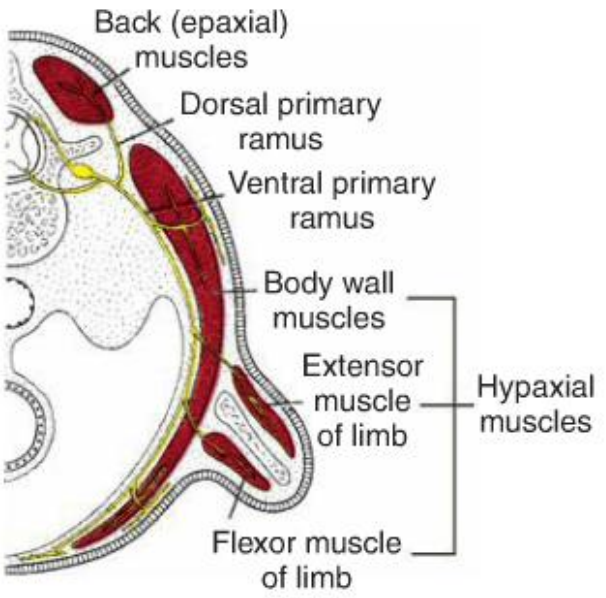
- The **upper limb buds** lie opposite the **lower five cervical** and **upper two thoracic segments**.
  The **lower limb** buds lie opposite the **lower four lumbar** and **upper two sacral segments**.


C4
C5
C6
T2
A
C4
C5
C6
T1
T2
C8
C7
B
Preaxial side of limb
Postaxial side of limb
C

As soon as the **buds** form, **ventral primary rami** from the appropriate spinal nerves and penetrate into the mesenchyme.

At first, each ventral ramus enters with **isolated dorsal and ventral branches**, but soon these branches unite to form large dorsal and ventral nerves.

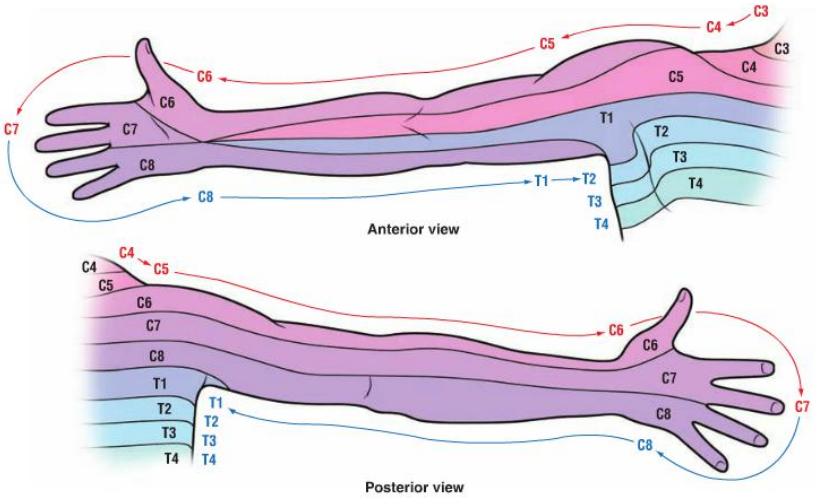
Thus, the ***radial nerve***, which supplies the extensor musculature, is formed by a combination of the dorsal segmental branches, whereas the ***ulnar*** and ***median nerves***, which supply the flexor musculature, are formed by a combination of the ventral branches.



Immediately after the nerves have entered the limb buds, they establish an intimate contact with the differentiating mesodermal condensations, and the early contact between the nerve and muscle cells is a prerequisite for their complete functional differentiation.

Sensory innervation for dermatomes

Spinal nerves provide sensory innervation for the dermatomes. Although the original dermatomal pattern changes with growth of the extremities, an orderly sequence can still be recognized in the adult.

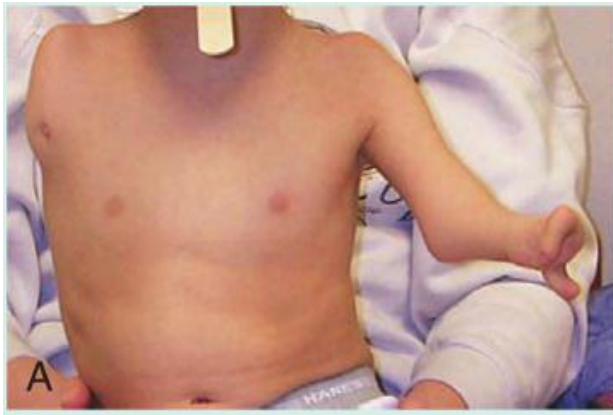


Bone Age

- **Radiologists** use the appearance of various ossification centers to determine whether a child has reached his or her proper maturation age. Useful information about **bone age** is obtained from **ossification studies** in the **hands** and **wrists** of children.
- Prenatal analysis of fetal bones by **ultrasonography** provides information about fetal growth and **gestational age**.

Limb Defects

- Abnormalities of the limbs vary greatly, and they may be represented by partial (**meromelia**) or complete absence (**amelia)** of one or more of the extremities.
- Sometimes the long bones are absent, and rudimentary hands and feet are attached to the trunk by small, irregularly shaped bones (**phocomelia**, a form of meromelia)
- Sometimes all segments of the extrimities are present but abnormally short: **micromelia**



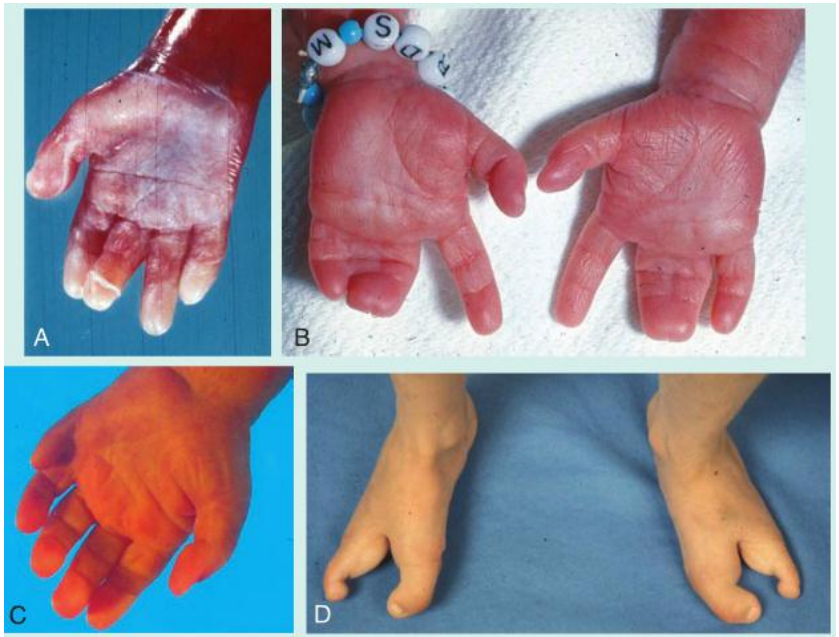
Unilateral amelia

phocomelia

- **Thalidomide**: a drug widely used as a sleeping pill and antinauseant. It was subsequently established that thalidomide causes a characteristic syndrome of malformations consisting of absence or gross deformities of the long bones, intestinal atresia, and cardiac anomalies.
- Because the drug is now being used to treat AIDS and cancer patients, there is concern that its return will result in a new wave of limb defects.
- Studies indicate that the **most sensitive period for teratogen-induced limb malformations** is the **fourth and fifth weeks** of development.

Defects involving the digits

Digital defects. **A.** Brachydactyly, short digits. **B.** Syndactyly, fused digits. **C.** Polydactyly, extra digits. **D.** Cleft foot, lobster claw deformity. Any of these defects may involve either the hands or feet or both.



AMNIOTIC BANDS

- Amniotic bands may cause ring constrictions and amputations of the limbs or digits.
- The origin of the bands is not clear, but they may represent adhesions between the amnion and affected structures in the fetus.
- Other investigators believe that bands originate from tears in the amnion that detach and surround part of the fetus.

Digit amputations resulting from amniotic bands.

Congenital hip dislocation

- Consists of under development of the acetabulum and head of the femur.
- It is rather common and occurs mostly in female newborns.
- Although dislocation usually occurs after birth, the abnormality of the bones develops prenatally. Because many babies with congenital hip dislocation are breech deliveries, it has been thought that breech posture may interfere with development of the hip joint. It is frequently associated with laxity of the joint capsule.