Movement Disorders Fox & Hedgehog

- Video Show & Tell (Fox Part) -

- Focus on Essential Tremor and Parkinson's Disease (Hedgehog Part) -

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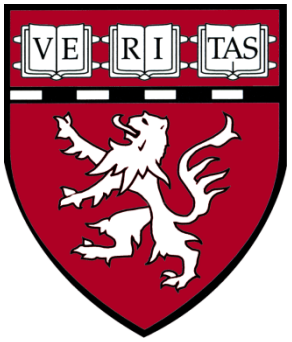

Outline

1. Introduction to movement disorders
2. Case presentations
3. Hyperkinesias
4. Case study: approach to essential tremor
5. Hypokinesias
6. The spectrum of parkinsonism
7. Case study: approach to idiopathic Parkinson's disease
8. Video ballad of movement disorders

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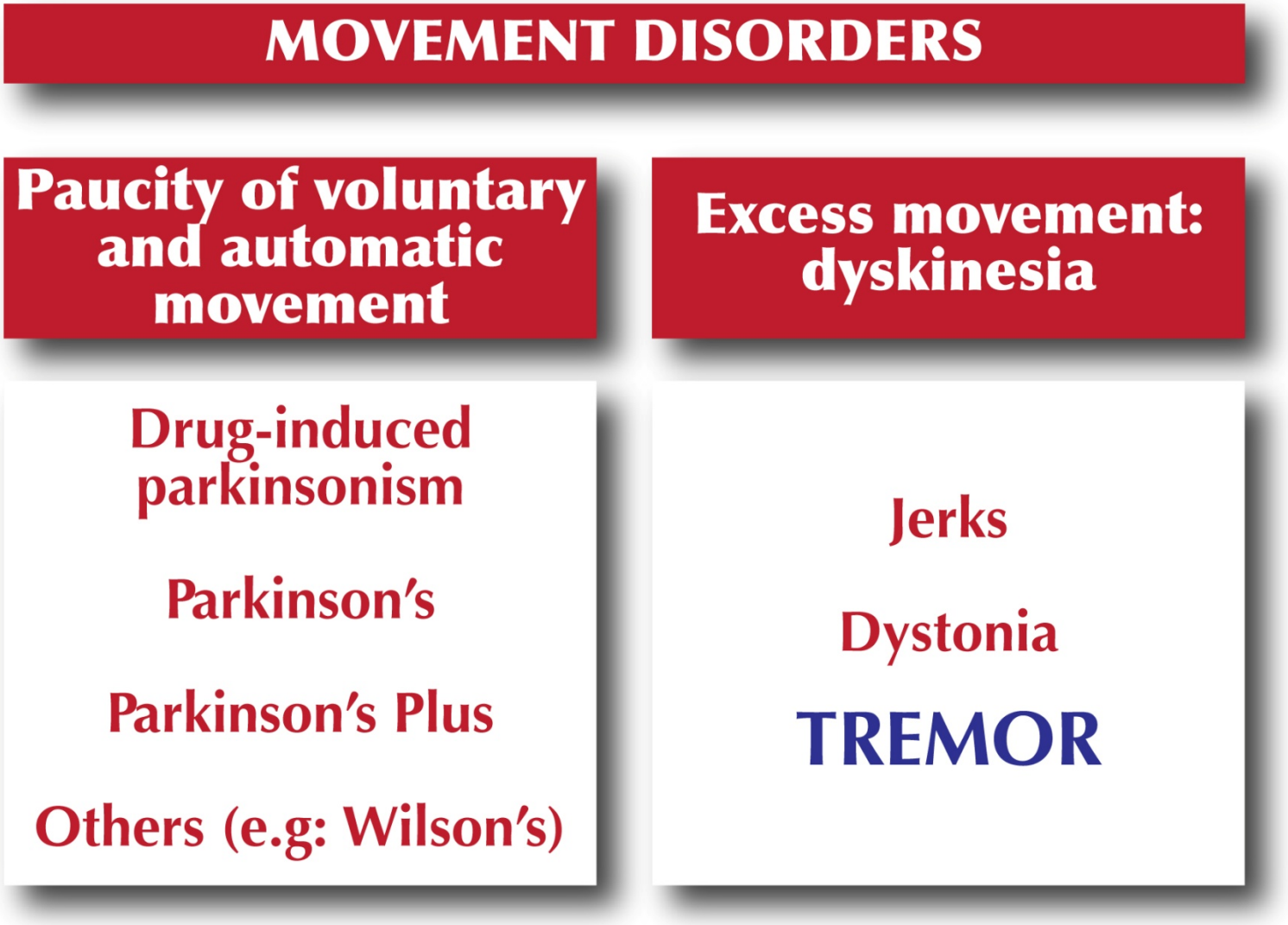
Movement Disorders: A Phenomenological Category



The 3 Most Important Things in Movement Disorders

- Observation
- History
- Examination

Describing Movement Disorders

- Anyone can describe a movement disorder
- Observe patient at rest, in waiting room
- Hypokinetic? Hyperkinetic?
- Spontaneous movements, also while distracted
- If any movements present, **be descriptive!**
- Describe location, frequency, speed, amplitude
- Aggravating/alleviating factors

Prevalence of Movement Disorders: Population Studies

Movement Disorder	Prevalence (100,000) in population	Reference
Restless legs syndrome	5,000 - 15,000	Yeh et *al., Sleep Breath* (2012) 16: 987-1007
Essential tremor	900	Louis & Ferreira, *Mov Dis* (2010) 25: 534-541
Tourette's syndrome	770 (children); 50 (adults)	Knight et *al., Ped Neuro* (2012) 47: 77-90
Parkinson's disease	300	de Lau & Breteler, *Lancet Neuro* (2006) 5: 525-35; Nussbaum & Ellis, *New Eng J Med* (2003) 348: 1356-64
Primary dystonia	33	Nutt et al., *Mov Dis* (1988) 3: 188-194
Blepharospasm	13.3	Defazio *et al., Neurology* (2001) 56: 1579-1581
Hemifacial spasm	7.4 - 14.5	Auger & Wishnant, *Arch Neurol* (1990) 47: 1233-34
Hereditary ataxia	6	Schoenberg et al., *The Inherited Ataxias - Adv Neurol* (1978) 21: 15-32
Huntington's disease	5.7	Pringsheim *et al., Mov Dis* (2012) 27: 1083-1091
Wilson's disease	3	Reilly *et al., J Neurol Neurosurg & Psych* (1993) 56: 298-300

Updated Fahn & Jankovic *Principles and Practice of Movement Disorders* (2007) Churchill Livingstone Elsevier

Case mix in Movement Disorders Clinic Cohorts

Movement Disorder	% cases
Parkinsonism	32.9
Dystonia	31.3
Tremor	13.9
Tics (Tourette's)	4.7
Chorea	3.1
Tardive syndromes	2.7
Myoclonus	2.5
Psychogenic movement disorder	2
Hemifacial spasm	1.7
Ataxia	1.5
Paroxysmal dyskinesias	0.8
Stereotypies (other than tardive dyskinesias)	0.7
Restless legs syndrome	0.5
Stiff-person syndrome	0.1

Fahn & Jankovic *Principles and Practice of Movement Disorders* (2007) Churchill Livingstone Elsevier

Need to know: muscle tone

- Testing: manipulate joint through full range of movement
- Normal tone
- Rigidity
  - *constant = "lead pipe"*
  - *intermittent = "cogwheeling"*
- Spasticity usually indicates corticospinal damage
- Hypotonia: can be a sign of cerebellar disease
- contractures in hypokinetic disorders, dystonia

Case 1: "I cannot hold my coffee cup!"

- HPI: 52 yo RHW with increasing difficulty performing activities of daily living due to bilateral hand shaking. Continues to work as a computer analyst.
- FHx: "My whole family shakes at Thanksgiving dinner…"
- SocHx: Non-smoker, rare alcohol

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Case 2: “My tennis partner is getting better than me!”

- HPI: 65 yo LHM with 6-month history of gradually slowing gait has noticed intermittent tremor in R hand x 3 months. Continues to play tennis twice weekly, but losing to his long-time partner.
- FHx: Mother had ‘shakes’ in her old age
- SocHx: Nonsmoker, -EtOH, works as CPA

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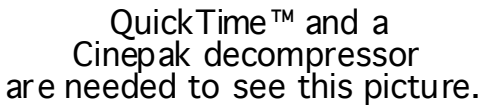
What's This Type of "Shake"?



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- Sudden, brief, shock-like involuntary movements
- Caused by muscular contractions: positive […]
- Caused by inhibitions: negative […], *e.g.* asterixis
- Can be a form of seizure

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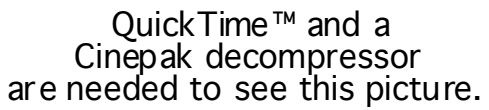
What's This Type of "Shake"?



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- "Voluntary" in nature
- Abnormal movements (motor […]), abnormal sounds (phonic […]), or combination
- Simple or complex. Simple […] difficult to distinguish from myoclonic or choreic jerks, but tend to be repetitive.

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What's This Type of "Shake"?

QuickTime™ and a
Cinepak decompressor
are needed to see this picture.

- Twisting movements which tend to be sustained at the peak of movement
- Frequently repetitive, often progress to abnormal postures
- Simultaneous contraction of agonist and antagonist muscles

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What's This Type of "Shake"?

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Cinepak decompressor
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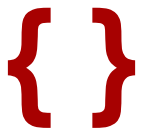

- Involuntary, irregular, purposeless, non-rhythmic, abrupt, rapid, unsustained movements that flow from one body part to another
- To be differentiated from: tics, myoclonus, dystonia
- Prototype: Huntington's

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{DISCUSSION}

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Classification of Hyperkinesias

- Akathisia
- Ataxia
- Athetosis
- Ballism
- Chorea
- Dysmetria
- Dystonia
- Hemifacial spasm
- Hyperekplexia
- Hypnogenic dyskinesias
- Myoclonus
- Moving toes/fingers
- Paroxysmal dyskinesias
- Restless legs
- Stereotypy
- Stiff-muscles
- Tics
- Tremor

Definition of Tremor

- An oscillating movement affecting one or more body parts
- Rhythmic and regular

Types of Tremor

- Rest tremor
- Action tremor
- Postural tremor
- Intention tremor
- Task-specific tremor

Drug-Induced Tremor

- Anti epileptic drugs
- Tetrabenazine (dopamine depleting)
- Antidepressants
- Lithium
- Methylphenidate
- Antibiotics: fluoroquinolones (levoflox; cipro etc)

Enhanced Physiologic Tremor

- Affects most individuals
- Affected by a number of stressors including fatigue, anxiety etc

Case 1: Essential Tremor - Need to Know

- Symmetric postural tremor - 4 to 10 Hz
- Arms most predominant; other body parts also affected
- In most, beneficial response to alcohol
- 10% > 70 yo affected
- Strong family history

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Case 1: Essential Tremor - Management

- Is tremor affecting activities of daily living? Social interactions?
- Know when to refer to a neurologist

Essential Tremor - Propanolol and Other Beta Blockers

- Perhaps most effective drug for ET
- Other beta blockers may also be effective
- Despite conventional wisdom, no increased risk of depression; small risk of fatigue and sexual dysfunction
- Contraindications: asthma; second-degree atrioventricular block; insulin-dependent diabetes
- Prn use: 20-80 mg before event

Essential Tremor - Primidone

- Another effective medication
- Start low, at bedtime, increase slowly (rarely need to go beyond 250 mg a day)
- In difficult cases, can be used in combination with beta blocker

Essential Tremor - Topiramate and other anti-epileptics

- Good evidence of efficacy
- Start low dose at night - some studies have found benefit in up to 400 mg/day, but 100 mg/day divided in bid dosing could work well
- Side effects: weight loss (22%); paresthesias; cognitive blunting
- Other AEDs: zonisamide and leviteracetam

Essential Tremor - Gabapentin

- Studies have broad efficacy profile of gabapentin (effective to no effect)
- Together with leviteracetam, is excreted by kidney; so a consideration in patients with compromised liver, for example

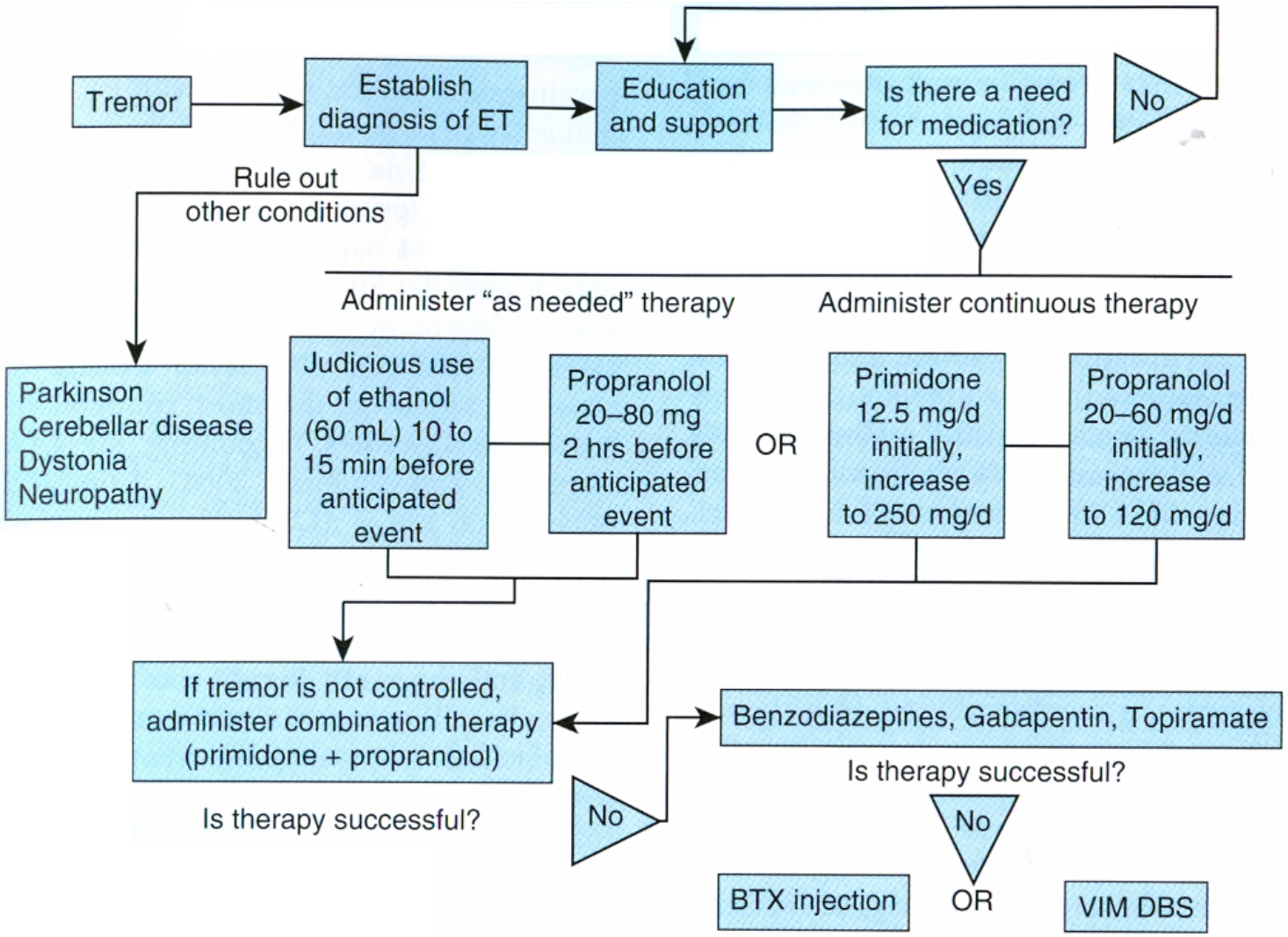
Essential Tremor - Benzodiazepines

- Effective
- Abuse potential
- Consider in patients who need therapy prn -- need trial runs!

Essential Tremor - deep brain stimulation

- For refractory cases
- Thalamus - Vim

Essential Tremor - Fahn-Jankovic Algorithm



Principles and Practice of Movement Disorders
Fahn & Jankovic (Eds.) (Elsevier)

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Not to miss: Wilson's disease

- Copper-transporting P-type ATPase (ATP7B)
- The wing-beating tremor; postural and intention
- Other presenting features: liver disease; dystonia; parkinsonism; cognitive impairment; dementia; psychosis
- Diagnosis: Kayser-Fleischer rings; Serum ceruloplasmin; 24-hour urine copper
- Reversible! Not so straightforward. Avoid copper-rich foods. D-penicillamine along with pyridoxine (controversial); others; liver transplant; symptomatic treatment

Case 2: “My tennis partner is getting better than me!”

- HPI: 65 yo LHM with 6-month history of gradually slowing gait has noticed intermittent tremor in R hand x 3 months. Continues to play tennis twice weekly, but losing to his long-time partner.
- FHx: Mother had ‘shakes’ in her old age
- SocHx: Nonsmoker, -EtOH, works as CPA

{DISCUSSION}

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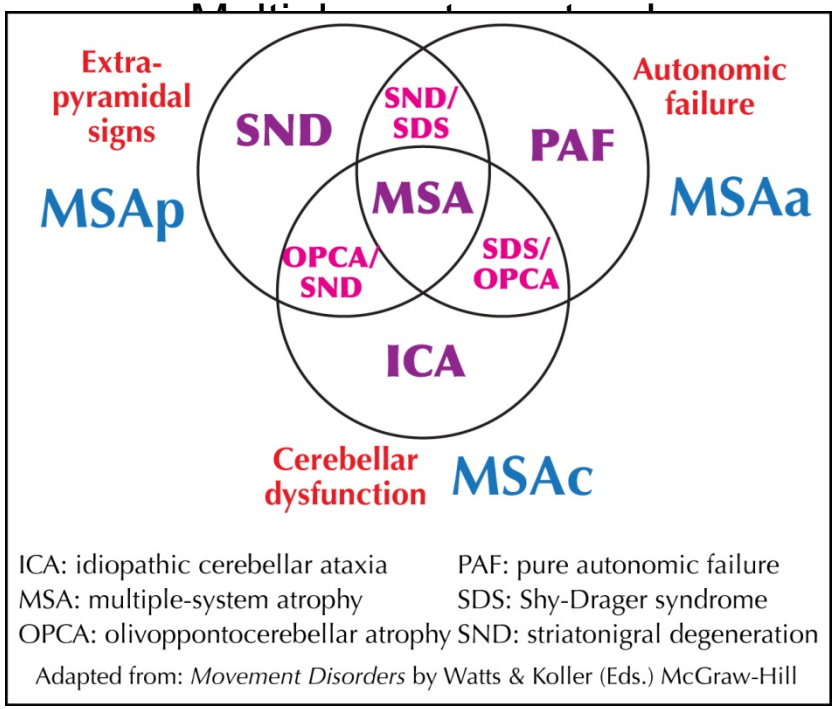
Classification of Hypokinesias

- Parkinson's disease
- Symptomatic parkinsonism
- "Parkinson's Plus syndromes"
  - Progressive supranuclear palsy



  - Corticobasal degeneration

- Dementia syndromes
  - Alzheimer's disease
  - NPH
  - ALS/dementia/PD complex of Guam
- Hereditary disorders
  - Wilson's disease
  - Huntington's disease
  - NBIA (Neurodegeneration with Brain Iron Accumulation)

The TRAP of parkinsonism

- **T**remor
- **R**igidity
- **A**kinesia
- **P**ostural Instability

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Idiopathic Parkinson's Disease

- Prototype of a 'hypokinetic" disorder
- Most common human movement disorder…in the Movement Disorder clinic. Less common than ET.
- Characterized by cardinal triad:
  - Bradykinesia
  - Rigidity
  - Tremor
- Also:
  - Disturbance of Balance
  - Response to L-DOPA
- Loss of neurons in ventral tier of the substantia nigra *pars compacta* (SNc) / ventral tegmental area (VTA) complex mainly

Case 2: Is it Parkinson's Disease? Ddx

Entity	How to differentiate from PD
Med-induced parkinsonism	Careful screening, including neuroleptics (including **atypicals**) and GI motility drugs
Essential tremor (ET)	+ FHx, **symmetric tremor**, - rigidity, - bradykinesia, - tremor at rest, tremor worsens with movement
Dementia with Lewy bodies (DLB)	Early memory impairment, **delusions and hallucinations**
Progressive Supranuclear Palsy (PSP)	Lack of tremor, **impaired voluntary saccades, early falls**
Corticobasal degeneration (CBD)	Alien hand, prominent dystonia, asymmetrical
Shy-Drager (MSAa)	Orthostasis, early autonomic dysfunction
Olivopontocerebellar Atrophy (OPCA; MSAc)	Brainstem signs such as dysphonia and swallowing difficulties; cerebellar signs
Striatonigral degeneration (SND; MSAp)	No response to L-DOPA

Case 2: Parkinson's Disease Initial Management

- Dopamine agents: either L-DOPA (Sinemet) or dopamine agonists.
- The right dose? Enough. Like adding salt to soup.
- L-DOPA
  - Better tolerated in older folks
  - Concern over dyskinesias not huge concern
  - Start Sinemet 25/100 one tab tid (qid) increase to effect. Push to 800-1,000 mg LVD/day before concluding no effect
- Dopamine agonists
  - Pramipexole (Mirapex), Ropinirole (Requip), avoid Parlodel (bromocriptine)
  - Start low, go slow. Start with suggested doses

Case 2: Dopamine Replacement Strategies

- Replace precursor (Levodopa)
  - With peripheral dopa decarboxylase inhibitor (carbidopa)
  - Sinemet 25/100 and other formulations – *'without emesis'*
- Dopamine agonists
  - Pramipexole (Mirapex®), ropinirole (Requip®), bromocriptine
  - Extended release versions of dopamine agonists
- Inhibit breakdown: COMT
  - Tolcapone (Tasmar®), entacapone (Comtan®)
- Inhibit breakdown: MAO
  - Selegiline (Eldepryl®, Zelapar®)
  - Rasagiline (Azilect®)
- Delivery
  - Duodenal levodopa pump

Case 2: When to Refer

- Not Parkinson's
- Motor fluctuations
- Dementia
- Medication complications: now on Sinemet 11.5 tabs a day, Comtan, Requip, Eldepryl, Midodrine, Seroquel …time to refer
- Surgical therapies: Deep brain stimulation
- Access to clinical trials

Let's Go to Moving Movies…

What's this "Shake"?

This woman had a pressure injury to one sciatic nerve

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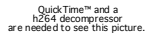
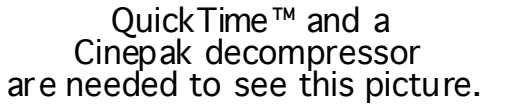
- Severe pain in one or both feet
- Characteristic writhing movement of toes and sometimes of feet



- Patients have history of lumbosacral root damage
- Includes cases of lumbar herpes zoster, generalized peripheral neuropathy or minor trauma to legs
- Onset middle or late in life; pathophysiology unclear
- Therapy: difficult; various AEDs, TENS, sympathetic blockage

What's this "Shake"?



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- Aka palatal myoclonus
- Guillain-Mollaret triangle (red nucleus / ipsi inferior olive / contra dendate nucleus)
- Associated with stroke; multiple sclerosis; Behçet's; dialysis encephalopathy etc
- 25% "idiopathic"
- Persists during sleep
- Tharapy:
  various; carbamezapine

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Cinepak decompressor
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What's this "Shake"?

- A feeding dystonia…

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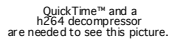

- Most are autosomal recessive; feeding dystonia characteristic; acanthocytes in blood smear
- Chorea; cognitive and personality changes; seizures; dystonia; parkinsonism; bulbar signs
- Rarely associated with lipoprotein metabolism disorders

What's this "Shake"?

QuickTime™ and a
H.264 decompressor
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- A focal dystonia
- Up to 25% of cases of focal dystonia in clinic
- EMG-guided unilateral or bilateral injection of botulinum in vocal cords or posterior crycoarytenoid muscle

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H.264 decompressor
are needed to see this picture.

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{Turn Sound Off}

What's this "Shake"?

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h264 decompressor
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- Can be post spinal infection

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h264 decompressor
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- Appears to be due to loss of inhibitory in the posterior horns
- Clonazepam; Keppra; other AEDs

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What's this "Shake"?

QuickTime™ and a
decompressor
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- Lumbar lordosis

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- Progressive fluctuating rigidity of axial muscles in the back, abdomen, hips and shoulders leading to lordosis emerging in 4th and 5th decades
- Painful spasms
- Up to 2/3 affected are insulin-dependent diabetics
- Anti GAD antibodies in > 60% patients (GABA metabolism affected in spinal cord?); anti amphimysin ab in breast ca
- Progressive encephalomyelitis with rigidity a very aggressive form of SPS
- Therapy: benzos; baclofen; steroids; IVIg

What's this "Shake"?

- Responds to zolpidem (Ambien)

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QuickTime™ and a
h264 decompressor
are needed to see this picture.

- Can occur 40+ years after amputation; may be preceded by pain at the stump months previously
- Is this a segmental myoclonus?
- Responds to zolpidem (Ambien)

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What's this "Shake"?

Call the neurosurgeon

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- 95% primary, due to vascular compression of VIIth nerve exit from the brainstem
- 5% secondary, s/p Bell's palsy, cerebellopontine angle mass lesion or brainstem lesions
- Remissions rare
- Therapy: posterior fossa exploration and facial nerve protection
  (chemical denervation)

Resources

Movement Disorders in Clinical Practice

By Guy Sawle (Isis Press)

Principles and Practice of Movement Disorders

By Stanley Fahn & Joseph Jankovic (Churchill Livingstone Elsevier)

Movement Disorders Neurologic Principles & Practice

By Ray L. Watts & William C. Koller (McGraw Hill)

A Great Movement Disorders Website

www.wemove.org

Worldwide Education in Movement Disorders

- Basically a one-stop website for background, workup and treatment for all movement disorders
- For patients and practitioners

The End

Thank you for your attention!

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Appendix

The following topics shall not be covered unless they arise as points of discussion.

Dystonic Tremor

- Postural, localized, irregular in amplitude and periodicity
- Typically in patients with dystonia
- Some patients with family history of dystonia may have dystonic tremor *without* any evidence of dystonia
- Difficult to distinguish sometimes from essential tremor
- Consider trihexyphenidyl

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Cinepak decompressor
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Primary Writing Tremor

- Usually a tremor part of writer's cramp (a focal dystonia) progression
- If no evidence of dystonia, then consider a primary writing tremor
- Can also be present with other manual activity (holding cup etc)
- Therapy: essential tremor vs. dystonia management paradigm; writing enabler; Vim DBS

Primary Orthostatic Tremor

- 14-16 Hz tremor in legs upon standing but not while ambulating
- Tremor is too fast to be visible at times -- auscultate quads (distant helicopter sound)
- Therapy: clonazepam; gabapentin

Cerebellar and Midbrain Tremors

- Typically a kinetic tremor - increased amplitude on target approach
- Sometimes mixed with postural tremor
- Rubral tremor - 2-5Hz may have rest and or postural component. Look for oculomotor nerve palsy and hemiparesis
- Therapy: difficult; supportive
- Riluzole

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Tremor in Neuropathy

- Some peripheral neuropathies: hereditary motor and sensory neuropathy; chronic inflammatory demyelinating polyneuropathy; IgM demyelinating paraproteinemic neuropathy etc
- In patients with known neuropathies beware of independent causes such as vitamin E deficiency and drug toxicity
- Therapy: address underlying cause; propranolol

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Cinepak decompressor
are needed to see this picture.

Post-traumatic Tremor

- Usually in children after head trauma
- 1.5 - 3Hz; midbrain tremor?
- Therapy: trihexyphenidyl; levodopa; essential tremor modalities