Neural Tube Disorders (s. Dysraphism)

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**Neurenteric Cyst, Epidermoid Cyst, Dermoid Cyst** → see [p. Onc30 >>](http://www.neurosurgeryresident.net/Onc.%20Oncology\Onc30.%20Dermoid,%20Epidermoid,%20Cysts,%20Lipoma.pdf)

**Neural Tube Disorders** **(s. neurulation defects, s. dysraphia)** – most common CNS malformations!

Classification

→ see [p. Dev1 >>](http://www.neurosurgeryresident.net/Dev.%20Developmental%20anomalies\Dev1.%20Congenital%20Anomalies%20(GENERAL).pdf)

Etiopathophysiology

embryology → see [p. A13 (1) >>](http://www.neurosurgeryresident.net/A.%20Neuroscience%20Basics\A13.%20Development\A13%20(1).jpg)

Theories

1. **reopening** of closed neural tube – questionable.
2. **nonclosure** (failure of neural folds to come together) – probably correct theory!

* normal closure begins on **20th day** after fertilization and is complete by **28th day** – i.e. ≈ 1-2 weeks beyond expected normal menstrual cycle - *women is frequently unaware that she is pregnant* during this critical time!

Etiology

– classic **multifactorial**;

* + epidemiological-experimental investigations have *failed to identify obvious source*.
  + **genetic factors** certainly play important role in at least conferring predisposition (*monoallelic disorders* are occasionally associated with neural tube defects).
  + at least in cranial region, neural tube closure ***occurs not in single continuous closure*** but *at* *multiple sites* and *in coordinated pattern* - each defined site is ***under control of different genes*** (susceptible to different factors).

Epidemiology

* among most common major malformations (0.001-1% of all human malformations).
* incidence - overall decline in past decades.

**Myelomeningocele** – 1 in 1000\* live births – most common anomaly of nervous system!

\*3-4 in 1000 in England, Ireland, Scotland, and Wales

**Encephalocele** – 1 in 5000-10000 live births.

**Anencephaly** – 0,1-1 in 1000 live births (greatest frequency is in Ireland and Wales)

Risk factors:

* 1. maternal hyperthermia
  2. maternal diabetes
  3. anticonvulsants (esp. *valproic acid* – causes dysraphism in 1-2% patients, *carbamazepine*)
  4. previous infant / fetus with neural tube defect (risk increases 10-fold)
  5. low socioeconomic status.

Classification, Pathology, Clinical Features

All cases involve bone / soft tissues ± underlying neural tissue. [see p. Dev1 >>](http://www.neurosurgeryresident.net/Dev.%20Developmental%20anomalies\Dev1.%20Congenital%20Anomalies%20(GENERAL).pdf)

Cranioschisis

**Anencephaly** (“absence of head”) - ***cranial neuropore closure defect*** (develops at ≈ 28th day of gestation) - absence of brain and calvarium; no epidermal covering.

* vast majority of cases show **complete absence of most of brain**.
  + anterior pituitary, eyes, brainstem are usually spared.
  + spinal cord pyramidal tracts are missing due to absence of cerebral cortex.
* neural epithelium is present in embryo, but direct contact with amniotic fluid results in degeneration of neural epithelium.
* remaining tissue covering basal cranium is highly vascular and friable membrane (*area cerebrovasculosa*).

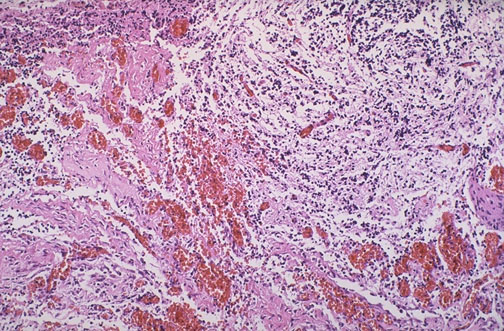
Clinical Signs

1. **polyhydramnios**.
2. neurological function is limited to ***brainstem & spinal reflexes*** (seizures, at times resembling infantile spasms, have been observed in some infants).
3. significant proportion are **stillborn**; infants who are born alive **do not survive** (survival can be prolonged with life support systems, creating controversy over use of anencephalic infants as organ donors).



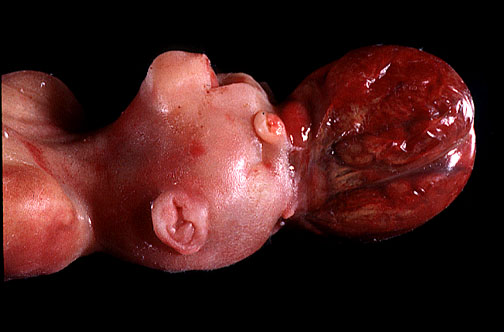
[Source of pictures: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>](http://library.med.utah.edu/WebPath/webpath.html" \t "_blank)

"Area cerebrovasculosa" from skull base - scattered primitive neuroglial tissue elements within irregular vascular proliferation:



[Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>](http://library.med.utah.edu/WebPath/webpath.html" \t "_blank)

**Exencephaly** – defect in calvarium (dura, bone, skin) – exposed brain (degenerated due to exposure to amniotic fluid):



**Cranium Bifidum - encephaloceles, cranial meningoceles** - defect in skull & dura (but often intact **epidermal covering**!; vs. anencephaly, myelomeningocele) with protrusion of:

* 1. leptomeninges (**cranial meningocele**)
  2. leptomeninges and underlying brain tissue (**encephalocele**); neural tissue (cerebral, cerebellar) within encephalocele is often abnormal and ischemic.
* in few cases portions of ventricles are also included - **encephalocystocele**.
* ***transillumination*** of sac may indicate presence of neural tissue within.
* incidence - 1:5 ratio to MMC.

Encephalocele (s. Cephalocele)

Pathogenetic theories:

1. ***cranial neuropore closure defect***
2. correct theory - ***mesenchymal defect*** → local herniation of fully neurulated neural tissue (at 8-12 weeks of gestation).

Pathogenetic theory for acquired cephaloceles in **adults** - most commonly associated either with trauma (incl. iatrogenic) or increased ICP (most common locations - where bone is already thin - tegmen tympani, middle fossa into sphenoid sinus).

Location (usually midline):

occipital encephaloceles (85% in North America) - often large and have variable contents

* 1. **Meckel-Gruber syndrome** - rare autosomal recessive condition: occipital encephalocele, microcephaly, microphthalmia, cleft lip / palate, abnormal genitalia, polycystic kidneys, polydactyly.
  2. **Walker-Warburg syndrome** - autosomal recessive congenital muscular dystrophy. [see p. Mus5 >>](http://www.neurosurgeryresident.net/Mus.%20Muscular,%20Neuromuscular%20disorders\Mus5.%20Muscular%20Dystrophies.pdf)

anterior encephaloceles:

1. most common isolated malformation in southeast Asia.
2. Robert's syndrome

parietal encephaloceles – less common.

sphenoidal encephaloceles – endocrine dysfunction.

Classification (Suwanwela and Suwanwela)

* + - 1. **Occipital**: often involves vascular structures
      2. **Cranial vault** (comprises ≈ 80% of encephaloceles in Western hemisphere):
  1. interfrontal
  2. anterior fontanelle
  3. interparietal: often involves vascular structures
  4. temporal
  5. posterior fontanelle
     + 1. **Fronto-ethmoidal s. sincipital** (15% of encephaloceles); external opening into face in one of the following 3 regions:

1. nasofrontal: external defect in the nasion
2. naso-ethmoidal: defect between nasal bone and nasal cartilage
3. naso-orbital: defect in the antero-inferior portion of medial orbital wall.
   * + 1. **Basal** (1.5% of encephaloceles; the only group that does not produce a visible soft tissue mass; may present as CSF leak or recurrent meningitis; may be associated with other craniofacial deformities, including: cleft lip, bifid nose, optic-nerve dysplasia, coloboma and microphthalmia, hypothalamic-pituitary dysfunction):
4. transethmoidal: protrudes into nasal cavity through defect in cribriform plate
5. spheno-ethmoidal: protrudes into posterior nasal cavity
6. transsphenoidal: protrudes into sphenoid sinus or nasopharynx through patent craniopharyngeal canal (foramen cecum)
7. fronto-sphenoidal or spheno-orbital: protrudes into orbit through superior orbital fissure.
   * + 1. **Posterior fossa**: usually contains cerebellar tissue and ventricular component.

Clinical Features

1. **protuberant mass** that may be pulsatile (except basal encephaloceles); **size** of encephalocele varies: barely visible bulge\* ÷ larger than infant's head.

\*may resemble cephalhematoma

1. **neurological deficits** correlate with extent of ***cortex that is herniated*** into cele: motor deficits, visual defects, psychomotor developmental delay.
2. ***malformed cortex*** (within / adjacent to cele) → **seizures**.
3. frequently associated with *other intracranial abnormalities* (e.g. hydrocephalus!, agenesis of corpus callosum, Dandy-Walker malformations, holoprosencephaly).
4. prognosis is good for many patients.

N.B. encephaloceles that contain large amount of neural tissue have poor prognosis!

**Nasal glioma** (misleading term - not neoplasm!; better term - **nasal glial heterotopia**) - form of **frontonasal encephalocele** with no clear bony defect - may not be immediately obvious on external examination.

* may present as **intranasal mass** (CSF rhinorrhea following removal of nasal polyp vs. Greenberg states that it does not communicate with subarachnoid space), **pharyngeal obstruction**, or recurrent **meningitis**.
* can be associated with hypertelorism, median cleft lip, hypothalamic dysfunction.
* requires immediate imaging and prophylactic antibiotics → surgical repair.

A nasal polypoid mass in a newborn is an encephalocele until proven otherwise!

Spina Bifida

* most common form of neural tube defects!
* mostly occurs in ***lumbar region***, followed by *lumbosacral region* (can also be located in cervical, thoracic, or sacral regions).
* spinal dysraphism is occasionally associated with *other spinal defects* (tethered spinal cord, spinal lipomas, sacral teratomas).
  1. **Spina bifida occulta** - defect in vertebral arch without any other associated defect (i.e. without involvement of cord or meninges; skin is intact over malformation).
* most commonly - L5 & S1 (up to 24% of population!), C1, Th1.
* defect is nearly always narrow and asymmetric.
* **asymptomatic** or subtle clinical signs - **cutaneous markings in** **midline of back** (mark defect location): **tuft of hair**, cutaneous **angioma** or **lipoma**; rarely, sinus tract may communicate from skin to underlying dura.
* no clinical significance\* - often found incidentally on radiographic studies.

\*occasionally associated with more significant spinal abnormalities (e.g. syringomyelia, diastematomyelia, tethered cord)

* does not seem to increase risk of neural tube malformations in that individual's progeny.
  1. **Spina bifida manifesta (s. aperta, cystica)** - defect in vertebral arch plus:

1. **meningocele** - involves meninges alone (i.e. postneurulation disorder - neural elements are intact)

* transilluminating protruding / herniating meningeal sac is covered by skin; may be asymptomatic!
* meningocele distends with crying.

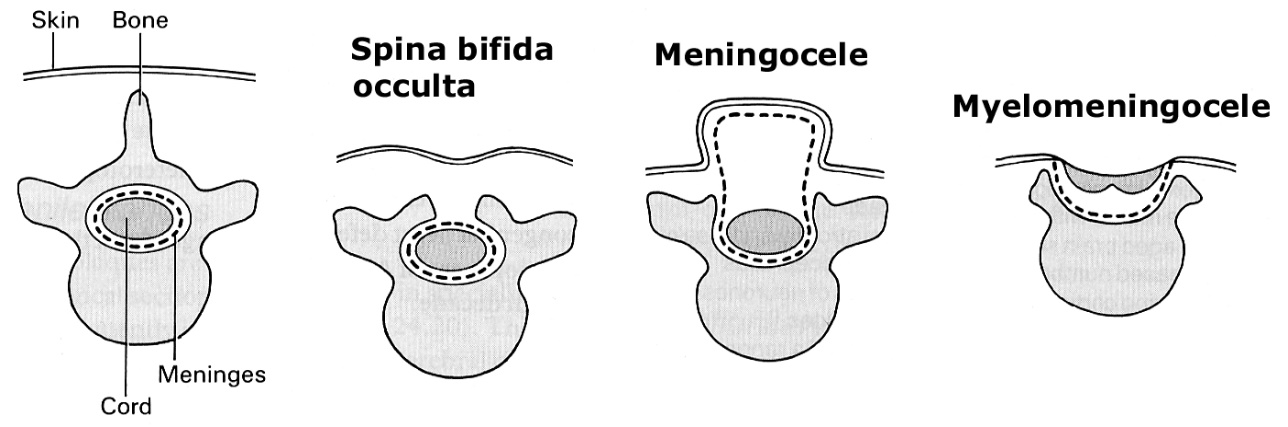
Atypical meningoceles(differentiate from dural ectasias in spondyloarthropathies):

* 1. **anterior sacral** **meningocele** – presacral cystic mass projecting into pelvis through anterior eccentric defect in sacrum\* → constipation, bladder dysfunction, anomalies of female genital tract (e.g. rectovaginal fistula, vaginal septa).

\*pathognomonic scimitar [riestas rytietiškas kardas] appearance on plain X-ray

* 1. **intrasacral meningocele** – sacral canal is expanded by meningocele which lies below normal level of termination of thecal sac.
  2. **lateral thoracic meningocele** – intrathoracic posterior mediastinal mass through eroded intervertebral foramen; occurs (70-85%) in association with neurofibromatosis.
  3. **anterior thoracic meningocele** with ventral spinal cord herniation; midsagittal MRI - spinal cord is displaced sharply forwards in contact with vertebral body at or very near intervertebral disc.

1. **myelomeningocele** (most common derangement of neurulation!) - involves meninges and underlying spinal cord; no skin covering over defect.



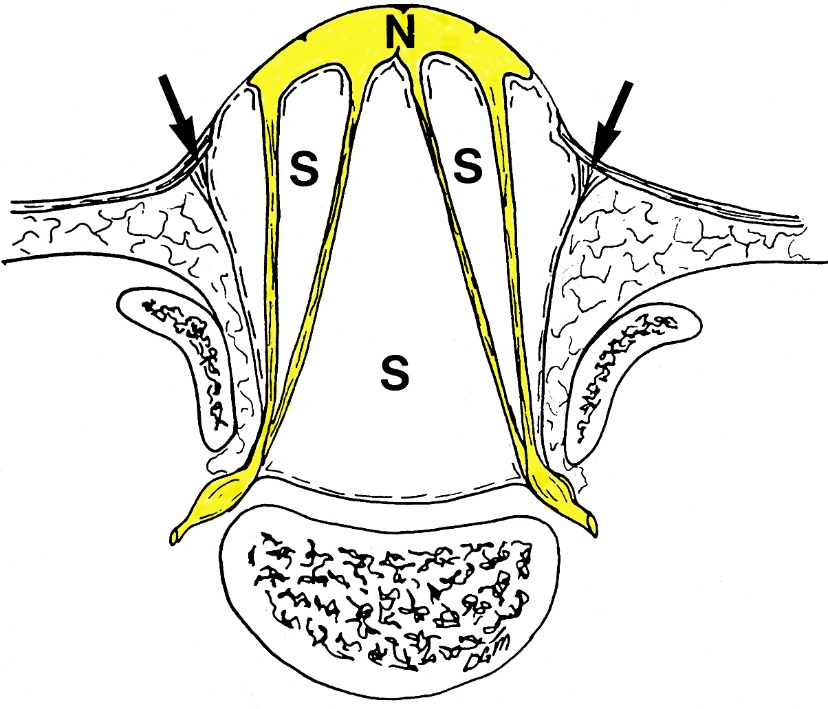
Myelomeningocele

Greatest disability of spinal dysraphism!

Pathology:

* focal segment of spinal cord fails to roll up and form tube (most commonly - failure of closure of caudal neuropore) - neural folds persist as flat plate of tissue referred to as *neural placode*.
* since neural tube does not fuse, cutaneous ectoderm does not come to cover neural tube (remains attached and lateral to neural plate, leaving cutaneous defect) - raw, exposed dorsal surface of *neural placode* represents tissue that should have formed ***interior of spinal cord*** (i.e. filleted spinal cord with visibly open central canal).
* CSF exiting from proximally formed central canal floods dorsal surface of placode.
* surrounding *neural placode* is thin layer of skin and arachnoid tissue, below which is subarachnoid space; enlarged ***subarachnoid space*** ventral to placode results in dorsally protruding sac on which neural placode is visible.
* nerve roots lie inferior to neural placode, with ventral roots lying medial to dorsal roots (i.e. dorsal roots exit from anterior surface of spinal cord just lateral to ventral roots).
* spinal cord is always tethered!

Transverse section through myelomeningocele: arrows demonstrate junction of neural placode (N) with dura mater and skin; subarachnoid space (S):



[Source of picture: David C. Sabiston “Sabiston Textbook of Surgery: the Biological Basis of Modern Surgical Practice”, 15th ed. (1997); W.B. Saunders Company; ISBN-13: 978-0721658872 >>](http://www.amazon.com/gp/product/141605233X?ie=UTF8&tag=viktsnotefort-20&linkCode=as2&camp=1789&creative=9325&creativeASIN=141605233X)

Level of defect: thoracolumbar junction (45%) > lumbar (20%) > lumbosacral (20%\*) > sacral (10%) > more rostral locations (5%).

\*according to Nelson – 75% cases are lumbosacral; according to Grainger – 80-90%

# Clinical Features:

1. Saclike **cystic structure** covered by thin layer of partially epithelialized tissue.

* remnants of neural tissue are visible beneath membrane, which may occasionally rupture and leak CSF.

1. **Spinal cord dysfunction**:
   1. **flaccid paralysis & sensory deficits** below level of lesion:

defects above L3 - deficits preclude ambulation (wheelchair dependent);

defects between S1 and L3 - assisting devices may allow ambulation;

defects below S1 - unaided ambulation.

* 1. **GU tract** involvement (≈ 90% patients) - constant urinary dribbling, relaxed anal sphincter.

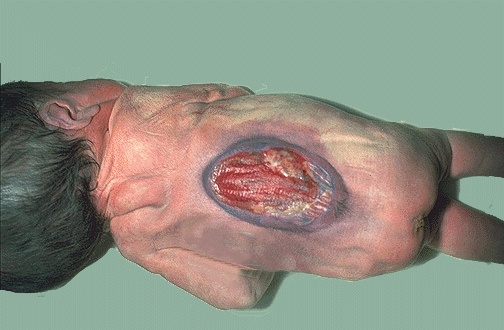
1. Superimposed **infection** (sac rupture → meningitis; UTI)
2. 75% patients have **normal intelligence**.
3. Other defects along neuraxis and surrounding mesoderm:
   1. **Chiari II (s. Arnold-Chiari) malformation** – most common (> 95%) finding associated with myelomeningocele! – most common cause of death!
   2. **hydrocephalus** (80-95%; esp. with myelomeningoceles in lumbosacral region) - ventricular *outlet obstruction* and *obliteration of posterior fossa subarachnoid cisterns* are likely causes.
   3. **lückenschädel** (> 50% cases) - regional thinning of cranial bones (radiographic and transilluminative lucencies); rarely found after 2 years of age.
   4. **platybasia**.
   5. **cerebral hemisphere malformations** - enlarged massa intermedia (frequent finding), agenesis of corpus callosum, polymicrogyria, pachygyria.
   6. **diastematomyelia**, diplomyelia.
   7. **skeletal deformities** (kyphosis, scoliosis, dislocated hips, clubfeet, Klippel-Feil syndrome) – esp. in defects above L3 – due to intrauterine paralysis.

N.B. patients with *myelomeningocele in upper thoracic* ÷ *cervical region* usually have very minimal neurologic deficit and in most cases do not have hydrocephalus!

Late complications of myelomeningoceles:

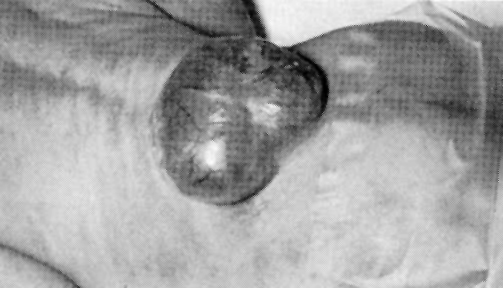
1. Scoliosis (esp. with lesions above L3)
2. Traction on cord.
3. Urological complications - continue to be leading cause of morbidity in myelomeningocele!

Usual causes of death: loss of renal function, shunt complications.



[Source of picture: “WebPath - The Internet Pathology Laboratory for Medical Education” (by Edward C. Klatt, MD) >>](http://library.med.utah.edu/WebPath/webpath.html" \t "_blank)

Lumbar myelomeningocele covered by thin layer of skin:



Myelomeningocele (*arrow*); note flaccid anal sphincter and poorly developed lower extremity musculature:



Diagnosis

Prenatal diagnosis

1. **Serum chemistry** - through routine screening programs: see [p. 71-72 (3) >>](http://www.neurosurgeryresident.net/USMLE%202\Histology%20(1-150)\71.jpg), [p. 2700 >>](http://www.neurosurgeryresident.net/USMLE%202\Urogenital%20system%20(2401-2700)\2700.%20Tests%20and%20Actions%20during%20Pregnancy%20and%20Puerperium.pdf)

* serum **α-fetoprotein (AFP)**↑ - ***specificity*** is much lower than amniotic fluid; peak of ***sensitivity*** somewhat later than amniotic fluid (i.e. ≈ 16-18 weeks' gestation – normal AFP peak; before that time, levels may be normal).
* most common causes of *false-positive* AFP↑: incorrect dat­ing of pregnancy, multiple gestation.
* further course is **detailed (level II) ultrasound** or **amniocentesis**.

1. **Amniotic fluid chemistry**:
   1. amniotic fluid **α-fetoprotein (AFP)**↑ (in almost all **open** neural tube defects, but also in gastroschisis, etc).
   2. amniotic fluid **acetylcholinesterase (AchE)**↑ (only in almost all **open** neural tube defects).

Amniotic fluid **AFP**↑ + amniotic fluid **AchE**↑ - sensitivity for open defects ≈ 100% → **detailed (level II) ultrasound**

1. **Ultrasound** - very high sensitivity at even 14-16 weeks' gestation.

* **lemon sign** (indirect sign) - symmetrical bifrontal narrowing of skull – risk of neural tube defects.

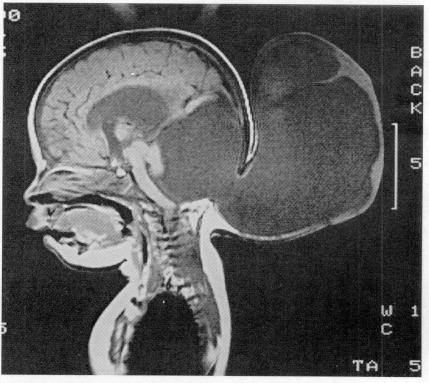
Postnatal diagnosis

- careful **MRI** (!) and **CT**.

Encephalocele

* **ultrasound** is most helpful in determining contents of sac.

Occipital encephalocele (MRI in newborn); at surgery, sac contained herniated dysplastic cerebellar tissue as well as CSF:



Spina bifida

* **cervical spine** – absence of cortical line on anterior surface of spinous process (on lateral and AP X-ray).
* **lumbosacral spine** – defect best seen on AP X-ray.

Myelomeningocele

* imaging is not necessary preoperatively – diagnosis is obvious clinically.
* do not overlook *Chiari II*, *tethered spinal cord*.
* every child must be screened for *hydrocephalus* (daily ***occipital-frontal circumference*** measurements and baseline **transfontanellar ultrasound**).
* ***orthopedic*** & ***urological assessment***.

Lumbosacral myelomeningocele - MRI shows spinal dysraphism and tethered cord:  


Meningocele

* US - subcutaneous cystic mass in continuity with spinal canal through bone defect.

Management

Prevention of meningitis / ventriculitis is extremely important (intellectual outcome is inversely related to occurrence of such complications) - **antibiotic prophylaxis** before and around time of surgery (esp. with open defects).

**Atraumatic delivery** (damaged CNS is more vulnerable to perinatal insults)

* prelabor **Cesarian section** significantly improves neurological outcome in large encephaloceles, myelomeningoceles.

Encephaloceles

**Surgical management** – as early as clinical conditions permit: [more details – see p. Op300 >>](../Op.%20Operative%20Techniques/300-399.%20Cranial/Op300.%20Craniotomies.pdf#Encephalocele_repair_middle_fossa)

1. Encephalocele contents:
2. **relocation** into cranium
3. **resection (amputation)**
4. Watertight **dural closure**
5. **Bone grafting** to cover calvarial defect (usually at later operation).

* indicated in most situations (exceptions – very small defects\*, large defects with associated microcephaly) even if there are significant associated malformations\*\*

\*may decrease with time

\*\*goal of surgery here - to simply improve caregiving for such infant.

* CSF leak → urgent surgery within 12-24 hours (to prevent meningitis).
* surgical prognosis is best in sporadic frontal encephaloceles; occipital encephaloceles are more commonly associated with hydrocephalus → worse cognitive outcome.
  + temporal encephalocele has high epileptogenicity - excellent outcome with resection and is commonly missed if not specifically looked for.

Myelomeningocele

* child is kept ***prone*** or in ***lateral*** recumbent position.
* defect is covered with ***warm saline-moistened nonadherent dressing*** (e.g. Telfa - to prevent injury and desiccation of neural placode).
* ***antibiotics*** (nafcillin + gentamicin), esp. if defect is leaking CSF; continue until clear that shunt is not needed.
* HUS then daily HC.
* genitourinary system evaluation.

**Surgical management** - **closing** all but prognostically worst cases. [see p. Op250 >>](HTTP://WWW.NEUROSURGERYRESIDENT.NET/Op.%20Operative%20Techniques/200-299.%20Spine/Op250.%20Cord%20and%20Spine%20Developmental%20Anomalies%20(techniques).pdf#MMC)

**Conservative management**

* **urological management** plays prominent role:
* regularly catheterize neurogenic bladder - avoid secondary dilatation of proximal urinary system → pyelonephritis, hydronephrosis.
* periodic urine cultures, assessment of renal function, renal imaging.
* some can become continent with implantation of artificial urinary sphincter at later age.
* **incontinence of fecal matter** is common and socially unacceptable (but does not pose same risks as urinary incontinence); many children can be "bowel-trained" with timed enemas or suppositories that allows evacuation at predetermined time once or twice day.
* **ambulatory aids**, **orthopedic care**.

Meningocele

**Surgical repair** – for cosmetic reasons: amputation of herniating sac, and closing dura; remainder of wound is closed in layers.

* prior to surgery, patient must be thoroughly imaged (MRI) for neural tissue involvement, if any, and associated anomalies.
* if CSF is leaking → immediate surgery (to prevent meningitis).

Prognosis

Recurrence rate for neural tube defect in subsequent pregnancy ≈ 3-5%\*; raises to 7-10% after two previous abnormal pregnancies

\*it is general recurrence risk for *multifactorial disorders*

Mortality rate:

**myelomeningocele** (treated aggressively) ≈ 10-15% (most deaths occur before 4 yrs).

Prophylaxis

* + 1. **Folate supplementation** 4 mg/day before conception\* and during early pregnancy (until 12th week).

\*general diet fortification with folate in case of unplanned pregnancy

* esp. for women who have had infant / fetus with neural tube defect.
* folate mechanisms are poorly understood.

U.S. Public Health Service 1992 recommendation:

1. all women of childbearing age capable of becoming pregnant must take **0.4 mg folate** daily (dose should not exceed 1.0 mg/d to avoid secondary vit. B12 deficiency).
2. women who had pregnancy with in neural tube defect must take **4 mg folate** daily (beginning 1 month prior to time pregnancy is planned).
   * 1. **Avoid heat exposure** (esp. hot tub).
     2. **Change** valproate to another anticonvulsant.

Bibliography for ch. “Developmental Anomalies” → follow this [link >>](http://www.neurosurgeryresident.net/Dev.%20Developmental%20anomalies\Dev.%20Bibliography.pdf)

[Viktor’s Notes℠ for the Neurosurgery Resident](http://www.neurosurgeryresident.net/)

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