Introduction

Head lice have been a common companion of the human species since antiquity and continue to be an annoying and common problem, particularly among children 3–12 years of age, and members of their families. Estimates of the incidence of head lice range from 6–12 million infestations annually in the US alone.

One of the leading factors for the increasing number of infestations is resistance of lice to topical therapies. Since the introduction of insecticides years ago, the louse has adapted by genetic alterations. Similar to antibiotic resistance, alternative therapies are continually being needed to offset the adaptations made by this species of insect. For example, although most infected individuals try over-the-counter (OTC) pediculicides initially, the agents with the highest success rates, namely malathion and ivermectin, are prescription products. Thus, with resistance to pyrethrins increasing, physician involvement is becoming more essential for proper distribution of these prescription insecticides.

Cause and Transmission of Pediculosis Capitis

Head lice are bloodsucking, wingless insects that are found worldwide with no strict limitations on their host in terms of age, sex, race, or socioeconomic class. They are highly host-specific and are approximately the size of a sesame seed, or 2–3mm.

The female louse lays her eggs, or nits, on the hair shaft within 6mm of the scalp. They are cemented to individual hairs by means of a proteinaceous matrix that closely resembles amino acid constituents of the human hair shaft itself. Thus, it would appear unlikely that a simple compound will be forthcoming that will easily dissolve the nit sheath without damaging hair. The nits remain affixed to the hair even after the hatching of the adult louse. Head lice partake in frequent blood meals, and lice mortality occurs after 24–36 hours off the host due to physiologic desiccation. The eggs, or nits, can survive and hatch after 10 days away from the host.

Transmission is by means of direct head-to-head contact or by indirect (fomite) transmission such as combs, brushes, blow-dryers, hair accessories, bedding, helmets, and other headgear. Several field studies in which investigators had no head-to-head contact with subject, found lice on themselves after combing the hair of infested individuals. Inasmuch as head lice harbor various blood-born pathogens within their gut, they remain unproven, yet likely, vectors of various human pathogens similar to body lice. Additionally, head lice are an occasional cause of impetigo as they carry coagulase-positive Staphylococcus aureus and group A Streptococcus pyogenes on their external surfaces.

Clinical Signs of Disease

Skin findings of head lice are limited to the scalp and surrounding tissue. The classic symptom is pruritus, but the intensity can vary greatly. Indeed, some patients will experience no symptoms of the infestation and could be considered ‘carriers’. More commonly, the first infestation takes 2–6 weeks before pruritus is evident, which is caused by the host’s immunologic response to the proteaceous components of the lice saliva or excreta. If re-infested, pruritus normally develops within the first 24–48 hours. The diagnosis is usually made by the identification of nits and/or adult lice in the scalp hair. Viable eggs are usually tan to brown in color, while hatched eggs are clear to white. The eggs and hatched nits strongly adhere to, and are not easily displaced from, the hair shaft. They are much more quickly observed on physical examination than mature lice for diagnostic purposes. Nits have to be differentiated from hair casts, dandruff, hair gel, and white piedra.

Louse Adaptations

Given the number of anecdotal and market-driven reported studies, assessment of topical lice therapies should include some simple, basic in vitro testing. To accurately evaluate pediculicidal activity of any compound, one must appreciate that head lice have the ability to ‘resurrect’ from a state of seeming death, in which respiratory and motor function appear to have...
These insects are less dependent than mammals for continuous nervous control of respiration and circulation, and the exact point of death is not readily defined. Indeed, the World Health Organization (WHO) recommends pediculidal testing to be read 24 hours after application of insecticide since otherwise mortality rates are overestimated.

**OTC Insecticides**

Any treatment for head lice should be ideally based on efficacy, potential toxicity, louse resistance patterns to various insecticides in a particular geographic area, and ease of access to preferred prescription remedies. The mainstay of head lice therapy remains pediculicides. With all topical preparations (regardless of package instructions), two applications seven to ten days apart are advisable so as to kill any nits that survived treatment, to better defend against the seemingly growing resistance to most pediculicides, and to reduce the risk of reinfestation by means of fomites.

**Pyrethrins and Permethrins**

Due to restrictions imposed by the US Food and Drug Administration (FDA), the bulk of topical OTC insecticides available for head lice are pyrethrins, which are insecticides derived from the extract of chrysanthemum flowers. Pyrethroids are synthetic forms of pyrethrins, which can be chemically altered for heat and light stability and improved insecticidal efficacy. Permethrin is the only synthetic form of pyrethrin that has been FDA-approved for human usage. These agents act on the sodium channels of the neuromuscular junctions of head lice. Pyrethrins have been formulated into lotions, shampoos, foam mousse, and cream rinses, and are usually applied to the head for 10 minutes then rinsed off. Pyrethrins usually also contain a synergist, namely piperonyl butoxide, which restricts the insects’ normal enzyme to detoxify the pyrethrin.

Although pyrethrins and permethrin were nearly 100% effective in the mid 1980s, recent studies indicate that efficacy has decreased substantially due to resistance, with some communities experiencing success rates of around 50%. In vitro analysis of head lice from infested individuals also reveal the decreased lethality of the product. As with pyrethrin, the efficacy of permethrin has decreased over time with clinical failure rates over 50% reported in some communities.

Pyrethrin and permethrin have favorable safety profiles. Percutaneous absorption of these insecticides are minimal, so mammalian toxicity is very low. Patients who are allergic to ragweed may experience wheezing and dyspnea, and those who are allergic to chrysanthemums should not use pyrethrin-based products.

As with all pediculicides, safety profiles are based on proper use according to package instructions. A 5% concentration of permethrin for overnight application is available for scabies, and the product has been used in a similar fashion to the scalp for resistant cases with some success.

**Prescription pediculicides**

**Lindane**

Lindane is a chlorinated hydrocarbon, which has been available as a 1% shampoo for the treatment of head lice for 50 years. Lindane has neurotoxic properties similar to those of dichlorodiphenyltrichloroethane (DDT), killing lice by over-stimulation of the parasite’s central nervous system (CNS). As late as July 1999, lindane shampoo was the only prescription product with a claim for the treatment of lice.

Resistance to lindane has developed. In a recent comparison of lindane, malathion, pyrethrin, and permethrin used to treat both treatment-sensitive and treatment-resistant lice collected from a patient population in Florida, lindane 1% was the slowest and least effective product, apparently killing no lice after 10 minutes, which is the recommended application time for lindane shampoo. After three hours of exposure, only 17% of lice were dead. Although the cure rates were between 76 and 88% in the mid 1980s, an in vitro study revealed only a 17% mortality in Florida, while Panama and South Korea still maintain success rates of 61% and 93%, respectfully.

Lindane does have significant problems for the host in terms of potential CNS toxicity, convulsions, seizures, paresthesia, and possible carcinogenicity. The FDA evaluated reports of adverse events and determined that most occurred in patients who used lindane in excessive amounts or misused the product. However, serious adverse events also occurred among patients who used the product according to label directions. Indeed, the sale of any product containing lindane for the treatment of lice or scabies in humans has recently been banned by the State of California.

In March 2003, the FDA issued a public health advisory with box warnings and restrictive labeling changes of lindane products to reduce use of this insecticide for scabies and lice. The doctrine stated that, “Lindane is a second-line treatment that should be used only in patients who cannot tolerate or have failed first-line
treatment with safer products. Lindane should not be re-applied if initial treatment fails.”

Certain patients are at increased risk for adverse events, including infants, children who weigh less than 110 pounds, the elderly, and persons with skin conditions that might increase systemic absorption. Lindane is contraindicated for patients with uncontrolled seizure disorders and for those with known sensitivity to lindane or its components.

Given the continual high sales of lindane, it seems likely that many physicians remain unaware of these labeling changes. In light of the warnings about this product and the legal ramifications, the place of lindane in the treatment algorithm would appear to be extremely limited. In short, it should only be used in patients who fail to respond to all other approved lice therapies as more effective and less toxic alternatives are available.

**Malathion**

Malathion was reintroduced into the marketplace in 1999 with FDA approval, given the increasing resistance to pyrethrin and permethrin. Of note, the FDA prior approval recommendation for an 8–12-hour application is still listed in the package insert, although a 20-minute treatment is sufficient. Currently marketed in a 0.5% concentration, malathion is the fastest and most effective pediculicide currently available, killing 88% of lice in 10 minutes and 100% in 20 minutes.

Studies in the UK, using malathion as the sole insecticide in the formulation reveal significant drops in sensitivity to head lice. Significantly, in the US, the malathion-containing prescription pediculicide Ovide® contains two insecticides, and has not met resistance to date. Specifically, the vehicle in the US has measurable pediculicidal and ovicidal effects by itself, in the form of terpineol, dipentene, and pine needle oil. These monoterpenoids are found in a wide variety of plant extracts with natural insecticidal properties.

The safety profile of malathion is favorable, with a pregnancy category B designation. Two safety issues related to malathion continue to concern both consumers and healthcare professionals. One concern relates to the high alcohol content (78%) in malathion 0.5% lotion, which makes it potentially flammable. Another concern is related to confusion about the difference between agricultural and pharmaceutical grades of malathion. Malathion products not intended for human use normally contain considerable more impurities, translating into significantly more toxicities.

**Ivermectin**

Ivermectin (Stromectol, Merck) is an antihelmintic agent derived from a class of compounds known as avermectins. It has been used in veterinary medicine since 1981, and has been an excellent antiparasitic drug for humans for various diseases including onchocerciasis and scabies.

Although not currently approved, ivermectin has had encouraging results both topically and orally for head lice. Oral ivermectin exerts its insecticidal effects only on lice that feed from their hosts. Since the plasma half-life of oral ivermectin is 28 hours, a second dose on day 8 is recommended to kill lice nymphs that hatch after the initial dose. Orally, 200μg/kg given at two separate time times, one week apart, is an effective treatment for head lice, especially for patients resistant to topical OTC therapies. Topical ivermectin has proved to be highly successful in the management of infestations in a few initial studies for head lice using a 1% concentration.

**Summary**

Pediculosis capitis remains a problematic parasitic infestation. During the last few years, considerable attention has been paid to the potential neurotoxicity and reduced efficacy with OTC insecticides and prescription lindane. Among prescription products, the US version of malathion, with an additional insecticidal agent in its vehicle, appears to provide superior efficacy and safety, and is currently the best topically available treatment for head lice. Other insecticidal treatments such as topical ivermectin will have to be developed given the insects’ ability to foster resistance to all various insecticides with time.

There is a market-driven emphasis to promote agents for head lice, which are non-insecticides as an alternative therapy. Such products must be evaluated with standardized in vitro testing, as well as clinical evaluations to ensure that they are more than hype and can assist the public in controlling this age-long nemesis, the head louse. The search for nontoxic treatment may have merit as an adjunct, possibly allowing lower concentrations of insecticides to be used. In a similar scenario, entire saturation with oil-based liquid paraffin has been definitely shown to be lethal to bird eggs. Lastly, there remains a lack of appreciation and lack of discussion with patients about fomite control, which is important for both avoiding the spread of the disease, as well as reinfesting oneself.

*A version of this article, with references, can be found in the Reference Section on the website supporting this briefing (www.touchbriefings.com)*