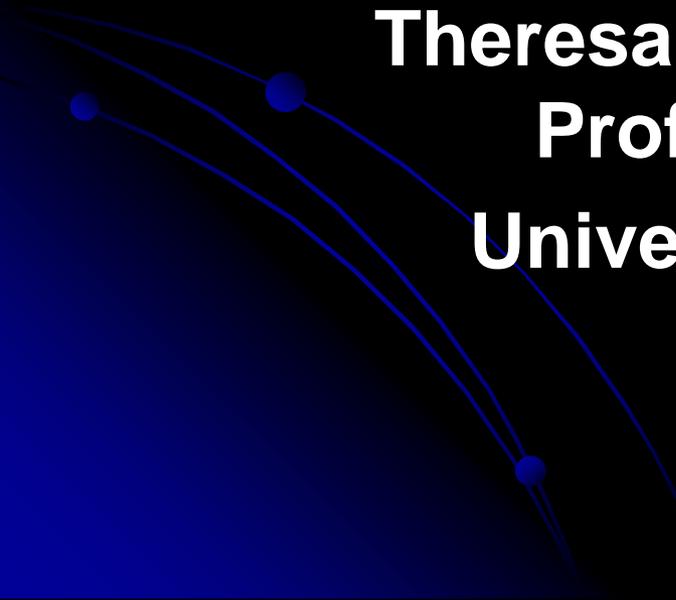
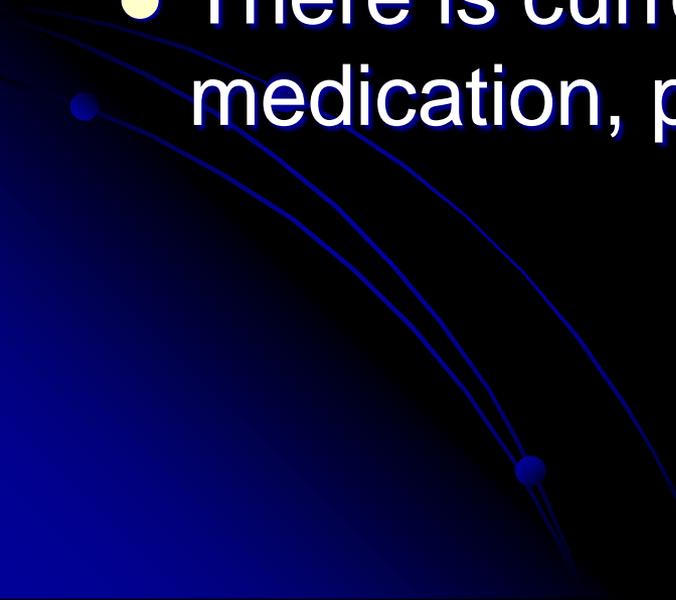


Diagnosis, Pathophysiology, and Treatment of Essential Tremor

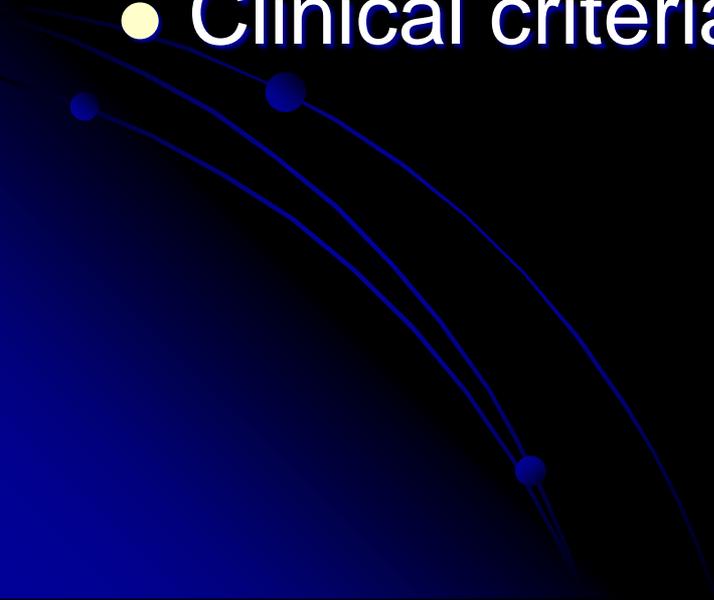
Theresa A. Zesiewicz, MD FAAN
Professor of Neurology
University of South Florida



Essential Tremor

- Essential tremor is characterized by a postural and/or kinetic tremor and is one of the most common tremor disorders in the world.
 - There is currently only one FDA approved medication, propranolol, for its treatment.
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Diagnosis

- There currently are no lab test or radiological scans to aid in the diagnosis.
 - It is estimated that 30 % to 50 % of cases are misdiagnosed.
 - Clinical criteria is used in the diagnosis.
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Clinical Criteria

1. Bilateral action (postural or kinetic) tremor of the hands and forearms (not a rest tremor) or an isolated head tremor without signs of dystonia.
2. The absence of other neurologic signs, with the exception of the cogwheel phenomenon (an oscillation of resistance during passive movement that is thought to be secondary to the tremor).
3. Secondary diagnostic criteria include long duration of disease (usually greater than 3 years), positive family history, and beneficial response to alcohol. The diagnosis of ET is made clinically, and there are no biomarkers or neuroimaging tools available to assist in the diagnosis.
4. Exclusion criteria for ET include a unilateral rest tremor, rigidity, bradykinesia, a focal tremor with abnormal posture, or a sudden onset of tremor.

Non-motor Symptoms

- Mild cognitive changes
 - Depression
 - Anxiety
 - Social phobias
 - Olfactory and hearing deficiencies
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Treatment of Essential Tremor

- Make correct diagnosis and exclude other possible causes of tremor.
- Treatment is not a cure but may offer tremor improvement.
- It is estimated that there is a 50 % improvement in tremor magnitude.
- There still remains 30 % to 50 % of ET patients that will not respond to medical therapy.

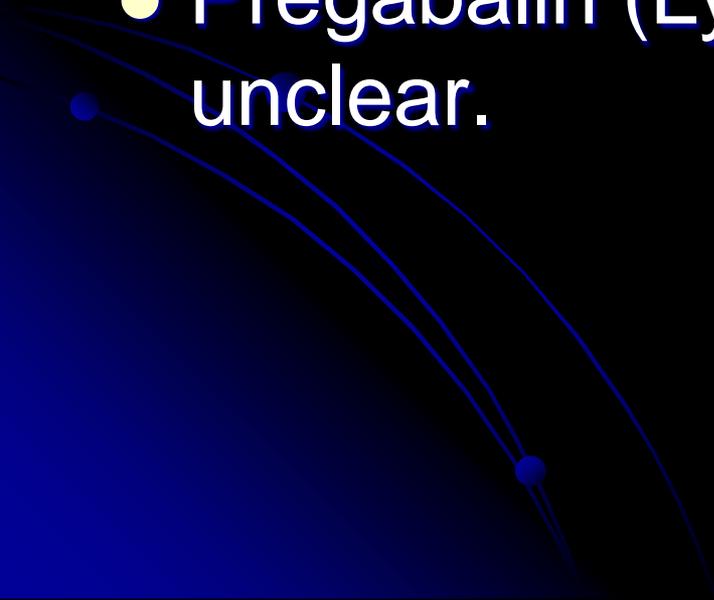
Antihypertensive Medications

- These include beta blockers and calcium channel blockers and are used to treat hypertension and other cardiovascular conditions.
- Two clinical studies suggests that propranolol (Inderal) reduces tremor in patients with ET.
- Others include atenolol (Tenormin) and sotalol (Sotacor).

Antiepileptics

- Primidone (Mysoline) is an anticonvulsant that effectively treats ET.
- Topiramate (Topamax) another anticonvulsant that has been shown to effectively reduce ET.
- Zonisamide (Zonegram) may have anti-tremor efficacy, although study results are mixed

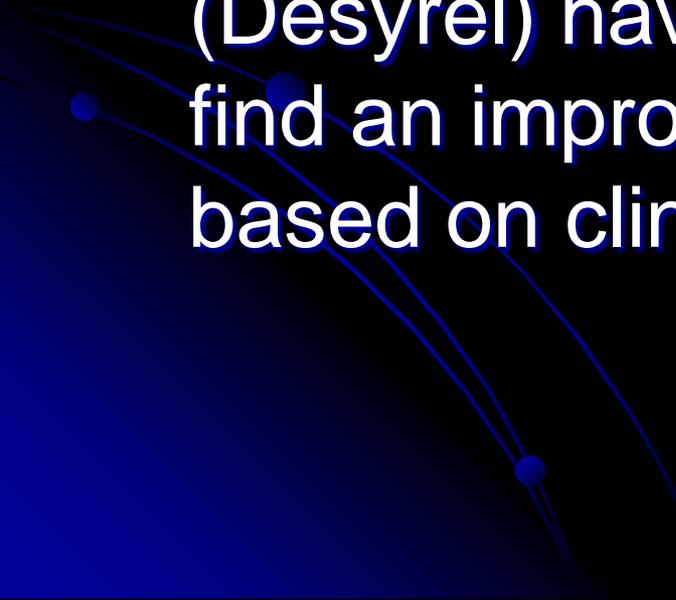
Antiepileptics

- Levetiracetam (Keppra), failed to show significant tremor reduction when tested several weeks compared to placebo in several controlled trials.
 - Pregabalin (Lyrica), the effect on ET is unclear.
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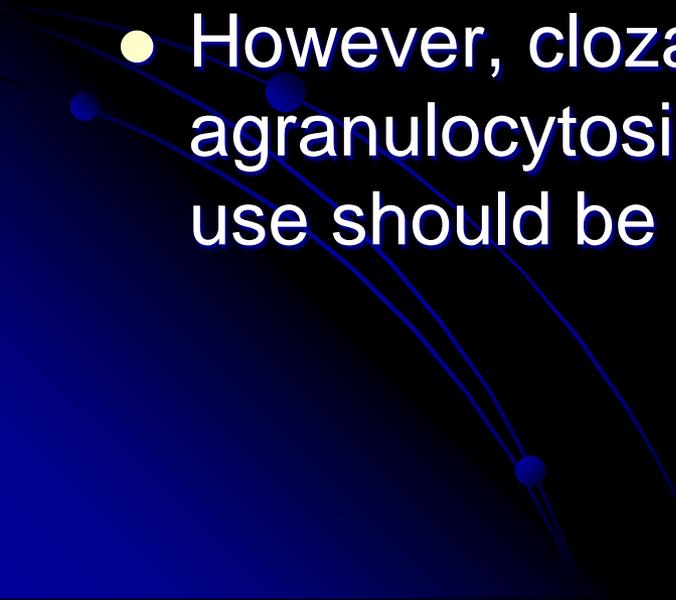
Antibiotics

- Isoniazid, an antituberculosis medication, was evaluated in a double blind, randomized placebo-controlled study of 11 patients with ET.
- At the end of the 4 week treatment period, only two patients experienced objective or subjective change in tremor.

Antidepressants

- Antidepressants have been used to treat ET without much success.
 - Mirtazapine (Remeron) and trazodone (Desyrel) have been studied but failed to find an improvement in tremor evaluations based on clinical rating scales.
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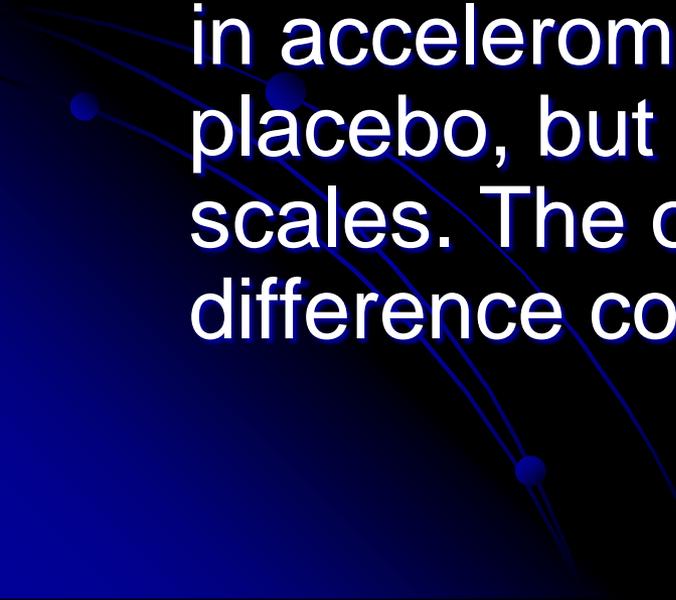
Antipsychotics

- Clozapine (Clozaril)) is an atypical neuroleptic with minimal extrapyramidal side effects that has been shown to reduce tremor by 45-50% in two controlled studies
 - However, clozapine use has a 1% risk of agranulocytosis, a serious side effect, and its use should be reserved for refractory cases.
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Antivirals

- Amantadine (Symmetrel) is an antiviral medication that is used to treat PD.
- One small open-label study evaluated the use of amantadine, an antiviral and antiparkinsonian agent, in 6 patients with ET. After a 1-month period there was no difference in accelerometric parameters compared to baseline.

Barbiturates

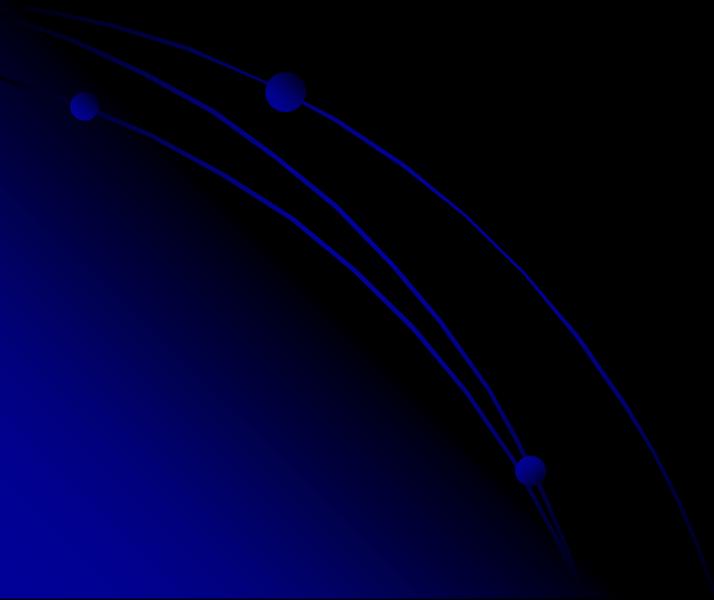
- Two double-blind, randomized, placebo-controlled crossover studies evaluated the effects of phenobarbital, an anticonvulsant and sedative, on tremor.
 - One study found a significant improvement in accelerometry parameters, compared to placebo, but no change in clinical rating scales. The other study failed to find a difference compared to placebo.
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Benzodiazepines

- Alprazolam (Xanax) has been shown to reduce clinical ratings of tremor in two double-blind, randomized, controlled studies.
- Although alprazolam has demonstrated effect in some patients with ET, it should be used cautiously as it has a high potential for abuse.
- Clonazepam (Klonopin) improved tremor compared to baseline in a blinded, controlled study. Another study failed to show any improvement in tremor, but had a 60% dropout rate due to side effects

Bronchodilators

- Studies of theophylline (Theo-dur), a xanthine derivative bronchodilator on ET, have found conflicting results.



Carbonic anhydrase inhibitors

- Controlled studies of two carbonic anhydrase inhibitors, acetazolamide (Diamox) and methazolamide (Glauctabs, Neptazane), failed to find a significant difference in tremor evaluations compared to placebo
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Botulinum Toxin

- Chemodenervation using botulinum toxin A (BTX) has been demonstrated to reduce hand tremor in patients with ET.
- Its use is hampered by side effects including hand weakness.
- Two controlled studies and 4 uncontrolled studies demonstrated improvement in limb tremor with BTX.

Surgical Treatment

- Thalamotomy is a stereotactic procedure that creates a lesion in the ventral intermediate nuclear (VIM) of the thalamus.
 - Studies have typically reported an 80–90% improvement in tremor symptoms compared to baseline.
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Surgical Treatment

- Deep brain stimulation (DBS) uses high frequency electrical stimulation from an implanted electrode to modify activity in the target area, usually the VIM thalamus.
- The electrode are connected to a pulse generator which is implanted in the chest wall.
- DBS is usually reserved for patients who are refractory to pharmacotherapy.