

**FAST FACTS AND CONCEPTS #37**  
**PRURITUS**

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**Background:** Pruritus (itching) is a common and often distressing symptom near the end of life. The itch sensation may arise from stimulation of the skin itch receptor via unmyelinated C fibers or arise as a central phenomenon without skin involvement (e.g. opioid-induced pruritus). Although histamine causes pruritus, many patients with pruritus show no signs of histamine release. Besides histamine, serotonin, prostaglandins, kinins, proteases, and physical stimuli have been implicated as mediators of pruritus.

**Common Causes**

- Dermatological (dryness, wetness, irritation, eczema, psoriasis)
- Metabolic (hepatic failure, renal failure, hypothyroidism)
- Hematologic (iron deficiency, polycythemia, thrombocytosis, leukemia, lymphoma)
- Drugs (opioids, aspirin, drug reactions)
- Infectious (scabies, lice, candida)
- Allergy (urticaria, contact dermatitis, drug reactions)
- Psychogenic
- The Itch-Scratch Cycle – scratching leads to cellular damage which results in more itching.

**Management:** Beyond eliminating the cause whenever possible, symptomatic strategies include:

- **Moisturizers:** Dryness (xerosis) is very common and may exacerbate other causes. The mainstay of treatment is skin hydration. Note: Most OTC preparations only have small amounts of moisturizer—they are mostly water. Serious dryness requires emollients and moisturizers (such as petroleum jelly) that patients find oily or greasy. Nevertheless, they may be applied after bathing, over damp skin, with a superficial covering. An older fashion remedy is immersion in an oatmeal bath (e.g. Aveeno).
- **Cooling agents** (e.g. Calamine and/or Menthol in aqueous cream, 0.5%-2%) are mildly antipruritic. They may act as a counterirritant or anesthetic. A more direct way to anesthetize the skin is with the eutectic mixture of local anesthetics lidocaine and prilocaine (EMLA cream). Simple application of cold compresses may also be helpful.
- **Antihistamines** may be helpful in relieving itch when associated with histamine release. Morphine causes non-immune mediated histamine release from mast cells. Although there is limited supporting evidence, many report benefits of combining H1 and H2 receptor subtype antihistamines. These may have central effects as well as peripheral antihistaminergic effects. Doxepin (10-30 mg PO at bedtime), a tricyclic antidepressant, also has very potent antihistamine and is often considered in refractory cases.
- **Topical steroids** may be helpful in the presence of skin inflammation. These are best applied in ointment rather than cream formulations to alleviate dryness. Systemic steroids have been used in refractory cases.
- **Topical tacrolimus** has shown benefit in reducing pruritus related to rashes from atopic dermatitis, genito-anal pruritus, and prurigo nodularis.
- **Antidepressants:** A systematic review of 35 studies showed benefit from initiation of antidepressants in most studies, with overall good tolerability. While their effectiveness may be a class effect, studies included in the systematic review suggested that paroxetine and mirtazapine were effective for paraneoplastic pruritus; sertraline, amitriptyline, and doxepin were effective for pruritus related to chronic kidney disease; and sertraline was effective for pruritus related to cholestasis.
- **Ondansetron and other 5HT<sub>3</sub> antagonists** have demonstrated benefit for patients with opioid-induced, cholestasis-induced, and renally-induced pruritus.
- **Cholestyramine** appears to benefit patients with cholestatic pruritus.
- **Gabapentin and pregabalin** have shown benefit in a variety of forms of refractory chronic pruritus including uremic pruritus, neuropathic pruritus, and itch of unknown origin. There is not conclusive evidence to support their use for opioid-induced pruritus or cholestatic pruritus.

- **Opioid Antagonists:** Continuous infusions of IV naloxone at low doses (e.g. 0.25-1 ug/kg/hr) has the largest body of data supporting its use in adult and pediatric patients with opioid induced pruritus without inducing opioid withdrawal. Small studies suggest a potential role for methylnaltrexone in opioid-induced pruritus. Mixed agonist-antagonist opioids (pentazocine, nalbuphine, buprenorphine) may also reduce opioid-induced pruritus.

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