The Hong Kong Society
of Child Neurology & Developmental Paediatrics

Annual Scientific Meeting

11-14 November, 2005
Hong Kong

Neuromuscular Disorders of Infancy, Childhood and Adolescence

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SCIENTIFIC PROGRAMME

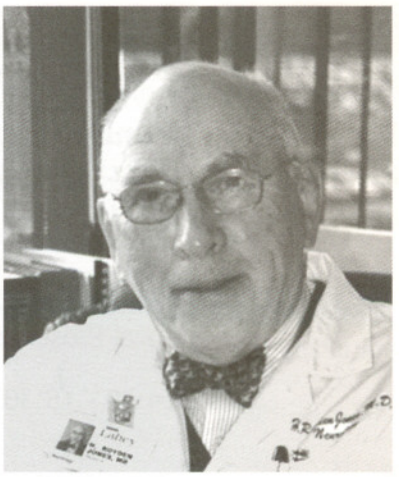
ANNUAL SCIENTIFIC MEETING 2005 ON "NEUROMUSCULAR DISORDERS OF INFANCY, CHILDHOOD AND ADOLESCENCE"

11 - 14th November 2005, Hong Kong

Date	Time	Session	Title	Speaker
11 Nov 2005 (FRI)	1900 – 2000	Dinner		
	2000 – 2200	Seminar I	Clinical and Laboratory Approach to the Infant and Child with a Neuromuscular Disorder	Dr Royden Jones
12 Nov 2005 (SAT)	0900 – 1000	Case Presentation	Interactive Case Studies (Kwong Wah Hospital, Nurse Quarter, 1/F Seminar room)	
	1000 – 1030	Tea break		
	1030 – 1130	Hospital Visit (Invited Guests)	Stroke Rehabilitation Centre & Department of Paediatrics (Kwong Wah Hospital)	
	1215 – 1400	Lunch		
	1400 – 1500	Seminar II	Electrodiagnostic Approach to Brachial and Lumbosacral Plexopathies and Peripheral Neuropathy	Dr Royden Jones
	1500 – 1600	Free Paper Session	Free Paper Presentation	
	1600 – 1630	Tea break		
	1630 – 1730	Seminar III	Paediatric Electromyography	Dr Royden Jones
13 Nov 2005 (SUN)	0930 – 1130	Seminar IV	Neuromuscular Disorders of the Critically Ill Neonate and Child	Dr Royden Jones
			Neuromuscular Disorders - Canadian Experience	Dr Lui Wai Ying
		Local Presentation I	Neuromuscular Disorders in Chinese Children - Prevalence and Functional Status	Dr Patrick Ip
			Multidisciplinary Assessment for Children with Neuromuscular Disorders	Dr Sharon Cherk
	1130 – 1200	Tea break		
	1200 – 1300	Seminar V	Common Lower Motor Neuron Disorders: Clinical Course and Diagnosis	Dr Royden Jones
	1300 – 1430	Lunch		
	1430 – 1530	Local Presentation II	Duchenne/Becker Muscular Dystrophy - Spectrum of DMD Gene Mutations and Genotype-Phenotype Correlation Among Southern Chinese Patients	Dr Ivan Lo
			Acute Flaccid Paralysis (AFP) Surveillance in HK	Dr Thomas Tsang
			Support of Children with Neuromuscular Disorder in Mainstream School	Mr Richard Ng Ms Peon Tang Ms Josephine Tong
	1530 – 1600	Tea break		
	1600 – 1700	Seminar VI	Guillain-Barre Syndrome – Clinical Presentation, Differential Diagnosis and Therapy	Dr Royden Jones
14 Nov 2005 (MON)	1900 – 2230	Keynote Lecture and Banquet	Childhood Neuromuscular Disorder From the Perspective of Adult Neurology	Dr Royden Jones

Venue: 11 – 13 November 2005: Lecture Theater, G/F, M Block, Queen Elizabeth Hospital
14 November 2005: Hong Kong Marco Polo Hotel, Tsim Sha Tsui

COURSE DIRECTOR



Dr. H. ROYDEN JONES, Jr., M.D.

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EDUCATION

1958 : BS: Tufts University, Medford, Massachusetts
1962 : MD: Northwestern University Medical School, Chicago, Illinois

POSTDOCTORAL TRAINING

1962 - 1963 Rotating Intern, Philadelphia General Hospital, Philadelphia, Pa.
1963 - 1965 Resident in Internal Medicine, Mayo Graduate School of Medicine, Rochester, Minnesota
1965 - 1966 Resident in Neurology, Mayo Graduate School of Medicine
1970 - 1972 Resident in Neurology, including Clinical Neurophysiology, Mayo Graduate School of Medicine

ACADEMIC APPOINTMENTS

Harvard Medical School: Harvard University
1973 - 1975 Clinical Instructor in Neurology
1975 Instructor in Neurology
1978 - 1980 Clinical Instructor in Neurology
1980 - 1988 Assistant Clinical Professor of Neurology
1988 - 1997 Associate Clinical Professor of Neurology
1997 - Clinical Professor of Neurology
Tufts Medical School: Tufts University
1998 - Lecturer in Neurology

MAJOR RESEARCH INTERESTS

1 Pediatric electromyography
2 Acute neuromuscular disorders of infancy and childhood
3 Guillain-Barre syndrome in children
4 Mononeuropathies in children
5 Lambert-Eaton Myasthenic Syndrome
6 Stiffman syndrome
7 Multifocal motor neuropathy

VISITING PROFESSORSHIPS

1995 : Visiting Professor of Neurology, University Western Ontario, London, Ontario
1995 : Visiting Professor of Neurology, University of Istanbul, Istanbul, Turkey
1995 : Visiting Professor of Neurology, Cornell University Medical School, NY, USA
1998 : Visiting Professor of Neurology University of Iceland,†Reykjavik, Iceland
1998 : Visiting Professor of Neurology Northwestern University Medical School, Evanston, Illinois, USA
2000 : Visiting Professor of Neurology Aristotle University Children's Hospital, Thessalonika, Greece
2003 : Visiting Professor of Neurology. University of Virginia, Charlottesville, Virginia, USA
The TR Johns memorial lecture.
2004 : Visiting Professor of Neurology. University of Lausanne, Lausanne, Switzerland
2004 : Visiting Professor of Neurology, Dartmouth Medical School, NH, USA

EDITORIAL BOARDS

1997-2003 CONTINUUM American Academy of Neurology
2004- Muscle and Nerve

AD HOC JOURNAL PEER REVIEWER

Neurology
Muscle Nerve
Clinical Neurophysiology
Journal of Child Neurology
Pediatrics
New England Journal of Medicine
Annals of Neurology

Dr. Royden Jones has been the editor and author of four major texts and the fifth one is now in publication. He edited the original Part II of Netter's Nervous System, Volume 1 in 1986 *Neurologic and Neuromuscular Disorders*, as well as three other monographs including *Clinical Pediatric Electromyography* in 1996 with Drs Bolton and Harper, *Neuromuscular Disorders of Infants, Childhood, and Adolescence* with his child neurology colleagues Drs. De Vivo and Darras in 2003, and *Netter's Neurology* just published this year. Currently Dr. Jones is the third editor with Gregory Holmes and Solomon Moshe on the first comprehensive pediatric neurophysiology volume *Clinical Neurophysiology of Infants, Children and Adolescence* to be published in late 2005. His other writings include more than 150 papers including over 70 original peer reviewed manuscripts and more than 90 book chapters.

KEYNOTE LECTURE

CHILDHOOD NEUROMUSCULAR DISORDERS FROM THE PERSPECTIVE OF AN ADULT NEUROLOGIST

Dr. H. ROYDEN JONES Jr., M.D.

How does one take residency training in internal medicine and adult neurology, practice adult neurology for 3.5 years, initially in Germany in the US Army, and than 6 more years at Lahey a major referral clinic, and than find themselves asked to perform pediatric electromyography at one of the most famous children's hospitals in the world...This occurred despite having seen only three children have an EMG during his training at the Mayo Clinic. Serendipity sometimes plays a major role in life. When one accepts the occasional unusual challenge we sometimes find such leads to interesting and very rewarding opportunities. Seizing the moment however may lead to a few intermediary challenges... to finally find the eventual goal.

In 1977, having had a modest clinical experience seeing occasional infants and more older children while in the Army, I offered to help cover the Children's Hospital Boston (CHB) patients for one of my colleagues. One year later I received a call from Cesare Lombroso, the world famous epileptologist who was a Professor of Neurology at Harvard Medical School and director of the neurophysiology unit at CHB. He had seen my curriculum vitae and noted I had trained at Mayo in the renowned electromyography laboratory of Edward Lambert MD, PhD. Cesare asked me to consider setting up such a facility at CHB, needless to say I was very shocked and quite surprised that this famous hospital didn't have their version of Dr. Lambert .

Initially I was reluctant on three counts. Firstly I didn't want to give electric stimuli or put needle electrodes into children. Secondly I had essentially no pediatric EMG experience. Lastly I could not find any reasonable in depth references to what was normal in pediatric EMG, let alone significant reviews similar to those already available for the assessment of the adult patient having various motor unit disorders. Furthermore I wondered how I would one perform EMGs on a very tiny newborn? Lastly I didn't even anticipate studies on the occasional premature in an old fashioned incubator. However having four of my own children, I felt compelled to accept the challenge finding a way to project my excellent training into the world of little people.

Certainly the principles of EMG are the same no matter what the age. Particularly important is the thought process always considering that the EMG is an extension of the clinical exam as well as the process of differential diagnosis. Fortunately both Lambert's lab at Mayo and Buchthal's lab in Copenhagen had established a few norms that allowed one to pursue EMG in the neonate and infant. When one evaluates a child there is the same clinical issue as the adult. One needs to define whether there is an abnormality within the peripheral motor unit. The diagnostic approach in children is similar to that of adults, starting with a careful clinical evaluation, followed by appropriate biochemical, genetic or imaging studies. I have been particularly blessed to have a very collegial and increasingly academic relationship with three outstanding child neuromuscular neurologists namely the late Michael Bresnan, Linda Specht, and most recently Basil Darras. They have continually enhanced my knowledge of pediatric neuromuscular disease thus making me a better child EMG'r.

Child neurologists and physiatrists may occasionally staff pediatric electromyography laboratories however it is significantly more common for adult neurologists or adult physiatrists to have this primary responsibility.

KEYNOTE LECTURE

Often during their EMG training these physicians have relatively limited experience with the broad spectrum of childhood neuromuscular illnesses, particularly those affecting infants. We are seeing a few more child neurologists take fellowships with us and occasionally our adult fellows get so stimulated by pediatric issues that they have essentially switched the emphasis of their careers...and very successfully so. Even at major academic centers, with reputations for expertise in the diagnosis and treatment of these disorders, the number of children evaluated in a PEMGL is relatively small compared with adults. This is often 10 % or less that of the total seen in most academic based adult neuromuscular programs.

We have witnessed a significant change in the diagnostic role for pediatric electromyography (EMG) in a number of instances during the last decades of the 20th century. Major scientific advances in the identification of the specific molecular pathogenesis for many peripheral nerve and muscle disorders has changed our initial testing for certain neuromuscular disorders. In 1979, when first performed EMGs at Children's Hospital Boston (CHB), boys with Duchenne or Becker muscular dystrophy were frequently evaluated. Soon thereafter the dystrophin gene was identified at CHB by Kunkel. This has made it possible to discontinue performing EMGs when boys present with a typical clinical phenotype of a dystrophinopathy. This seminal specific DNA study was repeatedly recapitulated with the identification of means to diagnose a number of other motor unit disorders. These now include the spinal muscular atrophies (SMA), Charcot-Marie-Tooth (CMT) type I peripheral neuropathies, as well as many other myopathies including myotonic dystrophy. The ability to utilize these very specific DNA tests depends on the pediatric neurologist's ability to reach a reasonable clinical diagnosis. These studies are relatively expensive, and presently no broad laboratory "profile" exists that economically and effectively screens children with common clinical profiles such as proximal weakness.

Other new testing modalities are also available that limit the need for EMG in certain clinical settings. Examples include antibody specific testing for myasthenia gravis, which often provides a very accurate means to study the subacute forms of this neuromuscular transmission disorder. However, in the acute clinical setting EMG still offers the opportunity to make a rapid neurophysiologic diagnosis. Within the past few years CHB colleagues are evaluating the role that MRI may provide to aid the diagnosis of children presenting with both Guillain-Barré syndrome and polymyositis. Thus there is an increasing clinical spectrum of neuromuscular disorders where traditional EMG studies are no longer routinely indicated. Despite this, our EMG laboratory still keeps reasonably busy evaluating various disorder of the peripheral motor unit. We are also more commonly consulted for an evolving spectrum of acute pediatric neuromuscular illnesses where EMG provides specific diagnostic help, particularly in the intensive care unit.3

Although many pediatric neuromuscular diseases are analogous to those seen in the adult, the relative frequency of certain disorders varies greatly with age. Many examples are available; for instance three of the most common clinical indications for adult EMG--carpal tunnel syndrome, nerve root lesions, and diabetic neuropathy --occur infrequently during childhood. The primary challenge remains whether one is an adult or child neurologist. Thus an adult neurologist brings diagnostic tools to the pediatric setting that are relatively easily utilized. However one needs to learn a new set of disorders in the younger child. To move into the child EMG lab one must have an open and inquiring mind that enjoys a new challenge, for those who do so there is a great satisfaction when you are able to solve a child's clinical neuromuscular problem...particularly one that contributes positively to their health.

SEMINAR I

OVERVIEW TO DIAGNOSTIC EVALUATION OF CHILDHOOD NEUROMUSCULAR DISORDERS

Dr. H. ROYDEN JONES Jr., M.D.

The rapidly evolving genetic discoveries vis-à-vis the molecular pathogenesis of many neuromuscular disorders (NMD) has led to a major diagnostic expansion and sometimes a concomitant re-classification of these various pathophysiologic entities, especially those having a, chronic clinical course with symmetric and proximal muscle weakness. An increasing number of these forms of pediatric motor unit disorders are now diagnosable utilizing a number of genetic DNA modalities. These particularly include myopathies such as Duchenne dystrophy, the spinal muscular atrophies, increasingly some of the polyneuropathies, and one anticipates similar modalities for diagnosing the rare congenital neuromuscular transmission disorders. These current diagnostic approaches emphasize the importance of newer non-neurophysiologic diagnostic techniques that in some instances are more specific and thus supplant both EMG and muscle nerve biopsy.

Various major genetic discoveries have provided the primary means for diagnosis. Dystrophin assessment for Duchenne or Becker muscular dystrophy has been the most widely utilized making both EMG and muscle biopsy no longer necessary in the evaluation of a young boy with a Duchenne/ Becker phenotype. This successful prototype there has led to an increasing emphasis on developing more specific DNA analyses for the many hereditable childhood NMD. Currently another useful DNA application occurs when there is a significant clinically suspicion of spinal muscular atrophy (SMA). Primary DNA analysis of the survival motor neuron (SMN) is often quite valuable. Here one initiates DNA testing via PCR/Southern blot assay (Crawford 2003). However tests such as this do not differentiate seemingly phenotypically and clinically dissimilar entities such as spinal muscular atrophies (SMA) types I and III. In addition there may be an occasional specific utility in continuing to use both the new DNA analyses as well as classic EMG as the latter is readily available and may provide time sensitive information. For example the baby with bronchiolitis who can not be weaned and the issue arises as to the presence of a specific underlying NMD.

Currently we also still utilize EMG for the initial evaluation of certain genetically defined polyneuropathies, such as the Charcot-Marie-Tooth (CMT) phenotype. EMG will define whether the primary pathophysiologic mechanism is demyelinating, such as in CMT 1a, where DNA analysis is available or axonal where few specific genetic defects are identified. This is also particularly relevant in babies where genetic analysis has failed to confirm a diagnosis (as in suspected SMA), and the infant may have a congenital polyneuropathy, or more likely a myopathy where a muscle biopsy or rarely DNA testing is than of value. Congenital myotonic dystrophy is an example of the latter where once the EMG identifies the classic needle EMG pattern; one can proceed with appropriate DNA testing rather than proceeding to biopsy. When there is also need for a muscle biopsy, or very much less likely a sural nerve biopsy, the standard histochemical techniques are now enhanced by immuno-histochemical / and Western blot assay utilizing antibodies against various muscle proteins.

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Electromyography is still essential for diagnosis of the Guillain-Barre Syndrome (GBS) or chronic inflammatory demyelinating polyneuropathy (CIDP). Similarly with certain pediatric neuromuscular transmission disorders, particularly infantile botulism, EMG is the primary means for early diagnosis although stool culture may eventually provide a specific diagnosis. When immediate diagnosis of myasthenia gravis (MG) is not of the essence, anti- acetylcholine receptor antibody testing is the most accurate means in both infants and children. These studies allow one to confirm the presumed clinical diagnosis very accurately and less invasively than standard NCS/ EMG. However repetitive motor nerve stimulation (RMNS) is still a very effective means to confirm a clinical diagnosis of MG as it is with infantile botulism. With the latter, Andrew Engel now anticipates that specific DNA testing will soon become available to provide a diagnostic means for some of the various congenital neuromuscular transmission defects.

The role of MRI for the evaluation of polymyositis rather than muscle biopsy or EMG is still being evaluated. Additionally as enhanced strength (3 Tesla) magnets become more readily available they will have more widespread utilization in children with other NMD. For example MRI may provide a major value for identifying sites of peripheral nerve damage in children with entrapment mononeuropathies.

SEMINAR II

PEDIATRIC PLEXOPATHIES AND MONONEUROPATHIES

Dr. H. ROYDEN JONES Jr., M.D.

Plexopathies

Paediatric brachial plexus lesions encompass two specific clinical sets. These include primary birth related lesions and a much broader spectrum of less common disorders sustained at any childhood age from infancy through late adolescence. Obstetrical brachial plexus palsies complicate a very small proportion of births. Despite this relatively low frequency, and concomitant major advances in prenatal planning and assessment, obstetrical brachial plexus palsies (OBP) continue to be a challenge in reference to a difficult labor and child birth.

Trauma is the primary paediatric mechanism for a brachial plexopathy. This is particularly so because of the superficial anatomic location of the brachial plexus (BP) with its close proximity to bony and vascular structures in the shoulder and neck. Various traumatic mechanisms occur including compression, traction, ischemia, and / or laceration. Sever's seminal 1925 study of 1100 newborns with brachial plexopathies provided the first detailed description of obstetrically related birth palsy.[Sever 1925]. The reported OBP incidence within industrialized countries varies today from 0.5 to 2 per 1000 live births. There is no specific delineation of the frequency of other pathophysiologic mechanisms for a pediatric brachial plexopathy. Of the 65 brachial plexopathies seen by me at Children's Hospital Boston (CHB) electromyography (EMG) laboratory between 1979 and 2001, 74% (48) were identified at birth. Almost all of the remaining 17 brachial plexus lesions (26% of the CHB brachial plexus population) had an acute onset between ages 3 weeks and 18 years.

Motorcycle and other motor vehicle accidents, sporting activities (Burner's or Stinger's from football, and other contact sports injuries), gun shot, knife wounds, and rarely falls are the most common inciting pathophysiologic causes. Child abuse is another all too frequent cause for neurological trauma; this always needs consideration in any presumed idiopathic plexopathy.

Post infectious inflammatory mechanisms (immune related neuralgic amyotrophy), and very uncommonly an osteomyelitis are the primary non-traumatic mechanisms in children. The very rare instance of a possible neoplasm requires consideration when there is a slowly ingravescent clinical course. A genetic predisposition to a hereditary brachial neuropathy (HBPN) is another unusual mechanism for a childhood brachial plexopathy.

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Lesions of the lumbosacral (LS) plexus are among the most uncommon peripheral nerve problems evaluated by our neuromuscular group at CHB. Most of these children usually have sustained a specific traumatic mechanism including motor vehicle accidents, pelvic fractures, and gun shot wounds. A post viral plexitis (immune related) may occur on rare occasions. Tumors are another unusual cause for a lumbosacral plexopathy in children. These may sometimes be benign such as a lipoma; however we have seen one instance of a malignant lymphoma presenting in a young adolescent. Additionally various iatrogenic etiologies are also described. Lumbosacral plexopathies are also rarely linked to some unusual predisposing factors including hereditary liability to pressure palsy (HNPP), and Ehlers-Danlos syndrome.

EMG studies in these children demand a very thorough evaluation that may include multiple nerve conduction studies as well as a more detailed needle EMG than is required in a number of other childhood NMDs. This group of disorders is one where we increasingly utilize a form of sedation.

Mononeuropathies (MNs)

These are exceeding rare in children, accounting for less than 10% of pediatric referrals for electroneuromyography (EMG) testing. This contrasts with adult MNs that account for about 30% of EMG referrals. The mechanisms of nerve injury are another major difference between focal neuropathies in children and adults. Traumatic injuries due to fractures and lacerations are a major cause of MNs in children accounting for 37-76% of cases; many are related to sports injuries. Compression injuries are the second most common cause of pediatric MNs while nerve entrapment injuries are relatively uncommon. In distinction, entrapment and compression injuries account for the majority of injuries in adults.

The particular nerve involvement also distinguishes focal neuropathies in children from those in adults. In children, nerve involvement is nearly equal in distribution among the median, ulnar, radial, peroneal, and sciatic nerves; whereas in adults, median MNs, mainly due to carpal tunnel syndrome (CTS), account for 65% of focal neuropathies. The major reason for this is the much lower incidence of CTS in children. In fact 50% of pediatric median neuropathies are located in the proximal segment in contrast to a similar location in just 1% of older individuals. Similarly if one considers the peroneal nerve as an extension of the sciatic nerve, sciatic nerve lesions in children occur with a frequency equal to peroneal neuropathies another major difference from adults where peroneal neuropathies are much more common. Definition of the etiology of some sciatic lesions sometimes provides a significant challenge to diagnose. We are hopeful that as 3 Tesla MRI units become a standard, uncommon sites of entrapment will be more easily identified.

SEMINAR III

THE ROLE OF ELECTROMYOGRAPHY IN PEDIATRIC NEUROMUSCULAR DISORDERS

Dr. H. ROYDEN JONES Jr., M.D.

Introduction

Electrodiagnostic evaluation serves as an important extension to the pediatric neurologic examination for children presenting with various motor unit disorders. The primary prerequisite to an EMG is a careful clinical evaluation, and sometimes certain biochemical / DNA studies. The exception is that on occasion the EMG must precede the genetic analysis such as to whether one finds a demyelinating or an axonal polyneuropathy. Subsequently the EMG may lead to a muscle and /or nerve.

The diagnostic role for pediatric electromyography (EMG) changed significantly during the last decades of the 20th century as previously noted. Major scientific advances occurred in the identification of the specific molecular pathogenesis for many peripheral nerve and muscle disorders. There is a continually evolving list of DNA laboratory methods capable of providing a precise explanation for some children's symptoms. These studies are relatively expensive and no broad laboratory "profile" exists that economically screens all children evaluated with a specific clinical presentation such as proximal weakness. In 1979, when I developed the Children's Hospital Boston (CHB) EMG laboratory, boys with Duchenne or Becker muscular dystrophy were frequently evaluated. In 1980s, at CHB, Kunkel identified the dystrophin gene. This seminal event has been increasingly recapitulated with the identification of specific DNA testing parameters for disorders such as the spinal muscular atrophies (SMA), Charcot-Marie-Tooth (CMT) type I peripheral neuropathies, and other myopathies including myotonic dystrophy. Subsequently we no longer perform EMGs when boys present with a clinical phenotype typical of a dystrophinopathy. Similarly antibody specific testing for myasthenia gravis providing a very accurate means to study the sub acute forms of this neuromuscular transmission disorder. However, in the acute clinical setting EMG still offers the opportunity to make a rapid neurophysiologic diagnosis. Within the past few years CHB colleagues are evaluating the role that MRI may provide to aid the diagnosis of children presenting with both Guillain-Barré syndrome and polymyositis.

However despite these variable advances our EMG laboratory continues to be challenged evaluating infants and children with various disorder of the peripheral motor unit. On average we perform 3-5 studies per week. Although pediatric neurologists may occasionally staff electromyography laboratories in children's hospitals typically adult clinical neurophysiologists or physiatrists are primarily responsible for performing these studies. Often, such physicians have had relatively little experience during their EMG training with evaluation of the broad spectrum of childhood neuromuscular illnesses, particularly those affecting infants. Even at major academic centers with reputations for expertise in the diagnosis and treatment of NMD, the number of children evaluated in an EMG laboratory is relatively small compared with adults. At Children's Hospital, Boston EMG lab we perform approximately 140-160 studies annually. This is about 10% of our

total adult EMG volume at the Lahey Clinic. Thus in many North American hospitals it requires a significant number of years to gain a broad clinical EMG perspective with a number of these pediatric neuromuscular disorders. However in some countries, clinical neurophysiologists such as Matthew Pitt at London's Great Ormond Street Hospital have rapidly acquired a broad experience. He evaluates 350-400 children annually. Although a number of pediatric neuromuscular diseases are analogous to the adult, the relative frequency of these illnesses varies greatly when different aged populations are compared. Two common clinical indications for an adult EMG infrequently occur in childhood; these include the carpal tunnel syndrome and nerve root lesions. In contrast, more infants are referred to our CHB laboratory for evaluation of the floppy infant syndrome (FIS) than mononeuropathies.

Because of the uncomfortable nature of this testing some highly respected colleagues are advocating the use of anesthesia for all children under age 12 who require any type invasive procedure including EMG. We have utilized this technique a number of years for any child needing repetitive motor nerve stimulation (RMNS), some toddlers requiring extensive testing, as well as mentally compromised children to whom one is not able to explain the purposes and nature of EMG testing. The issue that continues to concern us, in reference to the routine or required use of anesthesia, is the very rare but definite chance for a serious anesthesia complication. Additionally as the evaluation of motor unit potential (MUP) is particularly essential in many instances, we find that with we are best able to evaluate child's motor unit size and recruitment pattern when not anesthetized in comparison to careful attempts to have the anesthesiologist partially awaken the youngster by lightening the anesthetic concentration. Therefore, we often strive to reassure the child and their parents that we are making this study both practical to the clinical question, as well as friendly to the child, by getting the youngster interested in the sound of the MUPs.[13] It is often heart rendering to see how often one is able to develop very significant rapport with the cooperative child and subsequently achieve a clinically successful study.

This introductory chapter in this pediatric neuromuscular disorders section provides a clinically relevant, practical approach to the indications for and performance of EMGs in children. Initially we present a broad set of general neurophysiologic guidelines followed by more specific EMG concepts and recommendations. A few tables are included in Section XXXI of this text that provide[12, 13] various normative data for NCS/EMG in infants and children of different ages. Ideally, normative data for NCS and MUP parameters need to be independently established. When the EMG lab at TCHB opened in 1979, we considered collecting our own normal values for pediatric sensory and motor NCS as well as needle EMG. However, given the ethical considerations involved in the collection of such normative data for both infants and children we did not feel able to pursue this. Rather we extrapolated our initial normative data from various earlier somewhat limited evaluations [4-9] and later added other normative data.[10, 11] Each of these studies varied as to the numbers of children examined and specific techniques utilized. Miller and Kuntz's 1986 report, primarily from the Mayo Clinic, is frequently cited.[11] Unfortunately, this report was based on relatively small numbers of children, including only 23 infants; four neonates, six infants 1 to 6 months of age, and 13 babies ages 7 to 12

months.10 In 1993, another larger series was published from the Babies Hospital at Columbia in New York. This provided normative nerve conduction values for 155 healthy children ages 7 days to 14 years of age including 20 neonates, 23 infants 1 to 6 months old, and 25 babies 7 to 12 months of age. [12] The various studies attempting to establish pediatric norms are carefully collated by Harmon and his colleagues. [12, 16]

General Approach to Pediatric EMG

Initially, we personally review the youngster's history with the child and the parents, as well as performing a relevant neurologic examination, prior to the EMG. This information then serves as an extension to the clinical evaluation. The performance of a pediatric EMG always provides an added challenge to an electromyographer especially the study of the neonate and toddler.13-16 Prior to beginning the exam; the purpose of the EMG must be explained to both the parents and the child when he or she is old enough to comprehend. In this setting it is very important to gain their confidence as well as their appreciation that the pediatric electromyographer is empathetic to their various concerns. We tell the parents we will treat their child as we would our own, and this is always reassuring to them. The time utilized to assure that both the child and the parents are comfortable with the need for the EMG is repaid in not only the ease of performing the EMG as well as the reliability of the derived data. With older children we are always forthright explaining that the EMG has variable levels of discomfort. However we conclude by stating that we try to minimize this in every possible way. It is important to provide a quiet environment, encouraging the child to relax. ,[13-16] We also utilize a variety of toys such as a "TV" music box, stuffed animals, and books so that parents can read to their child making the laboratory a more friendly environment.

Although a number of my colleagues are comfortable having parents remain with their child during the study, one survey of pediatric EMG practice patterns reported that 32% of laboratory directors discouraged or prohibited parental presence.[17] However for us it is difficult to imagine any physician prohibiting a parent from being present during a pediatric EMG. There was even a more profound lack of parental presence during EMG of older children in that same study; only 30% were in attendance with school-aged children and just 14% while an adolescent was examined.[17] All parents have been asked to accompany their children. Good rapport with the parents, permitting them to interact with their child while providing the child with a secure environment, helps the electromyographer obtain a better than adequate examination. Having a parent sit on the edge of the examining table or comfortably in a lounge chair while holding an infant reassures the child and often enables the electromyographer to complete the EMG exam. When the parents recognize that the physician performing the study shares their concern for the well being of their child, they are almost always very cooperative. On occasion demonstrating a sensory NCS on the parent may relieve a child or parent's anxieties. Older children are encouraged to become participants in the process. Initially we perform sensory NCS studies, as these studies generally require a very minimal stimulus shock. This often helps the child to become comfortable with the electromyographer It is than easier to proceed to motor conduction studies where we have the child observe "the mountains" build up on the EMG

screen. Lastly many children can get through the needle portion by listening to the loudspeaker and concomitantly offering opinions as to what the sounds they make can be likened to. At times their responses are quite humorous; "out of the mouths of babes!"

Toddlers and preschoolers obviously do not appreciate the purpose for which they are being evaluated. Often one can study the young child without sedation by having the parent hold the child on his or her lap. At times, an assistant, such as a fellow, resident, or nurse, is extremely helpful if the infant's extremities occasionally must be restrained. However, we do not proceed past this stage-such as utilizing multiple restraints. We will reschedule the EMG and perform the study under nitrous oxide and propofol general anesthesia. Infants less than 1 year of age usually do not require anesthesia unless it is necessary to perform repetitive motor nerve stimulation (RMNS) to evaluate a potential neuromuscular transmission defect (NMTD) or with the pathologically irritable infant, such as may occur with Krabbe's disease, although today with DNA testing available we do not often see this type of child.

Our anesthesiologists pre-medicate the child with midazolam [(Versed) Roche Laboratories, Nutley, NJ] followed by induction with nitrous oxide and anesthesia maintenance with propafol [Diprivan (Stuart Pharmaceuticals, Wilmington, DE)]. . Both agents have a short duration of action and permit the child to be brought out of anesthesia rapidly. Midazolam is rapidly reversed with the benzodiazepine antagonist flumazenil. One is able to successfully evaluate insertional rest activity soon after the child falls asleep and complete the MUP evaluation at the end of the study when the child is more aroused. Anesthesia is also valuable for evaluation of NMTD's by performing RMNS at rapid and uncomfortable rates of 10 to 50 Hz. Stimulation of this intensity is often not well tolerated by the unsedated younger child who is too young to understand the purpose of the study. Our physicians follow the American Academy of Pediatrics Guidelines for Monitoring Infants and Children after Sedation.[18] The recently sedated child must not be permitted to walk alone because he or she could fall, resulting in serious injury. The child must not leave the nurse's supervision until he/she has satisfactorily recovered from the sedation.

The tiny extremities of the newborn present logistic challenges that make it technically difficult to perform NCS and EMG as outlined in detail in a prior text.[16] the peripheral nerves are relatively close to the surface in most children. It is important to keep the infant warm. With newborns the EMG is now almost always performed in the neonatal intensive care unit (NICU) and most times under infrared lamps. In general NCS require relatively minimal to modest stimuli when compared with the degree required for the average adult study. At CHB, we begin the EMG evaluation with sensory NCS, because these are generally easy to elicit with minimal stimulus intensity and therefore cause the least discomfort. During the motor portion of NCS, the child is encouraged to watch the response build on the oscilloscope. Often this is of help to distract them. Additionally children are often intrigued by watching their muscles contract.

SEMINAR III

Although the needle EMG portion of the study is usually not as well tolerated as NCS, on most occasions we are able to obtain an adequate examination without sedation. Older youngsters with whom you can gain good rapport need to have a reasonable discussion as to what to expect. Their concerns need to be assuaged about the anticipated discomfort before insertion of the first electrode. We attempt not to mention the word needle but simply state that we are putting tiny wire microphones or electrodes into the muscle. The feeling of discomfort is likened to a mosquito bite or a pinch. It is important to avoid having the child see any blood whenever possible by being certain hemostasis is achieved prior to moving on to the next site.

Overall the pediatric electromyographer needs to formulate the study similar to that of an adult. With diffuse processes, such as generalized peripheral neuropathies or myopathies but predominantly affecting the legs we often examine one leg and if normal we do not find it of value to examine other GBS or a potentially serious diagnosis such as spinal muscular atrophy (SMA) we usually examine another one to two extremities to demonstrate a diffuse or multifocal process. When the clinical issue involves a mononeuropathy versus a plexus level lesion in a single extremity, several motor and sensory nerves and multiple muscles need to be examined. In this setting at least 50% of these children seen at CHB have a traumatic etiology. Therefore only a single extremity needs to be evaluated. However when specific abnormalities are demonstrated without evidence of a traumatic cause, the similarly affected homologous area in the contralateral extremity is examined for comparison to look for concomitant "asymptomatic" similar lesions.

SEMINAR IV

NEUROMUSCULAR PROBLEMS OF THE CRITICALLY ILL NEONATE AND CHILD

Dr. H. ROYDEN JONES Jr., M.D.

SEMINAR

Introduction

Acute peripheral motor unit disorders occasionally confront the pediatric intensivist and / or the pediatric neurologist. These are best discussed as those related to either the infant or the older child. With babies the presentation can be a relatively broad and sometimes a challenging differential diagnostic set. Some processes are unique to this age including unsuspected Werdnig-Hofmann disease, Sabin vaccine related poliomyelitis, intrauterine acquired Guillain-Barre, and infantile botulism. The older child has a spectrum quite similar to the adult particularly Guillain-Barre and myasthenia gravis at times requiring urgent admission to a neurologic critical care unit. Another more newly recognized category relates to those processes that develop in a child already hospitalized and requiring intensive care for an acute systemic illness, such as status asthmaticus. This setting predisposes the child to another set of acute motor unit disorders.

Infants and Toddlers

The differential diagnosis here is a rather unique one; these disorders present either at birth, or shortly thereafter. A variety of congenital developmental or acquired lesions, at any level of the peripheral motor unit, may lead to this picture.

Werdnig-Hoffmann diseases spinal muscular atrophy (SMA-I) is one of the most common causes of the floppy infant syndrome. Occasionally SMA has not initially been recognized in these babies. And it is not until they are unable to cope with a respiratory illness such as a bronchiolitis that they present to the ICU requiring pulmonary support and later can not be weaned, that this sad diagnosis is made.

Fortunately poliomyelitis is now a very rare entity except in a few countries and in those settings still primarily using the Sabin immunization where there is a 1 x 106 incidence of a post vaccine event. Three cases of acute flaccid paralysis occurring in infants, secondary to immunization related poliomyelitis, became known to me within just a few years during the mid 1990s. All three babies were 3-4 months old, each having received type 3 polio immunization less than one month earlier. An acute febrile illness preceded a progressive asymmetric extremity weakness, head lag, irritability, and lethargy. A CSF pleocytosis with 100-580 WBC was associated with protein values between 82-143 mg/dl in all and glucose of 49 mg/dl in one.5 EMG demonstrated classic electrophysiologic evidence of an acute asymmetric anterior horn cell disorder. Our center for disease control has since mandated use of the Salk killed vaccine prior to giving the Sabin live vaccine and we have not heard of further similar cases....Unfortunately this standard is not met in some countries so that infantile polio needs consideration not only in this setting but also as new viruses appear also having a predilection for the motor neuron such as West Nile.

Some congenital hypomyelinating polyneuropathies present in the newborn period with a clinical phenotypic

appearance similar to SMA type I. Some of these rare disorders may be so severe that that they require intensivist support.

Although the Guillain-Barré syndrome (GBS) rarely affects newborn infants it needs consideration in the differential diagnosis of neonatal flaccid paralysis. In at least three instances GBS onset occurred soon after birth with hypotonia, marked respiratory distress, and feeding problems. One baby had a CSF protein was 243 mg/dl. An EMG was typical for GBS. Both the mother and child had IgG antibodies positive for recent CMV infection. Intravenous immunoglobulin therapy was associated with a complete symptomatic resolution in 2 weeks.

Infantile botulism rarely occurs in previously healthy infants. Most of these disorders usually present with severe hypotonia during the first 3-6 months of life. Other unique genetically determined congenital neuromuscular transmission disorders, such as familial myasthenia gravis now recognized to be secondary to an endplate deficiency of choline acetyltransferase, are rarely seen.

Very uncommonly some of the various myopathies have an infantile onset that leads to need for intensive care. These may particularly include myotonic dystrophy, and the glycogen storage disorders. Other congenital myopathies or dystrophies are less likely to require intensive support early on.

Older children and Adolescents

These boys and girls are predisposed to critical care peripheral motor unit disorders usually similar to the adult patient. These particularly include GBS and myasthenia gravis and are increasingly seen as children become older. However when GBS and MG affect children, both may vary significantly from their traditional presentation. The pseudoencephalopathic form of GBS is a good example. Some very uncommon entities, such as tick paralysis, or other agricultural or industrial toxins, always deserve careful consideration in the differential diagnosis of an acutely paretic child.

Intensive care Induced Neuromuscular disorders

Neuromuscular complications of extended intubation and sepsis affecting either the muscle cell or less commonly the peripheral nerve also occur in children. These relatively uncommon set of neuromuscular disorders typically develop in a child predominantly as various phenomena secondary to either sepsis or status asthmaticus independently affecting the peripheral nerve, neuromuscular junction, or muscle cell per se.

Diagnostic Approach to these patients

The differential diagnosis of these various motor unit disorders is significantly aided by utilizing clinical neurophysiology techniques, particularly nerve conduction studies and electromyography, (EMG) or electroencephalography (EEG), and cerebrospinal fluid (CSF) analysis. These studies provide the clinician an objective means to appropriately assign a specific patho-anatomic or neurophysiologic site for the child's illness.

SEMINAR V

LOWER MOTOR NEURON DISORDERS AND THE FLOPPY BABY SYNDROME

Dr. H. ROYDEN JONES Jr., M.D.

The floppy infant syndrome FIS is one of the most common reasons for referral of infants less than one year of age to a children's hospital electromyography (EMG) laboratory. These infants provide one of the major challenges confronting the pediatric electromyographer. This chapter provides a basis for performing a prudent EMG analysis of the floppy infant. Approximately 80% of floppy infants have a primary central nervous system (CNS) etiologic mechanism. Peripheral motor unit disorders comprise the other major diagnostic category for this uncommon clinical syndrome.

Central and peripheral nervous system abnormalities are not mutually exclusive as some infants have a neurologic disorder that produces lesions at both sites. Examples include babies with infantile neuronal degeneration, certain types of congenital muscular dystrophy, or infants with various metabolic disorders such as mitochondrial disease. Electrophysiologic evaluation of these infants is of value for two primary purposes. Firstly it can often distinguish between central and peripheral causes, and when a lesion of the peripheral motor unit is ascertained, EMG often provides an anatomic localization of the pathologic process to the anterior horn cell (AHC), the peripheral nerve, the neuromuscular junction (NMJ), or muscle. The results may offer therapeutic options, support the diagnosis of a specific genetic condition or provide prognostic information. With the rapidly expanding role of DNA analysis, we have a more sophisticated, specific testing method that will increasingly supplant the need for EMG in the evaluation of some floppy infants. This positive trend is currently evidenced in the evaluation of babies with suspected spinal muscular atrophy (SMA).

Pregnant mothers are aware of normal spontaneous fetal movements. Healthy newborns have purposeless extremity movements that are associated with well-defined muscular tone, a vigorous cry, and excellent ability to suck and swallow. In contrast during the pregnancy, sometimes the mother recognizes a paucity or significant diminution of fetal muscular activity. In these instances serious motor difficulties may be evident at or soon after birth. These infants characteristically have a paucity of limb movements, poor muscle tone, and a limp appearance leading to their designation of having the floppy infant syndrome. Lower bulbar motor dysfunction is also often present manifest by a weak cry and suck, with a compromised ability to protect the airway during feedings. Such infants are predisposed to episodes of aspiration and recurrent pneumonia. Although most floppy infants have recognizable signs of hypotonia at birth, initially such findings may be subtle. However, occasional newborns appear normal at birth but later demonstrate abnormal motor milestone development. A few months of observation by the parents, pediatrician, and pediatric neurologist may be necessary before the infant is referred for pediatric EMG. The differential diagnosis includes a broad spectrum of infantile neuromuscular disorders.

SEMINAR V

Experienced pediatric neurologists are able to select the infants who are most likely to have a peripheral motor unit disorder that may be further defined by an EMG evaluation. In some instances, e.g. spinal muscular atrophy (SMA) type I (Werdnig-Hoffmann disease), the clinical appearance is so stereotyped that the pediatric neurologist recognizes that the clinical problem is most likely secondary to an anterior horn cell lesion. The advent of survival motor neuron (SMN) gene testing makes EMG testing unnecessary in many infants with a classic clinical presentation. However, in some of these instances, EMG is still indicated to differentiate certain motor unit lesions including: 1) disorders that may clinically mimic SMA I, such as some of the congenital neuropathies 2) define the level of the motor unit abnormality in the rare instance of a spinal cord lesion, or 3) make an early diagnosis while awaiting the DNA analysis in an infant in whom SMA is the apparent clinical cause and who is quite ill wherein quality of life issues may need to be made.[3] When the clinical phenotype is less well-defined, or when there is a combination of features suggesting both brain and peripheral motor unit involvement, the EMG also provides useful differential diagnostic information.

It is also important for the electromyographer to observe whether the floppy infant has joint contractures compatible with the clinical designation of arthrogryposis multiplex congenita (AgMC). This floppy infant phenotype may result from lesions at any level of the neuroaxis, including upper and lower motor neuron, peripheral nerve, neuromuscular junction or muscle.[4-14] However, the concomitant presence of joint contractures is not specific to one disorder affecting any of the primary portions of the peripheral motor unit. AgMC occurs in association with any long-standing process associated with limited intrauterine mobility. EMG is helpful in defining if a peripheral motor unit problem is the etiologic mechanism in these infants.

SEMINAR VI

GUILLAIN-BARRE SYNDROME IN CHILDREN

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SEMINAR

The Guillain-Barre syndrome (GBS), an autoimmune, post infectious, primarily *demyelinating*, polyradiculoneuropathy, is the most frequent mechanism responsible for an acute rapidly evolving generalized weakness developing in a child at any age. In some parts of China, and very occasionally in western cultures, *axonal* lesions are the primary underlying pathophysiologic cause. The incidence of pediatric GBS for those <17 years of age in North America was studied in Olmstead County, Minnesota by Mayo Clinic researchers and found to be 0.8/100,000 person-years. This compares favorably with South America where the annual incidence rate was 1.1/100,000 children in Paraguay and 1.02/100,00 in Australia. With the continued decreasing incidence of poliomyelitis, GBS and transverse myelitis (TM) are currently the 2 most common causes for acute flaccid paralysis in children under age 15 in both Australia and China. GBS occurs with a little less than three times the frequency of TM.

The predominant pathophysiology is an immune response directed toward a prior infectious organism. Molecular mimicry occurs with the sharing of homologous epitopes between the prior microorganism and the Schwann cell ganglioside components of the affected peripheral nerve. This may induce both cellular and humoral immunologic defense mechanisms. In those with a predominant cellular mechanism there is a multifocal infiltration of the myelin sheath by inflammatory mononuclear cells. Macrophage generated breakdown of myelin results; secondary axonal damage follows in severe cases. In other forms of classic demyelinating pediatric GBS there may be an antibody binding to specific glycoconjugates in the abaxonal Schwann cell plasmalemma. There is consequent complement activation as demonstrated by complement activation products present on the outer surface of myelinated fibers and Schwann cells. This leads to vesicular demyelination, or a primary autoimmune antibody-mediated destruction of myelin. In the primary axonal variant there is an initial immunologic reaction against epitopes specific to the axonal membrane. The clinical course and eventual prognosis of either the demyelinating or axonal forms is determined by the extent of secondary or primary axonal damage

There are two primary criteria required to establish a GBS diagnosis. These are 1) progressive motor weakness ranging from minimal weakness of the legs to total paralysis of all 4 extremities and 2) areflexia. Typically older children have an acute rapidly evolving symmetric weakness frequently associated with varying degrees of distal paresthesiae and numbness. Sensory symptoms are usually less prominent, often just a vague tingling, but occasionally these may predominate early on.

One always needs to be cautious not to dismiss a GBS diagnosis early on into the illness, particularly when an adolescent presents with acute distal numbness and tingling. In this setting the attending physician

needs to avoid a premature diagnosis of hyperventilation syndrome, subsequent to the stress that is so common in this age group. The possibility of early GBS always must be a major consideration. It is wise to carefully observe such youngsters.

Some interesting clinical variants occur particularly amongst children. On occasion younger children present with an acute severe pain syndrome that may mask as a pseudo-encephalopathy with irritability, seeming confusion and such severe muscle pain that they hesitate to walk. Another clinical variant is the Miller-Fisher syndrome characterized by an acute ophthalmoplegia, ataxia, and areflexia. Some children present with an acute ophthalmoplegia without ataxia mimicking myasthenia gravis. Although the majority of children with GBS follow a relatively benign clinical course, a number initially require intensive care monitoring and occasionally intubation.

The differential diagnosis includes lesions at 1) the level of the spinal cord such as transverse myelitis, or even poliomyelitis variants, 2) at the peripheral nerve some of the toxic neuropathies, or even tick paralysis, 3) the neuromuscular junction infantile botulism, myasthenia gravis and rarely at 4) the muscle cell per se i.e. dermatomyositis, or even some of the channelopathies leading to periodic paralysis.

Both the demyelinating and axonal forms of GBS have the potential for an acute respiratory compromise. Therefore any child suspected of possibly having GBS must be immediately hospitalized. A significant weakness compromising ambulation is an immediate indication for immunomodulatory therapy. Ideally one likes to begin this in hopes of prevention of a respiratory compromise. To date, there is still no well-controlled study comparing the value of the two available therapeutic modalities i.e. intravenous immunoglobulin (IVIg) or plasmapheresis. However the ease of administration of the former has made it the choice today.