Hæmoglobinuria on the Indian Frontier.

A Second Communication.

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A paper on this subject was published in the Journal of the Royal Army Medical Corps, issues of March, April and May, 1934. For a proper appreciation of the present communication, the original paper should be consulted. This paper is merely in continuation of the original. It brings to notice a recent case which ended fatally. This case is the first to be reported since August 13, 1933. It forms number eleven in order of incidence, and furnishes the seventh death. As in all the former cases, the patient was an Indian; the total amount of plasmoquine administered was small; the illness was rapid and severe; and stoppage of the drug immediately after it became evident that something was amiss produced not the slightest effect on the progress of the malady.

Patient's Particulars.—A Mussulman (Pathan) sepoy of an infantry regiment. Aged 28. Service, eleven years; in Waziristan, five; in Burma, four; and two years in the N.W. Frontier Province, where the present attack took place.

Past Army Medical History.—In January, 1931, on out-patient treatment for enlarged spleen. Spleen two finger breadths below costal margin. No malaria parasites found.

In February, 1934, admitted to hospital, and diagnosed "Malaria, clinical relapse." No malaria parasites found.

Present History.—On August 19, 1934, again admitted to hospital with "Malaria, clinical, relapse." No malaria parasites found at this, or at any subsequent date.

Atebrin, 0.1 gramme, t.d.s., administered for seven days. Total atebrin taken, 2.1 grammes, spread evenly over one week.

Atebrin present in the urine on fourth day of the course. No toxic signs or symptoms.

On August 29, 1934, patient was discharged from hospital. Interval between cessation of atebrin course and commencement of plasmoquine course—four days.

On August 30 and 31, and on September 1, 0.01 gramme plasmoquine, b.d., was given. No more plasmoquine, or other antimalarial drugs were administered thereafter. Total plasmoquine taken, 0.06 gramme, spread evenly over three days.

Onset.—Sudden: one hour after administration of second dose of plasmoquine, on September 1.
Severe pain in epigastrium and back; severe nausea and vomiting; stools and urine black in colour.

Condition on Admission to Hospital, September 2.—Temperature 99.6° F. Pulse 82, of good volume and tension. Respiration 20. Mentally quiet and rational. Generalized icterus well marked in the conjunctivæ. Epigastrium painful and tender. Spleen enlarged to a hand-breadth below the costal margin. Liver palpable, but not tender.

Blood: Red blood cells, 3,125,000; haemoglobin, 60 per cent.; white blood cells 8,750; polymorphonuclears 68 per cent.; large mononuclears 5 per cent.; lymphocytes 27 per cent.; eosinophils nil.

Urine: Passed in small quantities; eight ounces this morning. Colour, smoky to black. Acid reaction. Albumin abundant. Granular and tube casts plentiful, and red blood corpuscles present in a heavy, brown, amorphous deposit. District Laboratory reported haemoglobin, as well as red blood cells.

Stools: Semi-solid, black. District Laboratory report on the presence of blood was negative.

Treatment: General, with two intravenous injections of saline, sod. bicarb. and glucose.

Progress.—On the morning of September 3, nausea and vomiting had ceased, but the jaundice had deepened, no urine had been passed and the stools remained black. A slight improvement in the general condition was recorded.

At noon 10 ounces of urine, and at 11 p.m. 15 ounces of urine were passed. Examination of the urine yielded the same results as on September 2.

On September 4, temperature 100° F. and pulse 104. General strength maintained.

This morning, two ounces of a one per cent solution of methylene blue were administered intravenously; and at noon an intravenous solution of saline, sod. bicarb.-glucose was given. The latter had to be cut short, owing to the onset of a very severe rigor.

From this date, suppression of urine set in.

September 5: From this day onwards, anuria was complete, and the patient's condition steadily deteriorated.

Saline injections were continued, and on September 7 the methylene blue injection was repeated.

On September 8 the red blood cells numbered only 2,400,000, and the haemoglobin percentage had fallen to 50. Blood transfusion was carried out.

A second blood transfusion was given on September 9, when the red blood cells count was down to 1,100,000, and the haemoglobin fell to 25 per cent.

The patient made no response to treatment, and death occurred on the morning of September 10.
Notes.—By the officer in command of the patient’s hospital:—
“A most exceptional case. . . . There is no question of an over-
dose of plasmoquine, as this drug is only in the hands of the sub-
assistant surgeon who personally gives it out.”

By the District Medical Specialist:—
“This man was under treatment for an attack of malaria; parasites
were not found in the blood, but the clinical condition left little doubt
about the diagnosis. . . . I saw the register of out-patient plasmo-
quine treatment, and there appears to be no doubt that the man
received only the prescribed dosage of the drug.”

Remarks.—This case bears a strong general resemblance to the cases
which were described in this Journal in March to May of 1934; and, in
individual characteristics, it is identical with some of these cases.

It is of great interest to note that methylene blue, even in heavy dosage
(it was given somewhat late in the attack), produced no effect.

This at once raises the question: did the haemoglobinuria take the form
of oxyhaemoglobinuria or methaemoglobinuria?

Although it is known that the former is no more pathognomonic of black-
water fever¹ than the latter is pathognomonic of plasmoquine poisoning,
still there is—in the light of our present knowledge of haemoglobinuria—a
balance of diagnostic probability when one or other of these two forms
occurs, or predominates, especially in the earlier stages of the attack.

In this case the clinical records give no indication as to whether the
medical attendants were dealing with oxy- or with methaemoglobinuria.
After all that has been written and said on this subject, it is disappointing
to find that the District Laboratory concerned failed to make the requisite
differentiation; and that the clinicians concerned failed to call for this most
important information.

Why is it of such importance to employ the spectroscope in these
obscure cases?
Because an early report of oxyhaemoglobinuria or of methaemoglobinuria,
as the case may be, will perhaps carry us a big step forward in the solution
of a vexing and vital problem.

This problem may be restated thus:—
(1) Does true blackwater fever occur, as an entity, amongst natives in
the west and north-west of India?
(2) Are these cases simply and solely due to plasmoquine poisoning?
(3) Can plasmoquine alone, or in combination with one or more
unknown factors, precipitate an attack of what we call blackwater fever?

¹ For the latest work on this subject, see “Laboratory Studies in Malaria and Black-
and R. J. Bromfield. Transactions of the Royal Society of Tropical Medicine and
Unfortunately, the case now recorded leads us no farther on the way to an answer to any one of the three questions comprising our present haemoglobinuric problem; but it presents certain features which have called forth this communication. It was a soldier—Napoleon—who said that: “Repetition is the figure of speech for the crowd”; and it seems to us that, at present, some hope of successful diagnosis lies in concentrating on the intimate blood changes which occur in this perplexing malady. And as for prophylaxis, why are these eleven patients all Indians? \(^1\) The answer to this question may provide a clue; but, to date, this riddle, too, remains unsolved.

\(^1\) In military medical practice in India, the sepoy only receives two-thirds of the dose of plasmoquine given to the British soldier; and his maximum daily dose is only 0.02 gramme.