

Disease	Onset, CMs	Cardiac	Other	Rx
<b><u>GENETIC</u></b>				
<b>Congenital Myotonic dystrophy</b>	<b>Adolescent or adult onset. AD (Chr. 19). Most common muscular dystrophy in whites. Myotonia=delayed relaxation post contraction</b>	<b>Conduction defects</b>	<b>Frontal balding, testicular atrophy, DM 2 (insulin insensitivity), mental retardation or dementia</b>	
<b>Becker's MD (dystrophin)</b>	<b>x-linked recessive (males) <u>child to young adult</u> Less severe</b>	<b>yes with chf</b>	<b>mental retardation, calf pseudohypertrophy ^^CK early.</b>	
<b>Limb Girdle MD</b>	<b>autosomal recessive <u>child to young adult</u></b>	<b>no</b>	<b>normal mentation ±calf pseudohypertrophy</b>	
Ducheyne's MD (dystrophin)	x-linked recessive (males) early childhood	palpitations, sudden death	mental retardation, calf pseudohypertrophy	Prednisone
Emery-Dreifus= humor-peroneal atrophy	childhood	50% severe cardiomyopathy, A-V block & sudden death.	Normal mentation	
<b><u>ACQUIRED</u></b>				
Dermatomyositis	Prox Muscle weakness + skin rash. B cell mediated against endothelial antigens, resulting in capillary destruction and necrosis.		CPK 50xNI Bx: perifascicular atrophy. ^CA: <u>W/U for breast, ovary, &amp; prostate ca</u>	IVIG Prednisone Immunosuppressives
Polymyositis	F>M. Prox Muscle. Onset acute - subacute. Cricopharyngeal involvement. T cell mediated against muscle fiber antigens.		CPK 5-50 x NI. Bx: Inflammation	Prednisone, azothioprine, methotrexate
<b>Inclusion body myositis</b>	<b>In 50+ y.o, this is more common than polymyositis. Onset in years. Fingers, wrists, knees, feet. No cricopharyngeal involvement.</b>		<b>CPK 2-5x NI EMG: myopathic or mixed myo &amp; neuropathic Bx: Rimmed vacuoles &amp; inclusions; inflammation</b>	<b>No Rx available.</b>
Cushing's OR steroids	Proximal muscle weakness. Legs> arms		Other stigmata	
Thyroid disease	hypothy: cramps;CK10xnl.		Hyperthy: prox atrophy	
Hyper-parathyroidism	CK nl, ^ reflexes		M biopsy is non-specific	
Hypo-parathyroidism	Chvostok's, ^ reflexes, CK nl,^			
Statins	Proximal muscle weakness		Increased risk with cyclosporine or renal failure	
Other drugs	clofibrate, zidovudine (AZT), alcohol		pencilliamine, cimetidine, procainamide, chloroquine	

\*See CPT II deficiency (carnitine palmitoyl transferase deficiency) and Muscle Glycolytic Defects (e.g., McCardle's disease) below. Both have myalgias.

Case

A 70-year-old man cc: pain and stiffness in both shoulders and hips.

PE: atrophic shoulder girdle and gluteal musculature. ± inflammatory arthritis.

Lab: CK is nl. May be ^ ESR.

DX: Polymyalgia rheumatica

M biopsy: atrophy without inflammation.

Rx: NSAIDs; if no improvement, then give low-dose prednisone.

## MYOPATHY VERSUS NEUROPATHY

Myopathy	Proximal	mild atrophy	normal sensation	preserved DTRS
Neuropathy	Distal	prominent atrophy	decreased sensation	loss of DTRS

**Brachial plexopathy** has decreased movement or sensation in the arm and shoulder, caused by impaired function of the brachial plexus. Classically,

Radiation induced brachial plexopathy is painless and effects motor function.

Carcinoma induced brachial plexopathy is painful and effects sensory function.

## CONGENITAL MYOGLOBINURIA

Disease	Cms	IFT*	Defect	
CPT II def (Acyl CoA)	AR. Child & young adult. Precipitants: Fatigue & malnutrition. Myalgia, dark urine.	Neg	Can't oxidise fats	Lo protein, lo fat diet
Muscle glycolytic defects	Childhood. Dark urine post exercise. Muscle cramps	Pos	Deficiencies in myophosphorylase & phosphofructokinase	Ex training Progein & glucose diet

\*Ischemic Forearm exercise test, when positive, does not cause a rise in venous lactate.

An example of cervical dystonia is spasmodic torticollis ("wry neck"). Writer's cramp is an example of a segmental dystonia. Often, treatment of the focal dystonias involves the use of botulinum toxin to induce muscular weakness sufficient to decrease the dystonia but not severe enough to prevent usual functions.

Frederich's ataxia: A familial AD or AR ataxia. Onset in childhood. Initially there is pes cavus and kyphoscoliosis, then ataxia, absent DTRs, and positive babinski's. There is degeneration of the dorsal columns, corticospinal tracts, and spinocerebellar tracts.

Case: 61 y.o. woman with onset of seizures and mental confusion was admitted with a stroke like syndrome. Over ensuing months she developed multi-focal cortical lesions, lactic acidosis, a disturbed gait and progressive dementia. Muscle biopsy showed ragged red fibers and abnormal NADH tetrazolium reductase staining. MRI showed left temporal lobe lesion and 8 months later a right temporal lobe region.

Dx: **Mitochondria Encephalo-myopathies**, subtype MELAS: Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke Like Episodes. This case is atypical because most are diagnosed before age 40. Mitochondrial Encephalomyopathies are a group of diverse metabolic diseases associated with genetic defects in oxidative mitochondrial function usually diagnosed in children and young adults with the common features being muscle weakness, myoclonus, and abnormal NADH tetrazolium reductase staining on muscle biopsy. Most have maternal inheritance (via mitochondria), seizures and ragged red fibers on muscle biopsy. Brain lesions are cortical and multifocal and hence MS can be in the differential diagnosis (NEJM 2005; 353: 271).

Lyme meningitis & facial palsy occur within 3 months.

Lyme encephalo-myelitis occurs within years: memory loss, spastic paraesis, ataxia, bladder dysfunction, depression.

Akathisia: repetitive, purposeless movement with restlessness, usually 2<sup>nd</sup>ary to neuroleptics.

ACUTE UNILATERAL BLINDNESS July 30, 2004

AGE	PATHOLOGY	ETIOLOGY
< 40	Optic neuritis	<b>MS</b> , Viral, ICA dissection (mksap 12,q73)(with Amaurosis fugax)
40+	Optic vasculopathy	Giant cell arteritis. Retinal vein thrombosis(1). Ophthalmic artery embolus="amaurosis fugax" (transient).

(1) Q18, MKSAP12: Acute HA (may be unilateral), lateralizing paresthesias, papilledema, increased CSF pressure. Abnormal optic disc July 10, 2005

Visual loss	apparent swelling of optic nerve head	Condition	pathology	MS
No	yes	papilledema	increased ICP	no
No/ yes*	yes	optic neuritis	autoimmune	yes

Testing for optic neuritis Hx, PE:

- 1) Increased dimness following exercise
- 2) Increased dimness with fever
- 3) Swinging flashlight test for Afferent Pupillary Defect (Marcus-Gunn pupil)

\*Isolated optic neuritis. No MS. Rx= i.v. methylprednisolone. 1gm/day x 3 days. Q46. MKSAP13.

Ptosis differential diagnosis

Ptosis	Cr N 3 paralysis	mydri-asis	Sensory V forehead (Cr N5)	Process	Disease
Mild	No	Miosis (1)	Anhydriosis (1 <sup>st</sup> & 2 <sup>nd</sup> order lesions)	Horner syndrome (1)	1 <sup>st</sup> order:PICA, MS, tumors. 2 <sup>nd</sup> order:Lung Ca,lymphoma. 3 <sup>rd</sup> order:ICA dissect, migraine
mild or none(2)	Yes (eye is down & out) (2)	No	No	Ischemia to central motor fibers of 3 <sup>rd</sup> nerve. (2)	DM, HPT, atherosclerotic disease, SLE
yes	Yes	Yes (3)	No	Pressure on peripheral parasympathetic and central motor fibers of 3 <sup>rd</sup> nerve	Post. Communicating Artery Aneurysm, herniation, Tumor, ^ ICP (4)
Yes	Yes (5)	Yes	Yes	Pressure on multiple nerves (5)	Herniation, Cavernous Sinus Thrombosis with coagulopathy & Infection.

(1)**Horner syndrome** has less severe ptosis (sympathetic nerve innervates the superior tarsal muscle) and miosis (due to paralysis of pupillary dilation by the sympathetic nerve dilator); **this oculo-sympathetic nerve** (different from Cr Nerve 3) has 3 orders: (1) From hypothalamus via lateral brainstem and cervical cord to synapse in the intermedio-lateral cells column just above C8-T1, (2) exits out of T1 nerve root, over the apex of the lung and up to synapse 2 near the branch of the internal and external carotid, and (3) while nerves to the face (anhidrosis) travel with the external carotid artery, the remaining nerves travel to the orbit to innervate the radial smooth muscle dilator of the iris (miosis) and the superior tarsal muscle (ptosis).

(2) No up, down, or inward gaze. Cranial nerve 3 exits the brainstem at the ventral rostral mid-brain between the posterior cerebral artery and the superior cerebellar artery and enters the cavernous sinus. Inner nerve ocular motor nerve fibers are served by small vessels and are effected by DM & HPT, which spare the peripheral pupillary constricting fibers. Ptosis occurs because the motor nerve also innervates the levator palpebrae superioris muscle.

(3)Peripheral nerve parasympathetic pupillary constricting nerve fibers are impinged by aneurysms or tumor causing mydriasis. The impingement also effects the cranial nerve 3 inner ocular motor nerve fibers (Cecil, chapter 462).

(4) In herniation, pupillary dilation occurs first and then decreased light reflex.

(5) Cavernous sinus thrombosis also typically involves the 4<sup>th</sup> and 6<sup>th</sup> nerves.

## SOME DEMENTIAS AND THEIR CHARACTERISTICS

	Onset	Criteria, other features and treatment
Alzheimers	Gradual	1. Remote and recent (most prominent) memory. 2. 1+ other cognitive problem: Agnosia, aphasia, apraxia, or decreased executive function; 3. No delirium; 4. Significant decrease in ADLS. CT: Atrophy of hippocampus then temporal, parietal, and frontal lobes. Risk factors: trauma, family history. Rx: Vit E 2,000 IU/day; NMDA antagonist+anti-chol'erase inh (2)
Vascular Multi-infarct	abrupt	step-wise progression. CVA is concurrent or precedes dementia within the past 3 months. Findings on imaging are asymmetric.
Dementia with Lewy Bodies		1) Concurrent or late memory loss; there may be decreased attention; fronto-cortical skills, visual-spatial defects; 2) 2+ of <b>hallucinations, parkinsonism</b> , 3) Other: syncope, falls, fluctuating consciousness, sensitivity to anti-cholinergics, REM behavior disorder. Sensitive to risperidone (avoid). Rx: Response to anti-cholinesterases may be dramatic. For movement disorder, give carbidopa/levo dopa but not if psychotic. SSRIs, valproate, or quetiapine (Seroquel).
Front-temporal Lobar Dementia (FTLD): FTD	"Insidious" Gradual	1. Social interpersonal defects, 2. Self regulation defect, 3. Loss of insight, and 4. Emotional blunting. Pronounced or asymmetric frontal atrophy on MRI. Rx: similar to DWLB.
FTLD: Semantic	"	Memory deficit
FTLD: progressive non-fluent aphasia	"	aphasia
Prion disease: Creutzfeldt Jakob(3)	Rapid: weeks to death in 3 to 6 months.	A) Rapid onset of dementia. B) Either EEG with periodic sharp waves OR CSF with 14-3-3 protein. C) 2+ of these: 1 myoclonus, 2 pyramidal (motor weakness) or extra-pyramidal (Parkinsonian) disease, 3 visual or cerebellar defects, 4 akinetic mutism. Ddx: angitis, Hashimoto's encephalitis, Lyme. If there is a question, do brain biopsy to r/o primary angitis and or do anti-microsomal (anti-peroxidase) and antithyroglobulin Antibodies to r/o Hashimoto's encephalitis, which is treated with steroids.
Depression		Immediate term memory is defective

(1) Epsilon 4 allele homozygosity on chromosome 21 elevates risk by 3 fold. Pathology: intracellular neurofibrillary tangles and extracellular neuritic plaques. The current Alzheimer's model of pathogenesis is that altered cleavage of the amyloid precursor protein generates the amyloid protein, A-beta peptide, which then binds to a protease inhibitor enzyme complex, permitting the accumulation of extracellular proteases, causing neuronal degeneration. A therapeutic strategy may be to inhibit the generation of amyloid. (NEJM 2005;352:862.)

(2) The Nmethyl DAspartate antagonist, memantine (Namenda) plus an anti-cholinesterase inhibitors (Donepezil) or rivastigmine (Exelon).

(2) Devoid of DNA or RNA, prions are infectious proteins that cause CNS degeneration. Prions reproduce by binding to the normal cellular isotype of the prion protein and causing a conformational change to a pathogenic isoform of the prion protein. The mechanism is unknown. \*Sporadic CJD cases account for 85% of human cases. \*The median age is in the 50s. \*Variant CJD, associated with bovine spongiform encephalopathy(mad cow) presents at any age.

HIV results in dementia complex, peripheral neuropathy, myopathy, and myelopathy, but not motor neuron disease.

Peripheral neuropathies common to HIV infection include distal sensory neuropathy, demyelinating motor, mononeuritis multiplex, and cytomegalovirus-associated neuropathy.

Myopathy is from either HIV infection itself or from azathioprine.

Binswanger's disease: Rare dementia/ insidious course/ long-standing hypertension and/or atherosclerosis

\*has diffuse subcortical white matter damage.

### Vitamin B12 deficiency (subacute combined degeneration)

\*Often in chronic alcoholics.

\*Loss of vibration and joint position sense

\*Brisk deep tendon reflexes (dorsal column and lateral corticospinal tract dysfunction)

\*A subcortical type of dementia.

“Up to 30% of patients with neurologic complications resulting from B 12 deficiency do not have a macrocytic anemia at the time of presentation. Furthermore, serum vitamin B12 levels may be in the normal range in these patients (200 - 800 pg/ml in 31-50% with clinical B12 def (Pennypacker, 1992; Lindenbaum, 1995)).

Methylmalonic acid and homocysteine levels are characteristically high in patients with physiologic vitamin B12 deficiency.” Also, see Q 11, mksap 12. In those over 65, prevalence of B12 deficiency is 14% .

## REVERSIBLE CAUSES OF CONFUSION, DEMENTIA, AND/OR MEMORY LOSS

**Mnemonic = Mid Cat. (Metabolic, Infectious, Deficiencies, CNS, Autoimmune, Toxins.**

### METABOLIC:

Hypoxemia: CO poisoning, Obstructive Sleep Apnea

Hypothyroidism

Electrolyte abnormalities, including glucose, Mg, & Ca

Ammonia (hepatic failure)

Azotemia (renal failure)

Wilson’s Disease: AR disease. Neurologic signs include movement disorders (dystonia, tremor), unsteady gait, dysarthria, rigidity, personality changes, and unstable behavior. (MRI deposits in basal ganglia; ^ AST, ALT, K-F rings in 99%; Liver BX is gold standard)

Minimal Work Up

Hgb, CO level, ABGs

TSH

lytes, Ca, Mg

LFTs

Bun/Creat

### INFECTIOUS

Lyme

Syphilis

HIV

Encephalitis

Meningitis

Brain Abscess

Whipple’s Disease: 4 cardinal CM’s: Weight loss, abdominal pain, diarrhea, arthralgias. Also, hypotension, skin pigmentation, lymphadenopathy. T. whipplei (gm + bacillus) PAS positive material in lamina propria and villous atrophy. PEN, Strep and TMP/SMX x 1 year.

Lyme titer

VDRL

ESR

### DEFICIENCIES

B1 Thiamine: Wernicke’s: Ophthalmoplegia, ataxia, mental deterioration (confabulation due to temporal lobe injury). Korsakoff’s anterograde memory loss. Causes are alcoholism, anorexia nervosa, hyper-emesis, gastrectomy, hemodialysis.

B6 Pyridoxine. Replace.

B12 deficiency : homocysteine and methyl malonic acid are ^ . B12 level is inadequate. Up to 30% lack macrocytosis. Q11, MKSAP12.

B complex (niacin): Pellagra: Dementia, Diarrhea, Dermatitis.

CNS Subdural hematoma

NPHC

Depression

Non-contrast CT scan

AUTOIMMUNE: Sarcoid; SLE; vasculitis; Hashimoto’s encephalitis. Anti-thyroid Abs

### TOXINS, DRUGS & DRUG WITHDRAWAL SYNDROMES

Drugs: Anticholinergics, sedative-hypnotics, NSAIDs (indomethacin), Anti-hypertensives, anti-Parkinson drugs

Substance withdrawal: ETOH, benzodiazepines, tricyclics, barbiturates.

Toxins: Metals: Lead (“lead colic”, arthralgias, myalgias, HA, anorexia, decreased short term memory, anemia, peripheral neuropathy, nephropathy). Mercury (memory loss, depression, anxiety, intention tremor, sialorrhea, nephrosis) Pb, Mg levels, Tox screen, History

NOTE: Vascular dementia responds to donepezil, an anti-cholinesterase inhibitor (MKSAP 13 update; Malouf, 2004).

DEMENTIA'S HALL MARK ASSOCIATED FINDINGS:

Associated symptom	Diagnosis
Abrupt onset + focal neurologic findings	Vascular dementia
Parkinsonian symptoms + visual hallucinations	Dementia with Lewy bodies
Psychiatric and personality changes	Fronto-temporal dementia.

FOUR TYPES OF MEMORY (NEJM 2005; 352: 692.

Memory type	Function	Anatomic location	Typical disease effecting
Episodic	Personal experiences: e.g., What did I eat for supper last night?	Medial temporal lobes, hippocampus, parahippocampus	Alzheimer's Korsakoff's [After an ictus, remote memories are best preserved (Ribot's law).]
Semantic	Store of knowledge: Who is the first President of the U.S.?	Infero-Temporal lobes	Alzheimer's Trauma
Procedural	Driving a stick shift. "Muscle memory"	Cerebellum and Basal Ganglia	Parkinson's/ Huntington's/ Depression
Working	Attention, concentration, and short term memory: Remembering a phone number from 411 to place a call the next minute.	Pre-frontal cortex	Normal aging/ Vascular/ Alzheimer's/ Vit B12 def C-P bypass MS

Fluid moves from choroid plexus into lateral ventricles to 3<sup>rd</sup> ventricle to 4<sup>th</sup> ventricle, thru medial and lateral apertures, to subarachnoid space and is absorbed by arachnoid granulations into the venous sinuses, especially the superior sagittal sinus.

MINI-MENTAL STATE EXAM

Orientation: Time 5/ Place 5

Name 3 objects, ask patient to repeat them.3  
Repeat until patient learns all three.

Serial sevens Or world backwards 5

Recall: ask for the 3 objects. 3  
Language and executive function  
Point to a pencil and a watch and ask patient to name them 2  
No ifs ands or buts 1  
Follow a 3 stage command: 3  
Read and obey the following written statement: "Close your eyes" 1  
Write a sentence 1  
Copy 2 intersecting pentagons 1

Total is 30.

Abnormal is less than 23. Positive LR =9.Negative LR 0.2

Case (Q68), Neuro, MKSAP 12.  
68 yo Woman, 1 yr fluctuating confusion, inattention & visual hallucinations. Has Sjogren's syndrome. Ataxic gait.  
B12, VDRL & MRI are normal.  
Dx: R/o treatable dementia:  
LP: Increased IgG index (IgG-CSF/PRotein-CSF) and synthesis rate (IgG-CSF/IfG-Serum)  
Brain Bx= Perivascular inflammation.  
Dx: Vasculitis  
Rx= hi dose prednisone.  
Dementia resolved within 10 days.

Disease	CM's	Lab	Ddx	Rx
Amyotrophic Lateral Sclerosis (Upper & lower motor neuron gliosis and loss). <b>Motor only, upper &amp; lower</b>	Bulbar (jaw, face, palate, larynx, tongue) + extremities and/or spine. Spasticity, ^ reflexes, + Babinski. Fasciculations, atrophy & weakness. <u>Profound Weakness</u> . DTRs <b>increased</b> . Familial ALS:AD	EMG: Nerve conduction + for N disorder. Excludes MFMN, N-M and muscular disorders. - CT of Head. (Glutamate accumulates in lateral columns due to transporter defect.)	Structural Tumor Deficiencies 2 Metabolic 2 Toxic Auto-immune Bulbar 3 (1)	Riluzole (modest increase in survival.)
Multiple sclerosis (Plaque formation on myelin of CNS, including brain, optic nerves, & Spinal cord.) Risk is 50 x in a child of an MS patient. Mononeuritis multiplex, caused by infections, autoimmunity, or DM, simulates MS. <b>Central sensory &amp; Upper Motor</b>	Age 20 - 50, peaks at age 30. Presentation: Weakness 35% Sensory loss 37% Paresthesias 24% Optic neuritis 36% Diplopia 15% Ataxia or vertigo 17% Bladder 4% Dementia 2% (then up to 70%) <b>Fluctuating. ^ T &gt; ^ Sx's.</b> Lhermitte's. Marcus Gunn pupil. Internuclear ophthalmoplegia (2) DTRs are <b>increased</b> .	CSF: TP <b>Normal or slight ^</b> . <b>^IgG/Albumin.</b> Oligoclonal bands in 75%. Free kappa light chains (more specific). WBC 10-20/uL. Myelin Basic Protein & myelin oligodendrocyte glycoprotein. <b>MRI, Brain: Hyper-intense periventricular white matter, &gt;0.5cm, ovoid.</b> "Clinical & Laboratory evidence of nervous system lesions disseminated in time & space." (RR=9 with hi EBV Ab titer (JAMA2005;293:2496)	Neuromyelitis optica; encephalomyelitis; transverse myelitis. VATIGPM: Vasculitis S-D AVM CADASIL SLE, Sjogren's, Neurosarcomoid, Behcet's, APLAS Paraneo; spine mets, lymphoma HIV, HTLV-1 Lyme, Syphilis. Mitoch cytopths Cervical spondy Conversion dsrdr B12, E or Cu def Leukodystrophy	<u>Depression</u> <u>Fatigue:</u> Cool, exercise, Amantadine. Methylphenidate, SSRIs <u>Pain:</u> Carbamazepine. <u>Spasms:</u> Baclofen (gaba a)diazepam. <u>Bladder:</u> oxybutynin <u>Acutely:</u> Steroids, plasma exchange. Rlpsng-remtng: Steroids IFN-B, Glatiramer natalizumab mitoxantrone,
Guillain Barre (Acute inflammatory demyelinating polyneuropathy... demyelination w/ lymphocytic infiltrate) <b>Peripheral Nerves &amp; Lower Motor neurons.</b>	Acute. Symmetric. Tingling & stabbing pains of <b>feet</b> ****>>>Ascending weakness in legs, arms, cranial nerves, &/or diaphragm within hours. Most severe in 14-30 ds. It often follows Cambylobacter inf'n's (also Mono, CMV, Herpes, mycoplasma). Decreased swallowing & Ventilating. Dysautonomia. <b>DTRs are decreased to absent.</b>	Diagnosis is established by EMG, which shows decreased conduction velocity and partial motor conduction block.  CSF: Protein is increased (e.g., above 50 mg/dL). WBC's normal.	Botulism(6) <b>Tick paralysis</b> <sup>7</sup> (asc par+ataxia) Lyme, Inf'n N-hexane inhal, Porphyria Cord comprssn Mononeuritis multiplex: DM, Vasculitis	HVIG. Then early Plasmapheresis to x complications. <u>Steroids can harm</u> <u>Intubate at VC</u> <u>&lt;15ml/kg. Death is via autonomic dysfunction; BP fluctuations.</u>
Myasthenia Gravis (Autoantibodies induce acetylcholine receptor deficiency at motor endplate.) <b>Lower Motor</b>	Age peaks: W:20s. M:50-70. Fluctuates hourly. Worsens by ^ T, excitement, menses or on repetition. Food remains in mouth after swallowing: LR+13. Snarl. Difficulty combing hair, climbing stairs. Dyspnea. Peek sign(sclerae show after closing eyes x30 sec):+LR30, -LR:0.9 Ice Cube Test:LR+28,LR-0.14 Sleep test:LR+53,LR-0.01(4) <b>DTRs are preserved.</b>	EMG is definitive. ACHR or MUSK (Muscle specific Kinase) Antibody is positive in >90% with moderate to severe disease. 50% in ocular disease. 25% in those in remission. Edrophonium, anticholinesterase, relieves sx's but may cause bradycardia or sinus arrest!! Do MRI for thymoma (present in 15%).	Lambert Eaton(3) Rare congenital defects. Botulism (6) Organo-phosphate poisoning.	Pyridostigmine. Neostigmine. <u>Thymectomy</u> (5) Induce remission: Steroids. Azothioprine. Cyclosporine. Mycophenolate mofetil. Intractable: Plasmapheresis HIVIG.

(1) Ddx: Limb Onset: Cervical spondylotic myelopathy, Paraneoplastics, heavy metal intoxication, hyperthyroidism, hyperparathyroidism, B12 v, hexosaminidase v, and MFMN. For Bulbar Onset think: Myasthenia Gravis, Brainstem Tumor. Not multifocal motor neuropathy. See below.

(2) Lhermitte's: Shock like pain on movement of neck. Marcus Gunn pupil: Afferent pupillary defect on swinging flashlight. Internuclear ophthalmoplegia: Adducting eye is weak, abducting eye has nystagmus, and normal convergence..

\*\*\*\***Check for decreased reflexes in lower extremities... early sign, which will tip off to serious illness and exclude anxiety.**

(3) Eaton Lambert Syndrome, in 60% is a paraneoplastic syndrome, associated with small cell lung cancer (so get a CXR) with 4 features distinguishing it from myasthenia gravis: 1) Typically absent ocular and pharyngeal weakness, 2) Dysautonomia: dry eyes, dry skin, postural hypotension, gastroparesis, incontinence, erectile dysfunction, 3) Increasing strength with repetition, 4) Pre-synaptic motor nerve antibodies to calcium channels (rather than post synaptic antibodies to ACH receptors).

(4) LR's are from JAMA 2005;293:1906. The Ice Cube test has latex finger with ice over ptotic eye for 2 minutes. The Sleep test puts patient in dark room for 30 min with resolution of ptosis or removal of peeking. Anticholin test:+LR:9-67;-LR:01-27

(5) For MG, by RCTs, thymectomy gives improvement in 85% and cures in 35% (less in elderly); in kids, it may harm immunity.

(6) Botulism has **descending** paralysis (diplopia, dysarthria, dysphonia, dysphagia) with autonomic signs, hypotension, and urinary or fecal retentin.

(7) Tick paralysis is also ascending with paralysis. Removing the tick can supposedly cure the paralysis !

### HEADACHE (1) July 9, 2005

Condition	Profile	Character	Location	Precipitants	Onset, duration, frequency	Movement	Other distinguishing features	RX
Migraine Criteria A. (3)	W>M FH in 80%	pulsating	unilateral or bilateral	stress	4 to 72 hours	Still.	See criteria (A). Autonomic features (see below) are less common than in cluster HA. Hemiplegic migraine, a variant, may take weeks to recover or be permanent. R/O TIA, ICA dissection, CADASIL	NSAIDs ASA-caffeine-butalbital. Ergotamine, Sumatriptan(4). Metachlopramide(8) Prophylaxis: Propranolol, topiramate(5), amitriptyline.
Cluster	M>W. FH in 70%	Boring	Always unilateral. Supra or peri-orbital.	alcohol	quick start 0.25-3 hrs 8x/day or QOD Circadian.	Pacing	Autonomic features: ptosis, miosis, tearing, rinnorrhea, lid edema	<b><u>O2 inhalation 7L/m mask.</u></b> Subcu sumatriptan Prophylaxis: Verapamil, lithium, prednisone 50/day with taper. Valproic acid.
Hemi-crania		Fluctuates	unilateral				Autonomic features: ptosis, miosis, tearing, rinnorrhea, lid edema	<b><u>Indomethacin</u></b> up to 150 mg. Specific !!
Tension (B)		bandlike	bilateral		minutes to days	mobile	Photo or phono phobia may occur but not both. There is <u>no</u> N or V.	NSAIDS. Biofeedback. Cognitive behavioral Rx. Preventive: tricyclics.
Trigeminal neuralgia	elderly	shocklike, stabbing	eye, maxilla, jaw	chewing, eating	seconds		facial spasms (tic doloreux). <b><u>Causes:</u></b> Temporal arteritis, Tumor, MS, aneurysmal compression. There is nerve irritation via artery in 85%.	Carbamazepine/ Baclofen Phenytoin/ Gabapentin Surgery
Idiopathic intra-cranial HPT(2)	young obese white	non-pulsating	diffuse	worse on wakening.	Daily. Lasts hours	Still	1. Mono or bilateral visual loss x 30 seconds. 2. Tinnitus. Also, papilledema & 6 <sup>th</sup> N palsy. LP opening pressure > 20 cm.	LPs Weight Loss Lo Na diet. Acetazolamide. Lasix. Neurosurgery if visual field loss.

A: Migraine w/o aura: 4-72 hrs. 5+ attacks. 2+ of Unilateral/Pulsating/Moderate to severe/Decreased activity. 1+ of N or V/Phono or photophobia.

Migraine w/ aura: 2+ attacks: 1+ change without motor weakness of: Sensory/Visual/Speech reversible defect. 2+: Unilateral visual or sensory change/ onset > 5 minutes/ duration 5-60 minutes/ HA within 60 minutes of onset/ No other explanation.

(1) EMERGENCIES or DON'T MISS (OTHER): Subarachnoid hemorrhage, CSF leak (gives postural headache), cerebral and cortical vein thrombosis, temporal arteritis, glaucoma, encephalitis, ICA dissection with scotoma simulating migraine, vertebral artery dissection, abscess, tumor, reversible cerebral vasoconstriction syndrome.

CHRONIC: cervical spondylosis, obstructive sleep apnea, CADASIL.

Headaches precipitated by cough, sneezing, or straining should prompt an investigation to rule out a posterior fossa mass.

(2) AKA: pseudo-tumor cerebri. (3) Secondary causes: Vit A, Tetracyclines, OCPs, Addison's disease, hypoparathyroidism.

(3) CADASIL, Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, presents in the 30 y.o. with migraines, mood disturbance, focal neurologic deficits, strokes and dementia; no lab confirmation is available, with possible exception of skin biopsy.

(4) Where there is hyperalgesia of the scalp (occurs in 70% of patients), taking the sumatriptan within 30 minutes of prodrome or onset will enhance success.



- (5) Topiramate has associated weight loss. Amitriptyline has associated weight gain.
- (6) Benign coital headache syndrome: repeated headaches during coitus, with each lasting about 1 h. If the patient had only a single sudden coital headache, an investigation for a cerebral aneurysm would be appropriate.
- (7) Postural Headache from intracranial hypo tension & spontaneous CSF leaks. MRI: Subdural fluid accumulation, sagging brain, cerebral vein congestion. Rx=Blood patch via injection of 10 - 100 cc of autologous blood. (Also diagnostic). See JAMA 2006; 295: 2286.
- (8) Metoclopramide, the anti-emetic, is effective to prevent allodynia (which usually takes 1-4 hours to occur after the migraine begins).

**Migraine criteria without aura:**

- A. Lasts 4 - 72 hrs;
- B. Must have 2 of the following: moderate-to-severe, throbbing, unilateral, interferes with activity.
- C. Must have 1 of the following: Nausea & vomiting, phono & photophobia.

**Migraine prodrome:** Premonitory phase: yawning, mood alteration, fatigue, neck stiffness.

**Migraine with aura:** Marching symptoms lasting 60 minutes, followed by headache of scotoma, flashing light, zig-zag light, paresthesias, face or expressive or receptive language dysfunction, paresthesias, odors.

**Migraine prevention** (Level I evidence...at least 2 RCTs):

- 1) anti-epileptics: topiramate (weight loss), valproic acid (divalproex sodium & sodium valproate)(weight gain);
- 2) Anti-depressant: amitriptylline (weight gain; pregn:C);
- 3) Beta blockers: Metoprolol; propranolol (C);
- 4) Herbal: extract of butterbur root (Petasites hybridus);
- 5) Non-pharmacologic: relaxation therapy; biofeedback.

**Migraine triggers:** alcohol, exercise, menstruation, stress, weather, sleep deprivation, hunger, high altitude, air travel.

No OCPs in patients with migraine with aura.

Anti-emetics can be used in pregnancy. The safety of triptans is not well established.

Case:

- \*Severe eye pain (usually unilateral) with
- \*nausea, vomiting.
- \*colored halos around lights,
- \*loss of visual acuity.
- \*red eye
- \*pupil is dilated and fixed.
- \*Emergency tonometry will verify the diagnosis.

**Dx=ACUTE CLOSED ANGLE GLAUCOMA:**

\*Rx: urgent treatment with hyperosmotic agents, then surgical or laser iridotomy.

Case: An elderly man with glaucoma.

New onset bronchospasm.or bradycardia

Dx=Side effect of Rx for Primary OAG, beta adrenergic agonists (betaxolol, carteolol, levobunolol, metipranolol, timolol. as a topical agent but systemically absorbed. (Angle-closure glaucoma is less common than is primary open-angle glaucoma, which is asymptomatic and is usually detectable only through measurements of intraocular pressure at a routine eye examination.)

**STROKE & TIA DIAGNOSIS:**

**Differential diagnosis of stroke:**

Acute facial paresis, arm drift and abnormal speech: (absence of all three makes CVA unlikely.)

Differential diagnosis:

Don't miss or urgent: Status epilepticus, encephalitis, drugs, tumor, myasthenia gravis, abscess, infection unmasking a prior stroke

Other: Syncope, MS

**Differential Diagnosis of stroke etiology:**

1. Hemorrhagic stroke (including cocaine induced)
2. Subarachnoid hemorrhage
3. Atherosclerosis, artery-to-artery embolism

4. Cardiac embolism: PFO, AFIB, abnormal valve, recent MI (<4 weeks), LV thrombus, atrial myxoma, endocarditis
5. Carotid dissection (age < 40& Horner's syndrome; occurs in setting of cocaine, marfan's, MVA, manipulation of neck)
6. Coagulopathies:
  - \*Deficiencies of Protein C, protein S, and anti-thrombin III.
  - \*Anti-phospholipid Antibody syndrome.
  - \*Homocysteine

Inflammatory arteriopathies: temporal arteritis; Takayasu arteritis

## NOTES ON STROKE MANAGEMENT:

**Evolving Stroke:** NOTE: Stroke unit care teams are more effective (MKSAP 13 Update).

1. I.V. t-PA (Tissue Plasminogen Activator) must be given within 3 hours of onset. Onset is rigidly defined. If patient slept at 10 PM, woke at 2 AM with right sided weakness, his stroke started at 10PM.
3. For MCA strokes in the 6 hour time frame, intraarterial delivery of rTPA shows benefit based on RCTs and is becoming the standard of care in stroke centers with qualified interventionalists.
4. Contraindications to tPA include 1) Improving or minor symptoms, concurrent seizure, BP >185 systolic or >110 diastolic, glucose <50 or >400, SBE, and recent MI. The others are bleeding related.
5. Give Normal saline; not: a) Glucose containing solutions (Rx hyperglycemia), or b) Hi O2 delivery.
- 6a. BP control only if Systolic >220 or diastolic >120, if thrombolysis is planned, or if other organ damage is occurring. Lower by 15%. Hypertension usually resolves in 24 hours. (MKSAP 15)
- 6b. BP target for thrombolysis is 185/110. After thrombolysis it is 180/105 (MKSAP 15 Upd.)
7. Protect the Airway. Avoid aspiration. Head of bed is ideally 0-15 degrees, but higher if dysphagia. Compromise is about 30 degrees.
8. Two absolute contraindications to heparin: SBE or hemorrhagic CVA.
9. Give minidose heparin and TEDs for DVT protection.
10. Also control glucose: give insulin if plasma glucose is > 140 mg/dL. Monitor to avoid hypoglycemia.
11. Avoid fever & dysphagia.
11. Post stroke hemiplegia: B12 and folate reduce fracture by 7% (absolute reduction), NNT%=13 (JAMA 2005;293:1082) possibly by changes in bone matrix but not by improving mineralization.
12. ASA 325mg; delay this by 24 hours when giving t-PA.
13. DVT prophylaxis: 5,000 Units unfractionated heparin BI. (Compression for patients who cannot receive anti-coagulation)
14. Recommendations on full dose heparin: American Stroke Association/American Heart Association– reaffirmed by American Academy of Neurology (Stroke, May 2007;38:1655): “urgent coagulation is not recommended for patients with acute ischemic stroke” (UpToDate 11/07). Possible exceptions: cardioembolism from ongoing thrombus (e.g., valvular lesions), large artery intramural thrombus, arterial dissection. Heparin is contraindicated in “large” infarcts (1/3 of MCA supply) or uncontrolled hypertension.
15. NIH Stroke scale. 15 items: Level OC/Orientation/Follow commands/Gaze paresis/Field cut/Facial paralysis/R-L-U-L weakness/Limb ataxia/Sensory/Aphasia/Dysarthria/Hemineglect.
 

Case: 50 yo man with 5 hour history of MCA stroke.

What is best management?

Rx: intraarterial delivery of rTPA
16. For cerebellar CVA (limb ataxia, dizziness, clumsiness, nausea, nystagmus) Obtain MRI. Consider possible need for evacuation.
17. Hydrocephalus : Headache, personality changes.

Lab studies: remember the PT, PTT & platelets. Consider Utox, alcohol, pregnancy test, LP, EEG.

**TIA (or Secondary Prevention.. Considerations are similar)**

A. Definition: 1. Brief symptoms (< 1 day (more rigorously less than 1 hour)), 2. No evidence of acute infarction on neuroimaging.

**B. Differential diagnosis of TIA:** BPV, MS, migraine, myasthenia, Todd's paralysis, syncope, subdural hemorrhage, TGA (amnesia resolving in 24 hours)

C. For hospitalization: ABCD2 score for hospitalization: age 60+ = 1/ BP 140+/90+ = 1/ Clinical, hemiparesis = 2, Speech = 1/ Duration 10-59 minutes = 1/ 60+ minutes = 2/ Diabetes = 1. Scores of 4-7 should be hospitalized.

D. Work up:

\*On Day 1:

Blood for hypercoagulability studies

EKG

TT Echo

Carotid US, including transcranial doppler

MRA

\*On Day 2: Get TEE (best for ascending aorta,

\*On Day 3: If no answer as to etiology, do gadolinium MRA.

**RX long term:**

\*Statin

\*ASA 325mg+Clopidogrel ER 75 mg (Aggrenox) prevent both MI +ischemic stroke(MKSAP 13).

\*ACEIs probably are beneficial, per PROGRESS and ALLHAT.

\*BP control.

\*Exercise lowers the risk of stroke.

\*No sympathomimetics, including ephedrin or pseudo ephedrine. (Note that cocaine can cause either ischemic stroke as well as hemorrhagic intracerebral stroke.)

**\*Indications for endarterectomy are:**

\*surgeon's complication rate < 6%

\*5 year life expectancy

\*Asymptomatic or symptomatic, 70% - 99% occlusion. (Do within 2 weeks of TIA).

\*Symptomatic, 60%-69% occlusion, men only, surgical complication rate <3%.

\*Do not do endarterectomy if the complication rate exceeds 3%

Indications for stenting (can be as effective as endarterectomy, NEJM 2004;351:1493) would be an inaccessible carotid lesion, significant co-morbidities, no prior ipsilateral arterectomy.

**Arterial dissection management:**

**Hemorrhage in the cortex ("lobar hemorrhage")?** Amyloid,vascular malformation, tumor or infection.

**Hemorrhage in basal ganglia (~50%), pons, cerebellum, or thalamus.** HTN.(Cecil, 1. Ch. 441)

**Hemorrhagic stroke– Intracerebral Hemorrhage**

Causes:

HPT (basal ganglia, thalamus, pons)

Meds: Anti-coagulants, thrombolytics, sympathomimetic (cocaine), ETOH

Coagulopathy.

Vascular: Aneurysm, Vasculitis, amyloid

Neoplasm

Trauma

Infection.

Case: Sudden focal Deficit

**Headache (>95% in subarachnoid hemorrhage and ~ 55% in intraparenchymal bleed).**

**Vomiting** (Early in the course, vomiting suggests increasing intracerebral hemorrhage)

**Dx: Intracerebral hemorrhage.**

Further w/u to exclude **tumor or vascular malformation** if age < 45, no h/o HPT, atypical location, unusual appearance, or cocaine use (associated with higher incidence of vascular malformations).

Note: CT can **not** reliably visualize the cerebellum and brainstem due to bony structures.

RX: >No Anti-coagulation. >Watch Airway. >BP Control.

>Surgical intervention for cerebellar hemorrhage (shown to be beneficial)

>For ICP due to intra-parenchymal hemorrhage the Rx includes:

\*Hyperventilation (short term efficacy)

\*Mannitol

\*Hypertonic saline

\*Ventriculostomy.

\*BP control is a controversial area. Do NOT use nitroprusside

\_\_\_\_\_ Case

**HA, nausea, vomiting, progressing to ipsilateral ataxia, dysarthria and gaze paresis, with contralateral hemiparesis, progressing to coma:**

**Dx= >> Cerebellar hemorrhage and swelling. Rx = EMERGENCY EVACUATION**

**Hemorrhagic stroke– Subarachnoid hemorrhage**

**Familial Aneurysm Syndrome:** If there is an aneurysm in 2 first degree relatives, what is the risk of aneurysm in the patient? Ans: 8%. It is unknown whether screening is cost effective.

Risk factors are: Polycystic kidneys, Ehlers Danlos Syndrome, Pseudo-xanthoma elasticum, corticosteroid remediable aldosteronism (a rare aldosteronism reversed by cortisol).

CM's: "Worst HA of my life." "New migraine", Sudden onset. N, V, neck pain, seizure.

Lab: Immediately do Non Contrast CT. If negative, do LP for RBCs and xanthochromia.

**This is often due to Arteriovenous malformations (AVMs)**, composed of tangles of arteries connected directly to veins without intervening capillaries, can be found anywhere in the brain.

Three complications of subarachnoid hemorrhage:

1. Rebleeding.
2. Vasospasm with delayed brain ischemia (Use Nimodipine)
4. Hydrocephalus.

Incidental berry aneurysms:

<7 mm: repeat imaging, yearly

7-10 mm: Consider intervention.

>10 mm: intervene.

Case (MKSAP 12, Neuro, Q 18). 18 yo woman on OCPs, severe L HA, N,V, photophobia, numb L arm & face x 10 min. PE: Blurry optic discs. CT and LP negative.

Dx: r/o/ cerebral vein thrombosis. Do MR venography.

Multifocal Motor Neuropathy (NEJM 2007; 357: 2707.)

Diagnostic criteria:

\*Weakness without objective sensory loss in two or more nerves.

\*In early stages, the absence of diffuse symmetric weakness.

\*Conduction block in 2 or more nerves outside entrapment sites.

- \*Normal sensory nerve conduction velocities across the same segments with motor deficit.
- \*Normal sensory nerve conduction studies in a minimum of 3 tested nerves.
- \*Absence of upper motor neuron signs (spastic tone, clonus, Babinskis, pseudobulbar palsy).

Treatments:

1. IVIG.
2. Helpful but less so: Plasma exchange; cyclophosphamide.  
(Prednisone is ineffective.)

STROKE SYNDROMES IN THE E.R.:

CEREBELLAR	BRAINSTEM	LEFT HEMISPHERE	RIGHT HEMISPHERE
Ataxia: Truncal	Diplopia (3,4,6)	<u>Aphasia</u>	<u>Left hemi-neglect</u>
Ataxia: Ipsilateral Limb	Gaze paresis (ditto)	Eyes prefer to look left	Eyes prefer to look right
	Dysphagia, Dysarthria (9)	Right visual field defect	Left visual field defect
	Tinnitus, Vertigo (8)	Right hemiparesis	Left hemiparesis
	N, V (10)	Right sensory loss	Left sensory loss
	Hiccups, abnormal Respirations (10)		
	Ipsilateral face, Contra-lateral body		
	Hemi or Quadri paresis		
	Hemi or Q sensory V		
	Decreased consciousness		

HORNER SYNDROME

- 1<sup>st</sup>: MS, brain stem inf. Tumor
- 2<sup>nd</sup>: Sup sulcus tumor, brachial plexus injury
- 3<sup>rd</sup>: ICA dissection, migraine



Case (Q50, Neuro, MKSAP 12)

42 yo 6 wk h/o/ weakness, lo grade fever, non-productive cough, arthralgias.

PE: Weak U & L face and mild weakness of proximal hip and shoulder.

CXR: Hilar adenopathy. Ca 12.3

Dx: Neuro sarcoid

Ddx: SLE, Paraneo, brain mets, lymphoma.

Case (Q 73, Neuro, MKSAP 12)

34 yo man 4days ago: acute right jaw, face & head pain. 2 ds ago transient visual loss of rt eye.

Today: Right Horner's and left hand numbness & weakness.

Dx: ICA dissection.

Case: Parkinsonian disorder with nocturnal stridor.

Dx: Multisystem Atrophy (see NEJM 2004;351:918). Stridor may be fatal. Types are:

1. Striatonigral degeneration: Parkinsonian.
2. Olivo-ponto-cerebellar dysfunction: Ataxia.
3. Autonomic failure: Severe orthostasis or persistent urinary incontinence with ED in men and reduced genital sensation in women, constipation, fecal incontinence, change in perspiration, discoloration of the extremities.
4. A combination of these.

From Harrison's and Cecil-Loeb ISCHEMIC CVAs.

Clinical manifestation	Distribution	Vessel
<b>TIA's w/ monocular blindness (amaurosis fugax).</b> <sup>1</sup>	Retina and optic nerve	Ophthalmic from ICA.
Abulia, stupor, hemiplegia (face=arm=leg), hemi-anesthesia, and either aphasia or agnosia	massive unilateral stroke	ICA to MCA + ACA
Contralateral hemiparesis, sensory loss ( <b>Face &amp; arm are worse</b> than leg) & homonymous hemianopsia or quadrantanopsia. <sup>2</sup> <b>If dominant:</b> Expressive (total) aphasia. <b>If non-dominant:</b> hemi-neglect, anosognosia (unaware of defect) and spatial disorientation.	2/3 of all ischemic CVAs. Lateral cerebral hemisph. Basal ganglia, int capsule. Motory & sensory cortex, optic radiations, auditory sensory cortex, and in dominant hemisphere, the language areas.	MCA (middle cerebral artery)
<b>Face weak;</b> non-fluent(slow, deletes words); can repeat.	DH, Brocca's area (Frontal cortex).	Superior div'n of MCA
<b>Not weak;</b> Fluent aphasia: can not repeat or comprehend. ± contralateral homonymous hemianopsia;	DH (dominant hemisphere), Wernicke's (posterior temporal) area	Inferior division. of MCA
Hemi-neglect with spatial agnosia; ± contralateral homonymous hemianopsia	Non-dominant hemisphere, posterior temporal area.	Lower MCA
Dysarthria and clumsy hand syndrome (i.e., face and hand) OR complete unilateral sensory-motor stroke:.F to A to L.	internal capsule ... Anterior to posterior (Lacunar infarcts)	lenticulostriate branches of MCA
Contralateral face-to-arm-to leg hemiplegia and homonymous hemianopsia, often transient. Goldberg, p69	anterior to posterior internal capsule including tracts to the leg and visual cortex	ant. choroidal artery from ICA
Contralateral hemiparesis, sensory loss ( <b>Leg is worse</b> than arm or face). <b>Grasp &amp; suck reflexes, urinary incontinence,</b> abulia (slow, deletes words)& motor aphasia.	Frontal poles, motory & sensory cortex of legs & feet. Broca's area (anterior temporal lobe)	ACA (anterior cerebral artery)
Ipsilat. 3 <sup>rd</sup> n. palsy +contralat. ataxia (Claude's syndrome)	mid-brain, red nucleus	P1 of PCA(3)
Ipsilat. 3 <sup>rd</sup> n. palsy +contralat. hemiplegia (Weber's syndr)	mid-brain, cerebral peduncle	P1 of PCA(3)
Contralateral hemiballismus	mid-brain, subthalamic nucleus	P1 of PCA(3)
Contralateral hemisensory loss progressing to severe pain	Thalamus	P1 of PCA(3)
Coma, unreactive pupils, bilateral weakness, decerebrate	Major infarct of midbrain & subthalamus	Bilateral P1 of PCA(3)
Contralateral homonymous hemi-anopsia with <u>macular sparing</u> . Visual hallucinations. Transient memory loss	Medial temporal and occipital lobes	P2 of PCA(3)
Bilateral cortical blindness (Pupillary reflex is preserved.)	bilateral occipital lobe infarction	Bilateral P2 of PCA (3)
Syncope, vertigo, alternating hemiplegia	Medulla, cerebellum	VA (vertebral artery)
Syncope with arm movement	Stenosis proximal to origin of VA from subclavian (left) or innominate (on right)	subclavian steal
<u>Ipsilateral:</u> Ataxia, nystagmus.  Locked in <u>Contralateral:</u> hemiparesis, sensory loss  syndrome	Medial Pons (complete infarction can cause locked in syndrome)	BA (basilar artery)
<u>Ipsilateral:</u> Ataxia, nystagmus, VIII, or paresis of V or VII. <u>Contralateral:</u> Pain and temperature loss.	Lateral Pons	BA
<u>Ipsilateral:</u> Ataxia, facial sensation loss, palate paresis, nystagmus, dysphagia, hoarseness, <u>Horner's syndrome</u> . <u>Contralateral:</u> Pain and temperature loss.=Wallenberg's S.	Lateral medulla ("Lateral medullary syndrome" = "Wallenberg's syndrome")	VA or Posterior inferior. Cerebellar artery (PICA)
Nausea, dizziness, <u>headache</u> progressing to ipsilateral <u>ataxia</u> , dysarthria, gaze paresis, contra-lateral hemi-paresis, & somnolence, progressing to coma	Caudal midbrain (Cr N 3 & 4) and cerebellum. <b><u>surgical emergency.</u></b>	Superior cerebellar artery <b><u>KNOW THIS ONE.</u></b>

<sup>1</sup> The CCA bifurcation to ICA and ECA "is the most frequent site for atherosclerotic lesions of the cerebral vasculature."

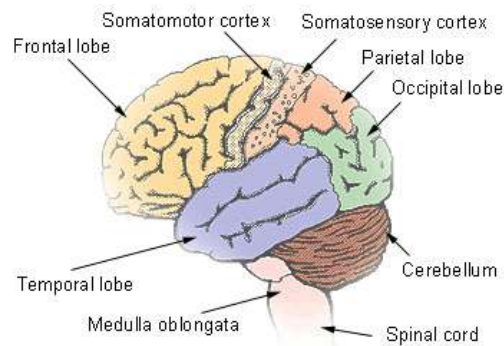
<sup>2</sup> An MCA ischemic infarct may be "virtually indistinguishable" from a **hemorrhagic** CVA of the putamen and internal capsule. ICA=Internal carotid artery; MCA=Middle cerebral artery, ACA=Anterior cerebral artery, PCA=Posterior cerebral artery.

<sup>3</sup> P1=branches are proximal to post. communicating art.; P2 branches are distal to it; Emboli are often cardiac or aortic in origin.

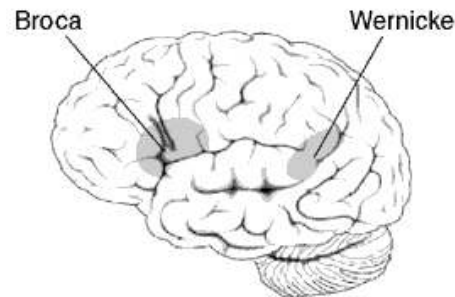
Name	Anatomy	Vascular defect	Type of Aphasia	Contralateral homonymous hemianopsia	Motor weakness
Broca's speech area	Dominant hemisphere in the frontal inferior cortex ( <u>superior</u> to the lateral fissure and hence there is a defect in the <u>superior</u> division of the MCA).	Superior division of the MCA (or a block in the ACA)	A non-fluent aphasia: *Slow speech *Deleted words *Poor syntax. Correct repetition with no word substitution.	NO. (Defect is too anterior to the visual fibers.)	Face, + or - arm (The defect is in the motor cortex.)
Wernicke's speech area	Dominant hemisphere, in the posterior superior portion of the temporal lobe ( <u>inferior</u> to the lateral fissure and hence there is a defect in the <u>inferior</u> division of the MCA).	Inferior division of the MCA	A fluent receptive aphasia: *Word salad (e.g., he obliviously substitutes "trable" for table). *He cannot repeat accurately "no ifs ands or buts" (e.g., go ivs, ants or futs") (1) Normal cadence with full and correct syntax.	Maybe. (Defect may involve the visual fibers near the occipital area.)	NO (The defect is not in the motor cortex.)
Both areas	Dominant hemisphere in the motor cortex and in the temporal lobe	proximal portion of the MCA	Total or "expressive" aphasia	Typical	Face and arm – relative sparing of the leg.

(1) Patients may also be paranoid, agitated and hostile.

Alexia without agraphia: Infarction of the left parieto-occipital region, a distribution of the left posterior cerebral artery.



**Lobes of the cerebrum**





## PORPHYRIAS

	Skin	Liver	Other Sx's	Precipitants	Urine	Serum	Other	Treatment
PCT: Porphyria Cutanea Tarda	Blisters on sun exposed areas	Increased AST, ALT.  Increased risk of liver cancer.  Increase in liver porphyrins.		Iron excess Sun exposure hemodialysis ETOH Smoking Estrogen use & pregnancy Hepatitis C infection.	Increase uroporphyrin	increase porphyrin (best diagnostic test) > 10 mcg/dL		Remove precipitants. Phlebotomy Low dose chloroquine
AIP: Acute Intermittent Porphyria		Increase risk of liver cancer	<b>GI</b> Abdominal pain 90% Vomiting 66% Constipation 66% <b>NEUROLOGIC</b> Trunk,limb,H,N pain 50% Paresis 50% (2) Psychiatric 50% (3) Convulsions 15% <b>Respiratory paralysis</b> <b>12%</b> <b>AUTONOMIC</b> HPT 45% Tachycardia 66% Fever 20%	Alcohol abuse Smoking Pre-menstrual Infection Starvation Drugs Surgery	Increase ALA & PBG, aminolevulinic acid, and porphobilinogen. (May be normal between attacks.)		Lo serum Na.  SIADH	Monitor peak flows. Avoid certain drugs: ACEIs, CCBs, sulfa drugs and many others. IV cimetidine. IV heme preparations. IV carbohydrates

(1) There are four types of acute porphyria: acute IP, Hereditary coproporpha, variegate porphyria, ALA-dehydratase deficient porphyria. The last is the most rare and requires a special assay.

(2) Muscle weakness is usually symmetric and usually involves the proximal muscles of the upper limbs first.

(3) This ranges from minor behavioral changes to depression, agitation, psychosis, and hallucinations.

(Symptoms are from Ann Int Med 2005; 142:441 and from UpToDate.)

## **TREATABLE SECONDARY CAUSES OF PARKINSONISM:**

### **Anti-dopaminergics (dopamine receptor blockers):**

Anti-psychotic drugs: chlorpromazine (Thorazine), haloperidol

Anti-emetic drugs: prochlorperazine (compazine)

Anti-heartburn & prokinetic: metoclopramide (Reglan)

Alpha methyl dopa

(The atypical neuroleptic, clozapine, is the least likely to have parkinsonism as a side effect. It is one choice for treating the psychiatric side effects of levodopa therapy in Parkinson's disease patients; however, the CBC should be closely monitored because agranulocytosis occurs in 1%.)

### **Treatable Diseases**

Wilson's disease

Hypothyroidism

Parathyroid abnormalities

Brain tumors

Normo pressure hydrocephalus

## **UNTREATABLE SECONDARY CAUSES OF PARKINSONISM:**

CVA

Creutzfeldt Jacob

Dementia with Lewy Bodies

Progressive supra nuclear palsy

Multi-system atrophy

Parkinson Drugs:

\*Levodopa/Carbidopa and limb and facial dyskinesias in most patients on chronic therapy

\*Bromocriptine and pergolide, dopamine agonists in the striatum, have similar side effects.

\*Selegiline, a MAO-B inhibitor, blocks the breakdown of intracerebral dopamine.

\*Anticholinergic agents, such as trihexyphenidyl (Artane) and benztropine mesylate (Cogentin), restore the balance between striatal dopamine and acetylcholine. Significant anticholinergic effects on the CNS are confusional states and hallucinations.

### **Chorea causes:**

Huntington's (CAG repeats).

Senile chorea

Metabolic: Hyperthyroid, hypoparathyroid, electrolyte abnormalities.

APLAS

Wilson's disease

Sydenham's chorea of rheumatic fever

Case

40 yo man with postural headache occurring within 15 minutes of becoming upright. Occ. Tinnitus, neck stiffness, & photophobia. Rx'd with sumatriptan. No relief.

Dx: Intracranial hypotension due to spontaneous CSF leak.

MRI: Epidural fluid accumulation, brain sagging, and venous congestion.

Rx: Blood patch via injection of 10 to 100 cc of autologous blood (also this is diagnostic).

PERIPHERAL POLY NEUROPATHIES:

**Axonal** Stocking glove. (EM: Decreased action potential, conduction slowing, positive sharp waves).

DM

Most Meds: INH, Cisplatinin, Amiodarone, metronidazole, DPH, B6

Uremia

B12

HIV

Lyme

Carcinoma (late)

Sepsis

Amyloidosis

Porphyria

**Demyelinating:** (EM: Conduction block)

Liver failure

Carcinoma

Lymphoma

Multiple Myeloma

Hypothyroidism (rare)

Sensory: HIV, B12.

Sensory then motor: Hypothyroidism, acromegaly.

Motor neuropathy: Critical illness.

Case: 26y.o. construction worker. 1 wk sudden onset, lifting-related, severe low back pain radiating down left leg to lateral foot.

PE: Full strength, except for inability to walk on left toe and absent left ankle jerk. Normal sensation.

Dx: S1 compression by herniated disc. R/O malignancy by history. S1 is little toe, L5 is big toe.

Plan: No MRI. "Do as much as you can." Conservative Rx for 6 weeks. Surgery generally no better in the long run than medical therapy.

Case: 55 y.o. man, poorly controlled DM 2. Numbness & tingling in lower legs x 6 months. Burning soles of feet, worse at night.

Tingling in right hand when he drives for long periods.

PE: Generally, decreased pain and temperature sensation to mid-shin, but increased sensation on soles of feet for pain and temperature. No ankle jerks and decreased knee jerks.

Dx: Diabetic polyneuropathy of lower extremities. Possible mononeuropathy (carpal tunnel... due to DM but different mechanism than stocking-glove polyneuropathy of lower extremities.) The lower extremity polyneuropathy must be present for several years before there is a comparable polyneuropathy of the upper extremities. The polyneuropathy is axonal (decreased amplitude on EMG), as opposed to myelin defect (decreased speed on EMG). It is small fiber primarily, which controls pain and temperature, as opposed to

large fiber, which effects position and vibratory sense.

Rx: mexilitine (don't use this — causes cardiac arrythmias !!!), capsaicin, and amitriptyline.  
(Carbamazepine is for sharp lancinating pain.)

Case: 62 y.o. alcoholic wakes with tingling in his right hand and right wrist drop. PE: Unable to elevate his right hand. The interosseus muscles (separating fingers when hand is placed flat on the table, not while wrist is flexed) are intact.

Dx: Radial nerve palsy. Ddx: Brachial plexopathy, radiculopathy, CVA. Rx: Supportive. Course: Many recover completely, particularly if this is primarily a demyelinating, rather than axonal, defect.

Case: 24 y.o. woman presents with severe burning pain and numbness on right thigh starting several weeks after birth of her 1<sup>st</sup> child. No back pain. PE: An **oval** shaped area of decreased pinprick on right lateral thigh.

Dx: Lateral femoral cutaneous nerve impingement at pelvic brim. Root is L2&L3. Causes are obesity, pregnancy, tight clothing, and diabetes. RX: Weight loss.

Causes of carpal tunnel: RA, hypothyroidism, DM, and Acromegaly.

**CMT (Charcot Marie Tooth) disease**, heterogenous inherited peripheral neuropathies, usually autosomal dominant but may be recessive or X-linked, very common, affecting up to 1 in 2500 persons. Onset usually in childhood but may be young adult.

Both motor and sensory nerves are involved.

Symptoms range from distal muscle weakness and severe atrophy and disability to only pes cavus and minimal weakness.

If patients have no sensory findings on exam or electrodiagnostics, consider an alternative diagnosis.

Case

45 yo man has a peripheral neuropathy

W/U is negative for DM, B12, uremia, HIV, Lyme, carcinoma, sepsis, amyloid & porphyria. And for axonal neuropathy: Liver, carcinoma, lymphoma, multiple myeloma, and hypothyroidism.

“Idiopathic diagnosis” is made. What other cause could there be?

Ans: Charcot-Marie-Tooth (often explains idiopathic.) Examine the family history.

### **CIDP (chronic inflammatory demyelinating polyneuropathy)**

\*Like GBS but chronic course

\*Also has CSF protein elevation as in GBS.

\*Rule out collagen vascular disease, HIV infection, and other systemic diseases.

\*25% of these patients have an MGUS present.

### **POEMS (=Osteosclerotic myeloma)**

P: Polyneuropathy in 100%. Initially sensory then motor. Distal, symmetric.

O: Organomegaly: HS megaly and/or lymphadenopathy.

E: Endocrinopathy: hypogonadism. Occasional hypothyroidism, adrenal insufficiency.

M: Monoclonal gammopathy with both lytic and sclerotic bone lesions (osteosclerotic)

S: Skin changes (2/3): hyperpigmentation, hypertrichosis, acrocyanosis, plethora. Responds to irradiation, melphalan, & prednisone.

**MFMN with CB: Multifocal motor neuropathy with conduction block:**

- \*The most important disease in the differential diagnosis of ALS.
- \*More gradual onset than ALS
- \*Most are male
- \*Confined to lower motor neurons (i.e., no spasticity and negative Babinski's)
- \*Sensory fibers are relatively spared.
- \*The upper extremities are affected more than the lower extremities.
- \*Initially asymmetric.
- \*1/2 have IgM antibodies to ganglioside GM1.
- \*Electrodiagnostic studies and pathology are consistent with an inflammatory demyelinating process.
- \*RX: IVIG, Plasmapheresis, Prednisone, Cyclophosphamide.

**Vasculitis:**

- \*Polyarteritis nodosa, etc.
- \*The most common pattern is mononeuritis multiplex caused by ischemic lesions of nerve trunks and roots.
- \*However, some types of vasculitic neuropathy present as a distal, symmetric motor-sensory neuropathy.

**Anti-Hu antibodies**

- \*An autoimmune neuronopathy
- \*Asymmetric sensory loss in the limbs, torso, and face.
- \*Marked sensory ataxia, pseudoathetosis, and inability to walk or stand.
- \*Idiopathic (majority) or 25% with small-cell lung cancer, sometimes preceding the diagnosis by 1 year.

**Case**

**40 y.o. woman s/p gastric by pass 10 years ago.**

**Skin depigmentation, kinky hair. Ataxia, lower extremity spasticity, positive Babinskis, decreased proprioceptive and vibratory sense.**

**Lab: NC, NC anemia. Normal B12 level, homocysteine, methyl malonic acid, serum vitamin E, VDRL negative, HIV negative, ESR, ANA, RF, paraneoplastic antibodies. Normal MRI of the brain and spine, normal CSF, and normal electromyographic study.**

**Dx: Copper deficiency. (Kumar, 2004).**

**MONONEURITIS MULTIPLEX**, inflammation of several nerves in unrelated parts of body:

DM (e.g., diplopia (Cr N3 &/or 6) with wrist drop (radial n.) or foot drop (peroneal n.). Can look like MS!

Vasculitis: polyarteritis

Connective tissue diseases: SLE, RA

Lyme Disease

## Transverse myelitis:

	X		
	XXX		
	XXX		(NOTE: CMs may also be <u>symmetric</u> .)
	XXX		
	X	X	
	X	X	
vPain &Temp	X	X	Weakness, & v position sense and radicular pain.
	X__	X__	

Def: A syndrome associated with neurologic defect related to one level of the spinal cord.

CM's: Acute onset in hours to weeks. ½ of patients develop maximal symptoms in 24 hours. Limb weakness (usually leg), below the level of the lesion there is ipsilateral loss of position sense, contralateral pain & temperature loss, and radicular pain, bowel and/or bladder dysfunction.

Causes: ANYTHING THAT CAUSES EDEMA OF THE CORD.

Infectious: Bacterial: **Lyme**, TB, mycoplasma, Syphilis.

Infectious: Viral: **HIV**, any of the Herpes viruses (Zoster, HSV, CMV), enteroviruses (coxsackie, echo, polio, influenza, rabies)  
Postvaccine: Rabies, cowpox.

Autoimmune: **SLE** (very important. See MKSAP 13, rheum. Q22, p70), Sjorgens, sarcoid.

MS

Paraneoplastic

Vascular: **Ischemia**: Spinal AVM, heroin abuse, thrombosis of spinal artery.

Idiopathic.

## MYELOPATHIES (= Disease or disturbance of the spinal cord):

### >COMPRESSIVE TYPE:

#### >MALIGNANCIES

#### >SYRINGOMYELIA (Fluid exerting pressure within the spinal cord):

\*Progressive myelopathy.

\*Onset in adolescence or early adulthood.

\*Chiari malformations in ½ of syringomyelia cases.

\*Acquired cavitations are due to trauma, myelitis, infection, or tumor.

CM's:

\*Sensory loss of pain and temperature. (Preserved vibration and position sense.)

\*Weakness of upper extremities. Muscle wasting. Asymmetric or absent DTRs reflect extension to anterior horns.

\*Subsequent spasticity, lower extremity weakness, and incontinence.

\*MRI is diagnostic.

RX: Decompression.

### >NON-COMPRESSIVE (5 types):

\*spinal cord infarction;

\*autoimmune: vasculitis, systemic lupus erythematosus (SLE), and sarcoidosis;

\*infections (particularly viral);

\*demyelinating disease such as multiple sclerosis;

\*idiopathic.

## Case

34-year-old female

CC: lower extremity weakness x 3 days

Decreased sensation "below the belly button"

Incontinence.

Low-grade fevers

PE: sensory level of the umbilicus.

Lower extremities +3/5 strength bilaterally proximally and distally.

Dx: a myelopathy. The rapidity of onset and the lack of other antecedent symptoms (e.g., pain) make a noncompressive etiology most likely.

Lab: MRI to identify a structural lesion such as a neoplasm or subluxation.

Noncompressive myelopathies result from five basic causes:

1. spinal cord infarction;
2. Vasculitis, systemic lupus erythematosus (SLE), and sarcoidosis;
3. infections (particularly viral): HIV & HTLV-I.
4. MS.
5. idiopathic.

Do: ANA, viral serologies for HIV and HTLV-I, LP

Myelopathy is not diagnosed with an EMG so don't do this test.

## Case

A 55-year-old woman cc: midthoracic back pain over the past several months. The pain is constant, dull in nature, and without radiation. Over the past month, she has noticed numbness beginning first in the feet and now extending up to her abdomen. Within the past week, she has experienced difficulty with walking. Her medical history is unremarkable, and her only medication is hormonal replacement.

Physical examination reveals a T-6 sensory level with increased tone and brisk reflexes in the lower extremities. Babinski signs are present bilaterally. Rectal exam is normal.

Which of the following statements is correct?

Dx: Myelopathy. A neurologic emergency. With MRI and then dexamethasone 100-mg bolus followed by 24 mg every 6 hours.

Causes: Spinal cord compression from a tumor.

Most common causes in a patient without known cancer: meningiomas or neurofibromas. These tumors are intradural and extramedullary. Intramedullary tumors, such as astrocytoma and ependymoma, are less common causes of cord compression. Metastatic disease leading to cord compression is typically extradural.

## EPILEPSY NOTES:

Ddx: TIA, transient global amnesia, syncope, migraine, psychogenic.

Seizure classification (PIER adaptation):

Simple partial seizure: Normal consciousness, single neuro modality involving a single region of body such as hand or arm.

Complex partial seizure: Altered awareness, staring, unresponsive. Automatism, preceding aura (especially autonomic). Post ictal focal neurologic deficit (hemiparesis or aphasia). Post ictal confusion.

Primary Generalized seizure: Loss of consciousness; no prodrome; Tonic-clonic seizure.

Epilepsy:

\*Tri-cyclics and tramadol lower seizure threshold.

\*70% of children and 60% of adults will be able to discontinue therapy eventually.

Patient factors include complete medical control of seizures for 1 to 5 years, a normal neurologic examination, a normal EEG, and single seizure type.

\*20% are completely refractory to medical therapy and should be considered for mesial temporal sclerosis resection

\*Depression, anxiety, and behavior problems may occur.

\*20% of epileptic patients have depression, with their suicide rate being higher than that of age-matched controls.

\*a twofold to threefold increase in mortality for patients with epilepsy compared with age-matched controls.

\*Due to MVAs, status epilepticus, a syndrome known as sudden unexpected death in epileptic patients (SUDEP). Research has centered on brainstem-mediated effects of seizures on cardiopulmonary function.

### SEIZURE MED SIDE EFFECTS

Medication	Side Effect
Levetiracetam (Keppra)	Psychiatric disturbances
Valproic acid (Depakote; Depekene)	Alopecia. Weight gain. Hepatic failure; bone marrow failure; teratogen
Carbamazepine	SIADH, hepatotoxicity, and agranulocytosis
Phenytoin	hirsutism, coarsening of features, gingival hyperplasia, lymphadenopathy, Stevens Johnson syndrome, and osteomalacia. Dizziness ataxia, deiploplia, and confusion. Teratogenic.

	Complex partial	Generalized Absence
Age	Begins in adolescence or adulthood	Begins in childhood, remits by adulthood
Frequency	once daily(except for frontal lobe seizure)	Multiple times daily
Aura	Yes	No
Post ictal	Yes	No
Cessation of activity and automatisms	Yes	Yes
Treatment		Levetiracetam (Keppra); Valproic Acid (Depakote; Depekene)

### Case

A 35-year-old woman cc: seizure. Feeling well, then right thumb retracting, then right hand, then right face, then generalized tonic clonic seizure, then loss of consciousness for 5 minutes, then post ictal state: amnesia and 6 hours of weakness in her right arm.

Dx: r/o tumor or abscess.

\*Initial laboratory screening of a 1<sup>st</sup> seizure should include, at a minimum, a toxicology screen, electrolytes (including calcium and magnesium), renal function studies, a CBC and a blood glucose level.

\*Tricyclics anti-depressants may lower the seizure threshold.



**\*EEG PATTERNS:**

Epilepsy: Spike and slow waves.

Metabolic encephalopathy: generalized slow waves.

**\*Primary Generalized Epilepsy:** First Line Therapy: **Valproic acid (Depakote)**. 2<sup>nd</sup> line includes Topiramate and lamotrigine.

**\*Partial seizures with or without Generalization:** First Line Therapy: **Carbamazepine, Phenytoin and oxcarbazepine**. 2<sup>nd</sup> line therapy includes: Topiramate, lamotrigine, and valproic acid..

\*70% of children and 60% of adults may be able to discontinue therapy. (?Not supported by mksap audio)

\*About 20% of these patients are completely refractory to medical therapy and should be considered for surgery, which is curative in 70% with mesial temporal sclerosis (complex partial seizures).

\*20% of epileptic patients have depression, with elevated suicide rates.

\*Titrate phenytoin anti-seizure medicine to efficacy and toxicity rather than to “normal therapeutic range”, and then add another drug if necessary.

\*Side effects of some anti-epileptics:

Valproic acid (Depakote): alopecia and weight gain

Phenytoin: hirsutism, gingival hyperplasia, coarsening of features, pseudolymphoma syndrome, teratogenic.

Carbamazepine: SIADH, hepatotoxic reaction and agranulocytosis.

\*The phenytoin idiosyncratic pseudolymphoma syndrome has diffuse lymphadenopathy, with mild elevations of liver enzymes and moderate fever.

**Febrile convulsions of childhood:**

\*Occur one or more times in 3 to 4% of children between the ages of ½ to 5 years of age.

\*Consist of brief tonic-clonic generalized seizures.

\*Re-occurrences occur in 5% without the presence of fever.

\*Although they can be recurrent, the syndrome is benign, unless there are durations longer than 10 minutes or focal abnormalities during the seizure.

**Transient Global Amnesia:**

CM's: Middle to older age adults; transient severe anterograde amnesia accompanied by repetitive questions asking where and why the patient is there, retaining ability to perform tasks such as driving or playing a musical instrument, lasting approximately 6 hours (1 to 10 hours). Risk of recurrence is low. The pathology involves the medial temporal lobes. MRI is obtained to rule out CVA.

**CHRONIC FATIGUE SYNDROME (CDC):**

1. Major criteria. All must be present:

\*Morning fatigue. (Fatigue does not resolve with bed rest. Fatigue worse in the PM suggests an organic cause.)

\*severity reduces average daily activity by 50%.

\*Exclusion of other chronic conditions, including preexisting psychiatric diseases.

2. The physical examination (must have 2 of 3 findings by a doctor on at least two occasions 1 month apart):

\*low-grade fever,

\*pharyngitis, and

\*palpable lymphadenopathy.

3. At least 6 of 10 common symptoms must be present

\*mild fever or chills,

\*sore throat,

\*painful lymph nodes in the cervical chains,

\*muscle weakness,

\*muscle discomfort,

\*fatigue after minimal exercise,

\*new headaches,

\*arthralgias,

- \*neuropsychological symptoms, and
- \*sleep disturbance.

4. Patients who do not have the required physical findings have to fulfill 8 of the symptoms.

Rx: NO acyclovir, vitamin B12, intravenous gamma globulin, and steroids.

Use NSAIDs, decongestants, and antidepressants, graded exercise program, minimal caffeine intake, and **avoidance** of complete rest, is advisable.

#### MENINGITIS

	Syndrome	WBC	Differential	Protein mg/dL	Glucose as % of serum	Staining etc
Bacteria	meningitis	1,000-10,000	neutrophilic	100 - 1,000	<30%	Positive in 70% of cases
	extra-meningeal sepsis	10- 1,000	“	100 - 1,000	nl	positive
Virus	meningitis, encephalitis	10- 1,000	lymph’c	50 - 200	nl	PCR of virus
TB or fungi	chronic meningitis	100- 1,000	“	100 - 500	<30%	Crypt Ag. Otherwise not helpful
Carcinoma	meningitis	> 5			<50%	
Normal	Normal	<5	<5Neut	< 45	50% - 80%	Negative

**Transient hypoxemia or hypotension** for a few minutes causes selective (for unclear reasons) necrosis of hippocampal neurons (most vulnerable) followed by cerebellar, striatal, and neocortical neurons, with cognitive impairment and/or movement disorders. (Cecil, 1. Ch. 440)

Romberg’s sign is present when a person, standing with feet together and eyes closed, can not maintain this position for more than 1 minute. It is supposed to test for dorsal column disease (e.g., due to Tabes dorsalis or pernicious anemia) but sensitivity is just above 50% and it will also be positive in ½ of patients with cerebellar disease (McGee).

The patellar deep tendon reflexes are commonly associated with the L4 nerve root level. The ankle jerk is commonly associated with the S-1 nerve root level.

Disease	CM's	MRI	Diagnosis	Rx	Preventive
Toxoplasmosis	CD4 < 100, HA, szrs, v cognition, focal signs	Multiple Ring enhancing lesions. Basal ganglia & cortex	CSF: Anti-IgG sensitivity >98% MRI typical, +serology, no prophylaxis then empiric criteria are met.	Pyrimethamine + folinic acid. Sulfadiazine. No steroids unless herniated.	TMP/SMX
Syphilitis Gummas	Meningitis Optic neuritis Stroke (vasculitis)	Multiple enhancing lesions in cortex and subcortex.	CSF VDRL S&S:30% & 95%		PEN G 4 M units i.v. q4hrs x 14 days
Bacterial abscess	focal lesions	One or multiple lesions. Ring enhancing late.	Surgical drainage. Bugs are in footnote (1)	Surgical drainage and antibiotics	
HIV encephalitis	Triad of subcortical dementia: Memory V, psychomotor V, Movement disorder.	Subcortical & periventricular enhancing lesions. Symmetric. Poorly demarcated.	HIV ELISA		
CMV neurologic disease	CD4 < 50/uL. Dementia and Focal signs are more common than in HIV. Can cause retinitis, myelitis, polyneuropathy	Scattered diffuse micronodules. Ventricular enlargement and periventricular inflammation. Meningeal enhancement.	CMV DNA by PCR in CSF	Gancyclovir or Foscarnet (no RCTs)	
PMFLE(1)(JC virus, a papova virus reactivated in 90% of us.)	Rapid focal deficits, motor, visual, ataxia, aphasia, and cognitive impairment	Patchy hypodense lesions in subcortical white matter, bilateral, asymmetric, well-demarcated. <b>Non-enhancing(3)</b>	PCR for JC virus sens 80% Spec > 91%		
Lymphoma	CD4 < 100 Mental v. Seizures Focal motor Sgs	Enhancing single or multiple lesions of corpus callosum, periventricles, or periventricular areas. >4 cm	EBV DNA by PCR on CSF. Sens 85%; spec >95%	RT + Steroids but little change in survival of 1-3 months. HAART does prolong survival if organism is sensitive.	

(1) Staph, Strep, Salmonella, nocardia, listeria, TB, peptostreptococcus, fusobacterium, bacteroides

(2) Progressive multifocal leukoencephalopathy; PMLFE is the only non enhancing lesion on this list.

SUMMARY

Disease	Cortex	Subcortex	Periventricle	Basal Gangl.	Corpus callo	meningeal	other
Toxo	Yes			Yes			Single ring enhancing
Abscess							1 or more. Late ring enhancing
Syphilis	Yes	Yes					Multiple enhancing lesions
HIV		Yes	Yes				Symmetric, poorly demarcated
CMV			Yes			Yes	Micronodules. ^ ventricular size.
PMFL		Yes					Non-enhancing. Asymmetric, well-demarcated.
Lymphoma			Yes		Yes		Enhancing. 1 or more lesions.

Ethical Issues:

\*Advanced directive controls where the patient is not able to communicate.

\*Advanced directives may be written or verbal.

\*Spouse has priority even where spouse is separated.

\*Withholding of food and hydration in a terminally ill patient is:

>Consistent and allowed by state law

>Consistent and allowed by Catholic Health care, where the Burdens outweigh the Benefits (Pope's elocutions).

>Not a painful or uncomfortable death where patient is aware of surroundings.

>Not euthanasia.

\*In euthanasia, the medical professional actively administers a lethal agent. This is only legal in the Netherlands.

\*In physician assisted suicide, the medical professional provides the agent to the patient, who administers the lethal agent.

Is the patient terminally ill? This is defined as a physician's judgement that the prognosis is less than 6 months.

A PEG tube is known not to prolong life.

**DIFFERENTIAL DIAGNOSIS OF STUPOR AND COMA.** There are 4 important entities: Brain death, coma, persistent vegetative state, and locked in syndrome.

**1) Brain death:** Cessation of cerebral and brain stem function.

1. No respiratory drive. Apnea off ventilator for 10+ minutes to achieve CO<sub>2</sub> of 50-60.

2. No cranial nerve function or motor function arising from brain. Test these reflexes: Pupillary(3), corneal(5 & 3), oculo-cephalic (doll's eyes: neck proprioceptors,8,3,4&6), vestibulo-cephalic (8,3,4,&6 via cold calories;eyes look toward cold), grimacing (7), gag(9&10), posturing, sucking.

\*\*\* (Spinal reflexes may be present!)

3. No reversible causes: rule out drugs, alcohol.

4. Temperature above 34 degrees.

**2) Coma:** Unarousable. Unaware of environment. The goal of exam in a comatose patient is to determine if the a lesion is structural or metabolic or both. Structural abnormalities are suggested by a) asymmetric findings; and b) abnormal reflexes pointing to specific points in the brain.

\*Oculo-cephalic reflex (doll's eyes): An alert patient does not have doll's eyes because they are suppressed. A comatose patients with intact circuits will move eyes with slight lag as head is moved. The afferent arc consists of the labyrinth, the 8<sup>th</sup> nerve, and neck muscle proprioceptors; the efferent arc has the Cranial nerves 3,4 & 6.

\*Response to noxious stimuli: press hard under superior orbital roof or twist nipple: Decorticate (flexor) posturing: adduction of upper arms, flexion of wrists and fingers (fists held over chest), extension of legs. Decerebrate (extensor) posturing: arms are adducted, extended and pronated and legs are extended. Decorticate posturing has a better prognosis. The signs are non-localizing.

Glasgow Coma Scale:

I. Motor response: 6 obeys commands/5 localizes to noxious stimuli/4 withdraws from noxious stimuli/ 3 decorticate (flexor) response/ 2 decerebrate (extensor) response/1 no response.

II. Verbal response: 5 alert and oriented/ 4 confused yet coherent speech/ 3 inappropriate words and jumbled phrases consisting of words/ 2 sounds but not words/ 1 no sounds.

III. Eye opening: 4 Spontaneous eye opening. 3. Opens to speech/ 2 Opens to pain/ 1 no eye opening.

## COMA EVALUATION

Stage	level of consciousness	pupils	oculocephalic reflex	respiratory pattern	motor tone and responses
diencephalon	lethargy to stupor	small & reactive	brisk	s7gh & yaws	semi-purposeful to decorticate
midbrain	coma	mpf	decreased to absent	tachypnea, hyperpenea	decerebrate
pons	coma	mpf	absent	eupnea	decerebrate to flaccid
medulla	coma mpf	mpf	absent	ataxic	flaccid

Modified from Plum and Posner

evaluation of the comatose patient

Causes:

- supratentorial structural disease (mass)
- infraterntorial structural disease
- diffuse brain disease (metabolic)
- psychogenic

PE to determine cause (see table)

3) **Pesistent vegetative state:** 1. Unaware of environment, 2. No purposeful activity, 3. Unable to communicate, 4. incontinent, 5. But is arousable, 6. has Sleep-Wake cycle, 7. There are functioning autonomies: GI, respiratory, and cardiac function present. 8. cranial and/or spinal reflexes may be present. 9. No change over 3 to 12 months. Pathology = **diffuse cortical injury**. Terry Schiavo case.

4) **Locked in syndrome:** complete paralysis of all motor function, with the exception of extra-ocular movements, with which communication may be possible. Patients are aware, rational, and communicable. Lesion is most often due to damage to the rostral ventral pons by massive infarction, trauma, ALS, or demyelination.

Herniation of a lower cervical disk: If the disk herniates laterally, it will generally compress the nerve route exiting the lower of the two vertebrae that account for the intervertebral space.

>C6 radiculopathy: absent biceps reflex; pain in trapezius, shoulder, radial forearm, and thumb.

>C7 radiculopathy: diminished triceps reflex; pain or paresthesia in shoulder blade and pectoral region, dorsal forearm elbow, upper arm, and 2<sup>nd</sup> and 3<sup>rd</sup> fingers or all fingertips.

>Coughing and sneezing often exacerbate the pain caused by a herniated cervical disk. Unlike the lateral disk syndromes mentioned above, a disk that herniates centrally may be painless but cause symptoms in the lower extremities.

Etiologies of tic douloureux(trigeminal neuralgia) are idiopathic (most common), multiple sclerosis, herpes zoster, or a tumor.

Grape fruit juice increases the toxicity of benzodiazepines.

## BLEEDS

Anatomy	A or V?	History
Epidural	arterial	trauma
Subdural	venous	trauma or deceleration, fluctuating Sx's.
Subarachnoid	arterial	“thunderclap”, worst HA in life. Woman, age 40-60
Brain (intracerebral)	arterial	dull HA.

Primary or inherited periodic paralyses may be classified according to serum potassium levels during an attack. Serum potassium levels may be increased, decreased, or normal.

Paraneoplastic syndromes include limbic encephalitis, sensory neuronopathy, Eaton-Lambert myasthenic syndrome, and cerebellar ataxia.

**What is limbic encephalitis?** The limbic system involves circuits surrounding the thalamus and includes the hippocampus, amygdala, dentate gyrus, mamillary body, anterior thalamus and medial forebrain bundle. It is **involved with emotions and autonomic functions.**

Leukoencephalopathy is the most common and serious neurotoxicity associated with methotrexate. The toxicity develops months to years after administration. The greatest risk is in patients who receive cranial irradiation before chemotherapy. Clinically, patients exhibit cognitive dysfunction and focal neurologic signs, which may progress to dementia, coma, and death. There is no treatment

In HIV, an indication for early brain biopsy is a single mass lesion with negative serology for toxoplasmosis.

The patellar deep tendon reflexes is associated with what nerve root? Ans: L4

The ankle jerk is associated with what nerve root: Ans: S-1.

.

Case

50 yo man with headaches precipitated by cough, sneezing.

Dx: r/o posterior fossa mass.

### **Spinal cord disorders:**

1. Inflammatory: SLE, Sjogren's, sarcoid
2. Infectious: HSV, HIV, West Nile virus, enteroviruses.
3. Deficiencies: B12, Copper (with zinc ingestion)
4. Vascular: Cord infarctions, dura based AV fistulas.

### TPN deficiencies

WEEKS	Vit's B & C, water soluble, except for B12	CHF, Nystagmus, ataxia, confabulation, memory loss (B1, B complex). Anemia (B2). Dermatitis & stomatitis (B2, B6, B Complex). Diarrhea (B complex). Petechial hemorrhages & echymoses (C)
	Mg	lethargy, anorexia, cramps, tetany
	Zinc	acrodermatitis, poor wound healing, and dysgeusia.
MONTHS	Copper	B12-like deficiency plus depigmented skin & kinky hair.
	Vit K	Increased INR
YEARS	Vit's A & D (fat soluble)	Night blindness; hypocalcemia
	Selenium	Myalgias, cardiomyopathy, anemia (hemolytic)
	Chromium	Hyperglycemia
	Iron, cobalt(?)	Anemia, microcytic
	B12	Anemia, macrocytic. Smooth tongue, degeneration of dorsal & lateral spinal cord: ataxia, spasticity, loss of position & vibration sense.

VITAMINS: B and C are water soluble. A, D, E & K are lipid soluble. DEFICIENCIES

B1, Thiamine	<b>Wet beriberi:</b> heart failure, ascites, peripheral edema <b>Dry beriberi:</b> > <b>Wernicke's</b> encephalopathy: vomiting, <b>nystagmus, ophthalmoplegia, ataxia, disorientation.(fully reversible with B<sub>1</sub>).</b> > <b>Korsakoff's</b> syndrome: <b>Retrograde amnesia, confabulation.(½ reversible with B<sub>1</sub>)</b>
B2, Riboflavin	NC, NC anemia, ST, glossitis, cheilosis, angular stomatitis, seborrheic dermatitis of perineum & scrotum. ( <u>Occurs with phenothiazines &amp; tricyclic antidepressants.</u> ). Prevents migraine.
B6, Pyridoxine	Glossitis, cheilosis, vomiting & seizures (rare. Relative B6 deficiency occurs in use of <b>INH</b> , cycloserine, penicillamine, & etoh'm.)
B complex, Niacin (part of NAD and NADP)	<b>Pellagra: "3 Ds: Dermatitis, Diarrhea, Dementia"</b> . Dermatitis, glossitis, stomatitis, proctitis, diarrhea, depression, dementia, psychosis. Made from tryptophan so not actually a vitamin. Seen in <b>carcinoid in which tryptophan is consumed</b> and in <b>INH</b> .
B12 (develops in years)	Macrocytic anemia, <b>smooth tongue, decreased DTRs</b> , decreased vibratory & position sense, spasticity, <b>ataxia, memory loss</b> .
Vit C, Ascorbic Acid.	<b>Scurvy: Petechial hemorrhages &amp; ecchymoses</b> . Then hyperkeratotic papules around hair follicles & Sjogren's syndrome.
Vit A	Night blindness
Vit D	hypocalcemia, increased PTH. Rickets in children.
Vit E	<b>Areflexia and decreased vibration &amp; position sense</b> are due to spinal cord deterioration.

### VITAMIN OVERDOSE

Vit A	Flaky skin, athralgias, alopecia, fever, HS megaly.
Vit B6	peripheral neuropathy: Absent position and vibration sense (NL motor & other sensory)
Vit D	Inc Ca, Hypercalcuria, renal stones(?) (Sarcoid & lymphomas have increased 1,25(OH)2 D
Vit E	Non toxic. Can reverse coagulation.
Vit C	Possible oxalate renal stones and interference with B12 absorption.
B complex, Niacin	Acanthosis nigricans, cholestatic jaundice.

## CHAPTER 5. THE VISUAL SYSTEM

Destruction of a cerebral hemisphere results in dense paralysis and sensory loss in the contralateral extremities. Such lesions do not result in corresponding visual loss or ocular paralysis confined to the contralateral eye. Rather, both eyes are affected partially. Neither eye can move to the contralateral side and neither eye sees the contralateral environment (Fig. 34).

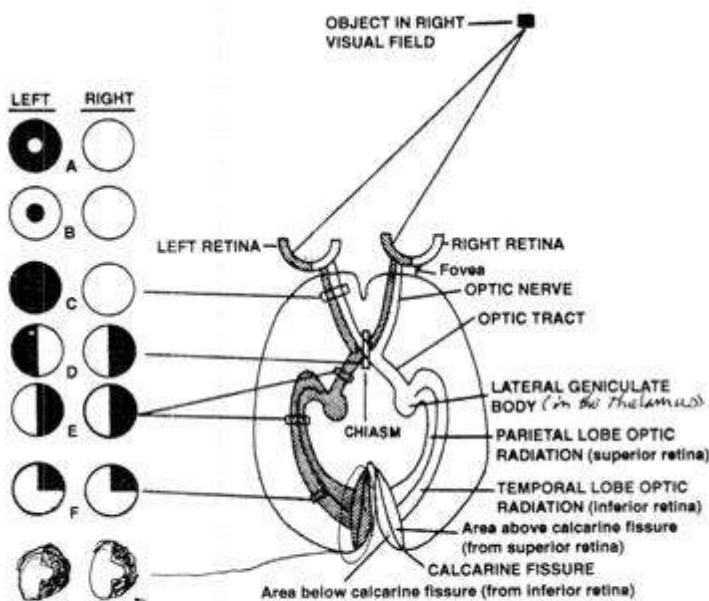


Fig. 34 The visual pathways as seen from above the brain. Letters A-F refer to visual field defects following lesions in the corresponding brain areas. Circles indicate what the left and right eyes see (the left and right visual fields). Black areas represent visual field defects. A. Constricted field left eye (e.g., end-stage glaucoma). When constricted fields are bilateral, it sometimes signifies hysteria. B. Central scotoma (e.g., optic neuritis in multiple sclerosis). C. Total blindness of the left eye. D. Bitemporal hemianopia (e.g., pituitary gland tumor). E. Right homonymous hemianopia (e.g., stroke). F. Right superior quadrantanopia.

*Homonymous hemianopsia with macular sparing due to collateral circulation*

*Named for the defects - not the remaining vision.*

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Picture Mr. HAL  
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JS CUNEATUS

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AMIC TRACT

Presbycusis, the hearing loss associated with aging, may affect 33% of people age 75 or older. The most common cause of this problem is presbycusis, which is manifested by a loss of discrimination for particular sounds and difficulty understanding speech in noisy environments. This is usually due to sensorineural deafness, with lesions in the neuroepithelial cells (hair cells), the neurons, or the stria vascularis of the peripheral auditory system. Rx: hearing aids

Case

45 yo man. Cc: imbalance

PE: wide-based gait and to sway forward and backward upon standing. Balance cannot be maintained when the patient is standing with the feet together and with the eyes open or closed.



No associated limb ataxia.

Dx: Alcoholic cerebellar degeneration in midline area of the cerebellum (vermis).

### Glaucoma

\*Open angle glaucoma is the leading cause of irreversible blindness in the world.

\*First visual loss (axonal) is peripheral.

\*Later is central visual loss.

\*Retinopathy due to glaucoma is irreversible.

Treatment is focused on lowering intraocular pressure.

\*Reduction in intraocular pressure protects against further damage to the optic nerve.

\*Closed-angle glaucoma is more common among Asians.

\*The Schitz tonometer is used in both hospitals and outpatient clinics.

\*Topical adrenergic antagonists are one of the more commonly used drugs

\* Excess drug is absorbed into the systemic circulation and can cause bronchospasm.

44 yo man cc: flu symptoms with n, v, d, headache and mild dyspnea. He felt better when he was shoveling snow. His wife has similar symptoms.

Dx: CO poisoning

### Case

66-year-old m man with difficulty walking. No back pain. The patient describes his problem as a feeling that he frequently trips. He has has tripped while climbing the stairs at home.

PMH: DM-2. hemoglobin A1C is 6.8%. Metformin 500 mg twice daily.

PE: no tenderness or deformity in the back.

Decreased left patellar reflex

Decreased dorsiflexion in the left foot.

When he walks he swings the left leg higher than the right.

Dx: a steppage gait due to weak ankle dorsiflexion most consistent with an L5 radiculopathy.

Diabetic neuropathy and vitamin B12 would be expected to cause bilateral sensory neuropathies.

The weakness after a cerebrovascular accident

### Case

29-year-old woman who uses OCPs.

Cc: Woke in the AM: Face was twisted, numb and swollen. At breakfast, she drooled out of the right side of her mouth when swallowing.

PE:

\*Dense right facial paresis equally involving the frontalis, orbicularis oculi, and orbicularis oris.

\*Finger rubbing is appreciated as louder in the right ear than in the left.

Dx: Bell's Palsy which may include ipsilateral hyperacusis resulting from involvement of fibers to the stapedius

Rx:

\*Artificial tears, ointment, eye patch to prevent corneal abrasion.

\*Standard practice with some conflicting data: a) Prednisone 60 mg/day + b) Vacyclovir 1 gm TID.

### Case

40 y.o. cc: Brief paroxysms of severe, sharp pains in the face without demonstrable lesions in the jaw, teeth, or sinuses are called tic douloureux, or trigeminal neuralgia. The pain may be brought on by stimuli applied to the face, lips, or tongue or by certain movements of those structures.

Dx: Trigeminal neuralgia

Ddx: Aneurysms, neurofibromas, and meningiomas impinging on the fifth cranial nerve.

will cause weakness of the jaw muscles

Rx:

\*Carbamazepine or phenytoin if carbamazepine is not tolerated.

\*Surgical therapy if no relief.

Case

35-year-old female. CC: intense vertigo that last several hours x 5 weeks.

\*tinnitus

\*Sense of fullness in the right ear

PE: Fine rotatory nystagmus maximal with gaze to the left.

\*Audiogram: high-tone hearing loss in the right ear, with recruitment but no tone decay.

Dx: Meniere's disease.

Paroxysmal vertigo results from labyrinthine lesions with nausea, vomiting, rotary nystagmus, tinnitus, high-tone hearing loss with recruitment, and, most characteristically, fullness in the ear.

Case 18 yo woman

FH in AD or AR pattern

Pes cavus and kyphoscoliosis

Then: ataxia of gait.

Then: action and intention tremors

Normal mentation.

DTRs absent

Positive Babinski's.

Dx: Friedreich's ataxia

Pathologically, there is degeneration of the dorsal columns, corticospinal tracts, and spinocerebellar tracts.

Case

45 y.o. woman with history of marijuana use presents with "the worst headache of my life.. Like a thunderclap... around my head and back of my head". She has 2/6 lower extremity weakness, which resolves after 2 weeks.

CT, LP negative. CTA and MRA both show multifocal segmental intracranial arteries (cerebellar, cerebral).

Dx: **Reversible cerebral vasoconstriction syndromes**. Ddx: SAH, cerebral angiitis.

Criteria:

\*Thunderclap headache (typically occipital or diffuse).

\*Negative CT for SAH

\*Negative CSF for SAH. Near normal CSF: <10WBCs/mm<sup>3</sup>; protein < 80 mg/dL(normal is <45; bacterial or TB/fungal >100; viral >50); normal glucose.

\*Multifocal segmental vasoconstriction on head MRA or CTA.

\*Reversibility of angiographic abnormalities with 12 weeks.

\*The typical patients is a middle aged female (2:1; F:M). Exposed to drugs such as pseudoephedrine, cocaine, amphetamines, marijuana or the cause is idiopathic.

\*There may be focal weakness, which often resolves completely. There may be parenchymal infarcts in up to 50%. A few deaths have been reported.

RCVS differs from SAH (positive CT and/or CSF; CTA: saccular aneurysm).

RCVS differs from migraine (not thunderclap; has recurrent course).

RCVS differs from cerebral artery dissection (localized).

RCVS differs primary cerebral angiitis(subacute or chronic).

The treatment for RCVS is high dose steroids (as is the treatment for cerebral angiitis) so if there is a question, give the steroids.

Nimodipine has also been used but risks watershed infarcts.

See Calabrese LH et al. Ann Int Med 2006;146:34-44

PRES syndrome, posterior reversible encephalopathy syndrome, can cause cortical blindness. This can occur postpartum.

#### Orientation Memory Concentration Test

	Maximum error	score x	Weight
1. What year is it now?	1	X4	
2. What month is it now?	1	X3	
. John Brown, 42 Market St, Chicago			
3. About what time is it?	2	X3	
4. Count Backwards 20 to 1	2	X2	
5. Say the months in reverse order	5	X2	
6. Repeat the phrase just given.	5	X2	

Total score = /28