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Avian development

THE avian embryo has a long and distinguished history as a subject of embryological study. The ancient Egyptians appear to have been the first to investigate its development in a systematic way; they incubated hens' eggs for varying periods of time and opened them to examine the state of development of the embryo. It was also a study of avian embryos that led William Harvey, in the 17th century, to the discovery of the circulation of the blood, and observations of the beating heart of the chick embryo that occupied René Descartes in part of his *Discours de la Méthode*. Notwithstanding this, the avian embryo is still one of the organisms of choice for modern developmental biology because it is easily obtained, large and relatively translucent, allows delicate microsurgical manipulations to be performed easily, and because its development is relatively well understood.

Birds are amniotes, like mammals, whose development they closely resemble (*see* MAMMALIAN DEVELOPMENT). The main differences are in the earliest stages; the avian embryo does not have a placenta and is a self-contained developing system.

To the modern developmental biologist, the avian embryo offers a very accessible system in which molecular studies can be combined with 'classical' embryology. Excellent staging systems are also available for the chick embryo. Transplantation, cell labelling, immunocytochemistry, and chemical treatments can now be combined with *in situ* HYBRIDIZATION and NORTHERN BLOTTING to examine changes in the patterns of gene expression resulting from experimental manipulations with well-studied effects. Moreover, with the advent of techniques for producing TRANSGENIC birds, which have recently become available, the developmental effects of targeted mutations can be studied in cellular as well as molecular detail.

The egg

Most of the material in the new laid egg (Fig. A52) [1,2] is nutrients, laid down by the mother to support the embryo. The embryo itself lies initially on the surface of the yolk, just under the vitelline membrane. The egg is designed to conserve water, to allow gaseous exchange and to prevent microorganisms from coming into contact with the embryo, as well as to provide nutrition and protection to the embryo.

It also provides a complex environment for the embryo to develop. For example, the pH of the yolk is slightly acid, while that of the albumen is quite alkaline. During early stages of development, the edges of the single-cell-thick embryo attach to the inner (yolk) face of the vitelline membrane, on which it expands, and it is thus poised in a pH gradient that may amount to as much as 3 pH units across a single cell.

Chick and quail embryos hatch 19–21 days after laying if incubated at 38°C; quail embryos develop slightly faster (19–20 days) than chicks (20–21 days).

Development *in utero*

After fertilization, which occurs internally in the mother, a hen's egg spends about 5 hours in the oviduct, and then moves to the uterus, where CLEAVAGE begins. This happens about 5.5 h after laying of the previous egg. The cleaving embryo remains in the uterus some 20 h before it is laid.

Cell division (cleavage) of the fertilized egg occurs in a planar way, with the daughter cells staying in the plane between the vitelline membrane and the yolk. Unlike mammalian embryos, which have holoblastic cleavage, cleavage in avian embryos is meroblastic. This means that the membranes separating new

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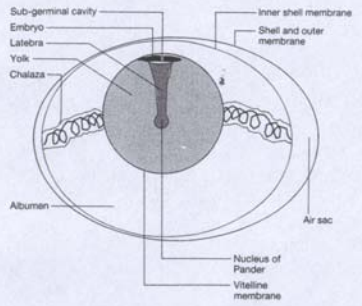

Fig. A52 Diagram of the principal components of a fertile hen's egg. The yolk is mainly PHOSPHOLIPIDS and is the main source of nutrients for the embryo. It is enveloped by a translucent, noncellular vitelline membrane and surrounded by albumen (egg white). The whole is contained within a calcareous shell, from which it is separated by two egg membranes. At the blunt end of the egg, between the two membranes, is an air sac. The embryo lies on the surface of the yolk, just under the vitelline membrane. The viscous albumen surrounding the vitelline membrane is connected with the inner membrane by two GLYCOPROTEIN threads called the chalazae, which allow the yolk to rotate so that the embryo always faces the top of the egg. In addition to nutritive components and GLYCOSAMINOGLYCANS to increase its viscosity, the albumen contains the enzyme LYSOZYME, a bacteriostatic agent. Egg albumen is therefore often used in embryo cultures to prevent the growth of microorganisms as well as to provide a source of nutrients.

cells arise as open cleavage planes, stretching into the yolk. As a result, the cells forming in the centre of the cleaving blastodisc are smaller than those around its periphery, and those around the edge contain more yolk. Because of this quirk, the MORULA and BLASTULA stages, as defined in lower vertebrates, are difficult to distinguish in avian embryos.

As the egg descends along the mother's reproductive system, it rotates while the albumen and shell components are secreted around it. During this rotation, the plane of the cleaving blastodisc remains at an angle of about 45° to the radius of the earth. This angle and the rotation are believed to be important in determining the polarity of the embryo. The edge of the blastodisc facing downwards will form the caudal (posterior) part of the embryo, under the influence of gravity.

It is possible to culture avian embryos out of the egg from late uterine stages until the formation of axial structures (head primordium, beating heart, somites, neural tube, notochord, etc.). Although it is still difficult to access the very earliest stages of development (cleavage) for experimental manipulation, several groups have recently developed techniques of 'total embryo culture' which allow access to the one-cell stage and incubation of the egg to the hatching-chick stage. Using this technique, it has been possible to inject a DNA construct into the single cell embryo and to study its expression at much later stages of development.

Formation of the embryonic axis and origin of the mesoderm

At the time of egg laying, the chick blastoderm consists of a disc of cells, some 2 mm in diameter, comprising an inner translucent area pellucida and an outer area opaca (Fig. A53). The latter region only contributes to extraembryonic structures. The first

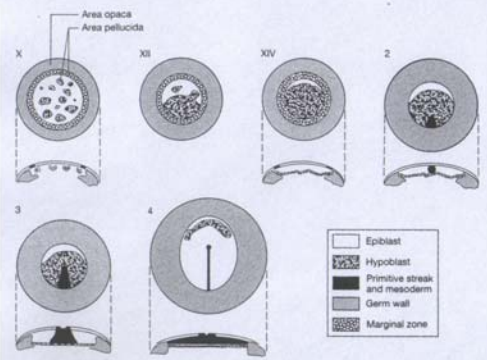

Fig. A53 Diagram illustrating the early stages of development of the chick embryo. Two staging systems are used [6]: Eyal-Giladi and Kochav's (in Roman numerals) for pre-primitive streak stages, and Hamburger and Hamilton's (in Arabic numerals) starting at stage 2 with the appearance of the primitive streak. Each diagram shows the embryo viewed from its dorsal (epiblast) side, with the posterior end of the blastodisc facing downwards. Some transverse sections through the blastodiscs are also shown.

cell layer to be present as such is the epiblast, which is continuous over both areae opaca and pellucida. It is an epithelium, one cell thick, which soon becomes pseudostratified and columnar, the apices of the cells facing the albumen. From this arises a second layer of cells, the hypoblast. At this time, the hypoblast is no more than several unconnected islands of 5–20 cells. However, by ~6 h of incubation, more cells are added to it and it becomes a loose but continuous epithelium. The source of these hypoblast cells is the deep (ENDODERMAL) portion of a crescent-shaped region, the marginal zone (Fig. A53), which separates areae pellucida and opaca at the future posterior (caudal) end of the embryo.

The embryo now consists of two layers: the epiblast proper, from which will arise all the embryonic tissues, and the hypoblast which will give rise only to extraembryonic tissues (mainly the yolk sac stalk) although it may also contain some PRIMORDIAL GERM CELLS. As the hypoblast continues to spread as a layer from posterior to anterior parts of the blastodisc, cells appear between the previous two germ layers. These are the first cells of the MESODERM [3]. As more of these accumulate, they coalesce in the first axial structure of the embryo, the **primitive streak**, which makes its appearance at the posterior margin of the area pellucida at about 10 h of incubation. Later, more mesodermal cells are recruited into the primitive streak by migration from the epiblast, as the streak elongates along the anteroposterior axis of the embryo.

All the mesoderm eventually migrates out of the streak to give rise to four mesodermal components: the lateral plates, intermediate mesoderm, paraxial mesoderm and the axial notochord. The lateral plates will give rise to the circulatory system, the lining of the coelom, the limb skeleton, and most of the remaining mesodermal organs. The intermediate mesoderm is a cord separating the lateral plate from the paraxial mesoderm, which gives rise to the transitory embryonic kidneys (pronephros and mesonephros). The paraxial mesoderm becomes subdivided into somites (see below), which give rise to the skeletal (voluntary) musculature, to the dermis, and to the skeleton of the trunk. The notochord forms a rod in the midline of the embryo and contributes to the vertebral bodies and intervertebral discs.

Before formation of the lateral plate, the mesoderm is packed densely at the primitive streak; as the lateral plate forms, it migrates massively, away from the axis of the streak. The left and right halves of the lateral plate later become separated from each other by the regression (shortening) of the primitive streak that occurs after the end of GASTRULATION. The notochord is laid down as a rod of mesoderm by the cranial tip of the primitive streak (Hensen's node), and elongates as the primitive streak regresses.

Some primitive streak cells insert into the hypoblast, displacing it towards the edges of the area pellucida (Fig. A52). These primitive streak derived, endodermal cells form the definitive endoderm, which will give rise to the lining of the gut. The elongation of the primitive streak and the expansion of the blastodisc, together with further recruitment of cells derived from the posterior marginal zone (this contribution now forming the junctional endoblast, which is also extraembryonic; Fig. A53), confine the original hypoblast to a crescent-shaped region underlying the anterior portion of the area pellucida; this region is known as the germinal crescent because it contains, transiently the primordial germ cells, which will later migrate into the gonads.

Regulation and induction

Higher vertebrate embryos are capable of extensive REGULATION. If a pre-streak chick blastoderm is cut into several portions, most of the portions are able to produce a complete, albeit somewhat smaller, embryo. Furthermore, if pieces derived from several embryos are combined, a fairly normal embryo develops which receives contributions from all the donor fragments. These findings indicate that at this stage of development, groups of cells are not committed to a preordained programme of development. Development at this stage must, therefore, transcend the CELL-AUTONOMOUS interpretation of a genetic programme: cell interactions are important in determining the pattern of gene expression in individual cells.

There are, in theory, two possible interpretations for these phenomena: the first is that cells in the embryo are PLURIPOTENT, and become specified to their ultimate fates by cell interactions; when a fragment is separated from the embryo, cells in the fragment interact so that the correct proportions of different cell types are generated. The second interpretation of the phenomenon of regulation requires the embryo to consist of a fairly random mix of cells already specified to their ultimate fates, which later sort to their correct destinations. According to this second interpretation, isolation of a fragment of embryo leads to sorting of the cell types to newly defined sites, but the cells do not change fates. We do not yet know which of these two interpretations is correct, although the first is generally favoured.

The hypoblast layer appears to be involved in the specification of embryonic polarity. If it is rotated by 180° about its anteroposterior axis, the primitive streak now forms from the opposite (anterior) pole of the blastodisc. The nature of the interactions between hypoblast and presumptive primitive streak cells in the epiblast is not understood, although it has been suggested that the hypoblast induces the formation of mesoderm from the epiblast, as the vegetal pole cells induce mesoderm from the animal cap in amphibian embryos (*see* INDUCTION). However, it has not yet been possible to demonstrate mesoderm induction in isolated fragments of avian embryos, as has been done in amphibians.

Origin of the nervous system

The cells of Hensen's node have rather special properties. If a node is grafted into the lateral region of a host embryo, a second nervous system is formed (Fig. A54), just like a graft of the dorsal lip of the blastopore generates a second nervous system in amphibians (*see* AMPHIBIAN DEVELOPMENT: INDUCTION). This is neural induction. It can be demonstrated, using chick/quail chimaeras or other methods of cell marking, that the supernumerary nervous system is derived from cells of the host epiblast rather than of the grafted node. Some signal from Hensen's node can therefore change the fate of the overlying epiblast cells to make them become nervous system, rather than epidermis.

After neural induction, the epiblast that will become neuro-

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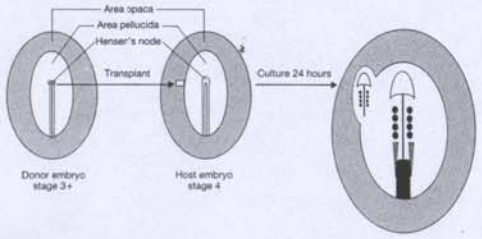

Fig. A54 When the tip of the primitive streak, known as Hensen's node, of a donor embryo is transplanted into another region of a host embryo, the transplant induces the formation of a secondary (ectopic) embryonic axis. The transplant itself differentiates into mesodermal cells (somites and notochord), while the nervous system comes from the epiblast of the host.

epithelium undergoes a series of dramatic changes. First, it becomes thickened. Then its edges elevate, forming the neural plate. This plate then rolls into a tube (Fig. A55). The whole process progresses roughly in an anterior-to-posterior direction so that the neural plate is still elevating in the tail region while it has already closed in cranial regions. The rims of the neural plate that meet during tube closure (the dorsal part of the neural tube) give rise to the neural crest, a special multipotent population of migratory cells that colonize many regions of the embryo and give rise to melanocytes, to the sensory component of the PERIPHERAL NERVOUS SYSTEM, to the autonomic ganglia (sympathetic and parasympathetic), to glial (Schwann) cells that accompany peripheral nerves, to the adrenal medulla, and to skeletal elements of the cranial vault and face. The motor nerves do not arise from the neural crest; instead, axons emerge from the ventral portion of the neural tube, from where they extend outwards to find their peripheral targets.

This stage of development is amenable to experimentation. The neural plate and neural tube can be extirpated, rotated, and transplanted, as can the notochord underlying it. Individual cells can be marked and their descendants followed, or they can be injected with antibodies or nucleic acids. Chick/quail chimaeras

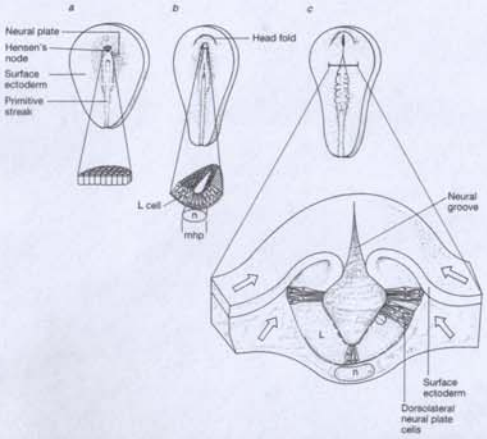

Fig. A55 Mechanism of formation of the neural tube in avian embryos. *a*, Stage 4; *b*, stage 6; *c*, between stages 6 and 8. Whole mounts of entire blastoderms and cross-sectional views are shown. The neural furrow begins to be generated (see *b*) as the neural plate becomes anchored to the notochord (n) and midline neural plate cells decrease in height and become wedge-shaped to form the median hinge point (mhp). Forces for these processes are thought to be intrinsic to the neural plate and to include microtubule-mediated cell elongation, cell division and cell rearrangement. Between stages 6 and 8 (*c*), bending of the neural plate is the predominant event. The dorsolateral neural plate becomes anchored to surface ectoderm, and dorsolateral neural plate cells increase in height and become wedge-shaped, resulting in neural plate furrowing, neural plate elevation around the mhp and neural fold convergence. Forces responsible are both intrinsic (cell wedging) and extrinsic (open arrows), the latter being provided by surrounding non-neuroepithelial tissues. Adapted from [5] with kind permission of Dr G.C. Schoenwolf.

can be constructed to study interactions between different groups of cells.

Segmentation

The segmental organization of vertebrate embryos is most obvious in the pattern of somites, from which derive the vertebrae and ribs of the axial skeleton, the dermis of the trunk, and all the voluntary musculature of the adult [4]. The metameric pattern of somites determines the segmental arrangement of other structures in the embryo, such as the peripheral nervous system.

In the chick embryo, some 55 pairs of somites form, each somite being, at first, an epithelial sphere that buds off the rostral (anterior) end of each of the paired segmental plates of paraxial mesoderm that appear about 1.5 days after the egg is laid. Each pair of somites takes about 1.5 h to form. Some 6–8 h after its initial appearance, each somite splits up into two further components (Fig. A56): the dermomyotome dorsally, which retains some epithelial characteristics and gives rise to the dermis of the trunk and to skeletal muscle, and the sclerotome ventromedially, which is a loose MESENCHYME that gives rise, along with the notochord, to the axial skeleton. Recent results suggest that the segmental pattern of somites is controlled at least in part by cell-autonomous properties depending on the cell division cycle.

Each sclerotome is subdivided into a rostral (anterior) and a caudal (posterior) half. Differences between the cells of the two halves determine the segmental organization of the peripheral nervous system: motor nerves and neural crest cells are restricted to the rostral half of each sclerotome and are unable to colonize the caudal half. There are numerous molecular differences between the two halves of the sclerotome, but it is not yet known which of these are directly responsible for the segmental pattern of components of the peripheral nervous system.

The subdivision of the sclerotome into rostral and caudal halves is maintained by mixing restrictions between the two kinds of cells. Rostral cells are able to mix with rostral cells, and caudal with caudal, but when rostral and caudal cells meet they generate a boundary that separates them. This is probably important in the morphogenesis of the vertebral column. Traditionally, it is thought that the rostral half of one sclerotome joins the caudal half of the preceding sclerotome to give rise to one vertebra, a model which accounts for the observation that the vertebrae are out of phase with the corresponding myotomes (axial muscle blocks). However, recent experimental work tracing the derivatives of individual somites has cast some doubt on this interpretation; it suggests that each somite gives rise to one vertebra, but that sclerotome cells may shift anteriorly by a half segment by migrating with the notochord.

Two portions of the CENTRAL NERVOUS SYSTEM are also organized in a segmental way (Fig. A57). The hindbrain (rhombencephalon) is subdivided into seven or eight segments (*see* VERTEBRATE NEURAL DEVELOPMENT) which display an alternating pattern of neuronal differentiation and other properties. These segments (rhombomeres), like the somites, are separated from each other by lineage restrictions that prevent cells from one rhombomere from crossing to the adjacent one. The diencephalon is similarly subdivided into four segments ('prosomeres' or 'diencephalic neuromeres'), again with an alternating pattern of neuronal differentiation and cell surface properties, and lineage restrictions maintaining the boundaries between adjacent prosomeres. However, the spinal cord does not appear to be truly segmented.

Limb development

The avian embryo has also been used extensively for studies on limb development. The limb buds begin to form at about 3 days

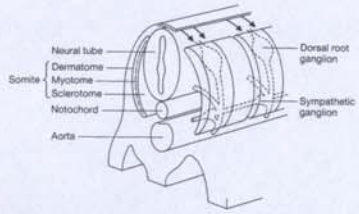

Fig. A56 Diagram illustrating the relationships between the developing nervous system in the trunk of avian embryos and the neighbouring mesodermal structures. All the components of the peripheral nervous system are confined to the anterior (rostral) halves of the somites. The thick arrows dorsally indicate the streams of migrating neural crest cells that will give rise to the dorsal root and sympathetic ganglia.

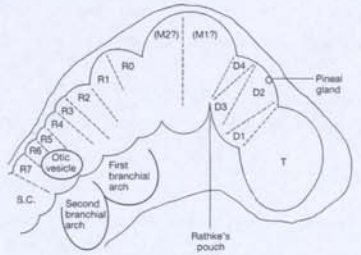

Fig. A57 Subdivisions of the central nervous system of the head of avian embryos. The diencephalon is subdivided into four neuromeres, D1–D4. The rhombencephalon (hindbrain) is subdivided into rhombomeres R1–R7, the first of which later subdivides into two further neuromeres R0 and R1. The midbrain may also be subdivided into two units (M1–M2) but the evidence for this is not yet strong. In the hindbrain, pairs of rhombomeres (R2–R3 and R4–R5) are aligned, respectively, with the first two branchial arches. The next pair of rhombomeres is aligned with the otic (ear) vesicle.

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after laying, when the ectoderm opposite somites 15–21 (wing bud) and 27–33 (leg bud) begins to elevate from the surface of the body, enclosing a mass of loosely packed lateral plate mesoderm. In time, the cells of this mesoderm will condense to form the primordia of the limb skeleton. The muscles and dermis arise from somite-derived cells which migrate into the limb buds.

Grafting experiments (*see* PATTERN FORMATION) have shown that the posterior margin of the chick limb bud contains special cells, able to respecify the pattern of the whole limb. This region has been called the zone of polarizing activity (ZPA). If such a region is grafted into the anterior margin of a host limb bud, a mirror-image pattern of bone and muscle elements is formed. It is believed that the ZPA produces a diffusible MORPHOGEN (thought to be related to RETINOIC ACID), the local concentration of which at different positions in the limb determines the type of bone and muscle elements that will develop at those positions.

The distal part of the developing limb bud is also special (*see* PATTERN FORMATION). It consists of a thickened ridge of surface ectoderm (the apical ectodermal ridge (AER)) which covers a region of special mesoderm, called the progress zone. The AER is required for continued growth and development of the limb, while the progress zone appears to be involved in controlling the proximodistal sequence of skeletal elements.

Because the chick limb bud is very accessible to such transplantation experiments, it is an ideal system in which, in the near future, such operations might be combined with molecular techniques.

C.D. STERN

1 Burley, R.W. & Vadehra, D.V. (1989) *The Avian Egg: Chemistry and Biology* (John Wiley, New York).
2 Tullet, S.G. (1991) Avian incubation. In *Poultry Science Symposium No. 22* (Butterworth-Heinemann, London).
3 Stern, C.D. (1991) Mesoderm formation in the chick embryo, revisited. In *Gastrulation: Movements, Patterns and Molecules* (Keller, R.A. et al., Eds) 29–41 (Plenum, New York).
4 Keynes, R.J. & Stern, C.D. (1988) Mechanisms of vertebrate segmentation. *Development* **103**, 413–429.
5 Shoenwolf, G.C. & Smith, J.L. (1990) Mechanisms of neurulation: traditional viewpoint and recent advances. *Development* **109**, 243–270.
6 Stern, C.D. & Holland, P.W.H. (Eds) (1993) *Essential Developmental Biology: a Practical Approach.* (IRL Press, Oxford).

avian erythroblastosis virus (AEV) An acutely transforming RETROVIRUS.

avian leukosis virus (ALV) *See:* ONCOGENES: RETROVIRUSES.

avian sarcoma virus Rous' sarcoma virus. *See:* ONCOGENES: RETROVIRUSES.

avidin A tetrameric glycoprotein from egg white that binds to BIOTIN. *See:* BIOTINYLATION: IMMUNOELECTRON MICROSCOPY.

avidity The strength of the interaction of a multivalent ANTIBODY with a multideterminant ANTIGEN. The net avidity is a complex function of the AFFINITIES of the various determinants and of the valencies of both reactants involved. Thus, when multivalent polyclonal antibody reacts with polyvalent antigen the avidity is determined by the sum of all of the individual interactions taking place between individual antigen-binding sites and antigenic determinants. Taking an antibody with a given affinity for a certain antigen, the strength of binding will be higher for pentameric IgM than for divalent IgG antibodies.

avirulence genes *See:* PLANT PATHOLOGY.

avirulent Applied to strains or mutants of pathogens that cause no or only mild disease. *See:* PLANT PATHOLOGY.

avr A genetic locus in some plant pathogenic microorganisms that determines race/cultivar-specific expression of disease symptoms in conjunction with the functionally complementary resistance gene in the host. *See:* PLANT PATHOLOGY.

axial mesoderm Portion of the MESODERM underlying the midline of the embryo. In the strict sense, the axial mesoderm comprises only the HEAD PROCESS under the brain and the NOTOCHORD posterior to the ear vesicle. Some authors also include the PARAXIAL MESODERM as an axial component. In amphibian embryos the term is only rarely used. Instead, the term dorsal mesoderm is used to describe the axial components; this is because after folding of the embryonic body, the axial mesoderm comes to lie most dorsally in the embryo. The axial mesoderm arises from HENSEN'S NODE in higher vertebrates and from the dorsal lip of the blastopore in amphibians and is the tissue capable of eliciting NEURAL INDUCTION. *See also:* AMPHIBIAN DEVELOPMENT.

axis determination The major model systems for the analysis of the molecular basis of the determination of the anterior–posterior and dorsal–ventral axes in early embryogenesis have been *Xenopus laevis* (*see* AMPHIBIAN DEVELOPMENT) and *Drosophila* (*see* DROSOPHILA DEVELOPMENT).

axon Elongated cellular process that carries electrical impulses away from the cell body of a NEURON. The axon is often much divided, each branch making a synapse on the dendrites or other parts of another neuron. *See:* SYNAPTIC TRANSMISSION.

axon hillock *See:* NEURON.

axon terminal *See:* NEURON: SYNAPTIC TRANSMISSION.

axonal transport (axoplasmic transport) Transport of material along an axon from the cell body of a neuron towards the terminal or synapse (anterograde transport) or in the reverse direction (retrograde transport). Substances such as neurotransmitters carried within lipid vesicles are transported bidirectionally at fast speeds (0.1–5 $\mu m\ s^{-1}$); CYTOSKELETAL components move *en bloc* only in the anterograde direction and more slowly (0.001–0.01 $\mu m\ s^{-1}$). Fast transport is attributed to KINESIN or DYNEIN attaching to the vesicles and moving them in one or the other direction along microtubule tracks; slow axonal transport consists of a steady movement of cytoskeletal polymers from cell body to

axon. Details of the mechanism are not understood. *See also:* MICROTUBULE-ASSOCIATED MOTORS.

Schnapp, B.J. & Reese, T.S. (1986) *Trends Neurosci.* **9**, 155–162.
Reinsch, S.S. et al. (1991) *J. Cell Biol.* **115**, 365–379.

axoneme Central core of eukaryotic cilium or flagellum. *See:* MICROTUBULES.

axoplasmic flow *See:* AXONAL TRANSPORT.

5-azacytidine Cytidine analogue (Fig. A58) which when incorporated into DNA cannot be methylated and leads to demethylated sites in DNA. Under certain circumstances it can induce changes in the state of cellular differentiation and activate genes on the silent X-chromosome, supporting a role for methylation in gene regulation. *See:* DNA METHYLATION: NUCLEOSIDES AND NUCLEOTIDES: X-CHROMOSOME INACTIVATION.

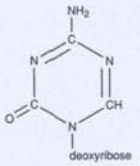

Fig. A58 5-Azacytidine.

Azorhizobium Genus of RHIZOBIA which can carry out NITROGEN FIXATION in association with the roots of leguminous plants. *See also:* NODULATION.

AZT The deoxyribonucleoside analogue 3′-azido, 3′-deoxythymidine, also known as zidovudine. It inhibits the activity of the retroviral enzyme REVERSE TRANSCRIPTASE and is used in the chemotherapy of HIV virus infection (*see* IMMUNODEFICIENCY VIRUSES). It appears to improve the quality of life in patients in which the symptoms of AIDS have appeared, and delays death, but it is now thought not to delay the time after infection at which symptoms appear. *See also:* DIDEOXYRIBONUCLEOSIDES.

azurin *See:* MOLECULAR EVOLUTION: SEQUENCES AND STRUCTURES.