THE PROPHYLACTIC USE OF QUININE IN MALARIA:

WITH SPECIAL REFERENCE TO EXPERIENCES
IN MACEDONIA.

BY

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BETWEEN the beginning of February and the end of April, 1917, I examined the various units of a certain division in Macedonia with a view to determining the proportion of men on duty who were infected with malaria. Smears from 540 men were stained and searched for parasites, and the results are summarized in Table I. Plasmodia were found in over 30 per cent. of the men who had been in Macedonia during the previous summer, while the altered differential leucocyte count suggested that over 60 per cent. of such men were in reality infected. Had it been possible to reckon the absentees in the Malta and Salonica hospitals, the total percentage of infected men would of course have been much greater. Parasites were found in nearly 8 per cent. of men with no history of fever; if we regard the increased hyaline count as evidence of infection, their number increases to over 37 per cent.

As no evidence of infection was found in recent drafts, it may be assumed that the great majority, if not all the men in whom parasites were present, had been infected during 1916 or earlier.

Technicalities.—The average time spent over each slide was about ten minutes, and no man's blood was examined more than once. Gametes were found in over 90 per cent. of the positive slides, and schizonts were also present in a large proportion. *P. vivax* was the common parasite found; *P. falciparum* was noticed on seven occasions, *P. vivax* being also present in four out of the seven; *P. malariae* was only diagnosed once. To simplify matters, *P. falciparum* and *P. malariae* have been reckoned in the table as *P. vivax*.

TABLE I.

Groups I to III are comprised of men who were in Macedonia during the summer of 1916; Group IV of drafts reaching Macedonia between September 1st and December 31st, 1916; and Group V of drafts reaching Macedonia in 1917. Members of the last two groups had never before been out of Britain.

Group.	Total Examined.	<i>P. vivax</i> Present.	Hyaline Leucocytes.*	
				Increasing presumably infected to
I. Fever within 3 months of examination	300	120=40%	89	69.6%
II. Fever during summer, but none within 3 months of examination	93	16=17.2%	33	52.6%
III. No history of fever ...	63	5=7.9%	20	39.6%
IV. No history of fever ...	40	3=7.5%	11	35.0%
V. No history of fever ...	44	—		

* 15 per cent. or over in men in whom no parasites were found.

The Results of Quinine Prophylaxis.

By quinine prophylaxis is meant the regular administration of quinine with a view to preventing the development or recrudescence of clinical malaria.

Method of Administration.—The salt employed was the sulphate, shown by analysis to be pure; the daily dose (gr. v-xxx) was given either in acid solution or in tablets.

The men in Groups I, II, and III of Table I had been taking quinine during the greater part of 1916, and I was assured by the regimental medical officers that many were taking it at the time I made the blood films. The kind of evidence available is illustrated by a group of twelve men belonging to the same brigade, the majority to a regiment whose medical officer had had considerable experience of malaria in the East, and who was positive that the prescribed dose was being taken; all the men had been taking daily doses of quinine varying from 30 to 10 grains. The length of time since the last relapse varied from eight days to three months. There was tinnitus and deafness in

three cases (one taking 30 and two taking 10 grains daily), and deafness in three cases (one taking 30 and two 10 grains daily). In all the 12 cases *vivax* schizonts and gametes were present in the peripheral circulation.

Owing to the varying amounts of quinine ordered by the medical officers attached to the different regiments it was possible to place 125 out of the 150 men examined during February into one or other of the following groups (Table II). Whether the quinine was given in small or large doses or not at all, seemed to make little difference either to the number of relapses or to the proportion of cases in which parasites were found; many of these men were constantly relapsing.

TABLE II.

Groups.	No. of Cases Examined.	No. of Men in Whom Parasites were Found.
I. No quinine between attacks ...	26	16 = 61.5 %
II. 30 gr. daily	21	11 = 50.2 %
III. 20 gr. daily	9	6 = 66.6 %
IV. 15 gr. daily	6	4 = 66.6 %
V. 10 gr. daily	48	22 = 45.8 %
VI. 15 to 30 gr. biweekly ...	11	3 = 27.2 %
VII. 6 gr. daily and 12 gr. biweekly ...	4	3 = 75.0 %

The evidence so far considered indicates (1) that, despite infection, a fair proportion of men examined had, temporarily at any rate, resisted illness or got the upper hand of the disease. (2) That a great deal of sickness due to malaria nevertheless existed in the division, much of it being little influenced by the administration of quinine.

The figures available from French sources show an even higher degree of infection. For example, Garin¹ claims that plasmodia (usually gametes) can be found in the blood of from 60 to 80 per cent. of troops returning from Macedonia without a history of malaria, while Abrami² states that from 85 to 95 per cent. of the French Macedonian army was attacked by malaria in spite of early and general preventive quinization! An early and correct solution of the following problems is therefore urgently needed:

I. Is any appreciable proportion of the Macedonian force saved illness through the administration of prophylactic quinine? If so, what proportion?

II. Is the general course of the disease ever affected by the previous administration of prophylactic quinine? If so, is the sum of such influences favourable or the reverse?

To answer these questions demands an exact knowledge of the conditions upon which the usefulness of the drug, both as a prophylactic and as a curative agent, depend. Unfortunately these conditions have never been thoroughly investigated on scientific lines, and large gaps in our knowledge exist. In spite of these drawbacks I have been tempted to analyse and draw conclusions from the data available in the literature of the subject.

I.—WHAT PROPORTION OF THE MACEDONIAN FORCE IS SAVED ILLNESS THROUGH THE PROPHYLACTIC ADMINISTRATION OF QUININE?

A. General Considerations and Analysis of Statistical Evidence.

Altogether I had access to some two hundred original articles, reports of medical societies, etc., in which the question of quinine prophylaxis was either dealt with or discussed. Nearly all of them were written in English, French, or German, and all—with one exception—were published between the discovery of the malaria parasite in 1880 and the present time. Of the authors 52.2 per cent. gave no details of their personal experience, while only 16.9 per cent. made use of controls. Table III gives an idea of the opinions expressed by these different writers, no less than 80 per cent. of whom were in favour of quinine prophylaxis.

TABLE III.—Views of Writers on Quinine Prophylaxis.

	In Favour of Quinine.	In Favour of Quinine with Reservations.	Against.	Total.
No statistics ...	65	21	20	106
cs but no controls	43	6	12	61
cs with controls...	26	0	8	34
Total ...	134	27	40	201

The majority of these papers were, however, devoid of interest. No doubt a large number of writers were unfavourably influenced by the difficulties in the way of controlling their results, and realized the impossibility of appreciably increasing our knowledge in the absence of such controls; be this as it may, the difficulties in the way of experimental research have unfortunately brought extremists to the fore, and such statements as the following are scattered throughout the literature:

The whole trend of recent inquiry and the results of clinical experiment have been to show that at the present day, more than ever before, the scientific administration of quinine is established as a measure of very great value and that it is indispensable in the general prevention of the disease.³

Quinine has its position in relief and cure, but in sanitary administration it has none.⁴

Knowing as we do that resistance to malarial disease is considerably greater in the inhabitants of malarial countries than it is in immigrants from non-malarial ones, it would seem natural to suppose that, other things being equal, the benefit derived from the use of prophylactic quinine varies directly as the resistance of the individual taking it—in other words, the greater the resistance the better the statistics. The truth of this supposition can only be tested in the present state of our knowledge by analysing the statistical evidence from different countries, taking care to distinguish between the natives of such countries and immigrants.* This has been accordingly done in Tables IV to VII.

TABLE IV.—Countries bordering on Mediterranean Basin.

	Statistics but no Controls.	Statistics with Controls.
In favour of quinine ...	16	18
In favour of quinine with reservations	0	0
Against ...	1	0
Total ...	17	18

All thirty-four papers in favour of quinine prophylaxis deal with the question in so far as it affects the permanent inhabitants of the respective countries; the single paper against deals with temporary inhabitants—namely, the French army in Macedonia.

TABLE V.—Africa excluding the Mediterranean Area.

	Statistics but no Controls.	Statistics with Controls.
In favour of quinine ...	13	2
In favour of quinine with reservations	1	0
Against ...	3	2
Total ...	17	4

One of the four papers in which controls were used deals with natives and is in favour of quinine prophylaxis; the remaining three deal with immigrant whites, one paper being in favour and two against.

TABLE VI.—Southern Asia.

	Statistics but no Controls.	Statistics with Controls.
In favour of quinine ...	14	5
In favour of quinine with reservations	1	0
Against ...	6	4
Total... ..	21	9

Three out of the nine papers in which controls were used deal with natives, and are in favour of quinine prophylaxis. The remaining six deal either with immigrants or with partly immigrant populations, such as coolies on rubber plantations; two were in favour of quinine prophylaxis, four against.

* The full bibliography of the authors whose views are summarized in Tables IV to VII will be published in the *Journal of the Royal Army Medical Corps* for June.

TABLE VII.—North and South America, including West Indies.

	Statistics but no Controls.	Statistics with Controls.
In favour of quinine ...	3	1
In favour of quinine with reservations	3	0
Against ...	1	2
Total... ..	7	3

One out of the three papers in which controls were used deals with natives, and is in favour of quinine prophylaxis; the other two deal with immigrants, and are against.

A study of these tables reveals the existence of a state of affairs very different from what might have been anticipated from merely glancing over the opinions of the various writers summarized in Table III, especially when we remember that controlled results are the only results of any scientific value. When controls were used and natives of the respective countries investigated, no less than twenty-three, or 100 per cent. of workers, were in favour of prophylactic quinine. When controls were used and immigrants dealt with, only three out of eleven, or 27.2 per cent., were in its favour. The evidence available would therefore seem to justify the enunciation of the following conclusion: "Other things being equal, the natives of malarial districts derive more benefit from quinine prophylaxis than immigrants from non-malarial ones."

Value of Prophylactic Quinine to the Natives of Malarial Countries in the Mediterranean Area.

We have seen that all the available statistical evidence is in favour of administering prophylactic quinine to the inhabitants of Mediterranean districts in which malaria is endemic. What does this really amount to? Celli, one of the best known of the Italian workers, thus expresses himself:

The daily use of quinine is as necessary as daily bread during certain months.⁵

He who takes quinine every day, and therefore has always a supply of quinine in the blood stream, can undergo with impunity inoculations of blood full of malarial parasites, and can expose himself with little or no danger to the bites of infected mosquitoes.⁶

Yet at a later date the following analysis of very extensive clinical material was published by the same author.⁷

TABLE VIII.—Quinine and Mosquito Prophylaxis (Celli).

Mosquito prophylaxis plus quinine prophylaxis	Symptoms in 1.75 % = 1 in 57.
Mosquito prophylaxis only...	Symptoms in 2.5 % = 1 in 40.
Quinine prophylaxis only ...	Symptoms in 20 % = 1 in 5.
No protection ...	Symptoms in 33 % = 1 in 3.

Clearly the quinine given produced some effect, but compared with the results obtained by mosquito prophylaxis, its action was almost negligible.

The brothers Sergent, who have investigated the subject for many years in Algeria, seem less enthusiastic than they used to be. The last paper I have seen gives details of the quinine given to native children in 1910.⁸ One of their tables is reproduced, and the authors content themselves with the observation that all methods give appreciable results.

TABLE IX.—Quinine Prophylaxis with Controls (Ed. and E. Sergent).

Dose of Quinine.	Improvement.	No Change.	Worse.
0.2 gram daily ...	19 = 5.5 %	315 = 83.5 %	7 = 2.02 %
0.6 gram every 3 days ...	19 = 4.2 %	425 = 94.6 %	4 = 0.9 %
0.6 gram every 6 days ...	35 = 9.7 %	300 = 80.4 %	16 = 4.8 %
Controls (no quinine) ...	5 = 0.8 %	220 = 90.5 %	21 = 8.7 %

These Italian and North African results are not very impressive, especially when it be remembered that we are dealing with the only type of case in which a consideration of the general statistical evidence led us to suppose that really striking benefit would be uniformly attained—namely, natives who have presumably inherited and acquired a certain amount of immunity against the parasites of their own country.

B. Methods of Giving Prophylactic Quinine.

The two methods usually employed are: (1) A small daily dose (5 grains, for example); (2) a larger quantity (usually 15 grains, taken on two consecutive days at intervals of from a week to ten days).

The advocates of the first method claim that quinine taken in this way is always circulating in the blood, and object to the other because it leaves the individual defenceless for several days owing to the rapid excretion of the quinine absorbed. The partisans of the second method maintain that by giving quinine in this manner the curative effect of the drug is not interfered with, but that the use of the first method may lead to the production of quinine-proof strains of parasites. I have searched the literature, but can find no evidence of one method having any appreciable advantage over the other.

In Italy, Greece, and North Africa, 3 to 6 grains daily is the ordinary dose, and larger quantities are not usually supposed to give any better results. It is seen from Table II that, on the whole, the smallest percentage of cases was diagnosed in those who were taking least quinine. The possible significance of these facts will be considered later.

C. "Suggestion" in Quinine Prophylaxis.

In quinine prophylaxis, as in all forms of medical treatment, the personality of the physician is not without influence, while the extent of his confidence in the treatment proposed can usually be gauged by the patient with considerable accuracy.

Laveran,⁹ in his book on malaria, published in 1898, comments on the fact that the English, who previously wrote so much in favour of prophylactic quinine, seem to have got tired of it. The psychological aspect of malaria prophylaxis has received considerable attention from American writers, several of whom regard the co-operation of the public as essential, and agree that no means of stimulating its curiosity and of keeping its sympathy should be neglected.^{10, 11} In Macedonia the French authorities advertise the merits of quinine by means of humorous coloured posters and picture post cards, which must go far towards reconciling the *poilu* to his daily dose. In Algeria the brothers Sergent have initiated the use of pink tablets containing three parts of sugar and two of quinine bihydrochloride, and state that these are everywhere accepted by the natives with the greatest alacrity, in marked contrast to their attitude towards the classical method. The striking possibilities of suggestion are vividly brought home by the following incident, related in all seriousness by Henrot.¹²

Dr. Nouat, head of the military hospital, Calcutta, was consulted by the Governor of Bengal as to the best way of protecting messengers against malaria. So many died from pernicious malaria as a result of the unhealthy country they had to cross that messengers had become unobtainable. Dr. Nouat, acting on a theory prevalent at the time—that infection took place via the respiratory tract—constructed respirators containing finely divided animal charcoal, and made the messengers wear them; the effect was excellent, for the messengers, although taking exactly the same route as their predecessors, ceased being ill.

D. Conclusions as to the Effect of Quinine in Preventing Clinical Malaria in Macedonia.

1. *Primary Malaria.*—From Table I it is seen that some of the men exposed to the risk of infection escaped, evidently because: (a) They had never been bitten by infected mosquitos; or (b) if infected, their powers of resistance were equal to the occasion, and no clinical symptoms ensued. If it be asked to what extent the natural resistance of these latter had been reinforced by taking quinine, the answer is that although the drug must have been the decisive factor in a few cases, the evidence points to their number having been very limited. No matter what disease we take, a proportion of any population is always more or less refractory. Moreover, malaria may be a very chronic condition, and the presence of parasites in the blood of people who have never developed symptoms and who have never taken quinine is well known. As Bass¹³ says: "No doubt many people get infected without ever knowing anything about it; others infected under similar conditions may be ill, and in some cases die." Further, the absence of symptoms in such apyrexial carriers is no guarantee of permanent immunity; in many cases all that is needed to produce an attack is such slight lowering

of vitality as is produced, for example, by a chill, a surgical operation, or a broken bone.

2. *Recurrent Malaria.*—I have come across no evidence which leads me to suppose that quinine is any more efficient in preventing relapse than it is in aborting the initial attack (see Table II).

II.—IS THE GENERAL COURSE OF THE DISEASE EVER AFFECTED BY PREVIOUS QUININE PROPHYLAXIS?

A. The Clinical Evidence and Its Significance.

The following examples are taken from the literature of the subject:

1. Celli states that both doctors and patients are unanimous that daily prophylactic quinine very frequently aborts primary infections, notably diminishes relapses, and prevents cachexia.¹⁴

2. So far back as the American civil war the responsible medical authorities¹⁵ state that men were saved from attack and preserved in perfect health for the time being by the use of prophylactic quinine, but that the method was abandoned owing to the shortage of quinine and to the eventual sickness of such men.

3. Neiva (Brazil), who was in charge of 3,000 men in a highly malarial district, found that to obtain the same therapeutic effect the dose of quinine had to be increased in proportion to the length of exposure to infection.¹⁶

4. Bell (Panama) states that men who were receiving the drug, in comparison with those who were not, under otherwise identical conditions, furnished fewer cases in the proportion of three to four; that such men were, however, more refractory to treatment, had a more prolonged convalescence, and relapsed more frequently.¹⁷

5. Stitt¹⁸ is of the opinion that quinine in reasonable doses has little or no effect, while those who take it are less amenable to its curative action, and relapse more frequently than those who only take the drug at the time of an attack; he also maintains that quinine prophylaxis does not prevent either anaemia or splenic enlargement, while Jacobson¹⁹ goes so far as to say that although symptoms may be masked for a time, the actual damage is as great as though no quinine had been given.

6. We have seen that in Macedonia quinine alone is quite unable to prevent malaria, while very large doses have to be given in many cases to obtain clinical amelioration. Only a few weeks ago, at a meeting of the Society of Tropical Medicine and Hygiene, a paper was read by Sir Ronald Ross in which details were given of various intensive forms of quinine treatment in chronic cases of malaria invalidated from Macedonia. No matter how big the dose or what route was chosen for its administration, frequent relapses still occurred.

After studying this and similar evidence, we are bound to admit that the general course of the disease may be adversely influenced by the previous taking of quinine.

Why does Quinine give Variable Clinical Results?

In ordinary circumstances the key to the problem undoubtedly lies in the constitution of the patient and in his state of health both at the time of infection and subsequently. Under good social conditions intermittent malaria tends to cure itself both temporarily and permanently, and whether quinine be given or not the temperature returns to normal in a few days. If only a little outside help is required to change the balance in favour of the patient, good hygienic conditions, an enthusiastic physician, and a little quinine will suffice either definitely to cure the individual or, at any rate, to prevent his relapsing for a considerable time in the absence of reinfection. If, on the other hand, the resistance of the patient falls short of this, no marked benefit will result.

Clinical evidence favours the view that the course of malaria may be unfavourably affected by the previous taking of quinine, but we have seen that under relatively favourable conditions a small daily dose of quinine tends to prevent clinical malaria, or at all events to lengthen the incubation period. This, however, cuts both ways, and should an individual run the risk of being frequently infected, the tendency will be for him to receive more massive doses of sporozoites as the result of taking prophylactic quinine. Can we wonder if his malaria is of a severer type when it does develop? It is universally assumed that the sporozoites resulting from conjugation in the insect host possess a greater potential capacity for mischief in the vertebrate host than merozoites derived from many generations of asexual multiplication. A European in the tropics who stays out at night and is generally careless with regard to mosquito prophylaxis is much more likely to suffer from, and to be eventually invalidated home with, chronic malaria than the individual who is careful in these respects. Experiments on proteosoma

infections in sparrows are said to show that the severity of the disease largely depends on the dose, that is to say, on the number of sporozoites inoculated.²⁰

We are now in a position to appreciate the inadvisability of giving prophylactic quinine over long periods, and to realize that the severity of malaria in Macedonia has been increased in some cases by previous quinine prophylaxis.

B. *The Probable Mode of Action of Quinine in Malaria.*

1. *As a Prophylactic.*—Cushny says:

Quinine differs from most other important alkaloids in acting, not on some specialized form of living matter, but on the general nutrition of almost all forms of protoplasm. Experimental evidence indicates that a number of ferments act more vigorously in very dilute solutions of quinine, while their action is retarded by larger quantities.²¹

It is possible, therefore, that the lytic action of human plasma on malarial parasites is increased when quinine is present in suitable concentration. It is equally possible that too great a concentration of quinine retards this activity; also that the long-continued administration of the drug sets up a tolerance to its presence which necessitates an increase of concentration to get the original effect.

We have previously noted that certain doctors in Mediterranean countries regard 0.2 gram (about 3 grains) daily as sufficient; the few cases I had the opportunity of examining in Macedonia appeared to justify the view that a maximum daily dose for prophylactic quinine exists, and that it is not a very big one. It is also possible that the mechanism about to be considered is not without influence.

2. *The Action of Quinine as a Curative Agent.*—Barlow, as the result of experimental work, thinks that quinine in therapeutic doses does not directly destroy the plasmodium, but tends to poison infected red blood corpuscles in such a way that they are more easily acted upon by the excretory products of the parasite. This results in its liberation before segmentation has taken place and facilitates its destruction. Gametes escape because their less active metabolism does not liberate sufficient toxin to destroy even the quinine-poisoned cell.²²

This explanation is in harmony with the facts. We know, for example, that quinine, given at the beginning of an attack of intermittent malaria, does not appreciably influence the train of clinical events, but tends to prevent subsequent attacks. It would seem to do this by poisoning infected red corpuscles and accelerating their disintegration, thus making the conditions less favourable for the multiplication of the parasite, which is unlikely to be present in sufficient numbers to produce symptoms when the next attack is due. This would give the resisting powers of the individual time to rally. Should his vitality be insufficient to dispose of all the plasmodia the metabolism of the survivors may be assumed to slow down, and even very large doses of quinine may be unable to poison the red cells sufficiently for the parasitic toxins to destroy them with sufficient speed, the plasmodium reacting by slowing its metabolism still further. In many cases it successfully avoids extermination, and, in the event of the host's vitality being sufficiently lowered, a relapse occurs.

In severe and chronic cases resulting either from massive infection or from the feeble resisting power of the individual, or from a combination of the two, large doses of quinine are usually given over long periods; according to the above theory, the poor results obtained would be largely due to an increased tolerance of the red cells for quinine.

Both clinical and theoretical considerations compel us to admit that the general course of the disease may be noticeably affected by the previous taking of quinine, and that the sum of such influences is frequently unfavourable. So far as the allied armies in Macedonia are concerned, there is every reason to suppose that quinine taken daily over periods of many months has increased the severity and chronicity of the disease in a certain proportion of cases. Taking one thing with another, the available evidence indicates that in Macedonia, at any rate, the disadvantages of quinine prophylaxis outweigh the advantages.

GENERAL SUMMARY OF CONCLUSIONS.

1. Small doses of prophylactic quinine—not too long continued—are of proved utility to the natives of malarial

countries, both in the absence of antimosquito measures, and when such measures are incomplete.

2. Quinine may be given with advantage to immigrants under the following conditions:

(a) During short journeys when conditions with regard to mosquito prophylaxis are less favourable than usual.

(b) An occasional dose after an unusually tiring day.

(c) Nervous people may be advised to take an occasional course as an additional precaution in spite of efficient mosquito prophylaxis.

Speaking generally, it may be stated that quinine prophylaxis is usually a bad investment for immigrants in the absence of protection against mosquito bites; taking one thing with another, the practice would in their case seem to be little more than a pious fraud, which has been perpetuated from one generation to the next simply because public opinion throughout the world has never been sufficiently enlightened to encourage the working out of the problem on scientific lines. A few well-planned experiments, carefully and simultaneously conducted in several countries, and these conclusions might have been reached many years ago. We know the experimental method to be at the bottom of all scientific and industrial progress, yet we refuse to admit its very obvious utility in preventive medicine. The following observation applies only too literally to the subject under discussion: "En dehors des sujets dont le contrôle expérimental est facile, bien peu d'opinions s'appuient sur la logique rationnelle. Sur l'interprétation de faits au fond assez clairs, mais que n'étaient pas des expériences suffisamment tangibles, le désaccord est complet."²³ Surely this lamentable state of affairs cannot continue much longer. The experimental evidence exists, but unfortunately its neglected fragments lie embedded in a very extensive literature, much of which is of little value owing to lack of detail and to the impressions of the writers being uncontrolled by clinical experiment.

APPENDIX.

Although the difficulties in the way of efficient mosquito prophylaxis in non-immune armies operating in highly malarial countries are very great, the failure of quinine prophylaxis shows that more serious efforts must be made to overcome them. A few methods of procedure are therefore mentioned, and their value briefly discussed.

A. *The Destruction of Mosquito Larvae.*

1. *Subsoil Drainage.*—This is the ideal method, but finance and labour difficulties militate against its general adoption. In Panama, where both money and labour were available, this method was little used, because the engineering works constantly interfered with the drains.²⁴

2. *The Oiling of Surface Water.*—In Panama the system of oiling seems to have been perfect, the whole area for about half a mile round all dwelling places being oiled once a week so thoroughly that all mosquito larvae were killed.²⁴ The method is obviously good when sufficient oil can be obtained.

3. *The Piping of Streams.*—In ravine country, when mosquitoes breed in the pools associated with fast-running but temporary streams, such streams may be piped with advantage within half a mile of camps.

B. *Mechanical Prophylaxis against Mosquito Bites.*

In countries where the reduction of mosquito larvae is difficult the importance of mechanical prophylaxis can hardly be exaggerated. The question will be briefly considered under the following headings:

1. *The Screening of Dwellings.*—In the canal zone all houses occupied by Americans had double doors, the windows being protected with copper-bronze screens—18 mesh to the inch. Orenstein²⁵ concludes that properly screened dwellings alone can be depended upon to reduce by at least one-third the malaria incidence in a locality where malaria is endemic.

2. *Net Prophylaxis.*—Stott²⁶ and others have emphasized the great value of supervised net prophylaxis for soldiers.

3. *Veils and Gloves with Gauntlets.*—These have been employed on sentry duty, etc. If properly used, such methods should be fairly effective, but adequate supervision is obviously difficult or impossible.

4. *Essential Oils.*—Oil of citronella, etc., either pure or in the form of ointment, has been tried for men on night duty, but without much success. According to Celli and others, such methods have a very restricted action.

5. *Night Work.*—The employment of African or Greek troops for sentry duty and all forms of night work during the summer and autumn months would seem to be worthy of serious consideration. After going carefully into the matter, the advantages might be found to outweigh the disadvantages.

6. *Education*.—The last, but certainly not least important, method is the education of officers and men as to the habits of the mosquito and the means of avoiding infection. Pamphlets, posters, lectures, lantern slides, cinema films, all have their place according to circumstance and opportunity.

In conclusion, I should like to thank my brother, Captain H. A. Treadgold, R.A.M.C., for valuable assistance.

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INTERLOBAR EMPYEMA AND OTHER SURGICAL COMPLICATIONS OF THE THORAX.*

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EMPYEMA is the commonest complication in the thorax needing surgical treatment. In most cases it is quite easy to diagnose, as it occurs after pneumonia; an increasing rise of evening temperature, with morning remissions and dullness and silence at the base of the lung, with displacement of the heart, pointing definitely to it; but, in quite a number of cases, matters are not so simple.

In rare instances there is no history of pneumonia. This is more common in poor children with bad mothers. I can recollect instances of children being brought to the outpatient department with a chest half full of pus who have not been a day in bed. They have had a cough for some time, are short of breath, and have lost flesh. I have never seen it in better class children.

In an adult it is very rare. About five years ago I was asked to see a shopkeeper's wife who for some weeks had had night sweats, with a temperature of about 100° F. each night and 97° in the mornings. There had been no acute illness, and there was very little cough and no sputum. The suggested diagnosis was phthisis, but no physical signs had been found. The upper lungs were normal, but there was dullness and silence below the angle of the right scapula, and the heart was slightly displaced to the left. My diagnosis was pleural effusion, probably tuberculous, but on inserting a needle pus was found.

Difficulties may occur from the situation of an empyema; it is not altogether uncommon between the lobes of the lungs, where it is often undiagnosed. If untreated such an empyema may burst into a bronchus, and after weeks of coughing, sometimes of fetid sputum, may clear up, or chronic bronchiectasis may result.

CASE I.

A man, aged 47, was admitted under me this spring. He had had left-sided pneumonia six or seven months before, but had recovered and been working at Newhaven until shortly before admission. He had a severe cough and a good deal of expectoration; the temperature was 100° at night. There was dullness in the second and third right spaces in front and diminished resonance below; bronchial breathing at the apex, distant tubular breathing in the second and third spaces, weak breathing below, with coarse crepitations. Over the right back breathing was bronchial and rather weak in the upper half, but there was no dullness. The left chest was normal except for some rhonchi.

The previous pneumonia had been on the left side and was too long ago to count, but I thought the case was one of interlobar empyema. A needle was introduced in the second space, over the dull area, that afternoon without getting pus.

* Read before the Medical Society of London.

Owing to an attack of influenza I did not go up to the hospital again for a fortnight; by that time Captain Prowse had examined the man with x rays, and reported a large abscess cavity in the upper part of the right side of the thorax rather more than half filled with fluid, on which waves could be seen when the man was shaken. In the meantime the patient was coughing up large quantities of sputum, and, when I saw him again, all dullness had disappeared and breath sounds were almost normal over the right upper chest. He had coughed up the whole empyema.

These interlobar empyemata may burst into the general pleural cavity. Of this I have seen three cases.

CASE II.

A youth, aged about 18, had a very severe pneumonia, implicating both lobes of the left lung and part of the lower lobe of the right. His temperature came down gradually for ten days, and then began to rise in a hectic manner. The left chest remained dull, but tubular breathing and crepitations could be heard all over. I could not detect any special dullness over the interlobar area. One day his temperature and pulse-rate both fell and he said he felt better, but I was surprised to find a large area of absolute dullness and silence at the left base, where the day before had been breath sounds. On putting in a needle pus was found, and at the operation there was a good pint of it. I believe that his empyema was originally interlobar, and, when it burst into the general pleural cavity, the relief of tension caused the fall of pulse-rate and temperature.

CASE III.

A soldier, admitted under me last autumn with dullness from the spine of the left scapula down to the base. A needle drew off pus. Major Buck operated in the usual situation and found very little pus. A few days later the temperature was still high and the man was worse. I then found that the lower part of the back was slightly resonant, but just below the level of the spine of the scapula there was an area of absolute dullness about three inches in depth. An aspirator inserted here withdrew much pus, which, however, reaccumulated, and Major Buck removed a portion of the fourth rib between the scapula and the spine, and opened a large empyema between the upper and middle lobes of the lung. The operation was one of some difficulty owing to the depth of muscle. In this case the original empyema was evidently interlobar and some of the pus had leaked down over the lower lobe, where it was found at the first operation.

CASE IV.

In this case an operation for empyema of the right side of the chest in a child set free only a very small quantity of pus, but a few hours later a sudden gush of quite half a pint of pus soaked the dressings. This must have come from between the lobes.

My father, Sir William Broadbent, described three cases of interlobar empyema in the *Practitioner* in 1905.

In the first pus made its way to the surface above and just outside the left mamma, and the patient made a good recovery.

In the second several unsuccessful aspirations had been made in the lower part of the right chest before he saw the case. It had been noted that breath sounds could sometimes be heard lower on the right front one day than the day before. This led him to suspect interlobar empyema. He found a band of dullness above the spine of the scapula and in the apex of the axilla. Pus was found on passing in a needle high up in the axilla. A piece of rib was removed in this situation, and half a pint of pus was evacuated, with rapid recovery.

The third was a boy, aged 10, who had a left-sided influenzal pneumonia spreading from base to apex. After a crisis on the ninth day, the temperature assumed a suppurative type. The doctor, finding dullness on the whole left base up to the spine of the scapula, absence of vocal fremitus and marked oegophony, put in a needle in three different places, but without success. He noted that the upper part of the lung was becoming duller and more silent. When seen by my father there was absolute dullness with no vocal fremitus or resonance or breath sounds from the apex down to the fourth space, whereas the lower part of the chest in front was comparatively resonant. At his suggestion a needle was put in at the lower edge of the pectoralis with the arm at right angles to the chest. A whole pint of pus was withdrawn. After operation at the site of puncture, a large collection of sloughs came away, and the boy ultimately made a good recovery.

When much pus collects in an interlobar fissure the lower lobe of the lung is so compressed that it becomes dull and airless, leading to the belief that there is an ordinary empyema, until exploration in the usual areas finds no pus. In the last case mentioned both upper and lower lobes were so compressed.

The characteristic of interlobar empyema appears to be a very dull band, either in the second and third spaces in front or just below the spine of the scapula behind. As a rule, there is much diminished resonance over the lower part of the chest, but not the flat dullness of the band of fluid, and breath sounds are very weak and usually absent at the base. The best place to insert a needle is the