Evidence-Based Diagnosis and Management of Severe Pruritus

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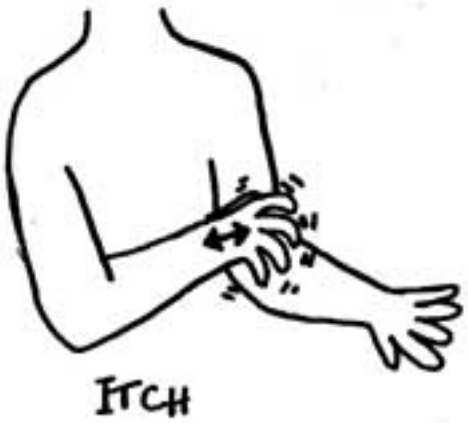
Disclaimer

- I have received honoraria from, have carried out clinical research with, and/or have served as a consultant for: AstraZeneca, Genentech/Novartis, GlaxoSmithKline, Meda, Merck.
- My presentation will include discussion of off-label uses of a number of FDA approved products, but not agents that are not FDA-approved.

Learning Objectives

After participation, the learner will be able to:

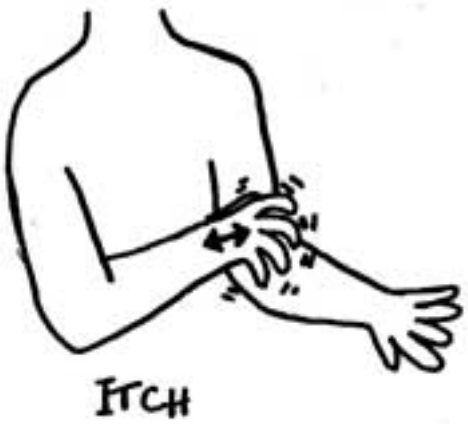
- Describe an evidence-based and cost-effective approach to diagnosis and management of patients with severe pruritus.



Pruritus

- an unpleasant sensation of the skin that provokes the urge to scratch
- a characteristic feature of many skin diseases
- an unusual sign of some systemic diseases
- Associated with impaired quality of life, as debilitating as chronic pain

Yosipovitch G, Bernhard JD. N Engl J Med 2013; 368: 1625-34.



Pruritus

- Acute / Chronic

Pruritus: The Evidence

- Pruritus is a symptom and not a disease.
- Wide range of etiologies
  - no single therapy can be recommended.
  - Each form of pruritus should be considered individually.
- Needs:
  - randomized controlled trials
  - well-defined outcome measures.

Weisshar, et al. European Guideline on chronic pruritus. Acta Derm Venereol 2012; 92: 563-81.

Pruritus: Prevalence

- Germany: population-based cross-sectional study
  - 12 months = 16.4%
  - Lifetime = 22.0%
- Chronic skin diseases
  - Atopic Dermatitis:100%
  - Urticaria: 100%
  - Chronic Renal Disease: 80-100%
  - Primary Biliary Cirrhosis: 40-70%
  - Hodgkin's Lymphoma: >30%

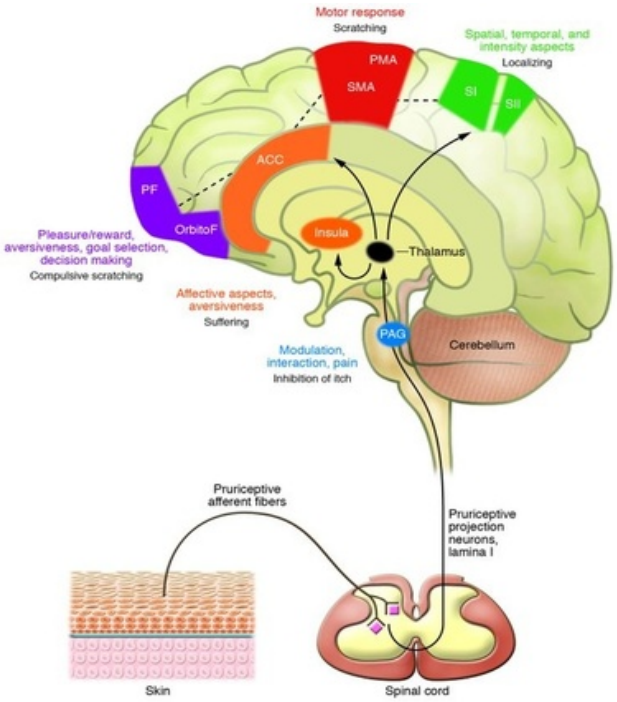
Matterne, et al. Acta Derm Venereol 2011; 91: 674–679.
Weisshar, et al. Acta Derm Venereol 2012; 92: 563-81.

Pruritus: Why?

- external stimulus
  - Insect
  - Clothing fibers
- defense mechanism
  - receptors in dermis become irritated
  - signal transmitted via C-fibers to dorsal horn of spinal cord and then via spinothalamic tract to cerebral cortex
  - Spinal reflex
    - ***scratch***
    - As innate a reflex as DTR.
- scratching: eliminates irritant sensation and / or provokes sensation of pain, thereby interrupting itch signal.
- pain and itch are separate
  - pain: withdraw
  - itch: scratch

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Why?



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Accessed August 30, 2015, at: https://www.quora.com.

Pruritus: Treatment?

- Pruriceptive itch
  - Cause: skin damage, inflammation
  - Atopic dermatitis, urticaria, psoriasis, drug reaction, etc.
  - **Antihistamines**
- Neuropathic itch
  - Cause: damage to nervous system
  - Post-shingles, stroke, burn injury.
  - **Non-narcotic analgesics, capsaicin**
- Neurogenic itch:
  - Cause: opioid neuropeptides
  - Cause: chronic liver or renal disease.
  - **Narcotic analgesics, non-narcotic analgesics**
- Psychogenic itch
  - Cause: serotonin, norepinephrine
  - Stress, depression, delusional parisitosis
  - **Anti-depressants, anti-psychotics**

http://www.aaaai.org/conditions-and-treatments/library/allergy-library/what-makes-us-Itch-.aspx

Pruritus: Management

- Initial step: identify underlying cause
- Treatments that are effective for one type of pruritus are ineffective for other types.
  - Ex: uremia
  - Ex: scabies
  - Ex: hyperthyroidism
  - Ex: cholinergic urticaria
  - Ex: xerosis

Yosipovitch G, Bernhard JD. N Engl J Med 2013; 368: 1625-34.

Antihistamines

- Act on H1 receptors on afferent C nerve fibers
- Often the initial therapy prescribed for patients with pruritus
- Soporific effects of 1st generation agents (e.g., hydroxyzine) may be beneficial in patients who have flares of pruritus at night.
- Data from RCTs are lacking to support efficacy in conditions other than urticaria.

Yosipovitch G, Bernhard JD. N Engl J Med 2013; 368: 1625-34.

Pruritus: Evaluation

- Comprehensive history
  - Recent exposures?
  - Recent travel?
  - Distribution of pruritus: generalized vs. localized

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Localized

- Notalgia paresthetica
  - Unilateral pruritus medial or inferior to the scapula.
  - Cutaneous sensory neuropathy, most likely caused by impingement of nerves as they exit the spinal column or traverse through muscles of the back.
  - Possibly the reason for the invention of the “back scratcher”
- Brachioradial pruritus
  - neurogenic pruritus affecting the upper extremities (either or both).
  - typically localized to the skin on the dorsolateral forearm overlying the proximal head of the brachioradialis muscle, but involvement of the upper arms and shoulders is also common
  - Associated with cervical spine disease and/or solar damage.

Lane J, et al. Cutis 2008; 81: 37-40.
Ellis C. Dermatol Pract Concept 2013; 3: 3-6.

Pruritus: Evaluation

- Comprehensive history
  - Recent exposures?
  - Recent travel?
  - Distribution of pruritus: generalized vs. localized
  - Onset
  - Duration
  - Effect on sleep
  - Response to treatment(s)
  - Medications
  - Other medical problems

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Systemic Causes

- Chronic renal failure
- Hodgkin's lymphoma
- Hyperthyroidism
- Malignant carcinoid
- Polycythemia vera
- Cholestasis
- HIV infection
- Others

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Yosipovitch G, Bernhard JD. N Engl J Med 2013; 368: 1625-34.

Pruritus: Evaluation

- Comprehensive history
  - Recent exposures?
  - Recent travel?
  - Distribution of pruritus?
- Complete physical exam
  - Associated dermatitis?
    - A characteristic rash can establish the diagnosis of a primary dermatologic disorder.
  - Other physical findings?

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Dermatologic Conditions

- Allergic Contact Dermatitis
- Atopic Dermatitis
- Bullous Pemphigoid
- Cutaneous T Cell Lymphoma
- Scabies
- Urticaria
- Others

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Laboratory Evaluation

- Directed by the findings of history and physical examination.
- Unremarkable →
  - Initial Labs:
    - Complete blood count with differential
    - Complete metabolic panel
    - Thyroid function tests
    - Chest x-ray.
  - Periodic re-evaluation

Yosipovitch G, Bernhard JD. N Engl J Med 2013; 368: 1625-34.

Pruritus: Laboratory Evaluation

Other studies, as indicated based on history, physical exam, clinical course:

- Antinuclear antibody
- Antimitochondrial antibodies
- Antitissue transglutaminase antibodies
- Calcium and phosphate levels
- Erythrocyte sedimentation rate
- HIV screen
- Pan–computed tomography scan
- Prick testing, patch testing
- Serum and urine immunofixation
- Serum and urine protein electrophoresis
- Serum iron and ferritin
- Skin biopsy with immunofluorescence
- Stool for occult blood, ova, and parasites

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Pruritus: Evaluation

- Comprehensive history
  - Recent exposures?
  - Recent travel?
  - Distribution of pruritus?
- Complete physical exam
  - Associated dermatitis?
  - Other physical findings?
- Management
  - Cause identified: prescribe specific therapy
  - No cause apparent: non-specific therapy

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritus: Non-Specific Management

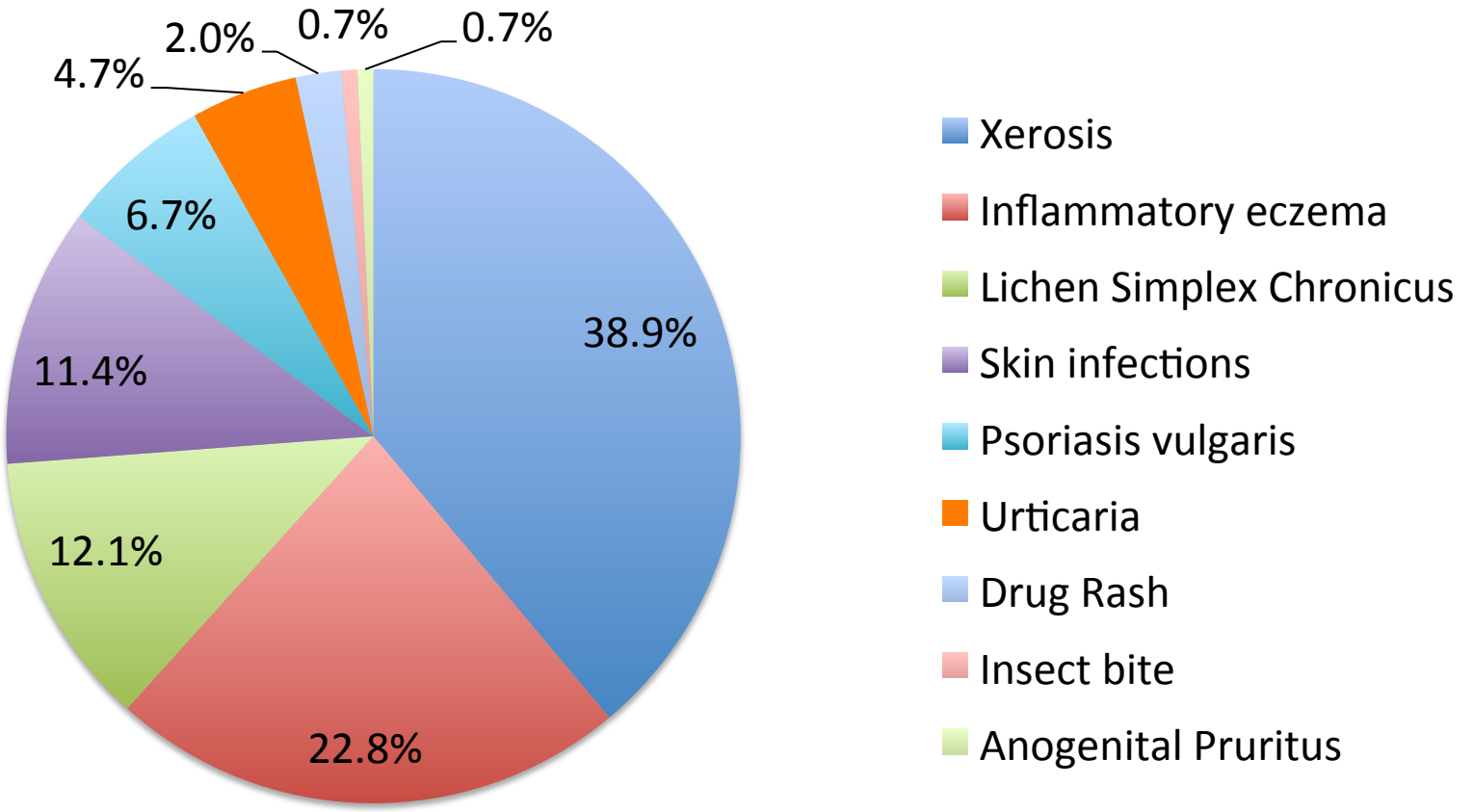
- Skin moisturization and cooling
  - Lubricants
  - Tepid baths, reduced frequency of bathing
  - Air conditioned environment
- Indoor humidification
- Avoidance of irritants
  - Non-irritating soaps
  - Non-irritating clothing
- Keep fingernails short
- Avoid vasodilators (caffeine, alcohol, etc.)
- Stress reduction

Moses, et al.. Amer Fam Physician 2003; 68: 1135-42.

Pruritic Skin Disease in Older Adults

149 older adults seen at Rajavithi General Hospital, Bangkok, Thailand.

- Xerosis usually occurred with increased bathing frequency & strong soaps/detergents
- "Inflammatory eczema": seborrheic dermatitis, dyshidrosis, allergic contact dermatitis.



Thaipisuttilkul. J Dermatol 1998; 25: 153-7.

Pruritus: Older Adults

- Pathophysiologic changes
  - Aging of skin
  - Decreased function of stratum corneum
  - Xerosis cutis
  - Co-morbidities
  - Polypharmacy

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Drugs Inducing/Maintaining Chronic Pruritus

Without Rash

- ACE Inhibitors
- Antiarrhythmic agents
- Antibiotics
- Antidepressants
- Antidiabetic drugs
- Anticonvulsants
- ASA/NSAIDs
- AT II Antagonists
- Benzodiazepines
- Beta Blockers
- Bronchodilators
- Calcium antagonists
- Diuretics
- Hormones
- Immunosuppressive drugs
- Neuroleptics
- Plasma expanders
- Statins
- Uricostatics

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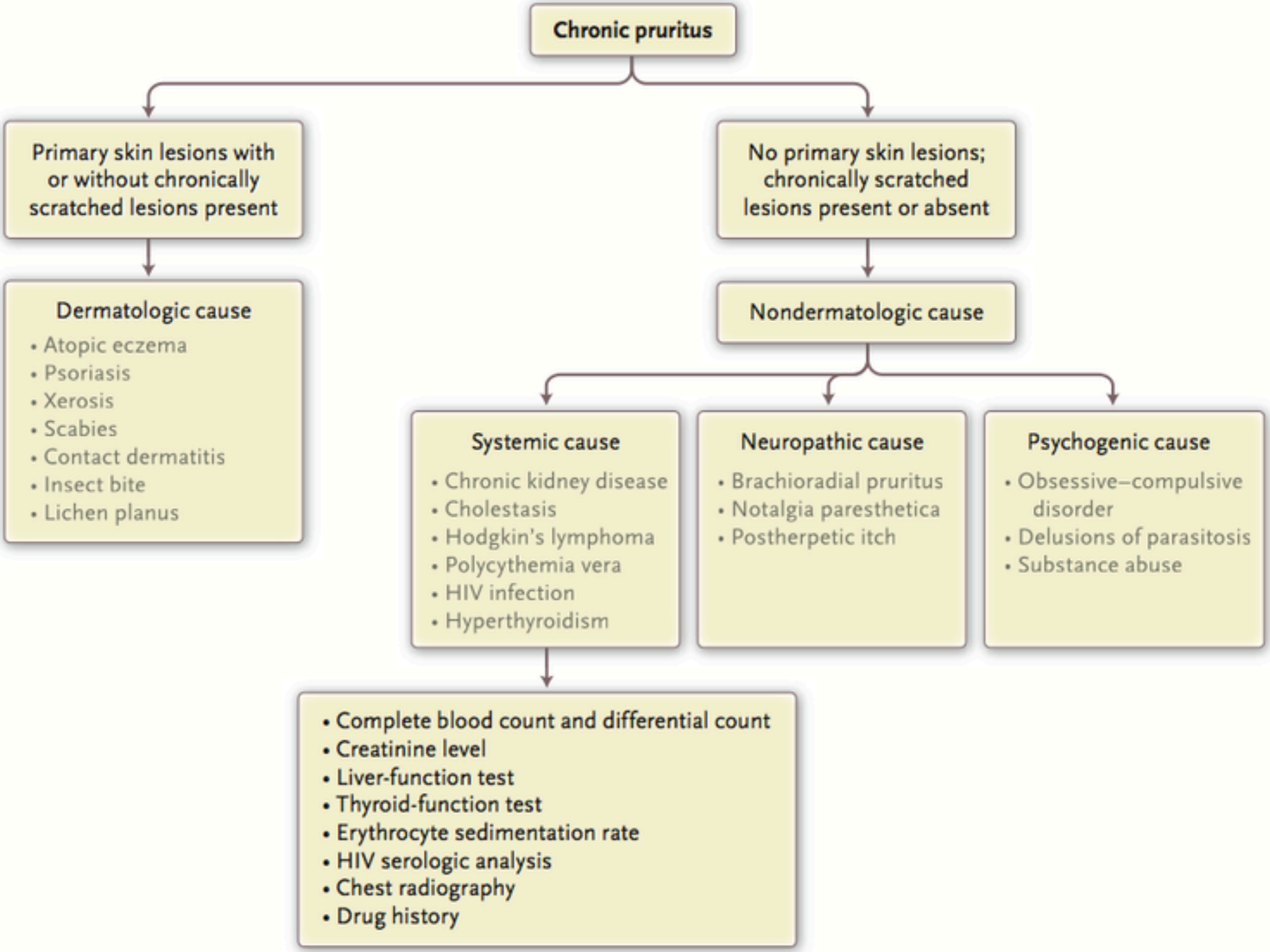

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Conclusion - 1

- Patients with pruritus are commonly encountered.
- Pruritus can be associated with substantial impairment in quality of life and incapacitating in severe cases.
- Etiologies include skin disorders, systemic diseases, psychogenic factors, and idiopathic.
- Initial step in management entails categorizing pruritus based on underlying cause

Conclusion - 2

- A variety of therapies can be utilized, depending on the cause for pruritus.
  - Non-pharmacologic measures
  - Antihistamines
  - Consider anticonvulsants, antidepressants, mu-opioid antagonists.
  - RCTs needed.
- Treatment for chronic disease is frequently long-term
- Treatment for idiopathic pruritus may be challenging
- Treatment of underlying cause can result in resolution