Carbaryl lotions for head lice — new laboratory tests show variations in efficacy

By IAN BURGESS, BSc, MSc, MPhil, FRSH

The efficacies of carbaryl lotions for head lice were tested using a new method. The new test appeared to be more sensitive than the method used when carbaryl lotions were first evaluated. The results suggest that carbaryl lotions should be applied for at least 10 hours or overnight and that all patients should have a second treatment after one week. The study also indicates that some marketed carbaryl products are more effective than others.

HEAD louse lotions containing carbaryl as the active ingredient have invoked debate about efficacy since their introduction around 1976. Many health districts now expect increased reporting of cases of head lice infestation when they change their recommended treatment to carbaryl formulations as part of the insecticide rotation policy.

In some districts, the public belief that carbaryl is less effective has forced the authorities to change back to malathion formulations after only a short period.[1] Furthermore, there has been concern in some districts that head lice may have developed resistance to carbaryl.

The reason for increased reporting is that carbaryl is now recognised to produce no residual effect, as may be obtained with malathion.

However, rather than being a detrimental property, this lack of residual effect should be regarded as advantageous since it provides the opportunity for contact tracing.[2] If a lotion has no residual effect, re-infection will be more likely to occur after contact with the carrier, thus making the association between carrier and re-infection easier to identify.

The lack of residual effect also reduces the risk of development of resistance following the exposure of lice to sub-lethal concentrations of insecticide as any residues wear off.

Hitherto, many of the reported failures of carbaryl-based lotions were accounted for by poor contact tracing and what is now called "insecticide abuse", in which the products are used inappropriately, incompletely or inadequately. However, in recent months the Medical Entomology Centre (MEC) has received an increase in inquiries about carbaryl efficacy and reported product failures. A high percentage of these inquiries reported newly hatched nymphs occurring shortly after an otherwise successful treatment. A second treatment one week later has been suggested as a possible solution to the problem.[3]

Clothing lice are used as a convenient laboratory test model for head lice, which are difficult to maintain in a laboratory. Although the clothing louse differs from the head louse in minor aspects of anatomy, they are closely enough related that they can interbreed. The clothing louse is, therefore, thought to be a suitable species for testing head lice preparations.

All of the lotion formulations in Britain were originally tested by the MEC on clothing lice using the methods then universally recognised. However, during the past three years, test methods of efficacy have been re-examined and the techniques used when the current lotions were developed are now considered inappropriate. This is particularly relevant to the effect of the formulations on eggs, since the original laboratory tests all showed 100 per cent efficacy. It is now known that this high mortality was achieved because the eggs were tested attached to corduroy cloth, which retains insecticide within the fibres after the formulation is washed off. This insecticide subsequently may pass into the eggs.

Current test methods use a non-absorbent gauze which does not retain insecticide, thus allowing the activity of different formulations to be assessed more accurately.

This paper describes tests of carbaryl-based head louse lotion formulations produced for the British market against laboratory-bred clothing lice and their eggs.

Materials and methods

Head louse lotions were obtained from local pharmacies, except Derbac-C, which was obtained directly from the manufacturer. All samples tested had a minimum of one year before their expiry date. Standard solutions were made using 99 per cent pure carbaryl crystals dissolved in a mixture of 60 per cent analytical grade propan-2-ol (isopropanol) and 40 per cent distilled water to give 1 per cent w/v and 0.5 per cent w/v concentrations.

Lice were obtained from the Cambridge reference strain culture colony of clothing lice maintained by MEC. Young adults and third instar nymphs were used and were not exposed to insecticide until at least five hours after feeding in order to avoid accidental death due to lice suffering spasms that rupture the gut. Louse eggs laid on close-mesh nylon gauze were obtained over a 48-hour period.

Lice and eggs were immersed in the test formulations for 10 seconds followed by incubation under normal maintenance conditions (30°C ± 2°C, 70 per cent relative humidity) throughout the test period. After the exposure time they were washed for one minute using a 1:15 mixture of Boots frequent wash shampoo (FWS 1:15) in tap water, rinsed in fresh tepid tap water then incubated until the results were recorded.

Controls performed concurrently were washed with FWS 1:15.

To mimic conditions of normal hair washing by consumers, the eggs were washed using FWS 1:15 on alternate days until the results were recorded.

Lice were examined approximately 18 hours and eggs 10 to 15 days after treatment. The hatching time of eggs varied with each batch. Any surviving lice or hatching nymphs were checked for their ability to feed. If they were unable to take a blood meal when placed on the back of the observer's hand they were considered incapable of survival and were recorded as dead. Nymphs that died in the process of escaping from the egg were recorded as half-hatched.

Treatments were compared using Chi-squared analysis.

Table 1: Efficacy of carbaryl-based lotions against clothing lice *in vitro*

	Treatment time			
	Two hours		"Overnight" (10 hours)	
Formulation and carbaryl concentration	Number of lice	Mortality (per cent)*	Number of lice	Mortality (per cent)*
Isopropanol (60 per cent)	103	5 (−0.10)	99	7 (2.23)
Carbaryl (0.5 per cent)	102	71 (68.02)	80	43 (51.34)
Carbaryl (1.0 per cent)	100	61 (58.96)	96	96 (100)
Carylderm (0.5 per cent)	161	161 (100)	—	—
Clinicide (0.5 per cent)	260	236 (90.29)	100	100 (100)
Derbac-C (1.0 per cent)	261	242 (92.34)	104	104 (100)
Suleo-C (0.5 per cent)	100	100 (100)		—

*Percentage mortality adjusted using "Abbott's correction" for control mortality[4]

► *Mr Burgess is deputy director of the Medical Entomology Centre at the University of Cambridge*

Table 2: Efficacy of carbaryl-based lotions against louse eggs *in vitro* (summary of six tests)

Formulation and carbaryl concentration	Treatment time: Two hours — Number of eggs: Total	Hatched	Half-hatched	Mortality per cent* (±SD)	"Overnight" (10 hours) — Number of eggs: Total	Hatched	Half-hatched	Mortality per cent* (±SD)
Isopropanol (60 per cent)	433	372	9	[−0.59] (2.2)	168	145	6	[−1.05] (2.02)
Carbaryl (0.5 per cent)	322	143	108	48.00 (17.44)	847	303	176	58.18 (21.30)
Carbaryl (1.0 per cent)	284	28	192	88.46 (2.93)	619	2	173	99.63 (0.36)
Carylderm (0.5 per cent)	1,223	435	226	58.35 (19.90)	1,171	199	311	80.11 (11.62)
Clinicide (0.5 per cent)	1,403	1,057	115	11.79 (7.11)	1,685	905	325	37.12 (17.64)
Derbac-C (1.0 per cent)	1,636	288	366	79.39 (9.98)	1,458	0	1	100
Suleo-C (0.5 per cent)	1,103	26	12	97.24 (5.01)	872	0	3	100

*Percentage mortality adjusted using "Abbott's correction" for control mortality[4]
Figures in square brackets indicate a lower mean mortality than the control group

Results

The effect of the lotions on lice are shown in Table 1. Both alcoholic lotions (Carylderm and Suleo-C) killed all lice within two hours with no sign of subsequent recovery. A two-hour treatment with either of the aqueous based lotions (Clinicide and Derbac-C) allowed some recovery, such that nearly 10 per cent of lice were able to take a blood meal. Overnight treatment killed all lice.

Simple solutions of carbaryl in isopropanol gave incomplete kills, except overnight at 1 per cent concentration, and some lice were sufficiently unaffected that they were able to lay eggs. Eggs were also laid by control lice and those treated with isopropanol.

Many of the lice were paralysed, even by treatments that failed to kill, and lost their grip on the gauze. In normal use, lice so affected may be washed from the patient's scalp during shampooing and not have the chance to recover.

When tested against louse eggs, none of the lotions achieved a complete kill after exposure for two hours (Table 2). Both aqueous based formulations killed significantly less eggs than the equivalent strength carbaryl solution ($p<0.001$) but this was not surprising since the manufacturers' instructions call for an overnight treatment period. Although Carylderm was significantly more effective than 0.5 per cent carbaryl in isopropanol ($p<0.001$) it was inconsistent, with egg mortality ranging from 25.3 per cent to 85.2 per cent over a series of six tests. Only Suleo-C gave consistently good results. Nevertheless, enough eggs survived this treatment to give a 50 per cent expectation of failure to cure completely with a single application. Some lice hatched from all groups were able to take blood.

With a single overnight treatment, complete kill was only achieved by Derbac-C and Suleo-C. The two lice hatched from eggs treated with 1 per cent carbaryl solution were able to bite but unable to ingest blood. They were, therefore, probably incapable of survival. Significant improvements were found in the performance of all other treatments over the respective two hours applications but in all cases fell short of an adequate egg kill. Lice from all these batches were able to feed.

Since a single application failed to kill all eggs in most tests, except for Derbac-C and Suleo-C, and in order to test the rationale for recommending a second treatment one week later, the formulations were also tested comparing a single dose treatment with two treatments one week apart. The results of these tests are shown in Table 3. Although significantly more effective than a single treatment ($p<0.001$), two treatments of two hours' duration did not kill all eggs. A significant improvement ($p<0.005$) was found when Carylderm and Clinicide were used twice overnight. However, in both cases complete egg kill was not achieved. Total kill was only consistently obtained with Derbac-C and Suleo-C using treatment times of 10 hours .

Discussion

Carbaryl is a crystalline solid at room temperatures and requires appropriate formulation to deliver it in an available form to an insect. The exposure time must also be long enough for it to take effect.[5] That carbaryl alone is not always sufficiently effective at penetrating lice is shown in Table 1.

However, the principal problem is not whether lotions will kill lice but rather whether they will kill eggs since surviving eggs, and the nymphs that hatch from them, are difficult to detect and will not be apparent until some time after treatment.

Carbaryl is not noted for its activity against insect eggs[6] and this was recognised when it was introduced for head louse treatment.[7] The results of this study suggest that formulation may sometimes render the insecticide less available to eggs than if presented as a simple solution. In most tests a high percentage of developing lice did not receive a lethal dose of insecticide until they had partially hatched, indicating that the carbaryl was trapped either on the shell surface or within its structure and only became available as the insect made its way out of the egg. This failure to penetrate the chorion has been observed in other species.[8]

Incomplete penetration of eggs by insecticide might account for consumer complaints of treatment failure where young and newly hatched lice are found within days of treatment.

The risk is increased if a shorter treatment time is used. Furthermore, the environment of the average scalp is likely to present more rigorous conditions for carbaryl than the laboratory. For instance, many consumers use hairdryers after routine hair washing. It has been suggested that if this is done following treatment it can increase the rate of hydrolysis of any remaining insecticide.[7]

One criticism of previously used testing methods and results is that laboratory bred clothing lice may be inherently more susceptible to insecticide formulations than "wild" lice because of the sheltered conditions under which they are reared[9] and that tests using them give a false idea of product efficacy. In the past, a false impression of some products was certainly obtained due to faults in the test method.

Since the strain maintained by the Medical Entomology Centre was cultured before the introduction of modern synthetic insecticides it is believed to be wholly susceptible to insecticides such as carbaryl and as such does not reflect the vigour or any other ability of "wild" head lice to render the insecticide ineffectual. Consequently I have made no attempt to extrapolate these results directly to normal use by consumers. The intention of the tests was to compare the efficacy of different formulations. However, if laboratory lice are more susceptible it is possible that some of these products may be even less effective in normal use than the results suggest. A field investigation is now necessary to confirm these findings.

Continued use of carbaryl is essential since it is generally agreed that insecticides should be rotated regularly to avoid the risk of lice developing resistance. The study has shown that some carbaryl products are more effective than others. This difference

Table 3: Efficacy of carbaryl-based lotions against louse eggs *in vitro* using either a single application or two treatments one week apart

Formulation	Treatment time: Two hours — Percentage mortality of eggs*: Single treatment	Two treatments	"Overnight" (10 hours) — Percentage mortality of eggs*: Single treatment	Two treatments
Carylderm	65.02	96.44	82.40	97.89
Clinicide	9.42	68.26	33.19	90.67
Derbac - C	79.49	99.87	100	100
Suleo - C	93.76	99.45	100	100

*Percentage mortality adjusted using "Abbott's correction" for control mortality.[4] The batches used to give mortality figures for single treatments were also two of the test replicates in Table 2

is not related specifically to the type of formulation since Derbac-C is water based and Suleo-C is based on isopropanol. These two lotions are, however, detectably different from their counterparts, Carylderm (isopropanol) and Clinicide (aqueous), in terms of characteristics such as smell and texture. The differences in efficacy between ostensibly similar formulations can only be attributed to the excipient components exerting synergistic, complementary or independent insecticidal effects on the lice or their eggs. The excipients are commercial secrets and consequently cannot be disclosed in detail. However, it seems that in the Clinicide lipid/water emulsion, the insecticide does not come out of the lipid phase into solution in the insect cuticle wax readily enough for efficient use. The emulsion might need to be more highly saturated.

One of the reasons for Suleo-C's higher efficacy might be its essential oil constituent, as these oils are themselves insecticidal compounds produced by plants to discourage pests from eating them.

In the light of these findings a change of approach to the use of carbaryl products is necessary, since even a minimal survival rate in the laboratory may mean that unacceptable survival of lice or eggs on patients is occurring. It will also increase the risk of resistance developing.

1. Lotions should be applied for at least 10 hours or overnight. (In both original field trials, a 24 hour treatment time was used. [6,10])
2. Patients should be treated a second time, seven days after the first application, to ensure the death of any eggs that survived the first treatment or young lice that hatched from them.[3,10]

Such measures, although cosmetically less elegant, will help ensure efficacy of carbaryl lotions into the future.

REFERENCES

1. Anon. NPA survey reveals treatment bias in district head lice policies. *Pharm J* 1989; **242**: 311.
2. Maunder JW. Updated community approach to head lice. *R Soc Health J* 1988; **108**: 201-2.
3. Roberts C. Ectoparasites examined. *Chemist and Pharmacy Update* 1989 (September): 12-15.
4. Abbott WS. A method of computing the effectiveness of an insecticide. *J Econ Entomol* 1925; **18**: 265-7.
5. Maunder JW. Insecticides in pediculosis capitis. *Arch Dis Child* 1989; **64**: 69-70.
6. Smith EH, Salkeld EH. The use and action of ovicides. *Annu Rev Entomol* 1966; **11**: 331-68.
7. Maunder JW. Clinical and laboratory trials employing carbaryl against the human head louse, *Pediculus humanus capitis* (de Geer). *Clin Exp Dermatol* 1981; **6**: 605-12.
8. Zschintzsch J, O'Brien RD, Smith EH. The relation between uptake and toxicity of organophosphates for eggs of the large milkweed bug. *J Econ Entomol* 1965; **58**: 614-21.
9. Meinking TL, Taplin D, Kalter DC, Eberle MW. Comparative efficacy of treatments for pediculosis capitis infestations. *Arch Dermatol* 1986; **122**: 267-71.
10. Maunder JW. Resistance to organochlorine insecticides in head lice, and trials using alternative compounds. *Medical Officer* 1971; **125**: 27-9.

ACKNOWLEDGEMENTS: This work was supported in part by the annual grant to the Medical Entomology Centre by the East Anglian regional health authority and also by International Laboratories Ltd. The sample of Derbac-C was kindly supplied by Charwell Pharmaceuticals Ltd. Thanks are also due to Dr John W. Maunder for his interest and encouragement throughout the study.

ABOUT PEOPLE

Professor Michael Newton, FRPharmS, head of the department of pharmaceutics at the school of pharmacy, University of London, has been awarded a DSc by the University of London.

Dr John Foster, MRPharmS, has been appointed chief pharmacist and technical services director of Nuffield hospitals. Dr Foster was formerly district pharmaceutical officer for Richmond, Twickenham and Roehampton, and Wandsworth health authorities. He is also chairman of the South West Thames regional postgraduate educational committee.

Mr Roger Tredree, MRPharmS, has been appointed district pharmaceutical officer in the Wandsworth and the Richmond, Twickenham and Roehampton district health authorities. He was formerly unit principal pharmacist at the University hospital of Wales, Cardiff.

Mr Mark Horsley, MRPharmS, has been appointed principal pharmacist, education and training, and assistant regional pharmaceutical officer, West Midlands regional health authority. He was formerly principal pharmacist, clinical services, at King's Mill hospital, Sutton-in-Ashfield.

Professor Ian Rodger, MRPharmS, professor of pharmacology at the University of Strathclyde, has been appointed to serve on the research committee of the National Asthma Campaign (formerly the Asthma Research Council) for a three-year period.

Mr Neil Slater, MRPharmS, has been awarded an MBA by the Warwick Business School. Mr Slater is central regional manager with the National Co-operative Chemists Ltd.

Mr William Gould, MRPharmS, has been elected chairman of Teesside Hospice Care Foundation, a charity which, with two health authorities, has developed a team of nine Macmillan nurses and a day centre for the terminally ill.