In recent years, there has been increasing recognition of the impact of childhood stroke and interest in the role of drugs in the acute, chronic, and prophylactic management of this condition. Most treatment strategies are based on studies in adults with stroke, and the relative infrequency of stroke and the heterogeneity of etiologies in childhood compared with adults present significant challenges in study design for childhood stroke studies. The presence of thrombophilia has been associated with stroke in children, strengthening the concept that antithrombotic, antiplatelet, and even thrombolytic agents have a role in stroke treatment and prevention. There are several potential roles for drugs in the treatment of childhood stroke including hyperacute therapy, antithrombotic medication, antiplatelet medication, and disease-specific medications. Herein, we review the use and rationale of these medications in childhood arterial ischemic stroke.

After arterial ischemic stroke (AIS), 10% of children will die, and 70% will be left with neurologic deficit; of the survivors, approximately 15% to 20% will have further strokes. However, despite such compelling numbers, optimal treatments for acute stroke and prophylaxis of children at high risk for initial or recurrent strokes are largely unknown.

In recent years, there has been increasing recognition of the impact of pediatric stroke and interest in the role of drugs in the acute, chronic, and prophylactic management of stroke in childhood. Most treatment strategies are based on studies in adults with stroke. Other than the use of transfusions to prevent stroke in high-risk patients with sickle cell disease (SCD), randomized controlled studies have not been completed in children. The relative infrequency of stroke and the heterogeneity of etiologies in childhood compared with adults present significant challenges in study design for childhood stroke studies. The presence of thrombophilia has been associated with stroke in children, strengthening the concept that antithrombotic, antiplatelet, and even thrombolytic agents have a role in stroke treatment and prevention. Nonetheless, the developmental nature of the hemostatic and fibrinolytic systems limits generalization of safety and efficacy data from adult studies of acute and prophylactic stroke interventions to children.

There is great variability in the use of antithrombotic and antiplatelet drugs after acute childhood AIS. Among 661 children with AIS reported to the International Pediatric Stroke Study, acute treatment consisted of anticoagulation alone in 27%, antiplatelet therapy alone in 28%, and a combination of anticoagulation and antiplatelet therapy in 16% of patients. Anticoagulation was more likely to be used in children with dissection and cardiac disease and less likely to be used in those with SCD and in those enrolled in centers in the United States.

There are several potential roles for drugs in the treatment of childhood stroke. Tissue plasminogen activator (tPA) as a hyperacute therapy has revolutionized the approach to stroke in adults; however, it is not known if tPA is safe or efficacious in childhood stroke. Antithrombotic medication is frequently used early while evaluation for an embolic source is ongoing and is used in children believed to be at high risk of recurrent embolic events. Aspirin is the most common antiplatelet medication used to prevent recurrent stroke in childhood, but other antiplatelet medications are being used more often for children who continue to have ischemic events despite aspirin. Finally, disease-specific medications are being developed for use in children with stroke caused by specific modifiable underlying etiologies, such as the use of hydroxyurea in SCD and folic acid in hyperhomocysteinemia.

Hyperacute Therapy in Childhood Stroke

Plasminogen activators are serine proteases that convert the inactive zymogen, plasminogen, to active plasmin, which in
Urokinase Isolated from human neonatal kidney cell cultures
Streptokinase Extracellular metalloenzyme produced by invasive bacteria
Staphylokinase Extracellular metalloenzyme produced by invasive bacteria
Symptomatic intracranial hemorrhage in 10.9% when given within 6 h
Beneficial at 0-4.5 hours when given at 0.9 mg/kg over 1 h
No benefit in stroke when given 3-9 h after stroke onset
Can be given as 2 boluses
Can be given as single bolus

<table>
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<th>Source</th>
<th>Clinical Experience</th>
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<td>Most widely used fibrinolytic, especially for myocardial infarction</td>
</tr>
<tr>
<td>Staphylokinase</td>
<td>Extracellular metalloenzyme produced by invasive bacteria</td>
<td>Phase II for myocardial infarction completed</td>
</tr>
<tr>
<td>Urokinase</td>
<td>Isolated from human neonatal kidney cell cultures</td>
<td>Symptomatic intracranial hemorrhage</td>
</tr>
<tr>
<td>tPA</td>
<td>Recombinant human tPA</td>
<td>Beneficial at 0-4.5 hours when given at 0.9 mg/kg over 1 h</td>
</tr>
<tr>
<td>Desmoteplase</td>
<td>DSPAα1 plasminogen activator from saliva of vampire bats, may be less neurotoxic than tPA because it does not interact with the NMDA receptor</td>
<td>No benefit in stroke when given 3-9 h after stroke onset</td>
</tr>
<tr>
<td>Reteplase</td>
<td>Recombinant nonglycolsylated form of human tPA</td>
<td>Can be given as 2 boluses</td>
</tr>
<tr>
<td>Tenecteplase</td>
<td>Genetically modified recombinant tPA</td>
<td>Can be given as single bolus</td>
</tr>
</tbody>
</table>

Table 1 Plasminogen Activators

<table>
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The developmental nature of the fibrinolytic system is now universally recognized. Plasminogen concentrations are approximately 50% of adult values at birth but reach adult values by 1 year of age. The blood concentration and stimulated release of endogenous tPA also show maturational differences. From 1 to 16 years of age, baseline tPA concentrations in blood are about 50% lower than in adults. A study of females aged 14 to 18 years showed that teenagers have lower venocclusive stimulated fibrinolytic activity (50%-70%) compared with adult men and women. Plasminogen activator inhibitor-1 (PAI-1) binds with tPA, thereby inhibiting tPA’s activity and influencing tPA’s hepatic clearance. PAI-1 concentrations overall are increased in women.29 Plasminogen activator inhibitor-1 (PAI-1) binds with tPA, thereby inhibiting tPA’s activity and influencing tPA’s hepatic clearance. PAI-1 concentrations overall are increased in children compared with adults. Furthermore, the ratio of tPA to PAI-1 is reversed throughout childhood compared with adults. In contrast, plasminogen and its inactivating protein, α2-antiplasmin (α2-AP), do not change significantly between 1 year and adulthood; however, there are no data regarding changes in concentration of these proteins during acute stroke in children. The lower baseline levels of tPA and increased PAI-1 concentrations in blood are about 50% lower than in adults. A study of females aged 14 to 18 years showed that teenagers have lower venocclusive stimulated fibrinolytic activity (50%-70%) compared with adult men and women. Plasminogen activator inhibitor-1 (PAI-1) binds with tPA, thereby inhibiting tPA’s activity and influencing tPA’s hepatic clearance. PAI-1 concentrations overall are increased in children compared with adults. Furthermore, the ratio of tPA to PAI-1 is reversed throughout childhood compared with adults. In contrast, plasminogen and its inactivating protein, α2-antiplasmin (α2-AP), do not change significantly between 1 year and adulthood; however, there are no data regarding changes in concentration of these proteins during acute stroke in children. The lower baseline levels of tPA and increased PAI-1 concentrations, which suggest a less active innate fibrinolytic system in children, suggest that an increased tPA dose relative to adults to promote fibrinolysis may be necessary.

Children have an increased volume of distribution, which may increase the necessary loading dose of intravenous tPA, and children have more rapid hepatic clearance of tPA than adults. However, there are no data to suggest that tPA is more effective in children than in adults.
or less safe in a particular pediatric age group, and dosing of fibrinolytic therapy in children cannot be safely or accurately extrapolated from adult data or existing pediatric data. Supratherapeutic doses of thrombolytics could lead to increased SICH and other less easily identified neurotoxicity. Inadequate dosing of thrombolytics, such as tPA, could theoretically lead to excessive bleeds and neurotoxicity without potential therapeutic benefit.

Other hyperacute therapies used in adult AIS include intra-arterial administration of tPA and other thrombolytics, such as urokinase,30,31 and endovascular clot retrieval devices. There are reports of the successful use of intra-arterial thrombolytics in childhood stroke,23,32-38 but there exist insufficient data on which to make recommendations.

Acute Treatment With Antithrombotic Agents

Short-term anticoagulation with unfractionated heparin (UFH) or low–molecular-weight heparin (LMWH) is often started in the acute period after a stroke while the initial evaluation of underlying stroke etiologies is pursued (Table 2). Children may be more likely than adults to have an underlying etiology that would be amenable to anticoagulation, such as cervicocephalic arterial dissection (CCAD), cardiac disease, or severe thrombophilia.

Unfractionated Heparin

Heparin is a glycosaminoglycan whose major anticoagulant effect is mediated through binding to antithrombin III (ATIII), which results in a conformational change in ATIII. This change markedly increases the rate of thrombin inactivation and, to a lesser extent, inactivation of factor Xa and factor IXa. Unfractionated heparin (UFH) has immediate onset when given intravenously.30 Importantly, there are age-related differences in activated partial thromboplastin time levels and antithrombin activity for identical anti-FXa concentrations of heparin.40

Immunoglobulin G–mediated heparin-induced thrombocytopenia (HIT) is a serious complication of heparin therapy and can result in severe thrombotic complications. It occurs more commonly with UFH than LMWH and usually within 5 to 10 days of the institution of therapy. HIT-associated thrombosis can be heralded by falling platelet counts without thrombocytopenia, and frequent platelet counts are recommended early in therapy.41

LMWH

UFH can be depolymerized into fragments, resulting in LMWH. This results in decreased plasma protein binding and improved bioavailability with more predictable pharmacokinetics. LMWH also has decreased platelet interactions.41 LMWH has been given in the acute poststroke period to a small series of children with AIS with no significant complications.42 In children older than 12 months, the usual initial therapeutic dose is 1 mg/kg subcutaneously twice daily and for prophylaxis 1 mg/kg daily.43

Long-Term Treatment With Antithrombotic Agents

Anticoagulation with LMWH has been used in some children with an increased risk of recurrent stroke, such as those with cardiac embolism or significant thrombophilic states. The use of therapeutic and prophylactic anticoagulation for at least 4 weeks’ duration was reported in 37 children after AIS associated with nonmoyamoya vasculopathy. During a total of 1,329 patient months of treatment, there were no major bleeds and 2 minor (ie, menorrhagia and soft-tissue hematoma) bleeds reported.44

Warfarin (4-hydroxycoumarin) is an oral agent commonly used in children requiring longer-term anticoagulation although

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**Table 2 UFH and LMWH**

<table>
<thead>
<tr>
<th>Type of Heparin</th>
<th>UFH (Standard)</th>
<th>LMWH</th>
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</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Accelerates ATIII inactivation of thrombin and factor Xa by inducing a conformational change in ATIII</td>
<td>Accelerates ATIII inactivation of factor Xa by inducing a conformational change in ATIII</td>
</tr>
<tr>
<td><strong>Initial dosage</strong></td>
<td>75-100 U/kg initial bolus dose, then 20 U/kg/h, higher dose in infants (25 U/kg/h)</td>
<td>Enoxaparin, 1.0 mg/kg/dose every 12 h SQ; higher dose in infants (1.5 mg/kg /dose)</td>
</tr>
<tr>
<td><strong>Monitoring</strong></td>
<td>aPTT; target aPTT should correlate with target antifactor Xa level of 0.3-0.7 U/mL</td>
<td>Target antifactor Xa level 4 h postdose: 0.5-1.0 because of minimal activity against thrombin, aPTT not useful</td>
</tr>
<tr>
<td><strong>Advantages</strong></td>
<td>Short half-life; Can be reversed with protamine</td>
<td>Stable pharmacokinetics because of lack of plasma protein binding</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Intravenous administration; Frequent blood draws for monitoring; Risk of IgG mediated HIT; Risk of hemorrhage</td>
<td>Administered by once or twice daily subcutaneous injection; Expensive; Risk of hemorrhage; Unable to immediately reverse</td>
</tr>
</tbody>
</table>

Ig, immunoglobulin.
subcutaneous LMWH is an option as well. The onset of the anticoagulant effect of warfarin occurs 36 to 72 hours after administration begins. Warfarin inhibits vitamin K, an essential cofactor for the posttranslational gamma-carboxylation of glutamic acid residues on factors II, VII, IX, and X. The prothrombin time (PT) is used to monitor warfarin because it is sensitive to reduction of factors II, VII, and X.

The international normalized ratio (INR) corrects for the differing sensitivities of PT reagents. The INR is equal to the patient PT divided by the normal PT raised to the power of the International Sensitivity Index (a value assigned to the lot of PT reagent that reflects the sensitivity of the PT reagent to decreases in the vitamin K–dependent coagulation factors). The therapeutic target INR is usually 2 to 3 except for patients with mechanical cardiac valves when an INR of 2.5 to 3.5 is recommended. The therapeutic dose of warfarin needed to achieve the target INR is usually age dependent, with infants requiring the highest doses and teenagers requiring doses comparable to adults.43 Plasma levels of warfarin are affected by several cytochrome P-450 enzyme polymorphisms as well as polymorphisms of vitamin K reductase (VKOR-C1). It can be difficult to maintain a stable INR because of the interaction of warfarin with many drugs and foods.

Warfarin is teratogenic in early pregnancy and results in osteoporosis with long-term use; the hemorrhagic risk is 0.5% to 3.2% per patient year. Notably, skin necrosis can occur shortly after the initiation of warfarin,46 particularly in patients with protein C deficiency; the risk of this complication can be reduced by the maintenance of therapeutic hep- arin until a therapeutic INR is achieved with warfarin. Loading doses of warfarin are no longer recommended.

Anticoagulation is rarely indicated for more than 3 to 6 months in patients with stroke but occasionally is warranted in patients with significant risk of recurrent thrombosis, usually because of congenital heart disease. There is no evidence that the presence of a single thrombophilic risk factor alone is an indication for long-term anticoagulation.

Long-Term Treatment With Antiplatelet Agents

Aspirin

Aspirin is routinely used acutely15 and chronically47 to reduce the risk of stroke in children although no trials assessing antiplatelet therapy in childhood stroke have been performed and treatment recommendations are based on extrapolation of adult experience and expert opinion. The optimal dose of aspirin in children is not known. The American College of Chest Physicians (ACCP) guidelines recommend 1 to 5 mg/kg/d for at least 2 years after dissection and cardioembolic source of stroke are excluded48; the RCP guidelines recommend a lower dose of 1 to 3 mg/kg/d. Some pediatric stroke experts use the higher dose acutely and the lower dose for chronic stroke prophylaxis.

Aspirin acetylates the enzyme cyclooxygenase, interfering with the production of thromboxane A2, thereby irreversibly inhibiting platelet aggregation. Aspirin at doses of 160 mg/d and 300 mg/d has been shown to reduce the risk of inhospital stroke recurrence in adults.49 The AHA recommends aspirin 50 to 325 mg/d as an option for secondary prevention of stroke.50 There is a small (2/1,000) increased risk of hemorrhagic stroke or hemorrhagic transformation of the stroke associated with aspirin use.50 Importantly, there is significant individual variability in effectiveness. Although it is clear that there is a subset of stroke patients who are clinically “resistant” to aspirin therapy (initiated to prevent recurrence by virtue of subsequent strokes), it is unclear how to monitor efficacy other than by clinical recurrence. In adults, data are only now becoming available regarding attempts to objectively evaluate the efficacy of aspirin by measuring “residual platelet responsiveness.” Several in vitro assays have been developed to determine individual responsiveness to aspirin; however, there are no convincing data to correlate these assays with clinical outcomes.51 Indeed, in patients who have had aspirin doses modified based on the assays, there is no evidence that dose modification changes clinical outcomes.52 At present, there are no data regarding resistance to antiplatelet agents available in the pediatric age group, and there is a lack of information to support the use of routine monitoring in this population.

A prospective nonrandomized comparison of aspirin 2 to 5 mg/kg/d versus low-dose LMWH (1.0–1.5 mg/kg/d of enoxaparin) for the prevention of stroke recurrence after the initial stroke showed no differences in the rate of stroke recurrence and no significant treatment complications in either group.47 The dose of LMWH used in the study was the lower prophy- lactic dose rather than a therapeutic dose.53

Aspirin use has been associated with Reye syndrome in childhood.54 The incidence of Reye syndrome in the United States has dropped markedly since 1980 when its association with aspirin was first reported.55 Although aspirin use is linked to Reye syndrome, the risk appears to be dose dependent, with clinical manifestation usually occurring with doses >20 mg/kg.56 Reye syndrome has not been reported in children taking aspirin for stroke prophylaxis. Because varicella and influenza57 have been associated with Reye syndrome, vaccines to prevent these disorders should be given to children on aspirin. In addition, other causes of encephalopathy and liver failure, such as certain inborn errors of metabolism, need to be investigated in patients presenting with possible Reye syndrome.

Clopidogrel

Clopidogrel is a thienopyridine derivative that selectively inhibits the binding of adenosine diphosphate to its platelet receptor and the subsequent adenosine diphosphate–mediated activation of the glycoprotein IIb/IIIa complex, thereby inhibiting platelet aggregation. It reduces the formation of arterial and venous thrombi. Clopidogrel alone may be an alternative to aspirin in some children for secondary stroke prevention. However, in the presence of aspirin and other risk factors, it may increase intracranial bleeding.58 Although children require a lower dose than adults for platelet inhibition, there is significant variability in platelet inhibition for a
given dose. For children receiving aspirin who have recurrent AIS or transient ischemic attacks, ACCP suggests changing to clopidogrel or, alternatively an anticoagulant, either LMWH or oral vitamin K antagonist therapy.

In adults, the presence of a polymorphism in the CYP 2C19 allele (genotype 2C19*2) is associated with decreased responsiveness of platelets to clopidogrel, and this reduced function allele is associated with increased adverse outcomes with clopidogrel. The effect of this genotype on platelet responsiveness and adverse outcomes in children has not been reported.

Dipyridamole

Dipyridamole inhibits the activity of adenosine deaminase and phosphodiesterase, which causes an accumulation of adenosine, adenine nucleotides, and cyclic adenosine monophosphate (cAMP) in platelets. These mediators then inhibit platelet aggregation and may also stimulate the release of prostacyclin from the endothelium, causing vasodilation. Dipyridamole has been used in children (1) with mechanical prosthetic heart valves at a dose of 2 to 5 mg/kg/d in combination with an oral vitamin K antagonist such as warfarin; (2) with systemic embolism despite adequate oral anticoagulant therapy (INR 2.5-3.5); and (3) for whom full-dose oral anticoagulation is contraindicated, specifically in combination with lower dose oral anticoagulation (INR 2-3) plus aspirin. In the latest guidelines, however, an oral anticoagulant plus aspirin is recommended for these patient groups.

Use of Medications for Specific Childhood Stroke Indications

Sickle Cell Disease (SCD)

Children with SCD have a significantly increased risk of ischemic stroke; hemorrhagic stroke is less common but also increased. SCD is the only condition in childhood in which there is a proven method for primary stroke prevention; the use of chronic transfusion in children found to be at risk for stroke on the basis of abnormal transcranial Doppler blood flow has resulted in a 90% reduction in stroke risk. Data from the International Pediatric Stroke Study show that an aggressive transfusion. Aspirin is used by some for vasculopathy, Moyamoya disease, acute chest syndrome, and overly aggressive transfusion. Aspirin is used by some for vasculopathy in SCD although there is concern about risk of hemorrhage, particularly in older children. Currently, there are trials planned to assess the safety and efficacy of low-dose aspirin in the prevention of stroke in children with SCD. However, both the RCP and the ACCP guidelines suggest aspirin as secondary prevention in childhood AIS when SCD has been excluded.

Hydroxyurea is an antimetabolite that induces fetal hemoglobin in patients with SCD, with a resultant increase in total hemoglobin and a decrease in hemolysis. It can be associated with hematologic toxicity, including neutropenia, thrombocytopenia, and severe anemia. It is currently being tested for the prevention of stroke in SCD in childhood.

Moyamoya

Moyamoya disease is a progressive cerebral arteriopathy associated with stenosis and occlusion of the intracranial internal carotid circulation with the development of collateralization. Aspirin is often given for moyamoya vasculopathy, particularly when the patient is considered a poor operative risk or has not yet progressed to requiring revascularization, but there are scant data showing efficacy. Aspirin may be continued long-term in patients who have undergone revascularization as the risk of embolus from proximal stenotic vessels persists. Anticoagulants, such as warfarin, are rarely used because of the concern about bleeding from abnormal moyamoya vessels and the risk of hemorrhage after inadvertent trauma. Nicardipine, a calcium channel blocker, at a dose of 10 mg 3 times a day, has been reported to improve headaches and to reduce the frequency and severity of refractory transient ischemic attacks in children after revascularization in case reports. Intravenous verapamil has been reported to acutely improve neurologic deficit in a child with moyamoya.

Cervicocephalic Arterial Dissection (CCAD)

CCAD is associated with embolic stroke and is routinely treated acutely with intravenous UFH or LMWH, followed by 3 to 6 months of warfarin; however, no prospective randomized studies supporting such use have been performed. The AHA recommendations for the treatment of extracranial arterial dissections include the use of warfarin for 3 to 6 months or the use of antiplatelet drugs. Antiplatelet therapy is often continued for longer than 6 months. There is, however, no evidence from randomized studies to support the choice of antithrombotic agents over antiplatelet drugs.

A review of 34 children with extracranial traumatic carotid artery dissection did not support anticoagulation therapy over antiplatelet therapy. The authors of this study recommended antiplatelet therapy over anticoagulation in these patients; however, only half of the patients reported received anticoagulation and/or antiplatelet therapy. In practice, antithrombotic medications appear to be used more often than antiplatelet medications for the initial treatment of cranio cervical arterial dissection.

Anticoagulation is not recommended for children with an intracranial dissection or intracranial extension of a dissection because of concerns about subarachnoid hemorrhage.
(SAH) or those with SAH resulting from CCAD. Antiplatelet agents are at times used for intracranial dissection.

Heart Disease
Cardiac disease accounts for approximately a third of all cases of stroke in childhood and can occur spontaneously or during cardiac surgery or catheterization. Although heart disease is a common cause of stroke, it is a less frequent cause of recurrent stroke. This is possibly because of more aggressive prophylaxis of children with known cardiac risk factors for recurrent stroke. Warfarin has been used in children with stroke believed to be caused by heart disease. Current AHA guidelines recommend that for children with a cardiac embolism unrelated to a patent foramen ovale (PFO) who are at high risk of recurrent embolism, it is reasonable to start UFH or LMWH while warfarin therapy is initiated and adjusted. Alternatively, LMWH could be continued longer-term. The optimal duration of treatment is unknown. Options considered include 1 year or until the cardiac lesion is corrected or indefinitely if correction is not possible. In children with a suspected cardiac embolism unrelated to a PFO who have a lower or unknown risk of stroke, aspirin is recommended for at least 1 year.

Hyperhomocysteinemia
Elevated homocysteine (ie, hyperhomocysteinemia) is a risk factor for arterial and venous thrombosis in adults presumably because of endothelial injury and has been associated with initial and recurrent stroke in adults. Hyperhomocysteinemia has been associated with stroke in childhood as well. Hyperhomocysteinemia results from genetic polymorphisms of methylenetetrahydrofolate reductase (MTHFR) and cystathionine B synthase. In adults, the C677T and A1298C polymorphisms of the MTHFR gene are risk factors for ischemic and hemorrhagic stroke although homocysteine levels were not determined. When both were evaluated, homocysteine levels rather than MTHFR C677T polymorphism were associated with stroke in adults. The C677T polymorphism has been found to be a risk factor for ischemic stroke; however, elevated homocysteine, which correlated with the C6777T polymorphism, was found to be a risk factor for ischemic and hemorrhagic stroke.

Based on adult experience, homocysteine levels and MTHFR mutation testing are often evaluated in children with stroke. In a study of Thai children with stroke, the mean plasma homocysteine level was elevated; however, there was no significant increase in MTHFR C677T polymorphism. Because low levels of B12 and folate are associated with elevated homocysteine, folic acid and B12 supplementation are recommended in patients with elevated homocysteine and thrombosis. In adults, lowering the homocysteine level with daily supplementation of 2.5 mg folic acid, 50 mg vitamin B6 (pyridoxine), and 1 mg vitamin B12 (cobalamin) reduced the risk of stroke by approximately 25%, with a trend toward greater benefit in patients younger than 69 years. Benefit was not seen until at least 3 years of therapy, which is consistent with an earlier study showing no benefit at 2 years of treatment. A meta-analysis of 13 randomized controlled studies of folic acid supplementation to prevent stroke did not show a benefit; however, in a stratified analysis, a greater benefit was seen when B6 and B12 were supplemented along with folic acid. It is likely that some children with hyperhomocysteinemia identified as a risk factor for thrombosis will benefit from long-term supplementation with folic acid, vitamin B6 and vitamin B12, particularly given the benign nature of the treatment and the potential impact of homocysteine levels over many decades of life. It is unlikely that routine MTHFR polymorphism testing in children with a history of thrombosis is indicated.

Conclusions
Stroke is a significant cause of morbidity and mortality in childhood with sequelae that frequently last throughout life. There have been no trials of acute or chronic treatment of childhood stroke nor of primary or secondary stroke prevention in childhood other than in SCD. Because of the high rate of stroke recurrent in childhood, antithrombotic and antiplatelet medications are frequently used, which is often based on extrapolation from adult studies and on consensus. There is a critical need for studies to provide evidence-based guidelines for the acute and chronic treatment of stroke in childhood.

References


