Desarrollo del sistema nervioso

- Desarrollo del cerebro
  - Inducción
  - Neurulacion primaria
  - Neurulacion secundaria
  - Vesículas cerebrales primarias
  - Vesículas cerebrales secundarias
  - Diencéfalo y hemisferios cerebrales
  - Sistema ventricular
- Desarrollo de la medula espinal
- Sistema nervioso periférico
  - Placodas
  - Ganglio de los pares craneales
  - Ganglios raquídeos

Procesos en el Desarrollo neuronal

- Inducción
- Proliferación
- Migración
- Agregación
- Diferenciación
- Formación de circuitos
- Apoptosis

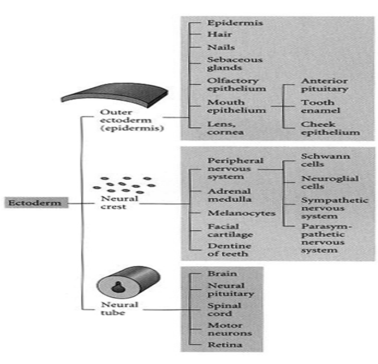

Figure 12.1. Major derivatives of the ectoderm germ layer. The ectoderm is divided into three major domains the surface ectoderm (primarily epidermis), the neural tube (brain and spinal cord), and the neural crest (peripheral neurons, pigment, facial cartilage).

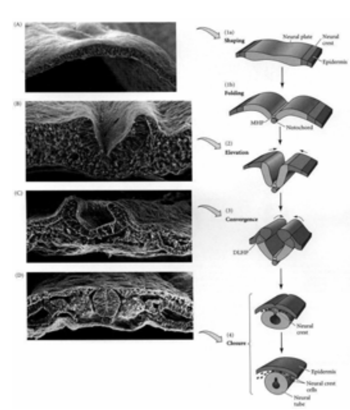

Figure 12.3
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Primary neurulation: neural tube formation in the chick embryo. (A, 1) Cells of the neural plate can be distinguished as elongated cells in the dorsal region of the ectoderm. Folding begins as the medial neural hinge point (MHP) cells anchor to notochord and change their shape, while the presumptive epidermal cells move towards the center. (B, 2) The neural folds are elevated as presumptive epidermis continues to move toward the dorsal midline. (C, 3) Convergence of the neural folds occurs as the dorsolateral hinge point (DLHP) cells become wedge-shaped and epidermal cells push toward the center. (D, 4) The neural folds are brought into contact with one another, and the neural crest cells link the neural tube with the epidermis. The neural crest cells then disperse, leaving the neural tube separate from the epidermis. (Photographs courtesy of K. Tosney and G. Schoenwolf; drawings after Smith and Schoenwolf 1997.)

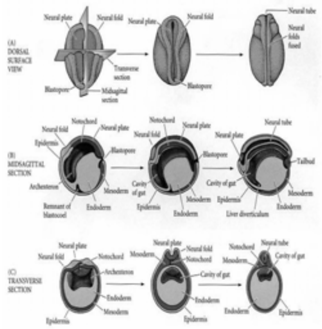

Figure 12.4

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Three views of neurulation in an amphibian embryo, showing early (left), middle (center), and late (right) neurulae in each case. (A) Looking down on the dorsal surface of the whole embryo. (B) Sagit-tal section through the medial plane of the embryo. (C) Transverse section through the center of the embryo. (After Balinsky 1975.)

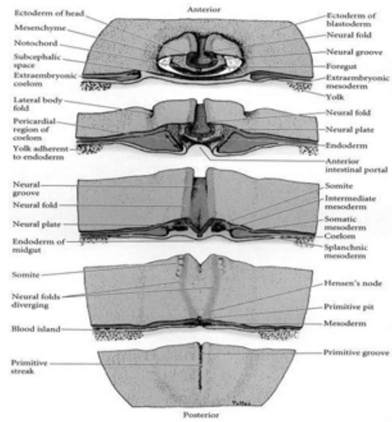

Figure 12.5

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Stereogram of a 24-hour chick embryo. Cephalic portions are finishing neurulation while the caudal portions are still undergoing gastrulation. (From Patten 1971; after Huettner 1949.)

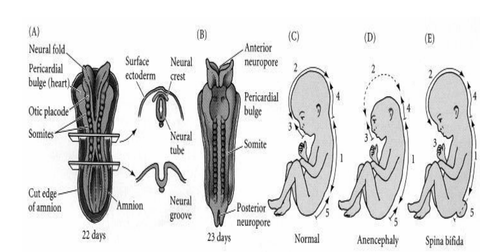

Figure 12.6

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Neurulation in the human embryo. (A) Dorsal and transverse sections of a 22-day human embryo initiating neurulation. Both anterior and posterior neuropores are open to the amniotic fluid. (B) Dorsal view of a neurulating human embryo a day later. The anterior neuropore region is closing while the posterior neuropore remains open. (C) Regions of neural tube closure postulated by genetic evidence (superimposed on newborn body). (D) Anencephaly is caused by the failure of neural plate fusion in region 2. (E) Spina bifida is caused by the failure of region 5 to fuse (or of the posterior neuropore to close). (C-E after Van Allen et al. 1993.)

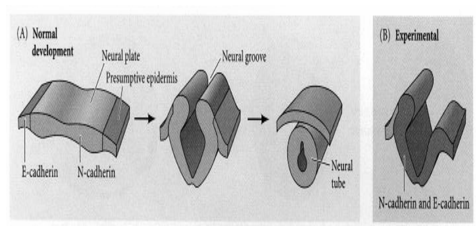

Figure 12.7

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Expression of N-cadherin and E-cadherin adhesion proteins during neurulation in *Xenopus.* (A) Normal development. In the neural plate stage, N-cadherin is seen in the neural plate, while E-cadherin is seen on the presumptive epidermis. Eventually, the N-cadherin-bearing neural cells separate from the E-cadherin-containing epidermal cells. (The neural crest cells have neither cadherin, and they disperse.) (B) No separation of the neural tube occurs when one side of the frog embryo is injected with N-cadherin mRNA, so that N-cadherin is expressed in the epidermal cells as well as in the presumptive neural tube.

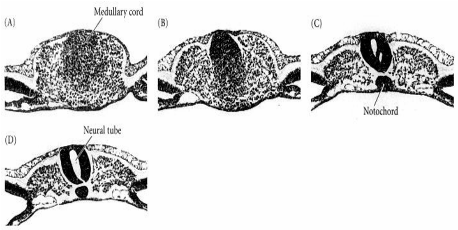

Figure 12.8

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Secondary neurulation in the caudal region of a 25-somite chick embryo. (A) The medullary cord forming at the most caudal end of the chick tailbud. (B) The medullary cord at a slightly more anterior position in the tailbud. (C) The neural tube is cavitating and the notochord forming. (D) The lumens coalesce to form the central canal of the neural tube. (From Catala et al. 1995; photographs courtesy of N. M. Le Douarin.)

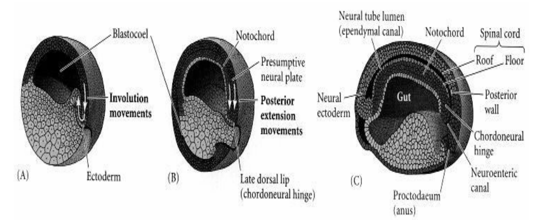

Figure 12.9

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Movements of cells during secondary neurulation in *Xenopus.* (A) Involution of the mesoderm at the mid-gastrula stage. (B) Movements of the dorsal blastopore lip at the late gastrula/early neurula stage. Involution has ceased, and both the ectoderm and the mesoderm of the late blastopore lip move posteriorly. (C) Early tadpole stage, wherein the cells lining the blastopore form the neurenteric canal, part of which becomes the lumen of the secondary neural tube. (From Gont et al. 1993.)

The anterior-posterior axis

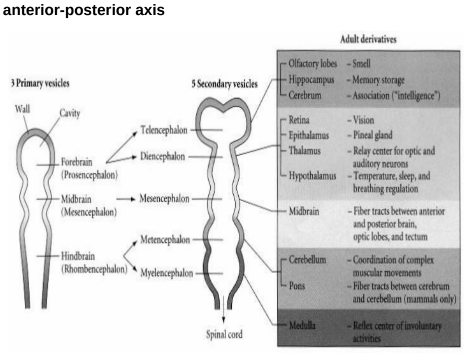

Figure 12.10

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Early human brain development. The three primary brain vesicles are subdivided as development continues. At the right is a list of the adult derivatives formed by the walls and cavities of the brain. (After Moore and Persaud 1993.)

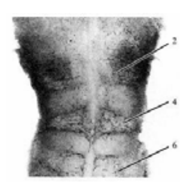

Figure 12.11

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A 2-day embryonic chick hindbrain, splayed to show the lateral walls. Neurons were visualized with an antibody staining neurofilament proteins. Rhombomeres 2, 4, and 6 are distinguished by the high density of axons at this early developmental stage. (From Lumsden and Keynes 1989; photograph courtesy of A. Keynes.)

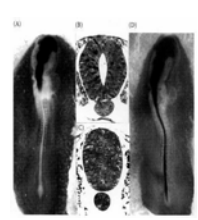

Figure 12.12

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Occlusion of the neural tube allows expansion of the future brain region. (A) Dye injected into the anterior portion of a 3-day chick neural tube fills the brain region, but does not pass into the spinal region. (B, C) Section of the chick neural tube at the base of the brain (B) before occlusion and (C) during occlusion. (D) Reopening of the occlusion after initial brain enlargement allows dye to pass from the brain region into the spinal cord region. (Photographs courtesy of M. Desmond.)

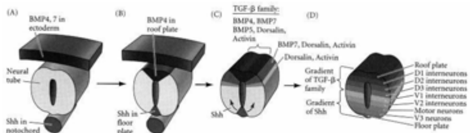

Figure 12.13

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Dorsal-ventral specification of the neural tube. (A) The newly formed neural tube is influenced by two signaling centers. The roof of the neural tube is exposed to BMP4 and BMP7 from the epidermis, and the floor of the neural tube is exposed to Sonic hedgehog protein from the notochord. (B) Secondary signaling centers are established within the neural tube. BMP4 is expressed and secreted from the roof plate cells; Sonic hedgehog is expressed and secreted from the floor plate cells. (C) BMP4 establishes a nested cascade of TGF-β-related factors, spreading ventrally into the neural tube from the roof plate. Sonic hedgehog diffuses dorsally as a gradient from the floor plate cells. (D) The neurons of the spinal cord are given their identities by their exposure to these gradients of paracrine factors. The amount and type of paracrine factors present cause different transcription factors to be activated in the nuclei of these cells, depending on their position in the neural tube. (E) Chick neural tube, showing areas of Sonic hedgehog (green) and Dorsalin expression (blue). Motor neurons induced by a particular concentration of Sonic hedgehog are stained orange/yellow. (Photograph courtesy of T. M. Jessell.)

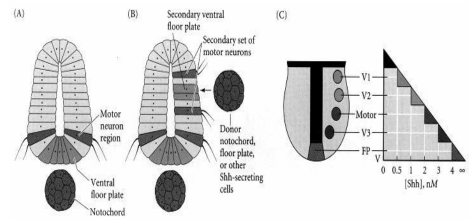

Figure 12.14

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Cascade of inductions initiated by the notochord in the ventral neural tube. (A) Two cell types in the newly formed neural tube. Those closest to the notochord become the ventral floor plate neurons; motor neurons emerge on the ventrolateral sides. (B) If a second notochord, floor plate, or any other Sonic hedgehog-secreting cell is placed adjacent to the neural tube, it induces a second set of ventral floor plate neurons, as well as two other sets of motor neurons. (C) Relationship between Sonic hedgehog concentrations, the generation of particular neuronal types in vitro, and distance from notochord. (A, B after Placzek et al. 1990; C after Briscoe et al. 1999.)

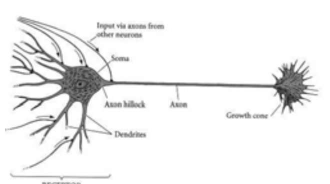

Figure 12.22

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Diagram of a motor neuron. Electrical impulses are received by the dendrites. and the stimulated neuron transmits impulses through the axon (which may be 2–3 feet long) to its target tissue. The axon is the cellular process through which the neuron sends its signals. The growth cone of the axon is both a locomotor and a sensory apparatus. It actively explores the environment and picks up directional cues as to where to go. Eventually it will form a synapse with its target tissue.

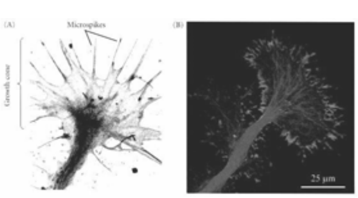

Figure 12.23

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Axon growth cones. (A) Actin microspikes in an axon growth cones, seen by transmission electron microscopy. (B) Growth cone of the hawkmoth *Manduca sexta* during axon extension and pathfinding. The actin in the filopodia is stained green with fluorescent phalloidin, while the microtubules are stained red with a fluorescent antibody to tubulin. (A from Letourneau 1979; B courtesy of R. B. Levin and R. Luedemanan.)

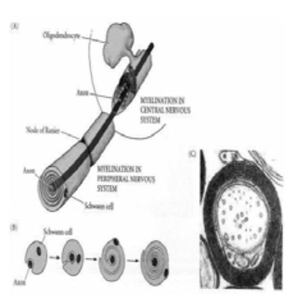

Figure 12.24

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Myelination in the central and peripheral nervous systems. (A) In the peripheral nervous system, Schwann cells wrap themselves around the axon; in the central nervous system, myelination is accomplished by the processes of oligodendrocytes. (B) The mechanism of this wrapping entails the production of an enormous membrane complex. (C) Micrograph of an axon enveloped by the myelin membrane of a Schwann cell. (Photograph courtesy of C. S. Raine.)

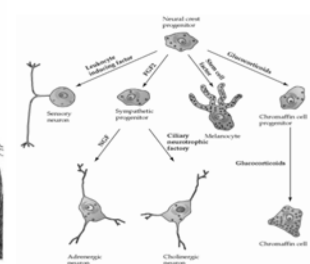


Figure 22.12. Cell signaling during the migration of neural crest cells. The establishment of each precursor type relies on signals provided by one of several specific peptide hormones. The availability of each signal depends on the migratory pathway.

Resumen

- 1 The neural tube forms from the shaping and folding of the neural plate. In primary neurulation, the surface ectoderm folds into a tube that separates from the surface. In secondary neurulation, the ectoderm forms a cord and then forms a cavity within it.
- 2 Primary neurulation is regulated by both intrinsic and extrinsic forces. Intrinsic wedging occurs within cells of the hinge regions to bend the neural plate. Extrinsic forces include the migration of the surface ectoderm towards the center of the embryo.
- 3 Neural tube closure is also a mixture of extrinsic and intrinsic forces. In humans, if the neural tube fails to close various diseases can result.
- 4 The neural crest cells arise at the lateral borders of the neural tube and surface ectoderm. They become located between the neural tube and surface ectoderm, and they migrate away from this region to become peripheral neural, glial, and pigment cells.
- 5 There is a gradient of maturity in many embryos, especially those of amniotes. The anterior develops earlier than the posterior.
- 6 The dorsal-ventral patterning of the neural tube is accomplished by proteins of the TGF-β family secreted from the surface ectoderm and roof of the neural tube, and from Sonic hedgehog protein secreted by the notochord and floor plate cells. Both types of protein appear to work through gradients.
- 7 The brain forms three primary vesicles: prosencephalon (forebrain), mesencephalon (midbrain), and rhombencephalon (hindbrain). The prosencephalon and rhombencephalon will become subdivided.
- 8 The brain expands through fluid secretion putting positive pressure on the vesicles.

9 The neurons of the brain are organized into cortices (layers) and nuclei (clusters).

10 New neurons are formed by mitosis in the neural tube. The neural precursors can migrate away from the neural tube and form a new layer. Neurons forming later have to migrate through the existing layers. This forms the cortical layers. The germinal zone at the lumen of the neural tube is called the ventricular zone. The new layer is called the mantle zone (gray matter).

11 In the cerebellum, a second germinal zone—the external granule layer—is formed. Other neurons migrate out of the ventricular zone on the processes of glial cells.

- 12 The cerebral cortex in humans has six layers, and the mantle zone is called the neocortex. Cell fates are often fixed as they undergo their last division. Neurons derived from the same stem cell may end up in different functional regions of the brain.
- 13 Neural stem cells have been observed in the adult human brain. We now believe humans can continue making neurons throughout life, although at nowhere near the fetal rate.
- 14 Dendrites receive signals from other neurons, while axons transmit them. The place where the signaling takes place (through the release of neurotransmitters) is called a synapse.
- 15 Axons grow from the nerve cell body, or soma. They are led by the growth cone.
- 16 The chordate and arthropod systems, though structurally very different, appear to be specified through the same set of genetic instructions.

Genética del desarrollo

Modelo : Droshophila Melanogaster

- Embriogénesis: 1 día
- 3 estados larvales en 4 días
- metamorfosis en 5 dias
- 9 días de vida como adulto
- total: alrededor de 19 días

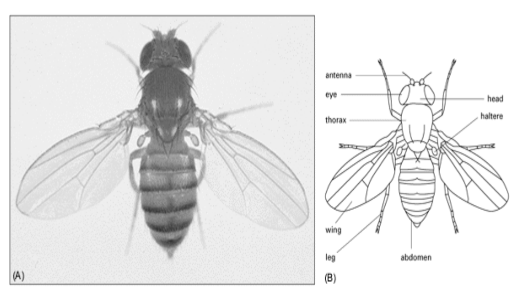
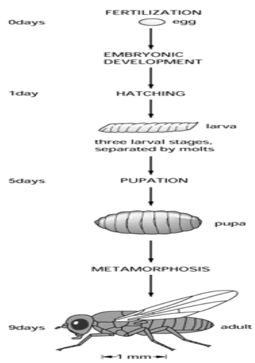
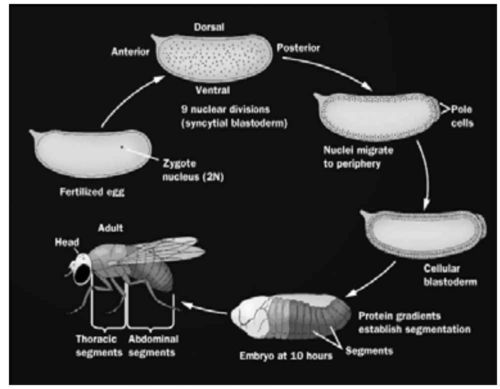


Figure 21-47. *Drosophila melanogaster*. Dorsal view of a normal adult fly. (A) Photograph. (B) Labeled drawing. (Photograph courtesy of E.B. Lewis.)



Synopsis of *Drosophila* development from egg to adult fly.



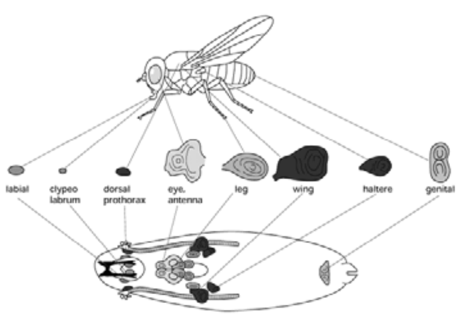
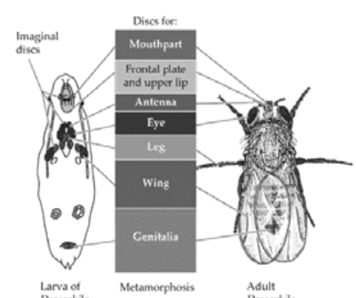


Figure 21-71. The imaginal discs in the *Drosophila* larva and the adult structures they give rise to. (After J.W. Fristrom et al., in Problems in Biology: RNA in Development [E.W. Hanley, ed.], p. 382. Salt Lake City: University of Utah Press, 1969.)



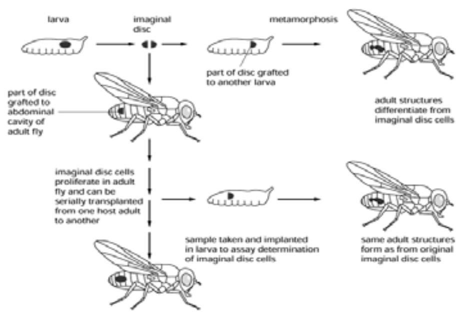


Figure 21-72. Experiments to test the state of determination of imaginal disc cells. The method of assay is to implant the cells in a larva that is about to undergo metamorphosis; the cells then differentiate to form recognizable adult structures, which lie, however, inside the body of the host fly after metamorphosis and are not integrated with it. The disc cells can either be assayed immediately or be implanted in the abdomen of adult flies, which serve as a natural culture chamber. Hormonal conditions in the adult allow the imaginal disc cells that have thus bypassed metamorphosis to continue to proliferate for an indefinite period, without differentiating, before the assay for cell determination is done. In both cases the cells generally differentiate to form the structures appropriate to the disc from which they derived originally.

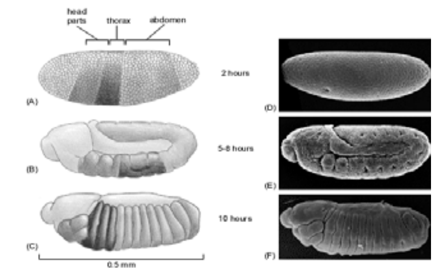


Figure 21-49. The origins of the *Drosophila* body segments during embryonic development. The embryos are seen in side view in drawings (A-C) and corresponding scanning electron micrographs (D-F). (A and D) At 2 hours the embryo is at the *syncytial blastoderm* stage (see Figure 21-51) and no segmentation is visible, although a fate map can be drawn showing the future segmented regions (*color* in A). (B and E) At 5-8 hours the embryo is at the *extended germ band*stage: gastrulation has occurred, segmentation has begun to be visible, and the segmented axis of the body has lengthened, curving back on itself at the tail end so as to fit into the egg shell. (C and F) At 10 hours the body axis has contracted and become straight again, and all the segments are clearly defined. The head structures, visible externally at this stage, will subsequently become tucked into the interior of the larva, to emerge again only when the larva goes through pupation to become an adult. (D and E, courtesy of Rudi Turner and Anthony Mahowald; F, courtesy of Jane Petschek.)

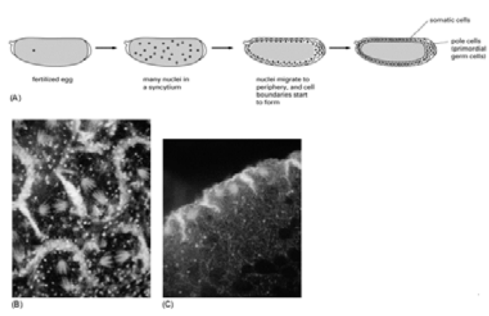


Figure 21-51. Development of the *Drosophila* egg from fertilization to the cellular blastoderm stage. (A) Schematic drawings. (B) Surface view and (C) optical section photographs of blastoderm nuclei undergoing mitosis at the transition from the syncytial to the cellular blastoderm stage. Actin is stained *green,* tubulin *orange.* (A, after H.A. Schneiderman, in Insect Development [P.A. Lawrence, ed.], pp. 3-34. Oxford, UK: Blackwell, 1976; B and C, courtesy of W. Theurkauf.)

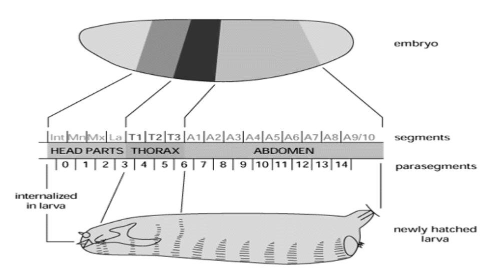


Figure 21-50. The segments of the *Drosophila* larva and their correspondence with regions of the blastoderm. Note that the ends of the blastoderm correspond to nonsegmental structures that form largely internal parts of the larva, as do the segmental rudiments of the adult head parts. Segmentation in *Drosophila* can be described in terms of either segments or parasegments: the relationship is shown in the middle part of the figure. Paraseg-ments often correspond more simply to patterns of gene expression. The exact number of abdominal segments is debatable: eight are clearly defined, and a ninth is probably present

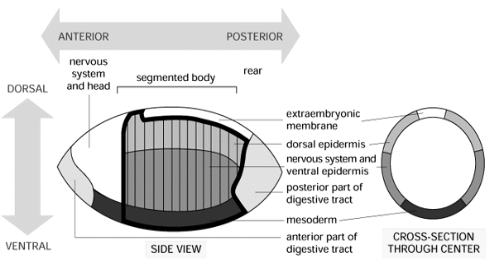


Figure 21-52. Fate map of a *Drosophila* embryo at the cellular blastoderm stage. The embryo is shown in side view and in cross-section, displaying the relationship between the dorsoventral subdivision into future major tissue types and the anteroposterior pattern of future segments. A heavy line encloses the region that will form segmental structures. During gastrulation the cells along the ventral midline invaginate to form mesoderm, while the cells fated to form the gut invaginate near each end of the embryo. Thus, with respect to their role in gut formation, the opposite ends of the embryo, although far apart in space, are close in function and in final fate. (After V. Hartenstein, G.M. Technau, and J.A. Campos-Ortega, *Wilhelm Roux' Arch. Dev. Biol.*194:213-216, 1985.)

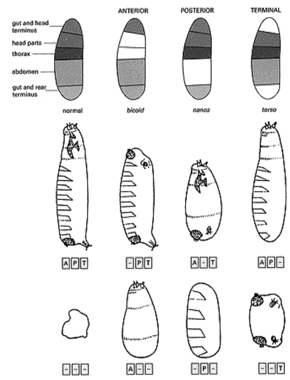


Figure 21-53. The domains of the anterior, posterior, and terminal systems of egg-polarity genes. The upper diagrams show the fates of the different regions of the egg/early embryo and indicate in (*white*) the parts that fail to develop if the anterior, posterior, or terminal system is defective. The middle row shows schematically the appearance of a normal larva and of mutant larvae that are defective in a gene of the anterior system (for example, *bicoid*), of the posterior system (for example, *nanos*), or of the terminal system (for example, *torso*). The bottom row of drawings shows the appearances of larvae in which none or only one of the three gene systems is functional. The lettering beneath each larva specifies which systems are intact (A P T for a normal larva, -PT for a larva where the anterior system is defective but the posterior and terminal systems are intact, and so on). Inactivation of a particular gene system causes loss of the corresponding set of body structures; the body parts that form correspond to the gene systems that remain functional. Note that larvae with a defect in the anterior system can still form terminal structures at their anterior end, but these are of the type normally found at the rear end of the body rather than the front of the head. (Slightly modified from D. St. Johnston and C. Nüsslein-Volhard, *Cell* 68:201-219, 1992.© Cell Press.)

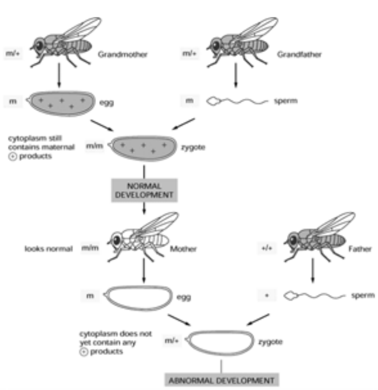


Figure 21-54. Inheritance of a recessive maternal-effect mutation. The pattern of inheritance is traced, starting with heterozygous (m/+) grandparents, for a mutation (m) that is recessive to the normal gene (+). The genotype of each animal or cell is shown to the left of it. *Red* color denotes presence of the normal (+) gene product. The gene product acts only at the beginning of development, and the appearance of the mature animal reflects the set of maternally specified components present in the egg. Note that the sperm makes no significant contribution of these gene products to the egg. The pattern of inheritance of a dominant maternal-effect mutation is different but can be worked out in a similar way.

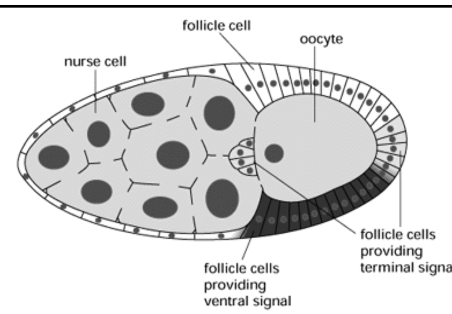


Figure 21-55. A *Drosophila* oocyte in its follicle. The oocyte is derived from a germ cell that divides four times to give a family of 16 cells that remain in communication with one another via cytoplasmic bridges. One member of the family group becomes the oocyte, while the others become nurse cells, which make many of the components required by the oocyte and pass them into it via the cytoplasmic bridges. The follicle cells that partially surround the oocyte have a separate ancestry; they are the sources of terminal and ventral egg-polarizing signals.

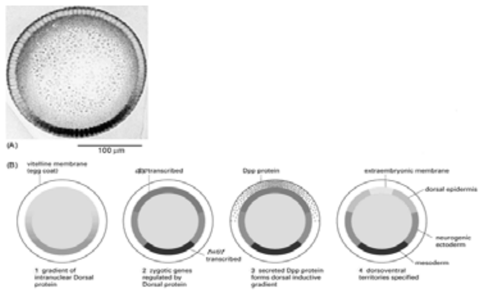
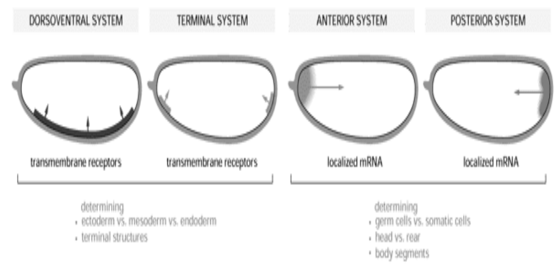


Figure 21-56. The gradient of the Dorsal protein and its interpretation. (A) The concentration gradient of Dorsal protein in the nuclei of the blastoderm, as revealed by an antibody. (B) The interpretation of the Dorsal gradient by genes that demarcate the different dorsoventral territories; for simplicity, only two representative genes are shown. Subsequent processes will further subdivide these territories. The *decapentaplegic (dpp)* gene in particular codes for a secreted factor that will act as a local morphogen to control the detailed patterning of the ectoderm. (A, from S. Roth, D. Stein, and C. Nüsslein-Volhard, *Cell* 59:1189-1202, 1989. © Cell Press.)



The organization of the four egg-polarity gradient systems.

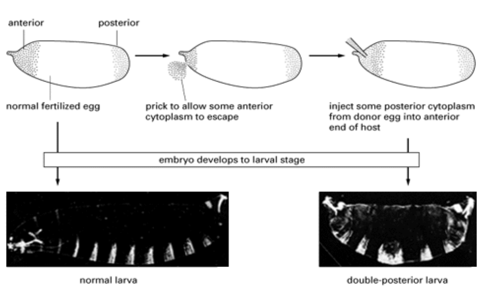


Figure 21-58. Localized determinants at the ends of the *Drosophila* egg control its anteroposterior polarity. A little anterior cytoplasm is allowed to leak out of the anterior end of the egg and is replaced by an injection of posterior cytoplasm. The resulting double-posterior larva (*photograph on right*) is compared with a normal control (*photograph on left*); the substitution of cytoplasm at one end of the egg has had a long-range effect, converting all the more anterior segments into a mirror-image duplicate of the last three abdominal segments. The larvae are shown in dark-field illumination. (From H.G. Frohnhöfer, R. Lehmann, and C. Nüsslein-Volhard, *J. Embryol. Exp. Morphol.* 97[Suppl]:169-179, 1986, by permission of the Company of Biologists Ltd.)

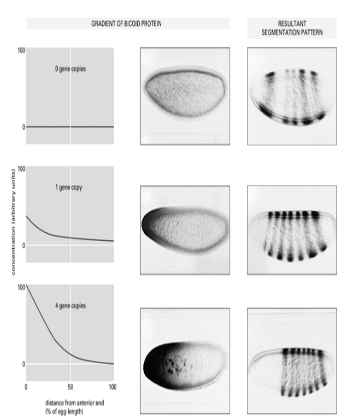


Figure 21-59. The gradient of Bicoid protein in the *Drosophila* egg and its effects on the pattern of segments. The gradient is revealed by staining with an antibody against the Bicoid protein; the segment pattern is revealed by an antibody against the product of a pair-rule gene, *even-skipped* (discussed later). Three embryos are compared, containing zero, one, and four copies, respectively, of the normal *bicoid* gene. With zero dosage of *bicoid*, segments with an anterior character do not form; with increasing gene dosage they form progressively farther from the anterior end of the egg, as expected if their position is determined by the local concentration of the Bicoid protein. Measurements of this concentration, as indicated by the intensity of staining, are shown in the graphs. Despite the considerable differences of position and spacing of the segment rudiments in the embryos with one and four doses of the gene, both embryos will develop into normally proportioned larvae and adults. A mechanism that may be responsible for this regulation is discussed on page 1064. (Slightly adapted from W. Driever and C. Nüsslein-Volhard, *Cell* 54:83-104, 1988. © Cell Press.)

Genes homeóticos

- Regulan la formación de estructuras específicas durante el desarrollo
- Se descubrieron en Drosophila melanogaster
- Son responsables de la determinación del eje antero-posterior en drosophila, diferenciación de neuronas en el gusano (Caenorhabditis elegans

Genes homeóticos

- Codifican para unas proteínas que poseen un **homeodominio** codificado por un **homeobox**
- **Homeobox:** (1983)Fragmento de DNA de 180 pares de bases, altamente conservado.
- No todos los genes con homeobox son genes homeóticos
- **Mutación homeótica**:Provoca substitución de estructuras que se encuentran en distintos segmentos corporales, Ejemplo Gen antennapedia

Figure 21-67. A homeotic mutation. The fly shown here is an *Antenna-pedia* mutant. Its antennae are converted into leg structures by a mutation in the *Antennapedia* gene that causes it to be expressed in the head. Compare with the normal fly shown in Figure 21-47. (Courtesy of Matthew Scott.)

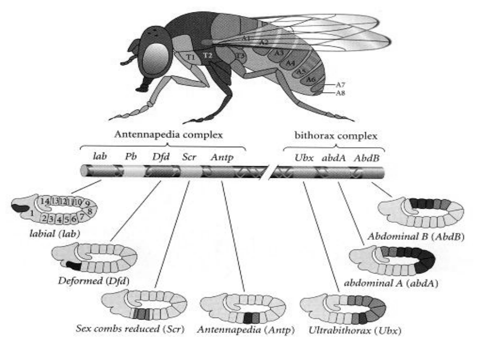


Figure 9.27. Homeotic gene expression in *Drosophila.* In the center are the genes of the Antennapedia and bithorax complexes and their functional domains. Below and above the gene map are the regions of homeotic gene expression (both mRNA and protein) in the blastoderm of the *Drosophila* embryo and the regions that form in the adult fly. Darker shaded areas are those segments or parasegments with the most product.

Category		Category	
Gap genes	***Krüppel (Kr)***	Pair-rule genes Secondary	***fushi tarazu (ftz)***
	knirps (kni)		***odd-paired (opa)***
	hunchback (hb)		***odd-skipped (slp)***
	giant (gt)		***sloppy-paired (slp)***
	tailless (tll)		***paired (prd)***
	huckendein (hkb)		
	buttonhead (btd)	Segment	***engrailed (en)***
	empty spiracles (ems)	polarity genes	***wingless (wg)***
	orthodenticle (otd)		***cubitus interruptus^D(ci^D)***
			hedgehog (hh)
Pair-rule genes Primary	***hairy (h)***		***fused (fu)***
	even-skipped (eve)		***armadillo (arm)***
	runt (run)		***patched (ptc)***
			gooseberry (gsb)
			pangolin (pan)

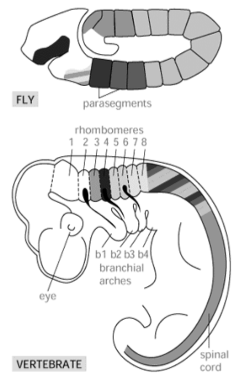


Figure 21-82. Correspondences between insect and vertebrate body regions as defined by HOM/Hox gene expression. A *Drosophila* embryo is shown at the extended germ band stage, with its parasegments colored according to the HOM genes that they express. The color code is as in Figure 21-80, and the same color code is used for the pattern of HoxB gene expression in the neural tube of a vertebrate embryo. For simplicity, the expression in other tissues of the vertebrate is not shown. Both in the fly and in the vertebrate, in regions where the expression domains of two or more HOM/Hox genes overlap, the coloring corresponds to the most "posterior" of the genes expressed. Where several genes have the same boundary to their expression domain, their common territory is shown striped. Note that just as the expression domains in the fly are related to parasegments, so the expression domains in the vertebrate are related to the rhombomeres (segments in the hindbrain). Each pair of rhombomeres is associated with a branchial arch (a modified gill rudiment), to which it sends innervation. The pattern of Hox gene expression in the branchial arches (not shown) matches that in the associated rhombomeres.