It is not possible to calculate accurately the number of cases of *M. canis* ringworm excluded from school in one year, but the figure must be high. Apart from the question of contagion, with which I have dealt, there can be no objection to these children being in school, because no subjective illness is produced in ringworm. The risk of child-to-child contagion is slight anyway, and it is virtually impossible if simple precautions are taken.

Summary

The importance and methods of distinguishing between *M. canis* and *M. audouini* scalp ringworm are indicated.

Some epidemiological considerations regarding *M. canis* ringworm are presented.

The role of microsporum ringworm as a cause of loss of schooling is discussed.

The results of a survey of the incidence of ringworm in the areas of the major education authorities of England and Wales are tabulated and analysed.

An experiment, carried out in Newport, where the scalp ringworm is almost exclusively of the *M. canis* type, and in Monmouthshire is described. Twenty-four children were allowed to continue at 19 schools, the exclusion rule being waived. In no case was the infection propagated.

The conclusion is reached that children with *M. canis* ringworm should neither be treated by *x*-ray epilation nor be excluded from school.

My thanks are due to Dr. David Lawrence, medical officer of health for Newport, for permitting me to carry out this investigation and for co-operating so helpfully. Also to Dr. Jacqueline Walker, of the Department of Medical Mycology, London School of Tropical Medicine and Hygiene, for carrying out the culture and identification of the fungi.

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FIELD TRIALS OF NEW ANTIMALARIALS IN WEST AFRICA

BY

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The value of new antimalarials has not always been assessed in the field in comparison with other similar drugs, and specific claims for one or another of the new compounds are difficult to judge when each has had only a limited number of clinical tests. Differences which are known to exist between geographical strains of malaria parasites justify comparative field trials in many tropical areas.

The present difficulties in carrying out chemotherapeutic tests of new compounds in temperate climates on cases of induced malaria and/or on non-immune volunteers increase the value of properly designed field trials in areas where indigenous malaria is common.

There has been little investigation, especially in tropical Africa, of the value of "camoquin" and pyrimethamine ("daraprim") in comparison with older antimalarials. The present paper reports on results of a chemotherapeutic trial of these drugs and of two other antimalarials, chloroquine sulphate ("nivaquine") and a new compound of the acridine series named "azacrin."

This last drug is a 2-methoxy-6-chloro-9-(5'-diethylamino-2'-pentyl) amino-3-aza-acridine dihydrochloride synthesized recently by Messrs. Ward, Blenkinsop and Co. jointly with Messrs. Howards and Sons, Ltd. The first laboratory tests against *Plasmodium gallinaceum* in chicks and *P. berghei* in mice have shown that this compound, given by the mouth, possesses good schizonticidal activity at a dose of 25 mg./kg. in chicks and at a dose of 5 mg./kg. in mice. Its toxicity for experimental animals was found to be low. No data on toxicity of this drug to man being hitherto available, it was taken as a precautionary measure by one of us before using it in field trials on children. The daily dose of 0.4 g. taken for five days having produced only minor side-effects (nausea), it was decided to use this drug for a field trial.

Present Investigation

The method of investigation was that developed by one of us (Bruce-Chwatt, 1951) and subsequently used in the first field trials of pyrimethamine (Archibald, 1951). This method is based on a preliminary selection of an adequate group of African schoolchildren, 5–10 years of age, all naturally infected with malaria. After the administration of a suitable therapeutic dose of the drug to be tested, daily blood examinations of each child are carried out. The parasite rate, parasite density, and any other malariometrical indices are calculated for each group from the results of daily examinations.

Blood slides (thin and thick film) were stained with Giemsa, and parasite rates and counts were based on the examination of thick films. Parasite counts were made from the parasite leucocyte ratio, and the number of parasites per c.mm. was calculated. No film was declared negative before the examination of at least 200 thick-film fields. Parasite density indices were computed as previously described (Bruce-Chwatt, 1951). The speed of decrease of the initial 100% parasitaemia of each group to the lowest level was used as a criterion of the comparative therapeutic activity of the investigated drug against the specific parasite.

For the purpose of the present trial 120 schoolchildren 5–10 years of age were selected after a preliminary investigation and divided into five groups. The first four groups were treated with chloroquine sulphate, pyrimethamine, camoquin and azacrin respectively. The fifth group was not given any drug and represented the control. The administration of each drug was invariably made under our personal supervision.

In the chloroquine sulphate group the drug was given in two different regimens. One-half received 0.75 g. (3 tablets) in a single dose on D day; the other half received 0.75 g. (three 0.25-g. tablets) on D day as a single dose, followed by 0.25 g. (1 tablet) on each of the two following days. In terms of chloroquine base the total dosage was 0.45 g. and 0.75 g. respectively.

The pyrimethamine group also received two different dosages of the drug. One-half had a single dose of 25 mg. (1 tablet) on D day, and the other half had 25 mg. on D day followed by the same dose on the next day. The camoquin group received one dosage only—0.4 g. (2 tablets) as a single dose on D day. The azacrin group was given 0.2 g. (2 tablets) on D day followed by 0.1 g. (1 tablet) on each of the two following days. The dosage of the four drugs is half the usual adult dose. The average age of the

children was 7.6 years. Apart from the preliminary selective examination every child was examined on D day immediately before the administration of the first dose and then on days D+1, D+2, D+3, D+4, D+7, and D+10. The results of the trial are shown in the Table.

Results of Comparative Field Trials of Four Antimalarial Drugs

Group and Day	No. of Cases	*P. falciparum*					*P. malariae*	
		Trophozoites			Gametocytes			
		No.	%	Density Index	No.	%	No.	%
Chloroquine sulphate I (0·75 g. single dose):								
D ..	15	15	100	3·14 (47/15)	0	0	4	26·6
D+1 ..	13	11	84·5	1·62 (21/13)	2	15·4	0	0
D+2 ..	15	0	0	0 0	4	26·6	1	6·7
D+3 ..	15	0	0	0 0	2	13·3	0	0
D+4 ..	14	0	0	0 0	1	7·2	0	0
D+7 ..	12	0	0	0 0	1	8·3	0	0
D+10 ..	13	0	0	0 0	2	15·4	0	0
Chloroquine sulphate II (1·25 g. in 3 days):								
D	18	18	100	3·00 (54/18)	1	5·6	1	5·6
D+1 ..	18	14	77·8	1·95 (35/18)	0	0	0	0
D+2 ..	18	3	16·7	0·33 (6/18)	1	5·6	0	0
D+3 ..	18	0	0	0 0	3	16·7	0	0
D+4 ..	16	0	0	0 0	1	6·2	0	0
D+7 ..	17	0	0	0 0	1	5·9	0	0
D+10 ..	16	0	0	0 0	3	18·7	0	0
Pyrimethamine I (25 mg. single dose):								
D	15	15	100	2·81 (42/15)	1	6·7	1	6·7
D+1 ..	15	10	66·5	1·67 (28/15)	0	0	0	0
D+2 ..	14	1	7·1	0·07 (1/14)	3	21·4	2	13·4
D+3 ..	15	0	0	0 0	3	20·0	0	0
D+4 ..	13	0	0	0 0	4	30·8	0	0
D+7 ..	14	0	0	0 0	5	35·7	0	0
D+10 ..	14	0	0	0 0	4	28·5	0	0
Pyrimethamine II (50 mg. in 2 days):								
D	17	17	100	3·70 (63/17)	1	5·9	2	11·7
D+1 ..	17	12	70·5	2·12 (36/17)	3	17·6	2	11·7
D+2 ..	17	1	5·9	0·06 (1/17)	5	29·5	1	5·9
D+3 ..	17	0	0	0 0	2	11·7	0	0
D+4 ..	16	0	0	0 0	6	37·4	0	0
D+7 ..	15	0	0	0 0	2	13·3	0	0
D+10 ..	15	0	0	0 0	4	26·6	0	0
Camoquin (0·4 g. single dose):								
D	28	28	100	3·2 (90/28)	5	17·8	3	11·7
D+1 ..	23	15	65·0	1·52 (35/23)	2	8·7	1	44·0
D+2 ..	27	1	3·7	0·04 (1/27)	6	22·2	0	0
D+3 ..	26	0	0	0 0	5	19·3	0	0
D+4 ..	27	0	0	0 0	6	22·2	0	0
D+7 ..	27	0	0	0 0	4	14·8	0	0
D+10 ..	27	0	0	0 0	4	14·8	0	0
Azacrin (0·4 g. in 3 days)								
D	12	12	100	3·8 (44/12)	4	33·3	1	0·09
D+1 ..	11	6	54·5	1·0 (11/11)	2	18·2	1	0·09
D+2 ..	12	1	8·3	0·08 (1/12)	4	33·3	1	0·09
D+3 ..	11	0	0	0 0	2	18·2	1	0·09
D+4 ..	5	0	0	0 0	2	40·0	0	0
D+7 ..	10	0	0	0 0	3	30·0	0	0
D+10 ..	11	0	0	0 0	3	27·3	0	0
Control:								
D	15	15	100	2·8 (42/15)	2	13·3	1	6·6
D+1 ..	14	11	78·2	2·7 (30/11)	1	7·1	1	7·1
D+2 ..	15	14	93·0	2·6 (37/14)	2	13·3	1	6·6
D+3 ..	14	11	78·2	2·0 (22/11)	2	14·2	1	7·1
D+4 ..	11	11	100	1·49 (16/11)	3	27·2	0	0
D+7 ..	13	10	77·8	2·1 (21/10)	2	15·4	1	7·7
D+10 ..	13	13	100	2·2 (29/13)	2	15·4	2	15·4

Discussion

These results show that all four drugs are very good schizonticides for *P. falciparum*. There seems to be relatively little difference between the speed with which in a selected group of African children each drug reduces the parasite rate for trophozoites of *P. falciparum* from 100% to 0 (clearance time).

The comparative clearance time of trophozoites of *P. falciparum* in each of the tested six groups was found to be as follows: chloroquine sulphate (dosage I), 1.78±0.41 days; chloroquine sulphate (dosage II), 1.95±0.39 days; pyrimethamine (dosage I), 1.74±0.26 days; pyrimethamine (dosage II), 1.77±0.24 days; camoquin, 1.69±0.43 days; azacrin, 1.58±0.42 days.

The clearance time found in this investigation for chloroquine is very close to the 1.80 days found for this drug in one of our first trials (Bruce-Chwatt, 1951). It was thought at first that the clearance time obtained in this type of trial with chloroquine is longer by about half a day when compared with figures quoted by investigators whose reports were based on clinical trials in East Africa (Handfield-Jones, 1949), in Tunisia (Durand, Schneider, and Dupoux, 1949), in Indo-China (Canet, 1950). Our average figures for the chloroquine clearance time of asexual parasitaemia due to *P. falciparum* are, however, almost identical with 1.84 days reported from India by Chaudhuri, Chakravarty, Rai Chaudhuri, and Poti (1952), and very close to 2 days observed by Singh and Kalyanum (1952).

In our present investigation camoquin appeared to have a faster action than any of the other drugs, except azacrin. This was somewhat unexpected, since in Bertagna's (1951) summary of information on camoquin the reported clearance time of asexual parasitaemia due to *P. falciparum* had a range between 24 and 120 hours, with an average duration of 53 hours, or 2.25 days. This is also the figure reported more recently by Mein (1951) from Brazil.

The camoquin clearance time of *P. falciparum* parasitaemia observed by us is slightly longer than 1.25 days reported by Hoekenga (1951) from Honduras, 1.2–1.4 days found in Bolivia (Villarejos, 1951), or 1.4–1.6 days reported by Singh and Kalyanum (1952) from India.

The clearance time for *P. falciparum* obtained with pyrimethamine is 1.74 days. This is close to the results obtained by the French workers in Tunisia (1.25 days) and in Indo-China (1.56 days) (Schneider, Canet, and Dupoux, 1952). In the Gambia, however, work by McGregor and Smith (1952) produced slower clearance times in cases of clinical *P. falciparum* malaria treated with pyrimethamine in doses different from those used in the present investigation. The clearance time in infants treated by them with an average dose of 2–4 mg. was 2.82 days even when two infants who failed to respond to therapy are excepted. In a similar series of young children it was 2.57 days, and in a small series of adults, it was 2.25 days.

None of the four antimalarials is an effective direct gametocide for *P. falciparum*, since the crescents persist in the peripheral blood for at least 10 days after the administration of the drugs and show no obvious and constant morphological changes.

In the camoquin series, in which gametocytes of *P. falciparum* were already present in the blood, there was little evidence of any gametocidal action. The observation supports the results quoted by Bertagna (1951) and by Mein (1951), and is in marked contrast to the findings of Singh and Kalyanum (1952), who found that 40% of their crescent carriers were cleared within six days.

Infections with *P. malariae* were too few and of a generally too-low density to obtain series of malariometrical data comparable with series of *P. falciparum*. Nevertheless it seems that chloroquine and camoquin have a more marked action on *P. malariae* (clearance time 1.2–1.3 days) than either pyrimethamine or azacrin (clearance time 2 days and 3 days respectively).

Two infections with *P. ovale* mixed with *P. falciparum* disappeared within 24 hours after the administration of camoquin and azacrin.

Of the four drugs used in the present trial pyrimethamine was tolerated best and no complaints of headache, nausea, or vomiting were made by any children who took it.

Chloroquine sulphate was also well tolerated, though two children complained of nausea after taking a single dose of three tablets. Four children out of 23 given camoquin complained of headache and nausea within four hours of taking 0.4 g. Azacrin was well tolerated in a single dose of two tablets (0.2 g.), but three tablets caused nausea, pain in the stomach, and vomiting in 7 out of 10 children.

It must be emphasized however, that some children had had little or no food in the morning when the drugs were administered and that the side-effects noted might have been less frequent if the drugs had been given after a meal.

Summary

Field trials with chloroquine sulphate, pyrimethamine, camoquin, and azacrin (an amino-aza-acridine) were carried out on 120 African schoolchildren with a subclinical natural infection with *P. falciparum* and *P. malariae*.

All four antimalarials have proved to be good schizonticides. The clearance time of parasitaemia due to trophozoites of *P. falciparum* was shortest with azacrin (1.58 days) and camoquin (1.69 days), closely followed by pyrimethamine (1.84 or 1.77 days) and chloroquine sulphate (1.78 or 1.95 days). None of the four drugs shows any direct gametocidal action.

It appears that chloroquine sulphate and camoquin have a more marked action on *P. malariae* than either pyrimethamine or azacrin.

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AN ASSESSMENT OF CHLOROPHYLL AS A DEODORANT

BY

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Between 1943 and 1950 many claims were made in published articles for the beneficial effect of water-soluble chlorophyll in stimulating the growth of granulation tissue and accelerating epithelization of skin ulcers. The work of Moss and his colleagues (1949) cast doubt on the validity of these claims. In 1951 the Council on Pharmacy and Chemistry of the American Medical Association could find no evidence that water-soluble chlorophyll stimulated granulation and healing beyond the normal rate.

Many reports also noted a deodorant property in chlorophyll when applied to skin ulcers. More recent workers have claimed that the alleged deodorant action of chlorophyll is effective against all kinds of body smells when the substance is taken orally. Such claims have received the widest publicity in the lay press. On the other hand, the *Journal of the American Medical Association* (1951) questions whether chlorophyll does in fact have deodorant properties at all.

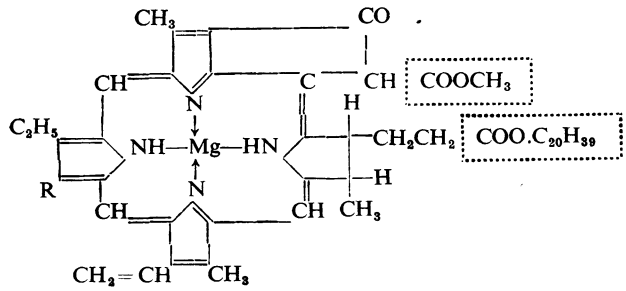
The present communication presents the results of a number of *in vitro* experiments designed to determine the effect of chlorophyll on a number of odours. Some clinical experiences with the drug are also recounted.

Full summaries of the earlier work with chlorophyll have appeared in recent leading articles in the *British Medical Journal* (1952) and the *Lancet* (1952). It is therefore unnecessary to review the literature again here. It may be noted, however, that all published findings of the action of chlorophyll as a deodorant have depended on the olfactory sense of the observer. Not only is the sense of smell notoriously inconstant from one observer to another, it is also apt to fluctuate in the one observer in different circumstances. Of all the human senses the sense of smell is the most easily affected by suggestion.

Chemistry

As there are various types of chlorophyll, a brief comment is required on the chemical composition of the substance used in these experiments.

Chlorophyll is extracted from plants (especially nettles, spinach, and alfalfa) with alcohol or acetone. This substance, which has the formula shown below, is oil-soluble



Chlorophyll formula. R=CH_3 (chlorophyll-*a*) or CHO (chlorophyll-*b*). Ester groups indicated by dotted boxes.

but not water-soluble. It has been described (*Lancet*, 1952) as "a system of four pyrrole rings pivoted on a central magnesium atom," and the formula is similar to that of haem, in which the pyrrole rings pivot in similar manner on an iron atom. Treatment of this substance with acid removes the magnesium atom. The magnesium atom is also easily displaced by other metals—for example, copper.

Treatment with alkali (hydrolysis) splits off the two ester groups shown in the diagram. The resulting substance is a salt of the dicarboxylic acid chlorophyllin. The sodium and potassium salts of this acid are soluble in water and constitute the active principles of the so-called water-soluble chlorophylls (Mitchell, 1952). The therapeutic substance called chloresium was defined by the Council on Pharmacy and Chemistry (1951) as consisting chiefly of the copper complex of the sodium and potassium salts of chlorophyllin. This is the substance used in those published trials in which the nature of the chlorophyll was disclosed. More often, proprietary preparations were used and no information was supplied about their chemical composition.

In the present experiments the substance hereafter called chlorophyll solution A consists chiefly of sodium copper chlorophyllin, and is made up in a solution containing 1 g. in 10 ml. The substance called chlorophyll solution B is a crude commercial preparation of water-soluble chlorophyll intended for use as colouring matter. Solution C is a proprietary preparation intended for use as an atmospheric deodorant, and is exposed to the atmosphere by means of a wick. Solution D is a proprietary water-soluble preparation sold for dispensing purposes. It is reported to contain 12.5% water-soluble chlorophyll.

Experiments

The principle of the first experiments is the same as that used by Alstead (1942) in assessing the deodorant properties of activated carbon. Methylmercaptan gas (one of the substances contributing to the odour of the gas normally present in the lower bowel) is evolved by adding 5N solution of