GLOSSARY

The terms are listed by their key nouns, e.g., Rhombic lip under Lip, rhombic.

Amygdala: See Nuclei, amygdaloid.

Apoptosis: A process of controlled cell elimination, e.g., many if not most postmitotic, postmigratory, well-differentiated neurons are eliminated during the formation of synapses. Defects in apoptosis may underlie various neurodegenerative disorders.

Archipallium: The cerebral cortex of the hippocampal formation. It is separated from the neopallium by the peri-archicortex (presubiculum), and it becomes distinguishable at stage 21 (Fig. 21-17).

Area dentata: The zone between the hippocampus senso stricto and the area epithelialis. It develops into the dentate gyrus and, during the embryonic period, is characterized by having only a ventricular layer (Fig. 21-4).

Area epithelialis: The field between the area dentata and the lamina terminalis (Figs. 21-4 and 21-17). It consists of one to two, and later more, rows of cells, which, as development proceeds, contain dark inclusions. In the fetal period, a part of it becomes the lamina affixa.

Area hippocampi: This is characterized at first by an early appearing telencephalic marginal layer, and this is the only part of the telencephalon that possesses a marginal layer (Fig. 16-11). A ventricular thickening forms in the dorsomedial wall of the cerebral hemisphere (Fig. 15-4). It is C-shaped already at stage 18.

Area reuniens: A term used by His for the junctional region of the prosencephalon, the hypophysial primordium, the tip of the notochord, the roof of the foregut, and the oropharyngeal membrane.

Areae membranaceae: Two very thin areas of endothelioid cells in the roof of the fourth ventricle (Fig. 17-5). The epithelium is thinnest at 6 weeks, whereas at the end of the embryonic period, the thin cells become replaced by cuboidal cells. The area membranacea rostralis is adjacent to the cerebellar primordium. The area membranacea caudalis corresponds to the central bulge of Brocklehurst (1969) and to the saccular ventricular diverticulum of Wilson (1937), and is believed to be the site of the future median aperture of the fourth ventricle.

Bundles, forebrain: See Fasciculi, prosencephalic.

Canal, neurenteric: A more or less vertical passage (perpendicular to the embryonic disc) that appears during stage 8 as a result of increasing breakdown of the floor of the notochordal canal (q.v.). Both canals commence in common, dorsally in the primitive pit, and the neurenteric canal may be regarded as the remains of the notochordal canal at the level of the primitive node. The neurenteric canal connects the amniotic cavity (at the primitive pit) with that of the umbilical vesicle (or so-called yolk sac) (Fig. 9-3E). The canal in stages 8 and 9 and its site in stages 10 to 12 are important landmarks in development and teratogenesis (Müller and O’Rahilly, 2004a).

Canal, notochordal: An oblique passage that appears in the notochordal process during stage 8 (Fig. 8-2).

Catecholamine cell groups (Tables 17-3 and 26-2): dopaminergic, noradrenergic, and adrenergic neurons (Zecevic and Verney, 1995). Monoamines have most probably also a trophic function (Verney et al., 2002).

Cells, Cajal-Retzius: Among the early-formed neurons (Fig. 17-19) as revealed by reeler-immunoreactivity (Zecevic et al., 1999). They are tangentially arranged bipolar neurons within the primordial plexiform layer. Those in the future molecular layer mature late in trimester 2 (Verney and Derer, 1995) and are most evident near the middle of prenatal life (Tsuru et al., 1996). Reelin produced by the Cajal-Retzius cells is responsible for the normal migration of the neurons from the ventricular layer to the periphery of the wall of the brain. Once the cortical plate develops, the Cajal-Retzius cells are external to (“above”) it. The

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fetal Cajal-Retzius cells are transformed embryonic C-R cells and have triangular, inverted pyramidal, or fusiform cells bodies from which two or more long horizontal dendrites emerge.

A distinction has been made between Cajal and Retzius cells (Meyer et al., 1999); the former lie closer to the pia, are smaller, and are frequently triangular or piriform, and they appear when the Retzius cells have already largely disappeared.

The thick horizontal fiber extends throughout the surface of the cerebral cortex for a considerable distance and establishes contacts with the apical dendrites of all pyramidal neurons, regardless of their location (layers 6, 5, 4, 3, 2) or different functional role.

The transfer of neuronal information from the Cajal-Retzius cells to all pyramidal neurons may be necessary for all of the latter to acquire and to maintain their functional activity (Marín-Padilla, 1988a). Here, as in other regions, the use of immunological neuronal markers would enable such cells to become identifiable at earlier stages, as is being found already in other species.

Cells, stem: See Stem cells, neural.

Cerebellum: This part of the hindbrain is derived mostly from the entire alar laminae of rhombomere 1 but partly from the isthmus rhombencephali. The sources of cellular production are mainly the rhombic lip of rhombomere 1 and the ventricular layer of the alar laminae (Fig. 18-18). The cerebellar primordium, distinguishable at stage 13 (Fig. 13-2), becomes the cerebellar plate (q.v.) at about stage 18 (Fig. 18-1), by which time cerebellar swellings (q.v.) have appeared. The cerebellar hemispheres develop early in the fetal period, and the vermis is formed from the medial portion of the hemispheres. See also Swellings, cerebellar.

Cerebrum: From Latin, meaning brain. In ancient usage the larger convoluted mass as distinct from the smaller (the cerebellum). At the time of His it included the mesencephalon (cf. cerebral peduncles), but became restricted to the prosencephalon, or to the telencephalon, or to the cerebral hemispheres. Hence the term has practically no scientific value, in contrast to the almost indispensable adjective (e.g., the middle cerebral artery).

Commissures of brain: In this book the term “commissure” is used as soon as fibers cross the median plane, although fibers growing medially are present long before they cross. Examples are the anterior and posterior commissures, and the corpus callosum. See also Decussation.

Cord, hypoglossal cell: A dense cellular prolongation formed by the dermatomyosomatic material of at least the rostralmost three occipital somites caudal to the rostral cardinal vein. The dermatomatic cells cannot be distinguished from the myotomatic cells, nor can possible contributions from neural crest and epipharyngeal material of the vagus nerve be excluded. The relocation of the cells in the tongue is achieved before the arrival of the hypoglossal nerve. (O’Rahilly and Müller, 1984b). The hypoglossal cord forms (at least some of) the muscles of the tongue. A reconstruction of the hypoglossal cell cord at stage 12 (Müller and O’Rahilly, 1987, Fig. 6B) is in agreement with experimental findings in the rat, in which, at a similar stage, neural crest and dermamyotomatic cells of the occipital somites migrate within and dorsal to pharyngeal arches 3 and 4.

Cord, neural: The neural tissue in the caudal eminence of embryos with a closed caudal neuropore. It becomes canalized secondarily. The development of spinal cord (at stages 12 to about 17–20) from this solid material is termed secondary neurulation (Fig. 12-13).

Cord, spinal: Embryologically, the part of the neural tube caudal to the last (the hypoglossal) rhombomere (Rh.D).

Corpus striatum (Fig. 19-6): The lentiform and caudate nuclei, which become connected by alternating striae of white and gray matter (hence the name), the putamen and the caudate nucleus are telencephalic and arise from the lateral ventricular eminence (experimental evidence exists in the rat), whereas the globus pallidus (externus and internus) is diencephalic and arises from the subthalamus.

Crest, neural: Cells that appear at the neurosomatic junction (i.e., between neural ectoderm and somatic ectoderm) and are probably almost exclusively derived from the neural ectoderm. Most of the crest cells of the brain leave the neural folds before closure of the neural tube (Figs. 10-5 to 7). They participate in the formation of the cranial ganglia (Fig. 11-2). The spinal ganglia appear as cellular condensations of neural crest only at stage 13 (Fig. 13-8B-C). The migration of neural crest cells depends on the extracellular matrix through which they travel. Migratory neural crest cells possess stem cell-like properties.

Decussation: An intersection, the two lines of the letter X, as in the optic chiasma. Further examples are the pyramidal decussation (Fig. 23-32), the decussation of the superior colliculi (e.g., of the tectobulbar fibers, Fig. 15-5), and that of the fibers of the trochlear nerves (Fig. 19-15). See also Commissures.

Dopaminergic centers: Early accumulations of dopaminergic cells that form the interpeduncular nucleus, the ventral tegmental area, the substantia nigra, and the amygdaloid complex (Fig. 17-13).
Ectoderm, neural (or neuroectoderm): The pseudostrati- 
ified epithelium derived from the embryonic ectoderm 
(which, in turn, comes from the epiblast) and that 
gives rise to the neural plate (Fig. 8-2) and to neural 
crest. The mitotic figures are found superficially, adja- 
cent to the amniotic cavity initially and, as the neural 
tube develops, beside the future ventricular cavity and 
central canal.

Eminence, caudal: the mesenchymal replacement of the 
primitive streak at stage 10 (Fig. 10-9), present until 
stages 14, 15 and providing caudal structures such as 
notochord, somites, neural cord, and hindgut (Fig. 12-15).

Eminences, ventricular (Table 19-1 and Fig. 15-2): two 
large intracerebral swellings characterized by an ex- 
ceptional persistence of their subventricular layer. 
The term ventricular eminences or elevations (G.J. 
Lammers) is preferred to the inaccurate designa- 
tions ganglionic eminence (Ganglienauge) or striatal 
ridges.

The medial ventricular eminence (Fig. 14-2) is a 
thickening of diencephalic origin. It expands rostrally, 
gives rise to most of the amygdaloid nuclei (exper- 
imental evidence exists in the rat), and in the fetal 
period contributes a part of the dorsal thalamus. (See 
Migration.)

The lateral ventricular eminence (Fig. 15-2), which 
appears after the medial, is a protuberance in the baso- 
lateral wall of the cerebral hemisphere. It represents 
the telencephalic part of the basal nuclei, and it ex- 
pands caudally (Fig. 17-4).

Later, the medial and lateral ventricular eminences 
overlap (Figs. 18-5 and 19-7) and expand towards the 
temporal pole (Fig. 22-6). At the end of the embry- 
onic period, both eminences lie along the floor of the 
lateral ventricle, separated from each other by a faint 
terminential sulcus (or paleoneostriatal fissure, or 
incorrectly striatoaudate sulcus). Exhaustion of their 
matrix, which proceeds caudorostrally, does not begin 
until trimester 2 (Sidman and Rakic, 1982).

Fasciculi, prosencephalic: Three chief bundles are de- 
scribed under this heading. The basal forebrain bun- 
dle (Fig. 19-23) contains descending fibers; it is “in 
part related to the olfactory system but also includes 
presumably non-olfactory channels of the vegetative 
nervous system present in macrosmatic, microsmatic, 
and anosmatic Mammals” and probably extends into 
the mesencephalic tegmentum (Kuhlenbeck, 1977).

The lateral forebrain bundle contains ascending as well 
as descending fibers, and corresponds in large mea- 
sure to the internal capsule (Fig. 19-23). The medial 
forebrain bundle (Fig. 19-23), which is predominantly 
descending, is described as the main pathway for lon- 
gitudinal connections in the hypothalamus.

Fissures: (1) In the forebrain a term reserved for three 
grooves, the floors of which are not completed by 
cortical tissue, i.e., the longitudinal, transverse, and 
choroid fissures; (2) the numerous grooves on the sur- 
face of the cerebellum.

Floor plate (Figs. 9-5 and 21-7): The ventromedial cells 
of the epithochochondal part (dorsal to the nottedorial 
plate or notochord) of the neural plate or tube. It 
is induced by the notochord. It expresses Shh, it 
motors neuron differentiation by contact- 
mediated diffusible factors, and acts commis- 
xural axes through the secretion of netrinproteins. 
The floor plate differs regionally: cells in the midbrain 
can induce the production of dopaminergic neurons, 
whereas those of the rhombencephalon develop into 
the septum medullae (Figs. 20-18 and 19).

Fovea isthm: See Recess, isthmic.

Formation, hippocampal: A congenite term for the den- 
tate gyrus, the hippocampus, the subiculum, and the 
parahippocampal gyrus. See also Hippocampus.

Ganglion, facio-vestibulocochlear: The common pri- 
midiurium (stage 10) that first appears for the ganglia 
of the facial and vestibulocochlear nerves (Fig. 11-2). 
It consists of neural crest to which the otic vesicle 
contributes. The facial and vestibulocochlear compo- 
nents become distinguishable from each other at stage 
13. It is not clear whether, at that time, the non-facial 
part contains both vestibular and cochlear elements.

Glia or neuroglia (a singular noun meaning glue): The 
non-neural interstitial tissue of the nervous system. 
The first glial cells to arise are the radial glial cells, 
from which other types may develop (Marin-Padilla, 
1995). Glia arises from three main sources: (1) the 
terminential and subterminial layers in the prosen- 
cephalon (from the intermediate zone of the devel- 
oping cerebral cortex in the ferret), and (2) the neu- 
ral crest in the mesencephalon, rhombencephalon, 
and spinal cord, and (3) the monocyte-producing 
 hematopoietic mesenchym. Glial growth factor, which 
is expressed by migrating cortical neurons, promotes 
their migration along radial glial fibers, and also aids 
in the maintenance and elongation of radial glial 
cells. The chief types of glial cells are astroglia, oligo-
dendroglia, microglia, and ependymal, satellite, and 
neurolental cells. Neurons and glial cells have the 
same precursor. Glia boosts synaptic communication 
and controls the number of synapses. Glial cells are 
about nine times more numerous than neurons.

Hippocampus (area hippocamp): The hippocampal pri- 
midiurium appears (at stage 14) as an early marginal 
layer (Fig. 16-11), followed by a ventricular thickening 
in the dorsomedial wall of the cerebral hemisphere. Its 
C-shaped form is soon evident (by stage 18, Fig. 18-2).
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It consists mainly of large pyramidal cells that are concentrated in a narrow band. The synapses per neuron are more than twice as numerous as elsewhere in the cortex. See also Formation, hippocampal.

Insula: The slight depression of the insula that becomes apparent in stage 23 is preceded by a flat area overlying the lateral ventricular eminence at stages 18–22 (Fig. 23–2).

Isthmus rhombencephali: A term introduced by His for an “independent part of the brain” (now acknowledged as a neuromere) during development and in the adult. At the beginning of its appearance (in stages 13 and 14) this is a short, narrow part of the neural tube between the midbrain and the hindbrain (Fig. 13–3). It contains nuclei and intramural and commissural fibers of the trochlear nerves. Then it expands and participates in the formation of the superior medullary velum dorsally. Its basal portion contains cerebellar tracts. The isthmus is believed to be a source of morphogens.

Lamina reuniens (Schlussplatte): A term used by His (1904) for what is here called the embryonic lamina terminalis (q.v.). Its ventral part becomes the Endplate (lamina terminalis sensu stricto), which remains thin and forms the rostral wall of the telencephalon medium. Its dorsal part is the Trapezplatte or massa commissuralis (q.v.).

Lamina terminalis, embryonic: The median wall of the telencephalon (Fig. 11–3) rostral to the chiasmatic plate (future optic chiasma). The commissural plate appears as a thickening in the embryonic lamina terminalis, and the remainder of the lamina then constitutes the adult lamina terminalis (Fig. 21–8) (Bossy, 1966).

Laminae, alar and basal (Fig. 21–7): Terms used by His for the dorsal and ventral zones of the neural tube, separated by the sulcus limitans. In the spinal cord, the alar plate, which has a broader ventricular layer, is essentially afferent, whereas the basal plate, which has a narrower ventricular layer but grows more rapidly, is fundamentally efferent (the “Bell–Magendie law”). An alar/basal distinction continues into the rhombencephalon and the mesencephalon, but not into the prosencephalon, where the sulcus limitans is absent. This point was long disputed in the past. The laminae express Pax genes (3 and 7 from the alar, 6 from the basal).

Layer, dural limiting (Fig. 22–14B): A layer of condensed cells appearing in the peripheral mesenchyme and forming the external boundary of the leptomeningeal primordium (O’Rahilly and Müller, 1986). See also Meninx, primary.

Layer, external germinal (or external granular) of cerebellum (Fig. 23–24B): A lamina on the surface of the cerebellar primordium. It arises from the rhombic lip, mainly of the isthmic segment and of Rh. 1. A special feature (at least in the rat) is that the migration of the cells in a lateromedial direction involves the use of axons as a substrate. It is frequently called the external granular layer because the granule cells arise from it. The transformation and migration of the cells of the external germinal layer as they become granule cells have been studied (Sidman and Rakic, 1982). These cells are believed to be the origin of medulloblastoma.

Layer, primordial plexiform (Figs. 21–7 and 17–19): The superficial stratum of the embryonic cerebral cortex. This layer contains horizontal (Cajal–Retzius) cells, unipolar as well as multipolar pluriform cells, tangentially arranged nerve fibers, horizontal branches of corticopetal fibers, and vertical cytoplasmic prolongations of the neuroepithelial cells. The long axes of the Cajal–Retzius cells run parallel to the cortical surface. Certain portions of the primordial plexiform layer are considered to be functionally active in the human embryo by stage 20 (Marín-Padilla and Marín-Padilla, 1982). It has been proposed that “an initial PPL may be a universal feature of the developing central nervous system” (Zecevic et al., 1989).

The earliest synapses seen in the human brain are in the primordial plexiform layer (Larroche, 1981; Choi, 1988) at about stages 17 to 19. They are formed by horizontal cells that correspond to those of Cajal–Retzius (Larroche and Houcine, 1982). After the subdivision of the primordial plexiform layer into subpial and subplate components, the synapses are present in those two layers, above and below the cortical plate but not within it (Molliver et al., 1973). Synapses have appeared within the cortical plate by the end of trimester 2 (Molliver et al., 1973).

The primordial plexiform layer is thought to play a significant role in the structural organization of the neocortex by determining the unique morphology of its pyramidal cells. “However, the nature of layer 1 remains enigmatic” (Marín-Padilla, 1992). A useful scheme of the development of the neocortical layers has been proposed (Rakic, 1984, Fig. 3), although the primordial plexiform layer was not included.

Layer, subpial granular (of Brun): A lamina that appears during trimester 2, and regresses and disappears during trimester 3 (Choi, 1988; Marín-Padilla, 1995). It is formed from the subventricular layer of the olfactory bulb by chain-migration, does not show mitotic figures, and contains precursors of astrocytes that...
later migrate into the gray matter of the insular region. The layer acts as a precursor pool for reelin-producing neurons that complement earlier-generated cells during the cortical migration (Meyer et al., 1999a).

**Layer, subventricular** (Fig. 21-7): Present only after the establishment of the cortical plate (at stage 21), this layer consists of cells at the interface between the ventricular and intermediate layers. These cells divide without interkinetic nuclear migration, and the cellular production constitutes the secondary proliferative phase. The subventricular layer of the neopallium remains active in the adult (mouse). Most glial cells are produced in the subventricular and intermediate layers.

**Layers, intermediate, marginal, and ventricular** (Fig. 21-6): The *ventricular layer* of the neural tube, which is adjacent to the ventricular cavity, contains most of the mitotic figures that generate neurons and glial cells. Mitotic division therein is characterized by interkinetic nuclear migration (Fig. 9-6). Later the lamina becomes the ependymal layer. Mitotic figures, however, are not restricted to the ventricular layer but can be found also more peripherally, in a *subventricular layer*, where cells apparently divide without movement of the nuclei during the mitotic cycle. It is believed that a temporal pattern of heterogeneity exists in the matrix. In early cerebral development, more neurons (Cajal–Retzius cells, subplate cells, secondary matrix cells of the subventricular layer) than glial cells are produced. The development continues with the production of neurons for layers 6 and 5, and finally of neurons for layers 4, 3, and 2. As development proceeds, the percentage of glial cells versus neurons increases.

The **intermediate layer** consists of several rows of postmitotic cells that appear peripheral to the ventricular layer and it corresponds approximately to the term mantle layer. The intermediate layer is poorly defined in routine histological sections, but very distinct in Golgi preparations. It is composed mainly of corticofugal and corticopetal fibers and their collaterals (Fig. 23-21) and is crossed by migrating neurons. Because of its richness in fibers the layer was named embryonic white matter by Marin-Padilla (1988a). It is the precursor of the internal white matter of the adult cerebral cortex.

The **marginal layer** is the cell-free peripheral zone of the neural tube. It is seen in the spinal cord and in most parts of the brain. In the telencephalon it may be considered to be present in the hippocampal primordium, whereas in the neopallium a primordial plexiform layer (q.v.) is found.

**LHRH neurons**: Gonadotropin-producing cells that contribute luteinizing-hormone-releasing hormone (LHRH; Schwanzel-Fukuda et al., 1996; Verney et al., 2002). They are derivatives of the olfactory neural crest and develop from the medial parts of the nasal pits (stage 16, Fig. 16-7A) and probably earlier from the nasal discs (stage 13). The cells are transported (stage 19) by fibers of the vomeronasal nerve and the nervus terminalis to the olfactory bulbs and to the forebrain septum (Fig. 19-11). The cells are accompanied by TH-positive neurons (Verney et al., 2002).

**Lip, rhombic**: A proliferative area persisting in the dorsalmost part of the alar plate of the rhombencephalon, including cells for the primordium of the cerebellum, and clearly defined at stage 17 (Fig. 17-3), when its mitotic figures are abundant and the remainder of the basal plate has differentiated into marginal and intermediate layers. The rhombic lip participates in the formation of the external germinal layer of the cerebellum (Figs. 23-28). Furthermore, it produces three superficial streams: a pontine, a cochlear, and the so-called olivo-arcuate migration of Esick (1912). The last-mentioned layer (Fig. 20-19) is ill-named because it has been shown (in the monkey) that the olivary nuclei arise mainly from the ventricular layer.

The term “rhombic lip,” which should not be used as a synonym for the primordium of the cerebellum, was introduced by His, who distinguished primary and secondary types. His primary lip (1890), which would be expected to appear at about stages 16 and 17, was not found in the present series and was in all likelihood artifactual, as pointed out by Hochstetter (1929) and Kuhlenbeck (1973). Subsequent usage of the term is twofold: (1) the junction between the thin roof plate and the much thicker alar lamina, i.e., more or less equivalent to the taenia of the fourth ventricle; (2) functionally, as used in this book, the dorsolateral portion of the alar lamina, which (characterized by mitotic figures from stage 16 on) acts as a proliferative zone (Figs. 20-20, 22-13, and 23-28).

**Massa commissuralis** (of Zuckerandl): A bed through which the fibers of two cerebral commissures pass: the commissura fornici and the corpus callosum. It develops early in the fetal period from the commissural plate and also from proliferating cells of the mesenchyme between the medial hemispheric walls in the region of the hippocampal primordium.

**Matrix, extracellular (ECM)**: Occupying 15–20% of the volume of the brain and associated with neurons and glia, the ECM preserves epithelial integrity and acts as a substrate for cellular migration and as a guide for
axonal extension. Fibronectin and laminin in the matrix facilitate migration, whereas chondroitin sulfate proteoglycans inhibit it.

**Meninx, primary:** The loose mesenchyme (*meninx primitiva* of Salvi) adjacent to the brain (Fig. 14-5) and spinal cord. From stage 17 onwards the leptomeningeal meshwork contains fluid that is believed to be derived from the adjacent blood vessels. Its peripheral border is represented by the dural limiting layer (q.v.). (O'Rahilly and Müller, 1986).

**Midline:** An undesirable term for the median plane (q.v.) (O'Rahilly, 1996).

**Migration:** Several types are described.

1. **Non-radial migration.** Neurons that do not use radial glia, as a migratory substrate have to glide across one glial fiber to another (O'Rourke et al., 1995).

2. **Radial migration,** mediated by radial glial cells, is prominent in the development of the telencephalic cortex (Sidman and Rakic, 1973). Cells within a given radial column share the same birthplace and migrate along a common pathway towards the pia mater. The number of radial columns determines the extent of the cortical surface, whereas the number of cells within the columns determines cortical thickness.

3. **Tangential migration** involves clonally related cells that are dispersed in a direction parallel to the pia mater. Tangential migration occurs in the cerebral cortex (Zecovic and Milosevic, 1997; Meyer and Wahle, 1999; Marin et al., 2001; Ullig et al., 2001) and in the rhombencephalon (Fig. 18-18).

4. **Combined radial and tangential migration.** In the cerebral cortex GABA-positive cells use both directions for dispersing from the ventricular zone: radial migration towards the pia, tangential migration parallel to the pia. The tangential “may be guided by glial fibers” (Ullig, 2002). In the cerebellum radial migration is from the ventricular zone, tangential from the rhombic lip (Fig. 18-18).

5. **“Chain migration”** by elongated neurons that are closely apposed and connected by membrane specializations, and ensheathed by a protective layer of glial cells. It provides “a steady supply of new GABAergic neurons destined for the olfactory bulb” and originating in the subventricular layer of the cortex (Verney et al., 2002).

**Myelination:** The process by which glial cells ensheathe the axons of neurons in layers of myelin. Rapid conduction of electrical impulses is thereby ensured. Both oligodendrocytes and astrocytes participate. The number of coverings is determined by the axon. Myelin accounts for approximately 70% of the dry weight of the mammalian CNS.

**Neopallium:** The cerebral cortex derived from the areas that possess a cortical plate, which latter begins to appear in stage 23 (Fig. 21-7).

**Nerve, vomeronasal (Fig. 18-13):** Nonmyelinated fibers from the vomeronasal organ (q.v.). The fibers enter the rostral medial wall of the olfactory bulb.

**Nervus terminalis** (Fig. 20-13): Fibers that enter the olfactory tube at stage 18 and that are probably autonomic. These fibers arise in the nasal mucosa and will later traverse the cribriform plate.

**Neuroectoderm:** See Ectoderm, neural.

**Neuroglia:** See Glia.

**Neuromeres:** Morphologically identifiable transverse subdivisions perpendicular to the longitudinal axis of the embryonic brain and extending onto both sides of the body (Müller and O'Rahilly, 1997b). The larger (primary) neuromeres appear early in the open neural folds (at stage 9), and the smaller (secondary) neuromeres are found both before and after closure of the neural tube. The full complement of 16 neuromeres is present at stage 14 (Table 10-1). Neuromeres are particularly clear in the hindbrain (Fig. 10-3), where they are termed rhombomeres (q.v.). In some instances the neuromeres are coextensive with domains of gene expression, whereas in others the domains cross interneuromeric boundaries.

**Neuropores:** Temporary rostral (stage 11, Fig. 11-7) and caudal (stages 11 and 12) openings that represent the remains of the neural groove before the fusion of the neural folds has been completed at each end. The neuropores close during stages 11 and 12, respectively. The rostral (or cephalic) neuropore has been studied particularly (O'Rahilly and Müller, 1989a, 2002).

**Neurulation:** The formation of the neural tube in the embryo (Fig. 9-5). Primary neurulation is the folding of the neural plate to form successively the neural groove and the neural tube. Secondary neurulation, which occurs without direct involvement of the ectoderm and without the intermediate phase of a neural plate, is the continuing formation of the spinal cord from the caudal eminence, which develops a neural cord (q.v.) (Müller and O'Rahilly, 2004).

**Nuclei:** The term is used here in the restricted meaning of areas of lower cellular density and slightly larger cellular size. As Dekaban (1954) pointed out, early and later neurons “group themselves into ‘centers’ or ‘nuclei,’ which will constitute functional systems or parts of the systems.” Rakic (1974), on the other hand, in delimiting diencephalic nuclei, maintains that subdivisions into discrete nuclear groups “appears to be based initially on the establishment of boundaries by fascicles of nerve fibers.”
Nuclei, amygdaloid: These dopaminergic nuclei are originally in a diencephalic position mostly in the medial ventricular eminence (Figs. 18-8), but later become telencephalic (Figs. 19-8 and 19-9).

Nuclei, basal (Fig. 19-6): An arbitrary group that generally includes the corpus striatum (q.v.), the amygdaloid complex, and the claustrum. To these are added, from a clinical point of view, the subthalamus and the substantia nigra, to complete the basal structures affected pathologically in so-called extrapyramidal motor diseases. The region of the future basal nuclei, which becomes compartmentalized into two entities by stage 19, extends to the preoptic sulcus caudally and to the prosencephalic septal area rostrally. The two compartments are, in order of appearance: (1) the medial ventricular eminence, and (2) the lateral ventricular eminence (Fig. 19-7). From the lateral eminence arise the caudate nucleus and the putamen; from the medial the amygdaloid complex; and from a basal thickening, the nucleus accumbens. The constituent cells of the basal nuclei are derived from the subventricular zone. These cells proliferate throughout the entire prenatal period (Kalas, 1969; Sidman and Rakic, 1982) by a special mode of division (investigated by Smart in the mouse). The basal nuclei are not ganglia, which, by definition, occur only in the peripheral nervous system.

Organ, vomeronasal: Epithelial pockets that appear bilaterally in the nasal septum in stage 17. They enlarge during the embryonic and fetal periods and are generally said to involute postnatally, although this has been queried (Smith et al., 1997, 2002). See also Nerve, vomeronasal.

Organs, circumventricular: Specialized ependymal regions in (chiefly) the third ventricle. They are practically all median in position and (with the exception of the subcommissural organ) are highly vascular and lack a blood-brain barrier. They vary in prominence and in structure with age, and some are difficult to find in the adult or may even disappear. Functions include secretion of substances (e.g., neuropeptides) into the cerebrospinal fluid, and transport of neurochemicals in both directions between neurons, glia, and blood cells and the CSF. The main structures that are generally included are: (1) the median eminence of the tuber cinereum (around the base of the infundibulum); (2) the neurohypophysis; (3) the organum vasculosum of the lamina terminalis (OVLT); supraoptic crest; intercolumnar tubercle; (4) the subfornical organ (at the level of the interventricular foramina); (5) the telencephalic (or paraventricular) paraplasia (a temporary ependymal thickening rostral to the velum transversum in trimester 1); (6) the epiphysis cerebri; (7) the subcommissural organ (modified ependyma in the roof of the aqueduct, beneath the posterior commissure); and (8) the area postrema (at the junction of the fourth ventricle and the central canal), which resembles the subfornical organ but differs from the strictly circumventricular organs in being related to the fourth rather than the third ventricle and in being bilateral.

 Paleopallium: The cerebral cortex of the piriform area, including the surface of the medial ventricular eminence with the amygdaloid complex. The piriform cortex represents the olfactory lobe in the paleopallium and neopallium. It becomes apparent when the cortical plate appears in stage 21 (Fig. 21-10).

Paraphysis: A telencephalic formation appearing first as a knob (stage 18, Fig. 18-8) and later developing one or more evaginations, which are in communication with the ventricle of the telencephalon medium and are lined by a single layer of ciliated cells. Further details: Ariens Kappers (1955); O’Rahilly and Müller (1990).

Parencephalon (Table 10-1): A part of the diencephalon (neurorome D2) which, together with the synencephalon (q.v.), becomes discernible at stage 13. Two portions can be distinguished at stage 14: the rostral parencephalon (including the infundibular region and the ventral thalamus) and the caudal parencephalon (containing the mammillary region and the dorsal thalamus).

Plane, median: This is considered to be a special region that is subject to a variety of anomalies, such as holoprosencephaly and agenesis of the corpus callosum. The median features of the developing brain are shown in Figures 17-5 and 24-32.

Plate, callosal commissural: See Massa commissuralis.

Plate, cerebellar: A term used when the cerebellar primordium becomes coronally oriented and more or less at a right angle to the remainder of the rhombencephalon (Fig. 18-1). See also Cerebellum and Swellings, cerebellar.

Plate, chiasmatic (or torus opticus): A bridge between the optic primordia across the median plane (Fig. 10-3). Its rostral end corresponds to the tip of the former neural plate. The fibers of the preoptic-hypothalamic tract cross in its caudal part at stage 18 (Fig. 18-2) and the optic fibers in its rostral portion at stage 19 (Figs. 19-3 and 20-2).

Plate, commissural (Fig. 12-3): A thickening in the embryonic lamina terminalis (q.v.) at the site of neuroporicus (q.v.). It is considered by some to be the bed through which commissural fibers of the anterior commissure, corpus callosum, and commissura fornici pass (Streeter, 1912; Hochstetter, 1928; Bartelmez and Dekaban, 1962). Others (e.g., His, 1904; Rakic and
Yakovlev, 1968) have maintained that the commissur-ation is preceded by the development of a massa com-missuralis (q.v.), which supplies some fusion of the me-dial hemispheric walls at the level of the hippocampal primordium.

**Plate, cortical** (Fig. 21-7): A neopallial feature first found in the embryo at stage 21 (Fig. 21-9). It consists of three to five rows of cells that have migrated radially from the ventricular layer and are arranged vertically. It increases in thickness and persists for long into the fetal period. Although formerly it was thought that only layers 2 to 5 develop from the cortical plate, it is now generally believed that layer 6 is also derived from the plate (Mrzljak et al., 1988). The migrating neurons that accumulate within the primordial plexiform layer are arranged in an outside-inside order. Synapses develop relatively late within the cortical plate, at about 23 weeks (Molliver et al., 1973), whereas they are already present in the primordial plexiform layer at stages 17–19.

**Plate, neural** (Fig. 8-2): The neural primordium that first becomes visible during stage 8 and is present in caudal areas up to stage 10. At the time of its first appearance it is slightly vaulted on each side of the neural groove. The prenotochordal part of the neural plate is the diencephalic region (neuromere D1 and the future rostral parencephalon). The epimorphic pillar of the neural plate (that overlying the notochord) develops a floor plate (q.v.).

**Plate, optic**: The median region that unites the optic primordia of the two sides (Fig. 10-3). It represents the rostral end of the neural plate, and it participates in the formation of neuromere D3.

**Plate, prechordal**: A multilayered accumulation of mesodermal cells in close contact with the median part of the future prosencephalon in the human embryo (Figs. 8-3 and 8-6). The plate differs appreciably in the mouse and in the chick embryo. It has been unequivocally found first at stage 7, and is usually detectable at stage 8. The plate lacks a clearly visible, complete underlying sheet of endoderm. At stages 9 and 10 the plate is related to neuromere D3 (Müller and O’Rahilly, 2003a).

**Plates, alar and basal**: See Laminae, alar and basal.

**Plexuses, choroid**: Intraventricular invaginations at stages 18–20 of choroidal (as distinct from ventricular) ependyma derived from the ventricular layer of the neural tube and characterized by tight junctions and tela choroidea (vascular pia mater). The plexuses are relatively very large in the embryo (Fig. 23-16). They are derived from choroidal fluid (in contrast to the ependymal fluid of earlier stages) and probably a variety of growth factors.

**Preplate**: A term that is sometimes used (e.g., by Bystron et al., 2005) for the early marginal zone of the cortical primordium.

**Prosomeres**: The neuromeres of the prosencephalon.

**Recess, isthmic (Fovea isthmi)**: The ventral limit of the meso-metencephalic sulcus (Fig. 17-5) (Bartelmez and Dekaban, 1962).

**Recess, postoptic**: The site where the optic sulci meet in the median plane (Fig. 10-3). This is the caudal limit of the chiasmal plate.

**Recess, preoptic**: In later stages this depression indicates the rostral limit of the chiasmal plate (Fig. 14-2).

**Rhombomeres**: The transverse swellings in the neural tube, known as neuromeres, are termed rhombomeres in the developing rhombencephalon, where they are clearly visible up to stage 17 (Müller and O’Rahilly, 2003b). They are originally four in number (Fig. 9-2C) and are termed A, B, C, and D. They increase in number by subdivision during stage 10 and are numbered 1, 2, 3 (from A), 4 (corresponding to B), 5, 6, 7 (from D), and 8 (corresponding to D and related to somites 1–4). Eight rhombomeres are generally identifiable from stage 11 to stage 17; in addition, the isthmus rhombencephali (q.v.) becomes apparent from stage 13 onwards. They are believed to result from transverse bands of high mitotic activity and they are maintained by cytoskeletal components, although their significance is still disputed. Cranial nerves 5 to 10 have a clear relationship to specific rhombomeres: the otic vesicle (Fig. 12-2 and 12-6), however, changes its position with regard to the rhombomeres, shifting from Rh.4 (in stage 10) to Rh.6 (in stages 14–17).

**Roof plate**: The plate consists of the dorsomedial cells of the neural tube (Fig. 21-7). It is believed to be induced by a morphogenic protein of ectodermal origin, and it may be important in causing differentiation of the dorsal part of the spinal cord.

**Septum, prosencephalic**: The septum verum (Andy and Stephan, 1968) is the basal part of the medial wall of the cerebral hemispheres. Hence it is formed at the time when the hemispheres expand beyond the lamina terminalis, beginning at stage 17. It is the area between the olfactory bulb and the commissural plate (Fig. 18-2). The nuclei arising in it during the embryonic period are the medial septal nucleus, the caudal nucleus of the diagonal band, and the nucleus accumbs.

**Sexual differentiation and brain development**: All embryos are exposed to maternal estrogen, and male fetuses additionally to their own testosterone; the hypothalamus is especially involved. Later, these hormones play a “housekeeping” role in the growth and maintenance of cells of the brain in both sexes.
The site of final closure of the rostral neuropore. It corresponds later to an area within the commissural plate (O'Rahilly and Müller, 1989a, 2002).

Situs neuroporicus (Fig. 12-7A): The site of final closure of the rostral neuropore. It corresponds later to an area within the commissural plate (O'Rahilly and Müller, 1989a, 2002).

Stalk, hemispheric: The original connection (Streifenhügelstiel, Hemisphärenstiel: His, 1904) between the diencephalon and the telencephalon, which becomes a stalk from about stage 17. It becomes greatly enlarged by fibers and tracts, especially by the continuation of the internal capsule (Figs. 21-6, 22-10, and 22-11), namely the lateral prosencephalic fasciculus (q.v.). See Sharp (1959) and Richter (1965).

Stammhügelstiel: The term used by His for the fibers (lateral prosencephalic fasciculus, q.v.) connecting the dorsal thalamus and telencephalon and continuing also to the epithalamus and to the mesencephalon.

Stem cells, neural: The pluripotential stem cells of the mammalian brain develop in the ventricular layer of the embryo and fetus, as well as from the neural crest. These cells develop into both neurons and glia. Neural stem cells persist in the adult mammalian central nervous system (e.g., in the endoderm) and participate in plasticity and regeneration, but they have the immunocytochemical markers of glia. The only site in the adult peripheral nervous system where production of neural stem cells is documented is the olfactory neuroepithelium. A pool of progenitor cells within the human dentate gyrus continues to produce new granule cells throughout life. Adult glial progenitors develop into oligodendrocytes and astrocytes (Compton et al., 1997). However, studies of embryonic and adult stem cells still contain “red herrings” (Quesenberry et al., 1997). However, studies of embryonic and adult progenitors developed into oligodendrocytes and astrocytes (Compton et al., 1997). However, studies of embryonic and adult stem cells still contain “red herrings” (Quesenberry et al., 2005) and much further work remains to be done.

Subplate (Figs. 21-7 and 23-22): A derivative of the primordial plexiform layer (q.v.), which may participate in the specification of the cortical plate (q.v.). It has been termed a waiting compartment for incoming afferent axons (Rakic). Catecholaminergic fibers and GABA-positive neurons are found bilaterally in the developing mesencephalon, rhombencephalon, and spinal cord. It is present at stage 12 and is the boundary between the alar and basal laminae (q.v.). In the human embryo the subplate limits ends rostrally near the rostral end of the mesencephalon (Fig. 17-4). This point was long disputed in the past (Fig. 21-8). See also Laminae, alar and basal.

Swellings, cerebellar: Bulges that are parts of the cerebellar plate, i.e., the alar lamina of the isthmic segment together with that of rhombomere 1. The earlier appearing internal cerebellar swelling (innerer Kleinhirnwulst) of Hochstetter, (1929) is inside the fourth ventricle (Fig. 17-4). The external cerebellar swelling (außerer Kleinhirnwulst) forms an expansion at the site of the rhombic lip (Fig. 17-3). It is delimited by a groove that corresponds to the later posterolateral fissure of the cerebellum. The internal and external cerebellar swellings are sometimes referred to, respectively, as the intraventricular and extraventricular portions of the developing cerebellum.

Synecephalon (Fig. 13-8A): The caudalmost part of the diencephalon, the portion that gives rise to the prethalamic and pretectal nuclei. It is delineated rostrally by the habenulo-interpeduncular tract (fasciculus retroflexus) and caudally by the di-mesencephalic borderline passing between the two constituents of the posterior commissure.

Telencephalon medium or impar: The first part of the telencephalon to appear (at stage 10, Fig. 10-3) is lateral in position. Only later (stage 14) do the lateral walls become domed and form the future cerebral hemispheres (Müller and O'Rahilly, 1985). The medial part of the telencephalon persists throughout life, so that a portion of the third ventricle remains telencephalic.
Torus hemisphericus: A ridge at the ventricular surface between the telencephalon and the diencephalon, and along which the cerebral hemispheres are evaginated (Fig. 14-2). An external di-telencephalic sulcus develops and accompanies it.

Torus opticus: See Plate, chiasmatic.

Velum transversum: A transverse ridge in the roof of the forebrain marking the limit between telencephalon and diencephalon (Fig. 14-2).

Ventricle, olfactory (Fig. 22-12): A prolongation of the lateral ventricle into the growing olfactory bulb at approximately stages 19 to 23, and also in the fetal period.

Ventricle, optic: At first (stage 13), the cavity of the optic vesicle, which is a prolongation of that of the diencephalon. Later it becomes the intraretinal slit between the external and internal strata of the optic cup, and ultimately the potential space (along which so-called detachment of the retina occurs) between layer 1 and layers 2–10 of the retina (Fig. 23-13).

Zona limitans intrathalamica: A zone that parallels the marginal ridge and sulcus medius between the dorsal and ventral thalami and is first recognizable as a thicker marginal layer at this site. Fibers of the zona are visible at stage 19 (Fig. 19-22). The zona is believed to form later the lamina medullaris externa. The marginal ridge, sulcus medius, and zona limitans intrathalamica are seen in Figure 21-14.