Managing Stroke in Children

Walter J. Molofsky, MD

Neonates, infants, and children all may suffer strokes. The incidence of stroke in the pediatric population is estimated at between 2 and 3 per 100,000 — highest in the younger age groups and decreasing through adolescence. Neonates and infants also may present with strokes that were prenatal in origin.

A stroke is a prolonged or permanent dysfunction of brain activity due to interruption of normal vascular flow or due to hemorrhage within the brain. Stroke symptoms that last less than 24 hours are called transient ischemic attacks.2 Strokes can be divided into two types: ischemic and hemorrhagic. Ischemic strokes are cerebrovascular insults.
### Risk Factors for Pediatric Stroke

<table>
<thead>
<tr>
<th>Cardiac Disease</th>
<th>Vascular Anomalies</th>
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<tbody>
<tr>
<td>• Congenital: Aortic stenosis, atrial septal defect, ventricular septal defect, coarctation, patent ductus arteriosus</td>
<td>• Aneurysm</td>
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<tr>
<td>• Acquired: Arrhythmias, endocarditis, myocarditis, rheumatic heart disease, myxoma</td>
<td>• Arteriovenous malformation</td>
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<td>• Moyamoya disease</td>
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<td>• Arterial dissection</td>
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<tr>
<th>Hematologic Disorders</th>
<th>Venous Infarcts</th>
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<tr>
<td>• Sickle cell disease</td>
<td>• Cerebral sinovenous thrombosis</td>
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<tr>
<td>• Leukemia or lymphoma</td>
<td>• Shock</td>
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<td>• Polycythemia</td>
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<td>• Thrombocytosis</td>
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<th>Coagulopathies</th>
<th>Metabolic Conditions</th>
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<tr>
<td>• Deficiency of proteins S or C, vitamin K, antithrombin III, Factor V Leiden, Factor VII, or Factor XIII</td>
<td>• Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)</td>
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<td>• Lupus anticoagulant</td>
<td>• Homocystinuria/methylene tetrahydrofolate reductase (MTHFR) mutation</td>
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<td>• Oral contraceptives</td>
<td>• Mitochondrial disorders</td>
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<td>• Pregnancy</td>
<td>• Lipid abnormalities</td>
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<tr>
<th>Vasculitis</th>
<th>Vasospasm</th>
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<td>• Post-infectious</td>
<td>• Migraine</td>
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<td>Meningitis</td>
<td>• Cocaine use</td>
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<td>Varicella</td>
<td>• Glue sniffing</td>
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<td>Mycoplasmas</td>
<td>• Phenylpropanolamine reaction</td>
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<td>HIV</td>
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<td>• Immune-mediated</td>
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<td>Henoch-Schönlein purpura</td>
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<tr>
<td>Systemic lupus erythematosus</td>
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<tr>
<td>• Post-radiation, post-chemotherapy</td>
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<td>• Drug abuse, reactions</td>
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<th>Trauma and Other Causes</th>
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<td>• Subdural hematoma</td>
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<td>• Epidural hemorrhage</td>
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<td>• Subarachnoid hemorrhage</td>
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<tr>
<td>• Dissection: Spontaneous or traumatic</td>
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<tr>
<td>• Dehydration</td>
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<td>• Brain tumor</td>
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that occur as a result of obstruction of cerebral blood flow. Hemorrhagic strokes are lesions resulting from extravasation of blood from normal, congenitally abnormal, or damaged blood vessels. Ischemic strokes can be associated with hemorrhagic infarction, and hemorrhagic strokes can have areas of surrounding ischemia, called penumbra. This can lead to clinical findings that initially exceed the area of primary hemorrhage or ischemia and offers an explanation for why improvement can occur following a stroke as the area of hemorrhage or transient ischemic impairment subsides.

The incidences of ischemic and hemorrhagic strokes are approximately the same (1 to 2 per 100,000) in pediatric patients, leading to a combined incidence of about 3 per 100,000. This is in contrast to the adult population, where ischemic strokes predominate by about 3 or 4 to 1.³

The underlying pathophysiology of stroke is similar in adults and children. Blood vessels are either obstructed or leak blood into surrounding brain tissue. However, the risk factors and specific disease entities responsible for ischemic and hemorrhagic stroke are much different in children than in adults. Hypertension and atherosclerotic vascular disease are the primary risk factors in adults. The risk factors for pediatric stroke are summarized in Sidebar 1.⁴ Despite comprehensive evaluation of stroke, there is a 10% to 20% incidence where no precipitating factor is found.⁴

**ISCHEMIC STROKE IN CHILDREN**

Major risk factors for ischemic pe-
diabetic stroke include cardiac disease, hematologic disorders, primary vaso-
litits, drug reactions or abuse, metabolic abnormalities (homocystinuria), lipid
abnormalities, migraine, and states of decreased perfusion, such as dehydra-
tion or shock. The most common clinical presentations of ischemic stroke in
children include sensory motor deficit, aphasia, dystonia, isolated motor hemi-
plegia, headache, and seizures.

Cardiac abnormalities account for almost one-third of the ischemic strokes
seen in children. These anomalies may be either congenital or acquired. Be-
tween 1.5% and 4% of children with uncorrected cyanotic heart disease, which
may be complicated by hypoxia, polycy-
themia, or cyanosis, can suffer strokes. These patients also are at high risk be-
cause of right to left shunting. Tetral-
ogy of Fallot, transposition of the great vessels, tricuspid atresia, and pulmonary
atresia are common cyanotic congenital cardiac anomalies that may lead to isch-
emic stroke. Thrombosis develop in the
atria in patients with mitral valve pro-
lapse, rheumatic heart disease, cardio-
myopathy, and endocarditis. Ischemic stroke also may result as a complication
of extracorporeal membrane oxygen-
ation procedures (ECMO).

Coagulation abnormalities account for
about 14% of ischemic strokes. Specific
abnormalities include hereditary defi-
cency of coagulation factors, erythrocyte
disorders such as sickle cell disease, and
disseminated intravascular coagulation.

HEMORRHAGIC STROKE IN
CHILDREN

Hemorrhagic strokes account for ap-
proximately 40% to 50% of strokes that
occur in the pediatric population. In ad-
dition, ischemic strokes also may have
a hemorrhagic component. The major
copathologies of nontraumatic brain hem-
orrhage in children include vascular mal-
formation (33%), cavernous malforma-
tion (2%), aneurysm (6%), brain tumor
(13%), hematologic disorders (17%),
coagulopathies (16%), hemorrhagic in-
farction (8%), and spontaneous dissec-
tion (2.9%). The clinical presentation of
hemorrhagic infarction includes headache, hemiplegia (60%), aphasia (30%), motor
seizures (39%), and lethargy and coma (21%). Seizures occur frequently, usually
occur within 48 hours of the hemorrhage. The areas most frequently involved by
intracerebral hemorrhage (ICH) are the
putamen 35%, cerebellum 15%, thalamus
10%, caudate 5%, and pons 5%.

Vein of Galen malformations are
common symptomatic vascular mal-
formations seen in infancy and the neo-
natal period. The choroidal type often
presents in newborns as congestive heart failure and hydrocephalus, usually due to in-
creased venous obstruction. The mural
type of malformation usually presents in
infancy with macrocephaly and develop-
ment delay.

Cavernous Malformation

Cavernous malformation, a well-cir-
cumscribed lesion with a reddish-purple
multilobulated appearance, is present

Vascular Malformation

Arteriovenousmalformations (AVMs)
are the most common cause of hemor-
rhagic strokes in infants. The neonate
with an AVM may present with macro-
cephaly, an audible bruit, and congestive
heart failure. The incidence of AVMs is
about 1 in 100,000 children, of which
12% to 18% become symptomatic dur-
ing childhood. Most AVMs are located
in the supratentorial compartment and
are localized to one hemisphere; 10% to
15% are found in the posterior fossa,
and about 5% to 10% in the midline. The
average yearly probability of hemor-
hage in these patients is about 2% to
4%. Following an initial hemorrhage,
the probability of rebleeding is approxi-
mately 1% to 2% per year. It is prob-
able that deep, small- to medium-sized
AVMs have a higher tendency to bleed.

The mortality in children with AVMs is
about 20% to 24%. Vein of Galen malformations are
in about 0.4% to 0.7% of the pediatric
population and represents about 5% to
13% of vascular hematomas. In contrast
to AVMs, cavernous malformations lack
large arterial feeders and draining veins.
They have a vascular wall that consists of
a single layer of endothelium. The lesion
is surrounded by gliotic tissue and
exhibits a characteristic lack of interven-
ning neural tissue. There is almost always
evidence of prior microhemorrhage.
The majority are supratentorial, 15% to
20% are infratentorial, and about 5% are
in a spinal location.

Cavernous malformations display a
wide range of symptoms, from asym-
omatic on one end to rarely reported
cases of cerebral hemorrhage on the
other. These lesions often present with
recurrent headaches or seizures. Asym-
ptomatic patients with mild complaints
such as headache without neurological
deficits often may be followed closely
without treatment.
Aneurysm

Intracranial aneurysms account for approximately 6% of nontraumatic intracranial hemorrhages in children. The overall incidence in the pediatric population is estimated at 0.5% to 4.6%. These aneurysms occur most frequently at a branching point of major blood vessels of the circle of Willis or in the middle cerebral artery. They are thought to develop as the consequence of hemodynamic stress at the site of congenital defects in the arterial medial or elastic. In children, there is a male predominance and a higher incidence of more unusual locations such as in the posterior circulation, peripheral region beyond the circle of Willis, and a carotid bifurcation.

The prevalence of multiple aneurysms (5%) is lower in children than in adults (15%). Presenting signs are related to mass effect and can include ophthalmoplegia, trigeminal neuralgia, headache, nausea, vomiting, seizures, and brain stem compression. Aneurysms also may be acquired as the result of intracranial trauma. These have been thought to arise from compression of the artery against stationary structures during a rapid deceleration injury.

The annual rupture rate of intracranial aneurysms has been estimated to be approximately 1%. There is a higher mortality associated with aneurysmal rupture and subarachnoid hemorrhage, as well as high incidence of rebleeding in the week following a hemorrhagic episode (20% to 50%).

The most common manifestation of a ruptured intracranial aneurysm is subarachnoid hemorrhage. The large vessels course through the subarachnoid space, and thus rupture allows the leakage of blood into the cerebrospinal space. Subarachnoid hemorrhage is often secondary to trauma and presents with a severe headache. Nausea, vomiting, and photophobia are associated symptoms, along with nuchal rigidity.

**MANAGEMENT**

The management of a patient with a stroke includes the prompt recognition that the often quite nonspecific findings may be related to possible cerebrovascular disease. Immediate stabilization followed by an evaluation for specific risk factors is essential. Following stabilization, prevention of recurrence and consideration of early rehabilitation should be instituted.

Pediatric cerebrovascular disorders may present with a variety of clinical scenarios. The classical presentation is rapid onset of clinical signs and symptoms related to an acute abnormality of brain function. The symptoms may include acute onset of mental status change, ataxia, language problems, motor impairment, or focal weakness in a previously normal child. A second presentation is slowly progressive or recurrent neurologic dysfunction. Examples of this include patients who have recurrent strokes or transient neurological dysfunction due to ischemic or microhemorrhagic events, underlying disorders such as AVMs, metabolic encephalopathy and lactic acidosis and stroke syndrome (MELAS), and sickle cell disease.

A third presentation is that of evolving focal neurological impairment related to a prenatal or perinatal stroke. This is especially common in the first year of life, presenting as the result of a fetus or neonate sustaining a cerebrovascular insult that was not recognized previously. During the first year of life as the infant develops, it may become apparent that there is an asymmetry of motor function. Imaging to evaluate this problem may reveal prior infarcts or strokes.

**SIDEBAR 3.**

**Initial Stroke Evaluation**

- Unstable patient: noncontrast computed tomography scan of the head
- Stable patient: magnetic resonance imaging scan of the head
- Complete blood cell count with platelets
- Electrolytes, calcium, magnesium, and phosphate levels
- Blood urea nitrogen and serum creatinine
- Liver function testing
- Prothrombin time
- Partial thromboplastin time
- Erythrocyte sedimentation rate
- Antinuclear antibody
- Chest x-ray
- Electrocardiogram
- Echocardiogram
- Urine toxicology screen
- Lumbar puncture (if infection is suspected)
It is important to determine the nature of the presenting clinical disorder before proceeding with further workup. Diagnostic considerations in infants and children presenting with the acute onset of focal neurological impairment are summarized in Sidebar 2 (see page 382). The differential diagnosis includes stroke, seizure, trauma, migraine, intracranial obstruction, abscess, metabolic disorder, toxic ingestion, drug reaction, meningitis, and syncope. The hallmark of a stroke is an acute event resulting in neurological impairment. Tumors classically present as slowly progressive disorders. Inflammatory and infectious disorders usually present with fever and other systemic findings. The focal impairment resulting from a seizure usually is transient. Once it has been confirmed that a cerebral vascular insult has occurred, the workup should focus on the specific disorder and risk factor responsible for the stroke.

The clinical evaluation of a child with recognized evolving or acutely acquired cerebrovascular events begins with stabilization of the patient’s airway, breathing, and cardiovascular status (ABCDs). A complete medical history and physical examination must then be performed. The purpose of the history is to determine if there are any underlying disorders that would predispose the neurovascular event. The physical examination serves to document the nature of neurological impairment. For example, a child with a heart murmur, history of sickle cell disease, or evidence of infection may have a cardiovascular
or hematological inflammatory process responsible for the stroke.

The initial investigation recommended for patients with a suspected cerebrovascular disorder is summarized in Sidebar 3 (see page 382). Thus, a complete blood cell count, liver function profile, erythrocyte sedimentation rate (ESR), electrocardiogram, and imaging study usually are the first steps in determining if one is dealing with a cerebrovascular disorder.

In the stable patient, the imaging technique of choice is magnetic resonance imaging (MRI). A computed tomography (CT) scan may not identify any area of ischemia or infarction within the first 24 hours. However, in unstable patients, a noncontrast CT scan of the head should be obtained, and if a vascular lesion is suspected, follow-up evaluation with an MRI and magnetic resonance angiography should be undertaken.

Following the initial evaluation and stabilization of the patient a more detailed workup may be pursued and is summarized in Sidebar 4 (see page 383). This includes a more comprehensive list of hematologic imaging, cardiac, and laboratory tests that may be included in the stroke evaluation. Selection of additional tests should be guided by the initial clinical history and laboratory and imaging assessments.

After the initial resuscitation and stabilization of the pediatric stroke patient, with particular attention paid to monitoring vital signs (ie, blood pressure, heart rate, temperature, respiratory rate), focused, disease-specific treatment modalities may be initiated (eg, partial exchange transfusion for sickle cell). Treatment of cerebrovascular abnormalities such as AVMs or aneurysms with intravascular hemorrhage may require embolization, surgery, or both. Thrombolytic and anticoagulant therapy for clearing obstructing vessels or preventing future clots is available, but no specific guidelines have been established in the pediatric population.

OUTCOMES

The outcome of children with strokes usually is much better than that of adults. The outcome is dependent on the size, location, extent, and etiology of the injury. Overall, mortality is approximately 20%, and 45% of pediatric patients with stroke have a persistent neurological deficit or seizure disorder.15

The cognitive deficit seen after congenital strokes in children also differs from that of adults. The effect of a left-sided congenital lesion produces a minimally depressed full-scale IQ with intact verbal IQ but depressed performance IQ. A left-sided lesion in adults generally produces a depressed full scale IQ with depressed verbal IQ but spares the performance IQ. A right congenital lesion in a child produces a depressed full scale and verbal IQ, whereas a right lesion in an adult spares the full scale and verbal IQ but decreases performance IQ. This is somewhat counterintuitive and thought to be due to variations in brain plasticity, with the right hemisphere being more able to take over left-sided function than the left hemisphere is able to take over right-sided function.16 Thus, the cognitive and language outcome in the neonatal population often is better for patients with left-sided stroke than a right-sided stroke.

SUMMARY

The incidence of stroke in the pediatric population is estimated at between 2 and 3 per 100,000. Strokes are divided into ischemic or hemorrhagic categories, depending on whether the primary cause is obstruction or bleeding into the brain. Strokes may present with acute, recurrent, or evolving neurological deficits. There is a long and varied list of causes of stroke in children. The major causes of ischemic stroke are cardiac abnormalities and coagulation disorders. Cerebrovascular malformations account for the majority of hemorrhagic strokes. The workup is guided by the initial history and imaging studies. Treatment is dependent on the specific risk factors identified, and outcome is dependent on the location and extent of the initial insult.

REFERENCES