serum; preparation of fluid and dried human serum suitable for administration to men wounded in the field; anti-malaria and anti-yellow fever measures, such as the preparation and testing of mosquito repellents, and surveying the geographic distribution of mosquito vectors in the Union and neighbouring territories; man-power research.

Research.—It was possible for most departments to continue investigations on which they were previously engaged. The volume of this research was large.

Leprosy.—The use of N.A.C. antigen, prepared from a new acid-fast variety of tubercle bacilli, in the treatment of certain forms of leprosy proved so encouraging that it was decided to follow up this work with further experiments. The clinical and immunological investigations on the treatment of leprosy by means of diphtheria toxoid according to the method introduced by Dr. Collier, of Thailand, were carried out. The 100 patients developed high anti-diphtheritic immunity as the result of a prolonged course of injections, but they failed to confirm Dr. Collier's claim for this form of treatment.

Pneumonia.—Cases of pneumonia clinically resistant to sulphapyridine therapy continue to be encountered. The majority of these are found to be associated with a *Staphylococcus aureus* either as the sole infecting agent or together with a pneumococcus or other organism. A number of these pneumonia cases have been treated with sulphathiazole with bacteriological control in these laboratories. In certain instances the results were highly satisfactory. It is concluded that, for the present, sulphathiazole, particularly in conjunction with an autogenous staphylococcus vaccine, is the best method of treating such resistant cases.

Typhus.—Dr. D. Ordman undertook the large-scale preparation of vaccine for prophylaxis in the typhus group of diseases. Vaccines will in future be available against exanthematic and murine typhus as well as against tick-bite fever. The vaccines are being prepared by the Zinsser-Castenada method involving the use of irradiated rodents including gerbilles and also the yolk-sac method in which the rickettsiæ for vaccine suspensions are harvested from the infected yolk-sacs of developing hens' eggs. The comparative immunizing value of the various vaccines is being investigated by protective and other tests and experiments are also being conducted to determine the most effective means of killing the rickettsiæ without impairing their immunizing value.

Relapsing fever.—The results of an investigation into the distribution of the *Ornithodorus moubata* tick and the occurrence of relapsing fever in South Africa have been published.

Lymphogranuloma inguinale.—The demand for Frei antigen in the diagnosis of cases of lymphogranuloma inguinale has led to interesting work with the bubo pus taken from cases of this disease. A large amount of this antigen was prepared.

A disease resembling tick-bite fever in its reactions in guinea-pigs was isolated from the tick *Amblyomma hebræum*. The ticks were collected on cattle found in the vicinity of the golf club at Lourenco Marques. The links of this golf club are notorious as a source of human tick-bite fever. Experiments to establish the identity of this strain are in progress.

Mycology.—A case of histoplasmosis, the first to be noted in Africa, has been investigated. The causal fungus, *Histoplasma capsulatum*, was isolated and successfully grown on artificial media and some animal experimental work has been carried out.

Routine work.—Diagnostic work expanded further during the year, the number of examinations and tests done being 274,101, an increase of 45,053 over that of the previous year.

Blood cultures from cases of suspected enteric fevers numbered 1,020. The following pathogens were isolated from 179 of these cultures :—

B. typhosus	150
B. paratyphosus A	14
B. paratyphosus B	14
B. paratyphosus C	1

From specimens of fæces and urine the following were isolated :—

	Fæces	Urine
B. typhosus ..	16	18
B. paratyphosus A ..	9	1
B. paratyphosus B ..	3	0
B. paratyphosus C ..	17	2

Widal agglutination test.—A total of 6,458 specimens were submitted to the Widal test. Positive reactions with *B. typhosus* 'H' and 'O' were given by 2,427; this figure includes those that gave in addition reactions with *B. paratyphosus A* and *B. paratyphosus B*, usually as the result of prophylactic inoculation. A number of bacteriologically proved cases of typhoid fever, however, gave some agglutination reaction with *B. paratyphosus A* without a history of previous inoculation. *B. paratyphosus C* was agglutinated to diagnostic titre with sera from thirty patients. The 'Vi' agglutination test was done on 6,479 specimens for the detection of typhoid carriers amongst persons handling food. Of these, 261 or 4 per cent gave a positive reaction. Most of these specimens came from a distance. It was not possible, therefore, to examine the reactors further as to the carrier state. Urine and fæces of fifteen positive reactors, examined on three successive days for *B. typhosus*, gave negative results. The serum of a native urinary carrier gave a positive 'Vi' agglutination test in dilutions up to one in eighty. His titre for 'O' was 1 in 200 and for 'H' 1 in 100. Tests done on different occasions showed that there was very little fluctuation in his 'Vi' agglutinin.

Typhoid complement fixation test.—Of 1,101 specimens submitted for the typhoid complement fixation test, 72 gave positive and 151 doubtful results.

Of 1,197 specimens examined by the Weil-Felix test, 138 gave positive reactions with *B. proteus* OX, 19 and 102 with *B. proteus* OX 2. Cross agglutination between these two types of *B. proteus* was common, while a number of specimens gave additional agglutination with *B. proteus*, OXK.

Of 873 specimens examined for the presence of agglutinins of *Br. melitensis* and *Br. abortus*, 26 specimens gave a positive diagnostic reaction. The serum of 1 patient who had a positive blood culture for *Br. abortus* showed a titre of 1 in 6,400 for this organism, and a titre of 1 in 200 for *Br. melitensis*.

Correspondence

QUININE AS A MALARIA PROPHYLACTIC

SIR,—At a meeting of the Royal Society of Tropical Medicine in London in 1925 (Yorke, 1925) at which the uses of quinine were being reviewed, the president remarked that the general position was hopeful 'save perhaps from the point of view of prophylactic quinine', and another doctor described this aspect of the subject as 'the eternal question', the implication being that it was one not yet settled.

This officially slams the door in the faces of those who have already made up their minds about the matter, one way or the other.

'Struth, there are many diverse reports on the subject. For instance, there is one of an experiment by Field, Niven and Hodgkin (1937), cited by Napier (1938), the outcome of which was successful, and on the other hand there are the accounts of the Army experiments during the last War when half battalions at Salonika were given 'prophylactic' quinine while the other half had nothing and the results were negative.

Now the diversity in the results of such experiments can, it is submitted here, be explained, and the explanation leads to this conclusion, that if 'prophylactic' quinine be given to an immigrant and susceptible population it has no effect on the malaria-rate, but if it be given to a settled population in a malaria-endemic area it will to a certain extent succeed, not that it is advisable even here.

The whole thing hinges on the observations in Holland by Korteweg (Swellengrebel and de Buck, 1931 and 1932) that during the stage of 'Korteweg's initial

fever' quinine has no action at all and on their explanation that it is only when there has been a certain initial systemic reaction that quinine can act as a parasiticide.

In other words, if quinine be given 'prophylactically' to a number of immigrants who have never had malaria, *e.g.*, to British soldiers, or to Tamil labour, no amount of the drug will prevent the primary manifestation of the fever, *viz*, 'Korteweg's initial stage', and this will run its course even during the concurrent administration of the quinine. If then, however, when that initial stage be over, and when that putative systemic reaction has taken place, quinine be still continued, it will stop the fever *quâ* therapeutic agent. 'Prophylactic' quinine in such communities therefore would show no results, as it did for all practical purposes at Salonika, but the course given, if continued, would as stated show therapeutic results, which means that the cost of that proportion of the total used, that had been used 'prophylactically', had been wasted.

On the other hand, if 'prophylactic' quinine be given to a settled community in which malaria is endemic, some infection will have previously occurred in a certain proportion of the population, and this infection will have already had a run, and produced the systemic reaction which is essential for the successful action of quinine, so that in this section of the population prophylactic quinine would be instrumental in averting a reappearance of *the same type of infection*. The success achieved by Field, Niven and Hodgkin (1937) in the F.M.S. can be explained in this way. But even in such a community there will be other persons becoming infected with a type from which they have never suffered before and prophylactic quinine will not save them, as has been explained above.

But granted that in such communities prophylactic quinine does reduce the malaria-rate, it does not appear reasonable to spend vast sums of money for this purpose, when a mere fraction of that used 'prophylactically' will be sufficient to cure immediately the cases of fever that develop. One postulates a person in whom systemic reaction to a particular strain of infection has already taken place and the question arises: Is it better to dose him for perhaps months on end with five grains a day or wait till he develops fever, when a few grains of quinine (provided the infection is not of a newly-acquired type) will immediately cure him? Many an Assam Planter answers this question by habitually refusing to take 'prophylactic quinine', and only on the onset of malarial malaise taking 5 grains, with some hot toddy, which usually puts him right again.

Sometimes in both sorts of community, the susceptible immigrants and the settled endemicized community, the systemic reaction to an infection does not take place, presumably due to environmental conditions such as insufficient food, or excessive labour, and then in both communities prophylactic quinine will have no apparent effect.

Now what are the processes that take place during that 'systemic reaction' to the invasion of the parasite, and also pertinent to this question is, how does quinine act as a parasiticide?

With regard to the latter point, the potency of the drug outside the body appears to be at best very low, for if a quinine solution be added to defibrinated malaria-infected blood and the mixture incubated at body-temperature for 12 hours, it is infective on injection into a susceptible person, even should the strength of the quinine in the mixture be much greater than ever can occur in the human circulation after the drug is taken therapeutically. In spite of this Yorke and Macfie (1924) think that quinine when given therapeutically does kill off a large number of the parasites (the quinine perhaps first becoming altered by the body-cells, but against this hypothesis is the fact that the drug is eventually excreted from the body not in any altered condition), those dead parasites act as antigen and excite the formation, by the tissues, of immune-bodies, which then deal with the parasites surviving from the first action of the quinine.

Now when the writer was a medical student he was warned against facilely diagnosing two, or even more, causes for a disease, and it seems that in an analogous situation Yorke and Macfie have not followed this wise principle, they have invoked two processes by which the parasites are killed off:—

(1) by the direct action of the quinine on the parasite,
(2) by the production of immune-bodies, by the tissues, which also act on the parasite.

Now it may be argued against these hypothetical processes that (*a*) if the quinine starts off by killing large numbers of parasites, why should it not go on doing so until all the parasites are killed off, and (*b*) is the unnatural destruction *by quinine* of a preliminary batch of parasites necessarily antecedent to the production of immune-body? the answer to which is 'no', for the *natural* reaction of the tissues to the infection is quite sufficient to account for the provision of all the antigen required for the formation of immune-body: because natural reaction alone, as is well known, leads to the state of tolerance that one finds in the inhabitants of highly endemic areas. Yorke and Macfie's hypothesis appears therefore to be at its best superfluous.

How quinine acts is therefore a question still remaining to be answered. Accepting the evidence that quinine in circulation acting on an early infection has no parasitic action (as *in vitro*), and that it is only when the *natural* systemic reaction or reaction of the tissue-cells has taken place that the drug acts—further that the reaction of the tissue cells in itself usually suffices to cure a malarial-infection, but that the cure appears to be hastened by quinine, it appears likely that immune-bodies like amboceptors have been produced by the tissues that enable the quinine to be shackled on to the parasite, and until such amboceptors are produced no such action can take place.

Quinine, therefore, can be taken at any rate as a working hypothesis, to be useless either therapeutically or prophylactically, until the necessary tissue-reactions have occurred, and it then follows that to give it therapeutically before 'Korteweg's initial stage' is over is to waste the drug, and to give it prophylactically is even much more wasteful, because for all practical purposes the fever can be stopped, if it can be at all, by minimal doses when it breaks out. Of course the prequisite tissue-reactions may not take place at all, and then quinine is completely useless and the only measures of any benefit are rest, good food, and so on.

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[*Note.*—We are not in agreement with the writer's conclusions; they are also opposed to those of most malarialogists of the present day. The Committee of the League of Nations Health Organization which was responsible for the Fourth Report were fully aware of the work of Swellengrebel and his colleagues.—EDITOR, *I. M. G.*]

TREATMENT OF NAGA SORE

SIR,—Since 1930 I have had occasion to treat numerous cases of Naga sore, and the routine treatment of the Naga sore with the strongest antiseptics, such as carbolic acid, has met with failure in my hands. The bacteriology of the disease led me to think of spirochæticidal treatment with N.A.B. As the germs