BLACKWATER FEVER IN MACEDONIA.*

BY

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THE nature of blackwater fever is at present undecided, but the work of the majority of recent observers may be summed up in the following conclusions stated by the Panama Canal Commission. Blackwater fever only occurs when a population not immune to malaria becomes exposed to extensive infection by it, when relapse and reinfection are therefore common, and owing to unfavourable conditions proper quinine treatment has not always been obtainable. It has also been found by many observers that quinine is in a very high percentage of cases the determining cause of an attack. When attacks have occurred under observation in hospital, the antecedent administration of quinine has been practically universal. The conditions quoted above were all present among the Allied Forces in the Balkan campaign from 1915 to 1918, and blackwater fever duly appeared. Conditions were especially favourable in the Serbian army, for not only was malaria a comparatively rare disease in Serbia, but also the army became highly infected when training in Salonica in 1916, and owing to various causes proper treatment could not be given.

The 41st General Hospital acted as base hospital to the Serbian army from August, 1916. During the autumn and winter of 1917-18, blackwater fever appeared in the Serbian army, and was treated both by us in this hospital and also by Parsons and Forbes¹ in two other base hospitals attached to the Serbian army.

The question of the existence of a quinine haemoglobinuria separable from true blackwater fever is answered in the negative by these observers, and experience at the 41st General Hospital confirmed this: both mild and severe attacks of haemoglobinuria occurred as a direct result of the administration of quinine, some of the latter proving rapidly fatal. The only possible differentiation would appear to lie in the severity of the attack, a severity which can undoubtedly be influenced by the treatment given. Experience in Macedonia, therefore, gave no justification for any such differentiation.

The relationship of malaria to blackwater fever was always close. By the beginning of August, 1916, when British base hospitals were first provided, the Serbian army had become widely infected with malaria; and the great number of patients admitted during the autumn were suffering from the disease, often in a very severe form. Nevertheless, though thousands of cases of malaria passed through the hospital during the winter, no cases of blackwater fever occurred. The latter disease did not appear till the autumn and winter of 1917-18, when the Serbian army had passed through two severe malarial seasons, and was heavily infected with chronic malaria. If blackwater fever is an independent disease, it is very remarkable that it did not appear in the winter of 1916-17, as the ground then occupied was practically the same as in the following year, and the conditions of existence in the second year were much improved.

The incidence can, however, be explained if the view be taken that blackwater fever only occurs in patients suffering from chronic malaria. The Serbian army was first extensively infected with malaria in 1916, so that the disease was not sufficiently chronic in the winter of 1916-17 for blackwater fever to appear. Evidence of chronic malaria was present in all cases that occurred at the 41st General Hospital.

The nature of the malaria parasite, whether benign or malignant, and the severity of the malarial attack for which quinine was given, did not appear to be of importance. It has been claimed that blackwater fever is only connected with the malignant form of malaria; but cases occurred in which the administration of quinine for a proved benign attack was followed by blackwater fever. It must be remembered that scarcity or absence of parasites in the peripheral blood cannot be taken as evidence that the infection is a malignant one, for both the

administration of quinine and the attack of blackwater fever itself cause rapid disappearance of the benign parasite. Some of the cases contracting blackwater fever did not show any great degree of malarial cachexia such as is usually found in the malignant type. Blackwater fever may therefore be associated also with a mild benign tertian infection.

All the cases in the hospital as well as most of those of Parsons and Forbes occurred between October, 1917, and April, 1918; no further cases were seen between April, 1918, and August, 1918; it was therefore a winter disease. The common sequence was a chill followed by malarial relapse, with which blackwater fever was associated.

The relationship of quinine administration to the attack was very definite. Eight attacks of blackwater fever occurred in patients who were already in hospital, and all rapidly followed the beginning of a course of quinine treatment. One attack was of especial interest:

The patient had already been treated for an attack of blackwater fever, but his temperature still remained irregularly raised. Although repeated examinations of the blood failed to demonstrate any parasites, it was thought possible that the condition was malarial in nature, so a further course of quinine was decided upon. On the second day of this course an attack of blackwater fever again took place. Shortly afterwards an abscess declared itself at the site of a subcutaneous saline injection, which had been given in treating the first attack, and the patient was also suffering from pyorrhoea. Subsequent malarial attacks proved to be benign tertian in nature, and parasites were easily found. It is therefore probable that the raised temperature was due to the abscess and the pyorrhoea, and was not malarial in nature. On this hypothesis, the administration of quinine was alone responsible for the attack of blackwater fever—that is to say, quinine can produce an attack in a patient with chronic malaria, though no malarial relapse is present.

The routine method of quinine administration was either 30 grains daily by mouth or 20 grains intramuscularly morning and evening. It was found that the amount of quinine administered before an attack of blackwater fever took place varied in different patients. From this the idea arose that each patient had a critical dose, and that amounts below this could be tolerated successfully. This was tested in three cases who had subsequent malarial attacks.

In one of these, the second known attack followed the administration of 30 grains of quinine by mouth within twenty-four hours. As a result of a theory that intramuscular quinine might be better tolerated than oral quinine, an attack of benign tertian malaria, which followed nineteen days later, was treated with 20 grains intramuscularly on the first day and 10 grains on the following morning. Blackwater fever again occurred. Two subsequent attacks of malaria were successfully treated with doses of 10 grains per day, given in the first instance intramuscularly and in the second orally.

The other two cases were also successfully treated for subsequent malarial attacks with doses below the critical dose. The occurrence of blackwater fever in a case of malaria does not, therefore, contraindicate treatment by quinine for further malarial relapses, if the critical dose is known, for doses smaller than this can be safely given. In a case known to have had blackwater fever, but whose critical dose is unknown, cautious administration of quinine is also justifiable for a malarial relapse, if careful watch is kept for the first signs of blackwater fever; for energetic treatment in the earliest stages, on lines to be given later, should avert the chief dangers of this complication.

The effects of continued administration of quinine, when blackwater fever has declared itself, were in every case very serious.

In one of the early cases a full course of quinine was continued after blackwater fever had occurred. This case died exactly one week later from a further attack, so acute that haemoglobin was only present in the tubules of the kidney and had not yet reached the bladder. In two other cases the administration of quinine for a period of twenty-four hours after the attack had begun caused suppression of urine, which reached a maximum in five days, and was, in one case, complete and fatal, in the other almost complete and only recovered from after a long and severe illness. Two other cases were even more rapidly fatal.

Continued administration of quinine would, therefore, appear to be most dangerous.

The course of the illness varied considerably, but in practically all cases the general condition of the patient on the first day did not appear dangerous. In the severe cases mental confusion and drowsiness became marked

* Abstract of a paper published in the *Annals of Tropical Medicine and Parasitology*, vol. xiv, No. 1, p. 3.