Resistance and the control of lice on humans and production animals

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Abstract

Phthiraptera (lice) are specialised insects adapted to parasitise many warm-blooded vertebrates, including domestic animals and humans. Often, attempts by the host to alleviate the irritation created by lice, causes derangement of the hair/fur coat. Unless treated, this derangement may cause economic losses due to hide damage and/or downgrading of wool/hair/fur. In 1981, application of aqueous insecticide solutions (dipping) for the control of sheep body lice (Bovicola ovis) was largely superseded by off-shears pyrethroid “pour-on” treatments. By 1985, several field failures with these products were found to be due to low-level (20×) insecticide resistance. In 1990, high-level (640×) resistance was diagnosed in a New South Wales population. However, despite 30+ years use, organophosphate-based products are still usually effective. Until recently, cattle lice caused little concern. Treatments were applied mainly for aesthetic reasons when cattle were to be presented for sale, and also to prevent damage to fences by rubbing cattle. However, the introduction of quality-management programmes have raised awareness of the economic losses due to hide damage associated with lice infestations. Emerging industries such as emu and alpaca farming have raised the pest status of other louse species, and necessitated insecticidal intervention. In humans, attempts to control head lice, Pediculus humanus capitis, infestations have repeatedly failed around the world. © 2000 Australian Society for Parasitology Inc. Published by Elsevier Science. All rights reserved.

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1. Introduction

Phthiraptera (lice) are specialised insects adapted to parasitise many warm-blooded vertebrates. Host specificity is generally high. Moreover, specificity to particular body regions of the host is a feature of a number of louse species. Humans have long been troubled by head and body lice and have expended much effort in an attempt to remove or alleviate the irritation caused by lice.

Lice are commonly spread by close contact among hosts, so the domestication and intensive farming of certain animals has elevated the status of some species of lice to that of pests. Most noteworthy among these are the biting louse of sheep, goats and poultry and the sucking lice of cattle, poultry and humans. Apart from grooming, washing and dust bathing by hosts to remove lice, insecticides belonging to various classes have been used to kill lice. Reasons for doing this have included attempts to increase productivity, or the quality of produce, aesthetic reasons including better appearance of stock at show, regulatory or quarantine requirements, and, complaints from staff working with lousy animals.

Before the development of synthetic insecticides and the widespread use of arsenic-based products, numerous remedies were used to treat lice. These included everything from date flour, cresol, naphthalene, sulphur, mercury, kerosene, oil and vinegar [1] to leaf extract from Indian hemp (Cannabis sativa) [2]. The development of the so called second-generation insecticides like DDT during the 1940s had enormous
impact. DDT was immediately used to dust prisoners of war to control body lice and soon gained wide acceptance, not only for use on humans but for animals as well. Organochlorine compounds like DDT, lindane, aldrin and dieldrin were successfully used to treat most domestic animal species for lice and other external parasitic infestations. Organochlorines were replaced by organophosphate, carbamate, pyrethroid and various insect growth regulator type insecticides, in line with prevailing insecticide technology and industry needs. There was a similar evolution in formulation and application. Originally, aqueous dips or oversprays were used, but later "pour-on" concentrates and injectable products were developed. These latter methods aimed to make treatment easier and to reduce the need for extra farm labour or rehandling of stock. In at least one case, however, misuse and overuse of pour-on pyrethroids led to the development of insecticide resistance.

2. Sheep body lice (Bovicola ovis)

In Australia, sheep body lice have received more attention than any other louse species. This is understandable when estimates of the costs and losses associated with louse infestation of sheep have been put at more than A$160 million annually [3]. Sheep have long been treated to remove lice. Dipping, either by swimming shorn sheep through a long bath of insecticide solution or by topical spraying in sheep showers have been in use since the insecticides that could be applied like this were available in the 1950s. Organochlorines were commonly used until banned in 1957. The organophosphates then became available. Arsenic was also widely used until it was deregistered in 1987. By that time, however, pyrethroid products had captured a considerable part of the sheep lice treatment market. Application of many pyrethroid products was by the innovative "pour-on" method. This entailed the delivery of a measured dose of insecticide concentrate along the backline of shorn sheep with a squeeze-action gun. The first of these products was Clout® , a deltamethrin-based product [4]. Similar products containing cypermethrin soon followed, and within a few years pour-on pyrethroid products had gained a 70% market share. This was not surprising given the apparent simplicity and labour-saving aspects of these products. Sheep could be treated immediately off-shears and returned to pasture. The alternative, wet dipping, has several disadvantages, including the need to remuster to treat optimally 10-14 days off-shears, reliance on complex machinery which may never have been appropriate for the task, the hazard of spray drift and dip use and, very importantly, complicated and poorly understood management of insecticide strength during dipping [5]. This latter difficulty prompted an investigation of an alternative dip management strategy [6], but there are difficulties with this proposal as well.

Only about 4 years after their registration, a number of complaints regarding pour-on failures were received, not only by the manufacturers of pyrethroid pour-ons but by the Australian Wool Corporation, Government Agriculture Departments and the media. Most State Departments of Agriculture still had the authority to quarantine flocks, so producers took some risks in reporting product failures. Nevertheless, complaints increased and pyrethroid resistance was suspected. It is interesting that despite 30+ years of regulatory control and the use of organophosphate and arsenic dips, and the fact that wool store surveys estimated the incidence of sheep lice in New South Wales at 20-30% of flocks, that resistance to these products was apparently never considered and certainly had not been investigated.

The pyrethroid situation was difficult in that the alternative treatments all entailed labour-intensive wet dipping. An investigation of the causes of pour-on failures was initiated in 1986. A laboratory bioassay was quickly developed [7]. The test exposed adult lice on treated cotton cloth squares under physiologically preferred conditions for 16 h. This was in spite of the fact that maximum louse response occurred within 2-4 h [8]. As is typical of pyrethroid intoxication of insects, the lice were knocked down but not dead at 4 h. Mortality had increased by 16 h, but the main reason for extending the bioassay was to make the test more versatile, particularly so that the slower-acting organophosphates could be tested as well (Levot, unpublished data).

Between mid-1986 and late-1991, 54 populations of B. ovis were tested for their toxicological responses to cypermethrin, deltamethrin, cyhalothrin and alphacypermethrin. Generally, responses were evenly distributed about a mean response. For cypermethrin, there was a 20-fold difference in the LC50 of the most- and least-susceptible populations tested (Fig. 1). These populations included lice from properties experiencing difficulties controlling lice, but also lice from untreated flocks. In most instances inappropriate flock management contributed to control failures, but problems also occurred on well-run properties. Concurrently, Johnson et al. [9] conducted pen trials with sheep infested with several of the same populations of lice to measure the effectiveness of some of the pour-on pyrethroid products against lice of known resistance status. Populations of lice originating from flocks with no history of pyrethroid use were eradicated in the trials. Conversely, four of the six populations derived from properties where pyrethroid treatments had previously failed, persisted for at least 12 weeks after treatment. Although generally causing greater than 80% re-
duction in lice numbers at 12 weeks after treatment, reductions of as little as 42% were recorded [9]. This is similar to the reduction expected after shearing alone (Levot, unpublished data). The laboratory bioassays had already demonstrated the strong (P < 0.01) correlations between population responses to the various registered pyrethroids [10]. These results highlighted the futility of changing to another pyrethroid-based product if the pyrethroid product of choice had previously failed to eradicate lice.

The standard recommendation given to woolgrowers who had experienced pyrethroid failure was to change to an organophosphate base product. Until a spray-on diazinon product was registered in late 1994, the only available organophosphate-only products were aqueous dips. There was concern that producers who had changed to using pyrethroid pour-ons in the early 1980s had done so because they had not been able to control lice beforehand with organophosphate dips. Moreover, with more and more farmers rejecting pyrethroids, the reliance on organophosphate products would again increase. Until this time no toxicological data existed for louse responses to diazinon or the other registered organophosphates. A survey of 28 of the louse populations that had been tested against the pyrethroids was used to describe the New South Wales field situation. With the exception of one population from Orange in central New South Wales, strain responses to diazinon varied only sixfold [11]. The responses of six populations to the other registered organophosphates coumaphos and propetamphos were similarly narrow. The Orange population response was significantly (P < 0.01) removed from those of the rest of the populations tested. Cross-resistance extended to coumaphos, but the response to propetamphos was similar to the other populations [11]. The Orange strain was susceptible to pyrethroids (Fig. 2).

In 1992, a population of lice was collected from sheep at Hartley in the central Tablelands of New South Wales. This louse population had experienced a haphazard and ineffective history of pyrethroid exposure. Anecdotal evidence suggested that sheep with various wool lengths had been treated with a deltamethrin backline whenever lice were found during yarning of the sheep. It is believed that this situation had persisted for some years. The Hartley strain had a heterogeneous response to cypermethrin in the laboratory bioassay (Fig. 3) [12]. Broadly speaking, some lice responded at concentrations that killed susceptible lice, but a large proportion survived concentrations that had been lethal to all populations tested up to that time. Some lice survived 1000 mg L⁻¹ [12]. The Resistance Factor at LC₅₀ was 642. A pen trial with small numbers of sheep infested with the Hartley strain highlighted the significance of this new level of resistance. Not only did a pyrethroid pour-on product fail to eradicate lice, but a full immersion plunge dip during which the cypermethrin solution was “mas-saged” into the short fleece of the shorn sheep also failed to eradicate lice (Fig. 4). Since then, several other high-resistance populations have been identified in New South Wales [5]; Levot unpublished data) and in South Australia [13] and Victoria [14, 15].

Resistance in the low-level resistance populations was completely suppressible in the in-vitro bioassays by co-treatment of lice with the monoxygenase inhibitor piperonyl butoxide [16]. Synergism ratios against these strains of up to around 20 were reported. Similar synergism of pyrethroids was also evident when Hartley strain lice were co-treated with piperonyl butoxide [16]. An experimental formulation containing cypermethrin and piperonyl butoxide (1:5) reduced lice numbers on sheep infested with Hartley strain lice by more than 95% for the first 6 weeks after treatment, but this had dropped to 80% by 10 weeks after treatment [17]. By this time, lice numbers on sheep

![Fig. 1. Louse strain responses to cypermethrin for the most- and least-susceptible populations tested between 1986 and 1989.](image1)

![Fig. 2. The Orange and Hartley strain responses to diazinon and cypermethrin compared with the other populations tested.](image2)
treated with cypermethrin alone had returned to pre-treatment levels.

Today, pyrethroid products have only a small portion of the market. Apart from loss of efficacy, persistent residues in the wool of treated sheep are jeopardising their use. Insect growth regulators like triflumuron and diflubenzuron have captured a large part of the market, but organophosphate products are still widely used.

3. Lice on other production animals

3.1. Cattle lice

There are two species of sucking lice (*Haematopinus eurysternus* and *Linognathus vituli*) and one biting louse species (*B. bovis*) that commonly infest cattle in Australia. Cattle in poor condition tend to carry more lice than well-nourished cattle, but lice infestations do not reduce normal growth rates when adequate feed is available [18]. Lice populations are highest in winter and fall to very low numbers in summer. This occurs whether or not insecticides are used. Consequently, without an economic incentive, the need to treat for cattle lice has been questioned [19] and cattle lice have remained low-profile. Damage to fencing due to lousy animals rubbing has always been a problem, but recently the adoption of quality assurance programmes such as Cattlecare® requires that producers take reasonable steps to improve hide quality. Lice eradication programmes integrating herd management and insecticide treatment of the herd is now being promoted, but has not gained wide acceptance. Pesticide application specifically for lice control is uncommon in most parts of Australia; however, several products aimed at other pests have, no doubt, impacted on cattle lice. Some treatments for cattle tick and/or buf-

Fig. 3. The heterogeneous response of the Hartley strain of *Bovicola ovis* to cypermethrin compared with the responses of the susceptible strain (Peak Hill) and a low-resistance strain (Claremont).

Fig. 4. Mean percentage reduction in lice numbers on sheep infested with the Hartley strain of *Bovicola ovis* following treatment with registered pyrethroid products.

falo fly also affect lice. The regularity of some of these treatments in certain areas have probably eradicated lice or at least reduced them to sub-clinical levels. Some products, notably the macrocyclic lactone anthelmintics, also affect sucking lice. Consequently, a secondary claim for sucking lice is seen of their product labels. Given the relatively low importance producers put on lice compared with intestinal worm parasites, and the high cost of these products, it is unlikely that they would be used specifically to treat lice. Registration of lousicides for use on cattle need to demonstrate greater than 95% reduction of louse numbers within a specified period, but proof of lice eradication from a herd is not mandatory. Kettle and Lukies [20] reported that some of the organophosphate pour-on products registered in New Zealand eliminated lice. These are the most popular products in Australia as well, and effectiveness is probably similar in most situations. Complaints from producers are very few. This suggests that adequate control can be obtained, that products perform to the satisfaction of most cattle producers and that resistance is not regarded as a problem. Resistance to DDT and lindane was reported in the USA [21], but no published reports of insecticide-resistant cattle lice were found in Australia. Interestingly, the related pig louse, *Haematopinus suis*, was reported to be resistant to the organophosphorus compound dichlorvos in Germany [22].

3.2. Poultry lice

McCossner [23] demonstrated that the systemic attributes of aldrin and dieldrin could be used to control
poultry body lice [Eomonocanthus (Menocanthus) stramineus] if applied s.c. or as a "spot" treatment. Pour-on treatment did not become common, but topical sprays of organophosphates and carbarlyl or dusta containing the same insecticides remain in common use today. Levot (Levot GW. Efficacy of insecticides for the control of external parasites of poultry. Final report of Project DAN25E supported by the Egg Industry Research Council, 1991) reported the results of small-scale trial of registered organophosphate treatments and permethrin when used to treat hens infested with several common poultry lice species. All treatments eradicated lice with a single treatment. Best practice flock husbandry recommends "all in all out" hen replacement strategy. Because lice cannot live away from the host for more than a few days, they can be eliminated from farms by "spelling" the sheds for a few days between batches of hens. Consequently, insecticides are rarely needed to control lice on commercial poultry. The situation is different with backyard poultry, but it is unlikely that there would be sufficient sustained selection pressure to lead to a resistance problem.

3.3. Goat lice

Several louse species infest goats worldwide, but the biting louse, Bovicola caprae and the sucking louse, Linognathus stenopus are the only species recorded from Australia. Goat lice submissions to our laboratory are rare, and only one complaint of failure of diazinon to eradicate a biting lice infestation has been received. Compared with the situation in sheep biting lice, nothing is known of the susceptibility of B. caprae to pyrethroids. However, the sheep pour-on Clout S, a water-based formulation of deltamethrin, is registered for goats as well as sheep, in Australia. Overseas, cypermethrin was effective against lice in Greece [24], but cypermethrin resistance was reported in two goat herds in England where pour-on products were no longer effective [25]. Goat lice have been recorded on lambs and sheep lice on goats [26]. As well, goat lice have been artificially established on sheep [27]. Although situations where cross-infestation could occur are not unusual in some areas of Australia, it is unlikely that it is a common occurrence. In the USA, the biting louse, Bovicola limbata, was adequately controlled with malathion or chlorfenvinphos applied to Angora goats [28].

4. Emerging industries

Alpaca farming is a small but growing industry in Australia. The camelid or chewing-biting louse, Bovicola breviceps, was first identified by Carmichael in 1996 from lice collected from an alpaca herd near Adelaide in South Australia [29]. It was speculated that the louse was already widespread, but at low levels in individual herds. Subsequently the Western Australian Department of Agriculture reported the occurrence of B. breviceps in alpacas that had been brought into Western Australia from Victoria. Since 1997 there have been increasing reports of lice on alpacas. Given the exotic nature of the pest, the existence of B. breviceps in Australia must question the adequacy of quarantine procedures for the importation of camelids at least. Alpaca herd management and the small and fragmented nature of the industry has favoured the transmission of lice between farms. Small-scale producers usually bring hembra (females) to working machos (breeding males). The hembra may infest, or be infested, during mating and will pass on the infestation to the cria (young alpacas) during lactation. Alpaca have communal rolling areas which may also favour the spread of lice between animals. Limited pen trials have demonstrated that three diazinon (100 mg l−1) oversprays, 14 days apart are effective [29], but no residue studies have been conducted to determine the consequences of such treatment. Pour-on pyrethroid and insect growth regulator sheep louse products and dog and cat "spot-on" organophosphate products have been rejected due to their failure to eradicate lice from alpacas and to peculiarities of alpaca husbandry such as deliberate partial shearing of individual animals.

Emu farming has gained some popularity among opportunists in recent years. Normally, the emu biting louse, Dahlmenhornia sp., is a minor pest of these birds, but when large numbers of birds are brought into intensive production runs the close contact between individuals can lead to higher incidence and heavier infestations. As with all emerging, or niche animal industries, there are no products registered specifically for treating ectoparasitic infestations of emus. Current industry recommended treatments are unknown, but products registered for use on other birds are the most likely candidates.

5. Human lice

Humans are host to three species of sucking lice: the body louse, Pediculus humanus; the head louse, Pediculus capitis; and the crab louse, Phthirus pubis. The body and head lice have variously been recognised as sub-species or distinct species. They are remarkably similar in appearance. Behaviourally they differ by infesting different parts of the body. The body louse may have evolved in association with the wearing of clothes, as it lives at the junction of the skin and cloth-
ing and females prefer to lay eggs in clothing next to the skin [30].

The head louse is very common in certain parts of the world, and has been the centre of much attention for many years, particularly among school children in both developed and developing countries [31]. Over the past 50 years a variety of compounds have been used to control head lice. Around the world today, products containing organochlorines (DDT, lindane), organophosphates (malathion), carbamates (carbaryl), pyrethrins (pyrethrum) and pyrethroids (permethrin, fenothrin, bioallethrin) are registered as pediculicides [32]. Despite this formidable array of insecticides, the number of cases of lice infestation has increased worldwide since the mid-1960s and now stands at hundreds of millions of people [32].

The organochlorines, DDT, lindane and dieldrin were the first of the synthetic organic insecticides used. Rupes et al. [33] found no resistance to DDT despite 25 years of use in Czechoslovakia, but resistance was demonstrated in lice from two Danish institutions for children in 1975. In 1976, Blommers et al. [34] found evidence of lindane resistance in lice infesting school children in two Dutch cities. Moreover, those authors quantified lice responses by laboratory bioassay and provided baseline data for malathion [34]. Lindane resistance was reported from Turkey [35], and Coates [36] reported lindane resistance in among lice infesting children in the north of England but noted that the then, new lotion containing malathion was very effective. This was also the case in Holland [37]. Organophosphate resistance was diagnosed in head lice from France in 1995 [38] and again in 1997 [39].

No doubt in an effort to move towards less cumulative or toxic compounds, pyrethrin and later pyrethroids became the preferred treatments in many countries. Within a few years, however, resistance was again suspected as the number of records of control failure increased. There were, however, some instances where these diagnoses were supported by the results of laboratory bioassays. Trials in France suggested that fenothrin provided only 40% control of head lice [40]. In England, 20-fold resistance to permethrin or fenothrin was reported within 4 years of use [41]. Greater than 100-fold resistance to permethrin was measured in Argentina [1] and over 500-fold resistance was found in 1993 in some areas of Czechoslovakia after 25 years of exclusive use [42]. Considerable research was undertaken in Israel. Muncuoglu et al. [43] reported the results of two resistance surveys conducted in 1989 and 1994. A fourfold decrease in susceptibility, as measured by time taken to kill lice exposed to permethrin-impregnated filter papers, occurred during the 5 years. By 1994, field failures were occurring. The 1994 responses were quite heterogeneous [43], as was seen when high-level pyrethroid resistance was first diagnosed in sheep lice in Australia [12]. Hemingway et al. [44] investigated the biochemical basis of resistance to insecticides in Israel. They found that permethrin resistance conferred side resistance to fenothrin which had never been used to control head lice in that country. A glutathione-S-transferase (GST) mechanism conferred resistance to DDT. However, it was clear that GSTs were not involved in resistance to pyrethroids as DDT resistance already existed in 1989, whereas permethrin resistance was not diagnosed until 1994 [44]. A weak monoxygenase resistance mechanism was found, but unlike the situation with sheep lice where resistance could be overcome by co-treatment with piperonyl butoxide [16,17], piperonyl butoxide synergism was not evident. The authors speculated that a nerve insensitivity (knock-down type resistance), together with the monoxygenase detoxification was responsible for resistance to permethrin.

Data for resistance in Australia are sadly lacking. This is not because head lice are not a problem. Jorm and Capon [45] listed head lice as the third most common communicable disease in Western Sydney long day care centres. Parents of many Australian school children will have confronted the problem of head lice on their children or the threat of contracting an infestation, at some time. Australian treatments are similar to those used elsewhere, although organochlorine products have disappeared. Shampoos, mousse and lotion products based on permethrin, synergised pyrethrum and malathion are available. However, as has plagued attempt to control head lice in other parts of the world, the lack of strategic treatment of all students in affected schools and the short prophylaxis from reinfection provided by most products have assured head lice a secure future.

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