NEONATAL EEG

Over the past several decades, electroencephalography (EEG) in newborn infants has become valuable as a serial, noninvasive screening tool for infants at high risk of perinatal injuries. The brain dynamics and connectivity in different states (awake or asleep) can be defined, and a whole range of acute or chronic cerebral disorders can be identified. Such information often reveals presymptomatic or subclinical conditions.

The EEG prognostic value at the time of continuous development is often greater than at a later stage. EEG testing can provide reassurance to the physician and parents at a time of potential catastrophic damage.

The continuous changes that occur during early brain development are often associated with striking changes in EEG patterns over short periods. This makes it difficult to interpret EEG results, which can discourage the use of EEG testing.

Given the close relationships between certain morphological aspects of the developing brain and EEG results, gestational age can be reliably estimated (to ±1 wk) by EEG criteria. In fact, CNS development of the immature brain proceeds at about the same
rate during fetal development as in the postnatal environment. The physiological substrate for these early EEG patterns is unknown, but is probably derived from cortical generators that are strongly influenced by subcortical (primarily thalamic) afferent input.

Rapid maturation of these structures (and not the corpus callosum) is most likely responsible for the interhemispheric synchrony that occurs close to full-term gestational age; in particular, rapid dendritic spine development and synaptogenesis are typical of the last month of fetal development. The complex development of cerebral sulci during this same period is probably responsible for the neonatal EEG results showing complex, more definitive patterns at term. At this age, easily recognizable and organized activity patterns appear. These continue with little change during the first month of life and are strictly characteristic of neonatal EEG.

There are several technical considerations when recording from a small (neonate) scalp. High skin resistance impedes low-resistance scalp-to-electrode contact. The state of activity (awake or quiet vs active sleep) can be selectively bound to certain aspects of pathology.

It is important to annotate the tracing with particular attention to the presence and type of eye movements, facial movements, respiration (regular or irregular), sucking, crying, grimacing, and so on. Extracerebral monitors are needed in routine recordings, including at least electrooculogram (EOG), respiration rate measurement, and electrocardiogram (ECG). Only a reduced number of scalp electrodes, generally never more than the set in a 16-channel recording, are applicable. A low time constant (0.25-0.60 s) is preferable to record the low-frequency background activity. Slow paper speed maximizes the slow background and the degree of interhemispheric synchrony.

Recent technologic advances have promoted the use of amplitude integrated EEG (aEEG) to offer an accessible tool for
bedside continuous cerebral monitoring. However, this easy-to-use device requires nonetheless careful management and a vigilant well-trained staff. It also needs to complement standard conventional electroencephalography to be interpreted by experienced readers to avoid inappropriate conclusions and false positives, especially in the domain of neonatal seizures. As for amplitude measurements, 2-channel aEEG appears considerably more sensitive in detecting cerebral injury in the term encephalopathic infant, in comparison with a single-channel aEEG, especially in the setting of unilateral injury.

THE NORMAL NEONATAL EEG

In the full-term born infant, ultradian sleep and waking cycles are well defined and easy to detect with polygraphic and behavioral criteria. On EEG, wakefulness characterized by eye opening, crying, and vigorous motor behavior accompanied by irregular vital signs on recordings (ECG, respiration) is marked by a low-amplitude activity and discontinuous 4-7 cps theta activity interspersed with low-voltage delta rhythms. Hence, the French name *activité moyenne*.

Active sleep (AS), the antecedent of rapid eye movement (REM) sleep, is usually indicated by irregular respiratory patterns with interspersed, brief apneic episodes that often precede clusters of eye movements. Contrary to adult physiology, prominent, subtle motor activity, especially of the face (e.g., grimacing, smiling), accompanies this state. These results are often interpreted as seizure activity by the inexperienced reader. On EEG, 2 patterns are observable, as follows:

- A continuous, low- to medium-voltage background with theta and delta activity and occasional anterior sharp-waves that occur primarily at sleep onset, or
- A lower amplitude, more continuous theta background is mostly seen between periods of quiet sleep (QS). The latter non-REM sleep is marked by a discontinuous pattern (*tracé alternant*) that is characterized by bursts of high-
amplitude (50-20 mV) synchronous delta activity and separated by intervals of lower mixed activity that resemble wake or AS activity.

Fig. Quiet sleep non–rapid eye movement tracé alternant.

Sleep state cyclicity is certainly achieved after 30 weeks’ postconceptional age (PCA), with stability over multiple cycles only at 36 weeks’ PCA.

Lately, the increased survival of extremely young premature babies has allowed to assess very early expression of sleep cyclicity by combining measures of REM and EEG discontinuity between 25 and 30 weeks’ PCA. Early forms of “transitional” sleep akin to “seismic sleep” in the rat represents an immature form of paradoxical sleep with mixed features of active and quiet sleep. It probably corresponds to a primitive form of brain activity characterized by a low level of inhibition progressively declining toward term. Near the end of the first month, a more diffuse pattern usually appears, consisting of continuous, high-to-moderate amplitude, slow activity that is not seen in the preterm infant. A high degree of synchrony between burst and interburst activity is desirable at term. This usually confirms normal maturational patterns.

Several morphological figures may occur with variable frequency. Random sharp-waves, most commonly temporal or
rolandic, are sporadically seen in QS. Nonrolandic, repetitive, highly focal spikes confined to a single location that occur during wakefulness usually indicate abnormalities. A burst of frontal delta and synchronous, frontal sharp waves are still abundant in the full-term born infant during AS. Spindle delta bursts (brushes) are seen with decreasing frequency in the full-term born infant and are usually confined to the central and temporal leads during QS. This state is the most vulnerable, being susceptible to various minor CNS insults that are only transiently apparent, depending on their expression. It is important to perform prolonged recordings, especially in stressed infants as they are likely to express less QS.

Several important milestones characterize EEG maturation patterns during the first months of life. The newborn progressively develops a circadian rhythm, resulting from the interaction of endogenous factors with external synchronizers such as light, eating, and sensory stimulation over the course of a day. At approximately the third month, sleep efficiently occurs in nocturnal intervals of at least 8 hours, reflecting mother-child interactions and the established activity of endogenous pacemakers.

With regard to EEG results, several important changes accompany this phase. From the second week of life, slow and continuous background activity (consisting of increasing amplitude delta waves whose frequency also decreases with the approaching first month of life) progressively replaces the discontinuous pattern (tracé alternant) that is typical of QS. Typical EEG characteristics disappear within the second month of life, including slow frontal biphasic spikes (encoches frontales) and negative rolandic spikes. The newborn still falls asleep in AS until the end of the third month. AS decreases from 50% to 40% by the end of the fourth month; likewise, QS progressively increases and becomes more defined due to the appearance of EEG hypnic features that are typical of adults. Vertex waves can be noted in the rolandic regions after the third month; sleep
spindles appear earlier, at about the sixth week, over the central regions.

The first sleep spindling samples are slower in frequency and more anteriorly distributed in newborns compared with older infants. These infrequently appear at the beginning of QS as rudimentary, low-voltage (< 25 mV), immature, asymmetric, and asynchronous 10-16 Hz EEG waveforms. The length, amplitude, and synchrony of these spindling samples increase during the first year of life and are more prominent in females and small for gestational age newborns, especially those with neonatal respiratory distress. Spindling maturation is prognostically valuable: their absence at the third month indicates abnormal maturation (eg, hypothyroidism, severe patterns of mental retardation). At the same time, the sawtooth waves that are typical of adult REM sleep make their first appearance in AS.

Around the sixth postnatal week, 75 mV occipital sharp waves characterize AS and increase in frequency from 2 to 4 Hz toward the end of the third month. At 3 months, a clearly defined 3-4 Hz, 50-75 mV occipital rhythm appears during wakefulness; this is interrupted by eye opening. It progressively evolves at about 5 months to a faster frequency of 6-7 Hz.

THE ABNORMAL NEONATAL EEG

Even more than in other epochs of life, in neonates the abnormal neonatal EEG has a prognostic value as opposed to a diagnostic value. Rarely, specific EEG patterns correspond to typical syndromes. Prognostic value can be increased with the following methods:

- Early recordings, possibly within the first 48 hours of life
  - Markedly abnormal EEG patterns usually last for a relatively short time, followed by less abnormal or even normal patterns despite the absence of clinical resolution.
- Prolonged recordings to include samples of different activity states - QS, for instance, is far more likely to show
valuable maturation pattern abnormalities and yet is less likely to occur within short recording intervals in a compromised infant.

- Serial EEGs obtained at short intervals to assess the rapid changes that are likely to occur in rapidly maturing, high-risk infants - Normalization of a previously abnormal pattern may indicate a minimal impact of a brain insult on maturation. Conversely, progressive deterioration of previously normal or moderately abnormal patterns favors the possibility of long-term neurological sequelae.

Because EEG abnormalities in neonates cover a broad spectrum, any classification is difficult and, in some cases, arbitrary. One possibility for classification would be to distinguish between diffuse and focal abnormalities and to categorize separately ictal and paroxysmal patterns in the presence of neonatal convulsions.

**DIFFUSE EEG ABNORMALITIES**

With regard to severity and prognosis, severe and irreversible abnormalities should be distinguished from moderate, reversible abnormalities. Severe abnormalities correspond to 2 main EEG patterns, inactive and paroxysmal, both of which are accompanied by a lack of sleep cycles and a lack of reactivity to internal or environmental stimuli.

The inactive or isoelectric pattern consists of cerebral activity below 10 mV that is continuously present throughout the record. Brief intervals of low-voltage activity, which are located over the posterior head regions, may occasionally be present. This pattern may occur in varying clinical conditions and often occurs with the following states:

- Early severe asphyxia or massive hemorrhage
- Severe inborn metabolic deficits
- CNS bacterial or viral infections
- Gross congenital malformations
Fig. Inactive or isoelectric pattern.

- Drug-induced state
- Hypothermia
- Postictal recording

In the absence of a drug-induced state, hypothermia, or postictal recording, the prognosis is poor but not necessarily fatal.

The paroxysmal or burst suppression EEG pattern is characterized by intervals of inactive background activity (< 10-15 mV) that alternate with synchronous or asynchronous activity bursts.

These include primarily high-voltage, irregular slow waves with or without sharp components. This pattern, which carries a highly unfavorable prognosis, must be clearly distinguished from a full-term newborn’s tracé alternant and a preterm infant’s tracé discontinue (TD), both of which are normal patterns. Serial recordings are essential to reach a reliable prognosis. Certain conditions (eg, Aicardi syndrome or uncommon dysgenetic conditions that involve the corpus callosum) rarely present as hemihypsarrhythmia.
Fig. Paroxysmal or burst suppression EEG. Notice prominent bursts of paroxysmal activity interspersed with an inactive background activity.

Severe but reversible diffuse abnormalities can occur and are exemplified by the so-called low-voltage pattern throughout the EEG record. QS and AS are only distinguishable by the slightly higher voltage in QS, where mixed frequencies under 10-50 mV are almost continuously recorded. This finding and a diffuse delta pattern with minimal theta rhythms throughout the entire EEG record hold an intermediate prognosis. When the abnormalities are compatible with these changes seen in sleep, they are generally considered moderate and reversible.
Diffuse EEG abnormalities can also be seen as irregularities in maturational indices and organizational states. In addition to the patterns of profound disruption to the ability to organize cyclic states (which are typical of the most severe abnormalities), several patterns of EEG dysmaturity can be recognized and identified. In newborns who are small for their gestational age, transient or persistent dysmaturity patterns can be distinguished by their duration. Quantification may include assessment of interhemispheric synchrony in *tracé alternant*, typical of QS, or the counting of premature features such as delta brushes.

Abnormalities of EEG patterns, noted in relation to sleep states and the instability of sleep-wake states during the newborn period, have some prognostic value. When different etiologies of the EEG pattern are considered, a few fundamental groups can be distinguished.

**Transient metabolic disorders**

Neonatal hypoglycemia can range from an asymptomatic state with a minimal EEG correlation to late-onset, idiopathic hypoglycemia accompanied by neurological symptoms and seizures. Toxemia and maternal diabetes are often encountered in high-risk pregnancies. These newborns usually present with decreased QS with a relative increase in AS. Transient hypocalcemia is often associated with barely abnormal interictal EEG and variable focal seizures (in 20% of patients). Convulsive patterns of hypomagnesemia, iatrogenic hypernatremia, and pyridoxine deficiency are described in EEG in Neonatal Seizures.

**Inborn errors of metabolism**

Periodic EEG patterns in newborns with uneventful deliveries strongly suggest the possibility of an inborn error of metabolism. The most frequent neurological symptoms are early movement disorders, convulsions, and cognitive dysfunction. In 1977, Mises accurately described periodic EEG patterns in methylmalonic aminoacidopathy. High interindividual variability characterizes
a pattern of periodic frontal or occipital sharp waves that are interspersed with rapid rhythms. In maple syrup urine disease, EEG complexes are low-voltage and less periodic; background activity is less depressed. Comb-like rhythms during the second and third postnatal weeks are pathognomonic of this disorder.

The highly peculiar EEG pattern of non-ketotic hyperglycemia distinguishes it from other forms. During the first 10 postnatal days, these infants, who present with hypotonia, respiratory distress, and myoclonic seizures, have EEGs characterized by periodic, highly stereotyped 1-3 Hz complexes with 4- to 18-second interburst intervals. Frontal, high-voltage slow waves are associated with characteristic rolandic and occipital early alpha rhythms.

Pyridoxine dependence (not to be confused with pyridoxine deficiency) is inherited as an autosomal recessive trait and is accompanied by severely abnormal EEGs and refractory seizures that only respond to pyridoxal supplementation.

RECORDING THE EEG: PREPARATION, PRECAUTIONS, AND TECHNICAL ASPECTS

Age of the neonate

Knowledge of the exact age of the baby undergoing EEG is important for a proper interpretation. Maturational changes occur fairly rapidly in the 25–48 week period and any discrepancy in the age-related EEG findings of more than two weeks is abnormal. The gestational age (GA) is defined as the time elapsed between the first day of the last menstrual period of the mother and the birth of the baby. A baby born prematurely at 32 weeks and having a chronological age of four weeks at the time of EEG recording is considered to have a postmenstrual age (PMA) of 36 weeks. This corresponds to a conceptional age (CA) of 34 weeks, assuming that conception occurred two weeks after the first day of the last menstrual period. However, in practice, the term CA is used interchangeably with PMA by many authors.
Clinical information

Time of birth, history of birth asphyxia, Apgar scores, occurrence of convulsions, etc. need to be noted by the technician before starting the recording.

Medication use

Medications like morphine, barbiturates, and benzodiazepines may influence the EEG findings, especially by lowering the voltage of the background activity. Their dosages, time of administration, and serum levels, if known, should be noted.

State of the patient

Noting the condition of the neonate, whether awake or asleep, on a ventilator, lying in an incubator, etc. is relevant. This helps not only in relating EEG phenomena to the state of the patient, but also in recognizing artifacts like those arising from high-frequency ventilation. Changes happening in the environment like loud noises, flashes of bright light, nursing care, etc. should also be noted, as these may produce transient attenuation of the background activity or produce movement artifacts.

RECORDING THE EEG

The timing of registration after birth

If the EEG is done to assess the degree of brain maturation, it can be done at least 24 hours after birth to ensure that transient EEG abnormalities caused by birth itself are not recorded. If however, the goal is to assess the degree of encephalopathy and detect subclinical seizures, in situations like perinatal asphyxia, it is advisable to start the EEG registration (as a part of serial EEGs or EEG monitoring) as early as possible (at least within 24 hours), after respiratory and hemodynamic stabilization.

The duration of recording

Recording with the child asleep as well as awake is needed
for the proper interpretation of neonatal EEG. A record made after feeding the baby is likely to succeed in this. The preparation for recording, like pasting of electrodes, can be done toward the end of the wake period so as to ensure that the neonate is not disturbed during sleep. The registration time should be 45 minutes or longer. Abnormal or absent sleep-wake cycling is sometimes the earliest indicator of brain dysfunction, and in such situations, it is required to record the EEG for a longer period (at least two to three hours).

Adequate skin preparation is required to achieve a scalp impedance of <5 kΩ. Mildly abrasive pastes (like NuPrep™ gel) applied using a cotton bud, followed by alcohol swabs generally give a good result. Enough time (at least 90 minutes) has to be scheduled for the EEG recording to avoid stressing the technician and the parents. This is preferable to registering an artifact-filled EEG, and later trying to minimize their influence, for instance by changing the filter settings.

Electrodes and montages

At our center, we use the full 10–20 system of electrodes for all neonatal EEGs done during working hours and the restricted system of electrode placement during emergency EEGs done outside the working hours. The restricted 10–20 system of electrode placement uses nine active scalp electrodes – Fp1, Fp2, Cz, C3, C4, T3, T4, O1, and O2 electrodes. Important spatial information is lost by using lesser number of electrodes. However, most clinical indications for an emergent EEG at this age do not call for a high degree of spatial resolution. Assessment of background activity is not affected by the reduced number of electrodes. The reduced montage has been shown to have a high sensitivity (96.8%) and 100% specificity when compared to a full 10–20 montage in detection of neonatal seizures. Silver–silver chloride EEG electrodes with conductive adhesive electrode paste (like 10–20™ paste) are used. In addition, at our center, we prefer using 3% collodion with small pieces of cotton or gauze for optimal
fixation of the electrodes. This gives a better quality registration and also ensures that there is no deterioration of electrode contact if the recording has to be extended to continuous EEG monitoring. In a period of more than 25 years of using this method, we have not encountered any allergic skin reactions or hazards due to flammability. Compressed cold air is used for drying. Fire hazard due to the flammable collodion has to be borne in mind, and a hair dryer should never be used. Removal of the electrodes is done using an acetone-free solvent (we use collodion-remover from Mavidon™ Medical Products). Acetone works equally well, but its fumes are quite irritating. We use the same technique in a baby lying in an incubator. However, the incubator is kept open for sometime after fixing the electrodes.

Many EEG transients have a preponderance at the vertex, and hence, inclusion of the Cz electrode as well as a coronal bipolar electrode derivation in addition to the bipolar anteroposterior derivation is meaningful. With digital EEG equipment, montage selection during registration of EEG is no longer very important.

**Electrode caps**

They help to save time, especially when a full 10–20 system of electrodes, or a more extensive recording (e.g., high-density EEG) has to be made. They also help to keep the electrode positions fairly accurate, especially in centers where there are no experienced technicians. The quality of the record depends on a snug fit, and thus, a wide range of cap sizes fitting different head sizes would have to be available. The electrode positions may show some change over time and with repeated use, much more than with conventional electrode application.

**Filters**

Very slow waves (0.2–0.5 Hz) occur in the neonate and hence the low-frequency filter is set at 0.005–0.01 Hz. This very low filter setting may make the EEG more vulnerable to slow artifacts like sweat potentials. The high-frequency filter is set at 70 Hz.
Polygraphy

Polygraphic registrations are the rule while recording neonatal EEG. Simultaneous recording of video is also becoming a standard practice. Video helps in assessing clinical seizures and in recognizing artifacts. Physiological variables like eye movements, ECG, breathing pattern, and muscle activity maximize information about different stages of arousal or sleep, as well as paroxysmal phenomena like seizures. Eye movements [EOG channel] are recorded using two surface electrodes, placed diagonally, one centimeter above and below the outer canthus of the left and right eyes. Muscle tone is registered using a surface electrode placed over the submental region (chin EMG). ECG is recorded by two electrodes kept over the right and left side of the anterior chest wall. Another option is to place these electrodes over the right and left arms, in which case they can, in addition to the ECG, also record the limb movements. Extra channels for registering movements (transducers or surface EEG electrodes) may be added, for instance in the presence of clonic movements, tremor, hiccups, etc. Respiration is monitored by a transducer kept over the abdomen or the chest. Cessation of breathing for 6-7 seconds may be normally seen in neonates and are considered to be pathological apneas meriting treatment only if they last longer than 10 seconds or occur frequently, or are associated with hemodynamic disturbances (like bradycardia or desaturations). Healthy premature infants may show short apneas as well as episodes of periodic breathing. Other polygraphic variables like nasal airflow (measured using a thermocouple) and oxygen saturation (pulse oximetry), if available, may add important information.

Reactivity

Transient attenuation of the EEG to external stimuli should be noted by the technician. Photic stimulation usually does not elicit photic driving in the term neonate and hence need not be done as a routine. However, in the premature infant, a striking
photic driving may sometimes be observed, especially with lower flash frequencies.

**EEG MONITORING IN NEONATAL EPILEPSIES**

Electroencephalographers often approach neonatal studies with trepidation. Neonatal studies vary from traditional electroencephalograms (EEGs) in both technical and visual aspects. Half of the full electrode set is used, placed at double distance, and the recording lasts for 60 minutes in order to catch a full sleep-wake cycle.

Extra electrodes are also essential for interpreting the recording, such as ocular leads, chin electromyogram (EMG), and cardiac and respiratory monitoring. When interpreting the neonatal EEG, the paper speed is slowed to 15 mm/sec in order to more easily recognize the slower delta frequencies, which dominate in neonatal records.

The low-frequency filter is set to 0.5 Hz in order to clearly interpret slow eye movements. Sensitivity is often lowered below the standard 7 mv/sec, given that amplitudes are not as high and scalp impedance is lower. Although these differences exist, with experience and knowledge of these EEG differences, interpretation in this age group is readily accomplished.

Much of the trepidation associated with the interpretation of neonatal EEG stems from the fact that “normal” background is somewhat of a moving target.

Findings that are acceptable at 30 weeks conceptional age (CA) are grossly abnormal at 36 weeks.

Therefore, neonatal EEG is best interpreted by first noting the infant’s current CA and then recognizing the characteristics that should be present in the EEG background of a normal neonate. CA is calculated by adding the estimated gestational age at birth to the current chronologic age (in weeks). If not given the correct gestational age, an age range can be estimated based on recognized patterns.
Neonatal EEG Background

Neonatal EEG studies should be systematically evaluated, with interpretation phrased in terms of several key features:

- Continuity
- Amplitude
- Symmetry
- Interhemispheric synchrony
- Normal named patterns

In extreme prematurity, normal electrographic findings are typically discontinuous, with bursts of continuous cerebral activity separated by intervals of relative quiescence and lower amplitude. This discontinuity improves with age, with the interburst interval becoming progressively shorter and higher in amplitude as the baby approaches full term. By 40 to 44 weeks CA, the EEG background becomes continuous in both wake and sleep.

Differentiation between wake and sleep states initially appears around 30 weeks CA. By definition, the infant is awake whenever his/her eyes are open and asleep when eyes are closed. Sleep is further subdivided into active sleep (AS, characterized by irregular respirations, occasional limb movements, and rapid horizontal eye movements) and quiet sleep (QS), characterized by deep, regular respirations and paucity of limb/trunk movement. Electrographically, wakefulness and AS in infants more than 30 weeks CA demonstrate fairly continuous cerebral activity, developing into a characteristic mixed frequency, moderate-amplitude activité moyenne pattern.

Because neonatal background abnormalities may become most apparent during deeper sleep stages, a complete assessment of the EEG background requires thorough evaluation of QS. To this end, continuous EEG (cEEG) provides a significant advantage over routine EEG in ensuring that a generous sample of QS is captured for review. As the invariant, nonreactive pattern of burst suppression seen in extremely preterm infants transitions into more defined wake-sleep stages around 30 weeks CA, the
final remnants of EEG discontinuity linger in QS. As development proceeds, QS discontinuity gradually resolves, with gradual improvement in the duration and amplitude of the interburst activity.

Between 30 and 32 weeks CA, QS activity consists of a tracé discontinuité pattern in which periods of cerebral activity are separated by nearly isoelectric periods of quiescence with voltage less than 25 µV.

With time, the voltage of the interburst intervals gradually increases such that by 35 to 36 weeks CA, QS typically transitions to a tracé alternant pattern, in which cerebral activity is consistently maintained above 25 µV but cycles between higher-amplitude bursts and more quiescent periods.

The interburst amplitude continues to increase until no periods of relative quiescence are perceived, and a continuous slow-wave sleep pattern is fully established around 44 weeks CA.

Bursts of activity appearing in one hemisphere within 1.5 seconds of the other hemisphere are considered to be synchronous. Prior to 30 weeks CA, cerebral activity occurs nearly simultaneously in both the right and left hemispheres, a phenomenon described as a hypersynchrony.

The reason for early interhemispheric hypersynchrony is unknown, though it has been postulated to be related to prominent thalamic drivers without significant cortical input. Following 30 weeks, occasional asynchronous bursts are seen, which progressively diminish until 100% synchrony is reestablished around 37 weeks CA.

**Background Patterns**

A. Excessive sharps
B. Excessive discontinuity
C. Brief ictal/interictal rhythmic/repetitive discharges (BIRDs)
D. Other patterns (depressed/undifferentiated, low voltage)
EEG background findings are also frequently employed to assess the functional integrity of the neonatal brain and to aid in the evaluation of neurologic prognosis. At the same time, however, many patterns are nonspecific and of uncertain clinical significance.

**TABLE: EEG Background in Prematurity**

<table>
<thead>
<tr>
<th>Conceptional Age (Weeks)</th>
<th>Maximum Interburst Duration (Sec)</th>
<th>EEG Background Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>24–25</td>
<td>60</td>
<td>No sleep organization or reactivity</td>
</tr>
<tr>
<td>27–30</td>
<td>35</td>
<td>Discontinuous in both wake and sleep, some reactivity</td>
</tr>
<tr>
<td>31–33</td>
<td>20</td>
<td>Differentiation between active and quiet sleep patternsWake and active sleep: mixed frequency continuous (<em>activité moyenne</em>)Quiet sleep: interburst intervals amplitude nearly isoelectric, &lt;25 µV (trace discontinue pattern)</td>
</tr>
<tr>
<td>34–36</td>
<td>10</td>
<td>Wake and active sleep: mixed frequency continuous (<em>activité moyenne</em>)Quiet sleep: Interburst intervals increase in amplitude, eventually exceeding 25 µV (trace alternant pattern)</td>
</tr>
<tr>
<td>37–40</td>
<td>6</td>
<td>Wake and active sleep: mixed frequency continuous (<em>activité moyenne</em>)Quiet sleep: Interburst intervals continue to increase in amplitude, increasing continuity (trace alternant) transitioning to continuous slow-wave sleep pattern</td>
</tr>
</tbody>
</table>
Excessive Sharps

Temporal sharp transients are normally seen during sleep in the term neonate, are often bilateral and asynchronous, and should be surface negative in polarity. If they occur in runs, are unilateral, or appear in wakefulness, they are more likely to be considered abnormal. Sharp waves occurring outside of the temporal or centrotemporal regions would also be considered abnormal. No official criteria exist in which temporal sharps are defined as excessive, and it has been proposed that greater than 13 over the course of a 60-minute recording in a term neonate would be considered excessive.

Excessive Discontinuity

In the term neonate, periods of attenuation during QS should not exceed 2 to 4 seconds in duration. Interburst intervals longer than this are considered excessively discontinuous. This pattern can be associated with dysmaturity or incorrect gestational dating but can also be a nonspecific marker for neonatal encephalopathy.

Brief Ictal/Interictal Rhythmic/Repetitive Discharges

First described by Shewmon in 1990, this pattern is considered interictal but on the ictal spectrum. It usually occurs in the context of electrographic seizures and is characterized by a run of epileptiform discharges with evolution but lasting less than 10 seconds. Their clinical significance is not yet completely understood, but given their presence in neonates with seizures, they may be associated with neurologic morbidity.

Depressed/Undifferentiated or Low Voltage

A depressed and undifferentiated pattern is most commonly associated with severe underlying neurologic injury to the cortical generators of electrocerebral activity. Low voltage is considered to be background activity persistently less than 10 µV without normal background features. The recording will also show poor reactivity, no alteration in frequencies with external stimulation, and no sleep-wake cycling.
SEIZURE DETECTION

Seizure is the most common neurologic disorder in the neonatal period. There are numerous potential etiologies for neonatal seizures, and timing of presentation as well as electrographic findings can be of potential use in elucidating their etiology. Seizures can be transient due to an acute injury, markers of an underlying genetic or metabolic disorder, or signs of an underlying structural abnormality.

![EEG Monitoring in Neonatal Epilepsies](image.png)

**FIGURE**: A 38-week-old baby boy born via emergency Caesarean-section (C-section) for polyhydramnios and nonreassuring fetal heart tracings with severe hypoxic-ischemic encephalopathy. Background shows low voltage (<10 µV) without reactivity.

EEG evaluation and confirmation of seizure activity is particularly important in the neonatal population, given the high rate of subclinical or subtly clinical seizures and because newborns may often have unusual movements that can be mistaken for seizure activity. For instance, a systematic video review of 526 electrographic seizures in nine infants revealed that only 34% of seizures were associated with clinical manifestations, and only 27% of these clinical seizures (9% of overall seizures) were
recognized by nursing staff. Of more concern, 73% of “seizures” documented by the neonatal intensive care unit (NICU) nursing staff were not epileptic seizures. Rather, the events marked by NICU nursing were not epileptic in nature. Instead, these movements commonly consisted of likely nonepileptic events such as jitteriness, mouthing, and fisting. Therefore neonatal seizure quantification solely by clinical observation is plagued by both high false-positive and high false-negative rates. To ensure an accurate assessment of seizure detection and treatment response, EEG monitoring is essential.

**Subclinical Seizures**

EEG confirmation of seizure cessation following anticonvulsant treatment is also recommended. Neonates are particularly vulnerable to the phenomenon of electroclinical uncoupling, in which clinical evidence of seizure activity ceases, following the administration of seizure medications, while subclinical electrographic seizure activity continues unabated. Although subclinical seizures are known to occur in critically ill children and adults, features of chloride homeostasis unique to the immature brain contribute to a high likelihood of electroclinical uncoupling.

The potassium-chloride cotransporter (KCC2), which is the predominant type of chloride channel in the adult brain, transport chloride ions outside of neurons and have a hyperpolarizing effect. In contrast, the predominant chloride channel in the immature brain is the sodium-potassium-chloride cotransporter (NKCC1), which transports chloride ions into neurons and has a depolarizing effect. Gamma aminobutyric acid (GABA), a neurotransmitter that activates chloride channels, can therefore have a paradoxically excitatory effect in developing neurons due to the predominance of NKCC1 channels. Because the transition from NKCC1 to KCC2 chloride channels occurs in a caudal-to-rostral progression, GABA initially becomes inhibitory in subcortical structures such as the brainstem and basal ganglia.
while remaining excitatory in the cortex. Commonly used medications such as phenobarbital, which exert their effects through GABA agonist activity, may therefore suppress brainstem motor output, while allowing electrographic seizure activity to continue in the cortex.

The high risk of subclinical seizures has been well documented in the NICU population. For instance, cEEG monitoring of neonates randomized to initial treatment with either phenobarbital or phenytoin demonstrated that while 24 of 50 infants responded completely to the first seizure medication administered, 15 of the remaining 26 neonates (58%) demonstrated electroclinical uncoupling, with suppression of clinical seizure activity during all or the majority of posttreatment electrographic seizures.

**Neonatal Seizure Semiology**

Seizure semiology in the newborn is variable but can be grouped into the following categories: clonic, tonic, and myoclonic. These are focal, repetitive, and cannot be suppressed by the examiner. Due to incomplete myelination, infants cannot generate generalized tonic-clonic seizures, but they can have multifocal seizures that can appear generalized to the untrained or inexperienced examiner. Infants can also have generalized epileptic spasms that are hypothesized to be more subcortically driven.

Because infants often have repetitive movements which can be difficult to interpret, EEG is often relied upon to distinguish stereotyped or rhythmic movements as epileptic or nonepileptic. Oral automatisms, bicycling, roving eye movements, and other nonrhythmic but repetitive movements are often seen in critically ill infants. Without clear electrographic correlate, these had been previously termed clinical only seizures, but are now more commonly presumed to be nonepileptic in nature. These movements tend to occur more often in encephalopathic infants and are also associated with poor prognosis.
Clinical Neurophysiology in Pediatrics

Table: Neonatal Seizure Types

<table>
<thead>
<tr>
<th>Movement Type</th>
<th>Localization/ Clinical Correlate</th>
<th>Electrographic Correlate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonic</td>
<td>Focal rhythmic jerking of an extremity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-suppressible</td>
<td>Yes</td>
</tr>
<tr>
<td>Tonic</td>
<td>Focal sustained extension or flexion of an extremity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not able to overcome with external manipulation</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Sustained extension of the whole body</td>
<td>Not usually</td>
</tr>
<tr>
<td>Myoclonic</td>
<td>Single jerk or multiple nonrhythmic jerks of an extremity</td>
<td>Usually</td>
</tr>
<tr>
<td>Spasms</td>
<td>Focal or generalized flexor, extensor, or mixed flexor-extensor</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Role of Amplitude-Integrated EEG

The use of amplitude-integrated EEG (aiEEG) is now growing in the NICU, because it offers an opportunity for continuous monitoring of cerebral activity in a manner that can be interpreted at the bedside by the neonatologist rather than requiring a certified electroencephalographer. With the growing use of therapeutic hypothermia for hypoxic-ischemic encephalopathy (HIE) in the NICU, aiEEG has become more widely used concurrently in monitoring for seizures and change in background activity.

aiEEG differs from conventional EEG in that it involves the use of only four electrodes and relies on the trending of voltage and comparison between the two hemispheres. The timescale is also broader, with the evaluation of 8 to 12 hours of data on one screen, as opposed to 20 to 30 seconds per screen of a conventional EEG.

Background activity on conventional EEG can be assessed using continuity, amplitude, and symmetry, all of which can also be assessed on aiEEG in a different manner. Interburst interval
cannot be precisely interpreted with this method, but voltage over time is averaged in order to give a range of activity, which can then be interpreted.

This is tightly linked to amplitude, where the peak-to-peak interval of minimum and maximum voltage ranges is represented as bandwidth. If the minimum voltages are consistently less than 5 µV and maximum less than 10 µV, this is considered a low-voltage, suppressed background. Normal activity is considered to be a minimum voltage of greater than 5 µV and maximum voltage greater than 10 µV.

Seizures are detected on aiEEG as a relative increase in overall amplitude over a given period of time. These can be detected by relative increases of the peak-to-peak amplitude with narrow bandwidth. Some indication of localization can be inferred if this occurs only in one hemisphere. Overall seizure burden can also be inferred, based on the number of peaks of increased voltage peaks.

However, a limitation of condensing this data and relying on voltage alone is that aiEEG can be ripe with artifact. When the baby is handled and high-amplitude electrode artifact is generated, this will appear as an amplitude spike on aiEEG.

Similarly, when continuous external artifacts such as EKG rhythm occur in the setting of a low-voltage, suppressed background, this can be misrepresented as a normal voltage range on aiEEG.

aiEEG has been shown in studies to be sensitive, but not very specific for the identification of an abnormal background and seizures. Regardless, given the ease of use, the widespread availability, and the ability for bedside interpretation, aiEEG has now become part of the standard of care during therapeutic hypothermia for HIE of the newborn. Studies have shown that the use of aiEEG may even be beneficial in that neonates are being treated for seizures only with electrographic confirmation, rather than purely on a clinical basis.
TRANSIENT OR “BENIGN” NEONATAL SEIZURES

Hypoxic-Ischemic Encephalopathy

HIE is the leading cause of seizures in the neonatal period, with an incidence of 2 to 5 per 1,000 live births. Seizures have been found in up to 80% of this population, but this may be an underestimation, given that continuous EEG monitoring is not routinely used. aiEEG is often used in the NICU to fulfill the need for continuous electrographic monitoring.

Therapeutic hypothermia has also become the standard of care in the treatment of infants with HIE and has been shown to improve neurodevelopmental background. Evaluation of background activity can be useful for prognostication in infants with HIE. Persistently abnormal background activity without evidence of improvement over time is more likely to be associated with a worse neurodevelopmental outcome. A normal background or improvement in background is less likely to be associated with poor neurodevelopmental outcome.

Recent studies have shown a high incidence of seizures in infants undergoing therapeutic hypothermia for HIE, up to 40% to 60%, with 35% to 75% of these being subclinical. The burden of seizures is highest in the first 24 to 48 hours, with a natural decline after 72 hours. It is presumed that a higher burden of seizures is associated with worse neurodevelopmental outcome; however, this is a topic of much debate, as infants with more severe HIE are also likely to have more refractory seizures. Additionally despite advances in antiepileptic drug development, relatively few advances have been made in the treatment of seizures due to HIE, and many treatments also have potential unwanted side effects in the developing brain.

Benign Familial Neonatal Convulsions

Benign familial neonatal convulsions are often seen around the fifth day of life, giving them the frequently used descriptive term of “fifth day fits.” Most are associated with a mutation in
EEG Monitoring in Neonatal Epilepsies

the KCNQ2 gene coding for a voltage-gated potassium channel, which has autosomal transmission, but other potassium channels as well as the sodium channel, such as SCN2A mutation, have also been implicated.

There is often a family history of neonatal seizures, and the electrographic background is frequently normal but can show excessive discontinuity and excessive sharp transients.

These were initially termed benign because there was thought to be no long-term consequence, although recent studies have shown that this is not always the case. KCNQ2 mutations have also been associated with Ohtahara syndrome, and the phenotype can be variable, with seizures persisting well beyond the neonatal period.

**Stroke**

Perinatal stroke is also a common cause of neurologic morbidity in the newborn period. The majority are arterial ischemic, although at least 30% can be venous in nature. Seizures are a common presentation of neonatal arterial ischemic stroke; up to 72% present with seizures. In a neonate with persistently unilateral seizures, arterial ischemic stroke should be strongly considered as an etiology and neuroimaging should be undertaken.

**Hypoglycemia and Other Reversible Causes**

Neonatal hypoglycemia is a frequent complication of infants of mothers with gestational diabetes, but can also be seen in well neonates with poor feeding. The occipital lobes are particularly at risk because of the high metabolic demand of the visual cortex. Persistent focal seizures can be seen emanating from either posterior quadrant. Imaging can show diffusion restriction in the areas affected, partly due to frequent seizures and increased local metabolism and partly due to watershed ischemia. These areas can later undergo laminar necrosis and develop the appearance of ulegyria.
Clinical Neurophysiology in Pediatrics

FIGURE: A 41+1-week-old baby boy with hypoxic-ischemic encephalopathy and meconium aspiration syndrome on selective hypothermia therapy, with seizures starting on the first day of life. This recording shows a seizure starting at T4.

Other electrolyte and metabolic disturbances can also precipitate seizures in the neonatal period, similar to adults. Hypomagnesemia, hypocalcemia, hyponatremia, and hyperbilirubinemia can also lead to neonatal seizures. In these
instances, correction of the underlying etiology is necessary to effectively treat the seizures.

CATASTROPHIC EPILEPTIC ENCEPHALOPATHIES

There are several conditions presenting in the neonatal period which have been termed “catastrophic,” in that they are associated with frequent seizures and severe interictal background abnormalities which, without prompt remedy, almost inevitably result in poor neurodevelopmental outcome.

Ohtahara Syndrome

Ohtahara syndrome, also known as early infantile epileptic encephalopathy with suppression-burst presents in early infancy. Initial symptoms are seen within the first 3 months, frequently within the first 2 weeks. Clinically this presents with brief (less than 10 seconds) tonic spasms (generalized or focal), which occur independently or in clusters. Other seizure types including focal seizures, hemiconvulsions, or tonic-clonic seizures are seen in approximately 33%. Most cases are related to a variety of structural brain lesions, although metabolic and genetic disorders have been reported. Mutations associated include syntaxin binding protein 1 (STXBP1), Aristaless-related homeobox (ARX), sodium channel SCN2A, and KCNQ2.

The typical EEG pattern is a consistent (wake and sleep) “suppression-burst” pattern with periods of diffuse amplitude suppression alternating with bursts of high amplitude spike and polyspike discharges.

Diagnosis of Ohtahara syndrome is based on the clinical picture and EEG findings. The prognosis is poor, with many affected children dying in infancy. Survivors have developmental impairment and many have chronic seizures or evolve into Lennox-Gastaut or West syndrome. Anti-seizure medications are used; however, there is no specific evidence-based therapy known. Surgery has been performed for cases with clear focal lesions.
### TABLE: Neonatal Epilepsy Syndromes

<table>
<thead>
<tr>
<th>Epilepsy Syndrome</th>
<th>Interictal EEG Background</th>
<th>Seizure Types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ohtahara syndrome</td>
<td>Burst-suppression (wake and sleep)</td>
<td>Tonic spasms Focal Tonic-clonic</td>
</tr>
<tr>
<td>Early myoclonic epilepsy of infancy</td>
<td>Burst-suppression (more prominent in sleep)</td>
<td>Multifocal myoclonic</td>
</tr>
<tr>
<td>Malignant migrating partial seizures of infancy</td>
<td>Multifocal sharps</td>
<td>Focal, arising from multiple regions</td>
</tr>
<tr>
<td>Pyridoxine-dependent epilepsy</td>
<td>Continuous spike-wave Burst suppression</td>
<td>Infantile spasms Multifocal myoclonic Focal Tonic</td>
</tr>
</tbody>
</table>

### Early Myoclonic Epilepsy of Infancy

Early myoclonic epilepsy of infancy (EMEI) was described shortly after Ohtahara syndrome and there are a number of similarities between them. EMEI also begins within the first 3 years, although it can present as early as a few hours after birth. Clinically this begins with focal myoclonus that can shift between different body parts often in an asynchronous and random pattern. A wide range of focal seizures (anything from tonic posturing to autonomic signs) is very common and tonic spasms are also seen. There is a range of underlying disorders associated with EMEI including structural lesions and metabolic and genetic abnormalities. In contrast to Ohtahara syndrome, diffuse cortical atrophy, rather than focal structural lesions, is typically seen. A variety of metabolic abnormalities have been associated, in particular, nonketotic hyperglycinemia. Mutation of the v-erb-a erythroblastic leukemia viral oncogene homologue 4 (ErbB4), which is associated with cortical migration, is also related.

The typical EEG pattern of EMEI is similar to the suppression-burst pattern seen in Ohtahara syndrome; however, in EMEI the suppression-burst pattern is not continuous and occurs more
prominently (or exclusively) in sleep. The myoclonic seizures are not generally associated with changes on the EEG.

EMEI is also diagnosed clinically and treated with antiseizure medications. Additionally, treatment of the underlying metabolic disorder may be helpful. The prognosis of EMEI is also very poor, with 50% of patients dying by 3 years and the survivors having severe developmental impairment.

**Malignant Migrating Partial Seizures of Infancy**

Malignant migrating partial seizures of infancy (MMPSIs) present in the first 6 months of life with multifocal, bilateral, independent seizures. Seizures are very difficult to control and are associated with progressive developmental impairment and a decrease in the head circumference. The underlying etiology is unknown; however, it is likely genetic. Mutations have been found in a number of genes including $\text{SCN1A}$, phospholipase C beta 1 ($\text{PLCB1}$), $\text{KCNT1}$, and $\text{TBC1D24}$.

The ictal EEG shows focal seizures initiating from different locations in both hemispheres that “migrate” from one area to another.

MMPSI is diagnosed by clinical presentation along with the typical EEG pattern and has a poor prognosis. Status epilepticus is common and may be related to patients dying in the first 2 years of life.

**OTHER EPILEPSY SYNDROMES PRESENTING IN NEONATES**

Hemimegalencephaly (HME) is a severe developmental brain anomaly characterized by the overgrowth of one hemisphere. This is associated with epilepsy, psychomotor retardation, and contralateral motor defect. Seizure types include focal motor seizures, asymmetric tonic or clonic seizures, and epileptic spasms. HME is one of the causes of Ohtahara syndrome and West syndrome and is associated with a variety of genetic abnormalities and neurocutaneous syndromes; however, it may
be an isolated syndrome. Patients with West syndrome associated with HME may have a unique EEG background called hemihypsarrhythmia (high amplitude, poorly organized with multifocal spikes over the affected side only).

Diagnosis of HME is based on imaging including asymmetry of the hemispheres and ventricles, loss of gray-white differentiation, neuronal heterotopia, thick cortex, and abnormalities in the gyri, basal ganglia, and internal capsule. The clinical course and prognosis is dependent on seizure control, the severity of the affected side, the ability of the contralateral side to compensate, and early surgery.

**Metabolic Epilepsies**

Pyridoxine-dependent epilepsy was first described by Hunt and colleagues in 1954. This syndrome is unique in that it is severe but treatable, and thus early recognition is of tantamount importance. This syndrome has an estimated birth incidence between 1:400,000 and 1:750,000. Seizures can be prenatal in onset and can include multiple seizure types, including infantile spasms and focal, multifocal myoclonic, and tonic seizures. There can also be an associated encephalopathy, which may manifest as tremulousness, irritability, or hypothermia. The baseline EEG will show a continuous spike-wave or burst-suppression pattern. Diagnosis is established by giving an intravenous dose of 100-mg pyridoxine during EEG monitoring, which will often lead to the resolution of epileptiform activity and improvement of the background. The response is often seen rapidly, although delayed responses have also been reported. Relapses can occur after a median of 9 days if pyridoxine therapy is withheld, and therefore patients need to remain on lifelong therapy.

Folinic acid-responsive seizures are another treatable cause of neonatal seizures. EEG background features and seizure types can be similar to pyridoxine-dependent seizures, and concurrent pyridoxine dependency can occur within individuals. Seizures respond to 2.5- to 5-mg folinic acid given twice daily, and daily
doses should be added for patients with an incomplete response to pyridoxine treatment.

**FIGURE:** (A) A 40+5–week-old baby boy who presented with “jitteriness” and episodes of flexor spasms 3 hours after birth. Initial background was discontinuous and asynchronous. (B) After pyridoxine administration, the background normalized, becoming synchronous and continuous.
Pediatric Febrile Seizures

A febrile seizure is a convulsion in a child that may be caused by a spike in body temperature, often from an infection. Your child’s having a febrile seizure can be alarming, and the few minutes it lasts can seem like an eternity.

Febrile seizures represent a unique response of a child’s brain to fever, usually the first day of a fever. Fortunately, they’re usually harmless and typically don’t indicate an ongoing problem. You can help by keeping your child safe during a febrile seizure and by comforting him or her afterward.

SYMPTOMS

Febrile seizure symptoms can range from mild — staring — to more severe shaking or tightening of the muscles.

A child having a febrile seizure may:
• Have a fever higher than 100.4 F (38.0 C)
• Lose consciousness
• Shake or jerk arms and legs

Febrile seizures are classified as simple or complex:
• Simple febrile seizures. This more common type lasts from a few seconds to 15 minutes. Simple febrile seizures do not recur within a 24-hour period and are generalized, not specific to one part of the body.
Pediatric Febrile Seizures

- Complex febrile seizures. This type lasts longer than 15 minutes, occurs more than once within 24 hours or is confined to one side of your child’s body.

Febrile seizures most often occur within 24 hours of the onset of a fever and can be the first sign that a child is ill.

When to see a doctor

See your child’s doctor as soon as possible after your child’s first febrile seizure, even if it lasts only a few seconds.

Call an ambulance to take your child to the emergency room if the seizure lasts longer than 10 minutes or is accompanied by:
- Vomiting
- A stiff neck
- Breathing problems
- Extreme sleepiness.

CAUSES

A high body temperature causes most febrile seizures.

Infection

Usually the fevers that trigger febrile seizures are caused by a viral infection, less commonly by a bacterial infection.

Viral infections such as the flu and roseola, which often are accompanied by high fever, appear to be most associated with febrile seizure.

Post-immunization seizures

The risk of febrile seizures may increase after some childhood immunizations, such as the diphtheria, tetanus and pertussis or measles-mumps-rubella vaccinations.

A child can develop a low-grade fever after a vaccination. The fever, not the vaccination, causes the seizure.
RISK FACTORS

Factors that increase the risk of having a febrile seizure include:

- Young age. Most febrile seizures occur in children between 6 months and 5 years of age. It’s unusual for children younger than 6 months to have a febrile seizure, and it’s rare for these seizures to occur after 3 years of age.
- Family history. Some children inherit a family’s tendency to have seizures with a fever. Additionally, researchers have linked several genes to a susceptibility to febrile seizures.

COMPLICATIONS

Most febrile seizures produce no lasting effects. Simple febrile seizures don’t cause brain damage, mental retardation or learning disabilities, and they don’t mean your child has a more serious underlying disorder. Febrile seizures don’t indicate epilepsy, a tendency to have recurrent seizures caused by abnormal electrical signals in the brain.

Recurrent febrile seizures

The most common complication is the possibility of more febrile seizures. The risk of recurrence is higher if:

- Your child’s first seizure resulted from a low fever.
- The period between the start of the fever and the seizure was short.
- An immediate family member has a history of febrile seizures.
- Your child was younger than 15 months at the time of the first febrile seizure.

ARE FEBRILE SEIZURES HARMFUL?

The vast majority of febrile seizures are short and do not cause any long-term damage. During a seizure, there is a small
chance that the child may be injured by falling or may choke on food or saliva in the mouth. Using proper first aid for seizures can help avoid these hazards.

There is no evidence that short febrile seizures cause brain damage. Large studies have found that even children with prolonged febrile seizures have normal school achievement and perform as well on intellectual tests as their siblings who do not have seizures. Even when the seizures last a long time, most children recover completely.

Multiple or prolonged seizures are a risk factor for epilepsy but most children who experience febrile seizures do not go on to develop the reoccurring seizures that are characteristic of epilepsy. Some children, including those with cerebral palsy, delayed development, or other neurological abnormalities as well as those with a family history of epilepsy are at increased risk of developing epilepsy whether or not they have febrile seizures. Febrile seizures may be more common in these children but do not contribute much to the overall risk of developing epilepsy.

Children who experience a brief, full body febrile seizure are slightly more likely to develop epilepsy than the general population. Children who have a febrile seizure that lasts longer than 10 minutes; a focal seizure (a seizure that starts on one side of the brain); or seizures that reoccur within 24 hours, have a moderately increased risk (about 10 percent) of developing epilepsy as compared to children who do not have febrile seizures.

Of greatest concern is the small group of children with very prolonged febrile seizures lasting longer than 30 minutes. In these children, the risk of epilepsy is as high as 30 to 40 percent though the condition may not occur for many years. Recent studies suggest that prolonged febrile seizures can injure the hippocampus, a brain structure involved with temporal lobe epilepsy (TLE).
How are febrile seizures evaluated?

Before diagnosing febrile seizures in infants and children, doctors sometimes perform tests to be sure that the seizures are not caused by an underlying or more serious health condition. For example, meningitis, an infection of the membranes surrounding the brain, can cause both fever and seizures that can look like febrile seizures but are much more serious. If a doctor suspects a child has meningitis a spinal tap may be needed to check for signs of the infection in the cerebrospinal fluid (fluid surrounding the brain and spinal cord). If there has been severe diarrhea or vomiting, dehydration could be responsible for seizures. Also, doctors often perform other tests such as examining the blood and urine to pinpoint the cause of the child’s fever.

If the seizure is either very prolonged or is accompanied by a serious infection, or if the child is younger than 6 months of age, the clinician may recommend hospitalization. In most cases, however, a child who has a febrile seizure usually will not need to be hospitalized.

Febrile seizures be prevente

Experts recommend that children who have experienced a febrile seizure not take any antiseizure medication to prevent future seizures, as the side effects of these daily medications outweigh any benefits. This is especially true since most febrile seizures are brief and harmless.

If a child has a fever, most parents will use fever-lowering drugs such as acetaminophen or ibuprofen to make the child more comfortable. However, available studies show this does not reduce the risk of having another febrile seizure.

Although the majority of children with febrile seizures do not need medication, children especially prone to febrile seizures may be treated with medication, such as diazepam, when they have a fever. This medication may lower the risk of having
another febrile seizure. It is usually well tolerated, although it occasionally can cause drowsiness, a lack of coordination, or hyperactivity. Children vary widely in their susceptibility to such side effects.

A child whose first febrile seizure is a prolonged one does not necessarily have a higher risk of having reoccurring prolonged seizures. But if the child has another seizure, it is likely to be prolonged. Because very long febrile seizures are associated with the potential for injury and an increased risk of developing epilepsy, some doctors may prescribe medication to these children to prevent prolonged seizures. The parents of children who have experienced a long febrile may wish to talk to their doctor about this treatment option.

**What research is being done on febrile seizures?**

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. The NINDS is a component of the National Institutes of Health (NIH), the leading supporter of biomedical research in the world.

Researchers are exploring the biological, environmental, and genetic risk factors that might make children susceptible to febrile seizures. They are also working to pinpoint factors that can help predict which children are likely to have reoccurring or prolonged febrile seizures.

Investigators continue to monitor the long-term impact that febrile seizures might have on intelligence, behavior, school achievement, and the development of epilepsy. For example, NINDS-funded scientists are assessing the effects of febrile seizures, especially very prolonged febrile seizures, on brain structures such as the hippocampus, an area of the brain that plays a role in memory and learning. They are also working to determine the impact of these seizures on the development of epilepsy and memory.
Children who have experienced prolonged febrile seizures are more likely to develop a particular type of epilepsy called temporal lobe epilepsy (TLE), which is often difficult to treat. TLE is associated with scarring of the hippocampus and usually presents in adolescents or young adults, some of whom have a history of long febrile seizures as young children. Scientists are trying to identify which children will go on to develop TLE in order to develop better treatments to prevent this condition. Investigators are also trying to develop drugs to prevent the occurrence of brain injury, epilepsy, and memory problems following prolonged febrile seizures.

**PRACTICE ESSENTIALS**

Pediatric febrile seizures, which represent the most common childhood seizure disorder, exist only in association with an elevated temperature. Evidence suggests, however, that they have little connection with cognitive function, so the prognosis for normal neurologic function is excellent in children with febrile seizures. Epidemiologic studies have led to the division of febrile seizures into 3 groups, as follows:

- Simple febrile seizures
- Complex febrile seizures
- Symptomatic febrile seizures

**Starting MMR/MMRV vaccination earlier may reduce seizure risk**

In a case-series analysis of a cohort of 323,247 US children born from 2004 to 2008, Hambidge et al found that delaying the first dose of measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) vaccine beyond the age of 15 months may more than double the risk of postvaccination seizures in the second year of life. In infants, there was no association between vaccination timing and postvaccination seizures. In the second year of life, however, the incident rate ratio (IRR) for seizures within 7-10 days was 2.65 (95% confidence interval [CI], 1.99-
Pediatric Febrile Seizures

3.55) after first MMR doses at 12-15 months of age, compared with 6.53 (95% CI, 3.15-13.53) after first MMR doses at 16-23 months.

For the MMRV vaccine, the IRR for seizures was 4.95 (95% CI, 3.68-6.66) after first doses at 12-15 months, compared with 9.80 (95% CI, 4.35-22.06) for first doses at 16-23 months.

Signs and symptoms

Simple febrile seizure:
• The setting is fever in a child aged 6 months to 5 years
• The single seizure is generalized and lasts less than 15 minutes
• The child is otherwise neurologically healthy and without neurologic abnormality by examination or by developmental history
• Fever (and seizure) is not caused by meningitis, encephalitis, or any other illness affecting the brain
• The seizure is described as either a generalized clonic or a generalized tonic-clonic seizure

Complex febrile seizure:
• Age, neurologic status before the illness, and fever are the same as for simple febrile seizure
• This seizure is either focal or prolonged (ie, >15 min), or multiple seizures occur in close succession

Symptomatic febrile seizure:
• Age and fever are the same as for simple febrile seizure
• The child has a preexisting neurologic abnormality or acute illness

Diagnosis

No specific laboratory studies are indicated for a simple febrile seizure. Physicians should instead focus on diagnosing the cause of fever. Other laboratory tests may be indicated by the nature of the underlying febrile illness. For example, a child
with severe diarrhea may benefit from blood studies for electrolytes.

With regard to lumbar puncture, the following should be kept in mind:

• Strongly consider lumbar puncture in children younger than 12 months, because the signs and symptoms of bacterial meningitis may be minimal or absent in this age group.
• Lumbar puncture should be considered in children aged 12-18 months, because clinical signs and symptoms of bacterial meningitis may be subtle in this age group.
• In children older than 18 months, the decision to perform lumbar puncture rests on the clinical suspicion of meningitis.

Management

On the basis of risk/benefit analysis, neither long-term nor intermittent anticonvulsant therapy is indicated for children who have experienced 1 or more simple febrile seizures.

If, however, preventing subsequent febrile seizures is essential, oral diazepam would be the treatment of choice. It can reduce the risk of febrile seizure recurrence and, because it is intermittent, probably has the fewest adverse effects.

FEBRILE SEIZURE OVERVIEW

Febrile seizures are convulsions that occur in a child who is between three months and six years of age and has a temperature greater than 100.4°F (38°C). The majority of febrile seizures occur in children between 12 and 18 months of age.

Febrile seizures occur in 2 to 4 percent of children younger than five years old. They can be frightening to watch, but do not cause brain damage or affect intelligence. Having a febrile seizure does not mean that a child has epilepsy; epilepsy is defined as having two or more seizures without fever present.
Causes Of Febrile Seizures

Infection — Febrile seizures can occur as a result of the fever that accompanies bacterial or viral infections, especially human herpesvirus-6 (also called roseola or sixth disease).

Immunizations — Fever can occur as a side effect of certain vaccines, particularly after measles mumps rubella (MMR) vaccination. The fever typically occurs 8 to 14 days after the injection.

Risk factors — A family history of febrile seizures increases a child’s risk of febrile seizures.

Febrile Seizure Symptoms

Febrile seizures usually occur on the first day of illness, and in some cases, the seizure is the first clue that the child is ill. Most seizures occur when the temperature is higher than 102.2°F (39°C). The table describes how to take a child’s temperature.

Febrile seizures are classified as being simple or complex.

Simple — Simple febrile seizures are the most common. Typically, the child loses consciousness and has a convulsion or rhythmic twitching of the arms or legs. Most seizures do not last more than one to two minutes, although they can last up to 15 minutes. After the seizure, the child may be confused or sleepy, but does not have arm or leg weakness.

Complex — Complex febrile seizures are less common and can last more than 15 minutes (or 30 minutes if in a series). The child may have temporary weakness of an arm or a leg after the seizure.

Febrile Seizure Evaluation And Treatment

A child who has a febrile seizure should be seen by a healthcare provider as soon as possible (in an emergency department or provider’s office) to determine the cause of the fever. Some children, particularly those less than 12 months of age, may require testing to ensure that the fever is not related
to meningitis, a serious infection of the lining of the brain. The best test for meningitis is a lumbar puncture (also known as a spinal tap), which involves inserting a needle into the low back to remove a small amount of fluid (cerebrospinal fluid or CSF) from around the spinal cord. Other tests may also be recommended.

Treatment for prolonged seizures usually involves giving an antiseizure medication and monitoring the child’s heart rate, blood pressure, and breathing. If the seizure stops on its own, antiseizure medication is not required. After a simple febrile seizure, most children do not need to stay in the hospital unless the seizure was caused by a serious infection requiring treatment in the hospital.

After the seizure has stopped, treatment for the fever is started, usually by giving oral or rectal acetaminophen or ibuprofen and sometimes by sponging with room temperature (not cold) water.

**Recurrent Febrile Seizure**

Children who have a febrile seizure are at risk for having another febrile seizure; this occurs in approximately 30 to 35 percent of cases. Recurrent febrile seizures do not necessarily occur at the same temperature as the first episode, and do not occur every time the child has a fever. Most recurrences occur within one year of the initial seizure and almost all occur within two years.

The risk of recurrent febrile seizures is higher for children who:

- Are young (less than 15 months)
- Have frequent fevers
- Have a parent or sibling who had febrile seizures or epilepsy
- Have a short time between the onset of fever and the seizure
- Had a low degree of fever before their seizure
Pediatric Febrile Seizures

Home treatment — Parents who witness their child’s febrile seizure should take a number of steps to prevent the child from harming him or herself.

• Place the child on their side but do not try to stop their movement or convulsions. Do not put anything in the child’s mouth.

• Keep an eye on a clock or watch. Seizures that last for more than five minutes require immediate treatment. One parent should stay with the child while another parent calls for emergency medical assistance, available by dialing 911 in most areas of the United States.

Parents of a child who is at risk of having a recurrent febrile seizure can be taught to give treatment at home for seizures that last longer than five minutes. Treatment usually involves giving one dose of diazepam gel (Diastat®) into the rectum. One dose is generally all that is required to stop a seizure.

Preventive treatment — In most cases, treatment to prevent future seizures is not recommended; the risks and potential side effects of daily antiseizure medications outweigh their benefit. In addition, giving medication (eg, acetaminophen or ibuprofen) to prevent fever is not recommended in a child without fever (eg, if the child has a cold but no fever) because it does not appear to reduce the risk of future febrile seizures.

Treatment for fever (temperature greater than 100.4°F or 38°C) is acceptable but not always required; parents should speak with their healthcare provider for help in deciding when to treat a child’s fever. A detailed discussion of fever in children is available separately.

Follow-up

Intelligence and other aspects of brain development do not appear to be affected by a febrile seizure, whether the seizure was simple, complex, or recurrent or whether it occurred in the setting of infection or after immunization.
Epilepsy occurs more frequently in children who have had febrile seizures. However, the risk that a child will develop epilepsy after a single, simple febrile seizure is only slightly higher than that of a child who never has a febrile seizure.

FEBRILE SEIZURES: RISKS, EVALUATION, AND PROGNOSIS

Febrile seizures are common in the first five years of life, and many factors that increase seizure risk have been identified. Initial evaluation should determine whether features of a complex seizure are present and identify the source of fever. Routine blood tests, neuroimaging, and electroencephalography are not recommended, and lumbar puncture is no longer recommended in patients with uncomplicated febrile seizures. In the unusual case of febrile status epilepticus, intravenous lorazepam and buccal midazolam are first-line agents. After an initial febrile seizure, physicians should reassure parents about the low risk of long-term effects, including neurologic sequelae, epilepsy, and death. However, there is a 15 to 70 percent risk of recurrence in the first two years after an initial febrile seizure. This risk is increased in patients younger than 18 months and those with a lower fever, short duration of fever before seizure onset, or a family history of febrile seizures. Continuous or intermittent antiepileptic or antipyretic medication is not recommended for the prevention of recurrent febrile seizures.

Febrile seizures are the most common seizures of childhood, occurring in 2 to 5 percent of children six months to five years of age. As defined by the American Academy of Pediatrics (AAP), febrile seizures occur in the absence of intracranial infection, metabolic disturbance, or history of afebrile seizures, and are classified as simple or complex. Simple febrile seizures represent 65 to 90 percent of febrile seizures and require all of the following features: a duration of less than 15 minutes, generalized in nature, a single occurrence in a 24-hour period, and no previous neurologic problems.
### Key Recommendations For Practice

<table>
<thead>
<tr>
<th>Clinical recommendation</th>
<th>Evidence rating</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routine laboratory tests, electroencephalography, and neuroimaging are not recommended in patients with simple febrile seizures.</td>
<td>C</td>
<td>Consensus guideline and retrospective cohort studies</td>
</tr>
<tr>
<td>Parents should be reassured after a simple febrile seizure that there is no negative impact on intellect or behavior, and no increased risk of death.</td>
<td>B</td>
<td>Consensus guideline and prospective cohort studies</td>
</tr>
<tr>
<td>Use of long-term continuous or intermittent antiepileptic medication after a first simple febrile seizure is not recommended because of potential adverse effects.</td>
<td>B</td>
<td>Consensus guideline and randomized controlled trials</td>
</tr>
<tr>
<td>Use of antipyretic agents at the onset of fever is not effective at reducing simple febrile seizure recurrence.</td>
<td>A</td>
<td>Consensus guideline and randomized controlled trial</td>
</tr>
</tbody>
</table>

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series.

### Classification of Febrile Seizures

Simple (all of the following)
- Duration of less than 15 minutes
- Generalized
- No previous neurologic problems
- Occur once in 24 hours

Complex (any of the following)
- Duration of more than 15 minutes
- Focal
- Recurs within 24 hours
Risk Factors

Risk factors for febrile seizures include developmental delay, discharge from a neonatal unit after 28 days, day care attendance, viral infections, a family history of febrile seizures, certain vaccinations, and possibly iron and zinc deficiencies. Febrile seizures may occur before or soon after the onset of fever, with the likelihood of seizure increasing with the child’s temperature and not with the rate of temperature rise.

Vaccinations associated with increased risk include 2010 Southern Hemisphere seasonal influenza trivalent inactivated vaccine (Fluvax Junior and Fluvax); diphtheria and tetanus toxoids and whole-cell pertussis (DTP); and measles, mumps, and rubella (MMR). A Cochrane review and a review of 530,000 children receiving the MMR vaccine showed that the risk of febrile seizures increased only during the first two weeks after vaccination, was small (an additional one or two febrile seizures per 1,000 vaccinations), and was likely related to fever from the vaccine.

A genetic predisposition for febrile seizures has been postulated, although no susceptibility gene has been identified. Genetic abnormalities have been reported in persons with febrile epilepsy syndromes, such as severe myoclonic epilepsy in infancy and generalized epilepsy with febrile seizures plus (GEFS+). Most causes of febrile seizures are multifactorial, with two or more genetic and contributing environmental factors.

Case-control studies suggest that iron and zinc deficiencies may also be risk factors for febrile seizures. One study of febrile seizures in Indian children three months to five years of age showed lower serum zinc levels in patients with seizures compared with age-matched febrile patients without seizures. In another study, children with febrile seizures had nearly two times the incidence of iron deficiency compared with febrile children who did not have seizures.

Viral infections are a common cause of fever that triggers febrile seizures. A particular risk for febrile seizure is associated
with primary human herpesvirus 6 infection, which is typically acquired during the first two years of life. In a case-control study, polymerase chain reaction testing and antibody titers suggested that 10 of 55 children (18 percent) who experienced a first febrile seizure had acute herpesvirus 6 infection, whereas none of the 85 children with fever but no seizure had evidence of such infection. Other common viral infections, such as influenza, adenovirus, and parainfluenza, are associated with simple and complex febrile seizures.

**Evaluation**

Children should be promptly evaluated after an initial seizure. Most patients with febrile seizures present for medical care after resolution of the seizure and return to full alertness within an hour of the seizure. The initial evaluation should focus on determining the source of the fever. Parents should be questioned about a family history of febrile seizures or epilepsy, immunizations, recent antibiotic use, duration of the seizure, a prolonged postictal phase, and any focal symptoms. During the examination, attention should be given to the presence of meningeal signs and to the child’s level of consciousness. In a 20-year retrospective review of 526 cases of bacterial meningitis, 93 percent of patients presented with altered consciousness.

Routine laboratory studies in patients with simple febrile seizures are discouraged because electrolyte abnormalities and serious bacterial illnesses are rare. In a retrospective review of 379 children with simple febrile seizures, only eight were found to have bacteremia. Streptococcus pneumoniae was isolated in seven of the eight children, in an era before routine pneumococcal vaccination.

The AAP recently updated its 1996 guideline regarding the use of lumbar puncture in children with simple febrile seizures. A lumbar puncture is now an option when evaluating children six to 12 months of age whose immunization status for Haemophilus influenzae type b and S. pneumoniae is incomplete.
or unknown, and in those pretreated with antibiotics. This differs from the previous recommendation that lumbar puncture be performed in all children younger than 12 months and strongly considered in those 12 to 18 months of age. Currently, as in the previous guideline, a lumbar puncture is strongly recommended in those with meningeal signs and in those with any other findings from the history or physical examination that are concerning for intracranial infection.

The AAP’s updated recommendations are supported by evidence from observational studies, as well as two reviews. In the 20-year retrospective review mentioned previously, no patients with bacterial meningitis presented with only fever and seizure.

In a more recent review of 704 patients with simple febrile seizures and no other findings concerning for bacterial meningitis, no cases of meningitis were identified. A second study reviewed 526 cases of complex febrile seizures and found only three cases of bacterial meningitis. Of these, one patient was unresponsive at presentation, and another had clear indications for lumbar puncture based on physical findings. The third was treated for bacterial meningitis after she had a negative lumbar puncture in the presence of S. pneumoniae bacteremia.

Electroencephalography has not been shown to predict recurrence of febrile seizures or future epilepsy in patients with simple febrile seizures. Routine neuroimaging after simple febrile seizures is discouraged; it also has no additional diagnostic or prognostic value, and in the case of computed tomography, carries a small increased risk of cancer. Even after first complex febrile seizures, neuroimaging is not likely to be helpful in well-appearing children. In a review of 71 patients with first complex seizures, none had intracranial findings necessitating acute medical or surgical intervention. Electroencephalography and neuroimaging may be considered in children with neurologic abnormalities on examination and in those with recurrent febrile seizures.
**Acute Treatment**

Although most febrile seizures have resolved by the time of presentation, physicians should be prepared to treat patients with febrile status epilepticus.

In the acute setting, intravenous lorazepam (Ativan) in a dose of 0.1 mg per kg is the treatment of choice for acute tonicclonic pediatric seizures.

A Cochrane review found lorazepam to be as effective as diazepam (Valium), with fewer adverse effects and less need for additional antiepileptic agents. The same study found buccal midazolam to be superior to rectal diazepam (Diastat) when intravenous administration is not possible.

**Prognosis and Long-term Management**

Physicians can play a vital role in reassuring families about the good prognosis after a febrile seizure. Key concerns to be addressed include the risks of neurologic morbidity (including epilepsy), mortality, and seizure recurrence.

Parents should be reassured that children without underlying developmental problems do not seem to have lasting neurologic effects from febrile seizures.

A population-based study in the United Kingdom that included 381 children with febrile seizures reported that those with febrile seizures perform as well as others academically, intellectually, and behaviorally when assessed at 10 years of age. Parents should be told that mortality from febrile seizures is very rare—so rare that it is difficult to assess accurately.

A large cohort study in Denmark examined mortality rates in 1.6 million children. There was a slight increase in mortality (adjusted mortality rate ratio of 1.99) during the two years after a complex febrile seizure, but no significant increase among those with simple febrile seizures.

Parents should be warned that febrile seizures reoccur frequently. One cohort study found that 32 percent of children
presenting with an initial febrile seizure later had additional febrile seizures, 75 percent of which occurred within one year. Risk factors and risk of recurrence after an initial febrile seizure are provided in Table below. The risk of recurrence is similar between simple and complex febrile seizures.

**Table : Risk of Recurrence After an Initial Febrile Seizure**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>2-year risk of recurrence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 18 months</td>
<td>14</td>
</tr>
<tr>
<td>Duration of fever &lt; 1 hour before seizure onset</td>
<td>&gt; 20</td>
</tr>
<tr>
<td>First-degree relative with febrile seizure</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>Temperature &lt; 104°F (40°C)</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>Number of risk factors</td>
<td>Number of risk factors</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>&gt; 20</td>
</tr>
<tr>
<td>2</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>3</td>
<td>&gt; 60</td>
</tr>
<tr>
<td>4</td>
<td>&gt; 70</td>
</tr>
</tbody>
</table>

Multiple agents have been evaluated in the prevention of recurrent simple febrile seizures. Continuous use of phenobarbital, primidone (Mysoline), and valproic acid (Depakene) has proved effective in reducing recurrence of simple febrile seizures. However, these agents are not recommended because of associated adverse effects, the burden of long-term compliance, and a lack of data showing a reduced risk of future epilepsy with prevention of recurrent simple febrile seizures.

Intermittent use of antipyretics or anticonvulsants at the onset of fever is not recommended. No studies have shown a reduction in recurrent simple febrile seizures when antipyretics are given at the onset of fever. In a randomized, placebo-controlled, double-blind trial, no decrease in febrile seizure recurrence was observed with scheduled administration of maximal doses of acetaminophen or ibuprofen. Although...
intermittent use of oral diazepam at the onset of fever is effective at reducing recurrence of simple febrile seizures, the AAP does not recommend it because of potential adverse effects and because many recurrent febrile seizures occur before recognition of fever. If parental anxiety is high, oral diazepam given at the onset of a child’s fever may be considered.

Additionally, rectal administration of diazepam for abortive use at home may be considered in those with an initial prolonged febrile seizure and in those at highest risk of recurrence.
Epileptic and Nonepileptic Paroxysmal Events in Childhood

NON-EPILEPTIC SEIZURE

Non-epileptic seizures are paroxysmal events that mimic an epileptic seizure but do not involve abnormal, rhythmic discharges of cortical neurons. They are caused by either physiological or psychological conditions. The latter is discussed more fully in psychogenic non-epileptic seizures.

Diagnosis

A wide array of phenomena may resemble epileptic seizures, which may lead to people who do not have epilepsy being misdiagnosed. Indeed, a significant percentage of people initially diagnosed with epilepsy will later have this revised. In one study, the majority of children referred to a secondary clinic with “fits, faints and funny turns” did not have epilepsy, with syncope (fainting) as the most common alternative. In another study, 39% of children referred to a tertiary epilepsy centre did not have epilepsy, with staring episodes in mentally challenged children as the most common alternative. In adults, the figures are similar, with one study reporting a 26% rate of misdiagnosis.
Differentiation of a non-epileptic attack from an epileptic seizure includes the patient keeping their eyes closed and rarely causing themselves harm (both more common in non-epileptic attacks).

**Terminology**

The International League Against Epilepsy (ILAE) define an epileptic seizure as “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.” Epileptic seizures can occur in someone who does not have epilepsy - as a consequence of head injury, drug overdose, toxins, eclampsia or febrile convulsions, for example.

Medically, when used on its own, the term seizure implies an epileptic seizure. The lay use of this word can also include sudden attacks of illness, loss of control, spasm or stroke. Where the physician is uncertain as to the diagnosis, the medical term paroxysmal event and the lay terms spells, funny turns or attacks may be used.

**Causes**

Possible causes include:

- Syncope (fainting)
  - Reflex anoxic seizures
- Breath-holding spells of childhood
- Cataplexy
- Hyperekplexia, also called startle syndrome
- Migraine
- Narcolepsy
- Non-epileptic myoclonus
- Opsoclonus
- Parasomnias, including night terrors
- Paroxysmal kinesigenic dyskinesia
- Repetitive or ritualistic behaviours
NARCOLEPSY

Narcolepsy is a long term neurological disorder that involves a decreased ability to regulate sleep-wake cycles. Symptoms include periods of excessive daytime sleepiness that usually lasts from seconds to minutes and may occur at any time. About 70% also have periods of sudden loss of muscle strength, known as cataplexy. These spells can be brought on by strong emotions. Less commonly there may be vivid dream like images or the inability to move for a period of time during falling asleep or upon waking-up. People with narcolepsy sleep about the same amount of hours per day as people without but the quality of sleep tends to be worse.

The cause of narcolepsy is unknown. In up to 10% of cases there is a family history of the disorder. Often those affected have low levels of the neurotransmitter hypocretin which may be due to an autoimmune disorder. Trauma, certain infections, toxins, or psychological stress may also play a role. Diagnosis is typically based on the symptoms and sleep studies, after ruling out other potential causes. Excessive daytime sleepiness can also be caused by other sleep disorders such as sleep apnea, major depressive disorder, anemia, heart failure, drinking alcohol, and not getting enough sleep. Cataplexy may be mistaken for seizures.

While there is no cure, a number of lifestyle changes and medications may help. Lifestyle changes include taking regular short naps and sleep hygiene. Medications used include modafinil, sodium oxybate, and methylphenidate. While initially fairly effective, tolerance to the benefits may develop. Tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) may improve cataplexy.

About 0.2 to 600 per 100,000 people are affected. The condition often begins in childhood. Men and women are affected equally.
Untreated narcolepsy increases the risk of motor vehicle collisions and falls. The term *narcolepsy* is from the French *narcolepsie*. The French term was first used in 1880 by Jean-Baptiste-Édouard Gélineau who used the Greek *narkē* (narkē) meaning “numbness” and *lepsis* (lepsis) meaning “attack”.

**Signs and symptoms**

There are two main characteristics of narcolepsy: excessive daytime sleepiness and abnormal REM sleep. The first, excessive daytime sleepiness (EDS), occurs even after adequate night time sleep. A person with narcolepsy is likely to become drowsy or fall asleep, often at inappropriate times and places, or just be very tired throughout the day. Narcoleptics are not able to experience the amount of restorative deep sleep that healthy people experience – they are not “over-sleeping”. In fact, narcoleptics live their entire lives in a constant state of extreme sleep deprivation. Daytime naps may occur with little warning and may be physically irresistible. These naps can occur several times a day. They are typically refreshing, but only for a few hours or less. Vivid dreams may be experienced on a constant or regular basis, even during very brief naps. Drowsiness may persist for prolonged periods of time or simply never cease. In addition, night-time sleep may be fragmented with frequent awakenings. A second prominent symptom of narcolepsy is abnormal REM sleep. Narcoleptics are unique in that they enter into the REM phase of sleep in the beginnings of sleep, even when sleeping during the day.

The classic symptoms of the disorder, often referred to as the “tetrad of narcolepsy,” are cataplexy, sleep paralysis, hypnagogic hallucinations, and excessive daytime sleepiness. Other symptoms may include automatic behaviors and night-time wakefulness. These symptoms may not occur in all patients.

- Cataplexy is episodic loss of muscle function, ranging from slight weakness such as limnness at the neck or knees, sagging facial muscles, weakness at the knees often
referred to as “knee buckling”, or inability to speak clearly, to a complete body collapse. Episodes may be triggered by sudden emotional reactions such as laughter, anger, surprise, or fear, and may last from a few seconds to several minutes. The person remains conscious throughout the episode. In some cases, cataplexy may resemble epileptic seizures. Usually speech is slurred and vision is impaired (double vision, inability to focus), but hearing and awareness remain normal. Cataplexy also has a severe emotional impact on narcoleptics, as it can cause extreme anxiety, fear, and avoidance of people or situations that might elicit an attack. Cataplexy is generally considered to be unique to narcolepsy and is analogous to sleep paralysis in that the usually protective paralysis mechanism occurring during sleep is inappropriately activated. The opposite of this situation (failure to activate this protective paralysis) occurs in rapid eye movement behavior disorder.

• Night-time wakefulness is characterized by periods of wakefulness at night. These periods may be accompanied by hot flashes, elevated heart rate, and at times intense alertness.

• Sleep paralysis is the temporary inability to talk or move when waking (or less often, when falling asleep). It may last a few seconds to minutes. This is often frightening but is not dangerous.

• Hypnagogic hallucinations are vivid, often frightening, dreamlike experiences that occur while dozing or falling asleep. Hypnopompic hallucinations refer to the same sensations while awakening from sleep. These hallucinations may manifest in the form of visual or auditory sensations.

• Automatic behaviors occur when a person continues to function (talking, putting things away, etc.) during sleep episodes, but awakens with no memory of performing
such activities. It is estimated that up to 40 percent of people with narcolepsy experience automatic behavior during sleep episodes.

In most cases, the first symptom of narcolepsy to appear is excessive and overwhelming daytime sleepiness. The other symptoms may begin alone or in combination months or years after the onset of the daytime naps. There are wide variations in the development, severity, and order of appearance of cataplexy, sleep paralysis, and hypnagogic hallucinations in individuals. Only about 20 to 25 percent of people with narcolepsy experience all four symptoms. The excessive daytime sleepiness generally persists throughout life, but sleep paralysis and hypnagogic hallucinations may not. A rare subset of narcoleptics also experience a heightened sense of taste and smell known as the supertaster phenomenon.

Many people with narcolepsy also suffer from insomnia for extended periods of time. The excessive daytime sleepiness and cataplexy often become severe enough to cause serious problems in a person’s social, personal, and professional life. Normally, when an individual is awake, brain waves show a regular rhythm. When a person first falls asleep, the brain waves become slower and less regular, which is called non-rapid eye movement (NREM) sleep. After about an hour and a half of NREM sleep, the brain waves begin to show a more active pattern again, called REM sleep (rapid eye movement sleep), when most remembered dreaming occurs. Associated with the EEG-observed waves during REM sleep, muscle atonia is present called REM atonia.

In narcolepsy, the order and length of NREM and REM sleep periods are disturbed, with REM sleep occurring at sleep onset instead of after a period of NREM sleep. Also, some aspects of REM sleep that normally occur only during sleep, like lack of muscular control, sleep paralysis, and vivid dreams, occur at other times in people with narcolepsy. For example, the lack of muscular control can occur during wakefulness in a cataplexy
episode; it is said that there is intrusion of REM atonia during wakefulness. Sleep paralysis and vivid dreams can occur while falling asleep or waking up. Simply put, the brain does not pass through the normal stages of dozing and deep sleep but goes directly into (and out of) rapid eye movement (REM) sleep.

As a consequence night time sleep does not include as much deep sleep, so the brain tries to "catch up" during the day, hence EDS. People with narcolepsy may visibly fall asleep at unpredicted moments (such motions as head bobbing are common). People with narcolepsy fall quickly into what appears to be very deep sleep, and they wake up suddenly and can be disoriented when they do (dizziness is a common occurrence). They have very vivid dreams, which they often remember in great detail. People with narcolepsy may dream even when they only fall asleep for a few seconds. Along with vivid dreaming, people with narcolepsy are known to have audio or visual hallucinations prior to falling asleep.

Narcoleptics can gain excess weight; children can gain 20 to 40 lb (9 to 18 kg) when they first develop narcolepsy; in adults the body-mass index is about 15% above average.

Causes

Although the cause of narcolepsy was not determined for many years after its discovery, scientists had discovered conditions that seemed to be associated with an increase in an individual’s risk of having the disorder. Specifically, there appeared to be a strong link between individuals with narcolepsy and certain genetic conditions. One factor that seemed to predispose an individual to narcolepsy involved an area of Chromosome 6 known as the HLA complex. There appeared to be a correlation between individuals with narcolepsy and certain variations in HLA genes, although it was not required for the condition to occur. Certain variations in the HLA complex were thought to increase the risk of an auto-immune response to protein-producing neurons in the brain. The protein produced,
called hypocretin or orexin, is responsible for controlling appetite and sleep patterns. Of the billions of cells in the human brain, only about 10,000 to 20,000 cells secrete hypocretin molecules. Low levels of hypocretin have been correlated with a past history of infection, diet, contact with toxins such as pesticides, and brain injuries due to brain tumors or strokes.

Individuals with narcolepsy often have reduced numbers of these protein-producing neurons in their brains. In 2009 the autoimmune hypothesis was supported by research carried out at Stanford University School of Medicine.

The neural control of normal sleep states and the relationship to narcolepsy are only partially understood. In humans, narcoleptic sleep is characterized by a tendency to go abruptly from a waking state to REM sleep with little or no intervening non-REM sleep. The changes in the motor and proprioceptive systems during REM sleep have been studied in both human and animal models. During normal REM sleep, spinal and brainstem alpha motor neuron hyperpolarization produces almost complete atonia of skeletal muscles via an inhibitory descending reticulospinal pathway. Acetylcholine may be one of the neurotransmitters involved in this pathway. In narcolepsy, the reflex inhibition of the motor system seen in cataplexy has features normally seen only in normal REM sleep.

In 2004 researchers in Australia induced narcolepsy-like symptoms in mice by injecting them with antibodies from narcoleptic humans. The research has been published in the Lancet providing strong evidence suggesting that some cases of narcolepsy might be caused by autoimmune disease. Narcolepsy is strongly associated with HLA-DQB1*0602 genotype. There is also an association with HLA-DR2 and HLA-DQ1. This may represent linkage disequilibrium. Despite the experimental evidence in human narcolepsy that there may be an inherited basis for at least some forms of narcolepsy, the mode of inheritance remains unknown. Some cases are associated with genetic diseases such as Niemann-Pick disease or Prader-Willi syndrome.
In December 2013, a study was published providing evidence that autoimmune CD4+ T-cells against HRCT epitopes may be a causative factor of the disease, as well as reinforcing the association with the influenza H1N1 vaccine; however, this study was retracted by the authors in July 2014.

A retrospective study of several hundred people in China reported that narcolepsy onset is highly correlated with seasonal patterns of upper airway infections, including H1N1 influenza.

**Evolution**

Narcolepsy may represent an evolutionary atavism. According to a hypothesis REM sleep is an evolutionary transformation of a well-known defensive mechanism, the tonic immobility reflex. This reflex, also known as animal hypnosis or death feigning, functions as the last line of defense against an attacking predator and consists of the total immobilization of the animal: the animal appears dead (cf. “playing possum”). The neurophysiology and phenomenology of this reaction shows striking similarities to REM sleep, a fact which betrays a potential evolutionary kinship. For example, both reactions exhibit brainstem control, paralysis, sympathetic activation, and thermoregulatory changes. This hypothesis, which integrates many research findings into a unified and evolutionarily well informed framework, also sheds light on the phenomenon of narcolepsy.

**Vaccine**

A link between GlaxoSmithKline’s H1N1 flu vaccine Pandemrix and childhood narcolepsy was investigated due to increased prevalence of narcolepsy in Irish, Finnish and Swedish children after vaccinations. Finland’s National Institute of Health and Welfare recommended that Pandemrix vaccinations be suspended pending further investigation into 15 reported cases of children developing narcolepsy. In Finland in mid-November 2010, 37 cases of children’s narcolepsy had been reported by
doctors. This can be compared to the normal average of 3 cases of children's narcolepsy per year. “The incidence of narcolepsy with cataplexy in children/adolescents in the Swedish population increased during the pandemic and vaccination period, with a rapid decline in incidence during the post pandemic period.” They concluded that these results “provide strengthened evidence that vaccination with Pandemrix during the pandemic period could be associated with an increase in the risk for narcolepsy with cataplexy in predisposed children/adolescents 19 years and younger.” In 2013, the link between Pandemrix and narcolepsy was confirmed by a registry study by the Swedish Medical Products Agency, with a three-fold increase in risk for people under the age of 20.

**Diagnosis**

Diagnosis is relatively easy when all the symptoms of narcolepsy are present, but if the sleep attacks are isolated and cataplexy is mild or absent, diagnosis is more difficult. It is also possible for cataplexy to occur in isolation. Three tests that are commonly used in diagnosing narcolepsy are the polysomnogram, the multiple sleep latency test (MSLT), and administration of the Epworth Sleepiness Scale. These tests are usually performed by a sleep specialist. The polysomnogram involves continuous recording of sleep brain waves and a number of nerve and muscle functions during nighttime sleep. When tested, people with narcolepsy fall asleep rapidly, enter REM sleep early, and may often awaken during the night. The polysomnogram also helps to detect other possible sleep disorders that could cause daytime sleepiness.

The Epworth Sleepiness Scale is a brief questionnaire that is administered to determine the likelihood of the presence of a sleep disorder, including narcolepsy. For the multiple sleep latency test, a person is given a chance to sleep every 2 hours during normal wake times. The patient is taken in usually for an overnight sleep study. The following day the patient will have
multiple tests where they will be told to nap after a full nights sleep (usually eight hours). Observations are made of the time taken to reach various stages of sleep (sleep onset latency). This test measures the degree of daytime sleepiness and also detects how soon REM sleep begins. Again, people with narcolepsy fall asleep rapidly and enter REM sleep early. Occasionally, a multiple sleep latency test can result in a false-negative for a narcoleptic.

The system which regulates sleep, arousal, and transitions between these states in humans is composed of three interconnected subsystems: the orexin projections from the lateral hypothalamus, the reticular activating system, and the ventrolateral preoptic nucleus. In narcoleptic individuals, these systems are all associated with impairments due to a greatly reduced number of hypothalamic orexin projection neurons and significantly fewer orexin neuropeptides in cerebrospinal fluid and neural tissue, compared to non-narcoleptic individuals. Those with narcolepsy generally experience the REM stage of sleep within five minutes of falling asleep, while people who do not have narcolepsy (unless they are significantly sleep deprived) do not experience REM until after a period of slow-wave sleep, which lasts for about the first hour or so of a sleep cycle.

Measuring hypocretin levels in a person’s cerebrospinal fluid sampled in a spinal tap may help in diagnosing narcolepsy, with abnormally low levels serving as an indicator of the disorder. This test can be useful when MSLT results are inconclusive or difficult to interpret.

Classification

The 2001 International Classification of Sleep Disorders (ICSD) divides primary hypersomnia syndromes between narcolepsy, idiopathic hypersomnia, and the recurrent hypersomnias (like Klein-Levin syndrome); it further divides narcolepsy into that with cataplexy and that without cataplexy. This ICSD version defines narcolepsy as “a disorder of unknown etiology that is characterized by excessive sleepiness that typically
is associated with cataplexy and other REM-sleep phenomena, such as sleep paralysis and hypnagogic hallucinations”. It also establishes baseline categorical standards for diagnosis of narcolepsy, through 2 sets of well defined criteria, as follows. Minimal narcolepsy diagnostic criteria set #2:

- A “complaint of excessive sleepiness or sudden muscle weakness.”
- Associated features that include: sleep paralysis; disrupted major sleep episode; hypnagogic hallucinations; automatic behaviors.
- Polysomnography with one or more of the following: “sleep latency less than 10 minutes;” “REM sleep latency less than 20 minutes;” an MSLT with a mean sleep latency less than 5 minutes; “two or more sleep-onset REM periods” (SOREMPs).
- “No medical or mental disorder accounts for the symptoms.”

In the absence of clear cataplexy, it becomes much more difficult to make a firm diagnosis of narcolepsy. “Various terms, such as essential hypersomnia, primary hypersomnia, ambiguous narcolepsy, atypical narcolepsy, etc., have been used to classify these patients, who may be in the developing phase of narcolepsy.”

Since the 2001 ICSD, the classification of primary hypersomnias has been steadily evolving, as further research has shown more overlap between narcolepsy and idiopathic hypersomnia. The 3rd edition of the ICSD is currently being finalized, and its new classification will label narcolepsy caused by hypocretin deficiency as “type 1 narcolepsy,” which is almost always associated with cataplexy. The other primary hypersomnias will remain subdivided based on the presence of SOREMPs. They will be labeled: “type 2 narcolepsy,” with 2 or more SOREMPs on MSLT; and “idiopathic hypersomnia,” with less than 2 SOREMPs.
However, “there is no evidence that the pathophysiology or therapeutic response is substantially different for hypersomnia with or without SOREMPs on the MSLT.” Given this currently understood overlap of idiopathic hypersomnia and narcolepsy, the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) is also updating its classification of the primary hypersomnias. It reclassifies narcolepsy without cataplexy as major somnolence disorder (MSD). Additionally, MSD will encompass all syndromes of hypersomnolence not explained by low hypocretin, including idiopathic hypersomnia (with and without long sleep time) and long sleepers (patients requiring >10 hours sleep/day).

Further complicating these updated classification schemes, overlap between narcolepsy with cataplexy and idiopathic hypersomnia has also been reported. A subgroup of narcoleptics with long sleep time, comprising 18% of narcoleptics in one study, had symptoms of both narcolepsy with cataplexy and idiopathic hypersomnia (long sleep time and unrefreshing naps). It is felt that this subgroup might have dysfunction in multiple arousal systems, including hypocretin and GABA.

**Treatment**

People with narcolepsy can be substantially helped, but not cured. Treatment is tailored to the individual, based on symptoms and therapeutic response. The time required to achieve optimal control of symptoms is highly variable, and may take several months or longer. Medication adjustments are frequently necessary, and complete control of symptoms is seldom possible. While oral medications are the mainstay of formal narcolepsy treatment, lifestyle changes are also important.

The main treatment of excessive daytime sleepiness in narcolepsy is central nervous system stimulants such as methylphenidate, amphetamine, dextroamphetamine, modafinil, and armodafinil. In late 2007 an alert for severe adverse skin reactions to modafinil was issued by the FDA.
Another drug that is used is atomoxetine, a non-stimulant and norepinephrine reuptake inhibitor (NRI), that has no addiction liability or recreational effects. In many cases, planned regular short naps can reduce the need for pharmacological treatment of the EDS, but only improve symptoms for a short duration. A 120 minute nap provided benefit for 3 hours in patient alertness whereas a 15 minute nap provided no benefit. Daytime naps are not a replacement for nighttime sleep. Ongoing communication between the health care provider, patient, and the patient’s family members is important for optimal management of narcolepsy.

Another FDA-approved treatment option for narcolepsy is sodium oxybate, also known as sodium gamma-hydroxybutyrate (GHB). It can be used for cataplexy associated with narcolepsy and excessive daytime sleepiness associated with narcolepsy.

Narcolepsy has sometimes been treated with selective serotonin reuptake inhibitors and tricyclic antidepressants, such as clomipramine, imipramine, or protriptyline, as well as other drugs that suppress REM sleep. Venlafaxine, an antidepressant which blocks the reuptake of serotonin and norepinephrine, has shown usefulness in managing symptoms of cataplexy, however, it has notable side-effects including sleep disruption.

**Epidemiology**

In the United States, it is estimated that this condition afflicts as many as 200,000 Americans, but fewer than 50,000 are diagnosed. It is as widespread as Parkinson’s disease or multiple sclerosis and more prevalent than cystic fibrosis, but it is less well known. Narcolepsy is often mistaken for depression, epilepsy, or the side effects of medications. It can also be mistaken for poor sleeping habits, recreational drug use, or laziness. Narcolepsy can occur in both men and women at any age, although its symptoms are usually first noticed in teenagers or young adults. There is strong evidence that narcolepsy may run in families; around 10 percent of people diagnosed with
narcolepsy with cataplexy have a close relative with this neurological disorder. While narcolepsy symptoms are often confused with depression, there is a link between the two disorders. Research studies have mixed results on co-occurrence of depression in narcolepsy patients - the numbers quoted by different studies are anywhere between 6% and 50%.

Narcolepsy has its typical onset in adolescence and young adulthood. There is an average 15-year delay between onset and correct diagnosis which may contribute substantially to the disabling features of the disorder. Cognitive, educational, occupational, and psychosocial problems associated with the excessive daytime sleepiness of narcolepsy have been documented. For these to occur in the crucial teen years when education, development of self-image, and development of occupational choice are taking place is especially devastating. While cognitive impairment does occur, it may only be a reflection of the excessive daytime somnolence.

The prevalence of narcolepsy is about 1 per 2,000 persons. It is a reason for patient visits to sleep disorder centers, and with its onset in adolescence, it is also a major cause of learning difficulty and absenteeism from school. Normal teenagers often already experience excessive daytime sleepiness because of a maturational increase in physiological sleep tendency accentuated by multiple educational and social pressures; this may be disabling with the addition of narcolepsy symptoms in susceptible teenagers. In clinical practice, the differentiation between narcolepsy and other conditions characterized by excessive somnolence may be difficult. Treatment options are currently limited. There is a paucity in the literature of controlled double-blind studies of possible effective drugs or other forms of therapy. Mechanisms of action of some few available therapeutic agents have been explored but detailed studies of mechanisms of action are needed before new classes of therapeutic agents can be developed. Narcolepsy is an underdiagnosed condition in the
general population. This is partly because its severity varies, so it can be mistaken for other illnesses very easily. Some people with narcolepsy do not suffer from loss of muscle control.

**Society and culture**

In the British television comedy-drama *Doc Martin*, the character Joe Penhale (played by John Marquez) is portrayed as having narcolepsy. In the 2007 video game *Little Busters!*, the protagonist Riki Naoe suffers from narcolepsy. In the 2001 film *Rat Race*, Enrico Pollini, played by Rowan Atkinson, suffers from narcolepsy, which is used to comic effect several times. In the 2014 Tamil movie *Naan Sigappu Manithan* (directed by Thiru) the lead character, played by Vishal, suffers from narcolepsy. In the season four episode of the 2010 television series *Rizzoli & Isles*, “Judge, Jury and Executioner”, the murder victim Judge Kathleen Harper (played by A’da Alison Woolfolk) suffers from narcolepsy, and uses the drug methylphenidate. This drug is later used to kill her through an overdose.

In 2015, it was reported that the British Department of Health was paying for sodium oxybate medication for 80 people who are taking legal action over problems linked to the use of the Pandemrix swine flu vaccine at a cost of £12,000 a year. Sodium oxybate is not available to people with narcolepsy through the National Health Service.

**EPILEPTIC SEIZURES**

Epileptic seizures are paroxysmal, abnormal behaviors caused by excessive, hypersynchronous firing of neurons in the brain. Most seizures arise in the cerebral cortex, although subcortical structures can also generate seizures. The incidence of epilepsy is highest in early childhood and peaks again late in life. When epilepsy is attributed to a brain abnormality (eg, mental retardation, cerebral palsy, malformation), it is classified as “symptomatic.” Epilepsy is considered “idiopathic” when there is no recognized brain abnormality.
Morbidity

The risk of recurrence within 2 years after a first-time, unprovoked seizure is approximately 35% to 40%. Increased risk of recurrence is associated with factors such as a remote, symptomatic cause (e.g., brain injury); abnormal EEG; and seizure during sleep. Treatment with antiepileptic medication reduces the risk of a recurrence after a first seizure, but there is little evidence that treatment prevents the later development of epilepsy.

Prolonged seizures can cause brain injury, but epidemiological studies have not provided evidence that prolonged first seizures in otherwise healthy persons increase the risk of subsequent seizures. Furthermore, the number of seizures that occur before treatment is initiated is not necessarily associated with a greater likelihood of medical intractability. Seizure frequency and whether the seizures are generalized or partial have stronger predictive power. Therefore, little advantage is gained by treating first-time seizures, whether they are provoked by an identified acute insult or they occur out of the blue. The rationale for treating persons with recurrent seizures is that treatment will ameliorate seizure recurrence.

Diagnostic Suspicion

Most often, seizure history related by the patient or family members and the physical findings will lead the physician to suspect epilepsy. For example, a history of febrile seizures (particularly if prolonged) is a well-recognized risk factor for the development of temporal lobe epilepsy caused by mesial temporal sclerosis. An additional helpful clue from the history is a past brain injury from trauma or infection. It is generally understood that relatively remote trauma of a minor degree confers very little risk, but prolonged loss of consciousness or a penetrating head injury are significant risk factors for seizure episodes. A family history is important, because epilepsy in first-degree relatives is another risk factor.
Physical examination findings that indicate an abnormality of brain function provide further evidence of an increased likelihood of seizures. They also help classify epilepsy as either symptomatic or idiopathic. For example, mental retardation, cerebral palsy, or the presence of neurocutaneous lesions is noteworthy. Cerebral imaging studies may demonstrate a structural brain abnormality, erroneously heighten suspicion of seizures by the patient, caregiver, and physician. Benign or at least nonepileptic behaviors may be mistakenly identified as seizures or described in rather dramatic terms.

Parents of children who have health challenges that may include previous seizures may be very sensitive to any perceived abnormality in the child’s health. Benign events, such as hypnic jerks, may prove very frightening to the parents of a child who recently suffered a febrile seizure. A child with autism may have stereotyped movements that convince a concerned parent that the child is having seizures. Munchausen syndrome and Munchausen syndrome by proxy also may present as seizures. When the history suggests seizure, a careful differential diagnosis is important.

Nonepileptic Events

Nonepileptic seizures are behavioral events that resemble epileptic seizures but are not caused by abnormal, hypersynchronous neuronal discharges in the brain. The term “pseudoseizure” is discouraged, since the events themselves are real and disabling. Nonepileptic events can be caused by psychological disorders, or they can be manifestations of other pathological or physiological neurological conditions.

Alternating hemiplegia. This is characterized by repeated bouts of dystonic posturing accompanied by nystagmus. Hemiplegia can occur on either side or bilaterally. It occurs in the presence of developmental regression and persistent developmental delay. Onset is usually during infancy. The condition has been variously attributed to a migrainous
mechanism, epilepsy, and movement disorder. The underlying cause has been linked to mitochondrial dysfunction, channelopathies, and small vessel disease. The calcium channel blocker flunarizine has been used in treatment, as has topiramate.

Benign sleep movements. Benign myoclonus or hypnic jerks often occur shortly after falling asleep. Movements during rapid eye movement sleep also may be mistaken for seizures. Correct identification of these events often will allay the anxiety of patients and caregivers. However, if a child has experienced a seizure (e.g., a febrile convulsion) previously, parents may be hypervigilant. Asking the parents to record a video of such movements may be helpful.

Breath-holding spells (BHS). These spells commonly begin between the ages of 6 and 18 months. They are characterized by hard crying in response to injury or anger and breath-holding, stiffening, and cyanosis (or sometimes pallor) followed by brief loss of muscle tone and consciousness.

Pallid BHS are a type of syncope. They are more likely to occur in reaction to an event causing injury, pain, or emotional distress. Some children hold their breath on inspiration before getting the first cry out. Others hold their breath in expiration. They usually stop the behavior by age 5 or 6 years. A family history of BHS is common.

BHS are generally benign but can occasionally provoke acute reactive seizures, presumably caused by transient cerebral hypoxia in much the same way syncope can provoke acute seizures. Recognition depends on taking a careful history that looks for consistent initial crying and cyanosis or pallor early in the attack. Treatment for routine BHS consists of reassurance. Some evidence suggests that iron supplementation helps some children.

Gastroesophageal reflux. Symptoms associated with gastroesophageal reflux may be mistaken for seizures. Infants may have stiffening and crying episodes suggestive of infantile
spasms. Older children and adults, particularly if they are cognitively impaired and not able to communicate well, may have reflux-related pain leading to stiffening episodes that are reminiscent of tonic seizures, or they may have sudden behavior changes suggesting partial seizures. Abnormal posturing in patients with gastroesophageal reflux is often referred to as Sandifer syndrome.

Syncope. The distinction between epileptic seizures and syncope can be particularly challenging. Transient loss of consciousness—particularly if accompanied by body stiffening—can suggest seizures, but positive motor signs are common in syncope. At the same time, transient cerebral hypoperfusion occurring during syncope can cause an acute reactive seizure (convulsive syncope).

Features suggesting syncope include preceding light-headedness, sweating, pallor, prolonged standing, sudden changes in posture—from lying down to sitting or standing—and precipitation by vagal stimuli, such as micturition. Conversely, typical aura (eg, epigastric rising sensation, déjà vu), postictal delirium, and focal physical features, such as head turning, are suggestive of seizure. An EEG showing epileptiform discharges or postictal slowing can help confirm the diagnosis. An ECG revealing an arrhythmia or a positive tilt table test suggests syncope.

There are also rare cases in which a seizure provokes asystole. When such cases are recognized, the insertion of a pacemaker is often recommended.

Conversion disorder. Conversion disorders can manifest as psychogenic nonepileptic seizures (PNES) in adults and children. A history of significant social stresses should alert a clinician to the possibility of PNES. Some apparent secondary gain usually will be associated with the spells, although in conversion disorder, the patient is not consciously producing the symptom. In children, such gains may include being sent home from school or averting physical abuse.
A history of physical or sexual abuse should be considered when PNES are diagnosed. In children, less severe stresses such as high academic pressure or bullying at school also may cause symptoms.

A number of physical features during seizure episodes are suggestive of PNES. The eyes are usually closed. Asynchronous clonic limb movements (flailing) are often present. Other symptoms include pelvic thrusting and prominent rotatory (horizontal back and forth) head movements. An unusual lack of concern about the symptoms (la belle indifference affect) is typical. Also, it is unusual for persons with PNES to have the seizures during sleep. Incontinence and self-injury also are less common during PNES than in epileptic seizures.

The above-noted symptoms are suggestive but not definitive. It is important to document the nonepileptic nature of these disabling events; video EEG monitoring is most trusted. It may be challenging to get the suspicious event to occur in the clinical setting. Various forms of suggestion have been used to trigger events, but ethical considerations need to be acknowledged. Hypnosis also has been successfully used in both adults and in children to provoke PNES.

It is never adequate to simply give a diagnosis of PNES without further treatment. The episodes remain disabling despite reassurance that the spells are not epilepsy. If the underlying stresses contributing to the spells go untreated, and if adequate coping mechanisms are not adopted, it is likely that the spells will continue. Referral for psychological counseling is necessary. Early diagnosis of PNES carries a better prognosis for remission.

**Epileptic Seizure Types**

Generalized motor seizures. The types of generalized motor seizures are relatively easy to diagnose based on patient history. However, there are physiological and psychogenic behaviors that can be mistaken for these relatively dramatic epileptic seizures. Nonepileptic events that suggest generalized motor
Epileptic and Nonepileptic Paroxysmal Events in Childhood

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seizures include chorea, athetosis, dystonia, and opisthotonus. Because such behaviors are frequently (but not exclusively) encountered in developmentally disabled persons, a history of normally maintained consciousness and awareness may be difficult to ascertain.

More complex movements, such as chorea or athetosis, are characterized by writhing or jerking. They are usually distinguishable from seizures because of the absence of a clear rhythmic component (unlike clonic seizures). The movements are often bilateral and awareness is maintained. Because the movements may be generalized or focal, they may be mistaken for either generalized or partial seizures.

Absence seizures. These seizures are characterized by discrete episodes of unresponsive staring and are sometimes accompanied by minor automatisms such as eye blinking or head titubation. In the untreated person, they usually occur many times a day. Each episode may last from a few to about 30 seconds. The frequency of the seizures, their short duration, and the relative absence of automatisms help distinguish absence seizures from complex partial seizures.

Behavioral nonepileptic events such as inattention or daydreaming may be hard to distinguish from absence seizures unless there is a clear history of a lack of response to physical stimulation. An EEG is helpful, because untreated persons with absence epilepsy will almost always have generalized spike wave discharges. Atypical absence seizures are usually longer and have more accompanying subtle motor symptoms. They are commonly seen in cognitively impaired persons who have other, more obvious seizure types. Lennox-Gastaut syndrome is a common setting for atypical absence seizures.

Partial seizures. These seizures present the greatest diagnostic challenge because of the many symptoms that can be manifestations of epileptic activity. Loss of awareness is a clinical feature that distinguishes complex from simple partial seizures.
A wide variety of automatisms can be present during partial seizures depending on the part of the brain involved. Seizures arising from the frontal convexity or parasagittal region often are associated with prominent motor signs. Subtler motor activity that may be mistaken for absence seizures is indicative of orbital frontal and frontopolar seizures. Typical temporal lobe symptoms may include dizziness, staring, autonomic changes, and subtler, semipurposeful automatisms such as picking at clothes and chewing. Parietal and occipital onset is suggested by initial sensory and visual symptoms, respectively.

Subtle Or Subclinical Seizures

There are some circumstances in which seizure manifestations may be quite subtle and may show up only on an EEG. Patients in an unexplained coma or with waxing and waning levels of consciousness may be experiencing subtle seizures or nonconvulsive status epilepticus. An unexplained acute encephalopathy, particularly in the setting of a brain insult, should raise the possibility of seizure and prompt an EEG evaluation.

Other conditions in which subtle or subclinical seizures should be suspected as part of the differential diagnosis are Landau-Kleffner syndrome (LKS) and continuous spike and waves during slow sleep (CSWS).

Landau-Kleffner syndrome. LKS affects children and its hallmark is aphasia in the setting of relatively mild epilepsy. To make this diagnosis, the child must demonstrate loss of language skills and have either a history of seizures or an EEG showing epileptiform abnormalities. Some 20% of affected children have epileptiform EEG abnormalities without a history of clinical seizures. No specific EEG pattern is pathognomonic, but temporal maximum spikes often are described. Treatment is aimed at reducing the frequency of interictal spike discharges using such medications as valproate, benzodiazepines, and corticosteroids. Multiple subpial transection also has been used for treatment of medically refractory cases.
Continuous spike and waves during slow sleep. CSWS, also known as electrical status epilepticus during slow-wave sleep, is a condition in which nearly continuous (more than 85%) spike-wave discharges are seen on the EEG during deep slowwave sleep. Age at onset is usually 2 to 9 years, and the phenomenon is associated with language, cognitive, and behavioral impairments. Although most affected children have a history of seizures (either generalized or partial), cases identified only through EEG findings have been described. The cause may be cryptogenic or symptomatic.

The Role Of EEG

A routine EEG performed in a patient with a presumed first seizure will show epileptiform abnormalities about 7% to 34% of the time. An EEG performed in the first 24 hours after an attack increases the EEG yield to 51%. Repeated EEGs, sleep deprivation before the EEG, and sleep recorded during the EEG all increase the likelihood of recording epileptiform discharges. Nevertheless, some patients with epilepsy will persistently have normal EEGs, and some persons with epileptiform spike discharges may have a statistically increased risk but never experience a seizure.

Ideally, a seizure event should be captured on EEG, but this is seldom practical in the outpatient laboratory. If the events are reasonably frequent, a long-term EEG that records the habitual attacks helps provide diagnostic certainty.38 Both inpatient and outpatient long-term EEG are feasible, and outpatient video recording during EEG is increasingly practical, but the inpatient setting provides much more control over video recording conditions.

For seizures with altered consciousness, the EEG will almost always show some paroxysmal change, and most of the time an evolving apparent if the seizures are epileptic. Exceptions include some frontal lobe seizures in which the epileptogenic cortex is distant from recording scalp electrodes, such as in the mesial
frontal or the orbital frontal region. Even in such cases, a paroxysmal EEG change, such as slowing, will be evident, but prominent movement artifacts may obscure the EEG. Other exceptions include auras or simple partial seizures. Not enough of the cortex may be synchronized to allow recording of the rhythmic discharges from the scalp electrodes.

Because it is important that patients who are hospitalized for video EEG recordings have their habitual seizures, antiepileptic drugs often are tapered.

For patients with mixed epileptic and nonepileptic events, drug tapering presents a problem because drug withdrawal may simply uncover the epileptic attacks that were pharmacologically controlled, although the patient may also experience nonepileptic spells. It is important to document the variety of attacks in question and make sure that the video EEG captures the habitual events and not anomalous seizures that are provoked solely by medication withdrawal.

Clinical Highlights

- The distinction between epileptic seizures and syncope can be particularly challenging. Transient loss of consciousness—particularly if accompanied by body stiffening—can suggest seizures, but positive motor signs are common in syncope.

- Conversion disorders can manifest as psychogenic nonepileptic seizures (PNES) in adults and children. A history of significant social stresses points to the possibility of PNES.

- Behavioral nonepileptic events such as inattention or daydreaming may be hard to distinguish from absence seizures unless there is a clear history of a lack of response to physical stimulation. An electroencephalogram (EEG) is helpful, because untreated persons with absence epilepsy will almost always have generalized spike wave discharges.
• An EEG performed in the first 24 hours after a presumed seizure will show epileptiform abnormalities 51% of the time. Repeated EEGs, sleep deprivation before the EEG, and sleep recorded during the EEG all increase the likelihood of recording epileptiform discharges.

**NON-EPILEPTIC PAROXYSMAL EVENTS**

There are many events that may mimic an epileptic seizure but are not caused by abnormal electrical activity of the brain. They are referred to in the medical literature as paroxysmal events of uncertain aetiology or cause, or nonepileptic paroxysmal events.

Paroxysmal events may be defined as “sudden fits or outbursts” which may be observed in various clinical conditions including, but not limited to, MS, Encephalitis, malaria, and stroke.

A seizure is usually defined as a transient occurrence of signs and/or symptoms due to abnormal excessive or simultaneous neuronal activity within the brain. Whereas epilepsy is considered to be a brain disorder characterised by the enduring predisposition to generate epileptic seizures and relates to the neurobiological, psychological, cognitive and social consequences of this condition.

Hence not all seizures are considered to be epilepsy. Neurologists who specialise in this field are best able to accurately diagnose a person’s condition as epilepsy.

It is not always an easy task to correctly diagnose epilepsy and a recent UK study has shown misdiagnosis of the condition was as high as 22%, other studies have found a misdiagnosis rate of between 10% and 30%. The location of patients in the UK study had a large bearing on their ability to obtain an accurate diagnosis. Factors affecting the diagnosis included access to specialists and the education level of primary specialists.
A correct diagnosis is extremely important as there are many implications, some very serious, for misdiagnoses including:

- Unnecessary or inappropriate lifestyle restrictions, medical treatments, investigations
- Failure to receive the correct treatment
- Inappropriate expectations of the patient’s abilities
- Large costs to the Health Care System
- Death through uncontrolled and untreated seizures or untreated cardiac arrhythmias

In order to make an accurate diagnosis Clinicians need to:

- Obtain a careful clinical history involving witness accounts, experiences of the patient and video footage where possible
- Possess a full knowledge of nonepileptic paroxysmal events
- Correlate the events with recognised seizure signals
- Avoid over-interpretation of EEG’s
- Not use epilepsy as a default diagnosis
- Constantly review the diagnosis and carefully consider video evidence in conjunction with EEG’s

Categories of Events in Childhood

Anoxic/Ischemic Events

Which may include the following:

- Reflex (pallid) anoxic seizures usually occur under 18 months of age (80%) and can be provoked by pain with minimal distress which results in loss of consciousness, stiffening, down beating of eyes and incontinence
- Vasovagal episodes are preceded by postural, emotional or situational factors which can result in lightheadedness, weakness, nausea, pallor, and sweating, visual distortion. The episode may involve
progressive loss of tone, shallow respiration, bradycardia, loss of consciousness, motor features such as eye deviation, incontinence, jerking. Following the episode lethargy accompanied by rapid mental recovery is evident (more so than with common seizures)

- Breath Holding is common in childhood and may be provoked by anger, frustration, pain or fright. Usually vigorous crying precedes
- Breath holding leading to loss of consciousness with brief stiffening and sometimes 2 or 3 clonic jerks. Bradycardia and EEG slowing can be detected and recovery is fairly rapid
- Cardiac Events can be related to cardiac outflow, disturbance of cardiac rhythm and autonomic dysregulation. Physical symptoms such as palpitations, sweating, pallor, posture, exertion or a family history can all be relevant factors
- If there is a history of seizures occurring during or after exercise, an ECG is mandatory to exclude a prolonged Q-T interval.

Sleep Related Phenomena

Sleep related-including events can include parasomnias, hypnic jerks, neonatal sleep myoclonus, somnambulism (sleep walking).

Behavioural Events

These may include daydreaming, motor mannerisms, self gratification, posturing, vocalizations, and aggressive outbursts. Day dreaming is quite common in childhood and may increase with tiredness, medications, or learning challenges. Many patients can “zone out” for prolonged periods of time. However distraction is possible using touch, voice, noise and there is usually no increase in motor activity such as eye flickering or automatisms.
Psychiatric Events

These may include:

- Tics (including Tourettes syndrome)
- Anxiety/panic attacks, hallucinations (auditory/visual)
- Psychogenic - non epileptic seizures (PNES) which are most common in young adolescents and manifest in different ways.

Other Non Epileptic Events

- Neurological disorders which may include migraine, transient ischemic attacks, narcolepsy/cataplexy, spinal myoclonus, benign paroxysmal vertigo, benign torticollis of infancy, benign tonic upglaze, channelopathies, movement disorders, motor disorders
- Hyperekplexia, a channelopathy which usually occurs in the neonatal period is characterized by excessive startle to touch or sound, episodes of apnoea, response to sodium valporate/ clonazepam
- Gastrointestinal feed-related events such as tonic stiffening colour change and occasionally vomiting (Sandifer’s syndrome)
- Metabolic disorders including hypoglycemia or organic acidemias.
The Evaluation of Pediatric Sleep Disorders

Sleep disorders are common in childhood and adolescence and are associated with neurocognitive and psychosocial impairments as well as an increase in caregiver burden. Sleep problems in infants, children, and adolescents present in a myriad of ways, often leading to significant impairments in multiple aspects of daytime functioning.

While bedtime settling difficulties and frequent nighttime awakenings tend to be predominant during infancy and early childhood, sleep difficulties due to insufficient sleep hygiene or circadian rhythm disorders tend to be more prominent in adolescence. Onset of specific sleep problems in children and adolescents could further complicate any underlying comorbid medical condition, such as obesity and asthma, and psychological problems, such as depression, anxiety, and substance abuse. Current evidence indicates that chronically disrupted sleep in children and adolescents can lead to problems in cognitive functioning, such as attention, learning, and memory. Behavioral interventions for pediatric sleep problems (e.g., graduated extinction, parent education, positive bedtime routines), especially in young children, have been shown to produce clinically significant improvements.
SPECIFIC SLEEP DISORDERS IN CHILDREN AND ADOLESCENTS

SRBD. SRBDs are best understood as occurring across a spectrum that includes habitual snoring at its least severe form and obstructive sleep apnea (OSA) at its most severe form. SRBD also includes upper airway resistance syndrome (UARS) and obstructive hypoventilation syndrome as part of this spectrum. In children and adolescents, concern for symptoms (e.g., snoring) suggestive of underlying SRBD, such as obstructive sleep apnea, needs further exploration into other associated features, including witnessed pauses in breathing, chronic morning headaches, dry mouth/throat, nocturia/nocturnal enuresis, early morning thirst, feelings of grogginess/fatigue upon awakening, history of chronic ear infections, recent weight gain, and compensatory mechanisms, such as hyperextension of neck during sleep and chronic mouth breathing.

The association between ADHD and SRBD is well documented in literature through investigations into animal models of SRBD, parental reports, objective measures (e.g., polysomnography), and neuropsychological assessments. Association of persistent SRBD with learning difficulties, low academic performance, and other behavioral disorders have also been shown in these studies.

Treatment outcome studies have shown significant improvement in neurocognitive and behavioral measures of ADHD following the treatment of SRBD, providing further evidence into this bidirectional relationship. It has been proposed that prefrontal cortical dysfunction due to chronic SRBD is associated with impaired executive functioning that explains daytime cognitive and behavioral difficulties in children.

Although obesity appears to be one of the leading causes of SRBD in adults, adenotonsillar hypertrophy is the predominant cause of SRBD in typically developing children. Characteristic physical exam finding of tonsillar enlargement is absent at times
in children with suspected SRBD, but other characteristic features, such as macroglossia, retrognathia, high-arched palate, and nasal septal deviation, can predispose a child to SRBD.

If presence of nasal polyps or posterior nasopharyngeal obstruction is suspected, a consultation with an otolaryngologist for endoscopic evaluation may be appropriate. It is also important to note that children with disorders such as Down’s syndrome or Prader-Willi syndrome present with craniofacial abnormalities, including mid-face hypoplasia or micrognathia, that predispose them to SRBD.

Other risk factors associated with development of SRBD include obesity (high BMI, large waist circumference), presence of chronic sinus problems, recurrent wheezing, nasal allergies, family history of OSA, and association with African-American race. If a child is suspected of having SRBD after an evaluation, then he or she should be referred for an overnight polysomnogram. A polysomnogram can measure apneas (cessation in airflow in spite of continued respiratory effort) or hypopneas (reduction in width of airflow waveform by 50%, duration greater than two respiratory cycles and association with hemoglobin desaturation by at least 3% or with an arousal).

Utilizing traditional adult criteria, these two measures are then used to determine the apnea-hypopnea index (AHI), which is the total number of apneas and hypopneas per hour of sleep. An AHI between 1 and 5 an hour is generally considered mild OSA, whereas an AHI of five or more an hour is considered to be in the moderate-to-severe range.

Adenotonsillectomy (AT) is considered the treatment of choice once moderate-to-severe AHI is documented on initial polysomnography. Symptom alleviation in SRBD after AT has been shown to be as high as 83 percent in a meta-analysis; but persistent symptoms are seen in patients who are obese or have craniofacial abnormalities. A polysomnogram may be repeated in a few months after AT to reassess severity of persistent SRBD.
If residual symptoms of sleep apnea appear severe after AT and are associated with significant functional impairments, initiation of nasal continuous positive airway pressure (CPAP) should be considered as an option. Use of leukotriene-receptor antagonists, such as montelukast, and topical intranasal corticosteroids, such as fluticasone spray, appear to hold some promise in treatment of milder forms of SRBD and post-AT residual symptoms and are attributed to reduction in size of adenoids and chronic nasal inflammation. Dental appliances and surgical procedures, such as uvulopalatopharyngoplasty, are available treatment options in adults with OSA that are rarely utilized in children. In summary, AT combined with weight loss is considered first-line treatment in pediatric SRBD; use of intranasal corticosteroids and leukotriene-receptor antagonists for milder forms of SRBD and nasal CPAP for more severe sleep apnea are other available treatment options. Additionally, screening for presence of SRBD in children with underlying ADHD and learning difficulties should be undertaken.

Sleep-related movement disorders. Sleep-related movement disorders of childhood encompass sleep myoclonus of infancy, rhythmic movement disorder, periodic limb movement disorder (PLMD), and restless legs syndrome (RLS). Sleep myoclonus of infancy is typically associated with clusters of myoclonic jerks that involve the whole body, trunk, or limbs. They are usually considered to be benign phenomena and gradually disappear after six months of age, necessitating no further treatment. In rhythmic movement disorder (RMD), a child exhibits repetitive and stereotyped motor behaviors involving large muscle groups and are predominantly sleep related. RMD can also be associated with significant daytime impairments and/or associated with self-inflicted bodily injuries. Diagnosis can be definitively made using video polysomnography, and treatment encompasses ensuring safety of the child during sleep and reassuring parents that RMD should gradually resolve by five years of age. Persistent symptoms beyond five years of age can
be seen in children with developmental disorders, but these appear to be a gradual extension of daytime stereotypies that are commonly seen in this subgroup of children. Treatment with benzodiazepines such as clonazepam has been shown to be useful in severe cases of RMD.

Periodic limb movements in sleep (PLMS) are brief jerks (movements) during sleep that can last up to five seconds in duration occurring at 20- to 40-second intervals (periodicity) and occur more commonly in the lower extremities than upper extremities. Patients are usually unaware of these symptoms, but bed partners like siblings and parents are affected by these movements. If sleep disruption due to PLMS is documented on polysomnography and PLMS cannot be explained by any other underlying sleep disorder, then such movements are considered PLMD.

RLS in childhood is diagnosed using adult criteria and is usually supported by other features, such as positive family history, PLMS on polysomnography, improvement with dopamine agents, and presence of iron deficiency. Adult criteria for RLS are as follows: 1) An urge to move the legs, 2) the urge to move begins or worsens when sitting or lying down, 3) the urge to move is partially or totally relieved by movement, and 4) the urge to move is worse in the evening or night than during the day or only occurs in the evening or night. Typically in children less than 2 years of age, diagnosis of RLS needs further support by a child’s own age-appropriate descriptors of sensorimotor symptoms, such as “spiders crawling” or “tickles in my legs,” along with adult criteria described above. Both sleep-onset and sleep maintenance insomnia can be a common occurrence in children with underlying RLS. This is thought to be due to concept of “negative associations” where children associate sleep with distressing sensations in their limbs thereby perpetuating fear and anxiety surrounding bedtime. It may, therefore, be useful to screen children for sensorimotor symptoms suggestive of RLS who present with insomnia. Behavioral
treatment options for RLS and associated sleep disturbances in children and adolescents include enforcing strict routines for bedtime and wake-up time, reducing environmental stimulation prior to/at bedtime (e.g., limiting TV and video games), and encouraging daily physical exercise. It is helpful to ascertain the child’s current serum iron status through measurement of serum ferritin levels as symptoms of RLS and PLMS have been shown to be associated with low serum ferritin levels (<50ng/dL).

Dopamine pathways have been implicated as the common pathophysiological link in comorbid RLS and ADHD. Low serum iron stores can affect levels of dopamine since iron is the cofactor for tyrosine hydroxylase, a rate-limiting enzyme, during production of dopamine. Iron supplementation has been shown to be effective in reducing symptoms of RLS and PLMD, as well as daytime symptoms consistent with ADHD. Iron therapy is usually initiated at doses of 1 to 2mg/kg (elemental iron) with a target to achieve ferritin levels more than 50ng/dL, and concomitant vitamin C supplementation can help in better iron absorption.

Clinicians should thoroughly assess for symptoms of ADHD in patients with RLS and vice versa. Dopaminergic agonists, such as pramipexole and ropinirole, are approved by the United States Food and Drug Administration (FDA) for treatment of RLS in adults, but are not approved for use in children.

Other pharmacological agents (clonidine, gabapentin, clonazepam, benzodiazepine) have been shown to be effective in treatment of adult RLS symptoms, but controlled trials in children are largely lacking. These medications may be useful to treat severe RLS associated with sleep disruption and daytime impairments in older children and adolescents.

Dopaminergics, such as pramipexole and ropinirole, have been shown to be useful in adults, and some limited data support their use in pediatric RLS (particularly comorbid ADHD). The sedating effects of these medications can be a potential advantage
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in children with RLS and sleep-onset/maintenance difficulties, but daytime grogginess and hyperactivity can be problematic (especially in children with underlying ADHD) and should be monitored.

Bupropion has been shown to be effective in reducing symptoms of PLMS in adults with comorbid depression, and is potentially useful in children and adolescents. Use of antidepressants, such as serotonin reuptake inhibitors, has been shown to exacerbate symptoms of RLS as well as increase periodic limb movements in sleep. However, one review concludes that the data to support antidepressant use as a potential etiological factor for RLS is “limited.” Nevertheless, antidepressants should be used with caution in children with RLS and PLMS, and other potential therapeutic agents described above should be explored in comorbid mental disorders and sleep-related movement disorders.

In summary, if clinical suspicion for RLS/PLMS exists through subjective data and objective findings (polysomnogram) during an evaluation of a child, behavioral interventions should be initiated along with evaluation of iron status followed by iron supplementation, if needed.

Childhood insomnia. Insomnia in children is defined as repeated difficulty with sleep initiation, duration, consolidation, or quality that occurs despite age-appropriate time and opportunity for sleep, which results in daytime functional impairment for the child and/or family. Behavioral insomnia of childhood (BIC) most often presents as bedtime refusal or resistance, delayed sleep onset, and/or prolonged night-time waking that requires parental intervention. BIC is classified into three categories: sleep-onset association type, limit-setting type, and combined type. In the sleep-onset association type, children have difficulty initiating sleep independently and associate falling asleep with certain circumstances, such as place (couch or parent’s bed), a person’s presence (parent), or an activity (feeding from a bottle, being rocked, watching television). Thus, these
circumstances are required for the child to re-initiate sleep in the middle of the night. In limit-setting type, the child delays bedtime with multiple requests or refusal, while the parent has difficulty setting limits, allowing bedtime to delay. If a child requires certain circumstances to initiate sleep and there are difficulties with parental limit-setting, the diagnosis is combined type.

Etiology of pediatric insomnia is almost always multifactorial, and this understanding helps guide the clinician toward a thorough assessment and formulating a treatment plan. Assessment should include screening for presence of concurrent medical, psychiatric, and developmental disorders; associated functional impairments at school and home; and any associated burden on caregivers. It is also vital to screen for presence of OSA or RLS, as these may be possible etiologies behind a presenting symptom such as insomnia.

It is also important to determine whether the difficulties with sleep onset and/or maintenance are due to inappropriate/inconsistent sleep schedules or napping schedules. For example, parents may have expectations of napping that may be outside of a child’s developmental need or implement inconsistent or inappropriate naps (e.g., naps closer to bedtime), which lead to difficulty regulating the child’s sleep-wake schedule. Eliminating the nap at an inappropriate age can also result in an increase in the child’s behavioral difficulties at bedtime rather than helping with earlier sleep onset and/or sleep maintenance. The same issues relate to teenagers. Variable sleep schedules, later bedtimes, and early school start times are strongly associated with inappropriate napping in adolescents. Adolescents who regularly take long naps will likely take longer to fall asleep at bedtime, further disrupting the sleep-wake cycle.

Behavioral interventions should be the mainstay of treatment of pediatric insomnia and should be offered as initial treatment (or in conjunction with medications) to parents and children. Behavioral interventions aim to help children initiate and maintain sleep independently, resulting in increased total sleep
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time and improved sleep quality. A recent review published by the American Academy of Sleep Medicine found that behavioral interventions produce both reliable and lasting improvements in bedtime problems and night wakings in infants and young children. Sleep problems in children younger than age 5 improved in 94 percent of the 54 studies reviewed, and over 80 percent of children benefited from treatment with most improvements continuing for 3 to 6 months. Extinction and parent education/prevention received strongest support after empirical review. Gradual extinction, bedtime fading, positive routines, and scheduled awakenings were also strongly supported as treatments for young children. It is important to note that the key component for success is parental consistency when implementing the specific techniques, particularly during the presence of an extinction burst once unmodified or gradual extinction is implemented. Some interventions may need to be tailored for the parent and child when taking into account issues such as siblings, room-sharing, parental stress, and parental skills in limit setting.

PEDIATRIC SLEEP DISORDERS

Pediatric sleep disorders represent highly common phenomena that often interfere with daily patient and family functioning. Interest in and treatment of sleep disturbances in youth continues to increase, but research continues to lag. A recent survey indicated that pediatricians were more likely to prescribe antidepressant medications for insomnia than psychiatrists. Further investigation is needed to develop empirically based detection and treatment of pediatric sleep disorders.

The consequences of untreated sleep problems may include significant emotional, behavioral, and cognitive dysfunction. The magnitude of these sequelae is inversely proportional to the child’s overall ability to adapt and develop in spite of the sleep disturbance. Nevertheless, sleep regulation remains a critical part of health for youths. Elevated rates of sleep problems exist
among children and adolescents with neurodevelopmental, nonpsychiatric medical conditions and psychiatric disorders.

Reciprocal relationships occur between sleep disorders and comorbid psychiatric disorders. For example, when a given child with recurrent depression has an exacerbation, sleep problems often increase simultaneously. On the other hand, disrupted and inadequate sleep alone can produce behavioral, affective, and cognitive dysfunction. Neurobiologically, closely linked modulatory systems appear to regulate sleep, alertness, and attention span. This chapter focuses on the most prevalent sleep problems among youths that are typical and distinctly unique from adult sleep disorders. Night terrors, nightmares, and sleep apnea are covered only briefly.

Major scientific advances have altered the understanding of sleep disorders, which have resulted in major changes moving from Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition Text Revision (DSM-IV-TR) to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5). Sleep disorders were divided into 3 categories: Dyssomnias, Parasomnias, and Medical Psychiatric Disorders. These categorical differences were eliminated in the DSM-5 to encourage the understanding that medical disorders and sleep disorders are intertwined and primary causation is usually not important. The entire section has been renamed Sleep-Wake Disorders to highlight that etiology may be based in the inability to maintain alertness during the waking period. The definition of dyssomnia versus parasomnia is provided to highlight the developmental differences of sleep-wake disorders.

Patients with dyssomnias present with difficulty initiating or maintaining sleep or with excessive daytime somnolence. The DSM-IV-TR defines dyssomnias as primary disturbances in the quantity, quality, or timing of sleep. These disorders are believed to be a consequence of central nervous system (CNS) abnormalities that alter the sleep process. Adolescents with and without substance use disorders represent a significant proportion of
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sleep-disordered youths. This is an excellent example how difficult it may be to distinguish a primary sleep disorder from those induced by medical conditions.

Parasomnias result in disruption of an existing state of sleep. Arousals, partial arousals, and sleep-stage transition impositions define this category. An alternative definition of these phenomena describes deviated behavioral or physiologic events that transpire during sleep, specific sleep stages, or sleep-wake transitions. Insomnia or excessive sleepiness is uncommon in parasomnias despite intrusion upon sleep; these symptoms are characteristic of dyssomnia. Most parasomnias affect otherwise healthy youths and commonly subside over the course of adolescence. These disorders are typically viewed as transient developmental phenomena, though children with parasomnias have been found to display higher rates of sleep-onset delay, night awakenings, bedtime resistance, and reduced sleep duration compared to a community control group.

DIAGNOSIS OF PEDIATRIC SLEEP DISORDERS

Evaluation and treatment for pediatric sleep disorders begins in our outpatient pediatric sleep medicine clinics.
Outpatient Pediatric Sleep Medicine Clinic

Parents/caretakers of children who need a sleep evaluation may be required to complete a sleep questionnaire and a two-week sleep diary (PDF). This information will help the sleep medicine physician better understand your child’s sleep problems prior to the sleep clinic visit.

During a clinic visit, a board-certified pediatric sleep medicine specialist will obtain additional necessary information from the parents about the child’s sleep problem and will conduct a thorough physical examination of the child. If necessary, additional blood tests may be performed, particularly for overweight and obese children. These tests measure fasting blood sugar, insulin, cholesterol, and triglyceride levels. If it’s determined that an overnight sleep study (polysonomogram) is required, our team will work with parents/caretakers to schedule a convenient time for the study to take place at one of our sleep laboratories.

Overnight Sleep Studies & Sleep Laboratories

Often, the best way to diagnose a sleep disorder is to observe a child while they’re sleeping and to record several measures that can help pinpoint the cause of a sleep problem. University of Chicago pediatric sleep medicine experts oversee sleep medicine laboratories and provide expert interpretation of sleep studies.

Our comfortable, child-friendly sleep labs are equipped with the latest technology and are staffed by certified sleep technologists. Types of sleep studies offered include the following:

Overnight Sleep Study (Polysomnogram):

During a routine overnight sleep study, data are gathered from multiple tests to be analyzed together to determine a proper diagnosis. Electrodes are attached to the surface of the child’s skin and connected back to machines to record data for the following tests:
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- Electroencephalogram (EEG) to monitor brain activity and aid in diagnosis of possible seizure disorders
- Electroculeogram (EOG) to record eye movements and determine when REM sleep occurs
- Electrocardiogram (ECG or EKG) to monitor electrical activity of the heart
- Electromyogram (EMG) to measure muscle tension and to aid in the diagnosis of limb movement disorders

Additional body sensors will be placed to assess breathing and respiratory functions. We also perform pulse oximetry to measure blood oxygen levels. A video camera will record the study as well. A sleep technologist is always nearby throughout the study.

**Multiple Sleep Latency Testing (MSLT)**

Multiple sleep latency testing is a special type of sleep study that is performed during the day to examine reasons for excessive daytime sleepiness. The test also is used to determine if current treatments for sleep breathing disorders are working. Most of the same measures recorded for an overnight sleep study are taken during an MSLT. During the test, the child naps for a period of time and is awoken at periodic intervals. MSLT for children is best conducted in a sleep lab experienced in conducting pediatric sleep studies.

Additional Sleep Tests for Children with Complex Needs:
- Continuous positive airway pressure (CPAP) titration studies for children with sleep apnea
- Ventilator titration studies for children who rely on ventilators to breathe
- Studies for children who have tracheostomies, such as for severe sleep apnea or following surgery
- Oxygen titration studies for patients with severe lung disease
- Specialized tests to monitor seizure disorders (epilepsy)
• Studies to evaluate gastroesophageal reflux disease (GERD) during sleep

Home Sleep Studies

In some instances, a home sleep study be conducted in the convenience of the child’s own home. During an overnight home sleep test, the patient wears small, portable sleep devices that measure breathing effort, airflow levels and oxygen saturation. In the morning, a home health care professional will collect the device, download the data and send it to University of Chicago sleep medicine experts for analysis.

Sleep Research Studies

University of Chicago pediatric sleep scientists are conducting a variety of clinical research studies. Current patients and children who are not currently under care by one of our sleep specialists may enroll in these studies.

TREATMENT FOR PEDIATRIC SLEEP DISORDERS

Treatment is tailored to your child’s particular sleep disorder. Types of treatments offered through our program include the following, and more:

• Recommendations for proven methods and routines to help your child fall asleep and stay asleep, such as:
  o Behavioral treatments that address ways to reinforce good sleep habits
  o Techniques to calm children who suffer from sleep-related anxiety or night terrors/nightmares
  o Adjustments to sleep and feeding schedules

• Continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea. CPAP therapy involves the use of a machine and a special mask that delivers air to ensure unobstructed breathing during sleep. Our team is highly skilled in helping children acclimate to using the CPAP machine at home.
• Medications, if necessary, for children with complex medical problems. These medicines can help restore more normal sleep patterns, helping your child go to sleep or wake properly.
• Referrals to other pediatric specialists who can provide expert care for conditions that disrupt sleep. These conditions include obesity, gastroesophageal reflux disease (GERD), developmental disorders, epilepsy/seizure disorders, respiratory conditions, craniofacial disorders, and neuromuscular diseases. Many children can be helped with surgical treatments, such as tonsillectomy, adenoidectomy, or maxillofacial surgery.
• Our pediatric sleep medicine physicians work closely with other University of Chicago pediatric specialists, including pulmonologists, otolaryngologists (ENT surgeons), developmental experts, gastroenterologists, neurologists, craniofacial surgeons, psychologists, and psychiatrists.

SLEEP DISORDERS (PEDIATRIC)

Poor sleep can have a negative impact on a child, making it difficult to concentrate at school and causing behavioral problems, among other issues. The Pediatric Sleep Disorders Program at the University of Michigan Health System is the only pediatric sleep program that also offers a multidisciplinary sleep clinic in the state of Michigan, and one of the largest in the country. We are dedicated to providing comprehensive assessment and treatment of infants, children and adolescents with a variety of sleep problems.

We evaluate a large number of sleep issues, including:
• Snoring/breathing difficulties
• Sleep related breathing disorders, including:
  o Obstructive Sleep Apnea
  o Central Sleep Apnea
o Apnea of Infancy
o Sleep-related hypoventilation

- Insomnia
- Bedtime refusal
- Disorders of the sleep/wake schedule
- Unusual movements or behaviors during sleep
- Nightmares
- Night terrors
- Sleepwalking
- Excessive daytime sleepiness
- Teeth grinding
- Restless leg syndrome
- Circadian rhythm disorders, such as delayed sleep phase in teenagers
- Disorders associated with excessive daytime sleepiness, such as narcolepsy

We carefully evaluate your child and take a comprehensive history by our board-certified sleep physician. Our multidisciplinary team is made up of a board-certified sleep medicine specialist, a developmental/behavioral pediatrician and a pediatric psychologist, as well as sleep medicine and psychology fellows. Sleep studies are conducted at the Michael S. Aldrich Sleep Disorders Lab, one of the few centers of distinction for sleep medicine in the country, by sleep technicians trained in conducting sleep studies in children.

We also offer a multidisciplinary Prader-Willi clinic in conjunction with Pediatric Endocrinology and Orthopedics in the evaluation of sleep disorders in children with Prader-Willi syndrome.

Once a diagnosis is made, a wide range of effective treatment strategies is available. The majority of sleep problems can be improved, controlled or eliminated. For children with obstructive sleep apnea who are intolerant to with continuous positive airway
pressure (CPAP) or BiPAP, we will be offering an innovative alternative. We will offer in the one clinic visit, a visit with ear, nose and throat specialist, an orthodontist, a sleep medicine specialist and an oro-maxillofacial surgeon (specializes in bone and soft tissue reconstruction). The team of specialists will confer at the end of the visit and develops a treatment strategy that could include surgery, or a dental appliance to hold the jaw forward during sleep.

For children where sleep apnea (not breathing for two breaths or longer during sleep) is suspected but has never been identified, we offer esophageal pressure monitoring during a polysomnography sleep study. The procedure involves putting a thin tube down the nose to the esophagus with a little balloon on the end, which shows increased work during sleep. The procedure is well tolerated by patients. It allows us to diagnose sleep-related breathing disorders, even when other labs cannot identify them. Our sleep lab is one of very few in the country and the only one in Michigan to offer this type of monitoring.
Pediatric Muscular Dystrophies and Myopathies

Muscular dystrophy (MD) is a collective group of inherited noninflammatory but progressive muscle disorders without a central or peripheral nerve abnormality. The disease affects the muscles with definite fiber degeneration but without evidence of morphologic aberrations.

The first historical account of MD was reported by Conte and Gioja in 1836. They described two brothers with progressive weakness starting at age 10 years. These boys later developed generalized weakness and hypertrophy of multiple muscle groups, which are now known to be characteristic of the milder Becker MD. At the time, however, many thought that Conte and Gioja described tuberculosis; thus, they did not achieve recognition for their discovery.

In 1852, Meryon reported in vivid details a family with four boys, all of whom were affected by significant muscle changes but had no central nervous system abnormality when examined at necropsy. Meryon subsequently wrote a comprehensive monograph on MD and even went on to suggest a sarcolemmal defect to be at the root of the disorder. He further suspected that the disorder is genetically transmitted through females and affects only males.
Guillaume Duchenne was a French neurologist who was already famous for his application of faradism (the use of electric currents to stimulate muscles and nerves) in the treatment of neurologic disorders when he wrote about his first case of MD. In 1868, he gave a comprehensive account of 13 patients with the disease, which he called “paralysie musculaire pseudo-hypertrophique.” Because Duchenne was already held in high esteem for his work in faradism and for his contributions to the understanding of muscle diseases, one of the most severe and classic forms of MD, Duchenne MD, now bears his name.

The advancement of molecular biology techniques illuminates the genetic basis underlying all MD: defects in the genetic code for dystrophin, a 427-kd skeletal muscle protein (Dp427). These defects result in the various manifestations commonly associated with MD, such as weakness and pseudohypertrophy. Dystrophin can also be found in cardiac smooth muscles and in the brain (accounting for the slight mental retardation associated with this disease). Minor variations notwithstanding, all types of MD have in common progressive muscle weakness that tends to occur in a proximal-to-distal direction, though there are some rare distal myopathies that cause predominantly distal weakness. The decreasing muscle strength in those who are affected may compromise the patient’s ambulation potential and, eventually, cardiopulmonary function.

In addition, structural soft-tissue contractures and spinal deformities may develop from poor posturing caused by the progressive muscle weakness and imbalance, all of which can further compromise function and longevity. Equinovarus contractures start as flexible dynamic deformities and advance to rigid contractures. This altered anatomy prevents normal ambulation, proper shoe wear, and transfers (how patients can be picked up to transfer out of their chair).

Once wheelchair-bound, patients with MDs tend to develop worsening contractures and rapidly progressive scoliosis. On average, for each 10° of thoracic scoliosis curvature, the forced
vital capacity (FVC) decreases by 4%. In a patient with an already-weakened cardiopulmonary system, this decrease in FVC could rapidly become fatal.

The goal of orthopedic management is, therefore, to preserve or prolong patients’ ambulatory status for as long as possible. This goal can be achieved with soft-tissue releases for contractures. If the patient develops significant scoliosis, which generally occurs after they stop walking, early stabilization of the spine should be considered.

MUSCULAR DYSTROPHY

Muscular dystrophy (MD) is a group of muscle diseases that results in increasing weakening and breakdown of skeletal muscles over time. The disorders differ in which muscles are primarily affected, the degree of weakness, how fast they worsen, and when symptoms begin. Many people eventually become unable to walk. Some types are also associated with problems in other organs.

There are nine main categories of muscular dystrophy that contain more than thirty specific types. The most common type is Duchenne muscular dystrophy (DMD) which typically affects males beginning around the age of four. Other types include Becker muscular dystrophy, facioscapulohumeral muscular dystrophy, and myotonic dystrophy. They are due to mutations in genes that are involved in making muscle proteins. This can occur due to either inheriting the defect from one’s parents or the mutation occurring during early development. Disorders may be X-linked recessive, autosomal recessive, or autosomal dominant. Diagnosis often involves blood tests and genetic testing.

There is no cure for muscular dystrophy. Physical therapy, braces, and corrective surgery may help with some symptoms. Assisted ventilation may be required in those with weakness of breathing muscles. Medications used include steroids to slow muscle degeneration, anticonvulsants to control seizures and
some muscle activity, and immunosuppressants to delay damage to dying muscle cells. Outcomes depend on the specific type of disorder.

Duchenne muscular dystrophy, which represents about half of all cases of muscular dystrophy, affects about one in 5,000 males at birth. Muscular dystrophy was first described in the 1830s by Charles Bell. The word “dystrophy” is from the Greek dys, meaning “difficult” and troph meaning “nourish”. Gene therapy, as a treatment, is in the early stages of study in humans.

**Signs and symptoms**

The signs and symptoms consistent with muscular dystrophy are:

- Progressive muscular wasting
- Poor balance
- Scoliosis (curvature of the spine and the back)
- Progressive inability to walk
- Waddling gait
- Calf deformation
- Limited range of movement
- Respiratory difficulty
- Cardiomyopathy
- Muscle spasms
- Gowers’ sign

**Cause**

These conditions are generally inherited, and the different muscular dystrophies follow various inheritance patterns. Muscular dystrophy can be inherited by individuals as an X-linked disorder, a recessive or dominant disorder. Furthermore, it can be a spontaneous mutation which means errors in the replication of DNA and spontaneous lesions. Spontaneous lesions are due to natural damage to DNA, where the most common are depurination and deamination.
Dystrophin protein is found in muscle fibre membrane; its helical nature allows it to act like a spring or shock absorber. Dystrophin links actin in the cytoskeleton and dystroglycans of the muscle cell plasma membrane, known as the sarcolemma (extracellular). In addition to mechanical stabilization, dystrophin also regulates calcium levels.

Recent studies on the interaction of proteins with missense mutations and its neighbors showed high degree of rigidity associated with central hub proteins involved in protein binding and flexible subnetworks having molecular functions involved with calcium.

**Diagnosis**

The diagnosis of muscular dystrophy is based on the results of muscle biopsy, increased creatine phosphokinase (CPK3), electromyography, and genetic testing. A physical examination and the patient’s medical history will help the doctor determine the type of muscular dystrophy. Specific muscle groups are affected by different types of muscular dystrophy.

Other tests that can be done are chest X-ray, echocardiogram, CT scan, and magnetic resonance image scan, which via a magnetic field can produce images whose detail helps diagnose muscular dystrophy.

**Management**

Currently, there is no cure for muscular dystrophy. In terms of management, physical therapy, occupational therapy, orthotic intervention (e.g., ankle-foot orthosis), speech therapy, and respiratory therapy may be helpful. Low intensity corticosteroids such as prednisone, and deflazacort may help to maintain muscle tone. Orthoses (orthopedic appliances used for support) and corrective orthopedic surgery may be needed to improve the quality of life in some cases. The cardiac problems that occur with EDMD and myotonic muscular dystrophy may require a pacemaker. The myotonia (delayed relaxation of a muscle after...
a strong contraction) occurring in myotonic muscular dystrophy may be treated with medications such as quinine.

Occupational therapy assists the individual with MD to engage in activities of daily living (such as self-feeding and self-care activities) and leisure activities at the most independent level possible. This may be achieved with use of adaptive equipment or the use of energy-conservation techniques. Occupational therapy may implement changes to a person’s environment, both at home or work, to increase the individual’s function and accessibility; furthermore, it addresses psychosocial changes and cognitive decline which may accompany MD, and provides support and education about the disease to the family and individual.

**Prognosis**

Prognosis depends on the individual form of MD. In some cases, a person with a muscle disease will get progressively weaker to the extent that it shortens lifespan due to heart and breathing complications. However, some of the muscle diseases do not affect life expectancy at all, and ongoing research is attempting to find cures and treatments to slow muscle weakness.

**History**

In the 1860s, descriptions of boys who grew progressively weaker, lost the ability to walk, and died at an early age became more prominent in medical journals. In the following decade, French neurologist Guillaume Duchenne gave a comprehensive account of the most common and severe form of the disease, which now carries his name—Duchenne MD. It soon became evident that the disease had more than one form. The other major forms are Becker, limb-girdle, congenital, facioscapulohumeral, myotonic, oculopharyngeal, distal, and EDMD. Duchenne and Becker muscular dystrophies, being caused by a mutation of a gene located on the X chromosome, predominantly affect males, although females can sometimes have severe symptoms, as well. Most types of MD are multisystem disorders with manifestations
in body systems including the heart, gastrointestinal system, nervous system, endocrine glands, eyes, and brain.

**Research**

WHO International conducted trials on optimum steroid regimen for MD, in the UK in 2012. In terms of research within the United States, the primary federally funded organizations that focus on muscular dystrophy research, including gene therapy and regenerative medicine, are the National Institute of Neurological Disorders and Stroke, National Institute of Arthritis and Musculoskeletal and Skin Diseases, and National Institute of Child Health and Human Development.

In 1966, the Muscular Dystrophy Association began its annual Jerry Lewis MDA Telethon, which has probably done more to raise awareness of muscular dystrophy than any other event or initiative. Disability rights advocates, however, have criticized the telethon for portraying victims of the disease as deserving pity rather than respect.

On December 18, 2001, the MD CARE Act was signed into law in the USA; it amends the Public Health Service Act to provide research for the various muscular dystrophies. This law also established the Muscular Dystrophy Coordinating Committee to help focus research efforts through a coherent research strategy.

**PROGRESSIVE MUSCULAR DYSTROPHIES**

Muscular dystrophies are genetically transmitted diseases characterized pathologically by degeneration and loss of myofibers and clinically by inexorably progressive weakness and, many of them, by elevated CK. The pattern of weakness, tempo of evolution, and mode of inheritance vary among different dystrophies. Over 30 genes causing muscular dystrophy are known presently. Muscular dystrophies are clinically classified into the following groups:
Pediatric Muscular Dystrophies and Myopathies

- Dystrophinopathies (Duchenne and Becker muscular dystrophies)
- Limb-Girdle dystrophies
- Myotonic dystrophy
- Facioscapulohumeral and scapuloperoneal dystrophy
- Oculopharyngeal muscular dystrophy
- Distal myopathies
- Emery-Dreifuss muscular dystrophy
- Congenital muscular dystrophies.

Some of these groups contain several entities with different inheritance patterns. The most common muscular dystrophy in children is Duchenne muscular dystrophy. In adults, the most common dystrophies are myotonic dystrophy and the limb girdle dystrophies. The molecular pathogenesis and the basis for the genotypic and phenotypic diversity of muscular dystrophies are now beginning to be understood. The key structure in muscular dystrophies is the muscle membrane.

Most muscular dystrophies are due to break down of the dystrophin-glycoprotein complex, a network of fibrous proteins that bind myofibers to the matrix and stabilize the sarcolemma during contraction and relaxation. Some of these proteins are located in the muscle fiber just inside the sarcolemma (dystrophin); others are embedded in the sarcolemma (sarcoglycans); and others are located in the basement membrane outside the sarcolemma (alpha-dystroglycan, merosin). Loss of
the integrity of this network causes stress fractures of the sarcolemma to develop during muscle contraction. Influx of calcium through these breaks activates proteolytic enzymes leading to autodigestion of the sarcoplasm (myonecrosis). Defects of dystrophin cause the Duchenne and Becker muscular dystrophies. Abnormalities of sarcoglycans cause some limb girdle dystrophies. Deficiency of basement membrane proteins such as α2 laminin results in congenital muscular dystrophy. Based on these insights, the phenotypic classification is being replaced by a genetic-molecular classification. For instance, Duchenne and Becker muscular dystrophies are dystrophinopathies, several limb-girdle dystrophies are sarcoglycanopathies, etc. The clinical, pathological, and molecular aspects of the most common dystrophies are briefly described below.

DYSTROPHINOPATHIES

![Fig. Duchenne muscular dystrophy. Left:Dystrophin immunostain; right:Spectrin (control) immunostain.](image)

Duchenne and Becker muscular dystrophies (DMD-BMD) are caused by mutations of dystrophin, the largest known human gene, located on chromosome Xq21. They are transmitted in an X-linked pattern, i.e. from mother to son. Mothers and daughters are carriers. They have one normal and one abnormal copy of the gene. Male children who inherit the defective copy develop full blown disease. In DMD, dystrophin is absent. In BMD, it is severely reduced and of an abnormal molecular structure. The
abnormality can be demonstrated by treating sections of muscle with antibodies to dystrophin. In normal muscle, all muscle fibers show a strong reaction along the sarcolemma. In DMD (left), no reaction is seen. DMD muscle stained with antibodies to other membrane proteins such as spectrin (right) shows a normal reaction. In BMD, parts of muscle fibers have dystrophin, and other parts do not. The female carriers of DMD have a mixed population of myofibers, some with dystrophin and some without.

![Early Myonecrosis](image)

The key pathology of DMD is myonecrosis. At an early phase, necrotic fibers appear homogeneous and deeply eosinophilic. Macrophages then enter necrotic myofibers and remove the debris. Breaks of the sarcolemma allow also CK and other intramuscular proteins to leak out into the interstitial fluid and serum in massive amounts. Myofibers are huge cells. The membrane changes and myonecrosis in dystrophinopathies do not involve the entire muscle fiber, but only parts of it. Myonuclei in unaffected segments divide, activate synthesis of new myofilaments and repair the damage. However, because of the inherent molecular defect, repair is incomplete and cannot keep up with necrosis. Gradually muscle is lost, causing severe
weakness. Myonecrosis triggers inflammation. Inflammatory cytokines activate fibroblasts which lay down extracellular matrix proteins. This leads to fibrosis that permeates muscle and causes stiffness and contractures, major causes of disability in DMD. Lost muscle is replaced by fat.

These changes are most severe in DMD in which clinical abnormalities begin in early childhood. At an early stage, some muscles, especially the calves, may appear large (pseudohypertrophy) due to compensatory hypertrophy of non-affected myofibers and increased fat. As the disease progresses, muscle is gradually lost. Patients are usually confined to a wheelchair by 10-12 years. Treatment with prednisone prolongs ambulation by 2-4 years by some poorly understood mechanism. Death usually occurs by the end of the second decade due to respiratory insufficiency and other complications. In BMD, symptoms begin later and the disease is more protracted. Some patients have a nearly normal lifespan. Dystrophin mutations cause also dilated cardiomyopathy. Twenty percent to 40% of females with dystrophin mutations have mild muscle disease or a dilated left ventricle. Even if asymptomatic, they often show mild elevation of CK and subtle changes in the muscle biopsy.
Pediatric Muscular Dystrophies and Myopathies

Myofiber loss

Cardiomyopathy in DMD
Cardiomyopathy in DMD

The key laboratory abnormality of DMD and BMD is severe CK elevation. Because the fibers of each motor unit are destroyed gradually, the EMG shows low voltage and short duration motor unit potentials or polyphasic potentials corresponding to residual myofibers within each motor unit.

The muscle biopsy shows myonecrosis, phagocytosis of necrotic fibers, regeneration, and non-specific structural changes (central nuclei, split fibers, atrophic and deformed fibers). Increased endomysial connective tissue and fat are also seen. In BMD, the changes are milder. In a 5-year-old boy with proximal weakness, pseudohypertrophy of the calves, a CK of 6,000 and the above biopsy findings, the diagnosis is hardly in doubt. Dystrophinopathy can be confirmed by immunohistochemistry and DNA analysis.

The same methods can be used for carrier detection. Because dystrophin is also present in myocardial fibers, a similar process gradually damages the myocardium causing a clinically dilated cardiomyopathy (DCM). DCM develops late in the course of the disease but once begun, progresses rapidly and is the cause of death in 20% of DMD and 50% of BMD patients. Some individuals with dystrophin mutations have DCM but no skeletal myopathy (DMD-associated DCM).
LIMB GIRDLE MUSCULAR DYSTROPHIES

The limb-girdle muscular dystrophies (LGMDs) are a genetically heterogeneous group. Ninety percent are autosomal recessive and 10% autosomal dominant. As a group, they are less frequent than the dystrophinopathies and are milder clinically, i.e., they begin in adolescence or adulthood and have a slower progression. However, a subset of autosomal recessive LGMDs which has been called “severe childhood autosomal recessive muscular dystrophy” (SCARMD) is almost as severe as Duchenne dystrophy is. The molecular defects that cause most LGMDs are now known. Many cases in the SCARMD group are caused by deficiencies of sarcoglycans. Other LGMDs are caused by mutations of other proteins the function of which is poorly understood. Most of these proteins have a close association with the sarcolemma suggesting that the pathogenesis of muscle damage has to do with a membrane abnormality. A relatively large group of autosomal recessive LGMDs are caused by mutation of calpain 3, a protease located in the contractile portion of myofibers. Caveolin-3 and dysferlin mutations also cause LGMD.

Congenital Muscular Dystrophies (CMDs)

CMDs are a group of rare muscle diseases that present at birth or soon after with hypotonia, weakness, and developmental delay, similar to the congenital myopathies. Contractures develop early in some CMDs. Unlike muscular dystrophies and similar to congenital myopathies, CMDs are nonprogressive and patients are left with static, though in some cases severe muscle disease. CK is high in some and minimally elevated or normal in others. The muscle biopsy shows nonspecific findings, initially myofiber atrophy and later myofiber loss with fibrosis and fat replacement. The biopsy findings may not correlate with the clinical severity. The differential diagnosis of neonatal hypotonia includes SMA, CMD, and congenital myopathy. With the main finding of myofiber atrophy, it is sometimes difficult to distinguish SMA
from CMD In a very young infant. Some CMDs are associated with severe CNS abnormalities. CMDs are genetic diseases; most are autosomal recessive. The main CMDs are:

- Merosin-deficient CMD, due to deficiency of α-laminin (merosin), a component of the basal lamina of myocytes and other cells. This CMD is associated with white matter abnormalities.
- Ullrich CMD, due to deficiency of Collagen VI, also an extracellular matrix component.
- CMDs due to abnormal glycosylation of α-dystroglycan, a dystrophin-associated protein. This group includes Fukuyama CMD, which is common in Japan, Muscle-Eye-Brain (MEB) disease, described in Finland, and Walker-Warburg syndrome (WWS). The WWS is the most severe condition among the CMDs and is associated with lissencephaly. Dystroglycan is also expressed in brain tissue, and is important for the normal migration and layering of cortical neurons.

**MYOTONIC DYSTROPHY**
Myotonic Dystrophy is an autosomal dominant muscular dystrophy characterized by weakness and stiffness, more pronounced in facial and distal muscles, and by increased muscle excitability. Atrophy and weakness of facial muscles, ptosis, and frontal baldness produce a characteristic facial appearance. Myotonia (prolonged muscle contraction) occurs spontaneously or is elicited by voluntary activity or by mild stimulation, such as tapping on a muscle (percussion myotonia). The EMG shows characteristic repetitive discharges. In many cases, a handshake is enough to establish the diagnosis (the myotonic patient cannot let go). Symptoms appear in adolescents or young adults, but no age is spared. At times, congenital myotonic dystrophy, transmitted from the mother, causes severe, even fatal hypotonia, weakness, and respiratory insufficiency in newborn babies. In
addition to muscle disease, patients with myotonic dystrophy have cataracts, cardiac arrhythmias, testicular atrophy, and diabetes. Weakness is progressive. The biopsy shows atrophy of type 1 fibers, a profusion of central nuclei (normally myonuclei are under the sarcolemma), and ring fibers. None of these changes are diagnostic individually, but their combination strongly suggests myotonic dystrophy. Congenital myotonic dystrophy is characterised by small fibers with central nuclei, similar to centronuclear myopathy.

There are two genetic forms of myotonic dystrophy, DM1, and DM2. They are similar in most respects, except that in DM1 weakness is predominantly distal and in DM2 proximal. DM1 is caused by a CTG trinucleotide expansion in the DMPK (Dystrophia Myotonica Protein Kinase) gene on chromosome 19q13. In DM1, this gene is expanded over 37 CTG repeats. The more repeats, the more severe the dystrophy and the earlier the onset of symptoms. Thus, 100-150 repeats cause myotonia and cataracts, 150-1000 cause full blown myotonic dystrophy, and over 1500-2000 repeats cause neonatal myotonic dystrophy. As with other diseases caused by trinucleotide repeats, the onset of the disease is earlier with each successive generation (anticipation). DM2 is caused by a CCTG expansion of the ZNF9 (Zink Finger Protein 9) gene on 3q21. Neither mutation affects the coding portion of these proteins and it is not known how these mutations affect muscle and other organs.

CONGENITAL MYOPATHIES

Congenital myopathies are primary muscle disorders. Unlike muscular dystrophies, which are caused by defects of the muscle membrane, most congenital myopathies are due to mutations of contractile, structural and other proteins, which result in structural abnormalities of myofibers and accumulation of abnormal proteins in the sarcoplasm. There are several congenital myopathies. The most common ones are nemaline, centronuclear and central core myopathy.
Nemaline myopathy

Nemaline myopathy
Nemaline or rod body myopathy (NM) (Greek *nema*, thread) shows small and disorganized myofibers which contain rod-shaped structures composed of α-actinin, the main protein of Z-bands.

The rods are found in the sarcoplasm but in some cases they may also occur in nuclei. It is caused by autosomal dominant or recessive mutations of several genes that encode components of thin filaments.

There are 6 clinical forms of NM ranging from the severe neonatal form, which presents at birth with severe hypotonia and may be fatal in infancy to the adult-onset variant that has a milder phenotype. Nemaline rods occur infrequently in other neuromuscular disorders, including dematomyositis and HIV myopathy.
Centronuclear myopathy

Congenital myotonic dystrophy
Centronuclear (myotubular) myopathy (CM) is characterized by small myofibers with central nuclei, and central areas without contractile filaments, like immature fetal muscle. The most frequent CM is X-linked CM, caused by mutations of MTM1 on Xq28, but there are also autosomally inherited CMs. The severe/classic X-linked form of CM presents with severe hypotonia and weakness at birth or prenatally and may be fatal in infancy. Severe congenital myotonic dystrophy may have a similar appearance to CM.
In central core disease (CCD) myofibers have a central area (core) lacking oxidative enzyme activity. The cores consist of disorganized contractile filaments without mitochondria. A similar lesion, target fiber, occurs in denervation. Minicores and multiminicores are variations of the same pathology. CCD is caused by autosomal dominant or recessive mutations of RYR1 which encodes the skeletal muscle ryanodine receptor, a calcium channel on the sarcoplasmic reticulum. Some CCD variants with multiminicores are caused by mutations of SEPN1. The product of SEPN1 interacts with the ryanodine receptor in regulating calcium homeostasis in muscle. Patients with CCD have hypotonia and weakness at birth or starting in infancy. Most patients have a normal lifespan but severe forms of CCD may be fatal in infancy. Mutations of RYR1 (and CCD) confer susceptibility to malignant hyperthermia, a disorder of skeletal muscle calcium regulation.

Congenital fiber type disproportion (CFTD). The congenital myopathies described above share in common a predominance and smallness of type 1 fibers. Some children with the clinical phenotype of congenital myopathy only have type 1 fiber predominance and smallness without other structural abnormalities. These cases have been called CFTD. It is not clear if CFTD represents a disease entity or a “finding”. Genetic testing in CFTD cases reveals mutations of genes that are also associated with other congenital myopathies.

**MYOPATHIES**

PatientPlus articles are written by UK doctors and are based on research evidence, UK and European Guidelines. They are designed for health professionals to use, so you may find the language more technical than the condition leaflets.

Myopathies are a heterogeneous group of conditions with diverse aetiologies. They usually affect muscle without involving the nervous system or any disorder of the neuromuscular junction.
The muscular dystrophies are the most common of such disorders and Duchenne muscular dystrophy is the most common muscular dystrophy. However, the broad range of myopathies is outlined in the boxes below which include some of the rare primary disorders of muscle as well as acquired myopathies.

The subsequent sections put these conditions in context and highlight some contrasting diagnostic and clinical features. Most of the congenital myopathies are chronic and slowly progressive. However, metabolic, inflammatory, toxic and endocrine myopathies present subacutely or even acutely and this requires awareness amongst front-line physicians to recognise and diagnose myopathy.

Aetiology

There are many causes of myopathy, both inherited and acquired.

Inherited myopathies

- Muscular dystrophies: eg, Duchenne muscular dystrophy, Becker’s muscular dystrophy, myotonic dystrophy, facioscapulohumeral muscular dystrophy, limb-girdle muscular dystrophy, congenital muscular dystrophy, oculopharyngeal muscular dystrophy, distal myopathy.
- Inherited biochemical defects causing myopathy - eg, mitochondrial myopathy, lipid storage disease (eg, carnitine palmitoyltransferase deficiency, myopathic carnitine deficiency), disorders of purine nucleotide metabolism, glycogen storage disorders (eg, Pompe’s disease, McArdle’s disease).

Acquired myopathies

- Immunologically mediated: eg, polymyositis, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa, polymyalgia rheumatica, inclusion body myositis.
- Non inflammatory myopathies: eg, hyperthyroidism,
hypothyroidism, Cushing’s syndrome, diabetes mellitus, hypoparathyroidism, hyperparathyroidism, electrolyte disturbances (hypercalcaemia, hypokalaemia).

- Toxic and cachectic myopathies: eg, acute alcoholic myopathy with myoglobinuria, paraneoplastic myopathy, protein malnutrition, drugs (eg, steroids, statins, zidovudine, clofibrate, colchicine, cocaine).

- Infection: eg, trichinosis, toxoplasmosis, human immunodeficiency virus (HIV), Coxsackie viruses, influenza, Lyme disease.

Epidemiology

These are all relatively uncommon diseases:

- Duchenne muscular dystrophy is easily the most common childhood-onset muscular dystrophy and affects 1 in 3,300 boys. The prevalence of Duchenne muscular dystrophy is 63 cases per million.

- The prevalence of the Becker phenotype is 24 cases per million.

- Congenital muscular dystrophy is approximately 50% as common as Duchenne muscular dystrophy.

Presentation

Clinical features of myopathy:

- The hallmark symptom of myopathy (and neuromuscular disease) is weakness.

- Weakness predominantly affecting proximal muscle groups (shoulder and limb girdles) is typical.

- Weakness manifests itself in different ways at different ages:
  - Decreased fetal movements in utero.
  - Floppy infant neonatally.
  - Motor delay in the toddler years.
  - Reduced muscle strength and power in older children and adults.
• Myalgia may occur in inflammatory myopathies.
• Muscle-stretch reflexes are preserved.
• Somatosensory reflexes are preserved.
• Variation of strength with exercise (either increasing or decreasing) can occur:
  o Fluctuating muscle power suggests metabolic myopathy (for example, McArdle’s disease).
  o Fatigability (or progressive weakness with exertion, relieved by rest) is a feature of myasthenia gravis where the defect is in neuromuscular transmission.

History:
• Common symptoms:
  o Malaise, fatigue.
  o Symmetrical proximal muscle weakness with absence of sensory symptoms (paraesthesia).
  o Atrophy of muscles (and reduced reflexes) occurs late with myopathies (early with neuropathy).
  o Waddling gait of Duchenne muscular dystrophy at age 3-6 years is typical.
• Acuteness of symptoms:
  o Weakness over hours suggests a toxic cause or episodic paralysis.
  o Weakness developing over days - consider dermatomyositis or rhabdomyolysis.
  o Weakness over weeks suggests polymyositis, steroid myopathy, endocrine myopathy.
• Affected muscle groups:
  o Proximal muscle groups - difficulty rising from chair, climbing stairs, shaving, hair combing.
  o Distal muscles - difficulty walking (flapping gait), grasping, handwriting.
• Metabolic myopathies present with:
  o Difficulty with exercise.
o Cramps and myalgia with exercise (early with glycogen storage disorders and after prolonged exercise with lipid storage disorders).

o Myoglobinuria.

o Progressive muscle weakness in some metabolic myopathies.

• Past medical history, including autoimmune disease (eg, systemic lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa), endocrine disease, kidney disease, alcoholism

• Family history of muscular dystrophy or any other relevant conditions or myopathies.

• Medication - eg, steroids, lipid-lowering drugs, colchicine, heroin, zidovudine.

• Occupational history - eg, pottery industry - glazing salts can cause hypokalaemic paralysis.

Examination:

• Symmetrical proximal muscle weakness.

• Muscle tenderness is very rare with myopathy.

• Fever with inflammatory causes.

• There is usually no wasting but there may be hypertrophy of muscle (atrophy is a late sign).

• Reflexes and sensation are usually normal.

• Hypotonia is common in some myopathies (for example, congenital myopathies).

• There may be helpful additional signs such as the skin changes of dermatomyositis.

• Urine should be examined - myoglobinuria in acute alcoholic myopathy can cause renal tubular necrosis.

**Differential diagnosis**

This list includes other conditions causing weakness:

• Guillain-Barré syndrome.
Clinical Neurophysiology in Pediatrics

- Lambert-Eaton myasthenic syndrome.
- Myasthenia gravis.
- Cerebral palsy.
- Spinal muscular atrophy.
- Congenital hypomyelinating neuropathies.

It may be difficult to distinguish myopathy from peripheral neuropathy. The distinguishing clinical features of peripheral neuropathy are:

- Weakness affecting distal muscles - although there are exceptions:
  - Myopathy where distal muscle groups are affected (myotonic dystrophy, myopathy of Welander).
  - Peripheral neuropathies which affect proximal muscles (diabetic amyotrophy, motor neurone disease).
- Reduced muscle - stretch reflexes.
- Fasciculations.
- Somatosensory abnormalities.

Some complex cases may have both neurogenic and myopathic disorders which can lead to diagnostic confusion:

- Diabetes mellitus can cause both neuropathy and inflammatory myopathy.
- Cancer can cause dermatomyositis and chemotherapy may cause peripheral neuropathy in the same patient.
- Radiculopathy (from degenerative disc disease) can occur in patients with myopathy.

INVESTIGATIONS

Blood and urine tests

These, together with ECG examination, are most useful in acute situations.

- Creatine kinase (with isoenzymes) - level may be 50-100 x normal reference range.
Renal function and electrolytes including calcium and magnesium.
- FBC, ESR, TFTs, antinuclear antibodies.
- Serum myoglobin.
- Urinalysis and urine microscopy - myoglobinuria inferred by positive urinalysis with few red cells at microscopy.

**ECG**

May show:
- Changes of hypokalaemia - increased P-R interval, U waves, wide QRS and nonspecific ST-T changes.
- Sinus arrhythmias, deep Q waves and elevated R waves precordially (for example, in Duchenne muscular dystrophy).

**Muscle biopsy**

Muscle biopsy is important in diagnosis but findings under the microscope are rarely pathognomonic. Interpretation requires close consideration of the clinical history in conjunction with the microscopic features to make a diagnosis.

**Electromyography**

- Excludes primarily neurogenic processes (for example, spinal muscular atrophy).
- Proximal muscles of lower extremities often exhibit the most prominent features.
- Often helps to confirm diagnosis but is not in itself diagnostic.

**Magnetic resonance imaging (MRI)**

- May help to exclude neurological disease.
- May help in assessing complications (musculoskeletal or involving other organs).

**Genetic testing**

The genetic basis of the primary myopathies means that
genetic testing can be essential to the specific diagnosis. As defects are identified, repair strategies have been developed. Many are now at the stage of clinical testing.

Management

This depends on the diagnosis as well as the severity and extent of disease.

Emergency management

Myopathy can, rarely, present acutely or with acute complications. Examples include:

- Respiratory difficulties:
  - Respiratory failure can occur in a number of the myopathies.
  - Aspiration pneumonia may also occur.
  - Cardiac complications may be associated including cardiomyopathy and conduction defects.

- Some metabolic myopathies:
  - Hypokalaemia: oral supplements, cautious use of intravenous potassium, and prophylactic drugs (spironolactone and acetazolamide).
  - Hyperkalaemia: carbohydrate loading (for example, early in attacks with hyperkalaemic periodic paralysis), glucose and insulin.


- Polymyalgia rheumatica: treatment with corticosteroids. Be aware of associated giant cell arteritis.

Long-term care

- Myopathy associated with respiratory failure:
  - Monitor pulmonary function (early restrictive pattern may occur before onset of symptoms).
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- Beware of symptoms of nocturnal hypoxia (poor sleep, nightmares, headaches).
- Physiotherapy.
- May require tracheostomy and permanent ventilation.
- Specific medication: may be useful in particular situations for particular myopathies.
- Genetic counselling.
- Surgery (eg tendon release surgery): for example, to prolong the ability to walk.
- Physical aids: walking aids, wheelchairs, adaptive devices
- Family support.
- Dietary advice: both general (for example, to prevent obesity) and specific dietary advice may be required for the underlying cause of myopathy.

Prognosis

This depends on the specific diagnosis. The primary disorders are incurable conditions with varied prognosis. Secondary myopathy may be corrected by treating the underlying cause.

Prevention

Genetic counselling is, in some of the most common myopathies such as Duchenne muscular dystrophy, the only intervention that can prevent disease. In general:
- Give genetic counselling early.
- Test early for carrier status where appropriate.
- Consider prenatal diagnostic testing where appropriate.
- Advances in molecular genetics may help in the future.
Clinical Evaluation in Pediatric Peripheral Neuropathies

The prevalence of peripheral neuropathies in children from resource-poor countries (RPCs) is not known. A study of adult and pediatric patients with neuromuscular disorders in Libya identified that the largest group had forms of Charcot-Marie-Tooth (CMT) disease followed by acute inflammatory demyelinating polyradiculoneuropathy (AIDP).

In Senegal, adults between 20 and 40 years of age were reported to have undefined degenerative neuropathies, labeled ‘tropical neuropathies’, which were responsible for half of their cases, followed by toxic neuropathies (ethanol and isoniazid), then CMT disease and finally diabetes. The authors highlighted the challenges of gaining diagnostic closure in RPCs such that many of the progressive cases were placed under this generic label of ‘tropical neuropathies’.

Another study from the same group quoted that 8.16% of their neurology referrals aged 3–80 years were related to peripheral neuropathies. Children with peripheral neuropathies represented one-third of the patients seen in the out-patient neuromuscular service at the Red Cross War Memorial Children’s
Hospital in Cape Town, South Africa and 3% of the total group attending the service with neurological conditions.

In comparison with more ‘developed settings’, the disease spectra and the prevalences of pediatric peripheral neuropathies are different in RPCs. There are greater numbers of infections that lead to direct and indirect development of peripheral neuropathy, such as from tuberculosis, HIV type 1 (HIV-1), leprosy and diphtheria. Neurotoxins are seen more often, especially where access to optimal therapy may be limited; for example, some antiretroviral therapy regimens for HIV infection still included 2´-3´-didehydro-2´-3´-dideoxythymidine (stavudine), which is associated with an increased risk of peripheral neuropathy.

Nutritional deficiencies, such as vitamin B<sub>1</sub> and E deficiencies, remain an important aspect of RPCs. Unrecognized results of trauma will also be more evident with badly set fractures causing irreversible damage to nerves.

This reflects the poor socioeconomic settings where many children have limited access to health facilities, poor nutrition and frequent infections. The hereditary disorders – both those of ‘pure peripheral neuropathies’ and those related to neurodegenerative and systemic diseases – are also considered to be greatly underestimated in RPCs.

The capacity to screen these patients is almost nonexistent, with a lack of access to basic blood analysis, neurophysiology and neuroimaging in most centers in Africa; this is also the case for more complex neurometabolic and molecular genetic screens. Nerve biopsy should only be undertaken in centers with the capacity to perform the sample collection and to analyze the data accurately – this is often lacking, even in a developed world setting. Supportive management of any child with peripheral neuropathy is fairly standard, regardless of the underlying etiology. Limited access to ancillary services, orthopedic care and orthotic devices challenges this. Teaching parents an effective
home program is often more practical. Exclusion of reversible causes is essential, though challenging in many cases.

**CLINICAL FEATURES**

Most peripheral nerve disorders have a gradual and slowly progressive course. Acute presentation may occur with trauma, toxic exposure, or inflammatory conditions.

Most peripheral neuropathies show bilateral, symmetric, predominantly distal involvement, though focal neuropathies do occur in children from various causes such as trauma. The severity of diffuse nerve injuries is related directly to axon length; thus, longer axons are affected first, resulting in symptoms that typically have an earlier presentation and are more prominent in the distal lower extremities. Most neuropathies have combined sensory and motor involvement. However, some disorders have only motor or sensory abnormalities.

The most common motor symptom is weakness. It may present as clumsiness, difficulty with running or climbing stairs, or impaired fine motor skills such as writing, buttoning clothes, opening jars, or tying shoes. Ataxia, or balance difficulty, is another motor symptom associated with neuropathy. Sensory symptoms may include numbness or positive sensory symptoms such as paresthesia, pain, or burning sensations.

**Localization to the Peripheral Nervous System**

Although usually assumed, this layer deserves mention because not all symptoms of distal numbness, tingling and pain, and weakness are referable to the peripheral nervous system. Failure to consider this step can lead to diagnostic errors. Examples referable to the central nervous system include asymmetry, unusual symptom patterns, and pathological tendon reflexes.

It is also important to consider that some patterns of symptoms may not be attributable to definable lesions within either the central or peripheral nervous systems, and a
somatoform disorder should be considered. Somatoform disorders represent distressful physical symptoms causing impaired social or occupational dysfunction with no diagnosable condition to account for them. Symptoms of numbness, paresthesias, pain, weakness, and fatigue are considered to be “pseudoneurological” when no neurological basis can be found. Whether a patient fulfills full DSM-IV criteria for somatization or undifferentiated somatoform disorders is less important than recognizing that further evaluation is unlikely to lead to a physical diagnosis. Every patient deserves a considered evaluation because somatization can accompany true diseases, but when reasonable localization cannot be achieved, neurological and laboratory examinations are normal, and the temporal pattern does not fit known pathological processes, it is highly unlikely that the symptoms represent a definable pathology.

When this occurs, an understanding discussion seeking other factors is appropriate. Opening the conversation to consideration of internal factors that may be causative or contributory should be taken slowly. Conditions such as depression, anxiety, and panic disorders may coexist. Replacing long-standing symptoms with the “good news” of “good health” is rarely successful. With long-standing symptoms, the family milieu may have incorporated the patient’s symptoms, and giving the patient a therapeutic way out of their dilemma, such as physical therapy, should be considered.

Peripheral Neuropathy Pattern

There are several patterns of peripheral neuropathy. The prototypic and most common pattern is symmetric and length-dependent, involving sensory loss and pain and, less frequently, distal weakness. As progressively shorter nerves are affected, symptoms and signs unroll up the leg as a stocking. Nerve length at knee level is approximately equal to the length innervating the hand, and with further progression, symptoms and signs unroll up the arm as a long glove. In the extreme, a shield loss over the
chest and abdomen can be observed when nerve length involvement reaches the circumference of the thorax. Most length-dependent peripheral neuropathies are chronic and involve axonal pathology. Causes of peripheral neuropathy are many and are felt to reflect metabolic abnormalities. Diabetes mellitus is the most common underlying cause of this type of neuropathy, followed by hereditary (genetic) neuropathies. The cause for many neuropathies of this type is unknown, and idiopathic or cryptogenic neuropathies represent up to 25% of peripheral neuropathies.

When the pattern of symptoms and signs includes both proximal and distal limb segments, the pathological process is usually demyelination at multifocal sites along roots and nerves (inflammatory polyradiculoneuropathy). Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) occur.

Asymmetric patterns are less common and include different lesion sites and pathological processes. Unilateral and focal symptoms and signs in a limb must be distinguished from radiculopathy, plexopathy, or mononeuropathy (mononeuritis multiplex). In some situations, the most frequent being diabetes mellitus, length-dependent neuropathies coexist with radiculopathies, plexopathies, and mononeuropathies. Atrophic weakness without sensory loss that does not follow a radicular, plexopathy, or mononeuropathy pattern suggests motor neuron disease (amyotrophic lateral sclerosis).

**CLINICAL APPROACH**

The initial step is to confirm whether the signs and symptoms are related to peripheral nerve dysfunction. Occasionally, the patient with neuropathy may present with multiple pathologies. Spinal cord disease is the most common differential diagnosis in patients with neuropathic symptoms. In some patients with myelopathy, the sensory symptoms are present with few clinical
Clinical Evaluation in Pediatric Peripheral Neuropathies

signs; the classic signs of lower motor neuron involvement may be absent, simulating peripheral neuropathy. Patients with lacunar stroke may rarely present with sensory loss in median or ulnar nerve distribution. Although patients with spinal canal stenosis present classically with neurogenic claudication, in advanced stage, they may be associated with persistent symptoms and the condition may be confused with peripheral neuropathy.

In elderly patients, often there is a coexistence of cervical spondylotic myelopathy with late onset predominantly sensory axonal neuropathy. Similarly, spondylotic radiculopathy may occur with upper limb entrapment neuropathies, and the coexisting pathologies should be carefully diagnosed. Neuropathy may also occur with CNS involvement in vitamin B12 deficiency, adrenomyeloneuropathy and acanthocytosis.

The peripheral nerves comprise sensory, motor and autonomic fibers, which have different lengths, diameters, conduction characteristics and specialized functions. Their involvement therefore results in diverse symptoms, signs and EDx features. Focusing on these symptoms is helpful in the diagnosis of peripheral neuropathy.

History

Occasionally, simple history such as funny feet, unevenly worn shoes, and childhood clumsiness are important clues to a long-standing illness well beyond the presenting symptoms. The duration of symptoms is important in categorizing neuropathy into acute (<4 weeks), subacute (4–12 weeks) and chronic (>12 weeks). Vasculitis results in hyperacute mononeuropathies usually occurring by 24–72 h. Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) by definition peaks by 4 weeks of onset, and a progression beyond 8 weeks suggests chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The time course study helps in limiting the diagnosis for acute and demyelinating conditions, which have different diagnostic and therapeutic approaches. The diagnostic criteria of AIDP and
those of CIDP. Sensory symptoms are usually the presenting symptoms of neuropathy and include positive (burning, pain, walking on cotton wool, band-like sensation on feet or trunk, stumbling, tingling, pins and needles) and negative symptoms (numbness, loss of sensation) in hands and feet.

Motor symptoms include weakness and patient may complain of difficulty in turning keys in locks, unfasten button and opening bottles and jars. In the early stage, weakness in peripheral neuropathy is distal; however early proximal weakness is a feature of inflammatory neuropathy and porphyric neuropathy.

Autonomic symptoms such as postural hypotension, impotence, sphincter disturbance, diarrhea, constipation, dryness or excessive sweating point to the involvement of small myelinated or unmyelinated nerve fibers.

**Symptoms and Topography**

Precise details regarding the site and character of sensory symptoms are helpful in localizing and characterizing the neuropathy as in meralgia paresthetica and carpal tunnel syndrome. Distal dying back axonopathies have a characteristic length-dependent pattern of the evolution of symptoms, which are usually symmetrical and affect feet, hand and trunk. Demyelinating neuropathies may also have a length-dependent pattern of sensory evolution because in a diffuse process, longer fibers have a greater likelihood of being blocked. In a multisegmental pattern of sensory involvement, including trunk, suggests dorsal root gangioneuropathies, as observed in Sjogren’s syndrome-associated neuropathy.

Pain, loss of temperature sensation and autonomic symptoms are the features of small fiber neuropathy. Ataxia in the dark or on eye closure is suggestive of large fiber involvement. These sensory patterns do not localize the lesion even to the peripheral nerve but provide a notion regarding the involvement of fiber type and narrow down the diagnostic possibilities.
Examination

A number of important diagnostic clues can be identified on general examination, but often require a return visit to the patient. Umbilical keratomas of Fabry’s disease, Mee’s lines in arsenic and thallium poisoning, orange tonsils in Tangier’s disease are rare diagnostic opportunities available to well-trained clinicians. Maculoanesthetic patches with thickened nerves are the diagnostic characteristics of leprosy. On cranial nerve examination, anosmia is a feature of Refsum’s disease and vitamin B_{12} deficiency; impaired pupillary light reflex may indicate parasympathetic involvement and prompt a detailed search for dysautonomia which may occur in diabetic neuropathy and GB syndrome.

External ophthalmoplegia is a feature of Miller Fisher syndrome, facial weakness of GB syndrome and trigeminal sensory loss of Sjogren’s syndrome and lower cranial nerve palsy with gynecomastia of Kennedy’s syndrome. The presence of musculoskeletal abnormality such as pes cavus, high-arched feet and mutilation suggest hereditary neuropathy.

Muscle power testing in the context of nerve and root distribution is crucial. Difficulties arise when multiple mononeuropathies become confluent, thus making the differentiation from polyneuropathy difficult. In such a situation, electrodiagnostic (EDx) studies are invaluable. Tendon reflexes are important in the diagnosis of neuropathies. Distal reflex loss manifesting with absent ankle reflex but preserved reflexes elsewhere are characteristic of length-dependent axonopathies. In acquired demyelinating neuropathies, reflex loss is usually generalized as in CMT I.

The sensory examination is best performed by testing modalities that subserve large fibers (vibration and joint position) and small fiber (pinprick, pain and temperature) in conjunction with consideration for both focal and length-dependent features since it can provide important diagnostic clues to the likely cause.
PATHOPHYSIOLOGY AND NATURAL HISTORY

Despite the diverse array of medical disorders that cause peripheral neuropathies, peripheral nerves exhibit only a few distinct pathologic reactions to an insult or disease: wallerian degeneration, axonal degeneration, and segmental demyelination. The specific mechanisms by which the various disorders affecting peripheral nerves induce these pathologic changes are largely unknown. In wallerian degeneration, the axon degenerates distal to a focal lesion that interrupts the continuity of the axon. This reaction often occurs in focal mononeuropathies that result from trauma or nerve infarction.

Axonal degeneration, sometimes referred to as the dying-back phenomenon, results in axonal degeneration at the most distal extent of the axon. Axonal degenerative polyneuropathies are usually symmetrical, and as the disorder progresses, the axons typically degenerate in a distal-to-proximal gradient. Axonal degeneration is the most common type of pathologic reaction in generalized polyneuropathies, and it is often attributed to a metabolic cause.

Segmental demyelination refers to focal degeneration of the myelin sheath with sparing of the axon. This reaction can be seen in focal mononeuropathies and in generalized sensorimotor or predominantly motor neuropathies. Acquired segmental demyelinating polyneuropathies are often immune-mediated or inflammatory in origin. However, segmental demyelination can also occur in some hereditary polyneuropathies.

In peripheral nerve disorders that are characterized by either wallerian degeneration or axonal degeneration, prognosis is less favorable because the axon must regenerate and reinnervate muscle, the sensory organ, blood vessels, and other structures before clinical recovery is noted. Recovery may be more rapid with segmental demyelination because remyelination is accomplished more quickly, thereby re-establishing normal conductivity of the axon and return of function.
Symptoms and Signs

A host of symptoms and signs that reflect sensory, motor, and autonomic nerve fiber dysfunction are typical of peripheral neuropathies, and some combinations of symptoms and signs may be recognized as specific syndromes of peripheral nerve disease. Sensory symptoms include sensory loss, often described by patients as a sense of numbness or a “Novocain-like” feeling. In most generalized polyneuropathies, these symptoms begin in the most distal extent of the longest sensory fibers (i.e., those that subserve sensation in the toes and feet). The pathologic changes in most of these polyneuropathies are those of a distal-to-proximal axonal degeneration that have been referred to as distal axonopathies or dying-back neuropathies. Similar symptoms may be seen in hereditary or acquired demyelinating polyneuropathies.

Sensory Symptoms

Typically, all sensory modalities are affected to some extent, including light touch, pain, thermal sensation, vibratory sense, and joint position sense. As the disease progresses, sensory loss ascends the lower extremities, typically in a symmetrical fashion. When the sensory loss is at or above the level of the knee, the axons supplying the distal fingertips begin to be involved, and the length-dependent process then begins in the upper extremities. In addition to sensory loss, patients often complain of paresthesias and dysesthesias, often characterized by a sense of numbness, tingling, prickling, and pins-and-needles sensations. They might also complain of intense bandlike sensations and feelings of pressure.

The sensory examination often discloses a distal-to-proximal loss of the various sensory modalities. In certain polyneuropathies, pain predominates in the clinical picture, and the sensory examination tends to disclose deficits predominantly of pain and thermal sensation, conforming to an SFN. On occasion, when significant proprioceptive deafferentation occurs, patients are found to have altered joint position sense that can manifest as
an ataxia or tremor of the affected limbs and an imbalance of gait and station.

Pain is a serious symptom for many patients. It may be described as a dull aching sensation, an intense burning sensation or, occasionally, as intermittent lancinating pulses of pain. On occasion, patients notice that their skin is hypersensitive to tactile stimulation such as from the touch of bed sheets or clothing or from standing on their feet. Some patients note an exaggerated painful sensation resulting from any stimulus to the affected area, a form of pain termed *allodynia*.

**Weakness**

Impairment of motor function typically produces weakness in a distal-to-proximal gradient consistent with a length-dependent axonal degeneration. As with sensory loss, weakness begins in the toes, and as the polyneuropathy progresses, it ascends up the distal lower extremities to the level of the knees, at which time motor involvement in the hands may be observed. Similar patterns of weakness may be seen in demyelinating polyneuropathies. However, in the acquired segmental demyelinating polyneuropathies such as CIDP and related disorders, proximal muscle weakness resulting from root involvement may be observed outside the proximal-to-distal gradient of the dying-back mechanism. This pattern of involvement is termed a *polyradiculoneuropathy*.

Axonal degenerative polyneuropathies tend to produce weakness along with muscle atrophy, but atrophy is much less conspicuous in segmental demyelinating polyneuropathies because in these disorders the axon remains in continuity with the muscle, preventing denervation atrophy. The most common symptom in polyneuropathy is weakness in dorsiflexion of the feet at the ankles. This can result in a partial or complete foot drop that typically causes the feet to slap while walking and predisposes the patient to stumble and fall when the toes catch on an uneven surface.
Tendon reflexes are usually depressed or absent in a distal-to-proximal pattern of involvement, with the lower extremities affected more than the upper extremities. An exception to this is in SFN, in which the large-caliber sensory afferent fibers from muscle spindles are relatively preserved and the tendon reflexes might remain intact.

**Autonomic Symptoms**

In some polyneuropathies, typically in SFN, autonomic fibers are also affected. In these disorders, a variety of autonomic symptoms may be present, although certainly the most dramatic and incapacitating is orthostatic hypotension, which causes postural light-headedness, syncope, or both. However, orthostatic hypotension typically occurs only with advanced autonomic involvement.

Earlier in the course of autonomic neuropathy, patients might notice reduced or absent sweating (i.e., anhidrosis) often in a distal-to-proximal gradient. Some patients complain of excessive sweating confined to the head and neck region. This is most often secondary to anhidrosis in the limbs and thorax and reflects compensatory hyperhidrosis in the restricted areas that maintain normal sweating.

Other autonomic symptoms include dryness of the eyes and mouth and gastrointestinal dysmotility, often manifested by alternating constipation and diarrhea or by early satiety from gastroparesis. In addition, patients may have urinary bladder dysfunction caused by an atonic bladder, which results in overflow incontinence. In men, erectile dysfunction can represent an early autonomic symptom, reflecting parasympathetic autonomic nervous system involvement.

**Other Symptoms and Signs**

Various limb deformities and trophic changes may be observed in chronic polyneuropathies. Pes cavus, characterized by high arches and hammer toes and the clawfoot deformity, are
typical foot deformities in hereditary polyneuropathies with childhood onset. These deformities are a result of progressive weakness and atrophy of intrinsic foot muscles. A similar claw-like deformity may be observed in the hand.

Autonomic involvement of a limb may, at times, cause the affected area to appear warm, red, and swollen and at other times pale and cold because of abnormal regulation of small vessels as a result of autonomic denervation. Various trophic changes can occur including tight, shiny skin.

In patients who have had severe sensory loss in the limbs, the affected areas may be subject to incidental traumas, including burns, pressure sores, and other injuries that are not perceived by the patient. In these patients, repeated injuries and traumas can result in chronic infections, sometimes leading to osteomyelitis.

In peripheral nerve disorders that are focal and asymmetrical, sensory and motor—and occasionally autonomic—symptoms and signs may conform to a specific peripheral nerve distribution. For example, in carpal tunnel syndrome, patients might complain of intermittent numbness and tingling in the median nerve distribution in the hand or, as the entrapment progresses, atrophy and weakness of the thenar muscle group. In the mononeuritis multiplex syndrome, multiple individual peripheral nerves may be affected, and the sensory, motor, and autonomic symptoms and signs will be distributed in a multifocal pattern conforming to numerous individual peripheral nerve lesions. On occasion, some peripheral nerve disorders cause generalized sensory and motor fiber involvement with asymmetrical and focal features.

**Diagnosis**

Diagnosis begins by recognizing typical symptoms of peripheral nerve disease and identifying the pattern of peripheral nerve involvement. For example, if the symptoms are highly restricted and focal, they might conform to the distribution of an individual peripheral nerve or, possibly, to an individual root.
More-diffuse involvement of an entire limb might be caused by involvement of the brachial or lumbosacral plexus. Alternatively, if generalized symptoms are distributed in an asymmetrical and focal fashion, they may be consistent with a mononeuritis multiplex picture or possibly a polyradiculoneuropathy or polyradiculopathy syndrome. Most often, peripheral neuropathies produce symptoms that are generalized and relatively symmetrical, conforming to a distal-to-proximal gradient typical of a distal axonopathy.

**History and Physical Examination**

As soon as their distribution is recognized, the symptoms should be analyzed to determine which fiber types appear to be involved (i.e., sensory, motor, autonomic). In addition, the temporal profile of the disorder (i.e., chronic, subacute, acute) is noted. The neurologic examination is then helpful in confirming signs of sensory, motor, or autonomic dysfunction and in documenting the pattern and fiber type involved. These clinical features, which can be derived solely from the history and physical examination, are valuable for characterizing the nature of the peripheral nerve syndrome, which is essential in constructing a differential diagnosis.

**Electrodiagnostic Studies**

Another important component to the evaluation of peripheral nerve disease is electrodiagnostic studies, primarily nerve conduction studies and the needle electrode examination. Electrodiagnostic testing can document the presence of peripheral nerve disease, define the distribution and pattern of various sensory and motor fibers, and characterize the underlying pathologic processes (i.e., wallerian degeneration, axonal degeneration, segmental demyelination, or some mixture of these pathologic reactions). Characterizing the electrodiagnostic features, particularly whether the process is axonal or demyelinating, adds additional information.
Medical Studies

Other special studies include lumbar puncture for cerebrospinal fluid analysis, which may be useful in diagnosing inflammatory or infectious causes of polyneuropathy, in evaluating acquired demyelinating polyneuropathies such as those in GBS and CIDP, and in a variety of immune-mediated polyneuropathies.

Nerve biopsy, typically sural nerve biopsy, is most often recommended in patients with asymmetrical or focal polyneuropathies in whom a diagnosis of vasculitis is being considered. In addition, biopsies may be used to assist in the diagnosis of some inflammatory, infectious, and metabolic polyneuropathies.

Nerve biopsy can help to establish the pathologic basis of the polyneuropathy when electrodiagnostic studies cannot conclusively distinguish an axonal from an acquired segmental demyelinating disorder.

Special autonomic studies, particularly those that measure cardiovascular autonomic reflexes (including heart rate response to deep breathing, heart rate and blood pressure responses to the Valsalva maneuver, and heart rate and blood pressure responses to head-up-tilt) may also be valuable in documenting autonomic cardiovascular involvement.

Various tests of sudomotor function including the sympathetic skin response, quantitative sudomotor axon reflex test, and thermoregulatory sweat testing can provide valuable information regarding the extent and distribution of sudomotor impairment in polyneuropathy.

Skin biopsy to measure epidermal nerve fiber density is also a helpful test for the diagnosis of SFN. Quantitative sensory testing is a technique that allows precise measurement of sensory perception thresholds of various fiber types, which can also be helpful in assessing peripheral neuropathy, especially SFN, in which the electrodiagnostic studies are often normal.
Laboratory Studies

By recognizing the peripheral nerve syndrome and appreciating the potential differential diagnosis, one may systematically perform appropriate medical tests to explore the various possible causes. The most common peripheral nerve syndrome is the generalized sensorimotor polyneuropathy with electrodiagnostic features of a distal axonopathy. For this disorder, it is usually appropriate to pursue a history of toxin exposure and alcoholism with nutritional deficiency. It is also reasonable to perform routine laboratory screening studies including a complete blood cell count; erythrocyte sedimentation rate; a blood chemistry panel encompassing hepatic function, renal function, and electrolytes; thyroid function studies; and vitamin B$_{12}$ level.

It is important to screen patients for diabetes mellitus. In the past, a fasting blood sugar or hemoglobin A$_{1c}$, or both, was often performed, but recent reports suggest that impaired glucose tolerance detected on a glucose tolerance test might provide more meaningful information regarding diabetes as a potential cause for polyneuropathy.

Screening the serum and urine with protein electrophoresis with immunofixation is also important in assessing patients with generalized polyneuropathy. In one series, the only laboratory tests that were helpful in establishing a precise cause for the polyneuropathy were vitamin B$_{12}$, serum protein electrophoresis with immunofixation, and serum glucose. Additional laboratory and radiographic studies may be considered pending the specific clinical features, and may include chest radiograph, skeletal bone survey, antinuclear antibodies, rheumatoid factor, and angiotensin-converting enzyme level.

In patients with an aggressive, evolving polyneuropathy or a specific paraneoplastic syndrome, additional testing for an occult malignancy is often performed, usually in conjunction with autoantibodies, especially anti-Hu. A variety of autoantibodies have been associated with different
polyneuropathy syndromes. The most useful of these include anti-GM\textsubscript{1} antibodies in the setting of MMNCB, anti-Hu antibodies in the context of a sensory neuronopathy, and anti-myelin-associated glycoprotein antibodies in acquired demyelinating polyneuropathy with predominately sensory features and with a distal pattern of involvement. Most of the other antibodies are much less specific, and their roles in the mechanism of the polyneuropathies are less certain. Thus, the precise value of performing panels of antibody tests is unclear at this time.

Lumbar puncture is often reserved for patients with possible immune-mediated polyneuropathies, particularly those with demyelinating features on electrodiagnostic testing. However, CSF studies are also often assessed in cryptogenic axonal degeneration polyneuropathies and in patients with possible infectious or inflammatory disorders.
Electrodiagnosis in the pediatric population differs from that in adults with respect to the diagnoses, clinical presentations, set-ups, and normal values. In fact, it is probably easier to describe what is similar between pediatric and adult studies than what is different. The instruments and electrodes are similar, but the latter are smaller than those used with the adult.

The underlying physiology is similar, but development of the myelin and motor unit is incomplete in the pediatric patient. Due to the developing nervous system, normative data vary, as do the presenting abnormalities. The pediatric electromyographer must have an extensive knowledge of growth and development and a familiarity with pediatric differential diagnosis.

The knowledge of growth and development helps to narrow down the differential. The pediatric examiner’s understanding of “primitive” reflexes can be used to “trick” an infant into reflex movement, which will allow more rapid analysis of the motor unit potentials (MUPs). In keeping with this book’s title, “Practical Electromyography,” this chapter will approach the practical aspects of the pediatric electrodiagnostic medicine evaluation.
Development of the Motor Unit

The changes in the motor unit during growth are the basis for the differences between pediatric and adult normative data. Human fetal muscle development was studied in the 1960s, and with the current regulations regarding study of fetal tissue it is not likely to be studied again in the near future. Dubowitz found that muscle fiber diameters prior to 6 months of gestation are 10 to 25 μm, and after 6 months the diameter increases to 20 to 50 μm. He described three phases of muscle fiber development in utero. During phase I, from 12 to 20 weeks of gestation, the enzyme activity is equal in all fibers. In phase II, from 20 to 26 weeks, differentiation between fiber types commences. However, only a small number of type I fibers are present during this period. In phase III, later than 30 weeks of gestation, the fetus shows the same differentiation in muscle fiber types as are found in adult muscle.

Evaluation of fetal tissue also revealed that myelination of peripheral nerve axons begins toward the end of the first trimester. Myelination begins between weeks 10 and 15 and is completed by 2 years of age. Nerve conduction velocities (NCVs) increase with the diameter of the nerve fibers and with the increases in the distances between the nodes of Ranvier. The internodal distances reach their maximum lengths by age 5 years.

It is also important to be familiar with the normal maturation of the MUP as seen with needle electromyography (EMG). Normal infant MUPs are small in amplitude and duration, making it a challenge to differentiate them from potentials found in myopathies. Jablecki and Sacco et al reported that MUPs are similar in appearance to adults but increase 20% in both amplitude and duration between age 3 months and adulthood. The amplitudes of MUPs in nerve studies in children have been well researched. Nerve conduction velocities (NCV) increase 100 μV to 700 μV, with occasional units to 1,600 μV (5,6). The MUP durations range from 2 to 10 ms. The electromyographer must have experience to differentiate between the small motor units.
and fibrillations. One must focus on the initial deflection of the MUP and whether the potential is under voluntary control.

Many infants and children rapidly learn that contracting a muscle causes pain when a needle electrode is present in it. They will cease muscle movement as soon as an electrode is inserted. This further challenges the examiner, who must use normal infantile reflexes (and sorcery) to induce movement in the infant or child. Conversely, when evaluating resting membrane potentials, the child will frequently decide to move. Holding the joint in such a position that the muscle is at its shortest length is helpful in diminishing voluntary contraction.

Nerve conductions in children have been well studied. Motor and sensory NCVs increase with postconceptual age. Bougle reported that NCVs in preterm infants (d’31 weeks of gestation at birth) are about half that of adult normal values (usually about 25 m/s) and that the lower levels of adult normal values are reached by age 4 years. Full-term newborns have also been shown repeatedly to have NCVs half the adult normal values, and the NCVs also reach low adult normal values by age four years. Premature infants have been shown to have slower NCVs than full-term babies. The motor velocities are correlated with postconceptual age and are not affected by intrauterine growth retardation. A small study suggests that sensory NCVs are sensitive to growth retardation and cannot be used to determine the postconceptual age, which is possible with motor nerve conduction studies. Thus, it is possible to determine the postconceptual age of a small baby by motor nerve conduction studies. Gestational age is estimated by combining the velocities of the ulnar and posterior tibial nerves, as this is thought to be more accurate than that of a single nerve. Care in the positioning and measurement of the distances is critical. Skin temperature must be controlled. The technique is rarely if ever used as it is expensive and time-consuming. Alternative methods, such as the Dubowitz maturity scale, have been adequate for clinical purposes.
Setting up the EMG Laboratory

Once the physiology, growth, and development are mastered, the pediatric electromyographer must have appropriate space, instrumentation, and personnel to make an accurate diagnosis. The pediatric electromyographic laboratory should be large enough to accommodate a standard wooden plinth, electromyographic instrument, chairs, cabinets, warming lamps, sphygmomanometer, oxygen saturation instrument, and a table. The space must come equipped with a sink, suction, oxygen, and a telephone. Electrical shielding is often not necessary with modern instruments, but with the small distances encountered in pediatric patients, it is very helpful. Likewise, a telephone may not be needed in an adult laboratory, but if the physician is paged and is alone in the laboratory, he or she cannot leave the child to answer.

The pediatric laboratory must have space and seating for two or more parents or caregivers. There must be room for a nurse to help sedate, monitor, and distract the child. A resident or fellow will often be present as well. Additional room for a crib or wheelchair will smooth patient flow by preventing the need to move furniture. Blankets and gowns for different age groups should be stored close by. An otoscope, tongue blades, and stethoscope must be available for pre-sedation examinations. Of course, some means of cleansing toys and documenting this work must be developed. Scissors are needed to cut disposable electrodes into infant or small child sizes. The pediatric laboratory must have medicine cups and oral syringes available to administer sedatives and analgesics. Standard measuring devices and a calculator (to adjust medication doses) must be present as well. One must not forget a step-stool to help children reach the plinth.

Cupboards for toy storage are helpful because tubs of toys on the floor become cumbersome. Toys are necessary for distraction during the history but are just as valuable during the physical and the electrodiagnostic examination. A series of "cubbies" with toys for different ages would be ideal. Bubbles
make a mess but are good distraction for most young children. Contact your hospital’s Child Life Department; their members will be very helpful, as one of their goals is to help children through difficult procedures. A TV and a radio are beneficial, especially if they use batteries, as extra power cords create electrical noise. Older children and adolescents sometimes respond well to music CDs with headphones.

To become more specific regarding equipment, the pediatric EMG instrument must have the ability to deliver 20, 30, and 50 Hertz repetitive stimulation, as the diagnosis of botulism is encountered routinely in most pediatric laboratories. Be wary of the sales representative or purchasing department who assume that because you are studying children you will not need the capability for sophisticated testing. The less expensive instruments may not offer rapid repetitive stimulation. The sales representative and the purchasing department will try to make the most economical choice and during price negotiations may unknowingly acquire an instrument that is inappropriate for your needs.

Small, slender needles, 25 mm in length, are most frequently used, although the adult standard lengths of 37 mm are routinely used with adolescents. Both concentric and monopolar needles of small gauges must be available. The laboratory must carry electroencephalograph abrasive paste and alcohol swabs for cleansing. Cleaning the skin with the abrasive paste will decrease the impedance, which is helpful when dealing with the small stimulator-to-electrode distances encountered with pediatric patients. Disposable electrodes with embedded gel are almost a necessity for a pediatric laboratory. They are less likely to shift position than do simple metal electrodes, which require electrode gel and tape. Self-adhering electrodes are easier to use, so their use shortens the length of the examination, which secondarily allows the child to tolerate a more thorough study.

In summary, a large space in an electrically quiet room, but with a TV, telephone, and cupboard storage, is secondary only
to the choice of appropriate instrument and electrodes. A skilled nurse is invaluable in teaching, sedating, and reassuring patients and parents.

TECHNIQUES TO APPROACH THE PEDIATRIC PATIENT

The patient’s history, as with all medical evaluations, is critical. Physicians must ask about the birth history and development. Questions regarding whether a child is slowly progressing in development or actually regressing will often narrow the differential diagnosis. Age of presentation is helpful, as well as the reason for the first physician visit. Slowly progressive, painless disorders are often picked up by teachers or coaches when the child cannot keep up with peers. Extended family members who do not see the child except at holidays may also bring slowly progressive diseases to the parents’ attention.

Painful diseases are noticed immediately by parents. Questions regarding a child’s choice of activity after school can be helpful. Chronically weak children will not choose fatiguing activities. Parents may notice changes in their children’s choices, but this history is rarely offered spontaneously. Specific questions must be used to elicit information regarding changes in a child’s endurance and strength that parents may not be aware of initially. Inability of the child to enjoy field trips or visits to the mall is worrisome. Subacute presentations will be revealed in normally athletic children having difficulty participating in their chosen sport. Congenital problems usually prevent children from choosing vigorous sports. Once again, this history can direct an examiner toward a specific item in the differential diagnosis.

Physical Examination

The physical exam is a challenging portion of pediatric electrodiagnosis. Observing children in a parent’s lap and watching them play with toys is very helpful. I try to watch the child while getting a history from the caregiver and then proceed
with watching him or her crawl, walk, and run. Playing with toys will allow examination of coordination and strength. Sometimes we are lucky enough to be able to watch the child walk to the waiting room before he is even aware of us. Obtain as much of the physical examination as possible before touching a pediatric patient, because from that point on, the examination may reveal only what can be obtained from a crying and kicking child.

Observation of children’s movement patterns is critical since it substitutes for the child cooperating with the examiner during the physical examination. Children move in specific patterns when sitting down and arising from the floor normally, and these patterns differ in the presence of weakness. The most familiar example is the Gower’s sign, when a child will walk his hands up his legs when arising to stand. Though associated with Duchenne muscular dystrophy, this phenomenon occurs with any chronic proximal lower limb weakness. A quarter-turn from a sit to a prone four-point position is a more subtle hint and frequently occurs prior to the development of a full Gower’s sign. If you ask a chronically weak child to stand up from the floor, he or she will crawl over to a chair or a parent’s leg to pull up to stand rather than fall. In contrast, a child with a new-onset weakness will fall. This is often helpful to determine whether to proceed down a differential diagnosis for acute-onset abnormalities versus longstanding weakness that has just recently been noticed.

Children with weak necks will prop their occiput upon their shoulders; they appear to have lost their necks. This is seen in young children, as their heads are bigger in proportion to the rest of their body than are adult heads. Children will easily teach themselves to walk their fingers up a wall to turn on a light switch when they have weakened proximal upper limb strength. Children will also accommodate for weakness by using “primitive reflexes” in a functional manner. Children learn to use an asymmetric tonic neck reflex to facilitate elbow flexion. When in a supine position a child will reach out for a toy while looking
toward it, but will look toward the opposite shoulder when raising the toy to his or her chest. Watching a child sit up from a supine position is also helpful. A weak child will rotate his body around so his shoulders will come behind his pelvis for stability.

The Electrodiagnostic Exam

As with an adult examination, planning is critical to efficient performance of the procedure. Sedation is a controversial and important subject in this planning. An examiner will develop a sense for when distraction and verbal reassurance will be sufficient or whether sedation will be necessary. If sedation is going to be used, it is more effective to use it from the outset than to start it after a child has become agitated. It helps some children and their parents tolerate a more detailed examination than is possible without it. Parents know their child’s ability to tolerate procedures and are often the best source to consult if there is any question regarding the use of sedation. A pediatric laboratory must have medicine cups and oral syringes available to administer sedatives and analgesics. A policy and procedure for sedative use must be developed and followed to ensure safety. New pediatric electromyographers must become familiar with the conscious sedation protocol for their hospital and make sure that they have any certifications necessary. Some hospitals require pediatric life support (PALS) training, and specific medical staff privileges are necessary. Our pharmacy has put together a “tackle box” with our medications and documentation forms that our nurse signs out prior to each EMG clinic.

Sedation has the unfortunate potential to cause disinhibition and can occasionally make a child more easily agitated. I have found this to be more frequent with chloral hydrate (CH) than some other medications. CH is a pure sedative and in my experience does not offer relaxation: the child either sleeps or not. I have found the combination of lorazepam (0.07–0.1 mg/kg PO) and acetaminophen with codeine (10 mg/kg of
acetaminophen and 1 mg/kg of codeine PO) in liquid form to be the most helpful. It reduces stranger anxiety, and children will often relax during the set-ups between studies. Nasal midazolam provides excellent anxiolysis for short studies, but its duration of action is not long enough to do a thorough study. The nasal administration of midazolam causes nasal burning, and rectal administration can be used as an alternative route with similar doses. The oral route is also available.

Occasionally, general anesthesia is useful when there is need for extensive nerve conduction studies in cases of complicated peripheral injury or when performing repetitive nerve stimulation. Usually these children will have significant anxiety when the physical examination is done. Obviously, one cannot evaluate MUPs under general anesthesia. Anesthesiologists will usually be willing to use heavy conscious sedation for examination of MUPs and then put the child under general anesthesia to complete the nerve conduction studies. This technique is used infrequently, but occasional children have an aversion to needles or have been so traumatized by frequent and painful procedures that they cannot be studied while awake.

**Technical Considerations**

An electrically silent room, preferably with shielding, is helpful. All accessory electrical equipment should be unplugged and on a battery to prevent 60 Hz interference. If this is not possible, electrode wires need to be as short as possible and shielded. Needles can be monopolar or concentric. It is generally thought that monopolar needles are less painful, but short concentric needles used for small children are also very narrow in gauge. I do not believe they are more uncomfortable than monopolars, but this is a personal opinion based upon trial and clinical experience. Concentric needles cause more bleeding, and some children are very upset by the sight of blood, but the electrical baseline is so much quieter with a concentric needle that the examination can frequently be accomplished in a much
shorter time. In an intensive care unit (ICU) setting, concentric needles are usually necessary. ICUs have transport monitors available that run on batteries, and these can be used to diminish electrical interference. Respiratory therapists can also be asked to bag-ventilate a patient during an EMG. The ventilator should be shut off and disconnected from the AC source if interference continues to be a problem despite the use of the 60 Hz notch filter. Despite all these efforts, however, interference from equipment in neighboring cubicles is often a problem, and it is always easier to transport the child to the EMG laboratory if the child is stable enough.

**Instrumentation and Set-Ups**

In young children, distances are shorter between the reference and active electrodes than they are in adults. This is also true for the distances between the distal and proximal stimulation sites. Not only does stimulator interference increase with shorter distances, but shorter distances also introduce greater measurement error. An error of 1 cm in measuring an 8-cm latency introduces a 15% error in the NCV.

Sensory nerve conduction set-ups in adults are designed to have 4 cm between the reference (E2) and active (E1) electrodes. The latency measured to the first take-off varies less than the peak latency measured to the peak as the distance between the E1 and E2 electrodes narrows (15,16). On infants and young children, it is often impossible to obtain a distance of 4 cm between the electrodes; therefore, it is critical to evaluate the latency to the take-off as well as the peak.

Sensory nerve conduction responses are more easily obtained in children if the skin is prepared prior to starting the procedure. Rubbing the skin with a clean emery board or rubbing with EEG paste and then cleaning the skin with alcohol to remove oil and lotions increases the ability to record reproducible sensory nerve action potentials (SNAPs) by decreasing the skin impedance. Another trick is to hold the foot or hand while stimulating with
the other hand. This enables the examiner to determine when the child’s foot is relaxed so that the stimulation can be given when there is less background electrical interference from the patient’s voluntary activity. This takes some practice to feel. An alternate approach is to use the auditory feedback from the surface EMG signal to determine the amount of voluntary motor unit activity.

**Temperature**

Attention to temperature is critical when examining children. Babies have a greater surface area per kilogram than adults, which facilitates heat loss. The room must be warm and the child must be covered whenever possible. Heating lamps are helpful to maintain body temperature in infants as well as warming limbs of older children prior to nerve conduction studies. Heating lamps must be turned off and preferably unplugged during the actual examination, however, as they cause a great deal of 60-Hz interference. Pressure-activated heating pads can be helpful for local warming.

Control for skin temperature improves the accuracy of motor and sensory latencies as well as that of NCVs. Studies in adults have shown that NCVs change from 1.4 to 2.4 m/s/°C in the upper limbs and from 1.1 to 2.0 m/s/°C for the lower limbs. One may assume that temperature will affect the NCVs in young children, but the actual amount is not known. It is therefore critical to maintain a skin temperature close to the skin temperature of the normal children studied when the pediatric values were developed. Correction factors to adjust for skin temperature changes have not been developed for young children.

Volume conduction must also be considered, as it causes decreased latencies, which will affect the NCV calculation. Care must be taken not to overstimulate when trying to obtain a supramaximal compound motor action potential. The smaller size of our patients makes this error an even greater concern than it is in adults.
Normative data are essential in interpreting electrodiagnostic studies. It is difficult to collect such data due to the reluctance of both parents and physicians to cause discomfort to children. We must thank investigators who have published the data that they have collected. Careful attention to their protocols regarding electrode set-up and distances used is necessary to use their data clinically. It is best to refer to the original papers published to ensure the closest reproduction of their techniques possible. An invaluable reference is the chapter entitled “Pediatric Electromyography” in Neuromuscular Disorders of Infancy, Childhood, and Adolescence: A Clinician’s Approach, in which the authors collected normative data for children. From this list, the original articles can be found to determine the specific protocols for the normative data collected.

Clinical Problems

As in adult laboratories, there are groups of clinical problems that arise frequently. Children are frequently referred in the first year of life for evaluation of brachial plexus injuries, floppy tone, and decreasing strength. Less frequently, a child will be referred with regression of milestones in both cognitive and motor spheres.

Brachial Plexus Injury

Babies with brachial plexus injuries are frequently referred for evaluation during their second or third week of life. Injuries occur perinatally and are usually of the Erb type, an upper trunk injury. In more severe injuries the entire plexus will be involved. The classic Klumpke presentation of a lower trunk injury is rarely seen. The majority of Erb palsy injuries recover within the first 4 months, although Pondag’s review has refuted this premise. All EMG laboratories are referred a selected population of the more severe injuries. Microsurgery continues to be controversial, but children with the global brachial plexus injuries and a group of the severe classic Erb (C5–6 ± C7) will have a poor prognosis without surgery. The electrodiagnostic studies will be helpful to determine which babies are more likely to have a
spontaneous recovery. The parents’ history of the child’s movement and clinical observation are primary sources of information. Use of the Moro reflex is very useful to activate the muscles innervated by the upper trunk, including the shoulder abductors, external shoulder rotators, elbow flexors, and wrist extensors. If significant motion is elicited, an electrodagnostic study may not be indicated, as spontaneous recovery early frequently occurs. Heisse et al recently published a study that determined that the compound muscle action potential (CMAP) ratio (CMAP of the affected side as a percentage of the CMAP on the unaffected side) was predictive of motor prognosis.

The infant brachial plexus study starts with evaluation of the amplitude of the CMAPs of the axillary, radial, and suprascapular nerves. The stimulations are done from a supraclavicular position and responses are quite easy to elicit. If the amplitudes are questionable, then the contralateral side is stimulated for a comparison of amplitude and latency. Normal values for amplitude can vary up to 50% from side to side, but as Heisse reports, other normal values are not readily available. Sensory nerve conduction studies were previously thought to be necessary, as a normal response was considered diagnostic of a root avulsion. However, it has been found that they are not always helpful, as their absence does not exclude a root avulsion. A needle EMG is also necessary to identify active MUAPs. The electromyogram for a brachial plexus study is started within the sensory distribution of the axillary nerve. Babies with a significant upper trunk lesion cannot feel within the sensory distribution of the axillary nerve, so examination of the deltoid can be accomplished without discomfort to the child. It is, in fact, a good clinical piece of information if the child feels the electrode insertion, as it implies a less severe injury. Once again, if the electromyographer has any question regarding the size and recruitment of the MUAPs seen, then the child’s contralateral arm can be used as a control. The clinician should examine muscles that are obviously weak. Those muscles that are questionably weak will probably recovery
spontaneously. The prognosis and the discrimination among children who may benefit from surgery and those that will not are the goals of the study. Repeat studies can be done to see whether reinnervation is occurring electrically, if there is question left after the clinical examination. The preoperative study will not need to completely determine what surgical procedure is necessary, as an intraoperative study will be done to direct the surgical decisions.

The Hypotonic Infant

A frequent referral to a pediatric EMG laboratory is a request to evaluate a “floppy infant.” Since DNA testing is now available for many congenital syndromes, the frequency of these referrals has dropped.

Once again, a thorough history and physical examination should direct the examination. Primary central nervous system dysfunction causes 80% of cases of newborn hypotonia. A history of a difficult delivery frequently accompanies these children. Knowledge of the normal patterns of development is again necessary in the performance of the physical examination. Examination of muscle stretch reflexes and of distal motor control versus proximal motor control helps to guide the electrical examination. Children with central hypotonia almost invariably have muscle stretch reflexes. A spontaneous and persistent Babinski response is abnormal. All newborns have a positive Babinski response unless they are under influence of maternal sedation or they have severe weakness secondary to a peripheral neuropathy or another lower motor neuron lesion. Lower motor neuron paraplegia is usually secondary to myelomeningocele, but tumors are also possible.

Evaluate the alertness of the infant. Children with central hypotonia are usually not as alert and tend to have obligatory or persistent primitive reflexes. Distal strength is more difficult to appreciate in infants than in older children, as distal hand control does not develop until the latter half of the first year.
Distal ankle strength in children is usually examined during observation of gait, so special care must be taken to look for it in an infant. Most infants examined for a peripheral neuropathy will have generalized weakness; the weakness is just more profound distally than it is proximally.

ANAESTHESIA FOR NEUROSURGICAL PROCEDURES IN PAEDIATRIC PATIENTS

Neurophysiology

Accurate data pertaining to normal neurophysiological variables in paediatric patients are limited and often derived from the adult and animal data. Cerebral blood flow (CBF) affects the cerebral blood volume and the intracranial volume, thereby affecting the intracranial pressure (ICP). It varies with age in paediatric population, being lower in premature infants (12 ml/100 g/min) and full-term neonates (23-40 ml/100 g/min) and higher in infants and older children than in adults (50 ml/100 g/min). From 6 months to 3 years of age, CBF is 90 ml/100 g/min; and from 3 to 12 years of age, the CBF is 100 ml/100 g/min. CBF is coupled tightly with the metabolic demand known as cerebral metabolic rate of oxygen (CMRO\textsubscript{2}), and both increase proportionally after birth. In children, the CMRO\textsubscript{2} is higher at 5.2 ml/100g/min than the adults (3.5 ml/100 g/min) and hence, less tolerant to hypoxia. Neonates have a lower CMRO\textsubscript{2} (3.5 ml/100 g/ min) with a relative tolerance to hypoxaemia.

The autoregulation range of blood pressure in normal newborn is narrow between 20 and 60 mmHg. The autoregulatory slope drops and rises significantly at the lower and upper limits of the curve, respectively. Sudden hypotension and hypertension at either end of the autoregulatory curve places the neonate at risk for cerebral ischaemia and intraventricular haemorrhage (IVH), respectively.

The skull is a closed box with brain tissue, blood and cerebrospinal fluid (CSF) as its contents. An increase in volume
of one of these components with increase in ICP will result a compensatory reduction of other components (Monro-Kellie doctrine). In infants, open fontanel and cranial sutures lead to a compliant intracranial space. The mass effect of a space-occupying lesion can be masked by an increase in skull size. Hence, infants presenting with intracranial hypertension (ICH) may have a well-advanced pathology.

A large percentage of cardiac output is directed to brain in infants and children as the head accounts for large percentage of the body surface area and blood volume. This aspect places the infant at risk for significant haemodynamic instability during neurosurgery.

Preoperative Considerations

Preoperative evaluation and preparation

The evaluation must include history and physical examination pertaining to the conditions requiring special anaesthetic considerations. Assessment of neurological status should include evidence of raised ICP, altered sensorium and cranial nerve palsies. Infants with ICH might present with irritability, lethargy, decreased consciousness, failure to feed, bulging fontanel and cranial enlargement.

In children, it may present with early morning headache, vomiting without nausea, diplopia, and papilloedema, and in late stage, with Cushing’s triad. Frequent vomiting episodes may lead to dehydration and electrolyte imbalances, and increase the risk of aspiration. Hence, serum electrolytes should be determined to identify abnormalities of sodium and potassium following vomiting. Other laboratory investigations should include haemoglobin or haematocrit level, and typing and cross-matching of blood if the loss is expected to be considerable. Additional studies should include electrocardiogram (ECG), coagulation profile, renal and hepatic function, as deemed necessary. Children with pituitary tumours should undergo complete endocrine evaluation.
**EMG Considerations in the Pediatric Patient**

**Premedication**

Sedative and narcotic premedication should be avoided in all the children suspected of increased ICP as these medications decrease respiratory drive which may result in hypercapnia and further increase in ICP. However, patients with normal ICP, such as those scheduled for repair of vascular lesions, may be sedated so as to allay preoperative anxiety and avoid hypertension, thus preventing rupture of vascular abnormality. Oral benzodiazepines (midazolam) may be beneficial for small children as they provide sedation without respiratory depression and should be administered under supervision.

**Intraoperative Considerations**

**Induction**

The goal of anaesthetic induction is to avoid increase in ICP owing to associated hypoxia, hypercapnia and volatile anaesthetic-induced increases in CBF. An intravenous induction with thiopentone or propofol and neuromuscular block to facilitate endotracheal intubation is ideal in children with raised ICP. However, in children without IV access or with difficult IV access, inhalational induction by facemask with sevoflurane should be preferred as crying or struggling may lead to further increase in ICP.

After the IV access is secured, a bolus of thiopentone (1-2 mg/kg) or propofol may be given to prevent the pressure responses of tracheal intubation. Furthermore, the inhalational technique may subsequently be changed to an IV induction. All volatile anaesthetics cause an increase in CBF, and thence the ICP. Therefore, ventilation should be controlled as early as possible and mild hyperventilation be instituted to prevent rise in ICP. Children at risk for aspiration should undergo rapid-sequence anaesthetic induction with thiopentone or propofol followed by rapid-acting muscle relaxants such as succinylcholine or rocuronium.
**Maintenance of anaesthesia**

Anaesthesia is maintained either with low end-tidal volatile agents (minimum alveolar concentration (MAC) < 1) or with total IV anaesthesia (TIVA), along with short-acting opioids (fentanyl or remifentanil), inhaled nitrous oxide and controlled ventilation.

Sevoflurane has almost replaced halothane as an agent for induction; isoflurane, sevoflurane or desflurane is used for maintenance of anaesthesia during paediatric neurosurgical procedures. Sevoflurane provides smooth induction followed by a rapid recovery.

Neuromuscular blockade with non-depolarising muscle relaxants is given to prevent patient movement and minimise the amount of anaesthetic agent required. Children on chronic anti-convulsant therapy will require large doses of muscle relaxants and narcotics due to enzymatic induction of these drugs. Muscle relaxant should be withheld when assessment of motor function is carried out, e.g. during spinal cord surgery. Fentanyl is the most commonly used opioids, but its half-life increases with repeated dosing. It requires hepatic metabolism which is immature in premature infants. Hence, the sedative and respiratory depressive effects of fentanyl may be prolonged in these children. Remifentanil is unique in the sense it is cleared rapidly by the plasma esterases, but the associated rapid recovery may be accompanied by delirium and inadequate analgesia. Hence, it requires supplementation of other analgesics during postoperative period. Currently, it is not available in India.

**Positioning**

The neurosurgical procedures in children are carried out in different positions with certain challenges for each one of them. These surgeries are usually of prolonged duration during which the small child may disappear under the surgical drape and equipments. Hence, the anaesthesiologist must try to ensure unobstructed view of the part of child, proper padding of pressure
points, protection of the eyes from surgical cleaning solutions, and the access to IV line, airway and breathing circuits before commencement of surgery.

Supratentorial surgeries and ventriculoperitoneal (VP) shunt surgery are carried out with the patient lying supine with head probably turned to one side.

It is better to secure the endotracheal tube (ETT) in the non-dependant corner of the mouth to prevent oral secretions loosening the adhesive tapes used for fastening. The prone position is used during suboccipital craniotomy for posterior fossa lesions, spine surgery and repair of encephaloceles.

It must be ensured that the weight of the child is supported on bolsters under the chest and pelvis, and does not rest on the abdomen. Excessive pressure on the abdomen impedes ventilation, compresses vena cava and increases epidural venous pressure and bleeding.

There may be congestion of face and tongue, and pressure sore on malar prominences owing to horseshoe head rest. Extreme flexion of the neck may cause endobronchial intubation because of short trachea and intraoral kinking of ETT; hence, armoured ETTs are preferred. Excessive flexion or extension of head may cause brainstem compression in patients with Arnold-Chiari malformation (ACM). The sitting position is still being practiced in few centres across the globe.

In children more than 4 years of age, it is used for the exploration of the posterior fossa with the advantage to reduce intraoperative bleeding and to facilitate surgical exposure. Complications in relation to this position include cardiovascular instability, venous air embolism (VAE) and postoperative tension pneumocephalus. Extreme flexion of neck required in this position may be complicated by mid cervical flexion myelopathy and macroglossia. Lateral position is rarely used in paediatric patients with ipsilateral posterior lesions or cerebellopontine angle tumours.
Figure: Prone position in a 10-month-old child with occipital encephalocele

Figure: Sitting position in a 5-year-old child with posterior fossa tumour

Figure: Lateral position in a 2-year-old child undergoing retromastoid suboccipital craniotomy for excision of brainstem glioma
EMG Considerations in the Pediatric Patient

Monitoring

Intracranial surgery may be associated with haemodynamic changes owing to sudden blood loss, VAE and manipulation of cranial nerves. A part from the routine monitors, placement of an arterial cannula permits continuous monitoring of blood pressure, occasional estimation of arterial blood gas, electrolytes and haematocrit values. A central venous catheter provides large-bore access and aspiration of air during occurrence of VAE in sitting position. Precordial Doppler and trans-oesophageal echocardiography are sensitive monitors used to detect of VAE, but not available everywhere. Hence, the end-tidal CO$_2$ is commonly used in India for this purpose. Neurophysiological monitoring may be used with the goal to reduce morbidity by early detection of neurological insult when it is reversible, thereby improving the overall outcome. The monitoring modalities include electroencephalography (EEG), sensory evoked potentials (SSEP), motor evoked potentials (MEP) and brainstem auditory evoked potentials (BAEP).

Fluid management

The intraoperative goal is to maintain normovolaemia, and thus the haemodynamic stability. Normal saline is the most commonly administered crystalloid during paediatric neurosurgical procedures as it is mildly hyperosmolar and hence prevents cerebral oedema. However, infusion of large quantities (>60 ml/kg) of normal saline may cause hyperchloraemic metabolic acidosis and hypernatraemia. Ringer’s lactate is slightly hypo-osmolar and infusion of large quantities may increase cerebral oedema. Glucose-containing fluids should not be used during these procedures as hyperglycaemia worsens reperfusion injury. However, in neonates and premature infants, the danger of hypoglycaemia should be borne in mind. Blood glucose should be closely monitored in these patients, along with continuous infusion of glucose at 5-6 mg/kg/min. Children do not need exogenous glucose administration and are able to maintain normal levels along with the associated surgical stress. Blood transfusion
should be guided by the degree of blood loss and initial haematocrit values.

**Temperature management**

Although the experimental animal models favourably suggested the use of mild hypothermia in neurosurgical patients, it has not been extrapolated to humans. The associated complications prevent use of hypothermia in routine paediatric neurosurgical practice despite obtaining encouraging results following brain injury. The intraoperative goal is to maintain normothermia and avoid both hypothermia and hyperthermia with application of different methods.

**POSTOPERATIVE CONSIDERATIONS**

**Recovery and postoperative care**

The goal is “rapid awakening” in order to help early neurological assessment, haemodynamic stability, and minimal coughing and straining in the ETT. Sevoflurane provides better recovery profile, as compared to isoflurane in children. Trachea is extubated once the child responds to commands or infants open their eyes. However, there are circumstances where the children continue to remain intubated during the postoperative period. Surgeries that interfere with cranial nerve nuclei and brainstem function with depressed respiratory drive require postoperative mechanical ventilation till these functions are improved. Generally, the intracranial procedures require close observation in the intensive care unit (ICU). Children undergoing extracranial or minor procedures may be nursed in an inpatient unit (ward).

**SPECIFIC CONDITIONS**

**Hydrocephalus and shunt procedures**

Hydrocephalus is enlargement of ventricles by increased CSF secretion and decreased CSF drainage either by obstruction
EMG Considerations in the Pediatric Patient

It may be of communicating (non-obstructive) or non-communicative (obstructive) types.

The causes may be congenital (e.g. aqueductal stenosis, ACM, Dandy-Walker syndrome) or acquired (posterior fossa space-occupying lesions, infections, IVH of prematurity) origin. In infants and small children, hydrocephalus causes increase in head circumference.

The urgency of surgery depends on the degree of ICP rise. The surgical management includes CSF diversion procedures such as VP shunt surgery, which is the most commonly carried out paediatric neurosurgical procedure. The shunt may at times require revision due to normal growth to the child, malfunction, blockade or infection.

If the peritoneum is infected, the alternate extracranial sites include right atrium or pleura. CSF drainage may also be carried out internally with an endoscopic third ventriculostomy. During this procedure, warmed Ringer’s lactate or normal saline is used to irrigate the operating site.

Bradycardia and other arrhythmias have been reported to occur during irrigation phase and owing to manipulation of the floor of the third ventricle. The shunt surgery requires exposure of the body from head to abdomen; hence, heat conservation strategies need to be implemented. Children with features of ICH may be dehydrated (reduced intake following depressed mental status or frequent vomiting episodes) and require rehydration by securing an IV access before induction of anaesthesia (rapid sequence).

The haemodynamic and ICP changes during tunnelling phase of VP shunt insertion can be managed with increasing anaesthetic depth or addition of a narcotic agent. Rapid intraoperative drainage of CSF from the ventricular end should be avoided to prevent arrhythmia and haemodynamic disturbances. These children should be observed carefully in the postoperative period.
as they may have altered mental status which puts them at risk of aspiration of gastric contents following peritoneal handling.

![Figure: Hydrocephalus with increased head circumference in a 3-month-old child](image)

**Craniosynostosis**

It occurs due to premature intrauterine fusion of one or more cranial sutures, thereby causing an abnormal growth of skull. The sagittal suture is most commonly involved. Multiple suture craniosynostosis may present with associated craniofacial abnormalities such as Apert’s syndrome and Crouzen’s syndrome.

Surgical management includes strip craniectomy which should be carried out during the first 6 months of life to get the best result. Currently, endoscopic procedures for single suture involvement are being carried out to prevent morbidities of open suturectomy. However, management of multiple suture craniosynostosis requires a multidisciplinary approach for reconstruction of face with orbital advancements.
The anaesthetic considerations for craniosynostosis are as follows:

- Difficult airway associated with syndromic craniosynostosis
- Hydrocephalus and elevated ICP due to abnormal shape of skull; ICP reduction manoeuvres are to be undertaken
- Sudden and massive blood loss may occur, as the surgery is carried out in close proximity to major venous sinuses. Hence, large bore venous catheters must be secured before skin incision. Presence of an arterial cannula may help for continuous measurement of blood pressure, serial haematocrit and blood gas
- Venous air embolism: The reported incidence in children undergoing craniosynostosis repair is 82.6% with use of precordial Doppler, whereas it is 4.2% with the use of end-tidal CO$_2$ monitoring
- The Ocular (corneal) injury can be prevented by lubricating the eyes with wetting agents or antibiotic ointments
• Postoperative oozing of blood from the surgical site may need further transfusion of blood and blood components
• In children operated below the orbital ridge, a possible airway compromise owing to facial oedema should defer tracheal extubation by 24-48 h until resolution of oedema.

Brain tumours

These are most common solid tumours of childhood, two-thirds of which arise from the infratentorial compartment. Management of these posterior fossa tumours poses unique challenges to the neuroanaesthesiologist in the form of ICH due to obstructive hydrocephalus, the pressure responses to laryngoscopy and Mayfield head-pin fixation in children with deranged intracranial compliance, different positions (e.g. sitting position) and their related problems, and possible respiratory and cardiovascular changes during brainstem manipulations. Damage to respiratory centres and lower cranial nerves may cause apnoea and airway obstruction in the postoperative period. The head-pin fixation in children may cause skull fracture, dural tears, and even haematoma at pin sites.

In children, craniopharyngiomas are the most common tumours in the perisellar region. These tumours are associated with hypothalamo-pituitary dysfunction and require perioperative steroid replacement therapy. The children may present with endocrine abnormalities; preoperative thyroid and adrenal function should be obtained. Diabetes insipidus (DI) may occur during preoperative (8-35%), and rarely in intraoperative period; but is quite common (70-90%) in the postoperative period. DI causes large volume of urine which needs to be replaced on hourly basis. If the resultant hypovolaemia is not corrected with fluids, DI must be treated pharmacologically with synthetic vasopressin (DDAVP).

Meningomyelocele and encephalocele

Embryogenic neural tube fusion occurs during the first 4 weeks of gestation. Failure of fusion causes herniation of meninges
EMG Considerations in the Pediatric Patient

with (meningomyelocele (MMC)) or without (meningocele) neural elements in any level of the spinal cord. When this neural tube defect occurs in cranium, the meninges protrude through a bony defect on skull with (encephalocele) or without (cranial meningocele) brain tissue. All these defects require correction within first few days of life.

MMC is usually associated with ACM (most commonly Type II) and hydrocephalus. The characteristics of ACM include downward displacement of cerebellar vermis into upper cervical spinal canal, and elongation of brainstem and fourth ventricle.

These children may present with features of brainstem compression such as apnoea, vocal cord palsy causing stridor, autonomic instability and abnormal respiration. These children require surgical decompression of posterior fossa to accommodate the hind brain malformation.

Inhalational induction with sevoflurane is the commonly practiced technique as most of the children come to the operating room without an IV access.

Tracheal intubation is carried out with the child in supine position and the swelling is supported on a doughnut, or in case of large MMC, in lateral decubitus position. Excision and repair of MMC in prone position is combined with insertion of a VP shunt for hydrocephalus in supine.

The spinal cord below the defect of MMC is often tethered, which over a period of time results in distal neurological defects, scoliosis or kyphoscoliosis. Untethering of the cord needs Electromyography (EMG) monitoring to identify functional nerve roots. During the procedure, there may be sudden blood loss from an abnormal vessel or occurrence of VAE. These children have an increased risk of latex allergy, although it is rarely encountered in Indian context.

Occiput is the most common site for the occurrence of encephaloceles, although fronto-ethmoidal encephalocele is quite common in South-East Asia. There may be problems in mask
ventilation and potential rise in ICP due to compression of the sac during various manipulations in children with anterior encephalocele. Children with posterior encephalocele are intubated commonly in lateral decubitus position, or with the swelling supported by a doughnut, and even by placing the child’s head beyond the edge of the table, supported by an assistant.

Our experience suggests that placing the child in right lateral position helps in getting more space for laryngoscopy and intubation for a right-handed anaesthesiologist and vice versa. Intraoperative haemodynamic disturbances are commonly encountered during encephalocele repair. Apart from having a strong vagal tone, children with Chiari malformation may experience bradycardia during laryngoscopy and intubation due to compression of the brainstem. However, an event of cardiac arrest during these manipulations should not deter the neuroanaesthesiologist to continue with the procedure.

**Epilepsy surgery**

Surgical treatment offered to children with medically intractable epilepsy includes focal resection (of the area generating seizures), corpus callosotomy (two hemispheres surgically separated to reduce severity of seizures), hemispherectomy (disconnecting one side of the brain from rest) and vagal nerve stimulation (timed stimulation of left vagus nerve to blunt paroxysmal seizures).

The anaesthetic concerns include perioperative seizures and the effects of anticonvulsants. Chronic use of anticonvulsants induces rapid metabolism and clears anaesthetic agents such as neuromuscular blockers and opioids, thereby increasing the anaesthetic requirements. If intraoperative electrocorticographic (ECoG) monitoring is planned, sedatives and anticonvulsants should be withheld for 48 h preoperatively. Inhalational agents depress the cortical responses, hence should be avoided during ECoG recordings. An opioids-based technique is ideal during
such a scenario. Awake craniotomy offers the advantage of intraoperative ECoG monitoring, but is difficult to get the cooperation of children below 9 years of age.

Craniovertebral junction anomalies

Craniovertebral junction (CVJ) anomalies are developmental disorders that affect the skeleton and enclosed neuraxis at the junction of cranium and cervical spine. The clinical syndromes associated with these anomalies are attributable to the following: (i) pressure on the neuraxis by the bony abnormalities, (ii) intrinsic malformations of the nervous system and (iii) disturbance of the CSF circulation and blood supply.

Figure: T2-weighted magnetic resonance imaging of cervicomedullary junction shows basilar invagination (arrow)
The bony abnormalities usually encountered in CVJ anomalies are basilar invagination, occipitalisation and congenital atlanto-axial dislocation. The clinical manifestations may occur because of direct compression of the neural tissue by these osseous anomalies as the spine is grossly unstable.

The patients may present with respiratory dysfunction (restrictive lung disease) owing to compression of the brainstem by odontoid process of second cervical vertebra affecting the respiratory centre and weakening of the muscles of respiration including diaphragm.

The surgical management includes transoral odontoidectomy and occipito-cervical fixation, with both the procedures carried out in one setting. The anaesthetic considerations include securing the airway with minimal manipulation of neck, preferably by awake fibreoptic intubation, blood loss during odontoidectomy, haemodynamic changes during posterior fixation owing to prone position and handling near cervico-medullary junction.

Postoperatively, the tracheal intubation is continued for at least 12-24 h to prevent complications of potential reintubation due to pharyngeal oedema with a fixed cervical spine.

**Vascular malformations**

Arteriovenous malformations (AVMs) present with haemorrhage, seizure and hydrocephalus in infants and children, and with congestive heart failure (CHF) in newborns. AVMs are the most common cause of subarachnoid haemorrhage in children. Large AVMs, e.g. *vein of Galen malformation*, may present with high-output CHF. Usually intravascular embolisation is carried out in a neuroradiological suite as surgical excision is associated with considerable blood loss requiring adequate haemodynamic monitoring. The anaesthesiologist should be prepared to treat sudden hypertension and hyperaemic cerebral oedema following embolisation/excision of AVM with labatolol and sodium nitroprusside.
Moyamoya disease is a vaso-occlusive disorder of the distal internal carotid artery, present in children with transient ischaemic attacks or recurrent strokes. Surgery for this condition, encephalo-duro-arterial-synangiosis (EDAS), may be often complicated by cerebral ischaemia. Hence, the anaesthetic goal is to optimise cerebral perfusion pressure (CPP) by normovolaemia with preoperative hydration, normotension, normothermia and normocapnia, as both hypo and hypercapnia cause steal phenomena from the ischaemic region, thereby causing further cerebral ischaemia.

Neuroradiology

Most of the neuroradiological studies (computed tomography (CT) scan and magnetic resonance imaging (MRI)) can be carried out with light sedation. However, general anaesthesia (GA) is required in children who are uncooperative with co-existing medical conditions and during the procedure of intravascular embolisation which may be painful for a child.

Endotracheal intubation is not always required to secure the airway for the children undergoing these procedures under GA. Use of laryngeal mask airway has been suggested, although there is insufficient evidence to recommend its routine use.

Head trauma

Head injury may cause intracranial haematoma, diffuse axonal injury and oedema with deranged autoregulation and intracranial compliance.

Sometimes, the children with head trauma may present with depression of ST segment in the ECG. These ST-T changes are possibly due to sympathetic hyperactivity associated with raised ICP and should not deter the anaesthesiologist to continue with the anaesthetic plan. These changes revert back to normal once the decompressive procedure is carried out. The anaesthetic goal is to prevent secondary injuries such as hypoxia, hypotension, hyperthermia, hyperglycaemia, hypoglycaemia, etc.
matched blood must be available during emergency evacuation of an extradural haematoma. In a child, a small intracranial bleed may result in significant loss of circulating volume. Subsequent hypovolaemia and hypotension may be further aggravated by preoperative infusion of mannitol and diuretic therapy. Hence, precaution should be taken to prevent hypotension even it occurs for a brief time period.
Clinical Neurophysiology
in Pediatric Peripheral
Neuropathy

Neurophysiology studies are useful to differentiate between types of demyelinating disease, as well as between axonal and demyelinating disease. The presence of conduction block can support an early diagnosis of AIDP. These results are unlikely to alter management, but may assist with counseling for prognosis. This is most relevant to the hereditary group.

Useful neurophysiological markers, other than the typical demyelinating and axonal ranges described in CMT1 and CMT2, are the extreme slowing evident in CMT3 (usually <10 m/s motor conduction velocity) and most forms of CMT4, as well as the intermediate values seen in patients with distal-intermediate CMT disease and X-linked CMT (CMTX) disease.

The patients with early-onset neuronal hereditary motor sensory neurology can have values in the borderline axonal/demyelinating range. These patients present before 5 years of age with distal weakness, wheelchair dependency (occurring by the second decade in most) and markedly affected distal upper limb function. At presentation, these children appear to have a waddling gait with proximal weakness and foot drop. MFN2
mutations are reported in 50% of this group, placing them under the subcategory of CMT2A2. Patients with spinal muscular atrophy with respiratory distress typically have absent sensory responses and compound muscle action potentials are absent or markedly reduced. Electromyography detects denervation. The patients often present with intrauterine growth retardation, diaphragmatic dysfunction (becoming evident between 1 and 6 months of age), a weak cry, inspiratory stridor and earlier noted foot deformities. Sensory and autonomic nerve involvement can occur, leading to reduced pain perception, excessive sweating, constipation, cardiac arrhythmias and constipation. Fatty pads over the phalanges are an additional clinical marker. Peripheral electrophysiology must be performed in a center skilled in performing such studies. The interpretation must be made with caution, as the normal ranges vary significantly until 5 years of age, when the nerve conduction velocity approaches adult levels. In some infants with axonal degeneration and a paucity of large diameter fibers, nerve conduction velocity may be in the so-called ‘demyelinating range’. Furthermore, axonal pathology does not always result in measurable abnormality in nerve conduction. In patients with axonal degeneration, undamaged fibers will conduct with normal conduction velocities and the degenerating fibers do not conduct at all. This results in surface electrode measurements potentially in the normal range or only mildly slowed. However, the amplitude of the compound muscle action potential will be reduced due to the smaller number of conducting fibers and motor units activated by the stimulus. In patients with small fiber neuropathy, such as hereditary sensory and autonomic neuropathy types 4 and Fabry’s disease, nerve conduction studies will also be normal due to the absence of involvement of large myelinated fibers.

**MOLECULAR GENETIC ANALYSES**

Molecular genetic analyses for peripheral neuropathies are limited in South Africa to screening for CMT1A. This form is
described as the commonest subtype to affect children and adults, estimated at 50% in the former and 70% in the latter. However, this figure has not been assessed for RPCs.

There are little data describing the incidence of CMT1A in indigenous African populations. A study from Brazil reported that 13% of their cohort with CMT1A were of African descent (n = 6). In comparison with CMT1A, CMTX typically presents in the second decade.

Although it is more symptomatic in males affected, female carriers can manifest with signs of neuropathy potentially leading to diagnostic confusion with CMT1. Neurophysiology studies are typically in the intermediate range and the majority of patients have a mutation in CMTX1.

If there is access to brainstem auditory responses, these are often abnormal in patients with CMTX. CMT2B1, an axonal subtype of CMT with onset in the second decade of life, is prevalent in northwestern Africa (northwest Algeria and east of Morocco); a founder effect is suggested. In the neuromuscular clinic at the Red Cross War Memorial Children’s Hospital in South Africa, children with hereditary neuropathies in the indigenous African population are dominated by axonal forms of CMT.

Genetic analysis of this axonal group remains a challenge, even for international centers, and the group has previously had the lowest molecular genetic mutation detection rate. With the expanding identification of mutations associated with axonal forms of CMT, namely MFN2, TRPV4, GDAP1 and NEFL, the molecular genetic diagnostic closure is improving. Such screening is only available in equipped international centers.

Storing DNA should be considered, as genetic screening is becoming more cost effective and available and preparing for this may enable families to gain diagnostic closure. Several publications expand on the many identified subtypes of CMT and the specific phenotypes related to them. It is beyond the
scope of this chapter to cover descriptions of all subtypes; only those most relevant are addressed here. For most forms of CMT, the acute and chronic care is the same, and predominantly symptomatic.

**Peripheral Nerve Biopsy**

Most guidelines that discuss investigations of peripheral neuropathies recommend consideration of peripheral nerve biopsy if other routes have failed to confirm an underlying diagnosis. Peripheral nerve biopsy is a safe investigation, which, if performed and analyzed in an appropriate setting, can enhance the diagnostic yield of complex patients. However, most guidelines, are adult based and few exist with pediatric emphasis. Specific features on histology would include the giant axons of GAN, CMT2E/CMT1F, CMT4C and ‘glue sniffing’ neuropathy related to exposure to N-hexane, the myelin out folding of CMT4B, the unusual Schwann cell cytoplasmic chains of CMT4C, the extreme paucity of fibers in some cases of LMNA mutations and the mixed ultrastructural demyelinating/axonal degenerative picture of MFN2 mutations (CMT2A2) associated with abnormal mitochondria. In RPCs it may be more cost effective if, while the child undergoes a procedure (usually orthopedic), an ‘opportunistic biopsy’ is taken. This may enable diagnosis of suspected conditions, such as metachromatic leucodystrophy, GAN, CMT3, among others, to be confirmed. The biochemical and molecular genetic analyses for these conditions are costly and not readily available to RPCs. Prior to such screens being available overseas, histopathological analysis was a useful diagnostic tool. With regard to RPCs there is a case to maintain access to these screens.

**FACTS ABOUT PERIPHERAL NEUROPATHY**

Peripheral neuropathy has many different causes. Some people inherit the disorder from their parents, and others develop it because of an injury or another disorder. In many cases, a
A different type of medical problem, such as a kidney condition or a hormone imbalance, leads to peripheral neuropathy. One of the most common causes of peripheral neuropathy in the U.S. is diabetes. About 60 to 70 percent of Americans with diabetes have some form of nerve damage.

**Types of peripheral neuropathy**

There are more than 100 types of peripheral neuropathy, each with its own set of symptoms and prognosis. To help doctors classify them, they are often broken down into the following categories:

- **Motor neuropathy.** This is damage to the nerves that control muscles and movement in the body, such as moving your hands and arms or talking.
- **Sensory neuropathy.** Sensory nerves control what you feel, such as pain or a light touch. Sensory neuropathy affects these groups of nerves.
- **Autonomic nerve neuropathy.** Autonomic nerves control biological functions that you are not conscious of, such as breathing and heartbeat. Damage to these nerves can be serious.
- **Combination neuropathies.** A combination of two or three of these other types of neuropathies, such as a predominantly motor neuropathy or a sensory-motor neuropathy.

**Symptoms**

The symptoms of peripheral neuropathy vary based on the type that your child may have. Motor neuropathy symptoms may include:

- Muscle weakness
- Cramps
- Muscle twitching
- Loss of muscle and bone
- Changes in skin, hair, or nails
Sensory neuropathy symptoms may include:
- Numbness
- Loss of sensation or feeling in body parts
- Loss of balance or other functions as a side effect of the loss of feeling in the legs, arms, or other body parts
- Emotional disturbances
- Sleep disruptions

Autonomic neuropathy symptoms may include:
- Inability to sweat properly, leading to heat intolerance
- Loss of bladder control, leading to infection or incontinence
- Dizziness, lightheadedness, or fainting because of a loss of control over blood pressure
- Diarrhea, constipation or incontinence related to nerve damage in the intestines or digestive tract
- Difficulty eating or swallowing
- Life-threatening symptoms, such as difficulty breathing or irregular heartbeat

The symptoms of peripheral neuropathy may resemble other conditions or medical problems. Always consult your doctor for a diagnosis.

**Diagnosis**

The symptoms and body parts affected by peripheral neuropathy are so varied that it may be difficult to make a diagnosis. If your doctor suspects nerve damage, he or she will take an extensive patient history and conduct a number of neurological tests to determine the location and extent of your nerve damage. These may include:
- Blood tests
- Spinal fluid tests
- Muscle strength tests
- Tests of the ability to detect vibrations
Depending on what basic tests reveal, your doctor may want to perform more in-depth scanning and other tests to get a better look at your child’s nerve damage. Tests may include:

- CT scan
- MRI scan
- Electromyography
- Nerve and skin biopsy

**Treatment**

Usually a peripheral neuropathy can’t be cured, but you can do a lot of things to prevent it from getting worse. If an underlying condition like diabetes is at fault, your doctor will treat that first and then treat the pain and other symptoms of neuropathy. In some cases, over-the-counter (OTC) pain relievers can help. Other times, prescription drugs are needed. Some of these drugs include mexiletine, a medication developed to correct irregular heart rhythms; antiepileptic drugs, such as gabapentin, phenytoin, and carbamazepine; and some classes of antidepressants, including tricyclics such as amitriptyline. Lidocaine injections and patches may help with pain in other instances. And in extreme situations, surgery can be used to destroy nerves or repair injuries that are causing neuropathic pain and symptoms.

**Managing peripheral neuropathy**

Even if your child already has some form of peripheral neuropathy, a healthy diet and regular exercise can help reduce the pain and symptoms related to the disorder. You’ll also want to not let injuries go untreated and be meticulous about caring for your child’s feet and treating wounds to avoid complications, such as the loss of a limb.

**CAUSES PERIPHERAL NEUROPATHY?**

A 20-year-old right-handed male came to clinic with complaints of numbness and tingling in the right lower part of his forearm, 4th and 5th digit and lateral hand. The problem had
been increasing over the past month. In particular it increased over the day and was best in the morning. It also got worse day to day over the work week and was better on the weekends. He also complained of some general shoulder and neck muscle pain that he described as cramping, which also improved with rest. He had started a new summer job about 5 weeks previous where he did extensive computer work. He said that the keyboard and mousepad were on top of a solid desk with the monitor in front of the keyboard. He showed the examiner how he had to place the lateral aspect of his right lower forearm across the edge of the desk. He used other computers at home but said that he had a separate tray for his keyboard and mouse that were lower in height than the edge of the desk he worked on, and the edges of the tray were padded. He also played a variety of videogames with hand or lap controllers. He denies any new medications or toxin exposure. The past medical history was non-contributory. The family history revealed no neurological or genetic abnormalities.

The pertinent physical exam showed a healthy male with normal vital signs and growth parameters. His musculoskeletal examination showed very tight muscles of the neck and shoulder girdle bilaterally. His neurological examination was normal except for pain and numbness in the ulnar nerve distribution of the right lower forearm and hand. Strength was normal. The diagnosis of an acute, focal peripheral neuropathy secondary to ulnar nerve compression along with general muscle spasm of the neck and shoulders was made. He was instructed to suspend all computer work until he had normal sensation. He was given an information prescription of Internet resources on how to properly set-up a computer workstation so that it would be ergonomically appropriate for him. He was also instructed to take frequent short breaks, and to do intermittent stretching of his body. He was to return to clinic if the symptoms persisted or changed. At his next health supervision visit, he reported no problems after he had changed his workstation.
Discussion

Peripheral neuropathy is simply a disease of the peripheral nerves. They can be acute (30%) or chronic (about 67%). About 70% of chronic neuropathy in children is hereditary, 20% is indeterminant and 10% is acquired. Peripheral neuropathies are often present with predominantly distal involvement that is bilateral and symmetric. Sensory symptoms can include numbness, dysesthesia or ataxia. Motor symptoms often include weakness. The autonomic nervous system can also be affected with arrhythmias, hypotension, bowel or bladder problems or abnormal sweating.

Learning Point

The differential diagnosis of peripheral neuropathy includes:

- Neurologic
  - Abetaliproteinemia
  - Charcot-Marie Tooth Disease
  - Chronic Inflammatory Demyelinating Polyneuropathy
  - Dejerine-Sottas
  - Giant Axonal Neuropathy
  - Guillian-Barre Syndrome
  - Hereditary Sensory Neuropathies – Familial Dysautonomia
  - Ischemic Monomelic Neuropathy
  - Mononeuritis Multiplex
  - Metachromatic Leukodystrophy
  - Refsum Disease
- Infectious Disease
  - Chagas Disease
  - Diphtheria
  - Leprosy
  - Lyme Disease
- Rabies
- Tick Paralysis

- Rheumatic/Inflammatory
  - Churg-Strauss Syndrome
  - Henoch-Schonlein Purpura
  - Inflammatory Bowel Disease
  - Juvenile Rheumatoid Arthritis
  - Polyarteritis Nodosa
  - Sarcoidosis
  - Sjogren’s Syndrome
  - Systemic Lupus Erythematosus
  - Wegener’s Granulomatosis

- Specific Diseases
  - Celiac Disease
  - Chronic Illness Polyneuropathy
  - Cystic Fibrosis
  - Diabetes Mellitus
  - Hypothyroidism
  - Porphyria
  - Malignancy
  - Renal Failure/Uremia
  - Transplantation – Bone Marrow, Liver
  - Vitamin Deficiency – B1, B2, B6, B12, E

- Drugs
  - Alcohol
  - Anti-retroviral medications
  - Antibiotics – chloramphenicol, isoniazid, metronidazole, nitrofurantoin, penicillin, sulfonamide,
  - Chemotherapy
  - Phenytoin
  - Thalidomide
Toxins
- Arsenic
- Lead
- Mercury
- n-Hexane
- Organophosphates
- Thallium

Other
- Epidemic neuropathy
- Factitious
- Idiopathic – Bell’s palsy
- Mechanical – brachial plexus injury, injections, pressure,

SYMPTOMS OF PERIPHERAL NEUROPATHY
- Burning, tingling, or prickling sensation usually in the hands or feet
- Numbness or sensitivity to pain or temperature
- Extreme sensitivity to touch
- Sharp shooting pain
- Poor balance or coordination
- Loss of reflexes
- Muscle weakness
- Noticeable changes in the way you walk

Muscle weakness may begin around the arch of the foot and in the palm of the hand. It may be difficult to grip things or to perform certain tasks or activities such as writing, buttoning clothes, or tying shoes.

The muscles that pull the foot up may weaken and the reflexes may be lost, causing the front part of the foot to fall flat to the floor. This may result in poor balance or coordination, especially when tired. There may be a tendency to drag the feet or lift them high to prevent the feet from dragging.
Who is at Risk?

People who have received any of the following chemotherapy drugs may be at risk:

- Vincristine
- Vinblastine
- Cisplatin
- Carboplatin

People at highest risk for peripheral neuropathy are those who have received higher doses of these drugs or combinations of these drugs. Other risk factors include surgery, severe weight loss, and diabetes or a pre-existing nerve disease. Prolonged pressure on nerves from artificial limbs, wheelchairs, or crutches can also contribute to nerve damage.

Recommended Screening

Anyone who has received cancer treatment during childhood should have a yearly comprehensive medical check-up. If peripheral neuropathy is suspected, a thorough neurological examination should be included in this check-up. If a significant problem is detected, a referral to a neurologist (doctor who specializes in problems of the nervous system) may be needed for further testing. People with peripheral neuropathy may also benefit from physical and/or occupational therapy.

Rehabilitation services

There is no treatment that can cure or reverse nerve damage. Therefore, treatment is directed toward symptom management. Physical therapy is often helpful in providing exercises to improve strength, balance, and coordination. Occupational therapy can provide help to improve hand-eye coordination and other skills needed for daily life.

Orthotic Devices

Support for feet or ankles can be improved with orthotic devices. Arch supports or splints help prevent the arch from
flattening and help improve walking. Splints called ankle-foot orthoses (AFOs) may be recommended to prevent the ankle from moving too much from side-to-side and to support the foot when walking.

**Pain Management**

Healthcare providers can prescribe medication to control any pain, tingling, and burning sensation. The type of medication depends on the frequency and severity of pain. It is also important to know that some medications will have side effects of their own. Elastic stockings, warm packs, or exercise may also help with the discomfort. These measures will not replace medication but may decrease the need for them. They may also assist in improving mobility and independence.
EMG in Pediatric Brachial Plexopathy

Electromyography (EMG) is an electrodiagnostic medicine technique for evaluating and recording the electrical activity produced by skeletal muscles. EMG is performed using an instrument called an electromyograph to produce a record called an electromyogram. An electromyograph detects the electric potential generated by muscle cells when these cells are electrically or neurologically activated. The signals can be analyzed to detect medical abnormalities, activation level, or recruitment order, or to analyze the biomechanics of human or animal movement.

MEDICAL USES

EMG testing has a variety of clinical and biomedical applications. EMG is used as a diagnostics tool for identifying neuromuscular diseases, or as a research tool for studying kinesiology, and disorders of motor control. EMG signals are sometimes used to guide botulinum toxin or phenol injections into muscles. EMG signals are also used as a control signal for prosthetic devices such as prosthetic hands, arms, and lower limbs.

EMG then an acceleromyograph may be used for neuromuscular monitoring in general anesthesia with
neuromuscular-blocking drugs, in order to avoid postoperative residual curarization (PORC).

Except in the case of some purely primary myopathic conditions EMG is usually performed with another electrodiagnostic medicine test that measures the conducting function of nerves. This is called a nerve conduction studies (NCS). Needle EMG and NCSs are typically indicated when there is pain in the limbs, weakness from spinal nerve compression, or concern about some other neurologic injury or disorder. Spinal nerve injury does not cause neck, mid back pain or low back pain, and for this reason, evidence has not shown EMG or NCS to be helpful in diagnosing causes of axial lumbar pain, thoracic pain, or cervical spine pain. Needle EMG may aid with the diagnosis of nerve compression or injury (such as carpal tunnel syndrome), nerve root injury (such as sciatica), and with other problems of the muscles or nerves. Less common medical conditions include amyotrophic lateral sclerosis, myasthenia gravis, and muscular dystrophy.

TECHNIQUE

Skin preparation and Risks

The first step before insertion of the needle electrode is skin preparation. This typically involves simply cleaning the skin with an alcohol pad.

The actual placement of the needle electrode can be difficult and depends on a number of factors, such as specific muscle selection and the size of that muscle. Proper needle EMG placement is very important for accurate representation of the muscle of interest, although EMG is more effective on superficial muscles as it is unable to bypass the action potentials of superficial muscles and detect deeper muscles. Also, the more body fat an individual has, the weaker the EMG signal. When placing the EMG sensor, the ideal location is at the belly of the muscle: the longitudinal midline. The belly of the muscle can also be thought
of as in-between the motor point (middle) of the muscle and the
tendonous insertion point.

Cardiac pacemakers and implanted cardiac defibrillators
(ICDs) are used increasingly in clinical practice, and no evidence
exists indicating that performing routine electrodiagnostic studies
on patients with these devices pose a safety hazard. However,
there are theoretical concerns that electrical impulses of nerve
conduction studies (NCS) could be erroneously sensed by devices
and result in unintended inhibition or triggering of output or
reprogramming of the device. In general, the closer the stimulation
site is to the pacemaker and pacing leads, the greater the chance
for inducing a voltage of sufficient amplitude to inhibit the
pacemaker. Despite such concerns, no immediate or delayed
adverse effects have been reported with routine NCS.

No known contraindications exist from performing needle
EMG or NCS on pregnant patients. In addition, no complications
from these procedures have been reported in the literature.
Evoked potential testing, likewise, has not been reported to cause
any problems when it is performed during pregnancy.

Patients with lymphedema or patients at risk for lymphedema
are routinely cautioned to avoid percutaneous procedures in the
affected extremity, namely venipuncture, to prevent development
or worsening of lymphedema or cellulitis. Despite the potential
risk, the evidence for such complications subsequent to
venipuncture is limited. No published reports exist of cellulitis,
infection, or other complications related to EMG performed in
the setting of lymphedema or prior lymph node dissection.
However, given the unknown risk of cellulitis in patients with
lymphedema, reasonable caution should be exercised in
performing needle examinations in lymphedematous regions to
avoid complications. In patients with gross edema and taut skin,
skin puncture by needle electrodes may result in chronic weeping
of serous fluid. The potential bacterial media of such serous fluid
and the violation of skin integrity may increase the risk of cellulitis.
Prior to proceeding, the physician should weigh the potential
EMG in Pediatric Brachial Plexopathy

risks of performing the study with the need to obtain the information gained.

**Surface and intramuscular EMG recording electrodes**

There are two kinds of EMG: surface EMG and intramuscular EMG. Surface EMG assesses muscle function by recording muscle activity from the surface above the muscle on the skin. Surface electrodes are able to provide only a limited assessment of the muscle activity. Surface EMG can be recorded by a pair of electrodes or by a more complex array of multiple electrodes. More than one electrode is needed because EMG recordings display the potential difference (voltage difference) between two separate electrodes. Limitations of this approach are the fact that surface electrode recordings are restricted to superficial muscles, are influenced by the depth of the subcutaneous tissue at the site of the recording which can be highly variable depending on the weight of a patient, and cannot reliably discriminate between the discharges of adjacent muscles.

Intramuscular EMG can be performed using a variety of different types of recording electrodes. The simplest approach is a monopolar needle electrode. This can be a fine wire inserted into a muscle with a surface electrode as a reference; or two fine wires inserted into muscle referenced to each other. Most commonly fine wire recordings are for research or kinesiology studies. Diagnostic monopolar EMG electrodes are typically stiff enough to penetrate skin and insulated, with only the tip exposed using a surface electrode for reference. Needles for injecting therapeutic botulinum toxin or phenol are typically monopolar electrodes that use a surface reference, in this case, however, the metal shaft of a hypodermic needle, insulated so that only the tip is exposed, is used both to record signals and to inject. Slightly more complex in design is the concentric needle electrode. These needles have a fine wire, embedded in a layer of insulation that fills the barrel of a hypodermic needle, that has an exposed shaft, and the shaft serves as the reference electrode. The exposed tip
of the fine wire serves as the active electrode. As a result of this configuration, signals tend to be smaller when recorded from a concentric electrode than when recorded from a monopolar electrode and they are more resistant to electrical artifacts from tissue and measurements tend to be somewhat more reliable. However, because the shaft is exposed throughout its length, superficial muscle activity can contaminate the recording of deeper muscles. Single fiber EMG needle electrodes are designed to have very tiny recording areas, and allow for the discharges of individual muscle fibers to be discriminated.

To perform intramuscular EMG, typically either a monopolar or concentric needle electrode is inserted through the skin into the muscle tissue. The needle is then moved to multiple spots within a relaxed muscle to evaluate both insertional activity and resting activity in the muscle. Normal muscles exhibit a brief burst of muscle fiber activation when stimulated by needle movement, but this rarely lasts more than 100ms. The two most common pathologic types of resting activity in muscle are fasciculation and fibrillation potentials. A fasciculation potential is an involuntary activation of a motor unit within the muscle, sometimes visible with the naked eye as a muscle twitch or by surface electrodes. Fibrillations, however, are only detected by needle EMG, and represent the isolated activation of individual muscle fibers, usually as the result of nerve or muscle disease. Often, fibrillations are triggered by needle movement (insertional activity) and persist for several seconds or more after the movement ceases.

After assessing resting and insertional activity, the electromyographer assess the activity of muscle during voluntary contraction. The shape, size, and frequency of the resulting electrical signals are judged. Then the electrode is retracted a few millimetres, and again the activity is analyzed. This is repeated, sometimes until data on 10–20 motor units have been collected in order to draw conclusions about motor unit function. Each electrode track gives only a very local picture of the activity of
the whole muscle. Because skeletal muscles differ in the inner structure, the electrode has to be placed at various locations to obtain an accurate study.

Single fiber electromyography assessed the delay between the contractions of individual muscle fibers within a motor unit and is a sensitive test for dysfunction of the neuromuscular junction caused by drugs, poisons, or diseases such as myasthenia gravis. The technique is complicated and typically only performed by individuals with special advanced training. Surface EMG is used in a number of settings; for example, in the physiotherapy clinic, muscle activation is monitored using surface EMG and patients have an auditory or visual stimulus to help them know when they are activating the muscle (biofeedback). A review of the literature on surface EMG published in 2008 concluded that surface EMG may be useful to detect the presence of neuromuscular disease (level C rating, class III data), but there are insufficient data to support its utility for distinguishing between neuropathic and myopathic conditions or for the diagnosis of specific neuromuscular diseases. EMGs may be useful for additional study of fatigue associated with post-poliomyelitis syndrome and electromechanical function in myotonic dystrophy (level C rating, class III data).

Certain US states limit the performance of needle EMG by nonphysicians. New Jersey declared that it cannot be delegated to a physician’s assistant. Michigan has passed legislation saying needle EMG is the practice of medicine. Special training in diagnosing medical diseases with EMG is required only in residency and fellowship programs in neurology, clinical neurophysiology, neuromuscular medicine, and physical medicine and rehabilitation. There are certain subspecialists in otolaryngology who have had selective training in performing EMG of the laryngeal muscles, and subspecialists in urology, obstetrics and gynecology who have had selective training in performing EMG of muscles controlling bowel and bladder function.
Maximal voluntary contraction

One basic function of EMG is to see how well a muscle can be activated. The most common way that can be determined is by performing a maximal voluntary contraction (MVC) of the muscle that is being tested.

Muscle force, which is measured mechanically, typically correlates highly with measures of EMG activation of muscle. Most commonly this is assessed with surface electrodes, but it should be recognized that these typically only record from muscle fibers in close approximation to the surface.

Several analytical methods for determining muscle activation are commonly used depending on the application. The use of mean EMG activation or the peak contraction value is a debated topic. Most studies commonly use the maximal voluntary contraction as a means of analyzing peak force and force generated by target muscles. According to the article, Peak and average rectified EMG measures: Which method of data reduction should be used for assessing core training exercises?, concluded that the “average rectified EMG data (ARV) is significantly less variable when measuring the muscle activity of the core musculature compared to the peak EMG variable.” Therefore, these researchers would suggest that “ARV EMG data should be recorded alongside the peak EMG measure when assessing core exercises.” Providing the reader with both sets of data would result in enhanced validity of the study and potentially eradicate the contradictions within the research.

Other measurements

EMG can also be used for indicating the amount of fatigue in a muscle. The following changes in the EMG signal can signify muscle fatigue: an increase in the mean absolute value of the signal, increase in the amplitude and duration of the muscle action potential and an overall shift to lower frequencies. Monitoring the changes of different frequency changes the most common way of using EMG to determine levels of fatigue. The
lower conduction velocities enable the slower motor neurons to remain active.

A motor unit is defined as one motor neuron and all of the muscle fibers it innervates. When a motor unit fires, the impulse (called an action potential) is carried down the motor neuron to the muscle.

The area where the nerve contacts the muscle is called the neuromuscular junction, or the motor end plate. After the action potential is transmitted across the neuromuscular junction, an action potential is elicited in all of the innervated muscle fibers of that particular motor unit.

The sum of all this electrical activity is known as a motor unit action potential (MUAP). This electrophysiologic activity from multiple motor units is the signal typically evaluated during an EMG. The composition of the motor unit, the number of muscle fibres per motor unit, the metabolic type of muscle fibres and many other factors affect the shape of the motor unit potentials in the myogram.

Nerve conduction testing is also often done at the same time as an EMG to diagnose neurological diseases.

Some patients can find the procedure somewhat painful, whereas others experience only a small amount of discomfort when the needle is inserted. The muscle or muscles being tested may be slightly sore for a day or two after the procedure.

**EMG signal decomposition**

EMG signals are essentially made up of superimposed motor unit action potentials (MUAPs) from several motor units. For a thorough analysis, the measured EMG signals can be decomposed into their constituent MUAPs. MUAPs from different motor units tend to have different characteristic shapes, while MUAPs recorded by the same electrode from the same motor unit are typically similar. Notably MUAP size and shape depend on where the electrode is located with respect to the fibers and so
can appear to be different if the electrode moves position. EMG decomposition is non-trivial, although many methods have been proposed.

**EMG signal processing**

Rectification is the translation of the raw EMG signal to a single polarity frequency (usually positive). The purpose of rectifying a signal is to ensure the raw signal does not average zero, due to the raw EMG signal having positive and negative components. It facilitates the signals and process and calculates the mean, integration and the fast fourier transform (FFT). The two types of rectification of signals refer to what happens to the EMG wave when it is processed. These types include full length frequency and half length. Full length frequency adds the EMG signal below the baseline (usually negative polarity) to the signal above the baseline making a conditioned signal that is all positive. This is the preferred method of rectification because it conserves all signal energy for analysis, usually in the positive polarity. Half length rectification deletes the EMG signal below the baseline. In doing so, the average of the data is no longer zero therefore it can be used in statistical analyses. The only difference between the two types of rectification is that full-wave rectification takes the absolute value of the signal array of data points.

**Limitations**

Needle EMG use in clinical settings has practical applications such as helping to discover disease. Needle EMG has limitations, however, in that it does involve voluntary activation of muscle, and as such is less informative in patients unwilling or unable to cooperate, children and infants, and in individuals with paralysis. Surface EMG can have limited applications due to inherent problems associated with surface EMG. Adipose tissue (fat) can affect EMG recordings. Studies show that as adipose tissue increased the active muscle directly below the surface decreased. As adipose tissue increased, the amplitude of the surface EMG signal directly above the center of the active muscle
EMG in Pediatric Brachial Plexopathy

decreased. EMG signal recordings are typically more accurate with individuals who have lower body fat, and more compliant skin, such as young people when compared to old. Muscle cross talk occurs when the EMG signal from one muscle interferes with that of another limiting reliability of the signal of the muscle being tested. Surface EMG is limited due to lack of deep muscles reliability. Deep muscles require intramuscular wires that are intrusive and painful in order to achieve an EMG signal. Surface EMG can only measure superficial muscles and even then it is hard to narrow down the signal to a single muscle.

Electrical characteristics

The electrical source is the muscle membrane potential of about −90 mV. Measured EMG potentials range between less than 50 ìV and up to 20 to 30 mV, depending on the muscle under observation.

Typical repetition rate of muscle motor unit firing is about 7–20 Hz, depending on the size of the muscle (eye muscles versus seat (gluteal) muscles), previous axonal damage and other factors. Damage to motor units can be expected at ranges between 450 and 780 mV.

BRACHIAL PLEXUS INJURY

The brachial plexus is a network of nerves that conducts signals from the spinal cord, which is housed in the spinal canal of the vertebral column (or spine), to the shoulder, arm and hand. These nerves originate in the fifth, sixth, seventh and eighth cervical (C5–C8), and first thoracic (T1) spinal nerves, and innervate the muscles and skin of the chest, shoulder, arm and hand. Brachial plexus injuries, or lesions, are caused by damage to those nerves.

Brachial plexus injuries, or lesions, can occur as a result of shoulder trauma, tumours, or inflammation. The rare Parsonage-Turner Syndrome causes brachial plexus inflammation without obvious injury, but with nevertheless disabling symptoms. But
in general, brachial plexus lesions can be classified as either traumatic or obstetric. Obstetric injuries may occur from mechanical injury involving shoulder dystocia during difficult childbirth. Traumatic injury may arise from several causes. “The brachial plexus may be injured by falls from a height on to the side of the head and shoulder, whereby the nerves of the plexus are violently stretched....The brachial plexus may also be injured by direct violence or gunshot wounds, by violent traction on the arm, or by efforts at reducing a dislocation of the shoulder joint”.

**Signs and symptoms**

Signs and symptoms may include a limp or paralyzed arm, lack of muscle control in the arm, hand, or wrist, and lack of feeling or sensation in the arm or hand. Although several mechanisms account for brachial plexus injuries, the most common is nerve compression or stretch. Infants, in particular, may suffer brachial plexus injuries during delivery and these present with typical patterns of weakness, depending on which portion of the brachial plexus is involved. The most severe form of injury is nerve root avulsion, which results in complete weakness in corresponding muscles. This usually accompanies high-velocity impacts that commonly occur during motor-vehicle collisions or bicycle accidents.

**Disabilities**

Based on the location of the nerve damage, brachial plexus injuries can affect part of or the entire arm. For example, musculocutaneous nerve damage weakens elbow flexors, median nerve damage causes proximal forearm pain, and paralysis of the ulnar nerve causes weak grip and finger numbness. In some cases, these injuries can cause total and irreversible paralysis. In less severe cases, these injuries limit use of these limbs and cause pain.

The cardinal signs of brachial plexus injury then, are weakness in the arm, diminished reflexes, and corresponding sensory deficits.
1. Erb’s palsy. “The position of the limb, under such conditions, is characteristic: the arm hangs by the side and is rotated medially; the forearm is extended and pronated. The arm cannot be raised from the side; all power of flexion of the elbow is lost, as is also supination of the forearm”.

2. In Klumpke’s paralysis, a form of paralysis involving the muscles of the forearm and hand, a characteristic sign is the *clawed hand*, due to loss of function of the ulnar nerve and the intrinsic muscles of the hand it supplies.

**Causes**

In most cases the nerve roots are stretched or torn from their origin, since the meningeal covering of a nerve root is thinner than the sheath enclosing the nerve. The epineurium of the nerve is contiguous with the dura mater, providing extra support to the nerve.

Brachial plexus lesions typically result from excessive stretching; from rupture injury where the nerve is torn but not at the spinal cord; or from avulsion injuries, where the nerve is torn from its attachment at the spinal cord. A build-up of scar tissue around a brachial plexus injury site can also put pressure on the injured nerve, disrupting innervation of the muscles. Although injuries can occur at any time, many brachial plexus injuries happen during birth: the baby’s shoulders may become impacted during the birth process causing the brachial plexus nerves to stretch or tear. Obstetric injuries may occur from mechanical injury involving shoulder dystocia during difficult childbirth, the most common of which result from injurious stretching of the child’s brachial plexus during birth, mostly vaginal, but occasionally Caesarean section. The excessive stretch results in incomplete sensory and/or motor function of the injured nerve.

Injuries to the brachial plexus result from excessive stretching or tearing of the C5-T1 nerve fibers. These injuries can be located
in front of or behind the clavicle, nerve disruptions, or root avulsions from the spinal cord. These injuries are diagnosed based on clinical exams, axon reflex testing, and electrophysiological testing. Brachial plexus injuries require quick treatment in order for the patient to make a full functional recovery (Tung, 2003). These types of injuries are most common in young adult males.

Traumatic brachial plexus injuries may arise from several causes, including sports, high-velocity motor vehicle accidents, especially in motorcyclists, but also all-terrain-vehicle (ATV) accidents. Injury from a direct blow to the lateral side of the scapula is also possible. The severity of nerve injuries may vary from a mild stretch to the nerve root tearing away from the spinal cord (avulsion). “The brachial plexus may be injured by falls from a height on to the side of the head and shoulder, whereby the nerves of the plexus are violently stretched… The brachial plexus may also be injured by direct violence or gunshot wounds, by violent traction on the arm, or by efforts at reducing a dislocation of the shoulder joint”.

Brachial plexus lesions can be divided into three types:
1. An upper brachial plexus lesion, which occurs from excessive lateral neck flexion away from the shoulder. Most commonly, forceps delivery or falling on the neck at an angle causes upper plexus lesions leading to Erb’s palsy. This type of injury produces a very characteristic sign called Waiter’s tip deformity due to loss of the lateral rotators of the shoulder, arm flexors, and hand extensor muscles.
2. Less frequently, the whole brachial plexus lesion occurs;
3. most infrequently, sudden upward pulling on an abducted arm (as when someone breaks a fall by grasping a tree branch) produces a lower brachial plexus lesion, in which the eighth cervical (C8) and first thoracic (T1) nerves are injured “either before or after they have joined to form
the lower trunk. The subsequent paralysis affects, principally, the intrinsic muscles of the hand and the flexors of the wrist and fingers”. This results in a form of paralysis known as Klumpke’s paralysis.

Mechanism

Injury to the brachial plexus can happen in numerous environments. These may include contact sports, motor vehicle accidents and birth. Although these are but a common few events, there is one of two mechanisms of injury that remain constant during the point of injury. The two mechanisms that can occur are traction and heavy impact. These two methods disturb the nerves of the brachial plexus and cause the injury.

Traction, also known as stretch injury, is one of the mechanisms that cause brachial plexus injury. The nerves of the brachial plexus are damaged due to the forced pull by the widening of the shoulder and neck. This is a closer look at the traction mechanism at the cervical spine. The arrowed red line represents the stretch of the nerves. Depending on the force, lesions may occur.

Anatomy

The brachial plexus is made up of spinal nerves that are part of the peripheral nervous system. It includes sensory and motor nerves that innervate the upper limbs. The brachial plexus includes the last 4 cervical nerves (C5-C8) and the 1st thoracic nerve (T1). Each of those nerves splits into smaller trunks, divisions, and cords. The lateral cord includes the musculocutaneous nerve and lateral branch of the median nerve. The medial cord includes the medial branch of the median nerve and the ulnar nerve. The posterior cord includes the axillary nerve and radial nerve.

Traction

Traction occurs from severe movement and causes a pull or tension among the nerves. There are two types of traction:
downward traction and upward traction. In downward traction there is tension of the arm which forces the angle of the neck and shoulder to become broader. This tension is forced and can cause lesions of the upper roots and trunk of the nerves of the brachial plexus. Upward traction also results in the broadening of the neck and shoulder angle but this time the nerves of T1 and C8 are torn away.

**Impact**

Heavy impact to the shoulder is the second common mechanism to causing injury to the brachial plexus. Depending on the severity of the impact, lesions can occur at all nerves in the brachial plexus.

The location of impact also affects the severity of the injury and depending on the location the nerves of the brachial plexus may be ruptured or avulsed. Some forms of impact that affect the injury to the brachial plexus are shoulder dislocation, clavicle fractures, hyperextension of the arm and sometimes delivery at birth. During the delivery of a baby, the shoulder of the baby may graze against the pelvic bone of the mother. During this process, the brachial plexus can receive damage resulting in injury. The incidence of this happening at birth is 1 in 1000. This is very low compared to the other identified brachial plexus injuries.

**Classification**

The severity of brachial plexus injury is determined by the type of nerve damage. There are several different classification systems for grading the severity of nerve and brachial plexus injuries. Most systems attempt to correlate the degree of injury with symptoms, pathology and prognosis. Seddon’s classification, devised in 1943, continues to be used, and is based on three main types of nerve fiber injury, and whether there is continuity of the nerve.

1. Neurapraxia: The mildest form of nerve injury. It involves an interruption of the nerve conduction without loss of
continuity of the axon. Recovery takes place without wallerian degeneration.

2. Axonotmesis: Involves axonal degeneration, with loss of the relative continuity of the axon and its covering of myelin, but preservation of the connective tissue framework of the nerve (the encapsulating tissue, the epineurium and perineurium, are preserved).

3. Neurotmesis: The most severe form of nerve injury, in which the nerve is completely disrupted by contusion, traction or laceration. Not only the axon, but the encapsulating connective tissue lose their continuity. The most extreme degree of neurotmesis is transsection, although most neurotmetic injuries do not produce gross loss of continuity of the nerve but rather, internal disruption of the nerve architecture sufficient to involve perineurium and endoneurium as well as axons and their covering. It requires surgery, with unpredictable recovery.

A more recent and commonly used system described by the late Sir Sydney Sunderland, divides nerve injuries into five degrees: first degree or neurapraxia, following on from Seddon, in which the insulation around the nerve called myelin is damaged but the nerve itself is spared, and second through fifth degree, which denotes increasing severity of injury. With fifth degree injuries, the nerve is completely divided.

**Diagnosis**

The diagnosis may be confirmed by an EMG examination in 5 to 7 days. The evidence of denervation will be evident. If there is no nerve conduction 72 hours after the injury, then avulsion is most likely. The most advanced diagnostic method is MR imaging of the brachial plexus using a high Tesla MRI scanner like 1.5 T or more. MR helps aid in the assessment of the injuries in specific context of site, extent and the nerve roots involved. In addition, assessment of the cervical cord and post traumatic changes in soft tissues may also be visualised.
Treatment

Treatment for brachial plexus injuries includes orthosis/splinting, occupational or physical therapy and, in some cases, surgery. Some brachial plexus injuries may heal without treatment.

Many infants improve or recover within 6 months, but those that do not have a very poor outlook and will need further surgery to try to compensate for the nerve deficits. The ability to bend the elbow (biceps function) by the third month of life is considered an indicator of probable recovery, with additional upward movement of the wrist, as well as straightening of thumb and fingers an even stronger indicator of excellent spontaneous improvement. Gentle range of motion exercises performed by parents, accompanied by repeated examinations by a physician, may be all that is necessary for patients with strong indicators of recovery.

The exercises mentioned above can be done to help rehabilitate from mild cases of the injury. However, in more serious brachial plexus injuries surgical interventions can be used. Function can be restored by nerve repairs, nerve replacements, and surgery to remove tumors causing the injury. Another crucial factor to note is that psychological problems can hinder the rehabilitation process due to a lack of motivation from the patient. On top of promoting a lifetime process of physical healing, it is important to not overlook the psychological well-being of a patient. This is due to the possibility of depression or complications with head injuries.

Rehabilitation

There are many treatments to facilitate the process of recovery in people who have brachial plexus injuries. Improvements occur slowly and the rehabilitation process can take up to many years. Many factors should be considered when estimating recovery time, such as initial diagnosis of the injury, severity of the injury, and type of treatments used. Some forms of treatment include
nerve grafts, medication, surgical decompression, nerve transfer, physical therapy, and occupational therapy.

PHYSICAL Therapy

Having an effective Physical Therapy program is important when dealing with the unfortunate circumstances of brachial plexus injuries. One of the main goals of rehabilitation is to prevent muscle atrophy until the nerves regain function. Electrical stimulation is an effective treatment to help patients reach this fundamental goal. Exercises that involve shoulder extension, flexion, elevation, depression, abduction and adduction facilitate healing by engaging the nerves in the damaged sites as well as improve muscle function. Stretching is done on a daily basis to improve or maintain range of motion. Stretching is important in order to rehabilitate since it increases the blood flow to the injury as well as facilitates nerves in functioning properly.

A study has also shown that a sensory-motor deficit in the upper limbs after a brachial plexus injury can affect the corporal balance in the vertical positioning. Examined patients had a lower score in the Berg balance scale, a greater difficulty in maintaining in the unipodal stance during one minute and leaned the body weight distribution to the side affected by the lesion. Patients also exhibited a greater variability in the postural oscillation, evaluated by the directional stability index. The results alert the clinical community about the necessity to prevent and treat secondary effects of this condition.

Epidemiology

Adults

The epidemiology of brachial plexus injury also known as BPI is found in both children and adults, but there is a difference between children and adults with BPI. The occurrence of adult brachial plexus injuries in the 1900s multiple traumatic injuries for North America population is with a prevalence of about 1.2%. BPI is most commonly found with young healthy adults, from
ages 14 to 63 years old, along with 50% of patients between the ages of 19 and 34 years old, and with male patients being 89% at risk. Brachial plexus injury is a traumatic event and that has been shown to increase over the years.

**Children**

As for the epidemiology of brachial plexus injury in children, OBPP also known, as obstetrical brachial plexus palsy occurred the most for young children ranging from 0.38 to 1.56 per 1000 live births due to the type of care and the average birth weight of infants in different regions of the world. For example, a study done for the incidence of OBPP where United States is about 1.51 cases per 1000 live births, a Canadian study, where the incidence was between 0.5 and 3 injuries per 1000 live births, and European countries, such as a Dutch study reported an incidence of 4.6 per 1000 births.

Newborns with brachial plexus injury was most commonly found in Diabetic women whose babies weighed more than 4.5 kg at birth along with different types of deliveries. Brachial plexus injury risks for newborns are increased with gained birth weight, birth delivery where a vacuum is assisted, and not being able to handle glucose.

**Traumatic injuries**

BPI has shown to occur 44% through 70% with traumatic injuries, such as motorcycle accidents, sporting activities, or even at the work places. With 22% being motorcycle injuries and about 4.2% having plexus damage. People that have accidents with riding motorcycles and snowmobiles, have higher risks of getting BPI.

**Prognosis**

The site and type of brachial plexus injury determine the prognosis. Avulsion and rupture injuries require timely surgical intervention for any chance of recovery. For milder injuries involving build-up of scar tissue and for neurapraxia, the potential
for improvement varies, but there is a fair prognosis for spontaneous recovery, with a 90–100% return of function.

BRACHIAL PLEXUS AND PERIPHERAL NERVE INJURIES

Brachial plexus and peripheral nerve injury

The brachial plexus is a network of nerves running from the cervical spinal cord in the neck to the shoulder, arm, and hand. Brachial plexus and peripheral nerve injuries refer to injuries to the group of nerves that supply the arms and hands. These injuries include birth-related palsies, trauma, and peripheral tumors.

The brachial plexus is a network of nerves that run from the cervical spinal cord in the neck to the shoulder, arm, and hand. These nerves are responsible for stimulating the muscles of the upper extremity as well as signaling sensation or feeling of the arm. An injury to one or more of these nerves can result in varying degrees of upper extremity weakness or paralysis and numbness.

Types of injury include pulling, stretching, tearing, or compression of the nerve(s). Some nerve injury is temporary,
and patients recover most, if not all, function on their own with occupational therapy and time. However, some nerve damage is more severe, and patients with these conditions benefit from surgery and occupational therapy.

Causes

Brachial plexus injury caused during childbirth when nerves are stretched. Brachial plexus injuries may be related to the birthing process, when the nerves get pulled during delivery. Many of these babies recover well without needing surgery. Nevertheless, it is still important for them to be followed by a medical team early after the injury to monitor their recovery and ensure that additional treatment is not needed. Children treated at CHOP for brachial plexus injuries that happened during delivery are followed closely with regular office visits and occupational therapy sessions.

Older children can also have brachial plexus injuries. These injuries are often related to high impact trauma, such as sport collision or car accident. The brachial plexus can also be injured from a deep cut to the neck area. It is important for these patients to be evaluated and followed closely by a team that specializes
in brachial plexus injuries, as some surgical procedures should be done within several months after the injury.

**Signs and symptoms**

An injury to the brachial plexus or nerve(s) of the arm results in weakness or paralysis. Babies will not move their affected arm. In less severe injuries, some babies will regain function in the fingers and hands over the first few months after birth. They may have numbness in the arm, but this can be difficult to determine. Many babies with brachial plexus injuries hold the affected arm by their side, with the elbow straight, and the forearm and hand turned in.

Older children will also complain of weakness or no movement of the shoulder, arm, or hand. They may have numbness or tingling. For both babies and older children, other injuries may co-exist, such as broken bones of the ribs, collarbone, shoulder, or upper arm. There may also be other nerve injuries that can be seen as ptosis (droopy eyelid) and a smaller pupil on the affected side.

**Testing and diagnosis**

Your child’s initial evaluation is typically done by our pediatric specialists and our occupational therapist within the first month after injury. It starts with a medical history, a developmental history, a physical exam and a neurological exam.

Depending on your child’s age and cause of the injury, your child’s care will be coordinated through our Brachial Plexus Program, which can be initiated through any participating division: Neurology, Neurosurgery, Plastic Surgery, or Orthopedic Surgery. The Brachial Plexus Program brings together multiple pediatric subspecialists with experience treating children with brachial plexus and peripheral nerve injuries.

Some children may need additional tests during their care to help the team get a better understanding of their condition and determine the best treatment options.
An electromyogram (EMG) may be performed by our neurologist to assess muscle contraction.

Magnetic resonance imaging (MRI) of the brachial plexus and/or cervical spine, or a CT myelogram may also be ordered through CHOP’s Department of Radiology.

X-rays may be taken to look at bones or the chest, particularly if there is a history of a fracture or to evaluate the diaphragm for paralysis.

Ultrasound may be used as another way to evaluate the diaphragm or shoulder.

**Treatments**

**Occupational therapy**

Nerve transfer: A nerve fascicle is transferred from a functioning nerve (bottom) to a damaged distal nerve target (top), supplying the muscle with a new, functioning proximal nerve to power it. Many patients with birth-related brachial plexus injuries recover enough motion and strength and do not need early surgery. For all patients, we encourage regular sessions with occupational therapy, whether it is at The Children’s Hospital of Philadelphia or locally if patients live outside the Philadelphia region.

Goals for therapy focus on:

- Promoting nerve recovery
- Preventing joint contractures
- Maintaining range of motion in the upper extremities and neck
- Facilitating optimal use and typical movement patterns

Typical therapy interventions include:

- Range of motion exercises and stretching
- Splinting
- Joint compression and weight bearing to facilitate muscle contraction
• Bilateral motor planning activities
• Facilitating optimal alignment in the shoulder and scapula to promote smooth movement in all directions
• Aquatic therapy when indicated

Nerve repair: A damaged, scarred portion of a nerve, or neuroma, can be seen in the top image. This portion is resected, and, in the bottom image, nerve grafts are placed across the gap to repair the nerve. In addition to these regular sessions, your child’s occupational therapist will also teach you exercises that should be performed every day with your child to keep the joints supple and encourage normal motor development.

Patients are closely followed by our team for signs of functional recovery of the upper extremity. If there are no signs of recovery or not enough muscle recovery, then patients may get additional testing and evaluations to discuss surgical options to improve function.

Surgical intervention

Early surgical intervention for brachial plexus and other nerve damage is usually decided between three to six months after injury. We carefully follow each patient for signs of recovery and personalize treatment based on the type and degree of injury. Early surgical treatments include:
• Surgical exploration
• Neurolysis — releasing nerve from scar tissue
• Nerve grafting — taking nerve from elsewhere on the body to bridge a nerve gap after cutting away damaged nerve
• Nerve transfers — using working nerves to stimulate nerves and muscles that are not functioning well

Secondary procedures may be needed as children grow and are designed to augment their function. These surgeries include:
• Tendon or muscle transfers — using working tendons or muscles to power weak or non-working muscles
• Release of tight muscles or joints
• Osteotomies — cutting and repositioning the bones
• Joint fusions

Follow-up care

Children with brachial plexus and peripheral nerve injuries are followed by our Brachial Plexus Program, which brings together a variety of pediatric subspecialists who monitor each patient closely for recovery and additional nerve damage that may require further treatment.

Every patient’s care is tailored to meet their individual needs, and may include consultations with pediatric neurologists, neurosurgeons, occupational therapists, plastic and reconstructive surgeons, orthopedic surgeons and more.

NEONATAL BRACHIAL PLEXUS PALSIES TREATMENT & MANAGEMENT

Rehabilitation Program

Physical Therapy

The rehabilitation of children with brachial plexus palsy (BPP) must begin in infancy to achieve optimal functional returns. For the first 2 weeks, the child may have some pain in the affected shoulder and limb, either from the injury or from an associated clavicular or humeral fracture. The arm can be fixed across the child’s chest by pinning of his/her clothing to provide more comfort. However, some authors have discouraged this pinning in favor of immediate institution of gentle ROM exercises. Parents should be instructed in techniques for dressing the child to avoid further traction on the arm. Often a wrist extension splint is necessary to maintain proper wrist alignment and reduce the risk of progressive contractures.

Therapy is the cornerstone in the management of the symptoms of a child with BPP. The role of the treating physician is to guide the program and make critical decisions regarding
the need for further medical or surgical intervention. As the child gets older, bimanual activities (e.g., swimming, basketball, wheelbarrow walking, climbing) should be encouraged. A comprehensive therapy program that has been designed and implemented by a pediatric physical therapist is essential for children whose case is being managed conservatively, as well as for children who require surgical intervention.

A pediatric physical or occupational therapist’s role is 2-fold. The first responsibility of the therapist is to provide ongoing therapeutic treatment and parental instruction. By the very nature of therapy, the therapist’s second function is to provide precise and ongoing assessment of the infant’s functional status and recovery, to assist the physician in determining future medical and surgical considerations, and to assess the efficacy of these interventions.

When dealing with infants and young children, the pediatric therapist should evaluate the child based on normal development and age-appropriate skills. The therapist’s initial evaluation of an infant with BPP should include specific details about passive and active ROM, the strength of each muscle or muscle groups, and the posture of the affected limb compared with the other extremity, as well details regarding sensibility and overall function.

Formal goniometry should be employed to measure active and passive ROM. Standardized strength testing, although difficult in young children, is necessary for objective documentation of recovery. Physical therapists at the Hospital for Sick Children of Toronto have devised a simple observation tool that evaluates active joint movement against gravity. Based on observations of movement, a clinical grade is assigned to quantify the patient’s status, and progress can be tracked over time. Comparison of the movement patterns of the affected and unaffected arm also is useful. Testing of sensation, posture, and functional activity is performed through clinical observation.
A comprehensive therapy program should consist of ROM exercises, facilitation of active movement, strengthening, promotion of sensory awareness, and provision of instructions for home activities. Overall goals should focus on minimizing bony deformities and joint contractures associated with BPP, while optimizing functional outcomes.

Severe contractures should be avoidable with consistent therapeutic exercises, including passive and active stretching, flexibility activities, myofascial release techniques, and joint mobilization.

Over time, these contractures can lead to progressive bony deformity and shoulder dislocation. Early and consistent stretching of internal rotators should minimize the risk of this problem. External rotation, performed with the shoulder adducted alongside the chest and with the elbow flexed to 90°, provides maximum stretch of internal rotators (specifically, the subscapularis) and the anterior shoulder capsule. The scapula should be stabilized while stretching shoulder girdle muscles to maintain mobility and preserve some scapulohumeral rhythm. Early development of flexion contractures at the elbow is common and can be exacerbated by radial head dislocation caused by forced supination. Aggressive forearm supination, therefore, should be avoided.

Active mobility and strengthening initially are facilitated through age-appropriate developmental activities. As the child gets older, standard strengthening exercises are used and specific functional skills are introduced. Specific muscle groups can be targeted for strengthening through functional movement. Compensatory and substitute movements should be avoided, as they may perpetuate weak muscles and deformity.

Static and dynamic splinting of the arm is useful to reduce contractures, prevent further deformity, and in some cases, assist movement. Commonly prescribed splints include resting hand and wrist splints, elbow extension splints, dynamic elbow flexion
and supinator splints. Careful selection and timing of splint use is essential to optimization of the desired effect.

Taping techniques may be used by the therapist to control scapular instability and hence to promote improved shoulder mobility.

Sensory awareness activities are useful for enhancing active motor performance, as well as for minimizing neglect of the affected limb. Use of infant massage and drawing visual attention to the affected arm can be incorporated easily into play and daily activities. Weight-bearing activities with the affected arm in all positions not only provide necessary proprioceptive input but also can contribute to skeletal growth.

Instructing parents and family in a home exercise program is instrumental in effective management of BPP cases. A comprehensive program that includes stretching exercises, safe handling and early positioning techniques, developmental and strengthening activities, and sensory awareness should be developed and updated as needed. In older children with persistent disability, the focus on home instruction shifts to independence, with these patients learning self-stretching and strengthening exercises, as well as strategies for achieving specific life skills. The focus of therapy often is directed toward more recreational activities, such as swimming or basketball.

**BRACHIAL PLEXUS CLINIC**

A multidisciplinary, comprehensive center for the study of brachial plexus and peripheral nerve injuries in the pediatric population places particular emphasis on children who suffer these types of injuries during the birth process or via other types of trauma. A regional, centralized comprehensive clinic offers the expertise in the evaluation and treatment for these children. Further programming through education and clinical and basic science research allows the center to be on the forefront in the understanding of the pathophysiology of brachial plexus and peripheral nerve injuries and their treatment.
To provide the highest level of expertise, the members of the multidisciplinary service include pediatric neurosurgery, plastic surgery/microsurgery, neurology, social work, radiology, trauma surgery, and physical and occupational therapy. The patients are evaluated by the combined disciplines and electrophysiologic evaluation and imaging (both anatomic and functional) are able to be coordinated through the resource centers for these modalities. Treatment options including surgical intervention or physical or occupational therapy is decided following a comprehensive review of the evaluative information amongst the members of the center using established principles.

General Background

A brachial plexus and resultant upper extremity injury due to a difficult birth is one of the most common injuries during the birthing process. The incidence rate is 0.3 to 2 per 1,000 births, with most brachial plexus injuries identified immediately in the acute setting.

Brachial relates to the arm and plexus pertains to a network of nerves. The brachial plexus forms a network of nerves that conduct signals that control the muscles of the shoulder, arm, elbow, wrist, hand and fingers.

The mechanism(s) by which the brachial plexus is injured is most often attributed to severe lateral flexion of the neonate’s neck when the shoulder is stopped most often at the pubic bone ("shoulder dystocia") during delivery. The extent of the traction on the brachial plexus may result in various types of injuries to the nerves, from a simple mild stretch injury up to and including avulsion (separation) of the nerves from the spinal cord.

Although a vertex delivery with a shoulder dystocia is the most common cause, brachial plexus injuries can also occur following cesarean section delivery, probably due to intrauterine forces. Other predisposing factors associated with a brachial plexus injury include a mother who has given birth at least two times, high infant birth weight, prolonged labor, premature birth
and breech delivery. Although the results of studies involving recovery without intervention vary widely, the Collaborative Perinatal Study of 1973 documented a 90% to 95% rate of spontaneous good recovery, leaving approximately 5-10% of infants at risk for permanent functional disability.

Those that recovered showed some evidence of improvement by 4 months of age. A study from St. Louis found similar results. The challenge for physicians and families is to determine whether surgical intervention would be helpful to improve the function of the limb.

It is clear that the absence of any sign of recovery by 3-4 months of age is most predictive of an extremely poor functional prognosis with significant residual deficits.

As a rule of thumb, the rate of spontaneous recovery dictates the final functional outcome. Those infants who are slower to begin recovery and have slow progression of returning function are less likely to achieve complete functional use of the extremity.

**Anatomy of the Injury**

Approximately 75% of birth-related brachial plexus injuries involve the 5th-7th cervical nerve roots, including the upper and middle trunks of the plexus, and are clinically recognized as an “Erb’s palsy”.

The affected extremity is positioned in the classic “waiter’s tip” pose, adducted, internally rotated with elbow extension, forearm pronation and wrist and finger flexion. Up to 20-25% involves the entire brachial plexus (C5-T1), which is manifested by a completely flaccid upper extremity. Only 2% of injuries are isolated to C7-T1, also known as Klumpke’s palsy. With this type of injury, the flexors of the brachium are spared while the flexors and extensors of the fingers and wrist are weak or flaccid. A Horner’s syndrome may be associated with injuries that involve the C8-T1 levels due to injury of the sympathetic chain of the thoracic spinal cord. Most series cite a 4% incidence of bilateral injuries.
Examination and Diagnosis

The diagnosis of brachial plexus injuries relies heavily upon the clinical evaluation, which can be challenging in neonates and young children. The child’s functional use of the upper extremity, assessed clinically, is the most important indication for surgery. Ideally, children are first evaluated between birth and 6 weeks of age with physical and/or occupational therapy starting at 3-4 weeks of age; at 6 weeks, if there is a fracture to allow for adequate healing. Follow-up evaluations then occur at three-month intervals. Early evaluation is important in establishing a baseline physical examination and assessment of patient and family needs. This can often be accomplished by the pediatrician or family practitioner. Continued weakness of the limb or questions regarding the injury or function should be referred to a specialist for further evaluation.

The examination consists of a motor evaluation that scores both individual muscle groups (using the five-point British Research Council Grading System) and functional muscle group activities, including abduction, external rotation, and hand-to-head, hand-to-back and hand-to-mouth movements as well as sensory and reflex exams. Physicians should compare clinical assessments on subsequent visits every three months.

Children who recover partial function between examinations should continue to be followed at three-month intervals. Children who fail to improve on subsequent visits or who improve initially but then plateau at a nonfunctional level should be evaluated, initially via electromyography (EMG). This will assess the levels of injury and determine if there is evidence of early reinnervation.

Electrophysiologic studies, including EMG and somatosensory evoked potentials (SSEP) and imaging such as CT scans and MRI, are useful in confirming clinical diagnosis and extent of the injury. Electrodiagnostic tests, however, do not offer any prediction of ongoing or potential recovery. These studies are usually obtained at 4 to 6 months of age following
non-progression of recovery. In evaluating the possibility of a nerve root avulsion from the spinal cord, the standard had been a CT myelogram. With improved MRI formats, this non-invasive evaluation is more desirable for children. A pseudomeningocele or nonvisualization of the nerve roots is indicative of a preganglionic injury which at this time cannot be repaired with conventional techniques. Unfortunately, root avulsions have a poor prognosis for recovery and restoration of function to the extremity with current reparative techniques. If imaging does not reveal evidence of nerve root avulsion and the child has not had a significant partial or full return of function by 4 to 6 months of age, surgical intervention should be considered.

**Surgical Intervention**

It has been determined that early evaluation and intervention are important because functional results following surgery before 6 to 9 months are significantly better than those with intervention in older children (12 to 18 months). Children as young as 4 months of age can be considered for operative brachial plexus repairs. Though reparative surgery up to 18 to 24 months of age is possible, numerous studies have shown that children at that age are less likely to have good outcomes, though other operative interventions are available to improve outcome.

All of the surgical procedures are performed under general anesthesia. In the primary surgery, the initial phase consists of exploration, visualization and identification of the different elements of the brachial plexus. Following exposure, intra-operative EMG/SSEP studies are used to test the damaged segments. This is critical in determining the type of repair most suitable. The most common injury found through these means is an axontomesis or stretch injury. This damage involves only the perineurium (connective tissue cover surrounding a bundle of nerve fibers) and the axons. Though the nerve is viable, degeneration has disconnected it from the muscle. The natural regenerative effort of the nerve against scar results in a neuroma
when the pathway of the regenerating axons is blocked by the scarring, and the axons are prevented from successfully extending across the injured segment. The fibrotic scarring is most likely formed in response to hemorrhage and damage at the time of the initial injury and can partially or completely block conduction to the distal muscle groups. The EMG/SSEP studies confirm the extent of physiologic function passing through the neuroma as well as the existence of an avulsion if it was not diagnosed preoperatively.

The goal of all reparative procedures is to create an adequate pathway for the regenerating axons to reach their motor units and restore maximal function. The intervention following exploration is a neurolysis or the careful microsurgical dissection of the epineurial and perineurial scar tissue. With a neurolysis, the scar tissue compressing the injured segment of the nerve is released, allowing improved conduction of the existing neural elements and a wider conduit for improved regeneration.

Nerve grafts are used when there is minimal or no conduction across the scarred segment following the neurolysis. A “cable” or interpositional graft is performed by resecting the severely damaged segment of nerve and replacing it with a segment of the patient’s sural (relating to the calf of the leg) nerve. The “donor” sural nerve is a purely sensory nerve. It is obtained from the lateral aspect of the leg, just above the ankle, and leaves the patient with a small area of anesthesia on the lateral aspect of the foot. This area becomes smaller in children as they get older, due to ingrowth from surrounding areas. This graft is then sutured in line (end to end) following the resection of the damaged segment of nerve. The graft serves as a new conduit for the regeneration of axons across the scarred region into the distal end of the nerve. When reasonable electrophysiologic conduction across the damaged segment remains, the surgeon can use newer graft techniques that do not sacrifice the intact fibers. More recently, we have used end to side nerve grafts which preserves potentially intact fibers and lessens/eliminates any decrement
EMG in Pediatric Brachial Plexopathy

in baseline function since the nerve is not cut. Results have been similar to the published literature.

Recovery

Postoperatively, it has been determined that children quickly resume their usual routines and only remain on the hospital’s neurosurgical floor for one to three days for observation. Normally, they are discharged when they are eating well and no longer have significant need for pain medication.

If a graft was placed, the arm is kept in a sling for four weeks after the child is discharged. The main purpose of the sling is to remind the family to limit activity. Otherwise, movement of the limb is important to limit rescarring. Parents are able to remove the sling to change the dressing and inspect the incision.

The return of function is monitored one month postoperatively and every three to six months afterward. Following two or four weeks of recovery, children begin a physical and occupational therapy program. Though seen initially by therapists twice a week, the family is instructed to perform the range-of-motion interventions and other exercises each day. The goal is to maintain the musculature and joint movement until reinnervation.

Because regenerating axons grow approximately one millimeter per day, the reinnervation of a 10-centimeter nerve segment to the deltoid and/or biceps may take approximately three to four months. More distal reinnervation will take longer. Once the nerve reaches its target, there is a gradual refinement of its connections and a period of “retraining” that is required for maximal recovery of function. Recovery should be expected to continue 12 to 24 months postoperatively.

When a child has made some but not yet either a “functional” recovery (able to get their hand to their mouth) or less than “optimal” functional recovery, the secondary surgery can be considered. This has included possible operative interventions
such as nerve decompression, tendon releases and/or transfer, etc. to try to improve the outcomes in these children. Usually performed after 9 months of age up to 5-6 years old (or sometimes older), the goal is to improve the use of the extremity by improving nerve conduction and range of motion. Again, at our institution, the type of surgery is dependant on the affected segments and depends on the optimal approach either at one sitting or multiple procedures over time. The children postoperatively are either casted or splinted in a “statue of liberty” position with little overall discomfort.

**Outcomes**

To date, the results of brachial plexus injury repairs have been rewarding. Results in the Center for Brachial Plexus and Peripheral Nerve Injuries at Children’s Hospital and the few other institutions performing this work show that between 40% and 80% of patients will have improvement of one grade in at least two of three major muscle groups following the primary surgery neurolysis with or without grafting. Improvement of at least one grade translates into significant functional improvement in the use of the extremity, allowing children with brachial plexus injury to lead more normal and independent lives. While those with C5 and/or C6 injuries show better outcomes, gains in other neural territories remain promising.

For the secondary surgery, all of the patients will have some level of improvement, best in the patients who are functional but not optimal. Improvement usually involves better shoulder abduction/flexion and external rotation. There is a bit less improvement in supination. This poor response in supination is usually addressed later with tendon transfers.

Complications are few (less than 3%) and primarily include infection, bleeding and a worsened neurological condition. There is rarely a decrement in function with neurolysis alone. The risk of worsening functional status depends on the need for an interpositional graft. Given the natural history of these injuries,
these risks may well be outweighed by the possible benefits. These children may achieve significant improvement and long-term functional use of the limb.

Since the summer of 1995, the Center for Brachial Plexus and Peripheral Nerve Injuries at Children’s Hospital of Pittsburgh has evaluated and treated over 800 children with more than 200 undergoing surgery with all types of brachial plexus and peripheral nerve injuries, utilizing a multidisciplinary approach that includes professionals who specialize in neurosurgery, micro/hand surgery, neurology, physical and occupational therapy, neuroradiology and social work. Each of these specialties is available during an office visit to maximize the efficiency of a patient’s evaluation and to facilitate the collaboration among the different specialists. Patients with injuries to the brachial plexus and peripheral nerves due to all types of trauma are able to benefit from this approach by receiving comprehensive medical, surgical and psychosocial options throughout their ongoing evaluation.

**BRACHIAL PLEXUS INJURIES CAN BE DEVASTATING**

Injuries to the brachial plexus (the nerves that conduct signals to the shoulder, arm, and hand) can have devastating consequences, including loss of function and chronic pain. Fortunately, new advances in nerve surgery can yield marked improvement in movement and function of the shoulder, elbow, and hand, while simultaneously diminishing pain.

**Overview: The Nerves of the Brachial Plexus**

The nerves that make up the brachial plexus originate at the spinal cord and correspond to four cervical (neck) vertebrae and one thoracic (upper back) vertebra.

The nerves divide and join repeatedly before terminating in several peripheral nerves that branch out to supply the muscles of the shoulder, elbow, forearm, and hand. In addition to
“communicating” with the muscles that lift, lower, straighten, and bend the arm, the nerve complex serves as the pathway to communicate sensory perception to the brain.

In adults, brachial plexus injuries are almost always the result of a high impact injury, such as a motorcycle, skiing, or snowboarding accident. In some cases, however, a tumor or radiation may be the underlying cause. Brachial plexus injuries in children usually occur at birth.

**Diagnosis**

In addition to performing a physical examination, orthopedists evaluate brachial plexus injuries using MRIs, CT scans, and electro-diagnostic tests.

According to HSS physiatrist Joseph H. Feinberg, MD, electrodiagnostic testing (often known as EMG testing) assesses nerve function and is commonly used in the evaluation of brachial plexus injuries.

“The test is primarily used to assess the degree of nerve injury and determine the location of the injury, and the resulting information is used to help understand the likelihood and degree of recovery,” he explains. “A decision to perform surgery and the type of operation needed will often depend on this information.” He adds that the EMG test can also be used to monitor recovery.

The test entails stimulating the nerves with small electric shocks and inserting small acupuncture-like needles in certain muscles. The test can take anywhere from 30 to 60 minutes, depending on the complexity of the injury and the amount of information the physician requires.

Based on the surgeon’s findings, adult patients may be diagnosed with any one of the following conditions:

- **Neurapraxia**: a stretched nerve
- **Neuroma**: a condition in which scar tissue has grown around a disrupted nerve
• Rupture: one or more nerves are torn, but not at the spinal cord
• Avulsion: the roots of the nerves are torn away from the spinal cord. Multiple root avulsion is the most common diagnosis in high-energy traumatic brachial plexus injuries, such as occurs in a motorcycle or off-road vehicle accident.

Symptoms include numbness, an inability to use the muscles in the shoulder, arm, and hand, and a crushing or burning pain. Patients with a severe avulsion injury may also have a drooping eyelid, a phenomenon known as Horner’s Syndrome.

**Non-surgical Treatment**

Patients with a stretch neurapraxia may be able to regenerate healthy nerve tissue. However, recovery is unpredictable.

In such cases, the orthopedic surgeon conducts frequent and thorough examinations over the first three to six months following the injury and performs additional imaging and electro-diagnostic tests, as needed. If there is no recovery, the patient is assessed for internal damage to the nerve, and surgery may become necessary.

**Surgical Treatment**

Although nerve repairs and nerve grafts have been used in the past to reconstruct disrupted nerves in the brachial plexus, these surgeries have met with variable success, and were often inadequate to restore function in patients with severe injuries.

For the past decade, orthopedic surgeons at Hospital for Special Surgery (HSS) have used nerve transfers - in addition to nerve grafts and nerve repair - to restore function in these complex cases. While the concept of nerve transfer is not new – it was pioneered in the early 1900’s – novel techniques of nerve transfer have accelerated the pace and extent of recovery of shoulder and elbow function.
“The use of surgical nerve transfers has revolutionized our approach to these patients,” explains Scott W. Wolfe, MD, Chief of the Hand and Upper Extremity Service at HSS. “With the operating microscope, we can transfer a portion of an intact nerve from a functioning muscle and re-attach it to the undamaged portion of a nerve from another.”

Previously, the surgeon harvested healthy nerve tissue from an uninjured site in the arm or the leg. Occasionally, nerves from between the ribs were harvested and transferred to the arm. More recently, Dr. Wolfe and his colleagues have identified specific nerve transfer sites within the injured area that offer even better results than those previously achieved with nerve grafts or chest wall grafts. Timing of the surgery is essential.

“Ideally, we repair the nerves within three to six months following injury,” Dr. Wolfe says. “Surgery can still be done later with some improvement in function, although at 12 months and beyond, our results are much less predictable, as the muscles are less able to be revived.”

Some patients who seek treatment with a chronic injury years after their initial trauma may also benefit from a surgery in which working muscles with their blood and nerve supply are transferred from distant parts of the body. Read more about one patient’s experience with repair of a brachial plexus injury at HSS.

Results of nerve transfer surgery can be dramatic, especially with regard to function of the shoulder and the elbow, according to Dr. Wolfe. “What is amazing is the degree of redundancy within the peripheral nervous system that allows us to detach a portion of a functioning nerve without causing a loss of strength or sensation, but then re-attach the same nerve elsewhere and regain lost muscle function in a matter of months,” he explains.

Common examples include using a single fiber bundle of the ulnar nerve to revive the biceps muscle of the arm, or a portion
of the nerve to the triceps muscle to restore power to an atrophied deltoid muscle in the shoulder. While some advancements in the forearm and hand are on the horizon, it’s important for patients to realize that sensation and function below the elbow, if injured, may remain limited.

Moreover, patients need to understand that the first signs of muscle recovery may not be apparent until 6 to 12 months following surgery; gradual return of strength and mobility follow thereafter.
EVALUATION OF THE PEDIATRIC SURGICAL PATIENT

Comprehensive care of the pediatric surgical patient is multifaceted and requires a thorough understanding of the surgical diseases encountered, a detailed knowledge of the physiology of the pediatric population, and an awareness of the unique issues inherent in providing medical care for children. Establishing a healthy and trusting relationship with the child, as well as the child’s parents or guardian, is essential.

This chapter describes the general approach to treating the pediatric surgical patient. Care must be individualized; the approach may differ for newborns, infants, children, and adolescents and depends on the overall health of the patient.

Parental considerations

Complete care of the pediatric surgical patient includes establishing a good rapport not only with the child but also with the child’s parents or guardian. Parents and guardians are often anxious about the treatment of their child, and the responsibility
to allay their fears lies with the pediatric surgeon. Fostering a good relationship with the family can be accomplished with skilled communication.

The surgeon should always thoroughly explain the child’s problem. Reviewing the results of imaging studies with the parents and patient is helpful. Freehand drawings and diagrams from books can also be used to aid the surgeon in illustrating the anatomy and explaining the problem.

Parents often gain a better understanding of their child’s problem if the surgeon takes the time to explain how or why the problem arose. Be prepared to explain embryology in layperson’s terms when talking to parents of patients with congenital lesions or defects. Also, be familiar with basic genetics and modes of inheritance when counseling parents of a child with a genetic defect.

Knowledge of oncology is useful for discussing management of tumors; be prepared to answer general questions regarding chemotherapy and radiation regimens for tumors commonly encountered in pediatric surgery. Notify parents that the oncology staff is part of the team involved in their child’s care.

The explanation of the proposed surgical procedure in layperson’s terms includes describing where the incision will be made, the steps of the operation, how the incision will be closed, and the size of the scar. At this time, basic postoperative issues can also be addressed, including the anticipated length of hospital stay, the activity and dietary restrictions in the postoperative period, and the time the child will likely be away from school.

Of particular importance is explicitly explaining why the surgical procedure should be performed and what it should accomplish. This is also the time to discuss the risks of surgery. In addition, discussing options and alternative treatment plans is important. The consequences of not performing surgery should be addressed as well. Pause after providing important information so that parents have the opportunity to take it all
in. Leave time for questions at the end of the encounter, and give parents a means by which to contact you with questions. Refer parents to other resources (eg, support groups, the hospital’s family resource center, and reliable sources on the Internet). Caution parents about the information they find on the Internet; the accuracy of online information varies widely.

**History**

The surgeon must obtain a complete and detailed history from the patient and parents. The history, in concert with a well-performed physical examination, is the basis for a diagnosis and treatment plan. In an academic setting, the attending surgeon often sees the patient after a resident or medical student performs the initial evaluation. At this time, the surgeon must verify important points in the reported history and findings. This initial encounter with the surgeon also provides him or her with an opportunity to get to know the child and family.

The chief complaint (CC) is the reason why the child presents to the pediatric surgery service. Statement of the CC should always include the duration of symptoms. The history of present illness (HPI) should detail the course of the symptoms, including its acuity of onset, progression, and severity. Also include symptoms associated with the child’s CC. Document pertinent negative findings. Aggravating or relieving factors are important and must be noted, as should any treatment the child has received.

Any medical or surgical history relevant to the CC should be stated in the HPI. Birth history, medical conditions, and previous surgeries should be listed separately in the past medical history (PMH) and past surgical history (PSH). Of importance, a history of bleeding disorder or unusual bleeding should be noted, as well as any history of receiving anesthetics.

Note the names, doses, and frequency of all medications that the child is currently taking. Include both medications taken on a schedule and those taken as needed. Use of herbal supplements is increasingly popular, even in the pediatric population, and
these supplements should be included in the list of medications. Note drug allergies and reactions, along with symptoms that occur when the patient is given the drug. Food and environmental allergens may also be listed.

Document the family history and the social history. For many pediatric surgical patients, the family history is noncontributory. However, it is clinically significant in children with congenital malformations, genetic diseases, or malignancies. A child’s social history should address issues regarding the family and home environment and the child’s academic and social development.

**Physical Examination**

The goal of the physical examination is to identify the current surgical issues and to ensure that the organ systems other than the one being treated are healthy. Unlike the adult physical examination, in which one can often follow the same routine every time, the pediatric examination must be modified for each patient. Interacting with children of different ages and temperaments in different settings can be challenging.

Hand washing before and after performing the physical examination is essential. This serves purposes beyond infection control. On a psychological level, it conveys a reassuring message to the parent that hygiene is important to the surgeon. On a practical level, it warms the surgeon’s hands before he or she touches the child.

In an older and cooperative child, physical examination can be performed according to a standard routine. However, this routine may have to be modified in young children or infants who do not cooperate.

Infants should be positioned on the examination table for the entire examination. Toddlers and small children may sit in their parent’s lap for the initial part of the examination, and they may be moved to the examination table and positioned for the abdominal, inguinal, genital, and rectal examinations when
necessary. Having the parent by the examination table reduces the child’s anxiety and should be encouraged.

**Skin and integument**

Always ask the patient to undress completely. The pediatric surgeon is often consulted for evaluation of lesions or lumps and bumps. The lesion in question should be inspected for its size, shape, consistency, circumscription, and mobility. Thoroughly search for other, similar lesions on the body. Also inspect the skin for rashes, which may indicate an infectious process or vasculitis. Scars indicating previous surgery should be noted.

Cellulitis may arise after any trauma that interrupts the skin barrier (eg, scratch, laceration, foreign body, surgical wound). Erythema and warmth with induration and fluctuance indicates an abscess. Inspect the skin for birthmarks, noting any changes in their character. Bruises and burn scars, especially those resembling cigarette burns or burns that have a well-defined shape, should be suspected as signs of child abuse.

**Lymph nodes**

Lymphadenopathy can occur in many locations and often involves the cervical, axillary, epitrochlear, or inguinal chains. In children, lymphadenopathy most commonly has an infectious etiology, and a source of infection should be sought throughout the examination. The infection may be bacterial, viral, fungal, or protozoal. Enlarged lymph nodes may represent metastatic disease, or they may be the presenting sign of malignancies, such as acute lymphoblastic leukemia (ALL), Hodgkin disease, and non-Hodgkin lymphoma.

**Head, ears, eyes, nose, and throat**

On head, ears, eyes, nose, and throat (HEENT) examination, note the size and shape of the patient’s head. Children with abnormal fusion of the coronal sutures are not normocephalic. Microcephaly or macrocephaly may indicate a neurologic or intracranial process. An icteric sclera suggests hepatic or biliary
dysfunction. Otitis media can be excluded if tympanic membranes that are clear and if visible landmarks are found. Finding an erythematous oropharynx or inflamed nasal turbinates with associated rhinorrhea is common in upper respiratory tract infections. A quick dental examination to identify loose teeth is important in children scheduled to undergo surgery.

Chest wall

Breast tissue is commonly observed in infant boys and girls. This is normal and due to a slow decline in maternal hormones in the infant’s bloodstream. On a similar note, the pediatric surgeon may be asked to evaluate a male adolescent for gynecomastia, which is often due to the changing hormonal environment associated with puberty.

Evaluation of breast masses in girls requires particular attention. In preadolescent girls, one must distinguish a mass from a breast bud, keeping in mind that breast development does not occur at the same rate in both breasts. Normal breast tissue must be differentiated from a breast mass in female adolescents.

The pediatric surgeon may also encounter deformities in the chest wall, such as pectus excavatum and pectus carinatum. Apart from discerning the degree of deformity, performing cardiac and pulmonary examinations is important in children with these deformities.

Cardiovascular system

Heart rate and rhythm should be noted on the cardiovascular examination. Many children have an audible murmur at some point between infancy and adolescence. Most murmurs, fortunately, occur in normal hearts and are benign. Murmurs that have a structural cause may indicate a need for preoperative antibiotic prophylaxis. Consult a cardiologist if a new-onset murmur is in question. Check proximal and distal pulses. Expect strong pulses throughout. Suspect coarctation of the aorta if
pulses in the upper extremity are strong but pulses in the lower extremity are weak or absent.

**Lungs**

Good respiratory effort in a cooperative child is critical in the pulmonary examination. No layers of clothing should be present between the stethoscope and skin. Breath sounds should be clear on both sides. Abnormal breath sounds, such as rhonchi, wheezes, and crackles, indicate an underlying pulmonary process.

**Abdomen**

The abdominal examination should be performed systematically and gently.

First, observe the patient’s abdomen. If scars are present, their length and location can give the surgeon an idea of the previous surgical procedures performed. The shape of the abdomen may also be a clue to guide diagnosis. A scaphoid abdomen in a neonate or infant may suggest a diaphragmatic hernia but may be normal in a thin child. Intestinal obstruction, an abdominal mass, or ascitic fluid may cause abdominal distention.

Second, listen for bowel sounds. Be patient because up to 2 minutes may pass before bowel sounds are heard. The absence of bowel sounds may suggest peritonitis. The character of the bowel sounds is also important; high-pitched sounds are consistent with bowel obstruction.

While listening for bowel sounds in a young child, the clinician may use a stethoscope to palpate the abdomen, systematically covering the entire abdomen. Begin the palpation in an area away from the area of reported pain, leaving that area for last. Diffuse tenderness may suggest peritonitis or a generalized process. Focal points of tenderness often reflect the underlying pathology. Determine whether the pain is superficial, musculoskeletal, or visceral.
Gently evaluate the patient for peritoneal signs, such as rebound and guarding. Overly aggressive examination creates unnecessary pain and fear in the child. In young children, facial expressions and behavior are often more reliable indicators of pain than verbal reports are. Palpation can also give the surgeon an idea of the size, shape, and consistency of an abdominal mass. The size of the liver and spleen can be determined by percussion and palpation of their edges.

**Inguinal region**

The inguinal region is most commonly examined in the evaluation of a hernia or hydrocele. If an inguinal hernia is not visible on examination, the child should be coaxed to perform a Valsalva maneuver (e.g., coughing or straining as during a bowel movement). Intra-abdominal pressure is increased in crying infants. Hernias should be easily reducible and not incarcerated or strangulated; an incarcerated or strangulated hernia is a surgical emergency.

**Genitalia**

Children as young as 2 years understand the concept of modesty, and special attention must be given to modesty during the genital examination. In addition, always ensure that a staff person of the same sex as the patient is present in the room during the examination.

Genital examination in boys is necessary in the evaluation of a number of conditions, including hydroceles and undescended testes. The genital examination is one of the least comfortable parts of the physical examination; boys can assume the position most comfortable for them—lying down, sitting frog-legged, or standing.

Transillumination may be a useful technique to visualize the contents of an enlarged scrotum but cannot be relied on for a diagnosis, especially in infants. Note the size and shape of the testicle in the scrotal sac and the character of any fluid. Part of
the male genital examination includes checking for the presence of both testes in the scrotal sac.

The testis, epididymis, and spermatic cord should be appreciated as separate structures. Retractile testes can masquerade as undescended testes; always check to determine whether a testicle that is not in the scrotum can be brought down into the scrotum.

Performing a female genital examination to evaluate for fused labia, imperforate hymen, vaginal or perineal bleeding, and an assortment of other issues is not uncommon. Note that a pelvic examination performed by the surgeon is likely to be the first for a girl and has lasting psychological consequences. Always suspect sexual abuse when vaginal tears are present. Vaginal discharge can be a sign of a sexually transmitted disease and should raise the surgeon’s index of suspicion for abuse.

Rectum

The rectal examination may be traumatic to the child and their parents and should be performed quickly but thoroughly. Explaining the process to the child is useful to assure them that nothing will be done to them without first letting them know.

First, inspect the anus. Fissures, fistulas, skin tags, and other lesions can be seen by gently separating the anal opening.

Next, inform the child that he or she will feel a finger on the outside. Gentle external pressure often causes the anal sphincter to relax and facilitates passage into the anal canal. Condylomata acuminata, caused by human papillomavirus, are consistent with sexual abuse. Always use water-soluble lubricant on a gloved finger and obtain a stool sample for a guaiac test whenever feasible. The little finger may be used in infants and toddlers, and the index finger may be used in larger children.

Sphincter tone may be decreased in patients who have previously undergone anoplasty or have sustained traumatic injury to the sphincter muscle. Decreased sphincter tone is more
Intraoperative Considerations in the Pediatric Patient

alarming in the trauma setting because it indicates spinal cord injury.

Palpate the entire circumferences of the anal canal and rectum. Note the location, size, and texture of a palpated mass. Presacral tumors may be the cause of a child presenting with constipation. The examiner must differentiate discomfort due to the examination itself from tenderness due to an underlying process. Many children can make this differentiation if asked.

Pain on examination may be caused by anal fissures externally, appendicitis in a low-lying appendix, or pelvic inflammatory disease. The surgeon may also detect a fecal impaction during the rectal examination of a child with constipation.

**Back and spine**

Scoliosis and other spinal deformities are obvious during examinations of the back. Vertebral tenderness to palpation may be a sign of trauma. Costovertebral angle tenderness may be indicative of pyelonephritis or appendicitis in a patient with a retrocecal appendix.

**Extremities**

Clubbing is observed in many patients with chronic illness, especially patients who have pulmonary disease. Cyanosis is an indicator of poor oxygenation or perfusion, and efforts should be made to determine whether the cyanosis is chronic or acute. Edema may be a sign of impaired renal or cardiac function. Suspect abuse in patients with extremity deformities secondary to long-bone fractures.

**Nervous system**

Much can be gained from observing a child’s behavior. An interactive and playful child is likely to have no focal neurologic findings on examination. However, a basic neurologic examination, which only takes a minute with practice, should be
performed regardless. This comprises assessment of cranial nerve function, motor and sensory examination, reflex evaluation, and cognitive assessment.

**PEDIATRIC SURGICAL EMERGENCIES**

Surgical emergencies in children range from absolutely urgent to semi-elective, depending on the underlying problem. From an anesthetic standpoint, management of the patient may range from care of a critically ill premature infant to that of an otherwise healthy teenager. Understanding the differences in anatomy, physiology, and pharmacology of the different age groups, along with the underlying pathology of the surgical emergency will be the focus of this lecture.

**NEONATAL PERIOD—INCARCERATED INGUINAL HERNIA**

**Disease State**

The incidence of an indirect hernia in a full-term newborn is 3.5-5%, while the incidence in preterm infants is considerably higher, up to 30%. The greatest risk from a hernia is the development of intestinal incarceration and strangulation, with a reported incidence of up to 30% in infants less than 2 months of age. In 70% of incarcerated infant hernias, it may be possible to reduce the hernia and to convert an emergency operation to a semi-elective procedure. Because of a much higher complication rate following emergency surgery (22%) compared with elective surgery (1.7%), it is preferable to repair the hernia in an elective fashion.

**ANESTHETIC CONSIDERATIONS**

**Preoperative Assessment**

The postconceptual age PCA (gestational age plus the postnatal age) is important in considering the postoperative risks
of apnea due to general anesthesia or sedative drugs. Preterm infants who are less than 55 weeks PCA are at an increased risk of apnea following general anesthesia. Very small and very ill preemies may require postoperative ventilation and should have an ICU bed available. The metabolic and fluid status of the child should be assessed. A very small infant should not be NPO for longer than 2-3 hours without consideration of intravenous fluids. These infants are at risk for hypoglycemia, and appropriate glucose administration (5-8 mg/kg/min) should be provided both preoperatively and intraoperatively, usually with D-5 0.2 NS at 4 ml/kg/hr.

Laboratory studies that are ordered should reflect the underlying illnesses of the child and the surgical procedure. Most neonates having their hernia repair would benefit only from a preoperative hematocrit. Depending on the individual practice of neonatologists, many ex-preemies are allowed to have fairly low hematocrits (i.e., <28) without being prophylactically transfused. While anticipated blood loss should be minimal, anemia in the preterm infant is a predictor of postoperative apnea, regardless of the postconceptual age.

**Intraoperative Management**

Regardless of the anesthetic technique chosen for surgery, the operating room environment should be prepared with appropriate monitoring equipment and temperature regulation. The neonate will rapidly lose heat to a cold environment. Ambient room temperature should be increased to 80-85 degrees. Forced air warmers can dramatically improve the ability to maintain the neonate’s body temperature at a normal or even elevated level. Circuits, ventilators, and monitors are available for neonatal anesthesia.

Successful general anesthesia includes appropriate airway management, avoidance of hyperoxia to prevent retinopathy of prematurity, judicious fluid management, and avoidance of significant myocardial depression from the inhalation agents. In
MAC-equivalents, all the inhalation agents are myocardial depressants in neonates. All inhalation agents also predispose to postoperative apnea in the preterm infant, and intravenous caffeine (10 mg/kg) should be given to minimize this risk.

Depending upon factors such as the size of the hernia and the speed of the surgeon, regional anesthesia may be an option for this type of surgery. This is particularly appropriate if the hernia can be reduced, and the case can be done semi-electively. Both spinal (0.6-0.8 mg/kg tetracaine with epi) and caudal-epidural (1 ml/kg 0.375% bupivacaine with epi) anesthesia have been used in order to avoid general anesthesia and its attendant risks.

**Postoperative Care**

Analgesia should be provided. This can be done by the surgeon with a “splash technique” which involves bathing the wound with local anesthetic for 2-3 minutes prior to closure. Alternatively, the surgeon can infiltrate the ilioinguinal and iliohypogastric nerves prior to closure. The typical analgesia provided according to the recent survey of pediatric surgeons is a bupivacaine block (30%) and/or acetaminophen (30%).

All former preterm infants less than 55 weeks PCA should be monitored at least 24 hours for the risk of postoperative apnea.

**Infancy—Pyloric Stenosis**

**Disease State**

Hypertrophic pyloric stenosis is the most common surgical disorder producing emesis in infancy. It occurs in approximately 1/300 live births in the USA with an increased incidence in first born males. Parents with the disorder have a higher incidence of children born with pyloric stenosis.

The musculature of the pylorus is thickened and edematous. Obstruction usually develops by 2-4 weeks of age. Emesis is
usually projectile because of the high pressure generated by hypertrophied gastric muscles.

Diagnosis is often made by history and physical exam. An “olive” is sometimes palpated in the epigastrium just to the right of the midline. When the diagnosis cannot be made by exam, barium UGI or an ultrasound may be used to confirm the diagnosis. While many institutions are using ultrasound as the first diagnostic tool, recent cost-analysis shows the UGI to be more cost-effective.

**Anesthetic Considerations**

**Preoperative Assessment**

Preoperatively, the child should be assessed for signs and symptoms of dehydration. While it is becoming uncommon to see severe dehydration and malnutrition, it does occur. On admission, one may see tachycardia and hypotension which accompany significant dehydration. Other signs include decreased skin turgor, sunken fontanels, poorly perfused extremities, and lethargy.

In the case of extreme (15-20%) dehydration, a fluid bolus of 20 ml/kg of isotonic fluid should be administered for initial volume resuscitation. For mild to moderate dehydration, D5-0.45 NS with 20-40 mEq KCl/l is often used at a rate 1.5-2 times maintenance until volume is restored.

A second consideration involves the electrolyte status. Many infants present with some degree of metabolic alkalosis, hypochloremia, and hypokalemia. There may be a paradoxical aciduria which implies a significant potassium deficit. These electrolyte abnormalities should be mostly corrected prior to surgery.

Recognizing the push from insurance companies to rapidly diagnose, treat and discharge these infants, remember that pyloric stenosis is a medical emergency and not truly a surgical emergency.
Intraoperative Management

These children should arrive in the OR with an IV. Standard monitors are placed. The stomach should be emptied while the child is awake, as there is often residual stomach contents and barium. This does not guarantee that the stomach will be empty, however, and a rapid sequence induction should be performed following atropine administration.

A recent survey of anesthetists in the UK revealed that only 66% performed intravenous inductions, and of those, only 56% used cricoid pressure. There is also some controversy regarding the appropriateness of awake intubations in this situation. A recent study comparing awake, rapid-sequence, or modified rapid sequence inductions demonstrated faster, more successful intubations when the babies were paralyzed. In this study, atracurium (0.4-0.5 mg/kg), vecuronium (0.1-0.2 mg/kg) or rocuronium (0.6-1 mg/kg) were used for a modified rapid sequence induction. Generally, I use a rapid sequence induction with pentothal (4-6mg/kg)and succinylcholine (2 mg/kg).

While classically a Ramstedt procedure is used to open the pylorus, recently laparoscopic pyloromyotomy has been shown to be an acceptable alternative. It has been found to be associated with a faster time to full feeds. An alternative open approach uses a supraumbilical incision. Both of the latter procedures may increase the duration of surgery, but typically the procedure lasts less than 90 minutes, and requires an intermediate acting muscle relaxant in conjunction with an inhalation agent. Usually no narcotics are required. Surgeons can infiltrate the wound with local anesthesia prior to closure.

Postoperative Care

Respiratory depression has been reported in the immediate postoperative period and up to 7 hours after anesthesia in full term infants. This may be related to a delayed correction of CNS alkalosis. Narcotics are not usually needed for analgesia. Oral feeds are usually initiated 6-8 hours after surgery. The typical
time in hospital to return to full feeds is usually 2-3 days; HMO’s are pushing for a faster discharge.

**Toddler—Foreign Body Aspiration**

*Disease State*

Foreign body aspiration is the cause of death of more than 300 children yearly in the United States. While this can occur in any age group, the majority of children are between the ages of 1-3 years. In a recent large report, peanuts were by far the most commonly aspirated foreign body. This was followed by organic material, other nuts, popcorn, seeds, plastic objects and pins. Coughing, choking, and/or wheezing are present in the history and physical findings of over 90% of the children. A CXR may be helpful, particularly if inspiration/expiration films are done. Air trapping is the most common radiographic finding. Only a small proportion of inhaled objects will be opaque on the films. Fluoroscopy is less commonly performed. Most foreign bodies end up in a mainstem bronchus with a slight preponderance of the right side.

*Anesthetic Considerations*

*Preoperative Assessment*

A child in distress with cyanosis and wheezing will need urgent removal of the foreign body in the operating room. If the situation is not acute, and particularly if the child has recently eaten, consideration should be given to delay until some gastric emptying has occurred. The anesthesiologist should listen to the breath sounds for a baseline, as this may give an indication of where the foreign body is lodged. One should also view the preoperative CXR to determine the extent of known pathophysiology (air trapping, infiltrates, etc.) prior to induction. The decision whether to premedicate or to allow parental presence for the induction is dictated by the individual situation. In some situations it may be advantageous to allow the parent to be present.
Intraoperative Management

The decision to perform an inhalation induction versus an intravenous induction must be made according to the NPO and the airway status. Ideally, in order to maintain the airway and not dislodge the foreign body, an inhalation induction with sevoflurane or halothane and oxygen is performed. Once the child is deeply anesthetized, 2% lidocaine is used to topicalize the vocal cords and proximal trachea. The surgeons will usually use a rigid bronchoscope with a ventilating sideport to remove the foreign body. Airways that are particularly irritable may require additional boluses of propofol during the procedure, as ventilation is compromised, and rapidly changing the depth of anesthesia with an inhalation agent may not be possible. Be prepared to relax the vocal cords with either succinylcholine or propofol at the time the object is removed, to allow ease of passage. If it drops into the trachea, anticipate the worst.....Once the foreign body is removed, the child can be allowed to awaken with a mask, or an endotracheal tube can be inserted and subsequently removed when the child is fully awake. The latter is important for the child who had a full stomach, or one who was difficult to control because of all the wheezing, coughing and irritability.

Postoperative Care

Many of these children will have more wheezing and stridor following their surgery than prior to surgery. Rigid bronchoscopes, particularly if multiple insertions were performed, may cause subglottic edema. It is our routine policy to administer decadron 0.6-1 mg/kg intravenously during the procedure to minimize postoperative croup. Racemic epinephrine may be required in the PACU. Additionally, if the foreign body was fragmented or if infection and inflammation were noted distal to the obstruction, wheezing is common in the postoperative period. Nebulized albuterol and chest PT will improve the symptoms. Antibiotics are indicated if infection is suspected.
INTRAOPERATIVE CONSIDERATIONS

The anatomy of a young eye can present unique challenges.

1) Low scleral rigidity can cause collapse of the globe during surgery and a scleral fixation ring such as a Flieringa ring (or a double Flieringa ring) or the McNeill-Goldman scleral fixation ring and blepharostat should be used to stabilize the globe. The blepharostat also helps provide better exposure which can be a problem in infants with small interpaplebral spaces.

2) The younger the patient, the more pliable the tissue and more pliable or less rigid tissue is more difficult to handle and suture. Additional suturing challenges arise from the smaller size donor tissue that is used and the more shallow anterior chamber depth.

3) Higher posterior pressure can cause forward displacement of the lens and iris and there is an increased risk for iris prolapse, lens extrusion, and even suprachoroidal hemorrhage when the cornea is removed and the globe is open. Positioning of the patient with the head higher than the rest of the body can help to reduce this intraocular pressure. Preoperative ocular massage or use of the Honan balloon can reduce the risk of high posterior pressure. Many surgeons use IV mannitol as well. Retrobulbar blocks should be avoided. Anesthesiologists can help by not using succinylcholine and also by hyperventilating the patient if needed.

Other surgical differences between penetrating keratoplasty in adults vs children include the use of smaller donor grafts (usually between 5.5 and 7mm in diameter) in younger children.

Donor grafts should be oversized by .5 - 1mm. Interrupted or running sutures (or combinations) can be employed according to surgeon preference.
Postoperative Considerations

1) Young children generate stronger inflammatory responses to surgery than adults do. Increased fibrin release inside of the eye can cause iris-cornea adhesions. The much quicker healing time in infants can cause contraction of the tissue at the 360 degree interface between host and donor tissue. This contraction of tissue can then lead to loosening of the sutures which is a risk factor for suture abscesses and neovascularization of the corneal tissue, both of which can lead to rejection and failure of the new cornea. For this reason, frequent postoperative exams are essential. Parents should be taught how to look at their children’s corneas with a pen light every day and call if they notice signs of loose sutures or new infiltrates. Children should be brought in to see their surgeons frequently - maybe even 2-3 times per week for the first few weeks and then once per week for the next couple of months. In young infants, suture removal may begin as soon as 2 weeks after surgery and is often completed in about 3 months.

2) Eye drops: Frequent application of topical steroids is essential to reduce the high risk of rejection. Some authors advocate steroid drops every hour for the first few days followed by a very slow taper. Others advocate drops 10 times per day for the entire first month. Risk of infection is high in these children. Loose sutures, epithelial defects, wound dehiscence, and high doses of topical steroids are all risk factors for infection. One study found a 27% risk of infection for infants in the early postoperative period. For this reason, topical antibiotic drops are often used for a longer period compared with adult postoperative regimens.

3) Infants and young children are unable to cooperate with postoperative exams, instructions, or care. They can not be trusted to not rub their eyes during the healing period.
and this can lead to broken sutures and wound dehiscence. They may not tolerate the administration of necessary antibiotic and steroid drops and this can be a challenge for parents and other caregivers. Frequent exams under anesthesia are required during the postoperative period.

4) Adult patients who undergo penetrating keratoplasty are told to expect a sometimes lengthy visual recovery. Especially if they have good vision in the other eye, it can take many many months before sutures are removed and they are refracted and fit for rigid gas permeable contact lenses that might provide them with the best corrected visual acuity. In infants and young children, amblyopia can cause rapid and permanent vision loss and it is imperative that their visual rehabilitation begin as soon as possible with proper correction for the postoperative eye and amblyopia therapy, often including patching of the “good” eye. Collaboration with pediatric ophthalmologists and possibly optometrists is essential.

**Prognosis**

The prognosis for pediatric penetrating keratoplasty is guarded and is definitely not as good as for adults. The main reasons for this are the high rate of graft failure (most commonly due to rejection and infection) and also the high rate of vision loss from amblyopia despite maintaining a clear graft. A review of the published data reveals varied success with pediatric penetrating keratoplasty.

In 1977, Waring and Laibson reported 87% success for acquired corneal opacities but only 1/11 clear grafts among congenitally cloudy corneas. 4 out of 11 of their eyes were NLP (no light perception vision) and were either enucleated or phthisical. Because of their poor results, they recommended not performing surgery on patients with unilateral corneal disease.

In 1984, Stulting published data on 91 patients all aged 14 or younger. Although he reported clear grafts at one year in 60%
of patients with congenital opacities and 70-73% of patients with acquired causes of corneal opacities, only 29% of patients with congenital causes of opacities and only 45-67% of patients with acquired causes of opacities had vision better than 20/400. Only 3% of patients with congenital causes of opacities had vision better than 20/40; however, 17% of trauma patients had vision of 20/40 or better and so did 47% of patients with non-traumatic acquired opacities.

In 1990, Cowden published data from 66 surgeries in 57 eyes of 50 children aged 2 months to 14 years old. After a 1-10 years of follow-up, he reported 32 clear grafts, 30 failed grafts, and 4 eyes that were lost (one to endophthalmitis, 2 to phthisis, and one to a choroidal hemorrhage). Only about one third of the grafts performed for Peters’, sclerocornea, or intrauterine infection were clear at one year. Among his patients, those who were oldest at surgery tended to do best. In infants less than one year old, only 25% of grafts were clear at one year. In children between 1 and 4 years old, about one half were clear at one year. And in children older than 4 years old, about two thirds were clear at one year.

PREOPERATIVE CONSIDERATIONS

The majority of pediatric patients undergoing eye surgery are healthy and managed as day-cases. Only small percentage may have some underlying disorders, often of chromosomal or metabolic nature, which may provoke more challenges in anesthetic technique. Cases range from those, associated with mental, developmental delay and behavioral problems who should be treated kindly; and others, in whom associated disorders may be of more direct anesthetic impact. A number of syndromes in which there can be major difficulties with intubation are associated with cataracts, glaucoma or squints. These include the mucopolysaccharidoses, the craniosynostosis disorders (e.g. Crouzon’s, Apert’s and Pfeiffer’s syndromes) and the craniofacial syndromes (e.g. Goldenhar, Treacher–Collin and Smith–Lemli–
Intraoperative Considerations in the Pediatric Patient

Opitz). The Hallerman–Strieff syndrome, although rare, may present for cataract surgery in the neonatal period and invariably is associated with a particularly difficult airway. Stickler’s syndrome, which is associated with early retinal detachment and glaucoma, is a progressive connective tissue disorder that has some of the features of the Pierre Robin syndrome; it can also present intubation problems. Suitable precautions and techniques for patients with potential intubation difficulties should be induced in these patients.

Some patients need a thorough clinical examination specially those suffering from neurofibromatosis, von Hippel–Lindau disease, tuberous sclerosis and the Sturge–Weber syndrome. The congenital phakomatoses may show cardiac or intracranial lesions, seizures and frequently pheochromocytoma.

Ectopia lentis is a common presentation of Marfan syndrome and homocystinuria. These patients need surgical extraction of their dislocated lenses, patients with homocystinuria should receive aspirin before and after surgery as a prophylaxis against thromboembolic episodes. Preoperative intravenous glucose infusion is needed to counteract the hypoglycemia that may result in cases with homocystinuria due to the metabolic disorder. Aortic and valvular anomalies are common with Marfan syndrome, careful positioning and hypertension should be avoided in these patients.

Congenital and juvenile glaucoma patients are usually on beta blocker eye drops e.g. timolol, betaxolol etc. That may be sometimes absorbed systemically causing hemodynamic adverse effects.

Surgery during the first few days of life is indicated in an infant suffering from congenital cataract. The possibilities that this cataract maybe due to metabolic disorder or occurring following intrauterine infection should be taken into consideration and one should be ready for prompt management and monitoring if respiratory problems such as postoperative apneic episodes had occurred after surgery. Antibiotic prophylaxis is unnecessary.
in majority of ophthalmic surgeries in patients with cardiac anomalies as bacteremia is not expected. On the other hand a prophylactic antibiotic is given to patients with structural cardiac lesion and undergoing a nasolacrimal duct procedure in which the incidence of bacteremia is high, but it has become a debatable issue now. Fasting prior to surgery is required to reduce the risk of aspiration of food or liquids while under anesthesia. While rare, this is very serious complication and parents need to strictly follow recommendations and very specific policies regarding children’s ages and time periods for fasting, which are based on safety standards. The following guidelines for fasting times prior to surgery apply to healthy patients who are having elective surgery. A history of diabetes or reflux may require longer fasting times
- Clear liquids – two hours
- Breast milk – four hours
- Infant formula – six hours
- Nonhuman milk – six hours
- Light meal – six hours

**Pre-medication, Induction Of Anesthesia**

A plan should be made to pre-medicate the child and choose the induction technique either inhalational or intravenous that suits the child and preferred by the anesthesiologist. Child with poor vision should be handled in a careful manner.

Paracetamol, NSAIDs may be given as oral preparations or rectally preoperatively. If midazolam is used as a premedication there may be some anti-emetic benefit, other benzodiazepines, such as lorazepam and diazepam have shown to decrease PONV in strabismus patients; the use of oral clonidine 2-4 µg/kg as a premedication has shown mixed results.

**Airway Management**

If intraocular tension (IOP) has to be measured, intubation should be avoided as it raises the intraocular pressure, instead
a face mask may be used. Laryngeal mask airway (LMA) is used for simple procedures such as examination under anesthesia (EUA), specially in older children.

Some anesthesiologists find it more appropriate to maintain spontaneous respiration especially where a sterile field is required. It also has the benefit of reduced cough at the end of surgery and controlled ventilation with muscle relaxant can be used.

Very young children are best managed with intubation and controlled ventilation as well as in cases of intraocular surgery requiring a still eye with low intraocular pressure. Reinforced flexible tracheal tubes (ETT) are preferred to ensure airway security; also the tube should be firmly fixed in place as the access to the airway will be restricted during surgery.

**Maintenance Of Anesthesia**

Anesthesia maintenance technique widely depends upon the choice of the anesthesiologist and the availability of different agents, the depth of anesthesia should be considered. Sevoflurane anesthesia with bispectral index (BIS) 60 was associated with a higher incidence of oculocardiac reflex (OCR) compared with BIS of 40.

Incidence of bradycardia, dysrhythmias and ventilatory BIS disturbances, is higher with halothane specially when hypercarbia is present or preparations containing atropine or adrenaline are used during surgery. Isoflurane or sevoflurane may be preferable; whereas there is no difference between sevoflurane and desflurane and their effects on OCR.

Total intravenous anesthesia (TIVA) with propofol is effective in reducing the risk of PONV as propofol has anti-emetic effects. Remifentanil can reduce volatile requirements.

Hahnenkamp et al Compared four anesthetic techniques and their effect on OCR. The groups included: propofol and alfentanil infusions, ketamine and midazolam infusions, sevoflurane and halothane. The ketamine and midazolam group experienced the
least amount of hemodynamic changes due to OCR. Also a further study evaluating ketamine demonstrated that a single bolus of ketamine 1 or 2 mg/kg for induction lowered the incidence of OCR when compared with propofol and sevoflurane combination. A proposed mechanism may be the increased sympathetic tone associated with ketamine that counteracts parasympathetic stimulation of OCR.

Nitrous oxide should be avoided in ocular surgery Firstly; nitrous oxide is known to increase the risk of PONV. Secondly, in vitreoretinal surgery, where intraocular gas bubbles of sulphur hexachloride or perfluoropropane are introduced into the eye to tamponade detached surfaces, nitrous oxide diffuses from the blood into gas filled spaces cause a significant rise in intraocular pressure with subsequent ischemic damage. As well if nitrous oxide was used at the beginning of surgery, it will diffuse out of the bubble at the end of procedure, and the bubble will shrink which increase the incidence of recurrent detachment.

Fluids

Oral intake of clear fluids until two to three hours preoperatively is recommended to maintain hydration; liberal hydration with intravenous crystalloids intraoperatively is effective in reducing the risk of PONV. Recently a study demonstrated that an intraoperative lactated ringer’s solution at 50 ml/kg/hr is more effective in reducing PONV in strabismus surgery patients than a solution at 10 ml/kg/hr.

Anesthesia And IOP

Most anesthetic agents reduce IOP. Normally it ranges from 10-20 mmHg.

Anesthetic Agents Effect

Propofol, thiopentone: IOP reduced by 20-30% (3-7 mmHg)

Halothane, sevoflurane, isoflurane, desflurane: IOP reduced by 20-30% (3-7 mmHg)
Opioids: Minimal to no effect on IOP
Ketamine: Minor, dose dependent increase in IOP; marked effect when dose exceeds 5 mg/kg
Atropine: No effect on IOP
Non-depolarising muscle relaxants: Minimal to no effect on IOP
Suxamethonium: Significant increase in IOP within 30 sec of administration, effect lasts for 5-7 minutes, less if given with agents that reduce IOP
Acetazolamide, mannitol, dextans: Used for acute reduction of IOP preoperatively

Anesthetic Techniques And IOP
IOP affected by many physical and physiological events during anesthesia; coughing, straining, crying, bucking on the tube and the process of tracheal extubation may all cause a rise in IOP. A dose of lidocaine 1 mg/kg 3 min before intubation or extubation is beneficial in preventing acute increase in IOP.

The LMA has little effect on IOP, and allows smoother induction and emergence from anesthesia. IOP is increased by hypoxia and hypercapnia, and decreased by hypocapnia and hypothermia.

The Oculocardiac Reflex (OCR)
OCR is frequently encountered during ocular surgery in pediatrics particularly in strabismus surgery. It is defined by some authors as a 20% decrease in heart rate (HR), and by others as a 10-30% decrease in HR from baseline. Continuous ECG monitoring is mandatory during surgery.

A sinus bradycardia and occasionally junctional rhythms, atrioventricular block, atrial ectopics or ventricular ectopics may occur. Traction on extraocular muscles triggers OCR. Medial rectus muscle traction is more common to trigger OCR than traction on other extraocular muscles. However, Blanc et al were
unable to show that the medial rectus triggers OCR more often than the other extraocular muscles if the same type of stimulus is used. It is important to note that ocular trauma, increased intraorbital pressure from injection or hematoma or pressure on orbital apex after enucleation are also triggers of OCR.

The reflex takes its afferent innervations from the ophthalmic division of the trigeminal nerve, relays via the sensory nucleus in the 4th ventricle, with the efferent impulse in the vagus nerve. Vagal escape or OCR fatigue means disappearance of the response when the stimulus is discontinued.

It is a physiologic defense mechanism where the HR response weakens with repeated or sustained stimulation of extraocular muscles.

Intravenous atropine 20 µg/kg or glycopyrrolate 10 µg/kg at induction of anesthesia will block the OCR. Atropine can be given anytime during surgery if the OCR occurs, so it is important to have the drugs available and ready to use if bradycardia had occurred.

The reflex can be counteracted by applications of topical local anesthetic eye drops such as tetracaine, or by blocking the afferent limb of the reflex with a peribulbar block, which is not commonly used in pediatric patients due to the risk of globe perforation.

OCR is less common to occur with sevoflurane than with halothane, on the other hand more likely to occur with rocuronium rather than atracurium. Hypercarbia doubles the incidence of significant bradycardia, so controlled ventilation should be considered. PONV is more likely to occur in pediatric patients who experience OCR during surgery, therefore antiemetic drugs should be given during anesthesia.

**Oculo Respiratory Reflex**

Extraocular muscles manipulation can also provoke oculo respiratory reflex which results in reduction in tidal volume
and respiratory rate; consequent hypercapnia and hypoxemia may occur, which in turn increase the risk of OCR. Oculorespiratory reflex has the same afferent pathways as in OCR which relays in brainstem respiratory control area, and the efferent impulses travel along phrenic nerve and other nerves involved in respiration.

Extubation And Emergence From Anesthesia

Laryngeal mask airway is used in suitable pediatric patients in order to avoid straining and coughing on the tracheal tube at the end of surgery.

Intubated patients need deep extubation and smooth recovery but this is contraindicated with possibility of full stomach (e.g. in emergency surgery) or in cases with difficult airway management in whom awake extubation is indicated, 1mg/kg IV of lidocaine is given to minimize the effect of extubation on IOP.

Oral intake is resumed as early as possible as most pediatric patients undergoing ocular surgery are considered day cases but the high incidence of PONV sometimes favors hospital overnight admission.

Principles Of Pain Relief And Postoperative Care

To manage mild to moderate postoperative pain which occur in most ocular procedures, topical local anesthetic agents, NSAIDs or simple analgesics such as paracetamol may be given preoperatively either orally, rectally or IV at induction of anesthesia.

More severe pain as in vitreoretinal, enucleation and squint surgeries need strong analgesics given intraoperatively beside previously mentioned drugs such as intravenous fentanyl. Postoperative codeine phosphate or in older children tramadol or even morphine may be given if needed.

Opioid use increase the risk of PONV and antiemetics are indicated
Good analgesia can be produced by peribulbar block although most anesthesiologist avoids using this technique in children for fear of globe perforation and retrobulbar hemorrhage.

Tenon’s capsule is the fascial layer that extends from the limbus posteriorly to the optic nerve, separating the globe from orbital fat.

Sensation of the eye is provided by ciliary nerves that cross the episcleral space after emerging from the globe. Sub-Tenon block is very effective in pain relief if administrated at the end of surgery, strabismus surgery confined to this space and instilling local anesthetic can induce postoperative analgesia.

Optimal postoperative analgesia is crucial as pain may partly be responsible for PONV, emotional distress, and discharge delay if not properly treated.

The Association of Pediatric Anaesthetists of Great Britain and Ireland published guidelines for certain procedures, including, recommendations for strabismus surgery. There were three grade B recommendations:

1. Intraoperative local anesthetic blocks (sub-tenon or peribulbar) are effective in reducing PONV as well as improving preoperative analgesia when compared with intravenous opioids.

2. Topical nonsteroidal anti-inflammatory drugs (NSAIDs) have no extra beneficial effect on pain scores or postoperative analgesic requirements when compared with topical local anesthetics or placebo.

3. Intraoperative opioids and NSAIDs have same postoperative analgesic effect, but opioid use increases the risk of PONV.

The highest incidence of PONV was found in the meperidine group of patients when comparing the effect of fentanyl, meperidine, and peribulbar block, in combination with propofol infusion on PONV; the lowest was found in the peribulbar block, and fentanyl was in between. Practically, the use of opioids should
be minimized by administering acetaminophen and NSAIDs, in order to reduce the incidence. Other studies have shown that fentanyl increases PONV after strabismus surgery; but, a propofol and sufentanil technique showed less PONV compared with a propofol and isoflurane technique.

In comparison with sevoflurane and desflurane, bradycardia in response to OCR is more prominent with remifentanil. But it had the same incidence of PONV, when compared with fentanyl and as expected, higher pain scores were found in patients who received remifentanil.

Topical tetracaine proved to be effective in two separate studies; however this cannot be demonstrated by another study. Topical diclofenac has excellent analgesic effect with low incidence of PONV, however ketorolac did not show this benefit.

**Postoperative Nausea And Vomiting**

Nausea alone is difficult to be determined in children who usually had a higher incidence of PONV when compared to adults. Postoperative vomiting is very common in children after strabismus surgeries, especially in children over the age of 2 years.

About two-thirds of children vomit after strabismus surgery, if no preventive measures were taken. Most of the studies focus on prophylaxis rather than treatment. A systematic review of publications between 1981 and 1994 on vomiting in children after squint surgery demonstrated a mean incidence of vomiting within 6 hr of 54% in children receiving no prophylactic anti-emetic and 59% within 48 hr.

The exact mechanism of vomiting is not understood however it was suggested that it is a part of an ocular-emetic reflex, involving the ophthalmic division of the trigeminal nerve and the vomiting centre in the medulla, retrobulbar or peribulbar block reduces the incidence of postoperative vomiting probably due to local anatomical reasons for the reflex, as the incidence
of vomiting varies according to the surgical techniques, e.g. squint repair using the Faden myopexy technique has a significantly higher incidence of POV than the simpler muscle recession/resection technique.

Other prophylactic strategies to avoid postoperative vomiting included the use of anticholinergic agents, dexamethasone dimenhydrinate, clonidine, anti-emetics (e.g. metoclopramide, droperidol, ondansetron) or using the anti-emetic properties of propofol either as an induction agent or as part of TIVA technique. However, 5-HT₃ (serotonin) antagonists has led to marked reduction in the incidence of POV, if given intraoperatively.

Ondansetron 0.1 mg/kg is very effective and smaller doses have been proved to be equally effective. Combination therapy (e.g. ondansetron and dexamethasone) is better than ondansetron alone.

Cheaper 5-HT₃ antagonists (e.g. dolasetron 0.35 mg/kg) have been proved to be as effective as ondansetron, although dolasetron is not commonly available. Finally, acupressure to the P6 acupuncture point, a less common form of anti-emetic treatment, was found to be effective.

**Anesthesia For Specific Ophthalmic Procedures**

**Eye examination and measurement of IOP**

For eye examination under general anesthesia (EUA), either inhalational or intravenous induction technique with facemask to maintain the airway will be satisfactory. For longer time EUA it is better to use LMA.

Repeated examinations under GA are required in most of these children so it is recommended to manage them gently. Most anesthetic agents reduce IOP, so it can mask a high IOP and lead to mismanagement.

The use of ketamine in such cases is preferred by many anesthesiologists because it does not reduce IOP. A dose of 5-
10 mg/kg ketamine intramuscularly is sufficient to make a child calm and still enough within a few minutes to allow eye examination. It is reported that ketamine causes a slight increase in IOP; however, it is safer to have a falsely high rather than a falsely low IOP reading.

Atropine 20µg/kg or glycopyrrolate 10µg/kg is usually given as ketamine increases respiratory secretions. Maintenance of patent airway is mandatory, but instrumentation of the airway is rarely required.

Inhalational induction with sevoflurane via face mask with the presence of surgeon, is appropriate alternative technique to ketamine, and to measure the IOP as soon as the child is asleep. The sevoflurane should be kept at <5%, the child’s eyes should be central and pressure on the eyes by the facemask should be avoided.

It is recommended to measure IOP before airway instrumentation, however there is little evidence to prove that the latter significantly increases IOP. A proper technique should be maintained when serial measurements of IOP are to be made.

*Syringing and probing of nasolacrimal ducts*

Blocked nasolacrimal ducts in young children present early in life with increased tearing. For syringing and probing of nasolacrimal ducts the LMA will suffice if the surgeon does just probing.

But if the aim is to inject saline in the nasolacrimal duct then intubation is important to secure airway and avoid aspiration. In case of failure of simple probing, inferior turbinate bone may be fractured to or silicon catheter may be placed for few weeks to relieve the obstruction.

Dacrocystorhinostomy is more complicated procedure which involves exposure of the duct and creation of new opening through the nasal cavity. In order to reduce bleeding topical vasoconstrictor is applied on the nasal mucosa of the child and hypotensive anesthesia is induced, it is essential to secure the
airway by intubation and packing the throat; adequate suction of the nasopharynx before extubation is required. Postoperative analgesia with opioids is needed. Antibiotic prophylaxis in patient at risk of infective endocarditis is no longer given routinely in this procedure.

**Strabismus surgery**

Strabismus is usually idiopathic but secondary strabismus may occur in cases of trauma, infections, and space-occupying lesions, immunological, endocrine or inflammatory conditions that may result in muscle palsy.

Most children with strabismus are healthy, however some may present with disorders of central nervous system such as cerebral palsy, hydrocephalus and myelomeningocele. Other diseases or syndromes may be associated with strabismus such as cardiomyopathy and congenital heart diseases; each disease or syndrome has its specific anesthetic implication and should be considered during evaluation and management.

Possible incidence of malignant hyperthermia in patient with positive family history is common with strabismus surgery and the possibility is confirmed with a cuff muscle biopsy and caffeine test. Strabismus surgery is the most commonly performed pediatric eye surgery. It affects both males and females similarly.

During strabismus surgery the surgeon may use forcedduction testing to differentiate a paretic from restrictive squint. Sometimes botulinum toxin maybe injected into extraocular muscle requiring electromyelogram (EMG). Muscle relaxants are avoided in those cases. Topical local anesthetic can be used in fine adjustments after adjustable suture techniques in older children for minimum 24 to 48 hours after surgery.

Anesthetic technique, airway security and choice of ventilation vary according to the anesthesiologist choice. Both, TIVA or volatile anesthetics can be used for maintenance of anesthesia, however TIVA reduces the incidence of PONV.
PONV is very common up to 50–75% postoperatively. Combination of ondansetron 0.1 mg/kg IV and dexamethasone 0.1-0.2 mg/kg IV is effective in reducing this percentage by 10%. Atropine 20 µg/kg IV or glycopyrolate 10 µg/kg IV should also be considered to overcome this problem.

Deep extubation is preferred, it is better to avoid intraoperative opioids due to high risk of PONV, but fentanyl is considered.

If necessary, postoperative pain can be managed using NSAIDs, paracetamol and topical local anesthetics. A peribulbar block decreases the incidence of PONV by blocking the ophthalmic division of trigeminal nerve that passes to the vomiting centre in the medulla as well as providing analgesia after surgery, however it is not recommended by most anesthesiologist due to high risk of globe perforation.

Intraoperative sub-tenon block is very effective for analgesic requirements.

**Intraocular surgery**

Intraocular procedures are performed in pediatric patients mainly for management of glaucoma or for cataract aspiration with or without lens implantation.

Pediatric glaucoma surgeries include goniotomy, trabeculotomy and trabeculectomy, to maintain balance between production and drainage of aqueous humour and keep the normal IOP 10-22 mmHg.

For cases not corrected surgically a cryoprobe at “60 to “80°C behind the corneoscleral limbus is applied, the procedure is painful and opioid analgesia may be essential.

Any increase in venous pressure of the eye due to coughing or straining will cause an immediate rise in IOP by interfering with aqueous drainage via the canal of Schlemm and altering the volume of the choroid; on the other hand arterial pressure has little effect on IOP.
Neuromuscular blockade and controlled ventilation should be applied as it is important to keep the child’s eye central and motionless. Sudden rise in IOP should be avoided to prevent extrusion of the eye content through surgical incision especially in keratoplasty when cornea is penetrated and large defect should be covered with graft.

In order to prevent IOP rising, acetazolamide which decreases aqueous production, or IV mannitol can be given during these procedures. However, in penetrating keratoplasty IOP shouldn’t be lowered too much as it causes the eye to collapse. The surgeon may suture a ring around the cornea to support the eye during surgery.

Anesthesia is best maintained until neuromuscular blockade has been reversed, and patient is breathing spontaneously and extubation has been performed. Deep extubation is recommended, a small dose of propofol (0.5 mg/kg) immediately before extubation can be given in order to obtain smooth extubation and preventing increased IOP which be caused by coughing, straining on the endotracheal tube at the end of surgery.

In older children, topical anesthesia to the airway is effective although this should be avoided in infants.

Early resumption of oral intake is the simplest way to avoid the elevated IOP associated with crying in the immediate postoperative period.

LMA and pressure controlled ventilation is safe and effective, even though there is possibility of gastric insufflation and reflux, it can be used even in small children undergoing intraocular surgery. This has the benefit of smooth extubation with less coughing and decreased incidence of acute IOP elevation compared with the usual tracheal tube. LMA should be properly positioned and well secured otherwise tracheal tube should be used. Combination of paracetamol and diclofenac is usually effective to control postoperative pain as intraocular procedure is not particularly painful.
Combined general and local anesthesia can be done for older children undergoing intraocular surgeries using low volume single injection peribulbar block with short fine needle 25-27G to decrease anesthetic requirements and to allow rapid smooth recovery.

**Enucleation and evisceration**

Intraocular tumors such as retinoblastoma or endophthalmitis or cosmetic purposes, where there is an unsightly blind eye, removal of the whole eye is indicated. So long the procedure involves dissection of the extraocular muscles off the globe, OCR can be easily initiated, same anesthetic management as in squint surgery should be chosen. However, the risks of PONV are much lowered. In evisceration, the content of the globe are removed leaving the sclera behind with the extraocular muscles intact. Because the procedure is painful intraoperative fentanyl may be needed.

**Vitreoretinal surgery**

Retinal detachment in pediatrics may be primary due to retinal defect or secondary due to underlying disease. Repair of the detached retina is performed via vitreoretinal surgery, however this is unusual in children. The procedure involves creating a choreoretinal scar and placing a scleral buckle towards the back of the eye, which helps to oppose the neuroretina and retinal pigment epithelium. To tamponade the detached surfaces together, the surgeon injects an intraocular bubble of either sulphur hexafluoride or perfluoropropane. Nitrous oxide is avoided if intraocular gas is injected or in patients having intraocular bubble placed for several weeks after surgery. Mechanical ventilation and neuromuscular blockade are indicated to keep the eye motionless and avoid increased IOP during the surgery. Deep extubation is indicated for the same reason. Postoperative analgesics including opioids, and antiemetic should be considered for proper management of severe pain and PONV.
Emergency surgery

Emergency surgeries cannot be delayed for prompt repair of rapture globe with or without an intraocular foreign body; the faster the repair the less is the incidence of infection. In many cases the stomach is full and prompt intubation for airway protection is achieved by rapid sequence crush induction using succinylcholine and cricoid pressure. However, succinylcholine may cause transient increased IOP and subsequent extrusion of intraocular contents through even small wounds leading to the hazard of total loss of vision, although no well-documented reports have proven this. Intubation can be performed using a large dose of a non-depolarizing relaxant while maintaining cricoid pressure to avoid the effect of succinylcholine on IOP. To summarize, it is recommended to consider succinylcholine in cases of difficult airway management or there is high risk of regurgitation. If succinylcholine is contraindicated, or the risk of regurgitation is less concerned, a non-depolarizing relaxant with nerve stimulator monitoring can be used.

Retinopathy of prematurity

Retinopathy of prematurity (ROP) is common in babies of birth weight <1500 g and/or <31 weeks gestational age. ROP is classified in five stages ranging from mild (stage 1) to severe (stage 5). Infants with stage 3 or above are at high risk of retinal detachment and blindness. The abnormal peripheral retinal neovascularization should be abolished by the use of cryotherapy or laser therapy. Good results obtained when early interference is done, so early diagnosis and repeated examination of at risk infants should be considered between 6 and 7 weeks postnatal age 2-weekly until the risk has passed. Cryotherapy is a painful procedure and requires strong analgesic such as an opioid e.g. fentanyl. Postoperative ventilation with appropriate support is needed for the babies to avoid apneic episodes following anesthesia. In many infants other systemic disorders because of their extreme prematurity (e.g. bronchopulmonary dysplasia) need careful assessment.
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Preface

Neurophysiology studies are useful to differentiate between types of demyelinating disease, as well as between axonal and demyelinating disease. The presence of conduction block can support an early diagnosis of AIDP. These results are unlikely to alter management, but may assist with counseling for prognosis. This is most relevant to the hereditary group.

Neonatal seizures are a neurological emergency and prompt treatment is required. Seizure burden in neonates can be very high, status epilepticus a frequent occurrence, and the majority of seizures do not have any clinical correlate. Detection of neonatal seizures is only possible with continuous electroencephalogram (EEG) monitoring. EEG interpretation requires special expertise that is not available in most neonatal intensive care units (NICUs). As a result, a simplified method of EEG recording incorporating an easy-to-interpret compressed trend of the EEG output (amplitude integrated EEG) from one of the EEG output from one or two channels has emerged as a popular way to monitor neurological function in the NICU.

Peripheral neuropathy is caused by damage to, or an inflammation of, the nerves of the peripheral nervous system, according to Mayo Clinic. These nerves extend from the spinal cord to points throughout the body. The body-wide extent of the peripheral nervous system means that neuropathy can cause symptoms at almost any location, but most victims report pain, tingling and reduced sensation in the hands and feet. Sometimes, the symptoms are described by patients as feeling like they are wearing stockings or gloves due to the reduced sensitivity to touch.
Pediatric patients require special considerations in any neurophysiologic testing situation. Any technologist who performs routine EEG on a pediatric population will attest to the extra demands placed on the technologist, both technically and in additional training and experience required to produce a high quality, meaningful study. Technologists involved in routine nerve conduction and electromyography (NCV/EMG) know that these studies can be quite traumatic, even for adult patients. For many individuals, clinically induced pain can be compounded by the anxiety and fear surrounding the procedure, making the technologists’ job even harder. The demands placed on the technologist are even more evident when they are required to perform nerve conduction studies and assist in the needle examination in a pediatric patient. In addition to increased technical difficulty attributed to children’s small size and inability to cooperate fully with the examiners, pediatric NCV/EMG studies are almost always complicated by fear and stress experienced by both the parents and the child. These factors place additional demands on the technologist/physician team performing the pediatric electromyography. All the matter is just compiled and edited in nature. Taken from the various sources which are in public domain.

It is hoped that the book will serve the purpose of students and scholars on the subject and can be useful to them in allied fields.

—Editor
ABOUT THE BOOK

Neurophysiology studies are useful to differentiate between types of demyelinating disease, as well as between axonal and demyelinating disease. The presence of conduction block can support an early diagnosis of AIDP. These results are unlikely to alter management, but may assist with counseling for prognosis. This is most relevant to the hereditary group. Over the past several decades, electroencephalography (EEG) in newborn infants has become valuable as a serial, noninvasive screening tool for infants at high risk of perinatal injuries. The brain dynamics and connectivity in different states (awake or asleep) can be defined, and a whole range of acute or chronic cerebral disorders can be identified. Such information often reveals presymptomatic or subclinical conditions. The EEG prognostic value at the time of continuous development is often greater than at a later stage. EEG testing can provide reassurance to the physician and parents at a time of potential catastrophic damage. Peripheral neuropathy tends to get better over time, and this is especially true of cases with a definite cause, such as disease or exposure to toxins, that can be treated or managed. Doctors are also able to prescribe any of several medications to treat peripheral neuropathy, some of which focus on pain relief and others on the nerve damage itself or on relieving the underlying condition. It is hoped that the book will serve the purpose of students and scholars on the subject and can be useful to them in allied fields.

CONTENTS

EEG Monitoring in Neonatal Epilepsies; Pediatric Febrile Seizures; Epileptic and Nonepileptic Paroxysmal Events in Childhood; The Evaluation of Pediatric Sleep Disorders; Pediatric Muscular Dystrophies and Myopathies; Clinical Evaluation in Pediatric Peripheral Neuropathies; EMG Considerations in the Pediatric Patient; Clinical Neurophysiology in Pediatric Peripheral Neuropathy; EMG in Pediatric Brachial Plexopathy; Intraoperative Considerations in the Pediatric Patient