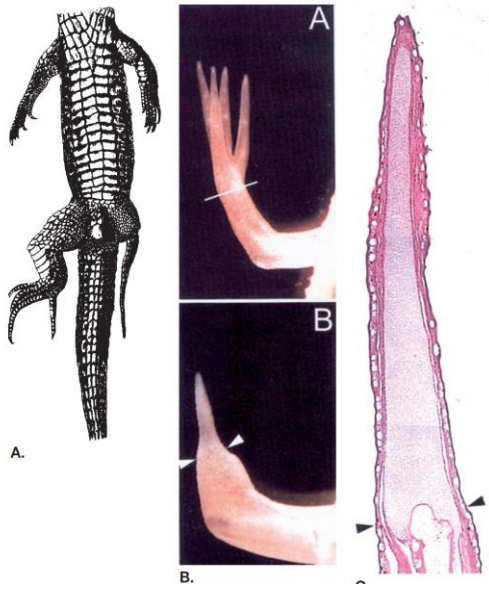
MORPHOGENESIS OF REGENERATING STRUCTURES

- Epimorphic regeneration→
  - perfect restoration of the structure anatomically

- Tissue regeneration →
  - restoring their original form, but the result is not perfect
  - follows a process that differs considerably from that seen in the embryonic development of the tissue at levels above that of the individual cell

TYPES OF MORPHOGENETIC PHENOMENA

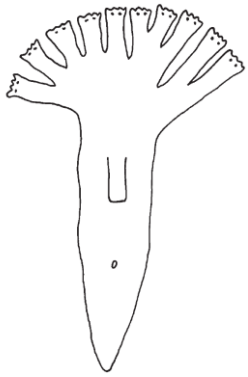
- **Absence of Regeneration**
  - a genetic deficiency or to the lack or deficiency of specific conditions
- **Perfect Restoration of Form**
  - an epimorphic regenerative process
- **Hypomorphic Regeneration**
  - incomplete formation of regenerating structures, occurs commonly throughout the animal kingdom
  - can be due to causes as diverse as nutritional deficiencies, delayed denervation, partial x-irradiation, or loss of regenerative power during metamorphosis
  - A result of deficiencies of or inappropriate morphogenetic information at the end of an amputated structure



TYPES OF MORPHOGENETIC PHENOMENA

- **Supernumerary Regeneration**
  - regeneration results in the formation of duplicated or supernumerary structures
  - can also be stimulated to form without loss of the original structure ➔amputation is not an absolute requirement for regeneration

Complete supernumerary limb in the newt, induced by the implantation of a piece of kidney from the frog, *Rana pipiens,* beneath the skin of the upper arm



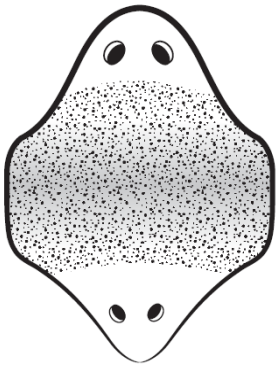
A ten-headed planarian *(Dendrocoelum lacteum)* that resulted from multiple cuts.

TYPES OF MORPHOGENETIC PHENOMENA

- **Heteromorphic Regeneration**
  - a regenerated structure is a close copy of what was originally lost, but certain classic experiments have produced striking examples of the regeneration of structures that are totally different from those that were amputated.
  - *homeotic regenerate* ➔ an amputated extremity is replaced by one appropriate for another body segment

Homeotic regeneration of a cluster of several hind limbs (right) from a regenerating tadpole tail after treatment with retinoic acid

A. Double-headed planaria



TYPES OF MORPHOGENETIC PHENOMENA

- **Morphallaxis**
  - remodeling the entire body according to the regenerative tissue size ➔ individual with a proportioned size

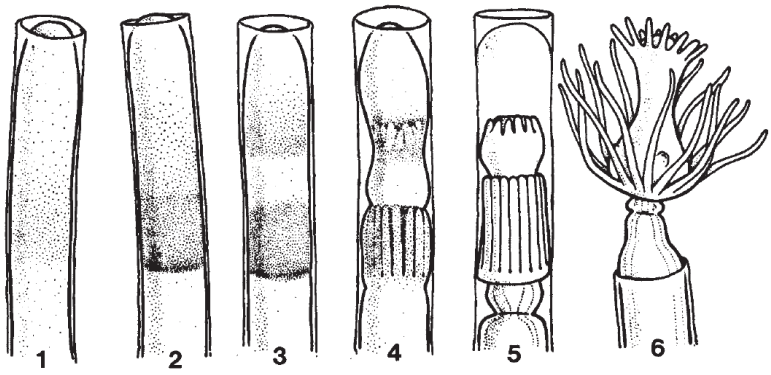
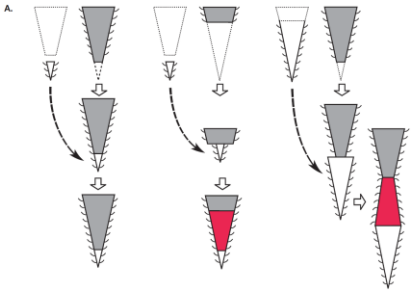


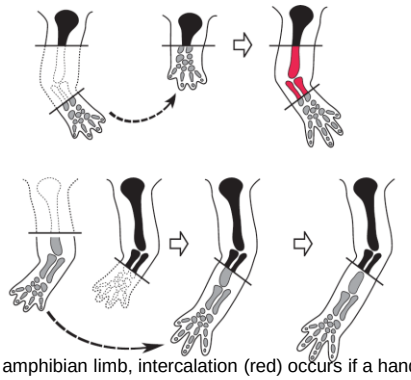
FIGURE 7-5 Anterior regeneration and morphallaxis in the hydroid *Tubularia:* (1) soon after amputation; (2) early formation of a pigment band presaging the formation of the proximal tentacles; (3) early formation of a second distal pigmented band above the proximal one; (4) and (5) early stages in the differentiation of proximal and distal tentacle rows; and (6) functional regenerated hydranth.

TYPES OF MORPHOGENETIC PHENOMENA

- **Somatic Embryogenesis**
  - formation of an entire individual from single cells or small parts of the body
- **Intercalary Regeneration**
  - the filling in of gaps along the proximodistal or cross-sectional axes of the limb ➔ It occurs when two nonadjacent tissues are placed next to one another.



Intercalary regeneration in cockroach and amphibian limbs. *(A)* In the cockroach, if the tip of a limb is grafted onto a corresponding level of a host limb (left), the graft heals in place, but no intercalation occurs. If a distal tip is grafted onto a proximal level of the host (middle), intercalation with normal polarity (red) takes place. If a proximal segment is grafted onto a distal segment (right), intercalation (red) also takes place, but the polarity is reversed.



In the amphibian limb, intercalation (red) occurs if a hand is grafted to an upper arm (top), but if an upper arm segment is grafted to a forearm, no intercalary regeneration takes place.

- **Growth as a Morphogenetic Phenomenon:**
  - growth, defi ned as an increase in mass or number of cells
  - growth commonly occurs after the overall form of the regenerate has been fully established

MAJOR CONCEPTS IN MORPHOGENESIS

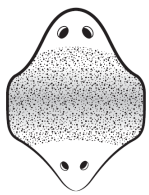
- **Organ Specificity**
  - the resulting regenerate is a replica of the original
  - Retinoic acid could change this phenomena
- **Tissue Specificity**
  - regeneration of complex structures is a tissue-specific phenomenon
- **Distalization**
  - only more distal, rather than proximal, structures form from an amputation surface

MAJOR CONCEPTS IN MORPHOGENESIS

- **Polarity:**
  - **Craniocaudal axis**
  - **Proximodistal axis of the limb**

  } Hox genes → Has been set during embryonic development
  - In regeneration : two possibility:
    - Reactivate some polarity system happened in embryonic development
    - Regenerate based on existing polarity in the remaining structure
  - In regeneration → polarity → linked to metabolic gradients / differences electric potential/ current flow
  - Polarity in regeneration can be reversed → ineffective regulators of the basis for polarity

A. Double-headed planaria



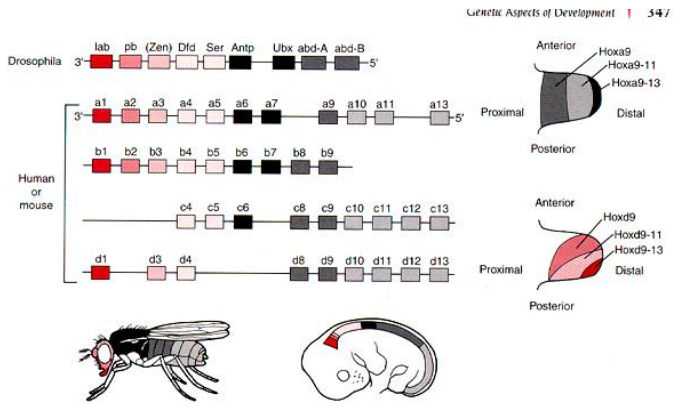
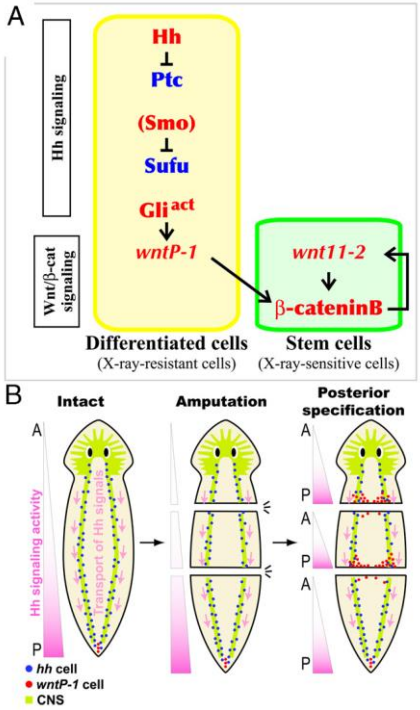
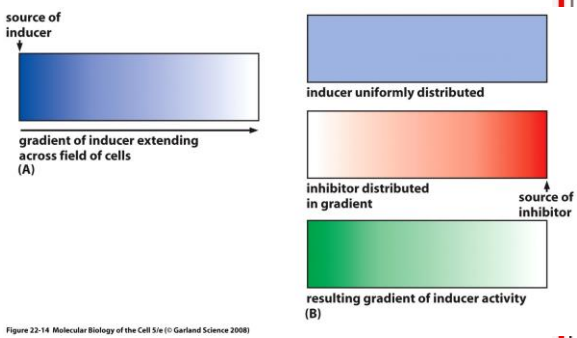


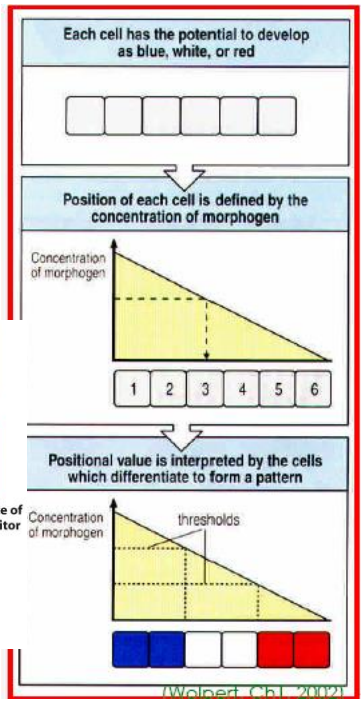
Figure 17–7. Action and arrangement of *HOX* genes. An ancestral *HOX* cluster in a common ancestor of vertebrates and invertebrates has been quadruplicated in mammals, and individual members of the ancestral cluster have been lost. The combination of *HOX* genes expressed in adjacent regions along the anteroposterior axis of developing embryos select a unique developmental fate. In the developing limbs, different combinations of *HOXA* and *HOXD* genes are expressed in adjacent zones that help select developmental fate along the proximal-distal and anterior-posterior axes. (Figure reprinted by permission from Wolpert L, Beddington R, Brockes J, et al [1998] Principles of Development. Copyright 1998, Oxford University Press, Oxford, England.)



Models for two aspect of the establishment of AP polarity by Hh signaling in planarians. (*A*) The signaling cascade model for posterior specification in planarian regeneration inferred from the present study. Hh signaling triggers posteriorization by inducing transcription of *Wnt* genes in differentiated cells (yellow-shaded box), from which the signal is transmitted to stem cells (green-shaded box) through Wnt/-cateninB signaling for tail regeneration.
Positive and negative regulators of posterior specification are written with red and blue letters, respectively. (*B*) A possible model for the establishment of AP polarity by Hh signaling in planarians. *DjwntP-1*-expressing cells (red dots) at the posterior end suggests that Hh signaling is exclusively activated there (pink gradients on the left), although *Djhh* expressing cells (neural cells; blue dots) are localized all along the VNCs (CNS is indicated by light green). In this model, *Djhh* gene products would be transported posteriorly via VNCs (pink arrows), leading to the induction of posterior specification at the posterior end. (Yazawa et al., PNAS 2009)

- Gradient
  - Metabolic gradients – annelids → polarity





- **Regulation**