PEARLS IN NEUROLOGY

Oklahoma Academy of Physician Assistants
42nd Annual Conference
September 21, 2016

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Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

David Lee Gordon, M.D.

I have no relevant financial relationships or affiliations with commercial interests to disclose.
PEARLS IN NEUROLOGY
LEARNING OBJECTIVES

- Describe the diagnosis & management of common neurologic emergencies
- Describe the diagnosis & management of common neurologic outpatient conditions
A 65-year-old man is in the ED of a hospital designated as an “acute-stroke-ready” stroke center. He has aphasia, right hemiplegia, and right visual field deficit and was last known normal 2 hours ago. Noncontrast CT brain is negative, fingerstick blood glucose is 92, and BP is 174/72. Which of the following represents optimal initial management of this patient?

A. Administer IV tPA and perform head CT angiography
B. Admit to a floor bed in the hospital for monitoring
C. Prescribe clonidine as needed for BP > 140/90
D. Transfer as soon as possible to a primary stroke center
E. Transfer quickly to a comprehensive stroke center
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QUESTION 1 – ANSWER

A. Administer IV tPA and perform head CT angiography
B. Admit to a floor bed in the hospital for monitoring
C. Prescribe clonidine as needed for BP > 140/90
D. Transfer as soon as possible to a primary stroke center
E. Transfer quickly to a comprehensive stroke center

- Stroke Centers
- The Penumbra & Core
- Thrombolysis & Mechanical Thrombectomy
TJC & OSDH STROKE CENTER LEVELS

Systems-Based Practice

- **Level 1 = Comprehensive Stroke Center** (TJC certification)
  - AIS, ICH, & SAH management including all therapeutic options and levels of care in ED, ASU, NSICU, neurointervention, surgery

- **Level 2 = Primary Stroke Center** (TJC certification)
  - AIS management in ED & ASU
    - Drip & *keep* if CTA negative = not thrombectomy candidate
    - Drip & *ship* if CTA positive = thrombectomy candidate

- **Level 3 = Acute Stroke-Ready Hospital** (TJC certification)
  - AIS management in ED – drip & *ship*

- **Level 4** – not prepared to manage acute stroke patients

_TJC = The Joint Commission; OSDH = Oklahoma State Department of Health; AIS = acute ischemic stroke; ICH = intracerebral hemorrhage; SAH = subarachnoid hemorrhage; ED = emergency department; ASU = acute stroke unit; NSICU = Neurosciences Intensive Care Unit; CTA = computed tomography angiography; “Drip” refers to administration of IV tPA_
ACUTE ISCHEMIC STROKE PATHOPHYSIOLOGY: THE PENUMBRA & CORE

- **Penumbra** is zone of **reversible ischemia** around **core** of irreversible infarction during **first few hours** after ischemic stroke onset.

- **Penumbra** is damaged by:
  - Low BP – hypoperfusion
  - Hyperglycemia – lactic acidosis
  - Fever – ↑ metabolic demand
  - Seizure – ↑ metabolic demand

*Note: Low BP & high blood glucose hurt the penumbra!*
AIS EMERGENCY THERAPIES
“Time is brain, save the penumbra!”

Tissue plasminogen activator (tPA) IV
- Thrombolytic (specifically fibrinolytic) agent
- Lyses clot & reperfuses penumbra
- Saves penumbra neurons & improves patient outcome if given within hours of stroke onset
- Different criteria for 3- and 4.5-h windows
- Excellent safety if given w/in time windows

Endovascular/IA therapy = Neurointervention
- Mechanical thrombectomy proven benefit w/:
  - IV tPA
  - Distal ICA/proximal MCA occlusion (by CTA)
  - Evidence of salvageable penumbra
  - Onset-to-groin-puncture time ≤ 6 h
  - Good prestroke neurologic status

pen (paene) = almost
umbra = shadow
AIS EMERGENCY THERAPY

**IV tissue plasminogen activator (tPA)**

- Stroke onset = last time known to be without symptoms
- FDA-approved \( \leq 3 \) h, consensus guidelines \( \leq 4.5 \) h, but:
  
  *The earlier you give IV tPA, the better the outcome*

- Do NOT give if:
  - Pt \( > 80 \) yo
  - Stroke too large (NIHSS > 25)
  - Ischemia > 1/3 MCA on scan
  - Taking warfarin at all
  - DM w/ previous stroke

- Disability risk ↓ 30% despite ~5% symptomatic ICH risk
- Lawsuits for not giving >>> lawsuits for giving

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**< 3.0 Hours**

- No upper age limit
- No limit on stroke size
- Can give if taking warfarin & INR \( \leq 1.7 \)

**3.0-4.5 Hours**

- Do NOT give if:
  - Pt \( > 80 \) yo
  - Stroke too large (NIHSS > 25)
  - Ischemia > 1/3 MCA on scan
  - Taking warfarin at all
  - DM w/ previous stroke

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*NINDS tPA Study*  
*ECASS II*
A 63-year-old man with hypertension, hyperlipidemia, and coronary artery disease is admitted to the hospital with a small right cerebral infarction manifested by left hemiparesis and new-onset atrial fibrillation. Preadmission, he took lisinopril and aspirin 81 mg daily. He has normal liver and renal function. Which of the following represents optimal management of this patient?

A. Add apixaban 5 mg twice daily to aspirin 81 mg daily
B. Add clopidogrel 75 mg daily to aspirin 81 mg daily
C. Change aspirin to warfarin with target INR 2.0-3.0
D. Continue current dose of aspirin 81 mg daily
E. Increase aspirin dose to 325 mg daily
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QUESTION 2 – ANSWER

A. Add apixaban 5 mg twice daily to aspirin 81 mg daily
B. Add clopidogrel 75 mg daily to aspirin 81 mg daily
C. Change aspirin to warfarin with target INR 2.0-3.0
D. Continue current dose of aspirin 81 mg daily
E. Increase aspirin dose to 325 mg daily

- Ischemic Stroke & TIA: Two types of Thromboemboli
- Antithrombotic Agent Options
USUALLY DUE TO 1 OF 2 TYPES OF THROMBOEMBOLI

- Thrombus = blood clot
- Embolus = floating plug
- Blood clot forms in vascular system (arteries or heart), travels downstream, plugs a brain artery

BLOOD CLOTS FORM FOR 1 OF 2 REASONS:

- **Platelets (Velcro, white clot)** – stick to bumpy pipes
- **Clotting factors (Jello, red clot)** – clump when blood stagnant

BLOOD CLOTS COME FROM 1 OF 3 LOCATIONS:

- **Artery** – esp. hardening of artery wall (atherosclerosis)
- **Heart** – esp. irregular heart rhythm (atrial fibrillation)
- **Blood** – blood too sticky (hypercoagulable state)
AIS/TIA SECONDARY PREVENTION

Antithrombotic therapy options

High-flow states: platelets cause clots

Platelets are like Velcro sticking to bumpy walls

- large-artery atherosclerosis
- small-artery disease

Low-flow & hypercoagulable states: clotting factors cause clots

Clotting factors are like dissolved powdered Jello that forms clumps of Jello when liquid is static

- cardioembolism
- hypercoagulable state

ANTIPATELET AGENT

- aspirin 81-325/d
- clopidogrel 75/d
- aspirin + dipyridamole XR 25/200 BID

ANTICOAGULANT

- warfarin (INR 2.0-3.0)
- apixaban 5 mg BID
- rivaroxaban 20 mg/d
- dabigatran 150 mg BID
- edoxaban 60 mg/d

Some patients need both types of antithrombotic therapy, e.g., a patient with coronary artery disease & atrial fibrillation.
Your 50-year-old male colleague suffers the sudden onset of right hemiparesis and difficulty speaking while at work. In the ED thirty minutes later, his symptoms have completely resolved and he wishes to return to work. The wisest course of action is:

A. Admit him to the hospital and arrange for a rapid ischemic stroke etiologic evaluation

B. Arrange for him to see his primary-care provider as an outpatient within the next month

C. Diagnose transient ischemic attack and prescribe daily aspirin for stroke prophylaxis

D. Obtain noncontrast head CT scan and, if normal, advise him that he may return to work

E. Tell him to take the rest of the day off, but not to worry since he is back to normal
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QUESTION 3 – ANSWER

A. Admit him to the hospital and arrange for a rapid ischemic stroke etiologic evaluation
B. Arrange for him to see his primary-care provider as an outpatient within the next month
C. Diagnose transient ischemic attack and prescribe daily aspirin for stroke prophylaxis
D. Obtain noncontrast head CT scan and, if normal, advise him that he may return to work
E. Tell him to take the rest of the day off, but not to worry since he is back to normal

- Acute Ischemic Stroke (AIS) & TIA Relationship
- AIS/TIA Etiologic Evaluation
ISCHEMIC STROKE & TIA
Both are usually caused by a traveling blood clot

### Acute ischemic stroke (AIS)
- Focal brain ischemia with infarction, usually with sequelae, because clot did not dissolve in time
- Equivalent term is “cerebral infarction”

### Transient ischemic attack (TIA)
- Focal brain ischemia with transient episode of neurologic dysfunction—but NO infarction or sequelae, because clot dissolved in time
- Signals that patient is at risk for an ischemic stroke in the near future—next time, the clot may not dissolve in time
- Partial seizures and migraine auras can mimic TIAs

*Long-term antithrombotic therapy for secondary stroke prevention depends on results of etiologic testing (Velcro or Jello clot?)*
## AIS/TIA ETIOLOGIC EVALUATION

Determine clot origin (artery, heart, or blood)

<table>
<thead>
<tr>
<th></th>
<th>NONINVASIVE</th>
<th>INVASIVE</th>
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<tbody>
<tr>
<td></td>
<td><strong>Day 1</strong></td>
<td><strong>Day 2</strong></td>
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<tr>
<td>BRAIN</td>
<td>MRI (w/ DWI &amp; ADC)</td>
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<td></td>
<td>(DWI &amp; ADC show very early ischemia)</td>
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<td>ARTERIES</td>
<td>CTA head &amp; neck</td>
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<td>(both with IV contrast)</td>
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<td>or MRA head &amp; carotid duplex (CD)</td>
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<td></td>
<td>(neither with IV contrast)</td>
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<tr>
<td>HEART</td>
<td>ECG &amp; monitor</td>
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<td></td>
<td>Cardiac biomarkers</td>
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<td></td>
<td>Transthoracic echo (TTE)</td>
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<td>(TTE for left ventricular source)</td>
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<tr>
<td>BLOOD</td>
<td>Hypercoagulable profile*</td>
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<td>(perform day 3 if artery &amp; heart evaluations negative)</td>
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<tr>
<td></td>
<td>Catheter angiography*</td>
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<td>(to clarify findings on CTA, MRA, or CD)</td>
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<tr>
<td></td>
<td>Transesophageal echo (TEE)*</td>
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<td>(TEE for left atrial, atrial septal, aortic arch sources)</td>
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*in select patients
A 79-year-old man falls out of bed due to weakness. He is able to call 911 and you see him in the ED. On your exam, he has normal mental status and language function, normal eye movements, mild bifacial weakness, mild weakness in all four extremities, normal sensation, absent reflexes throughout, and absent Babinski signs. You arrange for an admission and return to see him one hour later. At this time, he has quadriplegia—i.e., he cannot move any extremity at all. He still has absent reflexes and normal mental status, language, and sensation. His bowel and bladder function have been normal throughout this time. The most appropriate initial action you should take is to obtain STAT:

A. Blood glucose level and give IV D50 if glucose < 50
B. Electromyography and nerve conduction studies and give IVIG
C. Head CT scan and give IV tPA if there is no hemorrhage on CT
D. MRI scan of the cervical spine and consult neurosurgery
E. Pulmonary mechanics and intubate if forced vital capacity < 1-2 L
QUESTION 4 – ANSWER

A. Blood glucose level and give IV D50 if glucose < 50
B. Electromyography and nerve conduction studies and give IVIG
C. Head CT scan and give IV tPA if there is no hemorrhage on CT
D. MRI scan of the cervical spine and consult neurosurgery
E. **Pulmonary mechanics and intubate if forced vital capacity < 1-2 L**

- Guillain-Barré Syndrome Clinical Presentation
- Guillain-Barré Syndrome Acute Management
  - Lungs 1<sup>st</sup>
  - Nerves 2<sup>nd</sup>
GUILLAIN-BARRÉ SYNDROME (AIDP)

CLINICAL PRESENTATION

- Possible antecedent infection (esp. viral or Campylobacter)
- Acute history (symptoms plateau within 4 wks)
- Sensory symptoms common, but normal sensory exam
- Low-back pain common
- Distal weakness, often with “ascending paralysis”
- Absent reflexes
- Demyelinating neuropathy by EMG (electromyography) and NCS (nerve conduction studies) – findings peak at 2 wks
- Other possible findings
  - Dysautonomia (especially cardiac arrhythmias)
  - Cerebrospinal fluid – protein ↑ (peaks at 2 wks), no cells
GUILLAIN-BARRÉ SYNDROME (AIDP)
ACUTE MANAGEMENT—LUNGS 1ST

Cardiac & Pulmonary Management

- Admit to ICU (Neuroscience ICU if available)
- Monitor cardiac rhythm and blood pressure
- Elevate head of bed
  - Assist breathing in pt w/ diaphragm weakness
  - Prevent aspiration
- Pulmonary mechanics q 4-12 h
  - FVC = forced vital capacity
  - NIF = negative inspiratory force
- Intubation if FVC < 1-2 L (< 15-20 ml/kg)
GUILLAIN-BARRÉ SYNDROME (AIDP) ACUTE MANAGEMENT—NERVES 2\textsuperscript{ND}

- **Plasmapheresis vs. IVIG**
  - Exchange 2-3 liters of plasma every other day x 5 treatments
  - OR
  - IVIG at dose of 2 g/kg divided over 4-5 days (or 2 days for children & adolescents)

*Note: Steroids are ineffective in pts with AIDP*
A 23-year-old woman has intermittent episodes lasting 2-3 minutes manifested by losing consciousness and shaking all four extremities. For about an hour after each episode, she is sleepy and difficult to arouse. Upon careful questioning, you find that one time her father saw her staring at the ceiling and not responding to him for a few moments just prior to having one of these episodes. How would you best characterize the episodes she is having:

A. Absence seizures
B. Complex-partial seizures with secondary generalization
C. Juvenile myoclonic epilepsy
D. Primary generalized seizures
E. Pseudoseizures (psychiatric nonepileptic seizures)
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QUESTION 5 – ANSWER

A. Absence seizures
B. Complex-partial seizures with secondary generalization
C. Juvenile myoclonic epilepsy
D. Primary generalized seizures
E. Pseudoseizures (psychiatric nonepileptic seizures)

- Transient Loss of Consciousness Differential Diagnosis
- Types of Seizures
- Partial (Focal) Seizures & Secondary Spread
- Complex-Partial Seizures
DIFFERENTIAL DIAGNOSIS: TRANSIENT ALTERED CONSCIOUSNESS

- Complex-partial seizures
  - Change in consciousness, aura, and postictal state (lethargy, confusion, and/or focal deficit)
- Absence seizures (= petit mal) seizures
  - Childhood onset, automatisms, but no postictal state
- Syncope: loss of tone & no postictal state
- Migraine with aura: ↓ consciousness rare
- TIA: ↓ consciousness almost never occurs
SEIZURE TYPES: 
PARTIAL VS. GENERALIZED

- **Partial (Focal) Seizures**
  - Simple-partial (no change in awareness)
  - Complex-partial (change in awareness)

- **Generalized Seizures**
  - Generalized tonic-clonic (GTC = grand mal)
  - Juvenile myoclonic epilepsy (JME)
  - Absence (= petit mal)
  - Other – generalized tonic, generalized clonic, atonic
Complex-Partial Seizure
Focal (partial) seizure can spread to a portion of the opposite cerebral hemisphere with resultant “complex-partial seizure” and mild alteration of consciousness

Partial Seizure w/ 2° Generalization
Partial seizure can spread to the thalamus and then to both cerebral hemispheric cortices diffusely with resultant generalized seizure and complete loss of consciousness
Focal-onset seizures with change in consciousness
  - Staring
  - Amnesia for the event

Automatisms common
  - Eye blinking
  - Chewing
  - Lip smacking
  - Picking with fingers
  - Nose wiping

Presence of aura or focal postictal deficit imply a focal-onset (= partial) seizure

Causes include:
  - Tumor, AVM, abscess, stroke, posttrauma, mesial temporal sclerosis, HIV dementia, Alzheimer disease, idiopathic/cryptogenic

Evaluation
  - EEG may show focal spikes (epileptiform activity) or slowing due to underlying focal brain dysfunction
  - MRI brain without and with contrast with thin cuts through temporal lobe

Treatment:
  - Broad range of anticonvulsants
  - Surgical resection for refractory seizures
A 20-year-old male college student has a generalized tonic-clonic seizure in his hotel room while on spring break. The night before, he and three of his fellow students had stayed up all night driving from college in the midwestern U.S. to South Padre Island in Texas. He admits to a history of sudden jerking movements of his limbs in the morning. What is the most appropriate treatment for this patient?

A. Carbamazepine
B. Ethosuximide
C. Gabapentin
D. Phenytoin
E. Valproate
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QUESTION 6 – ANSWER

A. Carbamazepine
B. Ethosuximide
C. Gabapentin
D. Phenytoin
E. Valproate

- Juvenile Myoclonic Epilepsy
JUVENILE MYOCLONIC EPILEPSY (JME)

- Most common “idiopathic primary generalized epilepsy”
  - Starts in early adolescence, typically around age 15
  - Myoclonic jerks, GTC, or absence seizures in morning
  - Normal intelligence
  - Seizures commonly triggered by sleep deprivation
  - Family history of similar seizures

- Characteristic EEG
  - 4-6 Hz irregular polyspikes & waves

- Require lifelong antiepileptic drug use
  - Valproate (= valproic acid or divalproex) or lamotrigine

**NOTE:** Do not use phenytoin or carbamazepine—they may exacerbate JME
A 49-year-old man brought to the ED for confusion gets off a stretcher on his own and falls to the floor, whereupon he has generalized status epilepticus. Which of the following represents optimal management of this patient?

A. Administer fosphenytoin 20 mg PE/kg IV at ≤ 150 mg PE/min with cardiac monitoring

B. Administer phenobarbital 20 mg/kg IV before intubating the patient

C. Administer lorazepam 20 mg IV push after he stops shaking

D. Hold antiepileptic drug treatment pending results of laboratories and EEG

E. Place a tongue blade in his mouth to prevent him from swallowing his tongue
A. Administer fosphenytoin 20 mg PE/kg IV at ≤ 150 mg PE/min with cardiac monitoring
B. Administer phenobarbital 20 mg/kg IV before intubating the patient
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D. Hold antiepileptic drug treatment pending results of laboratories and EEG
E. Place a tongue blade in his mouth to prevent him from swallowing his tongue

- Generalized Tonic-Clonic Seizure
- Generalized Status Epilepticus Diagnosis & Evaluation
- Generalized Status Epilepticus Management
GENERALIZED TONIC-CLONIC (GTC) SEIZURE
(FORMERLY CALLED GRAND MAL SEIZURE)

- Tonic phase – stiff
  - Diffuse muscle contractions
  - Limbs stiffen, back arches, abdominal muscles contract, jaws clench
    
    Results in tongue biting, urinary or fecal incontinence, abnormal cry or shout

- Clonic phase – shaking
  - Shaking of 4 limbs
  - Injury to head & limbs can occur from striking hard surfaces
Prolonged or recurrent GTC seizures without return to consciousness

Differential diagnosis includes anything that affects cerebral cortex, either diffusely or focally:

- Subtherapeutic antiepileptic drug level, abnormal chemistries, drug toxicity, alcohol withdrawal, meningitis, sepsis, mass (tumor, abscess, AVM, hemorrhage), head trauma, encephalitis, encephalopathy (e.g., hypoxic-ischemic, HIV, Alzheimer)

Evaluate for subdural hematoma (may occur due to head trauma during seizure)
GENERALIZED STATUS EPILEPTICUS
MANAGEMENT

- Protect head & extremities from trauma
- Do NOT put anything into patient’s mouth (increases risk of aspiration and bitten tongues heal well)
- Correct underlying abnormalities (e.g., electrolyte abnormalities)
- Monitor blood pressure & ECG
- To abort a seizure, give:
  - Lorazepam 0.1 mg/kg IV push @< 2 mg/min only if pt actively having seizure (stops, but does not prevent seizures)
- To prevent further seizures, give:
  - Fosphenytoin 20 mg PE/kg IV @ < 150 mg PE/min (prevents future seizures if therapeutic)
A 58-year-old woman has a four-year history of progressive shaking and stiffness of her right arm and slowness of gait. She has a history of hypertension for which she takes lisinopril. Examination shows a normal mental status, diminished facial expression, normal eye movements, tremor of the right arm at rest, mild rigidity of both arms worse on the right, and a mildly slow, narrow-based gait. Which of the following is the most likely diagnosis?

A. Ischemic stroke
B. Lewy body disease
C. Medication-induced parkinsonism
D. Parkinson disease
E. Progressive supranuclear palsy
QUESTION 8 – ANSWER

A. Ischemic stroke
B. Lewy body disease
C. Medication-induced parkinsonism
D. Parkinson disease
E. Progressive supranuclear palsy

- Parkinson Disease Pathophysiology
- Parkinson Disease Diagnosis: Four Cardinal Features
PARKINSON DISEASE
PATHOPHYSIOLOGY

*Loss of dopamine cells*

Too little dopamine

Slow, stiff movements

*In upper brainstem
(specifically substantia nigra of midbrain)*
PARKINSON DISEASE DIAGNOSIS: FOUR CARDINAL FEATURES

Two equivalent ways to remember the 4 cardinal features of PD

“TRAP”
- Tremor (resting)
- Rigidity
- Akinesia (bradykinesia)
- Postural instability

“The 4 Ss”
- Shaking
- Stiff
- Slow
- Stooped

Bradykinesia (slowness) is most important feature in diagnosing PD
A 75-year-old man with Parkinson disease takes carbidopa/levodopa and has marked resting tremor, prominent dyskinesias, and increasing forgetfulness and memory loss. He says he is frequently visited at home by little white nurses who crawl in his bed, sit in his lap, and explore his room. He is not bothered by these nurses. Which of the following is the most appropriate action for you to take?

A. Add a dopamine agonist such as ropinirole
B. Add an antipsychotic agent such as quetiapine
C. Obtain MRI of the brain with contrast
D. Decrease his dose of levodopa
E. Schedule urgent deep brain stimulation
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QUESTION 9 – ANSWER

A. Add a dopamine agonist such as ropinirole
B. Add an antipsychotic agent such as quetiapine
C. Obtain MRI of the brain with contrast
D. **Decrease his dose of levodopa**
E. Schedule urgent deep brain stimulation

- Parkinson Disease Management Carbidopa/Levodopa (1 of 2)
- Parkinson Disease Management Carbidopa/Levodopa (2 of 2)
Levodopa (L-dopa)
- Crosses blood-brain barrier (dopamine does not)
- Maximum dose controversial, though most say 1000 - 1200mg/d

Carbidopa
- Inhibits peripheral decarboxylase (which turns L-dopa into dopamine)
- ↑s L-dopa available to brain
- ↓s dopamine peripheral side effects
- Minimum dose 75 mg/d
Starting dose 25/100 TID (carbidopa 25 mg/L-dopa 100 mg)

- May wish to start ½ tablet once daily and increase ½ tab every week to lowest effective dose—usually 25/100 TID

Good response implies Parkinson Disease diagnosis

Affects bradykinesia & rigidity >> tremor, postural instability

Dose-related side effects:

- Nausea / orthostatic hypotension
- Dyskinesias (with long-term use)
- Visual hallucinations (esp. people or animals) / psychosis

“Wearing-off” & “on-off” phenomena (w/ long-term use)

May need q2-4h, maximize drug effect in waking hours

Protein in gut decreases drug absorption
A 36-year-old man has a long history of intermittent severe headaches with nausea and vomiting and photophobia. Five days ago, he had the sudden onset of a dull, global, constant headache with no other symptoms. This morning, while lifting a box of books at home, the headache suddenly worsened to become the worst headache he has ever had and he vomited his breakfast. He came to the ED where he was mildly lethargic and kept his eyes closed due to photophobia. He had nuchal rigidity and an otherwise normal neurologic exam. A noncontrast CT scan of the brain was normal. The most appropriate action for you to take is:

A. Administer intramuscular ketorolac
B. Administer intravenous penicillin G
C. Administer subcutaneous sumatriptan
D. Obtain urgent MRI scan of the brain without and with contrast
E. Perform lumbar puncture for xanthochromia & cells in first & last tubes
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QUESTION 10 – ANSWER

A. Administer intramuscular ketorolac
B. Administer intravenous penicillin G
C. Administer subcutaneous sumatriptan
D. Obtain urgent MRI scan of the brain without and with contrast
E. Perform lumbar puncture for xanthochromia & cells in first & last tubes

- Subarachnoid Hemorrhage: History
- Subarachnoid Hemorrhage: Pathophysiology
- Subarachnoid Hemorrhage: Evaluation
SUBARACHNOID HEMORRHAGE: HISTORY

- **Headache**
  - Usually **sudden** onset, **severe**, **different** from past headaches
  - Often “worst headache of life,” possibly after Valsalva maneuver
  - Mild, persistent headache different for patient may occur due to “sentinel bleed” – initial slow leak of aneurysm

- **Neck pain & stiffness (anteroposterior)**

- **Lethargy &/or confusion**

- **Photophobia**

- **Nausea/vomiting**

- **Diplopia &/or ptosis**

- **Focal weakness**

- **Seizures**
SUBARACHNOID HEMORRHAGE: 
PATHOPHYSIOLOGY

- **Bleeding around brain** into CSF spaces
- **Saccular (= berry) aneurysm** rupture is most common cause of nontraumatic SAH
  - Saccular/berry aneurysm = weak outpouching in wall of intracranial artery, typically around circle of Willis
  - Arteriovenous malformations (AVMs), tumors, & bleeding abnormalities are much less common causes of nontraumatic SAH

- Nontraumatic SAH is an emergency!
- Two main goals of urgent evaluation:
  - Find the blood – by CT or LP
  - Find the aneurysm – by CTA or catheter angio
SUBARACHNOID HEMORRHAGE: EVALUATION  
*First priority is find the blood!*

- **Noncontrast CT scan**
  - Blood (white) in cisterns & ventricles
  - Detects 90% of cases

- **Lumbar puncture (if CT negative)**
  - Red blood cells
    - Check cells in first & last tubes
    - If SAH, same # in all tubes
  - Xanthochromia
    - CSF supernatant colored yellow with heme pigments in SAH pts

White blood in cisterns & 4th ventricle
While working out on a hot summer day, a 35-year-old man notes double vision and tingling in all four extremities that recur intermittently for the next week and he comes to see you in your office. On exam he has normal upgaze and right lateral gaze. On left lateral gaze, the left eye abducts normally but has left-beating nystagmus and he cannot adduct the right eye. He has mildly decreased sensation to all modalities below C5, diffuse hyperreflexia, and bilateral Babinski signs. The most appropriate action you should take is:

A. Arrange for emergent brain and spine MRI and likely administer IV methylprednisolone

B. Arrange for emergent electromyography and nerve conduction studies and likely administer IVIG

C. Arrange for emergent head CT scan and likely administer IV tPA

D. Prescribe oral prednisone 60 mg/day for 10-14 days and schedule return appointment

E. Schedule an appointment with a neurologist in four weeks
A. Arrange for emergent brain and spine MRI and likely administer IV methylprednisolone
B. Arrange for emergent electromyography and nerve conduction studies and likely administer IVIG
C. Arrange for emergent head CT scan and likely administer IV tPA
D. Prescribe oral prednisone 60 mg/day for 10-14 days and schedule return appointment
E. Schedule an appointment with a neurologist in four weeks

- Multiple Sclerosis Classic Clinical Presentations (1 of 2)
- Multiple Sclerosis Classic Clinical Presentations (2 of 2)
- Multiple Sclerosis Evaluation
- Multiple Sclerosis Management
MULTIPLE SCLEROSIS CLASSIC
CLINICAL PRESENTATIONS (1 of 2)

- Optic neuritis: typical symptoms & signs
  - Monocular visual loss or blurring (↓ visual acuity)
  - Colors look “washed out”
  - Eye pain on eye movement
  - Swollen optic disk (blurred disk margins)—though disk may be normal if inflammation involves optic nerve more posteriorly (retrobulbar neuritis)
  - RAPD (= Marcus Gunn pupil) on swinging light test

- Myelopathy: typical symptoms
  - Intermittent shock-like & vibratory sensations down back & into all 4 limbs (L’Hermitte sign)
  - Urinary frequency, hesitancy, urgency (UMN neurogenic bladder)
  - Constipation, sexual dysfunction
Internuclear ophthalmoplegia (INO)
- Also called MLF (medial longitudinal fasciculus) syndrome
- May have horizontal diplopia, vertical diplopia (from “skew deviation”), or no diplopia
- Right INO exam findings, for example:
  - Right gaze normal
  - Left gaze—R eye cannot adduct, L eye horizontal nystagmus

Multiple lesions over space and time

Symptoms worse when patient is hot
- With fever or on hot day or in hot bath
- Called Uhthoff phenomenon
MULTIPLE SCLEROSIS EVALUATION

- Urinalysis and urine culture
- MRI brain
- MRI cervical & thoracic spine
- Lumbar puncture

Always first check for and treat possible infection, esp. urinary tract infection since fever/infection may bring out MS deficits (Uhthoff phenomenon) and infection may worsen with steroids.

MRI brain and spine shows characteristic white-matter lesions on T2 and FLAIR images.

New lesions enhance with contrast on T1 images.

Specific MS panel abnormal in cerebrospinal fluid.
MULTIPLE SCLEROSIS MANAGEMENT

- Methylprednisolone 1 g/day IV x 3-5 days
  - May give 1 g/d, 500 mg q12h, or 250 mg q6h
- After IV methylprednisolone, may give:
  - Prednisone 60 mg/d PO & taper off over 10 days

NOTE: Do **NOT** give PO prednisone before giving IV methylprednisolone
After long days at work as a house cleaner, an 18-year-old woman complains of difficulty getting out of her car and difficulty getting food out of cabinets above her head. She does not have these symptoms in the morning. Where is the likely localization of the patient’s neurologic lesion?

A. Anterior horn cell
B. Muscle
C. Nerve root
D. Neuromuscular junction
E. Peripheral nerve
QUESTION 12 – ANSWER

A. Anterior horn cell
B. Muscle
C. Nerve root
D. Neuromuscular junction
E. Peripheral nerve

- Myasthenia Gravis
MYASTHENIA GRAVIS

Due to antibodies blocking neuromuscular junction

- Disease of **muscle** (myopathy) or **neuromuscular junction** (NMJ) disease may present with:
  - “Hair, chair, & stair” (proximal) weakness (when raising arms to do hair, rising from chair, or going up stairs)
  - Bilateral and symmetric weakness
  - Diplopia (= extraocular muscle weakness) & ptosis
  - Dyspnea, worse when supine (= orthopnea) due to diaphragm weakness
  - Normal sensation and reflexes

- **NMJ disease (myasthenia) more likely than myopathy when symptoms worsen with fatigue (e.g., at end of day or after exertion)**
A 92-year-old previously healthy woman who had been living independently without difficulty is found to be confused by her granddaughter and is brought to the ED. On exam, she is awake, but not attentive to the examiner. She is thrashing about using all four limbs and in fact needs to be restrained. She shouts repeatedly, “These damn people should just let me go home!” Based on this information alone, which of the following conditions is most likely to be responsible for her condition?

A. Alzheimer disease
B. Brain abscess
C. Brain tumor
D. Left cerebral infarction
E. Toxic-metabolic abnormality
PEARLS IN NEUROLOGY

QUESTION 13 – ANSWER

A. Alzheimer disease
B. Brain abscess
C. Brain tumor
D. Left cerebral infarction
E. Toxic-metabolic abnormality

- Delirium
DELIRIUM

- A syndrome of global cognitive dysfunction manifested by:
  - Confusion
  - Inattention
  - Change in consciousness
  - Disorientation (assuming normal language function)
  - Possible agitation and visual hallucinations

- Often reversible and fluctuating in severity

- Equivalent terms
  - Acute confusional state
  - Acute encephalopathy

- Toxic-metabolic encephalopathy is most common cause
  - Drugs/medications
  - Serum chemistry abnormalities
  - Systemic infection or fever
A 75-year-old man is found unconscious by paramedics and brought to the ED. On exam he is stuporous, withdrawing each limb only to deep painful stimuli. He has full extraocular movements on doll’s eye maneuver. Which of the following diagnostic tests or combination of tests are most likely to reveal the cause of this patient’s findings?

A. Complete blood count and serum chemistries
B. CT scan of brain with and without contrast
C. Electroencephalography (EEG)
D. MRI scan of brain with diffusion-weighted imaging (DWI)
E. Prothrombin time and partial thromboplastin time
PEARLS IN NEUROLOGY

QUESTION 14 – ANSWER

A. Complete blood count and serum chemistries
B. CT scan of brain with and without contrast
C. Electroencephalography (EEG)
D. MRI scan of brain with diffusion-weighted imaging (DWI)
E. Prothrombin time and partial thromboplastin time

- Depressed Consciousness Localization: Brainstem vs. Bicerebrum
- Depressed Consciousness Localization: Eye Movements Are the Key
DEPRESSED CONSCIOUSNESS LOCALIZATION: BRAINSTEM VS. BICEREBRUM

- Ascending Reticular Activating System (ARAS) is in the upper brainstem (midbrain/pons), hypothalamus, & basal forebrain
- ARAS axons diffusely innervate & stimulate thalami & cortex of both cerebral hemispheres
- Decreased consciousness is due to ARAS inhibition as a result of either:
  - **Brainstem** lesion (focal) or
    - Usually structural (stroke or mass)
  - **Bicerebral** dysfunction (diffuse)
    - Usually toxic-metabolic derangement
DEPRESSED CONSCIOUSNESS LOCALIZATION: EYE MOVEMENTS ARE THE KEY

- Upper brainstem contains both:
  - ARAS
  - Cranial nerves that control eye movements (3, 4, 6)

- Therefore, in patients with decreased consciousness, eye movements help localize lesion:
  - Brainstem dysfunction \(\rightarrow\) abnormal eye movements
  - Bicerebral dysfunction \(\rightarrow\) normal eye movements

ARAS & CNs 3, 4, 6 are near each other in upper brainstem
An 88-year-old previously healthy woman is found to be confused by her granddaughter and is brought to the ED. On exam, she is wide awake, alert, attentive to the examiner, and very talkative, but does not make sense and does not follow any commands. Which of the following diagnostic tests or combination of tests are most likely to reveal the cause of this patient’s findings?

A. Complete blood count and serum chemistries
B. Electroencephalography (EEG)
C. Lumbar puncture for cells
D. MRI scan of brain with DWI
E. Urinalysis and urine cultures
PEARLS IN NEUROLOGY
QUESTION 15 – ANSWER

A. Complete blood count and serum chemistries
B. Electroencephalography (EEG)
C. Lumbar puncture for cells
D. MRI scan of the brain with DWI
E. Urinalysis and urine cultures

“Altered Mental Status” = Aphasia (esp. Receptive) vs. Delirium
**“ALTERED MENTAL STATUS” = APHASIA (esp. RECEPTIVE) VS. DELIRIUM**

<table>
<thead>
<tr>
<th><strong>APHASIA</strong></th>
<th><strong>DELIRIUM</strong></th>
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<tbody>
<tr>
<td>✅ speech due to expressive aphasia or nonsensical speech due to receptive aphasia</td>
<td>✅ speech due to drowsiness or nonsensical speech due to confusion/disorientation</td>
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<tr>
<td><strong>Normal:</strong></td>
<td><strong>Abnormal:</strong></td>
</tr>
<tr>
<td>➢ Attention*</td>
<td>➢ Attention*</td>
</tr>
<tr>
<td>➢ Consciousness</td>
<td>➢ Consciousness</td>
</tr>
<tr>
<td>➢ Behavior</td>
<td>➢ Behavior</td>
</tr>
<tr>
<td>➢ Orientation</td>
<td>➢ Orientation</td>
</tr>
<tr>
<td>✅ Focal L brain dysfunction</td>
<td>✅ Diffuse brain dysfunction</td>
</tr>
<tr>
<td>✅ Often with R-sided signs</td>
<td>✅ Often due to toxic-metabolic etiology</td>
</tr>
<tr>
<td>➢ Expressive – motor</td>
<td>➢ Check serum, CSF</td>
</tr>
</tbody>
</table>
| ➢ Receptive – sensory, visual fields | }
A 72-year-old woman comes to the office with her husband because of a two-year history of progressive memory loss and confusion. She has gotten lost while driving, has left the stove on several times, and forgot where they went on vacation two months ago. She has a history of hypertension for which she takes hydrochlorothiazide. She is oriented to person and place, but not date. She recalls only 1 of 3 objects after three minutes. Her recall of current events is poor. Her calculations and interpretation of proverbs are mildly impaired. Examination is otherwise normal. MRI of the brain, B12 level, and thyroid function tests are normal. Which of the following is the most appropriate management of this patient?

A. Acyclovir  
B. Donepezil  
C. Estrogen  
D. Paroxetine  
E. Vitamin E
PEARLS IN NEUROLOGY
QUESTION 16 – ANSWER

A. Acyclovir
B. Donepezil
C. Estrogen
D. Paroxetine
E. Vitamin E

- “Confusion” Differential Diagnosis
- Alzheimer Disease – Pathophysiology & Clinical Course Early
- Alzheimer Disease – Pathophysiology & Clinical Course Late
- Alzheimer Disease Management – Disease-Specific Therapies
- Alzheimer Disease Management – Vascular Risk-Factor Modification
<table>
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<tr>
<th><strong>“CONFUSION” DIFFERENTIAL DIAGNOSIS</strong></th>
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<tbody>
<tr>
<td><strong>Delirium</strong></td>
</tr>
<tr>
<td>• Acute to subacute</td>
</tr>
<tr>
<td>• Associated with a change in level of consciousness</td>
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<td>• Patient says &amp; does strange things</td>
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<tr>
<td><strong>Aphasia</strong></td>
</tr>
<tr>
<td>• Only language is abnormal; patient is not confused</td>
</tr>
<tr>
<td>• Patient says strange things but does not do strange things</td>
</tr>
<tr>
<td><strong>Dementia</strong></td>
</tr>
<tr>
<td>• Subacute to chronic</td>
</tr>
<tr>
<td>• Not associated with change in level of consciousness</td>
</tr>
<tr>
<td>• Family complains of symptoms more than patient</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
</tr>
<tr>
<td>• “Pseudodementia”</td>
</tr>
<tr>
<td>• Patient notices symptoms more than others do</td>
</tr>
<tr>
<td>• Inattention &amp; distraction lead to memory recording problems</td>
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</table>
DEMENTIA DUE TO ALZHEIMER DISEASE
Pathophysiology & clinical course early

- Hippocampus (medial temporal lobe) degeneration occurs early:
  - Progressive memory loss first involving recent events is the hallmark of Alzheimer disease
  - As disease progresses, remote memory is affected
  - Disorientation to time and place occur first
  - Disorientation to person occurs in advanced stages

- Parietotemporal cortex degeneration follows:
  - Impaired word finding, calculations, spatial manipulation
Frontal cortex degeneration occurs late in the disease:

- Early in the disease, before the frontal lobe is involved, social behavior is preserved.
- Progressively poor judgment, delusions, agitation, inattention, indifference, and lack of initiation may progress to *akinetische Mutismus*.
- *Akinetic mutism* – increasing passiveness progresses to cessation of movement (akinesia) and speaking (mutism), but patient appears alert.
Currently available medications cannot cure Alzheimer disease, but slightly prolong patients’ abilities to maintain independence in daily activities.

- **Acetylcholinesterase inhibitors**
  - Donepezil (Aricept)
  - Rivastigmine (Exelon, Exelon Patch)
  - Galantamine (Razadyne, Razadyne ER)

- **NMDA antagonist**
  - Memantine (Namenda)

- **Follow-up neuropsychologic testing annually**
  - Follow cognitive decline
Alzheimer disease & vascular dementia frequently coexist. Regular exercise & tight control of vascular risk factors such as hypertension may slow the progression of dementia.

- Blood pressure management
  - Target BP < 120/80 with ARB or ACE-I

- Cholesterol management
  - Target LDL < 70 with statin

- Diabetes management
  - Target Hgb A1C < 6.5 with medications, diet, & exercise

- Regular aerobic exercise regimen
  - May slow dementia progression
  - Brisk walking, swimming, etc. 75 minutes per week

- Regular mental exercises (reading, writing, etc.)
A 65-year-old man with a long history of hypertension and diabetes mellitus type 2 complains of imbalance for the last several weeks. His symptoms are not present when seated or supine and are most pronounced when washing his hair in the shower or going out at night. He fell in a movie theater last weekend. He denies lightheadedness or a sense that the world is moving. Which of the following is the most likely diagnosis?

A. Chronic ear infection with vertigo
B. Elevated blood pressure with dizziness
C. Ischemic stroke in the cerebellum with ataxia
D. Orthostatic hypotension with near syncope
E. Peripheral neuropathy with sensory ataxia
PEARLS IN NEUROLOGY

QUESTION 17 – ANSWER

A. Chronic ear infection with vertigo
B. Elevated blood pressure with dizziness
C. Ischemic stroke in the cerebellum with ataxia
D. Orthostatic hypotension with near syncope
E. Peripheral neuropathy with sensory ataxia

- Differential Diagnosis of Dizziness or Imbalance
- Sensory Ataxia
DIFFERENTIAL DIAGNOSIS OF DIZZINESS OR IMBALANCE

- Vertigo
  - Hallucination of movement of patient or environment
  - Often spinning sensation, but may be side-to-side movement
  - Due to vestibular system dysfunction (inner ear, brainstem, cerebellum or temporal cortex)

- Ataxia
  - Gait imbalance or dysequilibrium
  - Motor ataxia—not affected by vision, due to cerebellar dysfunction
  - Sensory ataxia—worse when vision impaired (e.g., dark room, diabetic retinopathy), due to proprioceptive deficit

- Lightheadedness
  - Near syncope or syncope due to hypotension
  - Vibratory or buzzing sensation in head due to migraine
SENSORY ATAXIA

- Cerebellum requires 2 of 3 sensory inputs to function properly
  - Vision
  - Vestibular system
  - Proprioception (sensory input re: limb position)

- If proprioception is impaired:
  - Patient relies on vestibular system and vision
  - Patient only has 1 functioning system (vestibular) in the dark or when eyes are closed and, therefore, loses balance
A 50-year-old, right-handed man with BP 156/98 has a history of intermittent headaches with nausea, photophobia, and phonophobia since adolescence. For the last 6 years, however, he has had a constant, daily headache of fluctuating intensity with moderate nausea, sinus congestion, and profound photophobia and phonophobia for which he takes “Tylenol Sinus” 8 tablets daily. Three MRI scans of the brain without and with contrast were normal except for possible sinusitis, including a scan two months ago. Several migraine prophylactic agents have been ineffective. Which of the following represents optimal management of this patient?

A. Discontinue all analgesics and decongestants for at least one month
B. Prescribe antibiotics for likely chronic sinus infection
C. Prescribe clonidine as needed for headaches due to hypertension
D. Prescribe hydrocodone with acetaminophen four times daily
E. Refer patient to psychiatry for depression and anxiety
PEARLS IN NEUROLOGY

QUESTION 18 – ANSWER

A. Discontinue all analgesics and decongestants for at least one month
B. Prescribe antibiotics for likely chronic sinus infection
C. Prescribe clonidine as needed for headaches due to hypertension
D. Prescribe hydrocodone with acetaminophen four times daily
E. Refer patient to psychiatry for depression and anxiety

See the next lecture
THE END