QUININE PROPHYLAXIS IN NORTHERN INDIA.

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(Continued from p. 184.)

IV.—INDICATIONS AND TECHNIQUE.

Among the many methods described for administering quinine prophylactically are the following:—

Koch’s.—This is known as the “long interval prophylaxis” and consists of giving fifteen grains on the tenth and eleventh days.

Plehn’s.—“Double prophylaxis” consists of giving seven or eight grains of quinine every fourth and fifth, or fifth and sixth days.

Indian Method.—A medium size dose (ten grains) is given twice a week on two consecutive days.

Ziemann’s.—He gave 15 grains every four days.

Deeks [40] found that prophylactic doses of 15 to 20 grains twice a week greatly reduced the number and severity of the admissions by limiting the parasitic development sufficiently to prevent severe symptoms and to establish tolerance.

Stott [41] gave ten grains thrice weekly with unsatisfactory results.

In these methods the drug is given in fairly large doses intermittently, the object being to have the quinine in the blood in sufficient concentration to kill off easily and quickly any parasites which may have entered the body meanwhile and commenced their schizogonic cycle. The argument against this “large dose” method is that in a person bitten immediately after the effect of a dose has passed off, the parasite has a considerable time to multiply before the action of the second dose is felt.

The oldest method of giving quinine is by small doses daily, and originally it was hoped that with a small quantity of quinine constantly circulating in the blood any malaria parasites introduced into the body would be immediately destroyed. We now know that this is not the case. This method, however, continues to be the favourite, and it is generally held that the small amount of quinine always present in the blood exercises its effect on the malaria parasites after they have commenced multiplying by preventing or inhibiting subsequent schizogonic cycles. In Italy a dose of two to three grains daily has accomplished good results.

In Panama good results have been reported with a daily dose of three to six grains increased or decreased according to prevalence or virulence of the disease.

Celli’s method is to give three grains of quinine each morning and three
grains each evening. He holds that harmful effects from quinine are thus avoided and that quinine immunity does not occur.

Perhaps the most approved method is to give five grains daily in the evening. James recommends a further dose of five grains about midnight where a mosquito net is not being used. Castellani gives five grains daily and a double dose once a week.

Hehir [42] recommends five grains daily in stations where malaria is comparatively mild, and an extra five grains on the seventh day where the disease is moderately severe. Where severe, or very severe, ten grains is given daily for six days and twenty grains on the seventh. Watson [43] agrees that doses of less than six grains daily are of little value where malaria is intense—say where the spleen rate is over sixty. Where the malaria is intense and the population consists of immigrants he recommends ten-grain doses six days out of seven, and twenty-grain doses when suffering from pyrexia or not at work on account of ill-health. He states that 20 to 30 per cent of those taking quinine will be found to have parasites in the peripheral blood.

**The Experiment in the North-West Frontier Province.**

The reasons for the trial have already been discussed.

When considering the question of quinine prophylaxis originally in 1926 certain points were kept in mind:—

(1) That quinine prophylaxis was officially discredited, probably as the result of experiments carried out in Salonika during the war.

It was felt that conditions obtaining in Salonika might differ in essential factors from those affecting the North-West Frontier Province.

In Salonika, in addition to the trials and tribulations incidental to residence in a bad climate, the troops were exposed to the rigors and privations of a campaign. They were continuously under fire, life, apart from its dangers, was deadly monotonous and the vitality of the troops and their resistance to disease became lowered. Also it was appreciated that the type or the intensity of the infection might not be the same. In Nowshera, to which the trial was confined for the first two years, the malaria season is very short, and we can state quite definitely that, for practical purposes, infection takes place in the period between the second or third week of September and the first few days of November. (This is specially marked in an epidemic year.) There is quite a sharp line of demarcation, for while troops returning from the hills the last week in October usually contract a few cases of malaria, parties returning in November escape.

The same is true with certain modifications for other stations with which this paper deals. In Peshawar, it was found later, the season is not so well defined and is slightly earlier. In the Khyber stations the season is decidedly earlier.
Quinine Prophylaxis in Northern India

In ordinary years the infection is mainly benign tertian; in epidemic years malignant tertian is the prevailing type.

Though malaria infection is intense it has been attended by very little mortality in recent years. In Nowshera the morbidity rate has varied between 255 per mille in 1925 and 491 in 1922, whereas in Peshawar the worst year recently has been 1923 with an admission ratio per thousand of 479, and the best, 1922, with a corresponding figure of 371.

Hangu and Thal, which are included in the experiment in 1929, have an even worse record.

(2) That there was a firm belief in the lay mind, particularly among planters, that quinine prophylaxis was efficacious and that this belief was shared by many eminent and experienced malariologists.

(3) That in cases where quinine prophylaxis had been employed with success, there was considerable variation in the method of administration.

(4) That prolonged administration of quinine might have disadvantages, e.g., (a) it might be harmful, (b) quinine might lose its effect (i) either by being absorbed in decreasing quantities or (ii) by the parasites becoming quinine-fast.

Controls.—In view, therefore, of the strong body of opinion in the Service and outside opposed to this method of combating malaria, it was realized that the experiment must be well controlled. In Nowshera, in 1926, the British troops selected for the trial occupied ten barrack rooms. These were old buildings with electric punkahs in the main rooms and electric overhead fans in the verandahs. All the troops used mosquito nets. From each room half of the occupants were selected for a course of quinine and the remainder were kept as controls. Both groups lived under identical conditions as to work, play, messing and accommodation. Nominal rolls of both groups were drawn out—in 1926 the quinine group numbered 210 and the control group 228. Admissions to hospital for both groups were recorded as were also attendances at quinine parades of the quinine group.

Particulars of the Trial.—The chief mosquito breeding ground was the stony, gently shelving bed of the Kabul River slowly receding from its banks after the summer floods. It was found impossible to deal effectively with the mosquito-breeding in the river, which ran parallel to barracks and at a distance of about 400 yards. During October and November larvae of *A. stephensi*, *A. subpictus*, *A. culicifacies*, *A. maculatus*, *A. gigas* and *A. turkhudii* were all taken in this situation in large numbers.

It is interesting to note in this connection that in 1927, as late as December 3, the Kabul yielded larvae of the *A. stephensi*, *A. turkhudii* and *A. culicifacies*—the maximum and minimum dry bulb temperatures being 79°F and 39°F, respectively, and the temperature of the river water at the time of collection 58°F.

Another phenomenon in connection with this river, which I have not been able to explain, occurred in 1928. The river fell and the mosquito
breeding began as in previous years; and one awaited the commencement of the usual outbreak of malaria. Suddenly, for no apparent reason, mosquito breeding ceased and did not recommence. There was nothing to account for this in rainfall, humidity, temperature or wind, but the explanation may lie in some alteration in the chemical content of the water or in the failure of some necessary food supply. A welcome freedom from malaria resulted, and the year 1928 showed the lowest incidence of malaria on record.

In addition to the river, there were other sources of breeding in the immediate vicinity of barracks, e.g., wells, diggies, irrigation channels, pools after heavy rains. These, however, compared with the river, were comparatively easy to deal with.

The reservoir of infection was immense, for numerous bazaars, large and small, encroached on the barracks on all sides.

It was realized, therefore, that if the trial was to be successful, a comparatively large dose of quinine would be essential on account of the intensity of the infection to be dealt with. Watson's method, with certain modifications, was adopted.

*Dose and Salt.*—Ten grains of quinine sulphate. It was appreciated that quinine sulphate is not so readily absorbed as other salts, and that in treatment it sometimes fails to bring down the temperature, rendering a change of salt necessary. On the other hand, it is cheaper and it is more slowly excreted than other salts, and so its action is continued over a longer period.

The drug was made up in solution with the addition of citric acid.

*Frequency of Dosage.*—Daily for three weeks except Saturdays, when a purge was given with a view to stimulating the liver and increasing the power of the body to absorb quinine. It was hoped with this short course and one rest day per week that any disadvantages which might accrue from prolonged administration would not be encountered.

*Time of Administration*—Evening, between 6 and 7—exact time arranged so as to interfere as little as possible with games. This time also allowed for the maximum concentration of quinine in the blood during the period when the men were most likely to be bitten.

*Method of Administration.*—Quinine stations were established on a verandah in barracks. The parades were not held in hospital, so as to take up as little as possible of the time available for recreation. Bottles of quinine solution, a supply of one ounce gallipots and a basin of clean water were laid out on a table, and a bucket was placed alongside on the floor. One orderly filled a gallipot with quinine solution and handed it to the first soldier, who drank it down and then called out his name (this ensured that the quinine was actually drunk). An N.C.O. recorded the attendance.

The soldier handed the gallipot to a second orderly, who washed it. One hundred men could pass through each such station in less than ten minutes.
In the case of the Royal Artillery units the orderly officer was present at quinine parades. The C.O. of the infantry attended his own parade. A medical officer was present at the earlier parades and frequently later.

Absentees were accounted for and attended later, and arrangements were made for men on guard to receive their dose.

All cases of fever were admitted to hospital, and no quinine was given in barrack (outdoor) treatment except as part of the routine post-hospital malaria course. On admission, the urine of fever cases was subjected to the acid Tanret test to determine the presence, or absence, of quinine. A routine treatment was carried out. A diaphoretic mixture was given and a sharp purge. Thereafter salicylates were administered until the diagnosis had been definitely established. Two blood-films, a thick and a thin, were taken, stained and examined on admission, and twice daily thereafter until malaria parasites were found, when quinine treatment was commenced.

In the cases of benign tertian infections this consisted of quinine sulphate ten grains t.d.s. in acid solution during the first and third weeks, an iron and arsenic tonic only being given in the second week. During the fourth to eighth weeks inclusive the case received quinine sulphate ten grains once daily. The patient was discharged from hospital as soon as he was fit enough, and he continued the course of treatment in barracks, all doses being marked up on a treatment card. Malignant tertian cases received treatment on the same lines, but for three weeks only.

As soon as a diagnosis of malaria was made, the fact was entered up on the duplicate quinine or control roll kept in hospital. The rolls were again checked as cases were discharged.

In 1926 records were maintained till the end of November, though quinine prophylaxis was only given for three weeks in October, viz., 4th to 24th inclusive.

It was thought that any malaria "suppressed" by the quinine exhibited during the three weeks in October would reveal itself before the end of November.

The results of 1926 were considered encouraging, and instructions were received to continue the trials on a larger scale, and so in 1927 the scope of the experiment was extended to include Indian troops, as well as British, in Nowshera. The quinine mixture was given for three weeks during September, and again for three weeks during October, with an interval of ten days between the courses. Owing to the commencement of training camps, manoeuvres, etc., it was not considered practicable to continue observations during November. With these exceptions, the trial and the procedure carried out were exactly similar to those obtaining the previous year. The ten-day interval was adopted to eliminate or diminish any tendency for the production of quinine-fast parasites and to avoid any possible harmful effects which might result from ingestion of quinine by a large body of troops over a long and continuous period. It was recognized that the subjective effects of consumption of quinine pass
off in a few days, and it was felt that the action of quinine on the parasites might be correspondingly reduced for some reason other than the parasites becoming resistant to quinine.

In 1928, in addition to British and Indian units in Nowshera, certain British and Indian units in Peshawar were included in the experiment. The procedure was exactly the same as in the previous year, except that the dates were different, quinine being given from September 24 to October 13 and, after a ten-day interval, from October 24 to November 14. Actually, from November 1 onwards, owing to training, practice camps, etc., the issue of quinine became unreliable and records were not kept. This experiment, therefore, was considered to terminate on October 31, 1928.

In 1928 also, advantage was taken of the fact that the two-yearly relief of Chitral was taking place. On the outward journey one company of the 3/1st Punjab Regiment and one company of the 4/6th Punjab Regiment received prophylactic quinine. On the return journey the same company of the 3/1st Punjab Regiment and one company of the 3/8th Punjab Regiment received prophylactic quinine. The remainder of the force acted as a control.

The drug (bihydrochloride of quinine), two tablets of five grains each, was given in the evening during the concentration period at Dargai during the march from Dargai to Chakdara and for three days thereafter. On the return journey the tablets were given during the march from Chakdara to Dargai and for three days after the troops left Dargai. The Dargai-Chakdara zone was heavily infected with malaria. There was very little malaria in Chitral itself or in the country between Chitral and Chakdara.

Tablets of quinine were given because it was impracticable either to make up the solution or to carry it on the line of march. The bihydrochloride was used because of its greater solubility.

The diagnosis of malaria was on clinical grounds only, the detachment of a Field Ambulance accompanying the column having no facilities for microscopic examination.

(To be continued.)