Topic Area:
Itch in CTCL

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Itch in CTCL

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Itch in CTCL

- Worse in later stages of disease, more common in folliculotropic disease and Sezary Syndrome

- Patients with pruritus report more insomnia, fatigue, and have poor health-related quality of life scores

- Correlates negatively with disease

  specific survival

- What works?

Itch and QOL in CTCL

- Health related QOL decreases with more advanced disease
- Pruritus is more severe in advanced disease
- Recent study showed that QOL measured by the Skindex-29 correlated very strongly with pruritus measured on a 10 point visual analog scale of itch.
- Severe pruritus is associated with poor QOL

J Pain Symptom Manage 2013;45:114-119

Treatment and itch reduction

- **Skin** directed therapies
  - NBUVB and PUVA
    - Both shown to reduce pruritus
  - Nitrogen mustard
    - Improves pruritus in subset of patients but also may induce pruritus

Pathways mediating itch we can target with medications

- Histamine dependent pathway
  - Antihistamines, doxepin
- Pruritogenic interleukins
  - Duplimumab*, CIM331* (Anti-IL31)
- Protease pathway
  - Tetracyclines, nafemostat mesylate**
- Neurogenic inflammation
  - Capsaicin, aprepitant
- Opioid receptors.
  - Naloxone, butorphanol

*2017 FDA approved for atopic dermatitis
** In clinical trials

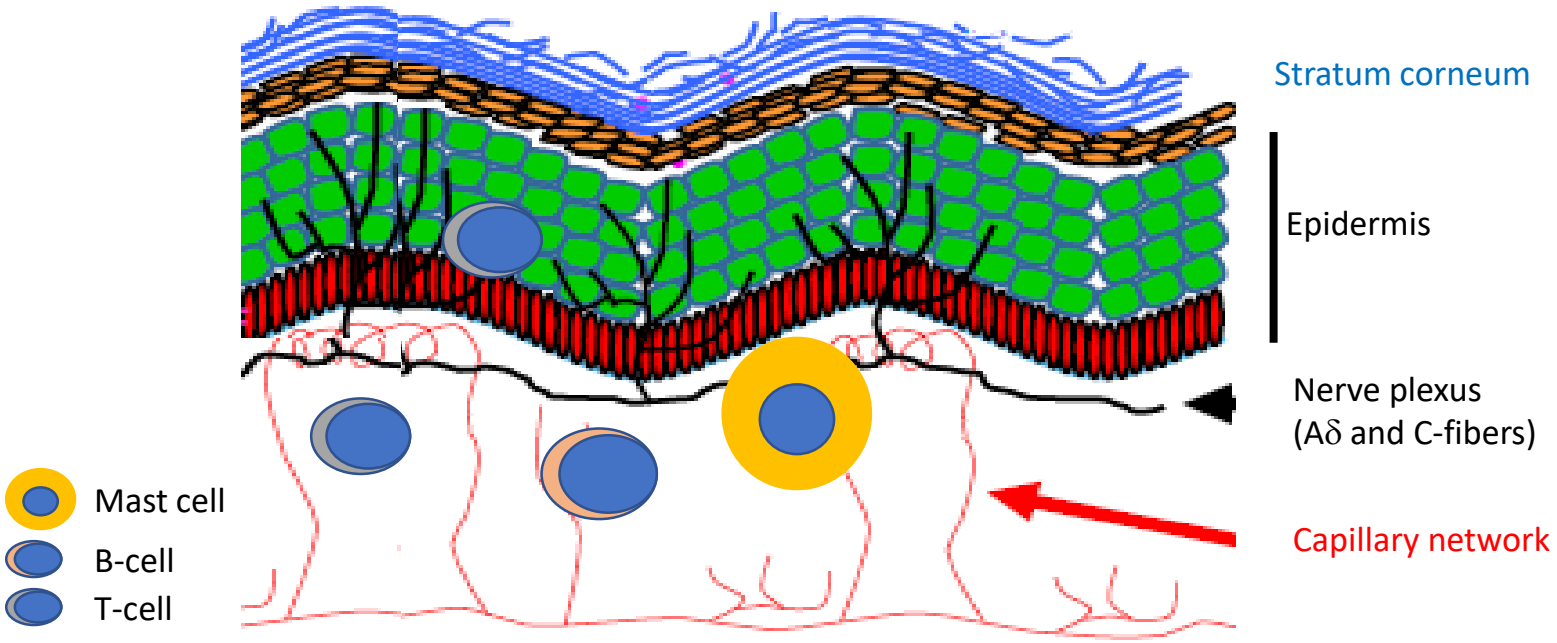
What are the mechanisms of pruritus in CTCL?

Primarily histamine independent pathways.

Treating the disease will treat the associated pruritus

While waiting for treatment response or when cases are refractory to treatment, what are our options for palliation?

Epidermal barrier



Antihistamines and CTCL

- Generally ineffective in controlling itch
    - Can try doxepin for enhanced antihistamine blockade compared to 1st and 2nd generation antihistamines but be wary of drug interactions

Understanding and Treating Pruritus in CTCL

Data from small studies, concepts borrowed from other diseases (like atopic dermatitis), and research that may lead to new and innovative therapies

Histamine (H4)

- H4 agonists induce pruritus that is independent of mast cells or other leukocytes
- May have an effect directly on peripheral nerves
- H4 antagonists also inhibit substance P induced pruritus

CNS-Targets for itch treatment

- Noradrenergic and specific serotonergic antidepressant (NaSSA)
  - Mirtazapine 15 mg PO qHS
- Drugs that release several neurotransmitters
  - Gabapentin
  - Pregabalin

Neuropeptides

- Substance P implicated in pruritus, released from terminal ends of cutaneous nerves in the skin
- It activates the neurokinin-1 receptor which is present on keratinocytes and dorsal horn neurons of rats

Opioid Antagonists

- 1 case report of naloxone treating itch in MF
- In the same patient, naltrexone (another opioid antagonist) actually EXACERBATED itch

- Imbalance of μ-opioid vs κ-opioid receptors?
- In one case series 3 of 4 patients with CTCL related pruritus had a substantial improvement in symptoms with naltrexone

Holistic approaches to itch

- Cognitive and behavioral therapies
  - Awareness training and habit reversal
  - Stress management education
  - Guided imagery
- Holistic Approaches
  - Acupuncture
  - Healing touch

Our therapeutic ladder for pruritus therapy

- Dry skin care must be optimized
- Treat the lymphoma
- Add antihistamines
- Add gabapentin if “burning” component in addition to itch
- Mirtazapine, lyrica or aprepitant next
- Naloxone last (we have the least experience with it)