NEUROSURGICAL MANAGEMENT OF SPINA BIFIDA: RESEARCH ISSUES

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The neurosurgical goal when treating children with spina bifida (predominantly myelomeningocele) is to maintain stable neurological functioning throughout the patient’s life time. Unfortunately, few long-term outcome studies are available to help direct the neurosurgical care of a child born with myelomeningocele and often treatment relies more heavily upon the experience of senior practitioners. This article reviews the current literature regarding neurosurgical treatment strategies, with recommendations concerning including prenatal diagnosis, in utero treatment and delivery modes, and postnatal management. Given the overall declining prevalence of open neural tube defects world-wide, research collaboration amongst practitioners through multicenter trial are essential to improving the lives of people born with this most complex congenital anomaly.

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Key Words: neural tube defect; myelomeningocele; hydrocephalus; spina bifida

Neural tube defects (NTDs) affect ~3,000 pregnancies per year in the United States [Centers for Disease Control, 2004; see Au et al., 2010]. Myelomeningocele (open spina bifida) is the most common NTD, and the most severe birth defect compatible with long-term survival. Although the incidence of myelomeningocele live births is declining, it continues to be the cause of significant chronic disability [Hunt and Poulton, 1995; Hunt et al., 1999; Hunt and Oakeshott, 2003; Oakeshott and Hunt, 2003]. In this review, we focus on myelomeningocele, but note that the methods used for assessing, treating (with modifications), and monitoring the spine also involve children with other spinal dysraphisms (e.g., meningocele, lipomyelomeningocele).

In the early 1950s, the survival rate for individuals with myelomeningocele was about 10% [Laurence, 1974]. Today, large numbers of children with myelomeningocele are surviving into adulthood because of advances in the management of several important complications [Hunt and Poulton, 1995; Bowman et al., 2001; Hunt and Oakeshott, 2003; Oakeshott and Hunt, 2003]. However, optimal treatment requires multispecialty care to prevent, monitor, and treat a variety of potential complications that can affect function, quality of life, and survival [Kaufman et al., 1994]. This care is ideally provided by a multidisciplinary team with expertise in pediatric subspecialties of neurosurgery, orthopedics, neurology, urology, and rehabilitation [Liptak and El Samra, 2010]. Access to physical and occupational therapists, nutritionists, social workers, wound specialists, and psychologists is also helpful.

The neurosurgical goal when treating children with spina bifida is to maintain stable neurological functioning throughout the patient’s lifetime. Unfortunately, few long-term outcome studies are available to help direct care of children born with this most complex congenital abnormality [Hunt and Poulton, 1995; Hunt et al., 1999; Bowman et al., 2001; Hunt and Oakeshott, 2003; Oakeshott and Hunt, 2003]. Often, the treatment of a child with this complex disease relies more heavily upon the experience of senior pediatric practitioners than multi-institutional, prospective, randomized clinical trials.

The aim of this article is to review the current literature regarding treatment strategy pertinent to neurosurgery. We will summarize the literature recommendations concerning prenatal diagnosis, in utero treatment and delivery modes. Lastly, we will highlight postnatal neurosurgical management.

OVERALL TREATMENT STRATEGY

Until the 1950s, hydrocephalus was an important cause of morbidity and mortality for individuals with myelomeningocele [Leck, 1966; Laurence, 1974]. The introduction of the valve for the ventricular cerebrospinal fluid (CSF) shunt in the 1950s offered effective treatment for hydrocephalus, and presented the possibility of long-term survival for some infants [Laurence, 1974]. At first, some providers, including John Lorber in England, advocated selective treatment for infants with myelomeningocele, reasoning that many of these children are a burden for themselves, their family, and society [Leck, 1966; Lorber, 1973, 1974; Lorber and Salfield, 1981]. They advocated active treatment only for infants whom they considered to have the best chance of a good neurological outcome, amounting to 30% of newborns with myelomeningocele. The remainder was selected for nontreatment based on criteria that included hydrocephalus, paraplegia, severe kyphosis, and associated congenital defects. These children were given only supportive nursing care, and antibiotics and artificial feeding were withheld. Survival of an untreated child was considered an unacceptable outcome.

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Received 15 February 2010; Accepted 18 March 2010
Published online in Wiley InterScience (www.interscience.wiley.com).
DOI: 10.1002/ddrr.100
In the Netherlands between 1997 and 2004, 22 children with spina bifida were euthanized during the neonatal period, following a protocol intended to reduce suffering in terminally ill infants known as the Groningen Protocol [see Verhagen and Sauer, 2005; Verhagen et al., 2005; Liptak and El Samra, 2010]. This form of active euthanasia has prompted intense controversy and criticism, in part because of the difficulties of objectively determining suffering in an infant, predicting survival and quality of life, and because the infant patient cannot participate in the decision about his or her treatment [Jotkowitz and Glick, 2006]. Hence, this protocol is not the standard of care for a newborn with myelomeningocele.

Today, most centers treat all viable newborns aggressively without selection [McLone, 2008]. Nonselective treatment increases overall survival several fold, and there is little difference in functionality as compared with individuals surviving selective treatment protocols. Nonselective treatment is the current standard of care in the United States [McLone, 1986, 2008]. We await the outcome of the Management of Myelomeningocele (MOMs) trial to determine if in utero closure affords advantages to the child with a myelomeningocele [Chescheir, 2009].

PRENATAL DIAGNOSIS

In addition to dietary fortification [see Au et al., 2010], a major impact on the declining birth rate of children with NTDs is likely elective termination of the pregnancy following prenatal diagnosis. The impact of termination on the overall incidence is impossible to determine in the USA, given the reason for termination is not reportable [Sutton, 2008]. Chan et al. [1993] reported a 75.7% decrease in live births with spina bifida in South Australia from 1966 to 1991 secondary to elective termination [Chan et al., 1993].

Prenatal diagnosis is accomplished by maternal screening of serum alpha fetoprotein (AFP) levels and the diagnosis is established by ultrasonography. Usually, the obstetrician who suspects a NTD in the fetus will also recommend an amniocentesis in order to complete a chromosomal analysis and obtain amniotic fluid for AFP and acetylcholinesterase [Shaer et al., 2007].

MATERNAL AFP SCREENING

Maternal serum AFP screening for NTDs is performed in the second trimester, between 15 and 20 weeks of gestation [Shaer et al., 2007]. AFP screening is primarily intended for the detection of myelomeningocele and anencephaly, but can also detect several nonneural fetal abnormalities [Shaer et al., 2007]. It does not detect skin covered lesions (occult spinal dysraphism). When the serum AFP is positive, it is important to repeat the serum AFP because repeat testing will be negative in many cases, and such findings are not associated with an increased frequency of false-negative NTD diagnoses.

No prospective randomized trials have been performed to determine the risks and benefits of labor and vaginal delivery for these infants. The optimal obstetrical mode of delivery in a fetus with myelomeningocele is indeterminate in the literature [Hadi et al., 1987; Shurtleff et al., 1987; Sakala and Andree, 1990; Luthy et al., 1991; Hill and Beatie, 1994; Merrill et al., 1998] and hence, is an obstetrical decision.

ULTRASOUND FINDINGS

Myelomeningocele can be detected before the 12th postmenstrual week by noting irregularities of the bony spine or a bulging within the posterior contour of the fetal back [Blumenfeld et al., 1993]. After the 12th postmenstrual week, sonographic fetal markers for open NTDs include cranial findings: the “lemon” sign and the “banana” sign [Blumenfeld et al., 1993; Canfield et al., 1996]. The lemon sign refers to a concave shape of the frontal calvarium. The banana sign describes the posterior convexity of the cerebellum in the presence of spina bifida. These changes result from the Chiari II malformation (i.e., herniation of the cerebellum and brainstem through the foramen magnum) [see Juraneck and Salman, 2010]. Other suggestive findings include ventriculomegaly, microcephaly, and obliteration of the cisterna magna.

FETAL SURGERY

Fetal surgery for myelomeningocele can arrest leakage of spinal fluid from the back, and might therefore prevent or reverse the Chiari II malformation and hydrocephalus [Tulipan et al., 1999; Chescheir, 2009; Hirose and Farmer, 2009]. The surgery has been performed at a few centers since the late 1990s. Preliminary results show that fetal intervention improves the radiographic appearance of the hindbrain, including reducing the incidence of Chiari II malformation; it may also decrease the need for CSF diversion. However, and the impact of fetal surgery on the Chiari II malformation, need for shunting, and other outcomes remain unproven because of varied selection criteria and lack of a comparable control group of children with myelomeningocele who did not receive fetal surgery [Johnson et al., 2003; Chen, 2008]. These issues are being addressed in a randomized, controlled study funded by the National Institutes of Health, the MOMs trial, which began in 2003 and is currently in progress at three institutions in the United States [Chescheir, 2009]. Infants are randomized to fetal surgery at 18–25 weeks gestation or neonatal repair. Outcomes include the need for a shunt at 1 year, neurological function, cognitive outcome, and maternal morbidity. The study is still enrolling participants, so results are not expected for some time.

LABOR AND DELIVERY

If a prenatal diagnosis of spina bifida has been made, delivery should occur at a hospital with personnel experienced in the neonatal management of these infants. In our experience, the necessity of preterm delivery is infrequently necessary; and usually is encountered when rapidly increasing ventriculomegaly is observed. The fetus would then be delivered once fetal lung maturity has been established. Otherwise, delivery can be postponed until term. No prospective randomized trials have been performed to determine the risks and benefits of labor and vaginal delivery for these infants. The optimal obstetrical mode of delivery in a fetus with myelomeningocele is indeterminate in the literature [Hadi et al., 1987;
MANAGEMENT OF THE NEONATE

Assessment

Immediately after birth, the open neural placode should be briefly assessed to note its location, size and whether it is leaking CSF [Cohen and Robinson, 2001]. Sterile nonlatex gloves should be used to minimize the risk of latex sensitization [Cremer et al., 1998; Rendeli et al., 2006]. The defect should be covered with a sterile saline-soaked dressing [McLone, 1998]. Large defects should also be covered in plastic wrap to prevent heat loss.

A thorough neurological examination should be performed. This should include the following:

- Observation of spontaneous activity—which has been noted to be depressed in children with myelomeningocele in comparison to normal controls [Rademacher et al., 2008].
- Extent of muscle weakness or paralysis, and/or presence of orthopedic deformities of the limbs or spine.
- Response to sensation.
- Deep tendon reflexes.
- Anocutaneous reflex (anal wink).
- Signs of hydrocephalus.
- Evidence of brainstem compression (Chiari II malformation).

In some infants, the neurological findings may improve during the first 72 hr of life [McLone, 1983]. The newborn should also be thoroughly assessed by the neonatology team for associated anomalies, including structural anomalies of the heart, airway, gastrointestinal tract, ribs, and kidneys [Whitaker and Hunt, 1987; Ritter et al., 1999]. Ritter et al. recommend screening echocardiograms for detection of associated congenital heart defects, present in 37% of his study cohort [Ritter et al., 1999]. A heart defect is more commonly noted in female infants with spina bifida and is unrelated to the presence of other congenital anomalies or the level of the spinal defect.

Although most coexisting anomalies are not immediately life-threatening and may be dealt with without much difficulty, it is important to remember that a few newborns with myelomeningocele may have potentially fatal associated malformations [McLone and Dias, 2003]. Intervention to prolong the lives of these patients is the setting of a dismal outlook makes little sense; they should be kept comfortable, and their family should be supported.

Antibiotics

Prophylaxis with broad spectrum antibiotics are commonly administered until at least the back wound is closed to reduce the risk of infection of the central nervous system (CNS) [McLone, 1983]. With this precaution and appropriate wound care, early CNS infection is rare. In a retrospective study of infants with back closure performed after 48 hr of age, ventriculitis occurred less often in infants given antibiotic prophylaxis as compared to those who were not [McLone et al., 1982].

Surgical Closure of the Spinal Lesion

Optimally, the back lesion should be closed within 72 hr following birth. In doing so, this further decreases the risk of CNS infection, and possibly improves neurological outcome [McLone, 1998; Tarcan et al., 2006]. In a retrospective review of a cohort stratified based upon timing of back closure, the children who underwent back closure within 72 hr of birth have significantly better bladder status on urodynamic testing as opposed to those children closed after 72 hr [Tarcan et al., 2006]. In the subgroup closed before 72 hr after birth, no benefit is noted if closure occurred before or after 24 hr of birth.

The microneurosurgical closure technique involves the approximation of the lateral edges of the open neural placode in the midline to reconstitute the neural tube [McLone, 1980; Gaskill, 2004]. This creates an outer layer of pia mater around the previously open neural tissue, or placode. It is unclear whether this decreases the incidence of retethering of the spinal cord, but it certainly facilitates untethering of the spinal cord later in life, should this be necessary [Bowman et al., 2009].

Occasionally, the defect is large requiring rotational, musculocutaneous flaps, acute tissue expansion, and/or skin grafting [Hadi et al., 1987; Orzenu et al., 2002; Muneuchi et al., 2005; Ulusoy et al., 2005; Arnell, 2006; Komuro et al., 2006; De Brito et al., 2007; Mutaf et al., 2007; Cole et al., 2008; Gumus, 2008]. Rarely, a newborn will have a severe spinal deformity requiring a kyphectomy simultaneously with placode closure [Reigel and McLone, 1988; Crawford et al., 2003]. Although there is considerable case report literature, no technique for closing the spinal lesion has been proven superior.

The mortality associated with closure is quite low [McLone and Dias, 1991–92]. However, the peri-operative complications can be extensive, with CSF leakage the predominant issue. Previously, newborns with myelomeningocele, who developed a CSF from the back closure, would undergo ventriculoperitoneal (VP) shunt placement. More recently, the authors successfully managed several neonates with only temporary diversion of their CSF with local wound care.

Other known complications include infections, missed associated spinal anomalies (such as: diastematomyelia, thickened filum terminalis) or inclusion dermoids [McLone and Dias, 1991–92; Chadduck and Roloson, 1993; Storrs, 1994; Harpold et al., 1997; Ramos et al., 2008]. Many authors have theorized that dermoids in the placode are secondary to retained dermal fragments included in the imbrication of the neural tissue [McLone and Dias, 1991–92; Chadduck and Roloson, 1993; Ramos et al., 2008]. Storrs reviewed the pathology of several resected placentas and tissue obtained during spinal cord untetherings and demonstrated that hamartomatous tissue is present within the placode [Storrs, 1994].

Hydrocephalus

In 10% of infants, hydrocephalus will be apparent at birth. In this group having macrocrania and massive ventriculomegaly, simultaneous myelomeno-
gocce repair and VP shunt placement may be appropriate. This approach is controversial, however, and may increase the complication rate [Reigel and McLone, 1988; Miller et al., 1996; Oktem et al., 2008].

In a retrospective review, the frequency of CSF infection, shunt malfunction and symptomatic Chiari II malformation is similar with simultaneous and sequential placode closure and shunt placement [Miller et al., 1996]. The rate of wound leak is lower and hospital length of stay is shorter in the cohort that underwent simultaneous operations. Oktem et al. [2008], however, note a higher rate of back wound infection and shunt infection in newborns undergoing simultaneous surgery for their myelomeningocele closure and shunt placement. Consequently, the conclusion in this retrospective review does not support concurrent surgical intervention in newborns with myelomeningocele and overt hydrocephalus. Larger, randomized clinical trials are needed to better determine the efficacy of this approach.

Following repair of the myelomeningocele, many infants will develop some degree of ventriculomegaly, which causes the head circumference to increase at a rate greater than the normal curve. In 2004, Wakhlu and associates reported on the prospective use of preoperative head ultrasounds (USs) to measure cranial ventricular size in predicting future need of CSF diversion after back closure [Wakhlu and Ansari, 2004]. Many pediatric neurosurgeons advocate active surveillance of the newborn with mild to moderate ventriculomegaly both clinically and radiographically to determine which infants will benefit from permanent CSF diversion [McLone and Dias, 1991–92; Chakroborty et al., 2008; Waf et al., 2009].

Ventricular size should be evaluated soon after birth by US, computerized tomography or magnetic resonance imaging. Serial neuroimaging, which is standard practice in most US centers, is then performed to identify any change in ventricular size.

In infants with rapidly progressive hydrocephalus, CSF management is mandatory [McLone and Dias, 1991–92; Chakroborty et al., 2008], both because of issues related to mortality and because of the effects of persistent hydrocephalus on the brain [Del Bigio, 2010]. Prompt CSF diversion is also indicated in infants who develop an acute neurological change, such as stridor, swallowing dysfunction or central apnea, with or without significant change in the ventricular size [McLone and Dias, 2003; Chakroborty et al., 2008]. Although the usual management of infants with hydrocephalus and spina bifida is VP shunt placement, Waf and others have found third ventriculostomy, with choroid plexus cauterization in Waf’s cohort a viable option [Teo and Jones, 1996; Waf et al., 2009].

By contrast, neurologically stable infants, with stable or slowly progressive increases in his/her ventricular size, should be followed clinically and undergo routine imaging [Chakroborty et al., 2008; Bowman et al., 2009; Waf et al., 2009]. If the infant is neurologically stable, a period of close observation and monitoring with serial imaging studies and head circumference measurements is warranted.

A multi-institutional study is warranted to assure that this management plan does not have long-term, deleterious effects upon the cognitive outcome of children with spina bifida who are living with mild to moderate ventriculomegaly and have not undergone CSF diversion.

Chiari II Malformation

The Chiari II malformation is characterized by herniation of the developing fetal cerebellum and medulla downward into the spinal canal and upward into the middle fossa, in association with myelomeningocele [Juranek and Salman, 2010]. This malformation is present in almost all patients with myelomeningocele. In young patients, particularly newborns, respiratory stridor, vocal cord palsy or central apnea are the most serious complications of the Chiari malformation [McLone and Dias, 2003].

There is significant literature regarding the appropriate management of infants who develop Chiari symptoms [Tubbs and Oakes, 2004]. Some authors advocate early posterior fossa decompression, or more appropriately upper cervical decompression, for relief of the Chiari symptoms. Unfortunately, a significant portion of patients will fail...
to respond to surgical decompression. Perhaps, this is because the symptoms are not caused by simple mechanical brain stem compression, but rather by an incomplete formation of the brain stem nuclei [Fujii et al., 1996].

If the patient is normal at birth, but deteriorates with stridor or opisthotonic posturing during infancy, decompression of the Chiari II malformation may be considered, but only after a shunt malfunction has been ruled out [McLone and Dias, 2003]. For a majority of patients demonstrating any type of neurological decline, a shunt revision will relieve or improve their symptoms [McLone and Dias, 2003]. In the extensive literature review by Tubbs and Oakes [2004], no treatment standard or guideline was able to be established. We concur with their conclusion; a randomized, prospective, multi-institutional study is needed to determine the optimal management of a child with myelomeningocele and a symptomatic Chiari II malformation.

**Challenges During Childhood**

For many children born with a myelomeningocele, surgical intervention throughout childhood is a common occurrence. The most common cause of decline in a child born with a myelomeningocele is a shunt malfunction. A long-term study of children born with myelomeningocele and hydrocephalus has shown an average shunt revision rate of 2–3 revisions during childhood [Bowman et al., 2001; Hunt and Oakeshott, 2003]. The greatest impedance to long-term independence and achievement in society may be the need for shunt revisions, especially after the age of 2 years [Hunt et al., 1999]. Hopefully, if the overall shunt dependency is able to be decreased—either by prenatal closure or more selective posterior shunt placement—the overall morbidity and mortality associated with this disease will also decline.

Given the overall prevailing prevalence of open NTDs world-wide [Shurtleff, 2004], only through research collaboration amongst practitioners will the science of medicine advance to improve the lives of these infants born with this most complex congenital anomaly. As we suggested in several places in this manuscript, multicenter studies are needed to address the following priority areas:

- The risks and benefits of labor and vaginal delivery.
- Concurrent versus sequential neurosurgical repair of the spine and shunting for hydrocephalus in newborns with myelomeningocele and overt hydrocephalus.
- Management of hydrocephalus through serial neuroimaging with delayed shunting so long as the child is neurologically stable to assure that this management plan does not have deleterious effects upon the outcomes of children with spina bifida with mild to moderate ventriculomegaly.
- The optimal management of a child with myelomeningocele and a symptomatic Chiari II malformation.

A research agenda of this sort, which prioritizes multicenter randomized trials, will lead to neurosurgical interventions that are grounded in an evidence base and not just the highly valued experience of senior practitioners.

**REFERENCES**


