# Biologi Regenerasi

2 SKS

Jumat 9.00-11.00

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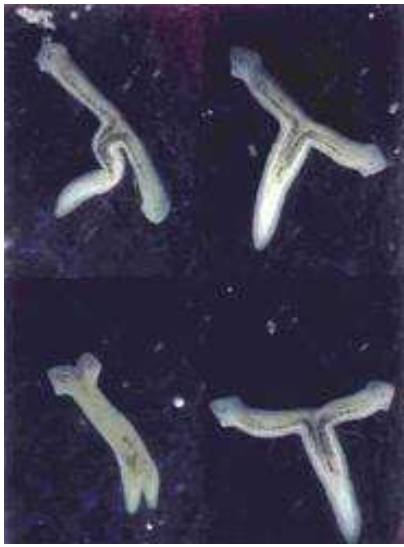
# History of Regeneration

- 1712 - René-Antoine Ferchault de Réaumur: limb regeneration in crayfish.
  Réaumur hypothesis: regenerating limbs from the expansion of tiny preformed limbs that resided at the base of the limb.



- 1740 - Abraham Trembley → hydra ,
- 1745 - Charles Bonnet → annelids,
- 1769 - Spallanzani → amphibians
- 1770 - P. S. Pallas → planarians.
- 1892 – Weismann → one of the first theories of morphogenesis in limb regeneration
- 1901 - Thomas Hunt Morgan

- *regeneration* is
  - the “reproduction or reconstitution of a lost or injured part” or “a form of asexual reproduction.”

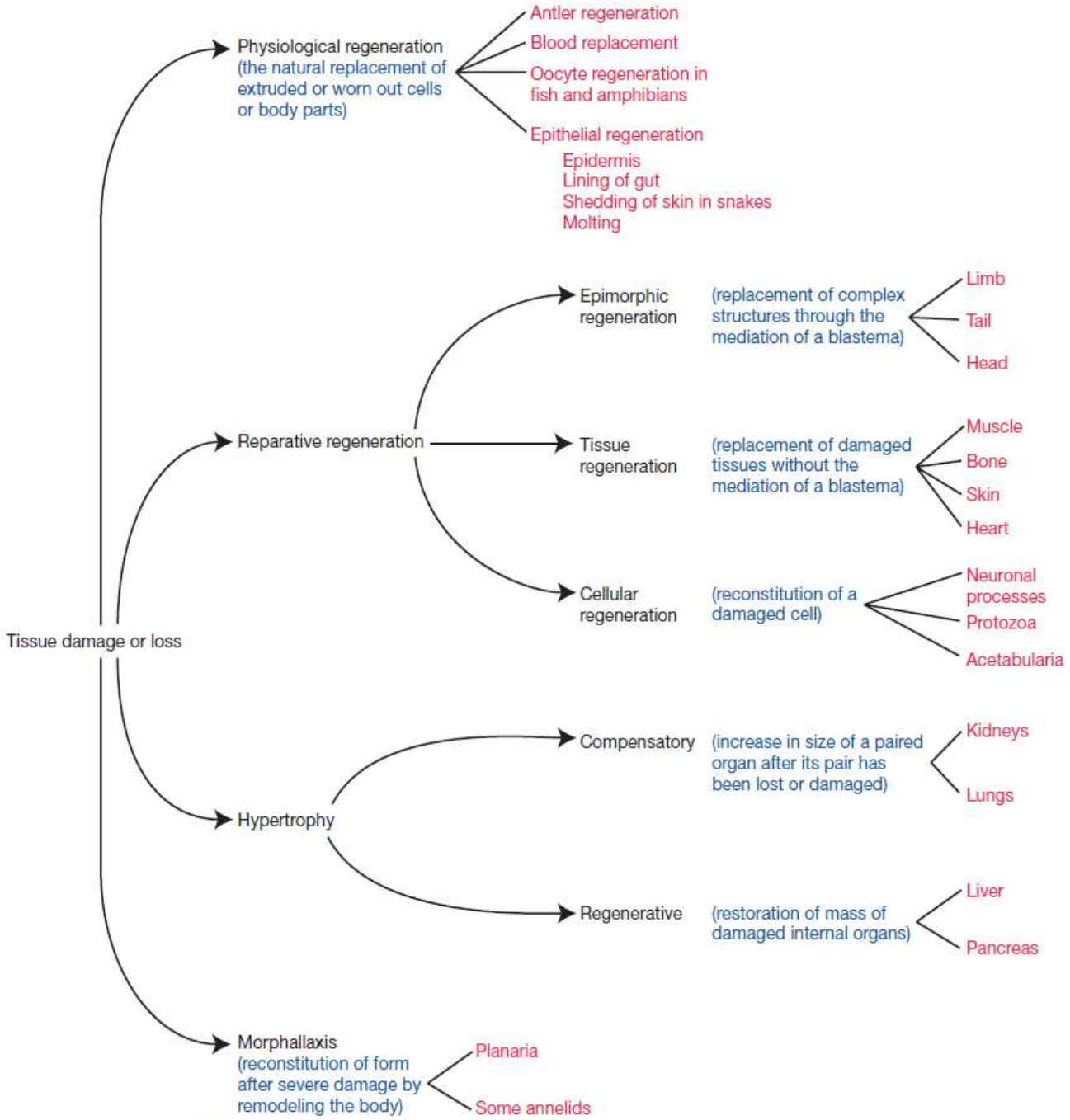


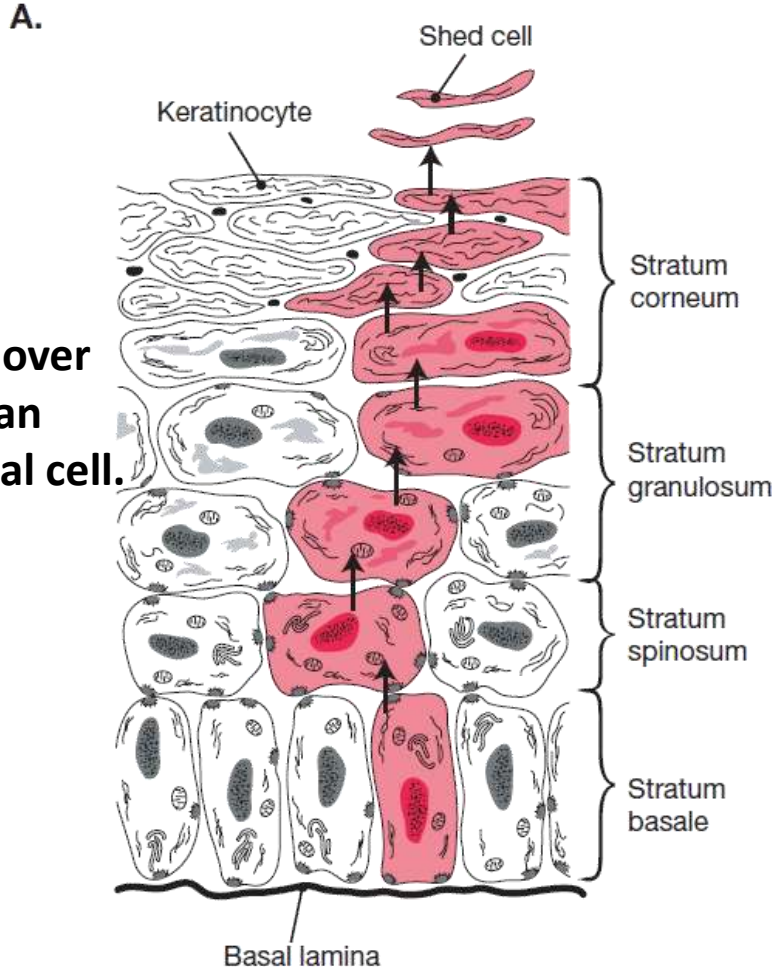

**FIGURE 1-1** Diagram illustrating the major types of named regenerative phenomena.

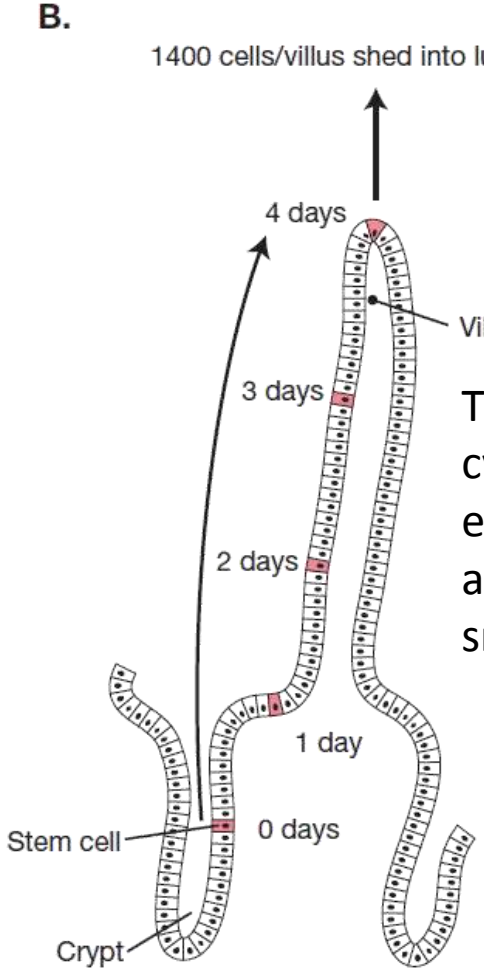
# Physiological Regeneration

- natural replacement of extruded or worn-out body parts, is a process that occurs in many of our body systems
  - cellular turnover shedding cycles of the epidermis or the epithelial cells lining the gut,
  - renewal of the endometrium after a menstrual period,
  - replacement of blood cells

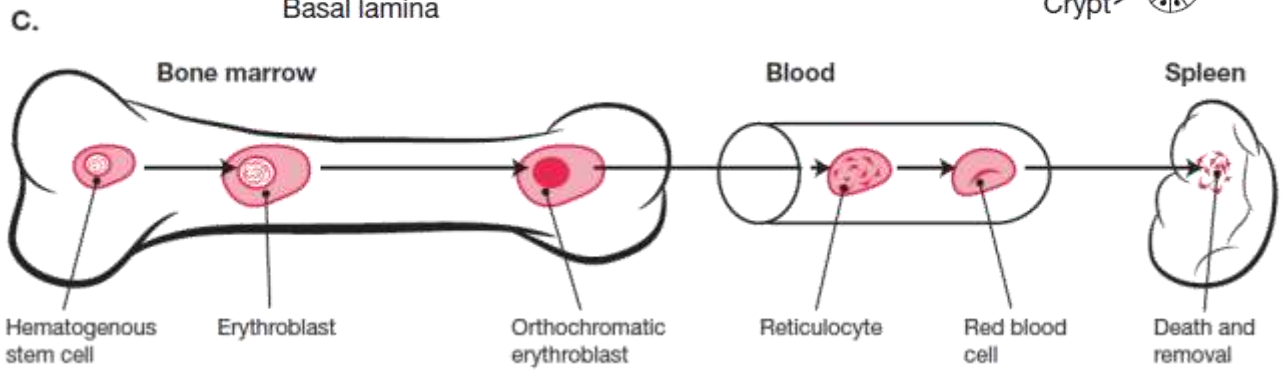
# THREE TYPES OF PHYSIOLOGICAL REGENERATION IN MAMMALS

**The turnover cycle of an epidermal cell.**




The shedding cycle of an epithelial cell on a villus in the small intestine.




**The replacement cycle of a red blood cell.**

# *Reparative regeneration*

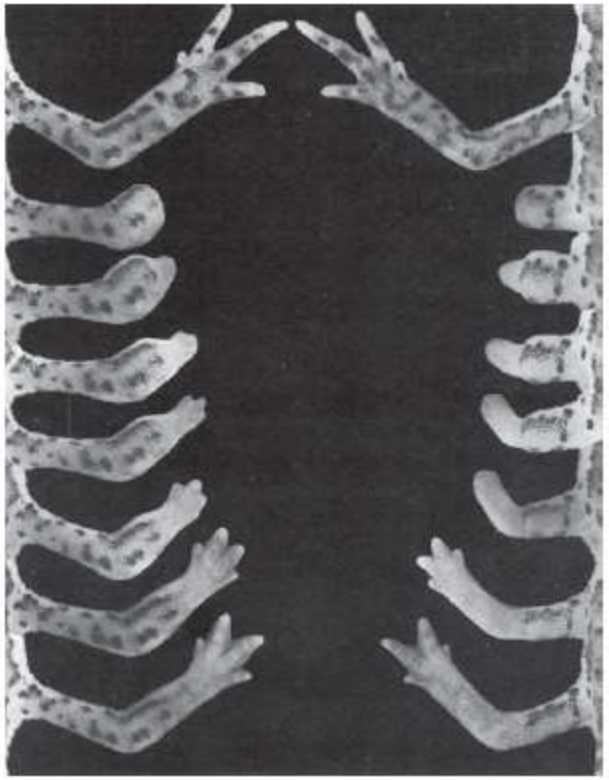
- replacement of a lost or damaged part of the body
- most varieties of posttraumatic regeneration.
  - regeneration of the amputated limb or tail of a salamander or newt,
  - reconstitution of the entire body of a planarian from a fragment less than 1/200 of the original mass

# Epimorphic Regeneration

- Thomas Hunt Morgan (1901)
  - proliferation of material precedes the development of the new part
  - formation of a regeneration blastema that arises through epithelial mesenchymal interactions and that contains and expresses intrinsic morphogenetic information.
  - The classic example of epimorphosis is the regenerating amphibian limb

- Epimorphic Regeneration ≠ *morphallaxis*
  - "in which a part is transformed directly into a new organism, or part of an organism without proliferation at the cut surfaces

- **Regenerating Amphibian Limb**
  - mobilizing cells at the amputation surface to form a regeneration blastema that then goes on to produce an almost exact replica of the amputated limb

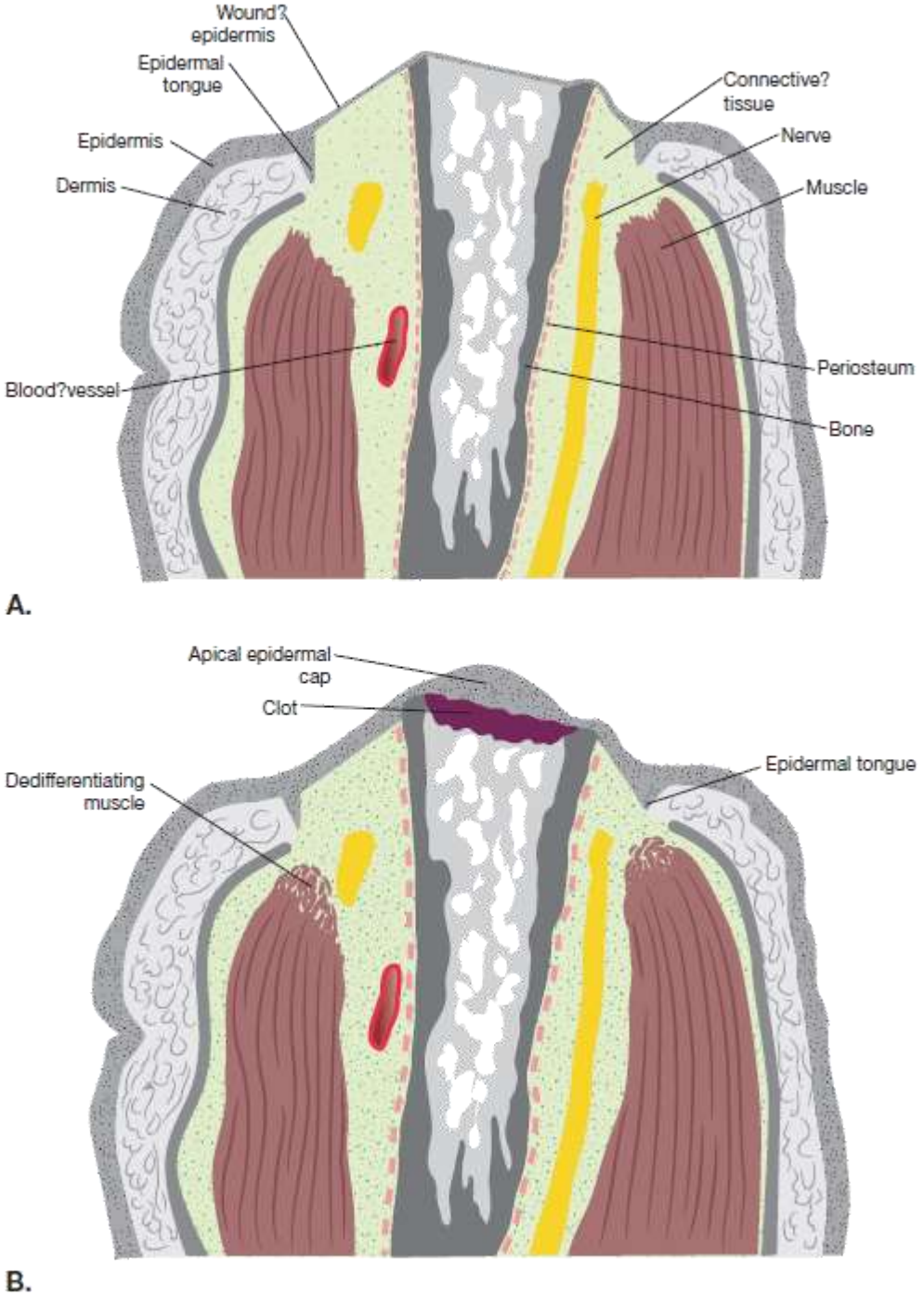


Successive stages in the regeneration of newt arms amputated at upper (right) and lower (left) arm levels. Starting below the normal arms at the top, the intervals of regeneration are 7, 21, 25, 28, 32, 42, and 70 days after amputation.

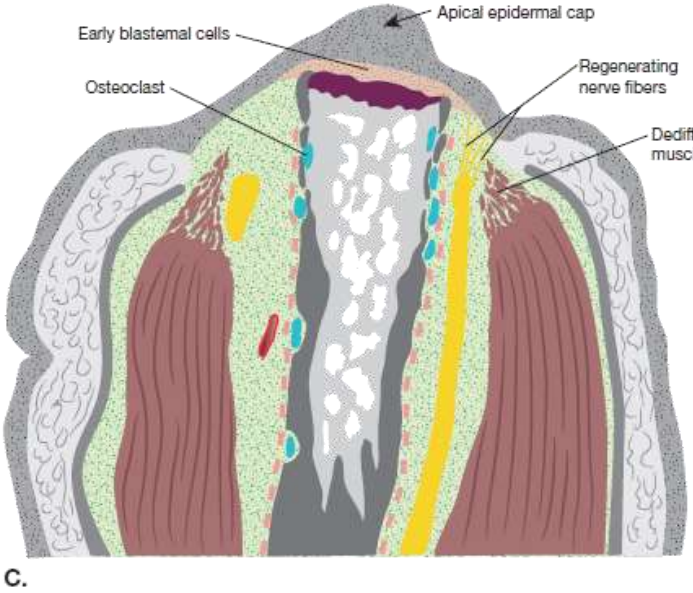
- **Epimorphic Regeneration** staging systems in limb regeneration
  - ***Phase of Wound Healing***
    - soft tissues retract → contractions of the muscle stumps within the limb
    - bleeding from major vessels stops through contractions of the vascular walls (
    - the epidermal cells at the margins of the amputation wound become mobilized and begin to migrate across the amputation surface

- ***Phagocytosis and Demolition***

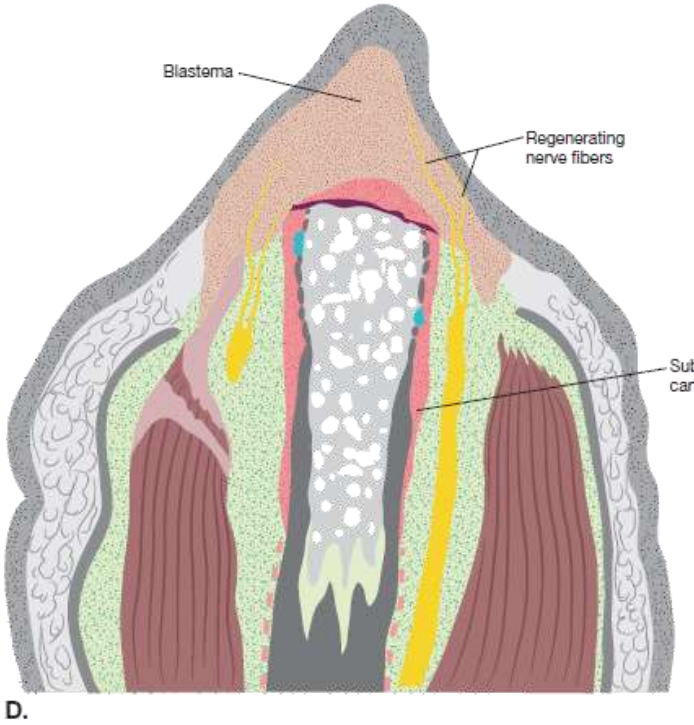
infi ltration of infl ammatory cells → demolition of tissue by matrix metalloproteinases & proteases,

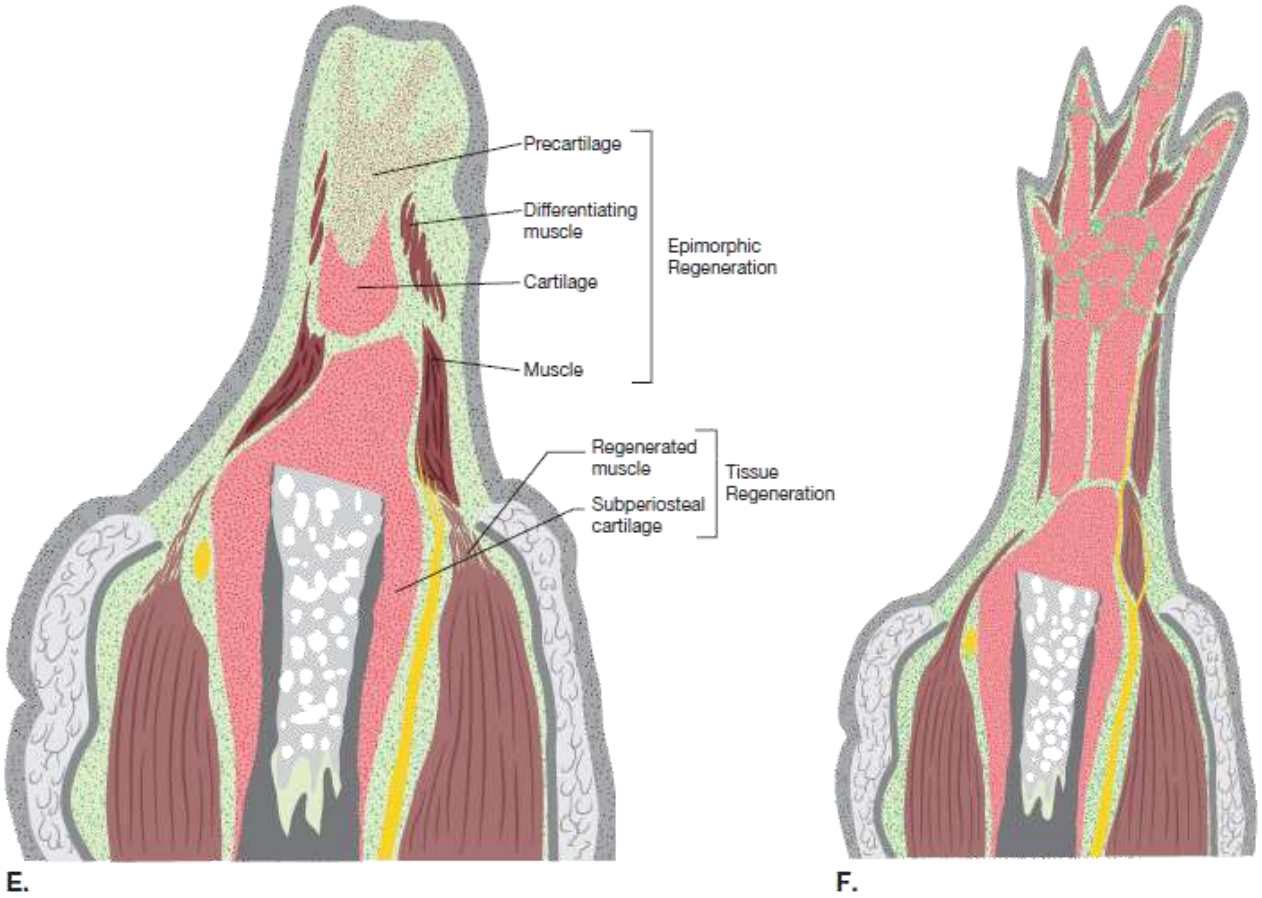


- ***Dedifferentiation***
  - tissues at the distal end of the stump have lost many of their mature histologic characteristics and have begun to produce cells of a more embryonic morphologic character




- ***Blastema Formation***
  - the immature-looking cells accumulate during late Dedifferentiation → become concentrated distally beneath the thickened apical epidermal cap → produces a budlike outgrowth at the tip of the limb stump, is called the *regeneration blastema*
  - the blastema is reminiscent of the embryonic limb bud.






***Morphogenesis.***

- Morphogenesis represents the morphologic fruition of the patternforming activity that has taken place within the regeneration blastema

***Growth***

growth of the regenerate

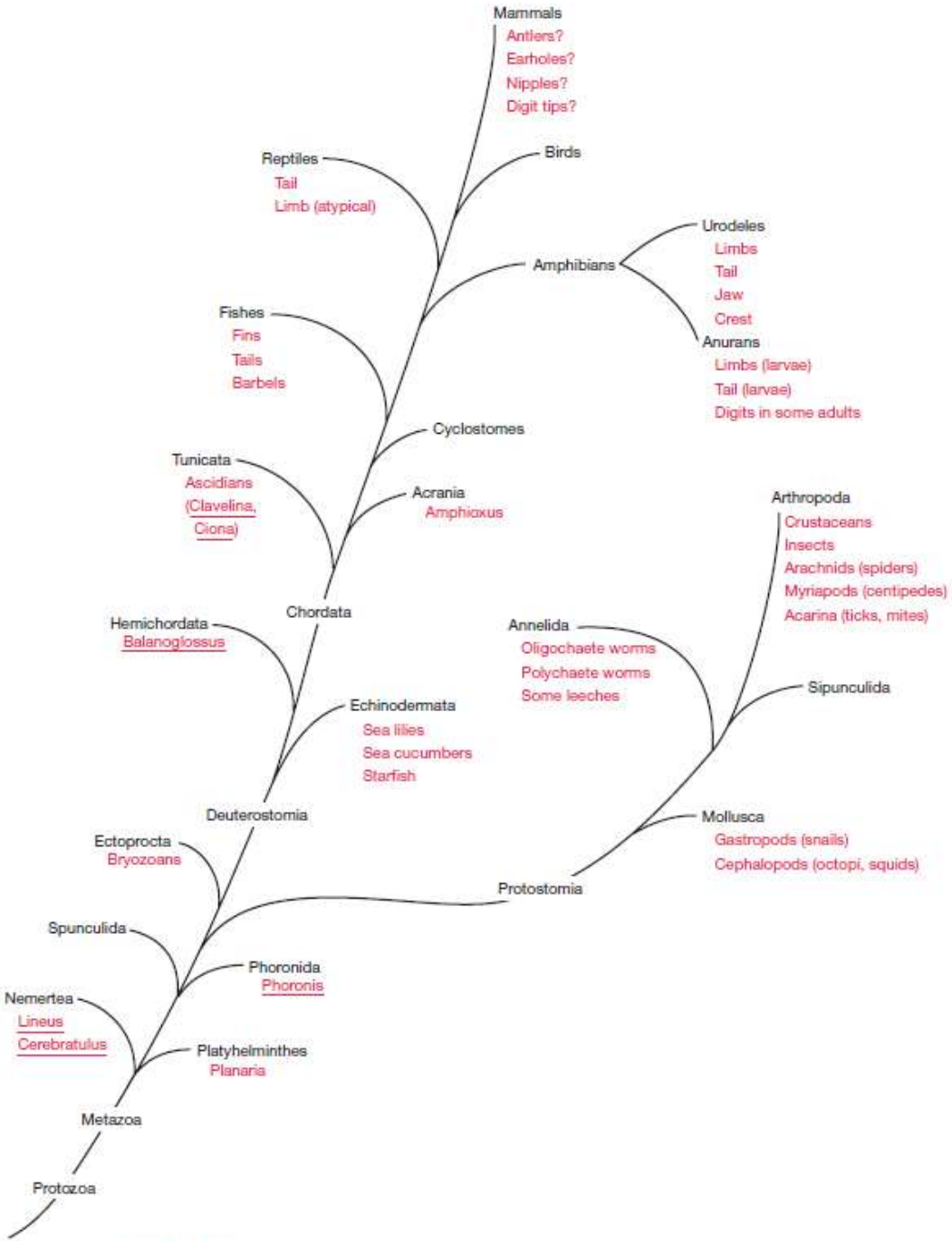



**FIGURE 1-5** Phylogenetic distribution of epimorphic regeneration.

# Tissue regeneration

- repair of most damaged tissues within the body, with the greatest emphasis on mammalian tissues because of the medical implications
- initiated by a wide variety of traumatic means
  - Mechanical trauma
  - Thermal trauma
  - Chemical trauma

## Common Features in Tissue Regenerative Processes

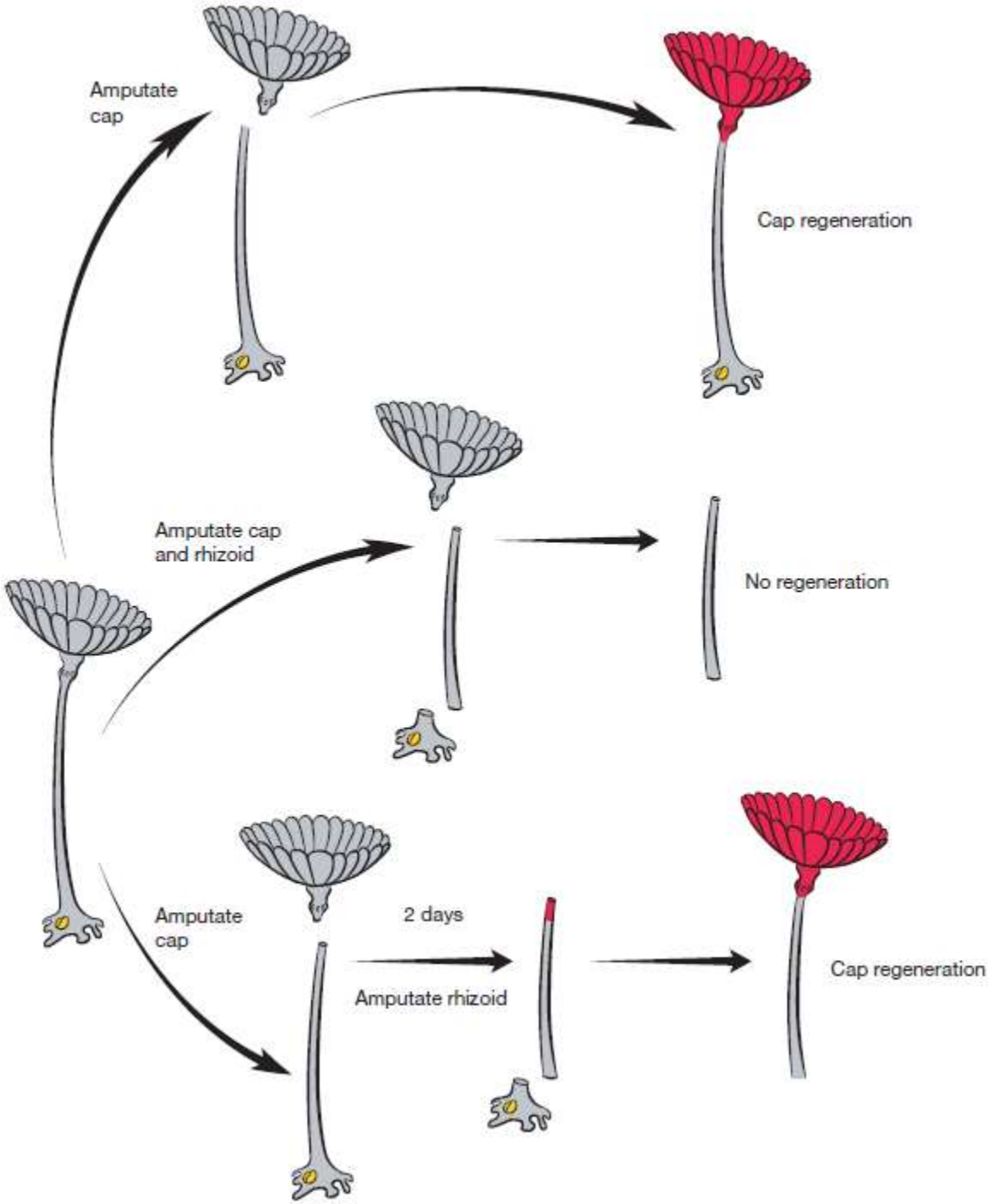
1. Trauma (e.g., mechanical, chemical, thermal)
2. Localized posttraumatic ischemia and edema
3. Local inflammation and the removal of damaged tissues by phagocytosis
4. Activation of the cellular precursors of regeneration
5. Revascularization of the traumatized region
6. The extracellular matrix as a substrate for regeneration
7. Increase in the number of regenerating cells by proliferation
8. Differentiation of the regenerating tissue
9. Morphogenesis of the regenerating tissue
10. Functional restoration

**Comparison of Tissue and Epimorphic Regeneration of Muscle**

| Characteristic | Tissue regeneration | Epimorphic regeneration |
|---|---|---|
| Initial stimulus | Muscle fiber damage | Anything that stimulates the regeneration of a limb |
| Cellular source of myoblasts | Satellite cells; marrow-derived stem cells; other? | Dedifferentiation; stem cells; other? |
| Removal of damaged cytoplasm | Phagocytosis plays a prominent role | Phagocytosis much less prominent |
| Regeneration blastema | Absent | Present |
| Relation of regenerating muscle cells to basal lamina | Most regeneration occurs within the confines of old basal laminae | Most regeneration occurs in the absence of old basal laminae |
| Time course | Fast | Slow |
| Relation to nerves | Early differentiation and morphogenesis independent of nerves. Final differentiation requires motor nerves | Nerves (any type) required for blastema formation; morphogenesis is independent of nerves |
| Relation between amount of damaged and regenerating muscle | Fairly direct between minimum and maximum thresholds | Amount of muscle in regenerates is independent of amount of damaged muscle in stump |
| Gradients | Related to patterns of blood supply, often centripetal | Pronounced proximodistal gradient of decreasing maturity. A lesser preaxial to postaxial gradient |
| Development of function | Development of contractile properties recapitulates the ontogenetic pattern | Unknown |
| Morphology of regenerate | Usually imperfect | Perfect |
| Amount of connective tissue | Above normal | Normal |
| Morphology of mature muscle fibers | Central nuclei commonly persist | Normal at the histologic level |
| Morphology of development | Unlike that in embryo above the cellular level | Close recapitulation of ontogenetic development |
| Morphogenetic control | Gross morphogenesis and internal architecture can be accounted for by physical factors | Morphogenetic controls similar to those operating in the embryo |
| Role of function in morphogenesis | Functional environment improves the quality of the regenerate | Function not needed for normal morphogenesis |
| Positional information | Present, but not expressed in amphibians | Present and expressed |
| Interactions between regenerative processes | Suppressed by epimorphic regeneration | Dominant over tissue regeneration |

# Cellular Regeneration

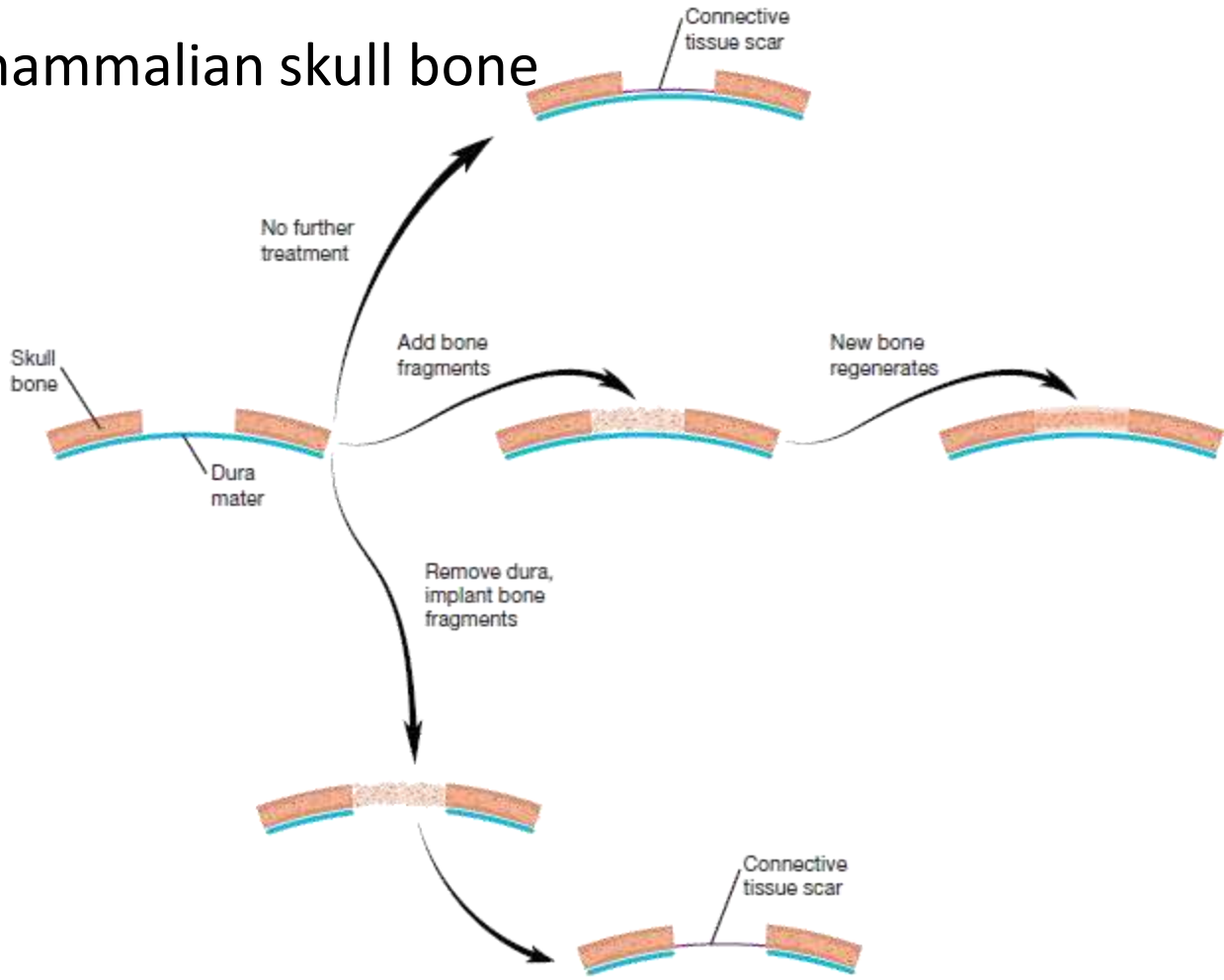
- the reconstruction of a single cell that has been traumatized
  - reconstitution of protozoa after resection or natural fission (~ asexual reproduction)
  - regeneration of transected or otherwise damaged axons of peripheral nerves




Regeneration in the unicellular marine alga, *Acetabularia*.

# Regeneration by Induction

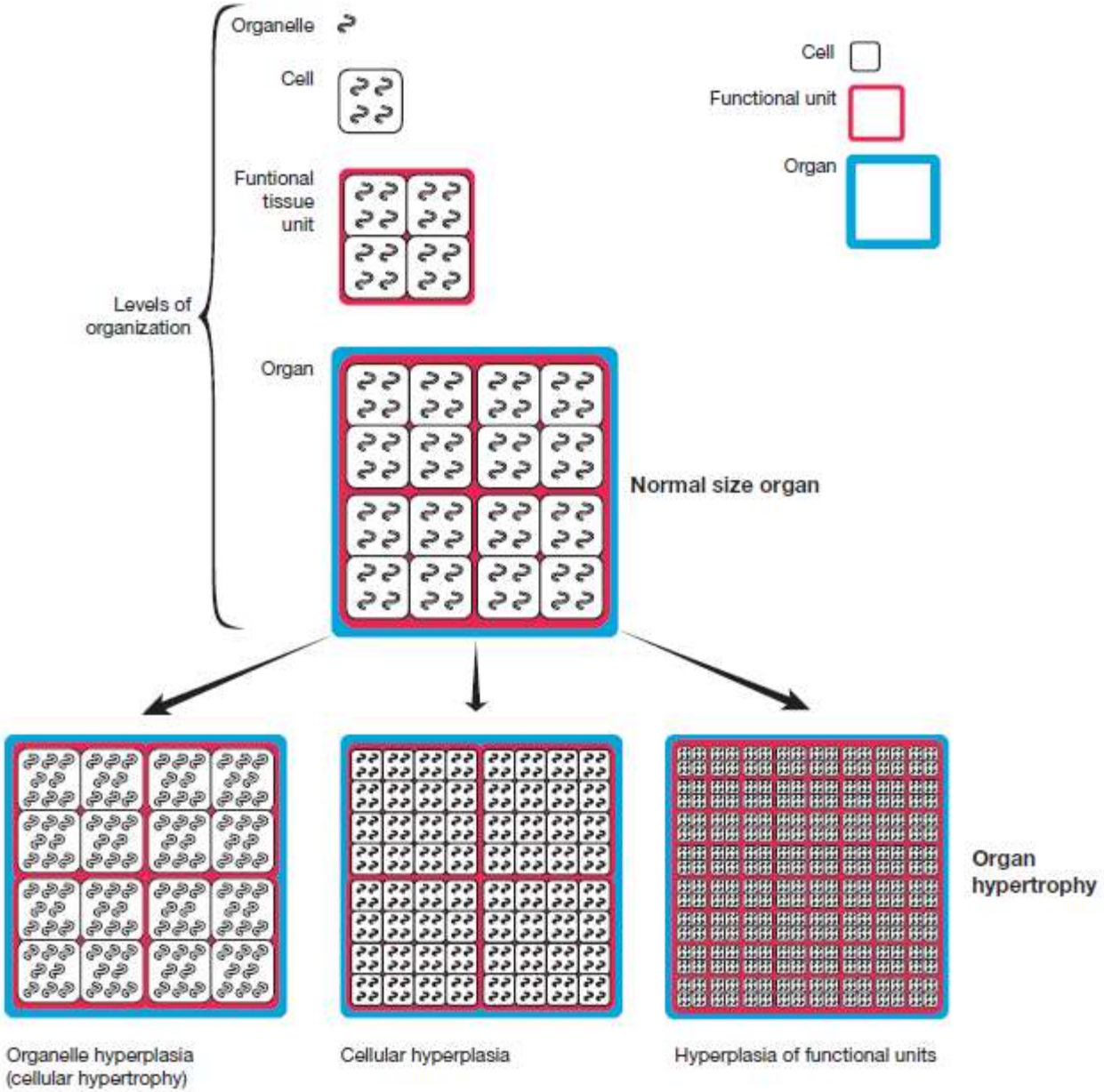
- tissue-specific regeneration can be stimulated by the application of tissues or materials with specific inductive properties
  - regeneration of mammalian skull bone




Regeneration by induction of a defect in the adult mammalian skull. Simple removal of bone results in the formation of a connective tissue scar. If the defect is fi led in with a mass of finely ground bone, new bone regenerates within a few weeks. If the dura mater is removed, regeneration fails to occur despite the addition of ground bone into the defect

# HYPERTROPHY

- Many internal organs have the capacity to increase their mass after damage or partial removal, or if one member of a pair (e.g., kidneys) is removed


Organelle
Cell
Funtional tissue unit
Levels of organization
Organ
Normal size organ
Cell
Functional unit
Organ
Organ hypertrophy
Organelle hyperplasia (cellular hypertrophy)
Cellular hyperplasia
Hyperplasia of functional units

# MORPHALLAXIS

- the “part is transformed directly into a new organism, or part of an organism,” and the other was that this occurs “without proliferation at the cut surfaces”
  - Invertebrate regenerating systems

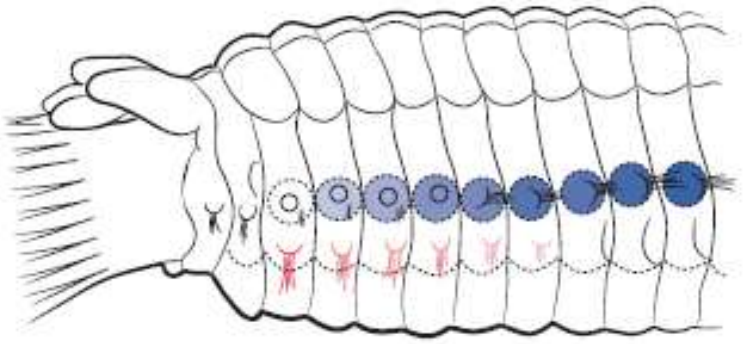


FIGURE 1-12 Morphallactic transformation of abdominal into thoracic segments during head regeneration in *Sabella*. Blue (from right to left): successive stages of dissolution of abdominal setae and setigerous bulbs. Red (from right to left): successive stages in the formation of thoracic setae. (Based on Berrill's (1931, 1978) experiments.)

# ASEXUAL REPRODUCTION

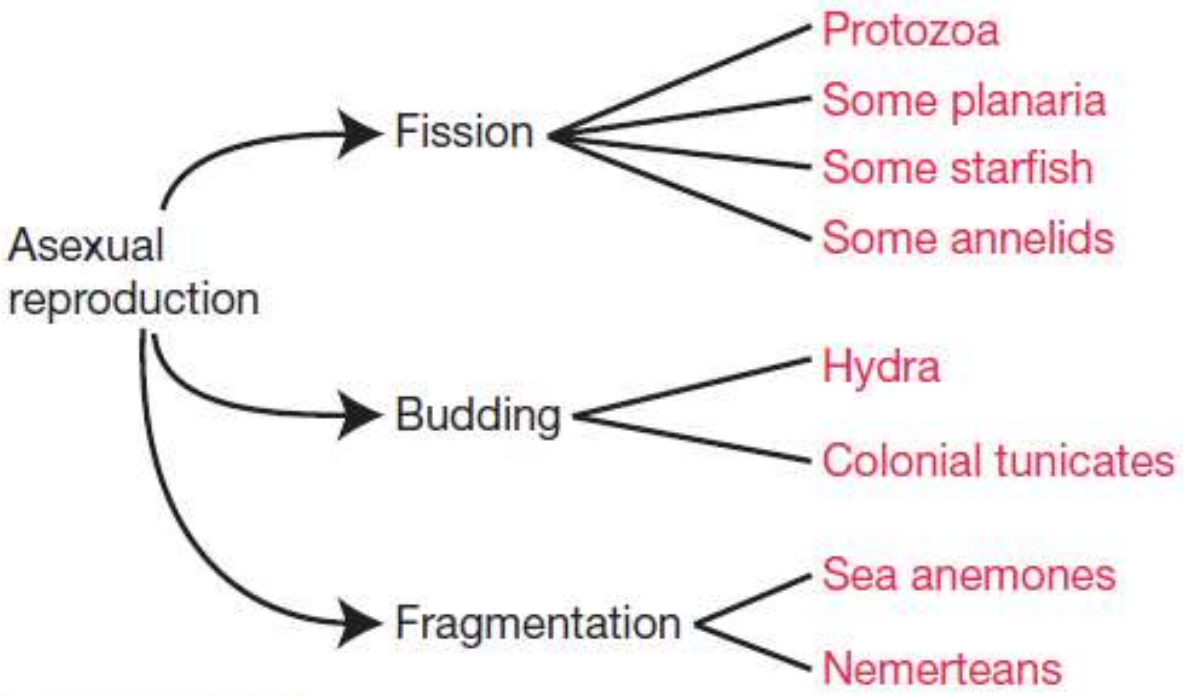



**FIGURE 1-13** Major modes of asexual reproduction among invertebrates.