Blackwater or Haemoglobinuric Fever: A Case Occurring upon the Middelvelt.

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At the mention of this disease the diversity of opinions held for many years as to its causation and treatment will alone, I am afraid, occur to most of us rather than any clear conception of its nature, cause, and remedy. Few of us, comparatively, have seen many or even a single case, our knowledge of the disease being confined to the fact of its occurrence in areas where malaria is rife in its worst forms, where malignant and remittent malaria predominate, and in people particularly prone to malarial attacks, and we connect it in some way with malaria.

We have read emphatic opinions that blackwater was a form of malaria by those who treat the disease throughout with quinine, others holding that it was solely caused by the administration of this drug—quinine poisoning, in fact—and its action upon the kidneys. Again, it has been asserted that blackwater was unconnected with malaria, a totally different disease, due to infection with an, as yet, unrecognized parasite, and it has been suggested that it was a piroplasmosis—the "malaria" of cattle, horses, and dogs—conveyed by ticks.

Previous to treating the case to be described I had only met with a very few mild cases of blackwater fever, occurring down upon the Lowveld during epidemics of remittent malaria; cases passing a portercoloured urine for from one to two days during the course of their attack, and passing through that phase without diminution of the amount of quinine they were taking.

Without any qualification, therefore, to be considered an expert, I would like to try and unravel these difficulties in this paper, and put forward a recent case in illustration. For whilst none of the opinions quoted are wholly true, as we now know, some of them are certainly half-truths.

Blackwater fever is not malaria in the sense of its being directly due to an invasion of the blood corpuscles by the malarial haemameba, nor to their breaking; it is not due to piroplasma infection, as it occurs where ticks do not exist; no causative parasite of any kind has been discovered; and as regards its causation by large doses of quinine, blackwater fever has occurred in those who have not taken quinine; it has occurred in those accustomed to take quinine when they have left it off, being unable to get it; and in some countries where it is the custom to give large doses of quinine during the after-attacks of malaria the disease has not been produced. The matter has been summed up by Daniels (in *Tropical Medicine and Hygiene*) as follows: Though quinine is not an essential or even a common cause of blackwater fever, it has been proved in many instances that a dose of quinine, even a small dose, has brought on an attack of haemoglobinuria; it may therefore be an occasional cause.

Blackwater fever is the result of a loss of the protective properties, an anaphylaxis, of red blood corpuscles leading to their death, with their contained haemameba, their breaking up and the solution of their haematin by the blood plasma, a hemolysis. The haematin acts as a diuretic, appearing in the urine and producing the characteristic known as hemoglobinuria. This condition of anaphylaxis results from repeated attacks of the severer infections of malaria.

A characteristic of the disease is the appearance of haemoglobin in the urine, unaccompanied by red corpuscles, as would occur were a hemorrhage to take place from the kidneys or bladder.

Those living down upon the Lowveld, unprotected against malarial infection, who suffer in consequence from repeated attacks of remittent and malignant malaria, are most certainly qualifying for blackwater fever sooner or later, and though such people may never have an attack in the areas where the disease is prevalent, they may have their first attack after leaving that area; it has occurred in them after their return to England, or after their removal to places where the disease is never seen, as in the case to be presently described.

Shortly, blackwater fever is an anaphylaxis occurring those chronically affected with the malignant varieties of malaria, and in such people a dose of quinine may precipitate an attack or cause a recurrence of it.

A word about the symptoms and treatment of the disease before describing the case.

The first phase is the occurrence of "blood" in the urine of a patient at the moment under treatment for a malarial attack. At first the urine contains such a quantity of haematin that in the ordinary china or enamelled chamber, when made to flow across the bottom, it looks to be pure venous blood; the urine is passed in small quantities, frequently with much strangury. There is much pain in the back and loins, in the region of the liver and spleen, and probably aching in the limbs and body. Jaundice suddenly appears with a marked anaemia, the yellow of the skin and conjunctive showing up brightly as a result of the anaemia.

The temperature is high and sustained, and hyperpyrexia may occur; there may be a rigor at the commencement only, or it may recur at intervals.

Nausea and constant vomiting is a most troublesome feature in this phase, which lasts from a few hours to a few days. Added to these symptoms, the patient has the general appearance of having just suffered a severe haemorrhage. He is restless to a degree, tossing his limbs about in first one direction, then in another, rolling from one side to the other, sighing, and palpitation of the heart at every movement. The general impression given is that of an early dissolution.

The second phase is led up to by a browning of the urine, which later becomes actually porter-
coloured (i.e., the haemoglobin loses its oxygen); the haemoglobin is giving place to methaemoglobin, and the destruction of the red cells has ceased, it may be temporarily or it may be permanently. Within a few hours the urine returns to a transparent yellow, and the patient feels that he is better and over the attack. He sweats profusely and constantly, feeling better each time. The temperature falls to the neighbourhood of the normal, and vomiting ceases. The amount of urine passed at this time now diminishes, for whilst it contained the diuretic haemoglobin, the amount was in excess of the normal.

After a few days of respite from dissolution, when it appears that convalescence has certainly set in, another phase is entered upon, that known as the secondary fever, and characterized by a thick sediment in the urine, which demonstrates the secretion of debris—of broken-down corpuscles—by the kidneys.

The temperature in this phase rises again, and falls a little to rise again, remaining sustained in this way, somewhere in the neighbourhood of 102°, for some days. It is caused by choking of the kidneys and the whole system by broken-down corpuscles, which the body is making every attempt to rid itself of. The kidney tubules are always more or less blocked, but the ureters may also become blocked, and this condition is the cause of all the troubles occurring in this phase, sometimes also of death.

In this phase hyperpyrexia may occur again, blood may again appear in the urine, and the first phase may more or less return. But if the detritus is satisfactorily got rid of, day by day, the heart has not been too much tried, and is not dilated by the predisposing, frequent, attacks of malaria—if these desirable conditions exist and continue, convalescence now really sets in.

The patient may succumb during any of the attacks of hyperpyrexia, but death is most common during the third phase, during the secondary fever, due to suppression of urine from blocking of the kidney tubules, even of the ureters, with the detritus of dead corpuscles.

Those who recover remain free from attacks of malaria for a considerable time, having apparently been cleared of the haemoglobin they harboured; but they are specially liable to further attacks of black-water fever if they remain in the area or return to the conditions which produced the first attack; if this was mild, further attacks will be mild; but if severe, they will be severe also, suggesting a constitutional predisposition.

When a lead in treatment is searched for but little assistance is found; there is no antidote, no sovereign remedy known, no particular drug which definitely benefits the anaphylaxis. Authorities still differ widely as to the wisdom of continuing quinine. Blood smears show a disappearance of the haemoglobin immediately after the onset of hemoglobinuria, but if future smears show a reappearance, a continuance of quinine is recommended. Again, should the patient become moribund during hyperpyrexia, a "heroic" dose of quinine is recommended intravenously, and credited with having saved a life sometimes. I should sum up treatment in an earnest recommendation to swell the patient with a weak solution of bicarbonate of soda from the first, continuously, throughout every phase until convalescence is really established—sod. bicarb. 1 drachm, ad aq. 20 ozs.; this is the most rational treatment of the disease.

When vomiting interferes with the water being taken by mouth at least 10 oz. of normal saline should be given by rectum every hour, and even subcutaneously if necessary.

Digitalis and strychnine will be constantly and regularly required, but antipyretics are dangerous, though I found an occasional dose of aspirine helpful.

The most distressing restlessness and vomiting are readily controlled by some preparation of opium, of which I found nepenthe beyond praise; it was constantly necessary to have recourse to doses of m.x., yet it always acted promptly, and never produced the least dryness of the tongue.

For the rest, hot packs were constantly used, by putting a number of hot bottles around the patient, to reduce the temperature and produce profuse perspiration; an ice-bag to the head throughout, and for hyperpyrexia cold baths are recommended strongly. Purging is strongly deprecated, even an initial dose of calomel, and the saline enemas and washing out of the bowel, previous to the administration of nutrient enema, were found to act quite satisfactorily.

I must here admit that had I been equipped with the above summary of blackwater fever and its treatment the other day, when I was suddenly called upon to treat a case developing in a patient at the moment under treatment for malaria, and in a place where this disease has never before been seen, I should have been spared much anxiety.

In the first week of September last Constable F. was transferred from the Barberton district to this town. He had been stationed for six years in that area, at Eureka City and Louw's Creek, which are but 15 miles apart, where malaria of the remittent and malignant type are rampant and blackwater fever not uncommon. He got on pretty well for the first three years, and then began to get regular attacks of malaria, which he staved off with quinine in the manner followed by the other residents. Latterly, however, these attacks had become more frequent, and tried him more and more—i.e., he became aware that he had a heart by its palpitation and precordial discomfort during attacks. He considered himself now "rotten with fever," and said that he felt that he could not stick much more of it.

On arrival here he was fat, flabby, anemic, with a yellowish tinge—most unhealthy-looking—and much debilitated, and I wondered how such a man was able to carry out his duties so long. Within a week of his arrival I was sent for to treat him in an attack of malaria, and found his heart much dilated, apex beating with a flabby, feeble, diffused impulse nearly 5
inches below, and to the left of, the nipple. His temperature was only 102° or so, yet he was sighing, restless, and "sticking it" very badly. Aches were severe in his limbs, and pain in his back; he had strangury, and passed about 2 ozs. of urine frequently with relief temporarily. He said he always had these symptoms with his attacks of malaria for some time past.

A blood-smear sent to the South African Institute brought a report of a malignant infection.

He was treated by Major Sinton's method, giving alkalies—sod. bicarb.—in larger doses than ordinary with the quinine, and was able to take gr.x. of quinine thrice daily with rapid relief to all symptoms, and with less evidence of quininism than he was accus-

tomed to. In addition, he was given an intramuscular injection of one of the preparations of organic arsenic as early as possible, and regular doses of strychnine and digitalis for his weak heart.

The attack lasted for a few days only, and as soon as he was up and about again I gave him an intravenous injection of one of the salvarsan preparations.

During the next two months, although he went down with further attacks, he steadily improved in every respect, and considered himself "another man"; he received two more intravenous injections of salvarsan, and took gr.x. of quinine at bedtime.

His further attacks were becoming milder and shorter in duration, and the more urgent symptoms—strangury, etc.—left him during the attacks, and were not now experienced.

His general appearance was much improved; he was stronger physically, and showed some energy in moving about, as well as mentally. He was only 31 years of age, but he said that he was rejuvenated.

He was enclosing his cottage with mosquito gauze, and just completed this when, on November 26th, he went down with another attack of malaria. At midday his temperature was 103.6°, and he appeared exhausted; he had taken gr.x. of quinine early, and again at midnight with his soda mixture, the latter dose having relieved his head and his aches, so that I expected his temperature to fall during the afternoon.

At 7 p.m. he was sweating profusely; his temperature had fallen to 99.8°, and he was decidedly better. I considered that he was over the attack, but enjoined him not to forget his last gr.x. dose of quinine, which he took.

At 3 a.m. I was hurriedly summoned, and found him passing what appeared to be pure venous blood, about 2 ozs. at a time, and preceded by strangury; pain in his back was very severe, and aches in his limbs, with severe headache. His temperature was 104°. Hot fomentations were applied to his back, and of his own accord he began to swill himself with water, adding half a packet of sod. bicarb. to about 1½
pints, as he said they always did on the Lowveld when
blood appeared. In an hour his symptoms appeared
to abate somewhat, and his temperature to fall; he
also showed an inclination to perspire, but he passed
urine—in the same state as described—five times
during that hour. I forbade further quinine, and left
him until morning, when I made arrangements to
admit him to hospital. On 27th arrived at the hos-
pital. He was immediately packed with hot-water
bottles, and soon perspired freely, even profusely,
with further ease and a fall of the temperature to
101.8°. But during the day his temperature jogged
up and down between this and 103°, appearing to be
controlled by tepid sponging, but at 2 a.m. on 28th
it was up to 103.4° again, whilst at 6 a.m. it was down
99.8°. Hopes were entertained that his fever was
disappearing, for his heart, even at this stage, re-
quired much stimulating with strychnine and digitalis,
but at mid-day he had a rigor and the temperature
went up to 104°, and he was very restless, and had
the appearance of having had a severe haemorrhage;
his face since the day before had become rapidly
yellow, whilst his lips were blue. He looked to be in
bad case, but another hot pack, and constant stimu-
ation with brandy to enable him to bear it long enough,
brought his temperature down to 100.6° by the even-
ing, and he seemed decidedly better.

On admission he had been supplied with abundance
of soda water, and drank about six pints during the
day, but during the night vomiting set in, and he
took less during the following day, the amount con-
sidered necessary being made up by saline enemata;
but with the fall of temperature the vomiting much
improved, and his supply of fluid was well maintained.
The urine showed blood on admission, or rather
haemoglobin, for a specimen taken at this time and
forwarded to the South African Institute brought
back the report that there were no corpuscles in it,
but only haemoglobin, and this condition continued
from midnight on 26th to midday on 20th, the colour
changing to brown with red on 27th, and only brown
—porter-coloured—during the morning of 20th, before
the colour stopped and dark yellow urine was passed.
Haemoglobin was therefore present, representing blood
destruction, for about 48 hours, when only methaemo-
globin—not fresh haemoglobin but old, having lost its
oxygen—appeared. This was the termination of the
first phase, caused by the destruction of blood cells.

On 20th and 20th all seemed well; he slept most
of the time and drank abundance of soda water.
Asked for butter milk, and took it and an ice; but we
took the precaution to give him a nutrient enema to
keep up his strength, as, in spite of strychnine and
digitalis four-hourly, his heart was very wobbly and
weak. He sweated well, but sponging was maintained.

On the evening of 30th he looked decidedly better:
the yellow had disappeared from his eyes and skin.
his heart was beginning to pick up again, his tempera-
ture was nearly normal, and he considered himself
through the attack and feeling "another man."

Then the next phase set in, and by 10 p.m. his tem-
perature had begun to rise again, reaching 104°
by 6 o’clock next morning. The urine, however,
remained clear, and was being passed in fair quantity,
without strangury or other trouble, and it seemed to
me that he was now suffering from another attack
of brooding parasites when, at 10 a.m., his tempera-
ture was still very high. Sponging had been tried,
and another hot pack, without any appreciable result.
I therefore determined to risk something and give him
quinine, which I did intravenously—gr.xv. of the
hydrochloride—and which seemed to answer, for his
temperature fell steadily until the evening.

But about six hours later haemoglobin again appeared
in the urine, only a definite colour, and not as at first;
it was evidently a mild recurrence only, but I have
no doubt caused by the quinine, for it disappeared
during the next ten hours after passing through the
brown stage.

The apparently good effects of this treatment did
not last long, for ten hours later his temperature was
on the upgrade again, and all the troublesome symp-
toms had returned except haemoglobinuria. Vomiting
again recurred, but appeared to be controlled by m.x.
doses of nepenthe, which also controlled the
distressing restlessess. Hot packing was again re-
sorted to, and had to be accompanied by much stimu-
lation, for the heart was by now distinctly giving
way, and not always responding to stimulation. He
was often wandering and delirious, and it was now diffi-
cult to maintain the inhibition of sufficient fluid, either
by mouth or by bowel, for the latter was returned at
once. The amount of urine secreted was definitely
diminishing, and the sediment of greyish detritus was
most marked in specimens set to deposit it; it was
nearly half the specimen.

By mid-day on December 2nd, in desperation lest
the maintained high temperature—it was then 104°
again—should end his life, and as the first injection
had given definite relief, I chancecl a slight return of
haemoglobinuria, and gave another gr.xv. of quinine
hydrochloride intravenously. It was administered
very slowly, for the patient was almost moribund, and
was attended with definite, though slight, jactitations
of arms and legs for about ten minutes after he had
received the dose.

Thereafter his temperature fell steadily, the delirium
passed off, and his constant complaint was of tiredness
and weakness: he took more fluid by mouth, and
needed constant stimulation hypodermically and by
mouth as well, and, strange to relate, no haemoglobin
appeared in the urine after this second exhibition of
quinine as it did after the first. After a fall to 101°
as a result of the injection, and a slight rise to 102°
the following morning, the temperature fell to 99.4°
at midday on 3rd. But towards evening the tempera-
ture was again on the upgrade, and in spite of stimu-
lation the weak heart failed before night, and he died
at 6,30 that evening.

The treatment of this case taxed the efforts and
resources of our little hospital to their utmost—con-
stant hot packing, sponging down, the administration
of constant saline and nutrient enemata, kept the
staff hard at work day and night; no man’s life was
ever more strenuously fought for.

When on the third day the temperature fell, and
everybody was pleased and smiling at the results of
their efforts, I alone still felt anxious, thinking of his
thin-walled, weak heart, which still must be kept
going and not allowed to drop; for in such cases it
has sometimes given way as they turned in bed to
urinate! The greatest precautions were enjoined
against this happening, and were carefully followed,
or he would never have survived the first phase; and
it is still a mystery to me how he existed day after
day, on December 1st and 2nd and throughout 3rd,
with a heart in the condition in which his was.

But for the extreme condition of dilatation of his
heart I feel sure that the splendid efforts of our staff
would have secured his recovery; the disappointment,
after the temporary success in the first phase, was
very keen, though efforts were never for a moment
relinquished throughout.

No doubt but that this constable was, on account
of his tendency to deposit fat in his muscles (his
heart muscle as well), quite unfit to be left for any
length of time on the Lowvelt in a malarious area,
and I have suggested that in future constables should
be transferred from such parts at the end of two
years, unless they show themselves specially resistant
to malaria, when they might be allowed to remain
for three years, but under no circumstances longer.

This constable’s temperature chart is reproduced,
as it is so typical of the usual course of blackwater
fever, and shows the phases through which they pass
so well.

Let none despair in these cases, when they meet
them, with hearts less dilated than was this one;
I am sure that they are curable!

Syphilis of the Stomach.

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Although the first mention in medical literature of
syphilis of the stomach is that of Anstral in 1834, the
modern study of the condition dates from the publica-
tion of Paters’ well-known thesis in 1907, in which
he considered some 122 recorded cases. Since that
date much has been written on the subject by
French, German and American observers, and
numerous cases have been investigated with the aid
of modern methods.

In England little attention has been paid to the
condition, but recently McNee has fully described a
case of gummatous syphilis of the stomach in which
the clinical diagnosis of carcinoma was corrected post
mortem on account of the absence of the features of
carcinoma and the discovery of numerous spiro-
chactes in the lesion in the stomach.

At the present time more or less well-authenticated
cases are being reported every week. Just as with
many other morbid states, once the condition has
been clearly appreciated and modern methods of in-
vestigation utilized in its differentiation, it is not by
any means the rarity that was at one time supposed,
and it has a definite clinical importance. It has long
been known, and has frequently been referred to in
medical literature, that gastric cases occurred which
resisted all treatment until put on anti-syphilitic
treatment, when these gastric symptoms rapidly dis-
appeared. Further, it occasionally happens that at
operation an apparently inoperable gastric carcinoma
is discovered, but the individual, instead of going
progressively downhill, ultimately perhaps completely
recovers.

In the earlier days, the diagnosis of syphilis of the
stomach chiefly rested in the history or other evidence
of syphilis and the disappearance of the gastric symp-
toms on anti-syphilitic treatment. As Fenwick and
others pointed out, many years ago, it does not follow
in all cases in which gastric symptoms disappear after
anti-syphilitic treatment that there was an actual
syphilitic lesion of the stomach; but in view of the
number of cases which are now being reported in
which large tumours shown, both by operation and
by radiography, to be in the stomach, rapidly dis-
appear under anti-syphilitic treatment, there can be
little doubt that syphilis of the stomach is a definite
clinical entity. Still more convincing evidence has,
however, been recently supplied by the discovery in
1920 by Wile of spirochactes in a syphilitic ulcer of
the stomach, and by McNee in 1923 of spirochactes in
a gummatous tumour of the stomach stimulating and
mislaced for carcinoma of the stomach.

Clinically, syphilis of the stomach has been de-
scribed in the following forms:
(1) Syphilitic gastritis. (2) Syphilitic ulcer. (3)
Gummatous syphilis leading to tumour formation and
hour-glass deformity of the stomach. (4) Leather
bottle stomach. (5) Perigastric syphilis with
secondary implication of the stomach.

Further, although not strictly syphilis of the
stomach, one must never forget the importance of
tubes dorsalis in the production of gastric crises—
crises which are nearly always early manifestations
of tubes, often appear long before the knee-jerks dis-
appear or the Argyll-Robertson pupil is present, and
in which the only other manifestation of tubes may
be some of the slighter sensory defects or changes in
the cerebro-spinal fluid. From my own experience,
I have no hesitation in saying that this is the most
important practical aspect of syphilis as it affects
the stomach, as it is so frequently overlooked and harmful
and unnecessary operations undertaken.

To return to syphilitic lesions proper of the
stomach, the question as to whether a true syphilitic
gastritis occurs or not has been a frequent source of
discussion in medical literature since Anstral first re-
ported in 1839 two cases of syphilis with gastric
symptoms cured by mercury. Some authorities, such
as Rudniew, are of opinion that it is frequent, and
claim that in the eruptive stage the stomach suffers