STROKE AND MULTIPLE SCLEROSIS

2017 ACOI Internal Medicine Review Course

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Stroke and Multiple Sclerosis

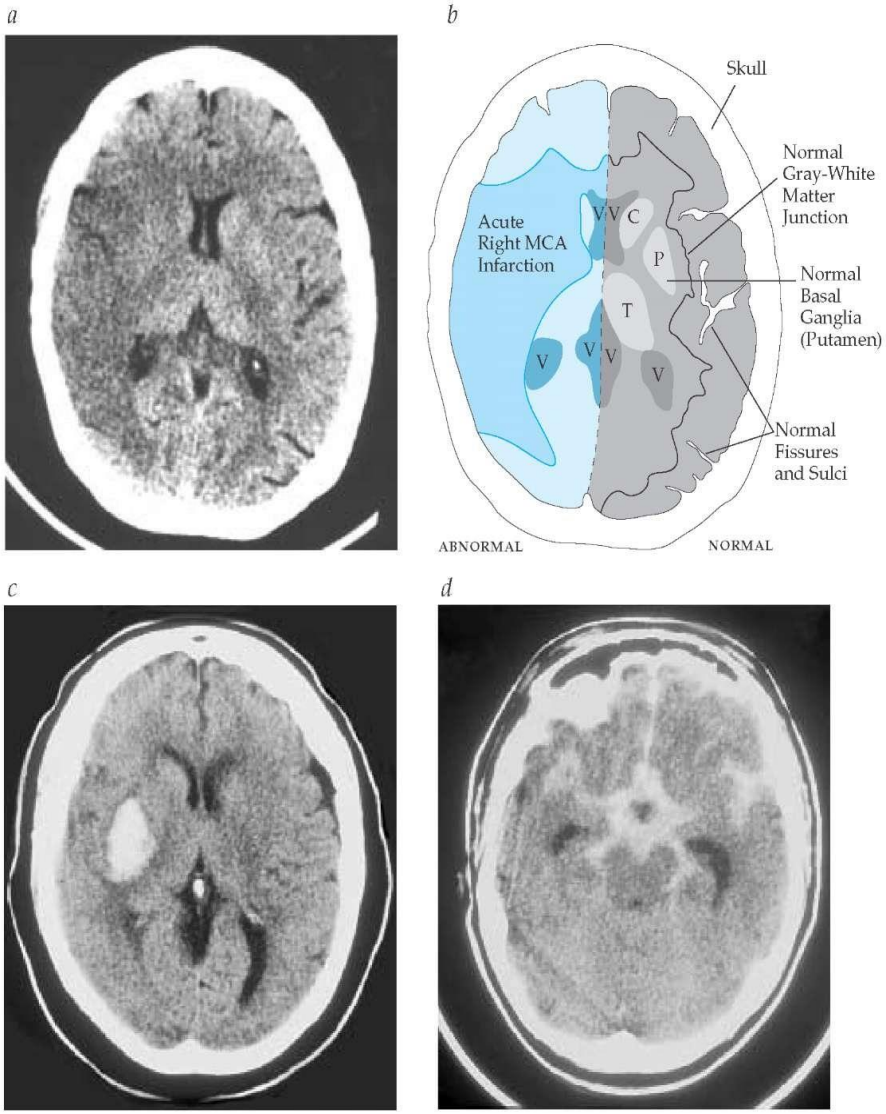
Stroke or Brain Attack

5th Leading cause of Death for men
4th leading cause of Death for women
3rd leading cause of death for Blacks
Acute brain injury due to a vascular etiology
Sudden onset
Persist at least 24 hours
Associated neurological deficit/deficits

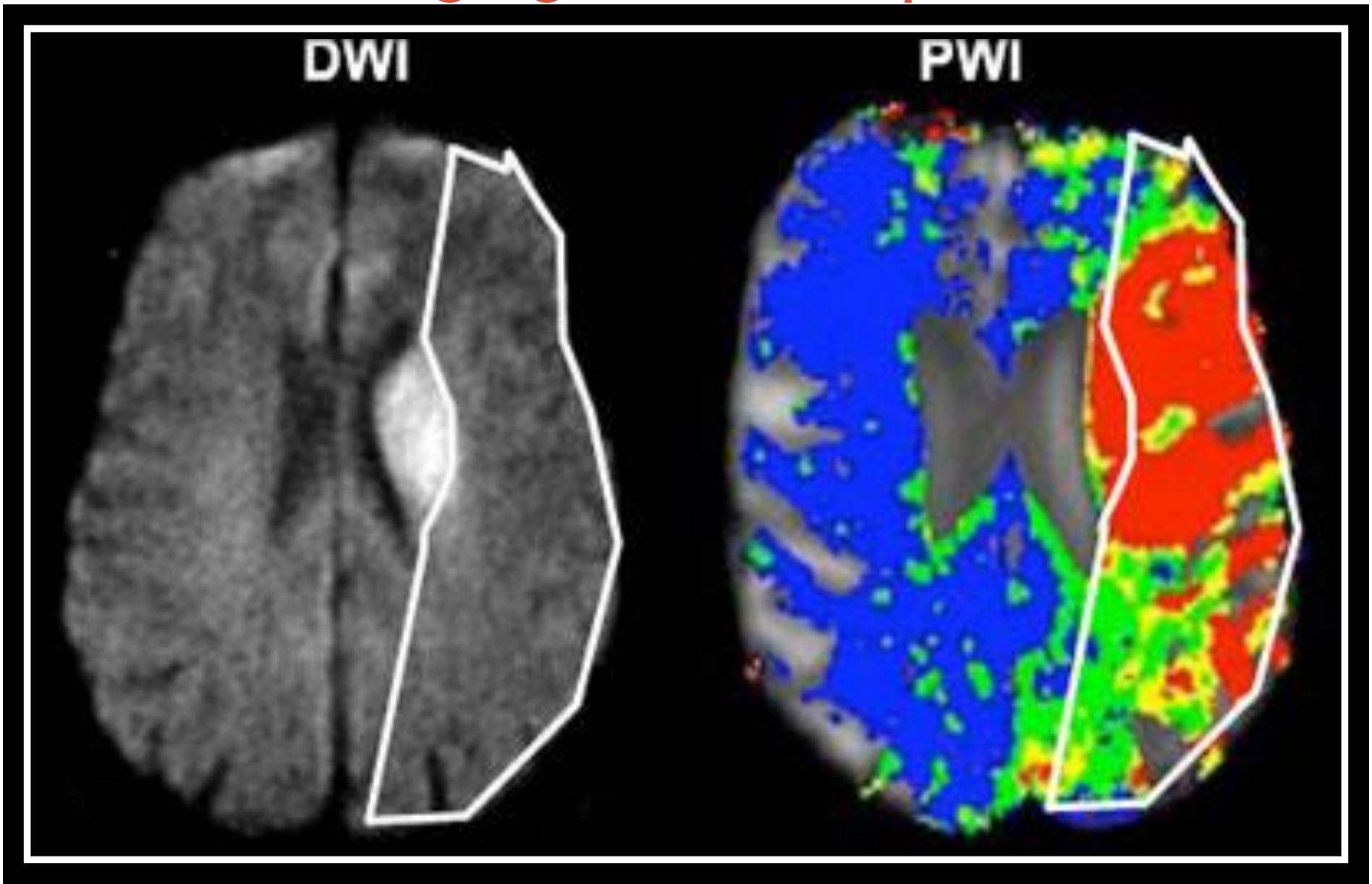
TIA

Neurological deficits lasting less than 24 hours

Stroke Imaging



Stroke Imaging- diffusion/perfusion



STROKE

- 795,000 Strokes Occur each year
- 87 percent of those strokes are ischemic
- Stroke kills 130,000 Americans/year
- Stroke costs the US an estimated 34 billion/yr
- Leading cause of serious long term disability

STROKE

- Race/Sex/Geography
  - Black risk of death is 1.49X Whites
  - Males greater risk than females
  - Hispanics higher risk for lacunar infarcts
  - Southeastern US has higher risk
- Age
  - Stroke occurs in all ages
  - Stroke increases with age
  - Age >64 is where 75% of occurrence

STROKE RISK FACTORS

- **Non-modifiable Risk Factors**
  - Age
  - Race
  - Sex
  - Ethnicity
  - History of Migraine
  - Sickle Cell Disease
  - Fibromuscular Dysplasia
  - Heredity

STROKE RISK FACTORS

- Laboratory Monitoring Risk
  - Glucose and Electrolytes
  - CBC with Platelets
  - Prothrombin Time/ Partial Thromboplastin Time
  - Cholesterol/LDL/HDL
  - ANA/RF/Homocysteine/ESR
  - Protein C/ Protein S/ Antithrombin III/ Leiden
  - Anticardiolipin Antibody
  - Lupus Inhibitor/ Antiphospholipid Antibodies

VASCULAR RISK FACTORS

- Modifiable conditions and lifestyle characteristics identified as a risk factors for stroke:

High blood pressure
Atrial fibrillation
Diabetes mellitus
Carotid artery disease
Myocardial infarction

High Cholesterol
Hyperhomocysteinemia
Smoking
Heavy alcohol use
Physical inactivity
Obesity

CIGARETTE SMOKING

- Background
  - Independent risk factor for ischemic stroke in men and women
  - 2-3 fold increased risk compared to non-smokers[1]
  - Spousal cigarette smoking may be associated with an increased stroke risk[2]
  - 50% risk reduction by 2 years after stopping smoking[3]

1: Shinton R et al.: BMJ (1989) 298:789-94.
2: Qureshi A et al.: Stroke (2005) 36:74-76
3: Colditz GA et al.: N Engl J Med (1988) 318:937-41.

ALCOHOL CONSUMPTION

- Background
  - Increased risk for both ischemic (RR 1.69) and hemorrhagic stroke (RR 2.18) with heavy alcohol consumption (>60g/day)[1]
  - BP elevation might be a reasonable explanation[3]
  - Light alcohol consumption (<12g/day) associated with reduced ischemic (RR 0.80) and hemorrhagic stroke[1]
  - Red wine consumption carries the lowest risk[2]

1: Reynolds K et al.: JAMA (2003) 289:579-88
2: Mukamal K et al.: Ann Intern Med (2005) 142:11-19
3: Bazzano LA et al.: Ann Neurol (2007)

PHYSICAL ACTIVITY

- Background
  - Regular exercise (at least 3x30min/week) is associated with a decreased risk of stroke
  - Physically active individuals have a lower risk of stroke or death than those with low activity (RR 0.73)[1]
  - This is mediated, in part, through beneficial effects on body weight, blood pressure, serum cholesterol, and glucose tolerance[2]

1: Lee C et al.: Stroke (2003) 34:2475-2481
2: Deplanque D et al.: Neurology (2006) 67:1403-1410)

BODY WEIGHT, DIET, NUTRITION

- Background
  - High body mass index (BMI ≥25) increases risk of stroke in men and women[1]
  - Abdominal adiposity is a risk factor for stroke in men but not women[2]
  - A randomized trial in women found no effect of dietary interventions to reduce the incidence of stroke[3]
  - Tocopherol and beta carotene supplementation do not reduce the risk of stroke. Vitamin E might increase mortality when used at high-dose (≥400 IU)

1: Kurth T et al.: Circulation (2005) 111:1992-1998
2: Hu G et al.: Arch Intern Med (2007) 167:1420-1427
3: Howard B et al.: JAMA (2006) 295:655-666

HORMONE REPLACEMENT THERAPY

- Background
  - Stroke rates rise rapidly in women after the menopause
  - Hormone replacement therapy in postmenopausal women is associated with an 44% increased risk of stroke[1]

1: Gabriel S et al.: Cochrane Review (2005) CD002229

ANTITHROMBOTIC THERAPY

- Background
  - In low risk persons low dose aspirin reduced coronary events, but not stroke[1]
  - In women over 45 years aspirin reduces the risk of ischemic stroke (OR 0.76; 95%CI 0.63-0.93) [2]
  - Aspirin reduces MI in patients with asymptomatic carotid artery disease[3]

1: Bartolucci A et al.: Am J Cardiol (2006) 98:746-750
2: Berger J et al.: JAMA (2006) 295:306-313
3: Hobson R, 2nd et al.: J Vasc Surg (1993) 17:257-263

VITAMINS

- Background
  - Beta carotene increased the risk (RR 1.10) of cardiovascular death[1]
  - Antioxidant supplements may increase mortality[2]
  - Folate, B12, B6 vitamins given to lower homocysteine levels may not reduce stroke recurrence and may increase vascular events[3]

1: Vivekananthan D et al.: Lancet (2003) 361:2017-2023
2: Bjelakovic G et al.: JAMA (2007) 297:842-857
3: Bonaa K et al.: N Engl J Med (2006) 354:1578-1588

SLEEP-DISORDERED BREATHING

- Background
  - Sleep-disordered breathing (SDB) is both a risk factor and a consequence of stroke
  - More than 50% of stroke patients have SDB, mostly in the form of obstructive sleep apnoea (OSA).
  - SDB is linked with poorer long-term outcome and increased long-term stroke mortality[1]
  - Continuous positive airway pressure is the treatment of choice for OSA.

1: Bassetti CL: Semin Neurol (2005) 25:19-32

MANAGEMENT OF COMPLICATIONS

- Falls
  - Are common in every stage of stroke treatment
  - Risk factors include cognitive impairment, depression, polypharmacy and sensory impairment[1]
  - A multidisciplinary package focusing on personal and environmental factors might be preventive[2]
  - Exercise, calcium supplements and bisphosphonates improve bone strength and decrease fracture rates in stroke patients[3,4]

1: Aizen E et al.: Arch Gerontol Geriatr (2007) 44:1-12
2: Oliver D et al.: BMJ (2007) 334:82
3: Pang MY et al.: Clin Rehabil (2006) 20:97-111
4: Sato Y et al.: Cerebrovasc Dis (2005) 20:187-92

MANAGEMENT OF COMPLICATIONS

- Dysphagia and feeding
  - Dysphagia occurs in up to 50% of patients with unilateral hemiplegic stroke and is an independent risk-factor for poor outcome[1]
  - For patients with continuing dysphagia, options for enteral nutrition include NG or PEG feeding
  - PEG does not provide better nutritional status or improved clinical outcome, compared to NG[2,3]

1: Martino R et al.: Stroke (2005) 36:2756-63
2: Dennis MS et al.: Lancet (2005) 365:764-72
3: Callahan CM et al.: J Am Geriatr Soc (2000) 48:1048-54

REHABILITATION

- Early rehabilitation
  - More than 40 % of stroke patients need active rehabilitation
  - Active rehabilitation should start early, providing the patient is clinically stable
  - Passive rehabilitation should be given if the patient is unconscious or paralyzed
  - Rehabilitation should be continued as long as perceptable recovery is taking place

REHABILITATION

- Multidisciplinary stroke team for rehabilitation
  - Stroke physician
  - Nurses experienced in stroke management
  - Physiotherapist trained in stroke rehabilitation
  - Occupational therapist skilled in stroke
  - Speech therapist familiar with speech problems in stroke patients
  - Neuropsychologist accustomed to stroke rehabilitation
  - Social worker familiar with the problems of stroke patients

Calculating Risk

ABCD2

To identify individuals at high early risk of stroke after transient ischemic attack.

A (Age); 1 point for age ≥60 years,

B (Blood pressure ≥ 140/90 mmHg); 1 point for hypertension at the acute evaluation,

C (Clinical features); 2 points for unilateral weakness, 1 for speech disturbance without weakness,

D (symptom Duration); 1 point for 10–59 minutes, 2 points for ≥60 minutes.

D (Diabetes); 1 point Total scores ranged from 0 (lowest risk) to 7 (highest risk).

Scale:

Stroke risk at 2 days, 7 days, and 90 days:

Scores 0-3: low risk

Scores 4-5: moderate risk

Scores 6-7: high risk

Stroke and Multiple Sclerosis

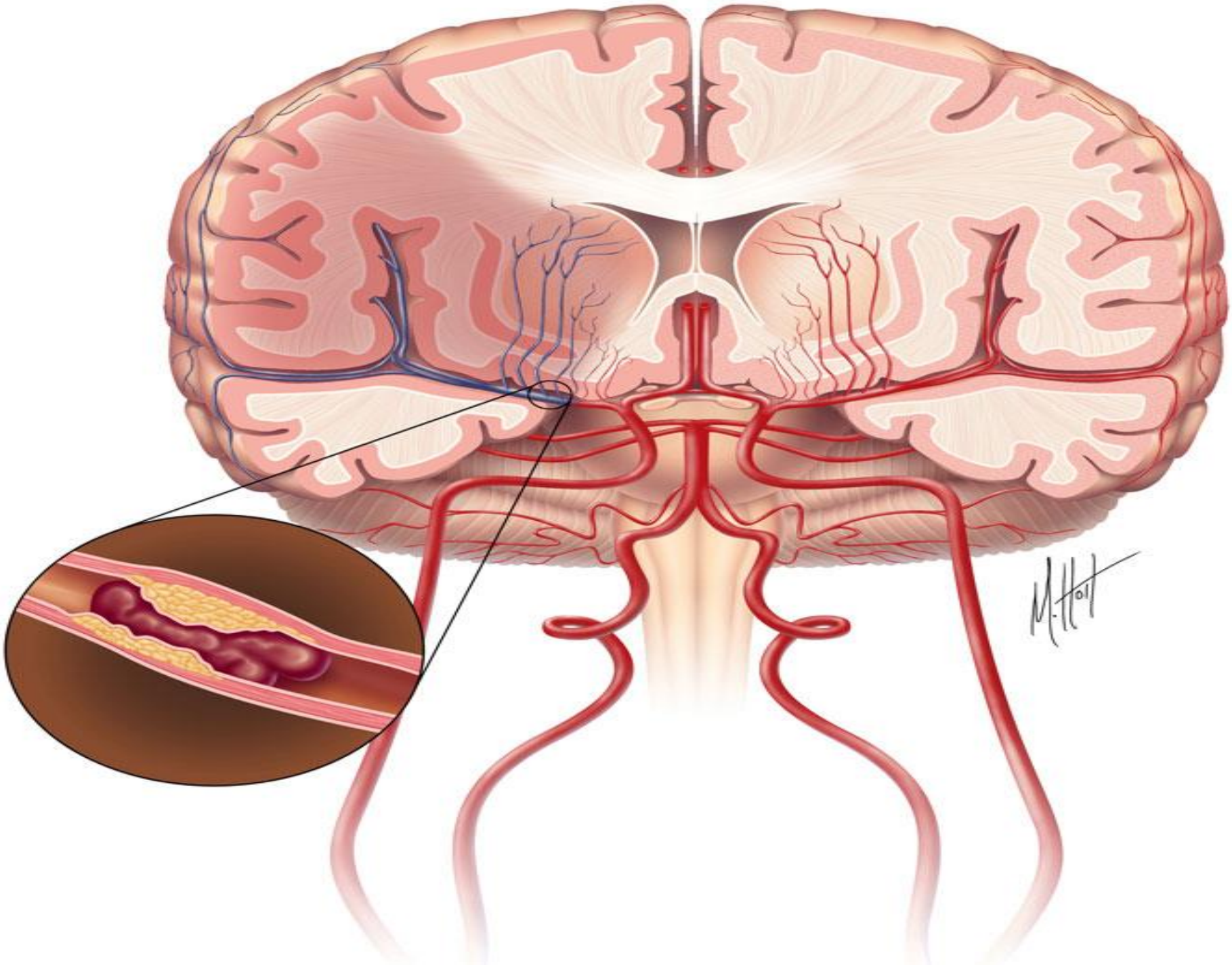
Types of Stroke

Ischemic- most common >70%

- Thrombotic
  - Atherosclerosis
- Embolic
  - Emboli form the Heart or Vessels

Hemorrhagic-

- Intracerebral
  - Hypertension or Amyloid Angiopathy
- Subarachnoid
  - Berry Aneurysms



Stroke and Multiple Sclerosis

Thrombotic Strokes

Atherosclerosis
- Internal Carotid
- Middle Cerebral
- Vertebrobasilar

Symptoms
- Slow stepwise progression of symptoms
- Usually preceded by TIA's

Other Causes
- Lupus anticoagulant
- Polycythemia
- Syphilis
- Thrombocytosis
- Dissecting Aortic Aneurysm

Stroke and Multiple Sclerosis

Embolic Stroke

- Not usually preceded by TIA
- Emboli
  - Heart
  - Large Blood vessel
  - Usually effects middle>posterior>anterior cerebral
- Symptoms
  - Neurodeficits worst at onset
  - Weakness is greater in distal extremities

Stroke and Multiple Sclerosis

Stroke Symptoms By Region

- Middle cerebral
- Anterior cerebral
- Posterior cerebral
- Single Hemisphere
- Vertebrobasilar
- Lateral Medullary syndrome
- Lacunar-small vessel

Stroke and Multiple Sclerosis

Middle Cerebral Artery Occlusion

- Contralateral hemiplegia
- Contralateral hemianesthesia
- Homonymous hemianopsia
- Impaired conjugate gaze in opposite direction
- Impaired spatial- nondominant
- Impaired language-dominant
- If lesion high- >loss face/upper ext
- If it is in the main trunk- same throughout

Stroke and Multiple Sclerosis

Anterior Cerebral Artery Occlusion

- Most affected in distal contralateral leg
- Urinary incontinence
- Gait abnormalities
- If includes corpus callosum the patient will have tactile anomia (*cannot name what they touch*)

Stroke and Multiple Sclerosis

Posterior Cerebral Artery Occlusion

- Contralateral homonymous hemianopsia
- Usually upper quadrantanopsia
- Mild contralateral hemiplegia/anesthesia
- Color anomia= corpus callosum damage
- Memory loss
- If occlusion bilateral memory will be severe/persistent

Stroke and Multiple Sclerosis

Single Hemisphere injury

- Does not affect paraspinal muscles
- Does not affect pharynx
- Does not affect jaw
- Does not affect the forehead
- If any or all of the above are affected think:
  - Bilateral hemispheric infarct
  - Brainstem infarct

Stroke and Multiple Sclerosis

Vertebrobasilar Artery Occlusion

- Associated with brain stem strokes
- Bilateral extremity motor/sensory dysfunction
- Quadraplegia in severe cases
- Crossed motor and sensory deficits
- Horner syndrome
- Cerebellar signs/stupor/coma
- Cranial nerve dysfunction

Stroke and Multiple Sclerosis

Lateral Medullary Syndrome

- Also called ***Wallenberg Syndrome***
- Nausea
- Vomiting
- Nystagmus
- Ipsilateral Horner Syndrome
- Ipsilateral palate and vocal cord weakness
- Ipsilateral face hemianesthesia
- Contralateral body hemianesthesia

Stroke and Multiple Sclerosis

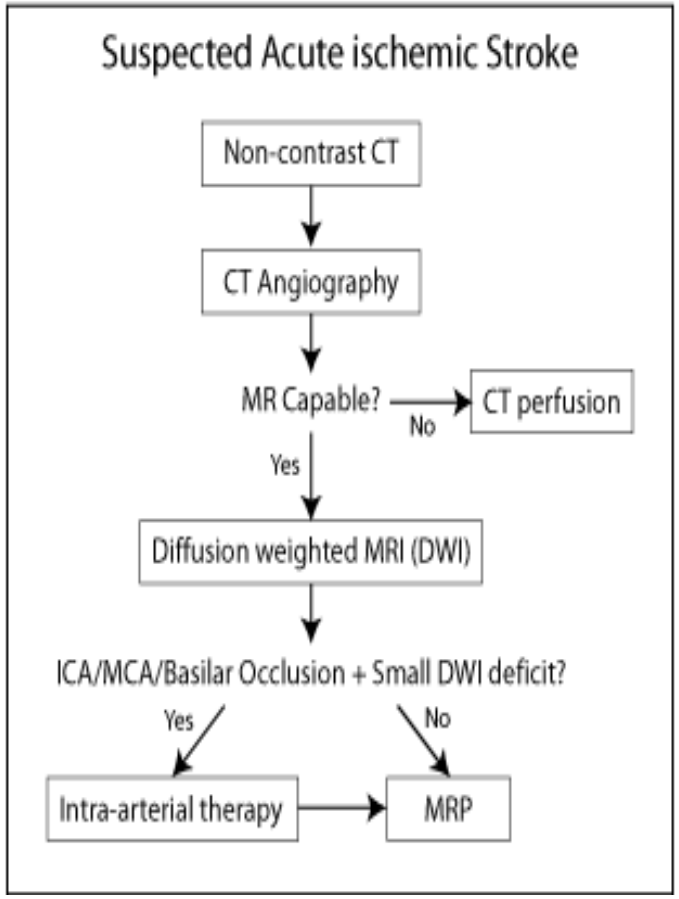
Lacunar Strokes

- Due to hypertension
- Occlusion of very small arterioles
- Over time they form cysts in the brain
- Pure hemiplegia
- Pure hemisensory
- Multiple bilateral frontal lobe “lacunes” can cause pseudobulbar palsy

Stroke and Multiple Sclerosis

Work up:

- History
- Computerized Tomography Brain
- CBC with platelets
- Troponin
- Electrolytes, Glucose, Bun, Cr,
- Coagulation profiles
- EKG
- Trans-thoracic Echocardiogram
- Carotid Ultrasound/Trans-cranial Doppler
- MRI/MRI Diffusion/Angiography



Stroke and Multiple Sclerosis

Ischemic Stroke Treatment

-Thrombolysis-Alteplase

>18 yrs old with an ischemic stroke Dx

Onset time – 3 hours(3-4.5 with caveats)

Oxygen

-Treat BP-gradually

-Aspirin/Antiplatelets

-Surgical Intervention

-intra-arterial therapy

-mechanical thrombectomy

Stroke and Multiple Sclerosis

- **CONTRAINDICATIONS TO ALTEPLASE(tPA)**

Absolute-
Intracranial hemorrhage on CT
Clinical Presentation suggests subarachnoid hemorrhage
Neurological surgery, serious head trauma, or previous stroke past 3 months
Uncontrolled hypertension(>185 mmHg SBP or >110 mm Hg DBP)
History of intracranial hemorrhage
Seizure at stroke onset
Known AVM, neoplasm , or aneurysm
Active internal bleeding
Suspected/confirmed endocarditis
Known bleeding diasthesis: plts<100,000, heparin with elevated PTT, oral anticoagulants and INR>1.7, thrombin inhibitors
Abnormal blood glucose(<50 or >400 mg/dl)

Relative –
Only minor or rapidly improving stroke symptoms
Patient has had major surgery or serious trauma excluding head trauma in previous 14 days
History of GI/Urinary hemorrhage in last 21 days
Recent arterial puncture at a noncompressible site
Recent lumbar puncture
Post myocardial infarction pericarditis
Pregnancy

Additional WARNINGS to tPA > 3 hr onset-
Age >80
History of prior stroke and diabetes
Any active anticoagulant use (even with INR <1.7)
NIHSS>25

Stroke and Multiple Sclerosis

- **Post Acute Care Therapy**

Antiplatelets

ASA (50-325 mg)/Aggrenox/Ticlodipine

Clopidogrel

Coumadin

Dabigatran, Apixaban, Rivaroxaben- (non valvular Atrial Fibrillation)

Manage underlying causes

Cardiac- ACC

HTN- JNC guidelines

Diabetes- HbA1C <6.5-7.0

Tobacco abuse

Hyperlipidemia- LDL <70

If >70% carotid stenosis- surgical evaluation/discussion

Stroke and Multiple Sclerosis

- **CHADS2**

Score for Atrial Fibrillation Stroke Risk

Congestive Heart Failure	1pt
Hypertension	1pt
Age>75	1pt
Diabetes Mellitus	1pt
Stroke or TIA Symptoms	2pt

Score >2	*High*	*oral anticoagulant*
Score >1 <2	*Moderate*	*oral anticoagulant or ASA*
Score 0	*Low*	*ASA 75-325mg*

Stroke and Multiple Sclerosis

Intracerebral Hemorrhage

- Amyloid Angiopathy
  - Commonly causes recurrent bleeds
  - >65 yrs old
  - Subcortical , rarely affects deep structures
  - Can cause multi-infarctional dementia
  - Also found in alzheimers patients- unclear association
  - Occasionally can be associated with subarachnoid

Stroke and Multiple Sclerosis

Intracerebral Hemorrhage

Hypertension

Gradual and smooth onset of symptoms

Putamen>Thalamus>Pons>Cerebellum

- Putamen
  - Contralateral hemiparesis/sensory loss/hemianopsia
  - Acts just like a middle cerebral infarct
- Thalamus
  - Contra hemiplegia/hemianesthesia/sensory>motor
- Pons
  - Coma/pinpoint pupils/complete paralysis
  - Can have decerebrate posturing bilaterally
- Cerebellum
  - Acute dizziness/ataxia/vomiting
  - No mentation change or loss of consciousness

Stroke and Multiple Sclerosis

Subarachnoid Hemorrhage

- Cerebral saccular aneurysm bleed
  - Usually Circle of Willis
  - IC=40%/AC=35%/MC=20%
- Hypertensive hemorrhages with ventricular rupture
- A-V Malformations
- Symptoms
  - Acute/Severe headache (thunderclap)-unresponsive to meds
  - May be alert/confused /comatose
  - No focal neurological signs
  - Neck stiffness is classic- but not always present

Stroke and Multiple Sclerosis

- **Hemorrhagic Stroke Work Up**

  Computerized Tomography

  (CT misses 10% of Bleeds)

  Lumbar Puncture

  Xanthochromic supernatent is diagnostic

  If LP (-) can be hours before blood gets in CSF

  Cerebral Angiography

  Can rebleed in 24 hours/Vasospasm

  Treatment

  -Neurosurgery consult/Intervention

  -ABC'S/ Intracranial Pressure monitoring

  -Hemodynamic and edema management/Nimodipine/Mannitol/Glycerol/Saline

  -Seizure management

Stroke and Multiple Sclerosis

- Multiple Sclerosis

Myelin deterioration

Brain-

Spinal Cord-

Optic Nerve -

Pathophysiology

10x more common in northern latitudes

May be viral in origin— Female2:1 Males

Autoimmune but does have genetic components

Onset 20-50 yrs of age

Plaques

Cause a mononuclear inflammation

Demyelination with axonal sparing

Oligodendrogial cell loss and astrocyte proliferation

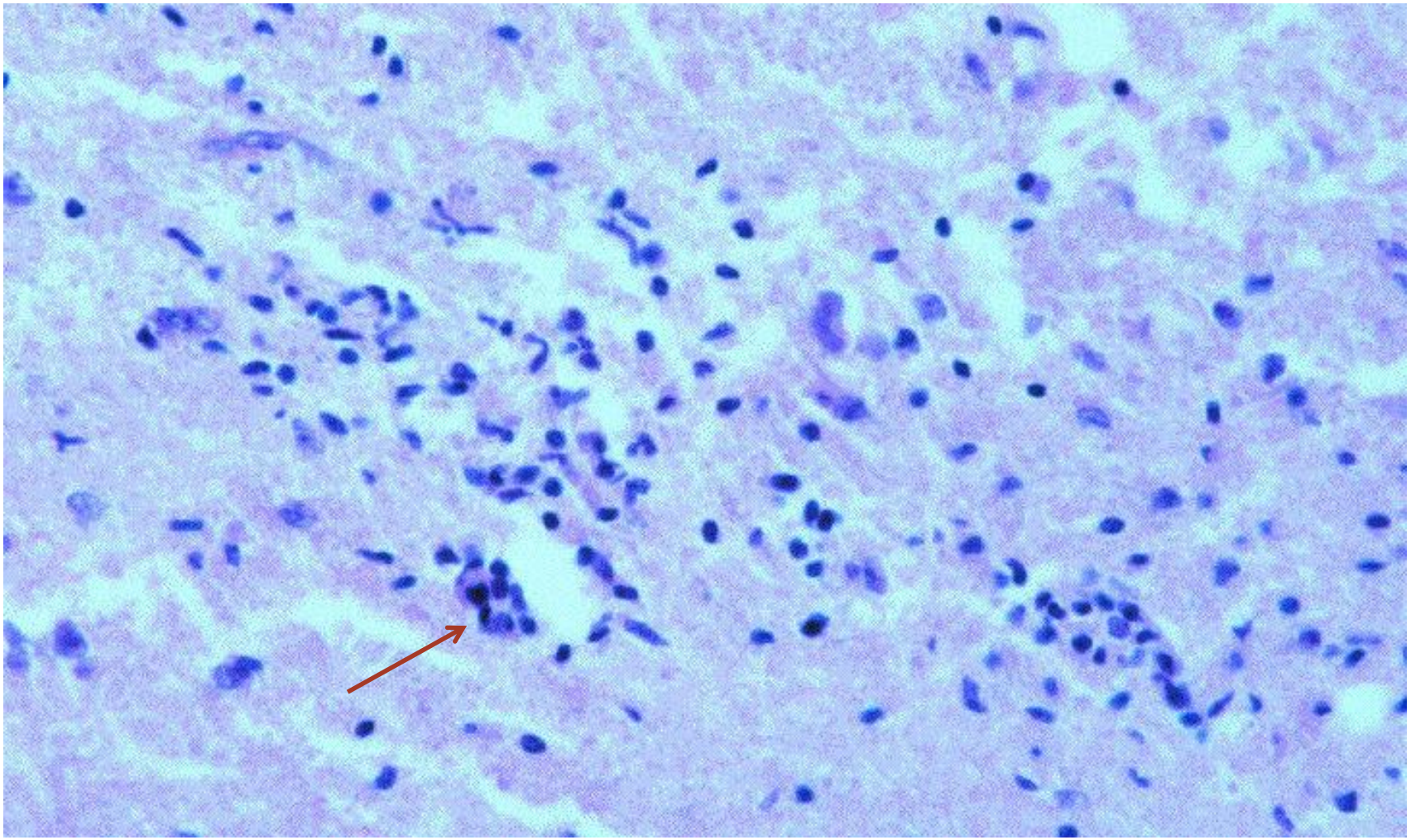
Long standing lesion Astrogliosis

Stroke and Multiple Sclerosis

Symptoms

- Mononeuropathy +/- multiplex
- Optic neuritis
- Ophthalmoplegia/Ophthalmoparalysis-
- Intermittent Diplopia
- Extremity weakness
- Tremors
- Lhermitte sign-
  - (Paresthesias radiating down the spine into extremities on neck flexion)

Multiple Sclerosis-H&E STAIN



Stroke and Multiple Sclerosis

- **Types of Multiple Sclerosis**

Clinically Isolated Syndrome(CIS)

No occurrence after initial

Relapsing-remitting

Most common

Has attacks followed by none then reoccurs

Primary-Progressive

Men

Gradual decline few plateaus

Secondary-progressive

Stage II relapsing-remitting. No periods of remission

Progressive-relapsing

Rare. Progressive form until the end

Malignant (Marburg Variant)

Very rare. Decline to death in few months

Stroke and Multiple Sclerosis

- McDonald Criteria: (attack must last 24 hours and 30 day interval)

Attacks	Lesions	Additional Information
2 or more	2 or more	none
2 or more	1	Dissemination in space or further attack
1	2	Dissemination in time or further attack
1	1	Dissemination space/time or further attack
0		1 yr of disease progression and 2 of below: Positive MRI Brain Positive MRI Spinal Cord Positive CSF

Stroke and Multiple Sclerosis

- **Diagnostic Tests**

  MRI –TEST OF CHOICE-Brain/Spinal Cord

  -White plaques lesions

  Evoked Action Potentials

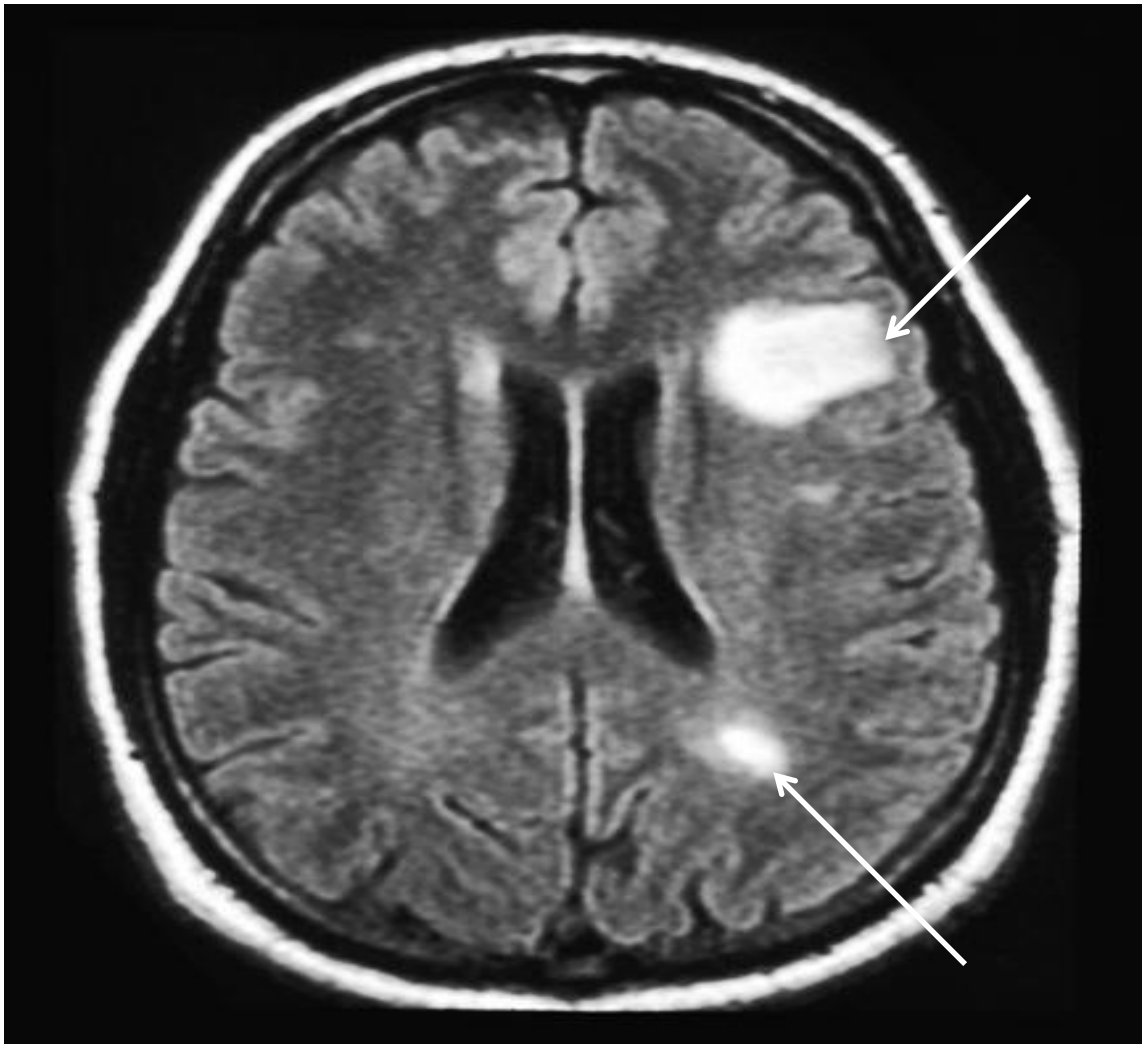
  -Silent lesions

  Lumbar Puncture

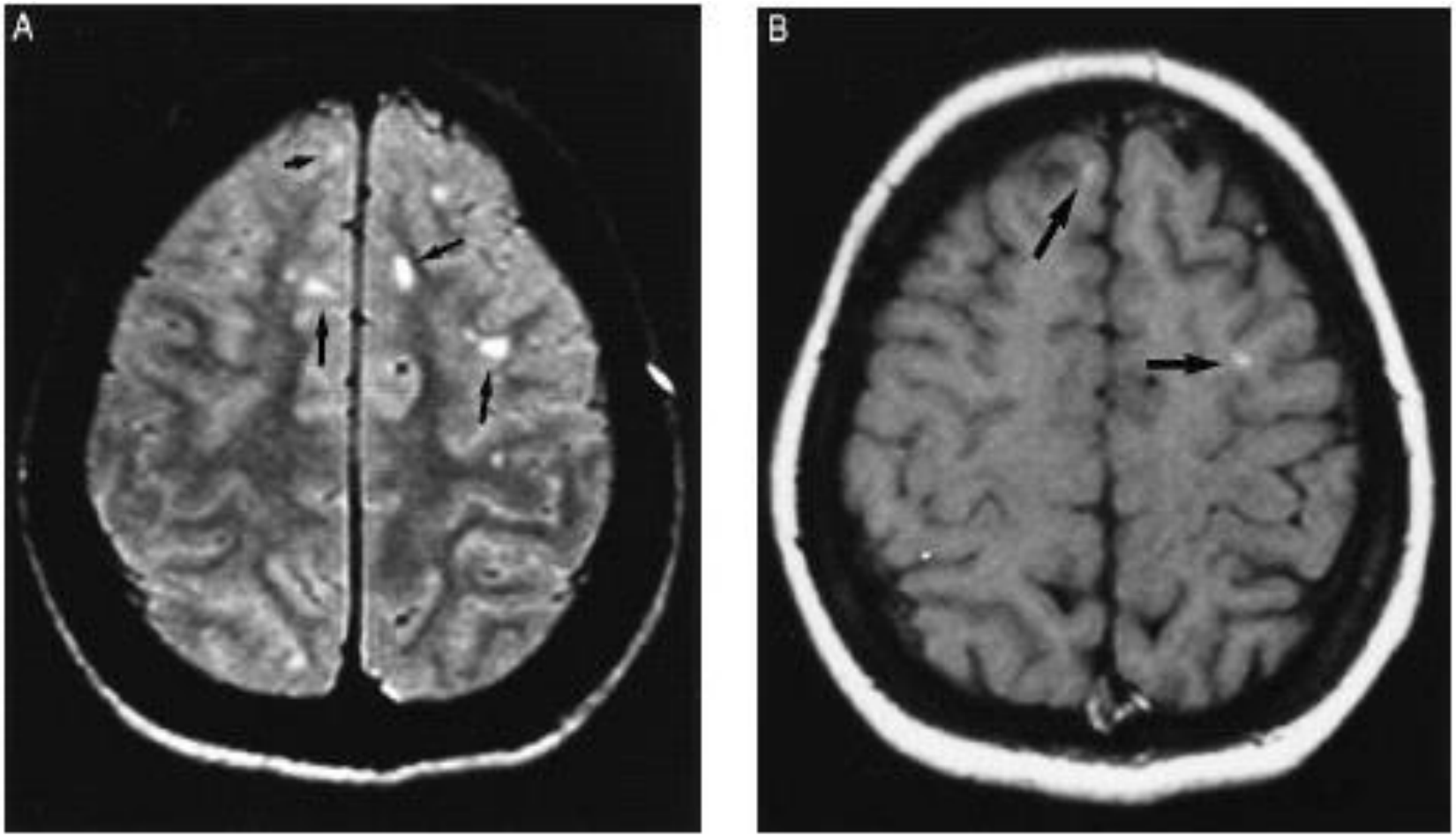
  -Increased IgG / Oligoclonal IgG bands CSF

  -Elevated protein

Stroke and Multiple Sclerosis



Stroke and Multiple Sclerosis



Stroke and Multiple Sclerosis

Treatment

Acute Phase/Initial

Steroids 500mg daily x 5 days

Plasma exchange for severe deficits with poor response to steroids

Oral Immunomodulator-

Fingolimod(*Gilenya*), *Ampyra,Aubagio,Tecfidera*

Relapsing-Remitting

Beta-interferons(1-a,1-b)-

Avonex/Rebif/Betaseron/Extavia/Plegridy

Monoclonal Antibodies-

Tysarbi-

Alemtuzumab (Lemtrada)- HIV negative

Copolymer-

Copaxone/Glatoba

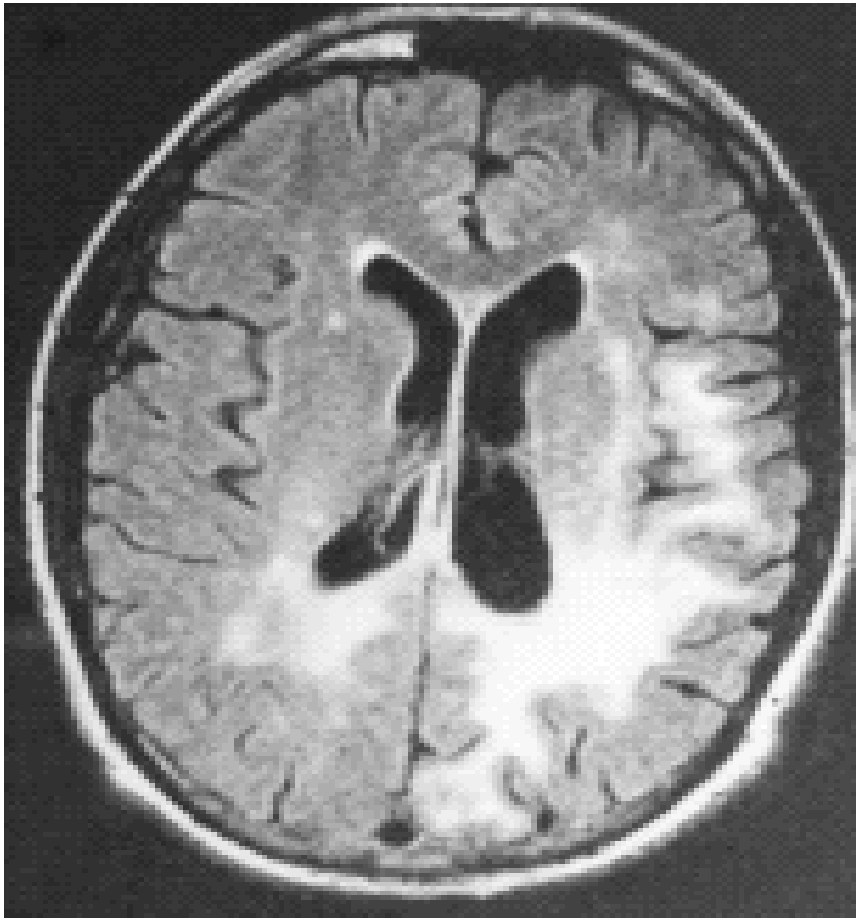
Chronic/Advanced

Novantrone(mitoxantrone)

Stroke and Multiple Sclerosis

- 34 yr old with history of ataxia, ophthalmoplegia and paresthesia of the legs intermittently with a massive weight loss over the past few months.
- His history is significant for HIV and has been on gancyclovir and protease inhibitors and T-cell counts have remained <200.
- His mentation is going quickly and he has no memory and has stopped eating.

- **What is your diagnosis?**



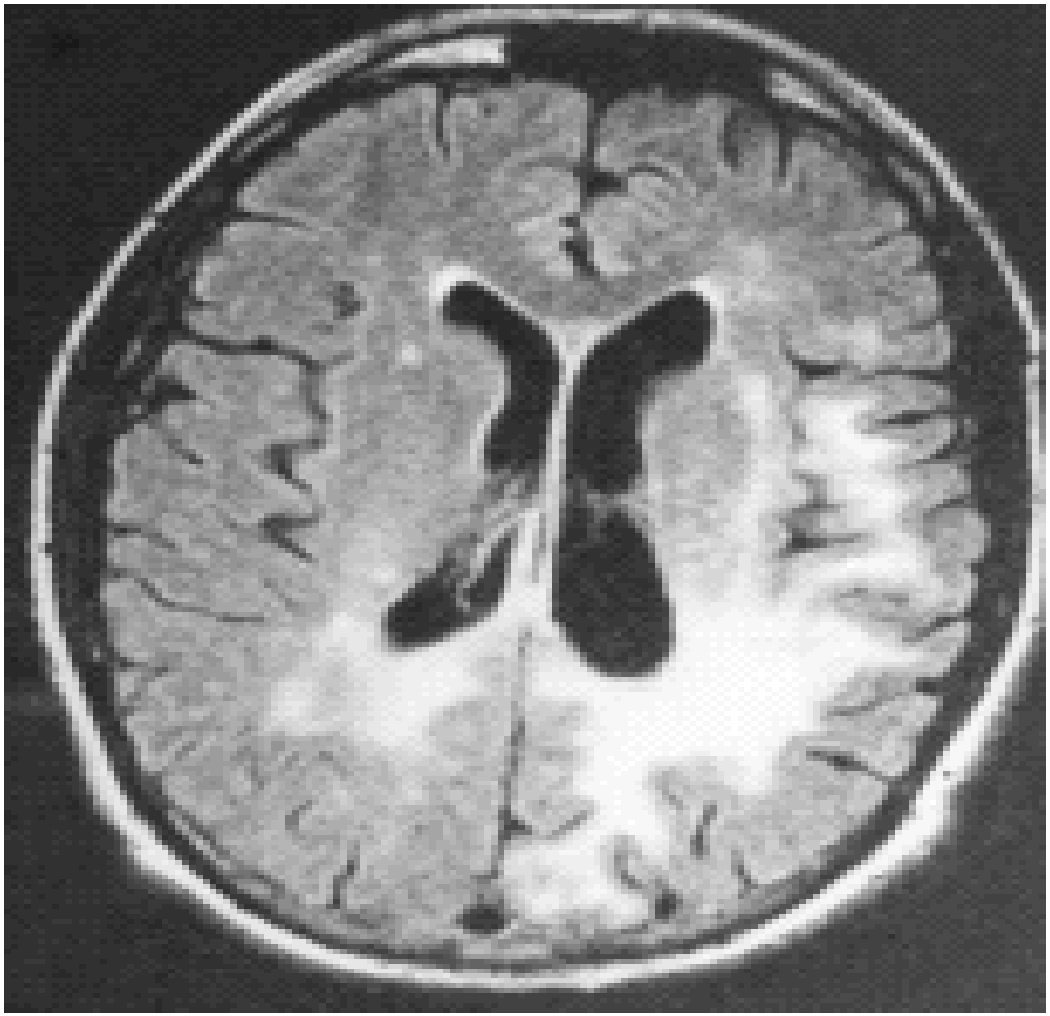
Stroke and Multiple Sclerosis

Answer

PML

Progressive Multifocal Leukencephalopathy

PML is caused by the JC Virus but there are some drugs that can create a reversible leukencephalopathy



Stroke and Multiple Sclerosis

Central Pontine Myelinolysis

Occurs in patients with severe hyponatremia

Their sodium is corrected too aggressively

-Quadraparesis

-Mutism

-Pseudobulbar palsy

-Swallowing dysfunction

Treatment

Correct Na slowly and treat underlying cause