

# What's bugging you? An update on the treatment of head lice infestation

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## ABSTRACT

Head lice infestation (*pediculosis capitis*) is a common problem in paediatric practice. It can cause considerable distress to children and their families and may lead to bullying and social stigmatisation. Therapy with "conventional" topical pediculicides with neurotoxic mode of action—such as malathion, permethrin, phenothrin and carbaryl—is increasingly associated with treatment failure as a result of the emergence of resistance within the parasite population. This review provides an overview of the natural history, clinical symptoms and diagnosis of head lice infestation. It also discusses general management principles and summarises the current data on novel treatment strategies, including wet combing, dimeticone, isopropyl myristate, benzyl alcohol, plant-based compounds and oral medication.

Head lice infestation (*pediculosis capitis*) is a common problem in children. It can cause considerable distress to affected children and their families and may have a profound impact on a child's well-being when associated with bullying and social stigmatisation. In recent years, with the abandoning of school nurse-based screening services, paediatricians and general practitioners in the UK have found themselves in the frontline in the fight against this parasite. Therapy with "conventional" topical pediculicides with a neurotoxic mode of action is increasingly associated with treatment failure as a result of the emergence of complex resistance mechanisms in the parasite population.<sup>1-4</sup> New treatment strategies are therefore needed.

## THE PARASITE

Head lice (*Pediculus humanus capitis*) are ectoparasites, with humans as the only known host. The lice almost exclusively live on the scalp and attach themselves to hair shafts by means of specialised claws (figure 1). Head lice are wingless insects and are unable to jump or fly. Transmission therefore occurs by close personal contact. The evidence that transmission can occur via fomites (eg, combs and hair accessories) is limited, and this route of transmission therefore remains controversial.

The female adult head louse has a relatively limited life span of around 3–4 weeks (potentially up to 3 months), but during this time, lays between 50 and 150 eggs, which are attached to the hair shafts.<sup>5-6</sup> After these eggs hatch, the parasite

undergoes several nymphal stages to finally reach the adult stage. Technically, "nits" are the remains of egg shells (ie, hatched eggs), although this term is frequently erroneously used for viable eggs. The life cycle, which forms the basis for the rationale behind all treatment approaches, is summarised in figure 2.

Adult lice are approximately 1–3 mm in length, and their eggs measure 0.8–1 mm but are still easily visible to the naked eye. All developmental stages, with the exception of the eggs, live off blood, obtained by piercing the host's skin.

## EPIDEMIOLOGY

As most health authorities in the UK have discontinued their routine screening programmes, large-scale epidemiological data has become scarce. Data from a small number of regional studies suggest that head lice infestation continues to be a significant problem throughout the country. A relatively recent population-based study reported that more than 2% of Essex school children had head lice infestation based on inspection<sup>7</sup>; based on additional survey results, the authors estimated that as many as 37% had been infested with head lice in the preceding year. A more recent study from Wales established a prevalence of 8.3%, while a group from Bristol reported a prevalence of 16.7% in school-age children.<sup>1-8</sup> Similar observations have been reported from other European countries, with prevalences ranging between 0.8% and 9.9%.<sup>9-16</sup> In the USA, estimates range from 6 to 12 million infestations per year.<sup>17-18</sup> In resource-poor countries, reported prevalences in school-age children often considerably exceed 10%.<sup>19-22</sup>

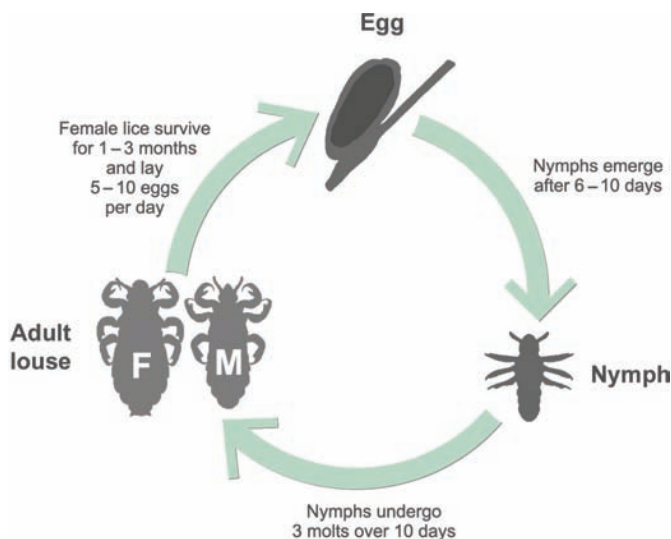
## SYMPTOMS AND SIGNS

Pruritus affecting the scalp, although not universally present, is the most characteristic, and frequently the only, symptom reported. Some patients with long-standing infestation report sleep disturbance resulting from intense pruritus. It appears that head louse-induced pruritus is caused by a delayed-type hypersensitivity reaction, as it tends to occur within 2–6 weeks during the first infestation, but develops considerably sooner during subsequent episodes—generally within 1–2 days.<sup>23-24</sup>

Pruritus may prompt scratching, which in turn can result in breaches of the skin barrier.



**Figure 1** Microscopy photograph of an adult head louse. Source: Head louse courtesy of Master Felix Curtis.



**Figure 2** The life-cycle of the head louse.

Secondary bacterial infections, occasionally in conjunction with regional lymphadenopathy, can therefore complicate the course of the infestation. Infection with *Staphylococcus aureus*, which is the most commonly implicated pathogen in this setting, can lead to impetigo, cellulitis, pyoderma and, less frequently, abscess formation.<sup>23 25</sup>

### DIAGNOSIS

The diagnosis of active head lice infestation is based on the detection of live lice.<sup>26</sup> Combing the entire scalp thoroughly with a specifically designed detection comb, which has fine teeth spaced 0.2–0.3 mm apart, has been shown to significantly increase detection rates compared to inspection alone.<sup>27–29</sup> This process is enhanced by wetting the hair or by using hair conditioner.<sup>30 31</sup> After each pass, the comb should be inspected for

the presence of lice, which may be aided by the use of a magnifying glass.

Eggs should also be searched for, although their presence does not necessarily indicate active infestation.<sup>26 32</sup> Viable eggs are tan- to brown-coloured, while hatched eggs are white or opaque. As head lice lay their eggs close to the scalp, eggs further than a few inches away from the scalp are unlikely to be viable. However, the distinction between viable and hatched eggs can not always reliably be made on inspection alone.<sup>26</sup>

### GENERAL TREATMENT PRINCIPLES

Other family members, most commonly siblings, are frequently also infested with head lice.<sup>31 33</sup> The entire family should therefore be screened and all affected individuals treated simultaneously to break the cycle of re-infestation within the same household.

General environmental “decontamination” measures are considered unnecessary, as head lice generally die within 1–2 days of leaving the host, being without access to a blood meal.<sup>24</sup> Nevertheless, head lice have been found on clothes, towels and bedlinen.<sup>34 35</sup> Although there is ongoing debate about the potential for re-infestation from these sources,<sup>36</sup> it seems advisable to change and wash these items regularly during the treatment phase. A recent study demonstrated that machine laundering at a minimum temperature of 50°C is sufficient to effectively decontaminate fabrics.<sup>37</sup>

### CONVENTIONAL PEDICULICIDES AND THE EMERGENCE OF RESISTANCE

“Conventional” topical pediculicides, which are essentially neurotoxic insecticides, remain the most commonly used form of treatment globally. The annual national expenditure for over-the-counter pediculicides is estimated to be around £27 million in the UK and exceeds \$350 million in the USA.<sup>38 39</sup>

Currently, four conventional pediculocidal agents are licensed for the treatment of head lice in the UK: malathion, permethrin, phenothrin and carbaryl (table 1). Carbaryl (CarylDerm) is no longer manufactured in the UK; since 1995, it has been available only on prescription because of concerns about possible carcinogenic effects.<sup>40</sup> The remaining three agents are available over the counter.

Pediculocidal treatment has to be applied on two occasions 7 days apart, as pediculocides primarily kill nymphs and adult lice, while their ovicidal activity is generally poor. This time gap allows surviving eggs to hatch, with the resulting nymphs subsequently being killed by the second application.

Prior to the mid-1990s, all four conventional pediculocides showed efficacies in excess of 80% in clinical trials. However, in the last 10 years, several studies have reported considerably lower cure rates for each of these agents, with varying

local patterns. The figures provided by several key studies are summarised in table 2.

In vitro studies have subsequently documented the emergence of resistance against these compounds in the parasite population and identified the underlying genetic basis.<sup>1 13 41–43</sup> Worryingly, relatively recent reports from the UK have described simultaneous resistance against malathion, phenothrin and permethrin,<sup>41 42</sup> potentially rendering all over-the-counter insecticidal products ineffective. Ultimately, knowledge of local resistance patterns may become crucial to improve treatment success rates.

In response to the rising number of treatment failures, a variety of strategies have been proposed. On a population level, one such strategy is to limit the use of pediculocides to one agent at a time and to rotate to another agent once treatment failure rates are increasing, heralding emergence of resistance. However, this approach is unfeasible when a whole range of agents are available over the counter, as is the case in most countries. Another approach is to use alternative forms of treatment, such as topical non-neurotoxic agents, oral drugs with pediculocidal activity, plant-based compounds and physical methods.

### TOPICAL NON-NEUROTOXIC AGENTS

Dimeticone, also used as treatment for infant colic, was the first therapeutic in this category to be licensed for the treatment of head lice infestation in the UK (4% dimeticone; Hedrin). It

is thought that dimeticone acts by coating the lice and causing disruption of their ability to manage water<sup>44 45</sup>; airway obstruction and suffocation has been proposed as another potential mechanism.<sup>46</sup> Two clinical trials evaluating this drug, both done in the UK, reported cure rates around 70%.<sup>44 47</sup> Notably, the cure rate of malathion, which was used as a comparator in one of the trials, was only 35%.<sup>47</sup> A more recent study in Turkey that evaluated two dimeticone-based lotions (4% dimeticone and 4% dimeticone with 2% nerolidol) reported cure rates of 92% and 83%, respectively.<sup>48</sup> The authors attributed the higher efficacy to the fact that the level of infestation was overall lighter than in the UK-based studies. Another large randomised trial conducted in Brazil, in which a different dimeticone-based formulation was used (92% dimeticone; identical to NYDA), reported a 97% cure rate, which compared favourably with the efficacy of permethrin used as the comparator drug (68% cure rate).<sup>49</sup> Given the different mode of action, it is unlikely that previously identified resistance mechanism will have an impact on the efficacy of this compound. In addition, the product is odourless, non-toxic and generally well tolerated.<sup>44</sup> Finally, its use should be acceptable to parents who have concerns regarding the safety of neurotoxic insecticidal compounds. In 2007, Hedrin was the market leader among licensed head lice treatments in the UK.<sup>50</sup>

More recently, a further preparation in this category, a 50% isopropyl myristate in cyclomethicone solution (Full Marks Solution), has been introduced in the UK. The only two published trials of this product, which were both sponsored by the manufacturer, are summarised in a single paper.<sup>51</sup> The authors report that 77% of the 111 patients treated with isopropyl myristate/cyclomethicone were free of head lice at the end of the treatment period, which compared favourably with a cure rate of only 19% with the comparator drug. However, the trials were discontinued early and had methodological limitations, as participants were not blinded and treatment was applied by investigators. In addition, the choice of comparator drug in these studies has been criticised previously, as the formulation (a 1% crème rinse) used in these trials was known to have low efficacy.<sup>50</sup> Notably, a trial in the USA, which included 30 patients treated with a different preparation of isopropyl myristate, reported cures in only 17 (57%), despite participants having received up to three treatment courses.<sup>52</sup>

In April 2009, the US Food and Drug Administration (FDA) approved a further preparation in this category, a 5% benzyl alcohol lotion (Ulesfia), which is currently not available in the UK. According to the FDA, the safety and efficacy of this lotion have been demonstrated in two clinical trials comprising more than 600 participants, with cure rates in excess of 75%.<sup>53</sup> The results of the phase II and phase III

**Table 1** Topical pediculocides currently available in the UK

Class	Generic name	Trade name	Formulation
Organophosphate	Malathion	Derbac-M	Liquid 0.5%
		Quellada-M	Liquid 0.5%, shampoo 1%
Pyrethroids	Permethrin	Lyclear	Cream rinse 1%
	Phenothrin	Full Marks*	Liquid 0.5%, lotion 0.2%, mousse 0.5%
Non-neurotoxic agents	Dimeticone	Hedrin	Lotion 4%, liquid gel 4%
	Dimeticone	NYDA	Spray 92%
	Isopropyl myristate/cyclomethicone	Full Marks	Solution, spray
Plant-based	Coconut, anise and ylang-ylang oils	Lyclear SprayAway	Spray

\*Production discontinued in the UK.

**Table 2** Efficacy of topical head lice treatment in clinical key trials

		Range of reported efficacy* (%)		
		Pre-1999	1999 to present	References
Conventional pediculocides	Carbaryl	78–92	–	86 87
	Malathion	83–93	17–98	47 79 82 88–91
	Phenothrin	88–96	13–75	44 81 86–88
	Permethrin	97–99	10–72	70 82 89 90 92–94
Other pediculocides	Dimeticone	–	69–97	44 47–49
	Isopropyl myristate	–	57–93**	51 52
	Coconut, anise and ylang-ylang oil combination	–	82–92	75 77

\*Note different methodologies and definitions for efficacy were used in different studies.

\*\*Upper limit based on a small non-randomised trial ( $n=30$ ) that did not include a comparator drug.

clinical trials have been summarised in a recent publication.<sup>54</sup>

### ORAL TREATMENT

A range of oral agents for the treatment of head lice, including the antiparasitic drugs albendazole,<sup>55</sup> thiabendazole,<sup>57</sup> levamisole<sup>58</sup> and diethylcarbamazine (DEC),<sup>56</sup> have been studied in recent years. All four compounds were shown to have some activity against head lice, but their effectiveness in clinical trials was generally disappointing, with reported cure rates well below 70%.

Another antiparasitic compound, which has shown more promising results, is ivermectin. In 1991, Dunne *et al* reported that the prevalence of head lice infestation in children treated with ivermectin during a study on oncocerciasis was significantly lower than in a control group that had received placebo.<sup>59</sup> A subsequent small phase II clinical study reported that a single oral dose was curative in some patients with head lice infestation.<sup>60</sup> A recent study in school-aged children in India that investigated the efficacy of a single dose of ivermectin combined with another antiparasitic drug (DEC or albendazole) reported that more than 90% of the participants who had received ivermectin were free of head lice at 15 days post-treatment.<sup>56</sup> A more recent double-blind, randomised controlled trial by Chosidow *et al*, which included both adults and children, reported that two doses of ivermectin given 1 week apart was effective in eradicating head lice in 95% of the participants when assessed on day 15.<sup>61</sup> This was higher than the 85% cure rate observed in the comparison group, who were treated with malathion lotion. However, the inclusion criteria included failure of previous treatment with a pyrethroid- or malathion-based topical pediculocide. This is important because this approach may have led to the selection of participants with malathion-resistant parasites, thus inevitably resulting in a lower cure rate in the comparison group. Furthermore, it is of note that the manufacturer had significant involvement in the study and the reporting of the results. Ivermectin is reported to have relatively few side effects in settings where it has been used to treat oncocerciasis.<sup>62</sup> However, the dose used for this purpose is considerably lower (150 µg/kg) than that used in the study by Chosidow *et al* (400 µg/kg). Also, it is disconcerting that an earlier publication reported an unexplained increase in deaths in elderly patients treated with ivermectin for scabies.<sup>63</sup> In addition, several publications have reported encephalopathy and other neurological abnormalities (including dysarthria, incontinence, abnormal tendon reflexes and seizures) in patients with *Loa loa* filariasis who received ivermectin, although this has been attributed to the parasite, rather than a side effect of the drug.<sup>64</sup> Accidental poisoning with ivermectin results in abnormal tendon reflexes and coma.<sup>66</sup>

Another drug, which has been investigated by several groups, is the antibiotic cotrimoxazole.<sup>67–70</sup>

Notably, one randomised study in children, which used a 10-day regimen, reported cure rates of 83% and 78% at 2 and 4 weeks post-treatment, respectively.<sup>70</sup> Although the treatment was generally well tolerated, a small number of children (4%) in this study developed allergic drug reactions, while others experienced gastrointestinal side effects.

To summarise, although several compounds have shown activity against head lice in a clinical setting, oral treatment is currently not recommended for first-line therapy. The use of ivermectin for head lice infestation unresponsive to topical treatment requires further evaluation, as its role in routine practice remains uncertain.<sup>95</sup> Sufficiently large trials, independent from commercial involvement, are needed to assess safety and efficacy in greater detail. Systemic treatment carries a greater risk of side effects, and in view of the availability of safe and effective topical treatment options, the risk/benefit ratio requires careful consideration.

### PLANT-BASED COMPOUNDS AND ESSENTIAL OILS

Several *in vitro* studies have evaluated the pediculocidal activity of a variety of natural compounds. Among the more promising substances are eucalyptus,<sup>71–73</sup> lavender<sup>72</sup> and tea tree oil.<sup>74</sup> None of these substances have been evaluated in published clinical trials, and currently, they can therefore not be recommended for the treatment of head lice infestation. However, three recently published studies, one investigating a coconut-derived emulsion shampoo and two evaluating a coconut anise spray (marketed as Lyclear SprayAway in the UK and as Paranix in continental Europe), have reported encouraging results.<sup>75–77</sup> Nevertheless, the available data are still limited, and the clinical efficacy of these agents remains to be confirmed in larger, well-designed studies that are done independent from commercial involvement.

### PHYSICAL METHODS

#### Wet combing

Wet combing as a treatment for head lice infestation has been reviewed by ourselves in detail in this journal previously.<sup>78</sup> In brief, a number of different combing kits are currently commercially available for this purpose, including the Bug Buster kit (Community Hygiene Concern, Milton Keynes, UK; available on NHS prescription) and the LiceMeister kit (National Pediculosis Association, Newton, Massachusetts, USA). This method relies solely on the physical removal of lice and eggs by means of a special comb, which is finer toothed than regular and detection combs. Simultaneous use of shampoo or conditioner, which merely acts as a lubricant, facilitates the process. It is recommended to carry out treatment sessions every 3 days for the duration of 14 days (ie, five sessions in total).



The cure rate in individual efficacy studies ranged from 38% to 75%.<sup>31 79–82</sup> However, most studies were small, and one study also had a very high drop-out rate (40%).<sup>80</sup> In addition, in one study, the wet combing was performed by a specifically trained research nurse,<sup>81</sup> therefore not reflecting a “real-life” situation.

A comparatively large study by Hill *et al* in the UK reported a cure rate of 57% with wet combing, which compared favourably with a cure rate of only 13% in children treated with pediculocides (malathion or permethrin).<sup>82</sup> However, the study design has been previously criticised, as the allocation concealment was inadequate, which may have skewed the results significantly.<sup>83</sup>

Nevertheless, there is sufficient evidence that wet combing alone can be an effective form of treatment when used correctly and consistently. The clear advantage of this method is the absence of potential side effects. Additionally, there are some data suggesting that parents frequently prefer wet combing to treatment with pediculocides.<sup>31</sup>

### Hot air

To date, only one trial has evaluated the use of hot air as a treatment for head lice infestation.<sup>84</sup> The authors investigated six different methods of delivery, including a conventional hand-held blow-dryer and a newly designed device the investigators called “LouseBuster”. For the majority of the 169 patients, the authors used an unconventional method to assess efficacy: following treatment, the lice and eggs were collected and their viability was assessed in the laboratory. The most effective method, the LouseBuster, was reported to have killed 80% of the lice and 98% of the eggs. However, only 11 children treated with this method had a follow-up assessment, and valid conclusions about the clinical effectiveness of this intervention can therefore not be made.<sup>85</sup> A further significant limitation of this study is that the authors excluded all subjects with a “high probability of reinfestation” (those with infested family members or classmates) from follow-up, which may have had a significant impact on the results.

### Electronic devices

A plethora of electronic devices, such as electronic combs, are enthusiastically advertised and marketed, particularly on the internet. Despite the claims made by most manufacturers that these devices have been evaluated in clinical trials, we were unable to identify a single publication providing trial data in a peer-reviewed journal. Therefore, these devices can currently not be recommended.

### CONCLUSIONS

Resistance of head lice against conventional neurotoxic topical pediculocides has become an increasingly common phenomenon over the last decade. While a large range of new treatment approaches have been evaluated over recent years, few have

consistently been shown to have high levels of efficacy. The majority of these interventions have been insufficiently assessed and consequently cannot be recommended at present. In contrast, both topical treatment with dimeticone and wet combing have been shown to be viable treatment options. Both methods have a high level of parental acceptance and practically no potential side effects. Topical, plant-based compounds are another promising option, although clinical efficacy data are still relatively limited. Nevertheless, for most interventions, cure rates are suboptimal, highlighting the need for continuing research into novel, more effective treatment strategies for head lice infestation.

### USEFUL WEBSITES WITH FURTHER INFORMATION

- ▶ Head lice (pediculosis). The Health Protection Agency (HPA). Available at: <http://www.hpa.org.uk/webw/HPAweb&Page&HPAwebAutoListName/Page/1204100452250?p=1204100452250>.
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