

GENERAL - Congenital CNS Anomalies

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CLASSIFICATION	1
ETIOPATHOPHYSIOLOGY	2
EPIDEMIOLOGY	2
DIAGNOSIS	2

CLASSIFICATION

ABNORMAL FORMATION OF NOTOCHORD (neurenteric canal disorders):

- 1) **neuro-enteric cyst** – due to neurenteric canal persistence.
- 2) **diastematomyelia, diplomyelia** – aberrant neuro-entodermal adhesions → split notochord and secondary splitting of neural plate and vertebral bodies.

NEURAL TUBE (s. NEURULATION) defects (s. dysraphia, abnormalities of DORSAL induction) - earliest to appear (17-27 days of gestation):

1. **CRANIORACHISCHISIS TOTALIS** - total failure of neural tube closure → brain and spinal cord necrosis secondary to exposure to amniotic fluid.
 - **iniencephaly** = occipital bone defect + cervical dysraphism + head retroflexion.
2. **CRANIOSCHISIS, s. CRANIUM BIFIDUM** (defects of cranial neuropore closure): **anencephaly, exencephaly, encephaloceles, cranial meningoceles**.
3. **SPINA BIFIDA**:
 - a) *spina bifida occulta* - skin is intact over malformation.
 - b) *spina bifida manifesta (s. aperta, cystica)*: **meningoceles, myelomeningoceles, myeloceles, rachischisis** (myeloschisis + spina bifida).

Spinal dysraphism may be classified pathogenetically:

- A) **nondisjunction of neural ectoderm from cutaneous ectoderm**:
 - 1) **myelomeningocele** (extensive failures of dysjunction)
 - 2) **dorsal dermal sinus** (punctate failures of dysjunction)
- B) **premature dysjunction of neural ectoderm from cutaneous ectoderm** – various fatty tissue inclusions:
 - 1) **lipomyelomeningodysplasia** (lipomyelomeningocele, lipomyelocele, lipomyeloschisis).
 - 2) **subpial lipoma, intramedullary lipoma**
- C) **disorders of secondary neurulation (s. abnormal retrogressive differentiation)** - **occult** dysraphic states (commonest malformations diagnosed in **adults!**):
 - 1) **tethered filum / tight filum / fatty filum** (failure of fibres in filum terminale to lengthen)
 - 2) **caudal regression syndromes** (failure to form terminal spinal cord, sacral agenesis)

Many spinal dysraphic malformations may cause **TETHERED SPINAL CORD!**

SEGMENTATION, CLEAVAGE and MIDLINE defects (s. malformations of VENTRAL INDUCTION) – appear during 5–8 weeks of gestation:

1. **Holoprosencephaly**
2. **Septo-optic dysplasia**
3. **Agenesis of corpus callosum**
4. **Arrhinencephaly** (incl. **KALLMANN'S syndrome**)

NEURONAL MIGRATION and CORTICAL FORMATION disorders - histogenetic period (2–5 months of gestation):

1. **Lissencephaly** (s. agyria) / **pachygyria** (s. macrogyria)
2. **Polymicrogyria**
3. Neuronal **heterotopia**
4. Focal **cortical dysplasia**
5. **Ulegyria***
6. **Schizencephaly***
7. **Porencephaly*, hydranencephaly***
8. **Megalencephaly**
9. **Hemimegalencephaly**
10. **Microencephaly**

*etiology - perinatal destructive insults (esp. vascular)

POSTERIOR FOSSA anomalies (posterior fossa structures are also formed during ventral induction period) – anomalies of **brainstem & cerebellum**:

1. **Chiari malformations**
2. **Dandy–Walker malformation**
3. **Mega cisterna magna**
4. **Vermian–cerebellar hypoplasia**
5. **Joubert's syndrome** see p. Mov50 >>
6. **Mobius' syndrome** see p. CN7 >>
7. **Marcus Gunn syndrome** see p. Eye64 >>
8. **Duane syndrome** see p. Eye64 >>

Abnormalities of CRANIUM

1. **Craniosynostosis**
2. **Microcephaly**
3. **Macrocephaly**

Abnormalities of CRANIOCERVICAL JUNCTION

1. **Basilar impression, basilar invagination, platybasia, convexobasia**
2. **Atlantoaxial instability**
3. **Occipitalization of atlas (s. assimilation of atlas)**
4. **Dens hypoplasia**
5. **Klippel-Feil anomaly**

Abnormalities of SPINE

1. **Vertebral fusion anomalies**
2. **Transitional vertebrae**
3. **Hemivertebrae**
4. **Butterfly vertebrae**
5. **Failure of fusion of secondary ossification centers**
6. **Limbus vertebra**
7. **Pedicle anomalies**

ETIOPATHOPHYSIOLOGY

- A. **Genetic** etiology (e.g. homeotic genes that control body patterning). see p. 83-92 >>
- B. **Environmental teratogenic insults** to antenatal brain:
- 1) **infections** (most commonly!)
 - 2) **irradiation**
 - 3) **toxins** (e.g. antiepileptics, alcohol)
 - 4) **metabolic disorders** (e.g. phenylketonuria)
- insults have different results depending on ***amount of brain affected*** and on ***time of insult during CNS development***.
 - several malformations are associated with block of CSF egress (through cerebral aqueduct or fourth ventricle) → congenital hydrocephalus.

Brain pathology depends on *TIMING OF INSULT* (and, to lesser degree, on *KIND OF INSULT*):

insult before 33-34 weeks → damage to ***periventricular structures*** in stereotypic manner.

cerebral blood supply has periventricular border zones; cerebral cortex during this period is protected by leptomeningeal anastomoses and low metabolic demand.

insult after 33-34 weeks → damage to ***cortical grey matter*** of more variable expression.

EPIDEMIOLOGY

Congenital CNS abnormalities:

- account for 75% **prenatal deaths**.
- occur in 1% **live births** (3% of all infants have at least one minor CNS malformation).
- 40% infants **dying in 1st year** of life have developmental nervous abnormality.

Most frequent malformations:

1. Neural tube defects
2. Posterior fossa malformations

DIAGNOSIS

PRENATAL diagnosis:

see p. 72 (2-3) >>, p. D45 >>

- 1) amniocentesis
 - 2) ultrasonography
 - 3) MRI
- **genetic counseling for parents** (of child with major neurologic abnormality) is important - ***risk of subsequent child's having such defect is high***.

Imaging in SPINAL malformations – rationale is EARLY DETECTION:

see p. D70 >>

- 50% patients have no neurological symptoms at diagnosis in infancy but without neurosurgical treatment 90% will develop neurological deficit!
 - most neurosurgeons repair closed spinal dysraphism as soon as malformation is diagnosed.
1. **Plain spinal X-ray** – not initially indicated (segmentation abnormalities are often isolated and lack of such bony anomalies does not exclude possibility of severe malformation); should be performed as preoperative study.
 2. **Spinal ultrasound** – highly accurate, but cannot completely exclude malformation; if malformation is found, further imaging is still indicated.
 3. **MRI** (!!!) - **can show most components of malformations**.
 - lengthy procedure and requires anaesthesia in all infants.
 - **CT myelography** may be necessary complementary investigation.
- radiologist is often asked to image child with ***midline skin lesion*** (dimple, lipoma, hair tuft, naevus, asymmetry of crena ani) – ***better not to perform any imaging*** - this may give false-negative result and lead clinician to have false sense of security (e.g. if there is previous ‘negative MR’, clinical signs may have progressed significantly before child has repeat study, thus delaying accurate diagnosis).

BIBLIOGRAPHY for ch. “Developmental Anomalies” → follow this [LINK](#) >>