Movement Disorders

Les troubles du mouvement

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Major Movement Disorders -
Les troubles du mouvement majeurs

To be covered in the next 30 minutes:

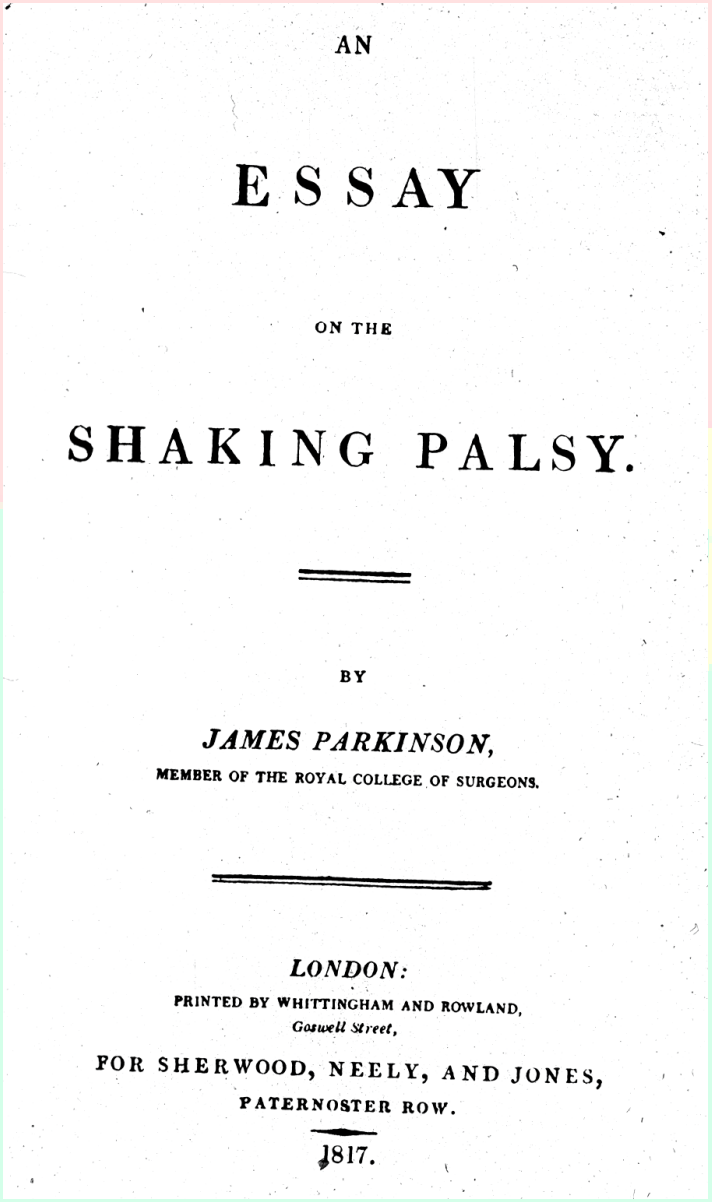
- Parkinson's disease – *la maladie de Parkinson*
- Other parkinsonian disorders – *d'autres maladies parkinsoniennes*
- Essential tremor – *le tremblement essentiel*
- Dystonia disorders – *les dystonies*
- Drug-induced disorders – *les dyskinésies d'origine médicamenteuse*

Parkinson's disease – *la maladie de Parkinson*

Outline:

1. The range of clinical manifestations
   - *La gamme de manifestations cliniques*
2. The diagnosis
   - *Le diagnostic*
3. Current treatment
   - *Le traitement actuel*

James Parkinson's monograph



AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.

Core clinical features (i.e., the syndrome of "parkinsonism"):

- Tremor
- Rigidity
- Akinesia
- Postural disturbances

Tremor

Rest tremor (characteristic)

- Occurs in repose
- 3-7 Hz (slow)
- ***TIP:*** Watch for rest tremor while walking, or during tasks of concentration (e.g., arithmetic, reciting months backward)

Action tremor (less common)

- Occurs with muscle activation
- 6-11 Hz (fast)

Rigidity

- Muscle tone: Increased passive resistance
  - A sign clinicians elicit, not a symptom
- Unlike spasticity, rigidity is uniform (1) in antagonists, (2) throughout a joint range, (3) regardless of speed
- ***TIP:*** Accentuated by contralateral activity
- "Cogwheeling": correlated with tremor, not rigidity

Akinesia

- "Akinesia": *from the Greek for* "lack of movement"
- Impairment of voluntary movement
- Typically causes most of the disability in Parkinson's disease (PD)

Akinesia

3 components:

Bradykinesia (decreased *speed* of movement)

- e.g. Slow initiation and execution of all movement

Hypokinesia (decreased *amplitude* of movement)

- e.g. Micrographia, decreased arm swing, short stride

Oligokinesia (decreased *quantity* of movement)

- e.g. Reduced blink and facial expression

- ***TIP:*** Tendency to progressive fatigue with repetition

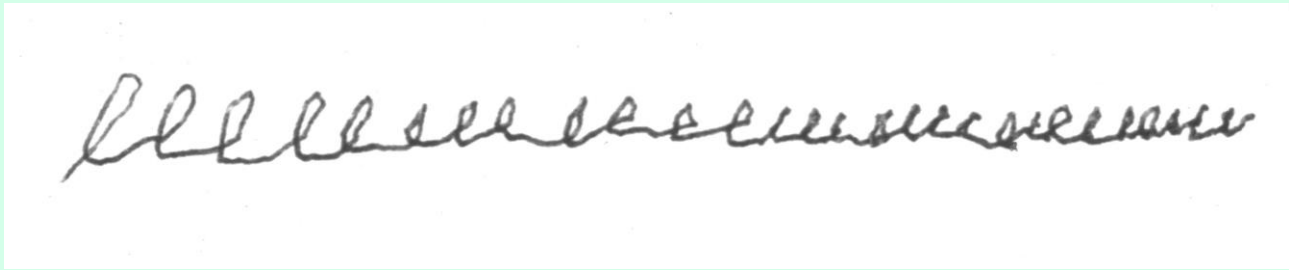
Micrographia

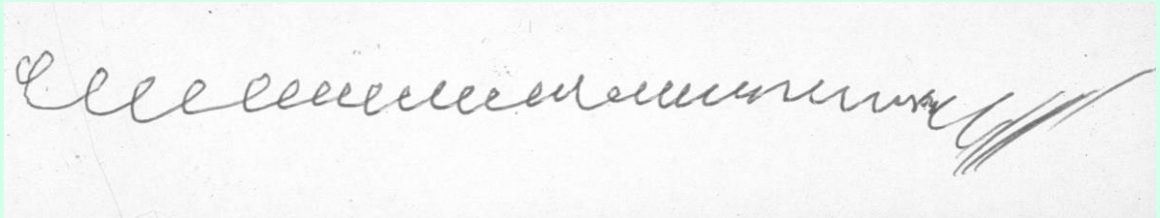
Drawing loops – *dessiner des boucles*

Right hand

Right-sided parkinsonism

Left hand





Postural Disturbances

2 components:

- Flexion posture, “stooping”
  - Neck, elbows, waist, knees
- Disorder of equilibrium, falls
  - *Exam:* Test for retropulsion
    - Pull backward on shoulders
    - Normal: recover balance in 2 steps

Parkinson's disease - Range of clinical manifestations *la maladie de Parkinson - la gamme de manifestations cliniques*

- Cardinal motor manifestations
  - Tremor, rigidity, akinesia, postural disturbances
- Non-motor manifestations *(les manifestations non-motrices)*
  - Cognitive (dementia, excess somnolence)
  - Autonomic (constipation, orthostatic hypotension/other cardiovascular instability, incontinence, sexual or sweat dysfunction/failure of temperature regulation)
  - Sensory (restless legs syndrome, loss of smell)
  - Miscellaneous (depression, REM-sleep behavior disorder)

"Premotor" Manifestations – *Les manifestations prémotrices*

- May precede motor onset by decades
- Strongest evidence established for:
  - Olfactory deficit
  - Constipation
  - REM-sleep behavior disorder
  - Excess daytime somnolence
  - Depression, anxiety

Savica et al. Arch Neurol 2010; 67: 798-801

Lang. Mov Disord 2011; 775-783

Typical Clinical Course of PD

- Starts in one limb
  - Dominant:non-dominant = 3:2
- Progresses slowly over months and years
  - Typically first to the other limb on the same side
  - Eventually becomes bilateral, but remains worse on the side first affected
- Tremor, rigidity and akinesia early; postural instability late (≥ 10 years)

Parkinson's disease - Diagnosis
la maladie de Parkinson - le diagnostic

Why do patients with PD go to doctors?

1. Involuntary movement
   - Is it a rest tremor?
   - Ask about and look for: Evidence of akinesia, rigidity
2. Trouble with voluntary movement
   - Is it akinesia?
   - Ask about and look for: Tremor, rigidity

Parkinson's disease - Diagnosis
la maladie de Parkinson - le diagnostic

- Clinical course: did it start unilaterally?
- Diagnosis can be supported by:
  - Non-motor features: REM-SBD, loss of smell
  - Imaging of dopaminergic nerve terminals
  - Response to medication
- Ultimately, we continue to diagnose PD by finding characteristic clinical motor features evolving in a characteristic way

Parkinson's disease – Current treatment
la maladie de Parkinson - le traitement actuel

- Medications
- Physical activity
- Surgery

Parkinson's disease – Medications
la maladie de Parkinson – les médicaments

- Medications
  - 6 categories currently available
  - General principles of medications for PD
    - drugs treat only symptoms; the disease progresses
    - all drugs are compatible with each other
    - using small doses of multiple drugs usually produces fewer side effects than large doses of a single drug
    - all side effects are reversible
    - laboratory tests for organ surveillance not required (exception: tolcapone)

Currently Available Medications

Modestly effective

- Anticholinergic drugs
  - diphenhydramine, trihexyphenidyl, benztropine, biperiden, etc.
- Amantadine

Most effective

- Levodopa (plus carbidopa or benserazide)
- Dopamine agonists
  - bromocriptine, pergolide, pramipexole, ropinirole, rotigotine, cabergoline, apomorphine, pirebidil, etc.

Levodopa boosters

- MAO (monoamine oxidase)-B inhibitors
  - selegiline, rasagiline, safinamide, etc.
- COMT (catechol-O-methyl transferase) inhibitors
  - tolcapone, entacapone

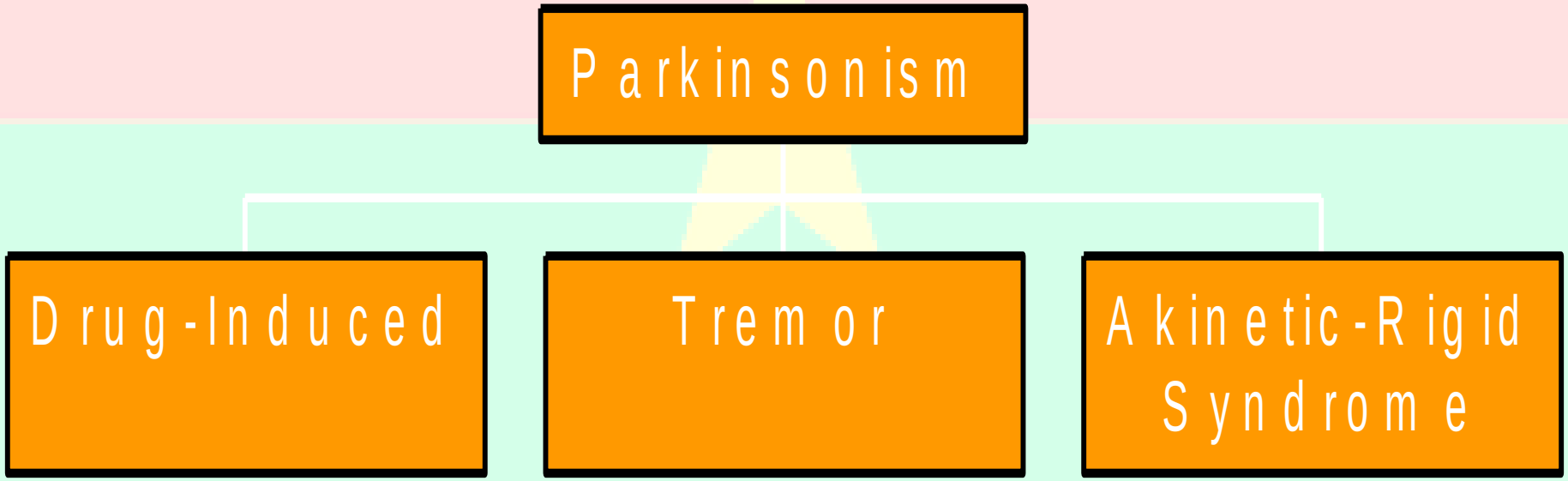
Physical activity for PD

- Numerous research studies over the last 15 years have established the value of physical activity
  - Aerobic exercise
  - Resistance exercise
  - Tai chi, yoga
  - Dance
  - Sports
- Every PD patient should be advised to get involved in regular physical ctivity of some kind

Surgery for PD

- Mainly for patients whose medications fail to control their symptoms consistently, or have intractable tremor
- Surgical options
  - Deep brain stimulation – *la stimulation cérébrale profonde*
  - Jejunal infusion of L-dopa – *infusion intestinale de la L-dopa*

Simplified Differential Diagnosis



Akinetic-Rigid Syndromes

- Infectious and postinfectious
- Toxic, metabolic
- Familial
- Young-onset, e.g., Wilson's
- Diagnosable by imaging studies
- Miscellaneous
- Degenerative

Degenerative Diseases

- Parkinson's disease
- Progressive supranuclear palsy
- Multiple system atrophy
- Corticobasal degeneration

Progressive supranuclear palsy - *la paralysie supranucléaire progressive*

Practical Clinical Diagnosis

- older patient
- vertical ocular motor disorder (slow saccades, restricted range)
- onset with gait disorder and disequilibrium
- no tremor
- rigidity in neck but not in limbs, relatively normal performance of repetitive movements
- little or no response to levodopa

Multiple system atrophy – *l'atrophie multisystématisée*

Practical Clinical Diagnosis

- younger patient (usually < 60 years old)
- no tremor
- early and prominent autonomic difficulty
- relatively rapid progression of parkinsonism
- poor, unsustained response to levodopa
- may have ataxia greater than parkinsonism
- REM-SBD

Corticobasal degeneration – *la dégénérescence corticobasale*

Practical Clinical Diagnosis

- patient in 7th decade
- asymmetric presentation
- combination of
  - basal ganglia signs (rigidity, dystonia, akinesia)
  - cerebral cortical dysfunction (apraxia, cortical sensory loss, alien limb)
  - other common features: action and focal reflex myoclonus, nonfluent aphasia

Essential tremor – *le tremblement essentiel*

- If a patient has a tremor, think of essential tremor (ET)
- Causes an action tremor of the hands
  - with sustained posture (“postural tremor”)
  - with movement (“kinetic tremor”)
- More disabling than rest tremor
- Typically interferes with eating, drinking, writing
- Distribution: upper limbs, head (50%), voice (25%)
- Progression is very slow

Essential tremor – *le tremblement essentiel*

- Frequency: 6-11 Hz (fast)
- Patients are usually neurologically normal, apart from tremor
  - Tremor is the sole source of disability
- Two distinctive features:
  - Responds to a low dose of alcohol
  - Positive family history (~75%), consistent with autosomal dominant inheritance

Essential tremor – *le tremblement essentiel*

- Examination – *l'examen*
  - Hold arms outstretched forward at shoulder level – *«la manoeuvre du serment»*
  - Finger-to-nose testing - *l'épreuve «doigt-nez»*
  - Optional: handwriting, drawing, drinking from a glass

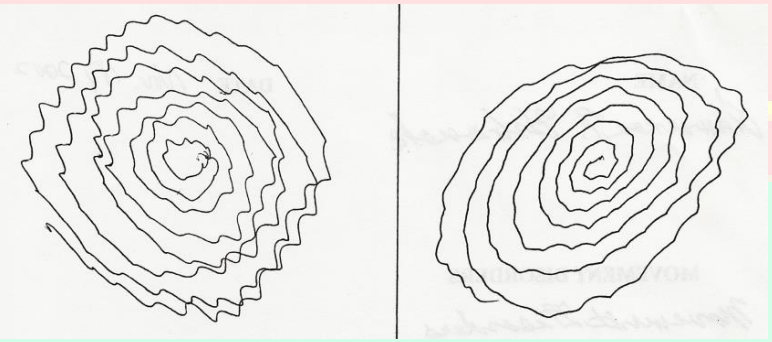
ET - Medical Treatment

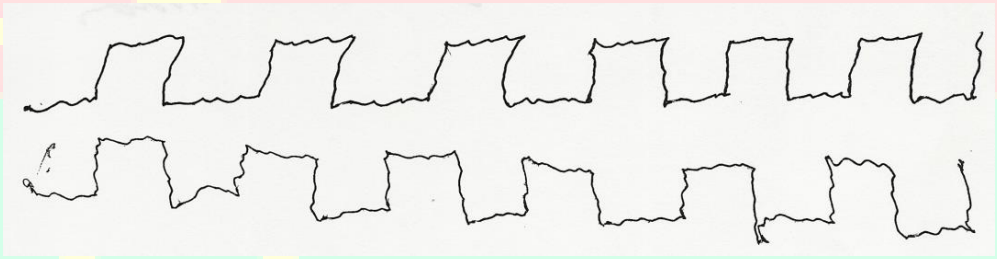
- 2 main agents used:
  1. Primidone: start 25 mg qHS; ↑ by 25 mg as tolerated or needed
     - Side effects: drowsiness, dizziness
  2. Propranolol: start 10 mg t.i.d. or 60 mg of long-acting preparation q.d.; titrate upward as needed and tolerated

Essential Tremor –
Response to Medication

An 84-year-old man with a 4-year history of essential tremor

Prior to treatment





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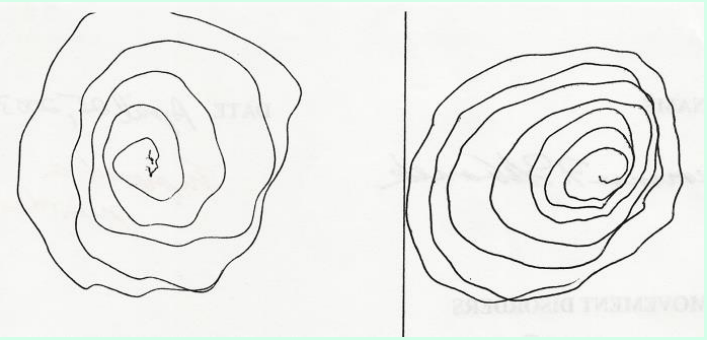

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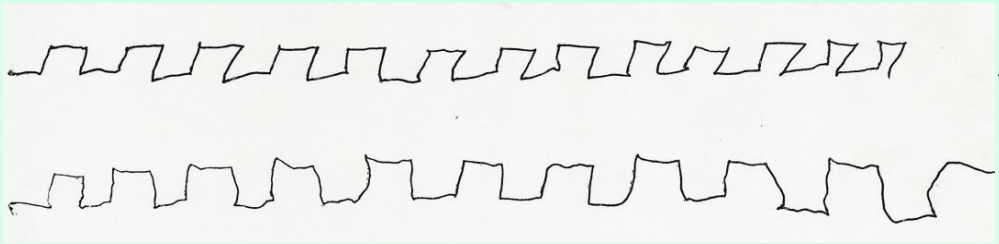

Right

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On primidone 500 mg qHS

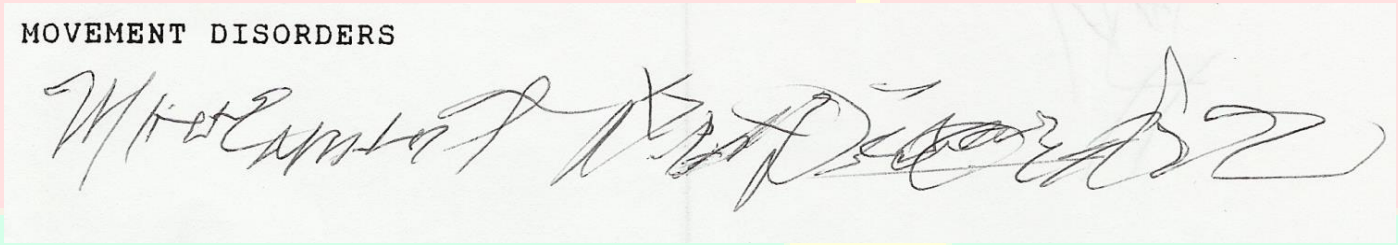
Essential Tremor

Medical treatment (others, less established)

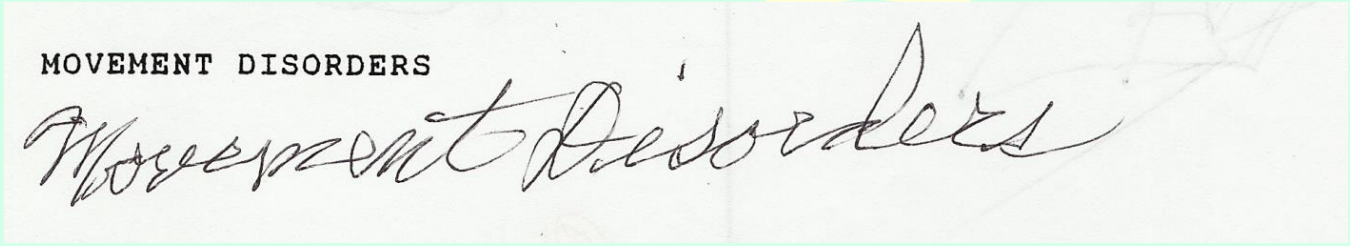
1. Methazolamide
2. Gabapentin
3. Mirtazapine
4. Topiramate
5. Clonazepam

Essential Tremor –
Response to Medication

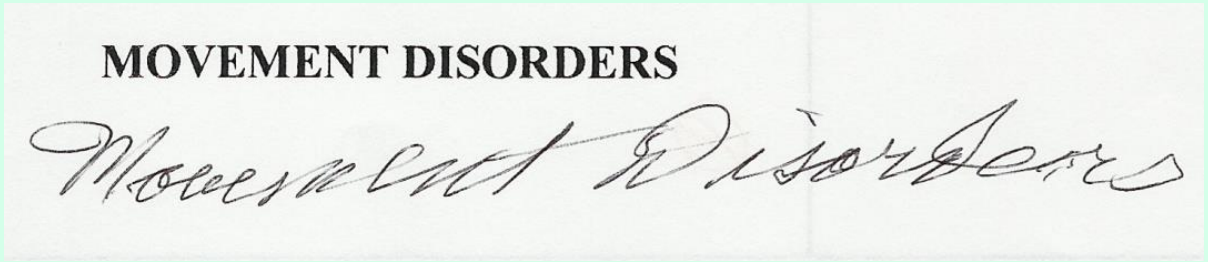
A 79-year-old woman with a 40-year history of essential tremor



Prior to treatment



On primidone 150 mg daily



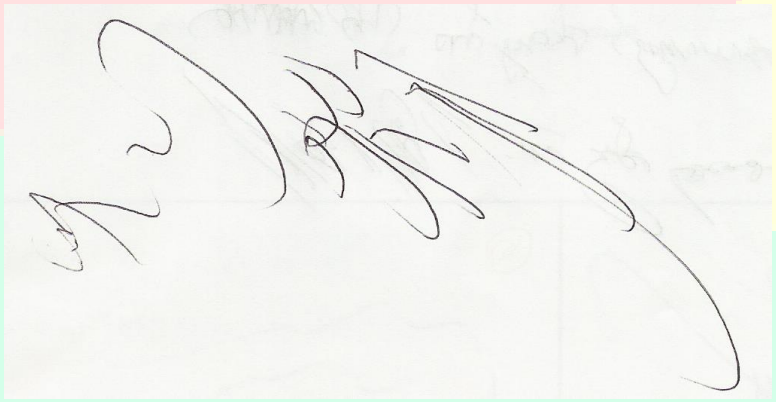
On primidone 250 mg, propranolol 120 mg, and methazolamide 225 mg daily

Essential Tremor –
Response to Medication

An 84-year-old man with a 56-year history of essential tremor

Prior to treatment

Left



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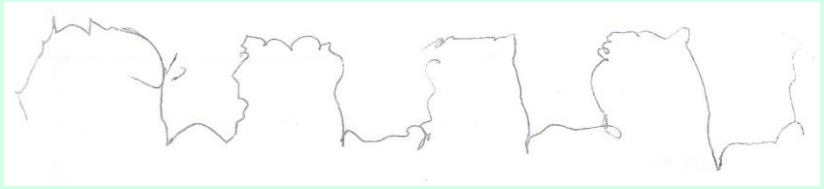

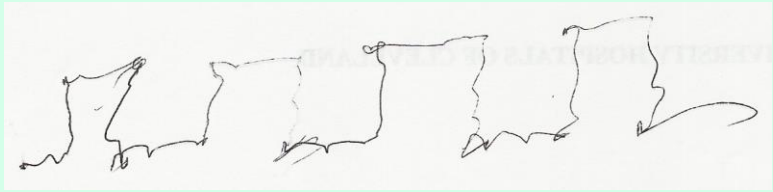

Right

On methazolamide 50 mg t.i.d.
and gabapentin 200 mg t.i.d.

Essential Tremor

Surgical Treatment – *le traitement chirurgical*

- Thalamotomy - *la thalamotomie*
- Deep brain stimulation of the thalamus - *la stimulation cérébrale profonde du noyau VIM du thalamus*
- Gamma knife therapy - *la thalamotomie par gamma knife*
- Focused ultrasound - *la thalamotomie par ultrasons focalisés*

Dystonia – Characteristic Features

- Continuous (tonic) or irregularly repetitive (clonic) muscle contractions, often resulting in sustained abnormal postures
- Two distinctive features:
  - Response to sensory "tricks" – *les gestes antagonistes*
  - Induced or ameliorated by specific actions ("task-specific" induction or suppression)

Dystonia - Classification

By etiology

- Primary: no identifiable pathology
- Secondary: identifiable cause

By distribution

- Focal
- Segmental
- Multifocal
- Generalized
- Hemidystonia

Primary Dystonia

Focal dystonia:

- Almost always sporadic
- Onset in adulthood
- Involves cranial, cervical or upper limb muscles
- Remains focal, rarely generalizes

Common Focal Dystonias

- Blepharospasm
- Oromandibular dystonia
- Spasmodic torticollis (cervical dystonia)
- Laryngeal dystonia (spasmodic dysphonia)
- Writer’s cramp

Secondary Dystonia

Dystonia may be due to a wide variety of causes of brain injury:

- Metabolic disorders (Wilson's, Leigh's, etc.)
- Trauma – central or peripheral
- Stroke
- Cerebral palsy
- Drugs
- Degenerative diseases (Parkinson's, CBGD, Hallevordern-Spatz, etc.)
- Psychogenic

Dystonia - Treatment

- Medications
  - Trial of levodopa in children
- Botulinum toxin injections
  - *les injections de toxine botulique*
- Surgery

Botulinum toxin - *la toxine botulique*

- “Chemodenervation” of muscle : Botulinum toxin prevents release of acetylcholine at neuromuscular junction
- Onset: within days, up to one week
- Duration: average 3 months
- Side effects: most commonly weakness in or near the region injected

Drug-Induced Disorders -Antidopaminergic Drugs

2 major drug categories involved:

- Antipsychotic drugs
  - Drugs used to treat hallucinations/delusions, or for behavioral modification (a.k.a. “neuroleptics”)
  - Haloperidol, risperidone, olanzapine, etc.
  - Typical antipsychotics cause more problems than atypical antipsychotics
- Antinauseant drugs
  - Drugs used as primary antiemetics, or as adjuncts for chemotherapy
  - Metoclopramide, prochlorperazine, etc.

Drug-Induced Disorders -Antidopaminergic Drugs

Neurologic Complications:

- Acute dystonic reaction
- Akathisia
- Parkinsonism
- Tardive dyskinesia and other tardive syndromes
- Neuroleptic malignant syndrome

Drug-Induced Disorders -Antidopaminergic Drugs

Acute Dystonic Reaction:

- Onset
  - Immediate (often after first dose) up to 72 hours
- Manifestations
  - Severe dystonia of face and/or neck muscles
  - *Oculogyric crisis*: forced gaze deviation
  - Importance: severe discomfort can be alleviated promptly
- Treatment
  - Withdraw the offending agent; resolves within days
  - I.V. or I.M. antihistamine (e.g. diphenhydramine 25 mg)
    - relief within 15 minutes
    - 72-hour prescription for pills to prevent recurrence

Drug-Induced Disorders -Antidopaminergic Drugs

Akathisia:

- Onset
  - Days to weeks after first dose
- Manifestations
  - Severe restlessness, agitation, intense discomfort
  - Unable to sit still, pacing, rubbing, repetitive behaviors
  - Importance: most common cause of neuroleptic noncompliance
- Treatment
  - Withdraw the offending agent; resolves within weeks
  - If needed, symptomatic Rx with propranolol, lorazepam

Drug-Induced Disorders – Antidopaminergic Drugs

Parkinsonism:

- Onset
  - Weeks to months after first dose
- Manifestations
  - Similar to Parkinson's disease
  - Less tremor, more symmetric
  - Importance: can be misdiagnosed and treated as Parkinson's
- Treatment
  - Withdraw the offending agent; resolves in up to 18 months
  - If needed, symptomatic Rx with amantadine, anticholinergics

Drug-Induced Disorders -Antidopaminergic Drugs

Tardive Dyskinesia:

- Onset
  - Usually a year or more after first dose *("tardive" = late)*
- Manifestations
  - Orolingual dyskinesias: chewing, licking, lip-smacking movements; head, trunk and limbs variably affected
  - Respiratory dyskinesias, pelvic thrusting: unusual but characteristic
  - Importance: may be irreversible
- Treatment
  - Withdraw offending agent (may worsen temporarily)
  - 50% chance of spontaneous remission

Tardive Dyskinesia

Other points:

- Traditional neuroleptics more liable than atypical neuroleptics to cause it
- Occurs in 20% of patients on chronic therapy
- Older women form the most vulnerable population

Other Tardive Syndromes

- Tardive dystonia
  - Consists mainly of cranial and cervical dystonia
  - Tends to occur in younger males
  - May not require as prolonged exposure; some cases occur within weeks of initiation of drug
  - Very low chance of spontaneous remission

Other Tardive Syndromes

- Tardive akathisia,
- Tardive myoclonus, and
- Tardive tremor have also been described;
- Recognized by “tardive” pharmacologic features:
  1. Onset after prolonged exposure
  2. Worsening after withdrawal of causative medication
  3. Suppression of symptoms by increased dose

Tardive Dyskinesia/Dystonia

Management:

- Prevention: avoid offending agents
- Use/switch to atypical antipsychotics
  - Best is clozapine
- Symptomatic therapy with presynaptic dopamine antagonists (reserpine, tetrabenazine)
- For dystonia: anticholinergics, botulinum toxin
- Alternatives: propranolol, clonidine, benzodiazepines

Drug-Induced Disorders -Antidopaminergic Drugs

Neuroleptic Malignant Syndrome:

- Onset
  - Any time during treatment, especially after ↑ dose
- Manifestations
  - Extreme rigidity, elevated CPK
  - Fever, dysautonomia
  - Impaired mental status
  - Importance: life-threatening
- Treatment
  - Withdraw offending agent
  - For rigidity: dopamine agonist, dantrolene

Final Words

- This is just a sample of the most important and treatable movement disorders
  - We did not even touch on chorea, tics, myoclonus, ballism, or athetosis
- Most movement disorders do not require any technology for diagnosis
- Using your ears and eyes (and occasionally your hands, and a pen and paper), you can be an excellent movement disorders neurologist