NOTES ON FOUR CASES OF BLACKWATER FEVER OCCURRING IN SOUTHERN NIGERIA.

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Blackwater fever is seldom encountered by Officers in the Royal Army Medical Corps. The writer has had the fortune to have had recently under his care four cases of this formidable disease. It is thought that short case notes and a summary of some interesting features observed may justify publication. Three of the four patients were officers who had been in Africa in a civilian capacity for some years before entering military service in this war. Two had suffered from blackwater fever previously. In none was there a really bad malarial history.

The clinical manifestations of the disease were quite different in each case, in fact haemoglobinuria was almost the only factor common to all.

Case 1.—Lieutenant W., aged 41, had lived in East Africa for seventeen years. His last attack of malaria was in December, 1940, in West Africa. Had blackwater fever in 1936. He had been noted to be pale and ill-looking for some time previous to admission. He stated that he had felt very unwell for some days but had undoubtedly been unwise in his alcoholic consumption, particularly of late. It was felt that the history that he had passed "black" urine for the first time two hours before admission was not to be relied on. He was admitted on the evening of November 29, 1941, and died of uræmia on December 6, 1941.

Case Notes.—29.11.41 — 19.00 hours. Condition on admission. Pale, slightly delirious, temperature 104°2. Pulse 120, liver slightly + and tender, spleen not enlarged. No prostration, and after settling down in hospital became quite sensible. Passed small quantity of urine which was dark red to black in colour. Blood films — no malarial parasites seen. Treatment absolute rest in bed—quinacrine tab. 1 four hourly. Copious fluids by mouth, fruit juice, glucose and weak tea. Alk. powder, 31 emulsified in water, to be taken hourly until urine becomes alkaline.

30.11.41: Seen at 02.30 hours—general condition much improved. Temperature 100° F. Sweating but no improvement in urine, of which he had passed a few ounces since admission. It was now almost black.

Pints vi fluids had been taken by mouth up to this time.

Later—10.00 hours. General condition fairly good but marked pallor, alert mentally and very co-operative. B.P. 128/90. Urine passed since admission ounces ix, uniformly black and in spite of intensive administration of alkali it was still slightly acid. Blood examination—total R.B.C. 3.75 ml., Hb. 80. Slightly jaundiced—pale yellow haemolytic type. Typed for blood transfusion and crossed typed with two donors with whom he was found to be compatible. Treatment—enema to be followed by rectal alkaline saline. Quinacrine was discontinued in evening as it was not considered safe on account of oliguria. Glucose fluids by mouth ad. lib. Alk. powder to be
Case 1.—Temperature Chart,
continued until urine alkaline. Urinary output entirely inadequate, always black.

13.00 hours: Condition satisfactory except for oliguria.


15.00 hours: Pints i, 2 per cent soda bicarb. in normal saline intravenously.

21.00 hours: Pints iss repeated intravenously. In addition intake by mouth pints v during day. Urinary output ounces ii only. Purgative given.

2.12.41. 10.00 hours. Urine ounces vi has redder tint pointing to fresh hæmolysis. No œdema—lungs clear. B.P. 105/60. Liver further enlarged. Vomiting frequently. Total R.B.C. 2.3 mil., Hb. 40 per cent. Blood urea 113 mg. per 100 c.c. No other uræmic manifestations.

15.00 hours: General deterioration. 450 c.c. citrated blood given by drip in 75 minutes. Felt better for this.

21.00 hours: I.S.Q. Day urine ounce ½. Condition appears hopeless. Urine contained heavy deposit of pus cells.

3.12.41: Night urine ounce i and showing evidence of fresh hæmolysis substantiated by blood-count. T.R.B.C. 2 mil., Hb. 38. Blood urea 210 mg. per 100 c.c. A drip infusion—soda bicarb. 3 per cent, glucose 5 per cent in normal saline—continued for four hours during which pints iii were given; no urine; patient now definitely uræmic, vomiting and twitching but showing no œdema. Prognosis almost hopeless.

4.12.41: Ounce 1 urine during last eighteen hours. Uremic manifestations ++, consciousness dulled. Further active treatment not indicated. Passed ounces iii of urine which raised fresh hopes, coloured pink though dearer—placed on continuous oxygen during night. If urinary output improves a further transfusion will be given in morning.

5.12.41. 06.00 hours: Complete suppression of urine, unconscious; shallow Cheyne Stokes respiration. Morphia gr. ½ i.v. as patient very restless.

12.17 hours. Died peacefully.

No necropsy performed.

Commentary.—This was the second attack of blackwater fever in a man who had spent eighteen years in Africa and who had been in very poor health previous to his illness. Hæmolysis was massive and recurrent. Intensive alkaline treatment by mouth and i.v. failed to prevent oliguria and later complete anuria or effectively to alkaline the urine. Intake of fluids by mouth in the seven days of illness was pints xxxviii, intravenously pints vss and by blood transfusion pint i. Total urinary output over whole period was ounces xxii. He lost approximately pints iii by vomit and a fair quantity, not more than pints v, by bowel. Diaphoresis was—seldom more than just obvious and yet (unless terminally) there was no œdema. The pulmonary bases remained dry and there was no ascites. It must be presumed that the renal tubules were effectively blocked by acid hæmatin crystals almost before admission. The clinical picture was one of progressive uræmia and anaemia and did not in any way react to treatment. I feel that the discon-
tinuation of quinacrine after first eighteen hours was inevitable owing to failure of excretion. He was a very excellent patient throughout and did all he could to keep cheerful and co-operate in his treatment.

Case 2.—Lieutenant G., aged 28.

Case Notes.—Had been employed by a trading firm in Nigeria from 1936 to 1940, when he was commissioned in the Royal West African Frontier Force. He did not suffer from malaria until October, 1940. There was a mild relapse in January, 1941. Except for this he had been in good health for the last five years. He states that he took his daily quinine regularly. He had not felt well for ten days before admission to hospital and had been under the care of his Regimental Medical Officer. Had suffered from lethargy and headaches. Three blood films were negative for malaria before admission.

Condition on Admission.—Afebrile. Complained of headache—examination N.A.D.

23.3.42: Blood film—negative malaria—urine normal—spleen not palpable.

24.3.42: Febrile during the day—very severe headache not relieved by veganin. Treated quinine grs. x t.d.s. Three blood films negative malarial parasites. Had fair night, vomited early morning and at 08.00 hours informed Sister that he had passed "black urine." Severe rigor, vomited. Temp. 104°. Conjunctivæ icteric. Passed ounces v urine, dark and opaque with heavy deposit suggesting severe massive hemolysis. Reaction neutral. Blood-typed—T.R.B.C. 38 mil. (Hæmogram p. 68. No further mention of hæmatological examination will be made.)

Treatment.—Absolute rest—copious fluids—water, fruit juice, dextrose, alkaline mixture g. ii (sodii bicarb. 2 parts, pot. cit. 2 parts, cal. carb. 1 part) two-hourly until urine alkaline and then regulated to maintain this. He had quinacrine g. 0.2 t.d.s. on this day. No further anti-malarial drugs were administered after this day.

26.3.42: Condition very grave—repeated rigors and vomiting. Skin and conjunctivæ rapidly showed severe hæmolytic jaundice—deepening from hour to hour. Passed ounces xcii urine in first twenty-four hours, every specimen showing results of gross hæmolysis—black to dark red—heavy amorphous deposit but remaining neutral or just alkaline. Intake pints x. B.P. 102/65. Morphia grs. ½ given at 10.00 hours with a markedly beneficial effect—rigors and vomiting ceased and patient got a badly needed rest. At 12.30 hours 400 c.c. homologous blood given by drip over three hours. Rigor at 16.00 hours. Vomiting again was incessant from 22.00 hours till midnight when morphia grs. ½ was repeated with good result. The vomit was usually deeply bile-stained. Later specimens of urine showed some improvement.

27.3.42: Very weak and anæmic—deeply jaundiced. B.P. 115/55. Fluid intake pints xiv, urine ounces lxvi definitely clearing but still showing hæmoglobin in progressively less amounts. Transfused 400 c.c. homologous blood drip three hours from 12.00 hours.

From this on there was a steady improvement, urine clearing, no further rigors, vomiting occasional, jaundice rapidly clearing; pulse improved, loud hæmotic murmurs heard at cardiac apex and over P.A. Passed ounces lxx urine, now almost clear. Further donors standing by.

28.3.42: Progress maintained—urine tinge of methæmoglobin. Feeling better and stronger, no evidence of air hunger or restlessness, pallor extreme, jaundice almost cleared. Feeds increased—jellies, Benger's, etc.
29.3.42: Progress as satisfactory as possible in circumstances, urine clear but contains albumin. No rigors or profuse diaphoresis. Desperately pale but transfusion withheld as no definite air hunger or restlessness present and fear of danger of further haemolysis. Intake and output satisfactory. Bowels opened well after enema. Still febrile.

30.3.42: Weak and apathetic, extreme pallor, vomited once. urine clear ounces lx. Three blood films negative malarial parasites. No evidence cardiac failure or air hunger. Later at 15.00 hours showed deterioration, muscular twitching generalized, restless and showing some respiratory distress. Blood 800 c.c. (400 c.c. from two homologous donors) drip from 17.00 hours to 23.00 hours when generalised muscular twitching became severe and second transfusion stopped with 0·10 c.c. to go. This was followed by a rigor and hyper-pyrexia.

31.3.42: Morphia grs. ½ repeated, slept well till morning. General condition improved, twitching slight, vomiting occasional, taking nourishment well, somewhat drowsy. Urine ounces lvi quite translucent but has faint black tinge quite unlike that seen when urine was clearing. Blood urea 213 mgs. per 100 c.c. and this in spite of free diuresis throughout.

1.4.42: Good night. Fluid intake ounces cxix, urine clear, ounces lxv, containing albumin. Is still showing uraemic manifestations—drowsy, occasional vomit and twitching. Still very exsanguinated. Blood urea 180 mg. Some guarding over right hypochondrium and liver dullness enlarged downwards but edge is not palpable. Slight lemon-yellow tint persists in skin and conjunctive. Recovery being retarded by uraemia and anaemia. Good result to enema.

2.4.42: Improved, looks and feels better. Muscular twitching now very slight, not so drowsy. Blood transfusion indicated, 400 c.c. three hour drip, followed by mild rigor, temp. 103° and profuse diaphoresis. Later progress satisfactory. Tremors slight and seldom, alert mentally.


4.4.42: Very satisfactory—no uraemic signs. Anahæmin 1 c.c.

5.4.42: Very satisfactory. Anahæmin 2 c.c.

7 & 8.4.42: General improvement persists. Developing troublesome superficial sepsis. Carbuncle on left buttock and right thigh and left index finger and on head. Ferri et ammon cit. gr. xxx t.d.s. Diet, restricted protein intake.


11.4.42: Satisfactory; superficial sepsis well localized and doing well.

12.4.42 to 14.4.42: Remittent pyrexia with some constitutional disturbance which could not, in ordinary circumstances, be attributable to the localized superficial sepsis. Chart shows coincidental deterioration in blood picture but blood urea dropping to 66 mg.

15.4.42 to 20.4.42: Occasional slight rises to 99° but general condition excellent. Campolon 2 c.c. I.M. Blood picture shows gradual improvement but R.B.C.s still under 2 mil. Blood urea on 20.4.42 was 87 mg.

21.4.42: All septic foci have now healed. Careful general examination, N.A.D., except spleen though not palpable is enlarged (percussion). Feels well. Good appetite, evening temp. 100°.

25.4.42: Afebrile last twenty-four hours. Progress very satisfactory.

27.4.42: Blood urea 49 mg. per 100 c.c. Pyrexia, vomiting. Malarial parasites seen in blood film. Reacted quickly to quinacrine g. 0·1 t.d.s.

12.5.42: Convalescence smooth. Blood urea:—30 mg. per 100 c.c.

The interesting features of this case were:

(i) Nitrogen retention combined with free diuresis and without evidence of nephritis or renal insufficiency. Uremic manifestations were first seen three days after haemoglobin had ceased to be present in the urine and after a very adequate urinary output had been maintained ab initio. Moreover, the blood urea did not return to anything like a normal figure until a month later. I cannot attempt to explain this except on the grounds that it was probably due to inadequate tubular function while glomurular function remained unimpaired.

(ii) The continued deterioration of the blood picture for six days after the urine and/or skin ceased to manifest any further evidence of haemolysis, and this despite blood transfusion. There seem to be two more obvious possible explanations of this (1) Haemodilution during early recovery stage; no blood volume estimations were carried out but clinically there was no evidence to suggest this. (2) That further slight haemolysis was taking place insufficient for haemoglobin to pass the renal threshold or produce any obvious haemolytic jaundice; this of course is possible but not convincing.

(iii). Value of repeated small slow blood transfusions. In this case it was felt that this was a life-saving procedure. There was undoubtedly a reaction on three occasions (rigor, pyrexia and diaphoresis) following transfusion in spite of the most careful matching of homologous blood but it did not reproduce haemoglobinuria. Nevertheless, the writer feels that transfusions are
not to be undertaken without carefully weighing up the pros and cons, always remembering that one is quite ignorant of the pathogenesis of the disease and what pulls the haemolysis trigger. The minimum time to administer an Army transfusion set bottle was never less than three hours. One aimed at 40 to 50 drops per minute.

(iv) Parenteral liver extract was given on the assumption that liver function was grossly upset and that it was possible that the intrinsic haemopoietic factor might not be mobilized as it would in an ordinary case of anaemia due to haemorrhage. The reticulocyte response was very striking—post or propter.

(v) Some factor other than the development of carbuncles retarded the recovery in this case and, though malarial parasites were not found until the thirty-third day, it is believed that malarial infection was probably the cause of this.

(vi) A very high colour index (1·6 to 1·2) was a persistent feature right into convalescence.

Case 3.—Captain T., aged 37.

Case Notes.—Had been employed by a trading firm in S. Provinces, Nigeria, since 1928. He suffered from blackwater fever on arrival in England on leave in 1932. Since then he has suffered from malaria of sufficient severity to need treatment in hospital once during each tour. He had felt unwell for about a week before admission. There had been low fever and diarrhœa during this period.

25.3.42: Temp. normal, later 101·2°. General examination; N.A.D. except slight icteric tinge in conjunctæ. Urine contained bile pigment and bile salts and a trace of albumin. No malarial parasites seen in blood film. Some diarrhœa, faces semi-liquid, hot dysenteric. Treated as case of infective hepatitis and, in view of history, quinacrine gr. 0·1 t.d.s. and quinine grs. x b.d.


27.3.42: Improved; urine only faintest tinge of bile pigment.

28.3.42: Felt much better in morning. Temp. normal. At 15.00 hours felt very unwell after a sleep and passed urine containing much haemoglobin and debris; it was opaque and dark red. Temp. 104·2°. Vomited once. Later there was profuse diaphoresis; soaked through mattress and dripped on to the floor. Treatment: Fluids; orange juice and dextrose ad lib., alkaline mixture two hourly, comp. alk. salts. Urine quickly became alkaline and diuresis was free from the onset of haemolysis.


30.3.42: Improvement maintained; urine clear. Pulse and temp. normal. R.B.C. 2·05 mil. Hb. 45 per cent.

31.3.42: Progress satisfactory. Was restless last night and had morphia gr. ¼ with benefit. Afefbrile. Blood-count, rather surprisingly, shows further deterioration but decided transfusion not indicated.
1.4.42: Had good night. Fluid intake ounces xcvii and urine ounces lxiv, quite clear, no albumin. Blood urea 40 mg. per 100 c.c. Blood shows further deterioration.

2.4.42: Satisfactory, appetite returning, diet increased, egg, fish, chicken, blood somewhat improved.

3.4.42: Progress maintained. Anahæmin i c.c. i.m.

4.4.42: Progress maintained. Anahæmin ii c.c. i.m.

5.4.42: Progress maintained. Campolon ii c.c. i.m.

6.4.42: Satisfactory in all respects. B.P. 104/50. Diet increased; lightly cooked steak. Ferri et ammon cit. grs. xc p.d.

7.4.42: Convalescence entirely satisfactory. Now allowed 4 pillows and is doing a little more for himself daily.

8.4.42: Progress very satisfactory; campolon ii c.c.

9.4.42: Progress excellent; up for long periods.

10.4.42 to 26.4.42: Relapse malaria. M.T. parasites in blood film. Treated, quinacrine g. 0·1 t.d.s. for seven days.


Commentary.—This was a case of one massive hämolysis (hæmoglobinuria lasting twenty-four hours) at the onset following a definite period of ill-health. There was no evidence of nitrogen retention and the convalescence was smooth except for a malarial (?) relapse on the twenty-seventh day when there was a rise in the temperature and malarial parasites seen. The presence of bile salts in the urine accompanying a very slight icterus in the conjunctivæ during the pre-blackwater period in hospital is suggestive that a mild infective hepatitis may have been a factor in precipitating the hämolysis. A surprising feature in these three cases was that the spleen was never palpable during or after the hämolysis.
Four Cases of Blackwater Fever Occurring in Southern Nigeria

Case 4.—C.S.M. S., aged 25.

This W.O. had spent thirteen months on the West Coast, principally in Gambia. He had only suffered from fever once and was treated in Quarters and no blood slides were examined. He stated that he had taken 5 grs. quinine daily. He felt ill for five days during a sea and train journey before he first noticed "black urine." Hæmoglobinuria had been present for twenty-four hours before admission off the train. His general condition was good. R.B.C. 3.0 mil. No malarial parasites were seen but the spleen was just palpable. He continued to pass port-coloured urine which was translucent and had none of the deposit seen in the other cases. The urine cleared in twenty-four hours but there were two short relapses before it remained clear. Lowest R.B.C. count was 1.7 mil. and the blood urea was 170 mg. per 100 c.c. on the second day. Blood urea on eighth day, 26 mg. He was afebrile and throughout, though he felt weak, showed no toxic manifestations.

His convalescence was rapid and entirely satisfactory until he left the station en route for England.

This case presented quite a different clinical picture to any of the previous three cases and represents what might almost be described as a benign form of the disease.

It will be noted that both Cases 2 and 3 were already in hospital before blackwater fever developed and that diuresis of alkaline urine was easily obtained. It is felt that these were factors of primary importance in prognosis.

The injection of morphia in gr. ½ doses undoubtedly exerted a favourable influence in Case 2 and it is felt that this drug, judiciously employed, is indicated in cases with adequate excretion but showing marked restlessness, apprehension and vomiting.

The experience gained by the care of four cases does not justify any dogmatism in the treatment of this disease so protean in its manifestations. This is particularly so regarding the wisdom of administering anti-malarial drugs. It is almost generally accepted that quinine is contraindicated. Malarial parasites are seldom seen and were never, until long afterwards, seen in these four cases. The writer feels that in the rare event of malarial parasites being found an atebrin substitute should be given but doubts whether routine administration is justified and certainly not in cases where oliguria is present.

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