

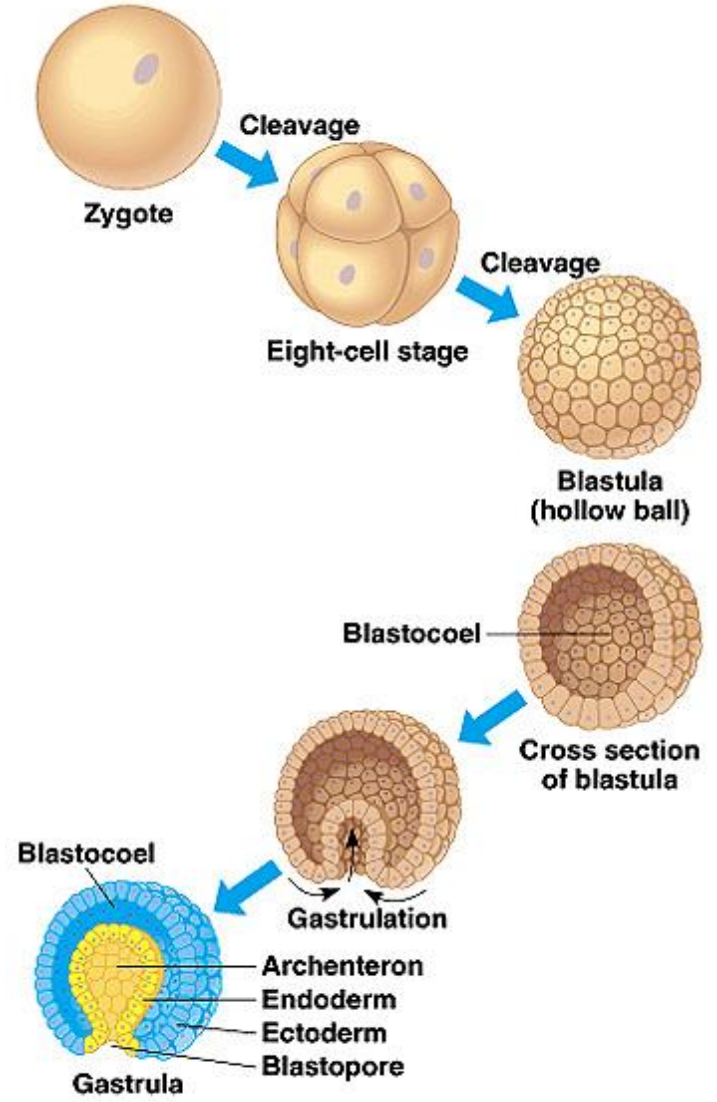
DEVELOPMENT OF THE LIMBS

Dr AMAL ALBTOOSH

https://youtu.be/VpbdqGJ9LWk?si=3regigaO_NxRs9qL



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ
 هَلْ أَتَى عَلَى الْإِنْسَانِ حِينٌ مِّنَ الدَّهْرِ لَمْ يَكُنْ
 شَيْئًا مَّذْكُورًا ﴿١﴾ إِنَّا خَلَقْنَا الْإِنْسَانَ مِنْ نُطْقَةٍ أَمْشَاجٍ
 نَّبْتَلِيهِ فَجَعَلْنَاهُ سَمِيعًا بَصِيرًا ﴿٢﴾



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Differentiation of germ layers

The three germ layers give rise to different cell types in the animal body:

✓ **The ectoderm** forms:

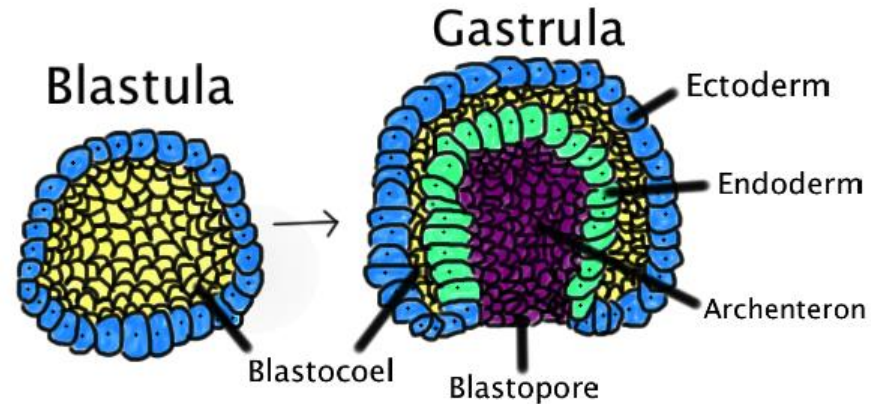
1. the nervous system
2. the outer layer of skin

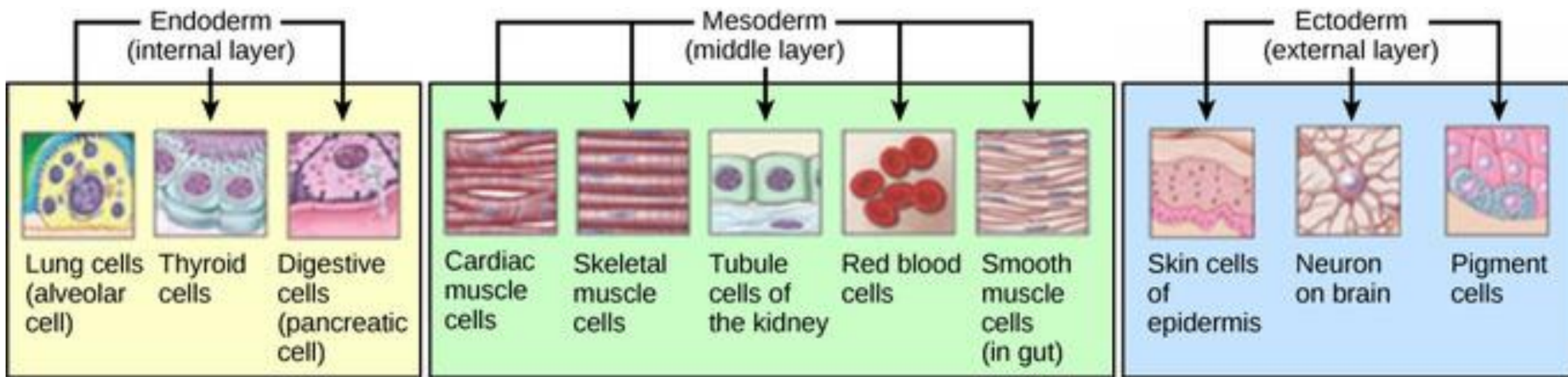
✓ **The mesoderm** gives rise to:

1. muscles
2. connective tissues

✓ **The endoderm** gives rise to the:

- columnar cells found in the digestive system and many internal organs.





Endoderm
(internal layer)

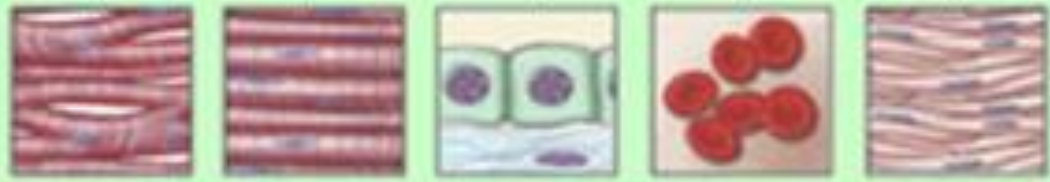


Lung cells
(alveolar cell)

Thyroid cells

Digestive cells
(pancreatic cell)

Mesoderm
(middle layer)



Cardiac muscle cells

Skeletal muscle cells

Tubule cells of the kidney

Red blood cells

Smooth muscle cells
(in gut)

Ectoderm
(external layer)



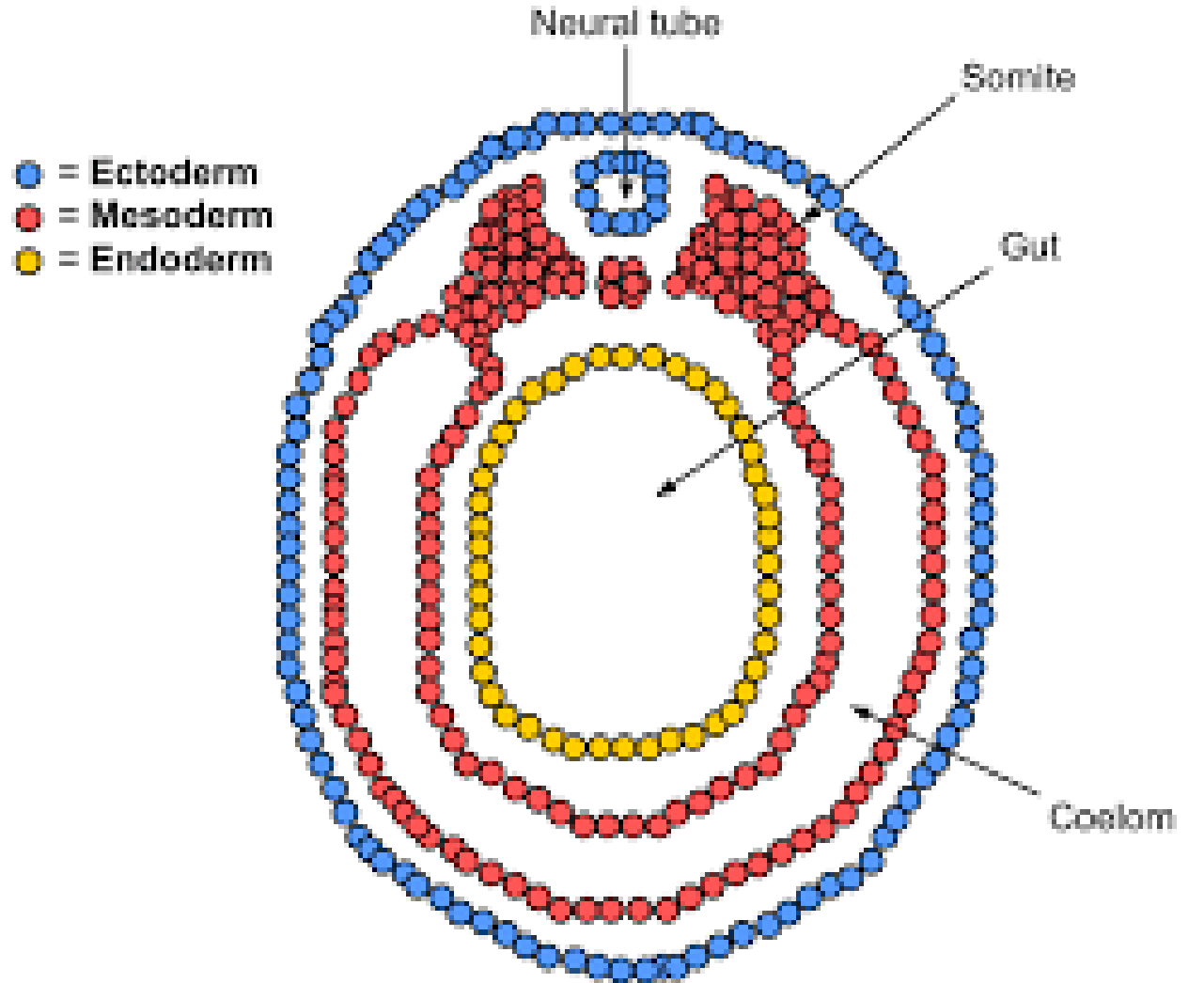
Skin cells of epidermis

Neuron on brain

Pigment cells

Limb's developments

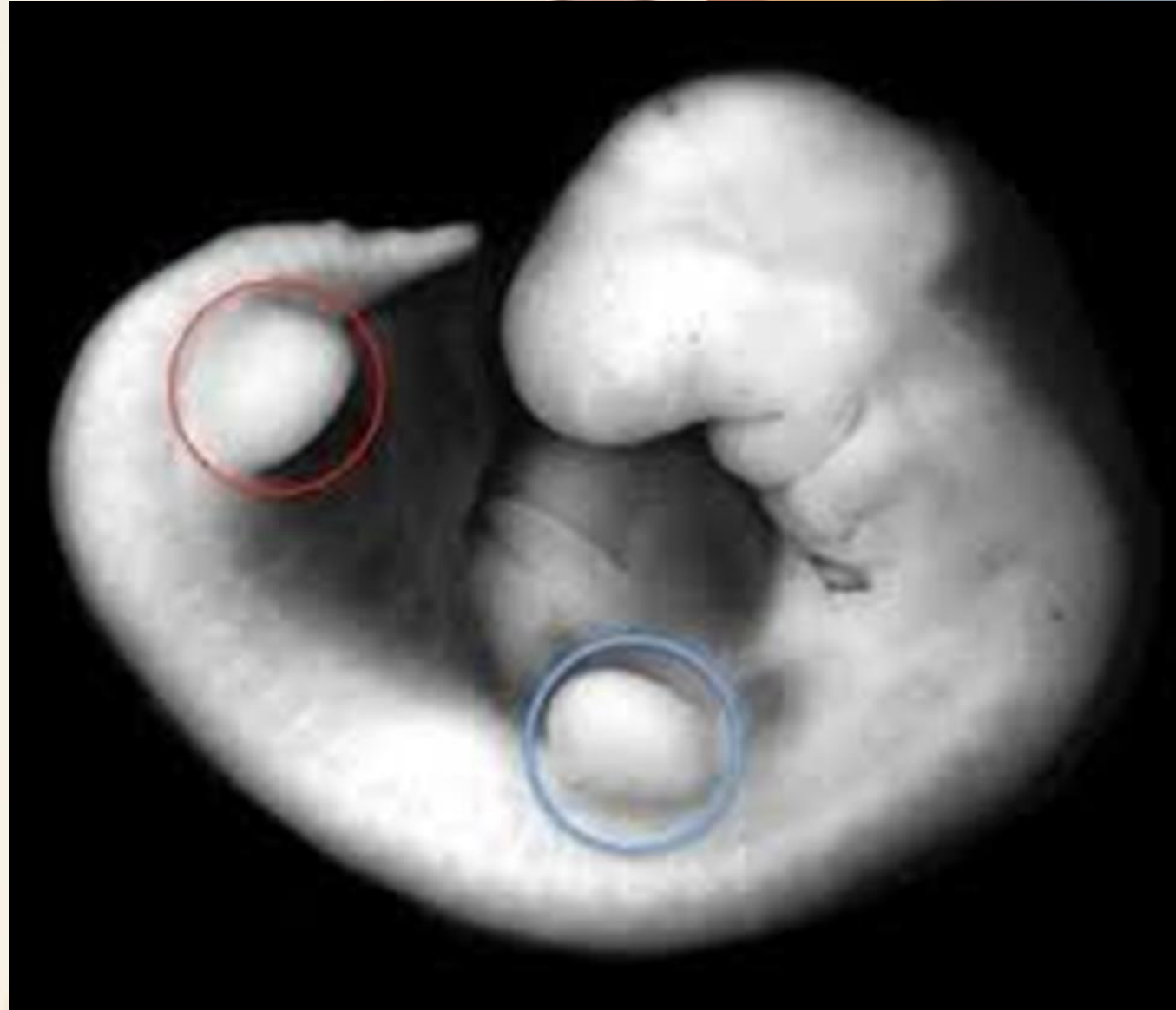
Begins with the activation of mesenchymal cells in the lateral plate somatic mesoderm.



Emergence of the Limb Buds

The biological sculpting of the limbs begins in Week 4. The upper limb buds appear first as small bulges oriented in a coronal plane, followed shortly by the lower limb buds.

Key Insight: Each bud consists of a core of somatic lateral plate mesoderm (which will condense to form the skeleton and vasculature), sheathed by a covering of ectoderm.

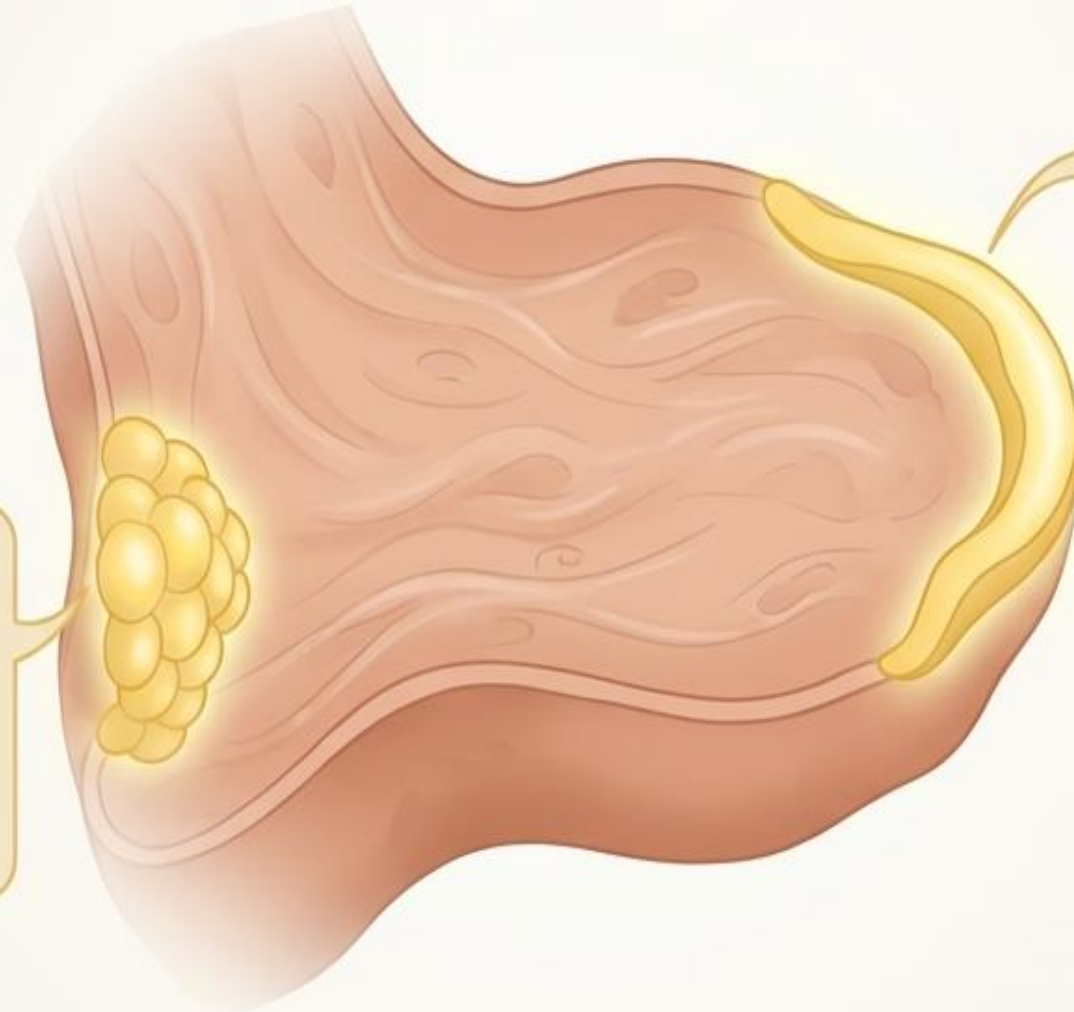


The Spatial Orchestrators of Limb Polarity

Two critical signaling centers coordinate the three-dimensional outgrowth and patterning of the limb.

ZPA (Zone of Polarizing Activity):

Mesodermal cells at the posterior base. Secretes Sonic hedgehog (Shh) to organize the anterior-posterior axis and pattern the digits.

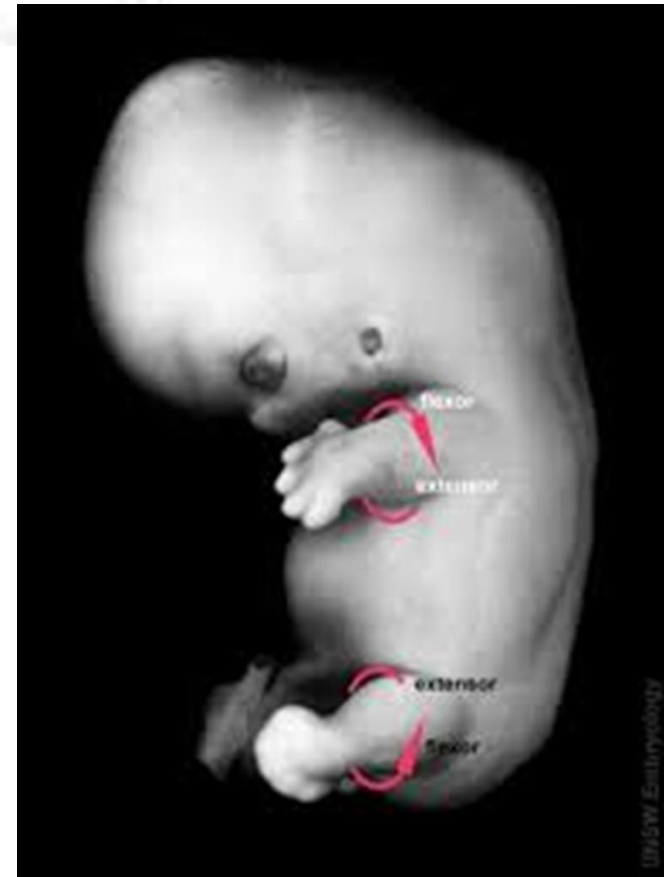
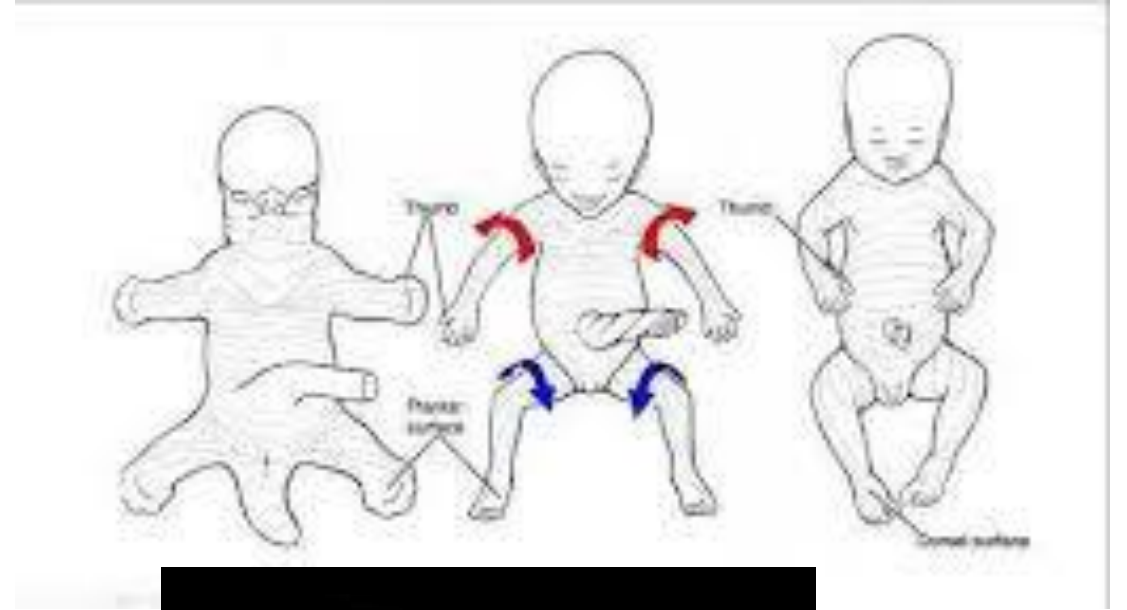


AER (Apical Ectodermal Ridge):
A ridge of thickened ectoderm at the limb apex. Secretes FGF to stimulate mitosis and prevent terminal differentiation of underlying mesoderm, driving proximal-distal outgrowth. Expresses Wnt7 to organize the dorsal-ventral axis.

A. Appendicular skeleton

(a) Upper limb buds rotate laterally through 90 degrees,

- ✓ whereas the lower limb buds rotate medially through almost 90 degrees.
- ✓ The upper limb buds become elongated by week 5
- ✓ and soon after they are subdivided into the precursors of the arm, forearm, and hand.



The Great Rotations: Morphological Inversion

During weeks 6–8, the limbs rotate 90 degrees in exactly opposite directions, permanently altering the spatial relationship of the flexor and extensor compartments.

Opposing Rotations Matrix

Upper Limb

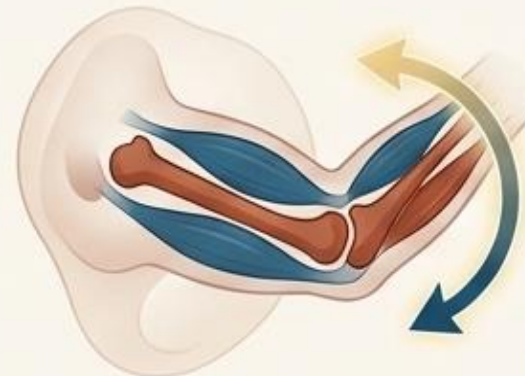


Rotates Laterally 90°
Elbow points posteriorly.

Flexor compartment moves
to the anterior position.

Extensor compartment
moves to the posterior
position.

Lower Limb



Rotates Medially 90°
Knee points anteriorly.

Flexor compartment moves
to the posterior position.

Extensor compartment
moves to the anterior
position.

Weeks 6–8

Sculpting the Digits via Apoptosis

The transition from a solid paddle to distinct human digits relies on precise, programmed cell death rather than isolated growth.



Flipper-like bud



Hand plate



Digital rays



Separated digits

Selected apoptosis within the AER leaves five separate, distinct AER regions at the tips of the future digits. This negative-space sculpting is mediated by BMP, Msx-1, and retinoic acid receptor signaling.

Week 5

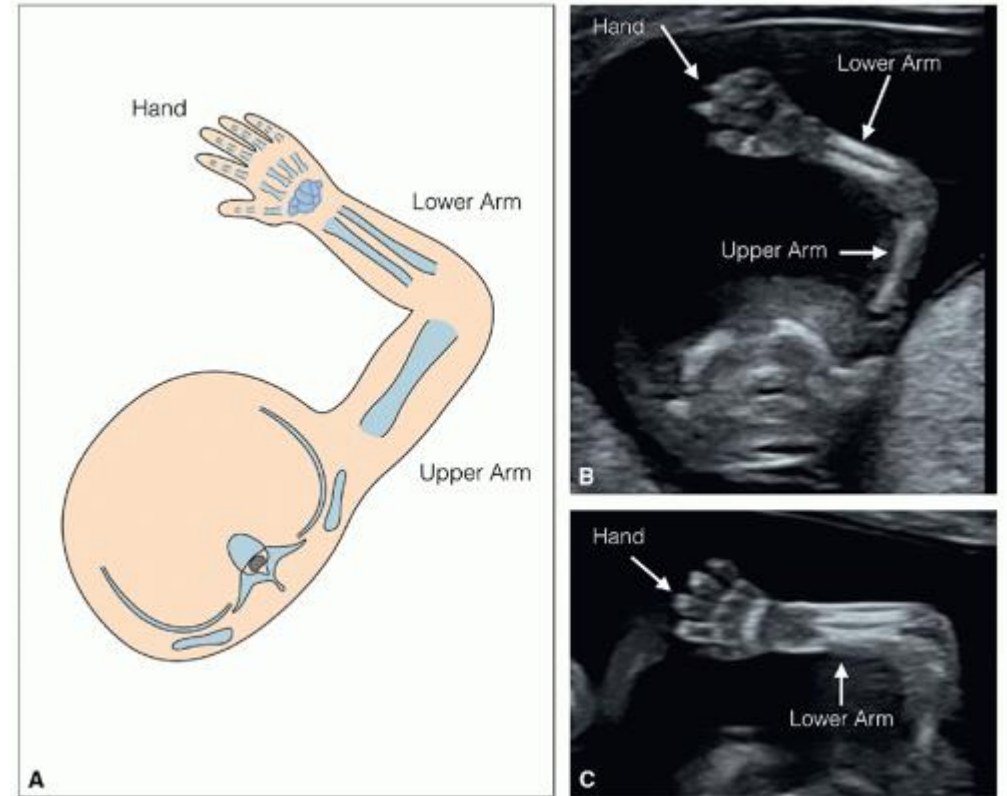
Week 6

Week 7

Week 8

2. Bones of limbs

- Are derived from the lateral plate somatic mesoderm. and develop by endochondral ossification **except for the clavicle**, which develops by intramembranous ossification.



Two Pathways of Osteogenesis

The conversion of preexisting connective tissue into bone occurs via two distinct mechanisms in the appendicular skeleton.

A Intramembranous Ossification (The Exception)

Mesoderm condenses into highly vascular sheets and directly forms a primary ossification center. In the limbs, this occurs only in the clavicle (the first bone in the body to ossify).



B Endochondral Ossification (The Rule)

Mesoderm first condenses into a hyaline cartilage model, which is subsequently replaced by a primary ossification center at the diaphysis. This forms all other limb and girdle bones.



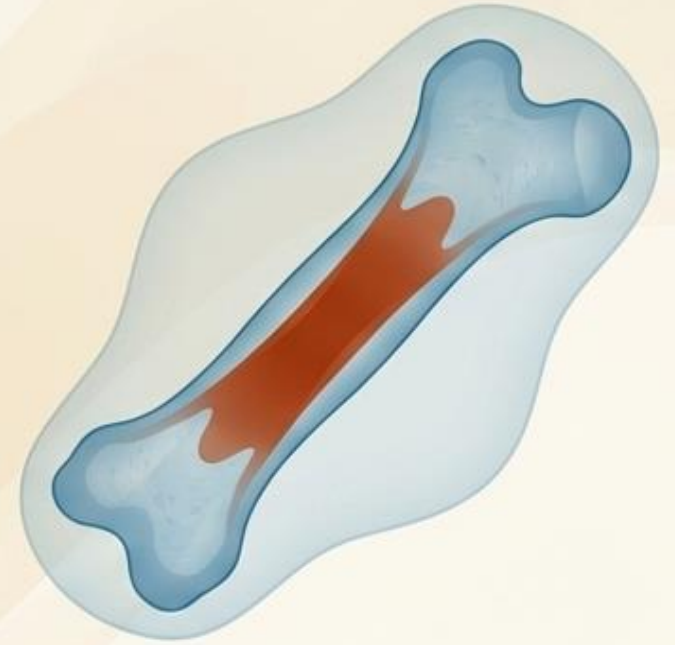
The Endochondral Timeline



Week 5 (Condensation):
Lateral plate mesoderm condenses along the central axis of the limb bud.



Week 6 (Chondrification):
The mesoderm converts to a complete hyaline cartilage model of the future bones.



Weeks 7–9 (Primary Ossification):
Primary ossification centers emerge within the diaphysis as osteogenesis replaces the cartilage model with true bone.

Weeks 5 to 9

Continued Sculpting: Epiphyseal Growth

The biological sculpting of the skeleton extends far beyond the embryonic period, continuing through childhood and adolescence.

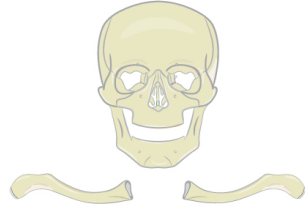
Clinical Insight: While primary centers form in the diaphysis before birth, secondary ossification centers form in the epiphyseal ends during childhood.

Radiographic Application: The radiolucent (dark) band visible on pediatric imaging is the epiphyseal growth plate—a vital remnant of the original hyaline cartilage model driving longitudinal bone growth.



Birth to Childhood

Intramembranous vs Endochondral Ossification

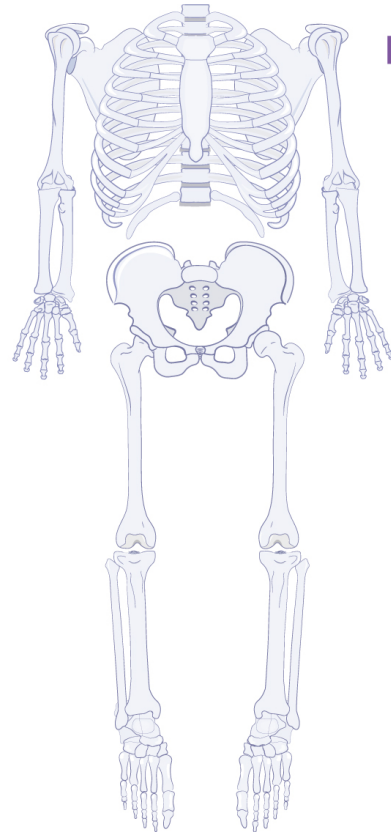


Intramembranous O.

- * Cranial vault
- * Facial bones
- * Clavicles

DIRECT ossification

NO hyaline cartilage model.



Endochondral O.

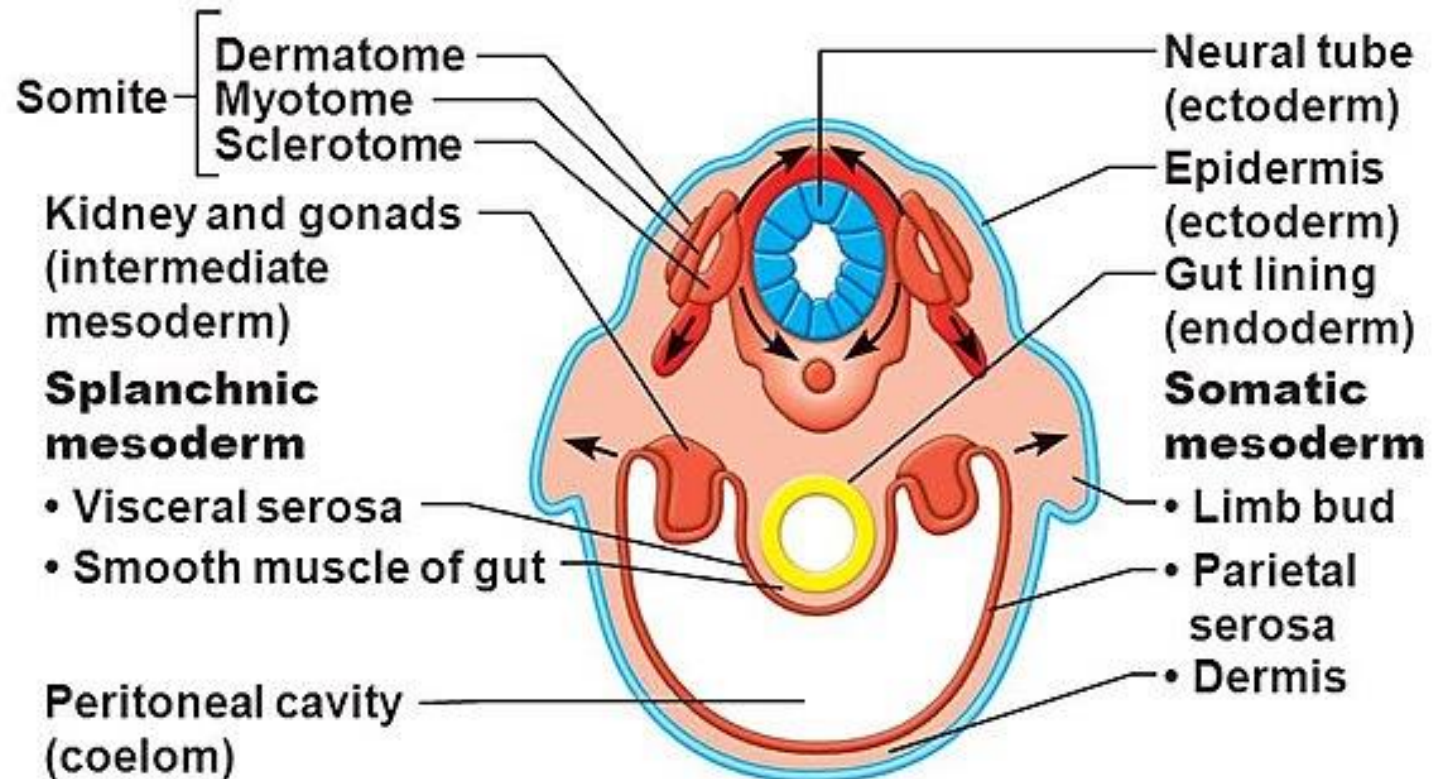
- * **Axial s.**
(except the head)
Sternum
Ribs
Vertebrae
- * **Appendicular s.**
(except the clavicles)
Shoulder & hip girdles
Limbs

INDIRECT ossification

Transitions through a hyaline cartilage model.

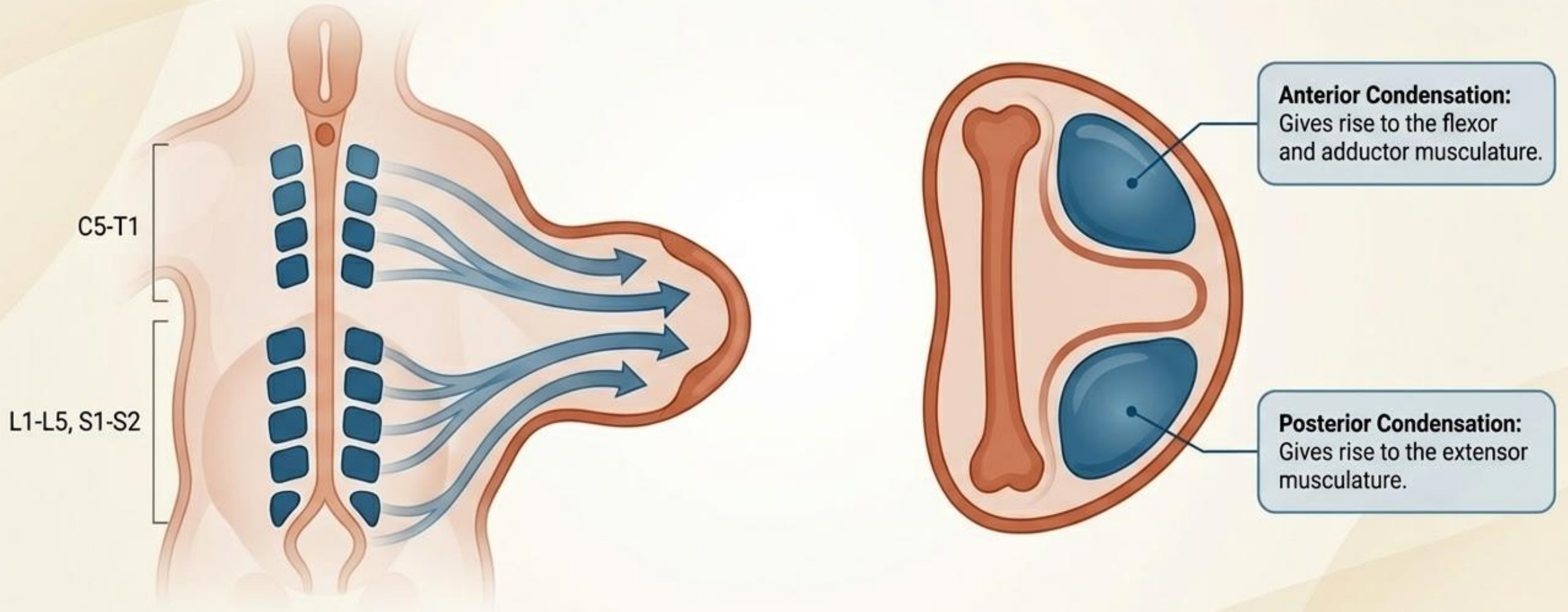
3. Muscles of limbs

- Develop exclusively from the myotomic portions of the somites (paraxial mesoderm) and form ventral (flexor) and dorsal (extensor) condensations of somites mesoderm.



Somitic Migration and Muscle Condensation

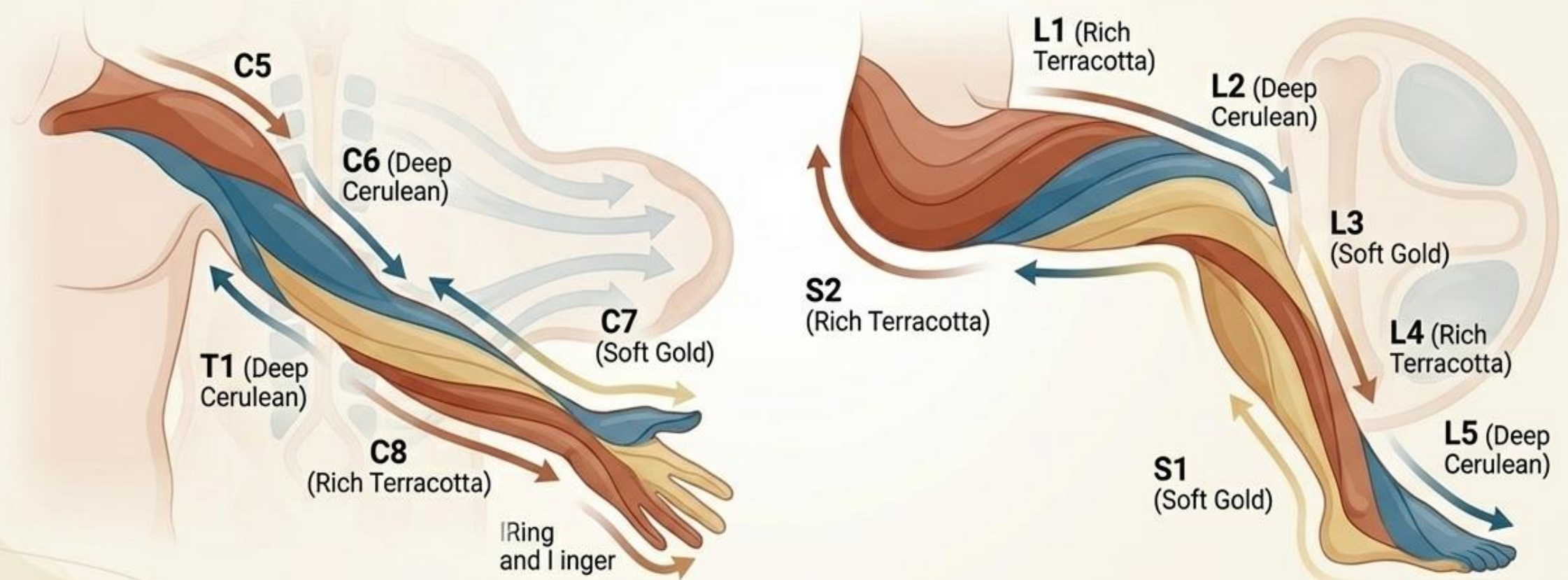
While lateral plate mesoderm forms the bones, mesoderm from the somites (myotomes) migrates into the limb bud during Week 5 to form the musculature.



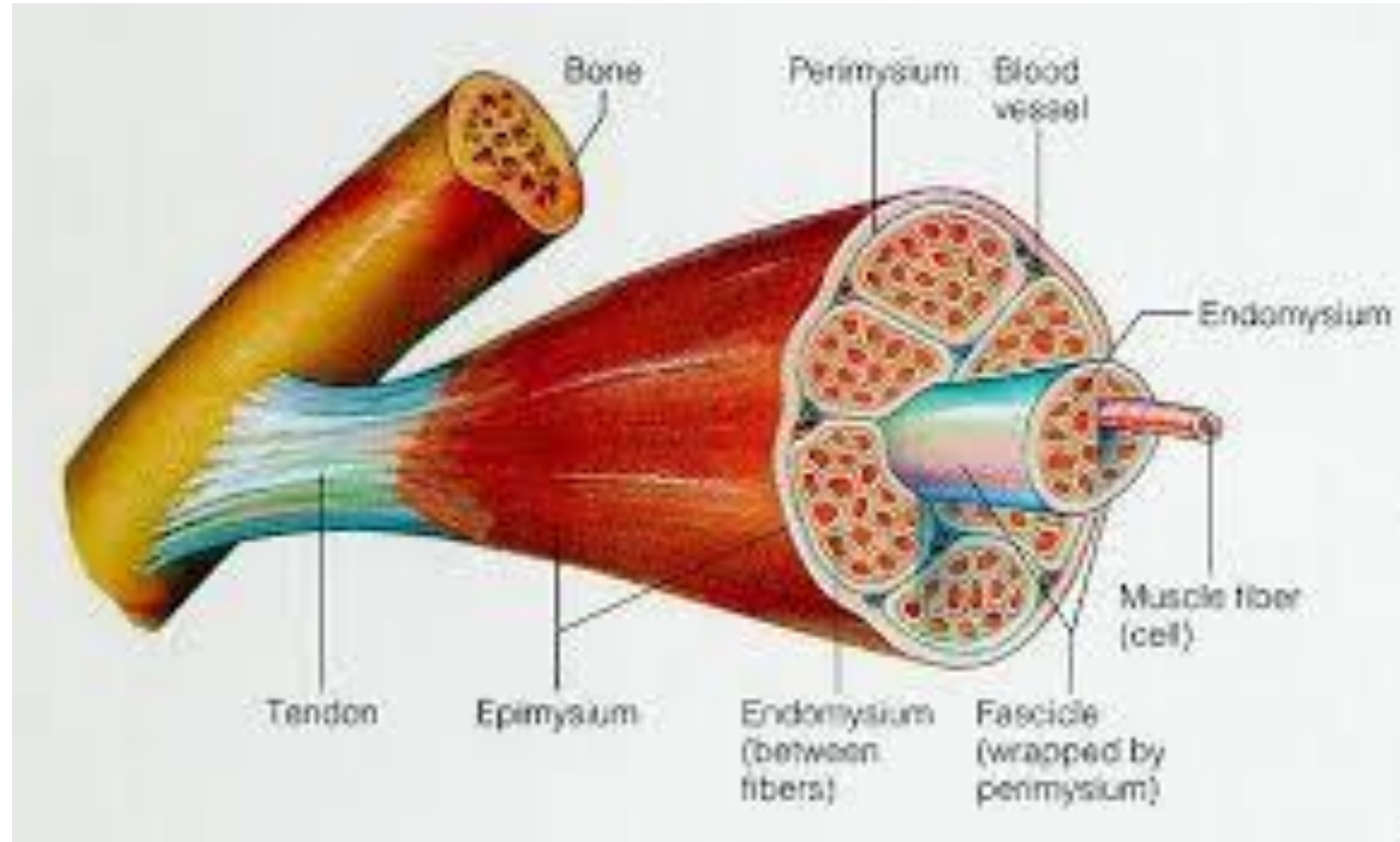
Dermatomal Spiraling

The opposing 90-degree rotations twist the originally straight, segmental pattern of embryonic innervation into a spiral pattern in the adult.

Takeaway: Ventral primary rami divide into posterior and anterior divisions, seamlessly following the posterior and anterior muscle condensations as they rotate into their final adult positions.



❖ Epimysium, perimysium, and tendons develop from the lateral plate somatic mesoderm.



قال تعالى: "وَلَقَدْ خَلَقْنَا الْإِنْسَانَ مِنْ سُلَالَةٍ مِّنْ طِينٍ * ثُمَّ جَعَلْنَاهُ نُطْفَةً فِي قَرَارٍ مَّكِينٍ * ثُمَّ نَحْنُ نَخْلُقُنَا الْنُطْفَةَ عَلَقَةً فَخَلَقْنَا الْعَلَقَةَ مُضْغَةً فَخَلَقْنَا الْمُضْغَةَ عِظَامًا فَكَسَوْنَا الْعِظَامَ لَحْمًا ثُمَّ أَنْشَأْنَاهُ خَلْقًا آخَرَ فَتَبَارَكَ اللَّهُ أَحْسَنُ الْخَالِقِينَ"

(المؤمنون، آية: 12 - 14)

The Embryonic Twist: Comparing Upper and Lower Limb Rotation

Initial Alignment (Weeks 4–6)



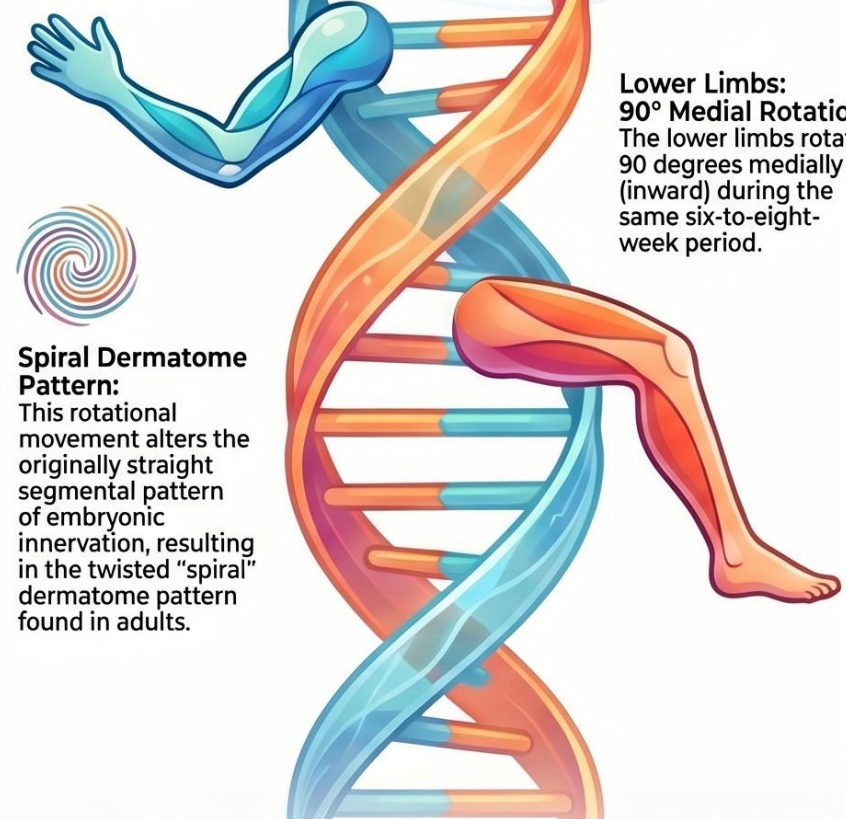
Appearance of Limb Buds (Week 4): Limb buds first appear as small bulges oriented in a coronal plane, with the upper limb buds appearing approximately four days before the lower limb buds.



Transition to the Sagittal Plane (Week 6): During week 6, both the upper and lower limb buds undergo a horizontal movement to transition from a coronal orientation to a sagittal plane.

The 90-Degree Divergence (Weeks 6–8)

Upper Limbs: 90° Lateral Rotation
The upper limbs rotate 90 degrees laterally (outward) during weeks 6–8 of development.



Lower Limbs: 90° Medial Rotation
The lower limbs rotate 90 degrees medially (inward) during the same six-to-eight-week period.



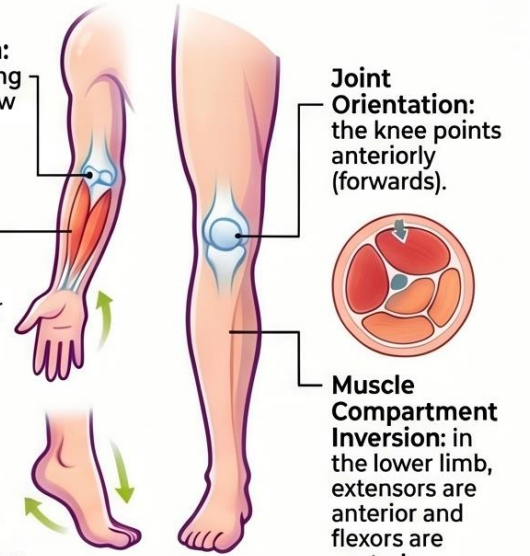
Spiral Dermatome Pattern: This rotational movement alters the originally straight segmental pattern of embryonic innervation, resulting in the twisted “spiral” dermatome pattern found in adults.

Anatomical Results (Post-Rotation)

Joint Orientation: Due to the opposing rotations, the elbow points posteriorly (backwards).

Muscle Compartment Inversion: In the upper limb, flexors are anterior and extensors are posterior.

Functional Equivalents: Because of these rotations, flexion at the wrist joint is embryologically analogous to plantar flexion at the ankle joint.



Joint Orientation: the knee points anteriorly (forwards).

Muscle Compartment Inversion: in the lower limb, extensors are anterior and flexors are posterior.

Limb Rotation Comparison

| Feature | Upper Limb | Lower Limb |
|-----------------------------|--------------------------|------------------------|
| Rotation Direction | 90° Lateral | 90° Medial |
| Joint Direction | Elbow points posteriorly | Knee points anteriorly |
| Extensor Compartment | Located posteriorly | Located anteriorly |
| Flexor Compartment | Located anteriorly | Located posteriorly |