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Neural Tube Defects in Iraq

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Embryonic Origin of Neural Tube Defects

Insaf Jasim Mahmoud

The Neural Tube is the origin of the central nervous system. It forms from embryonic ectoderm layer during weeks 3-4 of embryonic life. Neural tube defects (NTDs) happen when neural tube closure fails to occur. If closure fails to occur in the cranial region and most of the brain fails to form the condition is called Anencephaly. If closure fails anywhere from the cervical region caudally, then the defect is called Spina Bifida [1, 2].

NTD in the Occipital Region (Cranioschisis): when the cranial vault fails to form and brain tissue exposed to amniotic fluid degenerates, resulting in anencephaly. It is caused by failure of the cranial neuropore to close. Children with such severe skull and brain defects cannot survive. If the neural tube failed to close in cranial and upper spinal cord regions the result is massive necrosis of neural tissue. The defects can be prevented by maternal use of folic acid (400 microgram daily) prior to and during pregnancy. Abnormal Neural Tube Closure will lead to Skull Defects causing protrusion of Meningies and/or Neural Tissue: meningocele and meningo-encephalocele [3, 4].

NTDs in the Spinal Cord region: when neural tube closure fails to occur anywhere from the cervical region caudally, then the defect is called Spina Bifida**.** Most cases occur in the lumbosacral region, and seventy percent of all of these NTDs can be prevented by the vitamin folic acid [4].

NTDs are common, and severe congenital malformations are caused by multiple genes and environmental factors. Although more than 200 genes are known to cause NTDs in mice, there has been rather limited progress in delineating the molecular basis underlying most human NTDs. Numerous genetic studies are: Folate one-carbon metabolism, Homocysteine remethylation gene MTHFR: a risk factor in some human populations. More than 80 mutant mouse genes disrupt neurulation and allow an in-depth analysis of the underlying developmental mechanisms. Molecular pathways that are essential for normal neurulation include: The planar cell-polarity pathway, which is required for the initiation of neural tube closure, and the sonic hedgehog signaling pathway that regulates neural plate bending. Mutant mice also offer an opportunity to unravel the mechanisms by which folic acid prevents neural tube defects, and to develop new therapies for folate-resistant defects [5].

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Etiology of Neural Tube Defects

Ali Abdul Razzak Obed

Neural tube defects (NTDs) may result from genetic mutation or may be acquired deformities. Teratogens implicated in the etiology of NTD in experimental animals and in humans include: hyperthermia, low economic status, antihistamine and sulfonamide use, nutritional deficiencies, vitamin deficiencies, anticonvulsant use, and exposure to radiation before conception.

Of all the suspected teratogens, carbamazepine, valproic acid, and folate deficiency have been most strongly tied to the development of NTD. A woman taking valproic acid during pregnancy has an estimated risk of 1-2% of having a child with a NTD. Valproic acid is a known folate antagonist and its association with neural tube defects may be through that action.

The neural tube defects occur before day 26 post fertilization, often before many women have discovered their pregnancies. Thus, folic acid is not protective unless ingested in the periconception period. Other risk factors may include genetic factors do seem to play a role. The risk of one child having a NTD is approximately 0.1% to 0.2%. The risk increases to 2% to 5% with one affected sibling, and the risk for a third child increases to 10% to 15%. These rates do not suggest a Mendelian pattern of inheritance. Diabetes, especially when the mother's blood sugar is elevated early in her pregnancy. There is a link between pre-pregnancy obesity and neural tube birth defects, including spina bifida.

The effect of maternal age on risk of NTDs is generally considered to be small. When association with age can be found, risk tends to be elevated in older or very young mothers. Febrile illness during the first trimester has been associated with 2-3 fold increase risk for NTD. Any combination of hot tub use, febrile illness, or sauna use was associated with 6 fold increase in risk.

Recent study done by A.J.Agopian (Birth Defect Research Part 1, 2013) they found that known risk factors account for <50% of NTD cases.

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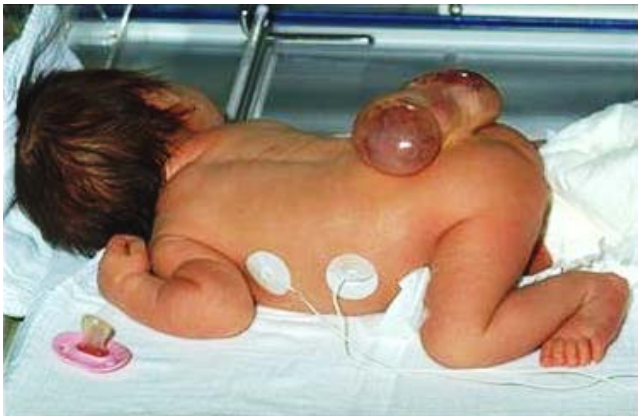

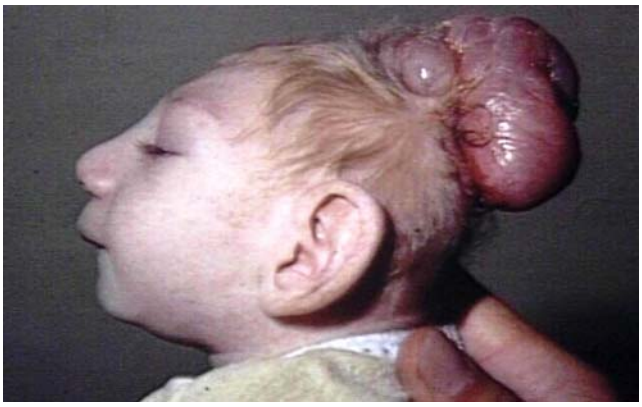

Epidemiology of Neural Tube Defects in Iraq

Mahmood Dhahir Al-Mendalawi

Neural tube defects (NTD), resulting from failure of the neural tube to close during the fourth week of embryogenesis, are one of the most prevalent congenital anomalies affecting around one in every 1000 pregnancies. Data on the prevalence of NTD in Iraq are not yet published by Ministry of Health. However, searching electronic database and locally publishing journals revealed remarkable increase in the prevalence of NTD in certain localities In Iraq compared to that reported worldwide. These include the following: Ramadi (3.3/1,000 live births, 3 fold) [1], Basra (4.3/1,000 live births, 4 fold) [2], Baghdad (4.4/1,000 live birth, 4 fold) [3], Diwaniah (8.5/1,000 live birth, 8 fold) [4], Najaf (27/1,000 live births, 27 fold) [5], and Fallujah (95/1,000 live births, 95 fold).[6] The cumulative effects of exposure to environmental toxicants, including depleted uranium, poor maternal nutrition, gestational folate deficiency, absent national programs on dietary folate supplementation, and psycho-social stress are thought to be related to the rise in the prevalence of NTDs in Iraq.

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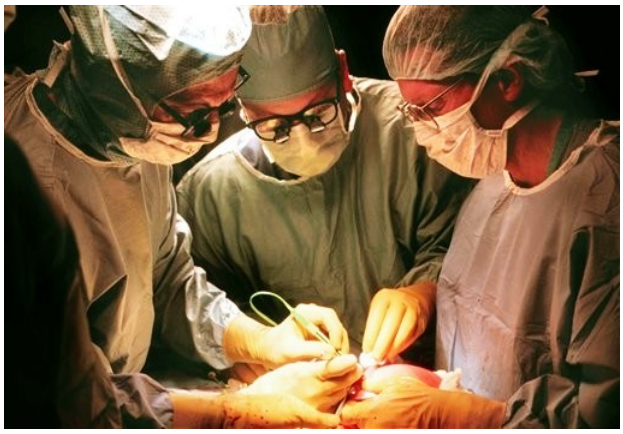

Surgical Management of Neural Tube Defects

Laith Thamer Al-Ameri

Management is usually surgical and to be started by a careful examination by a pediatrician and neurosurgeon to reveal any associated anomalies (cardiac and renal defects), head circumference must be measured as a large circumference or bulging fontanel suggest active hydrocephalus, Strider, apnea and/or bradycardia suggest Chiari II malformation [1].

Surgical repair of spina bifida cystica (the commonest type): After making anesthetic issues prone position is selected with transverse rolls tailored to patients allowing abdomen hanging free making sure no pressure applied to vital organs such as eyes and genitals. The repair then performed in following steps [2]:

- Dissecting the placode from skin removing abnormal epithelium circumferentially with care to avoid more trauma to neuronal element at rostral end
- Reconstruct the neural tube with Dural closure in a watertight manner
- Making a wide skin undermining to mobilize the skin and relive stress
- Vertical skin closure without tension with a flap to be considered if skin remains under tension.

In utero repair: A new rewarding advance is in-utero surgical repair of open spina bifida making less exposure of neural tissue to amniotic fluid and meconium and thus less neural toxicity and less negative hydrostatic pressure caused by cerebrospinal fluid leak decreasing incidence of hindbrain herniation and subsequent hydrocephalus. Procedure is done by approximation of two edges endoscopically early in pregnancy [1].

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Prevention of Neural Tube Defects in Iraq

Mahmood Dhahir Al-Mendalawi

Preventive programs involving primarily effective folate supplementation strategies [1] and regular antenatal visits together with secondary prevention using prenatal detection and termination of NTD pregnancies within the legal and religious frameworks [2] are indicated.

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