Acute hemiplegia in childhood

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Originally released June 19, 1995; last updated September 12, 2016; expires September 12, 2019

Introduction

Overview

Acute hemiplegia in childhood poses a diagnostic and management challenge for the clinician. Seizure and migraine are common etiologies. However, pediatric stroke is also a common cause of acute hemiplegia and needs to be promptly differentiated from other causes. In this recently updated article, the authors discuss recent advances in understanding the risk factors for and the etiology of stroke.

Key points

- Acute hemiplegia in children is often accompanied by headache. Tingling paresthesias as well as visual, sensory, or dysphasic auras are more common with headache associated with hemiplegic migraine than with acute hemiplegia due to stroke, where negative symptoms predominate.
- Acute hemiplegia after seizures is most frequently a Todd postictal paralysis, but stroke still needs to be considered when the paralysis is prolonged because children have seizures with stroke relatively frequently.
- Acute hemiplegia after a sports injury can be the result of trauma (hemorrhage or contusion), seizure with a Todd paralysis, hemiplegic migraine, or an arterial dissection. Appropriate imaging including MRA is required to evaluate for dissection because anticoagulation may be necessary to avoid progression.
- Focal cerebral arteriopathy is the most common cause of hemiplegia due to stroke in childhood. Onset of the hemiplegia is often subacute; preceding infections are relatively common especially in younger children; and recurrence risk is higher than with many other stroke types.
- Acute hemiplegia in childhood resulting from arterial ischemic stroke may eventually be regularly treated with thrombolytic therapy. This can currently be considered in children older than 12 years at institutions with stroke teams who are experienced in treating adult stroke in this manner. Clinical trials are in progress to determine the efficacy of thrombolytic therapy in children.

Historical note and terminology

The occurrence of unilateral weakness related to contralateral brain injury was already familiar to ancient physicians like Hippocrates and Aretaeus. Jusepe Ribera, a 17th century Spanish artist, painted a portrait of young soldier with hemiplegia. Early observations of acute hemiplegia were based on experience with penetrating head injury, intracranial hemorrhage, and epileptic seizures. In the late 18th century, Darwin experimented with electrical therapy for children with hemiplegia (Gardner-Thorpe and Pearn 2006). Todd described a post-epileptic hemiplegia in 1865 (Todd 1865), and in 1887 Freud described acute childhood hemiplegia associated with epilepsy (Pearce 2003). In 1916, Higier described hemiplegic seizures (Higier 1916). Seminal papers by Bickerstaff (Bickerstaff 1964), Aicardi and colleagues (Aicardi et al 1969), and Carter (Solomon et al 1970; Hilal et al 1971) focused mainly on childhood stroke and heralded the modern approach to evaluating acute childhood hemiplegia, caused by stroke. Our knowledge of the causes and treatment of both transient and permanent acute childhood hemiplegia have increased exponentially in the past decade due in no small measure to the International Pediatric Stroke Study (IPSS) initiative (Lynch et al 2002). In addition, structural and functional brain MRI, as well as traditional and MR angiography, have contributed to our understanding of the multiple causes and pathophysiology of acute hemiplegia in childhood.

Clinical manifestations

Presentation and course
Clinical manifestations, course, and outcome of acute hemiplegia vary depending on the etiology.

**Stroke.** Acute hemiplegia, a common presentation of arterial ischemic stroke (Mancini et al 1997; Ganesan et al 2011), appears suddenly in 50% of cases but is subacute (evolving over hours) in 35% and stuttering in onset in 15% (Dusser et al 1986). Arteriopathy in contrast to other causes for stroke almost always presents with hemiparesis as opposed to multifocal or bilateral symptoms (Mackay et al 2011). Subacute onset also suggests an underlying arteriopathy (Braun et al 2007). Duration of hemiplegia varies from days to weeks; deficits can be permanent. Etiology and location of lesion determine outcome. Seizures and headache may precede, present with, or follow arterial ischemic stroke in as many as a third of patients or more (Dusser et al 1986; Chadehumbe et al 2009; Hartman et al 2009; Abend et al 2011; Singh et al 2012) and may delay the proper diagnosis (Shellhaas et al 2006). Seizures are particularly common in children younger than 1 year of age who may or may not have an apparent hemiparesis (Zimmer et al 2007). Other neurologic signs can co-occur with hemiplegia, eg, hemisensory or visual deficit, aphasia, or constructional apraxia, depending on the location and type of the lesion. When seen in cerebral venous sinus thrombosis with associated infarction, acute hemiparesis is often accompanied by altered consciousness, headache, and seizures. Predisposing conditions are common, eg, dehydration and systemic diseases (Dlamini et al 2010).

**Hemorrhage.** Hemorrhage can occur in the setting of stroke (arterial or venous), vascular malformations and aneurysm, neoplasms, congenital heart disease, head and neck trauma, and hematologic disorders. Hemiplegia is generally abrupt in onset, except for hemorrhagic strokes, in a specific vascular territory. Headaches and seizures are common (Lo et al 2008; Chadehumbe et al 2009). In younger children, the clinical presentation may be nonspecific, whereas in older children (over 6 years of age) a focal deficit or hemiplegia is the rule (Lo et al 2008).

**Hemiplegic migraine.** Hemiplegic migraine usually has a slowly progressive onset evolving over 5 to 30 minutes, but in 5% to 10% of cases onset is abrupt, peaking in less than one minute (Thomsen et al 2003). In about 15%, the hemiplegia shifts sides during an attack. Weakness lasts less than 1 hour in 51% of cases, 1 to 24 hours in a subsequent 41%, and more than 24 hours in an additional 8% (Thomsen et al 2003). In hemiplegic migraine, positive symptoms (particularly paresthesias) often precede the hemiplegia (Gelfand et al 2010), and more typical auras (visual, sensory, or dysphasic) often co-occur with the hemiplegia. Headache can precede or occur at the same time as the aura or follow it—generally within an hour. A structural lesion needs to be ruled out as both arterial ischemic stroke and cerebral venous sinus thrombosis occur in migraineurs, at least in adulthood, at a greater frequency than in the general population, and headaches, especially in children, can occur at the onset of stroke. It is not known whether prolonged aura (more than 1 hour but less than 7 days) or persistent aura (more than 7 days) increases the risk for stroke. However, hemiplegic migraine does not specifically confer a greater risk of stroke than migraines with other auras (Klapper et al 2001).

**Seizures: ictal and Todd postictal paralysis.** Todd postictal paralysis is identified by its context; it occurs after a seizure. Duration ranges from minutes to days. Todd postictal paralysis usually resolves in less than 30 minutes (Gallmetzer et al 2004). Hemiplegia lasting more than 6 to 24 hours is unusual (Gelfand et al 2010). However, Todd himself reported episodes lasting for days (Todd 1865). Rarely, focal weakness may be the only manifestation of a seizure and generally lasts 30 minutes (Oestreich et al 1995; O’Donovan et al 2007). A hemiconvulsion-hemiplegia-epilepsy syndrome has been described and is characterized by a prolonged clonic seizure with unilateral predominance occurring during a febrile illness followed by subsequent hemiplegia (Auvin et al 2012). Mutations in sodium channel genes SCN1A and SCN2A are a predisposing factor for this syndrome. It is hypothesized that altered channel activity resulting from these mutations provokes both seizures and subsequent excitotoxic brain damage (Saitoh et al 2015).

**Demyelinating disorders.** Onset of hemiplegia in disorders affecting white matter, such as acute disseminated encephalomyelitis and leukoencephalopathy due to toxin or medication side effects, is more often subacute than acute and is often associated with an encephalopathy.

**Conversion disorder.** In conversion disorder, the hemiplegia usually appears suddenly and is typically temporally related to a psychological stressor (American Psychiatric Association 2000). Other psychiatric disorders (ie, depression and anxiety) may coexist.

**Prognosis and complications**

Outcome after acute hemiplegia is highly variable and depends on the underlying cause. Pooled data from several studies of children with arterial ischemic stroke indicate that 30% were neurologically normal, 61% had motor or
cognitive problems, and 9% died (Lynch and Han 2005). Epilepsy develops in 10% to 15% of children with arterial ischemic stroke (DeVeber 2003). Following intracerebral hemorrhage, 42% of children are normal and 32% have persistent deficits, with 25% mortality, and epilepsy in 11% (Lynch and Han 2005). Imaging studies suggest that acute involvement of the descending corticospinal tract on diffusion-weighted imaging is a harbinger of poor motor outcome (Domi et al 2009). In contrast, the outcomes in hemiplegic migraine, Todd postictal paralysis, and conversion disorder are generally excellent.

Clinical vignette

A previously healthy 9-year-old, right-handed boy was brought to the emergency room with left-sided weakness of subacute onset. He had complained of a generalized headache lasting for about an hour earlier that day. The hemiplegia began in his arm and progressed over the next half hour to involve his leg and face as well. He had a mild upper respiratory illness with a fever of 101˚F about 10 days before. There was no history of trauma, and there was no indication of a seizure. He was born at term without complications, his development was normal, and he was a good student at school. He had no chronic medical conditions, was taking no medications, and had never been hospitalized nor had surgery. Immunizations were up-to-date. There was a family history of migraine on the maternal side but no family history of epilepsy or stroke. On examination, he was afebrile with normal vital signs. He was 4 foot 6 inches and weighed 70 pounds; head circumference was 53 cm. There were no abnormal skin findings. General medical examination was unremarkable. He complained of a mild generalized non-pounding headache (3 of 10). He had difficulty copying a cube and showed a left hemineglect on a line bisection task. Cranial nerve examination revealed a left homonymous hemianopsia. Funduscopic examination was normal. Extraocular movements were full, and pupils were equal and reactive to light. There was flattening of the left nasolabial fold. Left arm and leg were flaccid with strength of 0/5; strength was 5/5 in the right arm and leg. Pinprick sensation on the left was probably slightly diminished, and he complained of some dysesthesia; graphesthesia and stereognosis were impaired. There was no dysmetria or dysdiadochokinesis on the normal right side. Gait could not be examined. Deep tendon reflexes were diminished on the left, and a Babinski sign was present. MRI of the brain obtained 2 hours after the ictus showed restricted diffusion in the right middle cerebral artery territory. The MRA revealed focal stenosis of the right middle cerebral artery. MRI of the neck was normal. His diagnosis was arterial ischemic stroke due to focal cerebral arteriopathy.

Workup including electrocardiogram, echocardiogram, thrombophilia studies, comprehensive chemistry panel, lactate, pyruvate, ammonia, urine organic acids, serum amino acids, rheumatologic studies (ESR, CRP), and urinalysis were all normal or negative.

Little improvement of his left hemiplegia occurred over the first week. He was discharged to a rehabilitation center on aspirin. At the 6-month follow-up, he was able to ambulate but still had a moderate hemiparesis with more involvement of the arm than the leg. MRI showed a chronic middle cerebral artery infarction. The MRA was unchanged from the time of the stroke.

Biological basis

Anatomic localization

The corticospinal tracts arise from somatotopically organized areas of primary motor cortex, lateral premotor cortex, and supplementary motor area as well as the primary sensory cortex in the postcentral gyrus, ie, the anterior paracentral gyrus, superior parietal lobule, and areas of the cingulate gyrus. The corticospinal tract descends in the corona radiata, the posterior limb of the internal capsule, the middle three fifths of the cerebral peduncle, the pons, and the medullary pyramids. Thus, lesions in any of these areas can result in hemiparesis of varying degree and distribution. Corticospinal neurons within the motor cortex are somatotopically organized in accordance with their functional importance; the size of the cortical representation in the motor homunculus varies with the functional importance of the body part represented. For example, isolated hand weakness of cortical origin may present with loss of thumb and finger movements and impaired hand flexion and extension, or it may occur with only partial involvement of a few digits. The corticospinal tract is also organized somatotopically in the posterior limb of the internal capsule with hand fibers lateral and slightly anterior to foot fibers, in the pons with fibers controlling the proximal muscles placed more dorsally than those controlling more distal muscles, and in the medullary pyramids with fibers of the lower extremities placed more laterally and decussating more rostrally than those of the upper extremities. Depending on the location of the lesion relative to the corticospinal tract pathway, a hemiparesis of
vascular origin may predominantly involve the upper or lower extremity with or without other associated findings, except for the pure motor hemiparesis of pontine lesions where the deficit is equal and spares the face (Brazis et al 2007). Cervical cord lesions can also cause hemiparesis secondary to compression of the corticospinal tracts.

**Stroke.** Most arterial ischemic strokes in children affect large vessels and occur in the distribution of the middle cerebral artery (Mancini et al 1997; Ganesan et al 2011); thus, these strokes not only produce hemiparesis but may also cause hemidysестhesia, hemianopsia, and aphasia (if it involves the dominant hemisphere) or constructional apraxia (if it involves the nondominant hemisphere). Infarction confined to the basal ganglia produces contralateral hemiparesis or movement disorder. Infarction of the small vessels penetrating the internal capsule typically presents with dysarthria, hyperalgesia, or decreased position sense along with hemiparesis. Lacunar strokes are rare in children. The anterior circulation is affected more often than the posterior circulation except in children with cardiac disease and in vertebral dissection (Ganesan et al 2002; Dowling and Ikemba 2011).

Among the arteriopathies (focal stenosis involving the distal internal carotid artery or proximal middle cerebral artery or anterior cerebral artery), localization of arterial ischemic stroke varies by type—moyamoya disease, arterial dissection, focal cerebral arteriopathy. In a focal cerebral arteriopathy series, children with a history of varicella infection were more likely to have basal ganglia infarcts and recurrent arterial ischemic stroke or transient ischemic attacks than those with no history of infection (Amlie-Lefond and Jubelt 2009). Children with moyamoya disease tend to have predominantly anterior distribution watershed infarcts. In adolescents and adults, early stage moyamoya disease is characterized by subcortical infarcts in regions supplied by the penetrating arteries. As moyamoya disease progresses, large cortical infarcts predominate in regions supplied by medullary arteries arising from the cortical branches. Hemorrhage occurs in the basal ganglia, with or without intraventricular extension, or can be primarily intraventricular. Subdural hematomas and subarachnoid hemorrhages are not uncommon in older patients with moyamoya disease (Scott and Smith 2009). Strokes in children with sickle cell disease and moyamoya arteriopathy generally occur in the anterior circulation (Pavlakis 1984). Dissections involve the anterior circulation of the intracranial carotid artery in about one half of patients and the posterior circulation originating at the C1/C2 level in the other half (Fullerton et al 2001). In cerebral venous sinus thrombosis, the associated stroke may be cortical or subcortical and often involves deep gray matter. Hemorrhagic infarcts are the rule. Subarachnoid and subdural hemorrhages also occur (Dlamini et al 2010).

**Hemorrhage.** Most nontraumatic hemorrhages are supratentorial, intraparenchymal, and lobar in location (Lo et al 2008). Subdural, subarachnoid, intraventricular, or a combination also occurs. Arteriovenous malformations are most often found along the middle cerebral artery in the parietal or frontal lobe. Hemorrhages are more common with small deep arteriovenous malformations than with large cortical arteriovenous malformations. Aneurysms occur predominantly in the anterior circulation (Hetts et al 2009).

**Hemiplegic migraine.** In hemiplegic migraine the neurologic deficits do not follow a traditional vascular pattern. Generally, the arm is more often affected or at least more involved than the leg (Gelfand et al 2010).

**Seizure: ictal and Todd postictal paralysis.** In Todd postictal paralysis, the severity and distribution of weakness are variable. Commonly, the arm and leg are affected to different degrees; unilateral facial weakness can occur. A unilateral Babinski sign can be present.

**Pathophysiology**

Acute hemiplegia in childhood is caused by an alteration in cerebral metabolism in a brain region involved in contralateral motor function. The specific mechanism of this metabolic derangement varies depending on the underlying cause.

**Stroke.** Although clinical history may be suggestive, neuroimaging is required to distinguish stroke from other causes of acute hemiplegia. The most common etiologies of stroke are arteriopathy (Amlie-Lefond and Jubelt 2009), infection, cardiac disorders, sickle cell disease, and thrombophilias (Jordan and Hillis 2011). Most children with stroke have multiple risk factors (Lanthier et al 2000).

The arteriopathies include focal cerebral arteriopathy, arterial dissection, moyamoya disease, and sickle cell disease as well as inflammatory conditions related to infection (meningitis, varicella) or immunologic vasculitic conditions. In cases of arterial ischemic stroke, excluding those due to sickle cell disease and cardiac disease, studies have revealed
cervical/cerebral arteriopathies characterized by dissection, occlusion, or stenosis in approximately 50% to 80% of previously healthy pediatric patients. In a retrospective review of 60 cases of pediatric arterial ischemic stroke that presented to a tertiary pediatric neurology center, cervical arteriopathy was demonstrated in 25%, and an additional 24% had intracranial arterial abnormalities (Ganesan et al 2011). A number of genetic disorders have associated arteriopathies (Munot et al 2011). Focal cerebral arteriopathy is the most common type (25%), followed closely by moyamoya disease (22%) and arterial dissection (20%). Recent upper respiratory tract infection appears to be a predictor for focal cerebral arteriopathy as the cause of arterial ischemic stroke, particularly in children 5 to 9 years of age (Amlie-Lefond and Jubelt 2009). Stroke from arterial dissections can be spontaneous, due to trauma or chiropractic manipulations to the neck or trauma to the soft palate (Fullerton et al 2001; Pierrot et al 2006). Arterial dissections are typically caused by emboli resulting from the migration of a thrombus that was originally located at the site of the subintimal dissection. Intracranial dissections account for 60% of pediatric anterior circulation dissections. Both intracranial and extracranial dissections can be associated with trauma (major or minor); however, children with severe trauma are more likely to have an extracranial dissection (Fullerton et al 2001). An indirect effect of infection on the blood vessels is suggested by the association between antecedent acute infection and spontaneous vertebral dissection. Thus, infectious agents or inflammatory reactions triggered by infections seem to have an important role in the pathophysiology of a number of the arteriopathies (Amlie-Lefond and Jubelt 2009).

Hemorrhagic stroke is due to disturbances of blood flow caused by occlusion of a cerebral artery or through rupture of a blood vessel, leading to diminished cerebral perfusion with concomitant ischemia. In cerebral venous sinus thrombosis with infarction, thrombosis within the venous system (more often superficial than deep) results in outflow obstruction, venous congestion, and an increase in hydrostatic pressure, which drives fluid into the interstitium and produces edema. Persistent increased hydrostatic pressure may result in venous infarction and hemorrhage and, if it is in excess of the arterial pressure, may also result in arterial ischemia. Predisposing conditions are common, including trauma, anemia, and acute and chronic medical problems like dehydration, infection, inflammatory bowel disease, thyrotoxicosis, and prothrombotic disorders (Dlamini et al 2010).

Most children with stroke due to cardiac disease have already been diagnosed at the time they have a stroke. Of approximately 200 children in the International Pediatric Stroke Study (IPSS) registry, 60% had congenital heart disease, 20% acquired heart disease, and 15% a patent foramen ovale. Strokes occur spontaneously, during catheterization, and during surgery. The presumed mechanism is cardioembolic, but as many congenital or acquired heart lesions can cause chronic hypoxia and polycythemia, it may be difficult to differentiate the contribution of embolic and thrombotic disease. In addition, children with cardiac disease have a higher frequency of thrombophilias than controls. Compared to other children with stroke, those with cardiac disorders are younger and are less likely to present with headache but are similar in terms of gender and presentation with focal deficits, seizures, or recent infection (Dowling and Ikemba 2011).

Prothrombotic conditions have been associated with stroke in children. These include activated protein C resistance (usually related to the factor V Leiden mutation), deficiencies of protein C or protein S, antithrombin III deficiency, prothrombin gene mutation, antiphospholipid antibody syndrome, elevated lipoprotein (a), and elevated homocysteine (Kenet et al 2000).

**Hemorrhage.** Hemorrhage causes hemiplegia as a result of mass effect or by specific involvement of the corticospinal tracts. Hemorrhages can be caused by vascular malformations (about 50%), brain tumors (10%), cardiac disease, hematological disorders, and medical illnesses (25%) (Lo et al 2008). In some cases, there is no definable cause. Intraparenchymal hemorrhages are generally due to vascular malformations or brain tumors (Lo et al 2008). Saccular aneurysms are 3 times more likely to hemorrhage than fusiform aneurysms (Hetts et al 2009). Subdural hemorrhages generally occur in the setting of hematological disorders or cardiac surgery. Subarachnoid hemorrhage is not associated with specific risk factors (Lo et al 2008). Sturge-Weber has been associated with spontaneous intracranial hemorrhages in some children (Nakajima et al 2014).

**Metabolic or genetic disorders.** Metabolic abnormalities such as hyper- and hypoglycemia and hypocalcemia result in inadequate energy supply to neurons. Inherited metabolic disorders can cause stroke-like episodes with hemiplegia, which are mediated by cellular energy failure, for example, in mitochondrial disorders like MELAS and organic acidemias. Disease-specific mechanisms for stroke have been documented in some genetic disorders (Testai and Gorelick 2010a; Testai and Gorelick 2010b; Munot et al 2011).

**Hemiplegic migraine.** Migraine auras of all types are due to cortical spreading depression characterized by brief
neuronal excitation, which initiates a depolarization wave that moves across the cortex at a rate of 3 to 5 mm/minute and is followed by a prolonged inhibition of neuronal activity. Whether hemiplegic migraine is qualitatively different from other migraines with aura is debatable. Mutations in 1 of 3 genes are responsible for 50% to 70% of familial hemiplegic migraine, ie, voltage-gated channels CACNA1A and SCN1A genes and the Na/K pump ATP1A2 gene (Russell and Ducros 2011).

Seizures: Todd postictal hemiplegia and ictal hemiplegia. In Todd postictal hemiplegia, neuronal exhaustion is considered the most likely cause. Todd believed in the context of his electrical theory of epilepsy that the hemiplegia resulted from undue exultation resulting in a state of depression or exhaustion (Binder 2004). Excessive inhibition is another proposed mechanism. Epileptic activity in the supplementary motor area or somatosensory cortex (Dale and Cross 1999) or temporopinsular area (Villani et al 2006) has been implicated in epileptic hemiparesis. Periodic lateralizing epileptiform discharges on EEG may be disproportionately frequent during ictal hemiparesis. Although the pathophysiological mechanism of hemiconvulsion-hemiplegia-epilepsy syndrome is not known, there are several factors that are believed to contribute to the pathogenesis. Inflammation and hyperthermia are known to worsen status epilepticus and prolonged status epilepticus damages the blood-brain barrier. The unilaterality may be due to regional maturation of the corpus callosum, focality of a neurotropic virus, and genetic predisposition (Auvin et al 2012). New research has identified missense mutations in sodium channel SCN1A and SCN2A that predispose children to encephalopathy with severe febrile seizures (Tenney and Schapiro 2012; Saitoh et al 2015).

Demyelinating disorders. Demyelination in the cerebral white matter or in the spinal cord results in hemiplegia primarily by slowing conduction through motor fibers.

Infection. Meningitis and encephalitis can cause hemiplegia via destruction of brain parenchyma (abscess), local inflammation, or vasculopathy (Chang et al 2003).

Neoplasm. A tumor may cause hemiplegia through compression of brain or cervical cord structures responsible for motor control by the mass lesion itself or surrounding edema or hemorrhage.

Head or neck trauma. Head trauma can cause acute hemiplegia through a variety of mechanisms, including shearing injury; intraparenchymal, epidural, subdural, or subarachnoid hemorrhage; or ischemic injury, which can be a primary effect due to dissection or secondary to vasospasm following subarachnoid hemorrhage. Repeated head trauma, as occurs in the setting of contact sports, may increase the risk of brain ischemia over time due to long-term vascular and neuronal changes (Brosch and Golomb 2011). Acute cervical cord compression causing hemiplegia may be spontaneous or the result of trauma (Fountas et al 2006).

Toxin or medication side effects. Toxic agents produce stroke via a range of mechanisms like vasculitis (eg, cocaine) or cause hemiplegia through myelin and axon loss, gliosis, and necrosis (eg, methotrexate leukoencephalopathy) (Lai et al 2004).

Conversion disorders. Atypical activation in motor cortex, basal ganglia, and thalamus in response to paretic limb stimulation (Liepert et al 2009) and atypical connectivity between the amygdala and the supplementary motor area (Voon et al 2010) as well as between the ventromedial and dorsolateral prefrontal cortex (de Lange et al 2010) are present in patients with conversion disorder. Motor mental imagery is impaired (Burgmer et al 2006). Together these data suggest an atypical relationship between emotion and motor function (Voon et al 2010).

Differential diagnosis

The differential diagnosis of acute hemiplegia is extremely broad, although stroke, migraine, and Todd postictal paralysis are the most common causes (Table 1).

Table 1. Causes of Acute Hemiplegia of Childhood
Stroke/hemorrhage
Epilepsy
Migraine
Alternating hemiplegia of childhood
Head or neck trauma
Neoplastic
Infectious
Metabolic disorders
Genetic disorders
Demyelinating disorders
Toxins and medications
Conversion disorder

Stroke. Stroke must be considered in any child presenting with acute hemiplegia. An etiology for stroke can currently be determined in about 80% of cases (Ganesan et al 2011) (see Table 2). Clinical clues are often present that permit a diagnosis even before imaging and workup.

Moyamoya disease and syndrome. Moyamoya disease can present with ischemia or hemorrhage. Transient ischemic attacks occur in approximately 40% of cases and ischemic stroke in approximately 30%. The transient ischemic attacks are usually motor but can be sensory; they may occur persistently on one side or may alternate sides. Transient ischemic attacks may be precipitated by fever, crying, coughing, or by activities that cause hyperventilation like exercise or playing wind instruments. Children with moyamoya disease sometimes have a history of seizures or migraine-like headaches (Scott and Smith 2009). A primary form of moyamoya disease is seen in Japanese and Korean people, whereas a secondary form occurs in a range of genetic and other disorders including: sickle cell disease, Down syndrome, neurofibromatosis, primordial dwarfism, PHACES, Alagille syndrome, osteogenesis imperfecta, Costello syndrome, antiphospholipid syndrome or lupus anticoagulant, Grave’s disease, and idiopathic thrombocytemia and thrombotic thrombocytopenic purpura as well as with cocaine and oral contraceptive usage and post-radiation (Ibrahimi et al 2010).

Sickle cell disease. Children with sickle cell disease are at high risk for stroke; 11% have a stroke by the age of 20 years. A moyamoya arteriopathy generally underlies stroke. Hemiparesis due to stroke is typically sudden in onset. Seizures, often focal, occur at the outset in approximately 20% of cases. A history of transient ischemic attacks is relatively uncommon, although it is possible they are under-recognized. Acute chest syndrome is a risk factor for stroke. Anemia or hypotension may trigger stroke in patients with severe stenosis as a result of worsening hemodynamic failure. Hemorrhage is less common than arterial ischemic stroke and occurs in older patients. Hemiparesis occurring in the setting of intraparenchymal hemorrhage, which is generally subcortical, presents with sudden severe headache, altered consciousness, and seizures (Ohene-Frempong et al 1998).

Arterial dissection. Headache commonly on the same side as the dissection predates by a few days or co-occurs with the hemiplegia, which can manifest as a transient ischemic attack or more often as a fixed deficit. In contrast to adults who are often diagnosed before the ischemic event because of headache, children generally present with hemiparesis (Amlie-Lefond and Jubelt 2009). Males predominate even when traumatic cases are excluded. Conditions associated with dissections include migraine, fibromuscular dysplasia (found in approximately 15% of patients) (Olin and Sealove 2011), Ehlers-Danlos type IV syndrome, Marfan syndrome, pseudoxanthoma elasticum, cystic medial necrosis, polycystic kidney disease, osteogenesis imperfecta (Debette and Leys 2009), alpha1-antitrypsin deficiency, and hypereosinophilic syndrome (van Gaalen et al 2011). The overall prognosis for carotid dissections is better than that of vertebral dissections, but all dissections need to be diagnosed promptly and treated as mortality and morbidity are not inconsequential (Rafay et al 2006; Tan et al 2009).

Table 2. Known Etiologies and Risk Factors of Stroke
Cardiac
• Congenital heart disease
- Septal defects
- Patent ductus arteriosus
- Valvular prolapsed or stenosis
- Coarctation of the aorta
- Patent foramen ovale

• Acquired heart disease
- Rheumatic heart disease
- Cardiomyopathy
- Endocarditis and myocarditis
- Arrhythmias
- Kawasaki disease
- Cardiac tumors
- Cardiac catheterization
- Recent cardiac or valvular surgery
- Prosthetic valve

Hematologic
• Iron deficiency anemia
• Sickle cell and other hemoglobinopathies
• Polycythemia
• Thrombocytosis
• Disseminated intravascular coagulation
• Idiopathic thrombocytopenic purpura
• Thrombotic thrombocytopenic purpura
• Vitamin K deficiency
• Drug-induced immune thrombocytopenia (heparin-induced)
• Hemophilia A
• Hemophilia B
• Von Willebrand disease (type I and type II)
• Antithrombin III deficiency
• Deficiency of protein C or S
• Activated protein C resistance (usually related to the factor V Leiden mutation)
• Prothrombin gene 20210A mutation
• Plasminogen activator promoter polymorphism
• Elevated lipoprotein (a)
• Antiphospholipid antibody syndrome
• Oral contraceptive use
• Hypereosinophilic syndrome
• Homocystinuria
• Methylene tetrahydrofolate reductase (MTHFR) C677T mutation
• Disorders of fibrinolysis
• Conditions associated with hematologic changes
  - Protein-losing enteropathy
  - Pregnancy
  - Solid cancer, leukemia, or lymphoma
  - Nephrotic syndrome
  - Inflammatory bowel disease
  - Behçet disease
  - Paroxysmal nocturnal hemoglobinuria

Infections
• Bacterial meningitis
• Viral meningitis/meningoencephalitis, including varicella
• Chronic fungal, tuberculosis, amebic meningitis
• HIV or AIDS
• Neuroborreliosis
• Syphilis
• Neurocysticercosis

Cerebral arteriopathies
• Focal cerebral arteriopathy
• Carotid and vertebral artery dissection
• Moyamoya disease and syndrome
• Inflammatory or immunological vasculitis:
  - Hashimoto encephalopathy with vasculitis
• Primary angitis of the CNS
  - Takayasu arteritis
  - Polyarteritis nodosa
  - Scleroderma
  - Systemic lupus erythematosus
  - Henoch-Schonlein purpura
  - Behçet disease
• Infectious arteritis

**Toxins or medications**
• L-Asparaginase
• Methotrexate
• Interferons
• Cocaine
• Heroin
• Amphetamines
• Sympathomimetics (eg, ephedrine, pseudoephedrine)
• Alcohol
• Cranial irradiation

**Neoplasm**
• Lymphoma
• Leukemia
• Brain tumors (primary or metastatic)
• Systemic tumors

**Cerebrovascular malformations**
• Arteriovenous malformations
• Vein of Galen malformations
• Cavernous malformations
• Venous angioma
• Intracranial aneurysms
• Sturge-Weber syndrome

**Head trauma**

**Genetic or inborn errors of metabolism**
• Aicardi-Goutieres syndrome
• Alagille syndrome
• Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
• Collagen disorders (BVSHD)
• Fabry disease
• Fibromuscular dysplasia
• Hereditary endotheliopathy with retinopathy, nephropathy, and stroke (HERNS)
• Mitochondrial encephalomyopathy (eg, MELAS, Leigh syndrome)
• Neurofibromatosis type I
• Osler-Weber-Rendu syndrome
• Osteogenesis imperfecta
• Posterior fossa anomalies, hemangioma, arterial lesions of the head and neck, cardiac abnormalities, eye anomalies and sternal defects (PHACES) syndrome
• Microcephaly, osteodysplastic primordial dwarfism type II (MOPD II)
• Sickle-cell disease
• Williams-Beuren syndrome

**Metabolic disorders**
• Diabetic ketoacidosis
• Hyper- and hypoglycemia
• Hypocalcemia

**Genetic disorders associated with stroke.** Recurrent hemiplegia often with incomplete recovery may be seen in a number of inherited conditions, such as MELAS, CADASIL, neurofibromatosis, Fabry disease, and homocystinuria (Saito et al 2010; Testai et al 2010a; Testai et al 2010b; Munot et al 2011). Many of these disorders are associated with arteriopathies. Table 3 details clinical features suggestive of particular diagnoses.
Table 3. Clinical Features of Genetic Disorders Associated With Stroke

<table>
<thead>
<tr>
<th>Disorder (Gene)</th>
<th>Non stroke neurologic presentation</th>
<th>Musculoskeletal Features</th>
<th>Ocular Features</th>
<th>Skin signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aicardi-Goutieres (SAMHD1)</td>
<td>Developmental delay or regression</td>
<td>Contractures</td>
<td></td>
<td>Raynaud sign</td>
</tr>
<tr>
<td>Alagille syndrome (JAG1)</td>
<td>Developmental delay</td>
<td>Butterfly vertebra</td>
<td>Posterior</td>
<td>Embryotoxin</td>
</tr>
<tr>
<td>ATS (SLC2A10)</td>
<td></td>
<td>Arachnodactyly</td>
<td></td>
<td>Joint laxity</td>
</tr>
<tr>
<td>CADASIL (NOTCH3)</td>
<td>Migraine with aura</td>
<td>Spondylosis</td>
<td></td>
<td>Alopecia</td>
</tr>
<tr>
<td>CARASIL (HTRA1)</td>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSVDH (COL4A1)</td>
<td>Migraine and Cerebral palsy</td>
<td>Cramps</td>
<td>Cataracts</td>
<td>Retinal tortuosity</td>
</tr>
<tr>
<td>Fabry disease (GLA)</td>
<td>Acroparesthesia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homocystinuria (CBS, MTHFR, MTR, and MTRR)</td>
<td></td>
<td>Tall stature</td>
<td>Dislocated lens</td>
<td></td>
</tr>
<tr>
<td>MELAS (MT-ND1, MT-ND5, MT-TH, MT-TL1, and MT-TV)</td>
<td>Seizures and Ataxia</td>
<td>Myopathy</td>
<td>Retinitis pigmentosa</td>
<td></td>
</tr>
<tr>
<td>Menkes disease (ATP7A)</td>
<td>Hypotonia</td>
<td>Developmental delay or regression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOPD II (PCNT)</td>
<td>Motor delay</td>
<td>Microcephaly</td>
<td>Café au lait spots</td>
<td></td>
</tr>
<tr>
<td>Neurofibromatosis (NF1)</td>
<td>Seizures and Optic glioma</td>
<td>Sphenoid dysplasia</td>
<td>Lisch nodules</td>
<td>Café au lait spots and Neurofibromas</td>
</tr>
<tr>
<td>PXE (ABCC6)</td>
<td>Skin laxity</td>
<td></td>
<td>Peau d’orange</td>
<td>Papular lesions</td>
</tr>
<tr>
<td>Williams-Beuren syndrome (CLIP2, ELN, GTF2I, GTF2IRD1, and LIMK1)</td>
<td>Developmental delay</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ATS = arterial tortuosity syndrome; BVSDH = brain small vessel disease with hemorrhage; CADASIL = cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CARASIL = cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy; MOPD II = Microcephalic, Osteoplastic Primordial Dwarfism type II; PXE = Pseudoxanthoma elasticum

Modified from (Testai et al 2010a; Testai et al 2010b; Munot et al 2011)

**Hemorrhage due to vascular malformations.** Arteriovenous malformations commonly present with hemorrhage and hemiplegia. In children, however, seizures are the most common initial presentation of arteriovenous malformations, whereas hemorrhage and acute hemiplegia with headache heralding the event is more common in young adults (Lo et al 2008). Notably, about one third of patients with arteriovenous malformations have a history of migraines predating the hemorrhage (Monteiro et al 1993). Progressive focal deficits, including hemiparesis, are thought to result from mass effect, steal phenomenon, or hypoxia and can occur in approximately 10% of patients (Mast et al 1995; Hoffman et al 1997). In infants and toddlers, Vein of Galen malformations can present with progressive hemiparesis due to ischemia or steal phenomenon. Hemorrhage can occur although this is not common (Golomb et al 2004).

**Hemiplegic migraine.** Both familial and sporadic hemiplegic migraines generally begin in childhood. In some cases, hemiplegia may be an aura similar to more common visual and sensory auras, as opposed to hemiplegic migraine...
being a separate entity (Levin 2008). Most patients also have another aura type (visual, sensory, or dysphasic) or at least paresthesias concomitant with the hemiplegia. Weakness is more common in the arm than the leg (Thomsen et al 2003). Symptoms usually resolve within 1 hour. Headache is usually present and is generally contralateral to the hemiplegia (Levin 2008; Silberstein et al 2008). The initial clinical distinction between hemiplegia due to stroke and hemiplegia due to migraine is complicated by the frequent occurrence of headache in association with cerebral venous sinus thrombosis and arterial ischemic stroke in children. Positive symptoms suggest migraine, in contrast to negative symptoms that are more characteristic of stroke (Gelfand et al 2010). The fact that migraine is a risk factor for stroke can also complicate the differential diagnosis in the acute phase. Mild head injury has been reported to precipitate hemiplegic migraine (Curtain et al 2006). Thus, traumatic hemiplegia may need to be ruled out. Alteration of consciousness, ranging from confusion to coma, occurs in up to one quarter of cases; meningismus and fever may be present, raising questions about infection. Ultimately, migraine is a diagnosis of exclusion. Relevant family illnesses include epilepsy, migraine (in 50%), hemiplegic migraine (in 25%), hypercoagulability, autoimmune disorders, and stroke. Migraine markers include a personal history of migraine or migraine equivalents of early childhood, motion sickness, somnambulism, and ice cream headache (Selekler et al 2004; Gelfand et al 2010).

**Alternating hemiplegia of childhood.** In alternating hemiplegia of childhood, episodes of hemiplegia, generally beginning prior to the age of 18 months, last for minutes to hours, sometimes alternating sides within the same episode, and are recurrent. Episodes may be triggered by bathing, light, or other environmental stress and are characteristically aborted by sleep. Episodes of abnormal eye movements often occur during the first few months of life. Most children are cognitively impaired and may be hypotonic or ataxic. About half of these children also have a seizure disorder (Saito et al 2010). Fifty percent of patients with alternating hemiplegia have a family history of migraine (Silberstein et al 2008).

**Seizures: ictal and Todd postictal hemiplegia.** Todd postictal paralysis can occur with partial seizures of any etiology. Notably, partial seizures and postictal hemiparesis occur in nonketotic hyperosmolar hyperglycemia more frequently than in other metabolic disorders. Prolonged hemiparesis lasting days, weeks, or months is reported after prolonged seizures in Sturge-Weber syndrome (Comi 2003). Patients with Sturge-Weber syndrome are uniquely susceptible to venous hypertension during status epilepticus (Coley et al 1998). Cerebral venous sinus thrombosis with infarction could underlie a prolonged postictal hemiparesis in this population. Transient focal weakness after a seizure may be more likely when there is an underlying structural lesion (Theodore 2010). Hemiplegic seizures may be difficult to distinguish from Todd paralysis without an EEG as consciousness may be maintained during the ictal paresis and duration is similar (O'Donovan et al 2007). Acutely, the clinical distinction between hemiplegia due to stroke and hemiplegia due to seizures is complicated by the frequent occurrence of focal seizures preceding or following cerebral venous sinus thrombosis and arterial ischemic stroke in children. In a prospective study performed at a tertiary care hospital, 21% of 77 pediatric patients who presented with arterial ischemic stroke, cerebral venous sinus thrombosis, or hemorrhagic stroke also had a clinical seizure at the time of presentation (Singh et al 2012). An additional 4% had a seizure within 24 hours of presentation, and 5% had seizure within 7 days of presentation. Of those who presented acutely with seizure, 43% had new-onset hemiparesis. In another prospective study of 60 children presenting with arterial ischemic stroke, 22% had a clinical seizure at presentation, and 100% of these patients had an associated hemiparesis at time of presentation (Abend et al 2011).

**Metabolic.** Metabolic abnormalities, particularly hypoglycemia, hyperglycemia and hypocalcemia, may present with hemiplegia, albeit uncommonly. Associated dizziness, tremor, confusion, and coma suggest insulin overdose. In children with diabetes mellitus, transient hemiplegia (affecting face and arm more than leg, lasting less than 24 hours) can occur during a mild respiratory illness and is often associated with headache and nausea; it often presents on awakening (Kossoff et al 2001).

**Infection.** Intracranial infections may cause acute hemiplegia due to compression and edema, eg, abscess or tuberculosis. Focal cerebritis or stroke with an associated hemiplegia can occur in the setting of meningitis or encephalitis and is often associated with fever, headache, and lethargy (Riela and Roach 1982; Griesemer et al 1994).

**Neoplasms.** Neoplasms typically cause progressive, as opposed to acute, hemiplegia secondary to destruction or compression. Signs of increased intracranial pressure, such as headache, vomiting, papilledema, or abducens nerve palsy, are often present. Arterial ischemic stroke can also result from direct compression or invasion of intracranial blood vessels. An acute hemorrhage into a brain tumor may cause acute hemiplegia or seizures with postictal hemiparesis (Lo et al 2008).
**Head and neck trauma.** Trauma with resulting hemorrhage (epidural and subdural hematomas, contusions, shear injuries, and intracerebral hemorrhages) can cause hemiplegia. In contrast to the acute hemiparesis that develops with traditional arterial epidural hematomas, children can develop venous epidurals where the onset of a hemiparesis can be delayed for hours to days (Schutzman et al 1993). The role of trauma in pediatric arterial ischemic stroke is significant (without hemorrhage), especially as it relates to contact sports. In a case series of stroke occurring in adolescent football players, 2 of the 3 presented with hemiplegia, and 2 had a delayed presentation (Brosch and Golomb 2011). The cause may be multifactorial and depends on individual risk factors.

**Demyelinating disorders.** Demyelinating disorders can cause acute hemiplegia. Acute disseminated encephalomyelitis frequently presents with hemiparesis often accompanied by headache, irritability, lethargy, and fever (Tenembaum et al 2002; Dale et al 2009). A minor illness in the preceding weeks is often reported.

**Toxin or medication side effects.** Multiple illicit drugs, including heroin, amphetamine (intranasal or intravenous), cocaine, phencyclidine, lysergic acid diethylamide, and marijuana as well as alcohol can increase the risk of stroke with associated hemiplegia (Brust 2011). Over-the-counter sympathomimetics such as ephedrine and pseudoephedrine and oral contraceptive agents also increase risk of stroke with associated hemiplegia.

**Chemotherapy.** Methotrexate-induced necrotizing leukoencephalopathy occurs several months after treatment, especially in patients receiving high cumulative doses of intrathecal methotrexate combined with whole-brain radiotherapy. The hemiplegia is sometimes associated with aphasia (Fisher et al 2005). L-asparaginase can affect coagulation with resulting hemorrhage, cerebral venous sinus thrombosis, or arterial ischemic stroke. Children generally present after several weeks of treatment with headaches, seizures, or hemiplegia. A number of other chemotherapeutic agents have also been implicated in hemorrhage or vasculopathy and stroke (Schiff et al 2009).

**Diagnostic workup**

History and clinical examination provide crucial clues about the cause of hemiplegia. Both family and personal history are relevant. Funduscopic examination may reveal signs of retinal hemorrhage, suggesting cerebral trauma, as well as signs of a genetic disorder like Lisch nodules or cataracts. Examination of the oropharynx and neck may reveal evidence of injury or inflammation. Examination of the heart facilitates the diagnosis of cardiac disease. Delayed or diminished femoral pulses suggest coarctation of the aorta, which has been associated with moyamoya disease. Examination of the skin may reveal lesions of varicella or herpes infection, abnormalities of Ehlers-Danlos syndrome or other connective tissue disorder, stigmata of neurocutaneous disorders, or lesions of conjunctivae and skin, suggesting Kawasaki or Behçet disease.

**Neuroimaging.** Neuroimaging is essential in the evaluation of a child with acute hemiplegia. CT is rapid and appropriate for emergent evaluation, but it is inadequate, except for perfusion-weighted imaging, to detect early
stroke or accurately distinguish the many mimickers of ischemic stroke in children (Shellhaas et al 2006; Abend et al 2011; Singh 2012). Magnetic resonance imaging with diffusion-weighted imaging sequences with apparent diffusion coefficient maps is the most sensitive test for arterial ischemic stroke (Albers et al 2006). Diffusion- and perfusion-weighted imaging can detect ischemia within minutes. Gradient echo imaging detects blood. Specific patterns on MRI may aid in defining etiology, especially in mitochondrial disorders. For example, complex I deficiency is a major cause of respiratory chain dysfunction and accounts for various clinical presentations, including Leigh syndrome and MELAS. Stroke-like lesions that do not conform to vascular territories, which are bilateral, and the presence/absence of basal ganglia signal abnormalities may be clues to an underlying mitochondrial disorder. Subsequent MR spectroscopy is useful to aid in identifying certain mitochondrial disorders by evaluating for lactate peaks in non-infarcted areas (Lebre et al 2011).

MRI can also provide some information about the presence of vasculopathies. Axial T1 MRI of the neck with fat saturation should be performed along with MRA to evaluate for arterial dissection or other vasculopathy. Moyamoya disease can be diagnosed on MRI based on its dilated, tortuous enhancing signal voids in the basal ganglia and the severe stenosis of the distal internal carotid artery (Bacigaluppi et al 2009).

In hemorrhagic stroke, CT may not identify underlying vascular abnormalities such as arteriovenous malformations and cavernomas, and it may poorly differentiate tumor from secondary hemorrhage. Therefore, MRI of the brain with gadolinium should be obtained. Multiple areas of hemorrhagic infarction suggest emboli. Tumor, demyelination, leukoencephalopathy, and evidence of trauma are best detected using MRI. Diffusion-weighted MRI can be similar in leukoencephalopathy and arterial ischemic stroke. However, in leukoencephalopathy the changes may not be confined to specific vascular territories (Baehring and Fulbright 2008); abnormalities can be present in subcortical or deep periventricular white matter, corpus callosum, cortex, cerebellum, and thalamus (Rollins et al 2004; Fisher et al 2005). Diffusion-weighted imaging changes may represent reversible cerebral dysfunction with associated cytotoxic edema and metabolic derangement rather than ischemic structural injury (Rollins et al 2004). Transient abnormalities have been described on MRI with both migraine and seizures. Longitudinal follow-up of a case of prolonged hemiplegic attack using MRI, DWI, MR spectroscopy, and single-photon emission computed tomography (SPECT) provided supportive evidence for primary neuronal dysfunction (Toldo et al 2011). The MRI revealed progressive signal alterations in the hemisphere affected. The MRS demonstrated neuronal loss (decreased N-acetylaspartate) without cerebral ischemia, and SPECT exhibited reversible impairment of neuronal function.

MRA is probably equivalent to standard angiography for carotid and middle cerebral artery angiopathies, but it is less sensitive for small vessel disease and distal angiopathy (Braun et al 2009). In some cases, cerebral angiography may be required to better delineate suspected arterial dissection, moyamoya disease, fibromuscular dysplasia, or vasculitis (Roach et al 2008). MRA can actually overestimate the length and severity of stenosis. MRA can also identify aneurysms larger than 3 mm. A 3-D CT angiography may have value in the evaluation of arterial ischemic stroke and arteriopathies, but the amount of radiation is relatively high, and its utility in pediatric cases is not well studied. The complication rate of conventional angiography is 0% to 1% in children.

**Electroencephalography.** EEG distinguishes between an ictal and postictal basis for hemiplegia. In moyamoya disease, hyperventilation can produce bursts of high-amplitude delta. Following cessation of hyperventilation, the delta activity can resolve and spontaneously recur, called “re-build up phenomenon” (Kurlemann et al 1992). Although EEG may be needed to evaluate seizures in sickle cell disease, hyperventilation is avoided because it leads to hypocapnia and vasoconstriction, which can precipitate decreased cerebral blood flow. Hypoxia and ischemia increase susceptibility to sickling and potential infarction (Millichap 2006). Prolonged video EEG monitoring may be high yield in arterial ischemic stroke, cerebral venous sinus thrombosis, or hemiplegic stroke as the reported incidence of non-convulsive seizures, including status epilepticus, in those who presented with seizure at the time of stroke ranges from 14% to 23% (Abend et al 2011; Singh et al 2012).

Complete blood count is required to evaluate for infection and hematologic disorders. Blood cultures are necessary for diagnosing bacterial endocarditis. Erythrocyte sedimentation rate, prothrombin time, and partial thromboplastin time may also suggest an etiology in some cases. Serum chemistries may help distinguish neurologic complications of hyperglycemia or hypoglycemia from stroke, whereas urine drug screen for cocaine and amphetamines may identify a toxicological cause of stroke. Routine urinalysis provides information about possible renal disease and dehydration. Pregnancy tests should be performed in adolescent females. When embolic disease is suspected, chest x-ray and echocardiography are essential to evaluate for possible cardiac disease. Cardiac rhythm monitoring can identify
arrhythmias as a source of emboli. When an acute or chronic meningitis or encephalitis is suspected, lumbar puncture is indicated. Children without evidence to suggest common causes of hemiplegia should undergo more extensive evaluation, such as a search for underlying prothrombotic state (Kenet et al 2000). A genetic workup should be undertaken when appropriate.

**Epidemiology**

The frequency of many disorders associated with acute childhood hemiplegia, as well as the frequency of hemiplegia occurring in these disorders is unknown. The incidence of stroke in children (including perinatal stroke) is estimated at 2.4 per 100,000 person-years. Inclusion of hemorrhagic stroke and transient ischemic attacks increases the total stroke incidence to 4.6 per 100,000 person-years (Agrawal et al 2009). The incidence of hemiplegic migraine ranges from 0.005% to 0.01% (Thomsen et al 2003); among migraineurs, the reported frequency ranges widely from 4% to 30% (Silberstein et al 2008).

**Prevention**

Risk factors for stroke in children differ significantly from those in adults. Widespread vaccination against *Haemophilus influenzae* and *Streptococcus pneumoniae* has decreased the incidence of bacterial meningitis and its complications, including stroke. Similarly, vaccination against varicella may have decreased the frequency of post-varicella focal cerebral arteriopathy. The best example of successful stroke prevention is the current management of sickle cell disease (Enninful-Eghan et al 2010). Children with metabolic and genetic disorders underlying stroke may benefit from treatment of their underlying condition, including possible gene therapy. Medication management to prevent migraine and seizure presumably decreases the frequency of hemiplegic migraine and Todd paralysis.

**Management**

Management depends on the cause of hemiplegia and differs significantly after stroke, hemorrhage, epilepsy, migraine, and infection as well as demyelinating, metabolic disease and genetic disease.

**Stroke.** Several consensus guidelines for the management of different types of stroke have been published (Monagle et al 2004; Paediatric Stroke Working Group 2004; Roach et al 2008). Acute management of all strokes includes standard supportive measures (Roach et al 2008). Thrombolytics for arterial ischemic stroke have not yet been adequately studied in children to be recommended for standard use (Roach et al 2008). Clinical trials are ongoing (Amlie-Lefond and Jubelt 2009). Decompressive hemicraniectomy should be considered for large strokes associated with mass effect and deterioration of consciousness (Smith et al 2004). Early heparinization is reasonable pending evaluation for the cause of the stroke because the likelihood of arterial dissection, undiagnosed cardiac disease, and coagulopathy is fairly high in children. Once these etiologies are ruled out, anticoagulation can be stopped and aspirin substituted for secondary stroke prevention. Even though the recurrence risk for most types of childhood stroke is relatively low (Ganesan et al 2011), treatment is recommended for at least 3 to 5 years (Roach et al 2008). If arterial ischemic stroke is due to cardiac embolism, extracranial arterial dissection, or hypercoagulable state, long-term anticoagulation is recommended (after arterial dissection for 3 to 6 months; after cardiac embolism for at least 1 year) (Roach et al 2008). In sickle cell disease, acute exchange transfusion (Monagle et al 2008; Roach et al 2008) followed by long-term transfusion therapy (Adams and Brambilla 2005; Lee et al 2006; Roach et al 2008) is standard care. Revascularization surgery is recommended for moyamoya disease if symptoms of ischemia increase or if cerebral perfusion is compromised (Roach et al 2008). With strokes due to cerebral venous sinus thrombosis, the precipitating illness and seizures and elevated intracranial pressure, if present, require treatment (Roach et al 2008). Anticoagulation both acutely and chronically is recommended (3 to 6 months) (Monagle et al 2004; Roach et al 2008), particularly given the fact that thrombus propagation may occur in over one third of untreated children (Moharir et al 2010). Based on a retrospective review of children with arterial ischemic syndrome who received anticoagulation acutely, the use of anticoagulation is relatively safe in children with arterial ischemic stroke, with a 4% risk of symptomatic intracerebral hemorrhage (Schechter et al 2012). Treatment of stroke due to genetic and metabolic conditions varies by disorder (Roach et al 2008).

Traditional rehabilitation is appropriate for hemiplegia of any cause. Both unimanual constraint therapy and bimanual therapy have been adapted for children and appear to improve function of the hemiparetic hand (Gordon et al 2008). Motor imagery training appears to enhance recovery of hemiplegia (Steenbergen et al 2009). The use of daily inhibitory, low frequency, repetitive transcranial magnetic stimulation to the unaffected M1 region may improve motor
function in children with chronic subcortical arterial ischemic stroke by rebalancing cortical inhibition of the contralateral motor cortex (Kirton et al 2008).

**Hemorrhage.** In the acute setting, children with cerebral hemorrhage should be stabilized medically. Surgical or endovascular intervention may be indicated in cases of large hemorrhage and arteriovenous malformations or aneurysm (Beslow and Jordan 2010).

**Seizures.** Appropriate EEG monitoring and choice of antiepileptic medication therapy is crucial to seizure control.

**Alternating hemiplegia of childhood.** Flunarizine, a calcium channel blocker, has been shown to reduce duration, severity, and frequency of episodes of alternating hemiplegia, but has no abortive effects (Mikati et al 2000). Theoretically, flunarizine works because alternating hemiplegia is a channelopathy involving CACNA1A and ATP1A2 (Chi et al 2012). However, flunarizine has not been shown to have a significant effect on the overall developmental outcome. Glutamate and N-methyl-D-aspartate (NMDA) receptors are thought to also be involved in the induction of attacks. Amantadine, an NMDA receptor antagonist, and topiramate are drugs that modulate ion channels and inhibit non-NMDA excitatory neurotransmission, and have been investigated as add-on agents (Chi et al 2012). Seizures are a rare side effect of amantadine (Tatli et al 2011).

**Hemiplegic migraine.** Flunarizine, valproate, and steroids have been used to treat prolonged auras acutely (Wheeler 2009). Intranasal ketamine has been used to treat hemiplegic aura (Kaube et al 2000). Calcium channel blockers and valproate are the most commonly used as preventative agents in hemiplegic migraine (Wheeler 2009; Peer Mohamed et al 2012). Beta blockers and triptans should be avoided (Klapper et al 2001; Gelfand et al 2010).

**Demelinating disorders.** Acute disseminated encephalomyelitis generally responds to treatment with corticosteroids or intravenous immunoglobulins (Dale et al 2009).

**Conversion disorder.** Physical therapy is an important part of treatment for conversion paralysis along with appropriate pharmacotherapy and psychotherapy to address the related psychological stressors and any comorbid psychiatric disorder (eg, depression, anxiety) (Ness 2007).

**Pregnancy**

Pregnancy is by definition a proinflammatory and hypercoagulable state. Postnatal infection, migraine, thrombophilias, lupus, heart disease, preeclampsia, smoking, obesity, older age, bed rest more than 4 days, and surgical delivery are specific risk factors (Feske 2007). Migraine frequency can increase or decrease during pregnancy; and migraine can also increase the risk of stroke during pregnancy (Bushnell et al 2009). Seizure control can be an issue during pregnancy.

**Anesthesia**

Specific anesthetic management is required in children who are at high risk for stroke due to moyamoya (Baykan et al 2005) or sickle cell disease (Marchant and Walker 2003).

**Outcomes**

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**References especially recommended by the author or editor for general reading.
Profile

Age range of presentation

0-01 month
01-23 months
02-05 years
06-12 years
13-18 years
19-44 years

Differential diagnosis list

hemiplegia due to stroke
hemiplegia due to epilepsy
hemiplegia due to Todd postictal paralysis
hemiplegic migraine
hemiplegia due to hypoglycemia
hemiplegia due to diabetes mellitus
hemiplegia due to tumor
hemiplegia due to trauma
hemiplegia due to infection
hemiplegia due to demyelination
hemiplegia due to toxin
hemiplegia due to metabolic disease
hemiplegia due to vasculopathy

Associated disorders

Aneurysm
Antiphospholipid antibody syndrome
Arteriovenous malformation
Atrial septal defect
Congenital heart disease
Endocarditis
Homocystinuria
Hyperlipidemia
Hypertension
Kawasaki disease
Leukemia
Mitochondrial encephalopathy, lactic acidosis, stroke
Mitral valve prolapse
Moyamoya disease
Patent ductus arteriosus
Rheumatic heart disease
Sickle cell anemia
Sickle cell disease
Thrombocytopenic purpura

Other topics to consider

Alternating hemiplegia of childhood
Cerebral palsy
Chemotherapy: neurologic complications
Hemiplegic migraine
Illicit drug use: neurologic complications
Moyamoya disease
Porencephaly
Stroke associated with sickle cell disease
Stroke in young adults
Sturge-Weber syndrome