

## Updates in Clinical Neurology

An overview

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PGY 4 - Neurology

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## Disclosures

- None yet



## Objectives

- Stroke
- Dementia
- Neuromuscular disease
- Headache and Pain
- Multiple Sclerosis
- Pediatric Neurology
- Neurogenetics
- Epilepsy
- Case



## Neurologist - Numbers

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### THE DOCTOR WON'T SEE YOU NOW? STUDY: US FACING A NEUROLOGIST SHORTAGE

Neurologists on Capitol Hill to Prevent Shortage, Longer Wait Times

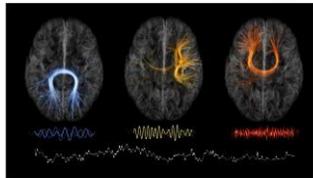
**ANNAPOLIS, Md.** - Americans with brain diseases such as Alzheimer's disease, Parkinson's disease or multiple sclerosis (MS) who need to see a neurologist may face longer wait times or have more difficulty finding a neurologist, according to a new study published in the April 17, 2013, online issue of *Neurology*, the medical journal of the American Academy of Neurology. The findings are being released as nearly 100 neurologists will descend on Capitol Hill next Tuesday, April 23, 2013, to encourage Congress to protect patients' access to neurologists and ensure there will be care for the one in six Americans currently affected by brain disease.



## Neurologist - Numbers

### One neurologist for 1 million Africans – scholar

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Sub-Saharan Africa suffers a huge deficit in neurologists, with only one specialist for a million people living on the continent, according to Professor Amadou Gallo Diop, head of the Neurology Department at Dakar's Fann University Hospital in Senegal.

The abstract for 0042 is one specialist for every 50,000 inhabitants said Professor Diop in an interview with the African Press Agency on Wednesday.



## Updates in Stroke

- **Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct.** N Eng J Med 2017
- **Findings:** Randomized 206 patients with acute ischemic stroke between six and 24 hours from symptom onset to **best medical treatment** with or without **thrombectomy**.
- **Findings:** The thrombectomy arm did substantially better. Functional independence was 49 percent with thrombectomy compared with 13 percent without, and there was no increased risk.



## Updates in Stroke

- **Long-term outcomes of patent foramen ovale closure or medical therapy after stroke.** N Engl J Med 2017
- **Findings:**  
The rates of subsequent strokes in the PFO closure group were low (about 1.0 percent per year), and about half as high as in the non-closure group. There was an increased risk of post-closure atrial fibrillation as well as deep vein thrombosis in the PFO closure patients.
- **Significance:**  
About 25 percent of strokes are “cryptogenic,” and many such patients are found to harbor a PFO. Though there is a statistical association between PFO and stroke, previous studies were inconclusive about the benefit of PFO closure for secondary stroke prevention.

## Updates in Stroke

- **Tenecteplase versus alteplase for management of acute ischemic stroke (NOR-TEST):** A phase 3, randomised, open-label, blinded endpoint trial. *Lancet Neuro* 2017;16:781-788.
- **Findings:**  
T1,100 patients presenting within 4.5 hours of acute ischemic stroke were randomized to tissue plasminogen activator (tPA) or tenecteplase (TNK). **There was no difference between the groups in the rate of good outcome or complications such as bleeding.**
- **Significance:**  
TNK has certain theoretical and practical advantages: It has higher fibrin specificity, and it is given as a single bolus not requiring subsequent infusion. In the US, it costs less than tPA. Did not show superiority over tPA; more studies needed

## Updates in Stroke

- **Guideline for the prevention, detection, evaluation and management of high blood pressure in adults:** AHA - Nov 7 2017
- **Findings:**  
A study of 9,000 people (SPRINT trial) showing that reducing systolic blood pressure (BP) from 130 to 120 could reduce the risk of heart attack and stroke. The main resultant guideline change is that the “normal” goal BP is set at 120/80, and the definition of “hypertension” is reduced from the previous threshold of 140/90 to 130/80 based on  $\geq 2$  readings on  $\geq 2$  occasions. That means that 46 percent of US adults have hypertension and a 45-year-old adult has a greater than 80 percent chance of developing hypertension over the next 40 years.
- **Significance:**  
The single most important modifiable risk factor for vascular disease and stroke is HTN. If the pressure is  $> 130/80$ , they should recommend rechecking outside of the doctor’s office, and if it is still elevated, lifestyle changes and possible pharmacotherapy should be prescribed.

## Updates in Dementia

- **A new potential biomarker for dementia with Lewy bodies.** *Neurology* 2017;89(4):318-326.
- **Findings:**  
Phosphorylate alpha-synuclein deposits in 100 percent of the cervical skin biopsies of 18 patients with dementia with Lewy bodies (DLB) compared to 23 non-DLB dementia cases and 25 age-matched controls. No deposits were identified in the comparator groups.
- **Significance:**  
This suggests that a simple skin biopsy could effectively identify DLB patients in a relatively non-invasive and inexpensive way. If replicated in populations more representative of the typical DLB cases seen in neurology clinics, it could be in highly effective diagnostic tool.

## Updates in Dementia

- **Dementia prevention, intervention, and care.** *Lancet* 2017.
- **Findings:**  
24 experts, highlighted the clear evidence that dementia represents a chronic disease that is potentially amenable to disease-modifying measures. The Commission determined that up to **one-third of future cases of dementia are preventable.**
- **Significance:**  
Improving early-child education, increasing physical activity, treating midlife and late-life hypertension, smoking cessation, preventing obesity and diabetes in midlife, and decreasing depression and social isolation. Although we have no effective disease-modifying therapies for dementia, we can modify the prevalence of the disease.

## Updates in Headache and Pain

- **Fremanezumab for the preventive treatment of chronic migraine.** N Engl J Med 2017
- **Findings:**  
With over 1,100 patients enrolled, the study by Silberstein, et al, demonstrated that fremanezumab, a humanized IgG2A monoclonal antibody that selectively binds to calcitonin-gene related peptide (CGRP), was effective over a 12-week trial in decreasing headache days compared to placebo in chronic migraine patients.
- **Significance:**  
Erenumab and fremanezumab are likely just the beginning of a new class of injectable drugs for migraine prevention. They offer the ability to target the migraine pathway in ways that we have never done before. Both trials excluded highly refractory patients, so we do not know now if these antibodies will be helpful for those most disabled from migraines; however, the potential is there.

## Updates in Multiple Sclerosis

- **Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis**
- **Ocrelizumab versus placebo in primary progressive multiple sclerosis.** N Engl J Med 2017
- **Findings:**  
In two identical phase 3 trials (by Hauser, et al), 821 and 835 patients with relapsing multiple sclerosis were randomized to intravenous ocrelizumab and subcutaneous interferon beta-1a for 96 weeks. Among patients with relapsing MS, ocrelizumab was associated with lower rates of disease activity and progression than interferon beta-1a over a period of 96 weeks.

## Updates in Multiple Sclerosis

- **Ocrelizumab versus interferon beta-1a in relapsing multiple sclerosis**
- **Ocrelizumab versus placebo in primary progressive multiple sclerosis.** N Engl J Med 2017
- **Significance:**  
The findings usher B-cell depleting agent in both relapsing MS as compared with interferon injections, and in primary progressive MS into the mainstream of MS therapeutics, leading to the first approved agent for the primary progressive form of the disease. Enormous attention will be paid to both the long-term extensions from these pivotal trials, as well as the real-world safety and efficacy of this agent as it is utilized in both relapsing and progressive patients with MS after US Food and Drug Administration (FDA) approval in March 2017.

## Updates in Pediatric Neurology

- **Trial of amitriptyline, topiramate, and placebo for pediatric migraine.** N Engl J Med 2017
- **Findings:**  
This randomized, double-blind placebo-controlled study evaluated amitriptyline, topiramate, and placebo in 8- to 17-year-old patients with migraine. **The study found no significant difference in the headache frequency or related disability with any of the three arms:** Additionally, there were more side effects in the patients that received amitriptyline and topiramate.
- **Significance:**  
The best medication approach to childhood headache has not been proven. The interim analysis revealed futility when there was no significance between groups in the primary endpoint of 50 percent reduction or greater. Additionally, the other secondary endpoints showed no difference. The medication-treated group had a higher rate of adverse events. Life style changes is an ignored strategy for headache management.

## Updates in Neurogenetics

- **Single-dose gene-replacement therapy for spinal muscular atrophy.** N Engl J Med 2017
- **Findings:**  
15 patients with spinal muscular atrophy 1 (SMA1) received a single dose of intravenous adeno-associated virus serotype 9 encoding the missing SMN protein, resulting in longer survival, achievement of motor milestones, and improved motor function..
- **Significance:**  
The study suggests the potential for an effective single-dose IV therapy for SMA, a leading genetic cause of infant death. It also illustrates the potential viability of gene replacement for long-term treatment of neuromuscular disorders

## Updates in Epilepsy

- **Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors** Epilepsy Curr 2017
- **Findings:**  
An association between SUDEP and the occurrence and frequency of tonic-clonic convulsions was reported. SUDEP is under-reported in death certificates, and there is a higher occurrence in children (specifically boys) than previously reported. The paper by Devinsky O, et al, provides evidence that medical examiners will under-report SUDEP
- **Significance:**  
SUDEP should be discussed with patients early in the relationship with patients, and patients should be counseled on avoidance of tonic-clonic convulsions.

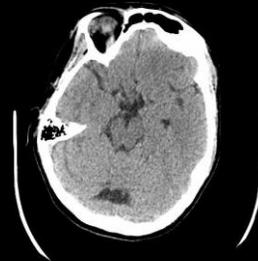
## Updates in Epilepsy

- **Position paper of the ILAE Commission for Classification and Terminology.** Epilepsia 2017
- **Findings:**  
A new classification system for epileptic seizures and epilepsy. For example, the term "complex partial seizure" has now become "focal seizure with impaired awareness." And epilepsy is now divided into four categories: focal, generalized, combined focal and generalized, and unknown. The category of "combined focal and generalized" did not exist before, and now will be used for "mixed" syndromes such as Lennox-Gastaut and Dravet syndromes. The terms "symptomatic generalized" and "cryptogenic" are no longer in use
- **Significance:**  
Clinicians will need to understand and start to use the new terminology. The revised classification system includes language and concepts that are much more patient-friendly.

## Case

- 35 year old gravida 2 para 1 who presented to Spectrum Hospital with acute right MCA syndrome (sudden left sided weakness)
- Neurological examination was significant for left-sided hemiplegia affecting face, upper and lower extremity.
- NIHSS of 12 on arrival prior to initiation of IV tPA at 1820 hours followed by mechanical thrombectomy with TIC13 outcome and NIHSS of 0.

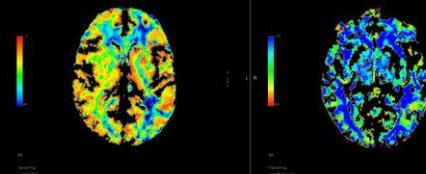
## Imaging



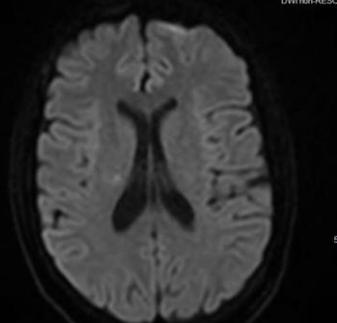
## Angio



## CT Perfusion



## DWI



## Clinical workup and impression

- Further workup for cryptogenic stroke revealed patient has a congenitally abnormally shaped mitral valve with HCM (SAM) and gestational hypertension.
- Hypercoagulable workup was negative.
- SAM (septal mitral valve leaflet defect) was noted. This is significant as HCM genotype with reduced penetrance or SAM is a possible independent risk factor for stroke.

## DWI

## Patient weeks later

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- Read the Neurology Today article, "New Practice Guideline Quantifies SUDEP: Incidence Rates and Risk Factors" (May 4, 2017):

