As we have already learned, time to thrombolysis is imperative [The ATLANTIS, ECASS, and NINDS r-tPA Study Group Investigators. *Lancet* 2004; SITS Investigators. *Stroke* 2008; SITS Investigators. *Stroke* 2009]. In past years, Prof. Kaste has seen a growth in thrombolysis rates within his hospital, and this trend continues. Last year, 276 stroke patients received thrombolysis in the neurological emergency room of his hospital. Twenty-eight percent of these patients were treated within 90 minutes of symptom onset. This is an indication of where stroke treatment is headed. Telemedicine is also provided for smaller hospitals, because it is more effective to transfer thrombolysis "know-how" than stroke patients, noted Prof. Kaste.

For optimal care to be provided, education, training, and up-to-date guidelines (both national and international) are necessary. Education must also include population-based education. Incorporating symptom recognition, how to act in a case of acute stroke, and risk information in the media setting to educate laypeople will have a huge impact on the burden of stroke.

Evidence-based information regarding the prevention and treatment of acute stroke is readily available, so it is time to transfer that knowledge into clinical practice, concluded Prof. Kaste. Wherever data are missing, it is our responsibility as clinicians to seek out new information and fill in the gaps. More readily available stroke units and faster response times will also contribute to better stroke outcomes in the future.

Stroke Prevention Among the Young with Heart Disease: Controversies in the Use of Antithrombotic Therapy

The neurodevelopmental sequelae of congenital heart disease (CHD) and its treatment are likely to limit the ultimate educational achievements, employability, insurability, and quality of life for these children, said J. William Gaynor, MD, Children's Hospital of Philadelphia, PA. The effects include cognitive deficits, such as a short attention span, delays in the development of motor skills, speech, and language; and impaired social competency and executive functions.

Children with CHD are at risk for stroke before and after surgery and even later in life. The frequency of vaso-occlusive stroke in children with CHD who undergo cardiac surgery is 5.4 cases per 1000 children. Age, duration of bypass, and reoperation may be associated with stroke risk [Domi T et al. *Pediatrics* 2008]. There remains an unmet need for data that concern the long-term prevalence of or specific risk factors for stroke, as well preventative therapies in the CHD population, concluded Dr. Gaynor.

The issue of whether to use antithrombotic therapy for stroke prevention in children with CHD remains unanswered due to a lack of data, said Fenella J. Kirkham, MD, UCL Institute of Child Health, University College London, London, UK. However, there is a 6-fold increased risk of stroke for these children compared with the general population [Fox C. 2010 unpublished]. According to Prof. Kirkham, although primary prevention may be difficult, we may be able to prevent recurrence if we understand the mechanisms, which include primary arterial disease, such as dissection and moyamoya, and cerebral sinovenous thrombosis, as well as embolus. Appropriate management of risk factors is then possible.

For all children with arterial ischemic stroke, including those with cardiac disease, the risk of clinical recurrence is increased in children with moyamoya and other vasculopathies and in those with genetic thrombophilia and raised lipoprotein (a) (Table 1).

Table 1. Multivariate Cox Regression for Risk of Recurrent Stroke in AIS.

Risk factor	Hazard ratio	CI for ratio	p value
Vasculopathy	3.1	1.9 to 4.9	0.001
Single prothrombotic	2.0	1.2 to 3.4	0.005
Raised Lp (a)	2.2	1.1 to 4.4	0.03

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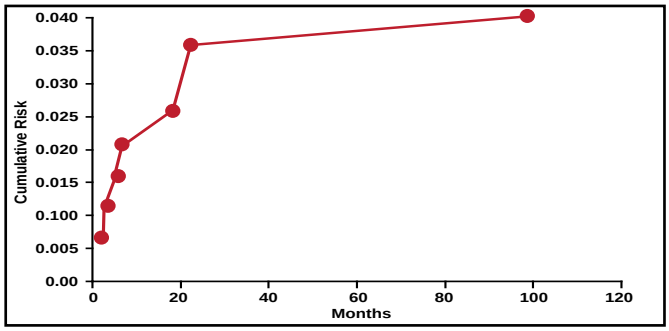
Recurrent thromboembolism in neonates is very low and occurs in the first year of life (Figure 1) [Gunther G et al. *Stroke* 2000]. Risk factors for recurrent sinovenous thrombosis include older age, presence of thrombophilia, and failure to recanalize affected venous sinuses. The current guidelines allow for anticoagulation of these patients. Prof. Kirkham is less inclined to use anticoagulation except in these children. She suggests the use of aspirin but would also exclude or treat iron deficiency. She cautions that before beginning therapy, it is important to fully investigate the patient.

There is a reasonably well-established link between patent foramen ovale (PFO) and cryptogenic stroke in young patients, according to Steven Messé, MD, Hospital of the University of Pennsylvania, Philadelphia, PA. However, the risk of recurrent stroke is relatively low (~1.5% per year on aspirin), while percutaneous PFO closure is expensive, has

a small but real risk of complication, does not replace other medical therapy, and is unproven.

Figure 1. Recurrent Thromboembolism in Neonates.



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The combination of PFO and atrial septal aneurysm (ASA) was associated with an increased risk of recurrent stroke in patients (OR 3.1; 95% CI, 2.3 to 4.2) in one Class I study but not in two other subsequent Class I studies.

The medical treatment options for PFO patients include antiplatelet drugs or anticoagulation, and there are no high-level data that confirm the superiority of either of these approaches, though anticoagulation is associated with more bleeding complications. Surgical or percutaneous closure can also be performed, but this does not preclude long-term medical therapy. At this time, there are no high-level data that support PFO closure. Randomized controlled trials are ongoing, but enrollment has been slowed by rampant use of off-label devices for PFO closure. Despite the lack of evidence, percutaneous septal closure procedures increased 50 times between 1998 and 2004.

Acute Stroke and the tPA Dilemma

There is some uncertainty regarding the appropriate treatment strategy for mild stroke and whether or not thrombolytic therapy with tissue plasminogen activator (tPA) is suitable for less severe stroke patients. Seizures at stroke onset, which occur in 4.2% to 7.7% of acute stroke patients, are generally exclusion criteria for tPA due to the possibility of injury or "stroke mimics," such as Todd paralysis [Sylaja *Stroke* 2006; Weir. *J Neurol Neurosurg Psychiatry* 2005; Mathews. *Neuroradiology* 2008]. Christopher Lewandowski, MD, Henry Ford Hospital, Detroit, MI, discussed methods for distinguishing stroke mimics from stroke and the ramifications of tPA in stroke mimics.

A thorough patient history to determine the time and duration of the seizure is imperative, as seizure duration is generally proportional to the duration of the postictal phase, except in the case of Todd paralysis, said Dr. Lewandowski. Physical exam and imaging can also assist the clinician in differentiating between mimics and authentic stroke. CT-perfusion imaging, CT-angiogram, and diffusion-weighted magnetic resonance imaging are highly sensitive and highly specific modalities for stroke assessment within minutes of stroke onset (Tables 1 & 2). However, the most rapidly available modality should be utilized due to time constraints that are related to stroke treatment. The risk of intracranial hemorrhage with tPA is dose-dependent, and the duration of action is relatively short. Therefore, the treatment of stroke mimics with tPA carries low risk, concluded Dr. Lewandowski.

Table 1. Comparison of Imaging Modalities for Acute Stroke.

Imaging Modality	Sensitivity Specificity	Details
CT-Angiogram	• 98% Sensitivity • 98% Specificity • for cerebral vessel occlusion in large branches	• Estimate of gross collateral blood flow • Provides source images that reflect cerebral blood flow • Provides diagnostic evaluation of the neck • Difficult to see smaller vessel occlusions
CT-Perfusion	• 90% to 95% Sensitivity within 6 hours • 100% Specificity	• Provides images that reflect cerebral blood volume and cerebral blood flow • Evaluates mean transit time • Low cost and widely available
MRI-DWI	• Approaching 100% Sensitivity • Approaching 100% Specificity within minutes after stroke symptom onset	• Benefits are similar to that of CT • Possibility of false negative DWIs occurring in brainstem stroke and lacunes

Table 2. CT-Perfusion Differences in Seizure versus Acute Stroke.

CT-Perfusion in Seizure/ Stroke Mimic	CT-Perfusion in Acute Stroke
Increased cerebral blood flow (hyperperfusion)	Decreased regional cerebral blood flow
Increased cerebral blood volume	Increased regional cerebral blood volume
Decreased mean transit time	Prolonged mean transit time