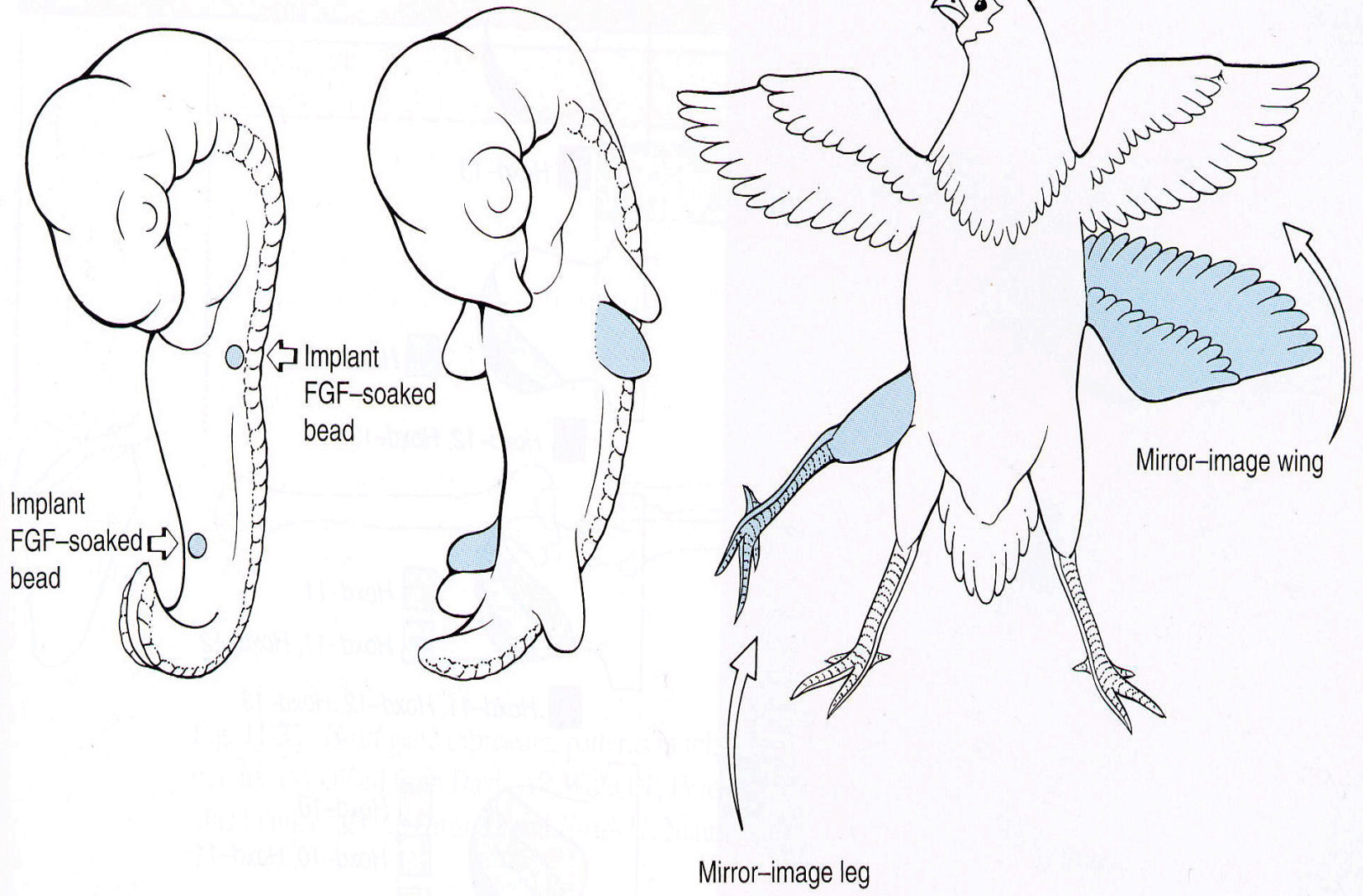
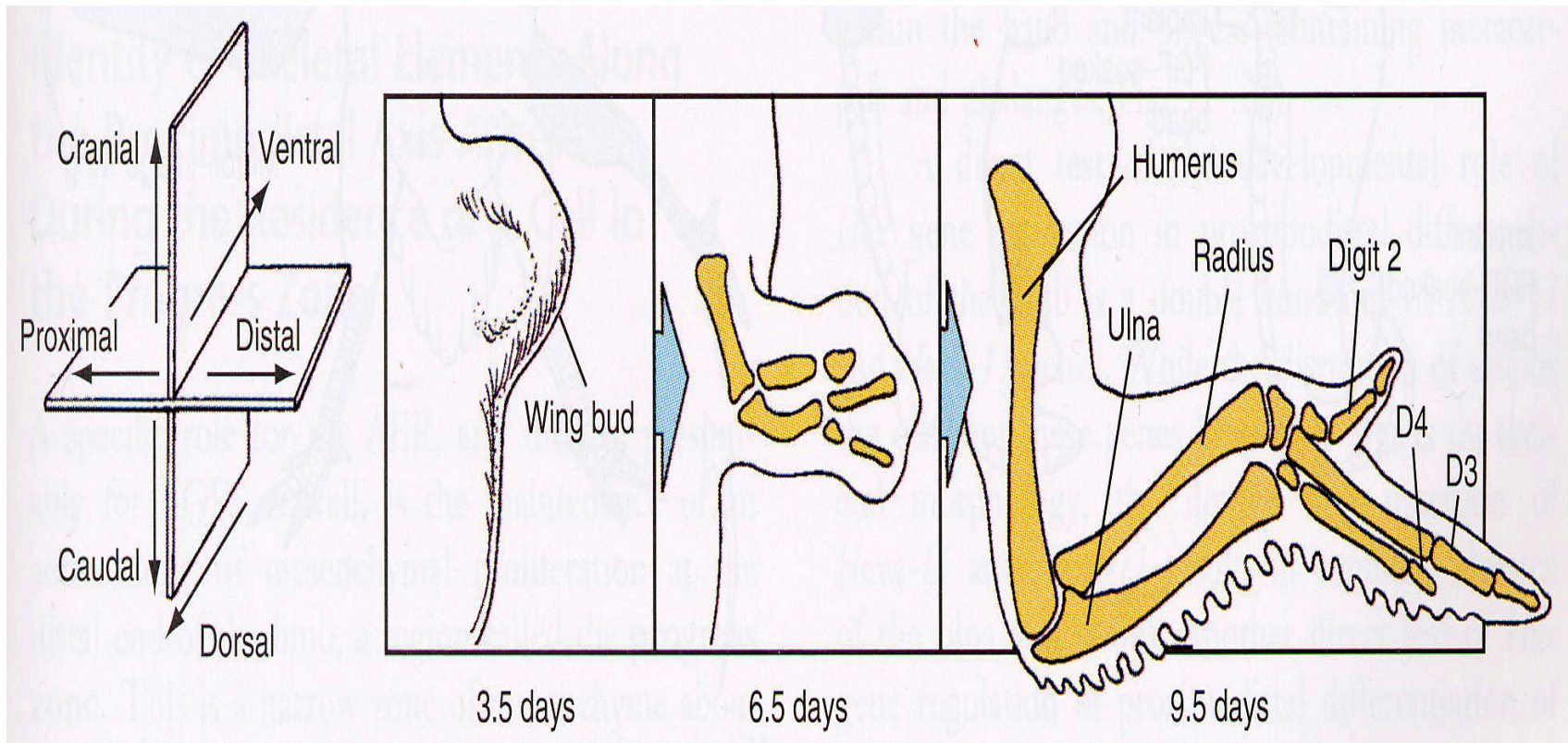


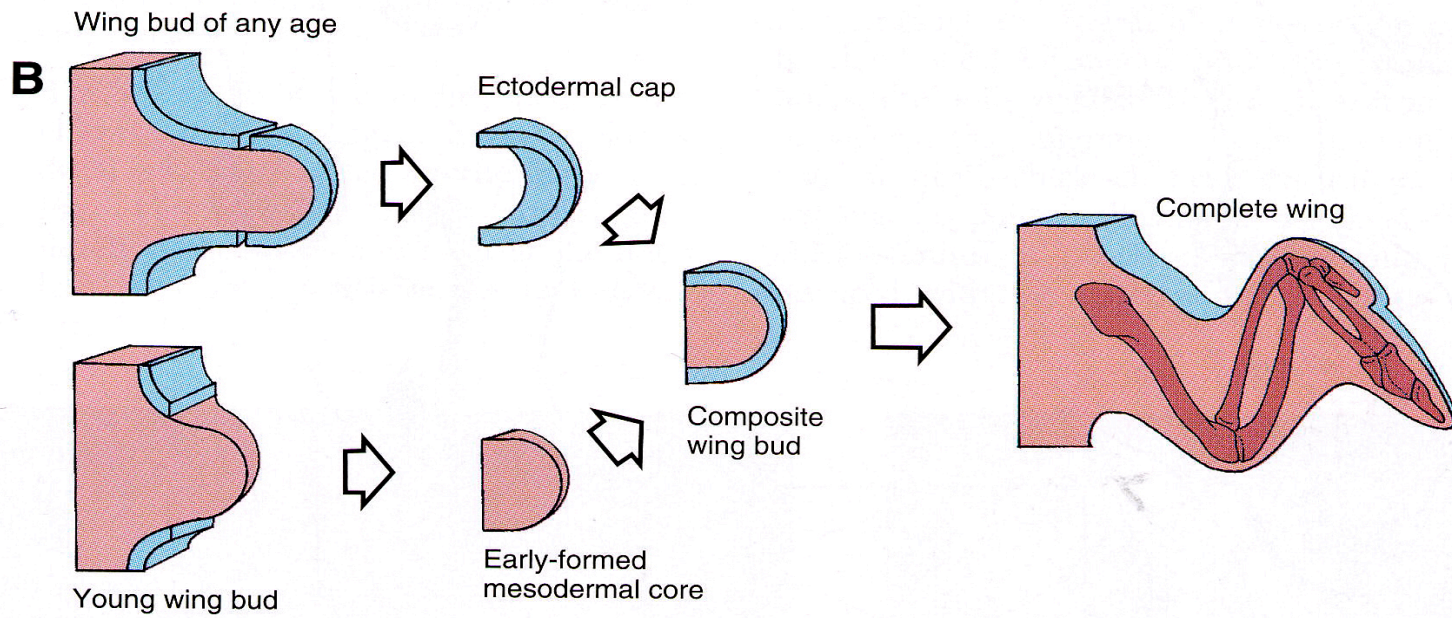
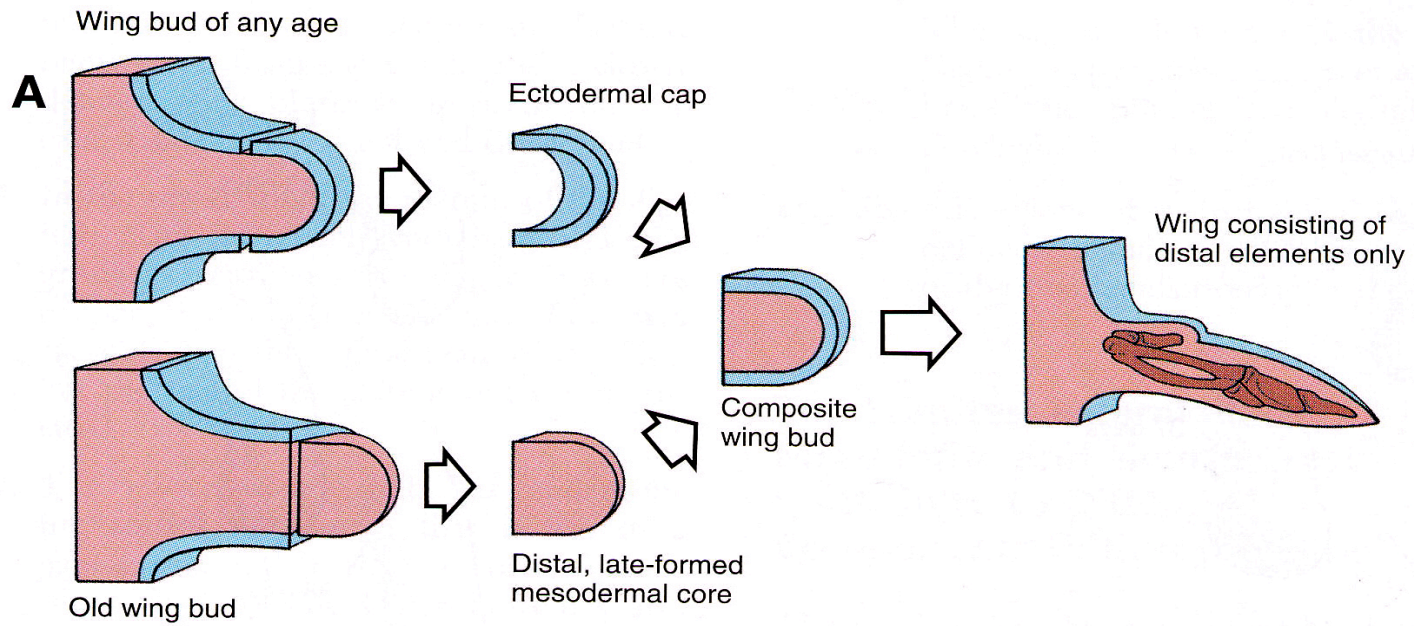
# Limb Field



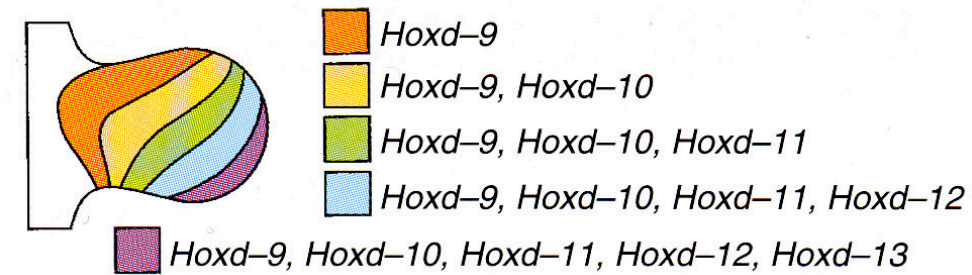
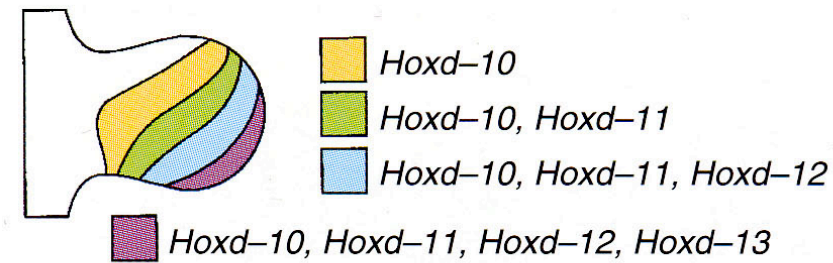
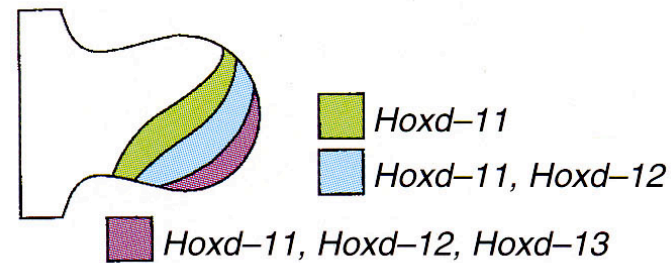
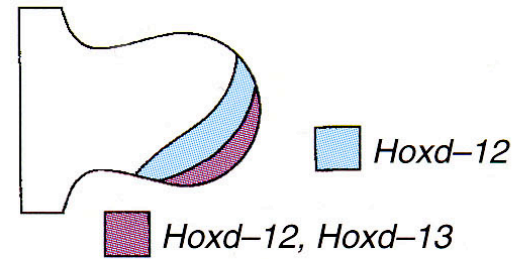
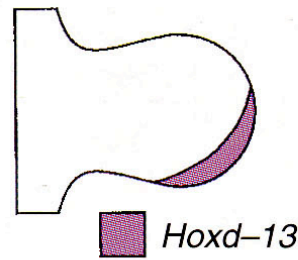
The same signal – FGF- induced the formation of either a wing or a leg. This signal is from the overlying ectoderm. This and other evidence indicates that identity of the limb (how it responds to signals) resides in the mesenchyme (lateral plate mesoderm) which gives rise to the skeleton.

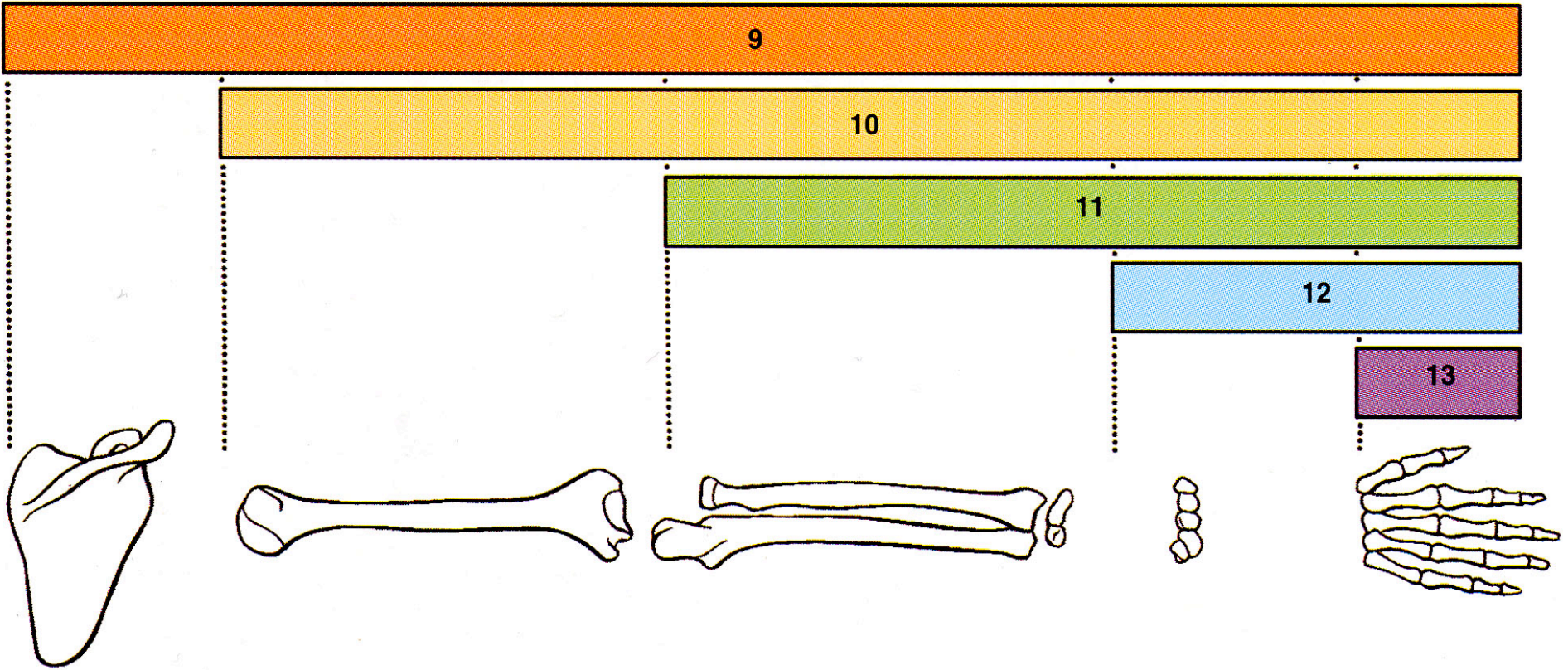
# Limb Elongation



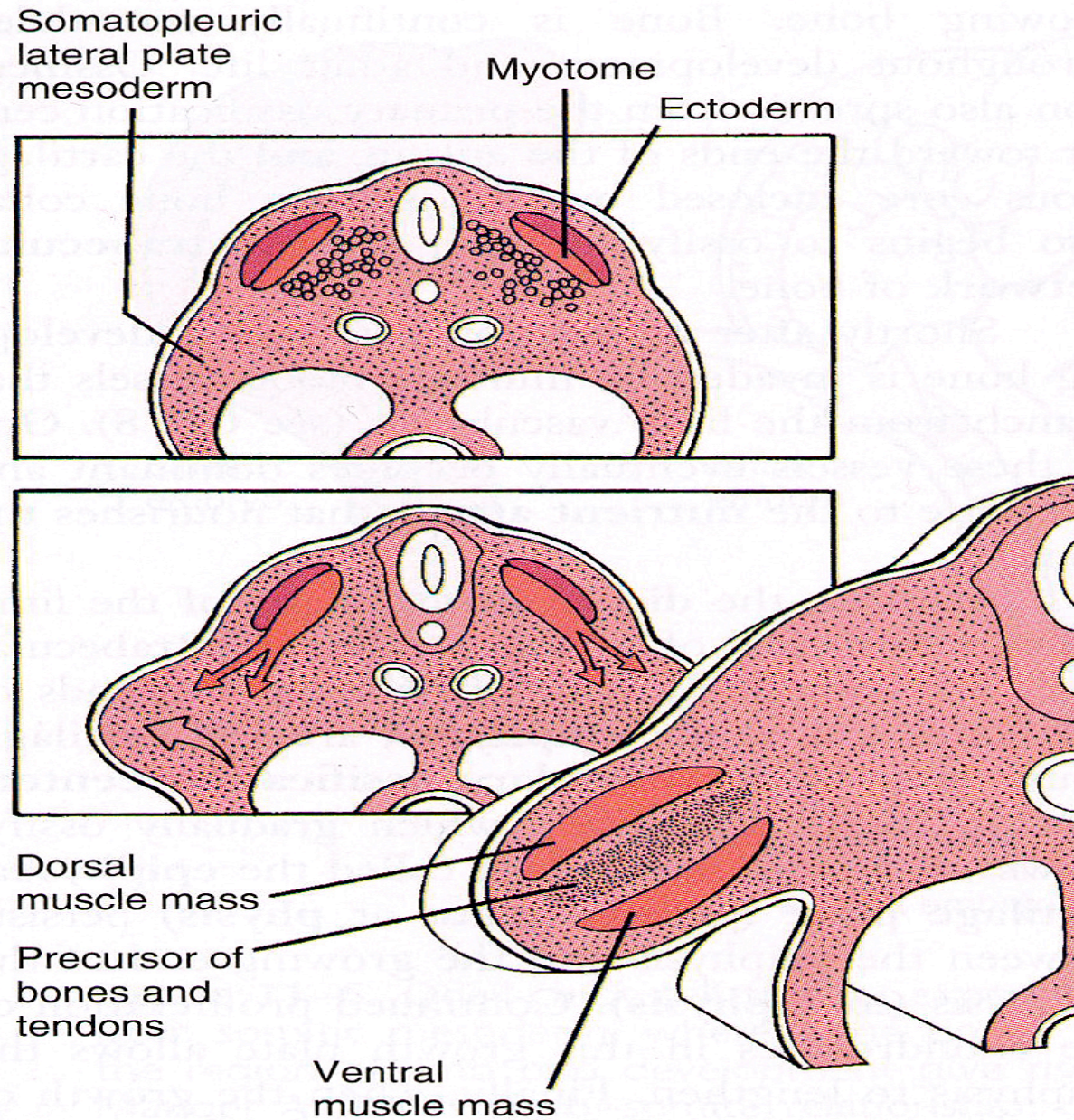


What would you predict would happen if you placed leg mesenchyme under the AER of the wing field?





# Muscles of limb are formed from migration of somitic cells

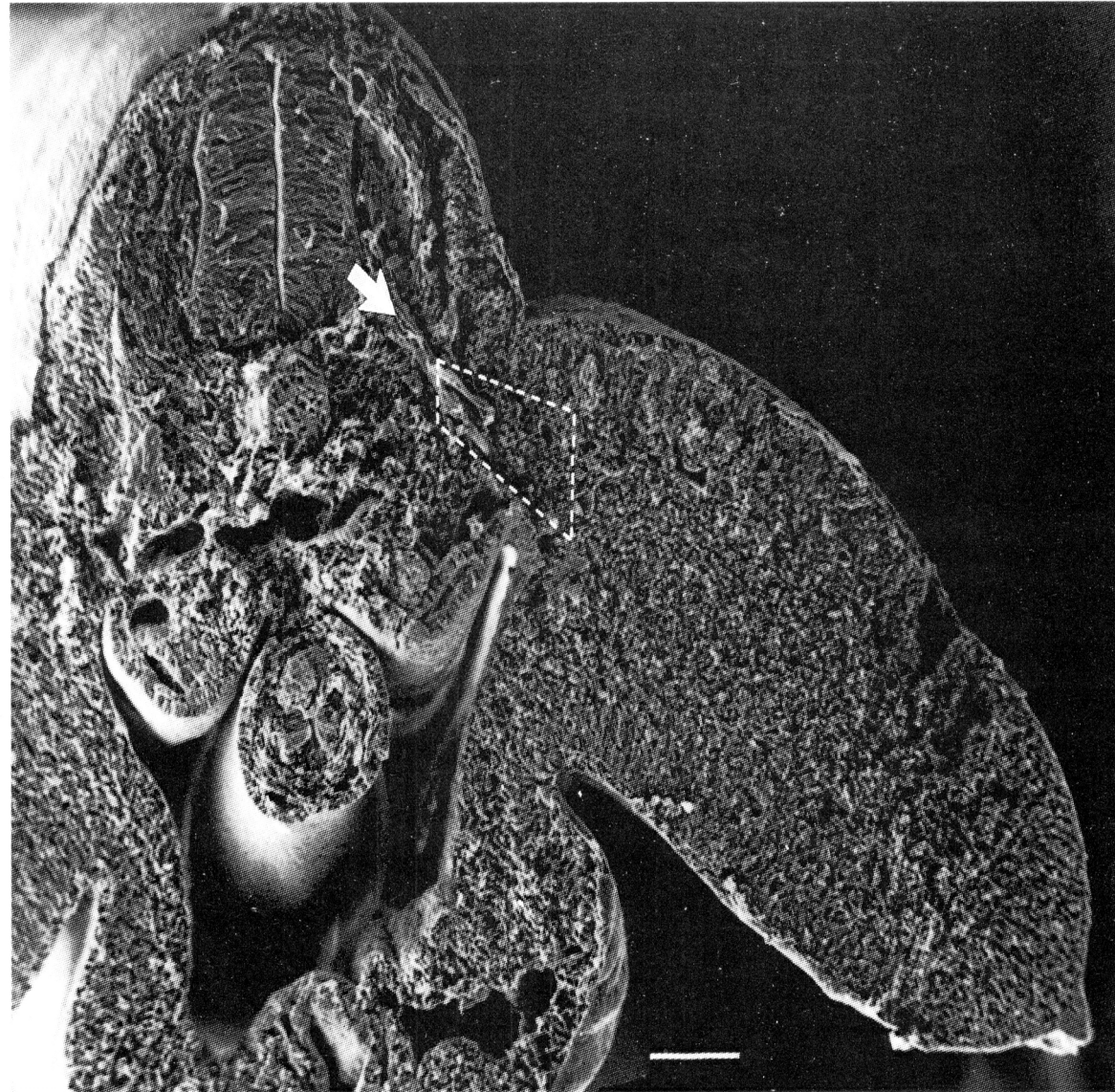


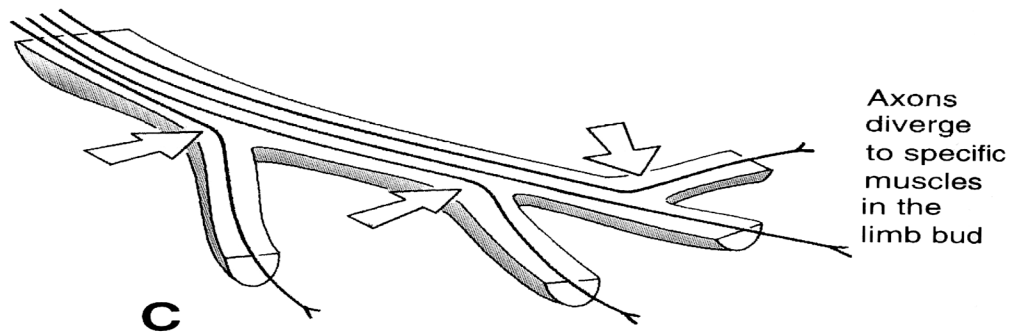
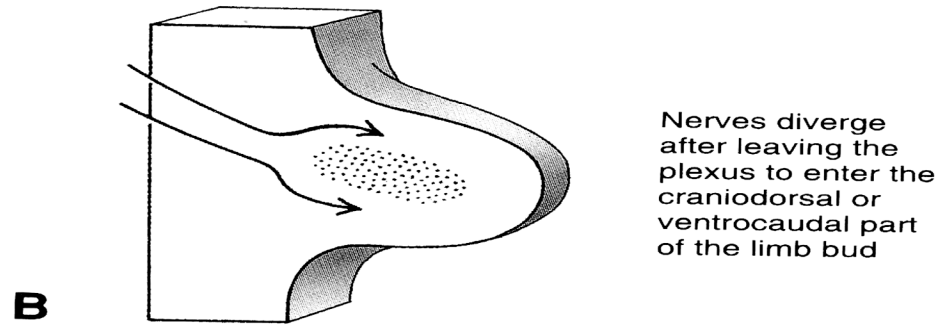
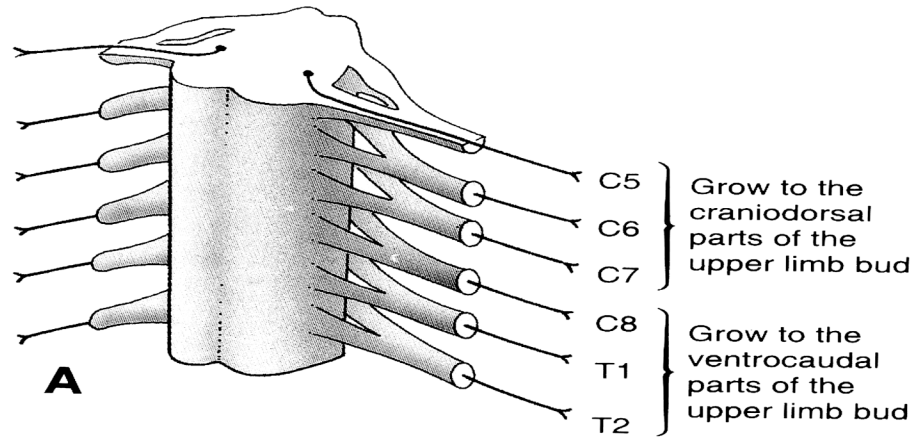
**Table 11-1**  
**Muscles Derived from the Ventral and Dorsal Muscle Masses of the Limb Buds**

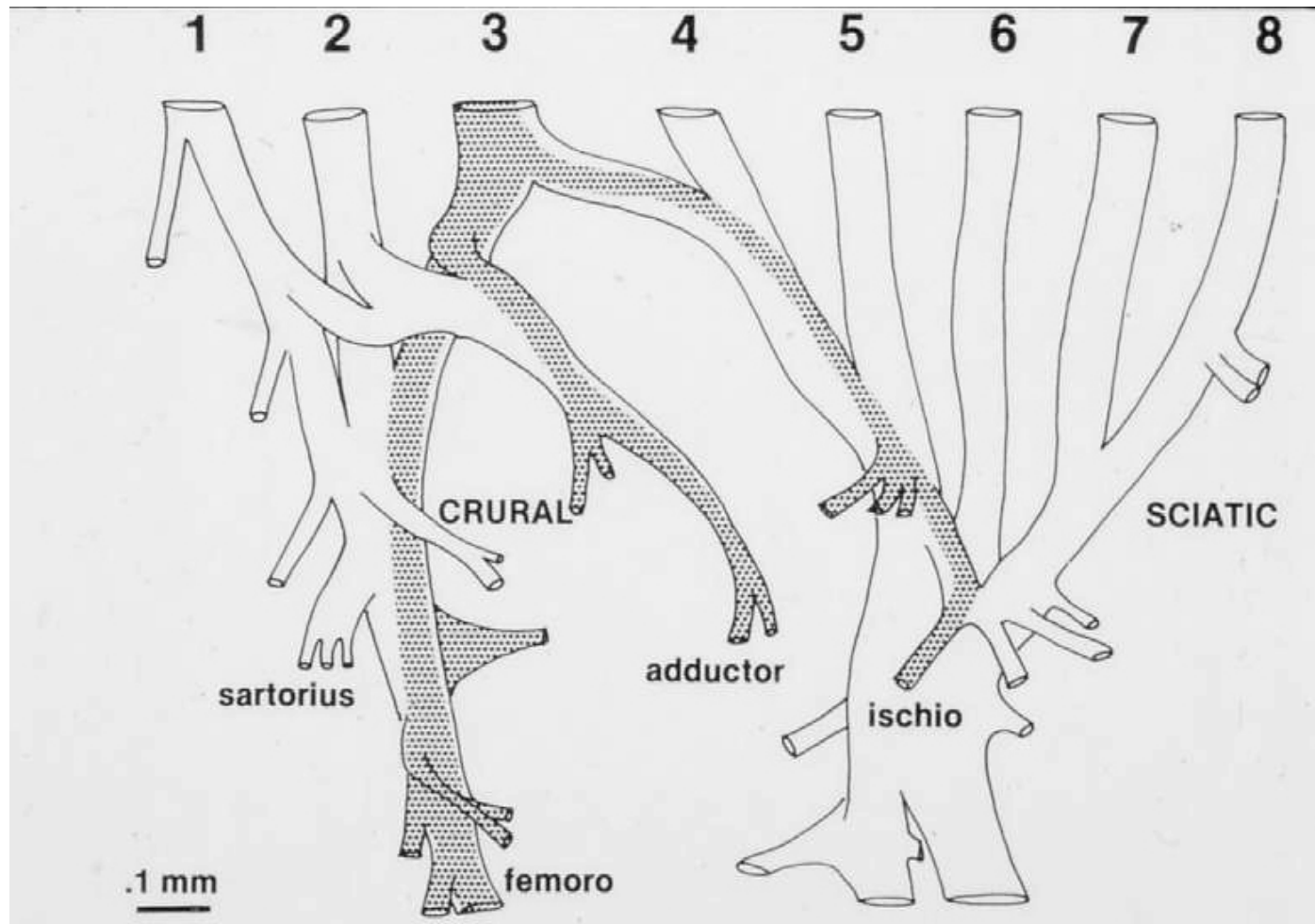
VENTRAL MUSCLE MASS	DORSAL MUSCLE MASS	
<i>Upper Limb</i>	<i>Upper Limb</i>	<i>Lower Limb</i>
Anterior compartment of the arm and forearm	Posterior compartment muscles of the arm and forearm	Anterior compartment muscles of the thigh and leg
All muscles on the palmar surface of hand	Deltoid	Tensor fasciae latae
<i>Lower Limb</i>	Lateral compartment muscles of the forearm and hand	Short head of the biceps femoris
Medial compartment muscles of the thigh	Latissimus dorsi	Lateral compartment muscles of the leg
Posterior compartment muscles of the thigh except for the short head of the biceps femoris	Rhomboids	Muscles of the dorsum of the foot
Posterior compartment muscles of the leg	Levator scapulae	Gluteus maximus, medius, and minimus
All muscles on the plantar surface of the foot	Serratus anterior	Piriformis
Obturator internus	Teres major and minor	Iliacus
Gemellus superior and inferior	Subscapularis	Psoas
Quadratus femoris	Supraspinatus (?)	
	Infraspinatus (?)	

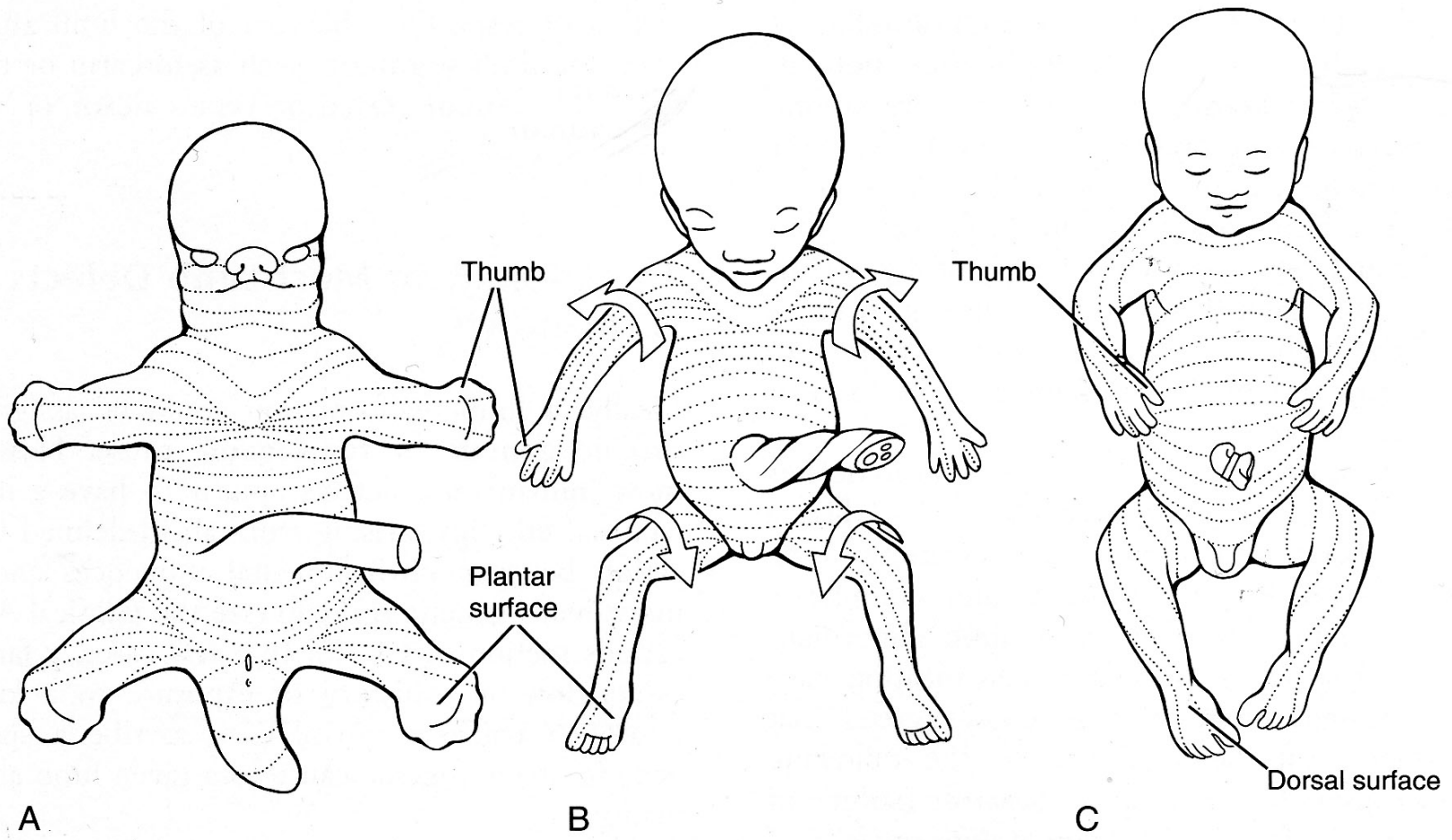
Data from Crafts RC. 1985. A Textbook of Human Anatomy. 3rd Ed. Churchill Livingstone, New York.

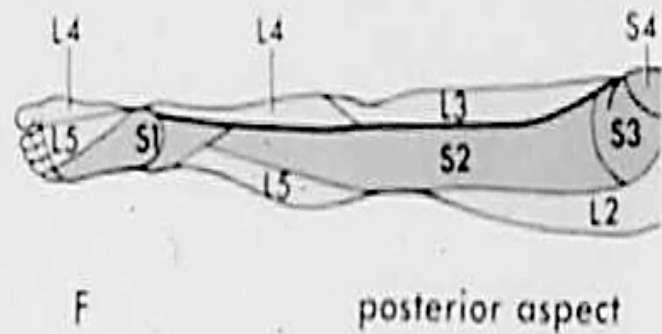
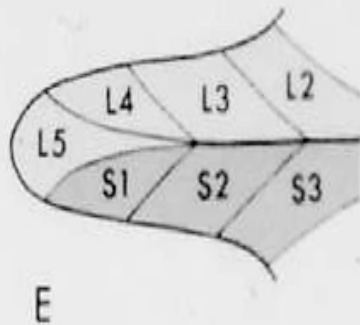
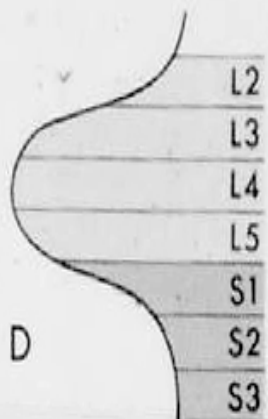
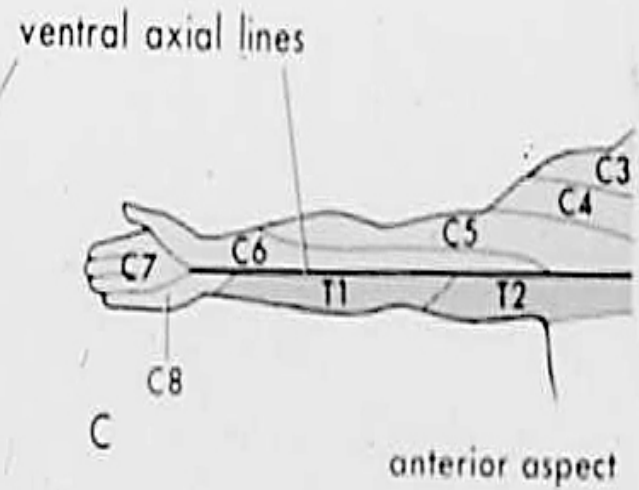
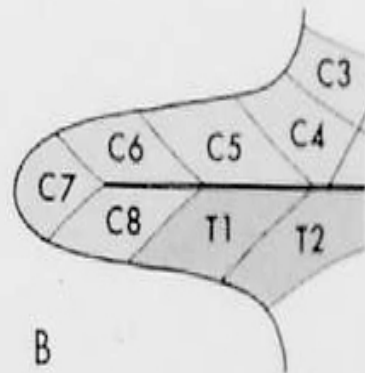
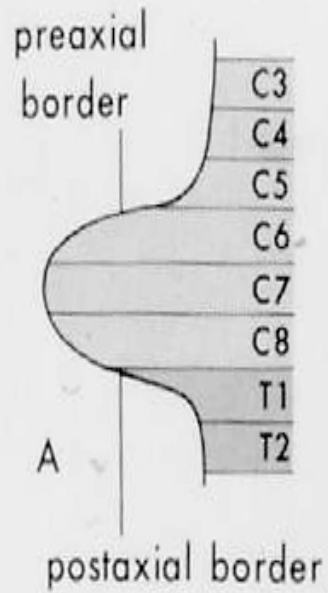
Axonal outgrowth to limb prior to muscle formation



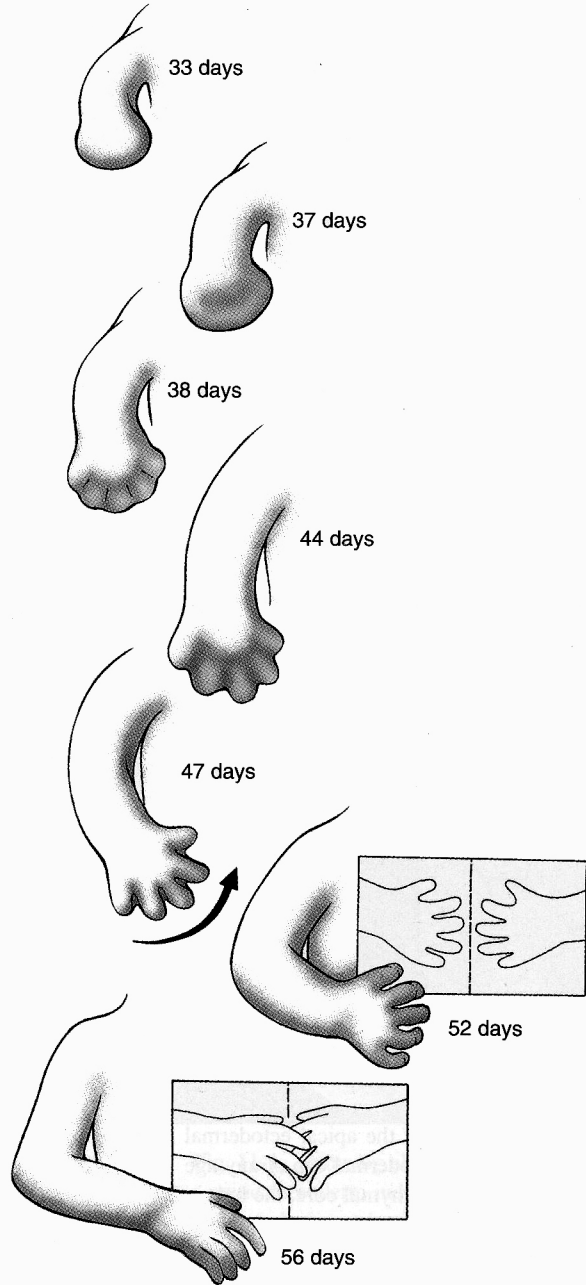




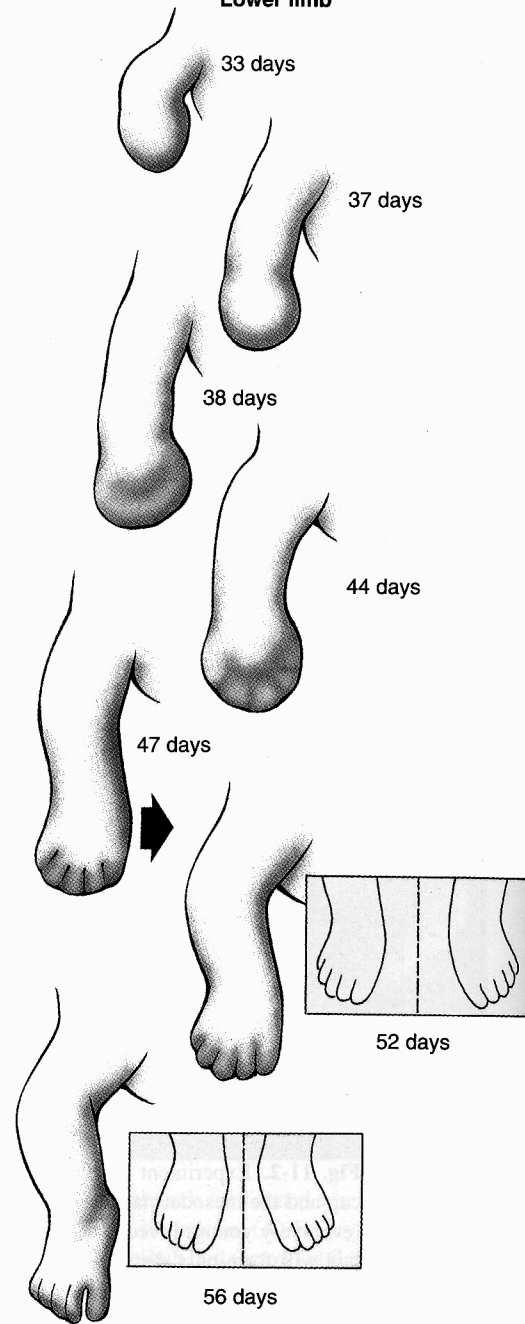




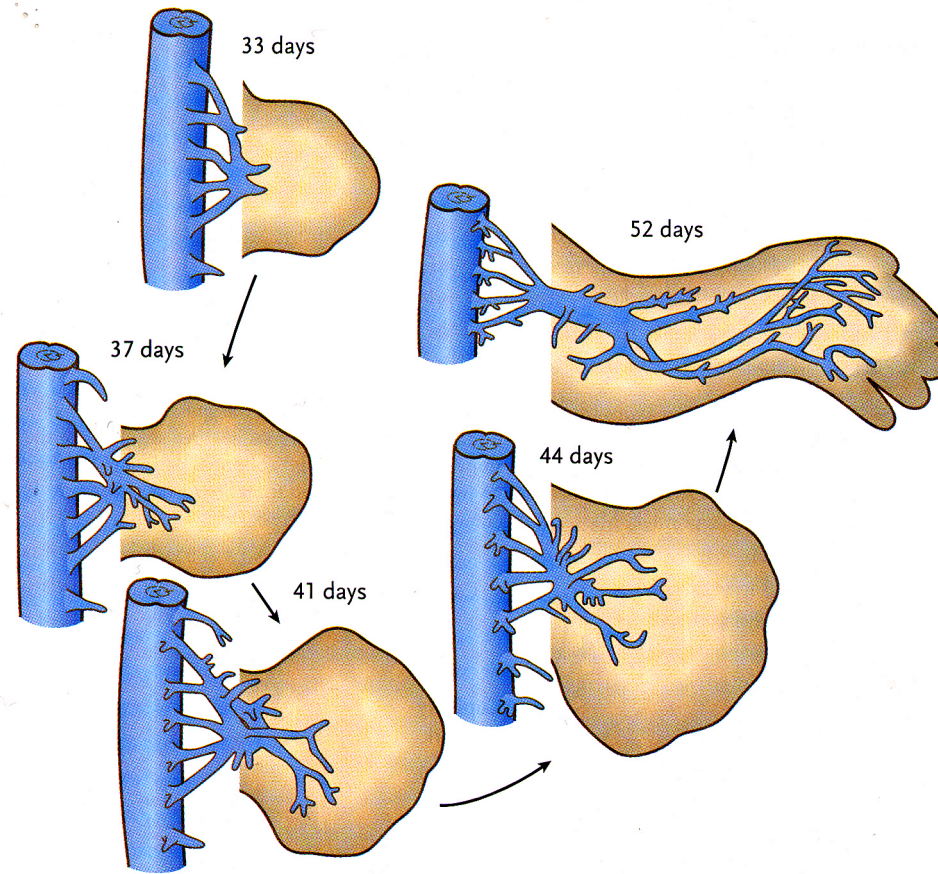
Upper limb



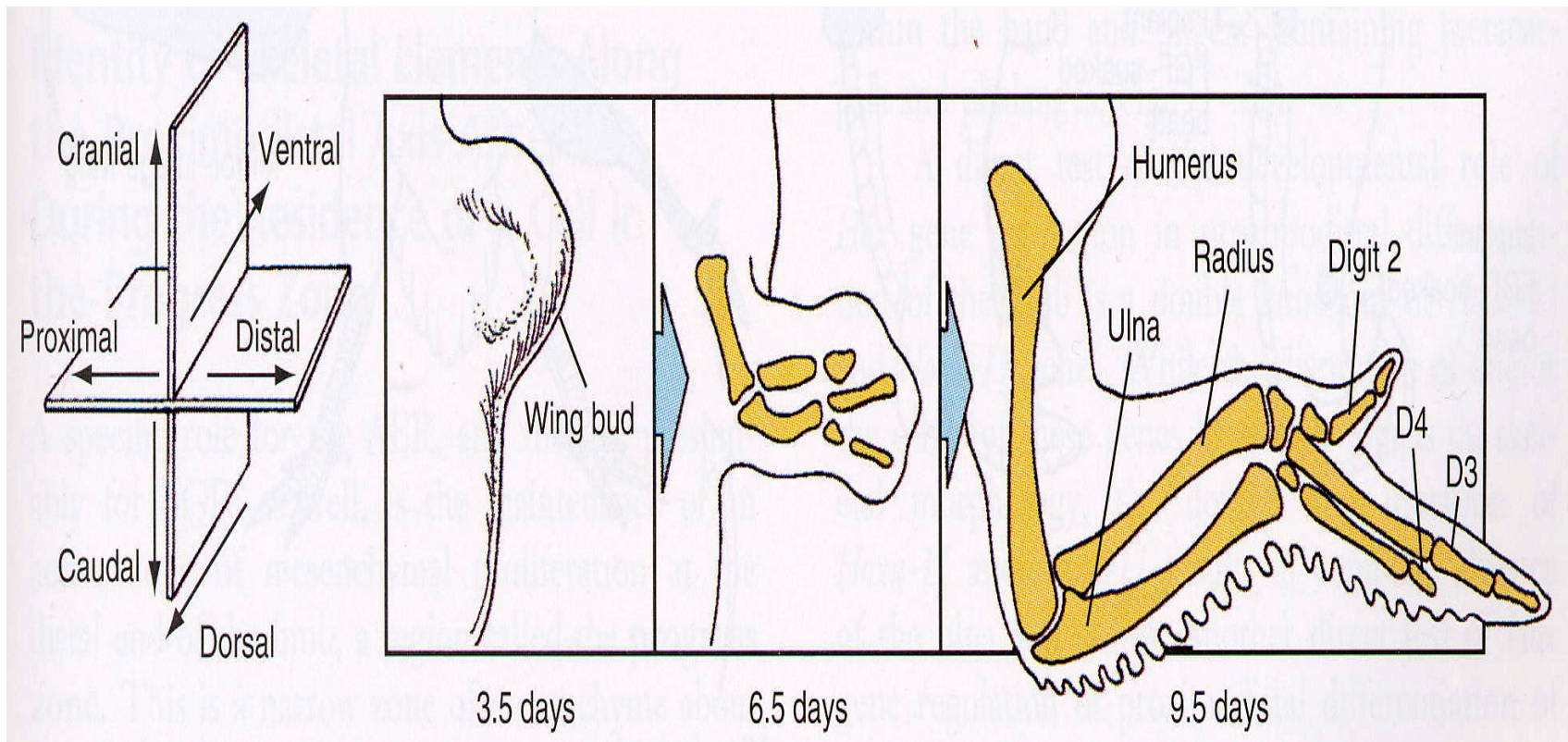
Lower limb

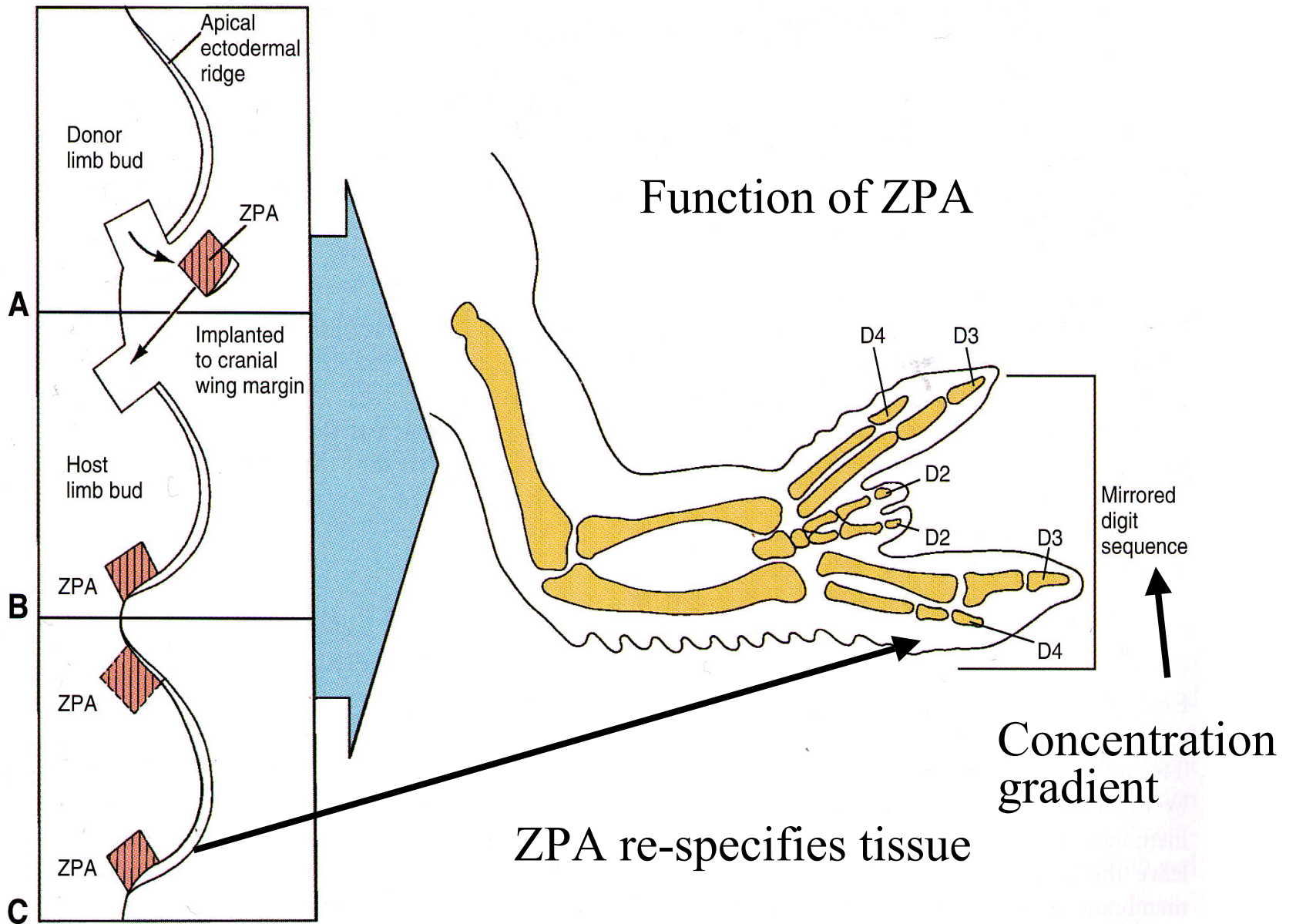


# Blood vessel growth into limb.



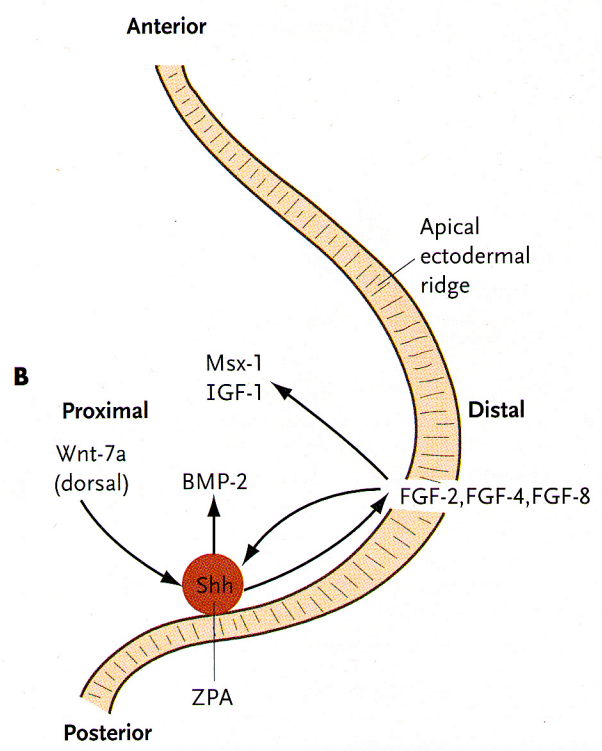
# Patterning of digits





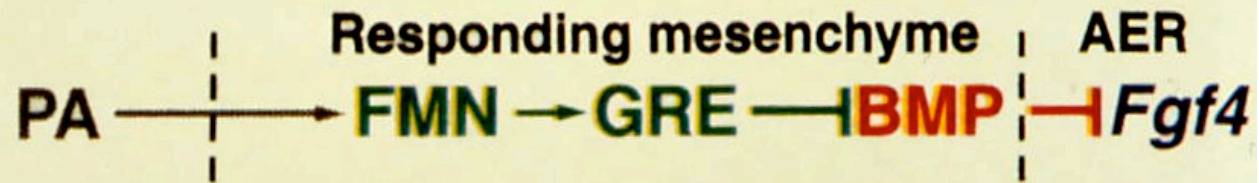
What are the known characteristics of the ZPA?

1. If ZPA is transplanted (at the correct time) to an ectopic site it will respecify tissue.
2. It acts to induce the correct A/P pattern via a concentration gradient.
3. Acts over a very narrow time frame.
4. The activity of the ZPA is universal among quadrupeds and is the same for the fore limb and hind limb.

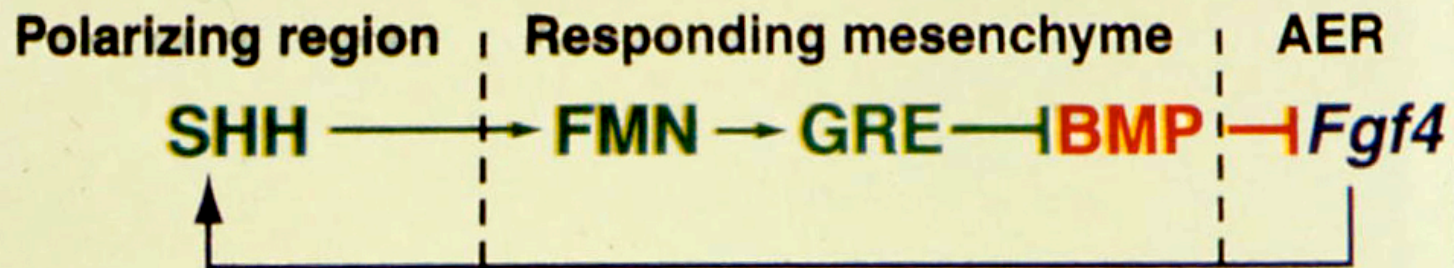


Shh dependent and independent signaling.

### SHH-independent



### SHH-dependent



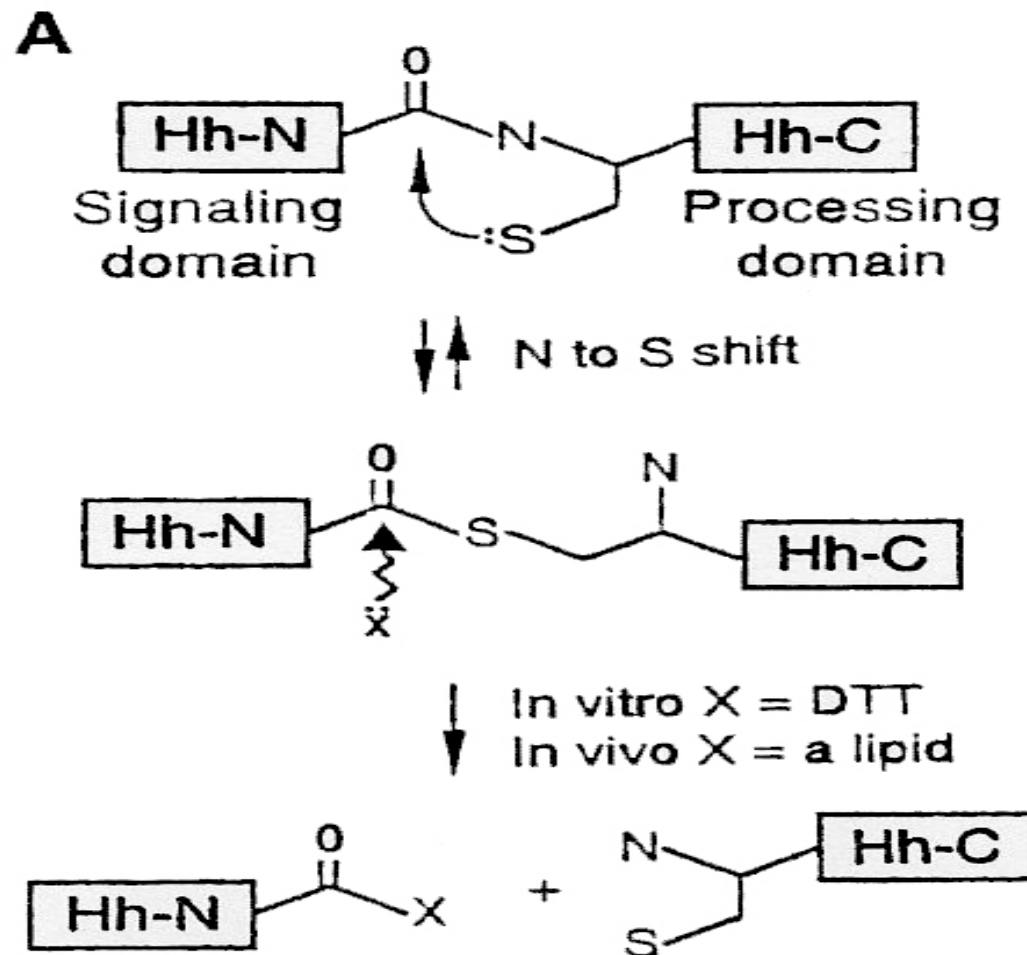
1. What is the polarizing signal?
  - (a) Sonic hedgehog (Shh) is the polarizing signal.
  - (b) Beads soaked in Shh can substitute for the ZPA.
  - (c) The notochord (which makes Shh) can substitute for the ZPA.

## 2. Concentration gradient.

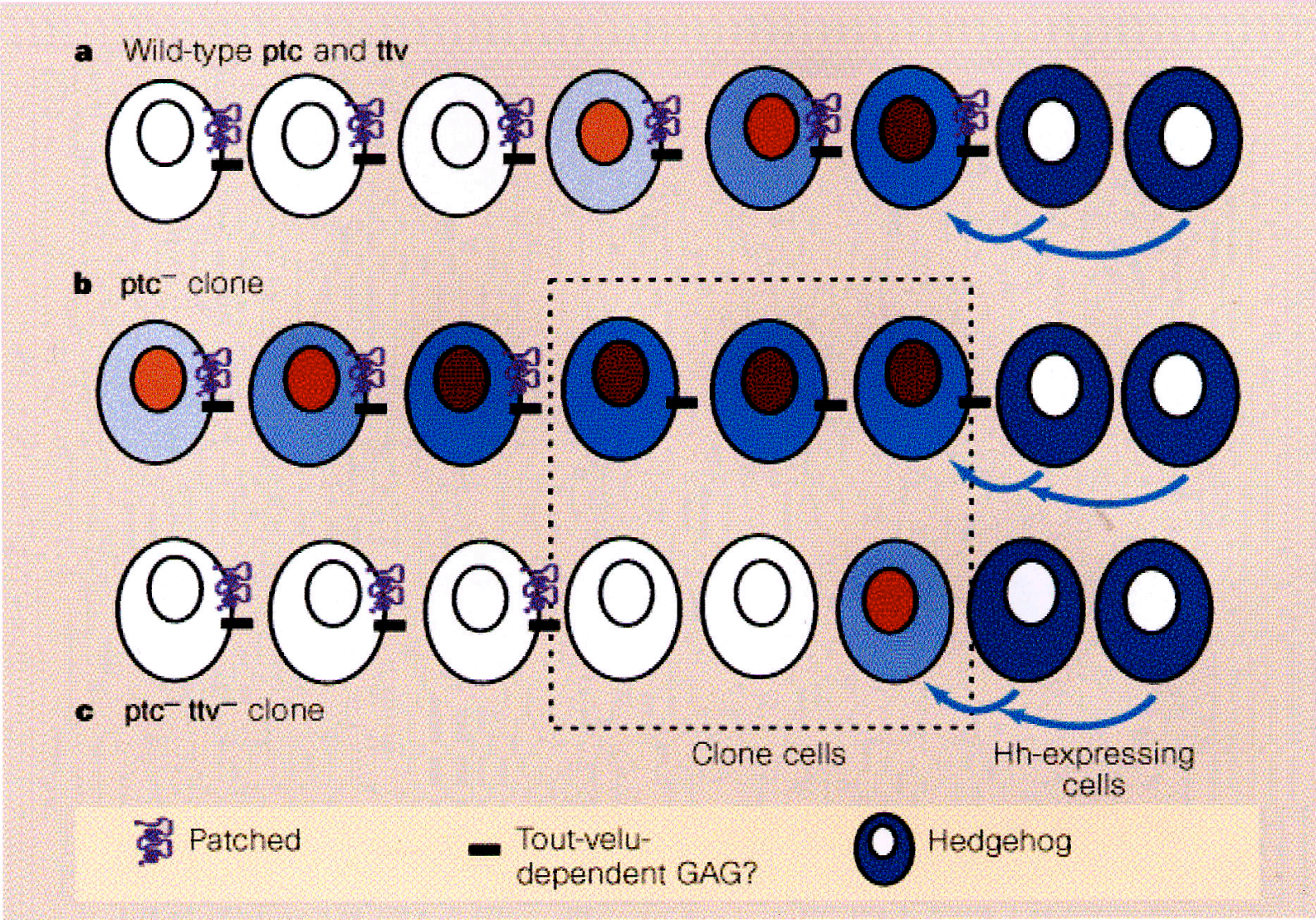
As suggested by the transplantation experiments, the polarizing activity stimulates differentiation of the mesenchyme in a concentration dependent manner.

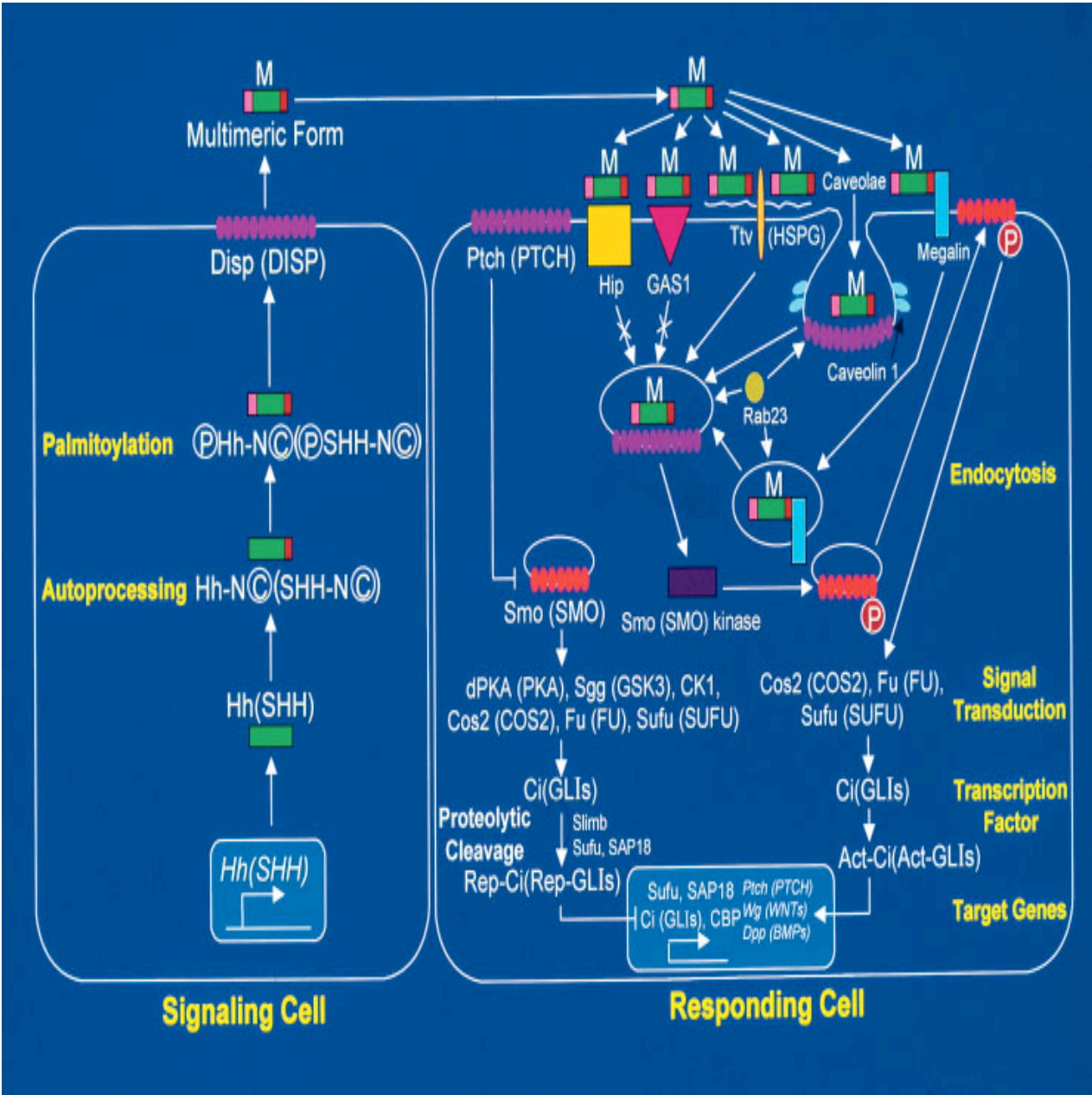
This has been verified by using fibroblasts that have been transfected with Shh. Depending on the number of cells used to substitute for the ZPA different patterns of digit formation occur.

How to limit diffusion of Shh.



Sharpening the concentration gradient but getting to where you need to go.





What maintains the ZPA?

*In vitro* ZPA loses polarizing activity if cultured alone.

*In vitro* ZPA retains activity if cultured with AER.

If one ablates the AER completely, the ZPA is lost.

As in the leg/wing experiment FGF (4/8) can replace the AER.

FGF is made in the right place (over ZPA)

FGF diffusion is limited by binding to ECM.

In summary:

1. Two sources of mesoderm limb: lateral plate forming cartilage and bone; somite-derived cells forming muscle.
2. The trunk level of the lateral plate mesoderm determines whether it become forelimb or hindlimb.
3. The ectoderm is a signaling center regulating growth and it participates in patterning this outgrowth.
4. Because limb innervation arrives just as the muscle masses are forming, the segmental pattern of innervation will be altered as limb rotate.