OBSERVATIONS ON FIFTEEN CASES OF HÆMOGLOBINURIC FEVER IN BRITISH CENTRAL AFRICA.

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HÆMOGLOBINURIC FEVER may be defined as an acute febrile disease, most probably of malarial origin, and characterised by the occurrence of an extensive and rapid hæmolytic.

ETIOLOGY.

Hæmoglobinuric fever is endemic in British Central Africa, but nothing definite appears to be known as to its causation. It occurs not only at the lake and river levels, but also in the Shiré highlands. There is no season of the year during which it can be said to be most prevalent. This much appears certain: that it does not usually occur until after about two to three years' residence in the country, is preceded by previous attacks of malarial fever, and in the large majority of cases quinine, antipyrin, or phenacetin have been taken by the patient during the febrile stage, and prior to the development of hæmoglobinuria. It would appear that certain constitutions are more liable than others, and it undoubtedly is the fact that one attack predisposes to another. Indians are much less susceptible than Europeans to this disease. The period of incubation is unknown.

SYMPTOMS AND COURSE.

The prodromata consist of a feeling of *malaise*, pains in the limbs, headache, discomfort in the epigastric region, and nausea. In a large number of cases hæmoglobinuria is preceded by a distinct rigor and vomiting of bilious matter. The vomiting increases in frequency, and is the main cause of distress to the patient. Presently he passes a quantity of dark-coloured urine, which varies in colour from a light claret to a dark porter. It is acid in reaction, always albuminous, and deposits on standing a dirty brown sediment, consisting of epithelium, red granules of hæmoglobin, some granular *débris*, and hyaline casts. Sometimes tube casts may be observed, containing blood pigment. The duration of hæmoglobinuria is usually about sixty hours, but it may be much shorter. With the occurrence of hæmoglobinuria the conjunctivæ and skin are stained a saffron colour, the icterus being slight, or in some cases very pronounced. The yellowness remains after the urine has cleared, but before the skin assumes its normal colour it has a peculiar ashy tint, from some change which the pigment has undergone in the tissues. In favourable cases the patient is well usually within a week, but in the more serious cases the bilious vomiting continues, and is followed by an obstinate hiccough. The urine is greatly diminished in quantity, so that not more than a few drachms are passed at one time. It is of a dirty brown colour, depositing much sediment, and in some cases it may be grumous-looking. Hæmorrhage may take place in the anterior and posterior nares; from the latter source it passes into the stomach and is immediately vomited. The patient gradually passes into an algid condition, death eventually resulting from syncope.

The temperature varies so much in different cases that it would serve no useful purpose to append charts. Broadly stated, before and shortly after the development of hæmoglobinuria there is generally severe pyrexia; later on, moderate pyrexia; during convalescence the temperature is sometimes subnormal. In suppression of urine, a temperature of collapse was noted in two cases.

DIAGNOSIS.

This presents no difficulty; but it should be remembered in this connection that sometimes patients passing "bilious urine" believe themselves to be suffering from "blackwater" fever. Apart from chemical tests, hæmoglobinuric urine can always be distinguished by the red colour of the froth, as contrasted with the bright saffron of bilious urine.

PROGNOSIS.

Although much depends upon the condition of the patient at the time of the attack, and on the severity of the attack

itself, the writer early recognised that the most important determining factor in prognosis, was the quantity and appearance of the urine passed. Shortly stated, if the urine is copious from the onset of hæmoglobinuria, the prognosis is good; on the other hand, if the quantity passed is suddenly diminished and the urine is of a dirty brown colour, depositing much sediment, the prognosis is bad. Persistent severe vomiting is also a bad symptom, especially if followed by hiccough. Profuse epistaxis has also been noticed in fatal cases.

TREATMENT.

This must be mainly symptomatic; but it is always advisable to administer a smart purge, such as calomel with compound jalap powder at the onset of the attack. Vomiting, being the most urgent symptom, early calls for relief. Various remedies have hitherto been tried, but without any apparent result. A mustard plaster to the epigastrium affords relief, and the sucking of ice would probably be of great value, but it cannot be obtained in this country. If the vomiting is severe it is advisable to give the stomach complete rest for a few hours, and peptonised nutrient enemata may then be used should the condition of the patient render this necessary.

Latterly I have successfully treated seven consecutive cases of hæmoglobinuric fever by administering every two hours during the first day a mixture consisting of sodii bicarb. gr. x, and liq. hydrarg. perchlor. m. xxx. During the four following days the mixture is given every three hours. This, I believe, effectually controls vomiting and increases the flow of urine. The alkali neutralises the acidity of the stomach and urine, and stimulates the renal epithelium; the mercury probably acting as a gastro-intestinal disinfectant, in the same manner as Sternberg's mixture does in yellow fever. This has, indeed, become the routine treatment of hæmoglobinuric fever in this country, and the results in other hands also have been so eminently satisfactory that I should like to see the mixture given a more extended trial.

No other drugs are given, and quinine is entirely withheld throughout the illness. Should the temperature cause any uneasiness, sponging affords great relief, and phenacetin in doses of gr. v to x may be given every four hours with the greatest safety.

The diet consists mainly of milk, to which a little Valentine's meat juice may be added, Brand's essence of chicken, and Benger's food. A tablespoonful of brandy is added to the milk if the condition of the heart renders this necessary. The nourishment is given frequently and in small quantity.

During convalescence, and in view of the anæmia, it is always advisable to administer a ferruginous tonic, and for this purpose ferri et ammonii citras and ferri et quiniæ citras are found most suitable.

CASE I.

P. H., aged 32, assistant collector, B.C.C.A., Zomba.
Length of Residence in Country.—Five years.
Number of Attack and Date of Present Attack.—Third, October 29th, 1896.
Urine.—Duration of Hæmoglobinuria.—Forty-eight hours; urine abundant.
Result.—Recovery.
Remarks.—Slight bilious vomiting; had taken no drugs prior to onset of hæmoglobinuria; made a rapid recovery.

CASE II.

J. B., aged 35, boatswain, B.C.C.A., Lake Nyassa, Fort Johnston.
Length of Residence in Country.—One year 7 months.
Number of Attack and Date of Present Attack.—First, November 4th, 1896.
Urine.—Duration of Hæmoglobinuria.—Forty-hours; urine abundant.
Result.—Death.
Remarks.—No notes of case, as patient was seen only 36 hours before death; had two severe attacks of rigor on ninth day of illness, and died of syncope; treated with quinine.

CASE III.

W. C., aged 28, agent, trading company, Fort Johnston.
Length of Residence in Country.—Two years.
Number of Attack and Date of Present Attack.—First, March 1st, 1897.
Urine.—Duration of Hæmoglobinuria.—Sixty hours; urine suppressed.
Result.—Death.
Remarks.—Has had a good deal of fever, and is a "bilious" subject; liver slightly enlarged; spleen normal; external hæmorrhoids. On the third day of illness urine suddenly diminished in quantity, and was of a brownish colour, depositing much sediment. On the fourth day 2 drachms of grumous-looking urine were passed; vomiting constant and sometimes attended with hiccough; frequent calls to stool. On the fifth day no urine was passed; had two attacks of syncope on attempting to stool. Died on the sixth day of illness. Treated with quinine.

CASE IV.

J. P., aged 30, engineer, trading company, Lake and Upper Shiré, Fort Johnston, and Lewonde Districts.

Length of Residence in Country.—Two years 6 months.

Number of Attack and Date of Present Attack.—First, November 27th, 1897.

Urine: Duration of Hæmoglobinuria.—Thirty-six hours; urine moderate.

Result.—Recovery.

Remarks.—Took calomel antipyrin, 20 grs. (in two doses), prior to onset of hæmoglobinuria; vomiting slight; bowels constipated; severe pyrexia during the first two days. Treated with quinine. Made a rapid recovery.

CASE V.

R. S., aged 25, Indian sepoy, Fort Johnston.

Length of Residence in Country.—Three years 3 months.

Number of Attack and Date of Present Attack.—First, February 23rd, 1898.

Urine: Duration of Hæmoglobinuria.—Fifty-eight hours; urine abundant.

Result.—Recovery.

Remarks.—Returning from expedition to Mpeseni's country; has suffered a good deal from fever lately; severe vomiting, and frequent calls to stool; nourished four entire days by nutrient enemata; treated with hypodermic injections of hydrobromate of quinine; made a slow recovery.

CASE VI.

J. G., aged 24, engineer, trading company, Lake Nyassa.

Length of Residence in Country.—One year 11 months.

Number of Attack and Date of Present Attack.—First, April 8th, 1898.

Urine: Duration of Hæmoglobinuria.—Fifty-four hours; urine abundant.

Result.—Recovery.

Remarks.—Has had good health except when temporarily employed on the Upper Shiré, when present attack occurred. Temperature on admission, 105.2; incessant vomiting; bowels constipated. Blood: No parasites; corpuscles "brassy," some shrunken, others swollen. Treated with quinine. Made a slow recovery.

CASE VII.

W. H., aged 25, engineer, trading company, Upper Shiré, Fort Johnston and Lewonde Districts.

Length of Residence in Country.—Two years 6 months.

Number of Attack and Date of Present Attack.—First, May 8th, 1898.

Urine: Duration of Hæmoglobinuria.—Thirty hours; urine suppressed.

Result.—Death.

Remarks.—Has suffered from constant attacks of fever; is very anæmic and emaciated; heart dilated; hæmoglobinuria preceded by fever of two days' duration. Took antipyrin and quinine. Prior to onset of hæmoglobinuria several attacks of shivering and lumbar pain; at night temperature 105°; passed bloody urine at 5 A.M.; first seen at 10 A.M.; temperature 104.8°; icterus prominent; passed a quantity of port wine coloured urine; constant vomiting of greenish-yellow bile. On the second day urine diminished in quantity, and altogether only about 8 ounces were passed; vomiting severe and persistent, causing patient much distress. On the third day about 10 ounces of urine passed, of a dirty brown colour, and loaded with sediment. Patient suddenly passed into a condition of collapse; temperature 95.4°; hot bottles to feet and abdomen, hypodermic injection of digitalin and strychnine. Temperature rose to 96.8°, and remained subnormal till death. On the fourth and fifth days no urine was passed, but a few drachms were with difficulty drawn off by means of a catheter; vomiting could not be checked, and all nourishment was given by enema. On the fifth day an obstinate hiccough developed, which persisted throughout the night and the following morning, when the patient died in a state of collapse. Treated with quinine by mouth and hypodermically.

CASE VIII.

J. C., aged 32, boatswain, B.C.C.A., Upper Shiré.

Length of Residence in Country.—Nine months.

Number of Attack and Date of Present Attack.—First, July 3rd, 1898.

Urine: Duration of Hæmoglobinuria.—Thirty-two hours; urine suppressed.

Result.—Death.

Remarks.—Has constantly been on sick list since arrival in the country; moderate drinker, but drinking heavily prior to attack; sent up by Dr. G. from Mpimbi to Fort Johnston for treatment, with a note that for past two days no urine had been passed. On admission about an ounce of urine was passed with difficulty; was of a chocolate colour and thick consistency. On the sixth day of illness patient had frequent attacks of epistaxis from both the anterior and posterior nares; no urine was passed. On the seventh day skin hot and dry, and patient drowsy, with slight muscular twitchings. As no urine had been passed, 1 gr. of pilocarpin injected, followed by profuse sweating. On the eighth day patient had three attacks of syncope; digitalin and strychnine were injected subcutaneously. Had a fourth attack of syncope at 7 P.M., to which he succumbed; treated with quinine.

CASE IX.

W. W., aged 35, tradesman's assistant, Fort Johnston.

Length of Residence in Country.—Four months.

Number of Attack and Date of Present Attack.—First, July 20th, 1899.

Urine: Duration of Hæmoglobinuria.—Sixty hours; urine moderate.

Result.—Recovery.

Remarks.—Prior to arrival in British Central Africa has been at Salisbury, Tete, and Blantyre, at all which places has suffered from malarial fever. Is very anæmic; liver dullness normal; spleen slightly enlarged, but not tender. Present attack commenced with an ill-defined rigor and bilious vomiting; before the development of hæmoglobinuria Dr. D. made an examination of the blood, and found parasites of malignant tertian infection; thereafter, no parasites. Placed immediately on a mixture of sodii bicarb. gr. x and liq. hydrarg. perchlor. mxxx, given every two hours during first day, and every three hours on following days. Corpuscle estimation: second day, 3½ millions; third day, about 2 millions. The corpuscles were "brassy" in appearance, some shrunken, others pale and swollen; urine casts granular, and contained yellow pigment. Made a slow recovery.

CASE X.

E. R., aged 32, naval officer, Fort Johnston.

Length of Residence in Country.—Five years.

Number of Attack and Date of Present Attack.—Third (?), November 3rd, 1899.

Urine: Duration of Hæmoglobinuria.—Sixty-two hours; urine abundant.

Result.—Recovery.

Remarks.—Suffering from mercurial pytalism at time of attack. Hæmoglobinuria preceded by a distinct rigor and pains in the limbs. Temperature 104.8°. Bilious vomiting; bowels constipated; placed on same mixture as previous case; made a good recovery. N.B.—Urine cleared after about 60 hours; remained clear for 12 hours; again became hæmoglobinuric, and remained so for about 8 hours.

CASE XI.

C. S., aged 40, Indian sepoy, Fort Johnston.

Length of Residence in Country.—One year.

Number of Attack and Date of Present Attack.—First, November 22nd, 1899.

Urine: Duration of Hæmoglobinuria.—Sixty-eight hours; urine moderate.

Result.—Recovery.

Remarks.—Has suffered from malarial fever in India, and has had three or four attacks since arrival in this country. Vomiting severe and persistent. Patient is anæmic and emaciated. Liver slightly enlarged; heart dilated. Placed on mixture as previous case. Recovery retarded owing to patient's exhausted condition.

CASE XII.

L. O., aged 23, tradesman's assistant, Fort Johnston.

Length of Residence in Country.—One year 10 months.

Number of Attack and Date of Present Attack.—Second, March 7th, 1900.

Urine: Duration of Hæmoglobinuria.—Sixty hours; urine abundant.

Result.—Recovery.

Remarks.—First attack after 8 months' residence at Kota-Kota on Lake Shiré; has had a moderate amount of fever since; is very anæmic; liver and spleen normal; had been feverish for two days prior to development of present attack, during which time he had taken about 20 grs. of quinine per diem; placed on same mixture as the preceding cases. On the eighth day of illness 5 grs. of quinine were given in the morning, and 5 grs. at noon. At 4 P.M. the patient again passed hæmoglobinuric urine. The quinine was discontinued, and the urine cleared in the course of a few hours. Recovery was retarded owing to persistent pyrexia, the temperature frequently rising beyond 105°.

CASE XIII.

J. C. B., aged 25, agent, trading company, Fort Johnston.

Length of Residence in Country.—Four years 10 months.

Number of Attack and Date of Present Attack.—First, April 13th, 1900.

Urine: Duration of Hæmoglobinuria.—Sixty-four hours; urine abundant.

Result.—Recovery.

Remarks.—Has resided mainly in the Shiré Highlands, and has had good health; developed present attack on arrival on the Upper Shiré; vomiting slight; treated with same mixture as preceding cases. Made a good recovery.

CASE XIV.

W. S., aged 32, planter, Zomba.

Length of Residence in Country.—Two years.

Number of Attack and Date of Present Attack.—Second, June 24th, 1900.

Urine: Duration of Hæmoglobinuria.—Sixty hours; urine abundant.

Result.—Recovery.

Remarks.—First attack six months previously; little or no vomiting. Placed on mixture as previous case. Made a good recovery.

CASE XV.

E. D., aged 29, transport work, Blantyre.

Length of Residence in Country.—Two years 9 months.

Number of Attack and Date of Present Attack.—Second, October 2nd, 1900.

Urine: Duration of Hæmoglobinuria.—Fifty-four hours; urine moderate.

Result.—Recovery.

Remarks.—First attack nine months previously. Present attack preceded by an ill-defined rigor and bilious vomiting. Took 10 grs. quinine in the evening; noticed black-water symptoms the following morning; persistent vomiting on admission; bowels constipated. Placed on the same mixture as preceding cases. Made a good recovery, but during convalescence suffered from pyrexia, the temperature ranging from 100° to 103° F.

NOTE ON THE STAINING OF FLAGELLA.

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It has been pointed out that the difficulty of discovering any single reliable method of staining the flagella of all kinds of bacteria probably means that for each species a special method is required. It is found in practice that a method which gives good results with one species will often fail to do so with another.

One of the best and easiest methods for general use is that introduced by Pitfield, and in working at the application of this method to the staining of the flagella of the typhoid bacillus, I found the modification now described more reliable than any given in the textbooks, and also very easily carried out. The mordant is made in the following manner:

A saturated solution of perchloride of mercury made by boiling, is poured while still hot into a bottle in which crystals of ammonia alum have been placed in quantity more than sufficient to saturate the fluid. The bottle is well shaken and then allowed to cool. In Richard Muir's modification of Pitfield's method, saturated solutions of ammonia alum and perchloride of mercury are added to each other in making the mordant. The method I have given provides a fluid saturated with both salts.

To 10 c.cm. of this fluid 10 c.cm. of a freshly-made 10 per cent. solution of tannic acid are added, and 5 c.cm. of carbol fuchsin. These are mixed