



Andres Deik, MD  
Assistant Professor of Clinical Neurology  
University of Pennsylvania

# MOVEMENT DISORDERS AND CNS INFECTION/INFLAMMATION

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# Outline

- CNS infections causing movement disorders
  - Viral infections
    - HIV/JC
    - West Nile virus
    - Viral parkinsonism
  - Bacterial infections
    - Whipple's disease
  - Parasitic infections
    - Toxoplasmosis
    - Cysticercosis
  - Prion diseases
    - CJD
- CNS inflammation causing movement disorders
  - Tremor in multiple sclerosis
  - Autoimmune ataxias
  - Autoimmune chorea
  - LGI1 encephalitis
  - Anti-NMDARAb encephalitis
  - Anti-GAD syndromes
  - Post-infectious movement disorders
    - Sydenham's chorea
    - Post infectious ataxia
    - Post encephalitic parkinsonism



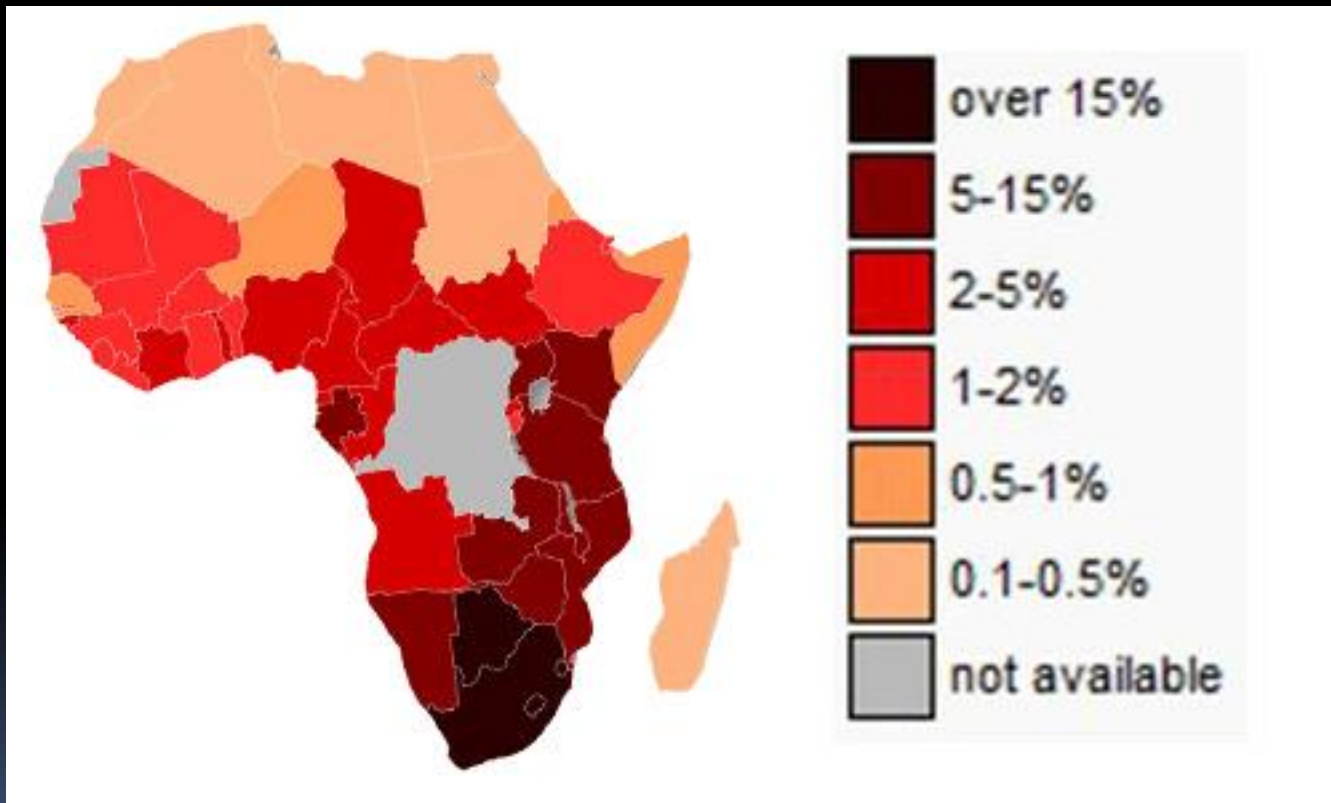
# Viral CNS infections



# HIV-related movement disorders

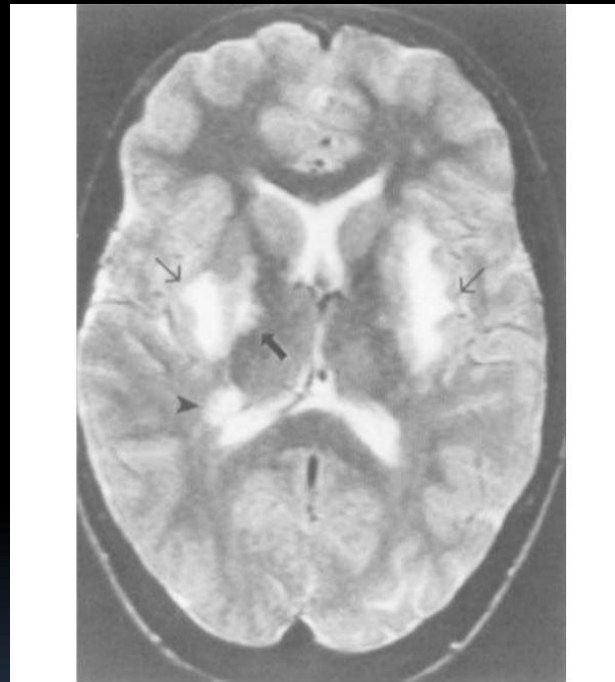
- 3% of HIV+ patients
- ~50% AIDS develop tremor or parkinsonism
- Mechanisms:
  - Opportunistic infections
  - Direct effect of HIV virus
  - Use of dopamine blockers
- Different movements have been described:
  - Hemichorea-hemiballism
  - Dystonia
  - Chorea
  - Myoclonus
  - Tics
  - Paroxysmal dyskinesias
  - Parkinsonism

# HIV demographics in Africa



# Akinetic-rigid syndrome in HIV-related PML

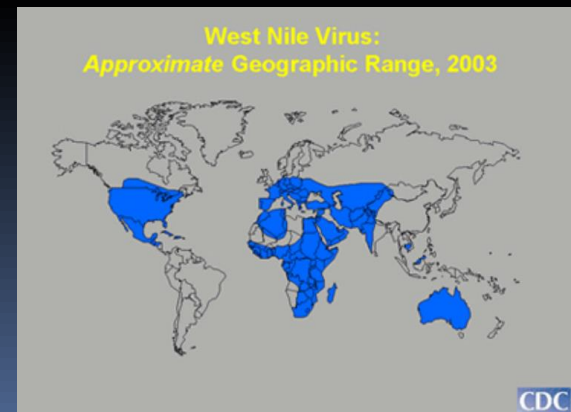
- JC virus (DNA polyomavirus)
- Present worldwide
- Asymptomatic infection in childhood
- Reactivates when immunosuppressed
- Tropism for oligodendrocytes



Progressive multifocal leukoencephalopathy involving the basal ganglia and deep white matter. The T2-weighted images demonstrate bilateral hyperintense lesions in the basal ganglia and external capsules (thin arrows), as well as involvement in the right internal capsule (thick arrow) and para-atrial white matter (arrowhead).

# WNV encephalitis causing opsoclonus-myoclonus

- Opsoclonus-myoclonus
  - 1:10,000,000/year
  - 2-3% of children with neuroblastoma
- Other causes of OM:
  - Celiac disease
  - Breast/Small Cell CA
  - Anti-Ri
- Treatment
  - Steroids
  - IVIG
  - Rituximab



# Viral parkinsonism

Virus	Family	Species
DNA	Herpesviridae	Herpes simplex virus
		Epstein-Barr virus
		Cytomegalovirus (CMV)
		Varicella zoster virus (VZV)
RNA	Bornaviridae	Borna disease virus
	Orthomyxoviridae	Influenza virus Type A
	Paramyxoviridae	Measles
	Picornaviridae	Coxsackie virus
		Echo virus
		Polio Virus
	Retroviridae	Human Immunodeficiency Virus (HIV)
	Flaviviridae	West Nile virus
		Japanese encephalitis B virus
		St. Louis Virus



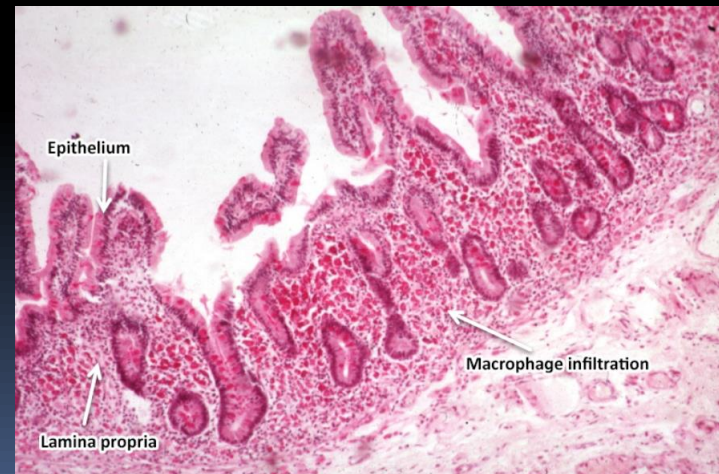


# Bacterial CNS infections



# Whipple's Disease

- *Tropheryma whippelii*
- Symptoms:
  - GI: arthralgias, weight loss, abdominal pain and diarrhea.
  - Neurologic: cognitive impairment, supranuclear gaze palsy, ataxia, *oculomasticatory myorhythmia*.
- Diagnosis: Duodenal biopsy.





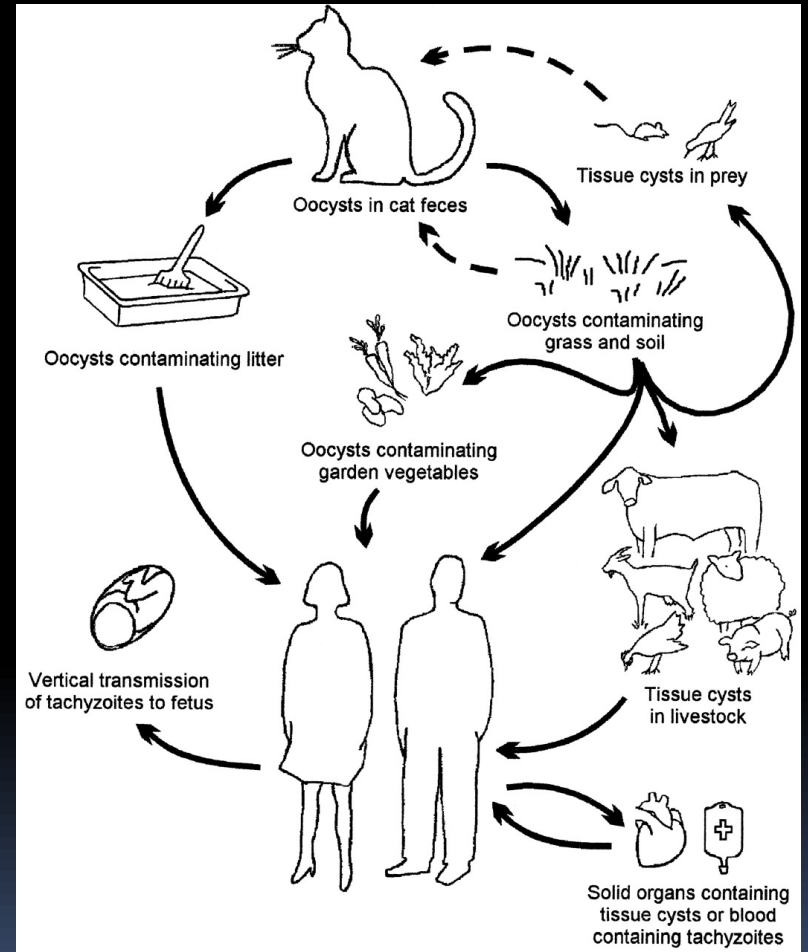
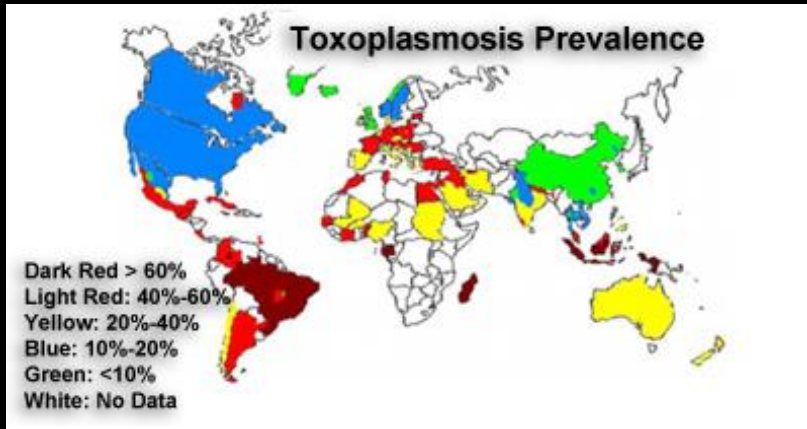
# Parasitic CNS infections



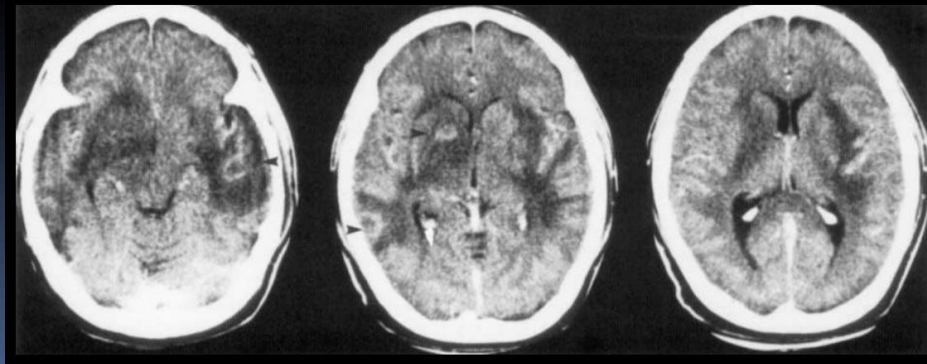
# CNS Toxoplasmosis

- Presenting symptoms
  - Fever
  - Headache
  - Altered mental status
  - Focal neurologic complaints or seizures
- Supporting laboratory findings
  - Toxoplasma antibodies
  - CD4 counts <100 cells/microL
- Typical CNS lesions are ring-enhancing at
  - Parietal or frontal lobes
  - Thalamus
  - Basal ganglia\*
  - Corticomedullary junction
- CNS lymphoma is main differential diagnosis

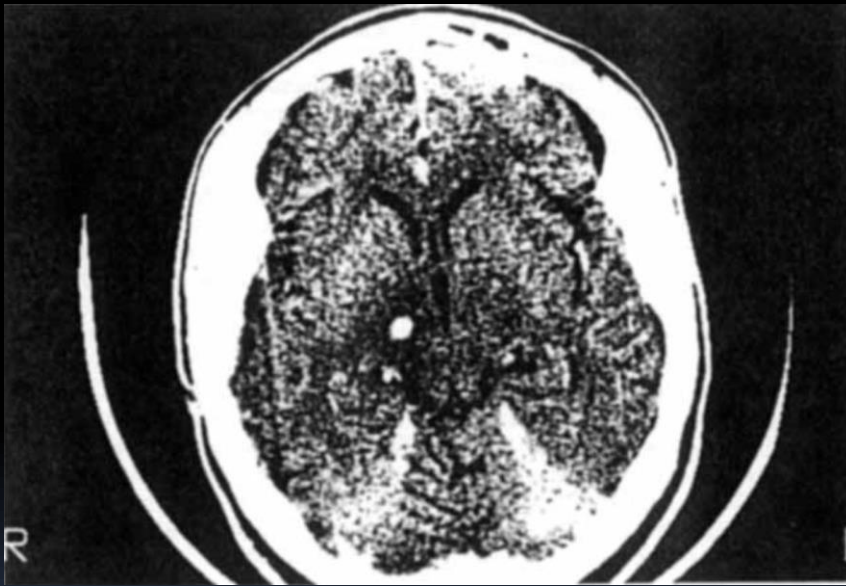
# CNS Toxoplasmosis



# Hemichorea in a patient with AIDS/CNS Toxoplasmosis

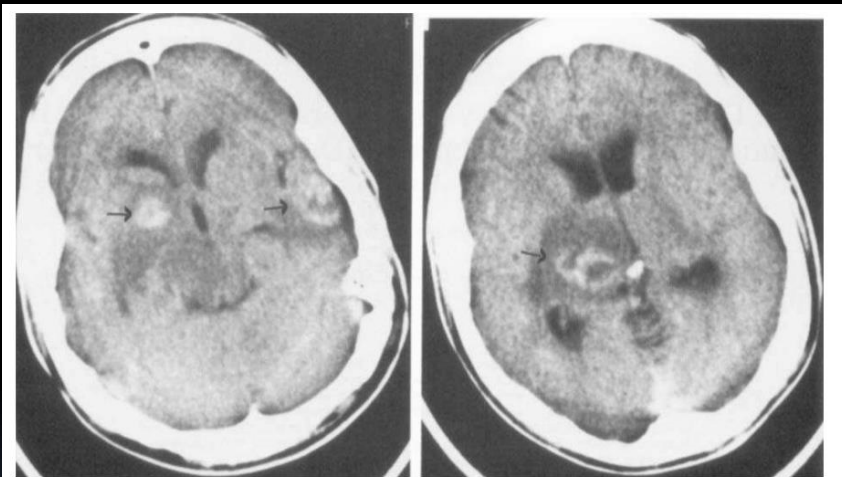


# Hemichorea-hemiballismus in a patient with AIDS/CNS Toxo



Enhancing lesion of the right STN

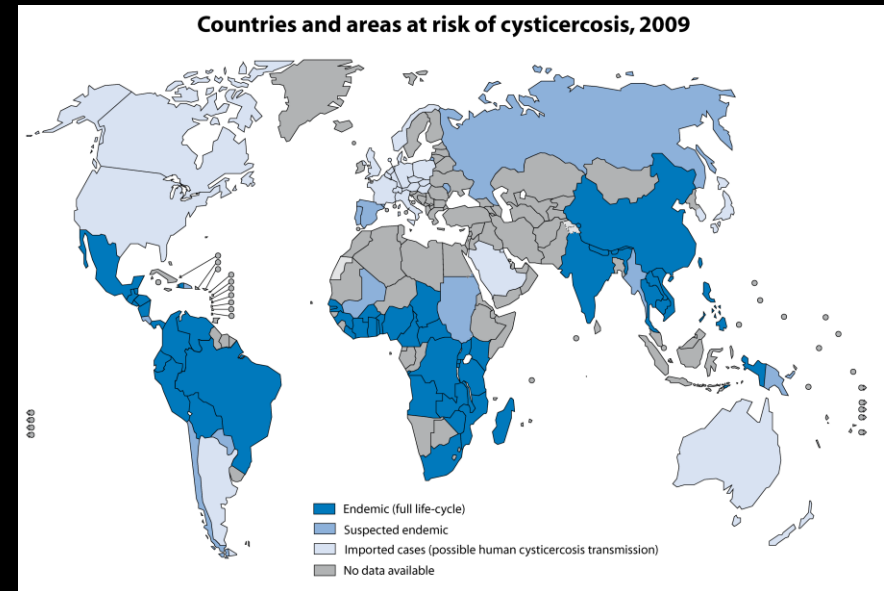
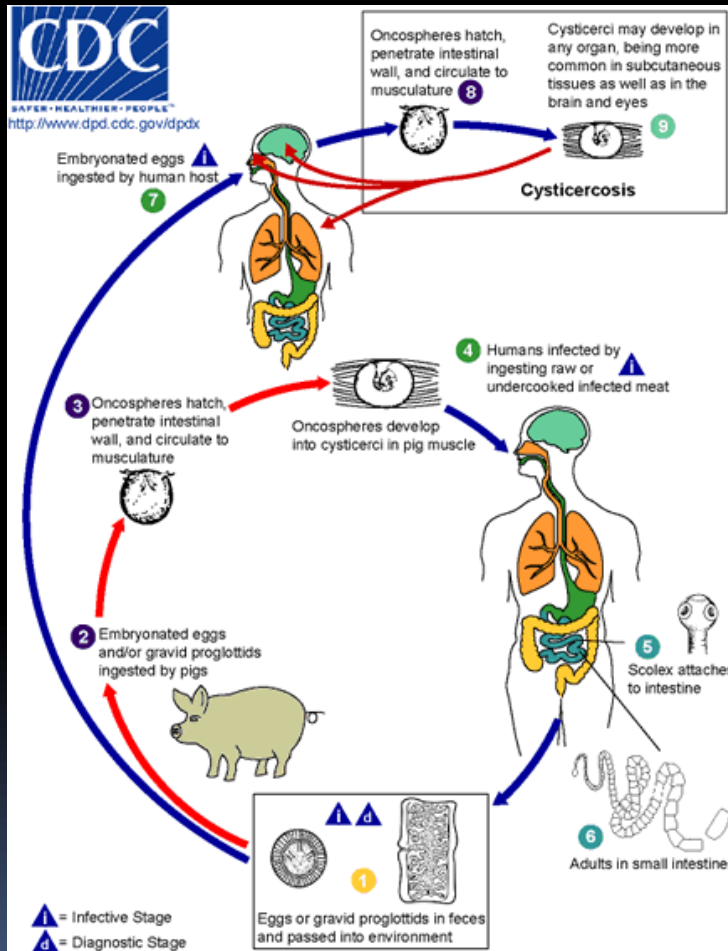
# Focal dystonia in a patient with AIDS/CNS Toxoplasmosis



Contrasted computed tomography scan showing enhanced toxoplasmosis abscesses in right lenticular nucleus and left temporal cortex (arrows) (A) and right thalamus (arrow) (B).

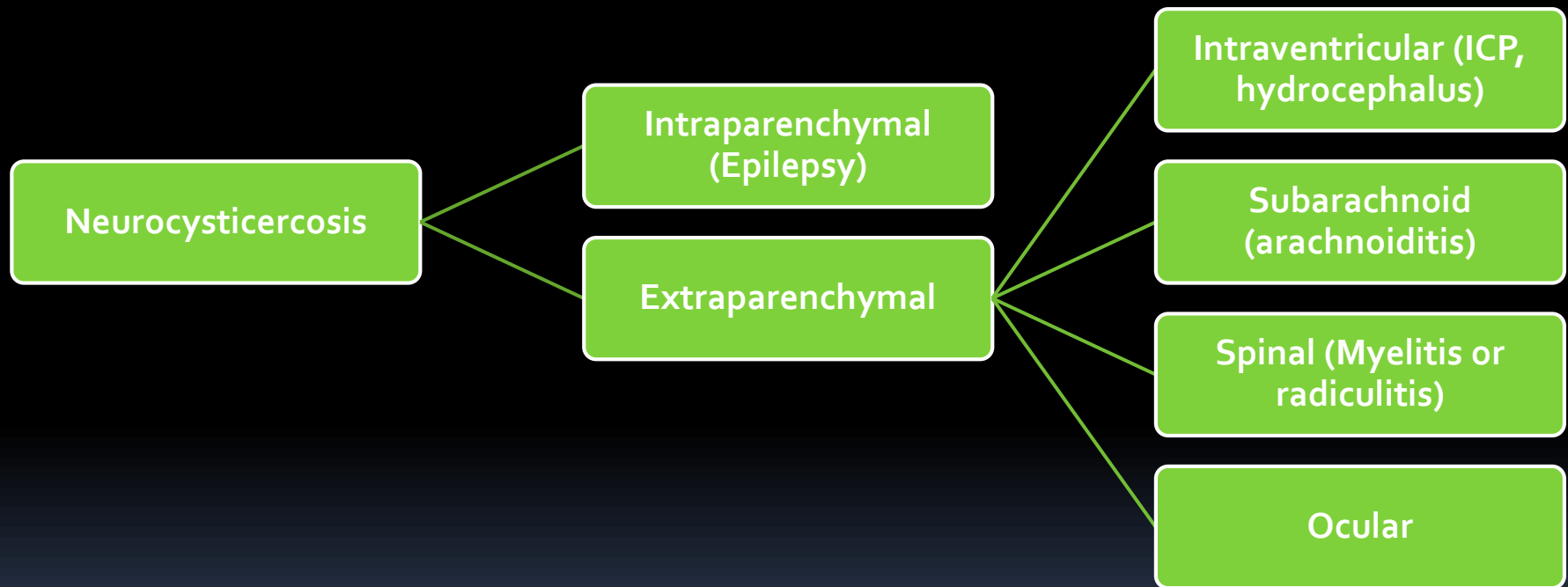


# Neurocysticercosis

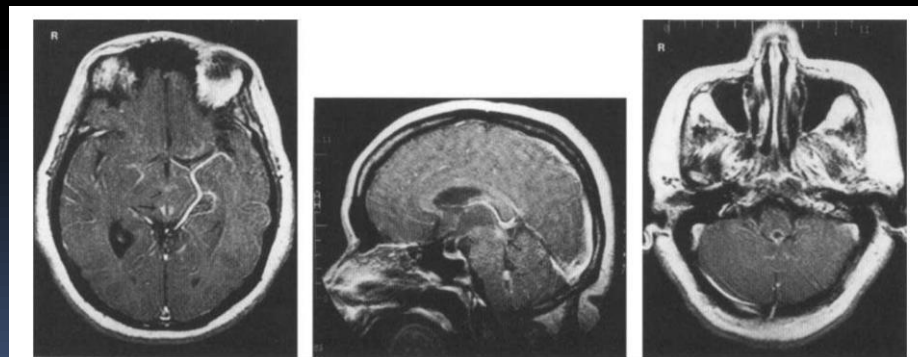


- Larval stage (metacestode) of the *Taenia solium*

# Neurocysticercosis

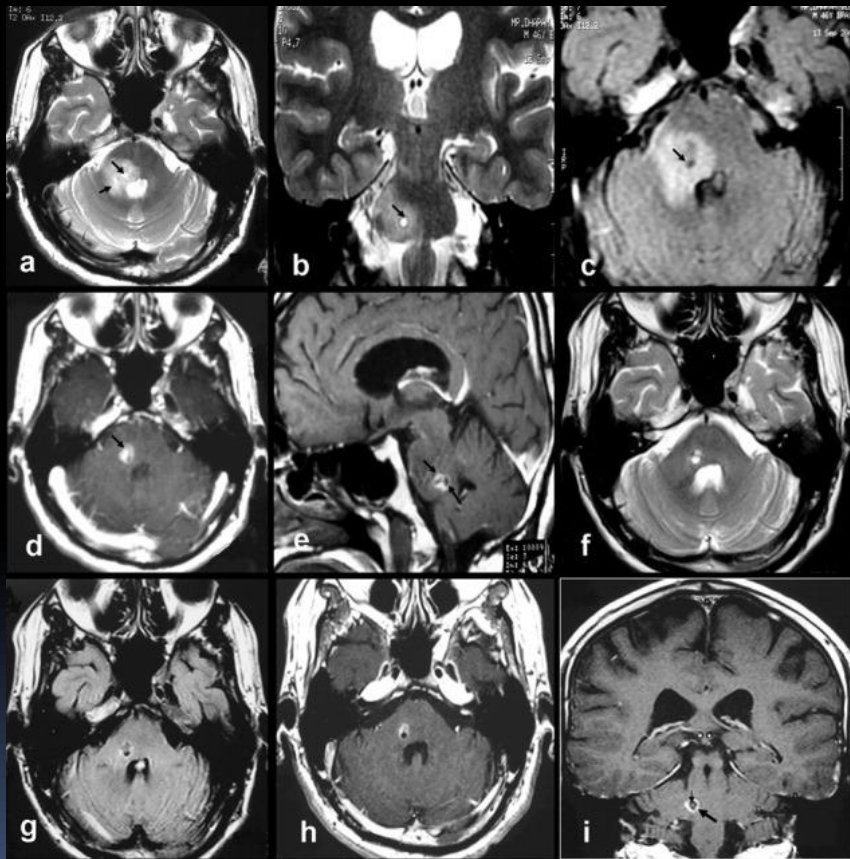


# Parkinsonism in midbrain neurocysticercosis



Cranial magnetic resonance scan (February 18). A: A postgadolinium axial T1-weighted image shows enhancement in the periaqueductal gray matter (long arrow) and the medial ventral midbrain (short arrow). B: A midsagittal section reveals contiguous areas of nodular (short arrow) and peripheral, cyst-like enhancement in the fourth ventricle. The enhancement in the periaqueductal region (long arrow) and ventral mesencephalon is also seen. C: An axial section through the medulla shows the cystic lesion within the fourth ventricle.

# Facial myokimia in pontine neurocysticercosis



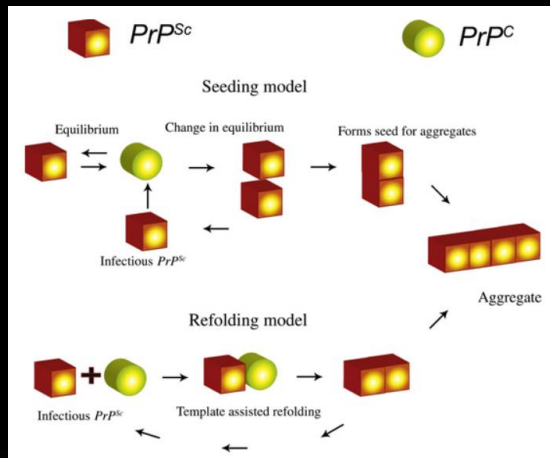


# Prion diseases

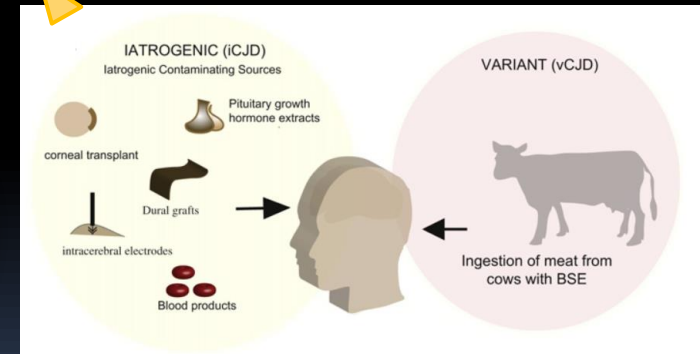
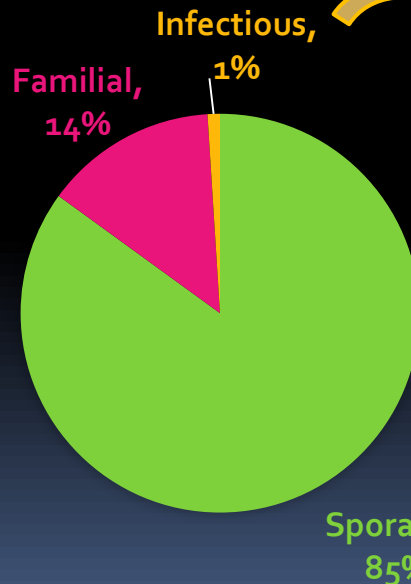


# Creutzfeldt-Jakob disease

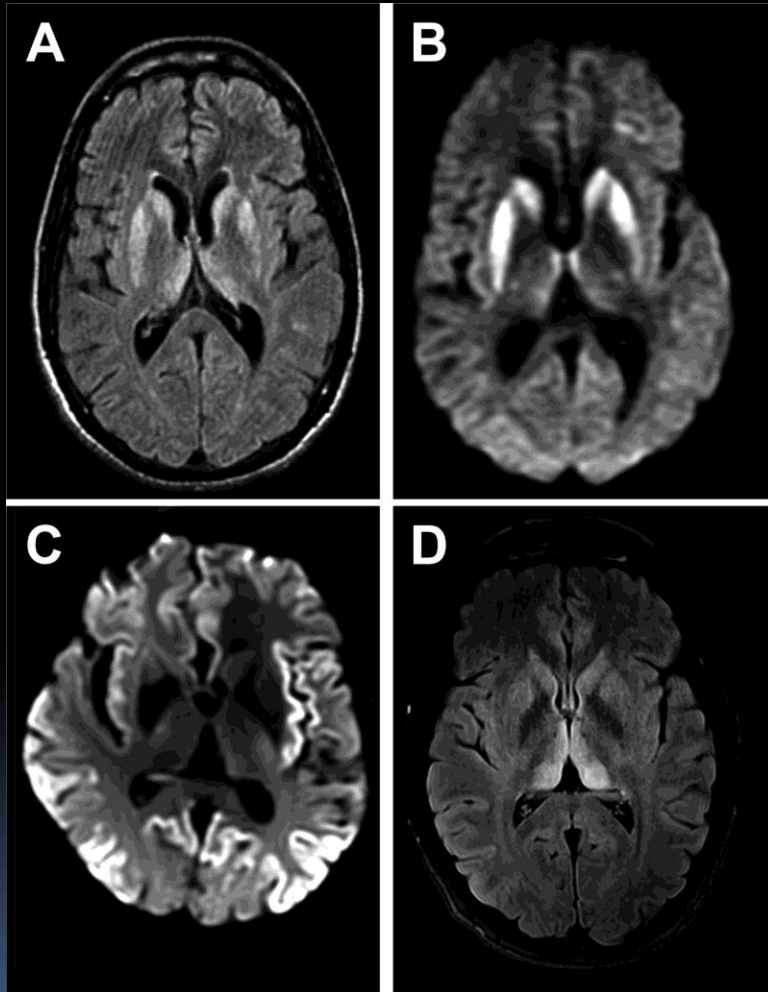
- 100% invariably fatal
- 250-300 cases/year in the US



## CAUSES



# Diagnosis of CJD



Typical MRI Changes

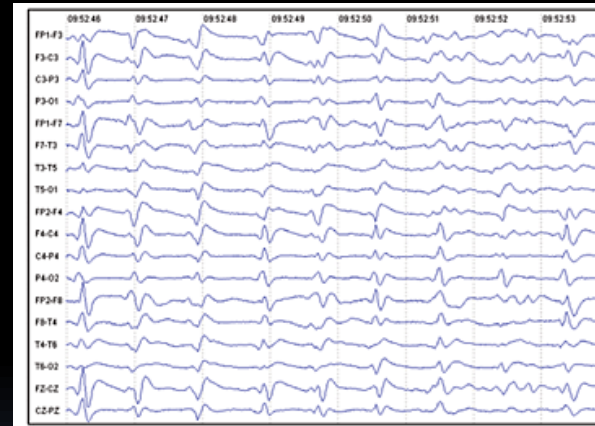
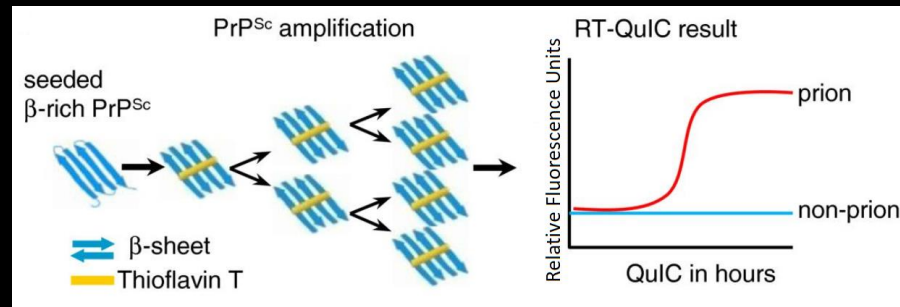


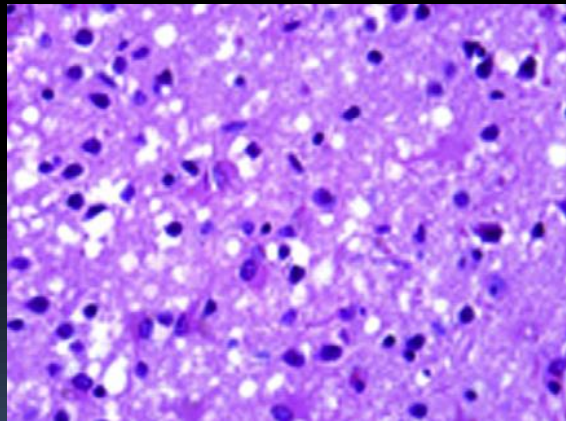
Figure 3. Periodic generalized triphasic wave complexes, moderate amplitude, at rest. Last EEG day-25.

1Hz periodic discharges

# Diagnosis of CJD



Quantitative real-time quaking-induced conversion



Spongiform changes on brain biopsy





# CNS Inflammatory diseases featuring Movement Disorders





# Autoimmune Movement Disorders



# Autoimmune ataxia

- Often paraneoplastic
- Most frequent cancers:
  - Lung (small cell)
  - Ovarian
  - Breast
  - Lymphoma
- Most frequent Abs:
  - Anti-Yo
  - Anti-Hu
  - Anti-Ri
  - Anti-Ma

Paraneoplastic cerebellar degeneration in a patient with Hodgkin's lymphoma with anti-Tr antibodies

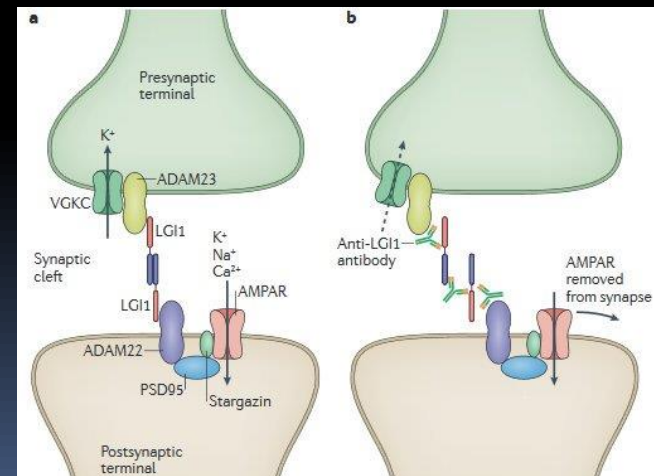
# Autoimmune Chorea

Paraneoplastic	Idiopathic
CRMP-5	CASPR2
ANA	ANA
aPL	aPL
TPO	TPO
ENA	ENA
RF	ASO
GAD65	GAD65
VGCC P/Q	dsDNA
ANNA-1	
ANNA-2	

	Paraneoplastic group (n = 14)	Idiopathic group (n = 22)	p Value
Age, median	72 y	45 y	0.001
Male sex	10/14	5/22	0.006
Moderate or severe chorea	9/11	9/22	0.06
Generalized onset	8/14	8/22	0.307
Weight loss (≥4 kg)	10/14	7/22	0.02
Coexisting neurologic disorder	12/14	14/22	0.25
Coexisting peripheral neuropathy <sup>a</sup>	6/14	1/22	0.008
Spontaneous remission/improvement	8/14	12/22	1.00

# LGI1 encephalitis

- Limbic encephalitis
  - Confusion
  - Disorientation
  - Seizures
- Medial temporal lobe inflammation
- Seizures semiology
  - Medial temporal lobe events
  - Bradycardia
  - Piloerection
  - Faciobrachial dystonic seizures (FBDS)



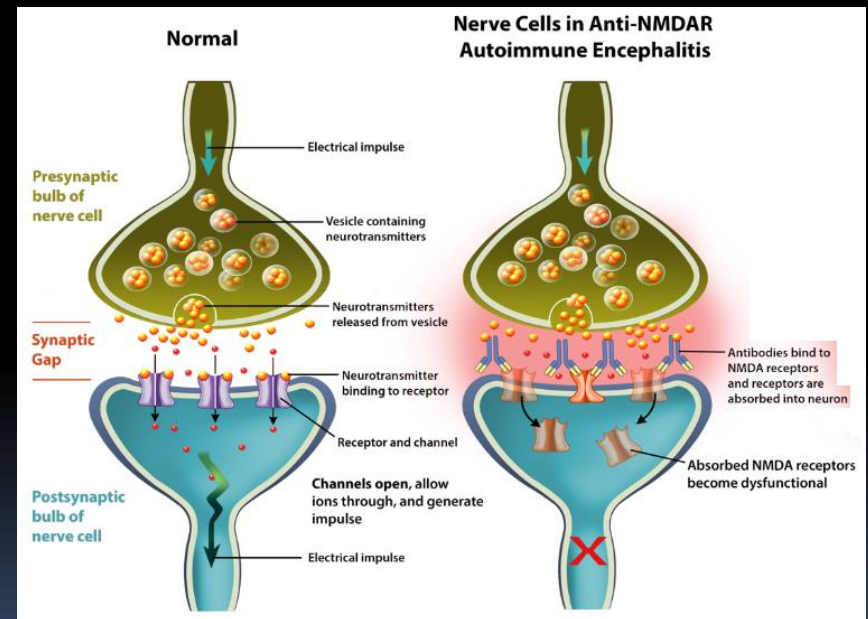
Watson, et al. DOI: <https://doi.org/10.1212/CPJ.000000000000016>

Aurangzeb, et al. *Seizure*. 2017 Aug; 50: 14–17.8

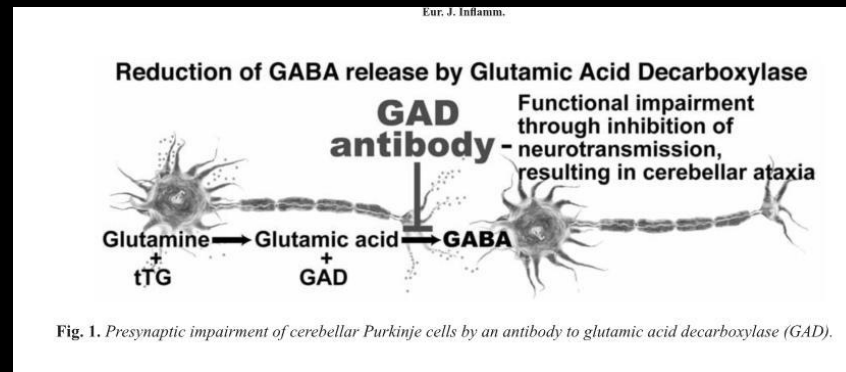
van Sonderen, et al. *Nature Reviews Neurology* volume 13, pages 290–301 (2017)

# Anti-NMDAR Ab encephalitis

- First described @ UPenn in 2007
- More common among young women
- Associated with ovarian teratomas
- Symptoms
  - Paranoia, hallucinations
  - Cognitive changes
  - Aphasia
  - Movement Disorder
  - Seizures
  - Dysautonomia



# Anti-GAD syndromes



- Stiff person syndrome was first described in 1956.
- GAD antibodies were documented in association with SPS in 1988.
- The spectrum of anti-GAD syndromes includes:
  - Stiff person syndrome
  - Stiff limb/trunk syndromes
  - Cerebellar ataxia
  - PERM
- Comorbid autoimmune disease and malignancy must be excluded.

# Anti-GAD syndromes

- Management

1. Exclude false positives results

- Confirm titer levels
- Check antibody levels in the CSF

2. Rule out malignant disease

3. Treatment

- No RCTs or Class I evidence
- Recommendations based on expert consensus
- Medications include:
  - Pulse steroids
  - IVIG
  - Rituximab



# Tremor

and Other Hyperkinetic Movements

## Clinical Spectrum of Stiff Person Syndrome: A Review of Recent Reports

*Harini Sarva, Andres Deik, Aman Ullah, William L. Severt*

Tremor Other Hyperkinet Mov (N Y). 2016 Mar 4;6:340. doi: 10.7916/D85M65GD. eCollection 2016.

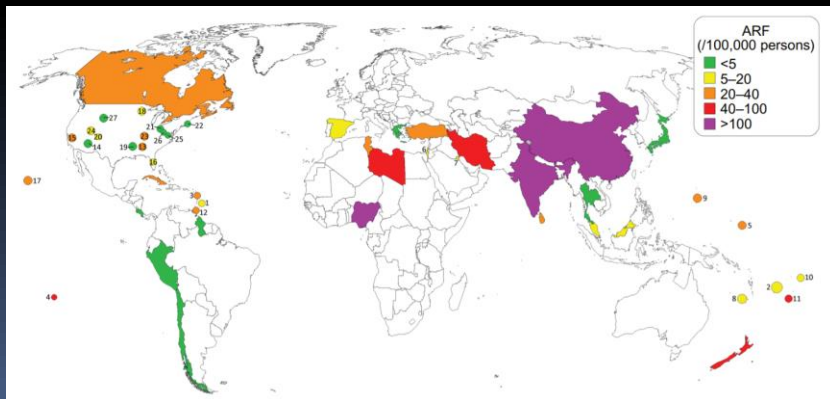


# Postinfectious Movement Disorders



# Sydenham's chorea

- Most common acquired chorea in childhood
- Mimicry against tubulin and lysoganglioside
- Chorea 1-8 mos after group A strep infection
- Testing
  - ASO titer (peaks 4 weeks after the infection)
  - antideoxyribonuclease (anti-DNAse) B titer
- Treatment
  - prednisone 1 mg/kg/d x 2 wks followed by a 2-3 wk taper

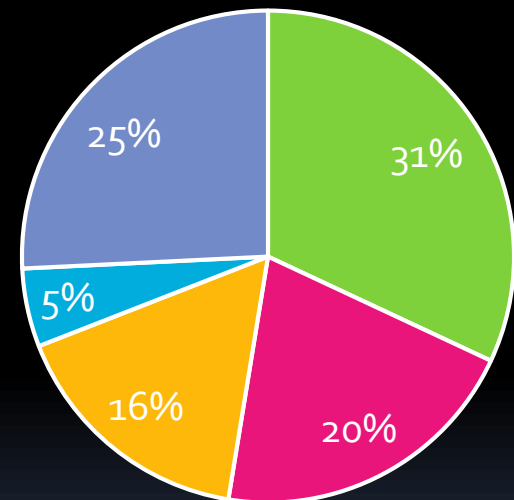


Worldwide epidemiology of acute rheumatic fever

# Postinfectious ataxia

- Postinfectious ataxia
  - Mean age of presentation: 5 +/- 4 yrs
  - Prodrome to ataxia onset: 9 +/- 7 day
  - Prodromal febrile illnesses are common
  - Patients exhibit nystagmus and dysmetria
  - Full recovery in 2-3 weeks

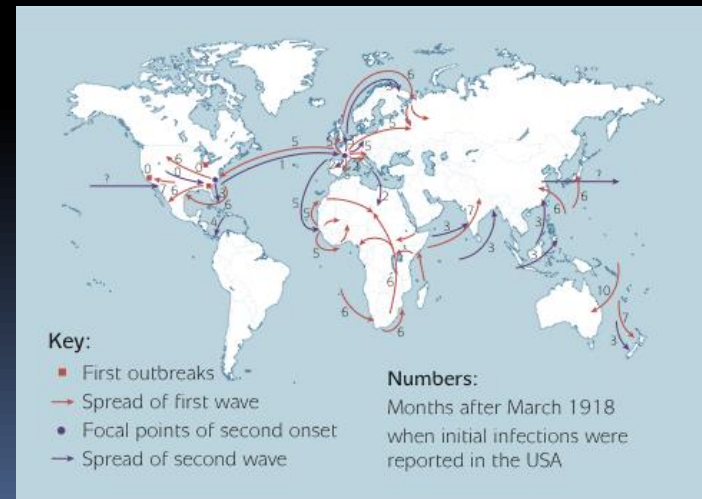
Common causes of postinfectious ataxia



■ Varicella                      ■ Mumps  
■ Nonspecific viral illness   ■ Mycoplasma  
■ Unknown

# Postencephalitic parkinsonism

- von Economo's disease
- 1916-1925
- Unclear link to the Spanish Flu Pandemia
- Pharyngitis followed by a sleep disorder, movement disorders and psychiatric disturbances





**THANK YOU!**