of the minute filterable virus frequently to be found in meningococcal cultures makes it impossible to be certain that in picking up a normal sized meningococcus one is not at the same time picking up some of this filterable virus. And this objection also applies to the presence of the very minute organisms described above. Now the smallest of these forms—and this is a point I have repeatedly tested—are quite invisible as organisms under a dry lens and the highest compensating ocular that will allow of good illumination. Even with a magnification of 3,000 obtained with a 1.5 mm. apochromatic oil-immersion lens and the appropriate tube length and compensating ocular it is still impossible to be certain that one organism, and one only, has been picked up. The photograph of the camera lucida drawings will illustrate the point of this objection, which applies both to Barber's method and to the fragmented cover-slip method. The only alternative, therefore, is actually to watch on the warm stage growth from a single organism, and even here—on account of these extremely minute forms—the problem is one of great difficulty, which is accentuated by the fact that growth and gemmation of asci is unsatisfactory on solid media, necessary as solid media may be for observing endosporeulation. It became necessary, therefore, to use methods of observation of individual organisms in liquid cultures other than the hanging drop method, which is, of course, useless for fine work owing to the curve and depth of drops.

The method I have adopted involves, as stated, the use of shallow cells covered with sterile slips, and the method ensures relative immobilization of the organisms under observation. On the whole it gives satisfactory results.

These results, however, require the greatest care in interpretation, owing to the presence, first, of the filterable virus and of the almost invisible organisms referred to, early gemmation and even endosporeulation being often exactly simulated by minute organisms brought into apposition by slight streaming movements still persisting; and owing, secondly, to slow rotatory and dipping movements. These movements lead to error, unless careful and prolonged watch is made, because an early bud, or a minute endospore, under observation may either temporarily vanish from view, or without having been previously seen may come into view for the first time, and simulate either a fresh bud or an endospore.

In all cases, therefore, most tedious and prolonged observation is necessary, which has to be repeated again and again with fresh cultures, as disappointment is frequent owing to death or arrest of growth of an individual organism under observation.

ILLUSTRATIVE FERMENTATION AND SEROLOGICAL TESTS OF THE SERUM-BROTH CULTURES EMPLOYED IN THE ABOVE OBSERVATIONS.

Fermentation Reactions.

In the case of all the fourteen cultures, details of which are here recorded, no reaction was observed in lactose, saccharose, mannite, or dulcitol.

In twelve of the cultures acid was produced quite definitely in glucose, in the remaining two cultures no acid being produced in glucose.

In every case incubation at 37° C. was continued for eight days.

Serum Reactions.

Dilutions:	1:4.	1:8.	1:16.	1:32.	1:64.	1:128.	1:256.	Control.
Culture 1 ...	C	C	C	C	C	C	C	NIL.
Culture 2 ...	C	C	C	C	C	P	NIL	NIL.
Culture 3 ...	C	C	C	C	P	NIL	NIL	NIL.
Culture 4 ...	C	C	C	C	C	NIL	NIL	NIL.

C = Complete agglutination. P = Partial agglutination.

In the case of these four cultures the dilutions were made from undiluted meningococcal serum supplied by the Lister Institute: Titre 1 in 250; No. cl.; date of tubing, February 9th, 1916; dates of agglutination, March 8th, 1916; March 4th, 1916; April 29th, 1916; April 29th, 1916.

Incubation at 37° C. was allowed for twenty-four hours before reading, plus one hour at room temperature.

The agglutination tests of the remaining ten cultures were kindly carried out by Dr. Lawes, using Gordon's method for identification of "strains."

The agglutination tubes and their contents were incubated at 56° C. for twenty-four hours before being read.

Serum Reactions.

	Normal.	I.			II.			III.			IV.		
		A	B	C	A	B	C	A	B	C	A	B	C
Culture 5 ...	-	++	++	++	-	-	-	+	-	-	-	-	-
Culture 6 ...	-	-	-	-	++	++	++	-	-	-	-	-	-
Culture 7 ...	-	-	-	-	-	-	-	-	-	-	-	-	-
Culture 8 ...	-	++	++	++	-	-	-	-	-	-	-	-	-
Culture 9 ...	-	++	++	+	-	-	-	-	-	-	-	-	-
Culture 10 ...	-	-	-	-	++	+	-	-	-	-	++	++	+
Culture 11 ...	-	-	-	-	++	++	+	-	-	-	-	-	-
Culture 12 ...	-	-	-	-	++	++	++	++	(+)	-	-	-	-
Culture 13 ...	-	-	-	-	++	++	++	-	-	-	-	-	-
Culture 14 ...	-	-	-	-	++	++	++	-	-	-	-	-	-

Cultures 8 and 9, 11 and 12, 13 and 14, were from three cases. Cultures 1 to 7, as well as culture 10, being from eight separate cases. A, B, C represent respectively dilutions 1 in 100, 1 in 200, 1 in 400.

Conclusions.

1. The so-called giant meningococcus is not a bacterium. It represents an ascual stage in the life-cycle of an organism allied to the ascomycetes.*

The ascus may be either large or small, or of any intermediate size (0.2 μ to 5 μ).

2. The meningococcus of Weichselbaum is not a bacterium. It is an ascospore, derived from the "giant meningococcus" by a process of endosporeulation.

3. The filterable meningococcal virus of my earlier papers probably represents a stage in the life-cycle of the ascomycetic organism described.

4. The true nature of the meningococcus and its alleged giant forms has hitherto been missed because of the practically exclusive use of solid media for purposes of identification, and because direct examination of unstained living organisms, including warm-stage development in liquid cultures, has not been carried out.

An Experimental Investigation

OF

THE SUITABILITY OF THE MORE SOLUBLE SALTS OF QUININE AND CINCHONINE FOR INTRAVENOUS INJECTION.

BY

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THE most soluble salt of quinine—namely, the bi-hydrochloride—has for many years been given intravenously in malaria, although only, as a rule, in very severe infections with cerebral symptoms. The method has gained a reputation for being dangerous, although I have long thought this to be due to the extreme class of cases in which it is generally used rather than to the method itself. Nevertheless, the intravenous route is apparently the most efficacious, as shown by the fact that some cerebral cases of malaria can be saved by it when quinine by the mouth or even subcutaneously would be too slow in its action to be trustworthy. The following experience helped to convince me of this fact. In a case with high continued fever, leading to a suspicion of typhoid, I found very numerous malignant tertian parasites in every field of the microscope, and, recognizing a very dangerous infection, 10 grains of bi-hydrochloride of quinine was at once given intravenously, with the result that the temperature fell finally to normal the next morning.† Some years later I found equally dangerous malignant tertian infections on

* The mycelial or "bacillary" phase is still the subject of study, and will be dealt with separately. Owing to the variable number of ascospores (meningospores) which the ascus (meningogascus) contains, and owing to the absence of perithecia, the organism here described is provisionally placed amongst the hemiascomycetes, instead of amongst the ascomycetes proper.

† See Chart 50, page 227 of my *Fever in the Tropics*.

examining blood slides of two fever cases in another hospital, and advised quinine intravenously. The medical man in charge, however, considered this method to be too dangerous, and gave large doses of quinine up to 50 grains a day by the mouth. One patient became comatose on the following day, and the other no less than three days later, and both died of cerebral malaria, in striking contrast with the above successful case.

At the present time there is urgent need, especially in connexion with military operations in malarial areas, for improvement in the treatment of malaria in the direction of trying to obtain complete elimination of the parasites with consequent prevention of recurrences of the disease, apart from new infections. In January last¹ I recorded having observed the disappearance of crescents from the blood in three consecutive cases following intravenous injections of tartar emetic, but pointed out that the drug had much less effect on the intracorpuseular stages of the parasites, and suggested its use during convalescence after the fever had been checked by quinine, in the hope of lessening subsequent relapses. Owing to the malarial season having barely commenced, I have not had any further opportunities of trying this method, but I have heard from two of the three first patients that they had remained free from malarial relapses for some time. On the other hand, Low and Newham² have recorded a failure in a single case, and Brodribb³ a success. The only report of an adequate test which I have yet seen is that of Captain A. J. Orenstein and Lieut.-Colonel W. Watkins-Pitchford, Director of the South African Institute for Medical Research,⁴ to whose courtesy I am indebted for a reprint of their paper. They record a series of 24 crescent cases among soldiers from German South-West Africa treated by quinine, followed by tartar emetic intravenously in accordance with my suggestion. In 10 of them the crescents disappeared after one injection of 0.04 gram, in 6 after two injections of 0.04 and 0.08 gram, and in the remaining 8 after one or two additional doses of 0.12 gram, no single failure having been met with. Quinine had previously been given for from twelve to forty-nine days without any effect on the crescents. Two cases examined one month and sixty-four days later respectively were still free from crescents. No cases had returned with a relapse at the time of their report. These results justify further trials of my method, while it would be of great interest to treat alternate cases during convalescence with tartar emetic, keeping the rest as controls. In benign tertian affections they obtained no such effects.*

At the suggestion of Sir Ronald Ross I have turned my attention to the investigation of methods of administering quinine, and, in view of the experience mentioned in the opening paragraph of this paper, I selected the intravenous route with a view to ascertaining in what form and strength the drug can be safely and conveniently administered in sufficient doses to afford hope of completely curing recently acquired infections so that relapses can be prevented. In the present paper I propose to record as briefly as possible the results I have obtained regarding the effects on the blood and the toxicity of the more soluble salts of quinine, and of two such salts of cinchonine in different dilutions when given intravenously in animals, and to mention trials of two of them on fever patients.

The Effects of the More Soluble Salts of Quinine and Cinchonine on Human Blood Serum.

The first point to be determined was the compatibility of different dilutions of the salts with human blood. MacGilchrist,⁵ who has done much work on the cinchonal alkaloids, has expressed the opinion that quinine salts are unsuitable for intravenous injection except in the extreme dilution of a single dose in several hundred cubic centimetres of saline, because he found that even in considerable dilution they caused gelatination or precipitation of blood serum *on standing*. As, however, solutions when injected intravenously do not stand in the blood, but are very greatly diluted within a few seconds, the immediate effect of given dilutions of the alkaloids on serum appears to be what we want to know. With the help of my friend Captain A. J. Shorten, I.M.S., I have tested this point, and

* Since writing the above I have heard from Sir Ronald Ross that no effect has been obtained with tartar emetic on any stage of the malarial parasites in a large number of relapsing cases in England, mainly of the benign tertian variety; so, in spite of the favourable South African results, it is now clear that tartar emetic will not solve the problem of malarial relapses.

have embodied the main data obtained in Table I, which gives the solubilities, quinine content, and the immediate and remote effects of adding the different dilutions noted to an equal quantity of human blood serum.

TABLE I.—*Immediate and Remote Effects of Quinine and Cinchona Salts on Human Blood Serum.*

Salt.	Solubility.	Quinine Content.	Dilution.	Immediate Effect.	Remote Effect.
Quinine bi-hydrochloride	1-1	81.6 %	1-2 1-10 1-100	Nil Nil Nil	Gelatinous. Ditto. Nil.
Quinine urea ...	1-1	59.2 %	1-2 1-5 1-10 1-100	Nil Nil Nil Nil	Gelatinous. Slightly turbid only. Ditto. Nil.
Quinine hydrochlor sulphate	1-2	74.3 %	1-2 1-10 1-100	Nil Nil Nil	Gelatinous and precipitated. Ditto. —
Quinine lactate ...	1-10	78.3 %	1-20 1-100	Thick precipitate Nil	Thick precipitate. Turbidity.
Quinine acid hydrobromide	1-7	60.0 %	1-10 1-20 1-100	Slight precipitate Slightly turbid Nil	Thick precipitate. Marked turbidity. Nil.
Quinine bisulphate	1-11	59.1 %	1-10 1-20 1-100	Slight precipitate Slight turbidity Nil	Thick precipitate. Marked turbidity. Nil.
Hydroquinine hydrochloride	—	—	1-10 1-20 1-100	Thick precipitate Ditto Turbid	Thick precipitate. Ditto. Some precipitate.
Quinine periodide.	1-20	48.4 %	1-20 1-100	Thick precipitate Slightly turbid	Thick precipitate. Precipitate.
Cinchonine bi-hydrochloride	1-1	—	1-3 1-10 1-100	Nil Nil Nil	Gelatinous and precipitated. Slightly turbid. Ditto.
Cinchonine acid hydrobromide	1-5	—	1-10 1-100	Nil Nil	Gelatinous and precipitated. Slightly turbid.

The data in Table I allow the more soluble salts of quinine and cinchonine to be divided into three classes. The first have no immediate effect on blood serum even in the strongest solutions, and include the bi-hydrochloride, urea, and hydrochlor sulphate of quinine and the bi-hydrochloride and acid hydrobromide of cinchonine, all of which are highly soluble. The second class produce an immediate turbidity of very slight degree of precipitation in concentrated solutions of 1 in 10, but no immediate or remote change in dilutions of 1 in 100, and include quinine acid hydrobromide and quinine bisulphate. The third class cause an immediate dense precipitate in blood serum in dilutions of 1 in 10 and 1 in 20, and include quinine lactate, quinine periodide, and hydroquinine hydrochloride, the last also producing an immediate turbidity in a dilution of 1 in 100.

As far as the effects on the blood serum are concerned, these data appear to indicate that the three quinine and two cinchonine salts in the first class would be quite safe for intravenous use in dilutions of 1 in 10, or even less, while the two in the next class would probably be safe, in view of their slight immediate effect on the serum in 1 in 10 solutions and their rapid dilution in the blood stream to below 1 in 100, which dilution has no great effect on the serum. The last three would not appear to be suitable for use intravenously as they produce an immediate dense precipitate in blood serum, although hydroquinine hydrochloride has been recommended for this purpose.

Effect of the More Soluble Salts of Quinine and Cinchonine on the Coagulability of the Blood.

This has been tested in order to exclude any possibility of intravascular clotting being produced by the injections. Equal quantities of solutions of different strengths in

normal saline were mixed with equal quantities of fresh finger blood in Wright's tubes and the coagulability times noted. The results showed such a uniform diminution of the coagulability time in the strong solutions and in 1 in 100 dilutions, as compared with controls in which normal saline took the place of the alkaloid solution, that it is unnecessary to give details of the experiments, which appear to exclude any danger of intravascular clotting following intravenous injection of these salts. Moreover, no immediate naked eye change was produced in the colour of the haemoglobin by any of them.

The above preliminary experiments on the action of the more soluble salts of quinine and cinchonine on blood, therefore, indicate that, with the exception of quinine lactate and periodide and hydroquinine hydrochloride salts, all those tested are likely to be safe for intravenous injection in concentrations of at least 1 in 10, which would allow of 1 gram being given in 10 c.cm. and so make the intravenous method quite convenient clinically.

The Toxic Action of the More Soluble Salts of Quinine and Cinchonine on Paramoecia.

A series of experiments has also been carried out with the more promising quinine and cinchonine salts with water paramoecia on similar lines to those I used in testing the alkaloids of ipecacuanha.⁶ MacGilchrist⁵ has recorded experiments on the action of cinchona alkaloids on paramoecia as observed under the microscope. I have found it more convenient, and I believe more accurate, to make the dilutions in small test-tubes and note the strengths which kill all the paramoecia in different times as observed with a hand lens, because some are killed much sooner than others, and as only a few can be watched under a microscope in a small drop of fluid, an accurate end point is difficult to obtain by that method. Table II gives the average figures obtained by four consecutive experiments with dilutions of 1 in 20,000, 1 in 30,000, etc., up to 1 in 70,000. Each set of experiments, including all the seven salts in the table, was completed at one time, so that the culture was exactly the same for each series. The dilutions were made in such a manner that the mixture contained the alkaloid in the strengths mentioned, and the results were noted up to eighteen hours.

TABLE II.—*The Relative Lethal Action of Quinine and Cinchonine Salts on the Protozoal Water Paramoecia.*

Salt.	Average Lethal Strength against Paramoecia.	Quinine Content.	Relative Toxicity against Paramoecia.
Quinine bi-hydrochloride ...	1 in 50,000	81.6%	614
Quinine urea	1 in 30,000	59.2%	507
Quinine hydrochlor sulphate	1 in 40,000	74.3%	537
Quinine acid hydrobromide	1 in 40,000	60.0%	666
Quinine bisulphate	1 in 30,000	59.1%	550
Cinchonine bi-hydrochloride	1 in 30,000	—	—
Cinchonine acid hydrobromide	1 in 37,500	—	—

The percentage of the alkaloid in each salt is shown in the third column of Table II, and by dividing this into the average dilution which killed all the paramoecia the relative lethal action of the different preparations on the protozoa in proportion to their quinine contents is obtained and shown in the last column. As far as this test goes, it shows that quinine bi-hydrochloride is actually, and the acid hydrobromide relatively, the most active of the quinine salts against protozoal paramoecia. Further, the acid hydrobromide of cinchonine gave slightly better results than the bi-hydrochloride. Both the cinchonine salts were weaker than the corresponding quinine ones against paramoecia, but it does not follow that they will prove less active against malarial parasites, which will be worth testing.

The Toxicity of the More Soluble Salts of Quinine and Cinchonine Intravenously in Animals.

A series of experiments was also carried out to ascertain the minimal lethal doses of solutions of these salts intra-

venously in pigeons and rabbits in strengths which would be convenient for administration in the case of man. The results are summarized in Table III.

TABLE III.—*Minimal Lethal Doses of Quinine and Cinchonine Salts Intravenously in Pigeons and Rabbits.*

Strength of Solution.	Minimal Lethal Doses in Pigeons in Grams per Kilo.			Relative Toxicity.	Minimal Lethal Doses in Rabbits in Grams per Kilo.		Relative Toxicity.	Relative Quinine Content.	Solubility.
	1-5	1-10	1-20		1-5	1-10			
Quinine bi-hydrochloride	0.065	0.07	0.07	1.26	0.035	0.035	2.57	0.90	1-1
Quinine urea ...	0.13	0.13	—	0.95	—	0.04	3.10	1.24	1-1
Quinine hydrochlor sulphate	0.11	0.11	—	0.90	—	0.0375	3.41	0.99	1-2
Quinine lactate ...	—	—	0.06	1.57	—	—	—	—	1-10
Quinine acid hydrobromide	—	0.13	0.13	0.94	—	0.045	2.73	—	1-7
Quinine bisulphate	—	0.12	0.12	1.03	—	0.0425	2.92	1.24	1-11
Hydroquinine (1)	—	0.10	—	0.90	—	0.035	2.57	0.90	1-2
hydrochlor (2)	0.12	0.13	0.13	—	—	—	—	—	—
Quinine periodide	—	—	0.075	2.03	—	—	—	1.52	1-20
Cinchonine bi-hydrochloride	0.07	0.08	—	—	—	0.035	—	—	—
Cinchonine acid hydrobromide	—	0.11	—	—	—	0.04	—	—	—

The minimal lethal dose in pigeons of quinine bi-hydrochloride in a solution of the strength of 1 in 100 was 0.07 gram per kilo.

A number of interesting points are brought out by the data in Table III. In the first place, it will be observed that the minimal lethal dose in pigeons of quinine bi-hydrochloride was the same, namely 0.07 gram per kilo, whether it was given in a dilution of 1 in 10, 1 in 20, or 1 in 100, but was slightly higher, 0.065, in a 1 in 5 solution. In rabbits the minimal lethal dose was the same in dilutions of 1 in 5 and 1 in 10. These observations confirm the conclusion derived from the absence of any immediate effect of strong solutions of this salt on human blood serum already dealt with, namely, that solutions of a strength of 1 in 10 may be safely injected intravenously.

The figures in Table III, giving the relative toxicity of the different salts in the case of rabbits and pigeons, have been obtained by dividing the minimal lethal doses into the relative quinine content as compared with quinine sulphate, the latter figures being given in the last column but one. Judged in this way, much the most toxic salts in pigeons were quinine periodide and quinine lactate, which I have shown above cause an immediate dense precipitate with blood serum. On the other hand, hydroquinine hydrochloride has one of the lowest relative toxicities in spite of its immediately precipitating blood serum. Possibly this is on account of its much greater solubility (1 in 2) than the lactate (1 in 10) and periodide (1 in 20). Relatively to their quinine contents quinine hydrochlor sulphate, quinine acid hydrobromide, and quinine urea gave the lowest toxicities in pigeons, and quinine bi-hydrochloride and acid hydrobromide in rabbits. I have so far only tried the bi-hydrochloride and acid hydrobromide intravenously in fever cases, and found the bromide salt can be given in from 10 to 15½ grain doses in adults without producing much dizziness, although half that amount of the bi-hydrochloride intravenously commonly produces cinchonism. In all probability the bromide radicle counteracts to some extent the action of quinine in the nervous system, hydrobromic acid having for long been used for that purpose. On the whole, the acid hydrobromide and the bi-hydrochloride of quinine appear to be the most suitable salts for intravenous injection. I had hoped to have been able to test quinine urethane and colloid quinine, but the expected supplies were lost through "enemy action."

Soluble Cinchonine Salts.

Mr. G. E. Shaw, Government of Bengal Quinologist, has very kindly prepared at my suggestion cinchonine bi-hydrochloride and acid hydrobromide, and their toxicities are also shown in Table III, while the data regarding their action on blood serum and on paramoecia have already been

given. Their toxicities are about the same as those of the corresponding quinine salts, while they are highly soluble, so appear to be suitable and well worth trying intravenously in the treatment of malaria. The acid hydrobromide salt is considerably the less toxic, but whether this combination will lessen the well known tendency of cinchonine salts to produce sickness remains to be tested. I am deeply indebted to Mr. Shaw for making these salts and also some hydroquinine hydrochloride (see (1) in Table III) for me at a time he was very short-handed.

Much of the experimental work in this paper was carried out at the Pasteur Institute, Shillong, thanks to the kindness of the director, Captain R. Knowles, I.M.S., and of Colonel H. E. Banatvala, C.S.I., I.M.S.

Suggestions for the Treatment of Malaria.

Owing to the lack of clinical material under my control at the present time I have only been able to try quinine intravenously in a very few cases of malaria, thanks once more to my friend Captain N. H. Hume, I.M.S. So far we have only given the bi-hydrochloride and the acid hydrobromide in $\frac{1}{2}$ -gram doses once a day for three or four days, but without observing more rapid disappearance of the fever and of the parasites than after quinine by the mouth, so larger doses will evidently be necessary if all the parasites are to be rapidly destroyed. As three grains of the bi-hydrochloride contain as much quinine as four of the acid hydrobromide, after commencing with $\frac{1}{2}$ -gram doses to ascertain whether the patient has any idiosyncrasy towards the drug, up to 12 grains of the bi-hydrochloride or 16 grains (approximately 1 gram) of the acid hydrobromide, in $7\frac{1}{2}$ and 10 c.cm. respectively of normal saline (making practically 10 per cent. solutions), may be given once daily for at least four days. It will probably be advisable to supplement the intravenous doses with quinine by the mouth, as the former is likely to be rapidly excreted through the kidneys—a point I am now investigating. In any case prolonged oral administration should follow the more active intravenous medication. Once the resistant relapse producing stages of the malarial parasite have been produced intravenous quinine is not so likely to be so effective, but the vigorous treatment of primary attacks of malaria by intravenous quinine appears to be worthy of careful trial to ascertain if the frequency of subsequent relapses can be reduced. Military hospitals in malarial areas should afford much more favourable opportunities for following up cases sufficiently long to enable this suggestion to be tested than civil practice. A further material advantage of such early intravenous administration is likely to be that dangerously large infections, which may terminate at any moment in fatal coma under oral administration of quinine, are likely to be rapidly controlled, and the present mortality from malaria to be reduced to practically nil.

The following is a very recent successful example of this line of treatment in the most intense malarial infection I have ever seen recovered from:

The patient was admitted at 4 p.m. in a collapsed and semi-conscious state for suspected cholera, but a low specific gravity of the blood, together with an axillary temperature of 99.4° and a rectal one of 105.6° , led to a blood examination, which revealed a malignant tertian infection of such extreme severity that a count actually showed the proportion of parasites to red corpuscles to be 46 per cent.—that is, almost one-half of them were infected. One gram of acid quinine hydrobromide in 10 c.cm. normal saline was at once injected intravenously. On the following morning the patient was conscious and much better, but the infection still amounted to 19 per cent. of the red corpuscles, so the gram dose was repeated morning and evening, and from the next morning no parasites could be found, and the patient is doing well three days later although deeply jaundiced.

Such a case speaks for itself.

Once repeated relapses have become established the only method of treatment which has given me satisfactory results is the daily administration of ten grains of quinine in one or two doses for at least three, and preferably six, months, always continuing until the end of the malarial season if in an endemic area. During the last seventeen years a number of malarial patients so treated by me have apparently lost their infections and remained free for long periods after omitting the quinine. For example, a medical man had suffered from repeated attacks of benign tertian malaria for several years, when I advised him to take ten grains of quinine a day for six months.

I saw him recently, and learnt that subsequently to that course he had remained free from fever for three years. By this plan, whenever resistant forms reproduce the fever-exciting cycle of the parasite, they will be destroyed by the continual dosage of quinine before they can multiply sufficiently to cause an actual attack of fever, and probably before they can form further resisting stages, which may thus be gradually eliminated from the system. However that may be, I believe this plan is at present the best method we have of checking malarial relapses, while it is one which should be feasible even on active service, if an abundant supply of readily-soluble quinine tabloids are at hand.

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THE SCABIES PROBLEM ON ACTIVE SERVICE.

BY

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EVERY man incapacitated from duty—it matters not by what means—is a gain to the enemy. From the point of view of the army, and of military efficiency, those diseases ought to rank highest in importance which cause most “casualties.” Judged from this aspect, diseases of the skin occupy one of the premier positions, for under the conditions of trench warfare it is inevitable that they are met with in large numbers. The exact extent of the wastage for which they are responsible is known only to the authorities, but it is apparent to all that, since many are contagious, successful efforts directed towards prevention and cure will amply repay by a very large gain of fighting men.

Of the skin diseases found amongst soldiers—excluding pediculosis—scabies is by far the commonest. When uncomplicated its effects incapacitate a man but little; but in consequence of the hard conditions of active service, secondary pyodermic complications are frequent and severe, and these are a very real cause of prolonged sickness. In contrast to the three or four days required for the complete cure of a simple case we have found that when pyodermic complications are established the period necessary is greatly prolonged—the average stay in hospital over a large number of cases being 31.67 days. It should be explained that this figure does not include either treatment elsewhere—which sometimes amounted to many weeks—or the days spent in journeying to the base.

CHARACTER AND DISTRIBUTION OF LESIONS.

Scabies as seen amongst soldiers differs in type from that usually met with in civil practice, and unless the differences are appreciated many cases will not be recognized, leading to dissemination by undetected carriers. The eruption is distributed much in the usual fashion, the sites of election being the wrists, hands, penis, lower abdomen, anterior axillary borders, elbows, and buttocks. The characteristic interdigital burrows, however, are rarely seen; they were present typically in only 13 per cent.* of our cases. Vesicles are much more common, though in quite a number of cases the hands are entirely free from lesions of any sort. A correct diagnosis can only be made after inspection of the whole body. In the majority of cases the penis is involved, and the discovery of papules or crusts on either skin or mucous membrane is almost pathognomonic. This serves in doubtful cases to distinguish scabies from the acute pediculosis so frequently seen, and is for this reason an extremely useful diagnostic sign.

Besides the primary lesions of scabies, others due to secondary coccal infection are common and important. They may be so severe as to mask the primary disease

* This figure does not include cases in which one or two indefinite lesions could be found after prolonged search; including these, the percentage would be about 45. It is our impression that lately burrows have been observed with more frequency than some months ago.