

# Skin Therapy Letter<sup>®</sup>

Volume 1 • Number 2 • September-October 2006

Clinical Evidence. Practical Advice.

Editor-in-Chief: Dr Stuart Maddin

**Dr. Stuart Maddin, MD, FRCPC**

## EDITOR-IN-CHIEF

Dr. Stuart Maddin, Chairman of SkinCareGuide, is one of North America's leading dermatologists, and is the author of numerous dermatologic journal articles, monographs and textbooks. In addition to providing consultative input to a number of pharmaceutical and biotech companies, he is the director of the clinical trials unit at the Division of Dermatology, University of British Columbia. Dr. Maddin has also acted in an advisory capacity to a number of drug regulatory agencies, such as the Health Protection Branch (Ottawa), the AAD-FDA Liaison Committee, and WHO (Geneva). He is the founder of the Dermatology Update symposia, now in its 21<sup>st</sup> year. As well, he is Past President of the Canadian Dermatology Association and served as Secretary-General of the International Committee of Dermatology — International League of Dermatological Societies.

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## PHARMACIST ADVISOR

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## The Management of Itchy Skin

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### Introduction

Itchy skin is a very common complaint seen in family practice as well as in dermatology practice. Causes of itchiness are extremely diverse and wide spread. A subset of nociceptive C neurons is responsible for the transmission of itch or pruritus, and these mediators (mainly histamine) can act centrally or peripherally. Skin disease that can mediate itchiness can originate in the skin or even in the central or peripheral nervous systems.

### Dermatologic Diseases With Pruritus

Numerous dermatologic diseases present initially or are associated with pruritus.

Dermatologic Disease	Cause
Infestation	<ul style="list-style-type: none"> <li>• Scabies</li> <li>• Pediculosis</li> <li>• Arthropod bites</li> <li>• Schistosomal cercarial dermatitis (swimmer's itch)</li> </ul>
Inflammation	<ul style="list-style-type: none"> <li>• Atopic dermatitis</li> <li>• Stasis dermatitis</li> <li>• Irritant or allergic contact dermatitis</li> <li>• Lichen simplex chronicus</li> <li>• Urticaria</li> <li>• Psoriasis, parapsoriasis</li> <li>• Prurigo nodularis</li> <li>• Drug hypersensitivity</li> <li>• Mastocytosis</li> <li>• Bullous disease, e.g., dermatitis herpetiformis, bullous pemphigoid</li> <li>• Pityriasis rubra pilaris</li> <li>• Polymorphous light eruption</li> <li>• Eosinophilic pustular folliculitis (Ofuji's disease)</li> <li>• Prurigo pigmentosa</li> <li>• PUPPP (pruritic urticaria papules and plaques of pregnancy)</li> </ul>

## Dermatologic Diseases With Pruritus (continued)

Dermatologic Disease	Cause
Infections	<ul style="list-style-type: none"> <li>• Fungal infections, e.g., inflammatory tinea</li> <li>• Bacterial infections, e.g., folliculitis</li> <li>• Viral infections, e.g., varicella</li> </ul>
Neoplastic	<ul style="list-style-type: none"> <li>• Cutaneous T-cell lymphoma</li> </ul>
Hereditary or Congenital	<ul style="list-style-type: none"> <li>• Darier-White disease</li> <li>• Hailey-Hailey disease</li> <li>• Inflammatory linear verrucous epidermal nevus (ILVEN)</li> </ul>
Others	<ul style="list-style-type: none"> <li>• Xerosis, eczema craquele</li> <li>• Senile pruritus</li> <li>• Anogenital pruritus</li> <li>• Itching in scars</li> <li>• Nostalgia paresthetica</li> <li>• Amyloidosis, mucinosis</li> <li>• Postburn and poststroke pruritus</li> <li>• Fiberglass dermatitis</li> <li>• Aquagenic pruritus</li> </ul>

## Categories of Pruritus Therapy

Causal therapy	<ul style="list-style-type: none"> <li>• Identification and treatment of the underlying disease</li> </ul>
Symptomatic treatment	<ul style="list-style-type: none"> <li>• Patient education</li> <li>• Elimination of provocative factors</li> <li>• Topical therapy               <ul style="list-style-type: none"> <li>- Corticosteroids for inflammatory conditions</li> <li>- Calcineurin inhibitors, e.g., tacrolimus (Protopic®) and pimecrolimus (Elidel®)</li> <li>- Crotamiton (Eurax®)</li> <li>- Moisturizers</li> </ul> </li> <li>• Systemic therapy               <ul style="list-style-type: none"> <li>- Antihistamines                   <ul style="list-style-type: none"> <li>• Sedation can be of benefit, especially in eczema</li> </ul> </li> <li>- Corticosteroids</li> </ul> </li> <li>• Physical modalities: e.g., phototherapy               <ul style="list-style-type: none"> <li>- UVB</li> <li>- UVA</li> <li>- PUVA</li> </ul> </li> </ul>

## Treatment of Specific Skin Disorders

### Atopic Dermatitis

Moisturizing is extremely important for replenishing the skin's water content and preventing water loss. Maintaining the barrier to keep out exacerbating factors from the skin, such as the external environment, is beneficial. Moisturizers should contain the following: emollients, humectants, occlusives, soothing agents and anti-irritants.

Oral antihistamines, especially those with sedating properties, e.g., hydroxyzine (Atarax®) or diphenhydramine (Benadryl®) may provide benefit for patients with pruritus. An antidepressant with potent antihistaminic properties, doxepin (Sinequan®), can also be useful. The role of histamine in eczema is questionable. Alpha hydroxy acids can reduce scaling and roughness. The use of topical vitamins and antioxidants is controversial because there is no strong evidence for effectiveness.

## Treatment of Specific Skin Disorders (continued)

### Urticaria

Histamine release has a central role in urticaria. There are many causes of urticaria that can be investigated by an allergist. Oral antihistamines, either sedating or nonsedating, are beneficial. Nonsedating antihistamines, such as loratadine (Claritin®), desloratadine (Aerius®), or fexofenadine (Allegra®), can be used in combination with sedating antihistamines at bedtime.

### Winter Itch

- The cold, dry air of Canadian winters increases transepidermal water loss and causes xerosis (severely dry skin).
- As we heat our homes, especially with electric heat, it reduces the humidity in the air.
- The skin tries to maintain an equilibrium, also causing an increase in transepidermal water loss.
- All ages can be affected.
- Can exacerbate underlying skin diseases associated with pruritus, which in turn can exacerbate pruritus further.
- Minimize soap. Nonsoap cleansers can be helpful (e.g., emulsifying ointment, Spectroge1®, Spectroderm®, Cetaphil®)
- Moisturizing after a bath is extremely important.

There is new evidence to show that niacinamide-containing moisturizers not only hydrate the skin but improve the skin resistance to external factors and improve the barrier function. Glycerin is required for moisturizers to work quickly and add moisture to the skin, but the niacinamide helps to sustain that benefit over a longer period of time.

## Management

- Treat underlying cause of pruritus
- Moisturizing
  - beneficial for most itchy disorders
- Antihistamines
  - sedating and nonsedating (sedating is necessary for atopics)
  - helpful for symptomatic relief
- Topical 5% doxepin cream
  - useful in neurodermatitis
- Capsaicin 0.025% cream, e.g., Zosterix®
  - used in postherpetic neuralgia
- Topical menthol and camphor lotion
  - best in adults
  - not well tolerated in children
- Crotamiton cream or lotion
  - beneficial for scabies
- Topical anesthetics such as EMLA®
  - useful in neurodermatitis
- Calcineurin inhibitors such as tacrolimus or pimecrolimus
  - approved for atopic dermatitis
- Systemic therapy such as ultraviolet B or narrowband UVB or PUVA
  - pruritus in pregnancy or systemic causes of itchiness
- Topical corticosteroids
  - most inflammatory skin diseases
- Topical Vitamin D3 analogs, e.g., Dovonex®
  - antipsoriatic
- Cholestyramine and colestipol resins used to control pruritus in patients with cholestatic liver disease.

## Conclusion

The causes and differential diagnoses are as diverse for pruritus as the treatment and management are nonspecific. This makes the workup of nonspecific itch difficult. With careful history and physical exam, as well as some laboratory investigations, most serious disorders can be ruled out and the patient's itch can be relieved.

# Treatment of Head Lice

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## Head Lice

An estimated 1 in 10 children in Canada will be affected by a lice infestation this year and it is more common worldwide than the common cold. Head lice infestations, i.e., *Pediculus humanus capitis*, is common, occurs worldwide and affects people of all ages and socioeconomic groups. Lice are wingless, bloodsucking insects. They are difficult to see because they are about the size of a sesame seed and they adapt to take on the color of their surroundings.

- The most common type of lice infestation.
- Occurs most commonly in school-aged children, especially girls between 3 and 11 years of age.
- Is often epidemic.
- Personal hygiene and socioeconomic status are not related to the likelihood of developing lice infestation.
- Not known to transmit bloodborne diseases.
- Spread through close head-to-head contact or through fomites (inanimate objects) which come into contact with the infested scalp and then are shared (e.g., combs, brushes, and hats).
- Most common places for outbreaks include schools, daycares, and play groups.

## Clinical Manifestations & Diagnosis

Head lice are typically confined to the scalp and while itching is the main symptom of lice infestation, the lice themselves are not itchy and the bites are generally painless. Itching is caused by the body's immune reaction to the saliva injected into the skin at the time of the blood meal. Redness and scaling may also be seen in the scalp as can small, itchy bumps on the posterior neck. Enlargement of lymph glands in the neck can occasionally be seen.

Diagnosis can be made ONLY by identification of a living louse. Nits or eggs are often empty shells and not an indication of an active infestation. Nits are also often mistaken for dandruff, sand or dirt, or dried hair gel.

## Myths and Facts

Myths about head lice are abundant. Belief in these myths is often why treatments are not used properly and why people believe their lice treatment has failed. The myths include:

- All children with lice scratch or itch. **Fact:** Initial infestation may produce no signs or symptoms for 4 – 6 weeks; only 1 in 3 children will complain of itching.
- Lice jump or fly from head to head. **Fact:** Lice do not jump or fly, but can be dislodged from hair by air movements giving the appearance of flying.
- Lice live in carpets, beds, clothes, and sofas. **Fact:** lice can only live for 24 hours away from a human host.
- Lice die immediately after treatment. **Fact:** lice may take several hours to die following treatment.
- One treatment is enough. **Fact:** due to loss of residual activity of pediculicides, two treatments, seven days apart, are recommended to kill newly hatched nymphs.
- Permethrin based products are 100% ovicidal. **Fact:** permethrin kills 70% of eggs with one treatment.
- Everyone in the family should be treated. **Fact:** only those with a proven infestation should be treated, although everyone should be checked daily to weekly.
- Head lice prefer long or dirty hair. **Fact:** lice do not care about hair length or cleanliness.

## Treatment Options

There are many proposed “natural” and alternative cures for treating head lice, including various oils, petroleum jelly, peanut butter and mayonnaise; the effectiveness of most are dubious. However, there are no clinical studies to demonstrate effectiveness of these agents and many are messy and difficult to use.

## Treatment Options (continued)

Most patients will need to be treated with a commercial product designed to kill lice. Most of these are available over-the-counter and work by attacking the central nervous system of the louse. No pediculicide is 100% ovicidal. In order to achieve maximum effectiveness of the pediculicide, it needs to be applied to dry or nearly dry hair. It should be saturated to allow sufficient pediculicide to penetrate lice and nits and left on for the entire recommended time.

- Permethrin 1% cream rinse (Nix®/Kwellada-P®)
  - Wash hair with conditioner-free shampoo and towel dry until hair is almost dry; then apply at least 25ml, and up to 50ml for thick or long hair, to hair and scalp especially behind the ears and the nape of the neck.
  - Leave product on for 10 minutes, then rinse with cool water over a sink (not in a shower or bath)
  - Comb wet hair with nit comb to remove any dying lice and nits
  - A second treatment in 7 days should be carried out for maximum efficacy
  - Minimal systemic absorption and low risk for toxicity
  - Contraindicated in patients with chrysanthemum allergy
- Synergized pyrethrins (R & C® shampoo)
  - Apply to dry hair and scalp, especially behind the ears and the nape of the neck. **Hair must be completely dry.**
  - Leave on 10 minutes, then add water to form lather. Rinse with cool water over a sink. Do not use conditioner.
  - A second treatment in 7 days should be carried out for maximum efficacy
  - Low risk of toxicity
  - Do not use if known allergy/sensitivity to chrysanthemum or ragweed
- Lindane shampoo 1%
  - Inexpensive
  - Apply to dry hair, leave on for 5 minutes and rinse with cool water over a sink (not in a shower or bath)
  - Comb wet hair with nit comb to remove any dying lice and nits
  - Concern re: neurotoxicity with high dose or repeated exposure
  - Contraindicated in neonates, young children (<2 years of age), pregnant women, and nursing mothers or those with a history of seizures.
  - Resistance has been seen for more than 2 decades.

Regardless of the type of treatment recommended, patients should be encouraged to use a nit comb (fine toothed metal comb) such as the LiceMeister® comb, on wet hair to manually remove the nits, which can become cemented to the hair shafts. Treated patients should also be monitored for reinfestation.

## Fomite Control

Following treatment, all clothing should be machine laundered and dried in the dryer (hot cycle). In addition, bed linens, towels, stuffed animals, and any headgear should be cleaned. Clothing that cannot be washed can be dry cleaned or sealed in a bag for 2 weeks. Combs and brushes can be covered in the pediculicide and then washed in hot water for 20 minutes; alternatively they can be soaked in a disinfectant solution (e.g., 2% Lysol for 1 hour). All interior areas should also be cleaned and vacuumed to remove any shed hairs.

## Reasons for Failure of Treatment

- Wrong diagnosis
- Poor adherence / improper use of chemical lice treatment (e.g., applied to wet hair, insufficient product applied)
- Inadequate time to evaluate treatment (lice do not die on contact with product)
- Poor manual removal of nits
- New exposure to lice (re-infestation)
- Not repeating treatment 1 week later

## Conclusion

Head lice are a common and embarrassing problem with many good treatments. Patients should be appropriately counseled to minimize spread of infestation and then advised on appropriate topical treatments. For further information about lice and lice eradication as well as counseling tips and patient material go to [www.SkinPharmacies.ca/CE](http://www.SkinPharmacies.ca/CE).

# Management of Eczema

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## Definition of Eczema

Often used interchangeably with the term atopic dermatitis (AD).

- Is a broad-spectrum condition that is subdivided into different clinical presentations, i.e., infantile, childhood and adult.
- Eczema is a clinical diagnosis that must meet a set of diagnostic criteria: [Williams HC, et al. *Br J Dermatol* 131(3):383-416 (1994 Sep).]
  - Pruritus, plus 3 or more of the following
  - Early age of onset
  - Typical distribution (i.e., extensors in infants and children, flexures in adults)
  - Personal or familial history of atopy (e.g., asthma, hay fever, eczema)
  - Xerosis (dry skin)
  - Chronicity and relapses
- Increased levels of IgE are not necessary to make the diagnosis.
- There are no diagnostic lab tests.

## Incidence

- The prevalence of eczema is increasing, especially over the past 30 years.
- Current studies find a prevalence of 20% in children in North America, Northern Europe, and Japan, [Laughter D, et al. *J Acad Dermatol* 43:649-55 (2000 Oct).] With lower figures elsewhere in the world, [Williams HC, et al. *J Allergy Clin Immunol* 103:125-38 (1999 Jan).] though reasons for this remain unclear.
- There is a strong genetic component.

## Presentation of Eczema

- Can either be acute or chronic in nature.
- Acute eczema shows marked inflammation of skin, erythema and juicy papules.
- Chronic eczema shows lichenification (thickening of the skin) from repeated rubbing or scratching, postinflammatory hyper- or hypopigmentation.
- Both types can show excoriations.
- There is commonly a secondary infection, usually with *Staphylococcus aureus* (*S. aureus*).

## Management

- Chronicity of disease must be emphasized – there is no cure for eczema.
- Preventative measures, including avoidance of trigger factors and skin hydration, are mainstays of treatment.
- Therapeutic measures include the use of topical and oral medications, and the treatment of secondary infections, if present.
- General strategy involves induction of remission, stabilization and maintenance, and the rescue of flares.

## Preventative Measures

- Avoid irritants and allergens such as harsh detergents, wool or other itch-inducing fabrics, and common allergens such as pet dander, dust, smoke, and pollens.
- The trigger need not be allergic in nature to induce eczema.
- Moisturizers
  - Need to be used on at least a daily basis because of the inherent xerosis of the skin.
  - Moisturizers that are occlusive prevent water loss.
  - Oils tend to stay on the surface of the skin and are not absorbed.

## Preventative Measures (continued)

- Maintain hydration of the skin
  - Use mild or soapless cleanser that does not disrupt the barrier of the skin.
- Bathing
  - Warm, not hot, baths or showers are encouraged.
  - It is crucial to moisturize immediately after bathing.
- Cool temperatures
  - Sweat is aggravating to eczematous skin, and can promote pruritus.

## Therapeutic Measures

### Topical Corticosteroids

- Most effective for an acute onset of eczema (flare) because of rapid onset of action.
- Potency of the agent depends on the location of the eczema (mild for face and groin, moderate for body).
  - Use the lowest potency possible to control the flare.
  - Greater potency exists when the drug is delivered as an ointment as compared to a cream or a lotion.
- Rarely, skin atrophy, tachyphylaxis (loss of effectiveness), or adrenal suppression is seen with prolonged, daily use. Use of more potent topical steroids is associated with increased risk of development of adverse effects. Risk is higher for younger children because of their surface area-to-weight ratio and because their skin is more permeable.
- To be applied only on the area of active disease.
- Can be used in combination with topical calcineurin inhibitors for local control of eczema.
- Allergic contact dermatitis to corticosteroids is rare.

### Topical Calcineurin Inhibitors

- New class of anti-inflammatory agents, available as pimecrolimus 1% cream (Elidel<sup>®</sup>), and tacrolimus 0.03% (children 2–12 years) and 0.1% (adults) ointment (Protopic<sup>®</sup>).
- Calcineurin inhibitors block cytokine transcription mediated by NF-AT in T cells.
- Pimecrolimus is approved for short-term and intermittent long-term therapy of mild-to-moderate eczema, whereas tacrolimus is approved for therapy of moderate-to-severe AD.
- Both are excellent for long-term management of AD [Meurer M, et al. *Dermatol* 205(3):271-7 (2002); Hanifin JM, et al. *J Am Acad Dermatol* 53(2 Suppl 2):S186-94 (2005 Aug).]
  - Reduces the intensity of the flare
  - Helps maintain remission
- Pimecrolimus has been shown to increase the time between flares.[Meurer M, et al. *Dermatol* 205:271-7 (2002).]
- To be applied only on areas of disease.
- Most common side-effects are local burning and stinging of the skin, which are transient.
- In response to black box warnings for calcineurin inhibitors initiated by Health Canada and the US FDA, the Canadian Dermatology Association has stated that the topical use of calcineurin inhibitors does not lead to an increased risk of malignancy, specifically lymphoma, and so can be used with the same precautions as with topical corticosteroids.[Maddin S. *Skin Therapy Lett* 10(4):1-3 (2005 May).] Their position still holds as of May 2006.

### Oral Anti-itch Medications:

- Sedating antihistamines, such as hydroxyzine or diphenhydramine, can be useful adjuncts when taken at bedtime, especially with flares.
- Mast cell stabilizers, such as ketotifen, can be useful when there are other atopic manifestations, such as asthma, rhinitis.

### Antibiotic Therapy:

- There may be a secondary infection with *S. aureus*, even without obvious impetigo, that can lead to a flare.
- Usually topical therapy, such as mupirocin (Bactroban<sup>®</sup>) or fusidic acid ointment (Fucidin<sup>®</sup>), is sufficient to help clear the eczema.
- In rare widespread cases, oral cloxacillin or a cephalosporin is required, after swabbing for cultures and sensitivities.

**Second-line Therapies** – For very resistant cases systemic treatments such as PUVA, UVB, cyclosporine, azathioprine, or methotrexate can be used. Systemic steroids are sometimes used short-term.

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Editor-in-Chief: Dr Stuart Maddin

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