



R.C.P.U. NEWSLETTER

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R.C. Philips Research and Education Unit

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A statewide commitment to the problems of mental retardation

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Neural Tube Defects

Introduction

Neural tube defects (NTD) are birth defects that may involve the vertebrae, spinal cord, and brain. The NTDs vary in severity from the typically asymptomatic spina bifida occulta to the lethal anencephaly. Survivors with significant NTDs typically have a plethora of medical as well as neurological/developmental problems.

NTDs occur in about 1/1000 to 1/2000 live births in the US. In Florida during 1996 (the most recent year we have complete data for) there were 105 live born infants with spina bifida and 13 liveborn infants with anencephaly reported to the Birth Defects Registry. Preliminary data from 1997 shows 80/5 infants respectively (these numbers are likely to increase before data is finalized). NTDs are a common and severe birth defect implicated in 1.3% of all neonatal deaths and second only to congenital heart defects as the leading cause of perinatal mortality from birth defects.

Embryology

During early embryonic development, the spine is open, but should close by the 4th week of prenatal development. If the neural tube does not close completely, then a NTD results. The type of NTD is determined by the location and degree of incomplete closure. In general, the higher along the neural tube the defect is and the larger the open area, the more complications result.

Types of NTDs

There are two major types of significant NTDs. Spina bifida is the most common, accounting for about 65% of all NTDs. With spina bifida, there

is a vertebral defect on the back through which cerebrospinal fluid, nerve roots, and the spinal cord may protrude. The defect is typically covered with a membrane. The exposed and stretched nerve roots and spinal cord may be damaged leading to neurological complications.

The other major type of NTD, anencephaly, is much more severe. Anencephaly is caused by lack of closure of the very top of the neural tube. There is incomplete development of the majority of the brain and the skull. Many of these babies are stillborn and the remainder die early in life. Anencephaly accounts for about 25% of all NTDs.

There are other defects which are sometimes classified as NTDs, including spina bifida occulta and encephalocele. Spina bifida occulta is a common finding in healthy people. There is a small gap in one or more of the vertebra of the spine, but the spinal cord and nerves are typically normal. Spina bifida occulta is usually asymptomatic. Occasionally, there is a small patch of hair or a fatty tumor covering the vertebral defect.

Encephalocele is a defect high in the neural tube leading to a skull defect, through which brain tissue protrudes. The protruding tissue is usually irreversibly damaged and thus there is a high mortality rate. Survivors typically have significant neurological complications including mental retardation.

Medical and Learning Problems

Since the vast majority of infants with anencephaly die early in life due to severe neurological complications, the remaining discussion will focus on children with spina bifida.

Clubfeet are a common complication of NTDs, and frequently require surgical intervention. Some degree of paralysis occurs in many children with spina bifida and braces may be required for ambulation. Bowel and bladder control problems are one of the most troubling aspects of spina bifida. Periodic catheterizations are often necessary to empty the bladder. Urinary tract infections occur frequently and kidney damage may occur. Decreased IQ scores and learning disabilities are also prevalent in children with spina bifida.

Many children with spina bifida develop latex allergies. This is a potentially life threatening reaction from contact with latex. This allergy may be related to the multiple surgeries and medical procedures required early in life exposing the infant to latex. Thus, children with spina bifida should be kept isolated from latex as much as possible.

Treatment

If the NTD is diagnosed before birth, Cesarean section delivery is typically recommended to minimize trauma to the exposed neural tissue. In addition, fetal surgery may be an option. It has been performed over 100 times for intrauterine repair of spina bifida. The surgery is performed based on the theory that closing the spinal defect will prevent further injury to the exposed neural tissue and perhaps improve outcome. Preliminary studies indicate that babies who had the fetal surgery are less likely to require shunts for hydrocephalus and have a decreased incidence of clubfeet. However, neurologic outcome does not appear to be improved and additional risks such as preterm delivery are substantial.

The standard treatment of spina bifida involves surgical closure of the NTD soon after birth, often within 48 hours, to prevent infection and further trauma to the nerves. During this surgery the spinal cord is replaced in the spinal canal and the defect in the back is covered with skin and muscle. Shunting may also be necessary to relieve the hydrocephalus ("water on the brain") which commonly occurs in children with spina bifida.

Further treatment is largely symptomatic and involves physical therapy, occupational therapy, and orthopedic bracing to help the child become independent and mobile. About 70% of children with spina bifida are able to walk independently

and the others use wheelchairs for mobility. In addition, evaluation and treatment by neurosurgeons, urologists, orthopedists, nutritionists, and psychologists may be necessary. Comprehensive spina bifida clinics can gather all of the medical specialists necessary for the care of children with spina bifida at one time in a central location, limiting the number of visits a family is required to make to the medical center.

Causes of NTDs

The exact cause of NTDs is not known. However, most NTDs are isolated, with no other problems present, and are felt to be multifactorial (caused by the interactions of multiple genes with environmental factors, such as low maternal folate levels). Although there is typically no one else in the family who has spina bifida, a family history should be taken because if other family members are affected then there is an increased chance of having another baby with a NTD.

NTDs, like other birth defects, show differing frequencies based on ethnicity and sex. NTDs occur most frequently among Caucasians (especially those from Ireland) and Hispanics. They are less frequent in African American and Asian babies. Female babies and twins are more likely than other babies to be born with NTDs.

NTDs may occur as a part of several syndromes including chromosomal disorders such as trisomy 13, trisomy 18, and specific deletions of chromosome 13. However, it is estimated that only 5-10% of fetuses with NTDs have a chromosomal disorder. Fetuses with NTDs and other accompanying congenital anomalies are more likely to have a chromosomal anomaly than those with isolated NTDs. Single gene disorders such as Meckel-Gruber syndrome and Roberts syndrome may also include NTDs.

Some specific risk factors for NTDs are known. For instance, mothers who have insulin dependent diabetes prior to pregnancy are at much higher risk to have a baby with a NTD than other women. Mothers who use specific medications during pregnancy to control seizure disorders and women who have very high fevers during pregnancy are also at increased risk. One of the most recent discoveries is that women with low folate levels are more likely to have children with NTDs.

Folic Acid

Folate is a natural vitamin belonging to the B-complex family. Its name is derived from "foliage" since it is abundant in leafy greens. In addition to being found in leafy green vegetables, some other folate-rich foods include certain fruits, beans, and fortified grain products. Folate must be converted to folic acid prior to utilization by the body. Folic acid plays an important role in energy production and in the formation of red blood cells.

The link between maternal folic acid deficiency and birth defects has been known for almost five decades. It was shown in 1965 that mothers of infants with birth defects, including central nervous system defects, more often had reduced folic acid levels than did control mothers. Ten years later, the idea that vitamin deficiencies had a direct role in the causation of defects related to the neural tube was proposed. Studies from the early 1980s raised the possibility that supplementation with vitamins (including folate) could help in the prevention of neural tube defects.

In 1991, the Medical Research Council (MRC) Vitamin Study Group reported the results of a well-designed prospective study of folic acid supplementation for the prevention of neural tube defects (NTD) in pregnancies of women who had a previous child with an NTD. The results of this study confirmed the role of folate alone in the prevention of NTDs and the recommendation was made by the Centers for Disease Control (CDC) that women who had a prior NTD affected pregnancy should consume 4000 (4 mg) micrograms of folic acid before pregnancy.

One year later, the CDC reported on a study involving women with no history of a previous NTD-affected pregnancy. They found that over 50% of NTDs could be prevented by supplementation with a multivitamin containing 400 (0.4) micrograms of folic acid when taken before conception and continued throughout the first trimester. This study led to the recommendation by the U.S. Public Health Service that all women of childbearing age who are capable of becoming pregnant take 400 micrograms of folic acid daily. Despite these recommendations, it is estimated that approximately 2/3 of nonpregnant women do not get the recommended daily allowance of folic acid.

In response to the inadequate amount of folic acid consumed by most women, the Food and Drug Administration mandated in 1996 that enriched cereal-grain products be fortified with 140 micrograms of folic acid per 100 grams of flour. Studies have shown that serum folate levels have increased since fortification has been instituted. However, it is estimated that fortification increases the average woman's consumption of folic acid by only about 100 micrograms, which is significantly less than the recommended 400 micrograms.

In addition to the prevention of NTDs, folic acid has other health benefits. Since folic acid plays an important role in the formation of red blood cells, it can be helpful for individuals with certain types of anemia. More recent studies suggest that folic acid may also help in the prevention of heart disease and stroke. Preliminary studies show that folic acid may also help prevent certain types of cancer, particularly colon cancer. In summary, other people, besides women of childbearing age, may benefit from taking folic acid.

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Parent Resources

Spina Bifida Assn of America
4590 MacArthur Blvd, NW
Suite 250
Washington, DC 20007-4226
800/621-3141

March of Dimes
PO Box 1657
Wilkes-Barre, PA 18703
800/MODIMES
www.modimes.org

About the RCPU

The Raymond C. Philips Research and Education Unit began in 1978 when the legislature established section 393.20 of what is now known as the "prevention" legislation. It is named after Raymond C. Philips, who was the Superintendent of Gainesville's Tacachale (formerly Sunland) Center for 38 years, and was an acknowledged state and national leader in services for mentally retarded persons. The Unit is located on the Tacachale campus and is funded through a contract with the Department of Children and Families.

The purpose of the R.C.P.U. is to treat, prevent, and/or ameliorate mental retardation through medical evaluations, education and research. The unit

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provides direct evaluations and counseling to families and promotes service, education, and prevention projects.

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Some of the conditions currently under study at the RCPU involve Angelman, Velo-Cardio-Facial, Prader-Willi, Fragile X, Williams and Smith-Lemli-Opitz syndromes.

The R.C. Philips Unit is a resource for all Floridians interested in the diagnosis, treatment and prevention of mental retardation. Staff members are available for consultation and for educational programs for health professionals and for the community at large.

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