An approach to patients with tremor

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Propranolol is the only FDA-approved medication for primary tremor.
Learning Objectives

1. Define tremor
2. Recognize different types & causes of tremor
3. Understand treatment options for the most common causes of tremor
Tremor

Tremor is rhythmic, periodic
Is the movement tremor?
Organic tremor (i.e., not functional)

The brain reverberating circuits driving tremor are constrained:

- Rhythmic
- Fixed frequency (may change over years)
- Consistent vector
- Not entrained by voluntary rhythms

Usually, but not always:

- Reproducible with similar postures or movements
- Not distractible
Rhythmic ?
Other clues to functional tremor

- Sudden onset of marked tremor in normal young people
- Rest required after marked tremor

Exception, Parkinson’s disease tremor

- Sometimes subacute onset
- Comes & goes (but AMRs provoke in opposite hand)
- Often all-or-none, sometimes with high amplitudes
Organic tremor?
Tremor

**Primary**
- Essential tremor (ET)
- ET variants
  - Orthostatic tremor
  - Task-specific tremor (e.g., writing)

**Brain lesions or diseases**
Associated with other neuro signs, such as:
- Parkinson’s disease
- Cerebellar outflow pathway damage

**Systemic**
- Medications (e.g. valproic acid; Li; sympathomimetics)
- Metabolic (e.g. metabolic encephalopathies, thyroid)
Essential tremor
Most common cause of tremor
(4-5% of adults)

1. Normal neurological exam except for tremor
2. No other cause
3. Family history of tremor in a little more than half
Essential tremor: hands
(Usually no resting tremor)
Treatment, essential tremor
Evidence-based guideline: Treatment of essential tremor *(Neurology 2011; 77:1752–1755)*

Report: Quality Standards Subcommittee, American Academy of Neurology

**Results & Recommendations:**

**Level A**, established as effective: propranolol, primidone

**Level B**, probably effective: alprazolam, atenolol, gabapentin, sotalol, topiramate

**Level C**, possibly effective: nadolol, nimodipine, clonazepam, botulinum toxin A, deep brain stimulation, thalamotomy

**Level U**, insufficient evidence: gamma knife thalamotomy, pregabalin, zonisamide, or clozapine
But committees can only help so much...

My approach
(balancing efficacy & side effects)
Beta-blocker: first choice for essential hand tremor

Two properties to note (Jefferson, JNNSP 42(1979) 904-909; Leigh, JNNSP 46(1983) 710-715)

1. Need beta-2 effect, i.e., non-selective $\beta$-blocker
2. Does not need to cross blood-brain-barrier

Propranolol & nadolol, both beta 1 & 2

Atenolol, metoprolol, beta-1
Nadolol does not cross the BBB (propranololol does)

Half-lives:

Propranolol (regular), $T_{1/2} = 4$ hours
Propranolol LA, $T_{1/2} = 10$ hours
Nadolol, $T_{1/2} = 20-24$ hours
Non-selective beta-blocker for tremor

Contraindications: Asthma, bradycardia, hypotension

If prominent beta-blockade needed, may be preferable to select drug with persistent effect (?)

**PRN use:**

Propranolol (regular) \( (T_{\frac{1}{2}} = 4 \text{ hrs}) 10 - 40 \text{ mg} \)

**Chronic, daily use:**

Propranolol LA \( (T_{\frac{1}{2}} = 10 \text{ hrs}) 60 - 160 \text{ mg twice/day} \)

Nadolol \( (40 - 240 \text{ mg once daily}; T_{\frac{1}{2}} = 20-24 \text{ hours}) \)

Nadolol & propranolol equally efficacious \( (Koller, Neurology (1983) 33:1076-7) \)
2nd-line drugs, essential hand tremor
Side effects may overshadow benefits

I infrequently prescribe

Primidone (barbiturate)
- Sedation, dizziness / clumsiness
- Start with ½ of 50 tablet in evening & raise slowly (Limit: 150 mg, 2-3 times daily)

Topiramate (carbonic anhydrase inhibitor)
- Dizzy, cognitive impairment, paresthesias
- Start, 25 mg daily, then bid; raised to 100 - 200 mg bid

Benzodiazepines
- Alprazolam (reasonable option for limited PRN use)
- Clonazepam
Essential tremor: voice (not PD)
Treatment, essential head tremor, voice tremor

• Medications rarely very helpful
  Exception: beta-blocker may attenuate exacerbations due to stress

• Botulinum toxin injections
  • Head tremor: Cervical paraspinal and splenius capitis muscles
  • Voice tremor: Thyroarytenoid muscles with ENT, EMG guidance
Long-standing essential tremor
Treatment of severe essential tremor

Severe hand tremor
- Drugs ineffective
- DBS, thalamus (Unilateral vs bilateral)
- Thalamotomy (ultrasound, gamma-knife)

Severe head, voice tremor
- Botulinum toxin
- Bilateral thalamic DBS (Putzke JNNSP 76(2005) 684-90)
Essential tremor drug therapy: Know when to quit

Strategies without pills:

1. Alcoholic beverage (1 per day)
   • Short-lived benefit (about an hour)
   • Must be timed: kicks-in quickly

2. Weighting of limb (modest effect)

3. Alternate hand postures
Orthostatic tremor (Heilman, Arch. Neurol. 1984)


Primary treatment: benzodiazepines (clonazepam)
Primary writing tremor
Not very responsive to medications
Mixed tremor; Combined resting-postural tremor syndrome *(Koller & Rubino, Arch. Neurol. 1985)*

Not very responsive to medications