7. Neurology

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I. Infarct

A. Terminology

1. Stroke ≡ a sudden, nonconvulsive focal neurologic deficit
2. TIAs ≡ deficit lasting ≤24 hr (usually <1 hr) & resolve completely
3. Emboli sources **= carotid atheroma (most common)**, cardiac & fat emboli, marantic endocarditis (metastasizing cancer cells)
4. Lacunar infarct = small infarct in deep gray matter, strongly associated with hypertension & atherosclerosis
5. Watershed infarcts occur at border of areas supplied by different arteries (e.g., MCA-ACA), often following prolonged hypotension

B. Presentation (See Figures 7-1 and 7-2)

1.

Table 7-1 Presentation of Stroke

Sign/Symptom	Artery	Region (Lobe)
Amaurosis fugax (monocular blind)	Carotid (emboli)	Ophthalmic artery
Drop attack/Vertigo/CN palsy/coma	Vertebrobasilar (emboli)	Brain stem
Aphasia	Middle cerebral	Dominant frontal or temporal[a]
Sensory neglect & apraxia[b]	Middle cerebral	Nondominant frontal or temporal[a]
Hemiplegia	Middle or anterior cerebral	Contralateral parietal
Urinary incontinence & grasp reflex	Middle or anterior cerebral	Frontal
Homonymous hemianopia	Middle or posterior cerebral	Temporal or occipital

[a] Dominant = left in 99% of right-handers & >50% of left-handers.
[b] Apraxia = patient cannot follow command even if it is understood & the pt is physically capable of it.

2. Wernicke's aphasia (temporal lobe lesion) = receptive, pt speaks fluently but words do not make sense: **Wernicke's is wordy**
3. Broca's aphasia (frontal lobe lesion) = expressive, pt is unable to verbalize: **Broca's is broken**
4. Edema occurs 2–4 days postinfarct, watch for this clinically (e.g., ↓ consciousness, projectile vomiting, pupillary changes)
5. Decorticate (cortical lesion) posturing → flexion of arms
6. Decerebrate (midbrain or lower lesion) posturing → arm extension

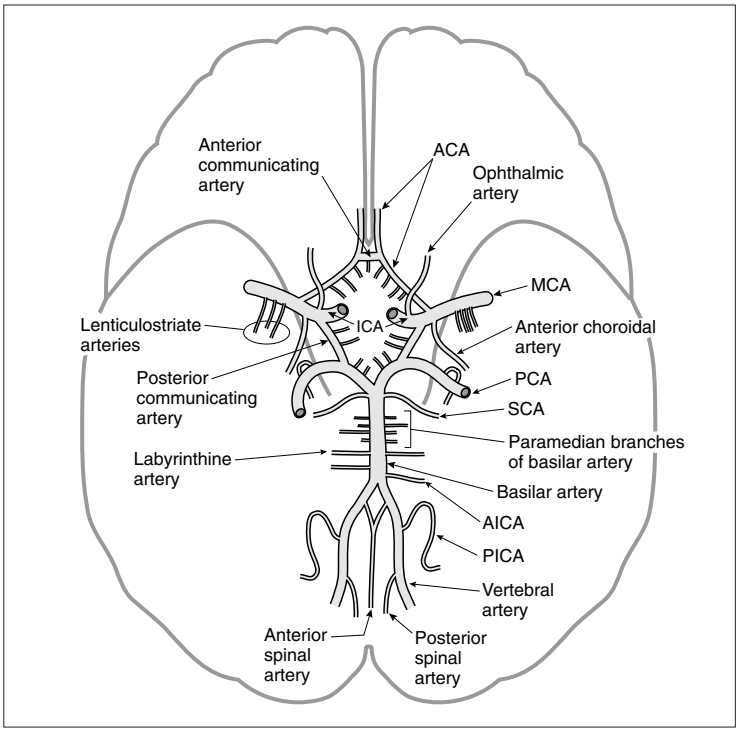

FIGURE 7-1 Circle of Willis. ACA = anterior cerebral artery; AICA = anterior inferior cerebellar artery; ICA = internal carotid artery; MCA = middle cerebral artery; PCA = posterior cerebral artery; PICA = posterior inferior cerebellar artery; SCA = superior cerebellar artery.
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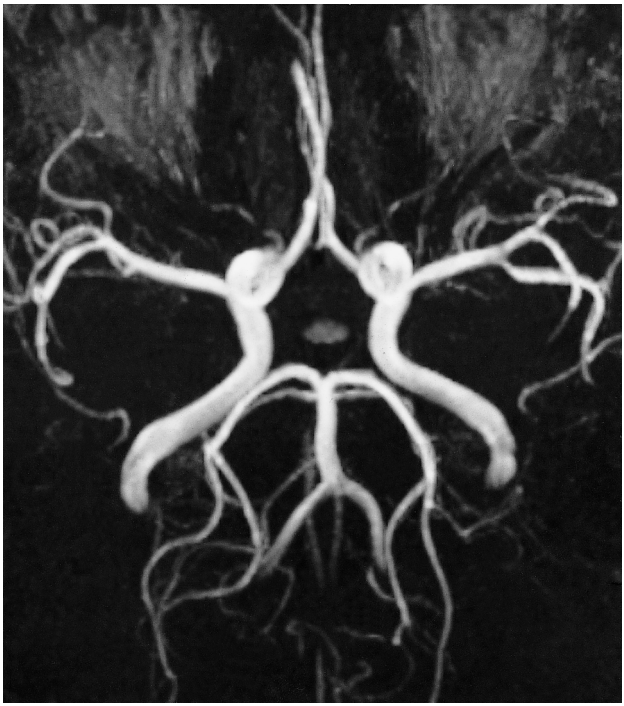
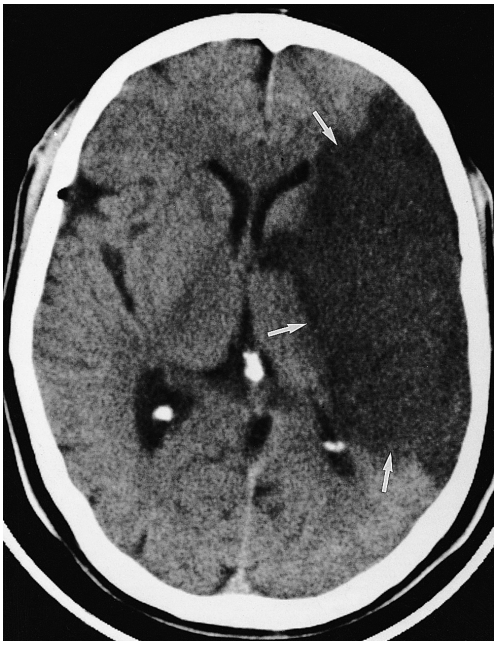


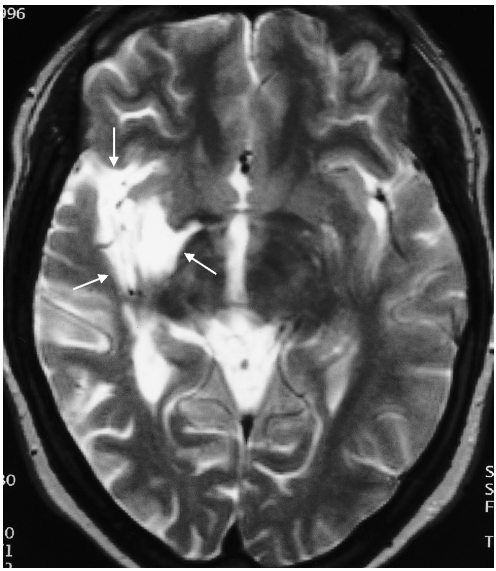
FIGURE 7-2 Magnetic resonance angiography (MRA). The arteries at the base of the brain, the circle of Willis, are very well shown by MRA without the use of any contrast agent.

C. DIFFERENTIAL DIAGNOSIS

1. Stroke, seizure, neoplasm, encephalitis, multiple sclerosis
2. Stroke causes = 35% local atheroembolic, 30% cardiac, 15% lacunar, 10% parenchymal hemorrhage, 10% subarachnoid hemorrhage, ≤1% other (e.g., vasculitis, temporal arteritis, etc.)
3. Dx = CT for acute, MRI for subacute infarct &/or hemorrhage (See Figure 7-3)
4. Rule out seizure → EEG, loss of bowel/bladder control & tongue injury
5. Lumbar puncture to rule out encephalitis & rule in intracranial bleed



(a)



(b)

FIGURE 7-3 Cerebral infarction. (a) Unenhanced CT scan showing a low-density region of the left cerebral hemisphere conforming to the distribution of the middle cerebral artery (arrows). (b) MRI scan of another patient with a right middle cerebral artery territory infarct. The infarcted area (arrows) shows patchy high-signal intensity on this T2-weighted image. The arrows point to the anterior and posterior extent of the infarcted brain tissue.

D. TREATMENT

1. tPA within 3–6 hours of onset (preferably 1 hr) for occlusive dz only!
2. **Intracranial bleeding is an absolute contraindication to tPA use!**
3. Correct underlying disorder, e.g., hyperlipidemia, hypertension, diabetes, valve abnormality, coagulopathy, atrial fibrillation
4. For embolic strokes give aspirin/warfarin anticoagulation for prophylaxis
5. If carotid is 70% occluded & patient has Sx → endarterectomy

E. PROGNOSIS

1. 20–40% mortality at 30 days (20% atheroemboli, 40% bleed)
2. Less than 1/3 patients achieve full recovery of lifestyle
3. Atheroembolic strokes recur at 10%/yr

II. Infection & Inflammation

A. MENINGITIS

1. 50% due to *Streptococcus pneumonia*, 25% due to *Neisseria meningitidis, Hemophilus influenza* is rare now due to vaccination, *Listeria* seen in neonates, elderly and immunocompromised pts, and Group B *Strep* (*S. agalactiae*) and *E. coli* are the #1 and #2 causes of neonatal meningitis
2. Si = **meningismus** (pt cannot touch chin to chest), ⊕ **Kernig's sign** (pt is supine with hip and knees flexed at 90°, examiner cannot extend knee), ⊕ **Brudzinski's sign** (pt is supine, when examiner flexes neck, pt involuntarily flexes hip and knees)
3. CSF differential for meningitis

TABLE 7-2 CSF Findings in Meningitis

	CELLS	PROTEIN	GLUCOSE
Bacterial	↑ **neutrophils**	↑↑	↓↓ (≤2/3 serum)
Viral	↑ mononuclear	± ↑	**Nml**
Subacute	↑ mononuclear	↑	↓

4. Can be acute, subacute, chronic presentations
5. Acute
   a. Send CSF for Gram's stain, bacterial cultures, HSV PCR
   b. Treat all patients empirically by age until specific tests return

TABLE 7-3 Empiric Therapy for Meningitis by Age

AGE	REGIMEN	COMMON ETIOLOGIES
Neonates (≤1 mo)	**Ampicillin + cefotaxime**	*Streptococcus agalactiae, Listeria, Escherichia coli*
Children to teens	**Cefotaxime + vancomycin**[a]	*Streptococcus pneumonia, Neisseria meningitidis*
Adults	**Cefotaxime + vancomycin**[a]	*S. pneumonia* by far most common

• Add acyclovir to any pt with possible HSV.
[a]Due to increasing rate of β-lactam resistance *S. pneumonia*

   c. Of viral causes, only HSV (acyclovir) & HIV (AZT) can be treated—otherwise treatment is supportive

d.

TABLE 7-4 Bacterial Meningitis

ORGANISM	PATIENTS	CHARACTERISTICS	TREATMENT
Streptococcus pneumoniae	**#1 cause in adults**: old age, asplenia, poor health predispose	Can progress from otitis media, sinusitis, or bacteremia	Pen G (if susceptible) Second line = cefotaxime, third line = vancomycin
Neisseria meningitidis	≥1 yr old or in adults in epidemics in close populations (military barracks)	**Petechiae on trunk, legs, conjunctivae**—beware of Waterhouse-Friderichsen syndrome (adrenal infarct)	Pen G Rifampin or fluoroquinolone prophylaxis for close contacts
Hemophilus influenzae type B	Formerly #1 cause in children, until vaccine	Now rare, but can cause epiglottitis	Cefotaxime
Streptococcus agalactiae	**#1 cause in neonates**	Acquired at birth	Ampicillin
Escherichia coli	Common in neonates	Acquired at birth	Cefotaxime
Listeria monocytogenes	Elderly/neonates, AIDS, diabetes, steroids	Difficult CSF Gram's stain/ Cx, Dx → blood Cx	Ampicillin
Staphylococcus aureus	Trauma/Neurosurgery	Wound infxn from skin	Oxacillin/Vancomycin

6. Subacute/chronic meningitis
   a. Si/Sx = per acute but evolves over wk → mo, +/– fever
   b. DDx = fungal, mycobacterial, noninfectious, other rare dzs
   c. Send CSF for fungal Cx, cytology, India Ink, TB PCR
   d. Fungal meningitis
      1) DDx = *Cryptococcus, Coccidioides,* other more rare dz
      2) ***Cryptococcus* commonly seen in AIDS**
         a) **India Ink stain will show *Cryptococcus* in CSF**
         b) **Opening pressure is commonly elevated**
      3) ***Coccidioides* blastocysts seen on CSF cytology**
      4) Tx = IV amphotericin B (intrathecal may be necessary)
   e. TB meningitis
      1) Usually occurs in elderly by reactivation, grave Px
      2) Dx is made by TB PCR of the CSF
      3) Tx = **RIPE: R**ifampin + **I**NH + **P**yrazinamide + **E**thambutol
   f. Other causes = sarcoid, cancer, collagen-vascular dz, drug reactions

B. ENCEPHALITIS

1. Si/Sx = similar to meningitis, but focal findings are evident

TABLE 7-5 Encephalitis

ETIOLOGY	DISEASE	SI/SX	TX/PX
Toxoplasmosis	1) Transplacental congenital dz → hydrocephalus/ mental retardation	**Multiple ring enhancing lesions → focal neurologic deficits**	Bactrim
	2) Adults exposed via cat feces get dz if immunosuppressed—**Toxo is the #1 CNS lesion in AIDS**	Toxoplasmosis antibody test very sensitive	Prophylax if CD4 ≤200/μL
HSV	**#1 cause of viral encephalitis**	**Olfactory hallucinations, bloody CSF, personality changes** EEG/MRI → temporal lobe dz	Acyclovir
Syphilis	**Meningovascular disease**	**Argyll-Robertson pupil**[a]	
	Parenchymal disease:		
	1) Tabes dorsalis = bilateral spinal cord demyelination	Pain, hypotonia, ↓ tone, ↓ DTRs ↓ proprioception, incontinence	IV penicillin
	2) Dementia paralytica = cortical atrophy, neuron loss, gliosis	Sx = psychosis, dementia, personality change	
PML[b]	Usually in AIDS, caused by JC virus	Diffuse neurologic dz	None, death inevitable

[a] Pupil accommodates but doesn't react to direct light.
[b] PML = progressive multifocal leukoencephalopathy.

C. ABSCESS

1. Si/Sx = headache, fever, ↑ ICP, focal neurologic findings
2. Risk factors = congenital R-L shunt (lung filtration bypassed), otitis, paranasal sinusitis, metastases, trauma & immunosuppression
3. Anaerobes & aerobes, gram-positive cocci & gram-negative rods can cause
4. Tx = antibiotics ⊕ **surgical drainage if >3 cm or if persists**
5. **Brain abscesses are invariably fatal if untreated**
6. Helminthic infections
   a. Cysticercosis (*Taenia solium*)
      1) Eggs transmitted by fecal-oral route
      2) **Encephalitis in Latin American immigrant is due to neurocysticercosis until proven otherwise**
      3) Tx = praziquantel ⊕ steroids (dead cyst → inflammation)
   b. Hydatid cysts (*Echinococcus*)
      1) Acquired by dog feces, can cause focal Sx & seizure
      2) If cysts rupture they can cause fatal anaphylaxis
      3) Tx = careful surgical excystation, mebendazole

III. Demyelinating Diseases

A. MULTIPLE SCLEROSIS (MS)

1. Unknown etiology, but ⊕ genetic & environmental predispositions, ↑ common in pts who lived first decade of life in northern latitudes

2. Si/Sx = relapsing asymmetric limb weakness, ↑ DTRs, nystagmus, tremor, scanning speech, paresthesias, optic neuritis, ⊕ Babinski sign
3. Dx = history, MRI, lumbar puncture
4. MRI → periventricular plaques, multiple focal demyelination scattered in brain & spinal cord (**lesions disseminated in space & time**)
5. **Lumbar puncture → ↑ CSF immunoglobulins manifested as multiple oligoclonal bands on electrophoresis**
6. Tx = interferon-β, may induce prolonged remissions in some pts
7. Px
   a. Variable types of disease, long remissions sometimes seen
   b. But can progressively decline → death in only a few years

B. GUILLAIN-BARRÉ SYNDROME

1. Acute autoimmune demyelinating dz involving peripheral nerves
2. **Si/Sx = muscle weakness & paralysis ascending up from lower limbs, ↓ reflexes, can cause bilateral facial nerve palsy**
3. **Most often preceded by gastroenteritis (classically *Campylobacter jejuni*)**, *Mycoplasma* or viral infection, immunization, or allergic reactions
4. Dx = Hx of antecedent stimuli (see above), CSF → **albumin-cytologic dissociation** (CSF protein ↑↑↑ without ↑ in cells seen)
5. Tx = plasmapheresis, IVIG, intubation for respiratory failure
6. Px is excellent for 80–90% of patients, will spontaneously regress
7. Respiratory failure & death can occur in remainder

C. CENTRAL PONTINE MYELINOLYSIS

1. Diamond-shaped region of demyelination in basis pontis
2. **Due to rapid correction of hyponatremia & in liver dz**
3. No Tx once condition has begun
4. Coma or death is a common outcome

IV. Metabolic & Nutritional Disorders

A. CARBON MONOXIDE POISONING

1. Seen in pts enclosed in burned areas, or during the start of a cold winter (people are using their new gas heaters) → bilateral pallidal necrosis
2. Si/Sx = headache, nausea, vomiting, delirium, cherry-red color of lips
3. Dx = elevated carboxyhemoglobin levels
4. Tx = hyperbaric oxygen (first line) or 100% O_2

B. THIAMINE DEFICIENCY

1. Usually 2° to alcoholism
2. Beriberi peripheral neuropathy due to Wallerian degeneration
3. Wernicke's encephalopathy: **Wernicke's triad = confusion (confabulation), ophthalmoplegia, ataxia**
4. Wernicke's is related to lesions of mamillary bodies
5. Tx: give thiamine prior to glucose (e.g., thiamine should be run in IV fluid without glucose) or will exacerbate mamillary body damage

C. B_{12} DEFICIENCY

1. Subacute degeneration of posterior columns & lateral corticospinal tract
2. Si/Sx = weakness & ↓ vibration sense (both worse in legs), paresthesias, hyper-

reflexia, ataxia, personality change, dementia—**note, neurological deficits can occur even if no hematologic abnormalities are present!**

3. Tx = B_{12} replacement (can use high-dose oral in lieu of injection)

D. WILSON'S DISEASE (HEPATOLENTICULAR DEGENERATION)

1. Defect in copper metabolism → lesions in basal ganglia
2. Si/Sx = extrapyramidal tremors & rigidity, psychosis, & manic-depression
3. **Pathognomonic → Kayser-Fleischer ring around the cornea**
4. Dx = ↓ serum ceruloplasmin
5. Tx = penicillamine or liver transplant if drug fails

E. HEPATIC ENCEPHALOPATHY

1. Seen in cirrhosis, may be due to brain toxicity 2° to excess ammonia & other toxins not degraded by malfunctioning liver
2. Sx = hyperreflexia, **asterixis** (flapping of extended wrists), dementia, seizures, obtundation/coma
3. Tx = lactulose, neomycin & protein restriction to ↓ ammonia-related toxins

F. TAY-SACHS DISEASE

1. Hexosaminidase A defect → ↑ ganglioside GM2
2. Si/Sx = **cherry-red spot on macula**, retardation, paralysis, blind
3. Dx by biopsy of rectum, or enzymatic assay, no Tx

V. Seizures (Sz)

A. TERMINOLOGY

1. Complex sz → loss of consciousness (LOC), simple sz does not
2. Generalized sz = entire brain involved, partial sz = focal area
3. Tonic sz → prolonged contraction, clonic sz → twitches
4. Absence = complex generalized sz → brief LOC
5. Grand mal = complex generalized tonic-clonic sz

B. PRESENTATION

1. Hx of prior head trauma, stroke, or other CNS disease ↑ risk for sz
2. Si/Sx = loss of bowel/bladder control, tongue maceration, postictal confusion/lethargy, focal findings indicate epileptogenic foci
3. If pt has Hx of seizures, always check blood level of medication

C. TREATMENT

1. Tx seizures if they recur or if pt has known epileptic focus

TABLE 7-6 Seizure Therapy

PARTIAL	GRAND MAL	ABSENCE	MYOCLONIC
Phenytoin*	Valproate*	Ethosuximide*	Valproate*
Carbamazepine*	Carbamazepine	Valproate	Clonazepam
Valproate	Phenytoin	Clonazepam	

*First-line choice.

2. Tx underlying cause: electrolyte, infxn, toxic ingestion, trauma, azotemia, stroke/bleed, delirium tremens, hypoglycemia, hypoxia
3. **Phenytoin causes gingival hyperplasia, hirsutism**
4. Carbamazepine causes leukopenia/aplastic anemia, hepatotoxic
5. Valproate causes neutropenia, thrombocytopenia, hepatotoxic
6. Stop Tx if no seizures for 2 yr & normal EEG

D. Status Epilepticus

1. Continuous seizing lasting >5 min
2. Tx with benzodiazepines for immediate control, followed by phenytoin loading & phenobarbitol for refractory cases
3. This is a medical emergency!

VI. Degenerative Diseases

A. Dementia vs. Delirium Differential

Table 7-7 Dementia versus Delirium

	Dementia	Delirium
Definition	Both cause global decline in cognition, memory, personality, motor, or sensory functions	
Course	Constant, progressive	Sudden onset, waxing/waning daily
Reversible?	Usually not	Almost always
Circadian?	Constant, no daily pattern	Usually worse at night (sun-downing)
Consciousness	Normal	Altered (obtunded)
Hallucination	Usually not	Often, classically visual
Tremor	Often not	Often present (i.e., asterixis)
Causes	Alzheimer's, multi-infarct, Pick's dz, alcohol, brain infxn/tumors, malnutrition (thiamine/B_{12} deficiency)	Systemic infection/neoplasm, drugs (**particularly narcotics & benzodiazepines**), stroke, heart dz, alcoholism, uremia, electrolyte imbalance, hyper/hypoglycemia
Treatment	Supportive—see below for specifics depending on the disease	Treat underlying cause, **control Sx with haloperidol instead of sedatives—**due to agitation pts are often given benzodiazepines or sedatives, but these drugs often exacerbate the delirium as they disorient the pt even more

B. Alzheimer's Disease (Senile Dementia of Alzheimer Type)

1. Most common cause of dementia—affects 5% of people over 70
2. Si/Sx = dementia, anxiety, hallucination/delusion, tremor
3. Occurs in Down's syndrome pts at younger ages (age 30–40)
4. Dx = clinical, with definitive diagnosis only possible at autopsy
5. Tx = anticholinesterase inhibitor can slow dementia, antidepressants & antipsychotics can be used for psychosis
6. Px = inevitable decline in function usually over about 10 yr

C. Multi-Infarct Dementia

1. Si/Sx = acute, step-wise ↓ in neurologic function, multiple focal deficits on exam, hypertension, old infarcts by CT or MRI

2. Dx = clinical, radiographic
3. Tx = prevent future infarcts by ↓ cardiovascular risks

D. PICK'S DISEASE

1. Clinically resembles Alzheimer's, more in women, younger age onset (50s)
2. Predominates in frontal (more personality changes seen) & temporal lobes
3. Dx = MRI → symmetrical frontal or temporal atrophy, confirm by autopsy
4. Tx/Px = as per Alzheimer's

E. PARKINSON'S DISEASE

1. Parkinson's disease = idiopathic Parkinsonism, mid- to late-age onset
2. Parkinsonism
   a. **Syndrome of tremor, cog-wheel rigidity, bradykinesia, classic shuffling gait, mask-like facies**, ± dementia due to loss of dopaminergic neurons in substantia nigra
   b. DDx = Parkinson's disease, severe depression (bradykinesia & flat affect), intoxication (e.g., manganese, synthetic heroin), phenothiazine side effects, rare neurodegenerative diseases
3. Dx = clinical, rule out other causes
4. Tx
   a. Sinemet (levodopa = carbidopa) best for bradykinesia
   b. Anticholinergics (benztropine/trihexyphenidyl) for tremor
   c. Amantadine → ↑ dopamine release, effective for mild dz
   d. Surgical pallidotomy for refractory cases
5. Px = typically progresses over years despite treatment

F. HUNTINGTON'S CHOREA

1. Si/Sx = progressive choreiform movements of all limbs, ataxic gait, grimacing → dementia, usually in 30s–50s (can be earlier or later)
2. Autosomal CAG triplet repeat expansion in HD gene → atrophy of striatum (especially caudate nucleus), with neuronal loss & gliosis
3. Dx = MRI → atrophy of caudate, ⊕ family history
4. Tx/Px = supportive, death inevitable

G. AMYOTROPHIC LATERAL SCLEROSIS (LOU GEHRIG'S DISEASE, MOTOR NEURON DISEASE)

1. Si/Sx = **upper & lower motor neuron dz** → muscle weakness with fasciculations (anterior motor neurons) progressing to denervation atrophy, hyperreflexia, spasticity, difficulty speaking/swallowing
2. Dx = clinical Hx & physical findings
3. Tx/Px = supportive, death inevitable, usually from respiratory failure