Chapter 13 – Common Problems in Pediatric Neurology

Section 1

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Abnormal Head Size

Introduction
All family practice physicians and pediatricians care for children who have abnormal head size. An organized approach coupled with a few simple tests reveal the diagnosis in many cases. These include serial measurements, developmental assessment and family history, awareness of unusual physical features, and measurement of the parent’s head size. Early diagnosis catches potentially treatable medical disorders and optimizes long-term management of the child.

Head size is defined clinically as the occipito-frontal circumference (OFC). OFC > 2 standard deviations (SD) above the mean defines macrocephaly; OFC equally far below the mean is microcephaly. Macrocephaly and microcephaly should raise immediate red flags during a child’s visit, but the context in which they occur may reveal their relative importance.

Macrocephaly
Mild macrocephaly (+2 to +3 SD) in an older child with normal intelligence, no other symptoms or abnormal neurologic signs, normal velocity of head growth, and a strong family history of isolated macrocephaly usually gives little cause for concern. The macrocephalic child who lacks these reassuring features or displays neurologic signs or symptoms may have underlying intracranial pathology. An infant or young toddler in whom OFC is increasing too fast (crossing lines on standard growth charts), demands further testing regardless of other factors. Macrocephaly in association with neurodevelopmental abnormalities also requires investigation. If either of these factors is present, a positive family history does not eliminate the need for further work-up, including
neuroimaging, even though asymptomatic familial macrocephaly and benign infantile extra-axial fluid collection may cause initially accelerated head growth. Other physical features such as unusual facial features, short stature, and pathologic heart murmurs suggest specific non-neurologic evaluations such as chromosomal karyotype, specific genetic or metabolic testing, x-rays, or echocardiogram respectively.

This further work-up is guided by possible causes. Selected causes for macrocephaly are listed in Table 13.1-1 and can be further divided into macrocephaly caused by increased spinal fluid (obstructive versus non-obstructive hydrocephalus, pseudotumor cerebri), and increased tissue. Tumors may cause macrocephaly by both mechanisms, whereas children with megalencephaly have large heads simply due to increased brain size. Evaluation of the young child under two to three years old, in whom increased intracranial pressure results most readily in increased OFC velocity, includes imaging of the brain. Head ultrasound in the neonate, and CT with contrast in the older child allow some assessment of ventricular size and brain parenchyma, as well as extra-axial spaces, but magnetic resonance imaging (MRI) is preferred. MRI allows better visualization of the cortical mantle, white matter abnormalities, small lesions, and abnormalities in the cerebellum and brainstem, including tumors. MRI requires sedation or general anesthesia in young or uncooperative children. Neuroimaging in pseudotumor cerebri, or benign intracranial hypertension, may reveal a "full" appearance to the brain, with smaller than usual ventricles. Diagnosis of pseudotumor cerebri requires lumbar puncture to demonstrate elevation of opening pressure but reveals normal CSF otherwise. Other ancillary tests important in the initial evaluation of the macrocephalic child are listed in Table 13.1-2. Otherwise uncharacterized macrocephaly with mental retardation or autism in a male suggests the need for Fragile X type A (FRAXA) DNA testing as well as more routine chromosomal karyotype. Further testing for cytogenetic microrearrangements may be fruitful as well, but the role of testing for specific autism-related genes (PTEN, NLG3, NLG4X) is unclear. This and other secondary testing may accompany referral to a subspecialist such as a child neurologist.

Table 13.1-1: Selected conditions associated with macrocephaly

- Obstructive, non-communicating, internal hydrocephalus
  - Tumor
  - Congenital infection (especially toxoplasmosis)
  - Posthemorrhagic
  - Aqueductal stenosis
  - Chiari II malformation
  - Dandy-Walker malformation
  - Tuberous sclerosis
  - Neurofibromatosis

- Non-obstructive, communicating, external hydrocephalus
  - Tumor (choroid plexus papilloma)
  - Hydranencephaly and other forms of hydrocephalus ex vacuo
  - Subdural hematoma/hygroma, non-accidental trauma
• Benign increased subdural space in infancy
• Cerebral malformations
• Cerebral vein/sinus thrombosis
• Post-meningitis
• Vein of Galen malformation/other arteriovenous malformations
• Chronic right-heart failure

• Pseudotumor cerebri (benign intracranial hypertension)
  • Toxicity—Lead, Vitamin A, Cyclosporin
  • Iron-deficiency anemia
  • Steroid use/withdrawal
  • Hypoparathyroidism
  • Metabolic disease
  • Renal disease
  • Venous sinus thrombosis

• Megalencephaly/increased tissue
  • Tumors
  • Hemimegalencephaly, other brain malformations
  • Fragile X syndrome
  • Neurocutaneous syndromes
  • Overgrowth syndromes (Sotos, Weaver, and Simpson-Golabi syndromes)
  • Leukodystrophies
  • Lysosomal storage diseases
  • Mucopolysaccharidoses
  • Glutaric acidurias
  • Canavan disease
  • Alexander disease
  • Skeletal dysplasias
  • Chromosome abnormalities
  • Autosomal dominant benign familial megalencephaly

Table 13.1-2: Selected valuable ancillary studies for macrocephaly

• Wood’s lamp examination (Tuberous sclerosis)
• Neuroimaging (MRI scan)
• CBC with RBC indices
• Lead level, iron studies
• Chromosomal karyotype
• Skeletal x-rays (for trauma and/or bone age assessment)
• Evaluation of cardiac function (in young children)
• Lumbar puncture with opening pressure (only after neuroimaging study)
• FRAXA DNA test
• Other specific gene testing when indicated
• Urine for metabolic screen, organic acids
• Lysosomal enzyme panel, other specific metabolic testing when indicated

The cause for the macrocephaly, once identified, dictates management. Obstructive hydrocephalus requires referral to a neurosurgeon for possible ventriculoperitoneal shunt placement, and correction of the underlying anatomic cause if it is amenable to treatment. Brain tumors and many metabolic diseases also require referral for specialized and complex therapy. As previously stated, management of other causes of macrocephaly requires only observation or simple interventions. Non-obstructive hydrocephalus may be due to increased cerebrospinal fluid production, decreased resorption, or loss of brain volume, and sometimes requires surgery. Symptomatic megalencephaly associated with either developmental delay or other unusual physical features, should be evaluated by a medical geneticist experienced in the diagnosis of dysmorphic syndromes. This is important not only for diagnosis, but to identify certain overgrowth syndromes that carry increased risk of malignancy.

Microcephaly
In the overwhelming majority of cases, microcephaly results from failure of the brain to grow at an appropriate rate at some point during development. As the degree of microcephaly increases, so does the probability of mental retardation. A young child with an OFC more than 3 SD below the mean for age has an approximately 50 percent chance of being mentally retarded, although this risk may be modified by OFC growth velocity and family history. It is important always to measure the parents’ OFCs when possible. Among individuals with microcephaly and cognitive disability, acquired causes, including fetal alcohol exposure, hypoxic-ischemic injury, congenital infections, and untreated maternal phenylketonuria (MPKU), are more common than inherited disorders. Despite this, there are hundreds of genetic syndromes that cause microcephaly. Genetic mutations associated with non-syndromic microcephaly have now been described and clinical testing likely will be available soon. Specific diagnosis, if possible, may require extensive testing, and referral to a pediatric neurologist or medical geneticist may be valuable. Selected disorders associated with microcephaly are listed in Table 13.1-3.

Table 13.1-3: Selected conditions associated with microcephaly

- Acquired causes
  - Alcohol-related birth defects
  - Hypoxic-ischemic injury (pre- and postnatal events)
  - Congenital infections (TORCHS, HIV)
  - Untreated Maternal phenylketonuria (MPKU)
  - Postnatal meningoencephalitis (bacterial and viral)
  - Early non-accidental trauma
  - Severe malnutrition
- Genetic forms
  - Nonsyndromic microcephaly (familial and non-familial)
  - Chromosome abnormalities
Devastating conditions such as severe brain malformations and neurodegenerative diseases may cause microcephaly. While CT scan may reveal intracranial calcifications in some congenital infections and a few other conditions, MRI scan allows better assessment of white matter and the cerebral cortex and may show cortical malformations and neuronal heterotopias that may not be evident on a CT scan. Other salient ancillary tests are listed in Table 13.1-4.

Table 13.1-4: Selected ancillary studies for microcephaly

- Neuroimaging (MRI scan)
- Ophthalmologic examination
- Hearing evaluation
- Neonatal titers for TORCHS infections, HIV
- CBC, chemistry panel (including cholesterol level)
- Thyroid studies
- Chromosomal karyotype, subtelomeric FISH or DNA microarray testing
- Urine for metabolic screen and organic acids
- Serum lactate, pyruvate
- Specific gene testing when indicated
- Specific metabolic testing, including testing of spinal fluid
- Maternal phenylalanine level

In most cases, microcephaly cannot be corrected. Two specific causes, however, represent significant family planning and public health issues. Fetal alcohol exposure may be the most common cause of mental retardation; alcohol-related birth defects occur in 9/1000 children born in the United States. Affected children may not have features sufficient for diagnosis of fetal alcohol syndrome, yet still suffer cognitive disability and have concomitant retardation of brain growth. Likewise phenylketonuria (PKU), a formerly significant cause of mental retardation, has an incidence of 1:12000 and usually is discovered due to abnormal newborn screens.

Unfortunately, some phenylketonuric females of reproductive age do not continue to follow the prescribed dietary restrictions. These females may have only subtle deficits themselves but they (when pregnant) may expose the fetus to high phenylalanine levels in utero. The untreated PKU female therefore has potent teratogenic consequences for the fetus. The risk for a child of an
untreated PKU female is proportional to maternal phenylalanine level and approaches 100 percent with maternal levels over 1200 mg/dl. It is estimated that left unchecked maternal PKU will result in the same number of affected infants as did PKU before widespread use of newborn screening and dietary management. Any mother who has a child with microcephaly for which an etiology has not been established and who has not previously had a normal child, should be tested for PKU. This is done not only to prevent future affected children, but also to prevent neuropsychiatric sequelae that occur in adults with PKU who do not maintain their diets.

Conclusion
Macrocephaly and microcephaly are common. Approximately 5 percent of children are either macro- or microcephalic. The primary care physician must be able to identify even subtle cases, and spot emergent causes, and diagnose major and easily treatable causes. Diagnosis in more complex cases is important from therapeutic, family and public health perspectives; a specialist can refine the differential and provide appropriate treatment.

Selected Reading

Questions and Answers
Cranial Abnormalities
1. Advantages of MRI scan over CT scan include all of the following EXCEPT (choose all that apply):
   A. better visualization of the cerebral cortex
   B. better visualization of the posterior fossa
   C. less need for sedation
   D. better visualization of intracranial calcifications
2. Which of these findings is incompatible with a diagnosis of asymptomatic familial megalencephaly?
   A. female gender
   B. OFC +2.5 SD from mean
   C. mild mental retardation
   D. brother and father with large heads
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3. In the case of a 10-year-old boy with normal development but an OFC 2.5 SD below the mean for age, what is the most likely additional finding?
   A. father’s OFC 2.5 SD
   B. intracranial calcifications on CT scan
   C. coronal and sagittal craniosynostoses
   D. positive gene test for Rett syndrome

4. In a 6-month-old infant with macrocephaly, which of the following by itself excludes the need for further evaluation?
   A. normal development
   B. normal appetite
   C. normal head growth velocity
   D. family history of macrocephaly
   E. none of the above

5. In the case of a newborn child with OFC —4SD from mean, which finding below would be least consistent with this head size?
   A. normal development
   B. maternal binge drinking during the first trimester of pregnancy
   C. the child’s parents are first cousins
   D. somatic growth retardation

Cranial Abnormalities
1. C, D
2. C
3. A
4. E
5. A

Paroxysmal Non-Epileptic Disorders in Children

Introduction
Paroxysmal non-epileptic events are frequently encountered in the pediatric patient population and can be mistaken for epileptic seizures. Up to 20–25 percent of patients referred with the diagnosis of seizures may have non-epileptic paroxysmal disorders and it is important to differentiate between them. Age-based classification of these non-epileptic disorders occur is given in Table 13.1-5 and some of the common non-epileptic events occurring in different age groups are described.

Breath-holding spells (cyanotic infantile syncope)
Breath holding spells may be cyanotic or pallid. Cyanotic breath holding spells are more common.
Cyanotic Breath-holding spells
Cyanotic breath-holding spells are seen in approximately 4.6 percent of children,
with a peak incidence between 6 and 18 months. There is a positive family history in 25–35 percent of patients. Episodes are commonly precipitated by minor injury, fright or frustration, resulting in vigorous crying. The infant becomes apneic (holds breath in expiration), cyanotic and loses consciousness and muscle tone. When prolonged, it may be associated with stiffening and brief clonic movements and maybe confused for a seizure. Following the breath holding spell, the child rapidly regains consciousness. Rarely a breath-holding spell may actually evolve into a true generalized tonic-clonic seizure, presumably triggered by cerebral anoxia.

It has been proposed that vigorous crying leads to hypocapneic cerebral ischemia, compounded by arterial oxygen desaturation from apnea and reduced cardiac output from raised intrathoracic pressure is the underlying pathophysiology.

**Pallid Breath-holding spells**

These episodes are precipitated by a sudden, unexpected unpleasant stimulus such as a mild injury, usually to the head (without associated crying) followed by collapse with pallor, diaphoresis, bradycardia and loss of consciousness. The patient may be limp, and have posturing and clonic movements. It may progress into a generalized tonic-clonic seizure presumably due to cerebral ischemia.

In these patients, ocular compression often induces prolonged asystole. A hypersensitive vagal mediated cardiac inhibitory reflex with transient cardiac asystole resulting in syncope due to cerebral ischemia is thought to be the underlying pathophysiology.

Breath-holding spells are often mistaken for epileptic seizures and it is important to differentiate the two to avoid unnecessary treatment with anticonvulsants. Breath-holding spells are always preceded by a precipitating event followed by a sequence of crying, apnea and cyanosis and do not occur spontaneously or during sleep. With a seizure, the child stiffens rather than becoming limp and may have clonic movements of the extremities (Table 13.1-6). Treatment of breath-holding spells involves parental reassurance that it is a benign and self-limited condition. Atropine and pacemaker implantation have been used in patients with pallid breath-holding spells with variable success.

**Shuddering attacks**

The onset is usually in infancy or early childhood. They are characterized by sudden flexion of head, trunk and elbows, with adduction of elbows and knees associated with rapid tremulous contraction of the musculature and no loss of consciousness. This is similar to a sudden brief shiver that occurs when exposed to cold. Frequency is variable and there may be multiple episodes in a day or there may be periods of several weeks without episodes. Episodes may also occur in clusters. Parents need to be reassured that this is a benign and self-limited condition and treatment is not required.

**Stool-withholding activity and constipation**

The child may exhibit episodic, abnormal behavior due to perineal discomfort experienced during stool withholding, usually associated with chronic constipation. It is characterized by sudden interruption of activity with assumption of a motionless posture of slight truncal flexion, occasionally with brief generalized jerks, seen when the child is experiencing paroxysmal
discomfort associated with withholding stool. The behavior resolves with treatment of constipation.

**Self-stimulatory behavior**

These are episodes of genital self-stimulation seen in infants and young children. The behavior is stereotypic, characterized by tightening of thighs with pressure to pubic or suprapubic area. These rocking, rhythmic movements may continue for minutes to hours, and are often accompanied by irregular breathing and flushing. They may be mistaken for episodes of abdominal pain or dystonia, resulting in unnecessary evaluation. Treatment includes parental reassurance.

**Rhythmic behavior disorder (Head banging, Jactatio Capitis Nocturnus, body rocking, Rhythmie du soleil)**

These are stereotypic repetitive movements involving the large muscles of the body (usually head and neck), occurring during transition from wake to sleep, continuing into light sleep. The intensity of the movements can vary from single turns of the head on pillow to involvement of entire body. They are seen in children between one to five years of age, usually starting before 18 months of age. These movements are seen in about 30 percent of children at 1 year, decreasing to only 2 percent at 5 years of age. They are more common in children with mental retardation. Usually, no specific treatment is indicated. The bed should be padded to avoid injury. Clonazepam may be used if the episodes are potentially injurious, or interfere with normal sleep.

**Stereotypies**

These are more complex motor behaviors that are not truly stereotypic and consist of different movements in each episode. The movements themselves are repetitive, rhythmic, coordinated, non-reflexive and seemingly purposeful, most commonly affecting the upper extremities. They are suppressed by distraction and are usually brief, lasting from seconds to less than 15 minutes. They occur several times a day, often in clusters, and are commonly provoked by excitement, stress, fatigue, and boredom. They do not occur during sleep, and daily activities are rarely affected. These complex physiologic motor stereotypies occur in children, usually starting before three years of age. They may be seen in children with normal development and intelligence though neurobehavioral problems such as learning disabilities and attention deficit hyperactivity disorder are commonly present. They may also be seen in children with autism, mental retardation and sensory deprivation. The movements are usually chronic, with resolution seen in only a small percentage of patients by 11–12 years. Stereotypies may be mistaken for tics and differences between these two disorders are outlined in Table 13.1-7.

**Tics**

Tics are sudden, brief, rapid, repetitive, non-rhythmic, involuntary movements that may be motor, vocal or both. Attempts to suppress these movements only results in an increasing urge to perform them, with relief upon doing so. They are enhanced by emotional excitement and stress and persist during sleep. Motor tics commonly involve face, neck and shoulders. They are divided into simple and complex types. The simple motor tics include sudden, brief, meaningless movements such as blinking, grimaces, head jerking, shoulder shrugs and arm or leg jerks. Complex motor tics include more purposeful appearing activity such as bruxism, jumping, skipping, touching or smelling objects or self. Vocal tics are
also divided into simple and complex, ranging from throat clearing, grunting, and coughing to uttering syllables, phrases and profanities (coprolalia). Tics may be transient or lifelong.

Tourette’s syndrome is an autosomal dominant disorder. It usually begins in childhood between 2–13 years of age. It is characterized by multiple motor tics and vocalizations which have been present for at least 12 months. Behavioral abnormalities such as attention deficit hyperactivity disorder and obsessive compulsive disorder are common. Dopamine antagonists (e.g. haloperidol) have been effective in controlling tics. Other drugs such as guanfacine, risperidone, and clonidine are also effective.

**Disorders with Paroxysmal dystonia/choreoathetosis**

**Paroxysmal kinesiogenic choreo-athetosis (PKC)**

PKC is characterized by brief episodes of dystonic and choreoathetotic movements induced by movement or fright. They may be unilateral or bilateral and are not associated with unresponsiveness or incontinence. The attacks are brief, lasting from few seconds to minutes. The attacks begin between 5 and 16 years of age. Idiopathic, familial (autosomal dominant and recessive patterns) and symptomatic forms have been described. Symptomatic cases are less common, and have been described in association with multiple sclerosis, head injury, hypoparathyroidism, basal ganglia calcification, and stroke. Even though the attacks are non-epileptic, they do respond to relatively low doses of anticonvulsants such as phenytoin, or carbamazepine.

Paroxysmal nonkinesiogenic dystonic choreoathetosis (PDC) is another paroxysmal disorder with dystonia/choreoathetosis. Differences between these disorders are outlined in Table 13.1-8.

**Nocturnal Paroxysmal Dystonia**

This is an uncommon disorder characterized by brief episodes in sleep of choreoathetoid, dystonic posturing or violent ballistic flailing of extremities lasting less than a minute. These movements are stereotypic, occurring several times each night in NREM (usually stage 2) sleep. These brief episodes are partial seizures arising from the supplementary motor cortex in the mesial frontal region. The EEG however is normal. Patients respond to carbamazepine.

**Pseudoseizures**

Pseudoseizures are episodic, behavioral spells that mimic true epileptic seizures. The term non-epileptic seizures is preferred, because it is more neutral. They are common, accounting for 5–20 percent of the outpatient epilepsy population 10–40 percent of patients with pseudoseizures also have epileptic seizures. Majority of the patients are female. Pseudoseizures commonly occur between 15–35 years of age, but are also seen in children. Clinical features that differentiate non-epileptic seizures from epileptic seizures are outlined in Table 13.1-9. Traumatic and stressful events such as sexual and physical abuse, bereavement, and parental divorce are commonly present. Psychiatric illness such as depression and dissociative disorders are more commonly seen in adults. Video-EEG is usually needed to make a definitive diagnosis. It is important to convey the diagnosis to the patient in a non-judgmental manner. The patient is referred for psychotherapy, to learn coping skills to deal with the ongoing stressors. Patients may have been mistakenly placed on anticonvulsant therapy for misdiagnosed pseudoseizures. In this case, anticonvulsants should be
weaned slowly, and it should be stressed that the patient-physician contact will be maintained so that the patient does not feel abandoned. Family involvement is important for a good outcome. Consultation with a neurologist is helpful in these cases.

Table 13.1-5: Classification of Paroxysmal Non-Epileptiform disorders based on age of onset

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Wake</th>
<th>Sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>Jitteriness</td>
<td>Benign neonatal sleep myoclonus</td>
</tr>
<tr>
<td>&lt;8wks</td>
<td>Stiff baby/hyperexplexia</td>
<td>Rhythmic movement disorder</td>
</tr>
<tr>
<td>Infants</td>
<td>Breath holding spells</td>
<td></td>
</tr>
<tr>
<td>2 months–2 years</td>
<td>Shuddering attacks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spasmus Nutans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stereotypies</td>
<td></td>
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<tr>
<td></td>
<td>Self-stimulatory behavior</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stool withholding/constipation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Benign myoclonus of early infancy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hyperexplexia</td>
<td></td>
</tr>
<tr>
<td>Children 2–12 years</td>
<td>Stereotypies</td>
<td>Head banging</td>
</tr>
<tr>
<td></td>
<td>Syncope</td>
<td>Parasomnias—Sleep terrors, sleep walking</td>
</tr>
<tr>
<td></td>
<td>Migraine/variants (cyclic vomiting, benign paroxysmal vertigo)</td>
<td>Hyptic jerks</td>
</tr>
<tr>
<td></td>
<td>Tics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paroxysmal torticollis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paroxysmal choreoathetosis (kinesiogenic, dystonic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastroesophageal reflux</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stool withholding/constipation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Self-stimulatory behavior</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudoseizures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Munchausen by proxy</td>
<td></td>
</tr>
<tr>
<td>Adolescents &gt;12 years</td>
<td>Syncope</td>
<td>Narcolepsy—sleep paralysis, hypnagogic hallucinations</td>
</tr>
<tr>
<td></td>
<td>Migraine and variants</td>
<td>Parasomnias</td>
</tr>
<tr>
<td></td>
<td>Paroxysmal choreoathetosis (kinesiogenic, dystonic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudoseizures</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tremor</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transient global amnesia</td>
<td></td>
</tr>
</tbody>
</table>

Table 13.1-6: Differentiation between Breath-holding spells and Epileptic seizures

|                               | Breath-holding spells                      | Epileptic seizures                           |
|                               | Trigger                                   | Spontaneous, fever, sleep deprivation        |
|                               | Occurrence during sleep                   | May occur during sleep                       |
|                               | Event                                      | Associated with stiffening and jerking of extremities |
|                               | Postictal state                           | Maybe prolonged                              |
|                               | Epileptiform abnormalities on EEG         | Usually present                              |
|                               | Treatment                                 | Anticonvulsant therapy                       |
Table 13.1-7: Differentiation between stereotypies and tics

<table>
<thead>
<tr>
<th>Stereotypies</th>
<th>Tics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>School age</td>
</tr>
<tr>
<td>Pattern</td>
<td>Patterned, predictable, identical</td>
</tr>
<tr>
<td>Movements</td>
<td>Flapping, waving arm/hand movements</td>
</tr>
<tr>
<td>Rhythm</td>
<td>Rhythmic</td>
</tr>
<tr>
<td>Duration</td>
<td>Prolonged, continuous</td>
</tr>
<tr>
<td>Premonitory urge</td>
<td>No</td>
</tr>
<tr>
<td>Trigger</td>
<td>Excitement, stress</td>
</tr>
<tr>
<td>Suppression</td>
<td>Distraction</td>
</tr>
<tr>
<td>Family History</td>
<td>Rarely positive</td>
</tr>
<tr>
<td>Treatment</td>
<td>Poor response</td>
</tr>
</tbody>
</table>

Table 13.1-8: Differentiation between paroxysmal kinesiogenic choreoathetosis (PKC) and paroxysmal nonkinesiogenic dystonic choreoathetosis (PDC)

<table>
<thead>
<tr>
<th>PKC</th>
<th>PDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Types</td>
<td>Idiopathic Familial (AR &gt; AD) Symtomatic (multiple sclerosis, stroke, head injury, hypoparathyroidism)</td>
</tr>
<tr>
<td>Precipitants</td>
<td>Movement, fright</td>
</tr>
<tr>
<td>Duration</td>
<td>Seconds to minutes</td>
</tr>
<tr>
<td>Daily frequency</td>
<td>Several</td>
</tr>
<tr>
<td>Response to anticonvulsants</td>
<td>Good</td>
</tr>
</tbody>
</table>

Table 13.1-9: Differentiation between non-epileptic seizures (pseudoseizures) and epileptic seizures

<table>
<thead>
<tr>
<th>Non-epileptic seizure</th>
<th>Epileptic seizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>Prolonged (several minutes)</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Fluctuating features</td>
</tr>
<tr>
<td></td>
<td>Usually during wakefulness</td>
</tr>
<tr>
<td></td>
<td>Preserved consciousness, avoidance behavior</td>
</tr>
<tr>
<td></td>
<td>Side to side head movements</td>
</tr>
<tr>
<td></td>
<td>Out of phase extremity movements</td>
</tr>
<tr>
<td></td>
<td>Forward pelvic thrusting</td>
</tr>
<tr>
<td></td>
<td>Emotional vocalization</td>
</tr>
<tr>
<td></td>
<td>Pupillary reflex retained</td>
</tr>
<tr>
<td>Incontinence</td>
<td>Rare</td>
</tr>
<tr>
<td>Tongue bite</td>
<td>Occasional</td>
</tr>
<tr>
<td>Postictal changes</td>
<td>None</td>
</tr>
<tr>
<td>Affect</td>
<td>La Belle indifference</td>
</tr>
</tbody>
</table>

References


Ataxia

Ataxia is incoordination of the muscles during a voluntary movement or that sustain a voluntary posture. Disturbance of coordination is caused by a dysfunction in the cerebellum or its connections (see Chapter 1). Damage to the cerebellar hemisphere causes a tendency to veer in the direction of the affected hemisphere with dystaxia and hypotonia of the ipsilateral limb. Abnormality of the cerebellar vermis results in head bobbing (titubation), gait and truncal ataxia and nystagmus. Involvement of the sensory pathways in the spinal cord and peripheral nerves results in a wide based gait and inability to maintain a standing posture with the eyes closed (Romberg’s sign). Based on duration and progression, ataxias can be classified into acute, subacute and chronic onset ataxias. Some of the common causes of acute ataxia are listed in Table 13.1-10.

Subacute and chronic onset ataxias are often hereditary in nature. Some of these are treatable and should be recognized. Some examples of treatable ataxias in this group include Bassen–Kornzweig or a-beta-lipoproteinemia syndrome and ataxia with vitamin E deficiency (both treatable with vitamin E supplementation), Hartnup disease (niacin supplementation), familial episodic ataxias (treated with acetazolamide), and Refsum disease (responds to dietary restriction of phytanic acid). There are several familial or hereditary ataxias that may have autosomal dominant or recessive inheritance. Friedreich’s ataxia and ataxia telangiectasia are inherited in an autosomal recessive manner while spinocerebellar ataxias of several types and dentatorubral-pallidoluysian atrophy (DPRLA) are autosomal dominant.

Friedreich’s ataxia

Friedreich’s ataxia is one of the more common inherited ataxias in children with an estimated prevalence of ~2 per 100,000 in the general population. It generally presents with progressive gait ataxia in the later half of first decade though the age of onset may be earlier or later in some children. As the disease progresses there is nystagmus, dysarthria, limb and head tremor, and incoordination and ataxia of the upper limbs. Auditory and ophthalmic involvement is common with hearing deficit and optic atrophy. Patients have scoliosis, and often associated pes cavus, and talipes equinovarus. Examination is characterized by absent deep tendon reflexes, Babinski signs, impairment of posterior column functions, and gait and upper limb ataxia. Axonal sensory neuropathy is demonstrable by electrodiagnostic studies. Diabetes mellitus and progressive cardiomyopathy complicate the course of the disease; hypertrophic cardiomyopathy is often the cause of death in these patients. Friedreich’s ataxia gene localizes to chromosome 9 and the disease is due to a trinucleotide expansion in the gene (FRDA) for frataxin. Diagnosis can be confirmed by demonstration of abnormally increased GAA trinucleotide repeats in the majority of patients and by point mutation in the gene in a distinct minority of patients when the clinical picture is characteristic. The normal number of GAA repeats is less than 33 while disease causing alleles contain more than 66 GAA repeats. The range of GAA repeats between 34–65 is labeled as premutation alleles.
Consultation with a geneticist or a genetic counselor is advisable. Alpha fetoprotein is often used as an initial screening test for ataxia telangiectasia. Molecular testing also is available for several of the dominantly inherited spinocerebellar ataxias.

**Acute Ataxias**

Acute ataxia has a rapid onset, reaching maximum severity in a period of hours to several days. The two most common childhood causes are drug intoxication and acute postinfectious cerebellitis. Rarely, bacterial meningitis may present with ataxia. Drugs that are commonly associated with ataxia include barbiturates, phenothiazines, anticonvulsants such as phenytoin and carbamazepine, antihistamines, benzodiazepines, tricyclic antidepressants and alcohol (Table 13.1-10). Ataxia is usually associated with some change in personality or sensorium. The parents should be carefully questioned concerning drugs accessible to the child in the home; urine and blood should be screened when intoxication is suspected. Poison control should be notified and appropriate treatment should be administered depending on the drug ingested and its blood levels.

**Acute Postinfectious Ataxia**

Acute ataxia following an infection (viral or bacterial) or immunization may be due to isolated postinfectious cerebellitis, acute demyelinating encephalomyelitis (ADEM), and sometimes ataxia may be the presenting complaint in Guillain-Barré syndrome (specifically the Miller Fisher type). The clinical picture is characterized by rapid onset of ataxia usually following a varicella infection, but other viral infections such as measles, mumps, Coxsackie B, and Epstein-Barr have also been implicated. Postvaricella cerebellitis usually affects preschool and elementary school age children. It begins approximately two weeks after the onset of the viral illness, often after the vesicles begin to clear, and evolves rapidly over two to three days. Rarely, ataxia may be concomitant with or precede a skin rash. Gait is prominently affected and ataxia varies from mild unsteadiness to complete inability to stand or walk; the child is otherwise normal. Other neurologic signs may be present when ataxia is part of the clinical picture in patients with ADEM and areflexia and a mild degree of ataxia may be present in children with Guillain-Barré syndrome (GBS).

CT scan and MRI of the head are usually normal in isolated acute ataxia. In patients with other neurological abnormalities associated with ataxia (such as in ADEM) the T2 weighted images of the MRI scan may show increased white matter signal. Spinal root enhancement may be seen in patients with Guillain-Barré syndrome. CSF is usually normal except for a possible mild pleocytosis. It is a self-limited disease with excellent prognosis and complete recovery in the vast majority of the children.

Ataxia is a major feature of the Miller-Fisher variant of the GBS syndrome that typically occurs 10–15 days following a viral illness. Miller-Fisher syndrome is characterized by areflexia, ataxia and ophthalmoplegia that commonly affects vertical gaze, especially upward gaze. Horizontal gaze is usually preserved. Elevation of CSF protein with mild or no pleocytosis is often present. Other conditions that may mimic the syndrome should be excluded (Table 13.1-10).

**Paraneoplastic Disorders**

A relatively acute onset ataxia associated with opsclocus (rapid chaotic
conjugate eye movements) and myoclonus (violent jerking of the limbs on attempted movements) should suggest the possibility of neuroblastoma. The association of eye and limb jerking has been termed “dancing eyes, dancing feet syndrome.” The tumor is often thoracic in location, but may be found in other regions such as the abdomen and pelvis. Diagnosis can be confirmed by CT or MRI of the chest and abdomen, and elevated urinary catecholamines (homovanillic acid—HVA and vanillylmandelic acid—VMA). The neuroblastoma should be surgically removed. Approximately half of these children will have an impairment of motor ability and one-third will have some disturbance in intellectual function. Similar syndromes may be seen following viral infections and may respond to ACTH or steroid treatment.

On rare occasions, posterior fossa tumors, anomalies of the cervico-occipital region such as Chiari I anomaly and hydrocephalus may present with acute ataxia. Thus, neuroimaging is warranted in almost all cases of acute ataxia, even though the yield of imaging in these patients is quite small. Ataxia may be the only manifestation of certain types of seizures such as absence seizures associated with Lennox-Gastaut syndrome, complex partial seizures or nonconvulsive status epilepticus. In these cases, ataxia may be paroxysmal and the child may appear confused and disoriented during the episode. The demonstration of epileptiform discharges on the EEG concurrent with the episodes is diagnostic, in which case appropriate anticonvulsants should be administered. Vascular and metabolic conditions (Table 13.1-10) may require appropriate investigations and treatment.

When faced with a child who is displaying unsteadiness or incoordination, the first task is to distinguish normal, age appropriate clumsiness from an abnormal examination. Once ataxia is identified and categorized as acute or chronic, appropriate laboratory studies should be ordered to establish the diagnosis. If the diagnosis remains unclear, referral to a specialist such as a child neurologist, neurosurgeon or geneticist may be appropriate.

Table 13.1-10: Selected etiologies of acute ataxia

Intoxication
Anticonvulsants (barbiturates, phenytoin, carbamazepine, clonazepam)
- antihistamines, benzodiazepines, phenothiazines, tricyclic
- antidepressants, alcohol, Tic paralysis poisoning

Infections
- brain stem encephalitis, bacterial meningitis, viral infections (varicella, mumps, measles, Coxsackie, Echo, Epstein-Barr), cerebellar abscess

Postinfectious
- acute postinfectious cerebellitis (varicella), Miller-Fisher syndrome, acute demyelinating encephalomyelitis

Neoplastic and paraneoplastic disorders
Neuroblastoma, cerebellar tumors

Traumatic and vascular
- postconcussion, cerebellar (and brainstem) infarction (ischemia and hemorrhage), posterior fossa hematoma
Multiple sclerosis

Epilepsy
  - nonconvulsive status epilepticus, Lennox-Gastaut syndrome, complex-partial seizures

Basilar migraine

Conversion reaction

Metabolic

Hypoglycemia, intermittent maple syrup urine disease, Familial episodic ataxia, mitochondrial cytopathies

**Selected Reading**


**Epilepsy in Children**

**Incidence**

Approximately 9 percent of the United States population will have a seizure sometime during their lives; 3 percent of these have epilepsy. At least 1 percent of children can be expected to have an afebrile seizure by 14 years of age. The risk of recurrent afebrile seizures ranges from 4–8.1 per 1000 by age 11. Principles of recognition, classification and treatment are similar in children and adults. Focal or partial seizures are perhaps more common than primary generalized seizures though recognition of focal onset is often difficult in young children. Some epilepsy syndromes are seen uniquely in children. The more common syndromes are described here.

**Neonatal Seizures**

Neonatal seizures differ from those in older children and adults. They are often fragmentary and generalized seizures are uncommon except in the term infants. Table 13.2-1 lists some of the common etiologies. Neonatal seizures may or may not always be associated with EEG changes. Neonatal seizures most frequently have subtle clinical manifestations, such as sucking, lip smacking or other oral-buccal-lingual movements, bicycling or pedaling movements, rhythmic ocular movements such as horizontal eye deviation and occasionally apneic spells. Other seizure manifestations include focal clonic, tonic and myoclonic seizures. Intracranial infection must be considered and excluded unless some other etiology is apparent. Management includes treatment of the underlying cause, eg, infection, electrolyte or metabolic abnormalities. Phenobarbital is the drug of choice for seizure control in this age group. Phenytoin maybe added if phenobarbital is not sufficient to control the seizures.
West Syndrome (Infantile spasms, Blitz-nick-salaam krampfe)

West syndrome comprises a triad of infantile spasms, arrest of psychomotor development and EEG features of hypsarrhythmia. Several infantile spasms occur in clusters. Spasms maybe flexor, extensor or, more commonly, mixed. Onset peaks between 4 and 7 months of age. West syndrome is divided into two groups: 1) the smaller cryptogenic group comprises 30–40 percent of the patients in whom no known etiology is identified, and 2) the symptomatic group is characterized by the existence of previous brain damage as evidenced by psychomotor retardation, neurological and radiologic signs or by a known etiology. Tuberous sclerosis may present as infantile spasms. Therefore, a careful examination of the skin for cutaneous stigmata of tuberous sclerosis such as adenoma sebaceum and ash-leaf spots is important.

Infantile spasms are treated with adrenocorticotrophic hormone (ACTH); early therapy is thought to improve prognosis. Other therapies are less effective and prednisone, valproic acid, topiramate, vigabatrin (not available in the USA) and pyridoxine (vitamin B6) have also been used with variable results. The prognosis is generally poor with 25–50 percent of the cases evolving into Lennox-Gastaut syndrome, with the spasms transforming into other seizure types (tonic, myoclonic and generalized tonic-clonic seizures). There is a high incidence of mental retardation.

Lennox-Gastaut Syndrome

This syndrome manifests in children from 1–7 years of age, and a significant number of patients have previous history of infantile spasms. Multiple seizure types are common in this syndrome. Most common seizures are tonic, atonic, and atypical absence seizures but myoclonic, generalized tonic-clonic seizures (GTCS) and partial seizures also occur. EEG exhibits slow background activity and generalized bisynchronous 1–2 cps (cycles per second) spike and slow wave discharges. The seizures are difficult to control and prognosis is poor with psychomotor retardation. Antiepileptic medications, which are often only partially effective, include valproic acid, lamotrigine, topiramate and levetiracetam. Sedative anticonvulsants should be avoided if possible, because these drugs may increase seizure frequency by decreasing alertness. These patients are best managed by epilepsy specialists.

Febrile Seizure

Febrile seizures occur in 2–5 percent of children with a peak between the age of 6 months to 2 years. Most children have a single febrile convulsion; only 0.5 percent have recurrent febrile seizures. The seizures are brief (< 1.5 minutes), generalized tonic clonic seizures that usually occur at the onset of a febrile illness in an otherwise healthy child and in the absence of intracranial infection or a defined cause such as severe metabolic disturbance. Most children have a single episode of febrile convulsion and there is no evidence that these brief events lead to later CNS damage. Treatment is normally withheld after the initial seizure. For a child with recurrent simple febrile seizures and in situations when parental anxiety is severe, intermittent oral diazepam at the onset of the febrile illness has been advocated by some to prevent recurrence. Rectal Diazepam may be used for prolonged seizures. Antipyretics may not be effective in preventing recurrent febrile seizures. There is no convincing evidence that therapy will alleviate the possibility of developing future epilepsy. Children with simple febrile seizures and normal development have only a 1.5 percent
chance of developing epilepsy. This increases to 3–4 percent in the presence of risk factors that include the occurrence of complex febrile seizure (prolonged seizure with focal features and more than one seizure in 24 hours), underlying developmental or neurological abnormalities and family history of nonfebrile seizures. Many physicians do not treat simple febrile seizures. In cases of complex febrile seizures treatment options include phenobarbital and valproic acid. It is important to differentiate febrile seizures from seizures that have been precipitated by fever in epileptic children.

**Benign Childhood Epilepsy with Centrotemporal Spikes**

Previously known as Benign Rolandic Epilepsy, this syndrome comprises 75 percent of the benign focal childhood epilepsies. It occurs most commonly between 6 and 16 years of age (peak 9–10 years), with male predominance and a genetic predisposition. The seizures usually occur during sleep and are brief, simple focal motor seizures characterized by hemifacial grimacing and twitching, inability to speak and salivation. Generalized tonic-clonic seizures are not uncommon. EEG shows high amplitude unilateral or bilateral centro-temporal spikes that are activated by sleep. Prognosis is excellent with approximately 13–20 percent of patients experiencing only a single seizure. Treatment is usually unnecessary after the first or even the second seizure. Most anticonvulsants have been reported to be successful. Carbamazepine is the drug of choice, but valproic acid is also effective. Antiepileptic medications are maintained up to 14–16 years of age at which time seizures spontaneously resolve.

**Childhood Absence Epilepsy (Pyknodeps)**

Childhood Absence Epilepsy has a peak age of 6–7 years and is more frequent in girls. It is characterized by frequent daily absence seizures; GTCS may occur during adolescence. Family history is often strongly positive. Though development and neurologic examination are normal, school performance may suffer because of frequent interruption of awareness, which may be misinterpreted as daydreaming or attention deficit. EEG reveals paroxysms of generalized bisynchronous high amplitude 3 cps spike and slow wave discharges, which are markedly activated by hyperventilation. Fifty percent of patients with absence seizures become seizure free, 35 percent develop GTCS in adolescence and absences persist in the rest. Absence seizures may be a harbinger of juvenile myoclonic epilepsy, appearing approximately 4.5 years prior to the appearance of the myoclonic seizures and GTCS. Ethosuximide and valproic acid are the drugs of choice. Lamotrigine and clonazepam have also been found to be effective. Ketogenic diet may be effective for intractable cases. Absence seizures are exacerbated by carbamazepine and therefore should be clinically differentiated from complex partial seizures prior to initiation of therapy. Patients whose seizures are refractory to ethosuximide and valproic acid may need management by a neurologist.