OPTIMAL DELIVERY METHOD FOR THE FETUS WITH MENINGOMYELOCELE

by

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ABSTRACT

Optimal Delivery Method for the Fetus with Meningomyelocele (MMC)

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Background: MMC is a congenital anomaly which leaves the spinal cord and nerve roots exposed through a bony defect in the spine, leaving infants at risk for infection, death, and paralysis.

Objectives: To determine if prelabour Cesarean section (CS) is preferable to trial of labour (TOL), and if CS after TOL is preferable to vaginal birth (VB) for infants with MMC.

Design: Retrospective cohort study

Methodology: Cases were identified at the birth hospital through a medical records search for infants born with the ICD-9 code 741 for spina bifida and then tracked to neurosurgical centres. Birth and neurosurgical data were collected on infants born with MMC over a 10 year period in Ontario.

Results: 370 infants with MMC were identified. After exclusions (n=89) and incomplete follow-up (n=62), 219 remained (20 died in the birth hospital). Prelabour CS was associated with a lower risk of infection than TOL [8/46 (17.4%) vs 51/150 (34.0%), odds ratio (95% CI): 0.41 (0.18-0.94)]. CS after TOL was associated with a higher mortality rate at 6 months of age than VB [10/43 (23.3%) vs 12/116 (10.3%), odds ratio (95% CI): 2.63 (1.04-6.63)].

Conclusions: Although delivery by prelabour CS appears beneficial for the fetus with MMC, further analyses of the data, controlling for confounding variables, are required to confirm these findings.

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Lastly, I would like to dedicate this work to children with MMC and to their parents and care-givers, who must face the constant and immense challenges brought on by this condition every single day. Their courage, hope, strength and determination will never be forgotten.

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1. INTRODUCTION

1.1 Overview of Study Protocol:

This study is a retrospective cohort study which identifies infants born with MMC at their birth hospitals and then follows them forward in time to the neurosurgical treatment centre and rehabilitation centre. This study determines the association between labour and the mode of delivery with outcomes such as infectious morbidity in the first 6 months of life and severe paralysis at 2 years of age. The research questions are as follows:

1. Is prelabour CS versus TOL, with VB or CS after labour, for the fetus with MMC associated with a decrease (or increase) in severe paralysis at two years of age?
2. Among women experiencing labour, is CS versus VB for the fetus with MMC, associated with a decrease (or increase) in severe paralysis at two years of age?
3. Is prelabour CS versus TOL for the fetus with MMC associated with decreased (or increased) mortality and/or morbidity in the infant during the first 6 months of life? Outcomes of morbidity assessed were the following: Apgar score <7 at 5 minutes, definite meningitis, definite wound infection or breakdown, sepsis, urinary tract infection, seizures, Chiari malformation symptoms, shunt malfunction and/or infection, respiratory support for >48 hours, number of hospitalizations, and number of days in hospital.
4. Is CS following a period of labour, compared with VB, associated with decreased

(or increased) mortality and/or morbidity in the infant with MMC during the first 6 months of life? Morbidity is defined as in research question 3.

1.2 Overview of the Problem of Meningomyelocele:

Meningomyelocele (MMC) is a congenital anomaly of the spinal cord resulting in herniation of the meninges, spinal cord and nerve roots through a bony defect in the spine to lie exposed in the midline spinal axis. The incidence of MMC is 4-8 per 10,000 births in North America (Edmonds and James, 1990) and it is considered to be one of the most incapacitating congenital anomalies still compatible with life. Infants are at risk for infection and death, and life-long disabilities such as spinal and limb joint deformities, muscle paralysis with limitations in independent mobility, mental retardation, bowel and bladder incontinence, and social problems.

Both labour and the actual mode of delivery, either by Cesarean Section (CS) or vaginal birth (VB), may affect mortality, infectious morbidity and ultimately the severity of paralysis and degree of independent mobility and functioning.

1.3 Development of the Meningomyelocele Study:

The Meningomyelocele Study (MMC Study) was initially designed by Dr. Lea Fairbanks to define the optimal delivery method for the fetus with MMC, by studying both the effect of exposure to labour and the effect of the actual mode of delivery, either by CS or VB after the onset of labour, on the severity of paralysis as assessed at the age of 2 years. Any effects of labour and mode of delivery on 6 month mortality and morbidity, such as meningitis, sepsis, and wound infections, would also be examined.

The MMC Study involves retrospectively collecting data on infants born with MMC in Ontario over a 10 year period. Data were to be collected from the birth hospital, the neurosurgical hospital to which the infant was transferred, and the rehabilitation centre where follow-up occurs at 2 years of age. Cohorts were established based on 1) whether or not avoidance of labour and vaginal birth occurred, with infants being born by elective CS being compared to those delivered after a trial of labour (TOL), and on 2) the actual mode of delivery after the onset of labour, with infants born by CS after TOL being compared to those born vaginally.

1.4 Objectives of this Thesis:

The objectives of this thesis in the context of the MMC Study are:

a) to describe modifications to the original study design made by myself and discuss the limitations of such a retrospective cohort study. The collection and analysis of the 2 year rehabilitation data will not be part of this thesis.

b) to design the data collection instruments, collect the data from birth and neurosurgical centres, set up a computerized database and discuss issues of database management as they pertained to this study

c) to examine the effects of labour and mode of delivery on the 6 month exploratory outcomes of neonatal morbidity and perinatal mortality.

2. BACKGROUND

2.1 Embryological Development of the Central Nervous System

The development of the central nervous system (CNS) in humans begins very early, prior to the first missed period and proceeds in 3 main stages: neurulation, canalization and retrogressive differentiation (Byrd et al, 1991). The stage of neurulation begins with thickening and rapid proliferation of a single layer of ectodermal cells to form a thick pseudostratified layer of cells called the neural plate. At about 18 days of embryonal age (about 4.5 weeks gestational age), a distinct depression, the neural groove, appears in this newly formed plate on the dorsal ectoderm of the embryo (Behrmann and Vaughan, 1983). This groove quickly deepens in a longitudinal direction such that its two margins become apposed and fuse to form the neural tube (Behrmann and Vaughan, 1983; Angtuaco et al, 1994). This fusion begins near the centre of the embryo at the cervico-medullary junction and progresses cephalad and caudad (Behrmann and Vaughan, 1983; Donnai et al, 1993). By about 23 days of embryonal age (5.5 weeks gestational age), the neural tube is complete, except for an opening at each end, the anterior and posterior neuropores. These neuropores close by about day 25 of embryonal age, completing the stage of neurulation (Byrd et al, 1991). Clusters of ectodermal cells are excluded from and remain on either side of the neural tube to later form the neural crests which will subsequently give rise to cranial nerves, sensory ganglia, and the sympathetic chain (Angtuaco et al, 1994). Also, simultaneous with the stage of neurulation, the overlying ectoderm of the skin separates from the neural tube and fuses in the midline forming the perineural mesenchyme which grows around the neural tube to form the meninges, bone and muscle (Byrd et al, 1991).

The cephalic portion of the neural tube undergoes further enlargement to form the early brain. During the fourth week of development, the early brain undergoes extensive differentiation into several brain segments which will eventually form the ventricular system, the cerebral hemispheres, thalamic areas, brain stem, cerebellum and the neurocranial (eyes, internal ears, and olfactory organs) and visceral (cephalad portion of the digestive and respiratory tracts and facial structures) portions of the head (Angtuaco et al, 1994).

The spinal cord is formed from the caudal portion of the neural tube and continues its development by entering the stage of canalization, which begins at approximately the 30th day of fetal life (Byrd et al, 1991). During this stage, the caudal end of the neural tube elongates just distal to the posterior closure into a caudal cell mass with ependyma lining this central tubular structure (Byrd et al, 1991). Finally at 5.5 weeks, during retrogressive differentiation, there is a decrease in the size of the central lumen and caudal cell mass, resulting in formation of the spinal cord, filum terminale, conus medullaris, and central canal (Byrd et al, 1991). Although there is a variety of theories as to the development of the different types of spinal abnormalities, the underlying cause is a result of an insult (whether genetic or acquired) that interferes with the normal process of neurulation, canalization, and/or retrogressive differentiation (Byrd et al, 1991).

Several developmental abnormalities of the CNS are possible depending on the site and timing of the insult. A closure defect of the posterior neuropore leads to spina bifida and MMC (Behrmann and Vaughan, 1993). The term rachischisis is sometimes used for very

widespread spinal closure defects involving most or all of the dorsal, lumbar, and sacral regions. It is believed that most of the spinal dysraphic states occur approximately at the stage of neurulation of the spine and spinal cord, particularly the MMC/myelocele and lipomyelomeningocele.

2.2 Classification of Neural Tube Defects

MMC belongs to a group of disorders classified as neural tube defects (NTDs) which are malformations of the brain and spinal cord originating at various stages of embryonal neural tube development (Lemire, 1988). Whether the defect is in the brain or spinal cord, it may be further characterized as either open (not skin covered or non-epithelialized) or closed (skin covered or epithelialized). Non-epithelialized lesions, such as MMC, occur prior to neurulation and carry a much worse prognosis than epithelialized lesions (Lemire, 1988).

NTDs of the spine are also referred to as spinal dysraphisms which encompass a variety of disorders that have an abnormal formation of the paediatric spine as a common feature (Byrd et al, 1991). The most commonly seen NTDs of the spine are defects with obvious back masses such as MMC, lipomyelomeningocele, meningocele, and "occult defects" with no mass in the back such as diastematomyelia, dermal sinus, and tight filum terminale (Byrd et al, 1991).

MMC is a midline defect of skin, vertebral arches and neural tube, usually in the lumbosacral region (Romero et al, 1987). The degree of skin covering is variable and lack of fusion of the vertebral arches in the spinal column extend beyond the visible

neural lesion. The abnormally placed neural tissue is surrounded in the middle of the defect by a vascular network, with epithelial tissue peripherally (Noetzel, 1989). The extent of neurologic dysfunction correlates with the level of the spinal cord lesion (McLaughlin, 1985).

Patients with MMC have associated anomalies of the brain such as: the Chiari II malformation (present in 99% of cases), which consists of downward herniation of portions of the medulla oblongata, fourth ventricle, and inferior cerebellum into the upper cervical canal posterior to the cervical spinal cord; dysgenesis of the corpus callosum; and dysplasia of the calvarium, meninges, cerebral hemispheres, and cerebellum (Paidas and Cohen, 1994). These patients may have hydromyelia (present in 40-80% of cases), arachnoid cyst of the spinal canal (present in 20% of cases), and diastematomyelia (present in 30-40% of cases). They may have or develop scoliosis or kyphoscoliosis usually secondary to large defects of the neural arches, abnormal bony alignment of the pedicles, and abnormal neuromuscular imbalance (Paidas and Cohen, 1994). Non-CNS abnormalities which are sometimes associated with MMC include disorders of the kidneys, gastro-intestinal tract, face, thorax and extremities (Paidas and Cohen, 1994). Chromosomal abnormalities are found in 10% of cases (Paidas and Cohen, 1994).

2.3 Epidemiology of Neural Tube Defects and Meningomyelocele

Marked variations in the incidence of NTDs, with the majority of cases being equally divided between MMC and anencephaly, have been demonstrated depending on the geographical area, both between and within countries, the type of people and historical time period (Leech and Payne, Jr., 1991). In Canada, the reported incidence of NTDs

range from 1.6 per 1000 live births in British Columbia and Ontario to 4.0 per 1000 live births in Newfoundland and Quebec (Canadian Task Force on the Periodic Health Examination, 1994). Women who have had a previously affected pregnancy are at the highest risk of recurrence in subsequent pregnancies; however, 95% of infants born with a neural tube defect are from families without a previous case. The reported risk of recurrence is 2.1% in British Columbia, 2.4% in Ontario, 4.5% in Quebec and 5% in Newfoundland (Canadian Task Force on the Periodic Health Examination, 1994).

The highest rates of NTDs have occurred in parts of the British Isles, mainly in Ireland and Wales, where an incidence of 3.05 to 6.79 cases per 1000 births has been reported for anencephaly, and 3.33 to 4.13 cases per 1000 births for MMC (Paidas and Cohen, 1994). Elsewhere in the British Isles, the incidence for each of these defects ranges between 1.0 and 3.5 per 1000 births. World wide, an average incidence of one case per 1000 births for both anencephaly and MMC exists, but France, Norway, Hungary, Czechoslovakia, Yugoslavia, and Japan have a low prevalence (0.1 to 0.6 per 1000 births) (Lemire, 1988).

Migration patterns and ethnic differences have been considered when studying geographic variation of NTDs. Offspring of parents who have migrated to the eastern United States from Ireland have a higher incidence than do offspring of nonimmigrants (Lemire, 1988). A similar situation exists in other areas. For example, within Singapore, the Chinese previously had a NTD rate of 0.62 per 1000 births; Eurasians, 1.45 per 1000 births; Europeans, 2.15 per 1000 births; and Sikhs, 6.5 per 1000 births. Tan et al (1984) found the incidence of anencephaly in Singapore to be 0.54 per 1000 births between 1976 and

1980. Chinese constituted 67 (72%) of the 93 cases, whereas Malays and Indians each constituted 14% (13 cases for each). No cases were reported among Europeans (Lemire, 1988).

Geographic variations in incidence are demonstrated, both within and between countries, by the decreasing incidence from east to west in the United States, and from north to south in the British Isles (Reigal and Rotenstein, 1994). There is an overall east-west gradient, with the highest incidence in the British Isles, the lowest in Japan, and with North America being in between (Lemire, 1988). In North America, the east-west gradient has been lost due to the decreasing incidence of NTDs although the incidence in Newfoundland remains high (Seller, 1994).

Variations in the incidence of MMC based on sex, race, and social status also exist. Incidence remains higher in females than in males and is much lower in blacks and Asians than in whites (Byrd et al, 1991; Greene et al, 1991). The incidence of spina bifida does seem to increase with poverty and poor nutrition but these observations may be explained by chance alone (Byrd et al, 1991). Studies of variations with season, maternal age, and parity do not seem to provide meaningful clues regarding etiology. There is difficulty in establishing what the true risk of MMC may be with conception for any given fetus since many fetuses with MMC may be aborted in early pregnancy. It has been reported that MMC is 13 times more common in spontaneously aborted fetuses than in full-term infants (Osaka et al, 1978).

During the past 50 years, the incidence of MMC has been reported to be declining in

many parts of the world. Prior to the early 1980's, the incidence was thought to be as high as 1 to 2 per 1000 live births in the United States and from 4 to 5 per 1000 live births in regions of Ireland (Elwood, 1972; Laurence, 1989). Current figures indicate a drop in the United States from 5.9 per 10,000 births in 1984 to 3.2 per 10,000 births in 1992 (CDC, 1992; Reigal and Rotenstein, 1994). There has been a dramatic fall in incidence in the Irish Republic since the mid-1970's from 6.2 per 1000 births to 2.3 per 1000 births in 1987 (Scott et al, 1992). In 1970, the birth incidence of NTDs for England and Wales was 4.5 per 1000; in 1991 it was only 0.18 per 1000 (Scott et al, 1992).

The declining incidence is not accounted for solely by changing demographic patterns or increased rates of termination of affected pregnancies. Rather, it may be the result of many factors and could include improved maternal nutrition, availability of prenatal screening and diagnosis, selective pregnancy termination, undetermined environmental changes and vitamin supplementation (Reigal and Rotenstein, 1994). The dramatic fall in the Irish republic may be explained by the increase in dietary intake of folic acid. Since 1985, breakfast cereals have been fortified with folic acid and these now constitute over one third of the daily folic acid intake (Scott et al, 1992). Since this folate is in a readily bioavailable form, the overall availability may have increased by a factor of 2 or 3. It is also possible that in the early 1980's, the increased consumption of cereals and milk may have started a trend which was subsequently enhanced by the advent of fortified cereals (Scott et al, 1992).

2.4 Etiology

MMC has been recognized to be an etiologically heterogeneous disorder with at least 85% of cases attributed to multifactorial inheritance (Noetzel, 1989). The cause of MMC may involve an interplay between genetic and environmental factors. There is a familial tendency, or predisposition, to the occurrence of MMC but the pattern of inheritance does not fit mendelian transmission, although NTDs attributable to single genes have been described (Reigal and Rotenstein, 1994). This type of inheritance pattern usually results in a polygenic predisposition where the effects of several minor genes combine to determine the actual occurrence of MMC (Noetzel, 1989). Genetic factors may be responsible for the baseline incidence of MMC with various environmental factors increasing this incidence over the baseline levels (Noetzel, 1989). In North America, the risk of having a child with MMC is about 0.05%. If there is one sibling with MMC, the risk of a subsequent child having spina bifida increases to about 5% and if there are two, the risk increases to approximately 12 to 15% (Noetzel, 1989). The known tendency of NTDs to recur in families suggests several possible genetic mechanisms, including a recessive gene, a dominant gene with reduced penetrance, a recessive X-linked gene, cytoplasmic inheritance, and polygenic inheritance (Reigal and Rotenstein, 1994). The fact that NTDs have been observed in chromosomal abnormality syndromes has added to the suspicion that there is a genetic form of spina bifida (Reigal and Rotenstein, 1994).

Numerous teratogens have been suggested in the etiology of MMC including clomiphene citrate, valproic acid, phenytoin, trimethadione, haloperidol, alcohol, viral and other infections, local anaesthetics, triamcinolone, hydroxyurea, hypervitaminosis, dextromethorphan, and maternal fever (Paidas and Cohen, 1994; Reigal and Rotenstein,

1994). Despite the abundance of teratogens suggested as being associated with MMC, conclusive supporting data for a causal factor is missing (Reigal and Rotenstein, 1994).

Both animal and human clinical research have provided increasing evidence that nutritional deficiency states, particularly for folic acid and zinc, play a role in the etiology of NTDs (Paidas and Cohen, 1994; Reigal and Rotenstein, 1994). In 1965, Hibbard and Smithells found a significant relationship between primarily neurologic malformations of the fetus and defective folate metabolism in the mother when compared to a group of control women who had given birth to normal infants. Some case-control studies have found an association between high peri-conceptional intake of folic acid or multi-vitamins and a reduced risk of NTDs (Mulinare et al, 1988; Werler et al, 1993), whereas others have not (Bower and Stanley, 1989; Mills et al, 1989). Several prospective cohort studies have found a reduced risk of NTDs in those women with periconceptional multi-vitamin or folic acid supplementation (Laurence et al, 1981; Smithells et al, 1989; Milunsky et al, 1989; Vergel et al, 1990). In many of these studies, intake of multi-vitamins or folic acid was considered to be peri-conceptional if it occurred from 4 weeks before to 4 weeks after the last menstrual period. The strongest evidence, however, linking periconceptional folic acid supplementation with a reduced risk of NTDs, comes from the MRC Vitamin Study, a large randomized controlled trial indicating a relative risk of NTDs of 0.28 for women on folate versus those who did not take folate (MRC Vitamin Study Group, 1991). Although folic acid appears to prevent MMC, inferring that folate deficiency causes MMC, there have been no studies indicating folate deficiency among mothers with children with spina bifida. As well, affected pregnancies, despite the use of folate supplementation, have been reported.

Thus, the mechanism appears to be protective rather than preventive because of deficiency. Current evidence has permitted the CDC and US Public Health Service to recommend that all women of childbearing age consume the equivalent of 0.4 mg of folic acid per day in order to reduce the risk of having a child with an MMC (Reigal and Rotenstein, 1994).

2.5 Quality of Life for Children With Neural Tube Defects

Although the management of infants with MMC has shifted between aggressive treatment for all newborns and selective treatment based on various physical characteristics (the degree of paralysis, the degree of increased head circumference, the presence of kyphosis and other associated congenital anomalies, and birth injuries), most authorities agree today that infants born with MMC should be aggressively treated with immediate closure of the lesion and insertion of a ventriculoperitoneal (VP) shunt for hydrocephalus which is present in more than 80% of infants (Ryan et al, 1991). Although prognosis used to be poor, in recent years, improved closure techniques and other medical advances and increased societal acceptance of the disability have contributed to a better quality of life for these individuals.

Management of the child with MMC is optimized in the tertiary care setting by a team of specialists including, a neurosurgeon, orthopaedic surgeon, urologist, paediatrician, nurse, physical therapist, occupational therapist, social worker, orthotist, nutritionist, speech and language pathologist, and psychologist (Ryan et al, 1991). The two major goals in the management of children with MMC are (1) to prevent the physiologic impairments from becoming disabilities (eg. not being able to walk) and (2) to prevent

the disabilities from becoming handicaps or social disadvantages (eg. not being able to get a job) (Liptak et al, 1988). Achieving these goals requires comprehensive, coordinated care (Liptak et al, 1988).

A. Mortality:

Reported mortality rates vary depending on whether or not case series were selected or unselected. For unselected cases which include infants with severe hydrocephalus and chromosomal anomalies, mortality ranges from 14% to 19% for up to 10 years of follow-up (Lorber, 1973; McLone et al, 1985; Steinbok et al, 1992). For selected cases with the best prognosis, mortality rates for similar length of follow-up range from 3% to 8% (Gross et al, 1983; McCullough and Johnson, 1988). Operative mortality rates have been low at less than 5% (Ames and Schut, 1971; McLone et al, 1985). Mortality usually results from complications of the Chiari-Malformation defect, CNS infection, sepsis, and shunt complications (McLone et al, 1985).

B. Infection:

Infants with MMC are at risk for developing infections, particularly wound infections or dehiscence at the MMC closure site, meningitis and/or ventriculitis, and sepsis. McCullough and Johnson (1988) reported a rate of wound dehiscence requiring surgical revision, of 4.4%, although rates of wound infection requiring conservative management only are probably higher. The reported rate of ventriculitis was 6.7% (McCullough and Johnson, 1988). Charney et al (1985) reported rates of ventriculitis ranging from 8.3% in infants not receiving surgery to 10.4% in those who did.

C. Hydrocephalus:

Problems with hydrocephalus, either present at birth or related to shunt occlusions, infection or disconnection, usually require surgical revision. Hydrocephalus not only causes immediate complications of increased intracranial pressure, reduced consciousness, and vomiting, but it may also lead to reduced intelligence and perceptual-motor problems (Ryan et al, 1991). Approximately 80 to 85% of infants born with MMC also have hydrocephalus and up to 87% of these infants will require insertion of a shunt (McCullough and Johnson, 1988; McLone et al, 1992; Blum and Pfaffinger, 1994). Approximately 50% of shunted children require shunt revisions in the first year of life but after 2 years of age, the shunt revision rate remains steady at about 10% per year (Steinbok et al, 1992).

D. Chiari Malformation:

Although every child with MMC has the Chiari defect, a malformation in which the lower brainstem and cerebellum herniate through the foramen magnum and into the spinal canal, 6-32% actually develop clinical symptoms of apnoea, stridor, vocal cord paralysis, upper extremity weakness and spasticity and sudden death (McLone et al, 1982 and 1985; Park et al, 1983; McCullough and Johnson, 1988; Liptak et al, 1988; Ryan et al, 1991). The development of these symptoms often requires either a shunt insertion or a cervical laminectomy and posterior fossa decompression surgery (Liptak et al, 1988; Ryan et al, 1991) although some authorities question the value of this surgery (McLone, 1992). This malformation is the principal cause of mortality (McLone, 1992).

E. Spinal deformities and Spinal Cord Complications:

Spinal deformities such as kyphoscoliosis, and spinal cord complications such as syringomyelia (dilatation of the central canal of the spinal cord) and tethered spinal cord (resulting from adhesion of the spinal cord to the bony spine) often require surgical correction because of deterioration in bowel and bladder function, back and leg pain, pulmonary dysfunction, progressive deterioration in motor function, development of orthopaedic deformities, and recurrent skin ulceration (Liptak et al, 1988; Ryan et al, 1991).

F. Bladder and Bowel Incontinence:

Neurogenic bladder is very common and is best managed with serial urodynamic investigations to monitor function as the child grows, and clean intermittent catheterizations with concurrent drug therapy to prevent complications, such as renal stone formation, ureteral reflux, hydronephrosis, recurrent urinary tract infections and renal failure (Liptak et al, 1988). About 81% of children with MMC using catheterization plus medication are able to achieve satisfactory dryness (Liptak et al, 1988). A new alternative available for the older child with urinary incontinence is the artificial sphincter. Success rates of 80% have been reported with patients ranging in age from 7 to 28 years who received artificial sphincters (Liptak et al, 1988). Clean intermittent catheterization is utilized by 90% of children with MMC and 75% perform self-catheterization (McLone, 1992).

G. Loss of Motor Function:

Loss of motor function in the lower extremities leads to loss of mobility and to

musculoskeletal deformities (Liptak et al, 1988). The ability to ambulate is closely related to the level of the lesion so that children with intact quadriceps (L2-3-4) are much more likely to be ambulatory through adolescence than are those who lack such function (Liptak et al, 1988). Children with high to mid thoracic (T1-T6) lesions will always require wheelchair for ambulation whereas children with lower lumbar (L5) and sacral lesions will often require little or no assistance (Liptak et al, 1988).

The current philosophy is that all children should be given the opportunity to be upright, regardless of their functional prognosis unless they have severe central nervous system involvement because weight bearing increases bone density, helps to maintain urinary tract function, enhances cardio-respiratory fitness, reduces obesity and develops self-esteem (Ryan et al, 1991). Initially, a standing frame is used followed by gait training on the parallel bars once the child expresses a desire to move in the frame (Ryan et al, 1991). Other activities designed to develop balance and weight shifting abilities are then introduced (Ryan et al, 1991). Once independent ambulation occurs in the parallel bars, a walker is introduced and consideration is given to orthotic devices to allow more functional ambulation (Ryan et al, 1991). The overall goal is to provide maximum mobility with the minimum amount of bracing although many children will require a wheelchair to improve access to the environment, despite optimal bracing and gait training (Ryan et al, 1991).

Considerable controversy exists surrounding the timing of the introduction of a wheelchair for children who are unlikely to achieve independent community ambulation (Liptak et al, 1988). The proponents for early wheelchair introduction have argued that

early training will maximize eventual wheelchair skills, allow movement with greater speed, encourage participation in sports, minimize interventional surgery and enable children to keep up with their peers (Liptak et al, 1988; Ryan et al, 1991). The proponents of early ambulation in the upright position have argued that early introduction of the wheelchair limits the child's ambulatory potential and that ambulation in the upright posture slows progression of kypho-scoliosis, enhances cardio-respiratory fitness, reduces obesity, enhances wheel-chair transfer and self-care skills and improves renal tract function (Liptak et al, 1988; McLone, 1992). Some investigators have found that the timing of the wheelchair introduction made no difference in the ultimate level of wheelchair skill or ambulation (Ryan et al, 1991).

A substantial amount of energy is required for ambulation in adolescents with thoracic and high to mid-lumbar neurosegmental levels, particularly because of the increasing body weight (Ryan et al, 1991). Ambulation becomes less efficient in adolescence making it difficult for adolescents to keep up with their peers. The adolescent, therefore, may choose the wheelchair for full-time functional mobility (Ryan et al, 1991). Ambulation is usually done for therapeutic reasons only, with standing used for the purpose of transfers (Ryan et al, 1991). Because it is more energy efficient to use a wheelchair as the child grows to adulthood, community ambulation, the ability to walk between classes and in the neighbourhood, declines from 75% for pre-adolescents to 50% as young adults (McLone, 1992).

H. Intellectual Functioning:

Eighty to 85% of children with MMC have average intelligence with IQ scores in the

normal range (Liptak et al, 1988; McLone, 1991). Only 9% will have an IQ less than 70 with the majority of these children having had severe hydrocephalus at birth and/or ventriculitis in the neonatal period (McLone, 1991). Cognitive impairments in children with hydrocephalus are generally mild and most will function above the mentally retarded range (McLone, 1992). Higher MMC lesions are generally associated with lower intellectual functioning (McLone, 1992). Individuals who have shunts and a history of bleeding or infections usually have the lowest intellectual attainment, usually in the mentally retarded range (McLone, 1992).

Most children with MMC have selective cognitive disabilities and score better on verbal than on performance scales (McLone, 1992). Some display a hyperverbal communication pattern ("cocktail party chatter") with good vocabulary and articulation but, overall, demonstrate low intellect, poor social skills, and low academic achievement (McLone, 1991). Children with this "cocktail party chatter" (found in 25-35% of individuals with hydrocephalus) are extroverted, have precise articulation and mimic mature phrasing and often lead others to have high expectations that cannot be met (McLone, 1992). Specific cognitive testing often reveals problems with visual attention, visual-spatial perception, tactile perception, and auditory concentration (Liptak et al, 1988). Common manifestations seen as a result of these problems include a short attention span, distractibility, and difficulty with subjects requiring visual-motor integration such as arithmetic (Liptak et al, 1988). Problems with perceptual-organizational skills, upper extremity co-ordination and visual-motor co-ordination are frequent and increase with age. These have important practical implications for a wide range of functional skills (McLone 1992).

I. Psychosocial Effects:

MMC causes major psychological and social stress on both the child and the family. The parents have lost the normal child they were expecting and must attend to the immediate and long term needs of an abnormal child (Liptak et al, 1988) At a time when parents are least able to cope with the many issues involved in caring for an infant with MMC, they must also deal with feelings of denial, anger, depression, anxiety, and guilt (Liptak et al, 1988). In addition to direct medical expenses, there are numerous indirect expenses, such as costs for transportation, time lost from work for medical appointments, illnesses and hospitalizations, structural changes to the home, special clothing and special child care arrangements (Liptak et al, 1988). As a result of the needs of the child, the family may become isolated, lose job or school opportunities, be unable to take family vacations, and may need to give up the enjoyment of going out to dinner or to the movies (Liptak et al, 1988). The siblings of children with a chronic illness may have more difficulty adjusting and coping and families may react to the threat the child poses with nonacceptance, abuse or overindulgence, resulting in eventual fragmentation of the family (Liptak et al, 1988).

Children with MMC often require frequent hospitalization, surgery and treatments that are painful or embarrassing. They have restricted physical development and decreased ability to participate in many of the activities that other children their age can do. These factors make them different from their peers and may lead to anxiety and loss of self-esteem (Liptak et al, 1988). Children may become manipulative and demanding or may demonstrate regression and withdrawal as a response to the stress (Liptak et al, 1988). Learning disabilities may lead to poor school performance, negative reinforcement, loss

of interest in school, and a downward spiral of failure (Liptak et al, 1988). Most communities are poorly designed to meet the needs of these children so that access to transportation, public and community buildings and other activities and services are usually limited (Liptak et al, 1988). Although a person with MMC may have normal intelligence and optimal functioning in a medical sense, she or he may still have difficulty functioning in society leading to high unemployment (Liptak et al, 1988). Studies with long term follow-up have shown that 75% may approach a predicted level of independence but between 10 and 20% are likely to require long-term care (McLone, 1992).

2.6 Antenatal Diagnosis of Neural Tube Defects

Health Canada's Health Protection Branch estimates that at least 800 NTD conceptions occur each year in Canada (Carroll, 1994). Some of these 800 are spontaneously aborted and some are therapeutically aborted after detection resulting in at least 400 NTD births each year for a national prevalence of approximately 1 per 1000 total births, similar to the rate of NTD births in the United States (Carroll, 1994). Although a family history of NTDs increases the risk of having similarly affected offspring, 90 to 95% of NTDs occur in families without such history. Thus, prenatal diagnosis of NTDs is offered to all pregnant women and allows parents to terminate the pregnancy or prepare for the birth of an affected infant (Carroll, 1994).

A. Maternal Serum Alpha-Fetoprotein (AFP):

The association between the maternal serum AFP value and fetal open NTDs, such as anencephaly and MMC, was first recognized in 1972 (Brock and Sutcliffe, 1972).

Subsequent studies supported this association (Milunsky and Alpert, 1974; Leighton et al, 1975; Brock et al, 1979) and the usefulness of maternal serum AFP as a prospective screening test for open NTDs was firmly established by the United Kingdom Collaborative Study in 1977 (Wald and Cuckle, 1977 and 1979). The theory is that when the fetus has an "open" or non-skin covered NTD, AFP leaks across the exposed capillaries from the fetal circulation into the amniotic fluid which is then transferred across the amnion and the placenta into the maternal circulation (Rose and Mennuti, 1993) reaching a maximum level by 16-18 weeks gestation (Cuckle, 1992). Elevated maternal serum AFP levels also occur with multiple pregnancies and certain fetal abnormalities such as omphalocele, congenital nephrosis, Turner's syndrome with cystic hygroma, fetal bowel obstruction, teratoma, congenital heart defect, hydatidiform mole, hydrocephalus, polycystic kidney disease, and renal agenesis (Carroll, 1994).

The result of the maternal serum AFP value is reported as a multiple of the median (MoM) for each week of gestation, a convention which was introduced by the First UK Collaborative Study on maternal serum AFP as a method for participating laboratories to compare individual test results (Wald and Cuckle, 1979). The absolute value of a pregnant woman's AFP level is modified by other factors, namely maternal weight (lower AFP levels with increasing weight), race (higher AFP levels in African Americans than in whites), and insulin-dependent diabetes mellitus (lower levels in women with diabetes) (Cuckle, 1992; Carroll, 1994). The median maternal serum AFP value for each week of gestation is designated as 1.0 MoM. The adjusted result is expressed as a multiple of the median by dividing the maternal serum AFP concentration by the median value for that week of gestation. Most screening programs establish a cutoff of

2.0 or 2.5 times the median value when compared with normal controls at the same week of gestation.

Using a cut-off level of 2.5 multiples of the median, positive results will be found in 90% of anencephalic pregnancies and 75% of open spina bifidas (64% of all spina bifidas) (Cuckle, 1992). Three per cent of unaffected pregnancies will be screen positive but in about half of these the raised level will be explained by twins, underestimated gestation or fetal death (Cuckle, 1992). Maternal serum AFP screening is most accurate when done between 16-18 weeks' gestation, but it can be done between 15-22 weeks. Screening earlier or later than the optimal gestational age decreases the sensitivity of the test (Rose and Mennuti, 1993).

B. Ultrasound:

Although the maternal serum AFP may be repeated if the first test is abnormal, the presence of an NTD can usually be confirmed by detailed high resolution obstetrical ultrasonography paying particular attention to the fetal intracranial and spinal anatomy (Rose and Mennuti, 1993). In addition, this examination can rule out multiple gestation, incorrect gestational age, fetal death, or other fetal anomalies that can result in an elevated maternal serum AFP level (Rose and Mennuti, 1993; Carroll, 1994). Depending on the nature of the ultrasound equipment and the degree to which the fetal spine can be visualized, a detailed ultrasound can detect 70% to 90% of moderate-sized spinal defects (Rose and Mennuti, 1993; Carroll, 1994). Small defects in the lumbar region are more difficult to detect (Carroll, 1994). When done selectively because of a high prior risk of a central nervous system disorder, detection is high: all cases of

anencephaly are detected, as are 80-90% of spina bifidas, with only 1-2% of unaffected pregnancies having suspicious findings. The detection rate is likely to be lower when scanning is routine (Cuckle, 1992). The combination of maternal serum AFP screening and ultrasonography will detect more than 99% of cases of anencephaly (Rose and Mennuti, 1993).

Most authorities agree that even routine fetal ultrasonography done in the second trimester should include a transthalamic, transventricular and transcerebellar view of the fetal cranium and a quick assessment of vertebral body alignment with longitudinal scanning in order to maximize the diagnosis of anomalies (Angtuaco et al, 1994). Fetal ultrasound findings of MMC may include small head size, deviation of the cerebellum into the cisterna magna (banana sign), virtually obliterating it, scalloping of the frontal bones (lemon sign), enlarged transverse cerebellar diameter greater than or equal to 2 SD below the mean for gestational age, enlargement of the atrium of the lateral ventricle (>10 mm), dangling of the choroid plexus in the dependent lateral ventricle, and divergence of the posterior ossification centres of the spine (Filly et al, 1989; Hill et al, 1991; Gomez and Copel, 1993; Angtuaco et al, 1994). Cerebellar abnormalities have been noted in 95% of cases of MMC regardless of gestational age, and these abnormalities are often more readily attained than detailed spinal views (Gomez and Copel, 1993). In a prospective study evaluating 905 cases referred with elevated maternal serum AFP and a single fetus, 49 out of 50 NTDs were diagnosed by ultrasound alone and one case required amniocentesis for a definitive diagnosis (Morrow et al, 1991; Gomez and Copel, 1993). Ultrasound screening with an elevated maternal serum AFP has a sensitivity of 98% and a specificity of 100%. The predictive value of

a positive ultrasound diagnosis was 100% and of a negative ultrasound, 99.9% (Morrow et al, 1991; Gomez and Copel, 1993).

C. Amniocentesis:

In cases where the ultrasound results are questionable or fail to explain the elevation in the maternal serum AFP, an amniocentesis for determination of amniotic fluid AFP and acetylcholinesterase levels, may be required to clarify the diagnosis (Gomez and Copel, 1993). High amniotic fluid AFP levels and, in particular, high acetylcholinesterase levels, virtually confirm the presence of an open NTD. However, this diagnostic procedure does carry a risk of abortion of 0.5 to 1% (Gomez and Copel, 1993). Of amniocentesis performed for specific evaluation of elevated maternal serum AFP, 90% to 95% will reveal normal amniotic fluid AFP and acetylcholinesterase (Gomez and Copel, 1993). However, because of the recent improvement in ultrasound imaging technology and the recognition of various ultrasound markers for neural tube defects, amniocentesis is rarely necessary in the evaluation of patients with elevated maternal serum AFP (Gomez and Copel, 1993).

Most patients with a high serum AFP level in whom no abnormality is detected will have normal offspring. However, it is appropriate to follow these patients closely because they have increased rates of stillbirth, neonatal death, low birth weight, and premature delivery (Rose and Mennuti, 1993; Carroll, 1994).

If an NTD is diagnosed, the pregnant woman is given detailed multi-disciplinary counselling with respect to the expected prognosis and natural history of the defect. A

fetal karyotype by amniocentesis and fetal echocardiography are recommended prior to discussing prognosis. The parents may elect to terminate the pregnancy without further investigations or they may wish to proceed with further testing to help determine prognosis prior to making a decision about whether or not to continue with the pregnancy (Rose and Mennuti, 1993).

2.7 Prognostic Factors in Neural Tube Defects

A. General Issues:

The issue of being able to accurately predict the short and long term outcome of infants born with MMC has been debated in the literature for over 30 years. Prior to the availability of shunts for hydrocephalus, children with MMC were usually managed without surgery with most dying by 2 months of age and one year survival being only 20% (Noetzel, 1989). Of those who survived, most had normal intelligence and 70% were able to ambulate, some requiring assistive devices (Noetzel, 1989). When ventriculo-atrial shunts became available in 1958 to control life-threatening hydrocephalus (Lorber, 1973), it became common to treat all infants with MMC by early closure of the back defect and shunting irrespective of their degree of handicap (Noetzel, 1989). Despite the technological improvements, treating all infants resulted in the prolongation of life in the most severely affected infants and although mortality improved with most children surviving until age 10 years, only 30% were intellectually competitive ($IQ > 85$) and about 55% were confined to a wheelchair (Noetzel, 1989). The survival of such severely handicapped children raised the question as to the ethics of treating every infant with MMC and led to the application of strict criteria for selective treatment in the 1970's (Noetzel, 1989). In 1973, Lorber proposed a set of prognostic criteria to be

applied to infants with MMC to decide whether or not treatment would be indicated. This author recommended that infants with one or more of the following criteria should not be treated: gross paralysis of the legs, thoracolumbar or thoracolumbosacral lesions, kyphosis or scoliosis, grossly enlarged head, intracerebral birth injury, and other gross congenital defects. His contra-indications to the continuation of active therapy after closure of the MMC, were the development of meningitis or ventriculitis in an infant who already had serious neurological handicap and hydrocephalus (Lorber, 1973). In studies which reported the results of the application of these selective criteria, about 50% of MMC infants received supportive therapy only (Noetzel, 1989). Those infants who were selected for active treatment did extremely well with about 75% surviving to age 5 to 7 years, about 80% being ambulatory, and more than 85% having an IQ greater than 75 (Noetzel, 1989). The usefulness of the criteria described by Lorber (1973) were questioned however, since it became obvious that they were not sensitive enough (Noetzel, 1989). Some infants with adverse prognostic features were excluded from treatment but survived with handicaps that would have been prevented with early treatment, (Noetzel, 1989) or did well both physically and mentally despite the lack of treatment (Steinberg, 1991). Although it is true that the extent of physical rehabilitation is limited by motor disability, the overall rehabilitation potential for a child with MMC is mainly determined by intellectual capabilities and psychosocial adjustment which are not necessarily related to the level of spinal cord involvement (Noetzel, 1989).

At present, the management approach to each newborn with MMC should be determined individually, although aggressive therapy should be recommended regardless of the level of spinal deficit (Noetzel, 1989). Most tertiary care centres now have returned to an

aggressive therapeutic approach for patients with MMC (Noetzel, 1989). In one series of 200 consecutive unselected patients treated aggressively and followed prospectively for 5 to 9 years, mortality was only 14% (Noetzel, 1989). Of the survivors, 73% were competitive intellectually, 75% were ambulatory and 87% were continent of urine (Noetzel, 1989). McLaughlin et al (1985) followed the outcome of 212 infants born with MMC over 3 different time periods who were classified into one of 3 groups: (1) those with a good prognosis who received early treatment (2) those with a bad prognosis who received supportive care and (3) those with a bad prognosis who were actively treated. There was a significant difference in survival between surgically treated children and those receiving only supportive care in all three periods (McLaughlin et al, 1985). There was no significant difference in survival between patients in the good-prognosis and poor-prognosis groups who received early surgical treatment. The progress of surviving patients in the three groups was examined. In the survivors of the good prognosis group, 78% had normal cognitive development, 76% were ambulatory and 96% were residing in their natural home (McLaughlin et al, 1985). In the poor-prognosis early surgery group, 62% had normal cognitive development, 18% were ambulatory, and 79% resided in the natural home. In the supportive care group, only 40% had normal cognitive development, 20% were ambulatory, 50% resided in the natural home and 60% had kyphoscoliosis. McLaughlin et al (1985) observed that in their treated patients, nearly 80% demonstrated normal cognitive development and nearly an equal number were ambulatory. In fact, the results of aggressive therapy employed in the last several years are comparable with and, in many ways, exceed the outcome reported previously for management based on strict selection criteria (McLaughlin et al, 1985). Some exceptions to the use of aggressive therapy are infants who have extremely advanced hydrocephalus

noted at birth, major irreversible parenchymal brain injury secondary to anoxia, active central nervous system infection, or other malformation or medical problems incompatible with long-term survival (Noetzel. 1989).

Factors responsible for this improvement in outcome probably include increased frequency of prenatal diagnosis and improved prenatal and perinatal care; regionalization of newborn services such that selected infants are referred more promptly to tertiary care centres and are arriving in better condition; prompt availability of noninvasive imaging studies, such as ultrasonography and computed tomography, that have improved the ability to detect, monitor, and treat hydrocephalus more effectively; advanced surgical techniques for back closure and shunting of CSF, especially the introduction of ventriculo-peritoneal shunts; early detection and more aggressive management of infection, resulting in reduced post-operative CSF infections and myofascial breakdown after back repair; improved methods promoting urinary function and continence; technical advances in braces and other assistive devices for ambulation; better technical options for the management of kyphoscoliosis; and increased social acceptance of infants with MMC (McLaughlin et al, 1985; Noetzel, 1989).

B. Level of the Lesion:

Many investigators have found that the anatomical spinal level of the MMC is not only an important determinant of eventual functional ambulation and wheelchair reliance, but it is also associated with the strength of lower-extremity muscles (Hoffer et al, 1973; Barden et al, 1975; DeSouza and Carroll, 1976; Feiwell et al 1978; Huff and Ramsey, 1983; Stillwell and Menelaus, 1983; Gaff et al 1984; Samuelsson and Skoog, 1988;

McDonald et al, 1991). Weak iliopsoas muscle strength ($\leq$grade 3) is associated with partial or complete wheelchair reliance (McDonald et al, 1991). If weak iliopsoas muscle strength is coupled with strong quadriceps function, partial (household) ambulation is still possible. Even with strong (grade 4 to 5) iliopsoas and quadriceps, the achievement of community ambulation without reliance on a wheelchair does depend on the presence of antigravity gluteal muscle strength (McDonald et al 1991). Knowledge of gluteus medius, gluteus maximus and anterior tibialis strength also helps in the prediction of ambulation, with or without aids or braces. The majority of patients with grade 4 to 5 gluteal strength and grade 4 to 5 ankle dorsiflexion ambulate without the use of aids or braces. These patients also tend to have strong peroneal and gastrocnemius-soleus muscles, providing adequate foot and ankle stability. Evaluation of anterior tibialis strength can be more reliably performed on the newborn than can gluteus medius and gluteus maximus assessment. Since anterior tibialis and gluteal muscle strength is correlated, anterior tibialis function can be useful for predicting whether or not infants and toddlers with strong iliopsoas and quadriceps will be likely to rely on aids or braces for their ambulation (McDonald et al, 1991).

Despite these specific findings, some physicians continue to determine prognosis based on broad categorization of the anatomical spinal level of the MMC lesion (Neotzel, 1989). In children with levels of L2 and above, ambulation with full braces may be possible but long-term mobility usually requires a wheelchair. Most patients with lesions below S1 are ultimately able to walk unaided. Those with lesions at L5 may require short leg braces for mobility. Patients with intermediate lesions (L3 and L4) are most likely capable of assisted ambulation with braces or crutches. Because deterioration to

a lower level of ambulatory function can readily occur, predicted achievement levels are dependent on careful long-term management (Noetzel, 1989).

C. Hydrocephalus:

Brumfield et al (1995) found that when antenatal ultrasound findings were correlated with complications in the neonatal period and subsequent infant outcome on follow-up testing, severe hydrocephalus proved to be the one antenatal ultrasound finding that correlated most with later poor outcome in infants with a MMC. Twenty-six pregnancies with a fetal MMC referred in the third trimester, were followed with ultrasound examinations every three weeks until delivery (Brumfield et al, 1995). The head size was classified into three categories based on standard tables of head circumference (HC) and biparietal diameter (BPD) for a given gestational age (GA) for normal fetuses: macrocephaly if the BPD and HC were $>$95th percentile for GA, normal if the BPD and HC fell within the 5th-95th percentile for GA, and small if the BPD and HC were $<$5th percentile for GA. At 37-38 weeks' gestation, elective CS was performed before labour after obtaining a mature fetal lung profile. If labour or rupture of membranes occurred before an elective delivery could be scheduled, a CS was done in early labour. If ultrasound documented severe progressive hydrocephalus, delivery was considered as early as 34-35 weeks' gestation after documenting fetal lung maturity. There were 5 infants with macrocephaly and 21 infants with a normal or small head size. The infants with macrocephaly had statistically significant delays in mental and motor performances on subsequent long-term follow-up testing (Brumfield et al, 1995). Only 1 infant in the group of fetuses with head size within or below the normal range had a significant delay in follow-up mental testing, and only 5 in this same group had significant delays in motor performance (Brumfield

et al, 1995). No fetus with macrocephaly, however, had a normal mental score or motor performance on subsequent long-term follow-up testing (Brumfield et al, 1995).

After analysing the records of 167 patients and categorizing them into non-shunted, shunted with no history of ventriculitis, and shunted with a history of ventriculitis, McLone et al (1982) found that IQ scores were significantly lower and visual motor integration was slower in those children who had ventriculitis when compared to those that did not, shunted or unshunted. These investigators concluded that the severity of hydrocephalus at the time of birth may not necessarily be predictive of future intelligence and that mental retardation which is often associated with MMC is likely an acquired deficit related primarily to the onset of ventriculitis and/or meningitis (McLone et al, 1982). The mechanism by which infection of the ventricular system and/or meninges affects the ultimate development of the child's intellect is likely multifactorial (McLone et al, 1982). Theories include: the exacerbation of the rate and severity of the hydrocephalus by the ventricular infection; spread of periventricular edema along the white matter tracts of the brain; spread of the ventricular infection to the subarachnoid space and the cortical surface of the cerebral hemispheres through the ventricular system with destruction of myelin and fragmentation of cellular processes (McLone et al, 1982).

D. Delay in closure of the defect (defined as >72 hours):

Early closure of the back appears to be central to the management of MMC and there is a general consensus to perform this surgery within the first 72 hours of life to avoid infectious complications, limit the loss of motor function from drying of the neural placode and to facilitate nursing and parental care (Noetzel, 1989). Sharrad et al (1962)

compared muscle strength at birth and 3 months later in a group of infants having surgery within 48 hours of birth to a group of infants having no surgery at all. In the operative group, muscle strength improved whereas in the group not receiving surgery, muscle strength deteriorated indicating an increase in paralysis (Sharrad et al, 1962). On the other hand, Smyth et al (1972) concluded that immediate closure (within 72 hours of birth) when compared to delayed closure (3 to 28 days) did not result in any significant reduction in mortality or any improvement in muscle power in the legs. Deans and Boston (1988) made more controversial conclusions from their study which found that non-closure resulted in a significantly lower incidence of hydrocephalus, shunt insertion and ventriculitis during the first few months of life although mortality was similar to infants who underwent closure. Charney et al (1985) compared infants who had early surgery in the first 48 hours of life, delayed surgery between 3 to 7 days, and late surgery between 1 week and 10 months of age. Survival rates were similar between those with early, delayed, or late surgery, 92%, 94%, and 100% respectively (Charney et al, 1985). No significant association was found between the timing of surgery and the development of ventriculitis and there were no differences in developmental progress or changes in paralysis (Charney et al, 1985).

Charney et al (1985) felt that the absence of significant differences in morbidity or mortality between the groups having early, delayed, or late surgery suggests that there is no urgency in surgical intervention for the initial management of newborns with MMC. Instead it is important to have time for comprehensive discussions, counselling, and emotional support for the parents of these infants. During this time both physician and parents could seek additional advice and support from other physicians and parents,

and if need be, from institutional ethical review committees (Charney et al, 1985). However, Charney et al (1985) did advise that surgery should not be delayed indefinitely because mortality increased between 1 and 2 years of age and survival dropped below 90% without surgical intervention.

E. Antenatal Diagnosis:

A couple whose fetus has been diagnosed antenatally with a NTD faces the difficult decision of whether to continue or terminate the pregnancy (Grevengood et al, 1994). This decision is particularly complicated because of the inability to accurately predict the outcome of an affected pregnancy based on the extent of the lesion, as well as candidacy for and response to surgical repair (Grevengood et al, 1994). However, some studies have shown that the severity of the NTD, as determined by antenatal ultrasonography, does appear to influence the decision to continue or terminate the affected pregnancy (Grevengood et al, 1994). Grevengood et al (1994) reported that out of 27 women carrying fetuses with spina bifida, the 9 women who elected pregnancy continuation were all carrying fetuses with lesions caudad to T9, who, in general, have a better prognosis than those with lesions craniad to this level (Grevengood et al, 1994). In addition, all women carrying fetuses with anencephaly, a uniformly lethal condition, elected pregnancy termination. Ames and Schut (1972) reported that 35% of infants with thoracolumbar lesions died and corresponding percentages for lumbosacral and sacral lesions were 11% and 0% respectively, confirming that the prognosis of spina bifida varies by location of the lesion. With antenatal diagnosis resulting in pregnancy termination for severely affected fetuses and with the standard of care in many tertiary care centres being prelabour CS for delivery of those fetuses selected for pregnancy

continuation, it follows that a predominance of fetuses with less severe lesions would be delivered by prelabour CS.

Hogge et al (1990) reported on the outcomes of 23 women whose pregnancies were complicated by MMC and who were referred to a prenatal diagnosis and treatment centre where they received further testing. These women were offered counselling with respect to pregnancy termination and received close pregnancy surveillance if pregnancy continuation was elected. In pregnancies in which termination was chosen, autopsies were performed and postmortem radiographs were obtained in all cases to confirm the ultrasound findings. The distribution of the level of the lesion and the incidence of associated abnormalities were similar for women continuing the pregnancy (n=14) and for those electing termination (n=9) (Hogge et al, 1990). However, in studying the published data carefully, there was a tendency towards higher level lesions in the group electing termination.

F. Obstetrical Factors:

Prematurity, multiple gestation and fetal malpresentations (breech, transverse lie) in themselves are factors which increase perinatal morbidity and mortality. When these factors are combined with the presence of a congenital anomaly such as MMC, there is an increased chance that the infant will do worse than if there had been no MMC.

Many investigators feel that the increased survival and reduction in morbidity seen in infants with MMC is partly related to the tendency to deliver these infants in tertiary care centres with a level III nursery. The explanation given is that there are expertly trained

professionals who rapidly institute treatment and arrange for transfer to a paediatric neurosurgical centre.

2.8 Intrapartum Management of Fetuses with Meningomyelocele

It has long been recognized that uterine contractions during labour create a physiological stress on the fetus resulting in reduced placental perfusion and mechanical compression of the fetal head during the contraction (Cochrane et al, 1991). Studies of cephalic presentations have shown that the pressure applied to the cervix by the head are 3 to 4 times greater than the intra-amniotic pressure (Cochrane et al, 1991). These forces are increased after rupture of the membranes and are repeatedly applied to the fetal head with each uterine contraction. It has been postulated that these forces are also applied to the exposed spinal cord in infants with MMC resulting in traumatic injury and further neurological deterioration (Cochrane et al, 1991). Labour may also increase the risk for bacteria in the maternal lower genital tract to contaminate and infect the exposed spinal cord and nerve roots of the fetus, potentially leading to decreased motor function.

The effect of labour and delivery in infants with MMC was first studied in a case series of infants with MMC by Stark and Drummond in 1970. They reviewed obstetrical and newborn data on 130 consecutive infants born with MMC after a TOL (114 VB; 14 CS) who were admitted to the Royal Hospital for Sick Children in Edinburgh between 1965 and 1969. They recorded a 53.6% incidence of birth injury which included cephalohaematoma, fractures, ruptured sacs, hyperexcitability, convulsions and cerebral birth injury. They attributed this high rate of injury to the increased risk of malpresentation (19%) when compared to the general population and to hydrocephalus

which was commonly seen in infants with MMC (Stark and Drummond, 1970) (Table 1).

In 1972, Ralis and Ralis performed dissections of peripheral nerves in 39 infants born with MMC and in 71 infants without spinal cord defects (19 had other severe multiple congenital deformities), who all died between birth and 7 years of age. Compared to the group of infants who did not have MMC, the sciatic nerve in infants and children with MMC, was thinner, contained more connective tissue and fewer fibres, and demonstrated delayed maturation, more haemorrhage and more damage (Ralis and Ralis, 1972). Apparently these changes were confined to premature babies and those born by breech delivery. Unfortunately the presence or absence of labour and mode of delivery (VB or CS) and cause of death were not reported for these infants such that no conclusions could be made with respect to the etiology of the increased trauma in infants with MMC (Table 1).

In 1975, Ralis carried out an anatomic dissection of individual muscles and nerves of the lower extremities and of all damaged areas in a case series of 64 infants with MMC who died between the ages of 10 minutes and 3 months. Although all infants experienced labour with 15 infants born breech and 49 born cephalic, it is not clear whether any were born by Cesarean section. Extensive muscle haemorrhage, infarction, and degeneration and necrosis, likely from local anoxia, were found superimposed on muscle changes related to denervation and muscle atrophy, particularly in the musculotendinous junctions and in the tendons themselves (Ralis, 1975). Nerve haemorrhage and atrophy were also seen particularly in the uppermost, extrapelvic segment of the sciatic nerve (Ralis, 1975).

Although Ralis (1975) believed that mechanical birth damage of muscles and nerves in the legs of an infant with spina bifida could cause permanent deterioration to motor function, it was not clear from this study whether the mode of delivery (CS vs VB) had an effect on this damage as no such comparisons were made (Table 1).

Guha-Ray (1977) reviewed obstetrical and newborn data on 21 infants born with MMC at the Grace General Hospital in St. John's Newfoundland between 1970 and 1975. Nineteen women underwent a TOL (13 VB; 6 CS) whereas 2 women had a prelabour CS. They found a 58% incidence of fetal distress in infants with MMC compared to a 2.3% incidence in a group of 3,000 historical control infants described as being "normal" and delivered at the same hospital during the year of 1974. The characteristics of the historical control group were not clearly defined (Table 1) and the definition of "normal" is not given. In addition, this study does not compare infants outcomes with respect to the presence or absence of labour and mode of delivery. Even if this had been done, the small sample size would limit the ability of this study to detect differences in outcomes if they existed (Table 1).

Chervenak et al (1984) reported on the outcomes of 4 infants with MMC delivered by prelabour CS after documented fetal lung maturity by amniocentesis. One infant had a lumbosacral MMC repaired on the day of birth but died 13 days later of recurrent apnoea and bradycardia. Although the other 3 infants (all with lumbosacral MMCs repaired on the day of birth), assessed between 5 and 17 months of age, were reported as "doing well", the outcomes were not defined.

Shurtleff et al (1987) retrospectively compared 35 infants born by prelabour CS to 98 infants born after a TOL with respect to severe paralysis (motor level between T12 and L3), minimal paralysis (sacral or no loss of motor function), and the number of segments the mean motor level was below the anatomic level. They found that the incidence of severe paralysis was 15% in the prelabour CS group versus 39% in the TOL group. The incidence of minimal paralysis was 48% for the infants in the prelabour CS group versus 14% for infants in the TOL group (Shurtleff et al, 1987). In addition, the infants in the prelabour CS group had a mean motor level of function 3.2 segments below the anatomic level of the lesion compared to only 1.2 segments for infants in the trial of labour group (Shurtleff et al, 1987).

It is not clear from this study how long after birth the assessments of motor function were made and whether the timing of this assessment was similar in both groups. Because the majority of infants born by prelabour CS were born to a group of women who participated in antenatal diagnosis and selective pregnancy termination (70%), it was possible that the infants born by prelabour CS had a better prognosis than infants in the TOL group. None of the women giving birth to infants in the TOL group had undergone prenatal diagnosis and all these infants were born in outlying hospitals and required transfer to the study centre. The authors attempted to correct for this differential treatment in the study groups by comparing separately, cases born by prelabour CS to a set of matched cases from the women in the TOL group. They still found a lower incidence of severe paralysis and a higher incidence of minimal paralysis in the infants in the prelabour CS group (Shurtleff et al, 1987). Even though cases were matched for age, sex, anatomic level and city of origin, these matching variables failed to address the

potentially confounding effects of prenatal diagnosis, selective pregnancy termination and differential prenatal and peri-partum care in a tertiary care referral centre.

Bensen et al (1988) retrospectively studied the effect of labour on infants born with MMC who were admitted to an intensive care nursery between 1979 and 1985, by comparing those delivered after prelabour CS (n=13) to those delivered after a TOL (13 CS; 40 VB) for several outcomes. They found no significant differences in mortality, meningitis, neurologic findings and developmental scores at 1 year of age between the two groups.

It is not clear whether any eligible infants died before having the opportunity to be transferred to the nursery and therefore, be included in the study. If labour was associated with increased perinatal mortality, the infants in the TOL groups would appear to have a more favourable prognosis simply because the most severely ill infants would die before they could be studied. Also, potential confounding variables, such as prenatal diagnosis, were not discussed and, thus, it is not possible to determine if they were accounted for in the statistical analysis. The sample size was small, limiting the power of the study and thus, its ability to find a statistically significant difference if one did exist.

Sakala and Andree (1990) did a retrospective cohort study on infants born with MMC and transferred to their unit between 1979 and 1988. They compared the outcomes of 15 infants born after CS to those of 20 infants born vaginally. There were no statistically significant differences between the two groups with respect to maternal age, gravidity,

parity, gestational age, birth weight and length, and the size and location of the MMC defect. Head circumference was statistically significantly larger for the CS group ($p < 0.05$). One and five-minute Apgar scores were not statistically significantly different between vaginal and CS groups. Both groups underwent similar rates of procedures to close the defect as well as placement of VP shunts. The incidence of neonatal hydrocephalus, neurogenic bladder, faecal incontinence, orthopaedic deformities, and seizure disorder were similar between groups (Sakala and Andree, 1990). One infant born by CS developed meningitis resulting in an incidence of meningitis of 3% (Sakala and Andree, 1990).

Although Sakala and Andree (1990) attempted to take into account the baseline differences between groups, all relevant confounders were not discussed or accounted for. As well, the issue of survival bias was present since infants dying prior to transfer were not included in the analysis. The power of this study to detect differences was low due to the small sample size and more relevant longer term outcomes, such as motor function and level of paralysis were not examined. In addition, the effect of the presence or absence of labour could not be determined since infants born vaginally were compared to infants born by CS, either elective or after TOL.

A case-control study by Cochrane et al (1991) reported the ambulatory function of 208 patients with MMC aged 2-18 years who had been selected from the spina bifida clinics serving the Universities of British Columbia and Alberta. The obstetrical records for each patient were reviewed, all patients were re-examined by the authors and all parents were interviewed. The authors were particularly interested in how obstetrical factors

(presentation, labour, fetal distress, mode of delivery) and postnatal factors (shunt infections, number of shunt revisions, spinal complications such as hydromyelia, diastematomyelia and cord tethering, school performance) influenced the motor and sensory neurologic function, both at the time of birth and at last follow-up, and the eventual ambulatory function achieved. Ambulatory status was categorized as either wheelchair dependent, or using aids (crutches and braces) or independent (no aids or ankle-foot orthoses only). With respect to labour and mode of delivery, there were 123 (50%) vaginal vertex births, 14 (7%) vaginal breech births, 34 (16%) elective CS and 37 (17%) CS after TOL.

No statistically significant differences in motor or sensory level, either at birth or at the most recent examination, were found when patients were compared on the basis of birth presentation (vertex vs breech), delivery method (see groups above), labour (present vs absent) or fetal distress (present vs absent) (Cochrane et al, 1991). With respect to postnatal factors, only the timing of the MMC closure of the neural placode and the occurrence of spinal complications was associated with reduced eventual motor function but according to the table in their publication, statistical significance was not achieved. Sixty percent of patients demonstrated a stable motor level from birth to the last follow-up visit (Cochrane et al, 1991). Fourteen percent deteriorated at least one level and in all cases an additional complicating spinal anomaly or post-closure cord tethering was present (Cochrane et al, 1991). The postnatal deterioration reported in this study could not be attributed to the method of delivery. Improvement in neurological status was found in 26% of patients and of these, 50% were born by vaginal breech delivery ($p<0.04$) (Cochrane et al, 1991).

The ambulation of children appeared to be directly related to their neurological motor status ($p=0.001$) although it is not clear whether this was motor status at birth or at the latest follow-up visit or both. Overall, 34% required the use of a wheelchair, 27% needed aids other than an ankle-foot orthosis, and 39% were independent (Cochrane et al, 1991).

Presentation at VB was associated with significant differences in ambulatory pattern. Of infants in the vaginal vertex group, 30% were wheelchair dependent and 43% independent, while for infants in the vaginal breech group, the proportions were 44% and 22% respectively ($p=0.005$) (Cochrane et al, 1991). Although not statistically significant, infants in the vaginal vertex group had the highest proportion of independent ambulators and infants in the elective CS group had the highest proportion of wheel-chair dependent patients. No statistically significant relationship was found between ambulation and the presence of prenatal diagnosis, shunt infections, number of shunt revisions, or child's school performance.

Ambulatory function was affected by the age of the child. While independent ambulators remained so, many of the teenagers with midlumbar lesions, who had ambulated with aids as children, eventually elected a wheelchair for community mobility (Cochrane et al, 1991). Although Cochrane et al (1991) acknowledge this fact in their publication, it is not clear if they took into account the age at which the child was assessed for ambulation into the statistical analysis when comparing the groups based on presence or absence of labour. Although the authors state that for inclusion in the study, subjects had to be old enough to have established their mobility patterns and requirements, a 2 year

old child may not have yet realized their full ambulatory potential. Also, because this study examines children between the ages of 2 and 18 years attending rehabilitation centres, the issue of survival bias becomes relevant. The effect of selection bias should also be considered in this study. It is not known how representative this sample was of all children born with MMC in the provinces of British Columbia and Alberta since those children with very good ambulatory function might not even attend the spina bifida clinics in this study. Referral bias might result in the more socially privileged children attending private clinics instead of a University affiliated clinic such as the ones in this study. On the other hand, disadvantaged children might not be able to afford the trip in to a major University centre for follow-up visits and would be referred to the local physician or occupational and/or physiotherapist.

In 1991, Luthy et al reported another large study which compared outcomes of infants with MMC with respect to exposure to labour and route of delivery. They identified 200 infants born with MMC, representing approximately 95% of such infants in the state of Washington, between 1979 and 1988. Eighty-one of the 200 infants were identified to have MMC through antenatal diagnosis and their mothers had received routine counselling which included maternal serum AFP, amniocentesis, ultrasonography, karyotyping and consideration for pregnancy termination. Twenty-five cases were terminated according to the parents' wishes and 12 infants were excluded because of severe hydrocephalus. Of the 44 remaining cases in this antenatal diagnosis group, 37 were delivered by prelabour CS according to their policy, 6 underwent a CS after TOL, and 1 delivered vaginally. Of the 119 cases where the diagnosis of MMC was made only at birth, 11 infants delivered by prelabour CS mainly for malpresentation or previous CS,

30 were delivered by CS after a TOL, and 78 infants delivered vaginally. After excluding 3 infants who died, Luthy et al (1991) then grouped the surviving infants with MMC according to mode of delivery resulting in 47 infants in the prelabour CS group, 35 infants in the CS after TOL group and 78 in the vaginal delivery group.

Several factors were measured and compared between the three groups at 2 years of age including the anatomical level of the MMC (the most caudal posterior vertebral arch appearing intact on X-ray; remains the same throughout life), the motor level of paralysis (lowest level of purposeful movement on either right or left side), the difference in the motor and anatomical levels (motor level is either equal to or lower than the anatomical level), the incidence of severe paralysis (level of motor function at the T12 to L3 level), and the incidence of minimal or no paralysis (level of motor function at the sacral level) (Luthy et al, 1991).

As determined by radiography, there was no significant difference in the mean anatomical level of spinal lesion between the children delivered by CS without labour and those delivered by CS after labour began (Luthy et al, 1991). The anatomical level among the children delivered vaginally was significantly lower than that for either CS group ($F=4.89$, $p<0.01$), indicating that there were less severe lesions in the vaginal delivery group (VD) at the time of birth (Luthy et al, 1991). The mean motor level at two years or age was not significantly different in the prelabour CS group and the VD group, but each was significantly lower than that in the CS after labour group ($F=5.03$, $P<0.01$) (Luthy et al, 1991).

When the anatomical levels were subtracted from the motor levels, the mean difference was greater for the prelabour CS group (3.3 with a SD of 3.0) than for either the VD group (1.1 with SD of 2.3) or the CS after labour group (0.9 with SD 4.1)($F=8.67$, $P<0.001$), indicating that the children in the prelabour CS group had better motor function than would be predicted by their anatomic level (Luthy et al, 1991). There was no significant difference between the two groups exposed to labour in the difference between the motor level and the anatomical level, but each of these groups differed significantly from the prelabour CS group (Luthy et al, 1991).

Significant differences in the severity of paralysis at two years of age were found between the infants delivered by prelabour CS and those who had a TOL (Luthy et al, 1991). Forty-five percent of the prelabour CS group had sacral levels of paralysis or no loss, as compared with 16 percent of the groups exposed to labour (chi square=2.6, $p=0.005$). The chance of severe paralysis was 2.2 times greater in the groups exposed to labour than in the prelabour CS group (95% CI 1.7 to 2.8). No significant differences were found between the vaginal delivery group and the CS after labour group with respect to either severe paralysis (T12 to L3) or minimal level of paralysis (sacral levels or no loss), but the likelihood of paralysis in each of these groups was significantly greater than in the prelabour CS groups [the relative risk of severe paralysis for the prelabour CS group was set to 1.0; the RR (95% CI) for the CS after labour group was 2.3 (1.7-3.0); the RR (95% CI) for the VD group was 2.1 (1.8-2.5); and the RR (95% CI) for TOL was 2.2 (1.7 to 2.8)] (Luthy et al, 1991).

No significant differences were found among the prelabour CS group, the labour after

CS group and the VD group in the frequency of placement of CNS shunts, serious wound dehiscence, CNS infections, death and intellectual performance (Luthy et al, 1991). No differences were found in the means for the highest score achieved up to and including 24 months of age on the Bayley Mental Development Index between the prelabour CS group and the TOL group (Luthy et al, 1991).

There are some drawbacks in the study by Luthy et al (1991) which could have affected the results. Infants who were not transferred to the study centre, either because a decision was made for supportive care only or because the infants died prior to transfer, were never identified, never accounted for nor studied and it is not known how inclusion of these infants would have affected the results. The majority of infants delivered by prelabour CS belonged to a group of women who had been given the benefit of prenatal diagnosis and counselling and selective pregnancy termination. Termination of pregnancies with the most severely affected fetuses could select for infants with the best prognosis to be carried to term and delivered by prelabour CS. In addition, those infants born through this selection process would have also had the benefit of close pregnancy surveillance by serial ultrasonography to monitor head size and delivery prior to the development of severe hydrocephalus, a potentially important confounding factor.

In 1994, Hill and Beattie reported the neurologic outcome of 10 infants with MMC born by prelabour CS and 15 infants with MMC born by other methods (2 emergency CS, 2 assisted breech, 1 forceps, 10 spontaneous vaginal vertex). There were 2 deaths in the prelabour CS group occurring within the first two months of life, one associated with a congenital heart defect and one from non-shunted hydrocephalus. There was no

difference in neurological function between the groups in relation to method of delivery with 50% of both groups having nervous functioning below L3 (Hill and Beattie, 1994). Mean motor and mean anatomical levels, as originally defined by Luthy et al (1991), were similar in the prelabour CS versus the TOL group (Hill and Beattie, 1994). Although the difference between the anatomical level and motor level was greater for the prelabour CS group, indicating better motor function in the prelabour CS group, the numbers were too small to find any of the differences statistically significant and potential confounding factors were not accounted for (Hill and Beattie, 1994) (Table 1).

Table 1: Effect of Labour and Delivery on Infants with MMC

Study	Design	# Subjects	Findings	Study Limitations
Stark 1970	Case Series	Infants with MMC 130 TOL (116 VB; 14 CS)	53.8% birth injuries	No controls
Ralis 1972	Retrospective cohort	39 with MMC 71 without MMC All died between birth and 7 yrs of age	Sciatic nerve in infants with MMC more damaged than in infants without MMC	Presence of absence of labour and mode of delivery not reported; causes of death not reported
Ralis 1975	Case Series	64 Infants with MMC dying after birth All TOL	extensive muscle and nerve damage with VB	No controls; mode of delivery (CS or VB) not reported; causes of death not reported
Guha-Ray 1977	Retrospective Cohort	2 prelabour CS 19 TOL (13 VB; 6 CS); 3000 historical controls	↑ risk fetal distress in infants with MMC	Historical controls; did not compare infant outcomes by presence or absence of labour and mode of delivery; small sample size
Chervenak 1984	Case Series	4 infants with MMC All born by prelabour CS	1 infant died at 13 days of age of bradycardia and apnoea; 3 were "well' as assessed between 5-17 months of age	No controls; Outcomes not defined
Shurtleff 1987	Retrospective Cohort	35 prelabour CS 98 TOL	↓ risk severe paralysis with prelabour CS	Timing of motor assessments may have been different in the two groups; women in prelabour CS group participated in antenatal diagnosis and selective pregnancy termination; failed to take into account all important confounders
Benson 1988	Retrospective Cohort	19 prelabour CS 13 CS after TOL 40 VB	No difference: meningitis, death, neurologic findings, developmental scores	Infants dying prior to transfer to neonatal ICU were not accounted for; all important confounders were not taken into account; small sample size

Table 1: Effect of Labour and Delivery on Infants with MMC

Study	Design	# Subjects	Findings	Study Limitations
Sakala 1990	Retrospective cohort	15 CS 20 VB	No differences in infection, death	Effect of labour vs no labour was not examined; all relevant confounders were not taken into account; small sample size; long term outcomes were not assessed
Cochrane 1991	Case-control	34 prelabour CS 37 CS after TOL 123 VB - Vertex 14 VB - Breech	↑ wheelchair dependency with VB breech vs VB vertex ↑ wheelchair dependency with prelabour CS vs VB vertex	Age at which ambulation was assessed may not have been the same in the two groups; infants who died prior to assessments at rehabilitation centres were not accounted for; children with good ambulatory function or socially advantaged may not have attended study spina bifida clinics and may have been referred to private clinics
Luthy 1991	Retrospective cohort	47 prelabour CS 35 CS after TOL 78 VB	↓ risk of severe paralysis with prelabour CS	Infants who died prior to transfer to study centre were not accounted for; majority of women in the prelabour CS group had the benefit of antenatal diagnosis and selective pregnancy termination; all important confounders were not taken into account
Hill 1994	Retrospective cohort	10 prelabour CS 15 TOL	No differences in percent of infants with nervous function below L3 between groups	Small sample size; potential confounders not accounted for

2.9 Rationale for Research

Many studies examining the outcomes in infants with MMC according to mode of delivery are either case series with no controls, retrospective cohort studies or case-control studies which have problems of selection bias, referral bias, survival bias, small numbers and inadequate and loss to follow-up. The studies by Luthy et al (1991) and Cochrane et al (1991) are the largest and most comprehensive studies done to date. The majority of infants born by prelabour CS in Luthy's study however, were selected for pregnancy continuation because of a perceived good prognosis based on prenatal testing. In addition, Luthy's study did not include those infants who died at the birth hospitals (thus not having the opportunity to be transferred) and those infants who had severe hydrocephalus (thus a worse prognosis). In the Cochrane study, it is not clear if subjects were assessed for wheelchair dependency around the same age which could have affected the results. Determination of long term wheelchair dependency may be difficult to determine by 2 years of age but becomes more well established as the child grows. The 2 largest and most recent studies report conflicting results, with one showing that prelabour CS is beneficial in reducing severe paralysis (Luthy et al, 1991) and the other showing that prelabour CS is associated with increased wheelchair dependency (Cochrane et al, 1991).

We felt that it would be helpful to undertake a retrospective cohort study in Ontario because cases in Ontario might be subject to less selection bias as there was no specific policy of prelabour CS for pregnancies in which the diagnosis of MMC was made antenatally in the 1980's. As well, in view of the large number of pregnancies in Ontario, we thought an adequate sample could be obtained. In addition, we thought it

would be possible to obtain information on the majority of cases because patients tended to be followed up on a regular basis, particularly in the first 2 years of life, at well known rehabilitation centres. By identifying cases at the birth hospitals, the potential for missing stillbirths and infants who died at the birth hospital, prior to having an opportunity to be transferred, would be minimized. Also, infants with severe hydrocephalus would not be excluded.

2.10 Selection of Study Design

The randomized controlled trial (RCT) design would produce the strongest evidence for determining if prelabour CS would reduce the risk of severe paralysis compared to a TOL. The RCT design allows for the elimination of bias through the prospective collection of data, the random assignment to intervention, and the precise definition of outcomes. The already low incidence of MMC is decreasing further due to the increasing availability and utilization of prenatal diagnosis, the increasing rate of termination of pregnancies affected by MMC, and the increasing use of folic acid for prevention of MMC. These factors affecting the incidence of MMC would seriously hamper the feasibility of an RCT. A large multi-centred trial would be required to recruit enough subjects to have a reasonable power of finding a clinically important difference in adverse outcome and a study of this magnitude would likely require a great degree of co-operation, commitment, and financial resources over an extended period of several years. Further problems could arise in a study of such long duration, in that there could be a change in other practices (apart from the mode of delivery) which could affect the prognosis of infants born with MMC, or the research question being posed by the study may become irrelevant (Table 2).

The use of a prospective cohort study design may eliminate the logistical problems of randomization, as it would be easier to recruit subjects if physicians and patients were given a choice on the method of delivery. However, this non-random selection into study groups introduces selection bias and the often unpredictable influences of confounding variables, some of which are known, others of which may not yet be identified. The prospective cohort design within the context of this study, is subject to the same limitations as the RCT, as it too would be very costly and require a great degree of commitment over a prolonged period of time due to the extremely low incidence of MMC (Table 2).

The main advantage of the retrospective cohort study design is its feasibility, particularly with rare conditions such as MMC. Although the retrospective cohort design may be less costly and less time consuming, information obtained from chart abstraction or recall may be incomplete or inaccurate, or recorded in ways which may not be ideal for answering the research question. Also, existing data from the past may not include the information which is considered to be important at the time the study is being carried out. Confounding variables may be different as new ones are identified and old ones are discovered to be unimportant. It is also possible that the sample of infants with MMC studied or the way in which they were treated 10 years ago may not reflect or be representative of infants with MMC and their management today. With changing practices, it is possible that the question with respect to the optimum delivery method for these infants may no loner be relevant in the future (Table 2).

A case-control study design could also have been considered for this study by comparing

a groups of infants with MMC having severe paralysis to those without severe paralysis at 2 years of age. Matching on several important confounding variables could be performed at the outset or these variables could be taken into account later by appropriate statistical analysis. Like the retrospective cohort design, the case-control design is also less costly and less time-consuming. It is well suited for studying the interaction of a large number of risk factors for severe paralysis in infants with a rare condition such as MMC. In addition to sharing the same problems of incomplete or inaccurate data collection as the retrospective cohort design, the case-control method is further flawed by the potential for survivor bias and referral bias, the inability to calculate incidence and or prevalence of outcomes, the inability to study the effect on one factor on several outcomes of interest, and the potential for unknown confounders to affect the selection of cases and their controls. Identifying infants with MMC at rehabilitation centres at 2 years of age would miss stillbirths and infants who died prior to age 2 years and thus, who would never attend a rehabilitation centre. Valuable information about the incidence of meningitis, sepsis, wound infections, death and severe paralysis in MMC infants could not be calculated from such a study and the effect of labour and mode of delivery on all these outcomes could not be examined. Also, information on important pregnancy, birth and neurosurgical confounders might not be found in the rehabilitation records and other sources of information such as parental interviews might not be completely reliable necessitating the additional task of returning to birth records anyway (Table 2).

Table 2: Strengths and Weaknesses of Study Designs with Respect to the MMC Study

Study Design	Strengths	Weaknesses
Randomized Controlled Trial	Eliminates bias Random assignment to intervention Prospective data collection Precise definition of outcomes	Feasibility Costly Time consuming
Prospective Cohort	Prospective data collection More control over definition of outcomes Avoids survival bias	Feasibility Costly Time-consuming Selection bias Non-random assignment of subjects to study groups
Retrospective Cohort	Feasibility Less expensive Less time-consuming	Existing data may be incomplete, inaccurate, not in necessary format or irrelevant to research question Selection bias Possible bias in confounders, interventions and outcomes
Case-Control	Feasibility Less expensive Less time-consuming Can study effect of many factors on one outcome	Existing data may be incomplete, inaccurate, not in necessary format or irrelevant to research question Survival bias Referral bias Possible bias is confounders, interventions and outcomes Only one outcome can be studied

3. STUDY DESIGN

A population based retrospective cohort study was undertaken. Infants with MMC were identified at their birth hospitals and information about outcomes was collected shortly after birth and after referral to the paediatric neurosurgical centres where definitive treatment was received. Outcome information at two years of age will be collected from rehabilitation centres and will not be part of this thesis.

3.1 Study Objectives

The general objective of this study was to determine if delivery by Cesarean section (CS) and the avoidance of labour would improve the outcome of infants born with MMC. To examine whether or not the avoidance of labour and vaginal birth would be beneficial to infant outcomes, those infants born by CS with no labour were compared with those infants born, either by CS or vaginal birth (VB), after a trial of labour (TOL). Secondly, to examine whether or not VB itself would be detrimental to infant outcomes, those infants born by VB were compared to those infants born by CS after labour, thus controlling for exposure to labour.

3.2 Research Questions

Analysis of the exploratory outcomes forms the basis for this thesis. The primary and secondary questions will be addressed subsequently after collection of the 2-year rehabilitation data and will not form part of this thesis.

3.2.1 Primary Research Question

Is prelabour CS versus TOL, with VB or CS after labour, for the fetus with MMC associated with a decrease (or increase) in severe paralysis at two years of age?

3.2.2 Secondary Research Question

Among women experiencing labour, is CS versus VB for the fetus with MMC, associated with a decrease (or increase) in severe paralysis at two years of age?

3.2.3 Exploratory Research Questions (Subject of Thesis)

1. Is prelabour CS versus TOL for the fetus with MMC associated with decreased (or increased) mortality and/or morbidity in the infant during the first 6 months of life? Outcomes of morbidity assessed were the following: Apgar score <7 at 5 minutes, definite meningitis, definite wound infection or breakdown, sepsis, urinary tract infection, seizures, Chiari malformation symptoms, shunt malfunction and/or infection, respiratory support for >48 hours, number of hospitalizations, and number of days in hospital.

3.2.3 Exploratory Questions (Subject of Thesis) - continued

2. Is CS following a period of labour, compared with VB, associated with decreased (or increased) mortality and/or morbidity in the infant with MMC during the first 6 months of life? Morbidity is defined as in exploratory question 1.

3.2.4 Correlation of Infection and Severe Paralysis

To explore the correlation between infection during the first 6 months of life with the neurological outcome of severe paralysis at 2 years of age.

3.3 Sample Specification

The population of interest was comprised of infants born with MMC in hospitals in the province of Ontario during the period January 1, 1980 to December 31, 1989 inclusive.

3.3.1 Inclusion Criteria

1. MMC identified at birth
2. Gestational age $\geq$ 25 weeks
3. Born in a hospital in Ontario during the period January 1, 1980 and December 31, 1989, inclusive.

3.3.2 Exclusion Criteria

1. Lethal or other severe anomalies (such as hypoplastic left heart syndrome, pulmonary hypoplasia, chromosomal abnormalities incompatible with life).
2. Infants later confirmed to have NTDs other than MMC (such as anencephaly, encephalocele, lipomyelomeningocele, meningocele, dermal sinus).
3. Stillbirths in which the fetus was dead prior to labour.
4. Cases in which a decision was made prior to labour that there would be no

intervention for fetal welfare.

5. For the comparison of the VB versus CS after TOL groups, those stillbirths or deaths in which there was no intention to intervene obstetrically for fetal welfare during labour or where a pre-delivery decision was made to not resuscitate the infant after birth.

Exclusions were determined by an individual blinded to the mode of delivery.

3.3.3 Confounding Variables

The following variables may have an effect on the outcome of the infant with a MMC which may be independent of delivery method:

1. Antenatal diagnosis of MMC
2. Birth in a Level 3 perinatal unit
3. Gestational age at delivery
4. Non-cephalic presentation
5. Multiple gestation
6. Severe hydrocephalus noted at or prior to birth (defined as head circumference greater then 4 SD above the mean for gestational age)
7. Severity of the anatomic lesion
   a. level of the lesion
   b. size of the base of the lesion (ie. neural placode)
8. Delay in closure of the defect (defined as >72 hours after birth).

3.4 Methodology and Data Collection

A. Identification of Infants for Inclusion:

A letter was sent to the medical records departments of all hospitals in Ontario with obstetric services. Each hospital was asked to identify infants that met the inclusion criteria using the ICD-9 code 741 for spina bifida and to abstract information about these infants and their mothers from the infant and maternal records. Completed data collection forms were then mailed to the MMC study office. The data collection forms were reviewed and inclusion and exclusion criteria were applied. If information was incomplete or inconsistent, the hospitals were recontacted for additional information.

B. Tracking of Infants to the Paediatric Neurosurgical Centres:

Further information was collected on those infants who survived after birth and were referred for paediatric neurosurgical treatment. The medical records departments of the paediatric neurosurgical centres to which the infants in this study had been referred, were contacted and provided with a list of the infants' names, dates of birth, birth hospitals, and dates of transfer. The charts of these infants were then retrieved, linkages were verified and data were abstracted.

C. Tracking of Infants to the Rehabilitation Centres (not part of thesis):

Tracking of infants to the rehabilitation centres will be accomplished by using the information obtained from the infants' medical records at the neurosurgical centres. Information on motor function and degree of paralysis at 2 years of age will be abstracted from the rehabilitation charts by an individual who is unaware of the labour and delivery history. This final step in the tracking process will not be undertaken as

part of the thesis.

3.5 Study Outcomes

3.5.1 Primary Outcome:

The primary outcome is severe paralysis at 2 years of age. Severe paralysis is defined as a level of motor function at or above L2. The level of motor function is the lowest level of purposeful movement, on either right or left side, exclusive of spastic or reflex activity. The research questions involving this outcome will be addressed subsequently and are not part of this thesis.

3.5.2 Exploratory Outcomes:

1. Apgar Score <7 at 5 minutes
2. Definite meningitis/ventriculitis defined as clinical signs and symptoms of meningitis and a positive cerebrospinal fluid (CSF) culture with the CSF obtained from a ventricular or shunt tap. CSF obtained from the leaking MMC wound is almost always contaminated and was not used for establishing meningitis.
3. Definite wound infection/wound breakdown defined as a wound which required any of the following:
   a. the removal of sutures to open it up for drainage
   b. the removal of pustular debris with soaks/compresses
   c. the administration of antibiotics for treatment of a wound infection
   d. the surgical revision of the wound because of breakdown
4. Definite sepsis defined as clinical signs and symptoms of sepsis with positive blood culture.
5. Urinary tract infection defined as clinical signs and symptoms of a urinary tract

infection with a positive urine culture from a suprapubic aspirate or urinary catheter specimen.

6. Seizures as documented in the chart.

7. Chiari malformation symptoms as documented in the chart with or without subsequent posterior fossa decompression surgery. This diagnosis is based on a constellation of symptoms such as poor feeding, gagging, weak cry, and periods of apnoea.

8. Shunt malfunction or infection defined by either: (a) the onset of a new episode of hydrocephalus with a head ultrasound showing increased ventricular dilatation or shunt testing demonstrating obstruction, or (b) the documentation of a shunt infection by positive cultures from the shunt tubing but not positive from the CSF.

9. Resource utilization outcomes defined as one or more of the following:
   a. Prolonged respiratory support (>48 hours of assisted ventilation).
   b. Number of hospitalizations and readmissions
   c. Number of days in hospital.

10. Mortality:
   a. Stillbirth
   b. Neonatal Death ($\leq$ 28 days)
   c. Early Infant Death (29 days to 6 months)

3.5.3 Grouping of Intermediate Exploratory Outcomes

Although data on several exploratory outcomes were collected, a decision was made during the course of the study to group three particular outcomes, meningitis/ventriculitis, wound infection/breakdown, and sepsis, as one

"intermediate" exploratory outcome of morbidity. This intermediate outcome is the main outcome of interest for this thesis. The decision to group these 3 outcomes into one intermediate outcome was made after consulting with a neurosurgeon who was involved on a daily basis in the clinical management of infants with MMC, both in the initial surgical treatment and the long term follow-up. The rationale for grouping these outcomes was that this particular group of infections could be caused by bacterial organisms picked up by the infant during labour and during passage through the maternal birth canal and that the occurrence of these infections could cause permanent damage to nerve root and increase the risk of severe paralysis at two years of age. There is no scientific proof for this relationship but there is a strong biological plausibility for this theory and from a clinical viewpoint, neurosurgeons feel that there may be a relationship between these infections and reduced motor function. Thus, one of the objectives of this study was to explore the correlation between infection during the first 6 months of life with the neurological outcome of severe paralysis at 2 years of age. The finding of a positive correlation might be useful in that appropriate measures may be taken to prevent these infections, such as intravenous antibiotic administration during labour to mothers carrying a fetus with MMC, and hopefully reduce the risk of severe paralysis later in life.

Other infections, such as urinary tract infections or shunt infections would most likely be caused by organisms which the infant harboured in his/her own body and not from organisms picked up from the birth canal. Also, according to the neurosurgical expert, the occurrence of other outcomes such as Chiari

malformation symptoms and seizures would not be expected to be associated with the route of delivery or exposure to labour since these outcomes are related to the actual anatomical lesion. All infants with MMC have a Chiari malformation, but only 20% of them will develop the symptom complex of apnoea, poor feeding, gagging and weak cry. Seizures are related to the intracranial anatomical lesion associated with MMC.

3.6 Sample Size Calculation

Sample size for the primary question was calculated based on the work of Luthy et al (1991). He found that the risk of severe paralysis was 21% in the group of infants delivered by prelabour CS and 37% in the group delivered after a TOL. Thus, to find a 50% reduction in the risk of severe paralysis (from p2 of 40% in the TOL group to p1 of 20% in the prelabour CS group), a total sample size of 162 infants would be required with 81 infants in each of the prelabour CS and TOL groups (2-tailed test of significance $\alpha=.05$, $\beta=.2$). The sample size was calculated (according to Friedman et al, 1985) as follows, where 2N is the total sample size, $\hat{p}=p1+p2/2$, $Z\alpha=1.96$ and $Z\beta=0.84$:

$$2N = \frac{2[(Z\alpha\sqrt{2(\hat{p})(1-\hat{p})} + Z\beta\sqrt{p1(1-p1) + p2(1-p2)}]^2}{[p1-p2]^2}$$

The sample size for the secondary question involving the effect of VB on severe paralysis at 2 years of age was calculated using the same formula and also based on the work of Luthy et al (1991) who found that the risk of severe paralysis was 30% (p1) in the group delivered by CS after TOL, compared to 50% (p2) in the group delivered vaginally. To find a 40% reduction in the risk of severe paralysis (from 50% in the VB group to 30%

in the CS after TOL group (two-tailed test of significance, $\alpha = .05$, and $\beta = .2$), a total sample size of 184 infants would be required with 92 infants per study group at 2 years of age.

In summary, 81 patients would be required in the prelabour CS group, 92 would be required in the CS after labour group and 92 would be required in the vaginal delivery group, creating a total sample size of 265.

3.7 Feasibility

The literature suggests the incidence of MMC to be 0.4 to 1 per 1000 births. Statistics from the Ministry of Health indicate that 123,217 births occurred in the Province of Ontario in the year 1979-1980 and 142,336 births occurred in the year 1988-1989. Assuming an incidence of 0.4 cases of MMC per 1000 births, we would expect a minimum of 48 cases per year or 480 cases over a 10 year period.

It is estimated that approximately 75% of those patients identified will meet the inclusion/exclusion criteria, with 10% being excluded for lethal chromosomal abnormalities and 15% being excluded for other system lethal anomalies. Of the 75% of cases that are eligible, it is estimated that data will not be available in 15% of cases and 15% will die before reaching 2 years of age. Thus, 54% of the 10 year sample would be available for collection of the rehabilitation data at two years of age. Fifty-four percent of 480 would provide 259 infants for evaluation at the two-year rehabilitation centre follow-up.

3.8 Statistical Methods

The portion of the MMC study described in this thesis results primarily in the presentation of descriptive data and in the univariate analysis of the data to answer the exploratory questions. Baseline characteristics of the pregnancies in both the TOL and prelabour CS groups and in the VB and CS after TOL groups are compared using the Student's t-test for continuous data (such as maternal age) and the chi-square test for categorical data (such as multiple gestation, level of newborn care, prenatal diagnosis of MMC etc) in order to identify the possibility of differences between the two groups. Similarly, birth characteristics of the infants, such as fetal presentation, birth weight, sex, head circumference, presence of hydrocephalus, presence of other birth defects and classification of the MMC lesion, are compared using the Student's t-test for continuous data and the chi-square test for categorical data.

All the infant outcomes (Apgar score, death, meningitis/ventriculitis, wound infection/breakdown, urinary tract infection, sepsis, seizures, Chiari malformation symptoms, shunt malfunction/infection, number of readmissions, total days spent in hospital) are described categorically and are individually compared between the TOL and prelabour CS groups and between the VB and CS after TOL groups using the chi-square test and odds ratio with 95% confidence intervals.

Although data on several exploratory outcomes were collected, one single intermediate outcome of morbidity (which includes meningitis/ventriculitis, wound infection/breakdown, and sepsis) is compared between the TOL and prelabour CS group and also between the VB and CS after TOL groups using the chi-square test and odds

ratio with 95% confidence intervals.

The level of significance was set at $p=0.05$. Since multiple comparisons of the data were made, the significance of these analyses should be restricted to a descriptive or exploratory nature.

3.9 Ethical Considerations

Information regarding the index pregnancy and subsequent infant outcomes were obtained through chart reviews after study approval by each individual hospital. Infant and parent names were requested to facilitate tracking of the infants from birth hospitals to neurosurgical centres. Centres were assured that no contact would be made with the patients or their parents and that complete confidentiality would be maintained. No centre refused to participate because of ethical reasons. Some centres agreed to participate with the understanding that infant and parental names would not be released. All records were coded and stored confidentially and securely and were available only to the author (FM).

3.10 Modification of Study Design for Thesis Requirements

This study was originally designed by Dr. Lea Fairbanks in September 1991, with supervision from Dr. Mary Hannah. After assuming responsibility for the study in July 1992, I modified the research questions and provided more detailed definitions of the outcome measures, including the grouping of intermediate exploratory outcomes. Dr. Fairbanks initiated the study by making contact with the hospitals in Ontario providing obstetrical services. She developed the original obstetrical data collection form which

was utilized by the medical records departments to record information abstracted from both the infant and maternal records at the birth hospitals.

My contributions to the study were as follows: I completed the contacts with the birth hospitals (90 of the 165 birth hospitals in Ontario), personally collected obstetrical data (118 of 370 cases), redesigned the obstetrical data collection form to facilitate data entry, designed the neurosurgical data collection form, made contact with the neurosurgical centres, personally collected all the neurosurgical data (176 cases at Hospital for Sick Children; 68 cases at Children's Hospital of Eastern Ontario), designed the database, carried out double data entry of all the obstetrical and neurosurgical data, checked data integrity and performed a descriptive analysis of the data.

4. STUDY AND DATA MANAGEMENT

4.1 Data Collection Forms

4.1.1 Obstetrical Form

The original obstetrical data collection form (OBS Form) was designed by Dr. Fairbanks and then redesigned by myself to facilitate data entry (Appendix 1). This form has 33 different variables and records the maternal, baby and physician names, hospital of birth and pregnancy, labour and birth data.

4.1.2 Neurosurgical Form

The neurosurgical data form (NEURO Form) was designed by myself, pilot tested on infant charts from the Hospital for Sick Children and appropriately revised (Appendix 1). This form has 75 variables and records information about the neurosurgical condition, its treatment and infant outcomes in the first 6 months of life.

4.2 Data Collection Process

OBS forms were mailed to the participating birth hospitals for the medical records personnel to complete by chart review and then return to the study office. For birth hospitals in the greater Metropolitan Toronto area, I was able to personally collect the obstetrical data.

Collection of the neurosurgical data was done by myself and restricted to chart reviews at the Hospital for Sick Children's in Toronto and the Children's Hospital of Eastern Ontario in Ottawa. These two paediatric hospitals received over 80% of the original sample of babies identified at the birth hospitals and then transferred for further care.

4.3 Database Structure

DBase IV was utilized for database organization and data storage. The OBS form and NEURO form data were stored in separate data bases. The variables from these forms were defined according to type, width, decimals, and ranges (Appendix 2). Then data entry screens were designed to resemble and thus follow the hard copy forms exactly to facilitate data entry.

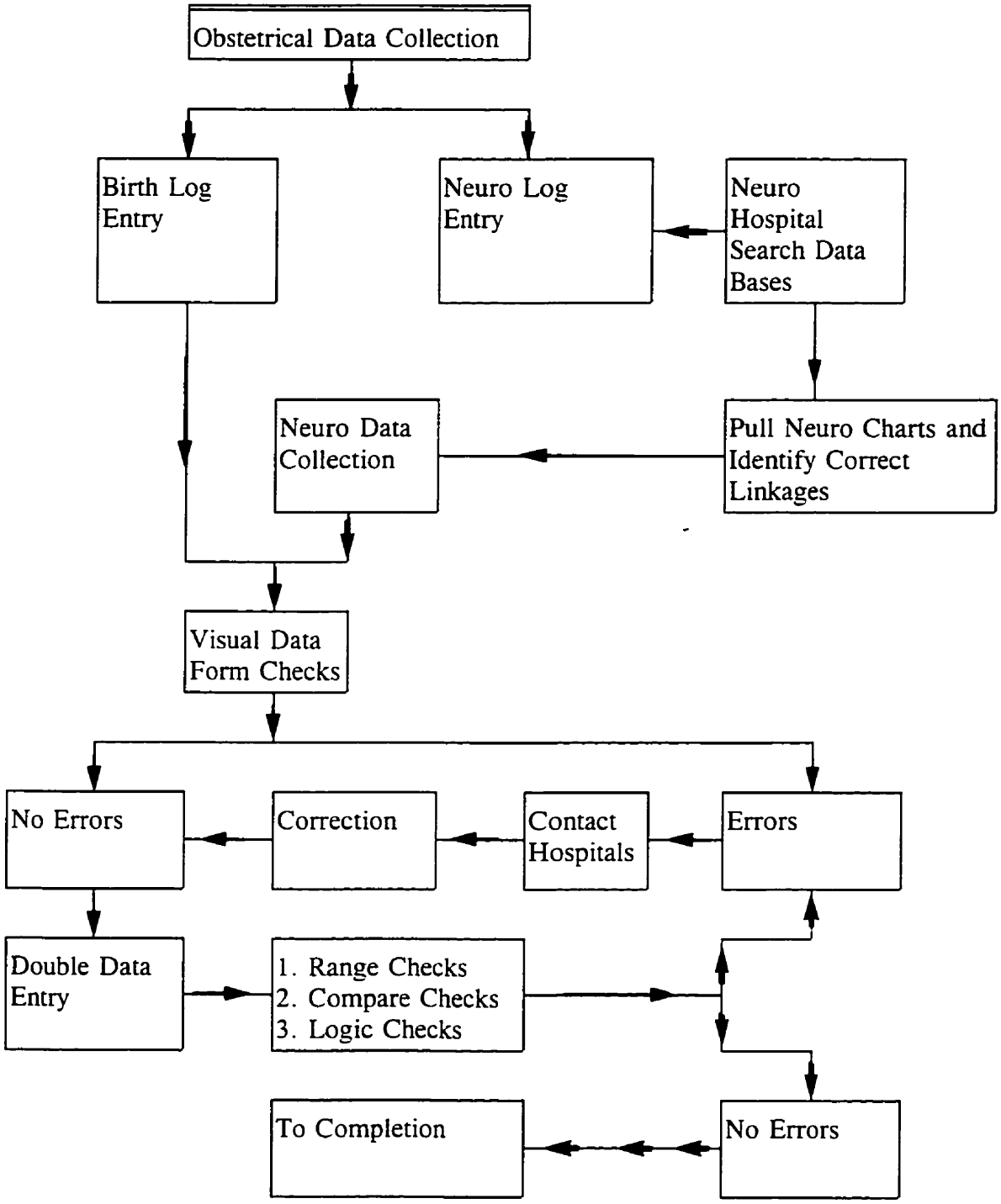
4.4 Data Flow and Data Entry (Figure 1)

As the OBS data forms arrived, a birth hospital log was created which recorded the baby's name, date of birth, hospital of birth, mode of delivery, type of lesion, and the initial outcome (ie: stillbirth, neonatal death, transfer to neurosurgical centre, discharge home etc.). The forms were visually assessed for major errors and discrepancies and if necessary, the birth hospital was contacted or re-visited to clarify the error. Missing data were not necessarily pursued. Just prior to data entry, each OBS form was assigned a baby code number. Each form underwent a double data entry process. Automatic range checks operated as the data were being entered to minimize data entry errors. Once the OBS data were double-entered, a comparison program was run and discrepancies in the two copies of entered data were corrected by comparing data to the original hard copy.

Infants transferred to the Hospital for Sick Children and the Children's Hospital of Eastern Ontario were entered into the "HSC log" and the "CHEO log" respectively. These logs listed the infants' names (if released), dates of birth, dates of transfer and hospital of birth. Using the information in these logs, the medical records personnel at the neurosurgical centres searched their computerized data bases for a matching infant

and its hospital number for each infant in the log. The charts of infants who appeared to match the ones in the logs were retrieved and visually inspected to ensure a correct link. After appropriate assignment of the baby code number, infant data from the neurosurgical charts were abstracted to the NEURO form. As in the case of the OBS form, a double data entry process was followed with range and comparison checks.

Figure 1: Data Flow Chart



4.5 Data Accuracy

Data accuracy was sought through several processes. Range checks were applied at the time of data entry and immediate corrections were often possible. In some cases the birth or neurosurgical hospital was contacted to check the information prior to correction.

With neurosurgical data entry, input of the baby code number and infant date of birth was automatically followed by computerized cross checking of the date of birth on the NEURO form with the date of birth on the OBS form with the same baby code number. If the dates of birth did not match, data entry could not proceed and hard copies of the corresponding NEURO and OBS forms were inspected.

Comparison checks were made after double data entry of all data and appropriate corrections were made by checking the hard copy. Post-entry logic checks of the data were performed using programs written in Dbase IV. These programs detected apparent discrepancies among different data fields, missing values, and suspicious values (variable values that although potentially valid are relatively rare and sufficiently important to warrant verification).

4.6 Database Closure

Finite dates were established after which no further data collection would occur. No further obstetrical data were collected as of December 1, 1995 and no further neurosurgical data were collected after January 8, 1996. Once all double-entry and logic check discrepancies were resolved, the databases were closed to allow data analysis to begin.

4.7 Database Integrity and Security

Hard copies of data were stored under lock and key in the Maternal, Infant and Reproductive Health Research Unit (MIRU). Both the hard copies and the entire computerized database were available only to me, the computer programmers (TL and CW) and the MIRU biostatistician (TM). The databases resided on a local area network file server (COMPAQ PROSIGNIA 75 MHz Pentium running Novell Netware 4.1 software) in the MIRU. This network is composed of the file server and approximately 40 personal computers. User passwords were required to access the directories containing the databases. The entire network was backed up onto magnetic tape overnight each Tuesday through Saturday by the senior computer programmer in the MIRU. Each week, one of the nightly backup tapes was stored in a fire-proof safe in the Information Systems Department at Women's College Hospital. These tapes were rotated to the safe using a 3-week schedule. That is, one tape from each of the previous two weeks would be in the safe at any given time. Quarterly backup tapes (prepared early in January, April, July, and October) were also stored in the safe and rotated.

5. STUDY RESULTS

5.1 Sample

5.1.1 Hospital Participation:

One hundred and sixty-five hospitals in Ontario were contacted with a letter explaining the study and requesting their participation (Figure 2). The response rate was 81% (133/165) with 19% of hospitals not responding even after a second mailing and a telephone call. Of the 133 hospitals responding, 47 did not have cases, 76 identified cases, 8 were not doing obstetrics during the study period and 2 refused to participate.

5.1.2 Cases:

Data were collected on 370 mothers and infants at 70 birth hospitals in Ontario (Figure 3). Fifty-two infants were excluded based on information on the obstetrical data form for the following reasons: less than 25 weeks (n=1), prelabour recognition of intra-uterine death (n=8), prelabour decision to not intervene for fetal welfare (n=10), congenital anomalies incompatible with life (n=6), hypoplastic lungs (n=3), chromosomal defects incompatible with life (2), lipomyelomeningocele (n=4), meningocele (n=5), encephalocele (n=4), spina bifida occulta (n=7), and lack of stated diagnosis (n=2). Of the remaining 318 infants, 3 were stillborn and 17 died in the immediate neonatal period at the birth hospital and the rest (n=298) were considered for neurosurgical care.

Of the 298 infants considered for neurosurgical care, 175 infants were transferred to the Hospital for Sick Children (HSC), Toronto, 68 infants were transferred to the Children's Hospital of Eastern Ontario (CHEO), Ottawa and 55 received neurosurgical care in

various other centres in the provinces of Ontario, Manitoba, and Quebec. For practical reasons, only those infants transferred to HSC and CHEO were followed up and they represented 82% of the sample of infants considered for neurosurgical care.

Of the 243 infants tracked to HSC and CHEO, 37 additional exclusions were made based on the information gathered from the neurosurgical records: 28 did not have MMC (11 had lipomyelomeningocele; 10 had meningocele; 2 had encephalocele; 1 had congenital aplasia of the cutis; 1 had hydrocephalus only; 1 had Dandy-Walker cyst; and 2 had occult spina bifida), and 9 had MMC with multiple anomalies which were very severe or incompatible with life (1 with pulmonary hypoplasia; 2 with Trisomy 18; 1 with hydrancephaly; 1 with sirenomelia; 1 with lobar holoprosencephaly, cleft lip and palate, and bladder extrophy; 2 with complex congenital heart disease; 1 with bladder extrophy, extensive omphalocele, and ambiguous genitalia). Also, 7 infants could not be identified at the neurosurgical centre despite scanning 3 different databases in the medical records department. There were 199 infants with neurosurgical data.

5.1.3 Sample Sizes of Study Groups:

For the comparison of cases in the prelabour CS group versus the TOL group, the total sample with perinatal outcome data was 219, which included the 20 deaths occurring at the birth hospitals and the 199 infants followed to neurosurgical centres (Figure 4). For the sample of 219, there were 53 women having prelabour CS and 166 women undergoing a TOL. For the sample of 199 infants transferred to neurosurgical centres, there were 46 delivered after prelabour CS and 153 delivered after a TOL (Figure 4). Obstetrical data were also available for the 62 cases which were transferred to neurosurgical centres but not followed up (7 cases for which a linkage was not found and

55 cases that went to neurosurgical centres other than CHEO and HSC).

For comparison of cases in the CS after TOL group versus the VB group, the total sample with perinatal outcome data was 163 after exclusion of 3 stillbirths from the TOL group (Figure 5). There were 45 women who had a CS after TOL and 118 women who had a vaginal birth. Of these 163 cases, 10 infants died at the birth hospital and 153 infants were tracked to neurosurgical centres (Figure 5). Of the 153 infants who were transferred to neurosurgical centres, 40 were delivered by a CS after TOL and 113 were delivered vaginally (Figure 5).

Figure 2: Hospital Participation

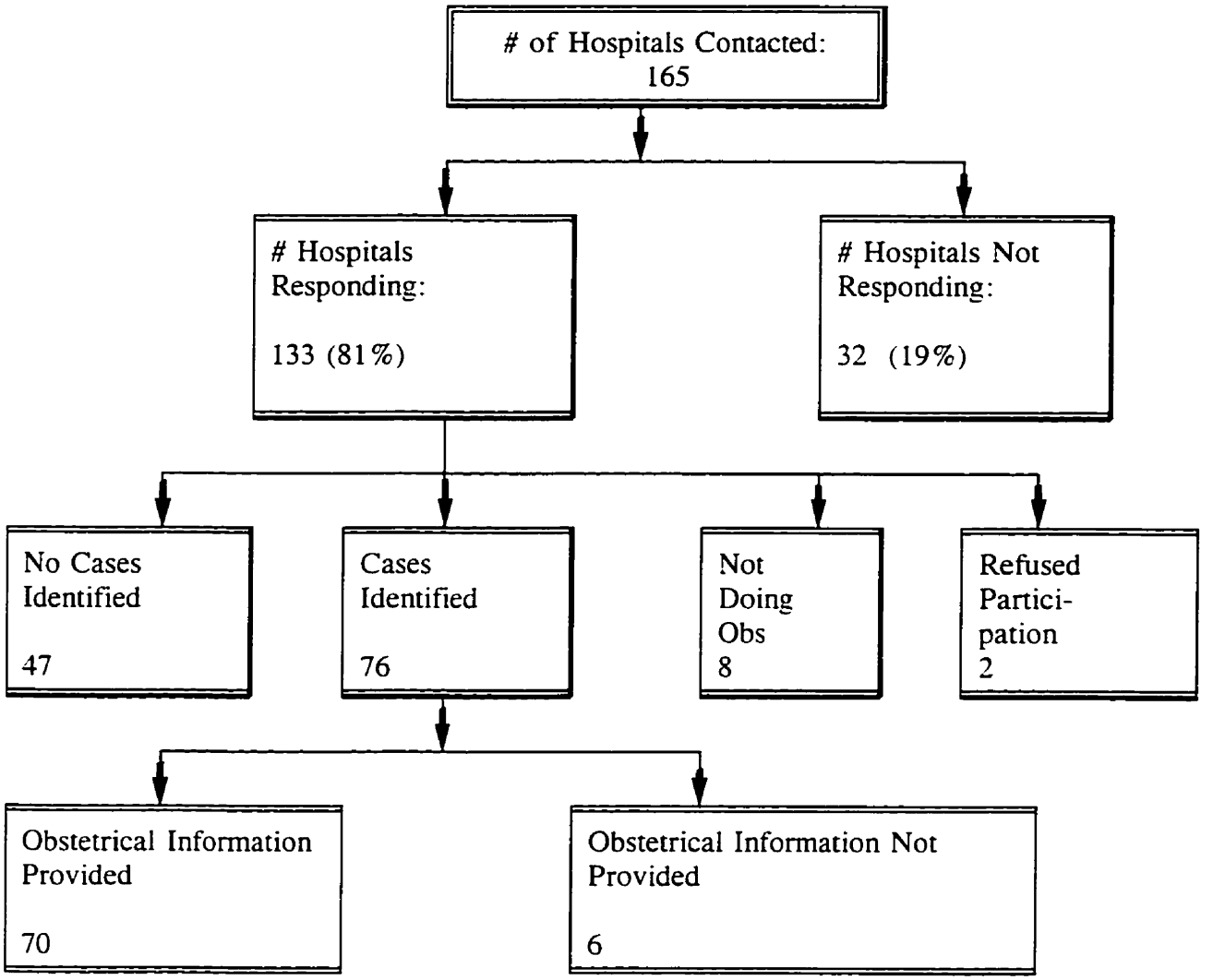
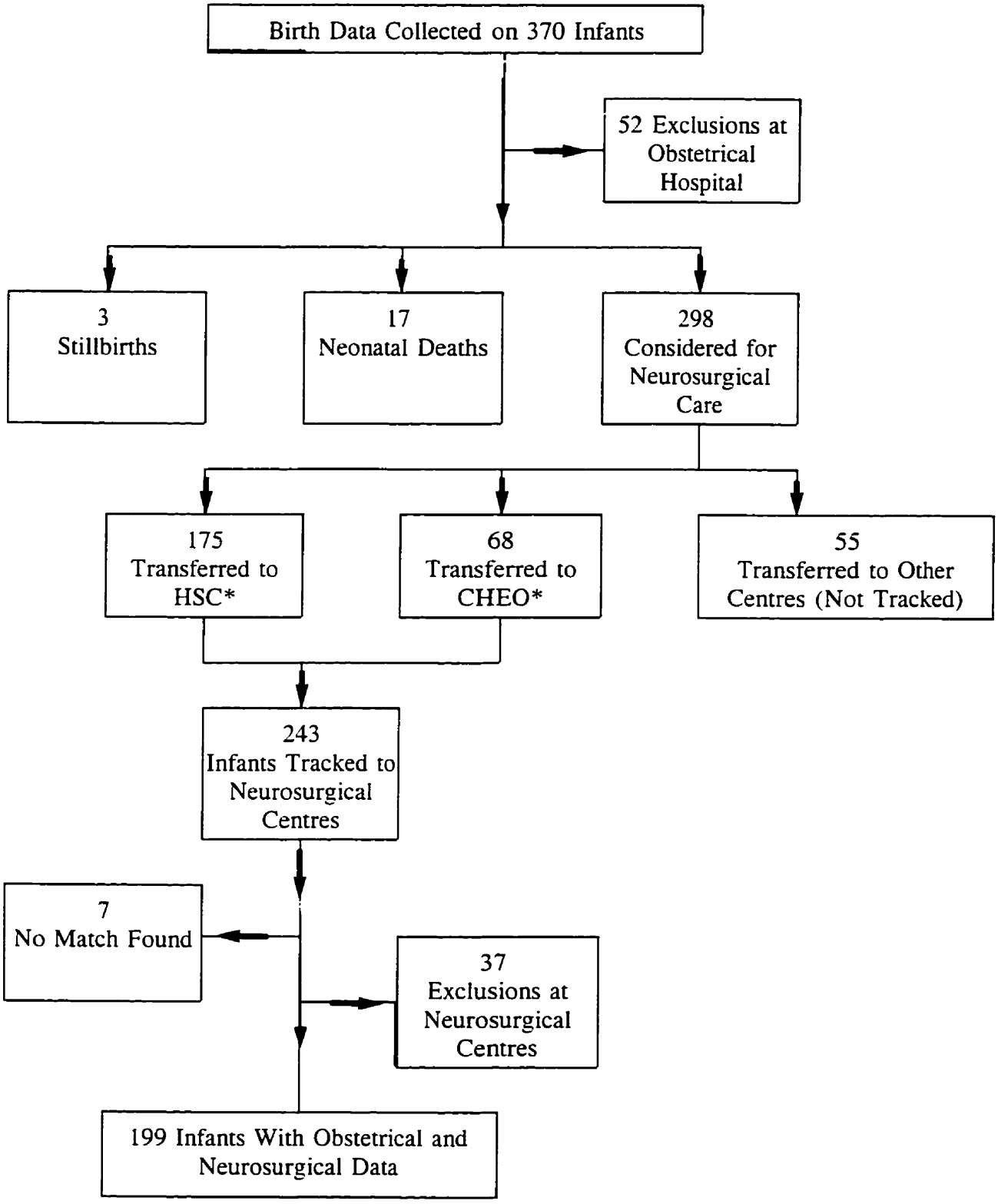


Figure 3: Cases



* HSC=Hospital for Sick Children; CHEO=Children's Hospital of Eastern Ontario

Figure 4: Study Group Sample Sizes for Prelabour CS versus TOL comparison

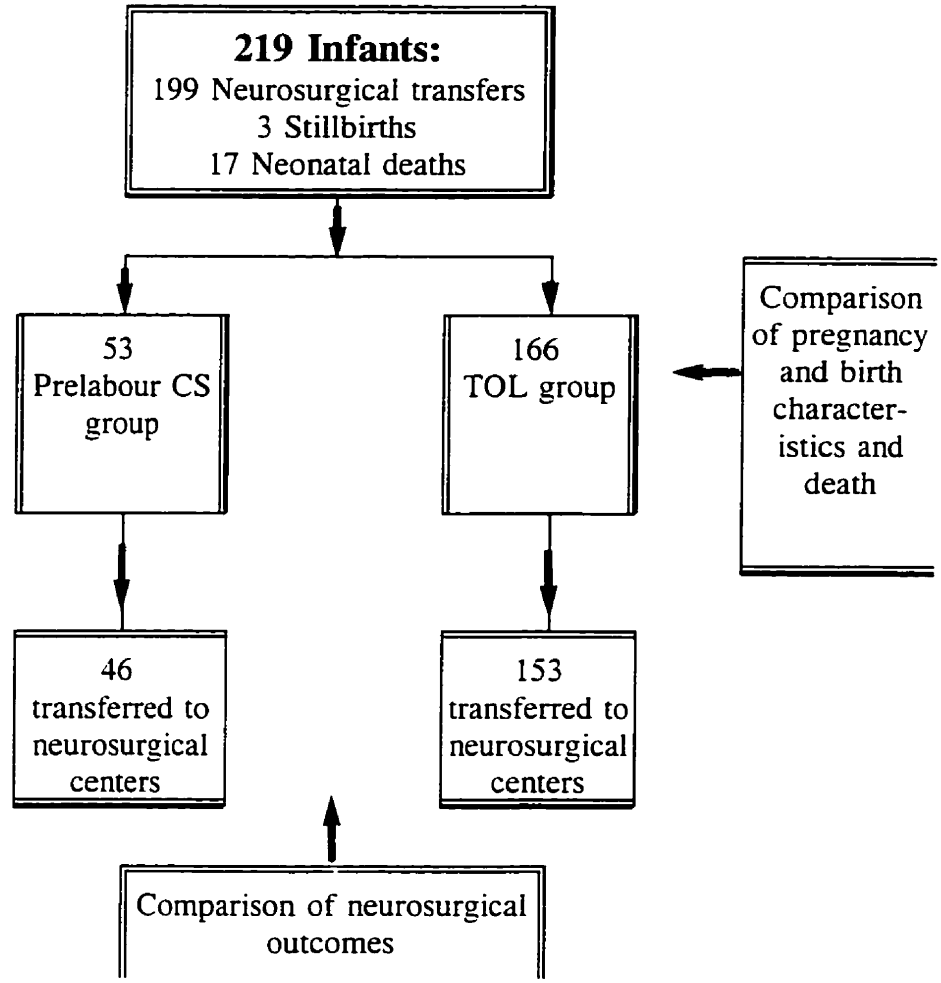
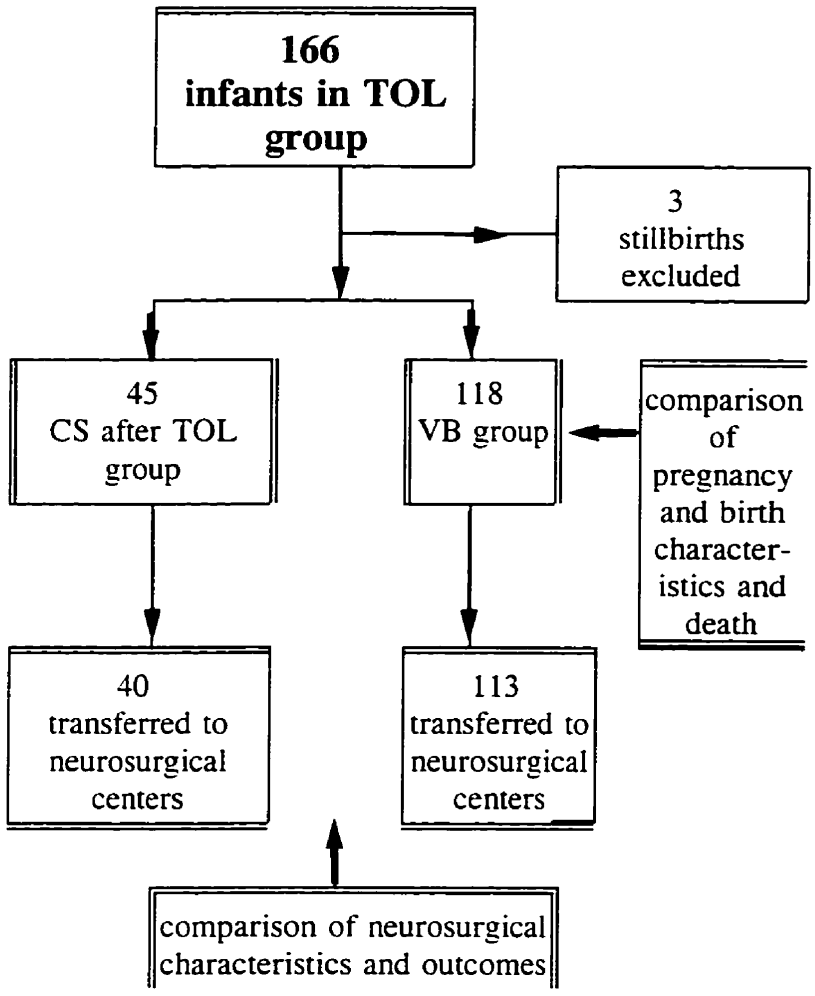


Figure 5: Study Group Sample Sizes for CS after TOL versus VB Comparison:



5.2 Prelabour Cesarean Section versus Trial of Labour Groups:

Of the total sample of 219 infants, 166 were delivered after a TOL and 53 were delivered by prelabour CS. In the group of infants not followed to neurosurgical centres, 52 were delivered after a TOL (38 vaginal; 14 Cesarean section) and 10 delivered by prelabour CS.

5.2.1 Pregnancy and Birth Characteristics:

Of the infants in the TOL group, 45 (27.1%) were delivered by CS after the onset of labour and 121 (72.9%) had a vaginal birth. All the infants in the prelabour CS group had a CS.

Table 3 presents the pregnancy characteristics for the 219 infants with birth data according to whether or not they were delivered after a TOL. Infants in the prelabour CS group were more likely to have been delivered in a level 3 perinatal unit (45.2% for prelabour CS group versus 26.5% for TOL group; $p=0.032$), have a neonatologist or neonatal nurse present at the delivery (44.4% for prelabour CS group versus 18.8% for TOL group; $p<0.001$) and have a prenatal diagnosis of MMC (52.8% for prelabour CS group versus 19.3% for TOL group; $p<0.001$). Antenatal chromosome analysis was performed in 2 (3.8%) of the pregnancies delivered by prelabour CS and in 5 (3.0%) of the pregnancies delivered after a TOL. All chromosome results were normal except for one case from the TOL group, in which the results were unknown.

Table 4 presents the birth characteristics of these 219 infants. The prelabour CS group had a higher rate of breech presentation (32.1% for prelabour CS group versus 12.6% for TOL group; $p=0.003$) and a higher rate of hydrocephalus (66.0% for prelabour CS

group versus 45.2% for TOL group; p=0.008).

Tables 5 and 6 present the pregnancy and birth characteristics of 62 infants who were not followed to neurosurgical centres. The infants in the prelabour CS group were more likely to be born in a level 3 obstetrical unit, have a neonatal nurse or neonatologist present, have a prenatal diagnosis of MMC, be in the breech presentation, and have hydrocephalus when compared to infants in the TOL group, suggesting that the characteristics of infants followed to the neurosurgical centres were similar to those not followed.

For those women having a CS in the prelabour CS and TOL groups, more than one reason was given for the CS in many cases (Table 7). With respect to CS for the indication of breech or other malpresentation, there were no differences between the two groups. However, the prelabour CS group, versus the TOL group, was less likely to have a CS for the indications of fetal distress ($p<0.001$), or feto-pelvic disproportion ($p<0.001$), and was more likely to have a CS for the indication of MMC ($p=0.011$) or previous CS ($p=0.009$).

Table 3: Pregnancy Characteristics (N=219) in the Prelabour Cesarean Section (CS) and the Trial of Labour (TOL) Groups

Characteristic	Prelabour CS N=53 n (%)	TOL N=166 n (%)	P	Odds Ratio[1] (95% CI)
Maternal age (yrs)				
Mean (±SD)	26.9 (±4.3)	28.2 (±5.0)	0.086	
# missing	3	11		
Gestational age at delivery				
<37 wks	5 (9.4)	17 (10.3)	0.855	0.91 (0.32-2.59)
≥37 wks	48 (90.6)	148 (89.7)		
Unknown		1		
Delivery				
Vaginal	0	121 (72.9)		
Cesarean	53 (100)	45 (27.1)		
Multiple birth				
Yes	1 (1.9)	7 (4.2)	0.431	0.44 (0.05-3.64)
No	52 (98.1)	159 (95.8)		
Level nursery available at birth hospital				
I	19 (35.9)	73 (44.0)	0.032	
II	10 (18.9)	49 (29.5)		
III	24 (45.2)	44 (26.5)		
Neonatologist/ neonatal nurse attending delivery				
Yes	20 (44.4)	29 (18.8)	<0.001	3.45 (1.69-7.04)
No	25 (55.6)	125 (81.2)		
Unknown	8	12		
Prenatal diagnosis of MMC				
Yes	28 (52.8)	32 (19.3)	<0.001	4.69 (2.42-9.09)
No	25 (47.2)	134 (80.7)		

[1]**For all the prelabour CS versus TOL comparisons, the odds ratio is calculated as prelabour CS/TOL for the uppermost factor in each row of the "Characteristics" column.**

Table 4: Birth Characteristics of Infants (N=219) in the Prelabour Cesarean Section (CS) and Trial Of Labour (TOL) Groups

Characteristic	Prelabour CS N=53 n (%)	TOL N=166 n (%)	P	Odds Ratio (95% CI)
Fetal presentation				
Cephalic	35 (66.0)	144 (86.8)	0.003	
Breech	17 (32.1)	21 (12.6)		
Other	1 (1.9)	1 (0.6)		
Birthweight (grams)				
Mean (±SD)	3308 (±587)	3256 (±693)	0.622	
# missing	0	8		
Sex of infant				
Male	21 (39.6)	76 (45.8)	0.432	0.78 (0.41-1.46)
Female	32 (60.4)	90 (54.2)		
Presence of hydrocephalus at birth hospital				
Yes	35 (66.0)	75 (45.2)	0.008	2.36 (1.24-4.50)
No	18 (34.0)	91 (54.8)		
Head circumference/ gestational age (birth hospital)				
>90th %	29 (54.7)	64 (38.8)	0.043	
10-90th %	23 (43.4)	84 (50.9)		
<10th %	1 (1.9)	17 (10.3)		
Unknown		1		
Presence of other defects (at birth hospital)				
Yes	11 (20.8)	36 (21.7)	0.886	0.95 (0.44-2.02)
No	42 (79.2)	130 (78.3)		

Table 5: Pregnancy Characteristics for Infants Not Followed to Neurosurgical Centres (N=62) in the Prelabour Cesarean Section (CS) and the Trial of Labour (TOL) Groups

Characteristic	Prelabour CS N=10 n (%)	TOL N=52 n (%)	P	Odds Ratio (95% CI)
Maternal age (years)				
Mean (±SD)	25.2 (±2.6)	24.9 (±4.5)	0.835	
# missing	1	2		
Gestational age at delivery				
<37 wks	2 (22.2)	2 (3.8)	0.040	7.14 (0.86-59.13)
≥37 wks	7 (77.8)	50 (96.2)		
Unknown	1			
Delivery				
Vaginal	0	38 (73.1)		
Cesarean	10 (100)	14 (26.9)		
Multiple birth				
Yes	0	1 (1.9)	0.658	
No	10 (100)	51 (98.1)		
Level nursery available at birth hospital				
I	3 (30.0)	31 (59.6)	0.132	
II	2 (20.0)	10 (19.2)		
III	5 (50.0)	11 (21.2)		
Neonatologist/ neonatal nurse attending delivery				
Yes	7 (70.0)	6 (11.5)	<0.001	17.86 (3.68-90.91)
No	3 (30.0)	46 (88.5)		
Prenatal diagnosis of MMC				
Yes	5 (50.0)	4 (7.7)	0.001	12.05 (2.41-58.82)
No	5 (50.0)	48 (92.3)		

Table 6: Birth Characteristics of Infants Not Followed to Neurosurgical Centres (N=62) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Characteristic	Prelabour CS N=10 n (%)	TOL N=52 n (%)	P	Odds Ratio (95% CI)
Fetal presentation				
Cephalic	5 (50.0)	47 (90.4)	0.002	
Breech	5 (50.0)	4 (7.7)		
Other	0	1 (1.9)		
Birthweight (grams)				
Mean (±SD)	3259 (±651)	3271 (±564)	0.956	
# missing	0	2		
Sex of infant				
Male	3 (30.0)	16 (30.8)	0.961	0.96 (0.22-4.22)
Female	7 (70.0)	36 (69.2)		
Presence of hydrocephalus at birth hospital				
Yes	9 (90.0)	22 (44.0)	0.008	11.49 (1.35-100)
No	1 (10.0)	28 (56.0)		
Unknown		2		
Head circumference/ gestational age (birth hospital)				
>90th %	3 (33.3)	29 (55.8)	0.127	
10-90th %	6 (66.7)	17 (32.7)		
<10th %	0	6 (11.5)		
Unknown	1			
Presence of other defects at birth hospital				
Yes	1 (10.0)	7 (13.5)	0.765	0.71 (0.08-6.54)
No	9 (90.0)	45 (86.5)		

Table 7: Indications for Cesarean Section for Women Having a Cesarean Section in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Indication for CS	Prelabour CS N=53 n (%)	TOL N=45 n (%)	P	Odds Ratio (95% CI)
Fetal distress				
Yes	1 (3.2)	15 (33.3)	<0.001	0.06 (0.01-0.41)
No	52 (96.8)	30 (66.7)		
Feto-pelvic disproportion				
Yes	4 (7.6)	18 (40.0)	<0.001	0.19 (0.07-0.52)
No	49 (92.4)	27 (60.0)		
Breech presentation				
Yes	12 (22.6)	10 (22.2)	0.960	1.02 (0.49-2.13)
No	46 (77.4)	35 (77.8)		
Malpresentation				
Yes	1 (1.9)	1 (2.2)	0.907	0.85 (0.06-13.19)
No	52 (98.1)	44 (97.8)		
Presence of MMC				
Yes	19 (35.9)	6 (13.3)	0.011	2.69 (1.18-6.15)
No	34 (64.2)	39 (86.7)		
Previous CS				
Yes	16 (30.2)	4 (8.9)	0.009	3.40 (1.22-9.43)
No	37 (69.8)	41 (91.1)		
Other				
Yes	12 (22.6)	9 (20.0)	0.751	1.13 (0.53-2.44)
No	41 (77.4)	36 (80.0)		

5.2.2 Neurosurgical Characteristics of Infants Transferred to Neurosurgical Centres:

For the 199 infants with neurosurgical data, there appears to be no significant differences in the characteristics of the MMC lesion and the initial neurosurgical management of the MMC between infants in the prelabour CS and TOL groups (Table 8). Although birth hospital data indicated a higher incidence of hydrocephalus for the prelabour CS group, neurosurgical hospital documentation of hydrocephalus demonstrated no significant differences in the incidence of hydrocephalus between the infants in the prelabour CS versus the TOL groups ($p=0.321$).

Although the size of the base of the MMC lesion or neural placode was not recorded in the chart for the majority of infants in this study, there did appear to be a predominance of lesions greater than 2.5 cms for infants in the TOL groups when compared to those in the prelabour CS group ($p=0.051$).

Table 8: Neurosurgical Characteristics of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Characteristic	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
Anatomic level of lesion				
Cervical	0	2 (1.3)	0.659	
Thoracic	3 (6.5)	6 (3.9)		
Thoraco-lumbar	9 (19.6)	44 (28.8)		
Lumbar	16 (34.8)	36 (23.5)		
Lumbo-sacral	15 (32.6)	48 (31.4)		
Sacral	3 (6.5)	15 (9.8)		
Cerv-thorac-lumbar	0	1 (0.65)		
Thorac-lumb-sacral	0	1 (0.65)		
X-ray level of the lesion				
Mean (±SD)	18.4 (±5.6)	19.6 (±4.1)	0.498	
# missing	32	114		
Level with respect to L2				
At/above L2	23 (53.5)	71 (51.1)	0.782	1.10 (0.56-2.19)
Below L2	20 (46.5)	68 (48.9)		
Unknown	3	14		
Size of base of lesion (neural placode)				
< 1.0 cm	3 (30.0)	4 (6.4)	0.051	
1.0 - 2.5 cms	5 (50.0)	34 (54.0)		
> 2.5 cms	2 (20.0)	25 (39.6)		
Unknown	36	90		
Intact sac				
Yes	24 (55.8)	76 (55.5)	0.969	0.99 (0.50-1.97)
No	19 (44.2)	61 (44.5)		
Unknown	3	16		
Hydrocephalus at neurosurgical hospital				
Yes	19 (41.3)	51 (33.3)	0.321	1.41 (0.72-2.77)
No	27 (58.7)	102 (66.7)		

Table 8: Neurosurgical Characteristics of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Characteristic	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
Head circumference/ gestational age (neurosurgical hospital)				
>90th %	21 (45.6)	51 (33.3)	0.109	
10-90th %	24 (52.2)	86 (56.2)		
<10th %	1 (2.2)	16 (10.5)		
Other congenital anomalies (neurosurgical hospital)				
Yes	8 (17.4)	30 (19.6)	0.737	0.86 (0.37-2.04)
No	38 (82.6)	123 (80.4)		
Surgical Procedure				
Closure of MMC	6 (13.0)	23 (15.1)	0.944	
Closure+Shunt	36 (78.3)	120 (78.4)		
Shunt Only	1 (2.2)	2 (1.3)		
No Surgery	3 (6.5)	8 (5.2)		
Timing of MMC closure				
Closure ≤ 3 days	40 (95.2)	141 (98.6)	0.188	0.28 (0.04-2.08)
Closure > 3 days	2 (4.8)	2 (1.4)		
No Closure	4	10		
Timing shunt insertion with MMC closure				
Simultaneous	7 (19.4)	13 (10.8)	0.175	1.99 (0.73-5.44)
Staged	29 (80.6)	107 (89.2)		
No MMC closure &/or no shunt	10	33		

5.2.3 Neonatal and Infant Outcomes:

(a) Death

There were no significant differences in the rate of death by 6 months of age and 2 years of age between infants in the prelabour CS and TOL groups (Table 9). The distribution of death, from stillbirth to late infant death, was also similar. All three stillborn infants were delivered vaginally in the TOL group. These fetuses, all alive at the onset of labour, died during the course of labour. In two infants, one cephalic and the other breech with cord prolapse, the fetal head was drained in order to allow for delivery. In the third case, the mother arrived to hospital with the fetus in breech presentation delivered to the head. Table 10 lists the causes of death in the first 6 months of life for both study groups with increasing hydrocephalus in infants not surgically treated, being the most common for both groups. The next most common cause of death for both groups was infection. In the prelabour CS group there were 2 deaths by 6 months of age from infection: one infant died of a shunt infection and one infant died of staphylococcal sepsis after supportive care only. There were a total of 7 deaths from infection in the TOL group: one infant who did not receive closure of the MMC developed Clostridium septic shock and necrotizing enterocolitis; 3 infants developed Group B Streptococcal sepsis (2 received closure of the MMC, one did not); one infant who received supportive care only developed Klebsiella meningitis; one infant who received supportive care only died of Staphylococcal sepsis; and one infant receiving supportive care only died of meningitis confirmed at autopsy.

Table 9: Mortality and Combined Adverse Outcomes of Infants (N=219) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome	Prelabour CS N=53 n (%)	TOL N=166 n (%)	P	Odds Ratio (95% CI)
Birth status				
Stillborn	0	3 (1.8)	0.324	
Liveborn	53 (100)	163 (98.2)		
Death by age 6 mos				
Yes	11 (21.2)	25 (15.4)	0.337	1.47 (0.67-3.24)
No	41 (78.8)	137 (84.6)		
Not followed	1			
Death by age 2 yrs				
Yes	11 (21.6)	31 (19.3)	0.718	1.15 (0.53-2.50)
No	40 (78.4)	130 (80.7)		
Not followed	2	5		
Distribution of death by age 2 yrs				
Stillbirth	0	3 (1.9)	0.126	
<28 days	7 (13.7)	19 (11.8)		
≥28 days-6 mos	4 (7.8)	3 (1.9)		
>6 mos-2 yrs	0	6 (3.7)		
Not dead	40 (78.5)	130 (80.7)		
Not followed	2	8		
Combined adverse outcomes (infection and/or death by age 6 mos)				
Yes	17 (32.1)	69 (42.3)	0.185	0.65 (0.50-1.24)
No	36 (67.9)	94 (57.7)		
Not followed		3		

Table 10: Causes of Infant Death (Excluding Stillbirth) In the First 6 Months (N=33) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Cause of Death	Prelabour CS N=11 n (%)	TOL N=22 n (%)
Increasing hydrocephalus after postpartum decision made not to surgically treat the infant	7 (64.0)	11 (50.0)
Infection (sepsis/meningitis/ ventriculitis/shunt)	2 (18.2)	7 (31.8)
Amniotic fluid arachnoiditis	0	1
Brainstem infarction in an infant whose MMC was closed	0	1
Meconium aspiration	0	1
Perinatal asphyxia	1	0
Prematurity and respiratory distress syndrome	1	1

5.2.3 Neonatal and Infant Outcomes - continued:

(b) Morbidity

Table 11 demonstrates no significant differences in one and five minute Apgar scores when comparing the TOL and prelabour CS groups. The occurrence of seizures at the birth hospital was similar in both groups.

Neurosurgical outcome data for the infants in the prelabour CS group versus those in the TOL group are presented in Table 12. No statistically significant differences were found between these two groups with respect to meningitis, sepsis, urinary tract infection, seizures, Chiari malformation symptoms, and shunt malfunction. The rate of wound infection/breakdown was lower for infants in the prelabour CS group (8.7%) when compared to those in the TOL group (22.7%), resulting in an odds ratio of 0.32 (95% CI 0.11-0.97). The rate of combined infectious morbidity was significantly lower for infants in the prelabour CS group (17.4%) than for those in the TOL group (34.0%), resulting in an odds ratio (95% CI) of 0.41 (0.18-0.94).

The bacterial organisms cultured from the CSF in the cases of meningitis and blood in the cases of sepsis are listed in Tables 13 and 14 respectively, with the TOL group having a greater variety of organisms found.

The readmission rate for urinary tract infection was higher in the prelabour CS group (17.4%) when compared to the TOL group (7.2%) [odds ratio (95% CI): 2.72 (CI 1.02-7.25)] as shown in Table 12. Ventilation for > 48 hours was less frequent in the infants in the prelabour CS group (0%) when compared to those delivered after a TOL (8.5%)

($p=0.041$).

Management of shunt malfunction, wound infection or breakdown and Chiari malformation symptoms, and total number days in hospital were similar in both groups (Table 12). The timing of the neurosurgical follow-up was similar in both groups (Table 15).

Table 11: Apgar and Seizures Outcomes of Infants (N=219) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome	Prelabour CS N=53 n (%)	TOL N=166 n (%)	P	Odds Ratio (95% CI)
Apgar 1 min				
<7	16 (30.2)	62 (39.5)	0.226	0.66 (0.34-1.29)
≥7	37 (69.8)	95 (60.5)		
Unknown		9		
Apgar 5 min				
<7	5 (9.6)	24 (15.3)	0.305	0.59 (0.21-1.63)
≥7	47 (90.4)	133 (84.7)		
Unknown	1	9		
Seizures at birth hospital				
Yes	0	4 (2.4)	0.254	
No	53 (100)	162 (97.6)		

Table 12: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome in First 6 Months of Life	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
Meningitis				
Yes	3 (6.7)	13 (8.7)	0.660	0.75 (0.20-2.75)
No	42 (93.3)	136 (91.3)		
Unknown	1	4		
Wound infection or breakdown				
Yes	4 (8.7)	34 (22.7)	0.036	0.32 (0.11-0.97)
No	42 (91.3)	116 (77.3)		
Unknown		3		
Sepsis				
Yes	1 (2.2)	16 (10.7)	0.077	0.19 (0.02-1.47)
No	44 (97.8)	133 (89.3)		
Unknown	1	4		
Urinary tract infection				
Yes	27 (60.0)	97 (64.2)	0.605	0.84 (0.42-1.65)
No	18 (40.0)	54 (35.8)		
Unknown	1	2		
Seizures				
Yes	1 (2.2)	10 (6.7)	0.254	0.32 (0.04-2.54)
No	44 (97.8)	139 (93.3)		
Unknown	1	4		
Diagnosis of Chiari malformation symptoms				
Yes	3 (6.7)	15 (10.0)	0.498	0.64 (0.18-2.33)
No	42 (93.3)	135 (90.0)		
Unknown	1	3		
Shunt malfunction				
Yes	17 (37.8)	45 (30.0)	0.326	1.42 (0.71-2.84)
No	28 (62.2)	105 (70.0)		
Unknown	1	3		

Table 12: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome in First 6 Months of Life	Prelabour CS N=46 n (%)	TOL N=153 n %	P	Odds Ratio (95% CI)
Infectious morbidity (meningitis/sepsis/wound)				
Yes	8 (17.4)	51 (34.0)	0.032	0.41 (0.18-0.94)
No	38 (82.6)	99 (66.0)		
Unknown		3		
Other complications				
Yes	6 (13.3)	24 (16.1)	0.652	0.80 (0.31-2.10)
No	39 (86.7)	125 (83.9)		
Unknown	1	4		
# Readmissions				
> 4	0 (0)	1 (0.6)	0.329	
3 - 4	2 (4.4)	7 (4.6)		
1 - 2	21 (46.6)	48 (31.4)		
None	23 (50.0)	97 (63.4)		
# Readmissions for meningitis				
One or More	3 (6.5)	4 (2.6)	0.207	2.60 (0.56-12.05)
None	43 (93.5)	149 (97.4)		
# Readmissions for wound infection or breakdown				
One or More	1 (2.2)	4 (2.6)	0.867	0.83 (0.09-7.58)
None	45 (97.8)	149 (97.4)		
# Readmissions for urinary tract infection				
One or More	8 (17.4)	11 (7.2)	0.039	2.72 (1.02-7.25)
None	38 (82.6)	142 (92.8)		
# Readmissions for sepsis				
One or More	1 (2.2)	2 (1.3)	0.672	1.68 (0.15-18.87)
None	45 (97.8)	151 (98.7)		

Table 12: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome in First 6 Months of Life	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
# Readmissions for seizures				
One or More	0	0		
None	46 (100)	153 (100)		
# Readmissions for Chiari malformation				
One or More	2 (4.3)	8 (5.2)	0.810	0.82 (0.17-4.02)
None	44 (95.7)	145 (94.8)		
# Readmissions for shunt malfunction				
Twice or More	0 (0.0)	7 (4.6)	0.059	
Once	14 (30.4)	26 (17.0)		
None	32 (69.6)	120 (78.4)		
# Readmissions for other reasons				
One or More	1 (2.2)	10 (6.5)	0.512	
None	45 (97.8)	143 (93.5)		
Ventilation > 48 hrs at neurosurgical hospital				
Yes	0	13 (8.5)	0.041	
No	46 (100)	140 (91.5)		

Table 12: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Outcome in the First 6 Months of Life	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
Total # days spent in hospital				
Mean (±SD)	34.8 (±18.6)	41.1 (±35.2)	0.113	
Shunt malfunction				
Infection	6 (35.3)	15 (33.3)	0.884	1.09 (0.34-3.52)
No infection	11 (64.7)	30 (66.7)		
No shunt malfunction	29	108		
Management of shunt malfunction				
Surgical/no antibiotics	5 (29.4)	10 (22.2)	0.711	
Surgical/with antibiotic	12 (70.6)	34 (75.6)		
Antibiotic only	0 (0.0)	1 (2.2)		
No shunt malfunction	29	108		
Surgical Revision of Wound Infection or Breakdown				
Yes	0	3 (8.8)	0.536	
No	4 (100)	31 (91.2)		
No wound infection	42	119		
Surgery decompression of Chiari malformation				
Yes	3 (100)	12 (80)	0.396	
No	0	3 (20)		
No Chiari symptoms	43	138		

Table 13: Cerebrospinal Fluid Culture Results in Cases of Meningitis (N=16) in the First 6 Months of Life for Infants in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Micro-organism cultured	Prelabour CS N=3	TOL N=13
Staphylococcus	3	5
Group B Streptococcus	0	4
Eschericia coli	0	1
Pseudomonas areuginosa	0	1
Klebsiella	0	1
Organism unknown but meningitis confirmed at autopsy	0	1

Table 14: Blood Culture Results in Cases of Sepsis (N=17) in the First 6 Months of Life for Infants in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Micro-organism cultured	Prelabour CS N=1	TOL N=16
Staphylococcus	1	5
Group B Streptococcus	0	3
Eschericia coli	0	2
Proteus mirabilis	0	1
Klebsiella	0	2
Diphtheroid organism	0	1
Clostridium species	0	1
Blood culture reported as positive but organism not recorded	0	1

Table 15: Timing of Neurosurgical Follow-up for Infants Receiving Neurosurgical Care (N=199) in the Prelabour Cesarean Section (CS) and Trial of Labour (TOL) Groups

Timing of Follow-up	Prelabour CS N=46 n (%)	TOL N=153 n (%)	P	Odds Ratio (95% CI)
Infant age at follow-up in first 6 months of life				
< 3 months	16 (34.8)	52 (34.0)	0.921	1.02 (0.65-1.61)
≥ 3 months	30 (65.2)	101 (66.0)		
Infant age at last follow-up				
< 2 years	6 (13.0)	25 (16.3)	0.107	
2 - 6 years	14 (30.4)	25 (16.3)		
> 6 years	26 (56.6)	103 (64.4)		

5.3 Cesarean Section after Trial of Labour versus Vaginal Birth Groups:

There were 166 infants in the TOL group: 121 (75.6%) were delivered vaginally and 45 (24.4%) were delivered by CS after the onset of labour. Three stillborn infants in the VB group were excluded from the analysis because they died during the course of labour and were thus committed to vaginal birth by the attending physician. In two infants, one cephalic and one breech with a cord prolapse, the fetal head was drained by puncturing the ventricles in order to allow for a vaginal birth. In the third infant, the mother arrived to hospital with the fetus in the breech presentation delivered to the head. Although a fetal heart rate was initially documented, the infant was stillborn. Autopsy revealed that this baby died of cord compression with resultant anoxia.

Of the 52 infants not followed to neurosurgical centres, 38 (71.9%) were delivered vaginally and 14 (28.1%) were delivered by CS after TOL.

5.3.1 Pregnancy and Birth Characteristics:

Table 16 presents the pregnancy characteristics for the 163 infants with birth data according to their mode of delivery. Infants in the CS after TOL group were significantly more likely to have a neonatologist or neonatal nurse present at the delivery ($p=0.011$). Rates of prenatal diagnosis were similar in the VB and CS after TOL groups. Chromosome analysis was done in 1 of the infants in the CS after TOL group and in 4 of infants in the VB group. All results were normal except for one infant in the VB group, the results for which were unknown.

Table 17 presents the birth characteristics of these 163 infants. The infants in the CS

after TOL group had a higher rate of breech presentation ($p=0.002$). The incidence of hydrocephalus was higher in the CS after TOL group (68.9%) when compared to the VB group (34.8%) ($p<0.001$).

Examination of the same pregnancy and birth characteristics according to mode of delivery for the 52 infants who were not tracked to neurosurgical centres (Tables 18 and 19, respectively) does not show the same statistically significant differences as above although similar trends as those who were followed, are evident for: having a neonatologist or neonatal nurse present at delivery, the incidence of hydrocephalus, and the incidence of head circumference > 90th percentile. Chromosome analyses were not done in any of these infants.

Table 16: Pregnancy Characteristics (N=163) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=45 n (%)	VB N=118 n (%)	P	Odds Ratio[2] (95% CI)
Maternal age (years)				
mean (±SD)	28.0 (±4.8)	28.3 (±5.1)	0.730	
# missing	0	11		
Gestational age at delivery				
<37 wks	6 (13.3)	11 (9.4)	0.465	1.48 (0.51-4.27)
≥37 wks	39 (86.7)	106 (90.6)		
Unknown	0	1		
Multiple birth				
Yes	2 (4.4)	5 (4.2)	0.953	1.05 (0.20-5.62)
No	43 (95.6)	113 (95.8)		
Level nursery available at birth hospital				
I	16 (35.6)	57 (48.3)	0.065	
II	19 (42.2)	28 (23.7)		
III	10 (22.2)	33 (28.0)		
Neonatologist/ neonatal nurse attending delivery				
Yes	14 (31.8)	15 (13.9)	0.011	2.89 (1.25-6.68)
No	30 (68.2)	93 (86.1)		
Unknown	1	10		
Prenatal diagnosis of MMC				
Yes	12 (26.7)	19 (16.1)	0.124	1.90 (0.83-4.32)
No	33 (73.3)	99 (83.9)		

[2]For all the CS after TOL versus VB comparisons, the odds ratio is calculated as CS after TOL/VB for the uppermost factor in each row of the "Characteristics" column.

Table 17: Birth Characteristics of Infants (N=163) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=45 n (%)	VB N=118 n (%)	P	Odds Ratio (95% CI)
Fetal presentation				
Cephalic	33 (73.3)	110 (93.2)	0.002	
Breech	11 (24.4)	8 (6.8)		
Other	1 (2.2)	0		
Birth weight (gms)				
mean (±SD)	3284 (±848)	3234 (±631)	0.729	
# missing	3	5		
Sex of infant				
Male	18 (40.0)	57 (48.3)	0.342	0.71 (0.36-1.43)
Female	27 (60.0)	61 (51.7)		
Presence of hydrocephalus at birth hospital				
Yes	31 (68.9)	41 (34.8)	<0.001	4.16 (2.09-8.68)
No	14 (31.1)	77 (65.3)		
Head circumference/ gestational age (birth hospital)				
>90th %				
10-90th %	29 (64.4)	32 (27.3)	<0.001	
<10th %	13 (28.9)	71 (60.7)		
Unknown	3 (6.7)	14 (12.0)		
	0	1		
Presence of other defects (at birth hospital)				
Yes	11 (24.4)	24 (20.3)	0.568	1.27 (0.56-2.86)
No	34 (75.6)	94 (79.6)		

Table 18: Pregnancy Characteristics for Infants Not Followed to Neurosurgical Centres (N=52) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=14 n (%)	VB N=38 n (%)	P	Odds Ratio (95% CI)
Maternal age (years)				
mean (±SD)	25.6 (±4.9)	24.6 (±4.3)	0.513	
# missing	0	2		
Gestational age at delivery				
<37 wks	0	2 (5.3)	0.381	
≥37 wks	14 (100.0)	36 (94.7)		
Multiple birth				
Yes	0	1 (2.6)	0.540	
No	14 (100)	37 (97.4)		
Level nursery available at birth hospital				
I	9 (64.3)	22 (57.9)	0.257	
II	4 (28.6)	6 (15.8)		
III	1 (7.1)	10 (26.3)		
Neonatologist/neonatal nurse attending delivery				
Yes	2 (14.3)	4 (10.5)	0.707	1.42 (0.23-8.75)
No	12 (85.7)	34 (89.5)		
Prenatal diagnosis of MMC				
Yes	0	4 (10.5)	0.206	
No	14 (100.0)	34 (89.5)		

Table 19: Birth Characteristics of Infants Not Followed to Neurosurgical Centres (N=52) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=14 n (%)	VB N=38 n (%)	P	Odds Ratio (95% CI)
Fetal presentation				
Cephalic	12 (85.8)	35 (92.1)	0.251	
Breech	1 (7.1)	3 (7.9)		
Other	1 (7.1)	0 (0.0)		
Birth weight (grams)				
mean (±SD)	3264 (±634)	3274 (±545)	0.956	
# missing	3	2		
Sex of infant				
Male	6 (42.9)	10 (26.3)	0.252	2.10 (0.58-7.58)
Female	8 (57.1)	28 (73.7)		
Presence of hydro-cephalus at birth hospital				
Yes	9 (64.3)	13 (36.1)	0.072	3.18 (0.88-11.54)
No	5 (35.7)	23 (63.9)		
Head circumference/ gestational age (birth hospital)				
>90th %	10 (71.4)	19 (50.0)	0.385	
10-90th %	3 (21.4)	14 (36.8)		
<10th %	1 (7.1)	5 (13.2)		
Unknown		1		
Presence of other defects at birth hospital				
Yes	2 (14.3)	5 (13.2)	0.916	1.10 (0.19-6.45)
No	12 (85.7)	33 (86.8)		

5.3.2 Neurosurgical Characteristics of Infants Transferred to Neurosurgical Centres:

For the 153 infants with obstetrical and neurosurgical data, the characteristics of the MMC lesion demonstrated some important differences between the VB and CS after TOL groups (see Table 20). Although the overall anatomical distribution of the MMC lesions was similar, there was a trend for a greater percentage of infants with thoraco-lumbar lesions in the CS after TOL group (40.0% for the CS group versus 24.8% for the VB group). With respect to the level of the lesion, 69.4% of infants had lesions at or above L2 in the CS after TOL group versus 44.7% of infants in the VB group [odds ratio (95% CI): 2.89 (1.25-6.33); p=0.01]. With respect to the size of the base of the lesion for those infants for which there was information on this variable, 70.6% in the CS after TOL group had lesions larger than 2.5 cms in comparison to 28.3% of infants in the VB group (p=0.008), although many infants were missing data on this variable in both groups (57.5% in the CS after TOL group and 59.2% in the VB group). A higher incidence of hydrocephalus was found in the infants born by CS after TOL (52.5%) versus infants born by VB (26.6%) [p=0.003].

Despite the differences in MMC lesion characteristics, initial neurosurgical management of the lesion was similar (Table 20).

Table 20: Neurosurgical Characteristics of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Anatomic Level of Lesion				
Cervical	0	2 (1.8)	0.320	
Thoracic	1 (2.5)	5 (4.4)		
Thoraco-lumbar	16 (40.0)	28 (24.8)		
Lumbar	8 (20.0)	28 (24.8)		
Lumbo-sacral	12 (30.0)	36 (31.9)		
Sacral	2 (5.0)	13 (11.5)		
Cerv-thor-lumbar	1 (2.5)	0 (0.0)		
Thor-lumb-sacral	0	1 (0.8)		
X-ray level of the lesion				
mean (±SD)	20.2 (±3.7)	19.3 (±4.3)	0.540	
# missing	29	85		
Level with respect to L2				
At/above L2	25 (69.4)	46 (44.7)	0.01	2.89 (1.25-6.33)
Below L2	11 (30.6)	57 (55.3)		
Unknown	4	10		
Size of base of lesion (neural placode)				
< 1.0 cm	1 (5.9)	3 (6.5)	0.008	
1.0 - 2.5 cms	4 (23.5)	30 (65.2)		
> 2.5 cms	12 (70.6)	13 (28.3)		
Unknown	23	67		
Intact sac				
Yes	17 (53.1)	59 (56.2)	0.760	0.88 (0.40-1.96)
No	15 (46.9)	46 (43.8)		
Unknown	8	8		
Hydrocephalus at neurosurgical hospital				
Yes	21 (52.5)	30 (26.6)	0.003	3.06 (1.45-6.46)
No	19 (47.5)	83 (73.5)		

Table 20: Neurosurgical Characteristics of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Characteristic	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Head circumference/ gestational age (neurosurgical hospital)				
>90th %	23 (57.5)	28 (24.8)	0.001	
10-90th %	15 (37.5)	71 (62.8)		
<10th %	2 (5.0)	14 (12.4)		
Other congenital anomalies (neurosurgical hospital)				
Yes	8 (20)	22 (19.5)	0.943	1.03 (0.42-2.55)
No	32 (80)	91 (80.5)		
Surgical procedure				
Closure of MMC	4 (10.0)	19 (16.8)	0.070	
Closure+shunt	30 (75.0)	90 (79.7)		
Shunt only	1 (2.5)	1 (0.9)		
No surgery	5 (12.5)	3 (2.6)		
Timing of MMC closure				
Closure ≤ 3 days	33 (97.1)	108 (99.1)	0.380	3.27 (0.20-53.77)
Closure > 3 days	1 (2.9)	1 (0.9)		
No closure	6	4		
Timing shunt insertion with MMC closure				
Simultaneous	6 (20)	7 (7.8)	0.062	2.97 (0.91-9.62)
Staged	24 (80)	83 (92.2)		
No MMC closure and/or no shunt	10	23		

5.3.3 Neonatal and Infant Outcomes:

(a) Death

The mortality rate by 6 months of age was 23.3% for infants in the CS after TOL group versus 10.3% for those in the VB group [odds ratio (95% CI): 2.63 (1.04-6.63)] as shown in Table 21. Death by 2 years of age was not statistically significantly different between groups. Table 22 lists the causes of death in the first 6 months of life for both groups. Increasing hydrocephalus in infants not surgically treated accounted for 70.0% of the 6 month mortality for infants in the CS after TOL group whereas this reason accounted for only 33.3% of the 6 month mortality for infants in the VB group. Infection accounted for 41.7% of deaths in the first 6 months for the infants in the VB group compared with 20.0% of deaths for infants in the CS after TOL group. Of the two infants dying of infection in the CS after TOL group, one infant, treated with surgical closure of the MMC, died of Clostridium septic shock and necrotizing enterocolitis and the other infant, receiving supportive care only, died of Staphylococcal sepsis. Of the 5 infants who died of infection in the VB group, 3 died of Group B streptococcal sepsis and/or meningitis, one died of Klebsiella meningitis after receiving supportive care only, and one died of meningitis, confirmed at autopsy, after receiving supportive care only.

Table 21: Mortality and Combined Adverse Outcomes of Infants (N=163) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome	CS after TOL N=45 n (%)	VB N=118 n (%)	P	Odds Ratio (95% CI)
Birth status				
Stillborn	0	0		
Liveborn	45 (100)	118 (100)		
Death by age 6 mos				
Yes	10 (23.3)	12 (10.3)	0.036	2.63 (1.04-6.63)
No	33 (76.7)	104 (89.7)		
Not followed	2	2		
Death by age 2 yrs				
Yes	10 (23.3)	18 (15.6)	0.265	1.63 (0.69-3.89)
No	33 (76.7)	97 (84.4)		
Not followed	2	3		
Distribution of death by age 2 yrs				
<28 days	9 (20.9)	10 (8.7)	0.093	
≥28 days-6 mos	1 (2.4)	2 (1.7)		
>6 mos-2 yrs	0 (0.0)	6 (5.2)		
Not dead	33 (76.7)	97 (84.4)		
Not followed	2	3		
Combined adverse outcomes (infection and/or death by age 6 mos.)				
Yes	21 (48.8)	45 (38.5)	0.237	1.53 (0.76-3.09)
No	22 (51.2)	72 (61.5)		
Not followed	2	1		

Table 22: Causes of Infant Death (Excluding Stillbirths) in the First 6 Months (N=22) in the Cesarean Section (CS) after Trial of Labour (TOL) and Vaginal Birth (VB) Groups

Cause of Death	CS after TOL N=10 n (%)	VB N=12 n (%)
Increasing hydrocephalus after postpartum decision made not to surgically treat the infant	7 (70.0)	4 (33.3)
Infection (sepsis/meningitis/ ventriculitis/shunt)	2 (20.0)	5 (41.7)
Amniotic fluid arachnoiditis	0	1
Brainstem infarction in an infant whose MMC was closed	0	1
Meconium aspiration	0	1
Prematurity and respiratory distress syndrome	1	0

5.3.3 Neonatal and Infant Outcomes - continued:

(b) Morbidity

Table 23 demonstrates that the infants in the CS after TOL group were more likely to have a one minute Apgar score <7 when compared to the infants in the VB group ($p=0.041$). There was no significant difference in five minute Apgar score <7 between groups. Seizures were not different between groups (Table 23).

Neurosurgical outcome data for the TOL versus prelabour CS groups are presented in Table 24. No statistically significant differences are found between the two groups with respect to meningitis, wound infection, urinary tract infection, sepsis, seizures, Chiari malformation symptoms, shunt malfunction, and the outcome of infectious morbidity. The differences seen in the comparison between the TOL and prelabour CS groups with respect to sepsis, wound infections/breakdown and overall infectious morbidity are not seen in the comparison between the VB and CS after TOL groups.

The organisms cultured in cases of meningitis and sepsis are listed in Tables 25 and 26 respectively.

Management of shunt malfunction, wound infection or breakdown and Chiari malformation symptoms, number of readmissions, reasons for readmissions, ventilation for more then 48 hours, and total number days in hospital were similar in both groups (Table 24). The length of follow-up was similar for infants in both groups (Table 27).

Table 23: Apgar and Seizure Outcomes of Infants (N=163) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome	CS after TOL N=45 n (%)	VB N=118 n (%)	P	Odds Ratio (95% CI)
Apgar 1 min				
<7	23 (52.3)	39 (34.5)	0.041	2.08 (1.03-4.22)
≥7	21 (47.7)	74 (65.5)		
Unknown	2	5		
Apgar 5 min				
<7	9 (20.9)	15 (13.2)	0.227	1.78 (0.70-4.38)
≥7	34 (79.1)	99 (86.8)		
Unknown	2	4		
Seizures at birth hospital				
Yes	0	4 (3.4)	0.211	
No	45 (100)	114 (96.8)		

Table 24: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome in the First 6 Months of Life	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Meningitis				
Yes	2 (5.3)	11 (9.9)	0.381	0.51 (0.11-2.39)
No	36 (94.7)	100 (90.1)		
Unknown	2	2		
Wound infection or breakdown				
Yes	8 (21.1)	26 (23.2)	0.783	0.88 (0.36-2.16)
No	30 (78.9)	86 (76.8)		
Unknown	2	1		
Sepsis				
Yes	5 (13.2)	11 (9.9)	0.577	1.38 (0.45-4.26)
No	33 (86.8)	100 (90.1)		
Unknown	2	2		
Urinary tract infection				
Yes	23 (60.5)	74 (65.5)	0.581	0.81 (0.38-1.72)
No	15 (39.5)	39 (34.5)		
Unknown	2			
Seizures				
Yes	4 (10.5)	6 (5.4)	0.276	2.06 (0.55-7.73)
No	33 (89.5)	105 (94.6)		
Unknown	2	2		
Diagnosis of Chiari malformation symptoms				
Yes	5 (12.8)	10 (9)	0.495	1.49 (0.47-4.65)
No	34 (87.2)	101 (91)		
Unknown	1	2		
Shunt malfunction				
Yes	7 (18.4)	38 (33.9)	0.071	0.44 (0.18-1.09)
No	31 (81.6)	74 (66.1)		
Unknown	2	1		

Table 24: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome in the First 6 Months of Life	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Infectious morbidity (meningitis/sepsis/ wound)				
Yes	13 (34.2)	38 (33.9)	0.975	1.01 (0.47-2.20)
No	25 (65.8)	74 (66.1)		
Unknown	2	1		
Other complications				
Yes	8 (21.1)	16 (14.4)	0.337	1.58 (0.62-4.06)
No	30 (78.9)	95 (85.6)		
Unknown	2	2		
# Readmissions				
>4	0 (0.0)	1 (0.9)	0.685	
3 - 4	3 (7.5)	4 (3.5)		
1 - 2	13 (32.5)	35 (31.0)		
None	24 (60.0)	73 (64.6)		
# Readmissions for meningitis				
One or More	2 (5.0)	2 (1.8)	0.271	2.92 (0.40-21.46)
None	111 (98.2)	38 (95.0)		
# Readmissions for wound infection or breakdown				
One or More	1 (2.5)	3 (2.6)	0.958	0.94 (0.10-9.31)
None	39 (97.5)	110 (97.4)		
# Readmissions for urinary tract infection				
One or More	4 (10.0)	7 (6.2)	0.423	1.68 (0.47-26.08)
None	36 (90.0)	106 (93.8)		
# Readmissions for sepsis				
One or More	0	2 (1.8)	0.397	
None	40 (100)	111 (98.2)		

Table 24: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome in the First 6 Months of Life	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
# Readmissions for seizures				
One or More	0	0		
None	40 (100)	113 (100)		
# Readmissions for Chiari malformation symptoms				
One or More	3 (7.5)	5 (4.4)	0.453	1.75 (0.40-7.69)
None	37 (92.5)	108 (95.6)		
# Readmissions for shunt malfunction				
Twice or More	2 (5.0)	5 (4.4)	0.391	
Once	4 (10.0)	22 (19.5)		
None	34 (85.0)	86 (76.1)		
# Readmissions for other reasons				
One or More	4 (10.0)	6 (5.3)	0.371	
None	36 (90.0)	107 (94.7)		
Ventilation > 48 hrs at the neurosurgical hospital				
Yes	2 (5)	11 (9.7)	0.356	0.49 (0.10-2.3)
No	38 (95)	102 (90.3)		

Table 24: Neurosurgical Outcomes of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Outcome in the First 6 Months of Life	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Total # days spent in hospital mean (±SD)	41.3 (±40.3)	41.0 (±33.3)	0.959	
Shunt malfunction				
Infection	2 (25)	13 (35.1)	0.581	0.62 (0.11-3.50)
No infection	6 (75)	24 (64.9)		
No shunt malfunction	32	76		
Management of shunt malfunction				
Surgical/no antibiotics	1 (12.5)	9 (24.3)	0.666	
Surgical/with antibiotics	7 (87.5)	27 (73.0)		
Antibiotics only	0	1 (2.7)		
No shunt malfunction	32	76		
Surgical revision of wound infection or breakdown				
Yes	0	3 (11.5)	0.314	
No	8 (100)	23 (88.5)		
No wound infection	32	87		
Surgery decompression of Chiari malformation				
Yes	4 (80)	8 (80)	1.000	1.00 (0.07-14.64)
No	1 (20)	2 (20)		
No Chiari symptoms	35	103		

Table 25: Cerebrospinal Fluid Culture Results in Cases of Meningitis (N=13) in the First 6 Months of Life for Infants in the Cesarean Section (CS) after Trial of Labour (TOL) and Vaginal Birth (VB) Groups

Micro-organism cultured	CS after TOL N=2	VB N=11
Staphylococcus	2	3
Group B Streptococcus	0	4
Eschericia coli	0	1
Pseudomonas areuginosa	0	1
Klebsiella and Pseudomonas	0	1
Organism unknown but meningitis confirmed at autopsy	0	1

Table 26: Blood Culture Results in Cases of Sepsis (N=16) in the First 6 Months of Life for Infants in the Cesarean Section (CS) after Trial Of Labour (TOL) and Vaginal Birth (VB) Groups

Micro-organism cultured	CS after TOL N=5	VB N=11
Staphylococcus	2	3
Group B Streptococcus	0	3
Eschericia coli	0	2
Proteus mirabilis	0	1
Klebsiella	1	1
Diphtheroid organism	0	1
Clostridium species	1	0
Blood culture reported as positive but organism not recorded	1	0

Table 27: Short Term and Long Term Neurosurgical Follow-up of Infants Receiving Neurosurgical Care (N=153) in the Cesarean Section after Trial Of Labour and Vaginal Birth Groups

Timing of Follow-up	CS after TOL N=40 n (%)	VB N=113 n (%)	P	Odds Ratio (95% CI)
Infant age at follow-up in first 6 months of life				
< 3 months	12 (30)	40 (35.4)	0.536	0.78 (0.36-1.70)
≥3 months	28 (70)	73 (64.6)		
Infant age at last follow-up				
< 2 years	8 (20.0)	17 (15.0)	0.290	
2 - 6 years	9 (22.5)	16 (14.2)		
> 6 years	23 (57.5)	80 (70.8)		

5.4 Summary of Results

Infants in the prelabour CS group were significantly more likely to be born in a level III obstetrical unit ($p=0.032$), have a prenatal diagnosis of MMC ($p<0.001$), present as breech ($p=0.003$) and have clinical hydrocephalus at birth ($p=0.008$) compared to infants in the TOL group. Infants in the prelabour CS group had a lower rate of infectious morbidity compared to infants in the TOL group [odds ratio (95% CI): 0.41 (0.18-0.94)]. Six month mortality was not significantly different between groups and causes of death, which were similar in both groups, were mostly related to increasing hydrocephalus after supportive care only or infection. The number of readmissions, total hospital days, 6 month and 2 year follow-up, rates of shunt insertion, shunt infections, shunt revisions, surgical wound revisions, and surgical decompression of Chiari malformation, were similar in both groups.

Infants born by CS after TOL were significantly more likely to have hydrocephalus ($p<0.001$), present as breech ($p=0.002$), and have more severe MMC ($p=0.01$) as compared to infants born vaginally. Infants born by CS after TOL had significantly higher 6 month mortality than the infants born vaginally [odds ratio (95% CI): 2.63 (1.04-6.63)]. Seventy percent of infants who died in the first 6 months of life in the CS after TOL group died from increasing hydrocephalus after supportive care only compared to 33.3% in the VB group. The number of readmissions, total hospital days, 6 month and 2 year follow-up, rates of surgical wound revisions, and surgical decompression of Chiari malformation, were similar in both groups. Although shunt insertion, infection and revision rates were similar in both groups, more infants in the CS after TOL group received their shunt simultaneously with closure of the MMC when compared to infants

in the VB group presumably due to the presence of more hydrocephalus at birth.

6. DISCUSSION

6.1 The Effect of Labour and Vaginal Delivery

Infants in the prelabour CS group had a lower rate of infectious morbidity compared to infants in the TOL group [odds ratio (95% CI): 0.41 (0.18-0.94)], suggesting that the avoidance of labour and delivery by CS may be beneficial for infants with MMC. Six month mortality was similar in both groups. In both groups, causes of death were mostly related to increasing hydrocephalus with supportive care only and infection. Number of readmissions, total hospital days, 6 month and 2 year follow-up, rates of shunt insertion, shunt infections, shunt revisions, surgical wound revisions, and surgical decompression of Chiari malformation, were similar in both groups.

Differences existed between infants in the prelabour CS group and those in the TOL group which may have had an effect on outcomes independent of the mode of delivery and the presence or absence of labour. Infants in the prelabour CS group were significantly more likely to be born in a level III obstetrical unit ($p=0.03$), have a neonatal nurse or neonatologist present at birth, have a prenatal diagnosis of MMC ($p=0.00$), have a higher rate of hydrocephalus at the time of birth ($p=0.008$), be in the breech presentation ($p=0.003$) and have smaller sized MMC lesions ($p=0.051$). Consideration must be given to whether or not any of these factors could have influenced the incidence of infectious morbidity in the study groups.

It is possible that birth in a level II or III obstetrical unit in the presence of a neonatologist or neonatal nurse could have resulted in more expert care in a more timely fashion with immediate coverage of the infant with intravenous broad spectrum

antibiotics, protection of the MMC wound with sterile dressings, and faster transfer to a neurosurgical centre in comparison to birth at a level I unit. However, common practice in the 1980's was to administer this type of management irrespective of the level of obstetrical unit and to transfer the infant to a neurosurgical centre within the first 12 to 24 hours of birth. In fact, of the infants followed to neurosurgical centres in this study, the majority arrived in neurosurgical centres within the first 12 to 24 hours of birth.

Most investigators comparing the outcome of MMC infants based on either immediate or delayed closure of the MMC lesion, have agreed that even a delay of up to one week in closure of the MMC will not increase the risk of meningitis, ventriculitis, or other serious infections, and will not increase the risk of mortality or the risk of paralysis later in life (Smyth et al, 1974:, Deans and Boston, 1988; Charney et al, 1985). Only one study by Sharrard et al (1962) demonstrated that infants not receiving surgery for MMC closure had a greater incidence of sepsis and deterioration of muscle function when compared to a group of infants receiving surgery within the first 48 hours of life. Although these authors claimed that the infants were randomized into operative and non-operative groups, this is not described in their publication, and statistical significance was not determined. Assessments of degree of paralysis were unblinded. It might not be appropriate to compare operation to no operation when most investigators agree that surgery should at least be done in the first week of life. The results from this thesis were that 95.2% of infants delivered by prelabour CS and 98.6% of infants delivered following TOL, received surgical closure of the MMC within 72 hours of birth ($p=0.188$) so that transfer and treatment occurred quickly in the majority of infants

irrespective of the level of unit in which they were born.

Antenatal diagnosis is believed to improve the prognosis of MMC infants for several reasons. It is possible that fetuses with the more severe lesions and thus the worst prognoses may be therapeutically aborted prior to viability, leaving those with the less severe lesions to progress to term. Increased fetal surveillance with serial ultrasonography for those pregnancies chosen for continuation may lead to a more timely delivery of the fetus. These interventions may improve mortality, but their contribution to reduced morbidity is questionable and unfounded. Grevengood et al (1994) found that the perceived severity of the MMC based on prenatal ultrasound does appear to influence the decision to continue or terminate an affected pregnancy. In their study, none of the women who elected pregnancy continuation were carrying fetuses with lesions craniad to T9 who, in general, have a 33% mortality rate and poorer prognosis than those with lesions caudad to this level. Corresponding mortality rates for lumbosacral and sacral lesions are 11% and 0% (Ames and Schut, 1972; Grevengood et al, 1994). There are no data to support the notion that infection is more likely to occur in infants with more severe lesions or more severe hydrocephalus, although mortality is higher with more severe lesions. The results of this research indicate that there was no significant difference in the overall anatomical distribution of the MMC lesions ($p=0.659$) or in the level of the lesions with respect to L2 ($p=0.782$) in the prelabour CS versus TOL groups, even though there was a higher likelihood of prenatal diagnosis in the prelabour CS group ($p=0.001$). However, there was a marked trend for smaller sized neural placodes in the prelabour CS group when compared to the TOL group ($p=0.051$) but with over 50% of infants having missing data for this variable, the significance of these

results is questionable. The size of the neural placode is more likely to be associated with the degree of neurologic deficit than with the risk of infection or death.

If prenatal diagnosis had truly resulted in pregnancy continuation for fetuses with the best prognosis, one would have at least expected to see less hydrocephalus and a lower mortality rate in infants born by prelabour CS, but this was not the case. Overall mortality rates at 6 months and at 2 years were similar and hydrocephalus at birth was present more often in infants born by prelabour CS. Rates of administering supportive care only, because of severe MMC, was similar in both groups, another indication that degree of severity of the lesion was similar in the prelabour CS versus TOL groups.

Breech presentation has been associated with a higher incidence of birth trauma and mortality but not necessarily a higher rate of infection in MMC infants. Although some investigators feel that babies presenting by the breech suffer more trauma no matter what the route of delivery, others feel that a CS for MMC infants presenting by the breech, allows for greater control and reduced trauma at the time of delivery (Chervenak et al, 1994).

It is thus unlikely that the differences in pregnancy and birth characteristics demonstrated between the two groups could entirely account for the significantly lower rate of infectious morbidity in the prelabour CS group. The avoidance of labour and vaginal delivery may therefore be effective in reducing this outcome.

6.2 The Effect of the Route of Delivery - Cesarean Section versus Vaginal

Infants born by CS after TOL had significantly higher 6 month mortality than the infants born vaginally [odds ratio (95% CI): 2.63 (1.04-6.63)]. No statistically significant difference was found in the rate of infectious morbidity between the two study groups [odds ratio (95% CI): 1.01 (0.47-2.2)]. Infants born by CS after TOL were significantly more likely to have hydrocephalus ($p<0.001$), present as breech ($p<0.001$), and have a neonatologist or neonatal nurse present at the delivery ($p=0.011$) when compared to the infants in the VB group.

The lack of difference in infectious morbidity between the two groups is interesting since one would expect to find a higher rate of infectious morbidity in those infants born vaginally since the fetus is actually passing through the birth canal and would be exposed to a higher concentration of bacteria. On the other hand, it is also possible that once labour is initiated and membranes are ruptured, the infant is exposed to bacteria in the maternal genital tract whether it occurs during vaginal delivery or from bacteria ascending into the uterus during the labour process. The differences in pregnancy and birth characteristics found between these two groups would be unlikely to affect infection rates as described earlier.

If vaginal birth is truly more traumatic than cesarean birth for infants with MMC, then one would expect the rate of mortality to be higher for the infants delivering vaginally. The results of this research indicate that the mortality rate was actually higher in the infants born by CS after the TOL and this is most likely related to a greater severity of lesions in this group. Although there was no statistically significant difference in the

overall anatomical distribution of the MMC lesions between the two groups, 40.0% of infants in the CS after TOL group had thoraco-lumbar lesions compared with 24.8% in the VB group. This clinically important difference in the severity of the lesions achieves statistical significance when the analysis is done comparing the level of the uppermost part of the lesion with respect to vertebral level L2. Infants born by CS after TOL were more likely to have lesions above L2 compared with infants in the VB group (69.4% vs 44.7%, $p=0.01$). This increased anatomical severity of the lesion, coupled with the higher rate of hydrocephalus in the infants born by CS after TOL, is likely to account for their increased rate of mortality when compared to infants born vaginally. More infants in the CS after TOL group died in the first 6 months of life from increasing hydrocephalus after supportive care only compared to the VB group, indirectly indicating that the severity of the lesions was, in fact, greater for infants in the CS after TOL group.

The number of readmissions, total hospital days, 6 month and 2 year follow-up, rates of surgical wound revisions, and surgical decompression of Chiari malformation, were similar in both groups. Although shunt insertion, infection and revision rates were similar in both groups, more infants in the CS after TOL group received their shunt simultaneously with closure of the MMC when compared to infants in the VB group, presumably due to the presence of more hydrocephalus at birth. This difference is clinically important but does not achieve statistical significance ($p=0.062$).

6.3 Study Limitations

A. Selection Bias

It is possible that mothers and infants who were meant to be in this study were never identified and how their exclusion might have affected the study results is unknown. Identification of MMC infants was dependent on the search of medical records for infants born with the ICD-9 code 741 for spina bifida in each birth hospital. It is possible that some infants were not coded properly and thus went unidentified. Indirect proof of this problem was found during the search for infants at the neurosurgical centres who were properly linked with infants identified at the birth hospitals. In some cases (n=10), neurosurgical records of infants with MMC born in the specified study period were identified at the neurosurgical hospital but did not link with any infants identified at the birth hospital. These infants were not included in the study since they were not identified by the methodology specified by this study. For the most part, the incorrect classification of disease occurred in the opposite direction. There were many infants classified in the general category of spina bifida but who in fact did not have the specific diagnosis of MMC.

B. Effect of Confounding Variables:

This study was designed as a retrospective cohort study in which exposure to labour and vaginal birth was determined in infants born with MMC in a retrospective manner by examining birth records at Ontario birth hospitals. These infants were then followed forward in time up to 6 months of age to determine the incidence of infectious morbidity, other neonatal morbidity and mortality after delivery by prelabour CS compared with delivery after TOL and delivery by CS after TOL compared with VB. The exposures

in this study were easily determined as labour and birth records objectively documented the presence or absence of labour and the eventual route of delivery, either vaginal or CS. Although the occurrence of labour and route of delivery were recorded in this study, the number of hours spent in labour were not. Taking into account the duration of labour in the statistical comparison of mortality and infection rates between the infants in the CS after TOL and the VB group, may be important if duration of labour is correlated with risk of death or infection. Such a relationship is expected since there exists similar situations in obstetrics, such as the increased risk of neonatal herpes with increased duration of membrane rupture. The absence of a statistically significant difference in infection rates between the infants in the CS after TOL group versus those in the VB group in this study, would suggest to most clinicians that once labour begins the risk of infection may not be reduced or averted. Had this study been able to investigate the possibility of a "dose-response" relationship between labour and infection or mortality in infants with MMC, the benefit of intervening with a CS even after labour has begun solely to reduce the risk of infection or death, would have been clarified.

Exposure to labour and selection of mode of delivery did not occur in a random manner and women were not equally likely to be in one group versus the other. Factors such as hydrocephalus, fetal presentation, and antenatal diagnosis, not only may influence the occurrence of labour and route of delivery, but may also be associated with the outcome of the infants. Women with a multiple gestation or those who have fetuses with severe hydrocephalus or a malpresentation, may not labour efficiently and may require a CS for delivery after the onset of labour. Twins, fetuses with severe hydrocephalus and fetuses in the breech presentation also have an increased risk of mortality.

Because of the ongoing controversy in the literature about the appropriate route of delivery for infants with MMC and the few studies which have indicated a benefit of prelabour CS, some clinicians in tertiary care centres in Ontario suggest that infants with MMC diagnosed antenatally, be delivered by prelabour CS. There is also some evidence to suggest that prenatal diagnosis of MMC increases the likelihood that pregnancies will be allowed to continue if fetuses have a better prognosis whereas fetuses with a worse prognosis may be terminated prior to viability. When one combines the issue of prenatal diagnosis and the preference of prelabour CS, it is clear that there is a potential for infants born by prelabour CS to do better, not because of the avoidance of labour, but simply because of prenatal diagnosis and selection of those with a better prognosis for continuing the pregnancy.

There has been no good evidence that birth in a level II or III unit with the constant availability of a neonatologist or neonatal nurse, reduces infectious morbidity and mortality but many clinicians intuitively feel that infants born in these circumstances would do better because of the availability of expert care and the perception that transfer to and treatment at a neurosurgical unit will be faster. When this issue is combined with the fact that infants with MMC in level II or III units are more likely to have had a prenatal diagnosis of MMC, better outcomes among those infants born in a higher level unit may just reflect the same selection as prenatal diagnosis.

In this study, information on what were considered to be the important confounding variables, based either on clinical practice or previous research, was collected and will be incorporated into a regression analysis as future research.

Despite recognizing what the confounding factors were and providing for proper collection of information regarding these factors, there were limitations in finding the information in the charts in this retrospective study. Information on most of the confounders, such as gestational age at delivery, fetal presentation, and multiple gestation were available because they were part of the normal routine documentation by medical personnel on established hospital obstetrical forms. Although the measurement and recording of head circumference should be routine at the birth hospital, it was often missing from the birth records. Since this was an anticipated problem, the head circumference measurement from the neurosurgical hospital, which was documented in all of the infants transferred and often taken only 12-24 hours after the infant's birth, was also recorded. Information regarding the level of nursery available at the birth hospital was checked against information obtained from the Ontario Ministry of Health. If there were discrepancies, the nursery at that birth hospital was contacted to verify the information. Although information regarding the general level of the MMC lesion with respect to vertebral level L2 was often available, the size of the base of the lesion was not recorded in the majority of the neurosurgical charts, even after carefully examining the admission notes by the neurosurgical resident and staff neurosurgeon and the operative note. Attempting to obtain this information accurately from interviewing the surgeons involved would be difficult due to recall bias. Timing of closure of the defect was obtained in all cases transferred to neurosurgical centres, since documentation of operative procedures, dates and times were very strict in these cases.

C. Outcome Ascertainment Bias:

One other problem in this study was that ascertainment of infectious morbidity and

mortality was not done in a blinded fashion. Although there was no knowledge of the exposure to labour or route of delivery from birth records when neurosurgical charts were abstracted, this information was often present in the initial neurosurgical history at the front of the chart. When abstraction of neurosurgical information was started, it was more common for me to accidently come across the delivery information. As I abstracted information from more charts I learned what part of the chart I had to stay away from in order to avoid this delivery information. None the less, for the comparison of the CS after TOL and VB groups, I was aware of the type of delivery in 27.5% of the CS after TOL cases and in 7.1% of the VB cases which is a significant difference ($p=0.001$). For the comparison of the prelabour CS and the TOL groups, I was aware of the type of delivery in 19.6% of the prelabour CS cases and in 12.4% of the TOL cases which was not statistically significant ($p=0.222$).

I believe it is unlikely that outcomes were determined differently in the groups despite the access to information in the chart on labour and mode of delivery as outcomes were clearly defined apriori and I made a major attempt to be consistent throughout the study.

D. Under-reporting of Outcomes:

In this thesis, the important outcomes were 6 month mortality and infectious morbidity which included meningitis or sepsis or wound infection. The historical nature of retrospective cohort studies often places constraints on the measurement of disease occurrence (Kelsey et al, 1986). In this study, an attempt was made to define the outcomes very carefully and in such a way that data on outcomes would be available in the medical record. Meningitis and sepsis were defined as the presence of clinical

symptoms and signs with positive cerebrospinal fluid and blood cultures respectively. It would be very unlikely for an infant to have either meningitis or sepsis and for this to go unrecognized. The use of blood cultures and CSF cultures was very liberal and these were done even for the most minimal symptoms. Thus, the majority of infants had evidence of these culture results on their charts. The documentation of wound infection was, unfortunately, more difficult and relied more heavily on subjective interpretation of how the wound looked by the attending physicians. Wound cultures were unreliable since they would often grow organisms even if there was no infection. The MMC wound is often contaminated by faeces from the diaper area and wound cultures are unreliable. Mortality was also quite easily established from either the birth hospital, if death occurred there, or the neurosurgical chart. In only a few cases, was follow-up for up to 6 months of age incomplete. In many cases, the cause of death was established by autopsy, but in some cases, autopsy was refused and the cause of death on the death certificate was utilized. I do not believe there was under-ascertainment of disease occurrence or mortality in this study.

E. Incomplete Follow-up:

The actual tracing of subjects involved a considerable amount of work. Birth hospitals in Ontario were contacted and a request was made to search their records for infants born with the ICD-9 code for spina bifida. Despite the potential for mis-classification of disease and failure to recognize all cases of MMC, in this study there were infants classified as having spina bifida who actually had other types of conditions such as hydrocephalus alone or congenital aplasia of the cutis. Tracing to neurosurgical centres was very successful since MMC is a disease which is usually treated in a paediatric

neurosurgical institution and records are very clear as to where the infant was transferred. As well, there are a limited number of paediatric neurosurgical centres which will treat these infants. In this study, I was able to track and collect neurosurgical information on 236 of the 243 infants transferred to the neurosurgical centres, Hospital for Sick Children (175 infants) and CHEO (68 infants). Although there were 298 infants considered for neurosurgical treatment, I only tracked those that went to HSC and CHEO which accounted for 82% of infants transferred for neurosurgical care. The loss to follow-up of 18% of the sample is unlikely to alter the results as the data on pregnancy and birth characteristics suggested the infants were similar.

F. Generalizability:

In this study, infants with MMC were identified at birth, and no information was obtained about pregnancies which were terminated prior to viability after a prenatal diagnosis of MMC. We therefore cannot generalize the findings to pregnancies less than 25 weeks gestation.

G. Random Error:

The results obtained in this study could be related to random error, in which chance alone could account for deviations from the true values. This study concludes from its observations that the combined infectious morbidity rate by 6 months of age is statistically significantly lower for infants in the prelabour CS group (17.4%) when compared to those in the TOL group (34.0%) [odds ratio (95% CI): 0.41 (0.18-0.94). The risk of concluding that prelabour CS is more beneficial (or less beneficial) compared to TOL when in actual fact there is no benefit (Type I error) in this study, is likely more

than 5% (at p=0.05) because of the multiple statistical comparisons made in the data.

No statistically significant difference was found in the combined infectious morbidity rate by age 6 months between the infants in the CS after TOL group (34.2%) versus those in the VB group (33.9%) group [odds ratio (95% CI): 1.01 (0.47-2.2)]. It is possible that this study result is due to the type II error of not being able to detect a difference when, in fact, one does exist. Using the methods provided by Fleiss (1981), the power of this study to detect a 50% reduction in the infection rate from 34% in the VB group to 17% in the CS after TOL group, with a 2.5:1 ratio in sample size between groups (113 infants in the VB group versus 45 infants in the CS after TOL group) would be 48.5% (2-tailed test, 5% significance). If the sample size was a 1:1 ratio between groups (45 infants in the VB group versus 45 infants in the CS after TOL group), the power of this study to detect the same 50% reduction would be even lower at 36%. Thus, this study had insufficient power to detect a 50% reduction in the infection rate between groups.

6.4 Need For A Randomized Controlled Trial

It is appropriate to study MMC using a retrospective cohort study design because MMC is relatively rare, easily recognized at birth and usually requires treatment in a major paediatric neurosurgical centre. Although a randomized controlled trial would be ideal to examine the effectiveness of prelabour CS on outcome in these infants, it would be very difficult to undertake. Because of its very low incidence, recruitment would need to be carried out on an international level and over several years. There is already evidence that the incidence of MMC is decreasing world-wide likely because of prenatal

diagnosis and termination, improved nutrition and other unknown factors. Other methods of dealing with the low incidence of MMC is to perform a multi-centred retrospective cohort study or to create or make use of existing fetal surveillance systems with databases which record antenatal and perinatal information about fetuses born with rare congenital abnormalities. Although there may be a cost for the start-up and regular maintenance of such databases, it may be relatively inexpensive to add on variables to an already existing database for important outcomes such as death, meningitis, sepsis, wound infections and severe paralysis for infants with MMC.

6.5 Future Research

Because of the potential for confounding factors to affect outcomes in a sometimes unpredictable way, it is crucial that further statistical analyses be performed to take these factors into consideration and examine their impact on the differences in outcomes between the study groups. In the comparison between the prelabour CS group versus the TOL groups, infectious morbidity was found to be significantly lower for the infants in the prelabour CS group. Confounding factors which I feel should be included in a multiple logistic regression include gestational age < 37 weeks, level of nursery, presence of neonatologist/neonatal nurse, prenatal diagnosis, breech presentation, presence of hydrocephalus, shunt insertion and whether or not supportive care only was given. Many of these factors were shown to be unbalanced between the two groups. Premature infants are more likely to develop infection because of their immature immune systems. There is a belief by clinicians that higher level care and presence of trained personnel may improve prognosis and reduce infectious morbidity; breech presentation may increase mortality; and investigators have provided evidence that hydrocephalus

requiring shunt insertion may increase the rate of infection, particularly meningitis and ventriculitis.

For the comparison between the CS after TOL and VB groups, mortality was found to be significantly higher for infants in the CS after TOL group. Factors which could account for this increased mortality in the CS after TOL group are the significantly increased incidence of hydrocephalus, increased breech presentation, and increased severity of the lesions. In addition to these factors, one must also examine the effect of other factors which could affect mortality even though they may be balanced between the two groups. These other factors include the presence of prematurity and treatment by supportive care only, which would both tend to increase the rate of mortality.

The final phase of the MMC study will be completed with collection of the rehabilitation data at 2 years of age and comparisons will be made in the severity of paralysis between the study groups.

7. CONCLUSIONS

The evidence from this study suggests that delivery by prelabour CS may reduce the risk of infectious morbidity in the first 6 months of life in infants with MMC when compared with infants delivered after a TOL. Once labour is initiated, however, there appears to be no difference in infectious morbidity between infants delivered by CS compared with those delivered vaginally. It is biologically plausible that infection of exposed nerve roots by bacterial organisms in the maternal genital tract which occurs during labour (irrespective of mode of delivery) may lead to permanent damage of these nerve roots, resulting in reduced motor function and a potentially increased risk of wheelchair dependency in later life. More sophisticated statistical analyses are required to take into account the effect of confounding factors and to eventually study the correlation between infectious morbidity in the first 6 months of life as defined in this study and severe paralysis at 6 months of age. Although, a randomized controlled design would be the ideal method to investigate the questions asked in this study, its feasibility remains questionable.

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APPENDIX 1

1. OBS DATA FORM
2. NEURO DATA FORM

MENINGOMYELOCELE STUDY-OBS DATA FORM

1. BABY CODE NO: _ _ _

2. BIRTH HOSPITAL:_____

MATERNAL INFORMATION:

3. Mother's Name:_____
LAST FIRST MIDDLE

4. Mother's Chart No: _ _ _ _ _ _ _ _ _ _ _ _ _

5. Mother's Physician:

NAME _____
LAST FIRST MIDDLE

ADDRESS_____

_____
TOWN/CITY PROVINCE POSTAL CODE

Telephone number (_ _ _) - _ _ _ - _ _ _ _

BABY INFORMATION:

6. Baby's Name_____
FIRST MIDDLE LAST

7. Baby's Obs Chart No: _ _ _ _ _ _ _ _ _ _ _ _

8. Physician caring for baby at birth hospital:

NAME:_____
LAST FIRST MIDDLE

ADDRESS:_____

_____
TOWN/CITY PROVINCE POSTAL CODE

TELEPHONE NO: (_ _ _) - _ _ _ - _ _ _ _

9. NAME OF HOSPITAL BABY TRANSFERRED TO IF APPLICABLE:

_____

10. Baby Chart No. Neuro Hosp:_ _ _ _ _ _ _ _ _ _ _ _

11. Name of physician accepting referral at neurosurgical centre:

_____

LAST FIRST MIDDLE

12. OTHER COMMENTS:

_____

_____

_____

HOSPITAL OF BIRTH FORM

1. BABY CODE NUMBER: _ _ _

2. Highest Level of newborn care at the birth hospital:

   [1] Level I Nursery
   [2] Level II Nursery
   [3] Level III Nursery

3. Maternal Date of Birth: _ _ / _ _ / _ _
   DD MM YY

4. Estimated Date of Confinement: _ _ / _ _ / _ _
   DD MM YY

5. Mode of Delivery:

   [1] Vaginal
   [2] Cesarean Section after Trial of Labour
   [3] Cesarean Section with No Labour

6. If a Cesarean Section was done, what were the primary indications (indicate "yes", "no" or "inapplicable" for each option)?

		Yes	No	Inapplicable
a.	Fetal Distress	[1]	[0]	[7]
b.	Fetopelvic Disproportion	[1]	[0]	[7]
c.	Breech Presentation	[1]	[0]	[7]
d.	Malpresentation (other than breech)	[1]	[0]	[7]
e.	Presence of Meningomyelocele	[1]	[0]	[7]
f.	Previous Cesarean Section	[1]	[0]	[7]
g.	Other	[1]	[0]	[7]

7. Was a neonatologist or neonatal nurse present at the delivery?

   [1] Yes
   [0] No

HOSPITAL OF BIRTH FORM

8. What was the fetal presentation at delivery?
   [1] cephalic
   [2] breech
   [3] other
   [8] information not available from chart

9. Was this a multiple pregnancy?
   [1] Yes
   [0] No

10. Was the diagnosis of meningomyelocele or spina bifida made by ultrasound scan prior to labour and delivery?
    [0] No
    [1] Yes

11. If answer to 10 was "yes", give the date of the first ultrasound making the diagnosis:

    _ _ / _ _ / _ _
    DD MM YY

12. Was antenatal or postnatal fetal chromosome analysis charted?
    [0] No
    [1] Yes

13. If the answer to 12 was "yes", indicate what the results were:

    [1] Normal Chromosomes
    [2] Abnormal Chromosomes
    [3] Results not interpretable or unavailable
    [7] Inapplicable

14. Baby's Date of Birth: _ _ / _ _ / _ _
    DD MM YY

15. Sex of Baby:

    [1] Male
    [2] Female
    [3] Unknown

16. Condition at birth:

    [1] Liveborn
    [2] Stillborn

HOSPITAL OF BIRTH FORM

17. Gestational age at birth in completed weeks: _ _

18. Birth weight in grams: _ _ _ _

19. Apgar Scores:

    a. 1 minute: _ _ b. 5 minute _ _

20. Did the chart state that hydrocephalus was present?

    [0] No
    [1] Yes

21. First head circumference after birth:

    _ _ . _ cms

22. Were there birth defects other than meningomyelocele and hydrocephalus? (If yes, please specify in the empty space).

    [0] No
    [1] Yes

23. Did assisted ventilation occur beyond 48 hours of birth?

    [0] No
    [1] Yes
    [2] Cannot be determined

24. Did seizures occur in the birth hospital?

    [0] No
    [1] Yes

25. Infant outcome:

    [1] Death at the birth hospital (Include Autopsy)
    [2] Transfer to another hospital/centre
    [3] Discharge home from birth hospital

26. Date of Baby's Death/Transfer/Discharge Home:

    _ _ / _ _ / _ _
    DD MM YY

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

Linking Data:

1. BABY CODE NO: __ __ __

2. Baby's Name: _____
   Last First Middle

3. Baby's Date of Birth: __ __ / __ __ / __ __
   DD MM YY

4. Baby's Sex:

   [1] Male
   [2] Female
   [8] Unknown

5. Birth Hospital: _____

6. Neurosurgical Hospital: _____

7. Neuro Hospital No: __ __ __ __ __ __ __ __ __ __

8. Date Admitted to Neurosurgical Hospital:

   __ __ / __ __ / __ __
   DD MM YY

9. Mother's Name: _____
   Last First

10. Mother's Address: _____

    _____

    _____

11. Possible Contact Physician: _____

    Physician's Address: _____

    _____

    Phone Number: ( ) __ __ __-__ __ __ __

12. Neurosurgeon: _____

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

ITEMS FOR DATA ENTRY

BABY CODE NO. ___ ___ ___

Baby's Date of Birth: ___ ___ / ___ ___ / ___ ___
DD MM YY

1. Neurosurgical Hospital:
   - [01] Hospital for Sick Children
   - [02] Children's Hospital of Eastern Ontario
   - [03] McMaster University Medical Centre
   - [04] Children's Hospital of Western Ontario
   - [05] Kingston General Hospital
   - [06] Victoria Hospital in London
   - [07] Montreal Children's Hospital
   - [08] Winnipeg - St. Boniface or Health Science Centre
   - [09] Other----> Specify:_____
   - [10] Not Treated in Neurosurgical Centre
   - [88] Unknown

2. Describe the Neurosurgical Diagnosis as Stated in the Neurosurgical Chart (for stillbirths or infants dying prior to obtaining neurosurgical care, use OBSFORM data):

   (More than one may apply)

	Yes	No
a. Meningomyelocele or Myelomeningocele	[1]	[0]
b. Lipomyelomeningocele	[1]	[0]
c. Dermal Sinus	[1]	[0]
d. Other (describe:_____	[1]	[0]

   _____)

3. Was this baby found to have other anomalies incompatible with life?

   - [0] No
   - [1] Yes-----> Specify:_____
   - [8] Don't Know

PLEASE FOLLOW THESE INSTRUCTIONS:

I. **IF 2a=0 AND/OR 2b, 2c, or 2d=1:**

EXCLUDE THIS CASE FROM THE STUDY.

II. **IF 3=[1] "Yes": EXCLUDE THIS CASE FROM THE STUDY.**

III. **OTHERWISE COMPLETE THE REST OF THIS FORM.**

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO. ___ ___ ___

4. Is the MMC anatomic level available from the Operative Note?
   [0] No (no OR note/OR note does not state level)
   [1] Yes

5. MMC anatomic level as described in the operative note if available or other notes if Qu.#4= No:
   [01] Cervical (rare)
   [02] Cervico-thoracic (often are normal)
   [03] Thoracic
   [04] Thoraco-lumbar (most frequent; #1 for severity)
   [05] Lumbar (second in frequency; #2 for severity)
   [06] Lumbo-sacral
   [07] Sacral (excellent prognosis)
   [08] Cervico-thoraco-lumbar (they die)
   [09] Thoraco-lumbar-sacral (#1 for severity)
   [88] Unknown

6. Upper X-RAY Level: The most caudal posterior vertebral arch that appears intact on x-ray films at the upper end of the lesion. ___ ___
   C1=01, C2=02, C3=03, C4=04, C5=05, C6=06, C7=7
   T1=08, T2=09, T3=10, T4=11, T5=12, T6=13
   T7=14, T8=15, T9=16, T10=17, T11=18, T12=19
   L1=20, L2=21, L3=22, L4=23, L5=24
   S1=25, S2=26, S3=27, S4=28, S5=29, coccygeal = 30
   unknown = 88

7. Size of base of lesion (**neural placode; not skin lesion):
   [1] < 1.0 cm
   [2] 1.0 - 2.5 cms
   [3] > 2.5 cms
   [8] Don't know

8. Was the sac intact at the time of surgery?
   [0] No
   [1] Yes
   [8] Don't know

9. Where is the anatomic level of the lesion wrt L2?
   [1] At or Above L2
   [2] Below L2
   [8] Don't Know

10. Head circumference measured on admission: ___ ___ . ___ (cm)

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO. ___ ___ ___

11. Was hydrocephalus present?
[0] No
[1] Yes
[8] Don't Know

12. Primary surgical procedure done on first admission:

[1] Closure of Meningomyelocele (MMC) Only

[2] Closure of MMC & Insertion of CSF Shunt ->

Circle One:
{1}. Simultaneous

{2}. Staged

{8}. Don't Know

[3] Insertion of CSF Shunt Only------>Supportive care

[4] No Surgery---------->Supportive care

[8] Don't Know

13. Date MMC closed: (if answer to #12 =[1] or [2]):

__ __ / __ __ / __ __
DD MM YY

14. Did this baby require ventilatory respiratory support for more that 48 hours at any time during its stay at the neurosurgical centre?
[0] No
[1] Yes
[8] Don't Know

15. Did this baby have any other congenital anomalies?
[0] No
[1] Yes; Specify:_____

_____

[8] Don't know

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO: ___ ___ ___

16. Was a chromosome analysis done?
    [0] No
    [1] Yes
    [8] Don't Know

17. If chromosomes were done, what were the results:
    [1] Normal chromosomes
    [2] Abnormal chromosomes:_____
    [3] Results not available or not interpretable
    [7] Inapplicable

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM
BABY CODE NO: ___ ___ ___

Enter the admission and discharge dates for each neurosurgical hospital admission for the first 6 months of life:

Admission #	**Admission Date**	**Discharge Date**	**Diagnosis**
18. Initial	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
19. Second	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
20. Third	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
21. Fourth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
22. Fifth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
23. Sixth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
24. Seventh	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
25. Eighth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
26. Ninth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____
27. Tenth	__ __/__ __/__ __ (DD MM YY)	__ __/__ __/__ __ (DD MM YY)	_____

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO: ___ ___ ___

28. Did the baby die prior to 2 years of age (If yes, remember to include autopsy record)?

[0] No

[1] Yes

[8] Unknown

29. If baby died prior to 2 years of age, date of death:

___ ___/___ ___/___ ___ ___ ___
DD MM YYYY

(Enter 01/01/8888 if unknown)
(Enter 01/01/7777 if inapplicable)

30. If baby died prior to 2 years of age, classify the category of death:

[1] Neonatal Death (< 28 days of life)

[2] Early Infant Death (28 days - 6 months)

[3] Late Infant Death (>6 months - <2 years)

[7] Inapplicable

[8] Unknown

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO: ___ ___ ___

Did this baby have any of the following complications (ie. outcomes) in the first 6 months of life?		**No**	**Yes**	**Don't know**
31.	Definite Meningitis	[0]	[1]	[8]
32.	Definite Wound Infection/ Wound Breakdown	[0]	[1]	[8]
33.	Definite Urinary Tract Inf.	[0]	[1]	[8]
34.	Definite Sepsis	[0]	[1]	[8]
35.	Seizures	[0]	[1]	[8]
36.	Diagnosis of Chiari Malformation Symptoms	[0]	[1]	[8]
37.	Definite Shunt Malfunction/ Shunt Infection	[0]	[1]	[8]
38.	Other:(_____)	[0]	[1]	[8]
39.	Other:(_____)	[0]	[1]	[8]

DEFINITE MENINGITIS (requires both):
(1) Clinical signs and symptoms of meningitis
(2) Positive CSF culture from ventricular, lumbar or shunt tap

DEFINITE WOUND INFECTION/BREAKDOWN (wound needing one of the following):
(1) removal of sutures to open it up for drainage
(2) removal of pustular debris with soaks/compresses
(3) administration of antibiotics for treatment of a wound infection
(4) surgical revision of the wound

DEFINITE SEPSIS: Clinical signs and symptoms of sepsis with positive blood culture or urine culture (suprapubic aspirate), or positive Ag detection test of blood or urine.

DEFINITE UTI: Positive Urine Cultures from a suprapubic aspirate with symptoms and signs of a UTI.

SEIZURES: Documentation of witnessed signs of a seizure

CHIARI MALFORMATION SYNDROME: Dx documented in chart based on poor feeding, gagging, weak cry, periods of apnoea, with or without decompression surgery for this diagnosis

SHUNT MALFUNCTION/INFECTION: Signs/symptoms/tests suggesting:
(1) Hydrocephalus and/or
(2) Shunt infection (ie. positive tube culture CSF culture -ve)
NB:If CSF is positive, outcome also includes meningitis with shunt infection

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM
BABY CODE NO: ___ ___ ___

How many times was this baby <u>readmitted</u> to the hospital in the first 6 months of age for any of the reasons listed below?

		None	Once	Twice	>Twice	Don't Know
40.	Meningitis	[0]	[1]	[2]	[3]	[8]
41.	Wound Infection or Breakdown	[0]	[1]	[2]	[3]	[8]
42.	Urinary Tract Infection	[0]	[1]	[2]	[3]	[8]
43.	Sepsis	[0]	[1]	[2]	[3]	[8]
44.	Seizures	[0]	[1]	[2]	[3]	[8]
45.	Diagnosis of Chiari Malformation Symptoms	[0]	[1]	[2]	[3]	[8]
46.	Shunt Mal-Function/ Infection (definite)	[0]	[1]	[2]	[3]	[8]
47.	Suspected Shunt Mal-function - Not Confirmed	[0]	[1]	[2]	[3]	[8]
48.	Other Describe: _____	[0]	[1]	[2]	[3]	[8]
49.	Other Describe: _____	[0]	[1]	[2]	[3]	[8]

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO: ___ ___ ___

50. What was the total number of readmissions to the neurosurgery hospital for this baby in the first 6 months of life?

___ ___

51. In the first 6 months of life, on what date was this infant last seen at the neurosurgical hospital?

___ ___ / ___ ___ / ___ ___
DD MM YY

52. On what date was this infant last seen at the neurosurgical hospital overall?

___ ___ / ___ ___ / ___ ___
DD MM YY

FOR BABIES IDENTIFIED WITH SHUNT MALFUNCTION, ANSWER #53 and 54:

53. Check the most appropriate response:

[1] The shunt malfunctioned in the presence of infection on at least one occasion (ie. bacteriology report of cerebrospinal fluid and/or tubing cultures indicate infection)

[2] The shunt malfunctioned with no infection on any occasion (ie. bacteriology report of cerebrospinal fluid and/or tubing cultures were negative)

[3] The shunt malfunctioned but infection status is unknown (ie. no bacteriology report of the cerebrospinal fluid and/or tubing cultures is available on the chart)

[7] Inapplicable

54. Indicate the most invasive management of the shunt malfunction (ie. [1] most invasive; [3] least invasive):

[1] Surgical shunt revision with antibiotics.
[2] Surgical shunt revision without antibiotics.
[3] Antibiotics without surgical shunt revision.
[7] Inapplicable
[8] Don't Know

MENINGOMYELOCELE STUDY - NEUROSURGICAL DATA FORM

BABY CODE NO: ___ ___ ___

55. For those babies identified as having had a wound infection/breakdown at the meningomyelocele closure site in the first 6 months of age, was a surgical revision of the wound ever done?

[0] No
[1] Yes
[7] Inapplicable
[8] Don't know

56. For those babies with a diagnosis of Chiari Malformation symptoms in the first 6 months of age, was surgery done for decompression of the Chiari malformation? (Chiari Malfn: poor feeding, gagging, weak cry, periods of apnoea)

[0] No
[1] Yes
[7] Inapplicable
[8] Don't know

57. What was the infant's outcome after the first admission to the neurosurgical centre?

[1] Death during the first admission.**(Please include Path)**
[2] Discharged back to birth hospital.
[3] Discharged to home.
[4] Discharged to a social agency (ie. CAS)
[5] Other -----> Specify:_____
[8] Don't Know

58. Did the chart indicate if this baby would be followed up at a rehabilitation unit or program?

[0] No
[1] Yes; if yes; which one(s)?_____
_____
_____
[7] Inapplicable
[8] Don't know

59. During review of this chart, was the mode of delivery encountered in the notes?

[0] No
[1] Yes

APPENDIX 2

1. SCHEMA FOR OBS FORM
2. SCHEMA FOR NEURO DATA FORM

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Value
BABYCODE UNIQUE CASE IDENTIFIER NUMBER This number uniquely identifies the infant in the study	Integer Number	3		Not Allowed
LEVELNUR HIGHEST LEVEL OF NEWBORN CARE GIVEN IN THE NURSERY This number indicates what is the highest level of newborn care available in the birth hospital	Coded Integer	1	1=Level 1 2=Level 2 3=Level 3	8 9
MATDOB MATERNAL DATE OF BIRTH This variable will be entered with the format DD/MM/YY	Date	8	01/01/30 - 01/01/78	01/01/99
EDC EXPECTED DATE OF CONFINEMENT This variable indicates the expected due date. It is entered in the format DD/MM/YY.	Date	8	01/11/70 - 01/06/90	01/01/99

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
MODEDEL MODE OF DELIVERY: Method by which the infant was delivered	Coded Integer	1	1=Vaginal 2=Cesarean Section after Trial of Labour 3=Cesarean Section with No Labour	8 9
FETDIS FETAL DISTRESS This number indicates whether or not a Cesarean Section was done for fetal distress.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9
CPD CEPHALOPELVIC DISPROPORTION This number indicates whether or not a Cesarean Section was done for relatively large baby for mother's pelvis.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9
BREECH BREECH PRESENTATION This number indicates whether or not a Cesarean Section was done because the infant was presenting with its buttocks first.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
MALPRES MALPRESENTATION (OTHER THAN BREECH) This number indicates whether or not a Cesarean Section was done because the infant was presenting in an unusual fashion (excluding breech) such as a shoulder or face presentation.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9
MMC PRESENCE OF MENINGOMYELOCELE This number indicates whether or not a Cesarean Section was done because of the presence of a meningomyelocele.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9
MATIND PREVIOUS CESAREAN SECTION This number indicates whether or not a Cesarean Section was done because mother had a previous one.	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9
OTHER OTHER INDICATIONS This number indicates whether or not a Cesarean Section was done for other reasons	Coded Integer	1	0=No 1=Yes 7=Inapplic-able	8 9

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Value
NEOPRES NEONATAL NURSE OR NEONATOLOGIST PRESENT This number indicates whether or not a neonatal nurse or neonatologist was present at the delivery	Coded Integer	1	0=No 1=Yes	8 9
FETPRES FETAL PRESENTATION This number indicates what part of the fetus delivered first	Coded Integer	1	1=Cephalic 2=Breech 3=Other	8 9
MULTPREG MULTIPLE PREGNANCY This number indicates whether this was a multiple pregnancy	Coded Integer	1	0=No 1=Yes	8 9
ANTEDX ANTENATAL DIAGNOSIS This number indicates whether or not a diagnosis of meningo-myelocele or spina bifida was made by ultrasound prior to labour and delivery.	Coded Integer	1	0=No 1=Yes	8 9
USSDATE ULTRASOUND DATE If antenatal diagnosis of MMC made, this variable indicates the date of the first ultrasound making the diagnosis. Format DD/MM/YY	Date	8	01/01/79 - 31/12/89	01/01/77 01/01/99

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
CHROMANA CHROMOSOME ANALYSIS This number indicates whether or not an antenatal or postnatal fetal chromosome analysis was available on the chart.	Coded Integer	1	0=No 1=Yes	9
RESLTCHR RESULTS OF CHROMOSOME ANALYSIS If results were available, this number indicates the results.	Coded Integer	1	1=Normal Chromosomes 2=Abnormal Chromosomes 3=Results not interpretable or unavailable 7=Inapplic-able	9
BABYDOB BABY'S DATE OF BIRTH This variable will be entered in the format DD/MM/YY	Date	8	01/01/80 - 31/12/89	01/01/99
BABYSEX BABY'S SEX	Coded Integer	1	1=Male 2=Female 3=Unknown	9
CONDBRTH CONDITION AT BIRTH This number indicates what the baby's condition was at birth	Coded Integer	1	1=Liveborn 2=Stillborn	9

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
GABIRTH GESTATION AGE AT BIRTH This number indicates the gestational age of the infant at birth in completed weeks	Integer Number	2	25-54	99
BIRTHWT BIRTH WEIGHT OF INFANT This number indicates the birth weight of the infant in grams	Integer Number	4	500-6000	8888 9999
APGAR1 ONE MINUTE APGAR SCORE	Integer Number	2	0-10	77 88 99
APGAR5 FIVE MINUTE APGAR SCORE	Integer Number	2	0-10	77 88 99
HYDRO HYDROCEPHALUS This number indicates whether or not the chart indicated that the infant had hydrocephalus	Coded Integer	1	0=No 1=Yes	8 9
HEADCIRC HEAD CIRCUMFERENCE This number indicates the first head circumference measured in centimeters after birth	Decimal Number XX.X	4	10.0-54.0	88.8 99.9

SCHEMA FOR OBS FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
DEFECTS OTHER CONGENITAL DEFECTS This number indicates whether or not the infant had any other congenital anomalies other than meningomyelocele and hydrocephalus	Coded Integer	1	0=No 1=Yes	8 9
VENT ASSISTED VENTILATION This number indicates whether or not the infant had assisted ventilation beyond 48 hours of birth	Coded Integer	1	0=No 1=Yes 2=Cannot be determined	8 9
SEIZURE This number indicates whether or not the infant had seizures at the birth hospital	Coded Integer	1	0=No 1=Yes	8 9
OBOUTCOM INFANT OUTCOME AT THE OBSTETRICAL HOSPITAL This number indicates what happened to the infant at the birth hospital.	Coded Integer	1	1=Death at the birth hospital 2=Transfer to another hospital/centre 3=Discharge home from birth hospital	8 9
DATEOB DATE OF BABY'S DEATH/TRANSFER/HOME Format: DD/MM/YY	Date	8	01/01/80 - 01/01/91	01/01/99

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
BABYCODE Unique Case Identifier Number	Integer Number	3		Not allowed
BABYDOB BABY'S DATE OF BIRTH This date will be entered in the format DD/MM/YYYY	Date	10	01/01/1980 - 31/12/1989	01/01/8888 01/01/9999
NEUROHOS NEUROSURGICAL HOSPITAL Neurosurgical centre to where baby was transferred for further care	Coded Integer	2	01=HSC 02=CHEO 03=MUMC 04=CHWO 05=Kingston 06=Victoria, London 07=Montreal Children's 08=Winnipeg 09=Other 10=Not treated in Neurosurgical Centre	88 99
MYELO MYELOMENINGOCELE Indicates whether or not the infant had this condition	Coded Integer	1	0=No 1=Yes	9
LIPOMYEL Lipomyelomeningocele Indicates whether or not the infant had this condition	Coded Integer	1	0=No 1=Yes	9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
DERMALSIN DERMAL SINUS Indicates whether or not the infant had this condition	Coded Integer	1	0=No 1=Yes	9
OTHERNEU OTHER NEUROSURGICAL CONDITIONS Indicates whether or not the infant had any other neurosurgical conditions	Coded Integer	1	0=No 1=Yes	9
INCLIFE INCOMPATIBLE WITH LIFE Indicates whether or not the infant had other congenital anomalies which were incompatible with life	Coded Integer	1	0=No 1=Yes	8 9
ORLEVEL OPERATIVE REPORT Indicates whether or not the anatomic level of the lesion is reported in the operative note	Coded Integer	1	0=No 1=Yes	9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
ANATLEV ANATOMICAL LEVEL Describes the anatomical level of the MMC lesion	Coded Integer	2	01=Cervical 02=Cervicothoracic 03=Thoracic 04=Thoracolumbar 05=Lumbar 06=Lumbosacral 07=Sacral 08=Cervicothoraco lumbar 09=Thoracolumbar sacral	88 99
XRAYLEV X-RAY LEVEL Describes the most caudal posterior vertebral arch that appears intact on radiological films at the upper end of the MMC lesion	Numeric Integer	2	01-30	88 99
SIZELES SIZE OF LESION Describes the size of the base of the MMC lesion also known as the neural placode	Coded Integer	1	1= < 1.0 cm 2= 1.0 - 2.5 cms 3= > 2.5 cms	8 9
SACINT SAC INTACT Indicates whether or not the sac of the MMC was intact or ruptured prior to treatment	Coded Integer	1	0=No 1=Yes	8 9
L2LEVEL LUMBAR 2 LEVEL Indicates where the anatomic level of the MMC was wrt lumbar vertebra no. 2	Coded Integer	1	1=At or above L2 2=Below L2	8 9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
CIRCHEAD HEAD CIRCUMFERENCE Measurement of the infant's head circumference on admission in cms	Numeric Decimal XX.X	4	20.0 - 58.0	88.8 99.9
HYDROCEP HYDROCEPHALUS Indicates whether or not clinical hydrocephalus was present	Coded Integer	1	0=No 1=Yes	8 9
SURGPROC SURGICAL PROCEDURE Indicates whether or not surgery was performed and if so, the type of surgical procedure done for treatment or supportive care.	Coded Integer	1	1=Closure of lesion 2=Closure of lesion and shunt insertion 3=Shunt only 4=No surgery	8 9
TYPESURG TYPE OF SURGERY In cases where treatment involved closure of the MMC and shunt insertion, indicates whether or not the procedures were done simultaneously or in stages.	Coded Integer	1	1=Simultaneous 2=Staged 7=Inapplicable	8 9
DATESURG DATE OF SURGERY Indicates the date of closure of the MMC lesion if this was performed. Date is indicated as DD/MM/YYYY.	Date	10	01/01/1980 - 01/01/1991	01/01/7777 01/01/8888 01/01/9999

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
VENTSUPP VENTILATORY SUPPORT Indicates whether or not the infant required ventilatory support for more than 48 hours at any time during its stay at the neurosurgical centre	Coded Integer	1	0=No 1-Yes	8 9
ANOMALY Indicates whether or not the infant had any other congenital anomalies	Coded Integer	1	0=No 1=Yes	8 9
CHRMSOME CHROMOSOME Indicates whether or not a chromosome analysis was done	Coded Integer	1	0=No 1=Yes	8 9
CHRMSES CHROMOSOME RESULTS Indicates the results of the chromosome analysis if it was done	Coded Integer	1	1=Normal 2=Abnormal 3=Results not available or not interpretable 7=Inapplicable	8 9
ADM1 ADMISSION 1 Indicates the date of the first admission to the neurosurgical centre. This date will be entered in the format DD/MM/YYYY.	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
DISCH1 DISCHARGE 1 Indicates the date of discharge after admission 1. This date will be entered in the format DD/MM/YYYY.	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM2 ADMISSION 2 Indicates the date of the second admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH2 DISCHARGE 2 Indicates the date of discharge after the second admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM3 ADMISSION 3 Indicates the date of the third admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH3 DISCHARGE 3 Indicates the date discharge after admission 3. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
ADM4 ADMISSION 4 Indicates the date of the fourth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH4 DISCHARGE 4 Indicates the date of discharge after admission 4. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM5 ADMISSION 5 Indicates the date of the fifth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH5 DISCHARGE 5 Indicates the date of discharge after admission 5. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM6 ADMISSION 6 Indicates the date of the sixth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH6 DISCHARGE 6 Indicates the date of discharge after admission 6. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
ADM7 ADMISSION 7 Indicates the date of the seventh admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH7 DISCHARGE 7 Indicates the date of discharge after admission 7. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM8 ADMISSION 8 Indicates the date of the eighth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH8 DISCHARGE 8 Indicates the date of discharge after admission 8. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
ADM9 ADMISSION 9 Indicates the date of the ninth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH9 DISCHARGE 9 Indicates the date of discharge after admission 9. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
ADM10 ADMISSION 10 Indicates the date of the tenth admission. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DISCH10 DISCHARGE 10 Indicates the date of discharge after admission 10. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	01/01/8888 01/01/9999
DEATH2YR DEATH AT 2 YEARS Indicates whether or not the baby died prior to 2 years of age.	Coded Integer	1	0=No 1=Yes	8 9
DATEDEAD DATE OF DEATH Indicates the date of death if the baby died prior to two years of age. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/2000	01/01/7777 01/01/8888 01/01/9999
CATEDEAD CATEGORY OF DEATH Indicates the category of death: neonatal death, early infant death, late infant death.	Coded Integer	1	1=Neonatal Death 2=Early Infant Death 3=Late Infant Death 7=Inapplicable	8 9
MENING MENINGITIS Indicates whether or not the infant had meningitis in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
WOUND WOUND INFECTION OR BREAKDOWN Indicates whether or not the infant had a wound infection or breakdown in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
UTI URINARY TRACT INFECTION Indicates whether or not the infant developed a UTI in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
SEPSIS Indicates whether or not the infant developed sepsis in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
SHAKES Indicates whether or not the infant had seizures in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
CHIARI CHIARI MALFORMATION Indicates whether or not the infant developed the symptoms of the chiari malformation	Coded Integer	1	0=No 1=Yes	8 9
SHUNTMAL SHUNT MALFUNCTION Indicates whether or not the infant had a shunt malfunction or infection in the first 6 months of life.	Coded Integer	1	0=No 1=Yes	8 9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
COMPLIC1 COMPLICATION 1 Indicates whether or not the infant had any other complications in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
COMPLIC2 COMPLICATION 2 Indicates whether or not the infant had any other complications in the first 6 months of life	Coded Integer	1	0=No 1=Yes	8 9
REMENING READMISSION FOR MENINGITIS: The number of readmissions for meningitis in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
REWOUND READMISSION FOR WOUND PROBLEMS: The number of readmissions for wound infection or breakdown in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
REUTI READMISSION FOR URINARY TRACT INFECTIONS: The number of readmissions for urinary tract infection in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
RESEPSIS READMISSIONS FOR SEPSIS: The number of readmissions for sepsis in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
RESHAKES READMISSIONS FOR SEIZURES: The number of readmissions for seizures in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
RECHIARI READMISSIONS FOR CHIARI MALFORMATION The number of readmissions for chiari malformation symptoms in the first 6 months of life.	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
RESHUNT READMISSIONS FOR SHUNT PROBLEMS: The number of readmissions for shunt infection or malfunction in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
REUNSHUNT READMISSIONS FOR SUSPECTED SHUNT PROBLEMS: The number of readmissions for suspected but unconfirmed shunt malfunction or infection in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9

SCHEMA FOR NEURO FORM

Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
REOTHER1 READMISSION FOR OTHER COMPLICATIONS 1: The number of readmissions for other complications in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
REOTHER2 READMISSION FOR OTHER COMPLICATIONS 2: The number of readmissions for other complications in the first 6 months of life	Coded Integer	1	0=None 1=Once 2=Twice 3= >Twice	8 9
TOTREAD TOTAL READMISSIONS The total number of readmissions in the first 6 months of life	Numeric Integer	2	00-10	88 99
DATLAST6 DATE LAST SEEN IN FIRST 6 MONTHS: Indicates the date on which the baby was last seen in the neurosurgical centre within the first 6 months of life. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/1991	88/88/8888 99/99/9999
DATEVER DATE LAST SEEN OVERALL: Indicates the date on which infant was last seen in the neurosurgical centre overall. Entry format is DD/MM/YYYY	Date	10	01/01/1980 - 01/01/2000	01/01/8888 01/01/9999

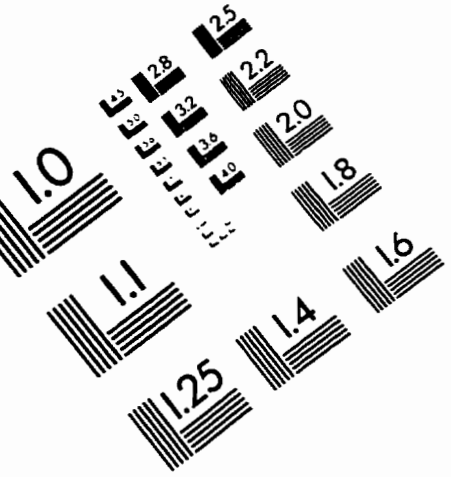
SCHEMA FOR NEURO FORM

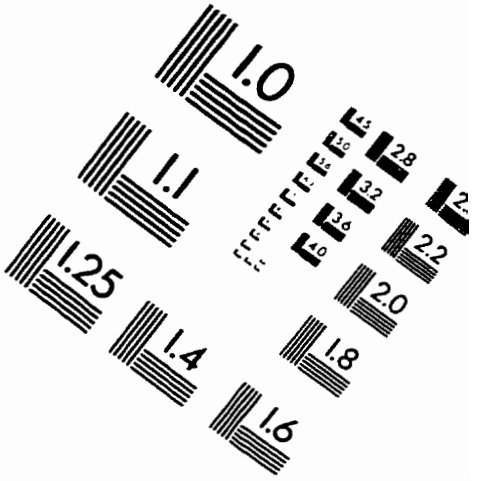
Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
SHUNTINF SHUNT INFECTION Indicates whether or not there was a shunt infection when the shunt malfunctioned in the first 6 months of life	Coded Integer	1	1=Shunt malfunction in presence of infection on at least one occasion 2=Shunt malfunction with no infection on any occasion 3=Shunt malfunction but infection status unknown 7=Inapplicable	8 9
SHUNTMAN MANAGEMENT OF SHUNT MALFUNCTION Indicates how the shunt malfunction was managed or treated in the first 6 months	Coded Integer	1	1=Surgical shunt revision with antibiotics 2=Surgical shunt revision without antibiotics 3=Antibiotics without surgical shunt revision 7=Inapplicable	8 9
WOUNDREV SURGICAL WOUND REVISION: Indicates whether or not a would infection or breakdown required surgical revision in the first 6 months of life	Coded Integer	1	0=No 1=Yes 7=Inapplicable	8 9

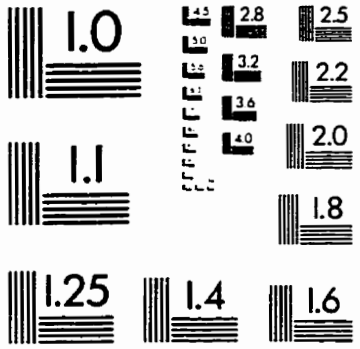
SCHEMA FOR NEURO FORM

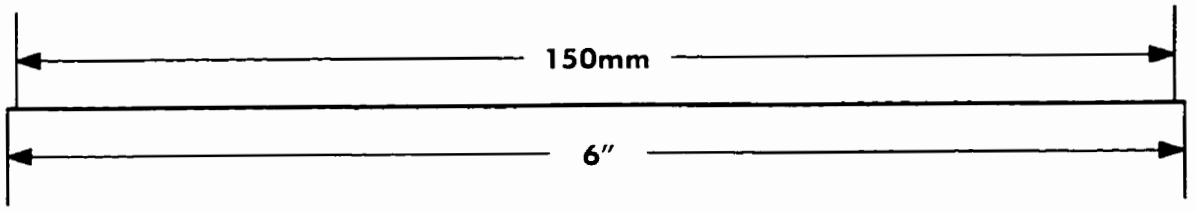
Variable Name and Description	Variable Type	Length	Variable Range Code and Label	Missing Values
CHIARSUR CHIARI SURGERY Indicates whether or not infant required cervical laminectomy for Chiari malformation symptoms in the first 6 months of life	Coded Integer	1	0=No 1=Yes 7=Inapplicable	8 9
NEUROUT NEUROSURGICAL OUTCOME Indicates what happened to the infant after treatment at the neurosurgical centre	Coded Integer	1	1=Death during first admission 2=Discharged back to birth hospital 3=Discharged to home 4=Discharged to social agency 5=Other	8 9
REHAB REHABILITATION CENTRE Indicates whether or not the infant was referred to a rehabilitation unit	Coded Integer	1	0=No 1=Yes 7=Inapplicable	8 9
TYPEDEL TYPE OF DELIVERY Indicates whether or not the mode of delivery was encountered in the neurosurgical chart as the chart was being abstracted	Coded Integer	1	0=No 1=Yes	9

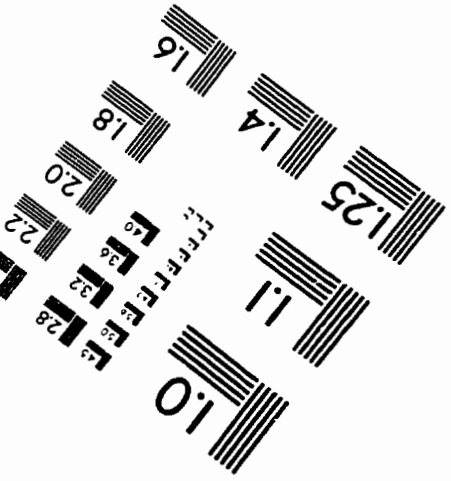
IMAGE EVALUATION
TEST TARGET (QA-3)

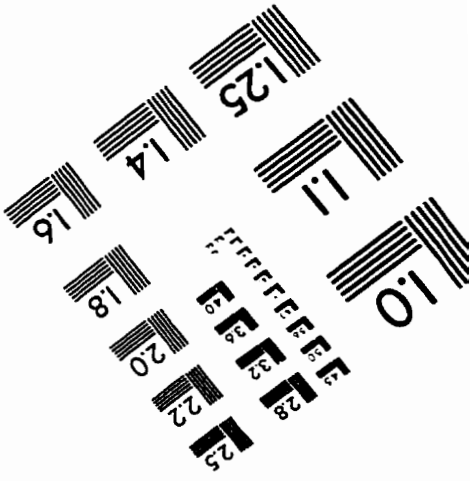












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