31

Pediculosis: Treatments on the Horizon

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The wide incidence of resistance to organochlorine insecticides in body lice seems to be extending to head lice. The simplest immediate alternative is to turn to other types of orthodox insecticides. Extensive tests on body lice of a considerable variety have been made during the last decade by Cole,[2,6] Hirst *et al.*[7] and Malhotra.[12] From these, it would seem that several organophosphorus compounds provide safe and effective dust treatments at 1 per cent, including malathion and temephos; also some carbamates, such as Mobam and perhaps carbaryl and propoxur. Natural and synthetic pyrethroids are alternatives not adequately field tested.

Malathion has been used in practice, against body lice and head lice; and it has suffered from resistant strains of the former, in parts of Africa. Preliminary evidence of the nature of this resistance indicates that it involves cross-resistance to several other organophosphorus insecticides, so that we cannot rely indefinitely on this group of compounds. Resistance, in fact, ultimately threatens all types of control by conventional insecticides and we are faced with the task of reviewing alternative control measures.

Ovicides

Ovicidal action involves different processes from normal insecticides and tends to require different toxicants. Most modern contact insecticides are poor ovicides, but tend to persist and kill emerging nymphs or larvae. Hence, the ovicides formerly added to less efficient insecticides have been omitted. But the threat of resistance should make us re-examine their possible value in postponing and possibly preventing this trouble, since it is generally thought that different stages in an

insect's life cycle should be attacked by different toxicants. The dinitroanisole ovicide used in the antilouse powder "MYL" of the U.S. Forces in World War II[9] should be remembered. Makara[11] reported the successful use of chlorphenamidine as a louse ovicide in Hungary.

Systemic Insecticides

At various times during the past 30 years, attempts have been made to find systemic poisons harmless to mammals, which would kill their ectoparasites.[10] Conventional insecticides were marginally successful, because their mammalian toxicity was too high for safety; some unusual compounds have shown promise. One was phenylbutazone (Butazolodin: monosodium 4-butyl-1,2-diphenyl-3,5,pyrazolodine dione).[3,13] This drug is an analgesic, antipyretic sometimes used for rheumatism. It was tried on louse infested men with some success;[15] but it is not sufficiently safe for prolonged administration. The use of systemic poisons for ectoparasites was still under examination by Cole *et al.*[5]

Antibiotics

It is unlikely that antibiotics would have any contact action against lice, so that it seems logical to consider them as possible systemic poisons. One possibility is that they might destroy microorganisms in the mycetome of the louse.

I do not think anyone has tried antibiotics as systemic poisons, but some Polish workers have investigated their stomach poison activity, by rectal injection of lice.[1] According to these experiments, the LC_{50} values (μg/mg) were: streptomycin, 2.8-4.9; chloramphenicol, 0.9-1.6; oxytetracyclin, 0.4-2.3. The lice were kept for 11 days after treatment at 1 μg/mg with daily feeds. Periodically they were killed and extracted and the residual antibiotic bioassayed. The lice usually destroyed most of the antibiotic in two to three days.

Insect Development Inhibitors

In discussing the chemicals which could be used to disrupt hormone-regulated activities in insects, Robbins *et al.*[14] point out that the most prolific candidates are hormone mimics. So far, there has been little progress in developing compounds to inhibit hormone synthesis. Of the hormone mimics, the most successful have been the juvenoids. The ecdysone mimics are more difficult to synthesize and, more importantly, do not act well by contact.

Juvenoids have the disadvantage that they only act efficiently at a relatively short part of the life cycle, just prior to metamorphosis. They can have an additional action in causing temporary sterility in the eggs

laid by treated adults. Several have been tested against body lice, in the U.S.A.[4,18] and in Japan.[16] Several showed promise, including methoprene and Staufer R-20458. Lice were dosed by topical application (.02 to 24 μg. per louse) or by confining them for 24 hours or continuously on cloth treated with 25 to about 300 μg./cm.^{2} No details are given about the persistence of these residues but it may be of interest to mention some unpublished experiments of a former worker in my department, Dr. J. W. Patterson. Using the bug *Rhodnius prolixus*, he found a distinct juvenilizing effect on filter papers treated with deposits of juvenoids at 10 μg./cm.^{2} These effects persisted in treated filter papers stored at room temperature for as long as 11 weeks.

There are other insect development inhibitors available which are not, apparently, hormone mimics; e.g. Dimilin and MON-0585. We hope to test these.

Two final points must be made. All insect development inhibitors tend to be slow in action and do not kill adults, which seriously limits their value for controlling lice. Insects are able to develop resistance to these chemicals, and are sometimes found to have already acquired it by cross-resistance from conventional insecticides.

Dehydrating Dusts

Certain fine dusts of chemically inert substances can kill arthropods by desiccation, either by absorbing lipids from the epicuticle or by abrading it. Tarshis and Blinstrub[17] showed in a small number of trials that silica aerogels were effective for controlling crab lice and head lice. A dust preparation is obviously unsightly and unsuitable for head louse treatments, but the substance might have promise for crab lice and, perhaps, resistant body lice. A possible disadvantage is that body treatments for crab lice were said to cause an uncomfortable sensation of dryness.

Miscellaneous Nonfeasible Methods

Because of the close association of lice with the human body, several noninsecticidal methods developed in recent years are clearly impractical. Biological control with arthropod parasites or predators would clearly not be tolerated, even if such forms were known. For the same reason, release of sterilized or genetically incompatible males is ruled out. Chemosterilants are too dangerous to place near the human body.

The use of microbial control by a virus, fungus or bacterium is just possible, but a survey of microorganisms found in lice by Jenkens[8] was not promising. The only organisms which were lethal to lice were pathogenic to man.

CONCLUSIONS

I cannot say that this survey has been encouraging. Most of the recent advances in arthropod control do not seem readily applicable to lice. It would be depressing to conclude that, on the horizon, the control measures would be those available prior to the introduction of modern contact insecticides. More hopefully, we must work toward improved hygiene in lousy people, which in turn depends on better education and general living standards.

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Epilogue

Although energetically studied over centuries, much of contemporary knowledge on scabies derives from the recent elegantly incisive studies of Mellanby and of Heilesen here summarized and elaborated on. A parasite thought dead, because of improved hygiene and efficient chemotherapy, revivified. What forgotten lessons has this pandemic retaught; what remains to be learned?

Improvement in social conditions, hygiene and chemotherapy may have influenced the post-World War II decrease in this infestation, yet can not be a complete explanation: the current pandemic developed with improved rather than deteriorating conditions. Contemporary sexual freedom, often glibly related to the recrudescence, fails to satisfy a cause and effect relationship.

Fashion suggests the popular explanation of herd immunity; this attractive hypothesis lacks verification. High priority must be given to understanding why the disease waxes and wanes in frequency; man remains subject to recurrent epidemics until laboratory and clinical investigations produce explanations leading to practical prophylaxis.

Inability to culture *Sarcoptes scabiei* impedes progress in defining the disease pathophysiology: e.g., cell-mediated or humoral antibody formation, experimental animal inoculations, and chemotherapy screening programs. The last two decades provided solutions for cultures of several fastidious organisms—the polio virus and the leprosy bacillus. Renewed cultural efforts should be energeticaly started *now*, when sufficient human clinical material is available to expedite this enterprise. Success would provide a building block critical to almost every basic science attack on scabies.

Few diseases present the happy situation in which several drugs are totally effective; this very efficiency led to an almost relaxed and casual attitude—why study a disease so readily cured? Philosophic and social changes, lay and scientific, produced a shift in interest from efficacy to safety. As delineated in the lindane sections (Chap. 19 and 20) considerable data permit outlining the profile of its pharmacology and toxicology. Much of this data stems from agriculture related endeavors; many gaps, especially as related to human topical application, must be filled.

Blending a detailed knowledge of cutaneous pharmacokinetics with judiciously chosen clinical trials should permit determination of the maximally effective but minimally toxic dose. Should the vehicles be altered, the concentrations lowered or duration of exposure decreased? These and related questions should be promptly answered.

The published toxicologic data for the remaining cosmetically acceptable and efficient scabicides is so scant that this has not been covered here. Responsible decisions on alternate drugs await the availability of this information. As suggested in Treatment on the Horizon (Chap. 21) the development of additional scabicides should proceed efficiently because of progress in dermatopharmacology and dermatotoxicology. Unfortunately no such programs exist. Equally important is the development of drugs to which lice will not become resistant. This is presently not an insurmountable problem for treatment alternatives exist; but now is the time to develop additional alternatives, so that they will be available when (and not after) the need exists.

Nephritis secondary to impetiginized scabies exists and has been studied in special populations (Chap. 6). If we do not succeed in eradicating scabies, we must learn more about the pathophysiology, epidemiology and prophylaxis of these impetiginized lesions, for at any time its prevalence may increase and produce more morbidity than scabies itself.

Much advancement has occurred in scientific methods, and scientific manpower has increased greatly; we need some of this productivity channelled into solving these and related problems. The cost should be minimal compared to the benefit.

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Index

Page numbers in *italics indicate figures*