Ischemic Stroke for the Non-Neurologist

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Disclosures

- None

Agenda

1. Define stroke and associated terminology
2. Discuss the code stroke and associated imaging
3. Overview of acute stroke management and decision making
4. Overview of stroke secondary prevention and decision making

Abbreviations

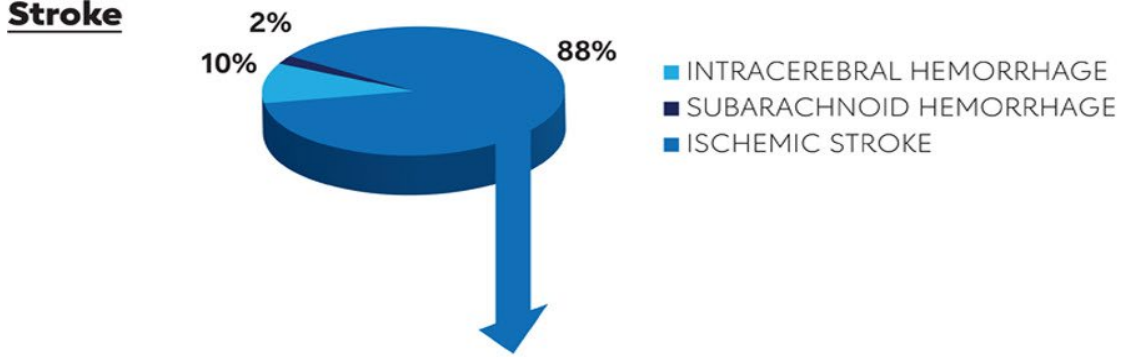
- AIS: Acute Ischemic Stroke
- CVA: Cerebrovascular Accident
- ICH: Intracerebral Hemorrhage
- IPH: Intraparenchymal Hemorrhage
- SAH: Subarachnoid Hemorrhage
- TIA: Transient Ischemic Attack
- ESUS: Embolic Stroke of Undetermined Source
- tPA: Tissue Plasminogen Activator
- TNK: Tenecteplase
- HTN: Hypertension
- CHF: Congestive Heart Failure
- HFrEF: Heart Failure with Reduced Ejection Fraction
- HFpEF: Heart Failure with Preserved Ejection Fraction
- HLD: Hyperlipidemia
- T2DM: Type 2 Diabetes Mellitus
- OSA: Obstructive Sleep Apnea
- OAC: Oral Anticoagulation
- DOAC: Direct Oral Anticoagulation
- ASA: Aspirin
- SAPT: Single Antiplatelet Therapy
- DAPT: Dual Antiplatelet Therapy
- NIHSS: National Institutes of Health Stroke Scale
- CTA: Computed tomography angiography
- MRA: Magnetic resonance angiography
- PFO: Patent Foramen Ovale
- LV: Left Ventricle
- EVT: Endovascular Thrombectomy
- MET/MT: Mechanical Thrombectomy
- IVT: Intravenous Thrombolysis
- LVO: Large Vessel Occlusion
- MeVO: Medium Vessel Occlusion
- DeVO: Distal Vessel Occlusion
- CEA: Carotid Endartectomy

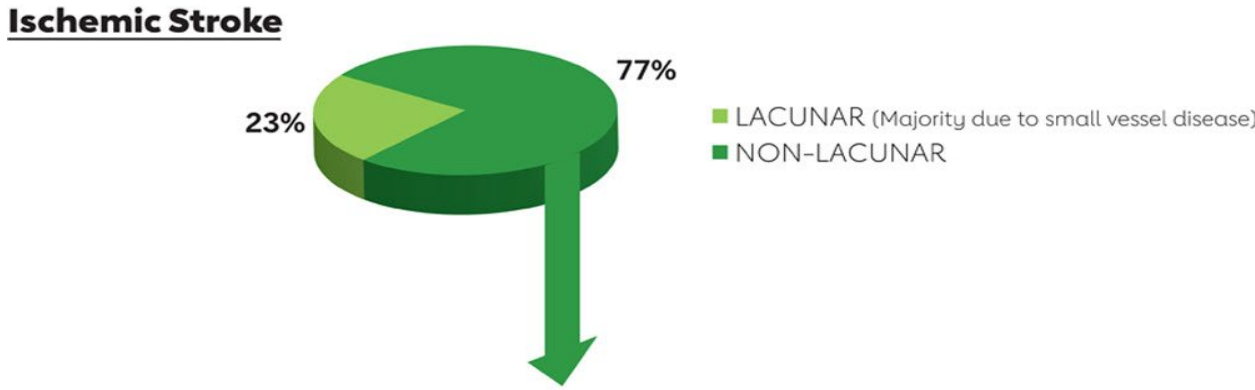
Exam abbreviations

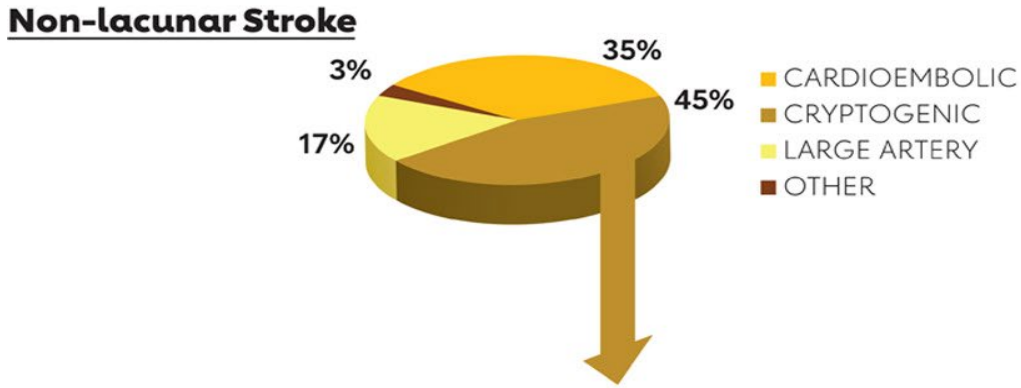
- LOC: Level of consciousness
- PERRLA: Pupils equal, round, and reactive to light and accomodation
- APD: Afferent pupillary defect
- LUE/LLE: Left upper/lower extremity
- RUE/RLE: Right upper/lower extremity
- DTR: Deep tendon reflex
- FTN: Finger to nose
- HTS: Heel to shin

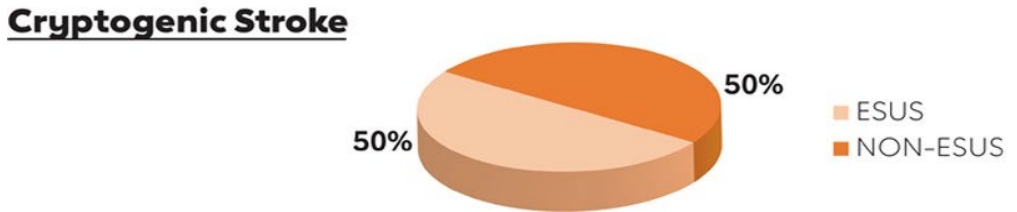
Stroke

- Neurological deficit attributed to an acute, focal injury of the central nervous system attributable to a vascular cause
- Types of Stroke
  - Ischemic (87%)
    - Impaired vascular flow due to occlusion or stenosis of an associated vessel
    - Lacunar Stroke: Blockage in deep, small arteries in the brain, <20 mm in size
    - Cryptogenic: Unknown cause based on workup, or more than 1 attributable cause
  - Hemorrhagic (13%)
    - Ruptured blood vessel
      - Intraparenchymal
      - Subarachnoid



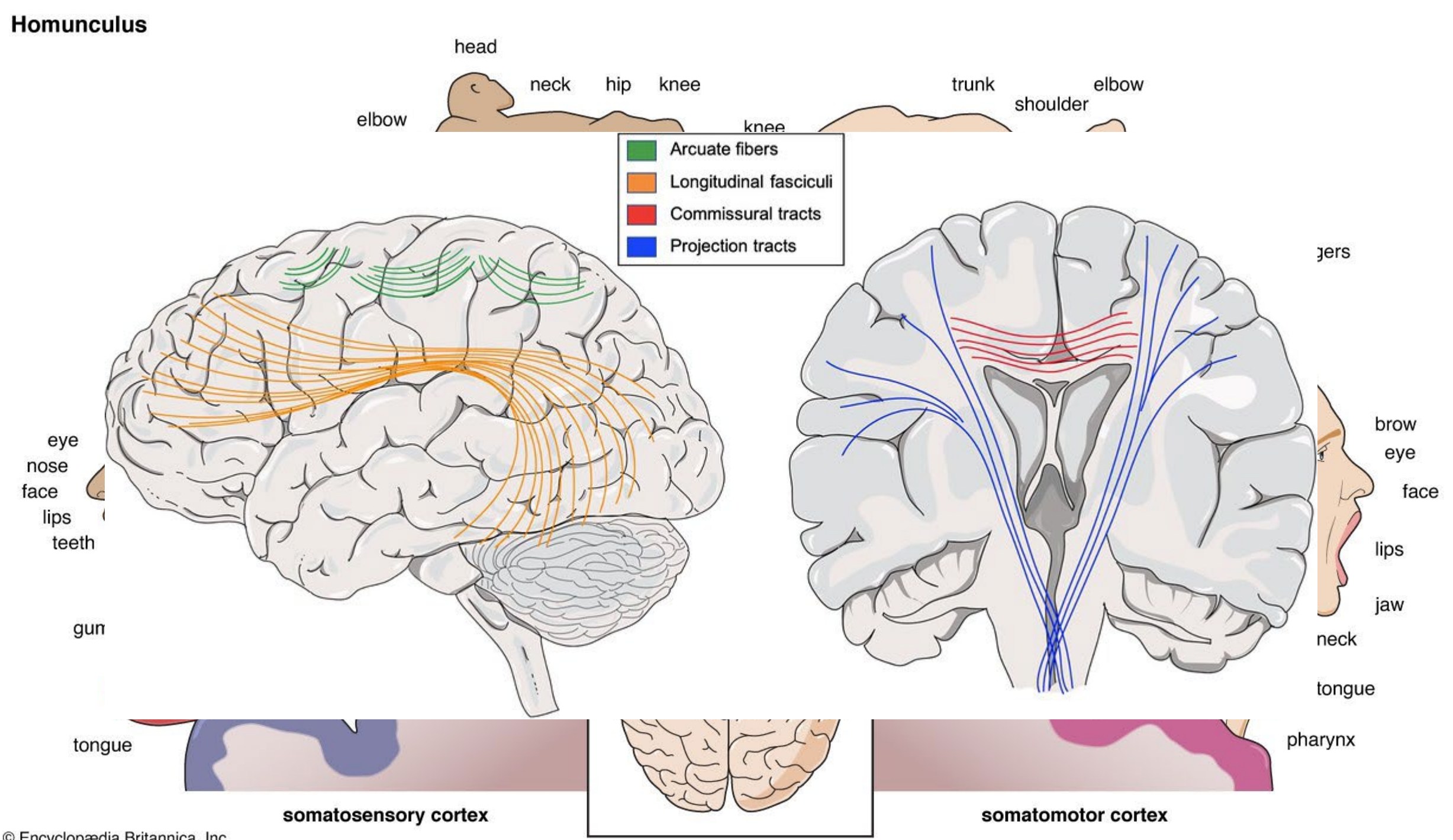


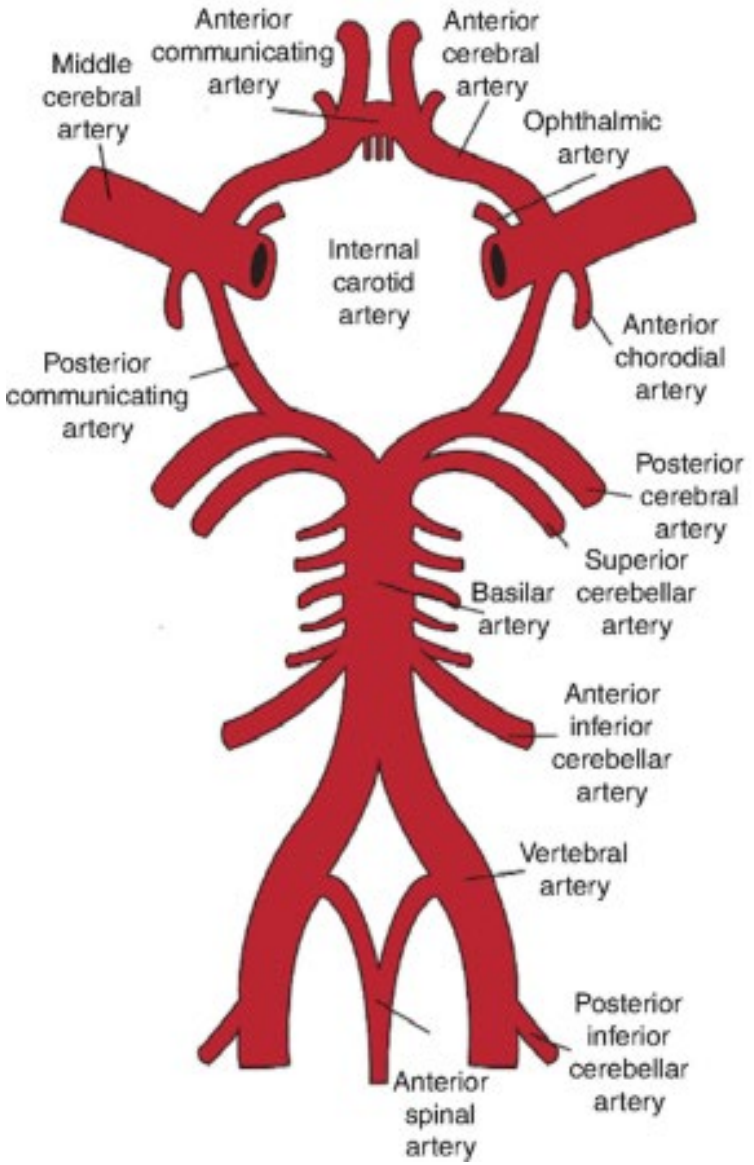


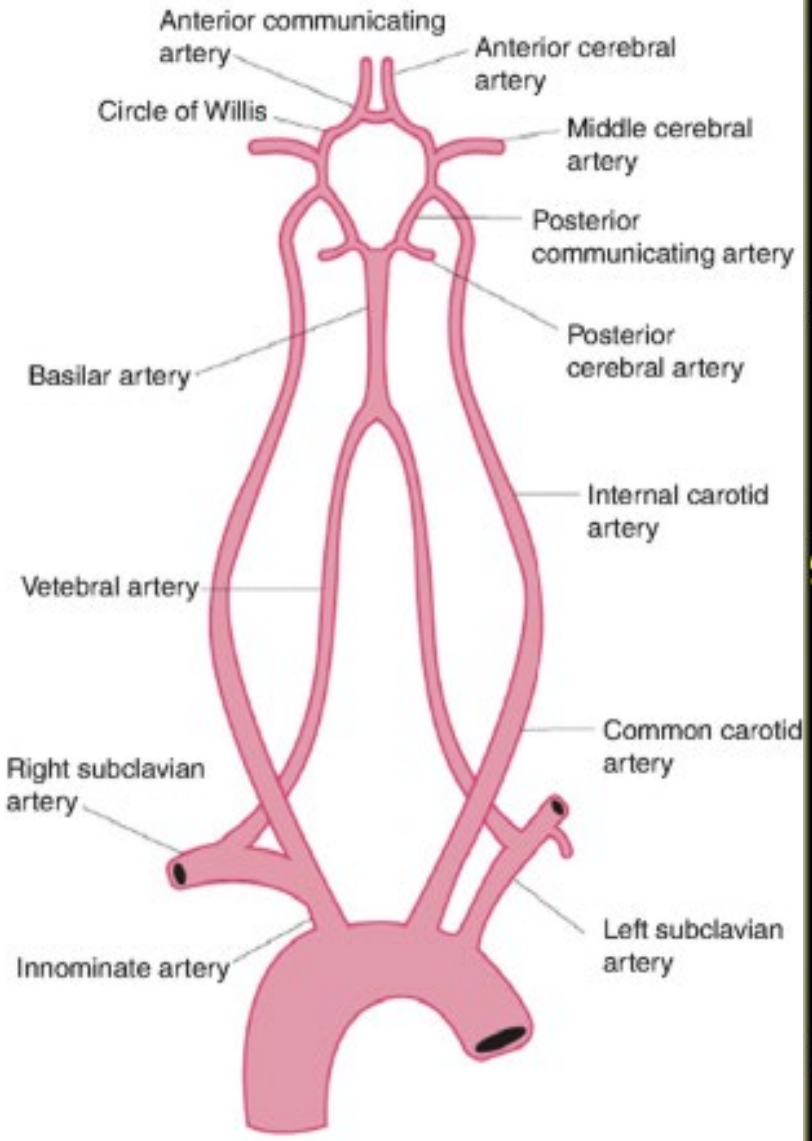


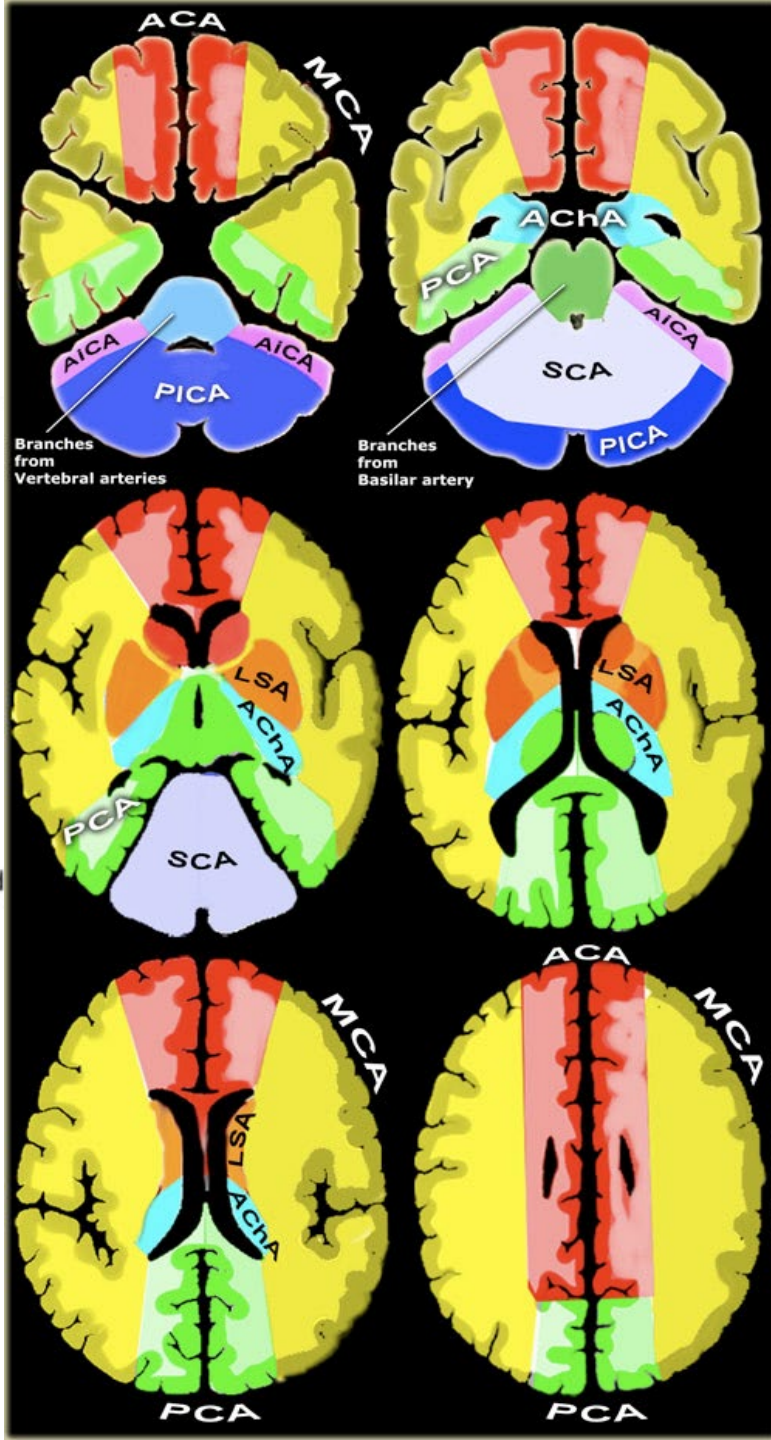
Stroke cont.

- Transient ischemic attack (TIA)
  - Transient focal neurologic deficit due to ischemia
  - Abrupt onset
  - Same symptoms as stroke with vascular localization
  - Usually <1 hour in duration, must resolve within 24 hours
  - No evidence of infarction on MRI
- Signify risk of impending stroke
  - Up to 8% risk of stroke in the next 48 hours
  - Requires **immediate medical attention**
- Be careful with this diagnosis
  - NOT ALL THAT IS TRANSIENT IS TIA




Middle cerebral artery
Anterior communicating artery
Anterior cerebral artery
Ophthalmic artery
Internal carotid artery
Anterior chorodial artery
Posterior communicating artery
Posterior cerebral artery
Superior cerebellar artery
Basilar artery
Anterior inferior cerebellar artery
Vertebral artery
Posterior inferior cerebellar artery
Anterior spinal artery


Anterior communicating artery
Anterior cerebral artery
Circle of Willis
Middle cerebral artery
Posterior communicating artery
Posterior cerebral artery
Basilar artery
Internal carotid artery
Vetebral artery
Common carotid artery
Right subclavian artery
Left subclavian artery
Innominate artery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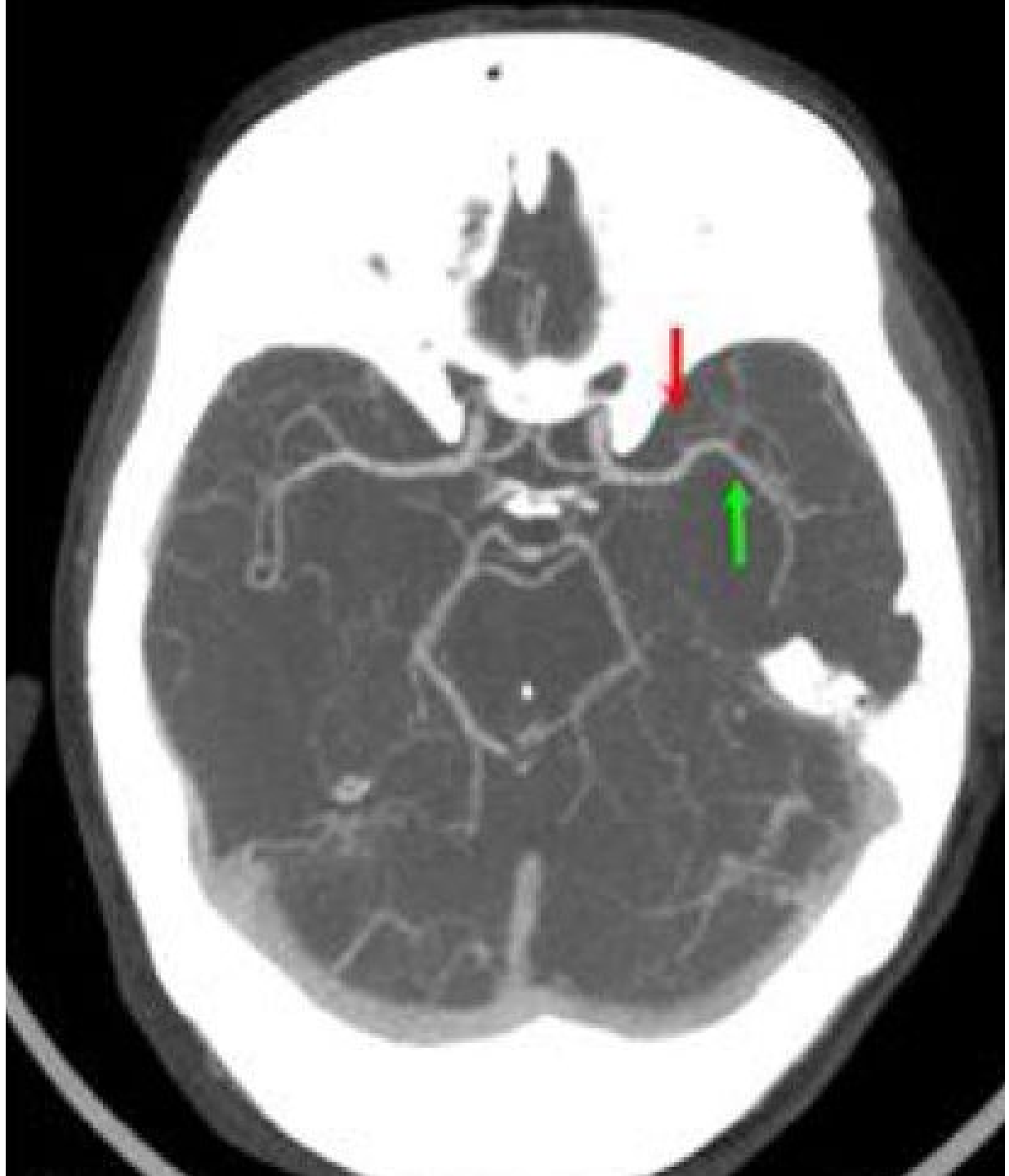
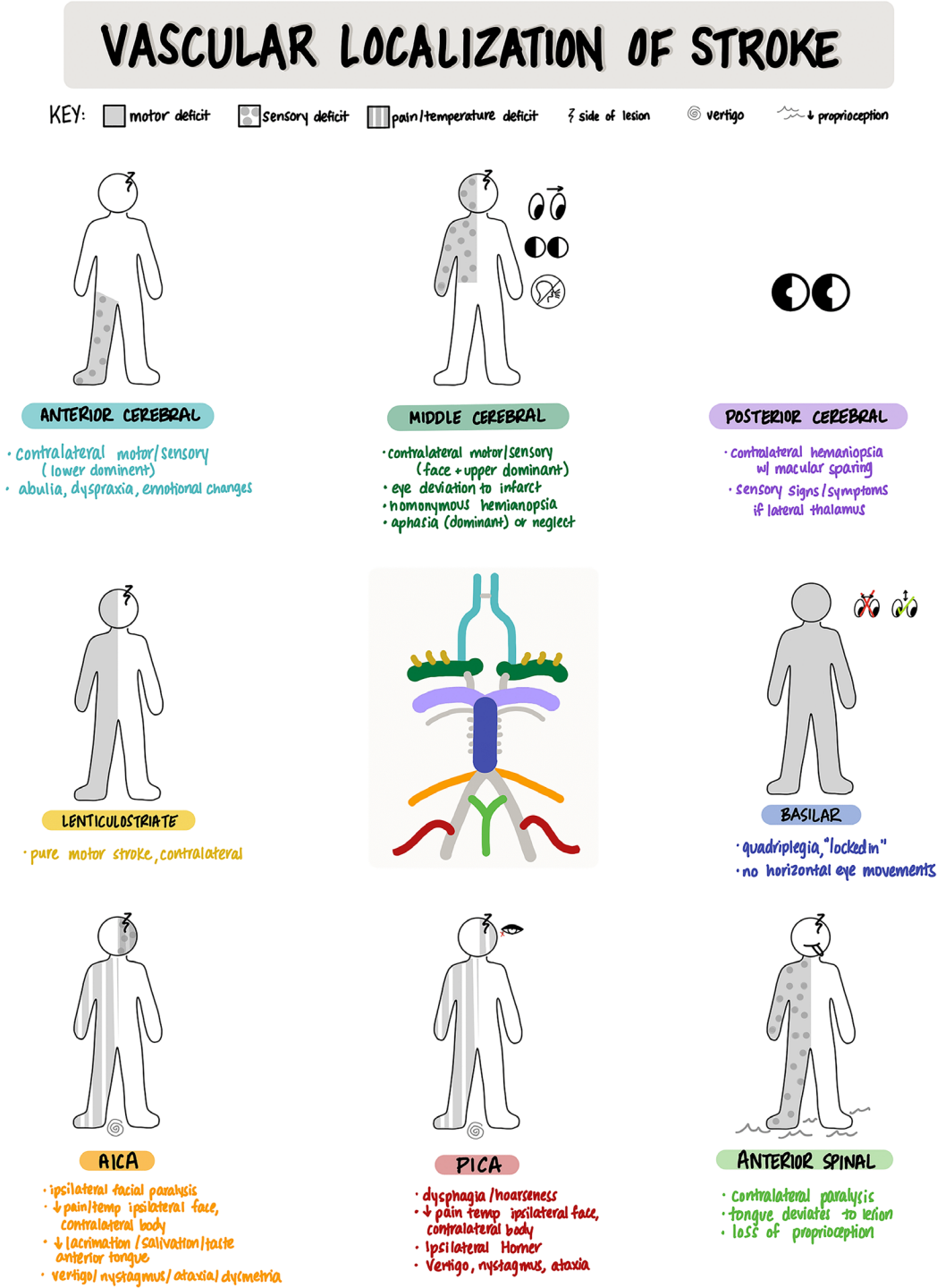


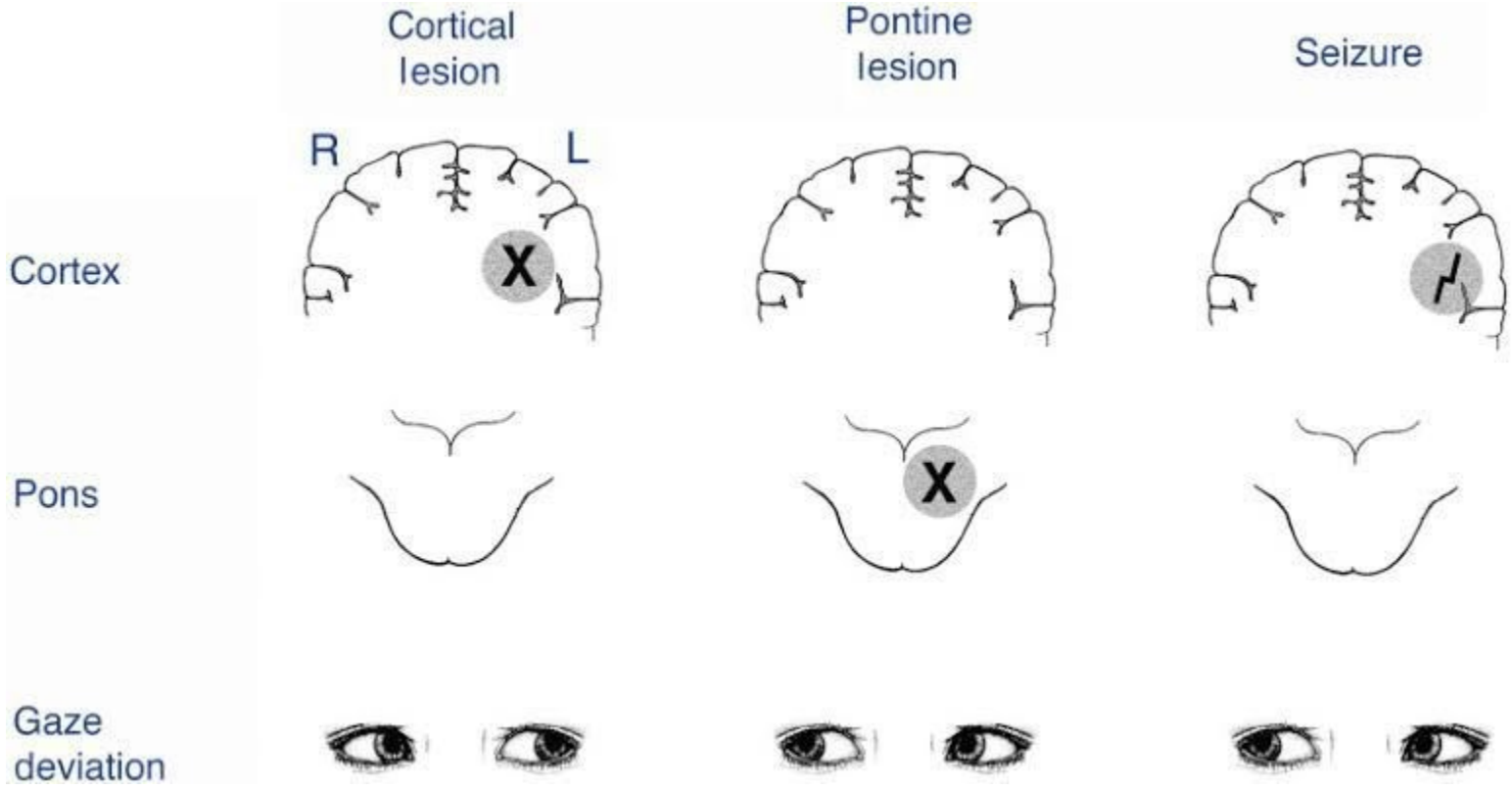
Quick and Dirty Localization Tips

- Cortical: Relating to the gray matter surface of the cerebrum
  - VAN (Vision, Aphasia, Neglect)
    - Can be helpful for LVO, but not isolated to cortex
- Subcortical: Referring to structures below the cortex
- Crossed symptoms (one side of face, opposite body): Think Brainstem
  - Lesion ipsilateral to facial involvement
- Lacunar syndromes:
  - Pure Motor: Internal Capsule, Pons
  - Pure Sensory: Thalamic (posterior circulation)
  - Sensorimotor: Thalamocapsular
  - Dysarthria-Clumsy Hand: Pons, corona radiata
  - Ataxic Hemiparesis: Pons, Internal Capsule



Gaze Preference

- More common in Right Hemispheric Lesions
  - Neglect phenomenon
- Right-way-eyes
  - Eyes toward lesion
- Wrong-way-eyes
  - Eyes away from lesion
    - Seizure
    - Pontine stroke
    - BL thalamic stroke



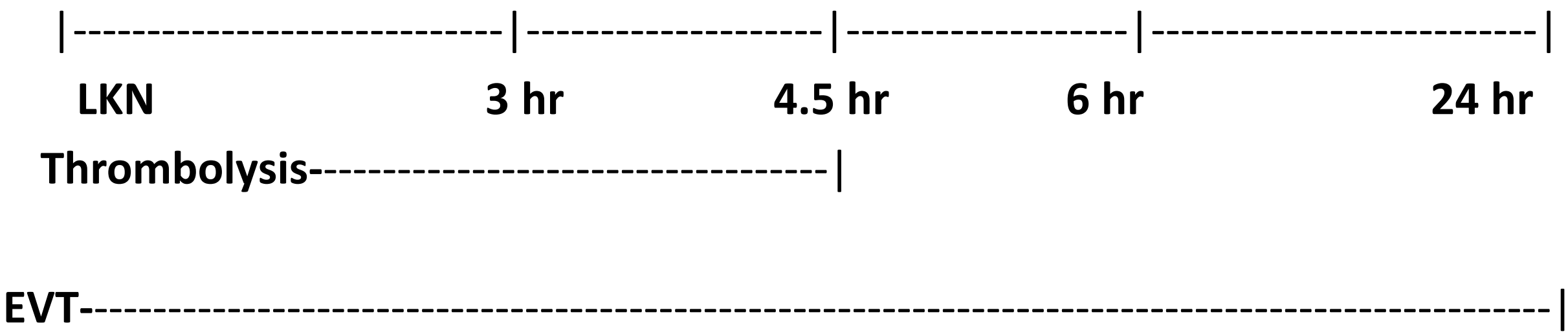
Stroke Alert

76 yoM admitted for COPD exacerbation is noted to be confused by nursing staff. He has a new R facial droop and is moving his right side less vigorously. He is unable to answer questions though appears awake.

Case cont.

- Stroke code/Alert
  - Activates neurology consult service and stroke coordinator
  - Activates neuro-interventional service
  - Holds CT imaging scanner for patient
- Stroke codes/alerts are not purely for acute imaging
  - The goal of a stroke code/alert is related to neurointervention

Interventional Timeline



What we want to know

- LAST KNOWN NORMAL
  - Not the time someone noticed the symptoms, but the last time someone saw them or documented the patient at their baseline
- Blood glucose
  - Hypoglycemia and hyperglycemia can mimic stroke
- Blood Pressure
- Antithrombotic use
- Recent surgical procedures
- Relevant vascular risk factors

NATIONAL INSTITUTES OF HEALTH STROKE SCALE (NIHSS)

Item	Title	Responses and Scores
1a.	Level of consciousness	0—alert 1—drowsy 2—obtunded 3—coma/unresponsive
1b.	Orientation questions (2)	0—answers both correctly 1—answers one correctly 2—answers neither correctly
1c.	Response to commands (2)	0—performs both tasks correctly 1—performs one task correctly 2—performs neither
2.	Gaze	0—normal horizontal movements 1—partial gaze palsy 2—complete gaze palsy
3.	Visual fields	0—no visual field defect 1—partial hemianopia 2—complete hemianopia 3—bilateral hemianopia
4.	Facial movement	0—normal 1—minor facial weakness 2—partial facial weakness 3—complete unilateral palsy
5.	Motor function (arm) a. Left b. Right	0—no drift 1—drift before 10 seconds 2—falls before 10 seconds 3—no effort against gravity 4—no movement
6.	Motor function (leg) a. Left b. Right	0—no drift 1—drift before 5 seconds 2—falls before 5 seconds 3—no effort against gravity 4—no movement
7.	Limb ataxia	0—no ataxia 1—ataxia in 1 limb 2—ataxia in 2 limbs
8.	Sensory	0—no sensory loss 1—mild sensory loss 2—severe sensory loss
9.	Language	0—normal 1—mild aphasia 2—severe aphasia 3—mute or global aphasia
10.	Articulation	0—normal 1—mild dysarthria 2—severe dysarthria
11.	Extinction or inattention	0—absent 1—mild loss (1 sensory modality lost) 2—severe loss (2 modalities lost)

Scoring range is 0-42 points.
The higher the number, the greater the severity.

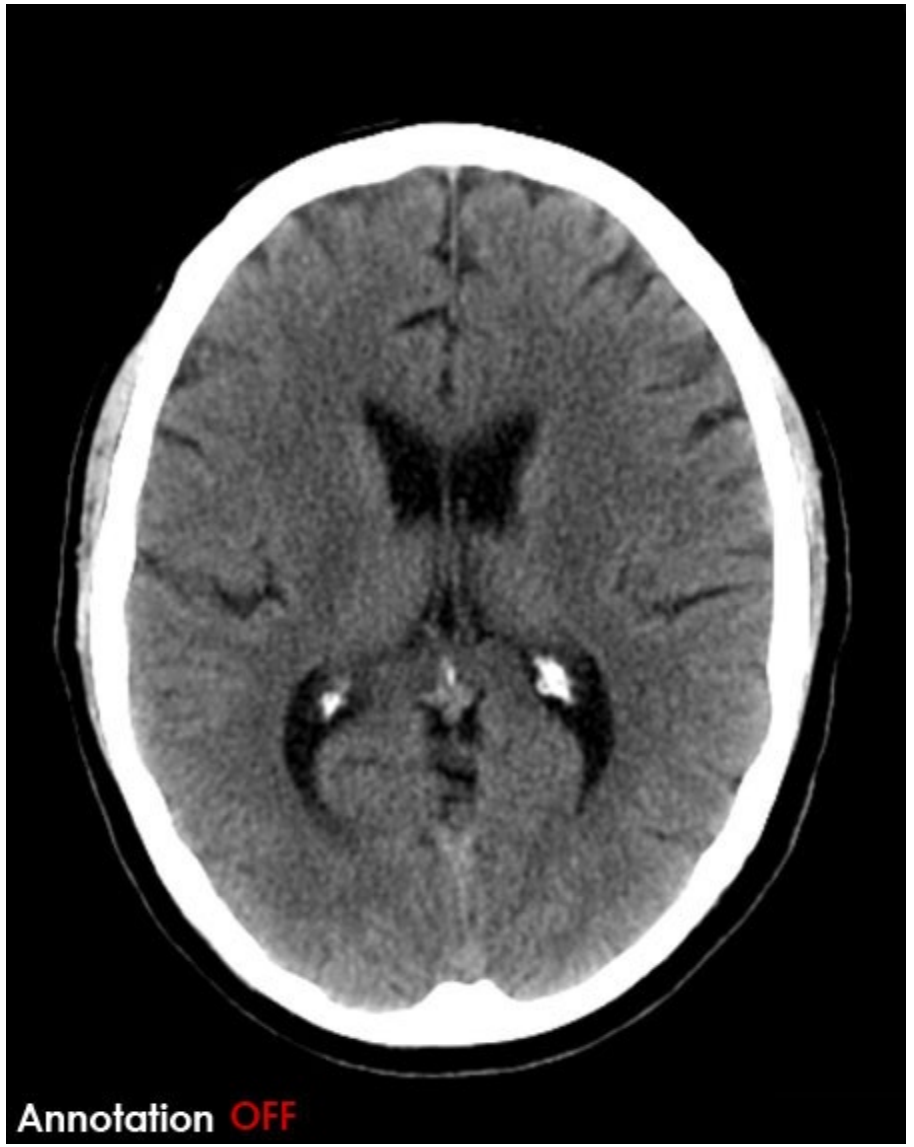
Score	Stroke Severity
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

Back to our case

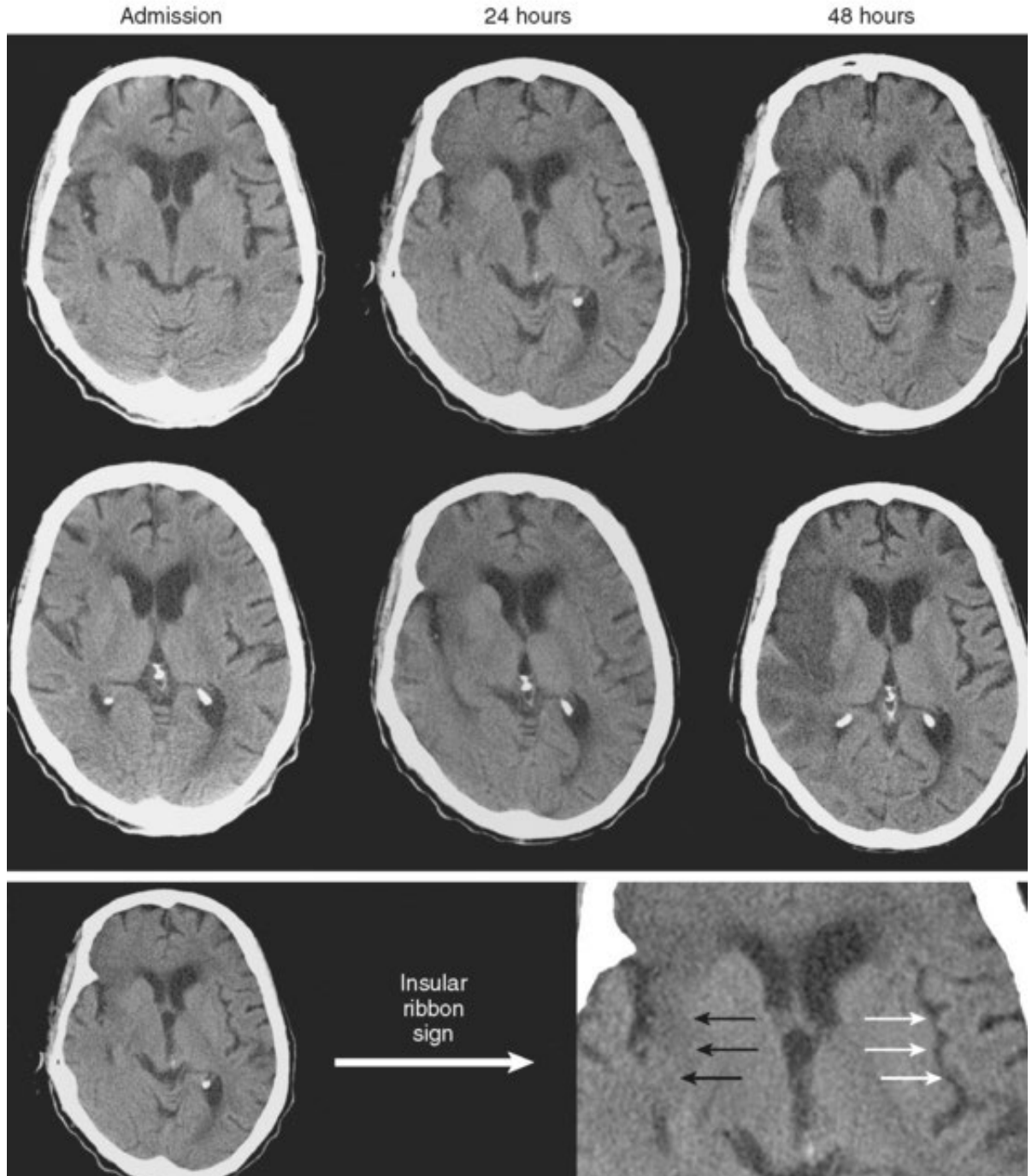
- Last known normal was documented by the nurse at 11:00 AM
- Fingerstick glucose: 120
- BP: 171/99
- PMH: HTN, HFrEF (EF 40%), COPD, tobacco use disorder, HLD
- Exam:
  - Left gaze preference
  - R facial weakness
  - No blink to threat on the R
  - RUE 0/5, RLE 3/5
  - No withdrawal of the RUE
  - Global aphasia
- NIHSS: 23

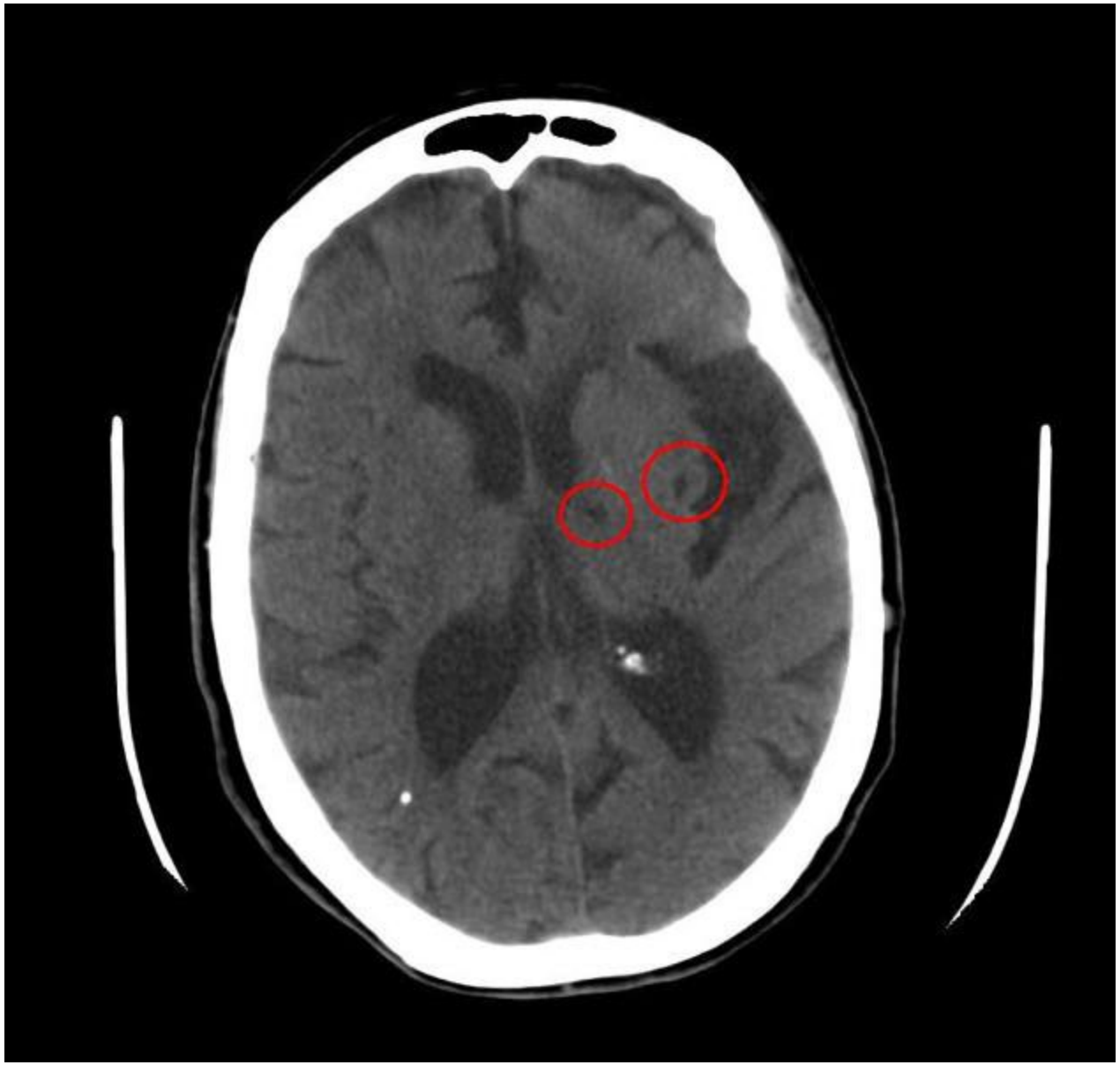
Noncontrast CT

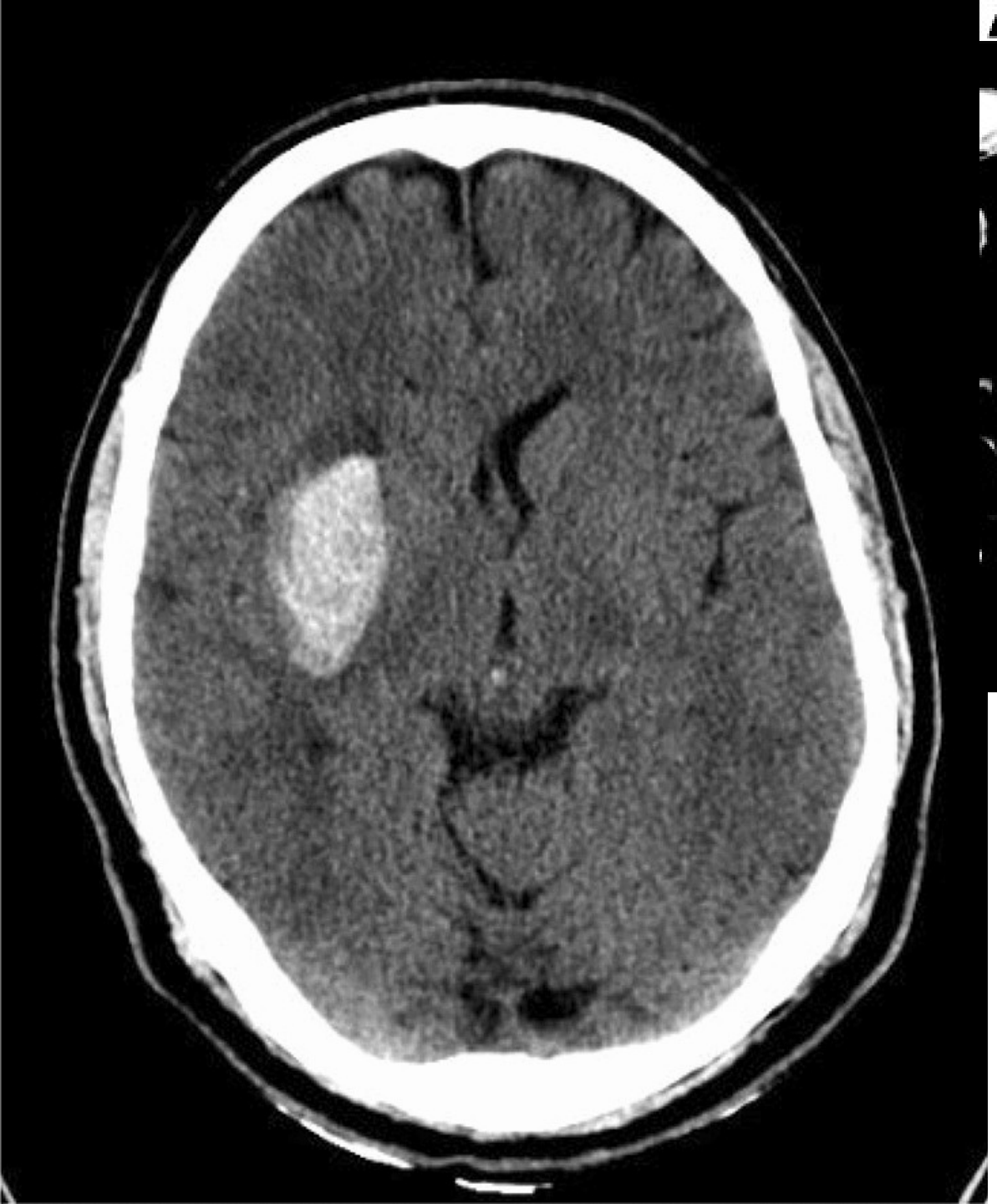
- Helps differentiate acute hemorrhage from non hemorrhage
  - Thrombolysis contraindicated in acute hemorrhage
- Sensitive and specific for acute hemorrhage
- First initial imaging study obtain during a stroke code
- Often negative early in ischemic stroke

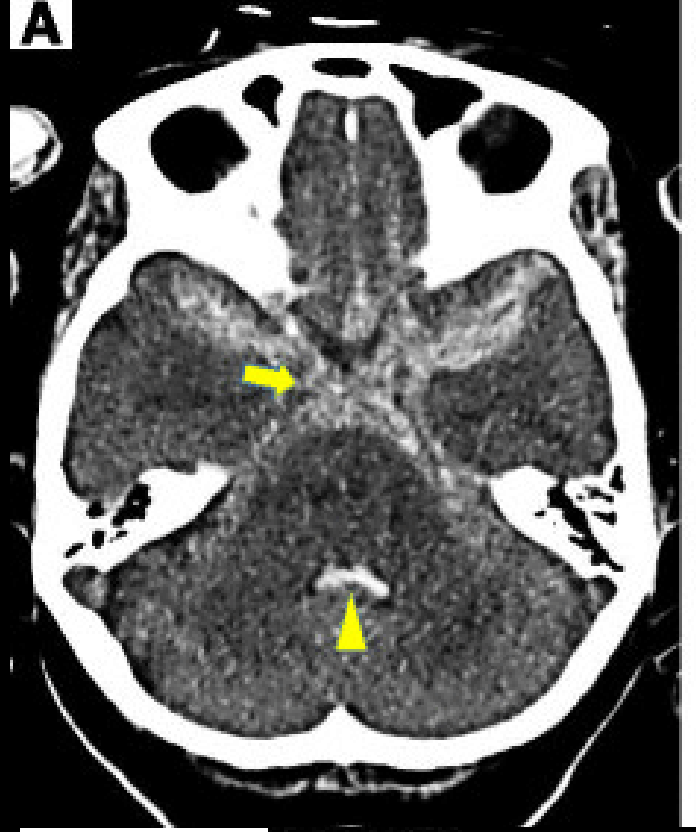


EARLY SIGNS OF ISCHEMIA ON CT SCAN





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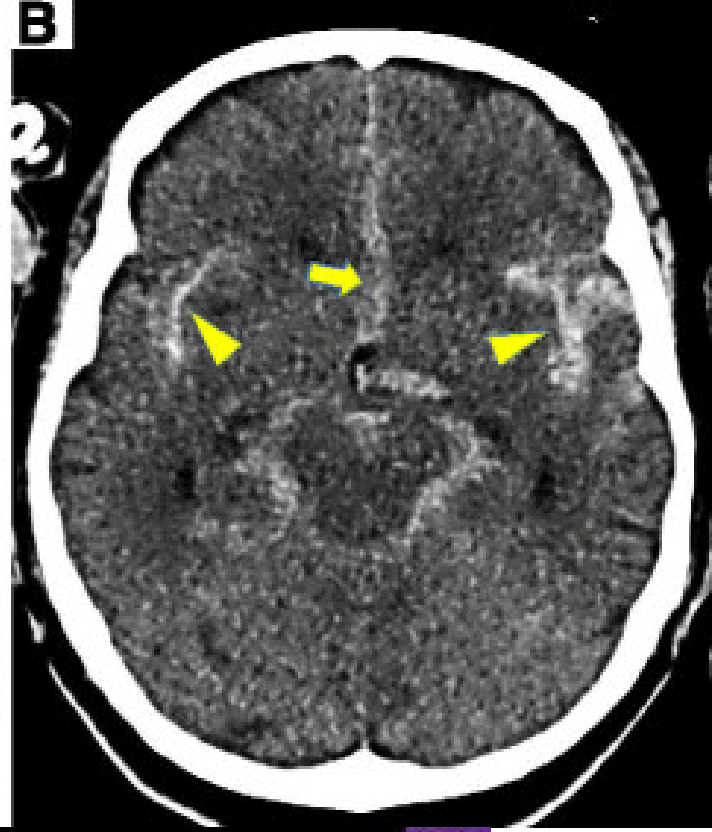
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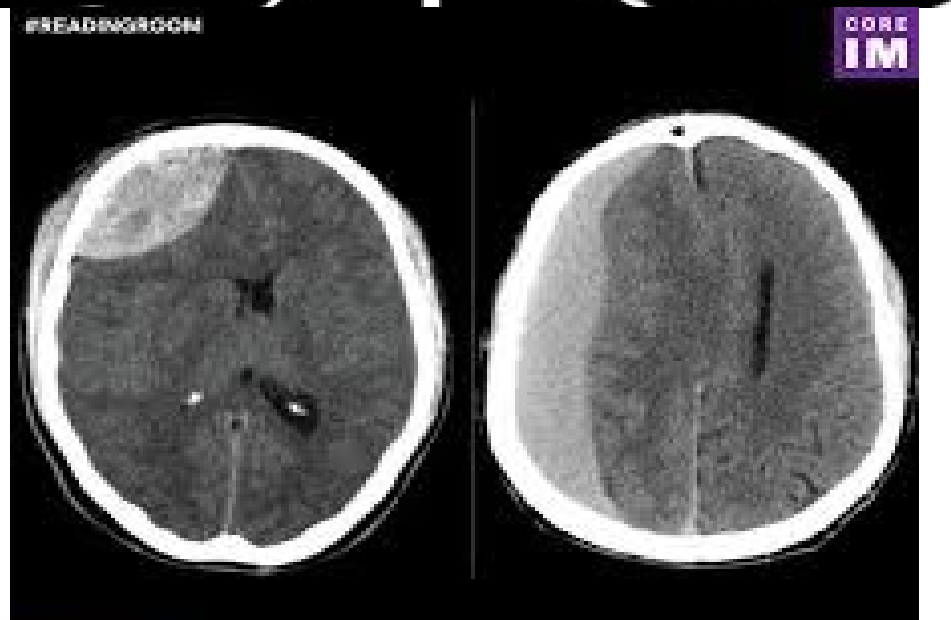

#READINGROOM
CORE IM

Thrombolysis

- Alteplase (tPA)
    - One hour IV administration
    - 0.9 mg/kg, max 90 mg IV
    - 10% bolus over 1 min
- Tenecteplase (TNK)
    - 5 second IV push
    - Weight-based tier dosing
    - 0.25 mg/kg, max 25 mg IV
    - Non-inferior to tPA
- Time dependent intervention
    - Benefit of therapy improves with earlier onset (be quick, but don’t hurry)
- Patients treated with thrombolytic have significantly improved odds of better outcomes 90 days post stroke

Contraindications (COR III: No Benefit)	And (COR III: Harm)
0- to 3-h window–Mild nondisabling stroke	For otherwise eligible patients with mild nondisabling stroke (NIHSS score 0–5), IV alteplase is not recommended for patients who could be treated within 3 h of ischemic stroke symptom onset or patient last known well or at baseline state. (*COR III: No Benefit, LOE B-R*)‡
3- to 4.5-h window–Mild nondisabling stroke	For otherwise eligible patients with mild nondisabling stroke (NIHSS score 0–5), IV alteplase is not recommended for patients who could be treated within 3 and 4.5 h of ischemic stroke symptom onset or patient last known well or at baseline state. (*COR III: No Benefit, LOE C-LD*)‡
CT	There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to alteplase. However, administering IV alteplase to patients whose CT brain imaging exhibits extensive regions of clear hypoattenuation is not recommended. These patients have a poor prognosis despite IV alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury.† (*COR III: No Benefit; LOE A*)‖
ICH	IV alteplase should not be administered to a patient whose CT reveals an acute intracranial hemorrhage.† (*COR III: Harm; LOE C-EO*)§‖
Ischemic stroke within 3 mo	Use of IV alteplase in patients presenting with AIS who have had a prior ischemic stroke within 3 mo may be harmful.† (*COR III: Harm; LOE B-NR*)§‖
Severe head trauma within 3 mo	In AIS patients with recent severe head trauma (within 3 mo), IV alteplase is contraindicated.† (*COR III: Harm; LOE C-EO*)§‖
Acute head trauma	Given the possibility of bleeding complications from the underlying severe head trauma, IV alteplase should not be administered in posttraumatic infarction that occurs during the acute in-hospital phase.† (*COR III: Harm; LOE C-EO*)§‖ (Recommendation wording modified to match COR III stratifications.)
Intracranial/intraspinal surgery within 3 mo	For patients with AIS and a history of intracranial/spinal surgery within the prior 3 mo, IV alteplase is potentially harmful.† (*COR III: Harm; LOE C-EO*)§‖
History of intracranial hemorrhage	IV alteplase administration in patients who have a history of intracranial hemorrhage is potentially harmful.† (*COR III: Harm; LOE C-EO*)§‖
Subarachnoid hemorrhage	IV alteplase is contraindicated in patients presenting with symptoms and signs most consistent with an SAH.† (*COR III: Harm; LOE C-EO*)§‖
GI malignancy or GI bleed within 21 d	Patients with a structural GI malignancy or recent bleeding event within 21 d of their stroke event should be considered high risk, and IV alteplase administration is potentially harmful.† (*COR III: Harm; LOE C-EO*)§‖
Coagulopathy	The safety and efficacy of IV alteplase for acute stroke patients with platelets <100 000/mm^3, INR >1.7, aPTT >40 s, or PT >15 s are unknown, and IV alteplase should not be administered.† (*COR III: Harm; LOE C-EO*)§‖ (In patients without history of thrombocytopenia, treatment with IV alteplase can be initiated before availability of platelet count but should be discontinued if platelet count is <100 000/mm^3. In patients without recent use of OACs or heparin, treatment with IV alteplase can be initiated before availability of coagulation test results but should be discontinued if INR is >1.7 or PT is abnormally elevated by local laboratory standards.) (Recommendation wording modified to match COR III stratifications.)
LMWH	IV alteplase should not be administered to patients who have received a full treatment dose of LMWH within the previous 24 h.† (*COR III: Harm; LOE B-NR*)§‡ (Recommendation wording modified to match COR III stratifications.)
Thrombin inhibitors or factor Xa inhibitors	The use of IV alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful.† (*COR III: Harm; LOE C-EO*)§‖ IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 h (assuming normal renal metabolizing function). (Alteplase could be considered when appropriate laboratory tests such as aPTT, INR, ecarin clotting time, thrombin time, or direct factor Xa activity assays are normal or when the patient has not taken a dose of these ACs for >48 h and renal function is normal.) (Recommendation wording modified to match COR III stratifications.)
Concomitant Abciximab	Abciximab should not be administered concurrently with IV alteplase. (*COR III: Harm; LOE B-R*)‡
Concomitant IV aspirin	IV aspirin should not be administered within 90 min after the start of IV alteplase. (*COR III: Harm; LOE B-R*)‡
Infective endocarditis	For patients with AIS and symptoms consistent with infective endocarditis, treatment with IV alteplase should not be administered because of the increased risk of intracranial hemorrhage.† (*COR III: Harm; LOE C-LD*)§‖ (Recommendation wording modified to match COR III stratifications.)
Aortic arch dissection	IV alteplase in AIS known or suspected to be associated with aortic arch dissection is potentially harmful and should not be administered.† (*COR III: Harm; LOE C-EO*)§‖ (Recommendation wording modified to match COR III stratifications.)
Intra-axial intracranial neoplasm	IV alteplase treatment for patients with AIS who harbor an intra-axial intracranial neoplasm is potentially harmful.† (*COR III: Harm; LOE C-EO*)§‖

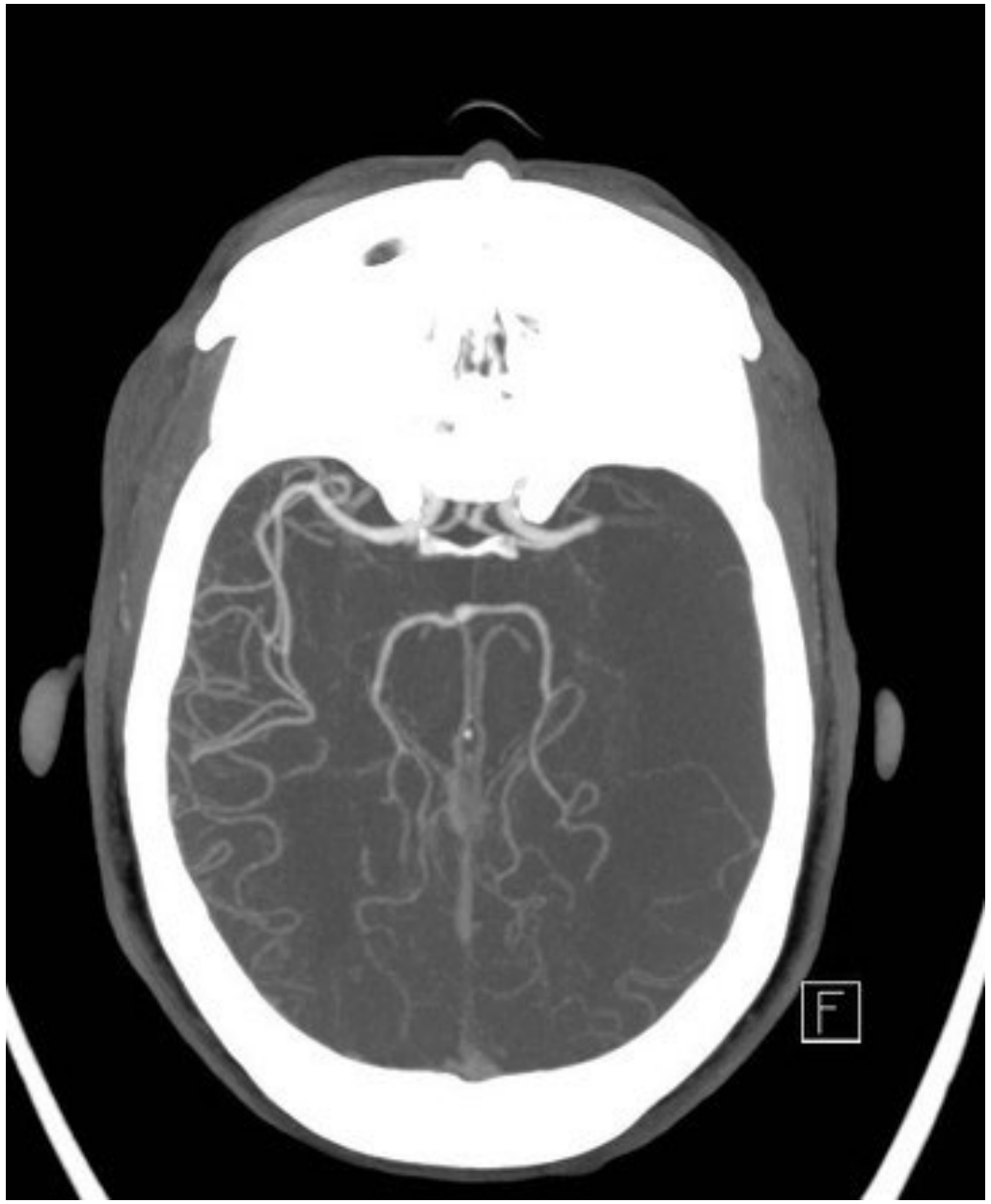
Back to our case

- The patient has no contraindications to thrombolysis
- Consented via family (could use two physician consent) and TNK is initiated

Now what?

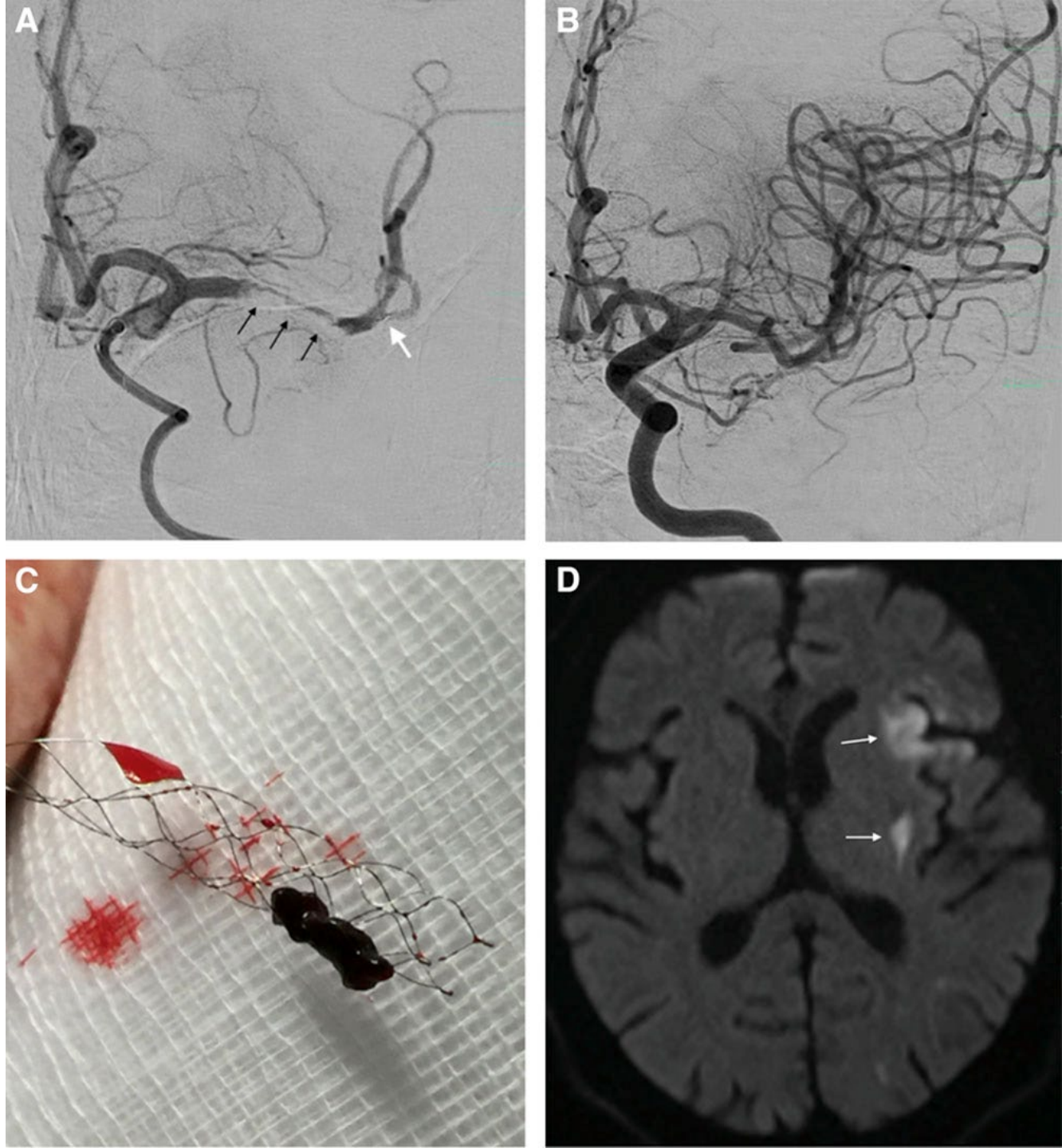
Angiography

- Most commonly obtained with CT angiography
- Sensitive and specific for detection of large vessel occlusion (ICA, M1, Basilar)
- Sensitive and specific for detection of ipsilateral carotid stenosis
- Can aid in decision making for intervention and secondary prevention



Endovascular Thrombectomy

- One of the more powerful interventions in medicine
- Guideline indications
  - LVO
    - Nondominant or co-dominant M2: **STEP**
  - NIHSS≥6
    - Low NIHSS consider for **STEP**
  - ASPECTS≥6
  - Prestroke mRS 0-1
  - <24 hours from LKN
- Use of advanced imaging beyond 6 hours LKN
- Data expanding use for “large core” infarcts
- If 4.5-24 hours with mismatch and not EVT candidate: **SISTER trial** (TS23 vs placebo)



Acute Post Stroke Care

- Permissive hypertension
  - Allows for BP 220/120 mmHg for first 24-48 hours
  - If thrombolysis, <180/105 mmHg
  - Begin to lower pressure after first 24 hours to goal normotension
- Administration of aspirin within 24-48 hours of onset
  - Hold 24 hours after thrombolysis
- DVT ppx within 24 hours of onset
  - Hold 24 hours after thrombolysis
- Avoid fever, hypoglycemia
- Dysphagia screening

Stroke risk factors

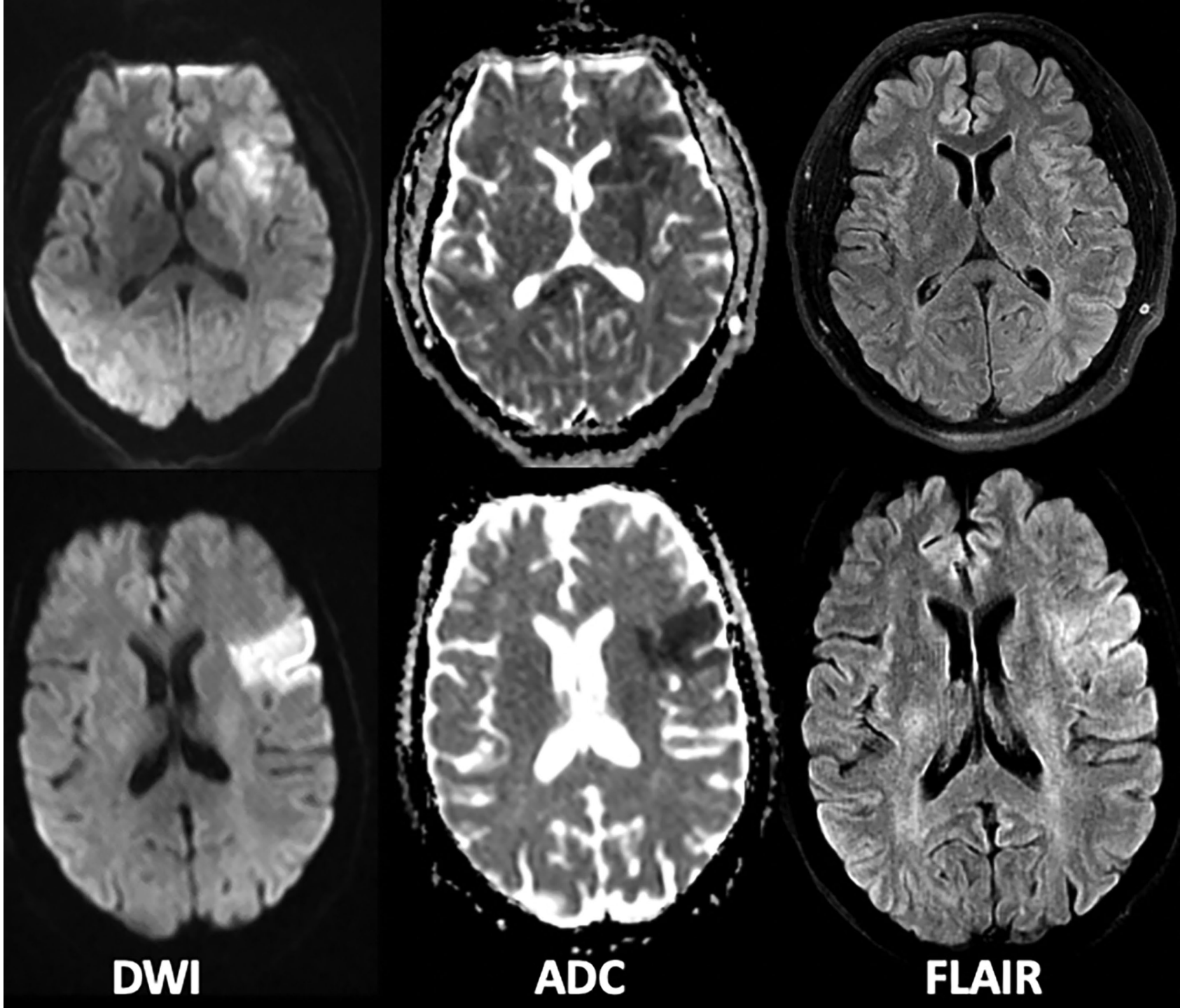
- Modifiable
  - Hypertension
  - Cardiac disease
  - Diabetes
  - Hyperlipidemia
  - Cigarette/alcohol
  - OSA
    - **SLEEP-SMART**: early use of CPAP post ischemic stroke
- Non-modifiable
  - Age
  - Gender
  - Race/ethnicity
  - Heredity

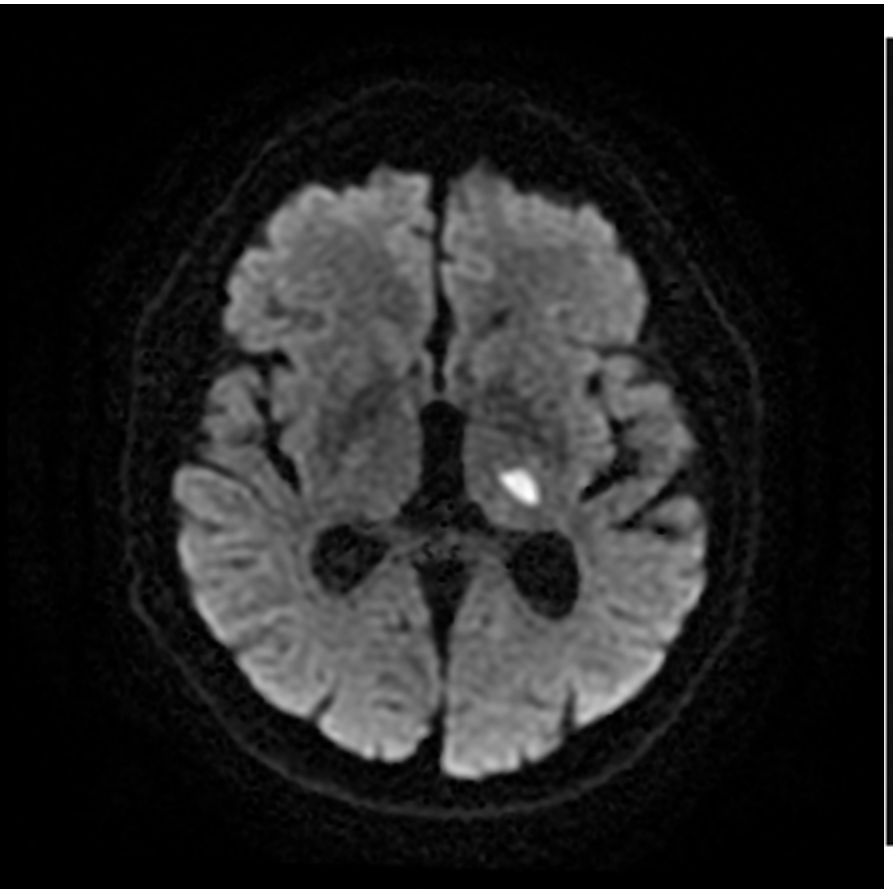
Initial Stroke Secondary Prevention Workup

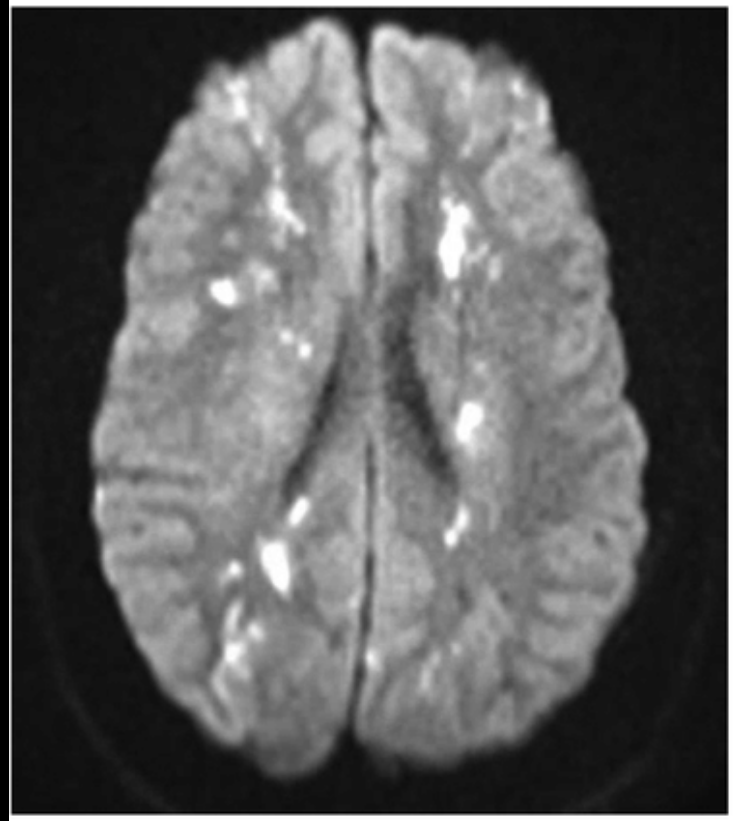
- Lipid Panel
  - LDL goal<70 for those with atherosclerotic disease
  - LDL goal<100 for those without evidence of atherosclerosis and stroke
- A1c
  - Long term secondary prevention goal A1c<7.0%
- TSH, Troponin
- Echocardiogram
  - Changes management around 1% of time
- MRI Brain w/o contrast
  - Not required, especially considering clinical diagnosis

MRI

- DWI most sensitive for early ischemia
- W/ ADC correlate: Acute
  - ADC begins to pseudonormalize around Day 7
- DWI-FLAIR mismatch
  - FLAIR signal delayed
    - Shown to be of utility for IVT in stroke of unknown LKN
- GRE/SWI
  - Useful for assessing hemorrhage, CAA







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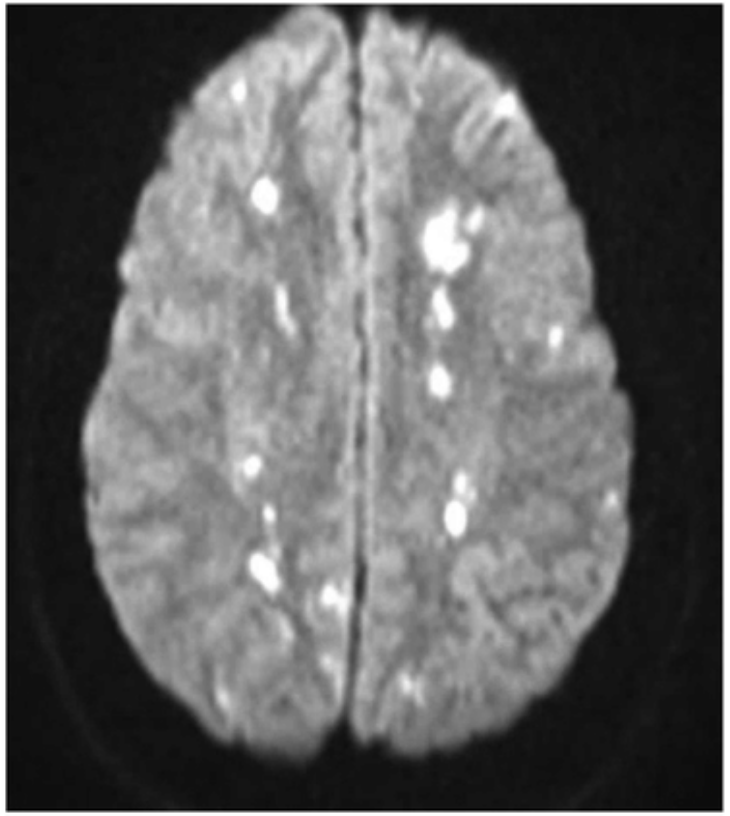

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Workup: unusual causes of stroke

- Dependent on patient's other comorbidities/systemic symptoms
- Toxicology screen
- Lumbar puncture
- Hypercoagulable evaluation
  - Antiphospholipid Antibody Syndrome
- Blood cultures
- Autoimmune evaluation

Stroke Etiology and Criteria

- Guidelines note investigating underlying stroke etiology
- TOAST subtype only "correct" around 60% of the time
- Personally more often break down stroke into stroke with associated conditions/risks
  - Evidence from trials based on specific indications rather than large etiologic subgroups

TABLE 1. TOAST Classification of Subtypes of Acute Ischemic Stroke

Large-artery atherosclerosis (embolus/thrombosis)*
Cardioembolism (high-risk/medium-risk)*
Small-vessel occlusion (lacune)*
Stroke of other determined etiology*
Stroke of undetermined etiology
a. Two or more causes identified
b. Negative evaluation
c. Incomplete evaluation

TOAST, Trial of Org 10172 in Acute Stroke Treatment.
*Possible or probable depending on results of ancillary studies.

General Stroke Secondary Prevention

- Antithrombotic management
  - Most commonly with aspirin 81-325 mg daily
- Lipid lowering therapy
  - Most commonly use of high intensity statins
  - Consider ezetimibe if cannot tolerate statins
  - If resistant, referral for PCSK9 inhibitor
- Blood pressure goal <130/80
- Hyperglycemic management (A1c<7.0)
- Smoking cessation
- Physical activity
- CPAP for patients with OSA **(SLEEP-SMART)**
- Mediterranean or DASH diet

DAPT-Specific Uses

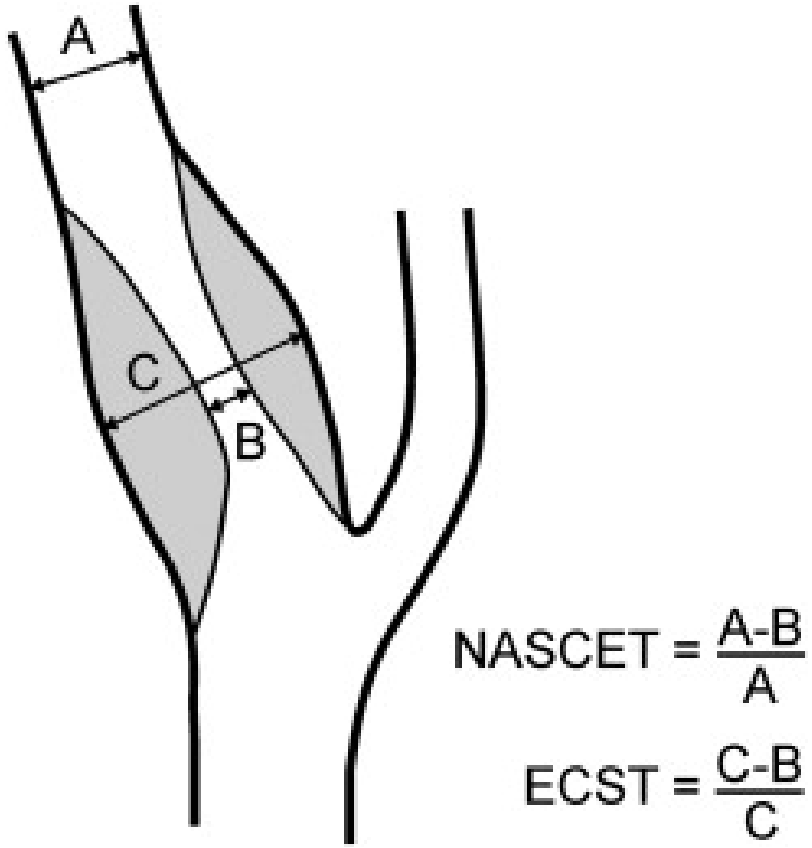
- High risk TIA or minor stroke
  - ABCD2 score≥4 or NIHSS<4 (up to 5 in some trials)
  - Can be implemented within 72 hours per INSPIRES
  - Aspirin 81 mg and Plavix 75 mg (after load) for 21 days then monotherapy
- Intracranial Atherosclerosis
  - Stenosis 70-99% with ipsilateral stroke attributable to disease
  - Up to 90 days of aspirin 81 mg and Plavix 75 mg daily then monotherapy
  - Patients eligible for **CAPTIVA**

Anticoagulation

- Atrial Fibrillation
  - Clear benefit in ECG diagnosed atrial fibrillation
  - Largest benefit in those with persistent and permanent atrial fibrillation
  - DOACs preferred over warfarin except in valvular AF
- Cardiac Thrombus
  - Recommend at least 3 months of therapeutic anticoagulation
- Cervical Artery Dissection
  - No clear consensus between anticoagulation and antiplatelet therapy
  - Increased bleeding risk after 6 months of continued AC use
- Mechanical valves
  - Warfarin
  - Addition of aspirin in patients with stroke preceding mechanical mitral valve
- LV noncompaction
  - Warfarin
- LVAD
  - Warfarin
- Started within 14 days of ischemic stroke
  - New evidence suggesting no increased risk with earlier initiation (4-7 days vs. 10-14 days)

Carotid Artery Stenosis

- Symptomatic carotid
  - Ipsilateral stroke with carotid with ≥50% stenosis
- Carotid revascularization shown to reduce all cause stroke
- Endarterectomy and transfemoral stenting with similar risk reduction
  - CEA with higher perioperative cardiac risk
    - Often preferred in older patients
  - Stenting with higher perioperative stroke risk



Patent Foramen Ovale

- Rare cause of ischemic stroke
  - 25% of the population with PFO
- Evidence in patients 18-60 with high ROPE score that PFO closure reduces risk of stroke
  - NNT approx. 40-45
- No clear benefit in patients with indication for OAC

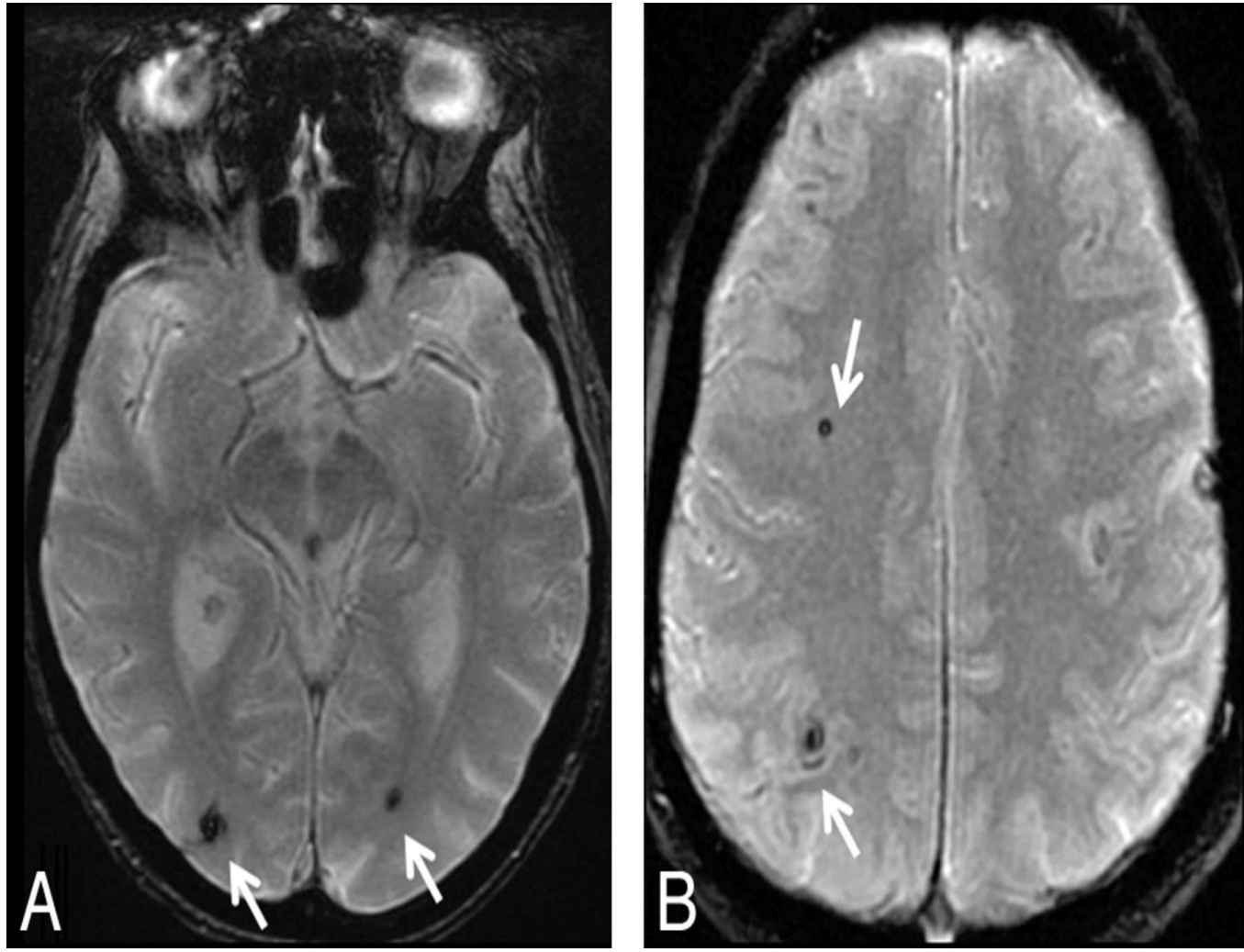
PFO-Associated Stroke Causal Likelihood (PASCAL) Classification System

	Likelihood that the PFO is causative of the ischemic stroke	
	RoPE score ≥7	RoPE score <7
PFO with straddling thrombus	Definite	Definite
Venous thromboembolism (DVT or PE) preceding the index infarct AND PFO with atrial septal aneurysm OR large shunt	Highly probable	Probable
PFO with atrial septal aneurysm or large shunt	Probable	Possible
PFO with small shunt and without an atrial septal aneurysm	Possible	Unlikely

DVT = deep vein thrombosis; PE = pulmonary embolism; PFO = patent foramen ovale; RoPE = Risk of Paradoxical Embolism.

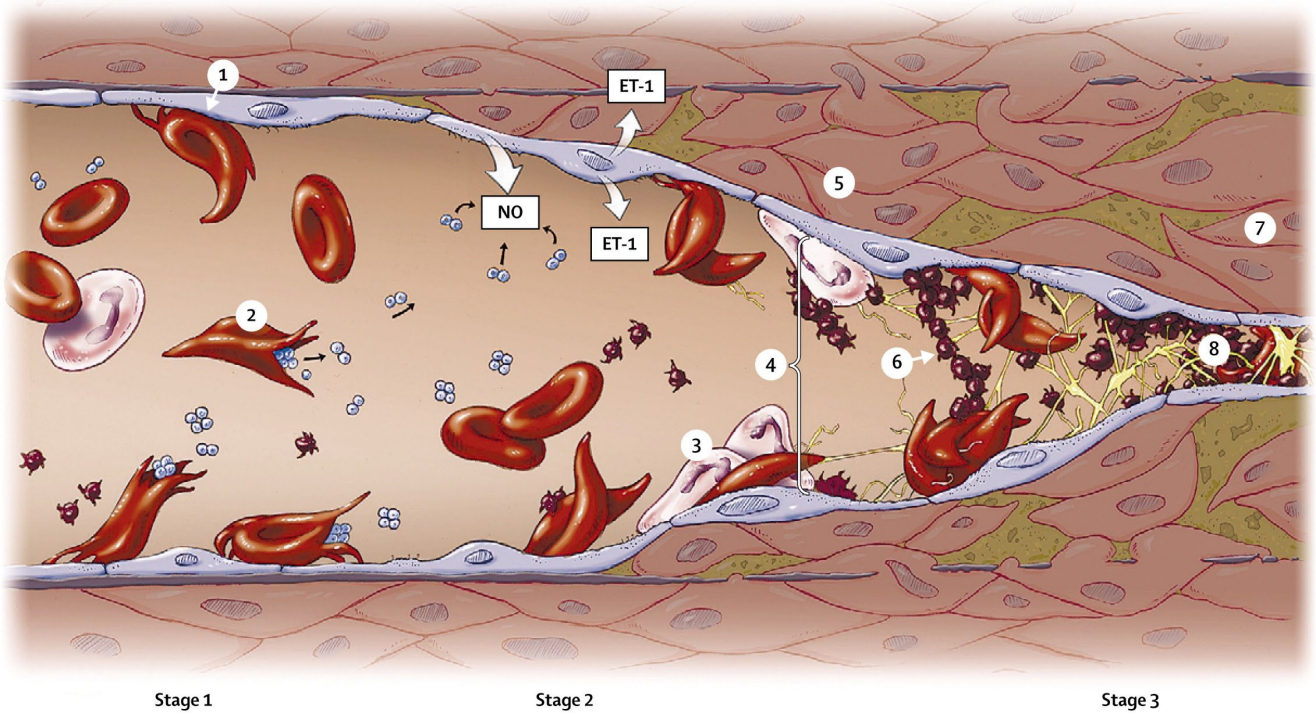
Infectious Endocarditis

- Use of appropriate antibiotics
- No primary role for antithrombotic therapy
  - Avoid AC as able up to 14 days due to increased risk of hemorrhage
- With recurrent stroke and emboli detection or veg>1.0 cm reasonable to pursue valve replacement prior to completion of antibiotics



Sickle Cell Disease

- Can receive thrombolysis and pursue endovascular therapy
- Exchange transfusion
- Chronic transfusions to reduce HgbS to <30% of total Hgb recommended for secondary stroke prevention
- Hydroxyurea

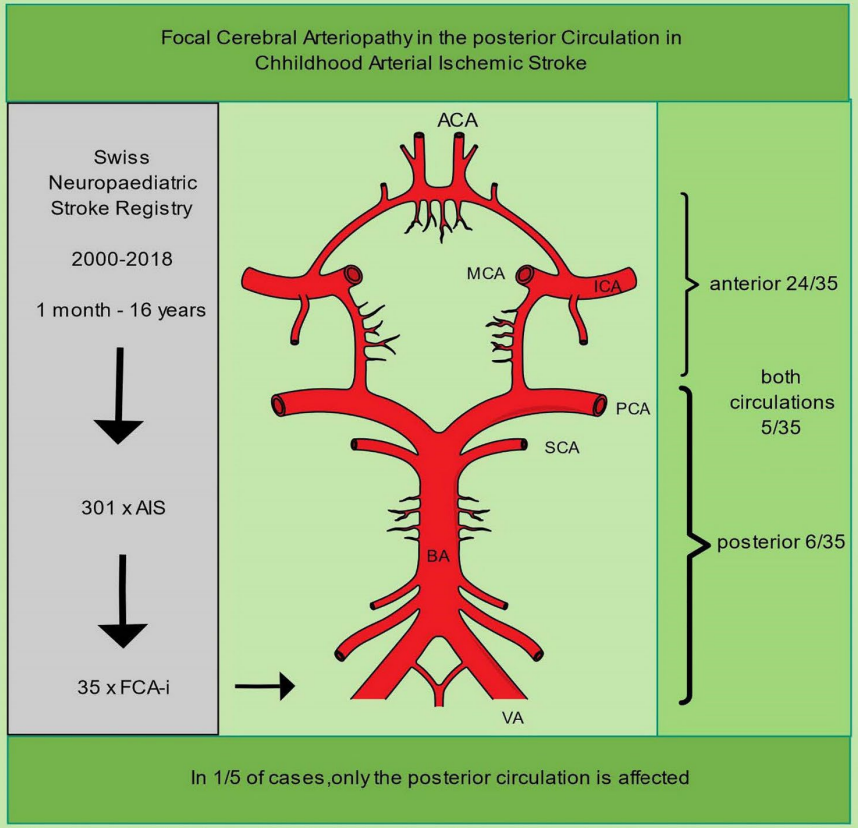


Pediatric Ischemic Stroke

- Perinatal Stroke: Acute neurologic syndrome with cerebral injury of vascular origin between 20 weeks gestation and 28 days postnatally
  - **i-ACQUIRE: Recovery using constraint induced movement therapy in infants with motor weakness**
- Childhood Stroke: Acute neurologic syndrome with cerebral injury of vascular origin between 29 days postnatally and 18 years old
- Different risk profile
- Use of tPA: Evidence in patients with LVO
- EVT in patients 2-18 years old
  - Case reports in neonatal stroke
- Variable use of antithrombotic therapy
  - Most commonly aspirin 3-5 mg/kg

Focal Cerebral Arteriopathy

- MRA with arterial wall imaging
- LP: VZV, HSV PCR
- Inflammatory markers
- Serial vascular follow up imaging
- Aspirin 3-5 mg/kg/day
- FOCAS trial:
  - Aspirin +/- glucocorticoids



Legend: AIS = Arterial Ischemic Stroke; FCA-i = Focal cerebral arteriopathy inflammatory type; ACA = Anterior cerebral artery; MCA = Middle Cerebral Artery; ICA: Internal Cerebral Artery; PCA: Posterior Cerebral Artery; SCA = Superior Cerebellar Artery; BA = Basilar Artery; VA = Vertebral Artery

FOCAS

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Questions?