

# Effective Pediculosis Management in the Era of Pesticide-Resistant Lice

By Cheryl Guttman Krader

**H**ead lice infestation, or pediculosis, is the most common human parasitic infestation. In the United States, its prevalence is highest among preschool and elementary schoolchildren, although pediculosis affects people of all ages and across all sociodemographic groups.<sup>1,2</sup>

Head lice do not carry disease, and pediculosis has no adverse health consequences other than a risk of secondary local infection if the skin barrier is compromised by scratching.<sup>2,3</sup> Pediculosis, however, is associated with significant economic and psychosocial burdens.<sup>3</sup> Therefore, effective, accessible treatment is important.

The optimal treatment for pediculosis should act rapidly and reliably to eliminate live lice and eggs and be easy to use, safe, and affordable.<sup>3</sup> Over-the-counter (OTC) agents are recommended as first-line intervention for pediculosis, and products containing pesticides that act chemically as neurotoxins have been used most commonly in the US. Traditional pesticide-based treatments, however, fall short of meeting the optimal treatment criteria. The pesticide-based products have been associated with increasing failure rates that are attributed to high levels of genetic-based louse resistance and low efficacy for eliminating eggs. Resulting failures with the pesticide products can lead to overuse, which compounds the burden for parents by increasing treatment cost and toxicity risks due to overexposure. OTC products with a physical mode of action are generating attention in the US as a valuable alternative treatment for pediculosis that can overcome the limitations of the traditional pesticide-based products. In Europe, lice treatments relying on a physical mode of action already have been the standard of care for nearly 20 years.

Customers trust pharmacists for their knowledge about OTC products and often ask for advice on product selection. This whitepaper presents updated information on pediculosis science and treatment that pharmacists can use to provide optimal counseling and OTC treatment recommendations.

## Basic biology facts

*Pediculus humanus capitis*, the etiologic agent in head lice infestation, is an ectoparasite with a life cycle defined by 3 stages.<sup>1,3</sup> The adult female louse deposits and glues eggs, also called nits, (~6/day) onto the hair shaft within 4 mm of the scalp. Depending on environmental conditions, the eggs hatch after 7 to 12 days (usually 8–9 days) to release nymphs. The hatched nymph molts 3 times over 9 to 12 days before maturing to become an adult. Females begin to lay eggs approximately 1.5 days after reaching the adult stage and fertilization, and the cycle restarts if the infestation is not treated.

Head lice feed exclusively on human blood.<sup>3</sup> Adults can live up to 30 days on the host's head, but die within 1 to 2 days off of the head.<sup>1</sup> Head lice cannot jump or fly. Transmission to other people occurs primarily by direct head-to-head contact that is particularly likely among children while playing at school, home, and elsewhere in the community.<sup>1,3</sup>

## Diagnosis

By understanding diagnostic criteria, pharmacists can play a role in confirming an active head lice infestation. They can also help parents understand the life cycle of head lice and select a successful treatment strategy.

Active infestation with head lice is confirmed by finding live nymphs or adult lice on the scalp or hair.<sup>1,3</sup> The presence of eggs on the hair shaft within ¼ inch of the scalp suggests the diagnosis, but it is not confirmatory because the eggs may not be viable.<sup>1</sup> In addition, because eggs, nits, and lice can be confused with dandruff or other debris, misdiagnosis is common.<sup>3,4</sup> Absence of itching does not rule out the diagnosis of pediculosis. Itching results from sensitization to components of louse saliva, but may take 4 to 6 weeks to develop in a primary case, if it occurs at all.<sup>3</sup>

## OTC TREATMENT

Treatment for head lice is generally recommended only for

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the individual with an active infestation.<sup>1,3</sup> Family members and other persons who have been in close contact with the infested individual should be checked for infestation, and in order to allow time for nymphs to hatch, they may be monitored for development of pediculosis for 7 to 10 days after contact with an infested individual.

### Pesticide products

OTC products approved for use in the US for treating pediculosis contain either permethrin (eg, Nix®) or synergized pyrethrins (pyrethrin + piperonyl butoxide; eg, A200®, Pronto®, R&C®, RID®, Triple X®).<sup>5</sup> Both permethrin and synergized pyrethrins are neurotoxins acting on the nervous system of the ectoparasite.<sup>6</sup>

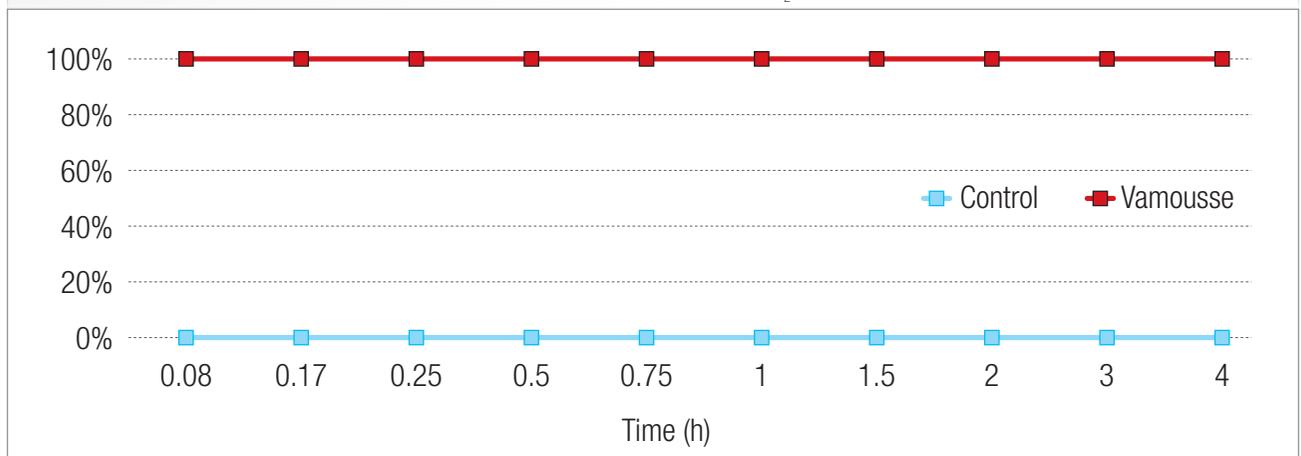
Resistance to these agents was noted soon after their introduction for head lice control more than 4 decades ago.<sup>7</sup> In recent North American studies, 97.1% to 99.6% of lice collected from infested individuals carried genes for resistance.<sup>7-10</sup> The increasing frequency of resistant genes has been linked

to a decline in clinical effectiveness of permethrin and synergized pyrethrin products that was documented in a recent systematic literature review.<sup>9,11</sup> Results of recent clinical trials conducted in the US show they have highly variable effectiveness rates of between 45% and 80%.<sup>12-15</sup>

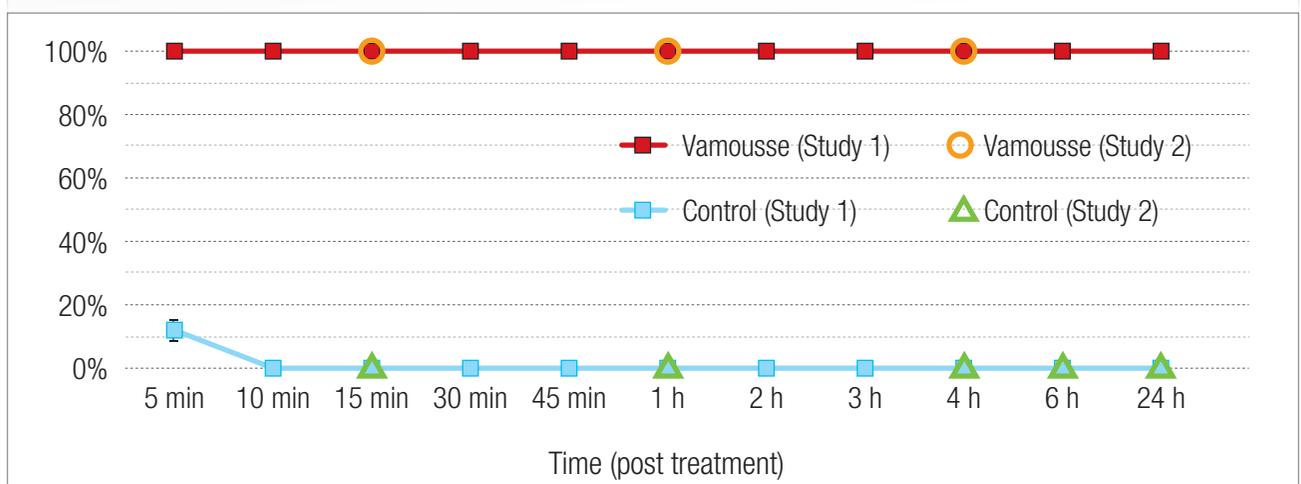
As another limitation, these pesticide-based products are largely not ovicidal.<sup>5</sup> This lack of activity against the developing eggs is explained both by the fact that the central nervous system target of the pesticides is absent during the first 4 days of development, and by the inability of the pesticide to penetrate the egg's chorionic membrane.<sup>6</sup> For this reason, products containing typical pesticide active ingredients require a second application after 7 to 10 days, targeting newly hatched nymphs.<sup>3</sup>

The second, required application is not to be administered sooner than 7 to 10 days following the first. This restriction, in place for safe, limited pesticide exposure, means that any failure in the first application puts the individual at risk of exposing others while waiting for the timing of the second application.

**Figure 1.** Mean ( $\pm 1$  SEM) percentage mortality of head lice treated with dH<sub>2</sub>O (n=6) control and Vamousse (n=6) over time.



**Figure 2.** Mean ( $\pm 1$  SEM) percentage mortality of human body lice treated with Vamousse and dH<sub>2</sub>O over time. (n=10 replicates of 10 lice per replicate, Study 1; n=5 replicates of 25 lice per replicate, Study 2).



Pesticide-based treatments for head lice are generally safe for humans when used as directed. Misuse (prolonged application) or overuse (>2 repeat applications) can occur, however, particularly in association with initial treatment failure and attempts to treat resistant or misdiagnosed pediculosis. Overuse appears to be common, as one study reported that people presenting to a lice and nit removal clinic in Florida had already treated themselves an average of 5 times.<sup>16</sup> A recent publication suggests a link between pyrethroid exposure in childhood and neurobehavioral development.<sup>17</sup> Although no cause and effect was identified, the practical recommendation is to ensure no greater exposure than required to control the target pest. With diminished efficacy of treatments containing these ingredients, overuse is certainly a risk that calls for innovations to be considered.

### Physical mode of action products

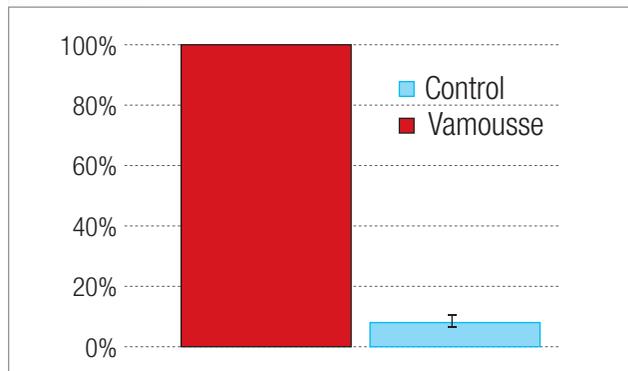
The inconsistent efficacy and safety concerns associated with pesticide-based treatments for pediculosis are driving a need for alternative treatments. Products with a physical mode of action offer a high safety profile and are less susceptible to the development of resistance.<sup>18</sup> From 2014 to 2016, unit sales in the US of such pesticide-free, physical mode of action products for treating pediculosis rose from 31% to 41% of total branded product sales.<sup>19</sup> Across Europe, lice treatments relying on traditional pesticides were almost completely replaced with products exhibiting a physical mode of action starting in the 1990s.

Vamousse® Lice Treatment, containing *natrum muriaticum* (sodium chloride) as its active ingredient, is one option in the category of pesticide-free OTC products for pediculosis. *Natrum muriaticum* is listed in the Homeopathic Pharmacopoeia of the United States, which is recognized as an official compendium by FDA, and it is both pediculicidal and ovicidal. Vamousse Lice Treatment is also safe, simple, and convenient to use. A treatment course involves a single 15-minute period of application followed by rinsing of the hair. There are no requirements to avoid use of shampoos or other hair care products, or for routine second application because unlike pesticide-based products, Vamousse Lice Treatment is ovicidal. The efficacy achieved with a single application minimizes the risk of lice transmission and avoids the possibility of noncompliance with a 2-part treatment.

The pediculicidal mechanism of action of *natrum muriaticum* involves rupture of the parasite's intestinal tract followed by dehydration.<sup>14</sup> Dehydration also explains its activity for rendering the lice eggs nonviable. The advanced formulation of Vamousse Lice Treatment enables fast penetration of the active ingredient to its target by compromising the protective lipid layer of the adult louse and the chorionic membrane of the egg.

As demonstrated by results of laboratory and clinical studies, Vamousse Lice Treatment is fast-acting and effective against pesticide-resistant organisms. All of the laboratory testing was performed using methods based on the American Society for Testing and Materials protocols. *Ex vivo* studies used adult

**Figure 3.** Mean ( $\pm 1$  SEM) percentage mortality of human head lice eggs treated with Vamousse and dH<sub>2</sub>O over time. (n=3 replicates of 25 lice per replicate)



head lice, immature human head lice, and confirmed viable eggs isolated from infested human volunteers residing in South Florida, where lice demonstrate a high level of genetic resistance to pyrethrin and permethrin.<sup>10</sup> *In vitro* testing was done with laboratory-reared body lice and eggs that are commonly used as surrogates for head lice. Testing was performed with a product exposure time of 15 minutes followed by rinsing with water, replicating instructions for human use. Results were evaluated at 24 hours post treatment to assess killing of live lice and after 15 days to evaluate ovicidal activity. In all laboratory tests, Vamousse Lice Treatment demonstrated 100% efficacy in killing lice and eggs (**Figures 1–3**).

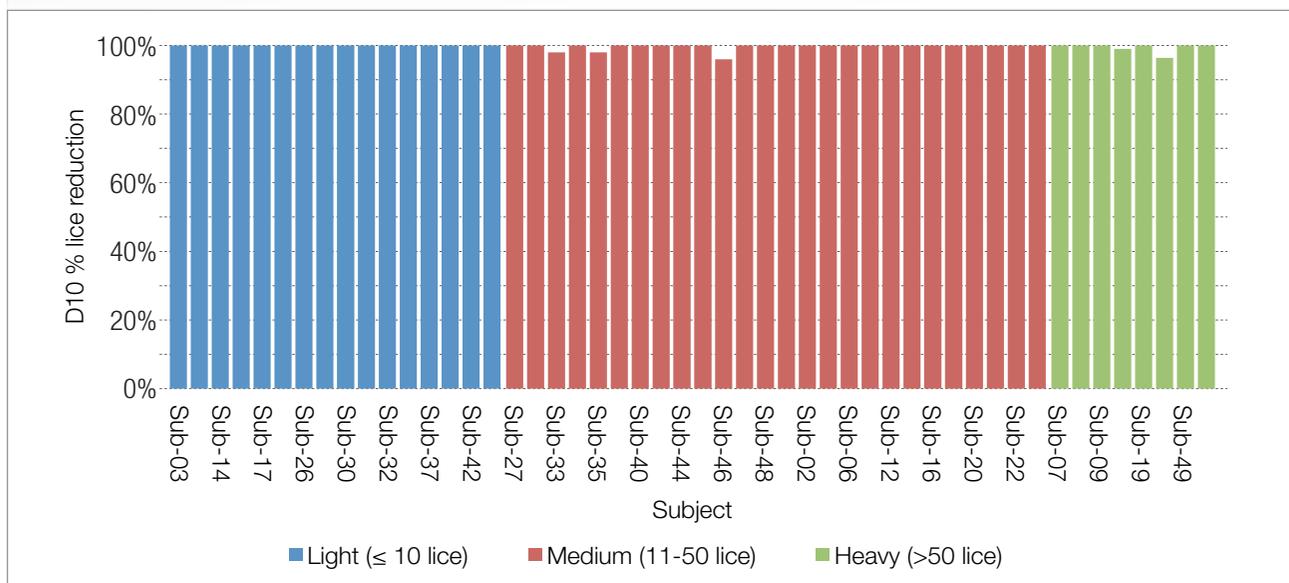
A clinical study of Vamousse Lice Treatment enrolled 50 patients. Cure, defined as being lice free, was achieved in 46 (92%) of the 50 study participants, including all 16 patients categorized as having “light” infestation (**Figure 4**). Analyses in the patients with incomplete cure indicated insufficient contact of product with 1 to 2 eggs, suggesting that the treatment will be successful in one application when all lice and nits are completely contacted. Nevertheless, treated individuals should be monitored for residual lice or signs of reinfestation. If reapplication is needed, it can be performed without safety concerns or the waiting period that a permethrin or synergized pyrethrin-based product requires.

### Conclusion

Pediculosis is a common and growing problem, with up to 12 million infestations estimated to occur annually among preschool and school-age children in the US.<sup>1</sup> Pharmacists have a role in helping parents/consumers select safe and successful treatment.

Louse resistance to permethrin and synergized pyrethrins has limited the efficacy of OTC products containing these pesticides and engendered their misuse and overuse, which raises safety concerns. Pesticide-free Vamousse Lice Treatment is easy to use, safe, and clinically proven. Pharmacists can recommend Vamousse with confidence when families seek professional advice about pediculosis management.

**Figure 4.** In vivo % reduction of lice in a 50 human subject clinical trial. Study volunteer infestation levels after a single 15-minute application of Vamousse, measured 10 days post treatment.



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