LABORATORY ACTIVITY: NEUROBEHAVIOR SYSTEM

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Resource Person : Tryando Bhatara, dr., M.Kes
Subject : Embryology
Department : Biomedical Sciences and Histology

A	Sequent			
	I	Introduction	:	40 menit
	II	Pretest	:	5 menit
	III	Laboratory activity	:	120 menit
	IV	Post test	:	5 menit
B	Topic			
	Date:			
	1. Discussion about Development of spinal cord, brain, cranial and spinal nerve, and autonomic nervous system 2. Chick Embryo Sections identification and drawing		: : :	40 menit 40 menit 40 menit
C	Venue			
	Biomedical Laboratory, Faculty of Medicine, Unisba, Jl. Tamansari No.22 Bandung 40116			
D	Equipment			
	1	1. Discussion about Development of spinal cord, brain, cranial and spinal nerve, and autonomic nervous system	1. Posters 2. Atlas	
	2	Preparate identification and drawing	1. Microscope 2. Immersion oil 3. Sections of chick embryo (24,48,72 hours)	
	3	Identification of congenital anomalies	Photos of (in manual lab act) 1. Spina Bifida 2. Anencephaly	
E	Task			
	Explain: 1. Development of brain 2. Development of spinal cord 3. Development of cranial and spinal nerve. 4. Development of autonomic nerve system			
F	Implementation			
	1. Students are divided into 6 groups 2. Each group is supervised by one tutor			

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Activity 1 : Discussions

Development of Brain

The first indications of the developing nervous system appear during the third week as the neural plate and neural groove develop on the posterior aspect of the trilaminar embryo. It is the notochord and paraxial mesenchyme that induce the overlying ectoderm to differentiate into the neural plate. *Signaling molecules transforming growth factor β family, Shh, and BMPs.*

- The neural tube differentiates into the CNS.
- The neural crest gives rise to cells that form most of the PNS and ANS.

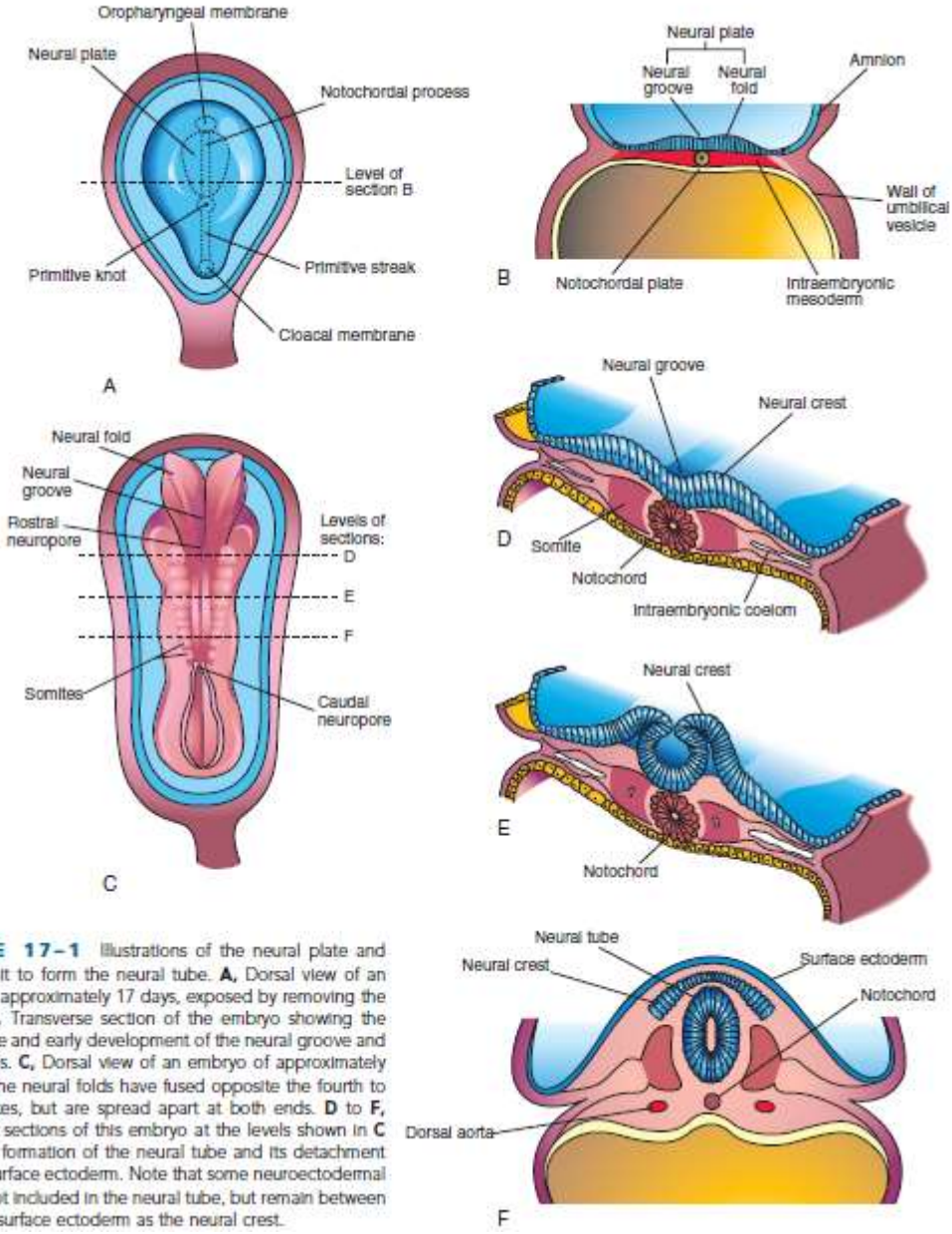


FIGURE 17–1 Illustrations of the neural plate and folding of it to form the neural tube. **A,** Dorsal view of an embryo of approximately 17 days, exposed by removing the amnion. **B,** Transverse section of the embryo showing the neural plate and early development of the neural groove and neural folds. **C,** Dorsal view of an embryo of approximately 22 days. The neural folds have fused opposite the fourth to sixth somites, but are spread apart at both ends. **D** to **F,** Transverse sections of this embryo at the levels shown in **C** illustrating formation of the neural tube and its detachment from the surface ectoderm. Note that some neuroectodermal cells are not included in the neural tube, but remain between it and the surface ectoderm as the neural crest.

Neurulation—formation of the neural plate and neural tube—begins during the fourth week (22–23 days) in the region of the fourth to sixth pairs of somites (Fig. 17-1*C* and *D*). At this stage, the cranial two thirds of the neural plate and tube, as far caudal as the fourth pair of somites, represent the future brain, and the caudal one third of the plate and tube represents the future spinal cord.

Fusion of the neural folds and formation of the **neural tube** begins at the fifth somite and proceeds in both cranial and caudal directions until only small areas of the tube remain open at both ends (Fig. 17-3*A* and *B*). The lumen of the neural tube becomes the **neural canal,** which communicates freely with the amniotic cavity (Fig. 17-3*C*). The cranial opening, the **rostral neuropore**, closes at approximately the 25th day and the **caudal neuropore** closes at approximately the 27th day (Fig. 17-3*D*).

Closure of the neuropores coincides with the establishment of a vascular circulation for the neural tube. The walls of the neural tube thicken to form the brain and spinal cord (Fig. 17-4). The neural canal forms the ventricular system of the brain and the central canal of the spinal cord.

Development of Brain

The brain begins to develop in the third week when the neural plate and tube are developing from the neuroectoderm (Fig. 17-1). The **neural tube**, cranial to the fourth pair of somites, develops into the brain. Fusion of the neural folds in the cranial region and closure of the rostral neuropore form three primary brain vesicles from which the brain develops (Fig. 17-18). The three **primary brain vesicles** form the:

- Forebrain (prosencephalon)
- Midbrain (mesencephalon)
- Hindbrain (rhombencephalon)

During the fifth week, the forebrain partly divides into two **secondary brain vesicles**, the *telencephalon* and *diencephalon*; the midbrain does not divide; and the hindbrain partly divides into two vesicles, the *metencephalon* and *myelencephalon*. Consequently, there are five secondary brain vesicles.

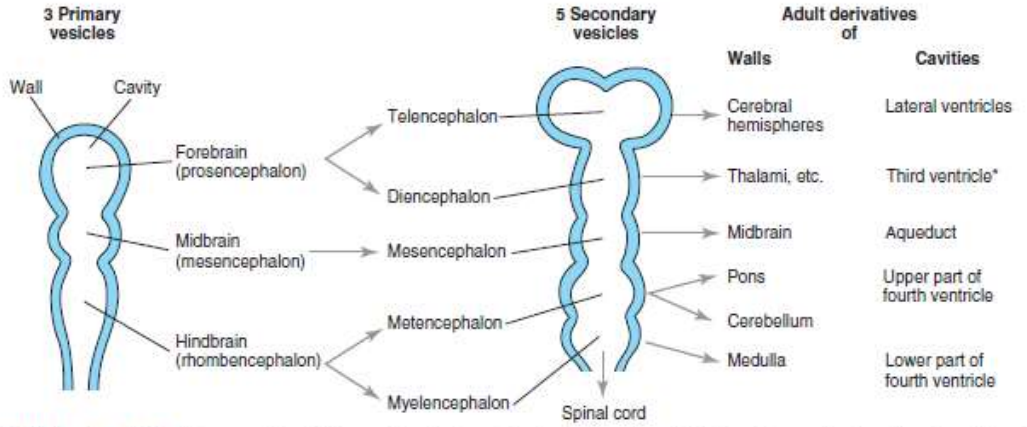
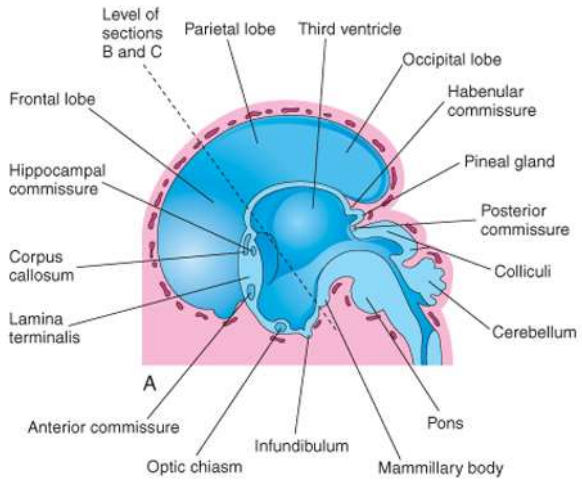
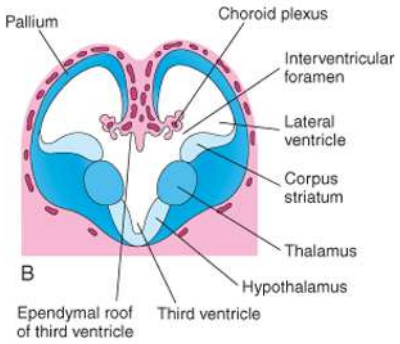
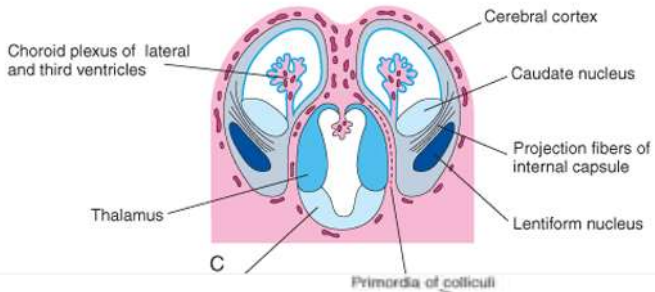
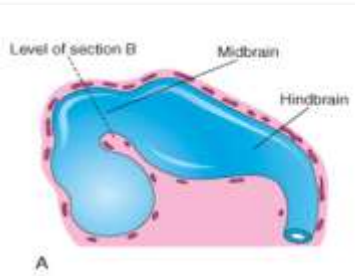


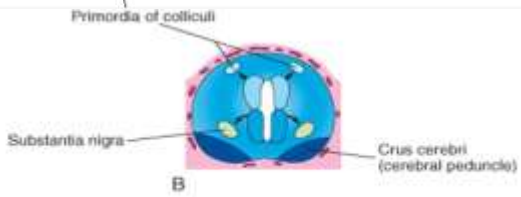
FIGURE 17–18 Diagrammatic sketches of the brain vesicles indicating the adult derivatives of their walls and cavities. The rostral part of the third ventricle (*) forms from the cavity of the telencephalon; most of this ventricle is derived from the cavity of the diencephalon.

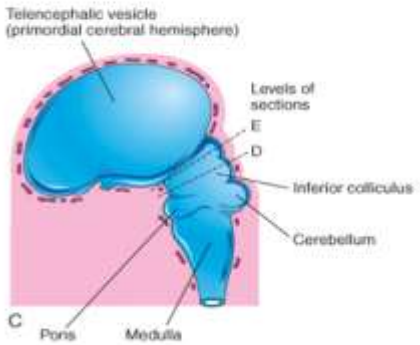

Level of sections B and C
Parietal lobe
Third ventricle
Occipital lobe
Frontal lobe
Habenular commissure
Hippocampal commissure
Pineal gland
Posterior commissure
Corpus callosum
Colliculi
Lamina terminalis
Cerebellum
A
Anterior commissure
Infundibulum
Pons
Optic chiasm
Mammillary body

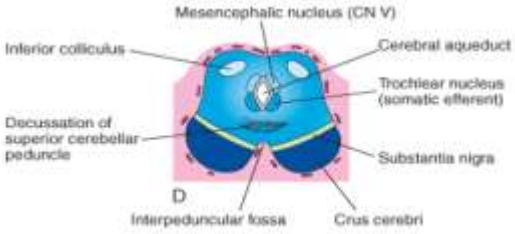

Pallium
Choroid plexus
Interventricular foramen
Lateral ventricle
Corpus striatum
Thalamus
B
Hypothalamus
Ependymal roof of third ventricle
Third ventricle

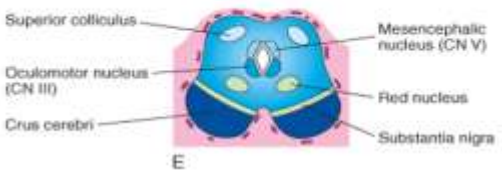

Cerebral cortex
Choroid plexus of lateral and third ventricles
Caudate nucleus
Projection fibers of internal capsule
Thalamus
Lentiform nucleus
C

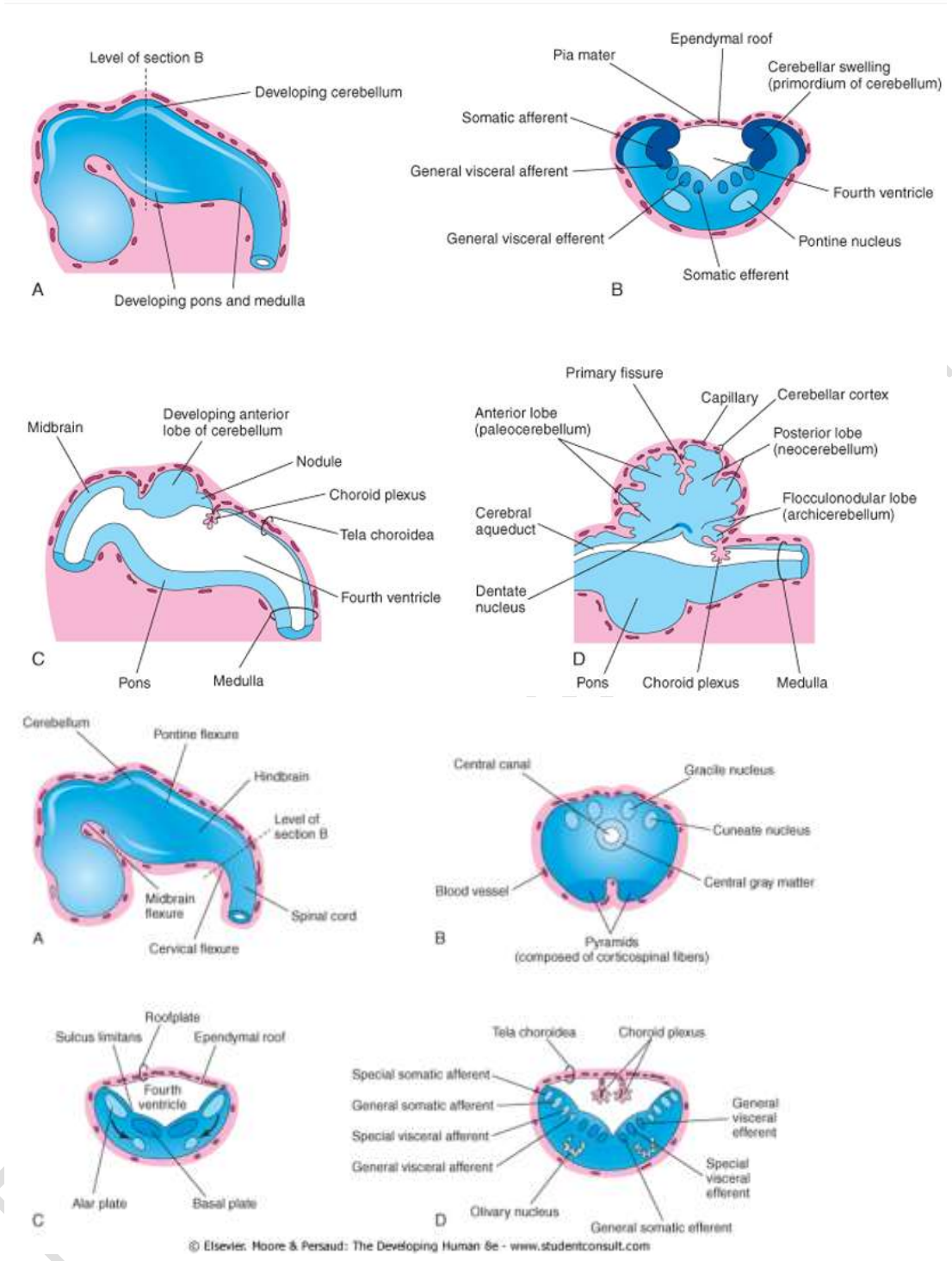

Level of section B
Midbrain
Hindbrain
A


Primordia of colliculi
Substantia nigra
Crus cerebri (cerebral peduncle)
B


Telencephalic vesicle (primordial cerebral hemisphere)
Levels of sections
E
D
Inferior colliculus
Cerebellum
C
Pons
Medulla


Mesencephalic nucleus (CN V)
Inferior colliculus
Cerebral aqueduct
Trochlear nucleus (somatic efferent)
Decussation of superior cerebellar peduncle
Substantia nigra
D
Interpeduncular fossa
Crus cerebri


Superior colliculus
Mesencephalic nucleus (CN V)
Oculomotor nucleus (CN III)
Red nucleus
Crus cerebri
Substantia nigra
E


Level of section B
Developing cerebellum
A
Developing pons and medulla
Ependymal roof
Pia mater
Cerebellar swelling
(primordium of cerebellum)
Somatic afferent
General visceral afferent
Fourth ventricle
General visceral efferent
Pontine nucleus
Somatic efferent
B
Midbrain
Developing anterior
lobe of cerebellum
Nodule
Choroid plexus
Tela choroidea
Fourth ventricle
C
Pons
Medulla
Primary fissure
Capillary
Cerebellar cortex
Anterior lobe
(paleocerebellum)
Posterior lobe
(neocerebellum)
Flocculonodular lobe
(archicerebellum)
Cerebral
aqueduct
Dentate
nucleus
D
Pons
Choroid plexus
Medulla
Cerebellum
Pontine flexure
Hindbrain
Level of
section B
Midbrain
flexure
Spinal cord
Cervical flexure
A
Central canal
Gracile nucleus
Cuneate nucleus
Central gray matter
Blood vessel
Pyramids
(composed of corticospinal fibers)
B
Roofplate
Sulcus limitans
Ependymal roof
Fourth
ventricle
Alar plate
Basal plate
C
Tela choroidea
Choroid plexus
Special somatic afferent
General somatic afferent
Special visceral afferent
General visceral afferent
General
visceral
efferent
Special
visceral
efferent
Olivary nucleus
General somatic efferent
D
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ENCEPHALOCELE

Encephalocele is a herniation of intracranial contents through a defect in the cranium (cranium bifidum). Encephaloceles are most common in the occipital region (Figs. 17-31A to D, 17-33, and 17-34). The hernia may contain meninges (**menigocele**), meninges and part of the brain (**meningoencephalocele**), or meninges, part of the brain, and part of the ventricular system (**meningohydroencephalocele**). Encephalocele occurs approximately once in every 2000 births.

MICROCEPHALY

Microcephaly is a neurodevelopmental disorder. The calvaria and brain are small, but the face is normal size (Fig. 17-36). These infants are grossly mentally deficient because the brain is underdeveloped. Microcephaly is the result of a reduction in brain growth. Inadequate pressure from the growing brain leads to the small size of the neurocranium. In the United States, about 25,000 infants are diagnosed annually.

Some cases appear to be genetic in origin. In autosomal recessive primary microcephaly, embryonic brain growth is reduced without affecting the structure of the brain. Exposure to large amounts of ionizing radiation, infectious agents (e.g., cytomegalovirus, rubella virus, and *Toxoplasma gondii* [see Chapter 20]), and certain drugs (maternal alcohol abuse) during the fetal period are contributing factors in some cases.

Microcephaly can be detected in utero by ultrasound scans carried out over the period of gestation. A small head may result from **premature synostosis** (osseous union) of all the cranial sutures (see Chapter 14); however, the neurocranium is thin with exaggerated convolutional markings.

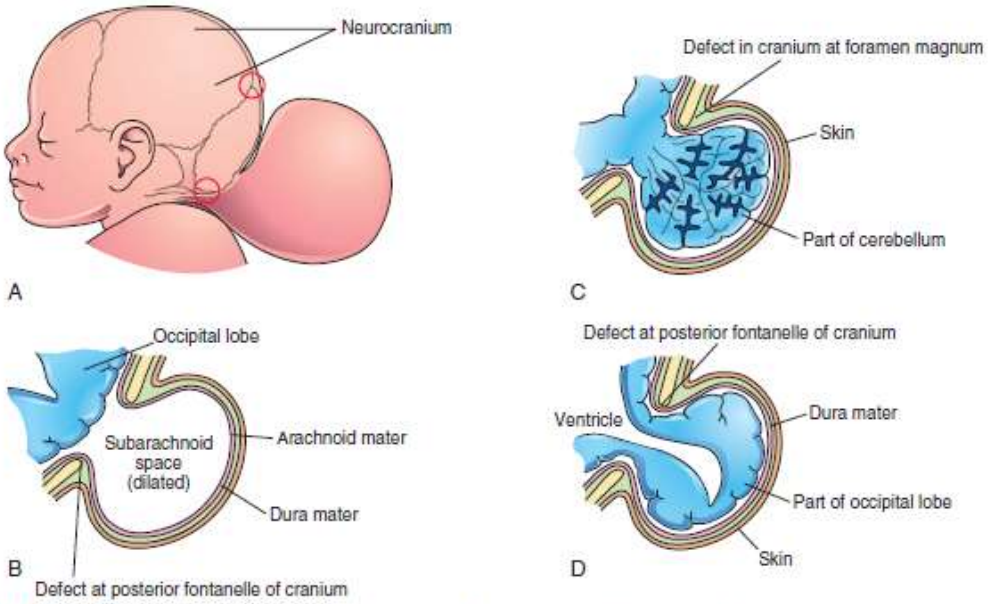


FIGURE 17–31 Schematic drawings illustrating encephalocele (cranium bifidum) and various types of herniation of the brain and/or meninges. **A,** Sketch of the head of a newborn infant with a large protrusion from the occipital region of the cranium. The *upper red circle* indicates a cranial defect at the posterior fontanelle (membranous interval between cranial bones). The *lower red circle* indicates a cranial defect near the foramen magnum. **B,** Meningocele consisting of a protrusion of the cranial meninges that is filled with cerebrospinal fluid (CSF). **C,** Meningoencephalocele consisting of a protrusion of part of the cerebellum that is covered by meninges and skin. **D,** Meningohydroencephalocele consisting of a protrusion of part of the occipital lobe that contains part of the posterior horn of a lateral ventricle.

HYDROCEPHALUS

Significant **enlargement of the head** results from an imbalance between the production and absorption of CSF; as a result, there is an excess of CSF in the ventricular system of the brain (Fig. 17-38). Hydrocephalus results from impaired circulation and absorption of CSF and, in rare cases, from increased production of CSF by a **choroid plexus adenoma** (benign tumor). Impaired circulation of CSF often results from **congenital aqueductal stenosis** (Figs. 17-38 and 17-39). The cerebral aqueduct is narrow or consists of several minute channels. In a few cases, aqueductal stenosis is transmitted by an X-linked recessive trait, but most cases appear to result from a fetal viral infection (e.g., cytomegalovirus or *Toxoplasma gondii* [see Chapter 20]), or prematurity associated with intraventricular hemorrhage. Blood in the subarachnoid space may cause obliteration of the cisterns or arachnoid villi.

Blockage of CSF circulation results in dilation of the ventricles proximal to the obstruction, internal accumulation of CSF, and pressure on the cerebral hemispheres (Fig. 17-39). This squeezes the brain between the ventricular fluid and the neurocranium. In infants, the internal pressure results in an accelerated rate of expansion of the brain and neurocranium because most of the fibrous sutures are not fused. Hydrocephalus usually refers to **obstructive or noncommunicating hydrocephalus,** in which all or part of the ventricular system is enlarged. All ventricles are enlarged if the apertures of the fourth ventricle or the subarachnoid spaces are blocked, whereas the lateral and third ventricles are dilated when only the **cerebral aqueduct** is obstructed (Fig. 17-39). Obstruction of an interventricular foramen can produce dilation of one ventricle.

Hydrocephalus resulting from obliteration of the subarachnoid cisterns or malfunction of the arachnoid villi is called **nonobstructive or communicating hydrocephalus**. Although hydrocephalus may be associated with spina bifida cystica, enlargement of the head may not be obvious at birth. Hydrocephalus often produces thinning of the bones of the calvaria, prominence of the forehead, atrophy of the cerebral cortex and white matter (Fig. 17-38*B* and *C*), and compression of the basal ganglia and diencephalon.

Development of Spinal Cord

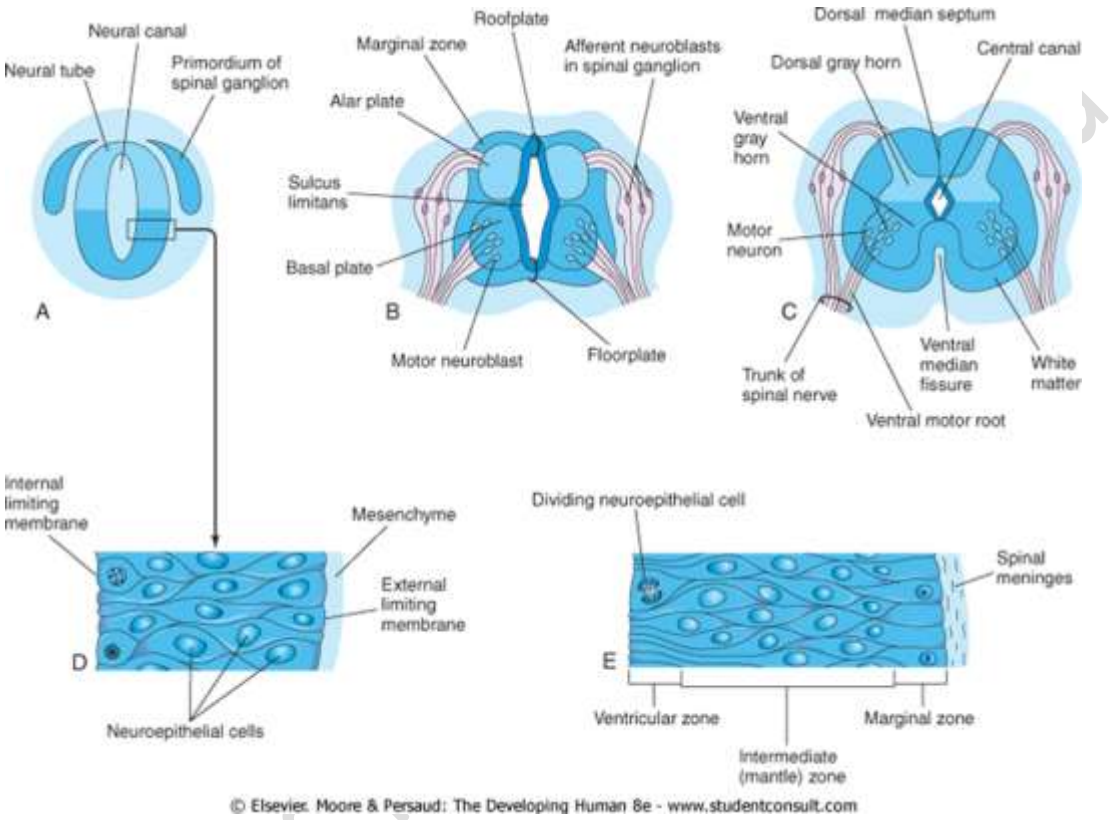
The spinal cord develops from the caudal part of the neural plate and the caudal eminence. The neural tube caudal to the fourth pair of somites develops into the spinal cord. The lateral walls of the neural tube thicken, gradually reducing the size of the **neural canal** until only a minute **central canal** of the spinal cord is present at 9 to 10 weeks. Initially, the wall of the neural tube is composed of a thick, pseudostratified, columnar neuroepithelium.

These neuroepithelial cells constitute the **ventricular zone** (ependymal layer), which gives rise to all neurons and macroglial cells (macroglia) in the spinal cord. Macroglial cells are the larger members of the neuroglial family of cells, which includes astrocytes and oligodendrocytes. Soon a **marginal zone** composed of the outer parts of the neuroepithelial cells becomes recognizable. This zone gradually becomes the white

matter of the spinal cord as axons grow into it from nerve cell bodies in the spinal cord, spinal ganglia, and brain.

Some dividing neuroepithelial cells in the ventricular zone differentiate into primordial neurons—**neuroblasts.** These embryonic cells form an **intermediate zone** (mantle layer) between the ventricular and marginal zones. Neuroblasts become neurons as they develop cytoplasmic processes

The supporting cells of the CNS—**glioblasts** (spongioblasts)—differentiate from neuroepithelial cells, mainly after neuroblast formation has ceased.



Proliferation and differentiation of neuroepithelial cells in the developing spinal cord produce thick walls and thin roof-plates and floor-plates. Differential thickening of the lateral walls of the spinal cord soon produces a shallow longitudinal groove on each side—the **sulcus limitans.** This groove separates the dorsal part, the **alar plate**, from the ventral part, the **basal plate**. The alar and basal plates produce longitudinal bulges extending through most of the length of the developing spinal cord. This regional separation is of fundamental importance because the alar and basal plates are later associated with afferent and efferent functions, respectively.

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Development of Spinal Ganglia

The unipolar neurons in the **spinal ganglia** (dorsal root ganglia) are derived from **neural crest cells**. The axons of cells in the spinal ganglia are at first bipolar, but the two processes soon unite in a T-shaped fashion. Both processes of spinal ganglion cells have the structural characteristics of axons, but the peripheral process is a dendrite in that there is conduction toward the cell body. The peripheral processes of **spinal ganglion cells** pass in the spinal nerves to sensory endings in somatic or visceral structures . The central processes enter the spinal cord and constitute the **dorsal roots of spinal nerves**.

Development of Meninges

The meninges (membranous coverings of brain and spinal cord) develop from cells of the neural crest and mesenchyme during days 20 and 35 days, which migrate to surround the neural tube (primordium of brain and spinal cord) and form the primordial meninges. The external layer of these membranes thickens to form the **dura mater** . and the internal layer, the *pia arachnoid* is composed of **pia mater** and **arachnoid mater** (**leptomeninges**). Fluid-filled spaces appear within the *leptomeninges* that soon coalesce to form the **subarachnoid space**. The origin of the pia mater and arachnoid from a single layer is indicated in the adult by **arachnoid. trabeculae**—numerous delicate strands of connective tissue that pass between the pia and arachnoid. Cerebrospinal fluid (CSF) begins to form during the fifth week.

Positional Changes of Spinal Cord

The spinal cord in the embryo extends the entire length of the vertebral canal. The spinal nerves pass through the intervertebral foramina opposite their levels of origin. Because the vertebral column and dura mater grow more rapidly than the spinal cord, this positional relationship of the spinal nerves does not persist. The caudal end of the **spinal cord in fetuses** gradually comes to lie at relatively higher levels. In a 24-week-old fetus, it lies at the level of the first sacral vertebra

The **spinal cord in the neonate** terminates at the level of the second or third lumbar vertebra **In an adult**, the cord usually terminates at the inferior border of the first lumbar vertebra

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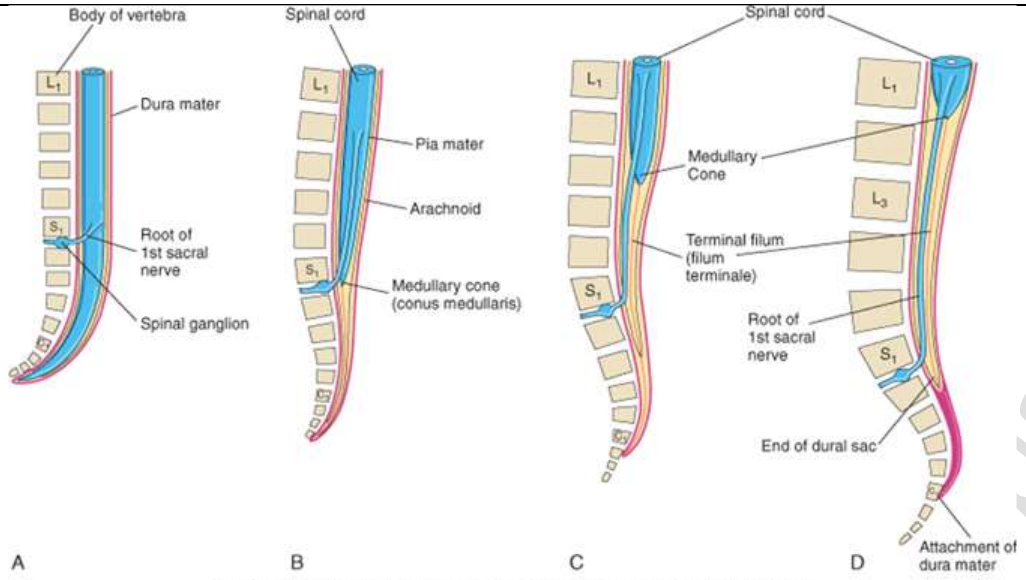

Birth Defects of Spinal Cord

Most defects result from failure of fusion of one or more neural arches of the developing vertebrae during the fourth week. **Neural tube defects** (**NTD**) affect the tissues overlying the spinal cord: meninges, vertebral arches, muscles, and skin. Birth defects involving the embryonic **neural arches** are referred to as **spina bifida**; subtypes of this defect are based on the degree and pattern of the NTD. The term—spina bifida—denotes nonfusion of the halves of the embryonic **neural arches**, which is common to all types of spina bifida. Severe defects also involve the spinal cord, meninges, and neurocranium—the bones of the cranium enclosing the brain. Spina bifida ranges from clinically significant types to minor defects that are functionally unimportant .

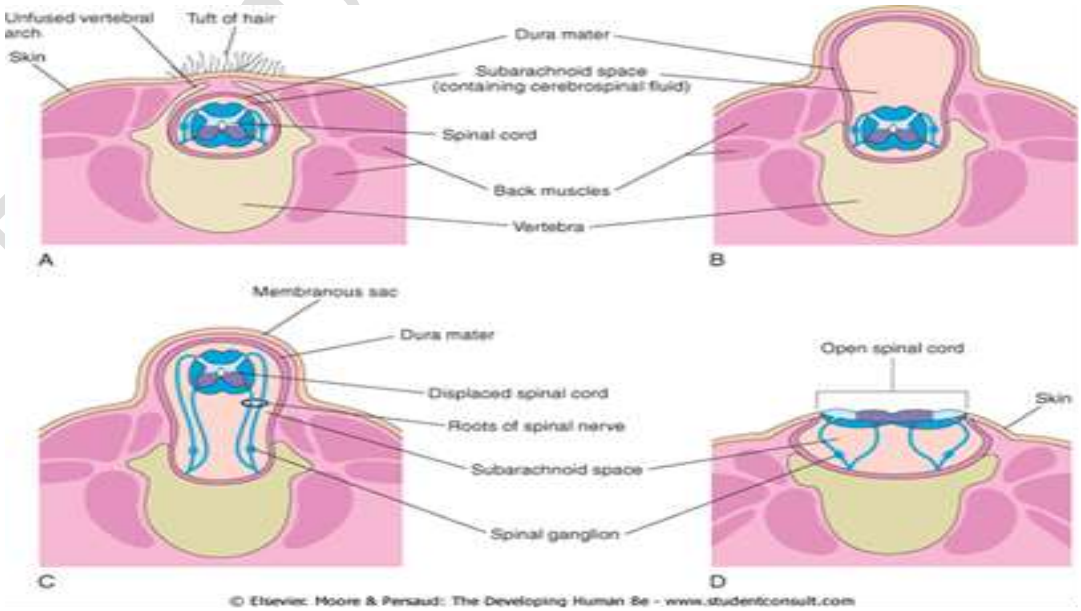

FIGURE 17–15 Infants with spina bifida cystica. **A,** Spina bifida with meningomyelocele in the lumbar region. **B,** Spina bifida with myeloschisis in the lumbar region. Note the nerve involvement has affected the lower limbs. *(Courtesy of the late Dr. Dwight Parkinson, Department of Surgery and Department of Human Anatomy and Cell Science, University of Manitoba, Winnipeg, Manitoba, Canada.)*

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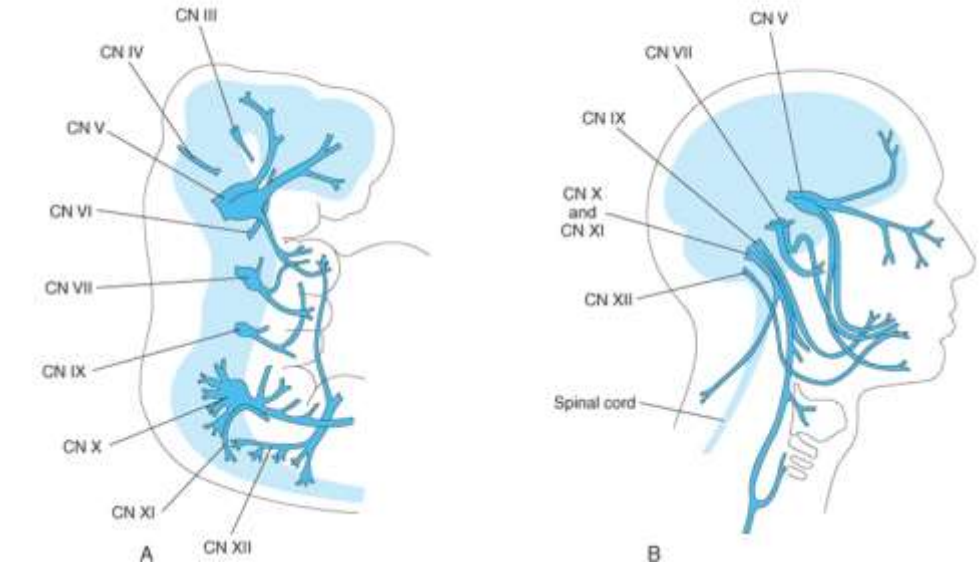
Development of Peripheral Nervous System

The Peripheral Nervous System (PNS) consists of cranial, spinal, and visceral nerves, and cranial, spinal, and autonomic ganglia. The PNS develops from various sources, mostly from the neural crest. All sensory cells (somatic and visceral) of the PNS are derived from **neural crest cells**. The cell bodies of these sensory cells are located outside the CNS. With the exception of the cells in the spiral ganglion of the cochlea and the vestibular ganglion of CN VIII (vestibulocochlear nerve), all peripheral sensory cells are at first bipolar. Later, the two processes unite to form a single process with peripheral and central components resulting in a unipolar type of neuron (Fig. 17-9*D*). The peripheral process terminates in a sensory ending, whereas the central process enters the spinal cord or brain (Fig. 17-8). The sensory cells in the ganglion of CN VIII remain bipolar.

Neural crest cells in the developing brain migrate to form sensory ganglia only in relation to the trigeminal (CN V), facial (CN VII), vestibulocochlear (CN VIII), glossopharyngeal (CN IX), and vagus (CN X) nerves. Neural crest cells also differentiate into multipolar neurons of the autonomic ganglia including ganglia of the sympathetic trunks that lie along the sides of the vertebral bodies; collateral, or prevertebral, ganglia in plexuses of the thorax and abdomen (e.g., cardiac, celiac, and mesenteric plexuses); and parasympathetic, or terminal, ganglia in or near the viscera (e.g., submucosal or Meissner plexus). Cells of the paraganglia—**chromaffin cells**—are also derived from the neural crest The term paraganglia includes several widely scattered groups of cells that are similar in many ways to medullary cells of the suprarenal glands. The cell groups largely lie retroperitoneally, often in association with sympathetic ganglia. The carotid and aortic bodies also have small islands of chromaffin cells associated with them. These widely scattered groups of cells constitute the **chromaffin system**. Neural crest cells also give rise to melanoblasts (precursors of melanocytes) and cells of the medulla of the suprarenal gland.



Spinal Nerves

Motor nerve fibers arising from the spinal cord begin to appear at the end of the fourth week (Figs. 17-4, 17-7, and 17-8). The nerve fibers arise from cells in the basal plates of the developing spinal cord and emerge as a continuous series of rootlets along its ventrolateral surface. The fibers destined for a particular developing muscle group become arranged in a bundle, forming a **ventral nerve root**. The nerve fibers of the **dorsal nerve root** are formed by axons derived from neural crest cells that migrate to the dorsolateral aspect of the spinal cord, where they differentiate into the cells of the **spinal ganglion** (Figs. 17-8 and 17-9).

The central processes of neurons in the spinal ganglion form a single bundle that grows into the spinal cord, opposite the apex of the dorsal horn of gray matter (Fig. 17-5*B* and *C*). The distal processes of spinal ganglion

cells grow toward the ventral nerve root and eventually join it to form a spinal nerve.
Immediately after being formed, a mixed spinal nerve divides into dorsal and ventral primary rami (Latin, branches). The **dorsal primary ramus**, the smaller division, innervates the dorsal axial musculature (Fig. 15-1), vertebrae, posterior intervertebral joints, and part of the skin of the back. The **ventral primary ramus**, the major division of each spinal nerve, contributes to the innervation of the limbs and ventrolateral parts of the body wall. The major nerve **plexuses** (cervical, brachial, and lumbosacral) are formed by ventral primary rami.
As the limb buds develop, the nerves from the spinal cord segments opposite to the bud elongate and grow into the limb. The nerve fibers are distributed to its muscles, which differentiate from myogenic cells that originate from the somites (see Chapter 15).
The skin of the developing limbs is also innervated in a segmental manner. Early in development, successive ventral primary rami are joined by connecting loops of nerve fibers, especially those supplying the limbs (e.g., the **brachial plexus**). The dorsal division of the trunks of these plexuses supplies the extensor muscles and the extensor surface of the limbs; the ventral divisions of the trunks supply the flexor muscles and the flexor surface.

DEVELOPMENT OF AUTONOMIC NERVOUS SYSTEM

Functionally, the ANS can be divided into sympathetic (thoracolumbar) and parasympathetic (craniosacral) parts. During the fifth week, **neural crest cells** in the thoracic region migrate along each side of the spinal cord, where they form paired cellular masses (ganglia) dorsolateral to the aorta. All these segmentally arranged **sympathetic ganglia** are connected in a bilateral chain by longitudinal nerve fibers. These ganglionated cords—**sympathetic trunks**—are located on each side of the vertebral bodies. Some neural crest cells migrate ventral to the aorta and form neurons in the **preaortic ganglia**, such as the celiac and mesenteric ganglia. Other neural crest cells migrate to the area of the heart, lungs, and gastrointestinal tract, where they form terminal ganglia in **sympathetic organ plexuses**, located near or within these organs. Parasympathetic Nervous System

The **presynaptic parasympathetic fibers** arise from neurons in nuclei of the brainstem and in the sacral region of the spinal cord. The fibers from the brainstem leave through the oculomotor (CN III), facial (CN VII), glossopharyngeal (CN IX), and vagus (CN X) nerves. The **postsynaptic neurons** are located in peripheral ganglia or in plexuses near or within the structure being innervated (e.g., the pupil of the eye and salivary glands).

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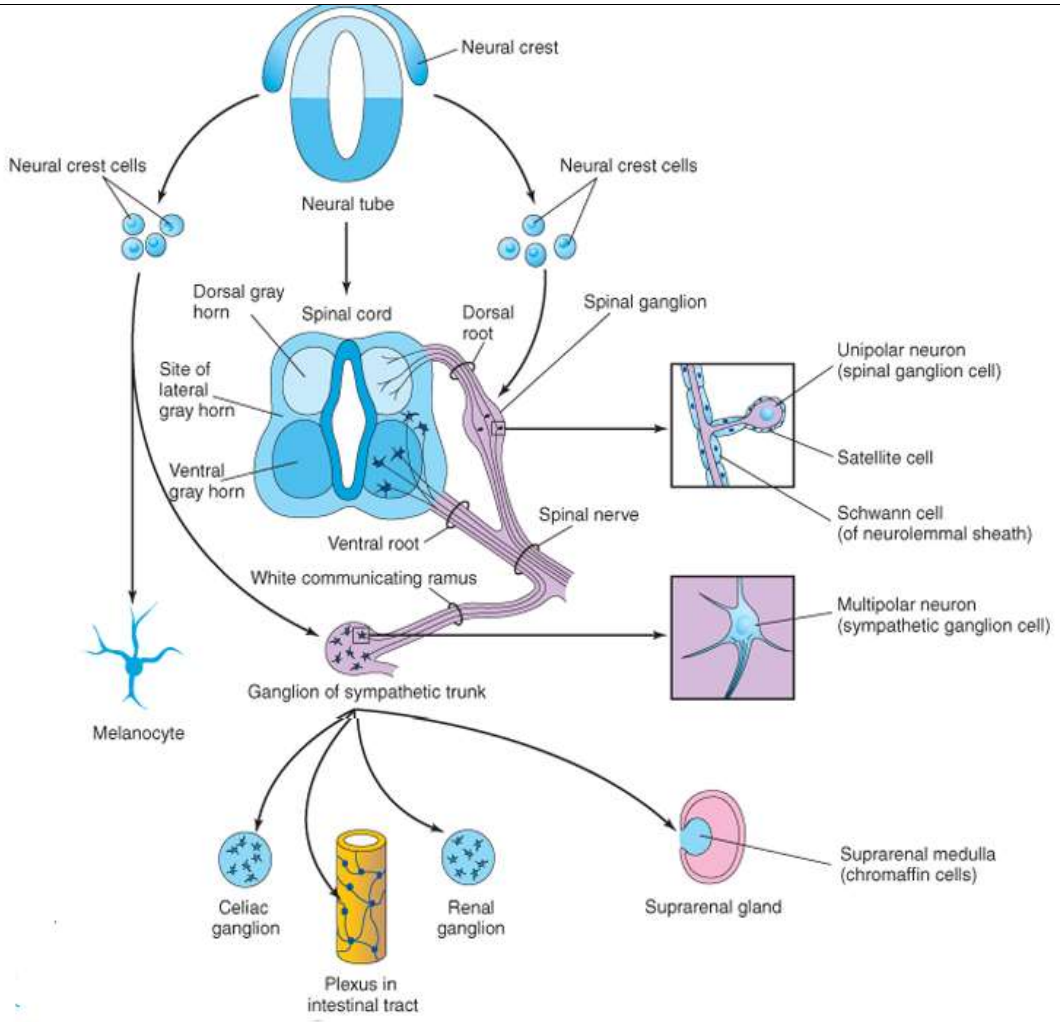
Neural crest
Neural crest cells
Neural crest cells
Neural tube
Dorsal gray horn
Spinal cord
Dorsal root
Spinal ganglion
Site of lateral gray horn
Ventral gray horn
Unipolar neuron (spinal ganglion cell)
Satellite cell
Schwann cell (of neurolemmal sheath)
Spinal nerve
Ventral root
White communicating ramus
Multipolar neuron (sympathetic ganglion cell)
Ganglion of sympathetic trunk
Melanocyte
Suprarenal medulla (chromaffin cells)
Celiac ganglion
Renal ganglion
Suprarenal gland
Plexus in intestinal tract

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Activity 2: Preparate identification and drawing	
	Chick Embryo 24 Hours
	Chick Embryo 48 Hours
	Chick Embryo 72 Hours

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Activity 3: Identify the picture
Explain the picture below

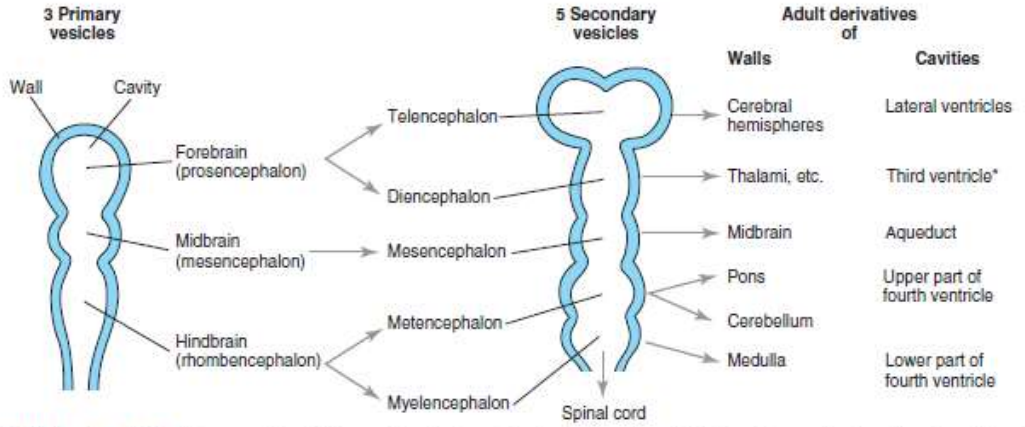

FIGURE 17–18 Diagrammatic sketches of the brain vesicles indicating the adult derivatives of their walls and cavities. The rostral part of the third ventricle (*) forms from the cavity of the telencephalon; most of this ventricle is derived from the cavity of the diencephalon.

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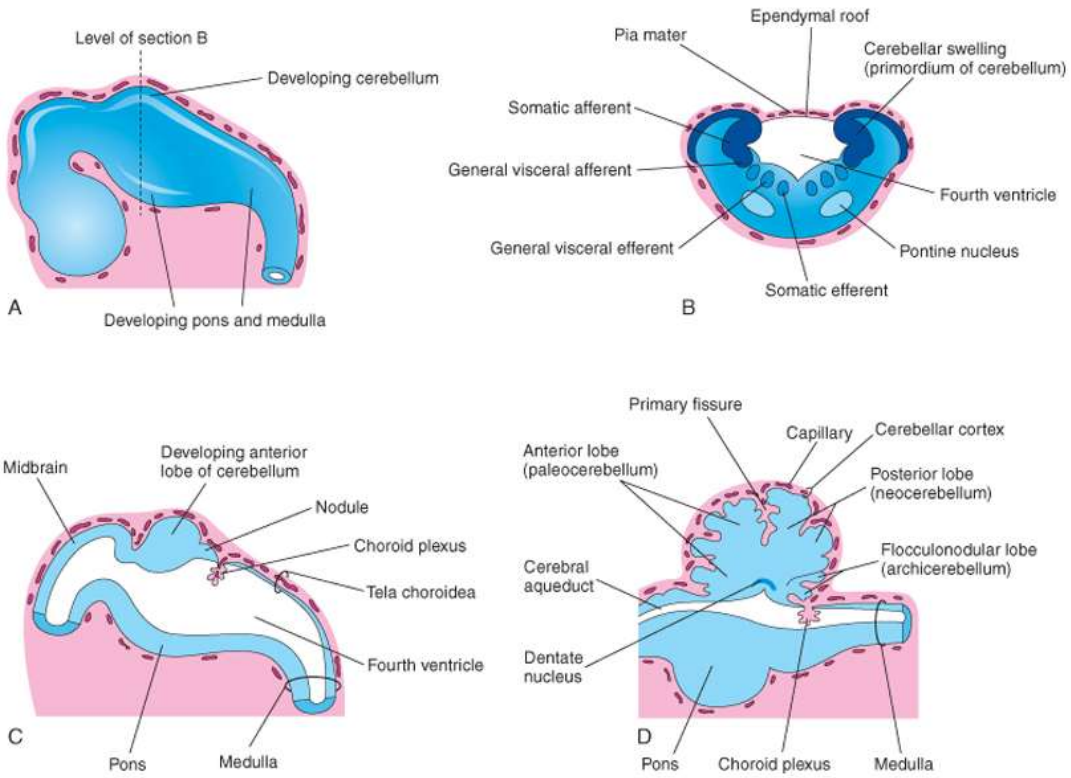

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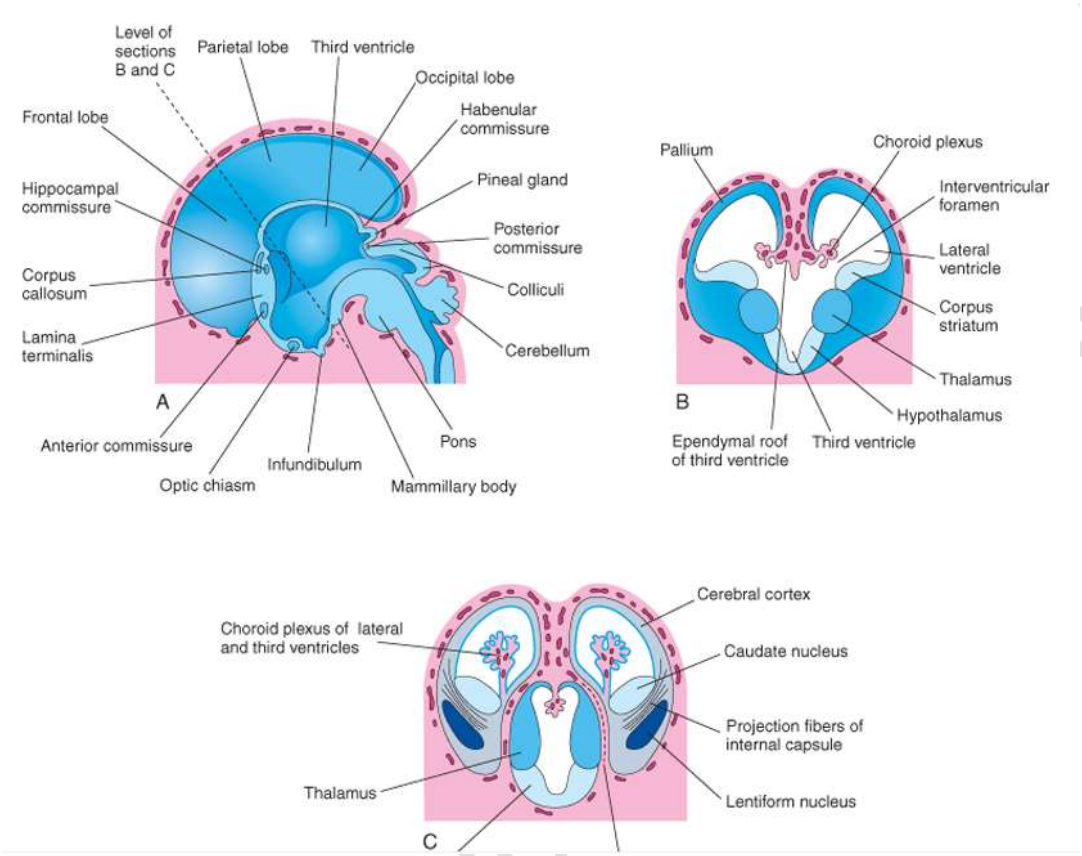
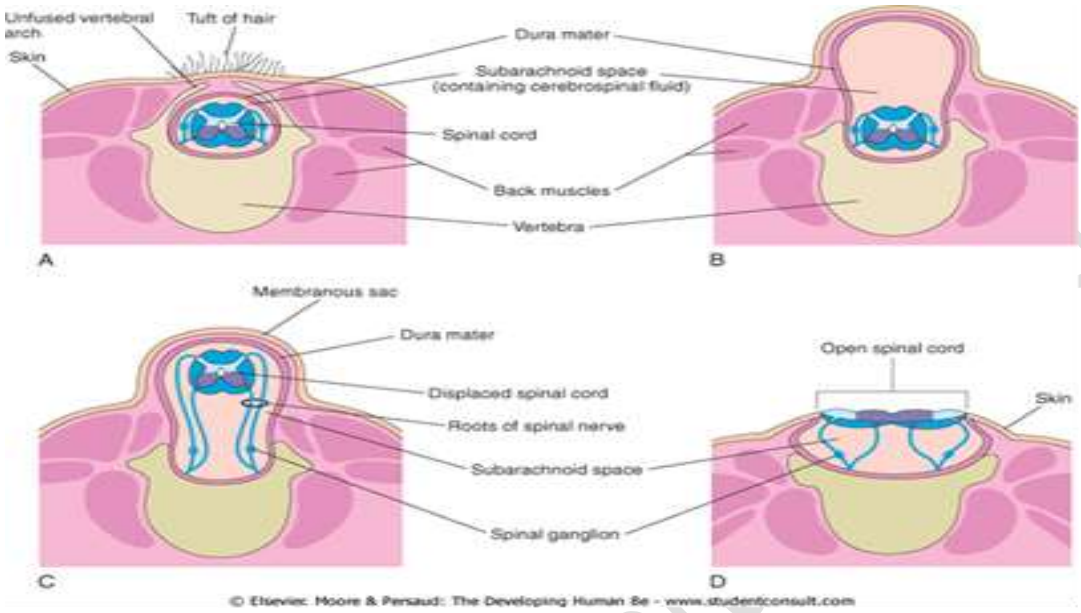
Explain The picture below



Fakultas Kedo

Explain the picture below and its risk factors / etiologies and functional consequences



Fakultas Kedokteran

Explain the picture below, its risk factors / etiologies and functional consequences

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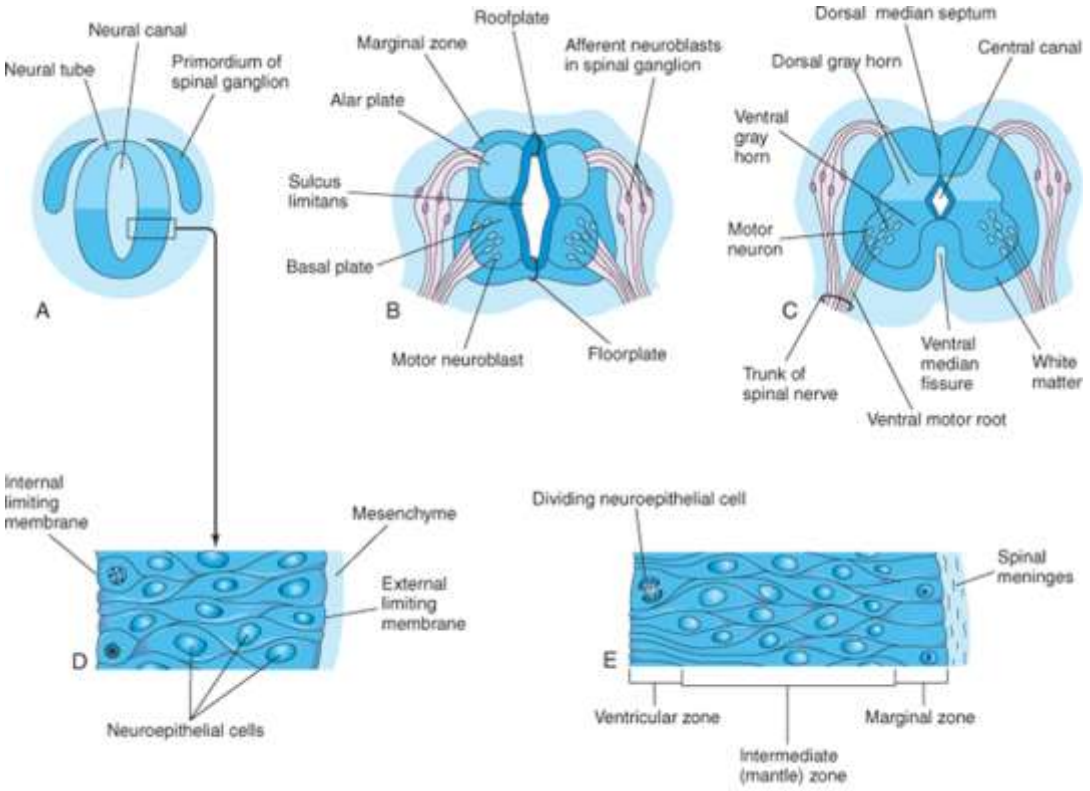
Explain the picture below



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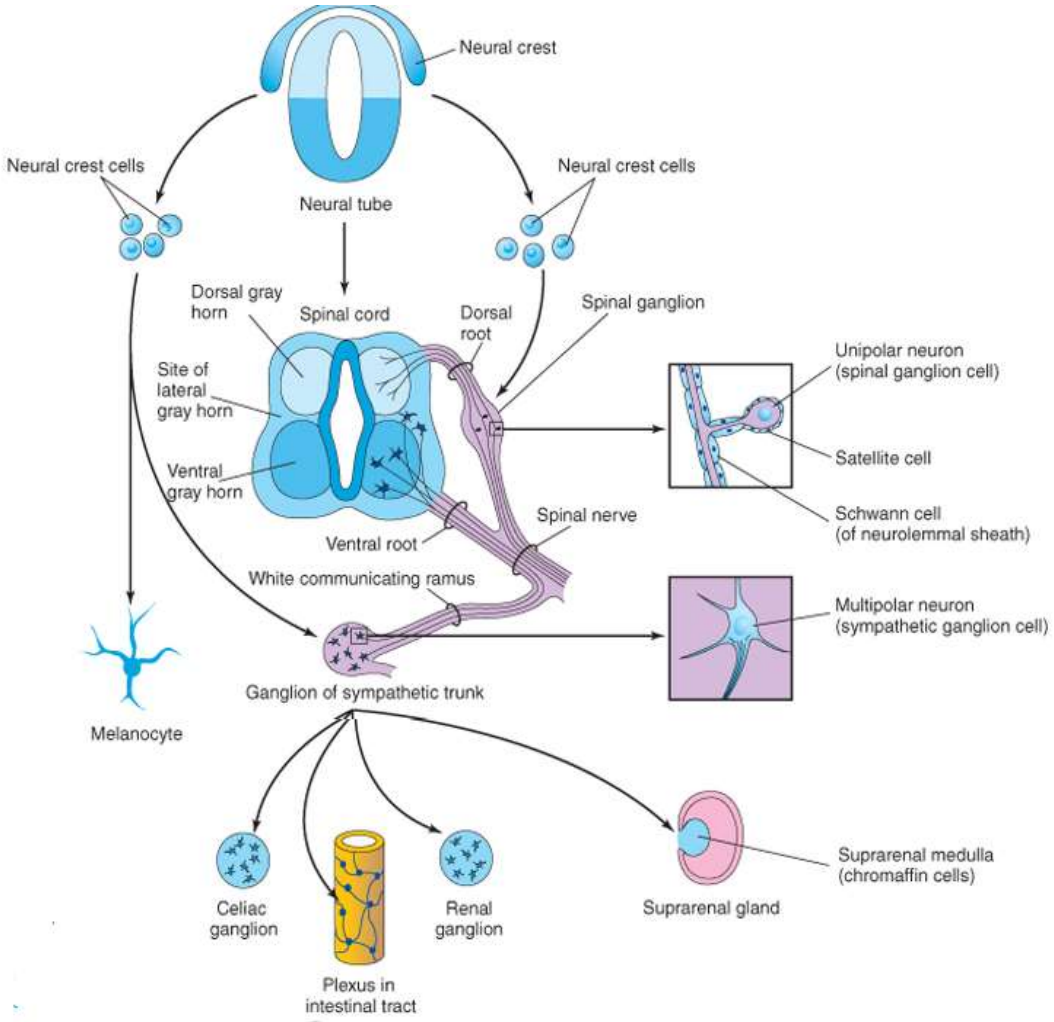
Explain the picture below



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G	References 1. Moore's The Developing Human: Clinically Oriented Embryology

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