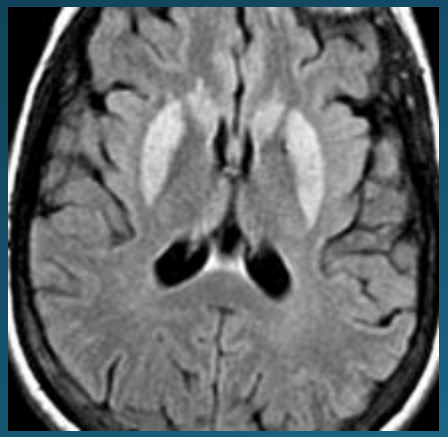
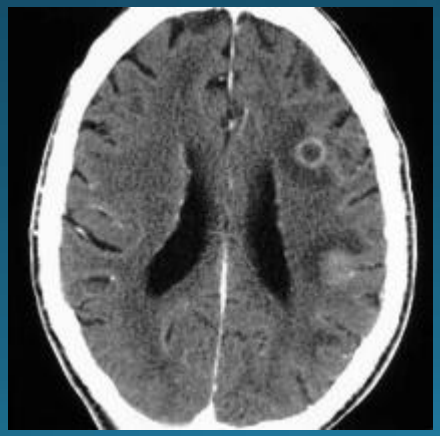
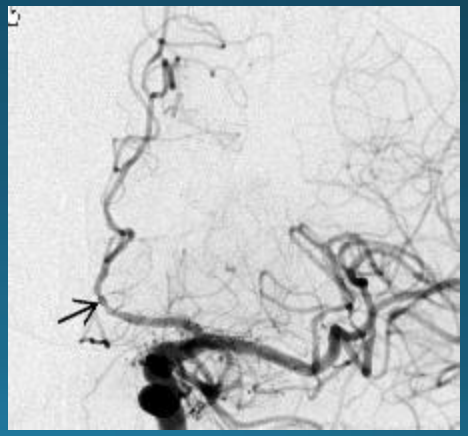
Prion Disease, Toxoplasmosis, and Vasculitis

Jarrod Dale, 9/8/11







Introduction

- CNS Prion Disease
- CNS Toxoplasmosis
- CNS Vasculitis

  - Etiology and Pathology
  - Patient presentation and Demographics
  - Types and Stages of Disease
  - Imaging Findings and DDx
  - Treatment and Prognosis

CNS Prion Disease

- aka: Creutzfeldt-Jakob Disease (CJD), transmissible spongiform encephalopathy
- Rapidly progressing, fatal, potentially transmissible dementing disorder caused by a prion
- Prion = proteinaceous infectious particle devoid of DNA or RNA

CNS Prion Disease

Etiology

- PrPSc = conformationally abnormal isoform of normal host encoded PrPc. It's insoluble and protease resistant
- Once introduced into cells, it starts a vicious self-perpetuating cycle turn normal PrPc into PrPSc

CNS Prion Disease

Pathology

- PcPSc is resistant to certain proteases on western blot
- variable accumulation of PrPSc in tissue
- spongiform encephalopathy with neuronal loss, and vacuolation with replacement gliosis

CNS Prion Disease

4 Types:

1. **sCJD** = spontaneous/somatic mutation of PrPc into PrPSc
2. **fCJD** = mutation in PRNP gene which encodes for abnormal PrPSc
3. **Iatrogenic CJD** = primarilly CNS surgery or human derived hormones (HGH, gonadotropins)
4. **vCJD** = (aka: nvCJD), infected beef

CNS Prion Disease

Clinical Presentation:

- rapidly progressive dementia associated with myoclonic jerks and akinetic mutism
- variable constellation of other neuro symptoms
- No gender preference
- Age: Young in vCJD, >60 for sCJD,
- sCJD all races/places, vCJD almost all in UK
- sCJD (85%), fCJD (15%), Infectious/Iatrogenic (<1%)

CNS Prion Disease

Imaging:

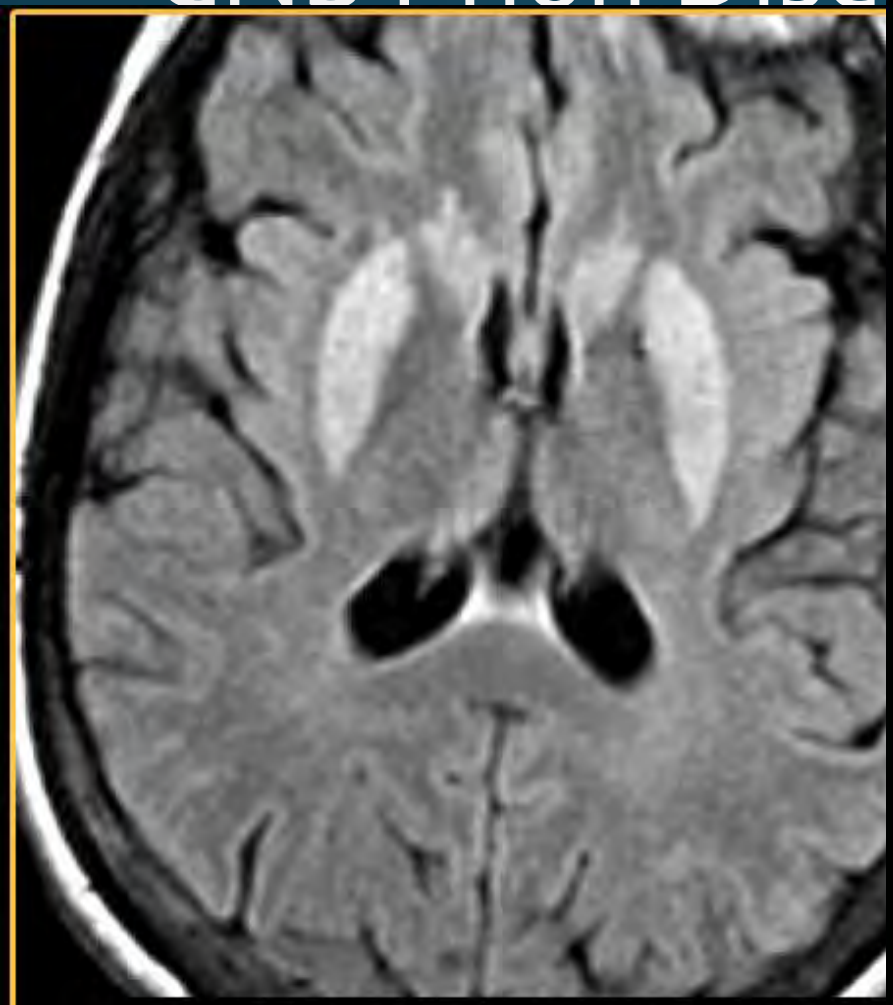
- Best tool = MR with FLAIR and DWI
- Best clue: progressive T2 hyperintensity in the BG, thalamus, and cerebral cortex
- CT has no real role, may show progressive ventriculomegally due to atrophy

CNS Prion Disease

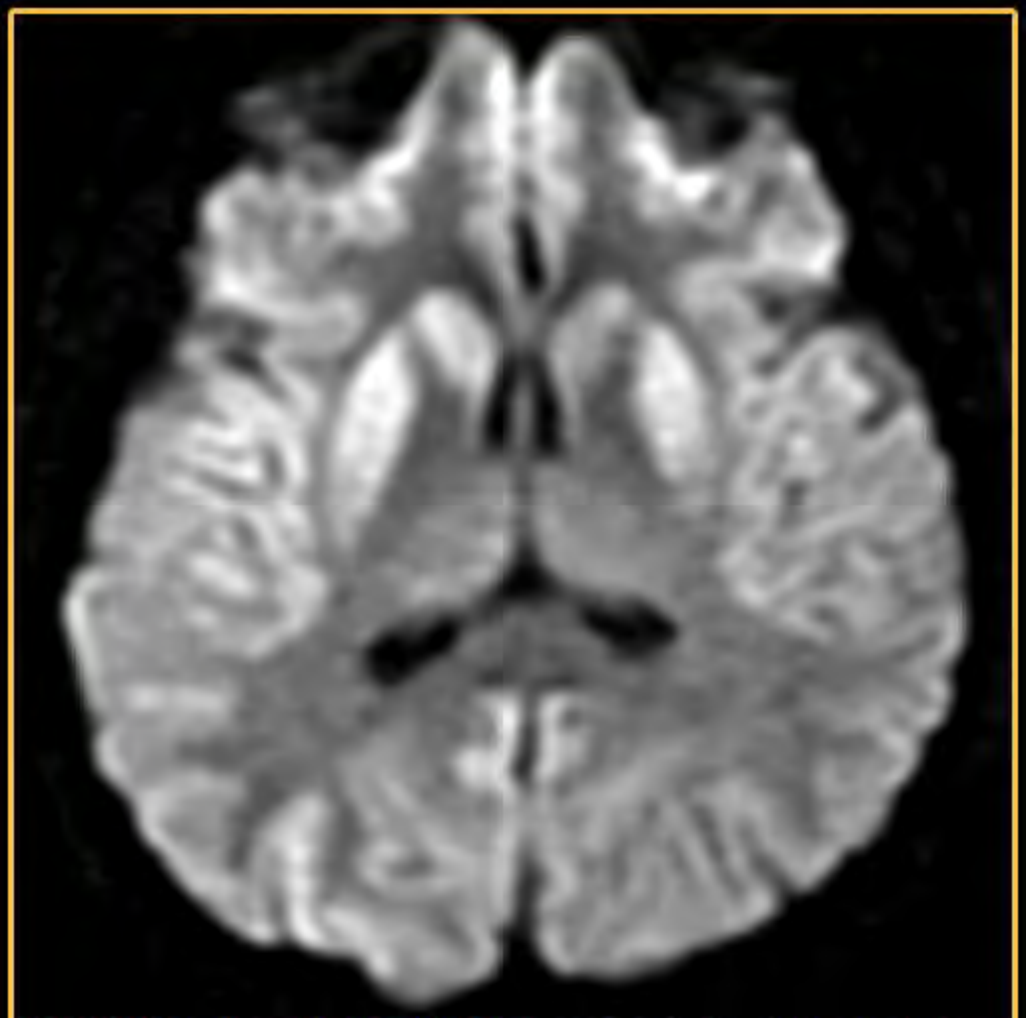
Imaging:

- T2WI/FLAIR/DWI
  - "Pulvinar Sign" = symmetrical hyperintensitiy in the posterior thalamus
  - "Hockey Stick Sign" = symmetrical pulvinar and dorsomedial thalamic hyperintensity
  - Cortical hyperintensity common in sCJD

CNS Prion Disease

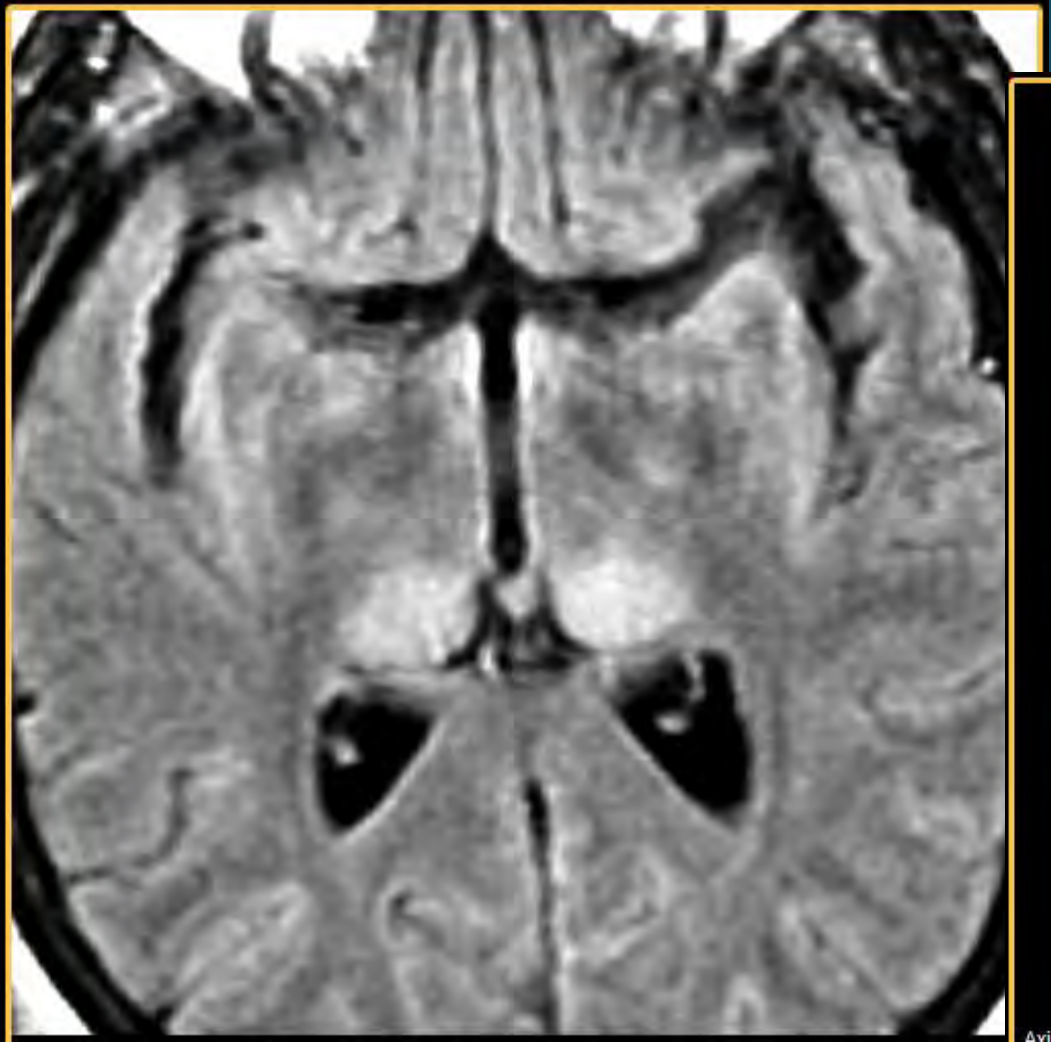


Axial FLAIR MR shows symmetric hyperintensity in the caudate and putamen, characteristic of sporadic CJD (sCJD). sCJD is the most common type of CJD, representing 85% of cases.

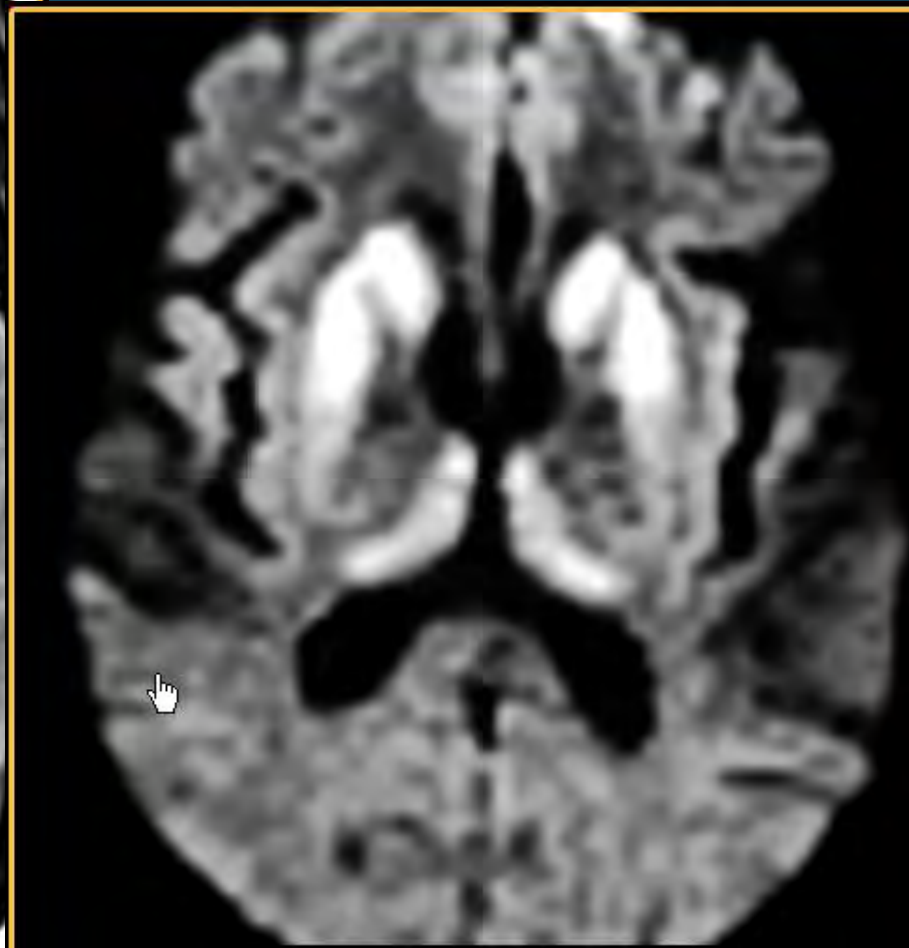


Axial DWI MR shows classic sCJD with diffusion restriction in the caudate and putamen as well as throughout the cortex. Frontal, temporal, and parietal cortical involvement is most common. Relative sparing of the pre- and postcentral gyri is typical of CJD.

CNS Prion Disease



Axial FLAIR MR shows bilateral, symmetric hyperintensities in the posterior thalami representing the "pulvinar" sign, which is characteristic of variant CJD. Another "pulvinar" sign is the T1 shortening seen in Fabry disease.



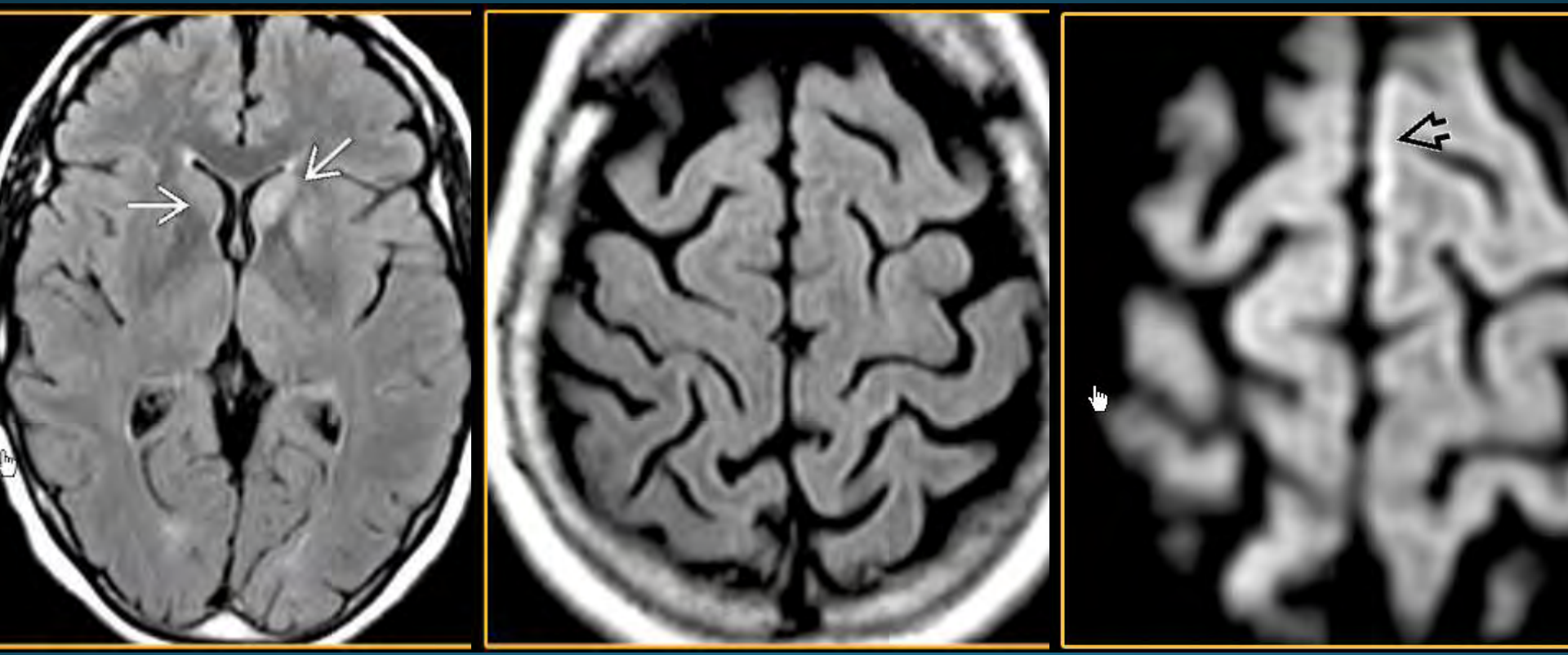
Axial DWI MR shows symmetric hyperintensity in the basal ganglia and thalami bilateral The thalamic involvement shows the "hockey stick" sign, which is symmetric pulvinar ar dorsomedial thalamus hyperintensity. This sign is most commonly seen in variant CJD but may also be present in sCJD, as in this case.

CNS Prion Disease

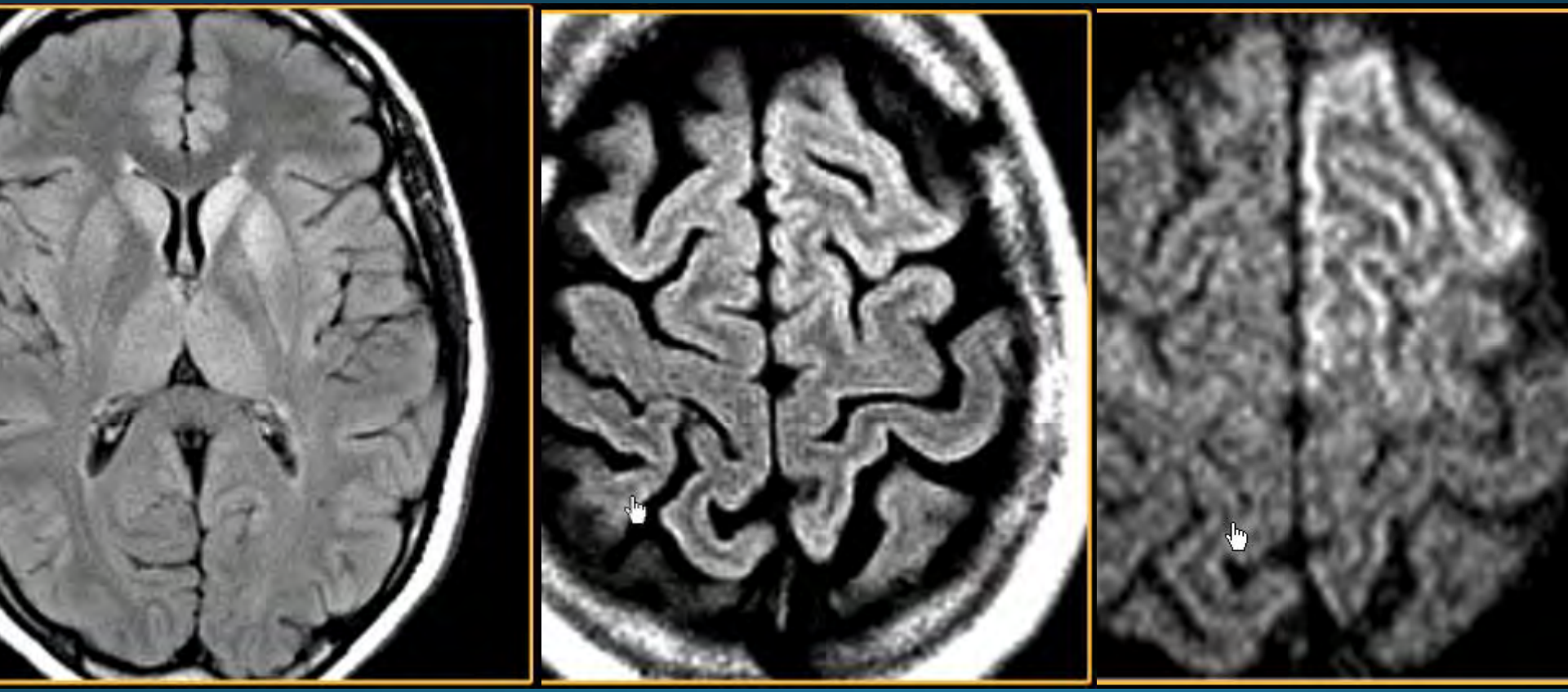
Imaging Pearls:

- DWI signal may disappear late in the disease
- No contrast enhancement
- Lack of basal ganglia findings doesn't exclude CJD if high clinical suspicion

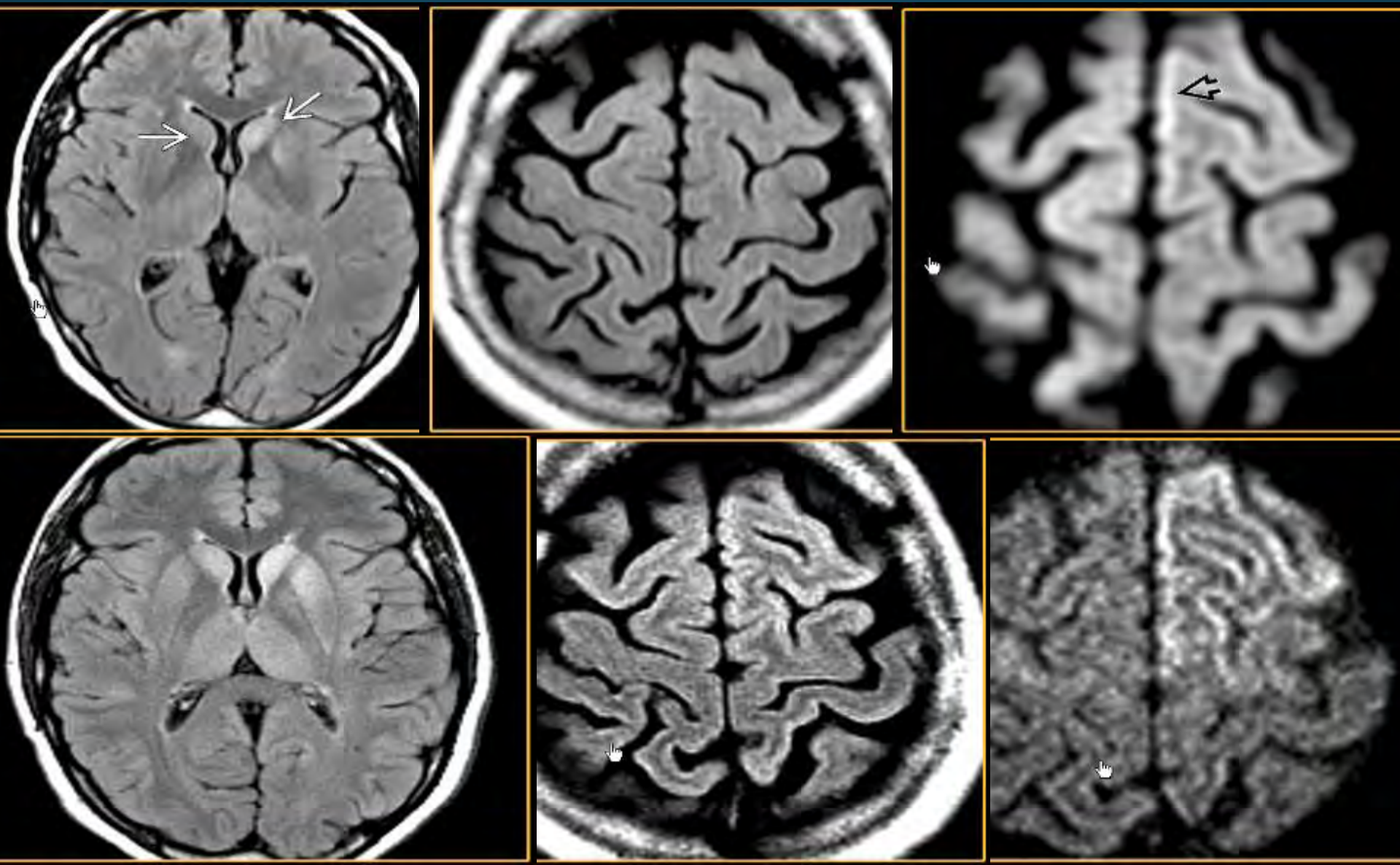
CNS Prion Disease



CNS Prion Disease



CNS Prion Disease



CNS Prion Disease

What about Nuc Med?

- Regional hypometabolism on PET correlates with lesions
- SPECT shows decreased uptake of various tracers and decreased absolute values of rCBF
  - can be asymmetrical
  - sensitive for early CJD

CNS Prion Disease

What about Nuc Med?

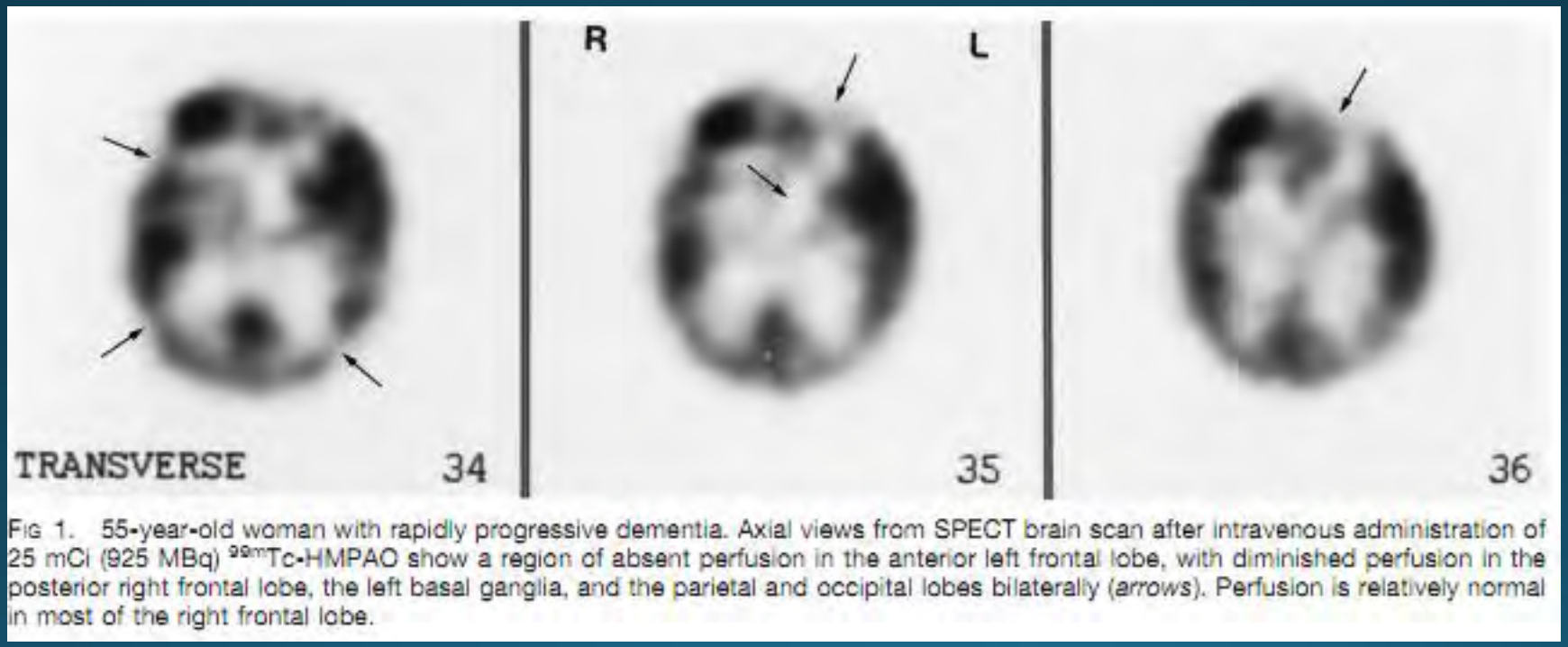


FIG 1. 55-year-old woman with rapidly progressive dementia. Axial views from SPECT brain scan after intravenous administration of 25 mCi (925 MBq) ^{99m}Tc-HMPAO show a region of absent perfusion in the anterior left frontal lobe, with diminished perfusion in the posterior right frontal lobe, the left basal ganglia, and the parietal and occipital lobes bilaterally (*arrows*). Perfusion is relatively normal in most of the right frontal lobe.

AJNR Am J Neuroradiol 19:454 –455, March 1998

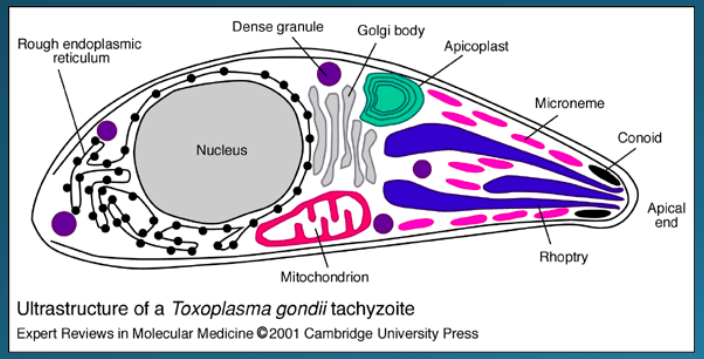
CNS Prion Disease

Treatment and Prognosis

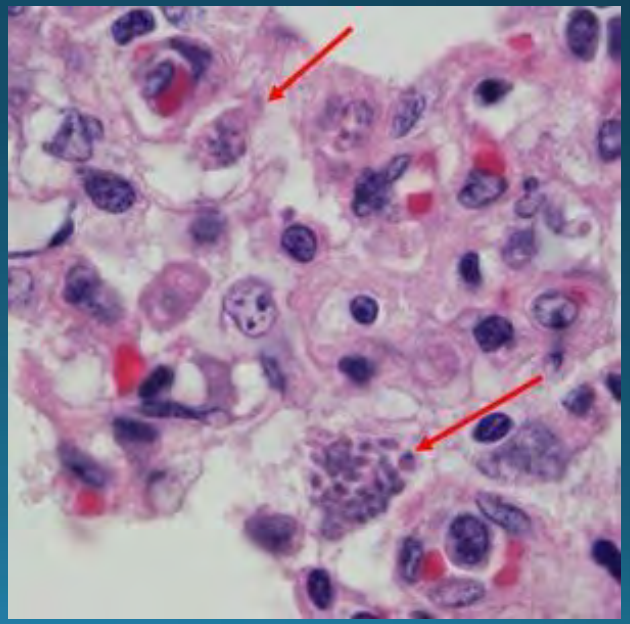
- **long incubation, but once symptoms start they are relentless, death usually within months**
- **Mean survival of sCJD = 8mos, vCJD = 16mos,** fCJD = 26mos
- **No effective treatment**

CNS Toxoplasmosis

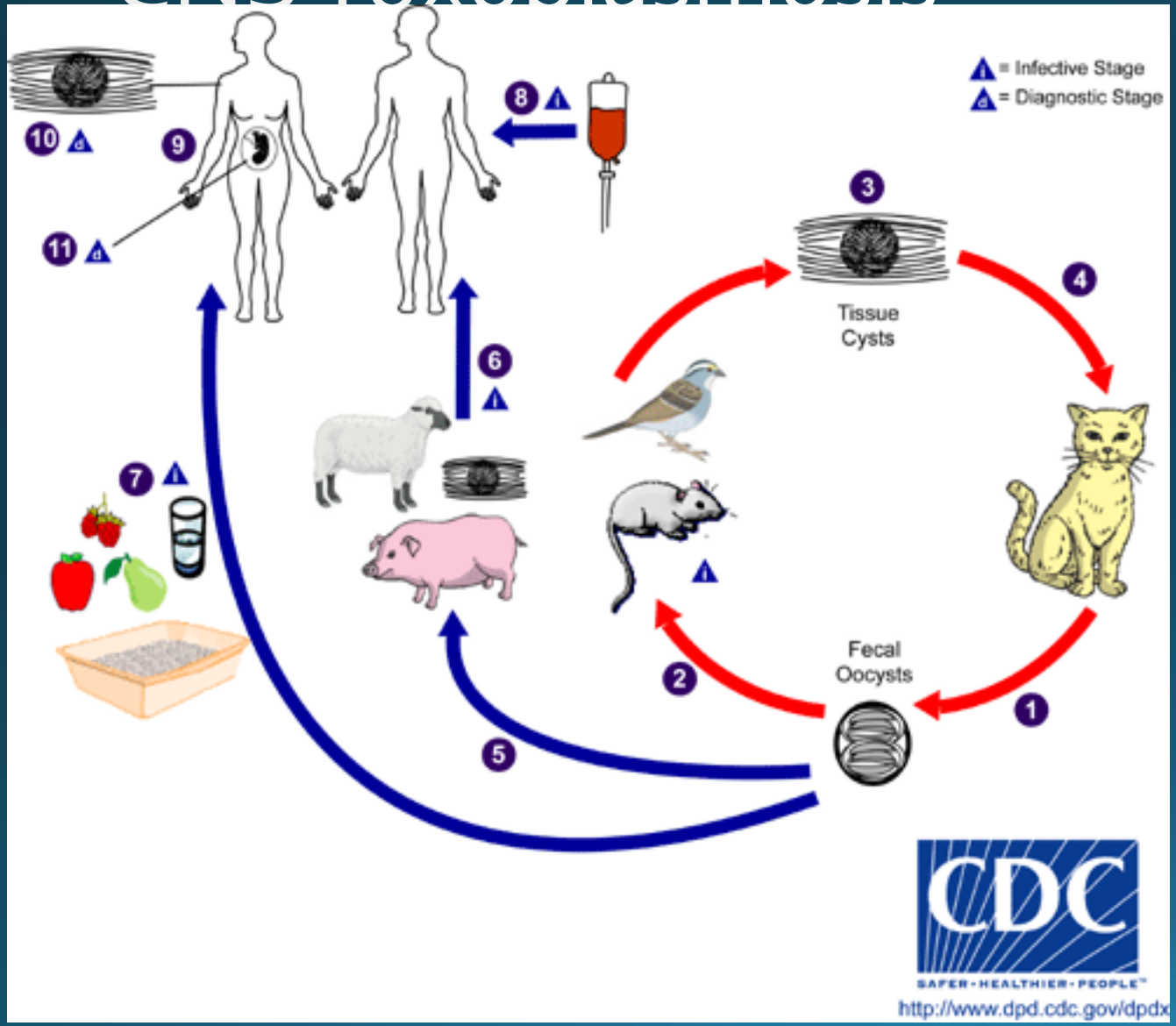
- *Toxoplasma gondii* = unicellular spore-forming protozoa
- 2 main forms: congenital or acquired
- Can be limited to the CNS or generalized

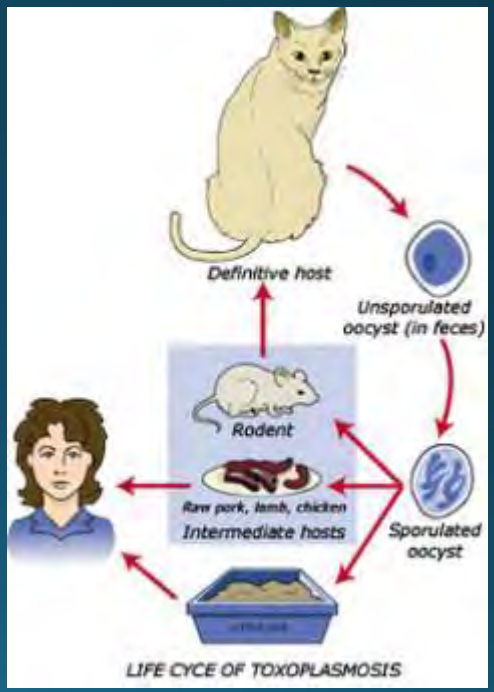


Ultrastructure of a *Toxoplasma gondii* tachyzoite



CNS Toxoplasmosis





CNS Toxoplasmosis

Congenital Toxoplasmosis

- **the "T" in TORCH**

- **transplacental infection only during "new" infections or if immunocompromised**
  - **most moms have circulating antibodies which protect the fetus**

- **the earlier in the gestation, the worse prognosis**

CNS Toxoplasmosis

Congenital Toxoplasmosis: Presentation

- **commonly diagnosed during pregnancy with labs and US**
- **newborn presents with seizures, chorioretinitis and hydrocephalus**
- **Hydrocephalus (and eventually encephalomalcia) due to ependymitis and obstruction of the aqueduct**

CNS Toxoplasmosis

Congenital Toxoplasmosis: Imaging

- multifocal, non-shadowing calcifications involving the basal ganglia, PVWM and cortex
- there can be large areas of parenchymal destruction
- Best first test is ultrasound

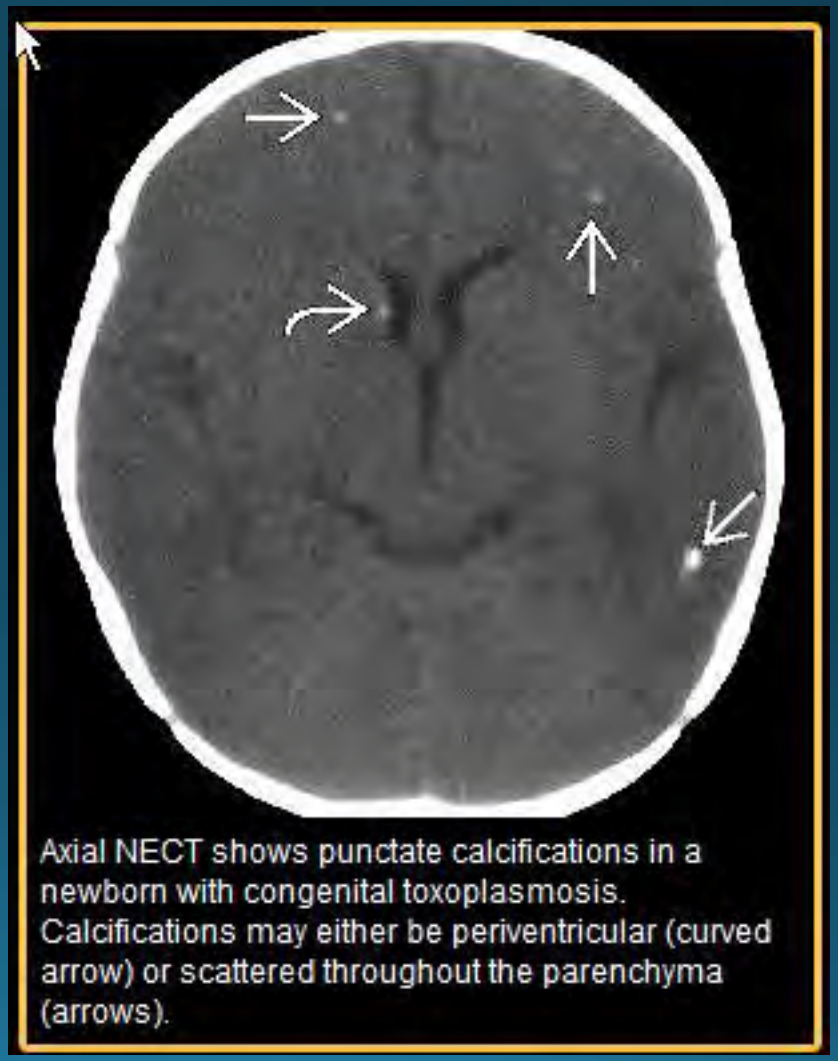
CNS Toxoplasmosis

Congenital Toxoplasmosis: Imaging

- **Protocol Recommendation:**
  - **monthly US to look for Ca and asses fetal growth (IUGR is common)**
  - **Fetal MRI to evaluate the brain**
  - **confirm infection with reference lab and amnio/cord blood viral PCR (to eval for other TORCH viruses)**

CNS Toxoplasmosis

Axial oblique ultrasound shows periventricular and intraparenchymal calcifications typically seen in congenital toxoplasmosis (arrows).

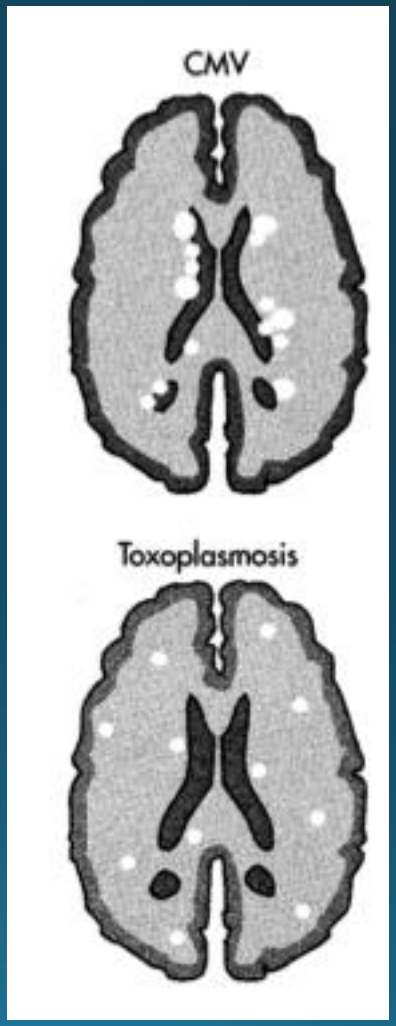


Axial NECT shows punctate calcifications in a newborn with congenital toxoplasmosis. Calcifications may either be periventricular (curved arrow) or scattered throughout the parenchyma (arrows).

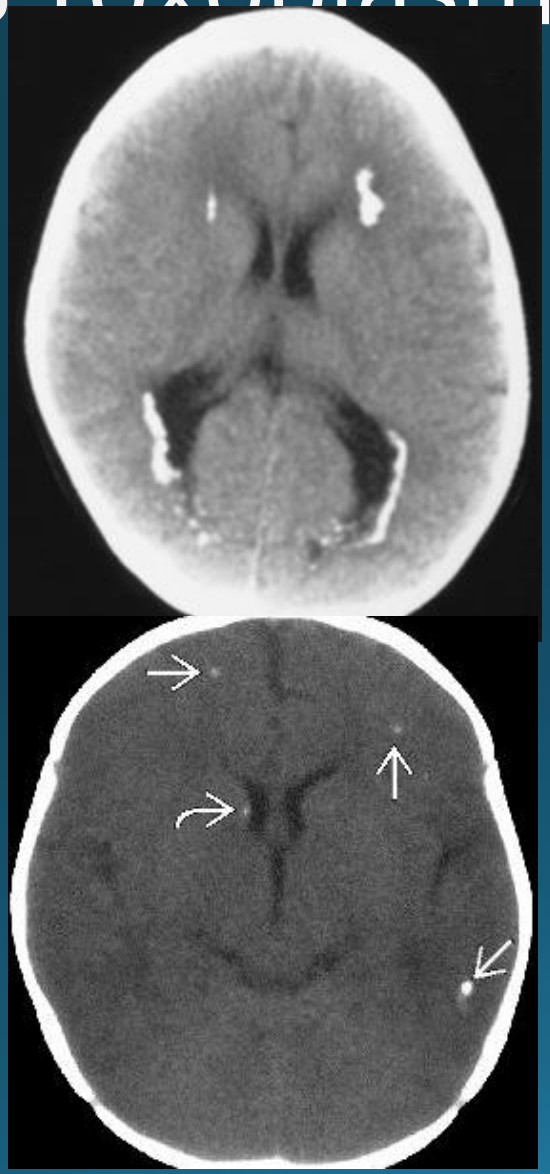
CNS Toxoplasmosis

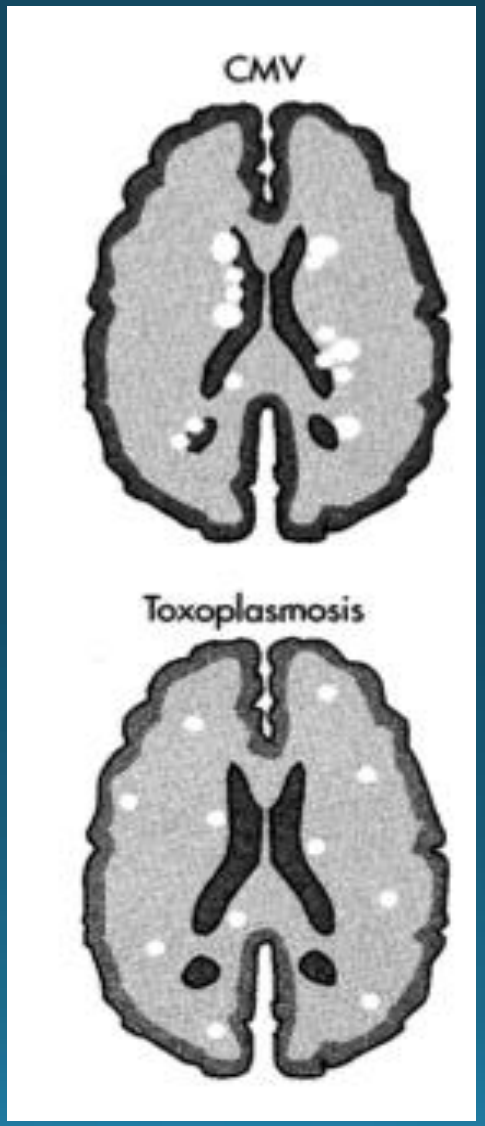
DDx in a fetus/neonate:

1. **Toxoplasmosis**
2. **CMV**



CNS Toxoplasmosis





CNS Toxoplasmosis

Congenital Toxoplasmosis:

- **1st trimester infection is rare, but more severe**
- **Infection at >20 weeks has higher likelihood of affecting the fetus but less severe**

- **blindness, epilepsy, mental retardation, if no brain abnormalities = better prognosis**

- **Rx = termination or folate synthesis inhibitors (pyrimethamine/sulfadiazine or sulfadioxine), which can cause severe pancytopenia.**

CNS Toxoplasmosis

Acquired Toxoplasmosis:

- **opportunistic infection**
- **most common CNS infection in AIDS pts**
- **usually a reactivation of a latent infection**
  - **20-70% of USA population is seropositive**

CNS Toxoplasmosis

Acquired Toxoplasmosis:

- **pts present with fever, malaise, headache**
  - **eventually develop personality changes or seizures**

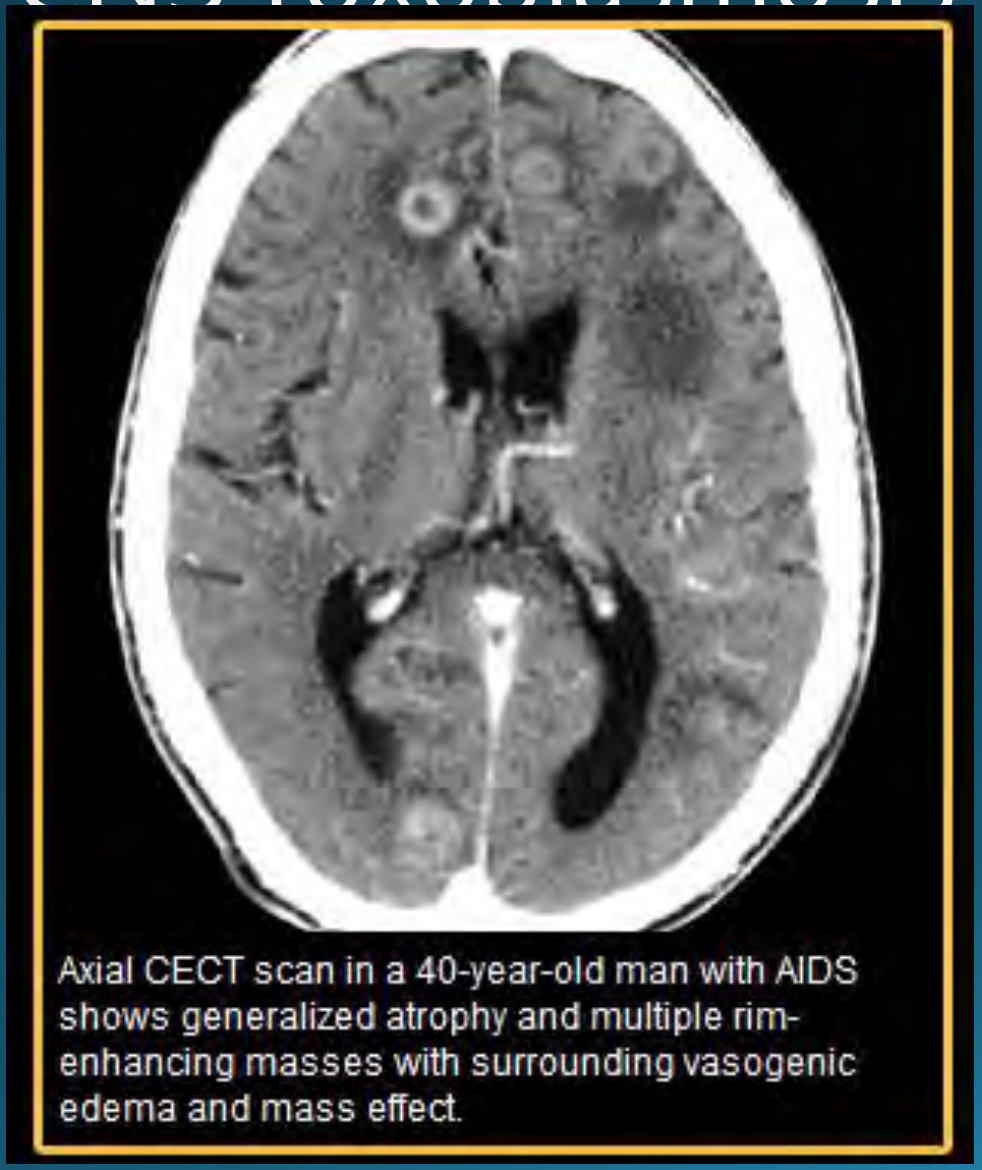
- **aka: Toxoplasmosis encephalitis (TE)**

CNS Toxoplasmosis

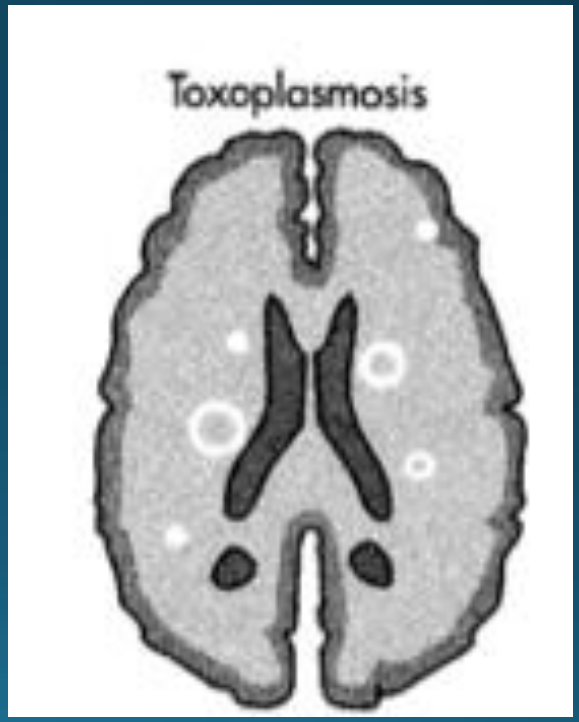
Acquired Toxoplasmosis: Imaging

- CT
  - ill-defined hyperdense lesions with edema
  - involves the BG, CMJxn, Thalamus, Cerebellum
  - Rim, nodular or targetoid enhancement
- MR
  - T2 hypOintense
  - T1 C+ "target" sign is highly suggestive

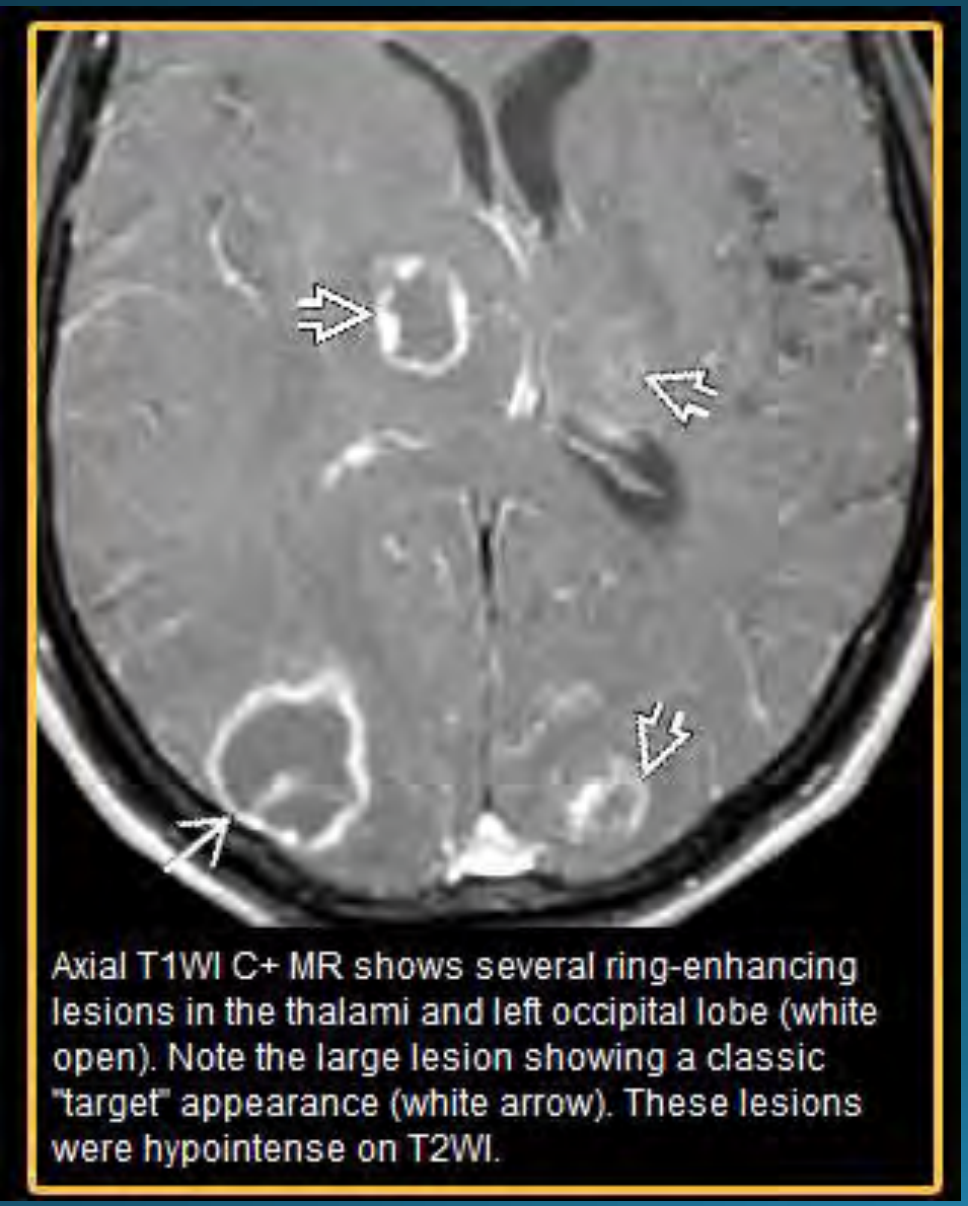
CNS Toxoplasmosis



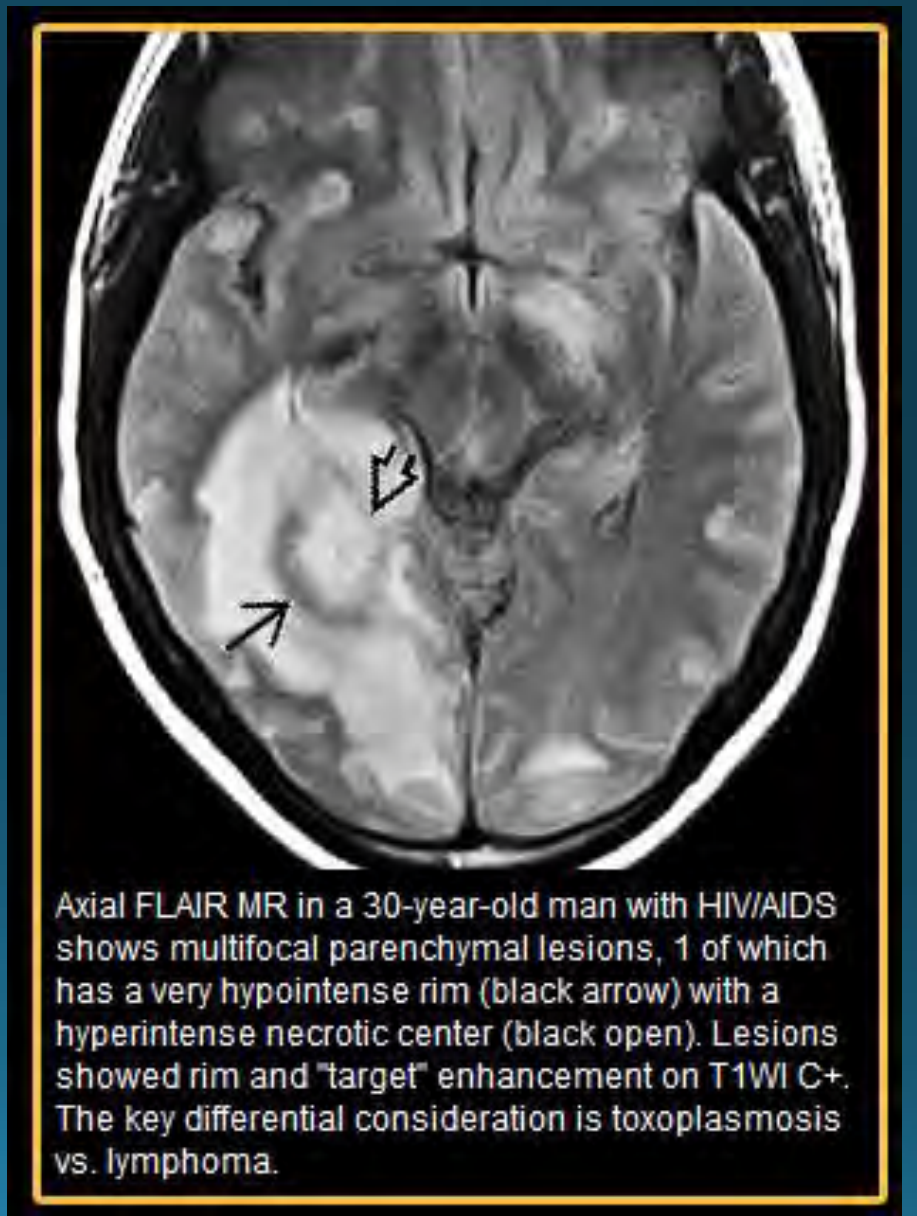
Axial CECT scan in a 40-year-old man with AIDS shows generalized atrophy and multiple rim-enhancing masses with surrounding vasogenic edema and mass effect.



CNS Toxoplasmosis



Axial T1WI C+ MR shows several ring-enhancing lesions in the thalami and left occipital lobe (white open). Note the large lesion showing a classic "target" appearance (white arrow). These lesions were hypointense on T2WI.

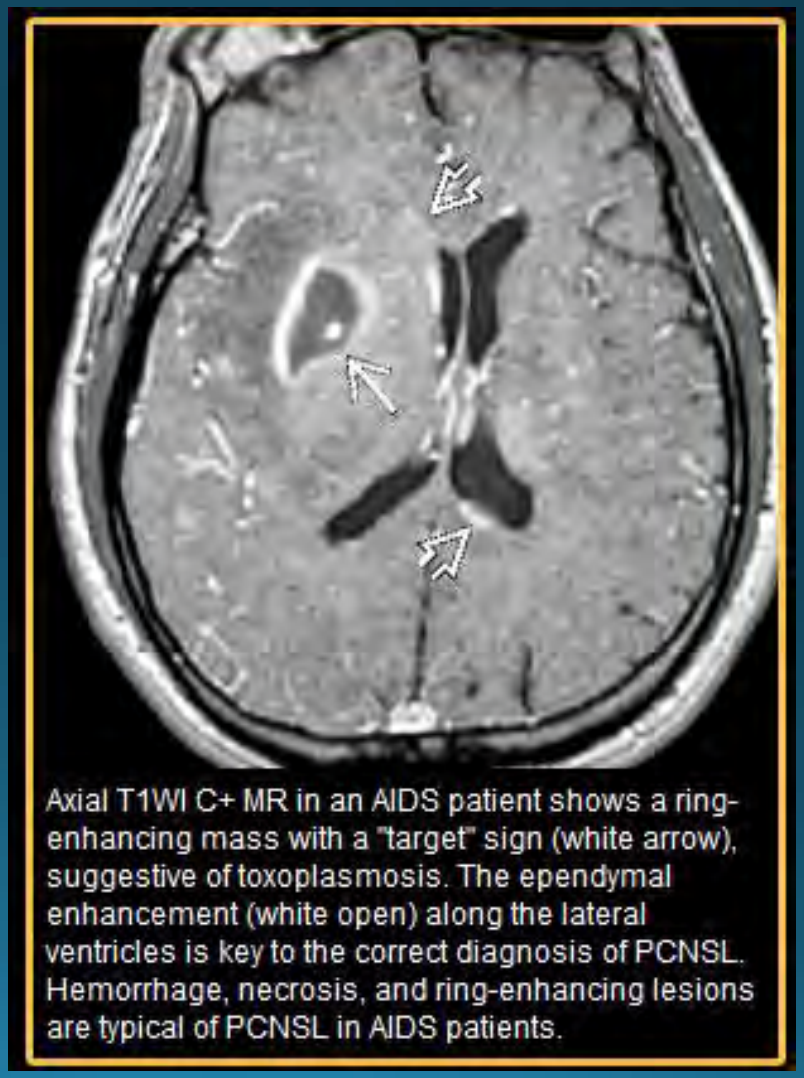


Axial FLAIR MR in a 30-year-old man with HIV/AIDS shows multifocal parenchymal lesions, 1 of which has a very hypointense rim (black arrow) with a hyperintense necrotic center (black open). Lesions showed rim and "target" enhancement on T1WI C+. The key differential consideration is toxoplasmosis vs. lymphoma.

CNS Toxoplasmosis

Toxoplasmosis vs CNS Lymphoma

Axial CECT shows extensive ependymal enhancement (white arrow) along the frontal horns of the lateral and 3rd ventricles. An additional frontal mass is present (white open) in this immunocompromised teen with PCNSL.



Axial T1WI C+ MR in an AIDS patient shows a ring-enhancing mass with a "target" sign (white arrow), suggestive of toxoplasmosis. The ependymal enhancement (white open) along the lateral ventricles is key to the correct diagnosis of PCNSL. Hemorrhage, necrosis, and ring-enhancing lesions are typical of PCNSL in AIDS patients.

CNS Toxoplasmosis

- **DDx = Primary CNS lymphoma**
- **TE lesions should resolve in 2-4 weeks**
- **Know whether treatment has been given, if poor response, suggest lymphoma**
- **PEARL:**

  Multiple "target" lesions on T1WI C+ that are dark on T2WI

CNS Vasculitis

- **Vasculitis = inflamatory changes in arterial walls**
- **Important to diagnose because they are potentially treatable**
- **There are dozens of different etiologies**

CNS Vasculitis

Examples of Potential Etiologies:

Infectious	Systemic	Granulomatous	Drug-related
Bacterial	Polyarteritis Nodosa	Sarcoidosis	Cocaine
Viral	Giant Cell/Temporal Arteritis	Wegener's	Amphetamines
Fungal	Takayasu's	Granulomatous angitis	Ergots
TB	Kawasaki's		Heroine
Syphilis	Behcet's Disease		
HIV-related	CVDs		
	Serum Sickness/Allergic		

CNS Vasculitis

Examples of Potential Etiologies:

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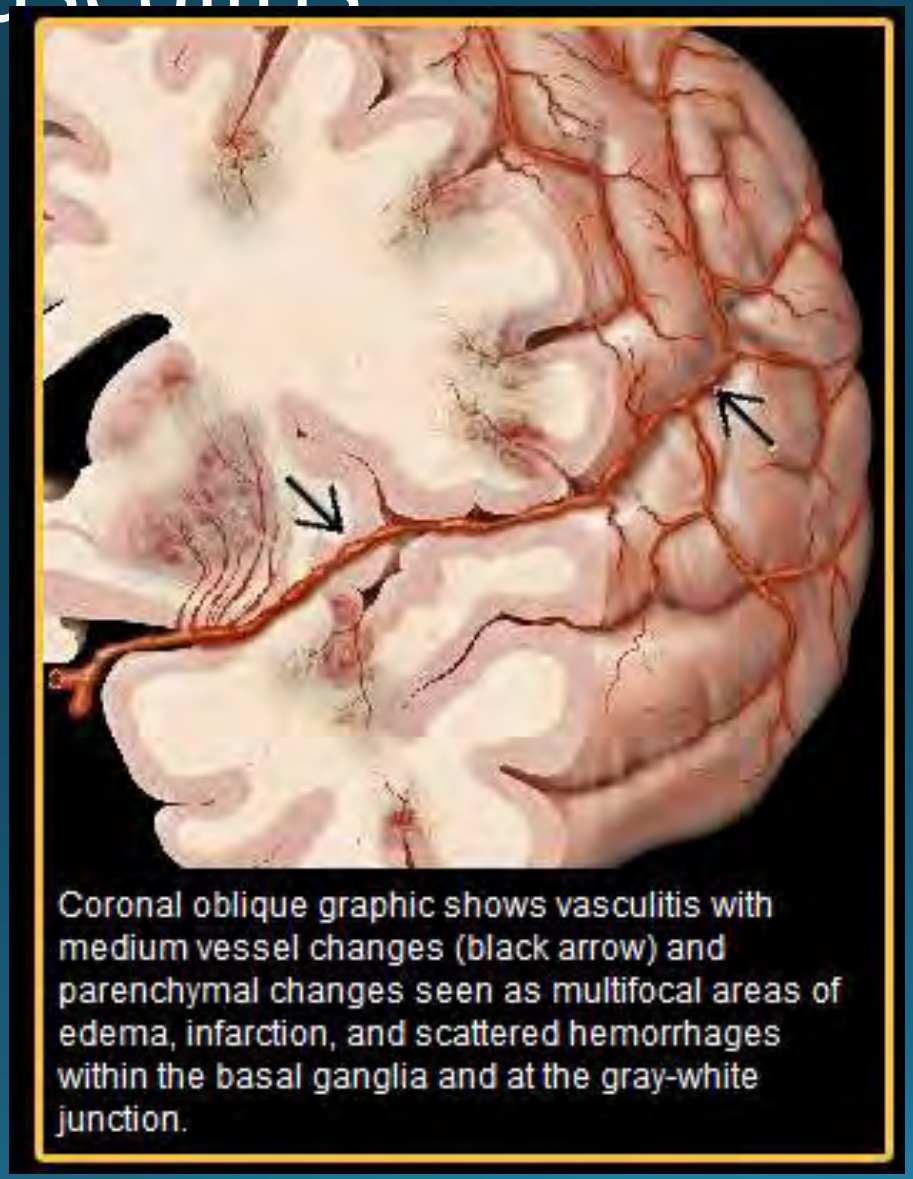
TB	Kawasaki's		Heroin
Syphilis	Behcet's Disease		
HIV related	CVDs		
	Serum Sickness/Allergic		

NOTE: This list is almost useless, the potential causes of vasculitis are too many to list on one slide

CNS Vasculitis

- **Evaluation with angiography, conventional or CTA/MRA**
- **look for irregular narrowing/stenosis of the vessels and secondary signs such as hemorrhage or aneurysms**
- **may need to biopsy depending on the clinical presentation**

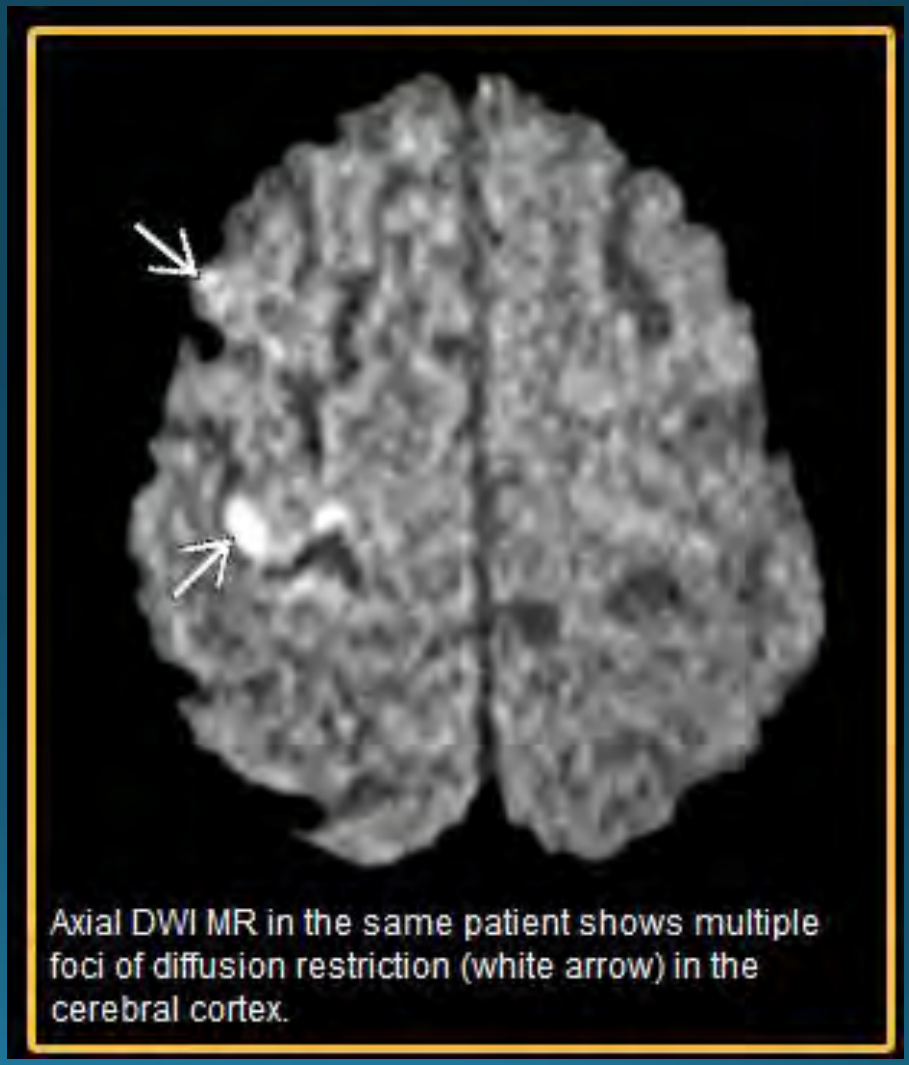
CNS Vasculitis



Coronal oblique graphic shows vasculitis with medium vessel changes (black arrow) and parenchymal changes seen as multifocal areas of edema, infarction, and scattered hemorrhages within the basal ganglia and at the gray-white junction.

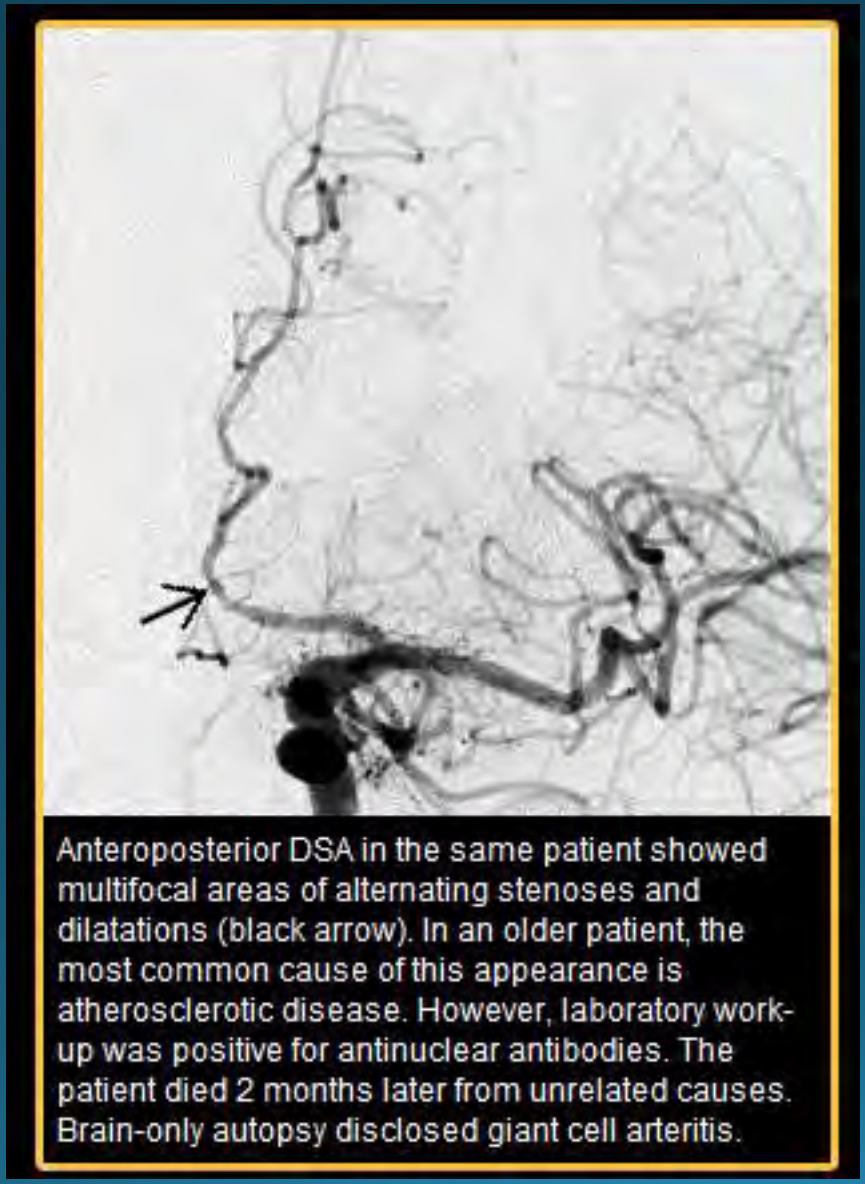
CNS Vasculitis

Axial FLAIR MR in a 71-year-old patient with TIA-like symptoms shows multifocal peripherally located hyperintensities (white arrow). Other scans (not shown) demonstrated similar lesions in the cortex and pons.



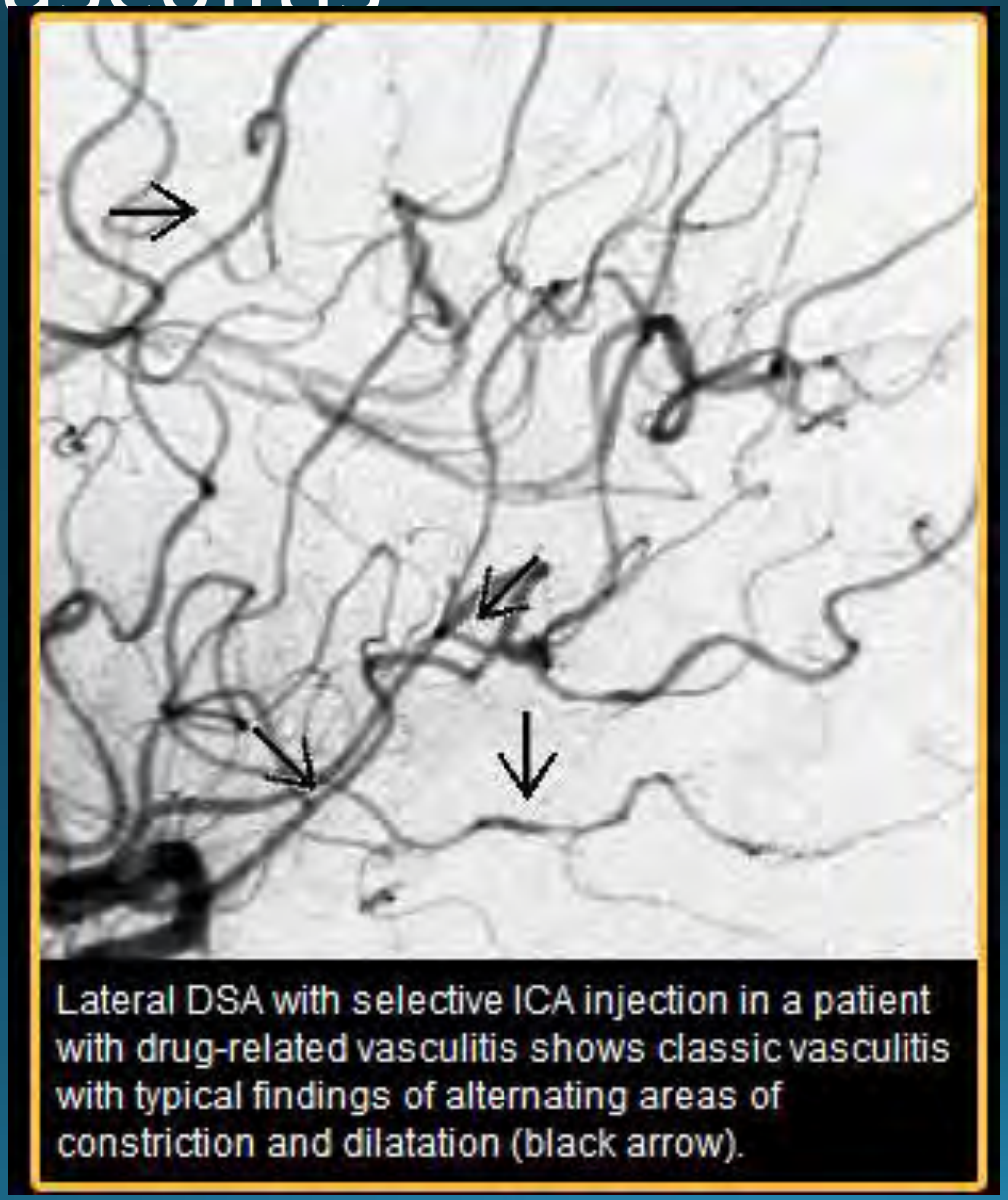
Axial DWI MR in the same patient shows multiple foci of diffusion restriction (white arrow) in the cerebral cortex.

CNS Vasculitis



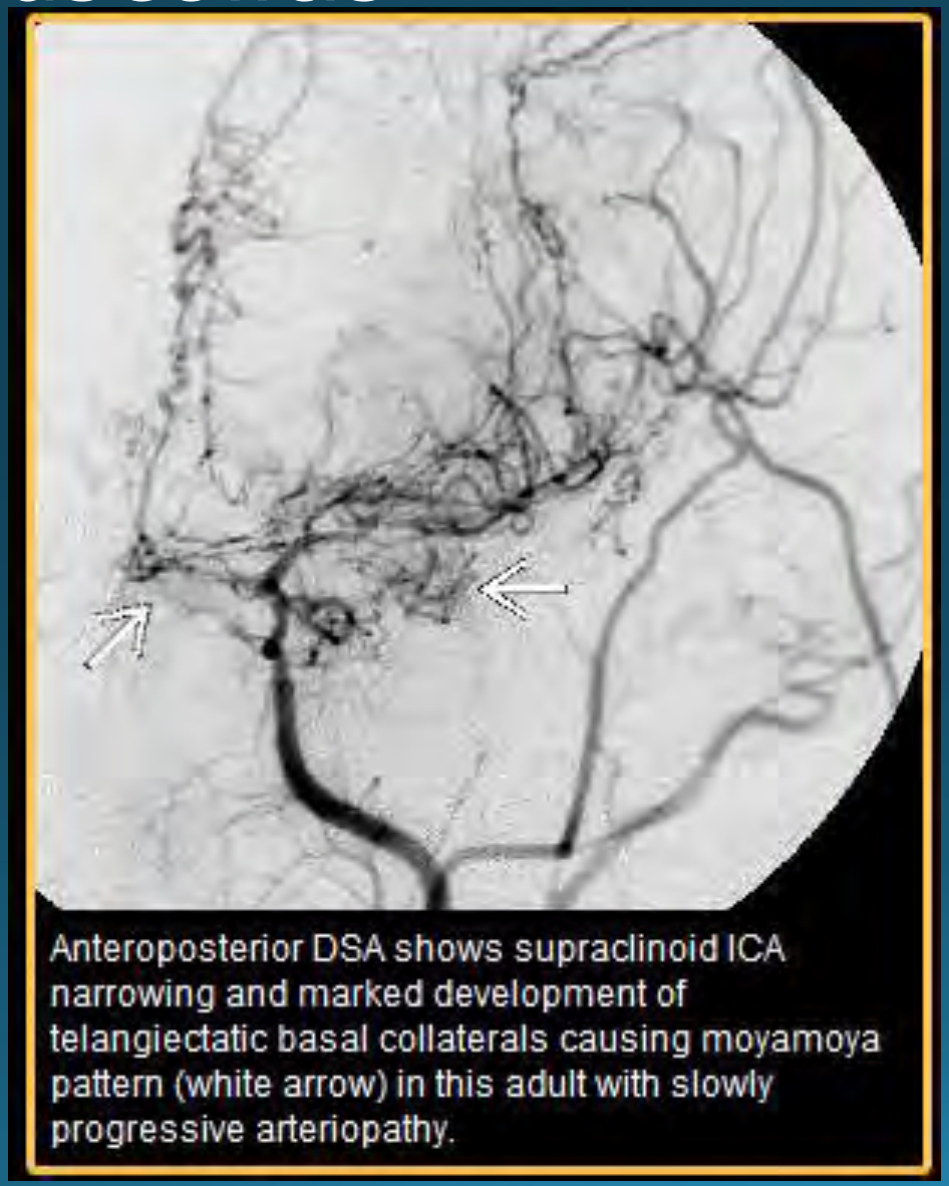
Anteroposterior DSA in the same patient showed multifocal areas of alternating stenoses and dilatations (black arrow). In an older patient, the most common cause of this appearance is atherosclerotic disease. However, laboratory work-up was positive for antinuclear antibodies. The patient died 2 months later from unrelated causes. Brain-only autopsy disclosed giant cell arteritis.

CNS Vasculitis



Lateral DSA with selective ICA injection in a patient with drug-related vasculitis shows classic vasculitis with typical findings of alternating areas of constriction and dilatation (black arrow).

CNS Vasculitis



Anteroposterior DSA shows supraclinoid ICA narrowing and marked development of telangiectatic basal collaterals causing moyamoya pattern (white arrow) in this adult with slowly progressive arteriopathy.

CNS Vasculitis

- **PEARL:**
  Multiple vascular territories producing an atypical pattern in various stages.

- **Most common "vasculitic" pattern on angio is atherosclerosis**

- **Most imaging findings are non-specific**
- **If you are thinking vasculitis, get a tox screen, LP, imaging and angiography.**
- **ONLY biopsy allows for definite diagnosis**

Thank you STATDx

- **CDC website**
- **Radiology Primer**