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"Understanding Spinal Muscular Atrophy: A Comprehensive Guide." *Families of Spinal Muscular Atrophy.* May 5, 2004 (May 27, 2004). <http://www.fsma.org/booklet.shtml#taking>.

ORGANIZATIONS

Families of SMA. PO Box 196, Libertyville, IL 60048-0196. (847) 367-7623 or (800) 886-1762. sma@fsma.org. <http://www.fsma.org>.

Borut Peterlin, MD, PhD

Spina bifida

Definition

Spina bifida belongs to a group of disorders known as neural tube defects (NTDs). These all involve problems in the development and closure of the neural tube, a structure in the human fetus that begins forming very early in a pregnancy. The neural tube eventually becomes the spinal column. When the neural tube does not close properly, it can lead to spina bifida, a disruption in the spinal column. Spina bifida occurs to varying degrees of severity, and in various forms.

Description

Spina bifida is also known by the name spinal dysraphism. It generally occurs in two major types. One types is spina bifida cystica or spina bifida aperta, which involves a sac filled with spinal contents along the spine. The other type is spina bifida occulta, in which the spinal cord stays inside the spinal canal and there is no sac.

Spina bifida ranges from having no or mild effects, to having severe effects and a significant impact upon a person's life. Physical symptoms can include weakness of limbs, paralysis, lack of bowel or bladder control, learning problems, **hydrocephalus**, **seizures**, central apnea, clubfeet, impaired vision, and latex sensitivity.

Depending upon the involvement of the spinal problem, spina bifida can also have psychological and emotional impacts upon the affected person and his or her family.

Demographics

Spina bifida is fairly common; it is thought to occur in about one in 2,000 live births in the United States. NTDs in general occur in about one in 1,000 live births in the United States. Many areas have an even higher prevalence, for somewhat unknown reasons. A population with a higher prevalence for NTDs is the United Kingdom, with an estimated rate of 2.8 per 1,000 live births in the 1970s. A similar study in Ireland at that time estimated the rate to be about 7.1 per 1,000 live births. Through the advent of prenatal screening, prenatal diagnosis, pregnancy management options, and unknown factors the prevalence in the British Isles has fallen somewhat in recent years.

Higher rates of NTDs have been reported in the northwest British Isles, with lower rates in the southeast. In Canada, higher prevalence rates for NTDs have been reported in the eastern region of the country, as compared to the western region. A higher prevalence of NTDs has been seen in China in the provinces north of the Yangtze River, and these may be as much as six times higher than in the southern provinces. Pockets of higher prevalence have also been seen in India, but these do not fit any clear geographic areas or regions.

In the United States, people of Hispanic ancestry have a higher chance for NTDs than other ethnic groups. Conversely, African Americans and some Asians have a lower risk than other ethnic groups. When those with high NTD risks immigrate to other countries, they do not keep their high risk for NTDs. When those with low NTD risks migrate, they tend to maintain their low risk status, as a group.

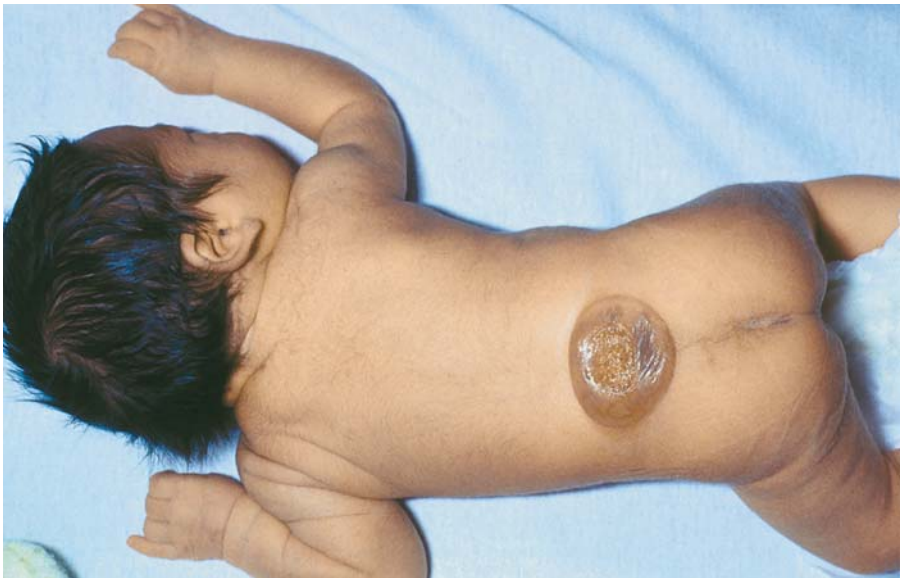
Spina bifida has been reported in males and females roughly equally.

Causes and symptoms

Spina bifida occurs because the neural tube, around the area of the spine, fails to close during fetal development. A multifactorial cause for this has been assumed, because multiple factors seem to be involved. It may best be described as an interaction between multiple genes and the environment. Many aspects of this interaction are still not well understood. As well, an exact neurological cause for spina bifida has not been identified.

Spina bifida can run in families. Multiple genes may be involved because identical twins, those with the exact same genetics, have been studied at length. Spina bifida also occurs as part of genetic syndromes and chromosome disorders.

Numerous families with NTDs have been studied to help identify recurrence risks. Generally, the risk is 3–5% for a couple to have another child with an NTD if they already have one. If a parent has an NTD, they have a 3–5% chance to have a child with one. If two or more children



An infant with spina bifida. *(© Custom Medical Stock Photo. Reproduced by permission.)*

already have NTDs, the risk is 6–9% for another one. If an NTD is in other more distant family members, the risk is somewhat higher than the average population, but probably not higher than 0.5%.

Environmental factors are also important in spina bifida. For example, taking the B vitamin folic acid before pregnancy conception has been shown to significantly reduce a woman's risk of having a child with the condition. Additionally, some medications can increase a woman's risk for spina bifida; these include some anti-seizures medications. As it turns out, many of these medications naturally reduce the levels of folic acid in one's body.

Neurological symptoms of spina bifida are varied. Many of them relate back to the early embryo's development, and how spina bifida occurs at this time. Three cell layers develop in the very early embryo; these are the ectoderm, mesoderm, and endoderm. The mesoderm normally sends signals to a region of the ectoderm to make it develop into neural tissue. Eventually, the neural ectoderm folds to form a tube, which runs for most of the length of the embryo. The top of the neural tube eventually forms the brain and top of the spinal column. The bottom of the neural tube eventually forms the lower back and bottom of the spinal column. This happens through very careful and controlled cell movements. The neural tube is usually completed forming by about 18 to 26 days after ovulation.

Failure of the neural tube to close causes spina bifida, and this disrupts the spinal column's structure and functioning. This disruption can be mild, as in spina bifida occulta. It may also be more severe with a large sac or cyst present, as in spina bifida cystica.

In about 80–90% of spina bifida cases, there is a cyst with parts of the spinal cord and spinal wall present. This is called a myelomeningocele (or meningomyelocele). This type of spina bifida can happen in a relatively high or low position on one's back. It often causes problems with bladder and bowel functioning, and sometimes paralysis or limb weaknesses. A neuropathic bladder can sometimes affect kidney functioning as well.

When a developing baby cannot move their limbs well *in utero*, this sometimes leads to feet and legs that turn inward, or clubfoot. As a result, some children with spina bifida are born with clubfoot.

Myelomeningoceles often cause spinal fluid to not flow properly through the system, and hydrocephalus may be a result. Head ultrasound scans may show hydrocephalus in about 90% of newborns with spina bifida. It is often associated with an **Arnold-Chiari malformation**, Type II. This occurs when the medulla pushes downward below the foramen magnum, and overlaps the spinal cord. This malformation is present in about 70% of people who have a meningomyelocele; it can cause distortion of the medulla and midbrain, as well as central apnea.

Hydrocephalus can eventually cause increased pressure to develop in the brain. This may ultimately lead to one's brain not being able to grow properly, and cause learning problems. Seizures may also be present. Learning problems are not a certainty with spina bifida, but when present they vary greatly. Their severity is impossible to predict. However, hydrocephalus and seizures put one at a higher risk for learning problems. Surveys on intellectual development have shown that children with hydrocephalus have lower IQs than their siblings without the condition.

In about 5% of spina bifida cases, there is no spinal tissue in the cyst wall; these are called meningoceles. Hydrocephalus is not usually present in this type of spina bifida, and a neurological examination may even be perfectly normal.

Optic atrophy and squinting may occur in people who have spina bifida, and a result of these may be poorer vision.

There is an association between spina bifida and latex sensitivity. Many have attributed this to the fact that people with the condition have a higher exposure to latex, since they may be in hospitals more often. Interestingly, a study in 2000 showed that 22% of children with spina bifida still had latex sensitivity, despite efforts to maintain latex-free environments for them.

Spina bifida occulta may cause mild symptoms, or none at all. Sometimes the only signs of it may in the lower spine area as a dimple, a small tuft of hair, or a small growth. If one has an imaging scan and a tethered spinal cord is noted, this can sometimes be a sign of spina bifida occulta as well.

Diagnosis

A early time to find spina bifida is during a detailed prenatal ultrasound scan, especially between 16 and 20 weeks gestation (from the last menstrual period). Ultrasounds cannot identify every structural problem in a developing baby, so some cases of spina bifida (especially mild forms) may be missed. However, it is a risk-free method to use that gives immediate results.

Prenatal blood screening is often offered to women between 15 and 21 weeks in a pregnancy. This screening measures the levels of various chemicals naturally found in a mother's blood, including alpha-fetoprotein (AFP). For this reason, the screening is often called AFP screening. AFP is a protein normally made by a developing fetus, so it is naturally present in maternal serum and called MS-AFP. When a fetus has spina bifida, the levels of MS-AFP may be higher than usual because it leaks out of the hole in the spine. If a woman's AFP screen comes back abnormal with a high MS-AFP value, she often is at a higher risk for having a baby with spina bifida. This may prompt her physician to offer her a detailed ultrasound, as well as other medical options that might give her more information about the baby.

One option to find spina bifida is a procedure called amniocentesis. Amniocentesis involves removing a small amount of fluid from around the baby, using a fine needle. This fluid naturally contains AFP, which may also be elevated if the baby has spina bifida. There is a small risk of miscarriage, about one in 200, with this procedure. As such, every women usually receives proper counseling through their doctor or a genetic counselor before having the test done.

Sometimes, spina bifida can only be seen at birth. A physical examination usually identifies spina bifida cystica fairly easily, especially if the sac is large. Spina bifida occulta can be more difficult to find, but clues can be a dimple in the lower back, a tuft of hair, or a small growth.

Once spina bifida is seen outwardly, imaging scans like x rays, ultrasound, **magnetic resonance imaging (MRI)**, or computed tomography (**CT**) can be helpful to see the extent of it. It is also a good way to identify whether someone has associated neurological complications like hydrocephalus.

Since spina bifida may occur as part of some genetic conditions, a medical geneticist should be involved to thoroughly examine a child with spina bifida. Identifying a particular syndrome in a child can help them receive more personalized medical care, and can help families identify a cause for why the spina bifida happened. It can also help to give families specific information about the chance of it happening again, for them or for other family members.

Some genetic testing, like chromosome studies, may identify a diagnosis or cause for the spina bifida. Abnormal genetic test results cannot be changed or reversed, but may provide answers about why the spina bifida occurred.

Treatment team

Treatment for people with spina bifida is highly dependent upon their symptoms. A multi-disciplinary team and approach is extremely helpful. Some hospitals offer day-long clinics devoted to people with spina bifida, which makes things much easier for families in terms of coordinating multiple appointments.

A treatment team for someone with spina bifida may include a **neurologist**, neurosurgeon, surgeon, **neuropsychologist**, medical geneticist, genetic counselor, orthopedic surgeon, physiatrist, physical therapist, occupational therapist, speech therapist, registered dietitian, social worker, nephrologist, ophthalmologist, audiologist, and a primary care provider. A neonatologist and pediatric specialists in those fields may be available to aid in the care for children. Those specializing in early childhood and development are particularly helpful, especially for issues related to attending school. Above all, good communication between the various specialists to coordinate care is essential.

Treatment

There is no known cure for spina bifida. Treatment primarily focuses on dealing with symptoms as they arise, since they vary so greatly from person to person.

Key Terms

Arnold-Chiari malformation, Type II Change in the brain when the medulla pushes downward below the foramen magnum, and overlaps the spinal cord.

Central apnea Abnormal breathing as a result of the medulla being pushed down, such as from an Arnold-Chiari malformation, Type II.

Chromosome Located in most cell nuclei, the genetic structure that contains all genes and DNA that make up an organism.

Clubfoot Abnormal positioning of the feet and legs, when they are turned inward towards each other.

Computed tomography (CT) scan Three-dimensional internal image of the body, created by combining x-ray images from different planes using a computer program.

Cyst Sac of tissue filled with fluid, gas or semi-solid material.

Foramen magnum Large opening in the back of the skull, where the spinal cord connects with the brain.

Hydrocephalus A state when fluid builds up in the brain, which may cause increased internal pressure and enlarged head size.

Magnetic resonance imaging (MRI) scan Three-dimensional internal image of the body, created using magnetic waves.

Medulla (spinalis) Elongated, cylindrical portion of the nervous system, which is contained in the spinal canal.

Neuropathic bladder Improper or lack of bladder function, due to a nerve problem.

Syndrome A well-recognized pattern of health problems or birth defects.

Ultrasound Two-dimensional internal image of the body, created using sound waves.

Ventriculoatrial (VA) shunt Tube that is placed from the brain to the chest cavity, in order to drain fluid.

Ventriculoperitoneal (VP) shunt Tube that is placed from the brain to the abdomen, in order to drain fluid.

X ray Two-dimensional internal image of the body, using radioactive waves.

Surgery to correct the spinal problem in spina bifida cystica is often done. This involves carefully tucking the spinal contents back into the spinal column, and closing the covering back up. This often happens shortly following birth to reduce the risk of developing an infection, and requires some time to heal afterward. Surgery has not been known to allow someone to regain functions they would not have had otherwise like movement, bowel, or bladder control.

A child with spina bifida is often carefully watched for signs of hydrocephalus. This may be done by measuring head circumference (which may enlarge) or with periodic head ultrasound or CT scans. If hydrocephalus is found, a procedure to put in a ventriculoperitoneal (VP) or ventriculoatrial (VA) shunt may be done. If a shunt is placed, it must be continually monitored and may need to be adjusted. Some people have their shunts removed later if the hydrocephalus never returns, and some people have a shunt for their entire lives.

Medications are widely available to treat those who develop seizures, and these may need periodic adjustments. Those who have problems with bowel or bladder control may require surgery, medications, or may never fully have these functions.

Babies and children with clubfoot often need to see an orthopedic surgeon and physiatrist, both of whom can recommend ways to correct them. Wearing braces on the legs can turn the feet back to their usual position, and this may be the only thing required. Sometimes surgery is necessary.

Surgery to correct the spinal problem during a pregnancy is experimental and not widely available. Since 1997, about 200 fetuses have had closure of myelomeningoceles during pregnancy. Since the surgery is so new, exact success rates, safety and long-term effects of the procedure are still not known as of early 2004.

Recovery and rehabilitation

Therapies and rehabilitation may be quite involved or relatively brief for people with spina bifida, depending on the severity of symptoms. Physical therapy is extremely important and can be ongoing. Speech and occupational therapies may be helpful if learning problems or delayed development are noted.

For those with wheelchairs, ramps and other assistive devices are helpful in their homes and places they frequent.

Clinical trials

As of early 2004, two **clinical trials** are under way in the United States to study spina bifida. National Institute of Child Health and Human Development (NICHD) sponsors both of these studies. One study is devoted to the genetics of spina bifida, recruiting many family members of an affected person to analyze and compare selected genes. The other study is attempting to identify the effectiveness and safety of spina bifida surgery during pregnancies. More information can be found at <http://www.clinicaltrials.gov>.

Prognosis

Prognosis in spina bifida is extremely varied and unpredictable. Years ago with far less intervention and fewer treatments available, someone with severe spina bifida had a high chance to die from complications. Mortality may still be high in complex cases even today. Conversely, those with a mild form of spina bifida may never even know they have it unless they have an internal imaging scan for an unrelated reason. As such, they may never have complications related to spina bifida and would have an average life span.

Today, there are far more options for helping those with spina bifida. Information can be learned during a pregnancy, allowing parents to make decisions and potentially prepare before birth. These treatments and therapies help maintain a better quality of life for those with spina bifida, and continue to offer hope.

Special concerns

Many couples who find their child has spina bifida during a pregnancy experience an array of emotional and psychological issues. They may be wondering how and why this happened, and may want some immediate answers. They also may be feeling guilt or wondering whether they could have caused it to happen. Issues related to these pregnancies, such as continuation or interrupting a pregnancy, can be complex and should be treated with sensitivity and care.

An important aspect of good prenatal care is regular folic acid supplementation, because this is known to reduce the risk for NTDs significantly. This can be gained through a prenatal vitamin, a separate supplement, or a healthy diet. Many breakfast cereals, breads, and other foods are now being supplemented with folic acid.

The current recommendation is for all women in their reproductive years to take 0.4 milligrams of folic acid daily, especially from about three to four months before conception. A woman with an affected child should take 4 milligrams of folic acid daily, beginning at least three to four months prior to conception. The reason for taking folic acid before conception is because the fetal spine forms very early, sometimes before a woman even knows she is pregnant.

Another tricky issue is managing the pregnancy of a woman with **epilepsy** or a seizure disorder. Many anti-seizure medications, like Depakote, cause an increased risk for NTDs and spina bifida. However, the risk of a woman having a seizure during pregnancy is also significant. The art is to find a balance between these two risks, in a way that makes everyone feel the most comfortable.

Resources

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Zipitis, Christos S., and Constantinos Paschalides. "Caring for a child with spina bifida: understanding the child and carer." *Journal of Child Health Care* 7, no. 2 (2003): 101–112.

WEBSITES

Children with Spina Bifida: A Resource Page for Parents. <www.waisman.wisc.edu/~rowley/sb-kids/index.htmlx>.

March of Dimes. <www.modimes.org>.

National Institute of Neurological Disorders and Stroke. <www.ninds.nih.gov/index.htm>.

ORGANIZATIONS

Association for Spina Bifida & Hydrocephalus (U.K.). ASBAH House, 42 Park Road, Peterborough, United Kingdom PE1 2UQ. (01733) 555988. (01733) 555985. info@asbah.org. <http://www.asbah.org>.

Spina Bifida and Hydrocephalus Association of Canada. 977-167 Lombard Avenue, Winnipeg, Manitoba, Canada R3B 0V3. 204-925-3650 or 800-565-9488; Fax: 204-925-3654. spinab@mts.net. <http://www.sbhac.ca/index.php?page=main>.

Spina Bifida Association of America. 4590 MacArthur Boulevard N.W., Suite 250, Washington, DC 20007-4226.

202-944-3285 or 800-621-3141; Fax: 202-944-3295.
sbaa@sbaa.org. <http://www.sbaa.org>.

Deepti Babu, MS, CGC

Spinocerebellar ataxia

Definition

Spinocerebellar **ataxia** is a genetically inherited disorder characterized by abnormal brain function that represents a varied group of disorders. It is most commonly inherited as a dominant trait, which means that any individual who is a carrier of one of the many different gene mutations is affected. It also means that a carrier will have a 50% percent chance of having an affected offspring, regardless of the genetic background of the reproductive mate. In this group of disorders, the brain and spinal cord degenerate.

Description

Individuals affected with spinocerebellar ataxia develop a degenerative condition that affects a region in the base of the brain called the **cerebellum** located behind the brainstem. The primary function of the cerebellum is to coordinate the body's ability to move. Loss of this quintessential function leads to a progressive atrophy, or wasting away of muscles. The spine also atrophies and this can lead to **spasticity**.

Spinocerebellar ataxia can be physically devastating and the progressive loss of the ability to coordinate movements in emotional complications and significant lifestyle changes. The adverse effects involve the legs, hands, and the speech. Currently, there are 11 types of spinocerebellar ataxia. As there are many different genes mutations that cause this disease, there are different names for each type. The different types have numerical assignments as nomenclature. For example, Spinocerebellar ataxia type 1 is also known as SCA1. The numbers span from 1-25 (there is no SCA9) and are designated based on the time at which they were identified and characterized. Spinocerebellar ataxia is the same disease as spinal cerebellar ataxia.

Demographics

There are several gene mutations on different chromosomes that cause Spinocerebellar ataxia and the frequency of these gene within different populations varies considerably. In fact, due to the number of different types it is often difficult to estimate the incidence of a specific type in a specific population. In general, the incidence is thought to be approximately one to five per 100,000 people. There is no known predilection for sex. As with virtually all autosomal dominant disorders, males and females are equally likely to inherit a defective gene.

Causes and symptoms

Spinocerebellar ataxia is caused by a genetic defect that involves an expansion in the DNA sequence called a trinucleotide repeat expansion for SCA types 1-3, 6-10, 12, and 17. In general, the type of DNA expansion involves three DNA letters (nucleotides). In these cases, the sequence CAG (C=cytosine, A=adenine, G=guanine) is repeated above the normal repeat length. The normal repeat number differs for different types, as does the expanded repeat sizes. By repeating this sequence of DNA too many times, function of the protein it encodes can be disrupted. Other types of repeat expansions that cause SCA have been discovered. For example, SCA10 involves an ATTCT repeat expansion of the SCA10 gene and SCA8 involves an expansion in the SCA8 gene with the nucleotides CTG repeated. Finally, SCA14 involves a mutation in a gene that does not involve a trinucleotide repeat expansion.

The most common types are SCA1 (6%), SCA2 (14%), SCA3 (21%), SCA6 (15%), SCA7 (5%), and SCA8 (2–5%). Age of onset for all of these types is on average from 20–30 years of age except for SCA6, which usually occurs between the ages of 40 and 50. People with SCA8 usually develop symptoms between in their late 30s. SCA2 patients usually develop **dementia** and slow eye movements. SCA8, which has a normal lifespan, and SCA1 patients are both characterized as having active reflexes. SCA7 patients develop visual loss. SCA3 is also known as **Machado-Joseph disease**.

In SCA types 1–3 and 7, there can be an earlier age of onset with increased severity (called anticipation) as the defect is passed from one generation to the next. This means that children can be more severely affect at an earlier age than their affected parent. The size of the repeat of nucleotides in the affected genes is thought to correlate with the severity and age of onset in offspring. As the repeat size expands, the severity worsens and age of onset becomes earlier compared with the affected parent. However, repeat size does not predict the exact age of onset or the specific symptoms that will develop.

Penetrance refers to the likelihood that individuals with a genetic defect will develop the disease. In spinocerebellar ataxia, the penetrance is quite high; however, there are rare cases in which people do not develop symptoms. The reason for the lack of complete penetrance is currently unknown.