Treatments in Stroke registries, the Virtual International Stroke Trials Archive, and the US FDA, age alone is not a barrier to thrombolysis with alteplase in adults, but patients over 80 years of age are excluded by European Regulatory Authorities. The Third International Stroke Trial revealed a significantly greater treatment effect of alteplase in patients over 80 years of age than in those aged 80 or younger. Alteplase treatment within 6 hours of stroke onset improved functional outcome. A risk of symptomatic intracerebral hemorrhage with alteplase is a deterrent to more frequent use, but further studies are indicated, especially in younger patients.

A PubMed search of the literature uncovers several single case reports of the successful use of thrombolysis in the treatment of childhood stroke. (Condie J, Shaibani A, Wainwright MS. Successful treatment of recurrent basilar artery occlusion with intra-arterial thrombolysis and vertebral artery coiling in a child. **Neurocrit Care** 2012 Feb;16(1):158-62). Coordination of neurology, critical care, and interventional radiology is recommended in management of ischemic stroke in children.

Currently, there are two treatment guidelines for therapy of childhood AIS (Royal College of Physicians in the UK, and American Heart Association and American College of Chest Physicians). Antithrombotic strategies are advocated, but the choice of agent varies with the guideline preference and risk factors. Thrombolytic treatment is not advocated. (Eleftheriou D, Ganesan V. Treatment strategies for childhood stroke. **Expert Opin Pharmacother** 2008 Dec;9(17):2955-67). In a multicenter, observational, cohort study, alteplase was used infrequently and the outcome was often poor; intracranial hemorrhage occurred in 4 of 15 patients. (Amlie-Lefond C, et al. International Pediatric Stroke Study. Use of alteplase in childhood arterial ischaemic stroke. **Lancet Neurol** 2009 Jun;8(6):530-6). Clinical trials are needed to determine optimal dose of alteplase in childhood stroke.

DEVELOPMENTAL DISORDERS

HEMIMEGALENCEPHALY: A FOETAL TAUOPATHY

Researchers at University of Calgary and Alberta Children's Hospital, Canada; and University of Pennsylvania, Philadelphia studied brain resections from 3 male infants with hemimegalencephaly (HME) and refractory epilepsy. One infant died at 2.5 months, and one has Proteus syndrome. The hippocampus and neocortex of HME showed cytoarchitectural abnormalities on electronmicroscopy and intense tau immuno-reactivity. The post-mortem non-HME hemisphere had sparse dysmorphic tau-reactive cortical neurons but none in subcortical regions. Numerous enlarged and dysmorphic cells exhibited immunoreactivity indicative of mTOR activation. Tau expression and mTOR activation were absent in control brains. Electron microscopy in each case showed lipid in neurons and lipid storage by light microscopy. The investigators propose that the pathogenesis of HME may involve an early defect in microtubules, probably related to the AKT3 gene. Lipidosis of neurons and glia suggests a metabolic impairment of undetermined type, related to tauopathy in HME. Perinatal treatment with everolimus (rapamycin), an inhibitor of mTOR pathway, might reduce the morbidity of HME, including epilepsy. (Sarnat H, Sarnat LF, Crino P, Hader W, Bello-Hespinosa L. Hemimegalencephaly: foetal tauopathy with mTOR hyperactivation and neuronal

lipidosis. **Folia Neuropathologica** 2012;50(4):330-45). (Response: Harvey Sarnat, MD, FRCP, Alberta Children's Hospital, 2888 Shaganappi Trail, NW, Calgary, AB T3B 6A8, Canada. E-mail: Harvey.sarnat@albertahealthservices.ca).

COMMENT. Hemimegalencephaly is a hamartomatous dysgenesis, sometimes associated with other neurocutaneous syndromes, especially epidermal nevus and Proteus syndromes. Infants with Proteus syndrome [alt: Wiedemann syndrome] are normal at birth and develop skin tumors and bone growths with increasing age, especially involving the skull and soles of feet. Neurological involvement in rare reports of Proteus syndrome includes HME, Ohtahara syndrome, syringomyelia, arachnoid cyst, craniocutaneous lipomatosis, vascular malformation, and meningioma. (Bastos H, da Silva PF, de Albuquerque MA, et al. **Seizure** 2008 Jun;17(4):378-82). (Opitz JJ. Hamartoma syndromes, exome sequencing, and a protean puzzle. **N Engl J Med** 2011 Aug 18;365(7):661-3). Proteus syndrome is caused by a mutation in AKT1, and is classed as a genetic mosaicism. A knowledge of neurological syndromes helps in the selection of diagnostic tests and our understanding of the cause of refractory epilepsies.

MORPHOLOGICAL VARIATIONS OF HIPPOCAMPAL FORMATION IN EPILEPSY

Researchers at Hospital Sao Paulo and other centers in Brazil compared the hippocampal formation (HF) morphology of healthy asymptomatic individuals (n=30) with that of patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE-HS)(n=68), of patients with malformations of cortical development (MCD)(n=34), and of patients with morphological HF variations without other structural signs (pure MVHF)(n=12). Morphological variations of HF were significantly more frequent in patients with MCD than in patients with MTLE-HS or in normal individuals. Febrile seizures occurred only in patients with MTLE-HS, supporting the hypothesis that febrile seizures cause the MTLE-HS. Refractory epilepsy is more associated with abnormalities like hippocampal sclerosis or malformations of cortical development than with variations of the hippocampal formation itself. Patients with pure morphological variations of the hippocampal formation showed higher incidence of extratemporal seizure onset. (Hamad APA, Carrete H Jr, Bianchin MM, et al. Morphological variations of hippocampal formation in epilepsy: Image, clinical and electrophysiological data. **Epilepsy & Behavior** 2013 Jan;26(1):67-70). (Response: Dr Hamad. E-mail: anahamad@gmail.com).

COMMENT. The authors conclude that morphological variations of hippocampal formation (HF) are rare in patients without seizures and that hippocampal formation malrotation is probably pathological. The development of HF is complete after 18 weeks gestation and is similar to the adult HF after 30 weeks gestation. Some authors suggest that febrile seizures might lead to hippocampal sclerosis or to hippocampal formation abnormalities but not to epilepsy. (Auer T, Barsi P, Bone B, et al. History of simple febrile seizures is associated with hippocampal abnormalities in adults. **Epilepsia** 2008 Sep;49(9):1562-9). The relationship between HF dysmorphism, febrile seizures and hippocampal sclerosis is still unclear.