Neural tube defects

What are neural tube defects?

Neural Tube Defects (NTDs) arise secondary to abnormal embryonic development of the future central nervous system. The two most common types of NTDs are spina bifida and anencephaly, affecting different levels of the brain and spine.[1]

The fusion of the neural tube occurs early in pregnancy from day 21 to day 28 after conception. Abnormal closure of the neural plate results in NTDs.[2] NTDs can be classified as:

- Open: frequently involve the entire central nervous system; neural tissue is exposed with associated leakage of cerebrospinal fluid (CSF).
- Closed: localised and confined to the spine with the brain rarely affected; neural tissue is not exposed although the skin covering the defect may be dysplastic.

NTDs can be classified on the basis of site of involvement (cranial and spinal) or into open (neural tissue exposed) or closed (neural tissue not exposed).

Cranial NTDs

- Anencephaly.
- Encephalocele (meningocele or meningomyelocele).
- Congenital dermal sinus.

Spinal NTDs

- Spina bifida.

- Spina bifida occulta.
- Myelomeningocele.
- Meningocele.
- Congenital dermal sinus.
- Caudal agenesis.

How common are neural tube defects? (Epidemiology)

NTDs are among the most common birth defects worldwide with a prevalence that varies from 0.5 to more than 10 per 1,000 pregnancies. This variance likely reflects differing contributions from risk factors such as nutritional status, prevalence of obesity and diabetes, usage of folic acid supplementation and/or fortification, the presence of environmental toxicants, and differing genetic predisposition among ethnic groups.[3]

Risk factors[1]

- Chromosomal anomalies such as trisomy 13, trisomy 18 and triploidy represent less than 10% of all NTDs cases, while non-syndromic isolated cases represent the vast majority of NTDs, exhibiting a sporadic pattern of occurrence.
- Women who have had an affected fetus have an empirical recurrence risk of 3% in any subsequent pregnancy; this risk rises to approximately 10% after conceiving a second NTD embryo.
- In twins, the NTDs' concordance rates among monozygotics is reported to be 7.7%, significantly higher than the rate for dizygotic twins (4.4%).
- Modifiable risk factors include maternal diabetes, maternal obesity, maternal hyperthermia (eg, sauna, fever), drugs (particularly valproate), and inadequate maternal nutritional status.

Neural tube defects presentation and management[1] [4]

See also separate articles Neonatal Examination and Paediatric Examination.

Cranial dysraphism

- Exencephaly:
    - Cranium (entire or significant portion) is absent but brain tissue is present.
    - Considered as embryologic predecessor of anencephaly.
- Anencephaly:
    - Cranial vault is absent.
    - Most cases are now terminated following prenatal diagnosis.
    - Up to 75% of the anencephalic fetuses are stillborn with the remainder dying shortly after birth.[5]
    - In live born babies, initial neurological examination may appear normal if brainstem structures are relatively intact and there may be seizures despite lack of cerebral hemispheres.

- Cephaloceles:

    - Brain matter herniates through a defect in skull. A cranial meningocele contains only meninges; an encephalocele contains brain tissue; a ventriculocele contains part of the ventricle within the herniated part of the brain.
    - These are rarer than anencephaly or spina bifida, with an incidence of 1-3/10,000 live births.
    - Associated with other brain abnormalities - eg, agenesis of corpus callosum or abnormal gyration - and may be part of a recognised syndrome.
    - Posterior cephaloceles are most common in western countries with most being occipital encephaloceles of variable size occurring above or below the tentorium. If below, they are associated with severe cerebellar defects - eg, Chiari III malformation.
    - Depending on size, site and associated abnormalities, there may be visual, sensorimotor disturbance, intellectual impairment and seizures.
    - In some parts of Asia, anterior cephaloceles are more common and may protrude into the nose, ethmoid or orbit. They often include olfactory tissue and frontal lobe tissue.
    - Cephalocele usually occurs as an isolated lesion but may be part of a syndrome such as Meckel-Gruber or Walker-Warburg syndrome.[6]

Spinal dysraphism

Spina bifida includes spina bifida occulta and spina bifida cystica. Spina bifida occulta is the most common form of spina bifida with isolated laminar defects being seen in 5% of spinal X-rays. Neurological deficit is rare and the only clinical sign is a tuft of hair or dimple at the site of defect.

Spina bifida cystica may be either a meningocele without neural tissue or a myelomeningocele where the spinal cord forms part of the cyst wall.

- Meningocele:
    - Protrusion of the meninges outside the spinal canal accounts for 5% of cases of spina bifida cystica.
    - There is no associated hydrocephalus, and neural examination is often normal.
- Myelomeningocele:
    - Occurs in 80-90% of spina bifida cystica cases.
    - 80% are lumbosacral consisting of a sac covered with a thin membrane that may leak CSF.
    - The level of lesion is best assessed by determining the upper limit of sensory loss; however, at all levels there is disturbance of bladder and bowel control.
    - Higher lesions are associated with bladder outlet obstruction with consequent dilatation of the upper urinary tract, and chronic pyelonephritis.
    - Hydrocephalus occurs in approximately 90% of cases at birth, even with normal head circumference.
    - It is usually associated with Chiari II malformation but it may also be due to aqueduct stenosis or have no clear cause.
    - It is usually detected by ultrasound.
    - If there are signs of progressive ventricular dilatation or rising intracranial pressure, there is usually a need for insertion of a ventriculoperitoneal shunt.

- Chiari II malformation:
    - Occurs in approximately 70% of cases of myelomeningocele.
    - It consists of downward protrusion of the medulla below the foramen magnum to overlap the spinal cord.
    - This causes the medulla to be kinked and the cerebellar vermis indented, the fourth ventricle elongated and the midbrain distorted.
    - Problems include palsies and central apnoea.
    - Treatment by closure of the defect remains controversial and is not always performed.
- Spina bifida occulta:
    - A defect of the posterior arch of one or more lumbar or sacral vertebrae (often L5 and S1).
    - It is often found incidentally on X-ray in children admitted to hospital; it may be considered as a normal variant.
    - However, if examination reveals a naevus, hairy patch, dimple, sinus or subcutaneous mass, MRI scan of the spinal cord is recommended even if there are no associated problems with sphincter or limb control.
    - It can cause asymmetrical lower motor neurone weakness associated with wasting, deformity and diminished reflexes.
    - There may also be progressive gait disturbance with spasticity and impaired bladder control.
- Dorsal dermal sinuses:
    - Often found in the occipital and lumbosacral areas and can connect the skin surface to the dura or to an intradural dermoid cyst.
    - If open, it can produce recurrent meningitis so should be explored and removed if possible, before infection occurs.

- Lipomyelomeningocele:
    - Seen as a bulge in the lumbosacral region normally lateral to the midline.
    - This is a lipoma or lipofibroma attached to the spinal cord, which is low-lying.
    - They are often associated with a meningocele.
- Diastematomyelia:
    - Sagittal cleft dividing the spinal cord into two halves, each surrounded by its pia mater.
    - The cord may be transfixed by a bony or cartilaginous spur.
    - Usually occurs in the low thoracic or lumbar regions.
    - Overlying skin abnormality is present in 75% of cases and X-rays show abnormalities in most cases, including abnormal segmentation of vertebrae, spina bifida and scoliosis.
    - Neurosurgery is normally indicated if abnormality involves cord or nerve roots, with the objective of freeing spinal cord from abnormal attachment to allow for normal growth and prevent further damage.

Investigations

- MRI is the study of choice for imaging neural tissue and for identifying contents of the defect in the newborn.
- CT scan allows direct visualisation of the bony defect and anatomy.
- Ultrasound is used antenatally for screening.

Prenatal screening

- Prenatal screening is possible by measurement of maternal serum alpha-fetoprotein or ultrasound.

- Alpha-fetoprotein in maternal serum: it is best detected at 16-18 weeks of pregnancy but may not detect closed defects and is less sensitive in women taking valproate.
- Ultrasound: is an effective technique for detecting NTDs and detects more NTDs than serum alpha-fetoprotein.[7] It can detect anencephaly from the 12th week and spina bifida from 16-20 weeks (may occasionally be missed, especially in the L5-S2 region).
- Second-trimester ultrasound examination increases detection rate of spina bifida to 92-95% and detection of anencephaly to 100%.[8]
- Amniocentesis: this is only used when it has not been possible to obtain adequate ultrasound images; it is used to measure alpha-fetoprotein and neuronal acetylcholinesterase.

Neural tube defects treatment and management

Affected children will require treatment from a multidisciplinary team to address any associated physical, developmental, hearing, and visual and learning difficulties that may occur in association with the NTD.

- The newborn with an open NTD should be kept warm and the defect covered with a sterile saline dressing.
- The baby should be positioned in the prone position to prevent pressure on the defect.
- Open NTDs should be closed promptly.
- Hydrocephalus: ventriculoperitoneal shunt placed at the time of myelomeningocele closure.
- Symptomatic Chiari malformations: suboccipital craniotomy and decompression of the posterior fossa and tonsils.
- Syrinx (a fluid-filled cavity within the spinal cord or brainstem): laminectomy and placement of a syringosubarachnoid stent to divert the CSF out of the central canal.

- In utero surgical repair has been practised in several centres in the USA for many years.[4] The Management of Myelomeningocele Study (MOMS) has shown short-term benefits for the newborn, including 50% reduction in the need for hydrocephalus shunting and significant improvement in spinal neurological function.[9]

Complications[4]

- Infections.
- Associated motor and sensory problems, particularly lower-limb.
- Associated general learning disability, developmental delay and hearing impairment.
- Bladder and bowel dysfunction.

Prognosis[4]

This depends on the nature of the defect and associated malformations:

- Open lesions affecting the brain (anencephaly, craniorachischisis) are invariably lethal before or at birth.
- Encephalocele can also be lethal depending on the extent of brain damage during herniation.
- Open spina bifida is generally compatible with postnatal survival, although the resulting neurological impairment below the level of the lesion can lead to lack of sensation, inability to walk and incontinence. Associated conditions include hydrocephalus, which often requires cerebrospinal fluid shunting, vertebral deformities, and genitourinary and gastrointestinal disorders.
- Closed spinal lesions are generally less severe and can be asymptomatic, as with spina bifida occulta which is considered a variant of normal. However, lumbosacral spinal cord tethering may be present in spinal dysraphism, and can lead to lower limb motor and sensory deficits, and a neuropathic bladder.

Prevention[10]

- Approximately 75% prevention of neural tube defects is possible prenatally if the prospective mothers can be provided with folic acid supplementation.[11]
- Pregnant women or women who wish to become pregnant should be advised to take supplementation with folic acid (400 micrograms) daily before conception and until week 12 of pregnancy.
- A higher daily dose (5 mg daily) is recommended for women at a high risk of conceiving a child with a neural tube defect, including women who have previously had an infant with a neural tube defect, who are receiving antiepileptic medication, or who have diabetes or sickle-cell disease.
- Healthy Start vitamins for women (containing folic acid, ascorbic acid, and vitamin D) are available for pregnant women through the Healthy Start scheme.[12]
- Food fortification with the addition of folate to grain products is considered the most effective method of ensuring adequate intake of folic acid in pregnant women in developing countries.[13]

Further reading

- Shine (Spina bifida, Hydrocephalus, Information, Networking, Equiality)
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