MARROW

2024 NEET-SS

# UPDATED PEDIATRICS NOTES

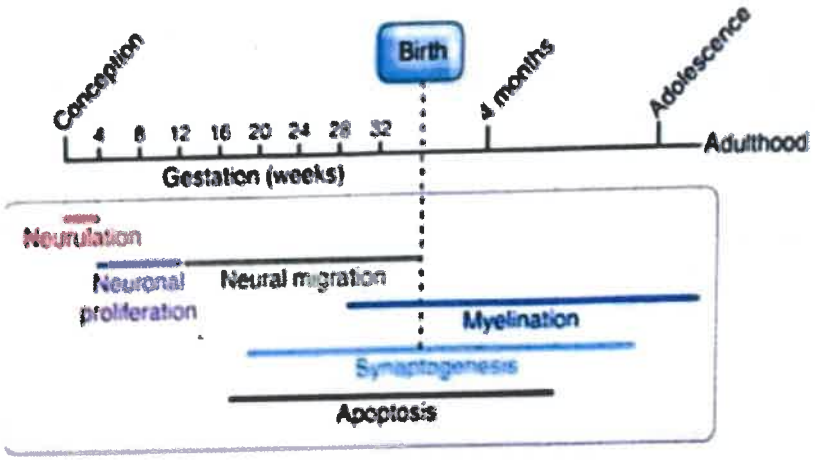
# NEUROLOGY

# CNS EMBRYOLOGY & BASICS OF MRI BRAIN

Active space

## Introduction

00:01:14




Embryology timeline.

Timeline :

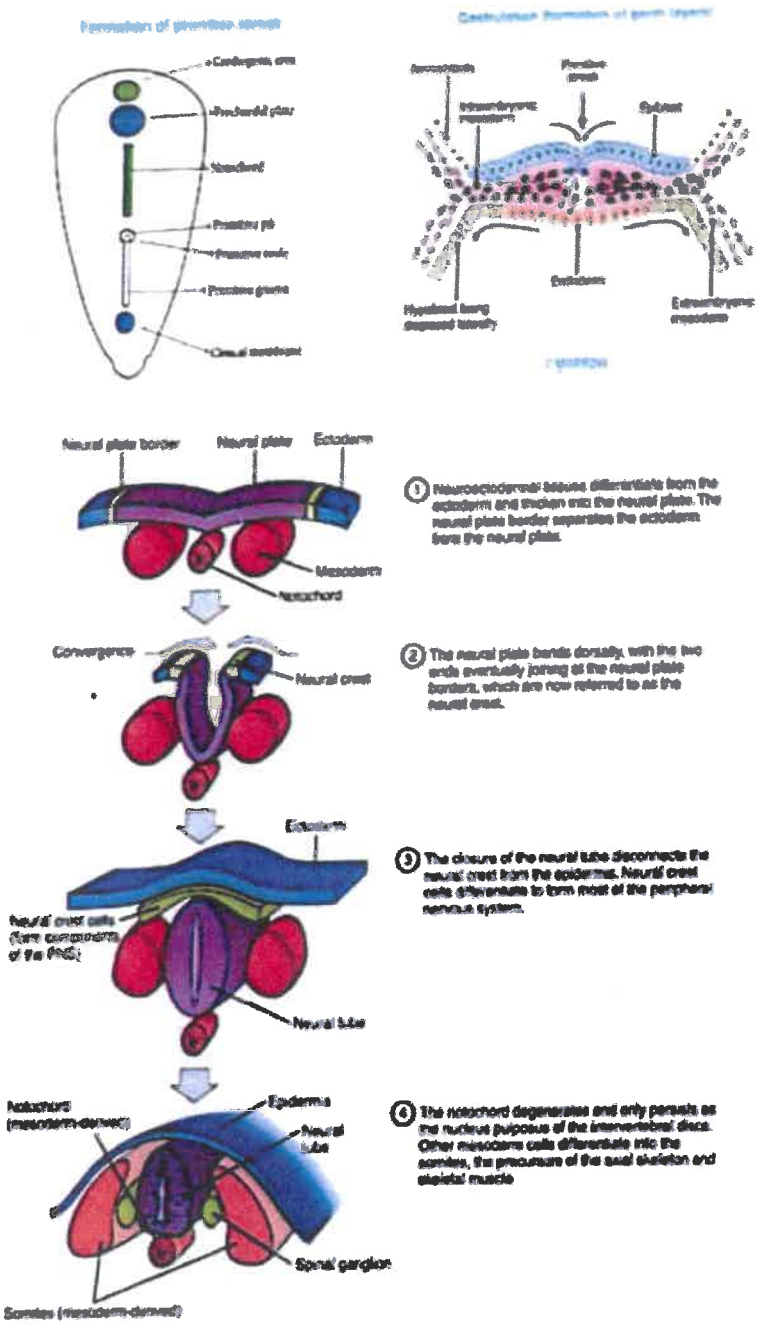
- Neurulation.
- Neuronal proliferation.
- Neural migration.
- myelination.
- Synaptogenesis.
- Apoptosis.

Gastrulation : 00:01:32

- Formation of a trilaminar embryonic disc : Endoderm, mesoderm and ectoderm.
- Gastrulation occurs in the 3rd week.
- Appearance of a primitive streak initiates gastrulation.
- It also defines the major body axes.
- Gastrulation precedes and is critical for neurulation.
- Cells from the primitive pit travel to the cephalad and form notochord in the mesoderm.
- Notochord induces formation of a plate of ectodermal cells dorsally in the midline : Neural ectoderm, which later develops into a neural plate.
- Ectoderm : Surface ectoderm and neural ectoderm.

Feedback

----- Active space -----




Formation of primitive streak, gastrulation & notocord

Neurulation : 00:10:11

- At day 17, lateral portions of the neural plate begin to thicken, forming neural folds.
- Contractile elements of neuroepithelial cells cause the neural tube to fold dorsally and fuse in the midline.
- Neurulation begins when the neural folds meet in the midline.
- Disjunction is the separation of the closed neural tube from the cutaneous

Feedback

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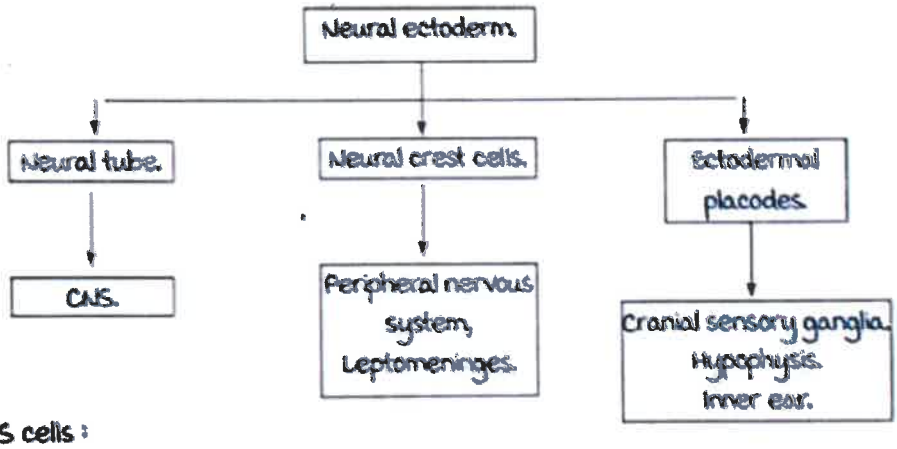
ectoderm.

- The anterior neuropore, the region that will eventually give rise to the brain, closes approximately by day 26. (If not closed : Encephalocele).
- The posterior neuropore, the region that will give rise to the caudal spinal column, closes approximately by day 29. (If not closed : meningomyelocele, Spina bifida).
- Neural crest cells arise from the neural plate's lateral edges during the neural tube formation.
- Some areas of neuroepithelium become incorporated into the surface ectoderm : Ectodermal placodes.




CNS cells :

1. Neuronal
2. Non neuronal :
   - Macroglia : Astrocytes, ependymal cells & oligodendrocytes.
   - Microglia.

Microglia : mesodermal in origin.

Neuronal cells and macroglia : Ectodermal in origin.

Leptomeninges : Origin is from surface ectoderm.

Duramater : mesodermal in origin.

## Development of brain

00:14:08

- By the time the neural tube is completely closed, it is divisible into an enlarged cranial part and an elongated caudal part, which later gives rise to the brain and spinal cord, respectively.
- With the closure of the anterior neuropore, three brain vesicles develop.

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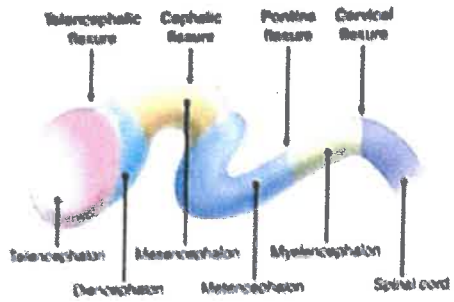
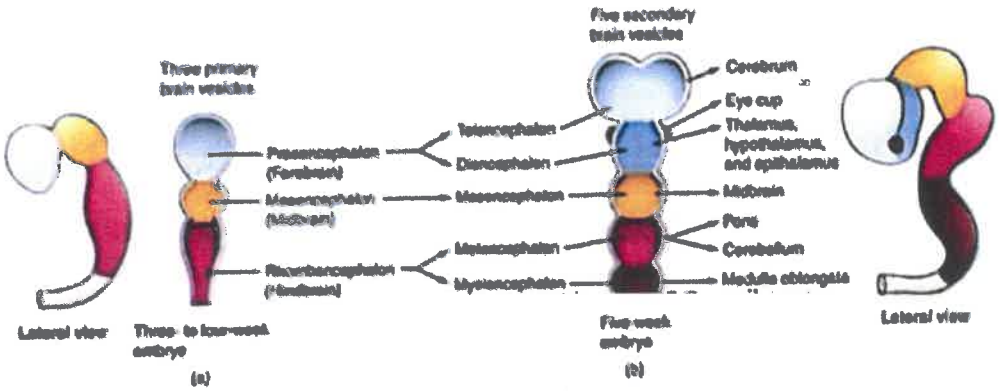
- The three subdivisions are prosencephalon, mesencephalon and rhombencephalon.
- 3 flexures : Cranial (mesencephalic), cervical flexures ventrally, and pontine flexure dorsally.

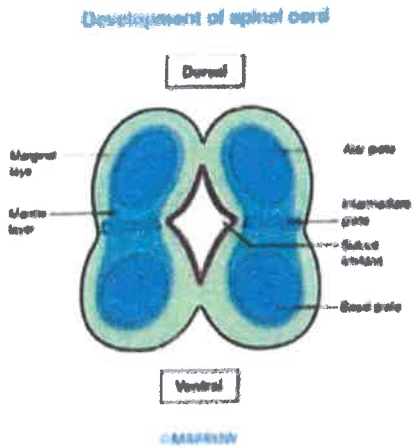



Development of brain.

Cross section of neural tube :

- A longitudinal groove (Sulcus limitans) divides the neural tube into two parts or laminae : Alar plate and basal plate.
- Alar plate lies dorsally and gives rise to sensory neurons (SAD).
- Basal plate lies ventrally and gives rise to motor neurons (MBV).
- marginal layer develops into white matter.
- mantle layer develops into grey matter.

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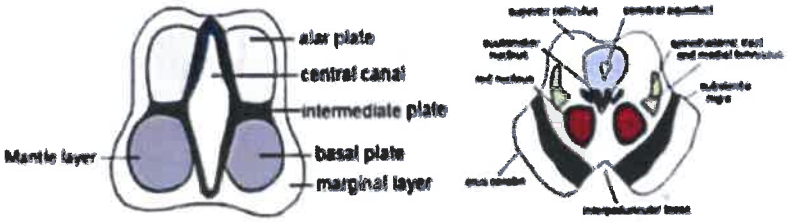
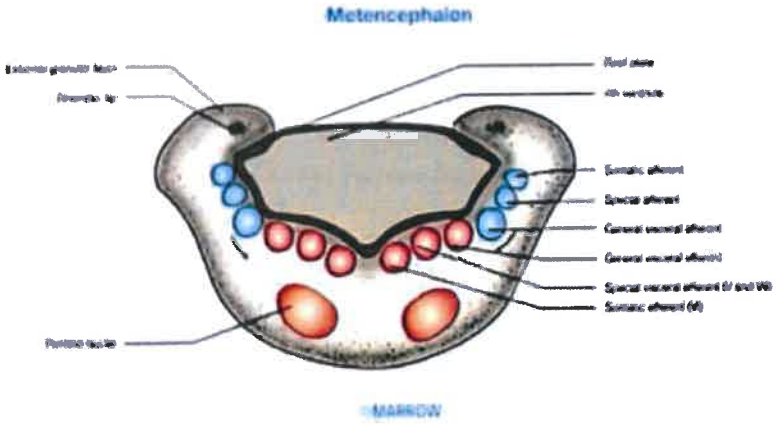
## Mesencephalon to midbrain :




- marginal layer develops into white matter.
- marginal layer proliferates ventrally and forms the crus cerebri

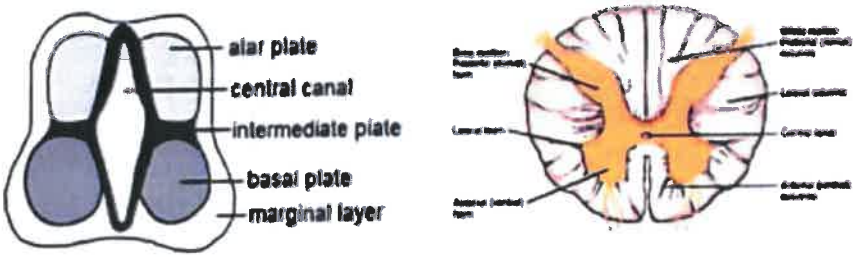
## Metencephalon to pons and cerebellum :

- In the rhombencephalon, the walls of the neural tube splay open dorsally so that the roof plate is stretched and widened.
- The dorsal margin of the alar plate, adjoining the massively expanded roof plate, is called the rhombic lip.
- The rhombic lip then develops cerebellar plates and, later, the cerebellum.
- The alar plate cells forms the pontine nuclei.




## myelencephalon to medulla oblongata :

Caudal to that develops into spinal cord.

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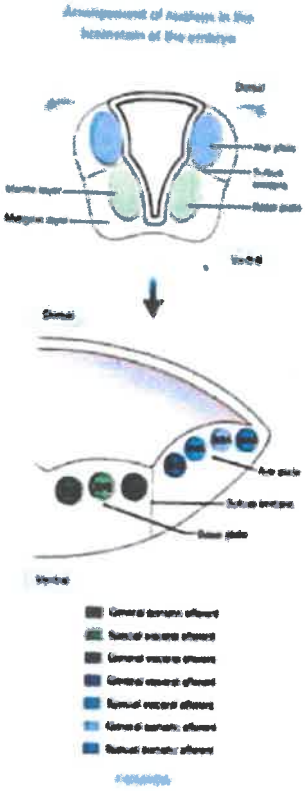
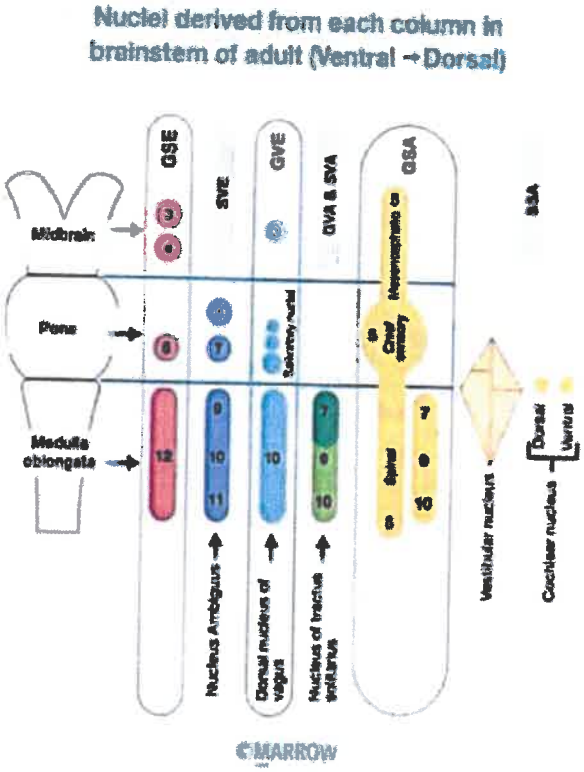
Brain stem nuclei orientation :

00:24:04

- Cells in each lamina (Alar and basal) organize into longitudinal columns : Visceral and somatic.
- Somatic components : Derivatives of 'somites' derived from mesoderm.
- All striated muscles of limbs and body wall and muscles of extraocular movements and tongue are somatic.
- Visceral components lie close to the sulcus limitans.
- Another special column appears between visceral and somatic columns : Supply derivatives of pharyngeal arches.



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Cranial nerve nuclei derived from various functional columns in the brainstem :

| GSE column | SVE column | GVE column | GVA/SVA column | GSA column | SSA column |
|---|---|---|---|---|---|
| Oculomotor nucleus | motor nucleus of trigeminal nerve | Edinger - Westphal nucleus | Nucleus of solitary tract (Nucleus tractus solitarius) | Sensory nuclei of trigeminal n. | Vestibular nuclei |
| Trochlear nucleus | motor nucleus of facial nerve | Lacrimatory nucleus | | 1. Chief | Cochlear nuclei |
| Abducent nucleus | Nucleus ambiguus | Superior salivatory nucleus | | 2. Mesencephalic | |
| Hypoglossal nucleus | | Inferior salivatory nucleus | | 3. Spinal | |
| | | Dorsal nucleus of vagus nerve | | | |

Major events in human brain development : 00:31:50

| Major events in human brain development : | |
|---|---|
| Gastrulation | 3 weeks POG |
| Primary neurulation | 3-4 weeks POG |
| Prosencephalic development | 2-3 months POG |
| Neuronal proliferation | 3-4 months POG |
| Neuronal migration | 3-5 months POG |
| Organisation | 5 months-years postnatally |
| Myelination | Birth to years postnatally |

Development of cerebral cortex :

- Neuroblasts proliferate in the ventricular zone & later in the subventricular zone.
- Then, they migrate towards the marginal layer through radial migration.
- Projection neurons undergo radial migration.
- Inhibitory interneurons undergo tangential migration.
- The early-generated neurons form the initial cortical plate, and later-generated neurons climb past them to become progressively more superficial.
- This gives an "inside-out" pattern.
- The marginal layer becomes the later layer I of the cortex.

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- The earliest neurons to migrate end up in layer 6, and the last to migrate end up in layer 2.
- The 6-layered cortex is formed by 24 to 27 weeks.
- Further organization in the form of myelination, synaptic maturation, gyri, sulci formation continues even postnatally.

## Basics of MRI brain 00:36:30

3 major sequences :

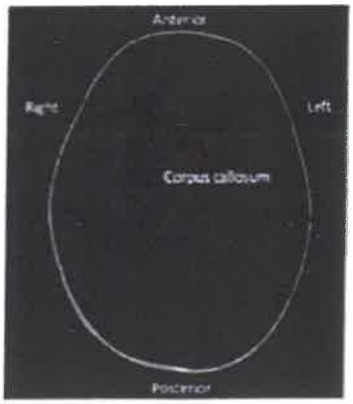
- T1.
- T2.
- T2 FLAIR.

3 views :

- Axial
- Sagittal.
- Coronal

Axial T1 :

- White matter is white.
- Grey matter is dark.
- CSF is black.
- Good for structural malformations.



Axial T1

T1 bright :

- Fat (myelin).
- melanin.
- Subacute bleed.
- manganese, copper.
- Contrast.
- Posterior pituitary gland.

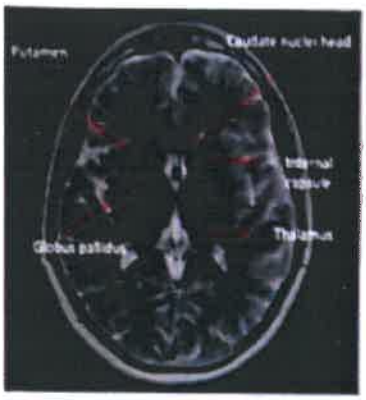
Axial T2 :

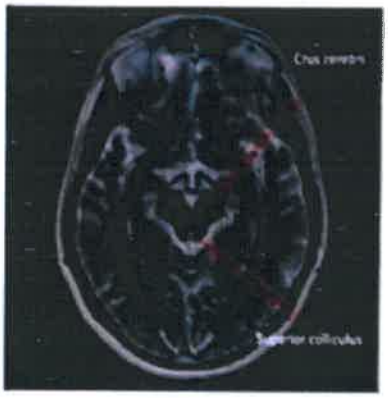
- White matter is dark.
- Grey matter is light.
- CSF is white.

WW2 : World War 2.

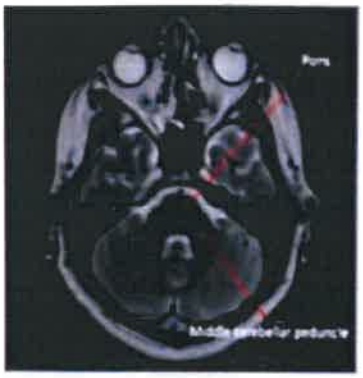
Water is white in T2.


Axial T2

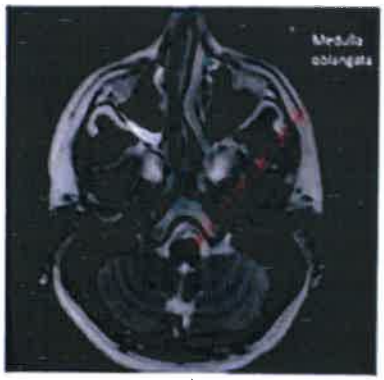


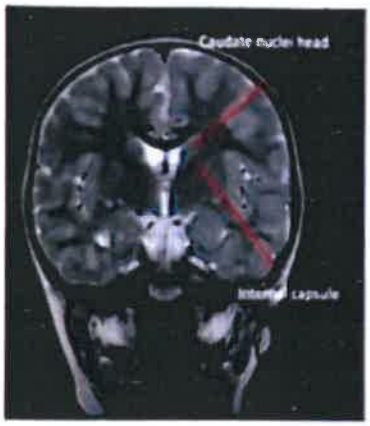

Midbrain



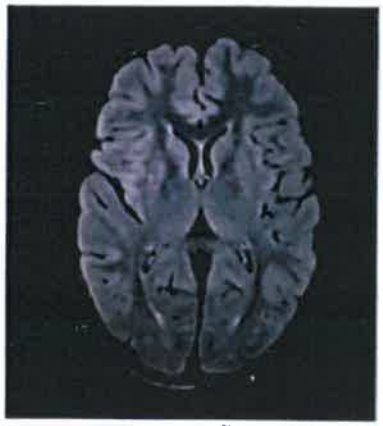

Pons




Medulla




Coronal T2



Axial T2 flair

**Axial T2 FLAIR :**

- T2 weighted sequence.
- Fluid/CSF : Dark.
- White matter lesions are highlighted

# CONGENITAL CNS STRUCTURAL MALFORMATIONS PART I

## Neural tube defects

00:00:21

Introduction :

- Results from the failure of the neural tube to close spontaneously between 3rd and 4th week of gestation.
- Most common congenital anomalies of CNS.
- Major NTDs (Neural Tube Defects) include : Spina bifida occulta, meningocele, myelomeningocele, encephalocele, anencephaly, caudal regression syndrome, dermal sinus, tethered cord, syringomyelia, diastematomyelia, lipoma involving the conus medullaris and/or filum terminale and iniencephaly.

Risk factors for NTD :

- Hyperthermia.
- Drugs : Valproic acid, phenytoin.
- Malnutrition.
- Low red cell folate levels, chemicals, maternal obesity or diabetes.
- Mutations in folate pathways.

Risk of recurrence :

- Affected child : 3-4%.
- 2 affected children : 10%.

Prevention :

- maternal periconceptional use of folic acid supplementation : Reduces the incidence of NTDs by at least 50%.
- Should be initiated before conception and continued until at least the 12th week of gestation, when neurulation is complete.
- Dose : 0.4 mg (4 mg in those with previous pregnancy with NTD).

Screening :

- Failure of closure of the neural tube allows excretion of fetal substances : Alpha-fetoprotein (AFP) and acetylcholinesterase into the amniotic fluid.
- Prenatal screening of maternal serum for AFP in the 16th-18th week of gesta-

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tion : Detect NTD.

**Closed spinal cord malformations :**

Spina bifida occulta :

midline fusion defect of posterior vertebral body with no spinal cord protrusion.

No clinical symptoms or neurological signs.

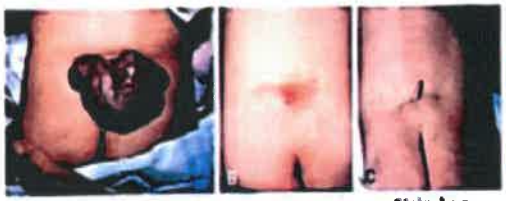
Occult spinal dysraphism :

Clinically significant closed spinal cord malformations.

Syringomyelia, diastematomyelia, lipoma, fatty filum, dermal sinus, tethered cord.

Most have cutaneous stigmata.

Hair patch.



Hemagioma. Patch. Skin tag.

Cutaneous Lesions associated with Occult Spinal Dysraphism

| |
|---|
| **Imaging Indicated** |
| Subcutaneous mass or lipoma |
| Hairy patch |
| Dermal sinus or cyst |
| Atypical dimples (deep, > 5 mm, > 25 mm from anal verge) |
| Vascular lesion, e.g., hemangioma or telangiectasia |
| Skin appendages or polypoid lesions, e.g., skin tags, tail-like appendages |
| Scar-like lesions (aplasia cutis) |
| **Imaging Uncertain** |
| Hyperpigmented patches |
| Deviation of the gluteal fold |
| **Imaging not Required** |
| Simple dimples (< 5 mm, < 25 mm from anal verge) |
| Coccygeal pits |

**Meningocele :**

- Meninges herniate through a defect in the posterior vertebral arches/anterior sacrum.
- Spinal cord : usually normal in position.
- Most have intact overlying skin.
- Patients with leaking CSF or a thin skin covering should undergo immediate surgical treatment to prevent meningitis.
- CT scan/MRI of the head is recommended for children with a meningocele because of the association with hydrocephalus.

**Myelomeningocele (MMC) :**

M/C neural tube defect.

Lumbosacral region : 75%.

Feedback

Clinical manifestations :

- Depend on location and associated lesions.
- Flaccid paralysis of the lower limbs, absent DTRs, loss of touch and pain.
- High incidence of lower-extremity deformities : Clubfeet, ankle and/or knee contractures and subluxation of the hips.
- Bowel and bladder incontinence.

Complications :

- Hydrocephalus with cerebellar herniation and thin elongated medulla in 90% cases : Chiari 2 malformation (Arnold Chiari malformation).
- Chiari crisis :
  Symptoms of brainstem dysfunctions in Chiari 2.
  Feeding difficulty, choking, stridor, apnea, vocal cord paralysis, pooling of secretions and spasticity.

Surgery :

- mmc repair within 72 hours in case of CSF leak.
- Followed by hydrocephalus management by ventriculoperitoneal (VP) shunt.

most important prognostic factors :

- Renal complications.
- Tethered cord.

**Skull dysraphisms :**

Cranial meningocele : CSF-filled sac protruding through skull defect.

Cranial meningoencephalocele :

- Part of the cerebral cortex or cerebellum or brainstem also along with the sac.
- Occipital region is the most common site.

meckel Gruber syndrome :

- Autosomal recessive.
- Triad of occipital encephalocele, polycystic kidney and post-axial polydactyly.

**moms study :**

- Management of Myelomeningocele Study.
- Randomized controlled trial.
- Prenatal repair of mmc vs post natal repair.

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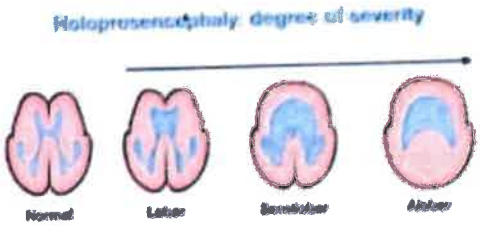
- Primary outcome : Death or need for VP shunt at 12 months.
- Statistically significant results in prenatal repair group.
- Study terminated based on the interim results of positive efficacy.

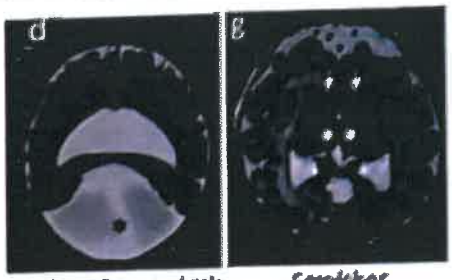
## Disorders of forebrain development

06.10.07

Holoprosencephaly :

- Defective formation of the prosencephalon and inadequate induction of forebrain structures.
- Types : Alobar, semi lobar, lobar and syntelencephaly.
- Facial abnormalities associated with severe cases : Cyclopia, synophthalmia, cebocephaly, single nostril, choanal atresia, solitary central incisor tooth and premaxillary agenesis.
- Associated with Sonic hedgehog gene (SHH) mutations.




Single midline ventricle : Alobar.

Semilobar.

Septooptic dysplasia :

Triad of optic nerve hypoplasia, pituitary abnormalities, and midline brain defects (involving septum pellucidum or corpus callosum).

Clinical presentation :

- Features of pituitary hormone abnormalities : Hypoglycemia, microphallus at birth, growth failure and other endocrine manifestations throughout childhood.
- Nystagmus, midline cranial defects: cleft lip or palate.

Any child with nystagmus should be evaluated for optic nerve hypoplasia and anterior pituitary insufficiency

Two genes : HESX1, SOX2.

Pituitary insufficiency management is crucial.

Agenesis of corpus callosum :

most common birth defect of CNS after spina bifida.

Development of corpus callosum : From commissural plate that lies in proximity

Feedback

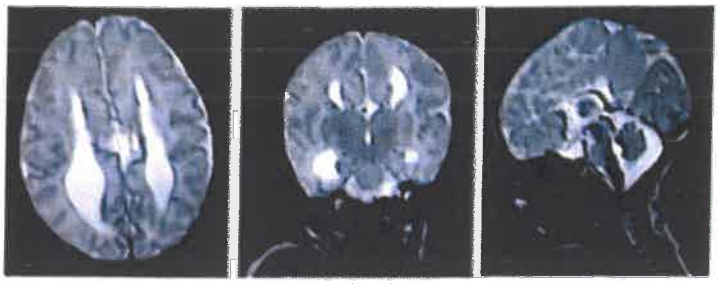
to the anterior neuropore.

MRI :

- Widely separated frontal horns with an abnormally high position of the third ventricle between the lateral ventricles.
- Racing car in axial section.
- Viking helmet appearance in coronal section.

Genetics : Trisomy 8 and 18.

Non-genetic factor : Fetal alcohol syndrome.



Parallel frontal horns of lateral ventricle. Viking helmet sign. No corpus callosum.

Aicardi syndrome :

- Triad : Corpus callosum agenesis, chorioretinal lacunae and infantile spasms.
- Exclusively seen in girls.

Feedback

# CONGENITAL CNS STRUCTURAL MALFORMATIONS PART II

Active space

## Disorders of cortical development 00.00:14

**Development of cortex :**

Three layers of neural tube :

- Neuroepithelial cell layer.
- mantle cell layer.
- marginal cell layer.

marginal cell layer later becomes → white matter.

mantle cell layer later become → Grey matter.

In the brain cortex → Cells from neuroepithelium proliferate and migrate to the surface → Grey matter forms the outer surface.

**Lissencephaly :**

- Absence of cerebral convolutions and a poorly formed sylvian fissure, giving the appearance of a 3 – 4 months fetal brain.
- Agyria : Complete, Pachygyria : Incomplete.
- Cortex is thick.
- Figure of 5 or hour-glass appearance in MRI.
- microcephaly, global developmental delay, epilepsy, dysmorphic facies.
- 15% associated with Miller-Dieker syndrome, 17p13.3 deletion.
- LIS1 gene mutation (PAFAH1B1 gene) : Posterior predominant lissencephaly.
- DCX gene mutation : Doublecortin (X-linked gene).
  - males : Anterior predominant lissencephaly.
  - Female relatives : Sub-cortical band heterotopia.
- ARX : XLAG (X-linked lissencephaly with abnormal genitalia).
- Type 2 lissencephaly/cobblestone lissencephaly : Associated with congenital muscular dystrophy (CMD).

MRI : Posterior predominant lissencephaly (PAFAH1B1 gene).

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## Schizencephaly :

Presence of unilateral or bilateral clefts within the cerebral hemispheres.

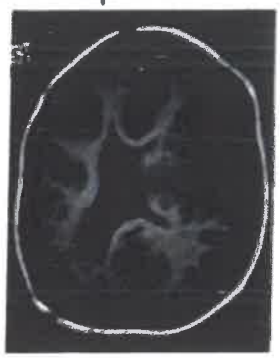
Closed lip :

- No communication with the ventricles.
- Presents with hemiparesis, good prognosis.

Open lip :

- Communicates with the ventricles.
- Presents with hydrocephalus or seizures.

mostly lined by polymicrogyria.



MRI : Schizencephaly.

Radiological differential :

- Porencephaly → Presence of cysts or cavities within the brain that result from developmental defects or acquired lesions like infarction or bleed.
- Differentiated by the presence of grey matter lining in schizencephaly.

Worst prognosis : Bilateral open lip schizencephaly.

## Porencephaly :

- Presence of cysts or cavities within the brain.
- most common site : Perisylvian region.
- most communicate with ventricles or subarachnoid space.
- differentiated from schizencephaly by the lining (Lined by white matter).
- Risk factors : Hemorrhagic venous infarctions, protein C deficiency and factor V Leiden mutations, perinatal alloimmune thrombocytopenia, von Willebrand disease, maternal warfarin use, maternal cocaine use, congenital infections, trauma such as amniocentesis and maternal abdominal trauma.
- Familial porencephaly : COL4A1 and COL4A2 genes.

## Neuronal heterotopia :

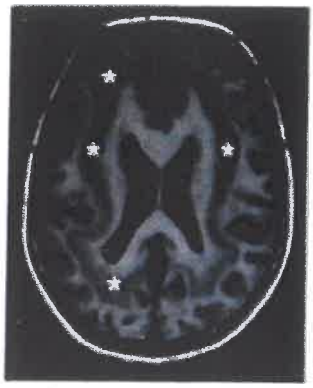
Presence of normal tissue in an abnormal location.

Types :

1. Periventricular nodular heterotopia : most common.
2. Subcortical and band heterotopia.
3. Glioneuronal heterotopia : Brain warts.

Seizures usually the presenting complaint.

FLNA gene : X-linked, more common in females.



MRI : Subcortical band heterotropia.

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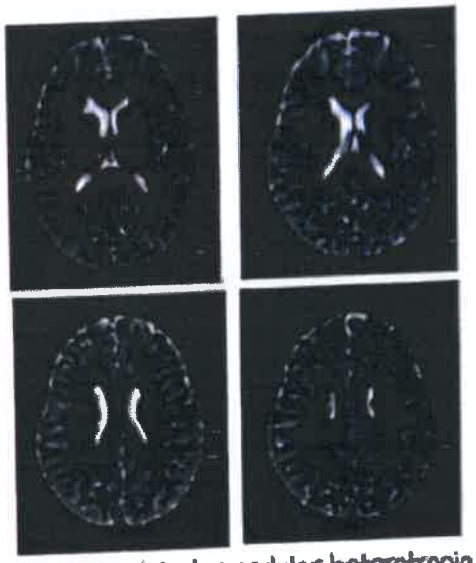


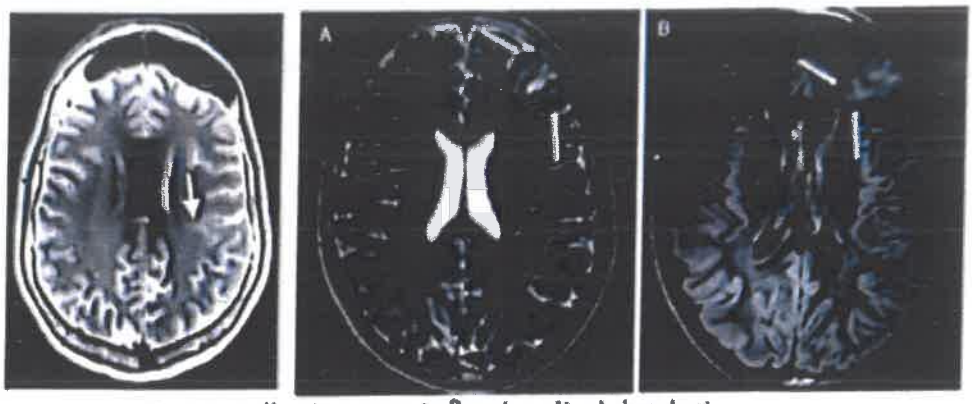
MRI : Periventricular nodular heterotropia.

Focal cortical dysplasia :

| Type | Subtype |
|---|---|
| FCD type I (Isolated) | 1a : Focal cortical dysplasia with abnormal radial cortical lamination.<br>1b : Focal cortical dysplasia with abnormal tangential cortical lamination.<br>1c : Focal cortical dysplasia with abnormal radial and tangential cortical lamination. |
| FCD type 2 (Isolated) | 2a : Focal cortical dysplasia with dysmorphic neurons.<br>2b : Focal cortical dysplasia with dysmorphic neurons and balloon cells. |
| FCD type 3 (Associated with principal lesion) | 3a : Cortical lamination abnormalities in the temporal lobe associated with hippocampal sclerosis.<br>3b : Cortical lamination abnormalities adjacent to a glial or glioneuronal tumor.<br>3c : Cortical lamination abnormalities adjacent to vascular malformation.<br>3d : Cortical lamination abnormalities adjacent ot any other lesion acquired during early life. Eg : Trauma, ischaemic injury, encephalitis.<br>3NOS : Cortical lamination abnormalities adjacent to a clinically or radiologically suspected principal lesion is not available for microscopic inspection. |

Classification of focal cortical dysplasia.

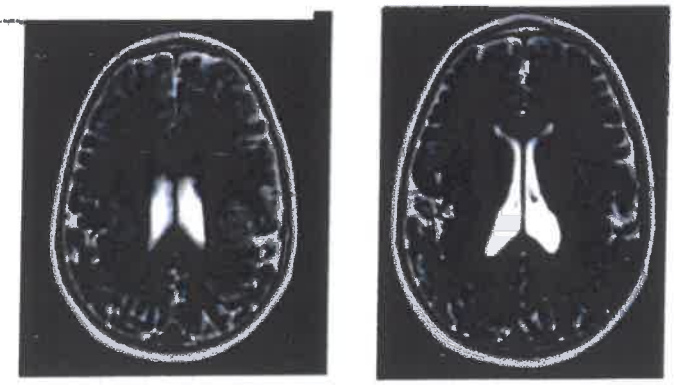
Active space



Transmantle sign seen in focal cortical dysplasia.

Polymicrogyria (PMG):

- The surface of the brain carries multiple and small convolutions separated by shallow enlarged sulci.
- May be found lining schizencephaly.
- Bilateral perisylvian: most common type.
- Congenital bilateral perisylvian syndrome: Bilateral perisylvian PMG, oromotor dysfunction and epilepsy.
- Non-genetic etiology: CMV.
- Genetic etiologies: 22q11.2 deletion (Di George syndrome), Zellweger syndrome, ADGRG1 (GPR56) leads to bilateral frontoparietal polymicrogyria (BFPP).



Perisylvian polymicrogyria.

Feedback

| Syndrome | PMG Pattern | Other Features | Genetic Basis |
|---|---|---|---|
| Aicardi | Variable, multifocal | Agenesis of corpus callosum, ocular lacunae | X-linked, *AIC1* deletion |
| Chudley-McCullough | Frontal | Sensorineural hearing loss, hydrocephalus, agenesis of corpus callosum | *CPSAQ* mutations |
| DiGeorge/velocardiofacial | Perisylvian, unilateral or bilateral | Cardiac defects, parathyroid hypoplasia, facial dysmorphism, thymus hypoplasia | 22q11.2 deletion |
| Ehlers-Danlos | Perisylvian and frontal | Skin fragility, cutaneous extensibility, joint laxity, bruising | Multiple genes |
| Kabuki make-up (Niikawa-Kuroki) | Perisylvian | Facial dysmorphism, digital anomalies, skeletal anomalies, microcephaly | *MLL2* and *KDM6A* mutations |
| Knobloch | Frontal | Eye abnormalities, occipital skull defects | *COL18A1* mutations |
| Leigh and other mitochondrial disorders, including PDH deficiency | Variable | Multiple CNS abnormalities, lactic acidosis, neurodegeneration, ocular microcomas | Mitochondrial, including respiratory chain disorders |
| Meckel-Gruber | Variable | Occipital meningoencephalocele, anencephaly, polycystic kidneys, polydactyly, bile duct abnormalities | Autosomal recessive, multiple genes |
| Megalencephaly capillary malformation polymicrogyria (MCAP) | Variable | Macrocephaly, vascular malformations, syndactyly, occasional hyperelasticity or thick skin | *PIK3CA* mutations |
| Megalencephaly polymicrogyria polydactyly hydrocephalus (MPPH) | Variable | Macrocephaly, polydactyly | *PIK3R2* and *AKT3* mutations |
| Warburg Micro | Frontal | Microcephaly, cataracts, microcornea, optic atrophy, hypogenitalism, hypoplasia of corpus callosum | *RAB3GAP* mutations |
| Oculocerebrocutaneous (Delleman) | Frontal | Orbital anomalies, skin defects, and multiple brain anomalies | Possibly autosomal dominant, gene unknown |
| Pena-Shokeir | Variable | IUGR, camptodactyly, multiple ankyloses, facial dysmorphism, pulmonary hypoplasia | Autosomal recessive, multiple genes |
| Sturge-Weber | Underlying cortical angiomatosis | Facial hemangioma, glaucoma | Somatic mutations in *GNAQ* |
| Thanatophoric dysplasia | Temporal | Skeletal anomalies, hypoplastic lungs, megalencephaly | Autosomal dominant, multiple genes |
| Zellweger and other peroxisomal disorders | Generalized | White matter dysmyelination, facial dysmorphism, intrahepatic biliary dysgenesis, stippled epiphyses, renal cysts | Peroxisomal (*PEX*, *PXMP*, and *PXR* gene family mutations) |

Syndromes with polymicrogyria.

## Disorders of posterior fossa development 00:19:50

Joubert syndrome :

- Autosomal recessive ciliopathy.
- Cerebellar vermis hypoplasia and the pontomesencephalic molar tooth sign (A deepening of the interpeduncular fossa with thick and straight superior cerebellar peduncles).
- Hypotonia, ataxia, characteristic breathing abnormalities including episodic apnea and hyperpnea (which improves with age), global developmental delay, nystagmus, strabismus, ptosis, and oculomotor apraxia.