

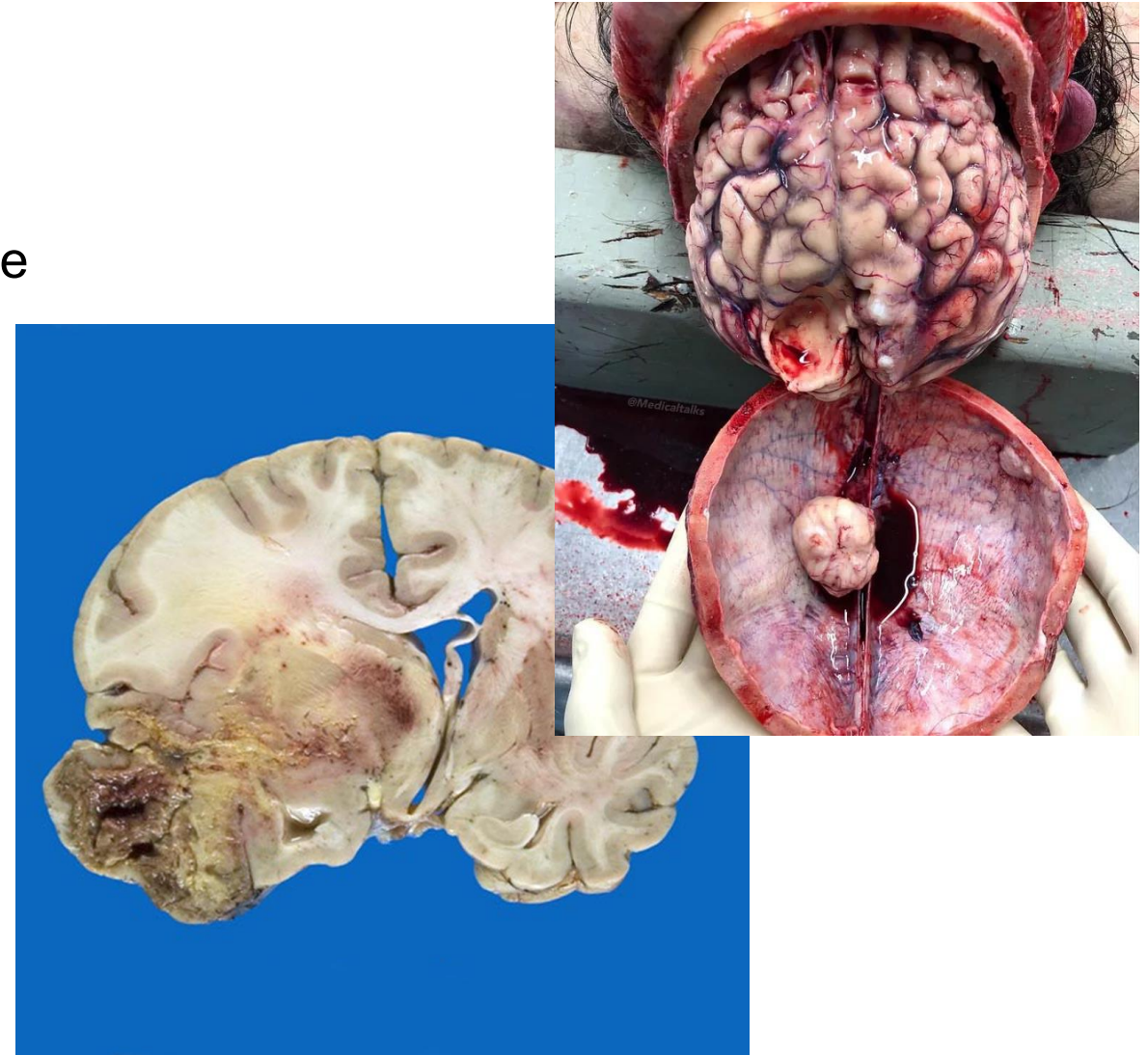
Brain Damage and Neuroplasticity

Can the Brain Recover
from Damage?



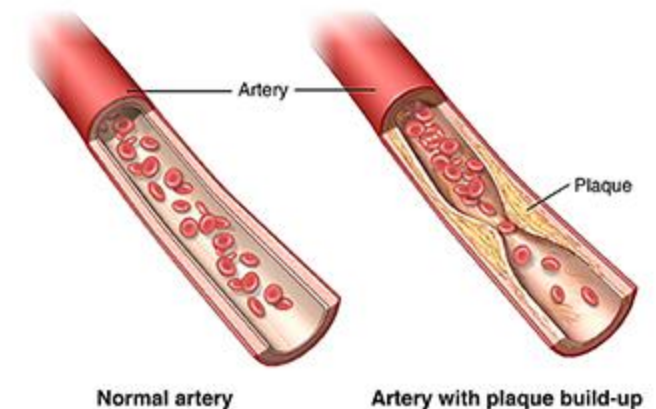
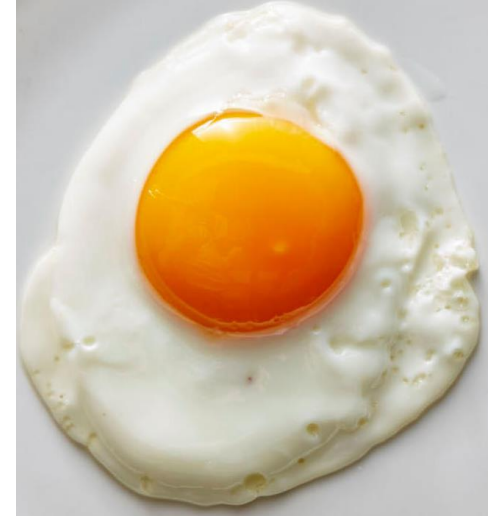
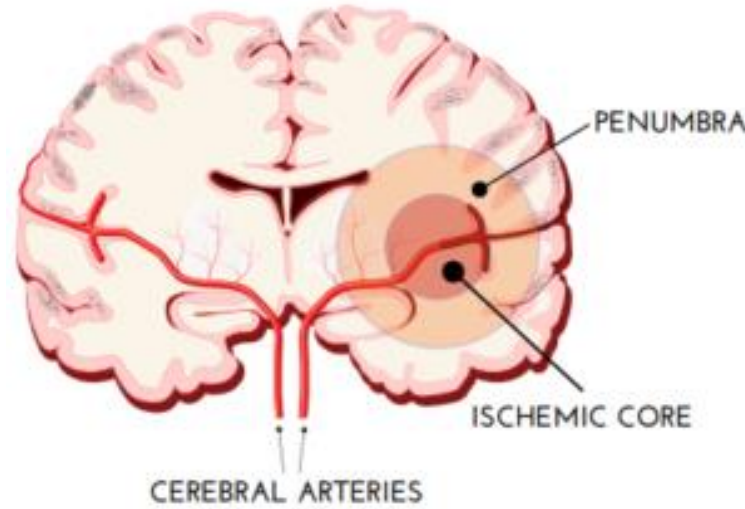
Brain Tumors

- Tumor types
 - Structure
 - Encapsulated grow within own membrane
 - Infiltrating grow diffusely through surrounding tissue
 - Benign or malignant
 - Origination
 - Gliomas originate from glial cells (often infiltrating)
 - Meningiomas grow in the meninges (encapsulated and benign)
 - Behavior
 - Metastatic originate in one organ and spread to another



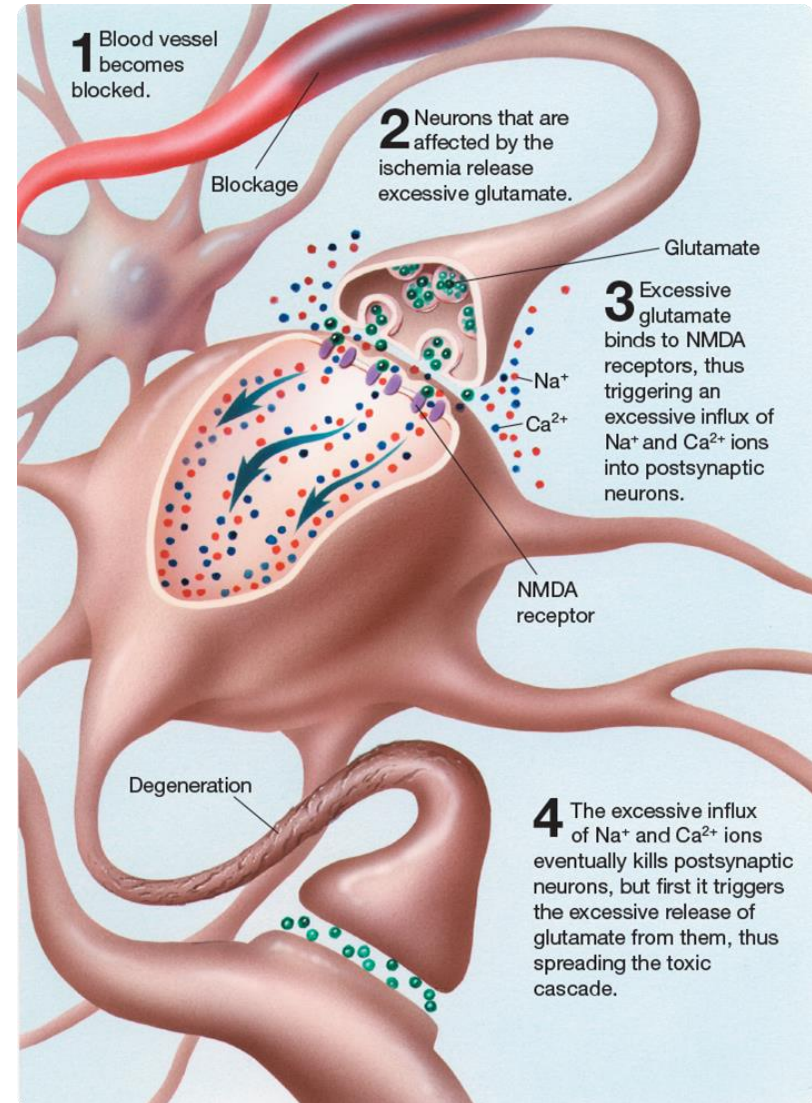
Strokes (1 of 2)

- Stroke defined
 - Cerebrovascular disorder of sudden onset
- Infarct
 - Area of dead or dying tissue surrounded by penumbra
- Causes
 - Cerebral hemorrhage
 - Can result from bursting aneurysms
 - Cerebral ischemia
 - Thrombosis
 - Embolism
 - Arteriosclerosis



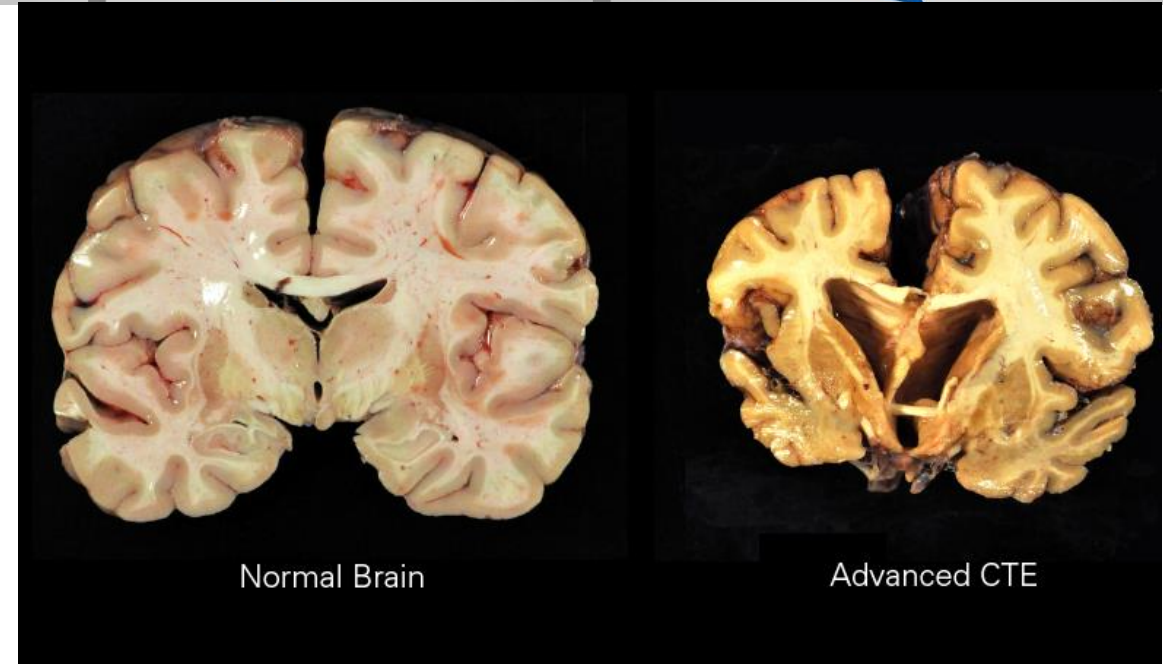
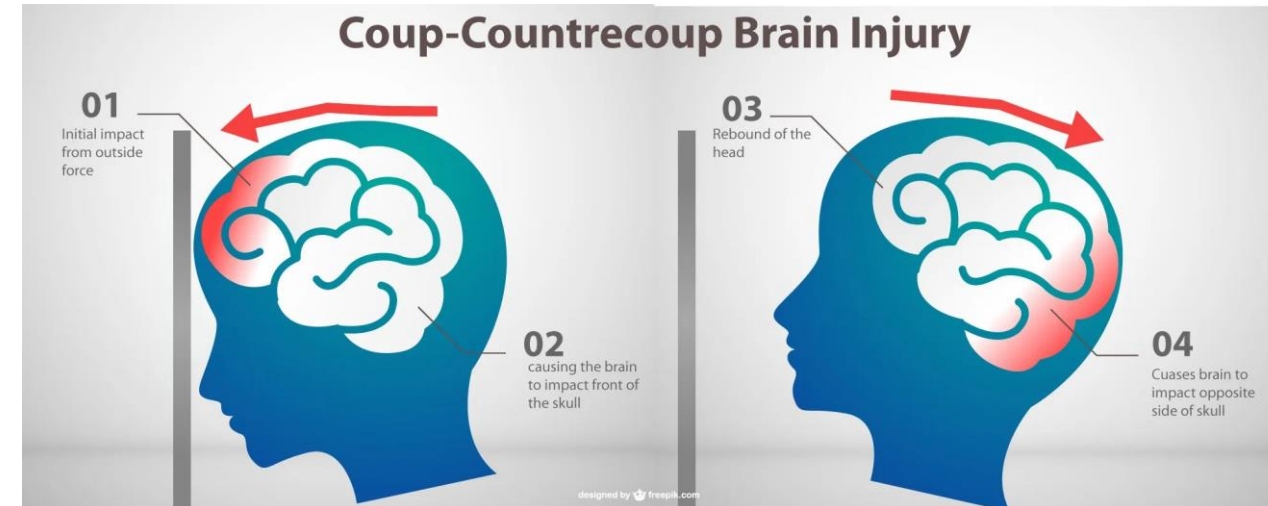
Strokes (2 of 2)

- Ischemic brain damage
 - Takes a while to develop
 - Does not occur equally in all regions of the brain
 - Physiological mechanism varies
- One mechanism of ischemia
 - Excessive release of excitatory amino acids
 - Glutamate released when blood vessels blocked
 - Excess glutamate release
 - Causes release of glutamate on receiving cell
 - Can kill postsynaptic cell
 - NMDA receptor blockers



Traumatic Brain Injuries

- Contusion
 - Injury includes bleeding without laceration
 - Results in hematoma
 - Caused by brain hitting skull
 - Can be countrecoup
- Mild TBI
 - When a blow to the head disrupts consciousness
 - No evidence of contusion or other structural damage
 - Effects on cognition, motor movements, and neurological function can last many years
 - Chronic traumatic encephalopathy (CTE) occurs in people who have had many mild TBIs over time



Infections of the Brain

- Infections

- Encephalitis

- Causative agents

- Bacterial

- Treated with antibiotics

- Can cause meningitis

- Brain abscesses

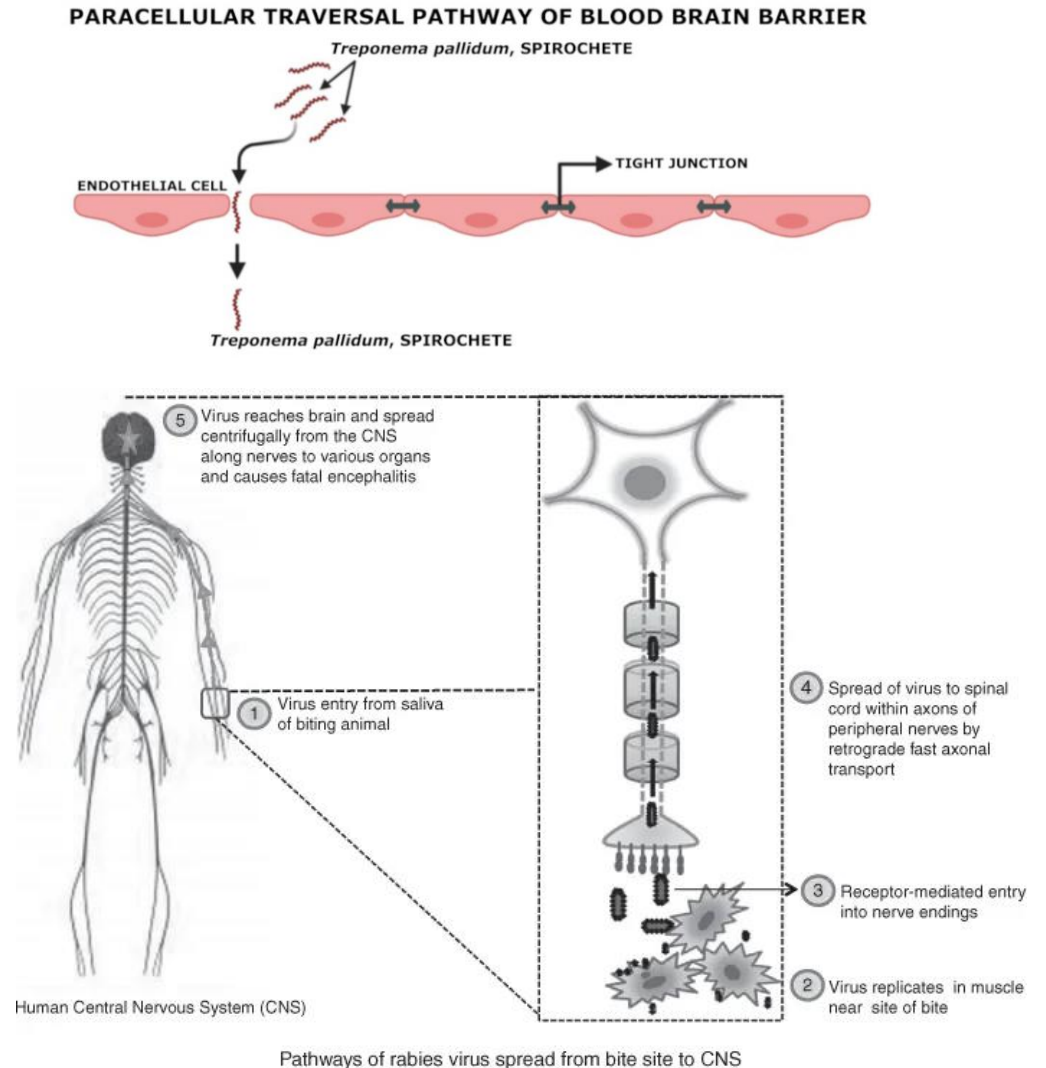
- General paresis (neurosyphilis)

- Viral

- Some preferentially attack CNS (rabies)

- May play a role in etiology of many disorders

- Can be dormant



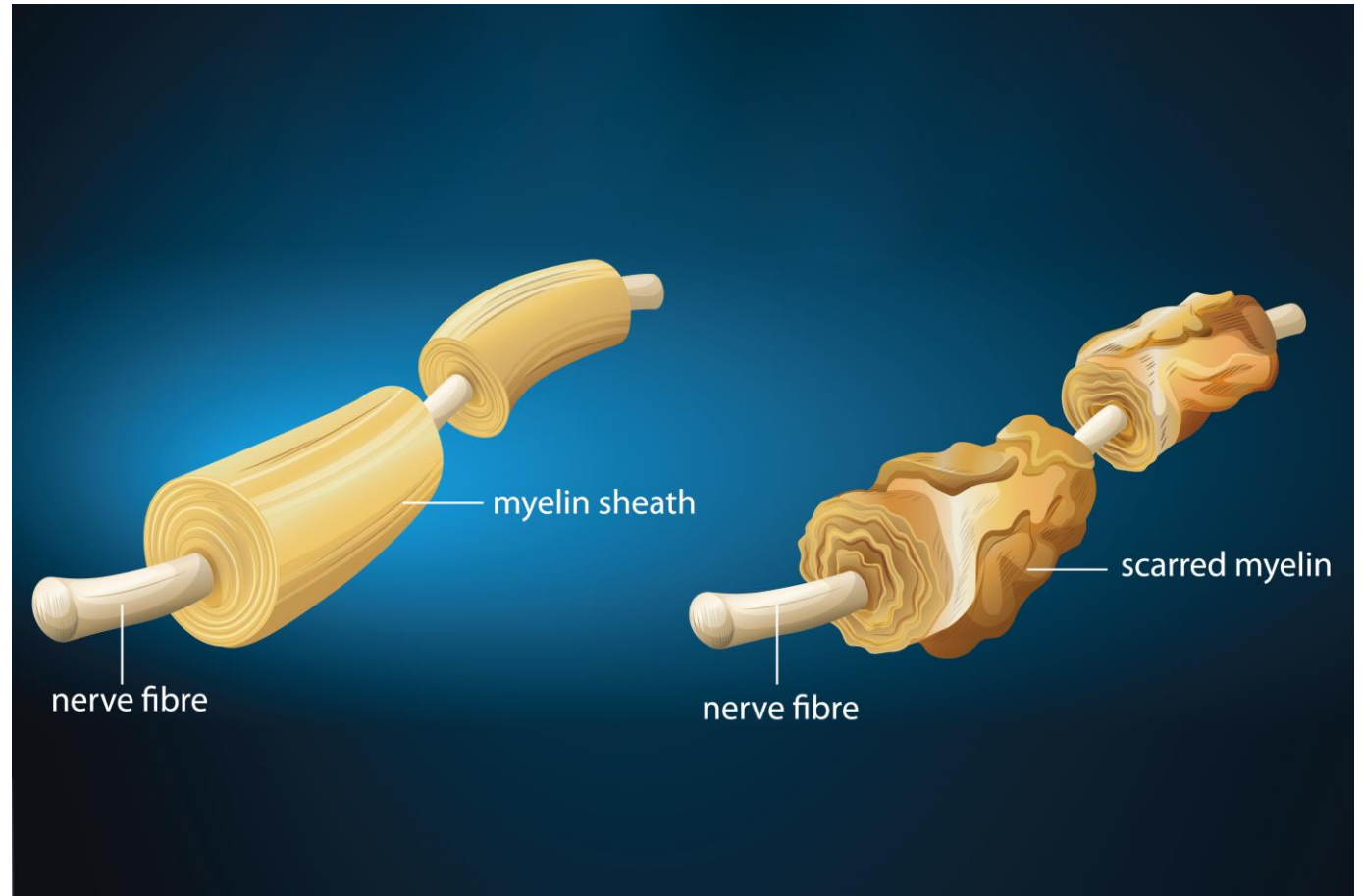
Neurotoxins

- Heavy metals
 - Toxic psychosis
- Drugs to treat neurological or psychiatric disorders
 - Tardive dyskinesia
- Endogenous
 - Antibodies against CNS components



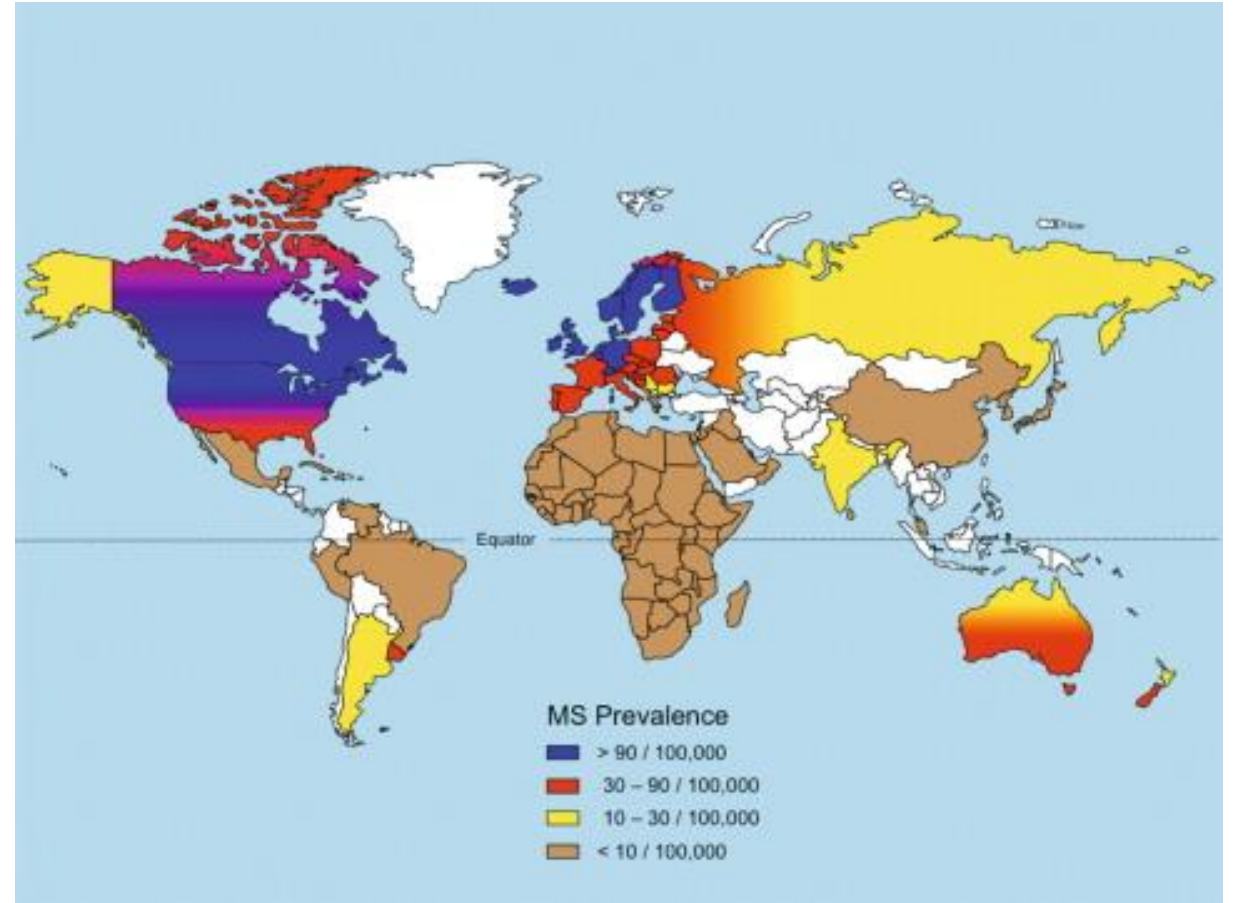
Multiple Sclerosis (1 of 2)

- Characteristics
 - Degeneration of myelin
- Symptoms
 - Ataxia
 - Weakness
 - Numbness
 - Tremor
 - Poor vision
- Causes
 - Perhaps faulty immune system
 - Experimental encephalomyelitis



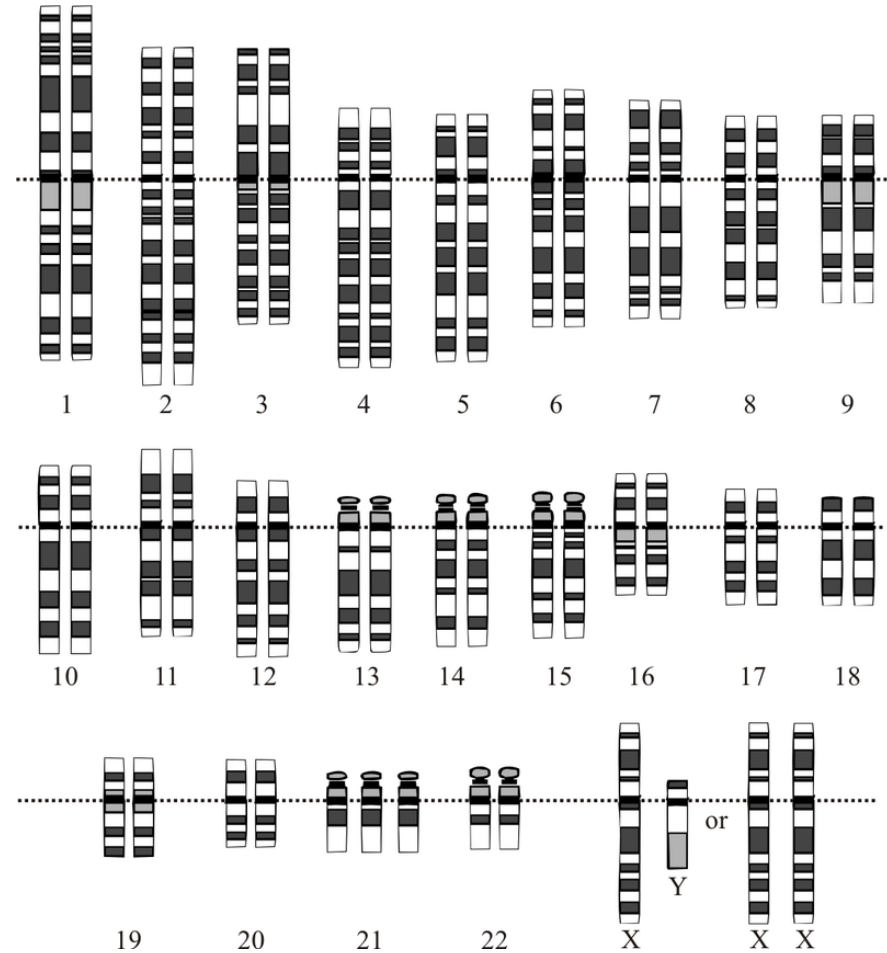
Multiple Sclerosis (2 of 2)

- Epidemiological studies
 - Higher concordance in monozygotic twins (35%) than dizygotic twins (6%)
 - Occurs substantially more in females
 - Higher in Caucasians
 - Higher among populations living in colder climates



Genetic Factors

- Can be accidents of cell division
- Down syndrome is an extra 21 chromosome
- Abnormal recessive or dominant genes
- Most diseases involve numerous loci on chromosomes



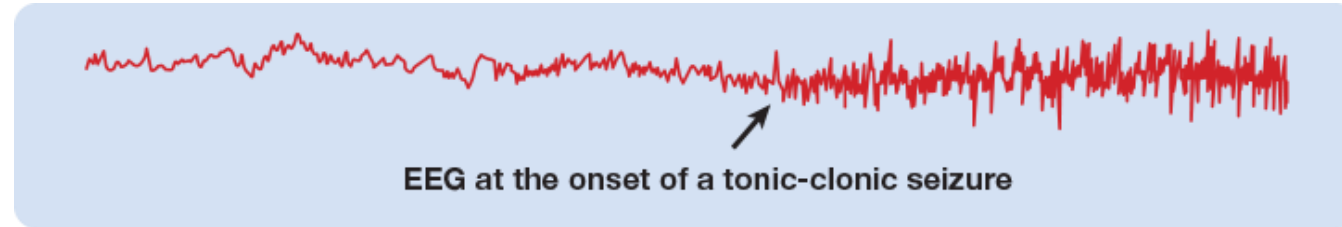
Programmed Cell Death

- Apoptosis
 - Programmed cell death
 - Occurs in cells that are dysfunctional
 - More adaptive than necrosis
 - Nucleus is impacted early in process
- Necrosis
 - Neuron dies passively due to injury
 - Can cause inflammation
 - Nucleus is impacted late in process



Epilepsy

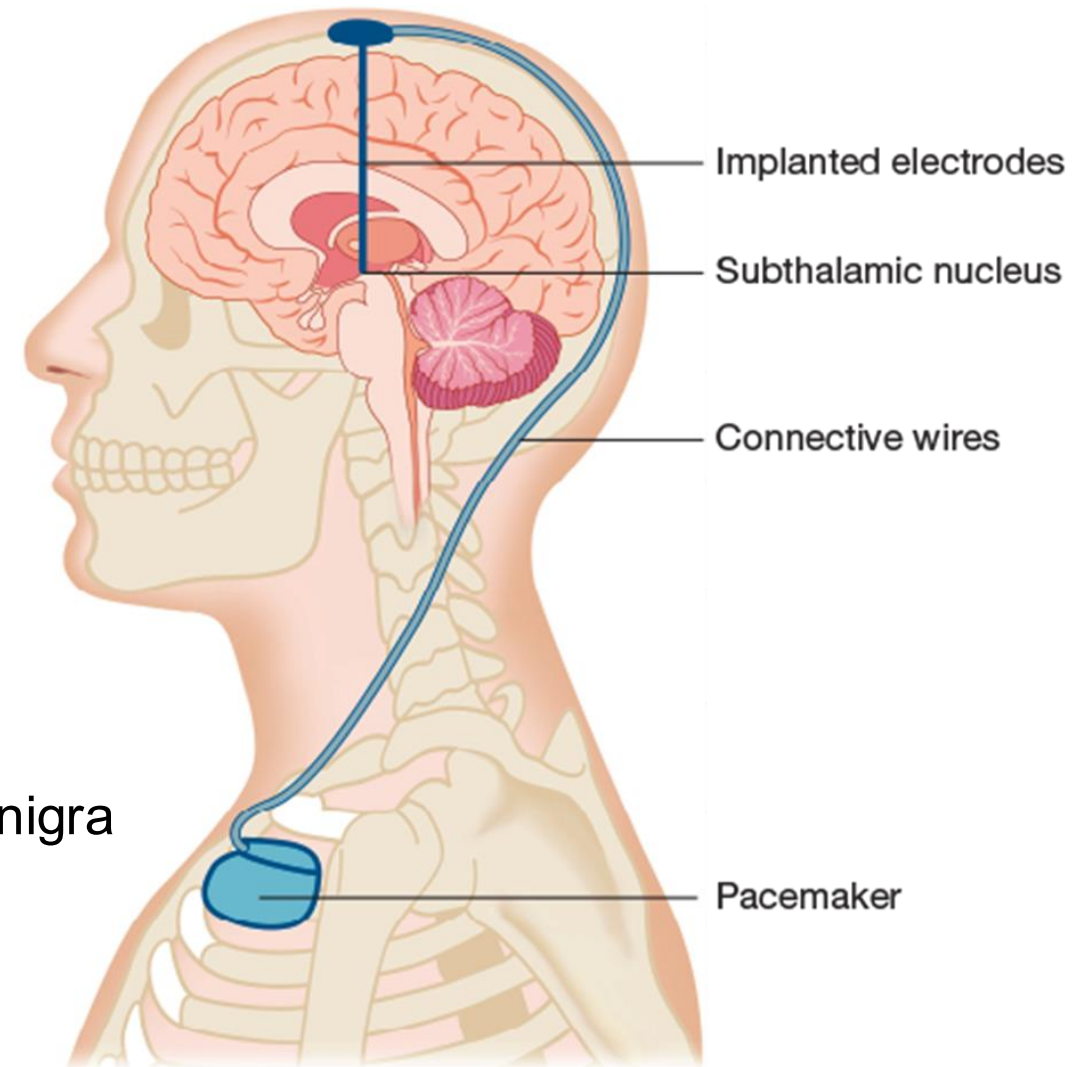
- Characteristics of epilepsy
 - Seizures recur spontaneously
 - Convulsions make diagnosis easier
 - Clonus/tonus
 - Loss of balance/loss of consciousness
 - Some seizures involve changes in thought, mood, and/or behavior with no convulsions
 - Epileptic spikes may be evident in EEG
 - Auras
 - Two main classes
 - Focal
 - Generalized



Parkinson's Disease

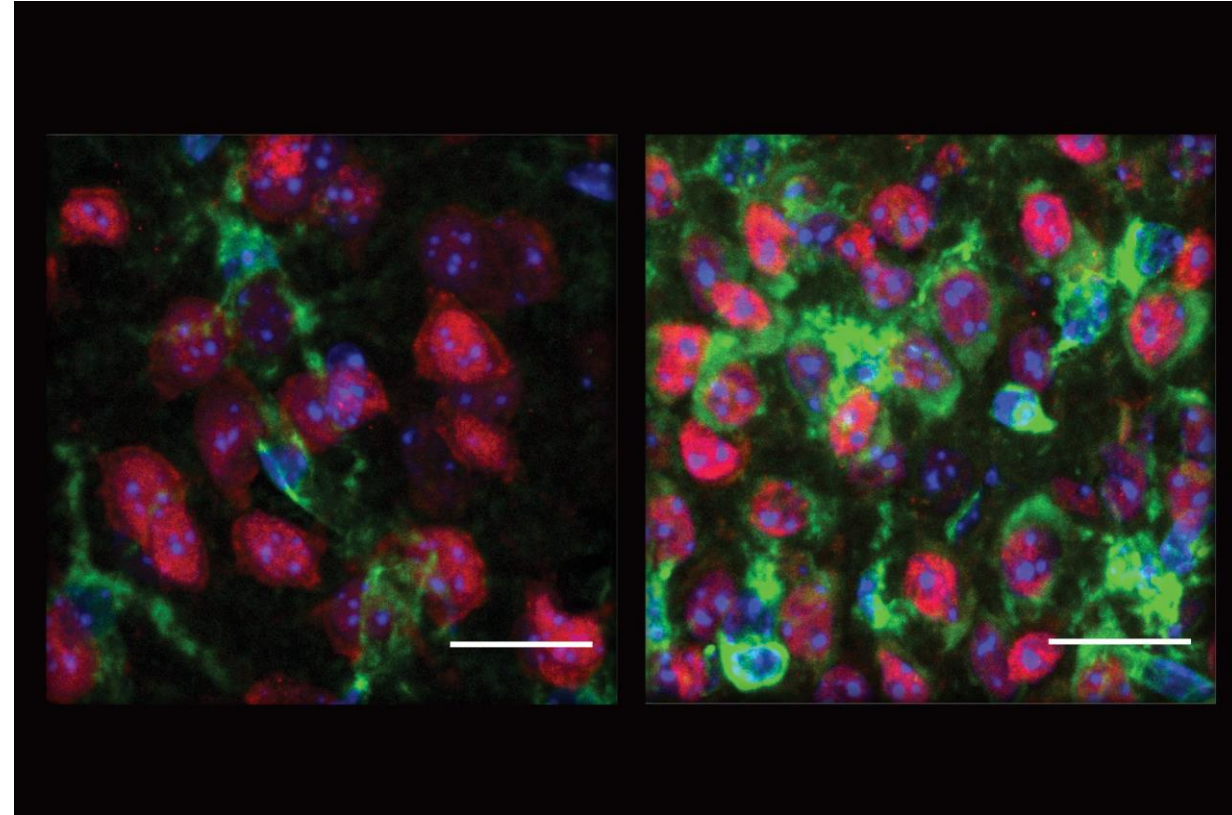
- Characteristics

- Occurs in 1–2% of population over age 65
- Slightly more often in males
- Symptoms
 - Tremor or stiffness in fingers
 - Tremor at rest
 - Muscular rigidity
 - Slowness of movement
 - Masklike face
- Causes
 - Degeneration of dopamine neurons in substantia nigra
- Treatments
 - L-dopa
 - Deep brain stimulation



Huntington's Disease

- Characteristics
 - Motor disorder
 - Inherited
 - Associated with dementia
- Symptoms
 - Complex jerky movements
 - Do not appear until 40 to 50 years of age
- Cause
 - Single mutated dominant gene (Huntingtin)



Alzheimer's Disease (1 of 2)

• Symptoms

- Decline in memory
- Emotional instability
- Loss of speech function
- Total dementia
- Loss of ability to do simple tasks (swallow)
- Terminal

• Diagnosis

– At autopsy

- Amyloid plaques
- Neurofibrillary tangles
- Loss of cells in hippocampus, amygdala, entorhinal cortex

TABLE 1. KEY CHARACTERISTICS OF ALZHEIMER'S DISEASE STAGES

	Preclinical	Prodromal	Dementia
Cognition	Subtle episodic memory loss (↓learning curve, possibly ↓delayed recall and false positive intrusions); subtle↓executive abilities	Obvious episodic memory loss ↓learning curve, ↓delayed recall, false positive intrusions, ↓clueing); repeats questions; misplaces items; disoriented to date; ↓executive abilities (problem solving, decision making)	Severe episodic memory loss (↓↓learning curve, ↓↓↓delayed recall, false positive intrusions, ↓↓↓clueing); repeats questions daily; misplaces items daily; disoriented to date, day, eventually month and year; ↑word finding difficulty; ↓comprehension; ↓↓↓executive abilities (problem solving, decision making, planning skills, abstraction, judgment); ↓finding their way; ↓drawing
Function	Normal	Struggles to be independent with instrumental ADLs (driving, finances, working, shopping, cooking, medication management); ↓engagement	Loss of independence of instrumental ADLs and eventually basic ADLs (dressing, grooming, bathing, feeding, toileting, and continence); ↓↓↓engagement
Behaviors	Apathy; irritability; dysphoria; ↓insight	Apathy; irritability; dysphoria; anxiety; ↓insight	Apathy; irritability; restiveness to care; anger; delusions; wandering/restless behaviors; depression; anxiety; sleep issues; ↓↓↓insight
Biomarkers	CSF amyloid and tau; amyloid PET; tau PET; FDG-PET	CSF amyloid and tau; amyloid PET; tau PET; FDG PET	Order only if clinical features questionable or atypical
Clinical considerations	Clinical trial participation; consider financial planning and advanced care directives	Cholinesterase inhibitor; clinical trial participation; ↑supervision (driving, medications, finances); financial planning and advanced care directives	Cholinesterase inhibitor; memantine; clinical trial participation; driving evaluations; ↑↑supervision; caregiver support; financial planning and advanced care directives

Abbreviations: AD, Alzheimer's disease; ADL, Activities of Daily Living; CSF, cerebrospinal fluid; FDG, fluorodeoxyglucose; PET, positron emission tomography

Alzheimer's Disease (2 of 2)

- Treatments
 - Increase acetylcholine function
 - Reduce amyloid plaques
 - Treatments based on relationship between Down syndrome and Alzheimer's
 - Treatments directed toward misfolded protein hypotheses

