Trying To Keep Ahead of Lice: A Therapeutic Challenge

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Background

The social, economic, and educational impact of head lice infestations is considerable. It is most commonly seen in school-aged children, and girls are more commonly affected than boys. New therapeutic options are now available that may help clinicians to keep ahead of lice.

Infestation

- Caused by the obligate ectoparasite *Pediculus humanus capitis*; can survive for 1–2 days away from the scalp.
- Transmission most commonly occurs through:
  - Close physical contact, especially head-to-head contact
  - Fomites, such as hats.
- Transfer is optimal when hairs are relatively stationary and parallel, i.e., while children are at rest.
- Eggs are glued to the hair close to the scalp in egg castings, or nits. Nits within 1 cm of the scalp should be counted as a sign of active infestation.

Clinical Presentation

- Most common symptom is pruritus.
- Occurs due to sensitization to either louse salivary or fecal antigens.
- May be so intense that excoriations and secondary bacterial infection may occur.
- Diagnostic gold standard is finding a live louse or nymph on the scalp, or a viable egg attached to the hair. Microscopic examination of the nit may aid in this determination.
- Nits alone are not proof of active infection.
- Not finding a louse does not completely rule out infestation.
- Louse combs increase the diagnostic yield.

Treatment Options

Pediculicides: Neurotoxic Agents

- Includes permethrin, permethrin-based products, malathion, and lindane.
- Not recommended for children < 2 years of age. Off-label use based on clinical judgement.
Treatment Options (continued)

- Avoid hair conditioner before applying; it may coat the hair and protect the lice and nits.

**Permethrin-based Products**
- OTC extracts of natural pyrethrins from chrysanthemums combined with piperonyl butoxide to increase stability and effect.
- Neurotoxic to lice, but not ovicidal; even after two treatments viable lice and eggs may remain.
- Contraindicated in patients allergic to ragweed, chrysanthemums, or other permethrin products.

**Permethrin 1%**
- Historically considered standard treatment; however issues of resistance have made it necessary to explore new alternatives.
- It is a poorly absorbed synthetic pyrethrin with pediculicidal and ovicidal activity.
- Leaves a residue on the hair and remains active for 2 weeks following application.
- Wash hair, rinse with water, towel dry, then apply to entire scalp and hair for 10 minutes and rinse out. Treat again 7-10 days later.

**Malathion 0.5%**
- Can be applied for 10 minutes or overnight and repeated in 1 week.
- Can cause stinging of the skin and eyes.
- Should be used with caution:
  - base is flammable.
  - may lead to respiratory depression if ingested (there are no reported cases).
- No significant resistance has been reported in the US.

**Lindane 1% Lotion**
- Second-line treatment to be used as an alternative when other treatments have failed.
- Has limited ovicidal activity; kills lice by causing CNS stimulation and respiratory paralysis.
- Higher side-effect potential including neurotoxicity and bone marrow suppression.
- Contraindicated in children <2 years, pregnant women, and nursing mothers.

**Oral Agent - Ivermectin**
- An anthelmintic drug and effective pediculicide
- Suggested for off-label use in the treatment of head lice at a dosage of 200µg/kg, to be repeated in 7-10 days.
- Possible neurotoxicity is a concern; safety and efficacy remain to be established.
- No resistance has been reported to date and it may be used after failure with topical pediculicides.

- May be useful for extensive infestations or infestations with multiple types of ectoparasites.
- Should not be used in children weighing <15kg.

**Non-neurotoxic Pediculicides**
- Exoskeleton Integrity Dehydration Pediculicides
- This is a new nonpesticide, nonprescription, behind-the-counter product containing isopropyl myristate 50% and ST-cycloheximethicone 50% (Resultz™).
- Recently approved by Health Canada for the treatment of lice in persons aged 4 years and older.
- Works by dissolving the waxy exoskeleton that covers the lice.
- Apply first to dry hair, scalp, and the nape of the neck, leave in place for 10 minutes, then rinse. Repeat in 1 week.
- Phase II clinical trials document a higher success rate (no live lice) compared with traditional pediculicides (57% isopropyl myristate 50% and ST-cycloheximethicone 50% vs. 22% with .33% pyrethrin + 4% piperonyl butoxide; 77.1% isopropyl myristate 50% and ST-cycloheximethicone 50% vs. 20% with permethrin 1%).
- Well tolerated with mild local erythema or pruritus being the main side-effect.

**Dry-on Suffocation Based Pediculicide**
- Originally marketed as Nuvo® Lotion; it was later discovered to be Cetaphil® Gentle Skin Cleanser.
- Reported 96% success rate when applied to the scalp, dried with a hair dryer (for ~30 minutes), and removed during the next day’s bath.[Pearlman DL. Pediatrics 114(3):e275-9 (2004 Sep).]
- Reviews found that the study did not use proper methods of diagnosing lice, was anecdotal, and was not a well-designed, randomized control study.[Roberts RJ, et al. Lancet 365(9453):8-10 (2005 Jan); Burkhart CG, et al. J Am Acad Dermatol 54(4):721-2 (2006 Apr).]
- Given encouraging preliminary results, further study is warranted.

**Mechanical**
- Nit combing is labor intensive and somewhat painful; should not be used alone.
- Application of a 8% formic acid rinse or a 1:1 mixture of white vinegar and water followed by combing with a nit comb can aid in nit removal.
- The only treatment recommended for children < 2 years of age.
**Environmental Interventions**

- Decontaminate clothing, linen and towels by washing in hot water (60°C) or dry-cleaning.
- Treat combs and brushes with boiling water, alcohol, bleach, or soak in a disinfectant solution (e.g., 2% Lysol®).
- Examine all household members and close contacts and treat concurrently if infested.
- Notify the school.
- Treat bedmates prophylactically.

### Treatment Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Comments</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pediculicides:</strong></td>
<td></td>
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<tr>
<td>standard</td>
<td>Historically considered standard treatment; however issues of resistance have made it necessary to explore new alternatives.</td>
<td>Permethrin</td>
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<tr>
<td></td>
<td></td>
<td>Permethrin-based products</td>
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<td></td>
<td></td>
<td>Malathion</td>
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<td></td>
<td></td>
<td>Lindane</td>
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<tr>
<td>Oral agents</td>
<td>Off-label use</td>
<td>Ivermectin</td>
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<tr>
<td></td>
<td></td>
<td>TMP/SMX*</td>
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<tr>
<td><strong>Pediculicides:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non-neurotoxic agents</td>
<td>Exoskeleton integrity dehydration pediculicide</td>
<td>Isopropyl myristate 50%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>and ST-cyclomethicone 50%</td>
</tr>
<tr>
<td></td>
<td>Dry-on suffocation-based pediculicide</td>
<td>Active agent unclear</td>
</tr>
<tr>
<td><strong>Mechanical removal</strong></td>
<td>Only treatment recommended for children under 2 years</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Environmental intervention</strong></td>
<td>Important to prevent recurrence</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Alternative treatments</strong></td>
<td>Published data is sparse</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Caution advised until more data is available.</td>
<td>N/A</td>
</tr>
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</table>

Table 1: Treatment categories for lice therapies; *TMP/SMX=Trimethoprim/ Sulfamethoxazole.

### Treatment Failures and Resistance

Resistance to permethrin and lindane is common in populations where these pediculicides have been heavily used. Treatment failures can also be a result of reinfestation from:
- an untreated classmate
- an inadequate quantity of pediculicide applied
- the improper duration of product application.

A second treatment of the prescribed pediculicide should be administered 7-10 days after the start of treatment to kill all active stages of the louse. Resistance should be suspected if live lice are still present 2-3 days after the second application of a product has been used correctly and no other cause for failure can be identified.
- If lice are present after 2 correctly applied treatments, resistance is certain.
- Resistant infestations should be treated with an agent from a different class of pediculicides

### Conclusion

Lice have developed resistance to some pediculicides and it is expected that with ongoing use, these pediculicides will probably become less effective. These products can still be used effectively to treat nonresistant lice. New products are now available in Canada that may prove to be equal to or more effective/safe than the standard neurotoxic pediculicides, while at the same time minimize the problem of treatment-resistant lice.
Combination Therapy for Acne Vulgaris

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The Disease

- Acne vulgaris is a complex skin disorder of the pilosebaceous unit affecting almost all people at some point in their lifetime, especially among people aged 15–24 years.
- Acne can be physically and emotionally scarring, causing significant psychosocial morbidity and reducing self esteem.
- All forms of acne involve one or more of these pathophysiologic factors:
  - Hyperkeratinization of the follicular epithelium with comedone formation
  - Increased sebum production
  - Bacterial proliferation of Propionibacterium acnes (P. acnes)
  - Local immune hypersensitivity causing inflammation.
- Acne may be classified according to predominance of specific skin lesions:
  - Comedonal (non-inflammatory) – mild
  - Papular (inflammatory) – mild-to-moderate
  - Pustular (inflammatory) – moderate
  - Nodulocystic – severe
- This order also follows increasing severity, with cutaneous scarring as the ultimate result.

Make a Diagnosis

Existing therapies for acne can be divided into one of the following categories:
1. Physical or mechanical modalities
   - Includes comedone extraction and other forms of acne surgery, chemical peels, and microdermabrasion.
2. Light-based therapy
   - Includes laser treatment, the usage of noncoherent light sources and photodynamic therapy
3. Topical or systemic medications
   - Includes retinoids, antibiotics, benzoyl peroxide, and hormonal therapy.
   - Two major categories based on primary mechanism of action:
     - Antimicrobials: reduce P. acnes growth
     - Comedolytics: reduce and/or prevent comedone formation
   - Formulations (i.e., gel vs. cream) may decrease sebum production.

Combination Therapy

- It is necessary to address all pathophysiologic factors of acne for effective treatment.
- Most medications do not act against all four major pathophysiologic features of acne.
- Combination therapy with a few logically chosen agents has a greater chance of addressing more pathophysiologic factors in acne development.
- Other benefits of combination therapy:
  - Some combinations have demonstrated synergy (i.e., the combined effect is better than that seen by the individual agents).
  - Potential to decrease individual drug doses and exposure times
  - Potential to reduce and prevent antibiotic resistance
  - Potential cost-savings by reducing the use of expensive medications.

Recommendations for Treatment

- Topical and systemic agents are the mainstay of acne therapy and maintenance.
- Physical and light-based modalities should be used as second-line or adjunctive therapy.
- Hormonal therapies may be used as second choice or adjunctive therapy in women with contributing androgenic factors for acne.
- Choose agents with different, but complementary mechanisms of action (e.g., antimicrobial + comedolytic agent).
Recommendations for Treatment (continued)

- Tolerability is related to compliance; choose agents with a good tolerability profile.
- Topical retinoids alone, or in combination with other medications, should be considered first-line therapy for both inflammatory and non-inflammatory acne.
  - Includes adapalene, tazarotene, tretinoin, and tretinoin gel microsphere.
  - Use early for best results.
  - Inhibits microcomedone formation, which is the precursor lesion in acne.
  - Clears mature comedones.
  - Improves inflammatory lesions.
  - Has synergistic effects with oral or topical antibiotics.
  - Induces remission of acne in maintenance therapy.
- Antibiotics are adjunctive therapy in inflammatory acne.
  - Oral antibiotics include minocycline, doxycycline, tetracycline, trimethoprim-sulfamethoxazole, and erythromycin.
  - Topical antibiotics include clindamycin and erythromycin.
  - Use only as long as necessary and combine with topical retinoids.
  - Antibiotics should not be used as monotherapy in order to prevent resistance and target more pathophysiologic factors.
  - Minimize duration of therapy to prevent resistance and side-effects.
- If there is need to continue antimicrobials, use benzoyl peroxide or benzoyl peroxide/antibiotic combinations.

<table>
<thead>
<tr>
<th>Acne Type</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild acne (comedonal)</td>
<td>• Topical retinoid</td>
</tr>
<tr>
<td>mild acne (papular)</td>
<td>• Topical retinoid + topical antibiotic +/- benzoyl peroxide</td>
</tr>
<tr>
<td>moderate acne (papular/pustular)</td>
<td>• Topical retinoid + oral antibiotic +/- benzoyl peroxide</td>
</tr>
<tr>
<td></td>
<td>• Topical retinoids act in synergy with antibiotic to hasten resolution of inflammatory lesions.</td>
</tr>
<tr>
<td></td>
<td>• Avoid antibiotic monotherapy.</td>
</tr>
<tr>
<td></td>
<td>• Discontinue antibiotic when inflammatory lesions resolve (usually no more than 6 months).</td>
</tr>
<tr>
<td></td>
<td>• Use topical retinoid to maintain remission post antibiotic.</td>
</tr>
<tr>
<td>severe acne (nodulocystic)</td>
<td>• Oral isotretinoin</td>
</tr>
</tbody>
</table>

Table 1: Treatment options for different acne types

Recommendations for Maintenance

<table>
<thead>
<tr>
<th>Acne Type</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild-to-moderate acne</td>
<td>• Topical retinoid</td>
</tr>
<tr>
<td>moderate-to-severe acne</td>
<td>• Topical retinoid +/- benzoyl peroxide</td>
</tr>
</tbody>
</table>

Table 2: Recommended maintenance for acne

Acne Medications and Pregnancy

Some acne medications must not be used by women who are pregnant or lactating, or who may become pregnant because of the potential harm to a fetus or breastfed infant. These medications include:
- Hormonal therapy
  - Estrogen and derivatives, flutamide, spironolactone
  - Oral and topical isotretinoin
  - Established teratogenicity
- Oral tetracyclines
  - Tetracycline, doxycycline, minocycline
  - Dental discoloration noted
- Oral sulfonamides
  - Trimethoprim-sulfamethoxazole
  - Theoretical risk of teratogenicity, anemia, jaundice
- Topical retinoids
  - Adapalene, tazarotene, tretinoin
  - Theoretical risk of teratogenicity

Conclusion

Acne vulgaris remains a therapeutic challenge, in large part due to its multifactorial pathophysiology. Evidence for improved and quicker efficacy with safety and longer remission has been noted with combination therapies.
Treatment Options for Excessive Sweating and Hyperhidrosis

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Excessive production of sweat, or hyperhidrosis, affects millions of people worldwide. Until recently, treatment was difficult. However, new advances have revolutionized the management options for many patients suffering from this condition.

Sweating is a necessary physiological mechanism, and under certain conditions, such as physical exertion or illness, it can become excessive. However, it is not necessarily hyperhidrosis, which is defined as nonphysiological, excessive sweating that is not caused by physical activity and occurs symmetrically in a localized fashion. In either case, it can have a significant negative impact on a patient’s quality of life, including difficulty with work, school, and social relationships. As a result, patients often shy away from situations that require shaking hands or other forms of close physical contact with other people.

Hyperhidrosis
Excessive Sweating vs. Hyperhidrosis

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Primary Focal Hyperhidrosis (PFHH)

• The most common form of hyperhidrosis
• Affects about 5% of the general population.
• Most frequently affects the axillae, hands, and feet; the face and the groins can also be involved.

Treatment Options

Several forms of treatment are now available for the management of PFHH. The options are slightly different and depend on the condition (excessive sweating vs. hyperhidrosis) and locations involved.

Axillary Excessive Sweating/ Hyperhidrosis

Topical Antiperspirants
• Available over-the-counter.
• The most commonly used first-line treatment for those who have regular sweating (deemed to be excessive by the patient) and hyperhidrosis who are seeking a less costly, noninvasive option.
• Preferred by patients due to relatively low cost.
• Aluminum chloride solutions
  • The effective ingredient frequently used in concentrations ranging from 10%–25%.
  • Rarely offers complete wetness control, but can be very helpful for many people.
  • Local irritation at the application site can limits tolerability.
• Aluminium zirconium trichlorohydrex complex
  • A new form of topical antiperspirant
  • Will be available soon in North America.
  • Similar efficacy, but may have less irritating side-effects than aluminum chloride-based products.

Subcutaneous Injection of Botulinum Toxin
• When injected by experienced physicians, it can be highly effective for the cessation of sweat production in areas of administration.
• It works by blocking acetylcholine release, a neurotransmitter secreted by the sympathetic nerves innervating the sweat glands.
• There is no spread of the toxin to other body systems, which could cause unwanted effects.
• There are no significant side-effects.
• More than 90% reduction in sweat production for more than 90% of patients.
• Repeated injections are necessary, usually one to two treatments each year.
• Relatively high in cost. However, most private health insurance carriers cover the cost of the drug for this indication with submission of appropriate paperwork.
• An injection of botulinum toxin eliminates the frequent use of topical antiperspirants and potentially saves costs associated with replacement of clothing.
Surgical Management of Axillary Hyperhidrosis

Surgical removal of the sweat glands in the axillae, or ablating the sympathetic chain supplying the sweat glands can also be performed for selected patients. However, unwanted effects of surgical treatment can include:

- With sweat gland removal
  - Necrosis
  - Scarring
  - Relapsed sweating
- With sympathectomy
  - Risk of intrathoracic injury to the lungs and other nerve structures
  - Compensatory hyperhidrosis.

Consequently, these procedures are reserved for those who do not respond to other treatment options.

Oral Anticholinergics

Oral anticholinergics such as glycopyrolate can offer mild-to-moderate relief for some patients suffering from PFHH. However, because of the systemic side-effects such as dry mouth, blurred vision, and reduced gastrointestinal motility, systemic anticholinergics have not been the accepted therapy for most patients.

Palmoplantar Hyperhidrosis

Hyperhidrosis affecting the hands and the feet is also very common, alone or in combination with axillary hyperhidrosis. The treatment options are similar to axillary hyperhidrosis.

Topical Antiperspirants

As for excessive sweating and axillary hyperhidrosis, antiperspirants containing aluminium salts in concentrations ranging from 10%–25% are considered the first-line therapies.

Botulinum Toxin Subdermal Injections

- It is highly effective for most patients.
- Cost of botulinum toxin therapy is significantly higher than for axillary hyperhidrosis because palmoplantar hyperhidrosis requires significantly larger doses.

Tap Water Iontophoresis

- Iontophoresis works by delivering micro-amounts of electric current through the medium of tap water.
- The mechanism of action is unknown, however, it may involve plugging the eccrine sweat gland pores.
- Initially, frequent treatment sessions are required to be effective.

- Once significant control of sweating is attained, infrequent maintenance therapy is all that is necessary for moderate-to-significant long-term control.
- It is relatively low in cost when compared with botulinum toxin, although the effect is also less pronounced.
- There are no significant side-effects.
- May be tried by patients before sympathectomy.

Oral Anticholinergics

As for axillary hyperhidrosis oral anticholinergics, such as glycopyrolate, can offer mild-to-moderate relief for some patients suffering from PFHH. However, because of systemic side-effects, systemic anticholinergics have not been considered as the accepted therapy for most patients.

Endoscopic Trans-Thoracic Sympathectomy

- Surgical ablation of the sympathetic nerve chain supplying the sweat glands to the hands can also be performed for selected patients.
- It can be very effective and long lasting for some patients.
- There are concerns of complications such as injury to other critical structures in the chest, and the troubling side-effect of compensatory hyperhidrosis. Therefore, this procedure is reserved for patients who cannot get adequate relief from other treatment options.

Conclusion

For most patients, antiperspirants containing aluminium salts are the first-line treatments. Other therapeutic options, especially for those with hyperhidrosis, include botulinum toxin injection, systemic anticholinergics, iontophoresis and surgery. Individualized patient counselling and careful attention to adverse effects are the keys to treatment satisfaction.
**Dermatologic Diagnostic Challenge**

**Question:** A 62 year-old man presented with an itchy rash on his right lower leg. He has used an OTC antifungal cream and his wife’s betamethasone cream without much relief. The plaques are well defined, slightly scaly, and thickened with some excoriations. He has had a history of recurrent jock itch. He has been taking a diuretic for 3 years for his hypertension.

**What is the diagnosis?**
- a. Psoriasis
- b. Discoid eczema
- c. Lichen simplex chronicus
- d. Basal cell carcinoma
- e. Fungal infection

Case study submitted by Richard Thomas, MD, Vancouver, Canada

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