OBSERVATIONS ON BLACKWATER FEVER.

BY SURGEON-MAJOR F. K. KLEINE,
Assistant in the Royal Institute for Infectious Diseases, Berlin.

DURING his stay in 1897 in German East Africa, which was occupied with the investigation of a plague-like disease that had broken out in that region, Robert Koch turned his attention also towards other infectious diseases, especially malaria and blackwater fever. In a report¹ dated March 2nd, 1898, he asserted that blackwater fever was not a special form of malaria, but a quinine intoxication. After his return, Koch found on looking through the literature of the subject that he was not alone in his opinion, but that similar views had been published here and there for some years. It appears as if a Greek physician, S. Verétas² had first observed and reported hæmoglobinuria in a malaria patient after the use of quinine in the year 1858. Konsolas, Papavassiliou, Karamipas, and others³ confirmed the assertion. But above all the credit is due to the Italian Tomasselli⁴ of having in 1874 convincingly shown the dangerous toxic action of the "chief of all remedies." His demonstration and those of his pupils are throughout adequately proven. Of German physicians, F. Plehn⁵ in particular has issued a warning against the use of quinine in blackwater fever, and has shown with examples how simple fever may be converted into hæmoglobinuria by this means. Nevertheless, with the exception of Tomasselli, the above-named authors, and indeed the majority of tropical physicians, regard quinine as at most one cause of blackwater fever; they hold that strain, chill, fatigue, excesses, psychical excitation, acute rheumatism,⁶ specific disease germs, and many other causes can likewise evoke hæmoglobinuria. R. Koch, on the other hand, regards the black urine as chiefly and preponderantly a direct consequence of the use of quinine, without at the same time denying that in many cases one remedy or another or even some other cause can produce hæmoglobinuria. Moreover, he does not accept Yersin's bacilli⁷ or F. Plehn's parasites.⁸ On the heels of Koch's publication followed numberless assaults, especially in English journals. One author⁹ expresses the wish that Koch had kept his unproved theory to himself and points out the great harm which it has ostensibly caused. A second¹⁰ regards the view that quinine is the cause of the melanuria in the absence of any scientific proof as a simple superstition on the level of the innumerable errors regarding diseases, etc. These opinions can be explained as the result of a superficial knowledge of Koch's arguments. Cases are frequently appealed to in which the patients took quinine "not abundantly or not more than ordinarily," and yet were attacked by blackwater fever and the authors thus forget that such histories support Koch, who has never maintained that it is necessarily only large or unusual doses of quinine which lead to melanuria. Dr. Crosse¹¹ most of all mistakes the question at issue. He considers the quinine theory completely erroneous, because he has never seen anyone develop melanuria during a course of quinine prophylaxis.

In opposition to these numerous objections and misapprehensions Koch lays down his views in a comprehensive paper.¹² He shows:

1. That malaria parasites are very often absent in blackwater fever.
2. That when they are present their number bears no relation to the hæmoglobinuria, as it should on the analogy of Texas fever.
3. That malaria with very numerous parasites may occur without giving rise to hæmoglobinuria.
4. That an exact comparison between the attack of malaria and that of blackwater fever reveals quite essential clinical differences.
5. That blackwater fever may be associated with two¹³ totally different kinds of malaria, namely, ordinary tertian and tropical fever.

These results, which were mainly obtained by systematic examination of the blood of 41 patients, prove that blackwater fever is not a variety of malaria. The true cause of the hæmoglobinuria was then convincingly demonstrated by the

histories of 17 cases of malaria. It was invariably quinine which even in small doses after some hours evoked melanuria. The characteristic symptoms of the attack, high fever, rigors, and hæmoglobinuria, as well as nausea and vomiting can all be explained as consequences of the dissolution of red blood corpuscles. Exactly the same symptoms are observed after transfusion of blood from lower animals into man, since the red blood corpuscles of the one animal species are at once destroyed in the blood of another.

R. Koch hence recognises not a direct but only an indirect connection between melanuria and malaria. The latter is the predisposing while quinine is the exciting cause. On account of the definite geographical distribution of blackwater fever, it appeared not improbable that another hitherto not certainly determined factor must accompany the predisposing malaria. With regard to the factors involved in the question, more may be seen in the paper of Koch's already referred to. His hope that in the not far distant future careful etiological researches would certainly establish quinine in the minds of all as the most potent determining cause of blackwater fever has been only partially fulfilled. The sole sufficient contribution to the knowledge of the disease has been published by the Royal Society's expedition; the valuable results of this will be further referred to below. At the International Medical Congress in Paris, on the other hand, the onus was thrown, in addition to the influence of the precedent malaria infection, upon unfavourable hygienic conditions, such as want of comfort, alcoholism, and demoralisation. The infectious theory of the nature of bilious fever seemed also to have not yet been given up.

In these circumstances Herr Geheimrath R. Koch has requested me to publish the following 15 cases, histories which powerfully support his views. These histories are not in any way selected, but refer to all the patients suffering with melanuria who have been treated by Herr Geheimrath Koch himself since his last communication on the subject or concerning whom he has received information from trustworthy observers.

1. * C., merchant. First attack of fever, October 4th, 1899, after three weeks' stay in Stephansort. Relapse. Blood on January 8th, 1900, showed large tropical rings and half-moons. Quinine treatment. Later, on every ninth or tenth day a gram of quinine by the mouth. When the patient remained lastingly free from fever he took from the middle of March on only half a gram of quinine, and this dose irregularly. On April 2nd he felt ill and took a gram of quinine. Next day at noon he had a chill (38.5° C.); at 7.30 P.M. he took another gram of quinine. About midnight the patient awoke with a violent rigor, which lasted two and

a-half hours, and was attended with vomiting. The urine passed next morning looked blackish-red; there was jaundice. During this day there were two more rigors, with vomiting. On the morning of April 5th the urine was somewhat clearer; nothing was found in the blood. The patient now took daily a small dose of quinine, beginning with a decigram by the mouth; the blood investigation remained negative, and the jaundice diminished. On April 14th he took a gram of quinine, and six hours later had a chill (39.9° C.). The urine passed in the night looked brownish, but contained no hæmoglobin; marked icterus. The dose of quinine was reduced to half and slowly raised. Gradual habituation to quinine followed without the recurrence of a blackwater fever attack.

2. W., machinist. Had first attack of fever, commencing without rigor and lasting only one day, twelve days after arrival in Friedrich-Wilhelmshafen. After the fall of temperature he took 1½ gram of quinine. Two days later he again had fever; he took another 1½ gram of quinine and

* All the histories relate to male patients between 22 and 40 years of age.

thereafter had fever about every eight days. From November, 1899, till the beginning of March, 1900, patient took as a prophylactic measure a gram of quinine every week. Then he stopped it, as the fever continued to recur in spite of everything. At 10.30 on the evening of April 6th, 1900, he felt ill and took a gram of quinine. Next morning he went to work, but was compelled to return home after half an hour on account of violent tinnitus aurium and vertigo. At 8 A.M. he had a severe rigor, with vomiting. The

urine was black, the temperature rose to 40.2°C. The patient was conveyed by boat to the hospital at Stephansort. On the way he micturated once, the urine being no longer black, but dark red. On his arrival (6 P.M.) he felt comparatively well, but had slight jaundice; examination of blood negative. On the night of April 7th-8th he had again suddenly a rigor and violent vomiting, and the urine became black. From April 12th on he took quinine in small but gradually increasing doses. On the 15th he had 0.8 gram by the mouth; in the afternoon he had chill, fever, brownish-black urine, and jaundice. After the urine had again become normal complete but still slower habituation to quinine was carried out.

3. (Personal observation by Surgeon-Major B.) During a stay of fourteen months in Togo had six attacks of fever (malaria tropica) while undergoing somewhat irregularly a prophylactic course of quinine. On September 22nd, 1900, felt ill and took in the morning 1 gram of quinine by the mouth. Three hours later had marked hæmoglobinuria which lasted four days, during which the hæmoglobin content of the blood sank to 38 per cent. Quinine treatment stopped. During the return journey to Europe there was another rise of temperature and 1 gram of quinine was taken as an experiment. Temporary hæmoglobinuria resulted. From February, 1901, onwards quinine in slowly increasing doses has been well borne.

4. O. G., officer, suffered for eight months in West Africa with fever about every four weeks, although he took half a gram of quinine every fifth day by way of prophylaxis. One evening he felt ill again, and on this account took next morning a whole gram of quinine instead of his customary half gram. Four or five hours later there was a rise of temperature to 40°C, and the urine was coloured with blood. Very slow convalescence, without the use of quinine. Return to Germany, and cure of the still persistent malaria with quinine, which was now well borne.

5. H., official, fell ill with fever after about eight months' stay in East Africa. Within eighteen months he had five malaria attacks of various duration which were treated with quinine. One evening he felt ill, and at 9 o'clock, before going to bed, took, for fear of a malaria attack, a gram of quinine. At 1 in the morning he was awakened by the need of micturition; he noticed a hæmorrhagic tint in the urine. The hæmoglobinuria lasted four days, during which he took no quinine. Three weeks later, on account of repeated attacks of fever, he had again recourse to the drug, but took only half a gram. Some hours later melanuria came on again with a rigor. He returned to Germany, and without quinine the attacks of fever completely subsided.

6. S., locksmith, after he had been three weeks in Cameroon, fell ill of fever which lasted four to five days, and was treated by a doctor with quinine. For prophylaxis he then took every fifth day half a gram of quinine. Despite this he had about six weeks later severe fever (no rigor) which lasted ten days. Later on he kept up the above-mentioned quinine prophylaxis for five months without escaping slight feverish attacks. After a rise of temperature to 41°C, the patient took next morning a whole gram of quinine, whereupon four hours later hæmoglobinuria supervened with a violent rigor. He returned to Europe, and was admitted into Koch's ward. The rings of tropical fever were found in the blood. Complete habituation to quinine was gradually established.

7. P., machinist, after living four weeks in Cameroon, was attacked with fever which set in without rigor, and was medically treated with quinine. Later on he took every fifth day for a year half a gram of quinine as a prophylactic, and then the same dose once a week. After the patient had followed this out for eight months he felt ill for some days, and without leaving off his work took accordingly half a gram of quinine; his temperature was then 37.5°C. Three hours later he could only pass a few drops of black urine. Severe rigors then set in, lasting four days at intervals of 12 hours. The urine retained its bloody appearance for two and a-half days. Convalescence occurred gradually, without the use of quinine. On the return journey to Europe the patient took a gram and a half of quinine in the course of five days, that is, 0.3 gram per diem. On this treatment the urine assumed, if not a bloody, at least a darker colour. Later on there was habituation to quinine.

8. P., a telegraph official, suffered during a stay of about five years in East Africa from numerous attacks of fever, returning at quite irregular intervals; they always came on with rigor, and were treated with quinine

in doses of from half a gram to three grams a day. From time to time the patient also took quinine in uncertain doses as a prophylactic. One day, about two hours after taking a gram of quinine through feeling out of sorts, he suffered from melanuria. After the colour of the urine had remained quite light for some days the patient, on the advice of his doctor, again took a gram of quinine, with the result that six hours later the urine once more was of a hæmorrhagic tint. Later on quinine was for some months taken every third or fourth day in half gram doses as a prophylactic. Melanuria certainly did not occur, but the fever attacks still did not cease. Return to Europe. Treatment of the malaria attacks with 1 to 1 gram quinine, which ordinarily resulted in no unpleasant consequences. Only once was the urine dark again and the skin yellowish. The next time he felt ill the patient, accordingly, by the advice of his doctor took two grams of salipyrin. The next day the urine was tinged with blood, and in the following twenty-four hours became almost black. Splenic tumour; jaundice; tertian parasites in the blood.

9. S., station official, fell ill of tropical malaria after three months' residence in the Togo District. Quinine treatment. Four months later, having felt well during the interval, the patient, thinking that he felt the prodromata of a febrile attack, took a gram of quinine. Two hours later he had melanuria; the urine cleared up again after four days. Within the space of about a year three attacks of blackwater fever followed. The bloody tinge of the urine occurred on each occasion about two hours after taking a gram of quinine; the temperature rose to 40.8°C. Return to Europe. After the last attack arsenical treatment.

10. L., sergeant, was taken ill three weeks after his arrival in Cameroon with a rigor followed by fever for five days. Quinine treatment. Monthly slight febrile attacks. No quinine prophylaxis. After two years in the interior severe blackwater fever. Patient had on account of indisposition taken half a gram of quinine; half an hour later he lost consciousness, and remained insensible for six hours. Dark urine, then anuria for two days. From the fourth day on the urine gradually cleared up. He lay ill three weeks, and then went by train to the coast, and was taken into the Cameroon lazaretto. Here the patient received half a gram of quinine on account of a slight attack of fever. Directly after a rigor came on, and he lost consciousness; the temperature rose to 41.7°C. Camphor and ether injections. Protracted convalescence.

11. K., missionary, returned to Europe after staying four years in East Africa. In Africa he had repeatedly suffered from malaria tropica, and had treated it with quinine both therapeutically and, for a time, prophylactically. On the journey from the interior to the coast he apparently contracted a fresh infection, for after being in perfect health for a year he suffered on board ship from slight weekly fever. The attacks recurred in similar fashion in Germany as well. Here the patient once, after the temperature had fallen, took a gram of quinine, and for the first time suffered from blackwater fever. He had a rigor, and the temperature rose to 39.5°C: the urine took on a dark hæmorrhagic coloration. The attack lasted three days and was repeated four weeks later. Patient had used half a gram of quinine as a remedy against neuralgic pains; three hours later the urine was bloody. The quinine treatment was counter-manned.

12. (Personal observation by Surgeon-Major H.). Repeated fever during two years in Dar-es-Salam. Irregular use of quinine. Arrived in Germany February 25th, 1901; last attacks on April 6th, 8th, and 10th. On April 17th patient felt indisposed, and at 10 A.M. took about 0.75 gram of quinine, repeating the dose at 3.30 P.M. Towards 9 o'clock in the evening a violent rigor came on again. Next morning the urine was of a blackish hæmorrhagic colour. The hæmoglobinuria continued for three days. In many preparations of the blood only quartan parasites of various generations were found.

13. Observation by Surgeon-Major Dempwolff. "During a four years' sojourn in South-West Africa the missionary S. suffered on three occasions, the last in March, 1900, from blackwater fever, always consequent upon the use of quinine. Taken into hospital (Outyo) and treated with methylene blue; increasing failure of strength; tropical rings in the blood. On this account a further experiment with quinine was made on April 22nd, 1900; the patient received 0.3 gram by the mouth in the morning. Hæmoglobinuria at once set in and was followed by anuria. Death."

14. S., petty officer. During seven months in the interior of German East Africa seven attacks of fever (malaria tropica). Treated with quinine. The patient to relieve a day's indisposition, took a gram of quinine hydrochloride and noticed two hours later that his urine was the colour of blood. Within five weeks this experience was repeated twice more. On each occasion the patient had previously taken a gram of quinine, as he believed he felt the signs of the onset of malarial fever. On the voyage home the patient suffered four times from fever without taking quinine; no melanuria. Admitted to Koch's wards on September

6th, 1900, on account of a return of the fever. Present state: a powerful man with faintly yellowish complexion, spleen palpable beneath the ribs. In the blood a few well-developed tropical rings, one half-moon. Nothing special in the urine. Temperature subfebrile. The patient was gradually accustomed to quinine. He received subcutaneously one-tenth gram of quinine hydrochloride, after some days one-fifth gram and so on. From September 27th on he had half a gram every seventh and eighth

day; temperature normal; no parasites remaining in the blood. As the patient wished to be discharged, and the continuance of the subcutaneous injections outside the hospital was inconvenient to him, he received on October 21st an experimental dose of a gram of quinine hydrochloride by the mouth. Eight hours later there was a rise of temperature; the urine was blood coloured; Heller's test gave a positive result. In the sediment were a few red blood corpuscles. Next morning the urine was clear. On November 8th half a gram of quinine hydrochloride was again given subcutaneously; no hæmorrhagic colour in the urine. If a gram of hydrochloride of quinine be given by the mouth when the stomach is almost empty about 30 per cent. (reckoned as anhydrous quinine) appears in the urine within twenty-four hours; of the half gram given subcutaneously only about 10 per cent. is thus recoverable. The quantity of quinine which our patient absorbed, and which caused his attack of blackwater fever, was thus six times as great as that which had previously been borne.

15. Observation by Dr. Nocht, Port Medical Officer at Hamburg. W., artisan. After three months' stay in Cameroon taken ill with remittent fever (apparently tropical). Patient was treated with quinine, and later on took every fifth day $\frac{1}{2}$ gram as a prophylactic. Almost a year free from fever. On October 1st, 1900, a fresh attack of fever; took three times on successive days $\frac{1}{2}$ gram of quinine. Four hours after patient had taken on the morning of October 7th $\frac{1}{2}$ gram of quinine (again as a prophylactic) he was attacked with a sudden rigor, with violent illness and fever. The urine was at first dark-red like blood; later on, after patient had been taken into the lazaretto, it assumed a blackish-brown coloration. After two months' further treatment without quinine patient started on the homeward journey. On the steamer he once, about December 10th, took $\frac{1}{2}$ gram of hydrochloride of quinine, which was followed next morning by an attack of blackwater fever. On January 4th, 1901, at Grabow (Mecklenburg), the patient's doctor gave him $\frac{1}{2}$ gram of quinine on account of fever. Six hours later there was a typical blackwater fever attack with marked jaundice. Rapid recovery. On

March 12th he was taken into the Seamen's Hospital at Hamburg. Condition: A man of medium strength, no jaundice; striking anemia of the skin; no fever, no oedema; liver slightly enlarged, spleen greatly enlarged. Blood examination showed 40 per cent. hæmoglobin, scattered large tropical rings and half-moons. In test tube experiments the blood of the patient dissolved quinine salts in the same concentration as normal blood. Nothing special in the urine. Treated with methylene blue. Since the presence of parasites in the blood continued the patient received at 8 o'clock on the morning of April 2nd, with his consent, a tenth of a gram of hydrochloride of quinine in a cachet. Two hours later the patient had a terrible rigor; he clung tight to the bed in order not to fall out. There was high fever; in the blood were a few large rings. He was collapsed in appearance, with rapidly increasing jaundice, violent vomiting, and a fluttering pulse. At 11 o'clock the urine looked ruby-red, and it soon became opaque. Heller's test for blood gave a positive result; in the sediment were no red blood corpuscles. Symptomatic treatment. After the cessation of the vomiting large quantities of fluid were given. On April 4th the hæmorrhagic colour of the urine had disappeared; the jaundice was also less, and the skin looked lemon-yellow. Treatment with methylene blue was again undertaken.

When we look through the histories of the patients we find that in each case the hæmoglobinuria followed more or less immediately the administration of quinine. This observation will be made the more frequently the more exactly inquiry is made into this particular point. Thus, in the sanitary report of the Royal Frontier Force in German East Africa for the year 1898-99, 33 attacks of blackwater fever are recorded, which affected 24 different patients. The onset of all the attacks was proved to be preceded by a shorter or longer use of quinine. In the report for the year 1899-1900, 19 attacks of blackwater fever in all came under observation, affecting 17 people. Two had admittedly taken quinine some time before—twelve days and six months respectively before the illness. One person—in spite of repeated intermittent fever—had never taken it (?). In 7 cases, on the other hand, quinine had been taken the day before, and in all the remainder the patients had partly on their own initiative, partly under medical advice, used the drug a few hours (three to seven) before the onset of hæmoglobinuria. Almost always it was expressly remarked

that the temperature was not febrile when the remedy was taken. In view of such facts the question arises why in our latitudes a man who suffers from any given disease,¹⁴ and takes quinine on that account, never has blood-coloured urine even after its abundant use. Against this it is to be remarked that in the first place so extensive and unregulated a use of quinine as in the tropics never occurs with us, thus we have absolutely no idea as to how, if at all, the prolonged administration of the drug influences the composition of the blood. In this second place the blood corpuscles which are destroyed in blackwater fever are not healthy, but have been already severely damaged by the preceding or still continuing disease of the blood—namely malaria. We often notice that patients who at once react to quinine with hæmoglobinuria, after some days bear the same dose without injury. This no longer appears accidental if we agree with Koch¹⁵ that the destruction of red blood corpuscles is proportional to the extent of the existing morbid changes and the amount of quinine administered. The second dose, which is well borne, has no longer to deal with severely injured blood corpuscles. If the dose of quinine be increased hæmoglobinuria can again eventually ensue, as long as the dose is great enough to destroy also slightly ailing red blood corpuscles.¹⁶ The so-called rehabilitation of convalescents from blackwater fever to quinine is nothing more than a gradual purification of the organism from all more or less diseased blood cells. Commencing with minimal doses of quinine, we stop at the dose which is empirically useful in the contest against malarial plasmodia.

The view that quinine exerts its toxic influence especially upon diseased blood corpuscles is nothing out of the ordinary. A weakened organism is more powerfully acted upon by poisons than a healthy one. This can be proved by many analogies, and thus one can completely dispense with the so-called individual predisposition, which perhaps also plays a part. In Case 8 hæmoglobinuria followed the use of salipyrin. If other drugs beside quinine, such as for instance anti-febrin, phenacetin, etc., were equally widely employed for malaria in the tropics, we should probably also obtain for observation blood-coloured urine after the use of these remedies. In the most recent literature on the subject a case is described¹⁷ in which after quinine had ceased to be used a blackwater fever patient suffered from renewed hæmoglobinuria when a gram of phenacetin was given him.

Regarding the reports concerning blackwater fever without preceding use of quinine, it must be mentioned that critical limitation is here often necessary. As I have been repeatedly and expressly assured by experienced tropical physicians the obtaining of a correct history is a matter of great difficulty. The question "Have you taken quinine?" is negatived while the patient involuntarily means, "I have not taken quinine abundantly or not more than usual," or "some time has already elapsed since I have taken it." Stephens¹⁸ refers to these difficulties. He states that in many cases the history given is in direct opposition to facts. He also maintains that the hæmoglobinuria of aborigines, who, according to the assurances of many observers, have never come into contact with quinine and yet suffer with this symptom, is in part certainly not identical with our blackwater fever, but is produced by the bilharzia hæmatobia. Among the blackwater fever cases of the English malaria expedition there is not a single one in which the use of quinine can be undoubtedly excluded. On the other hand, the hæmoglobinuria followed more or less rapidly on the heels of the quinine, and made the English observers certain that a causal relation existed between the two.¹⁹ They thereby confirmed the conclusions of R. Koch. Two Belgian physicians draw different deductions from the same observations. Van Campenhout and Dryepondt²⁰ quote in the report of the work of the Mission Médicale Belge au Congo 16 cases of blackwater fever; 13 of these could be straight away ranked with my cases as cogent proofs of the quinine theory. A few hours after taking moderate doses of quinine blackwater fever, with its well-known accompanying symptoms came on; three of the patients died. In spite of the clear state of affairs the authors instituted thorough investigations into the cause of the hæmoglobinuria, which they chiefly attributed to chill. They consider that Koch's theory is entirely wrong, and hold that he himself has been led away by his prejudices. Some sentences from the publication of

the English Malaria Expedition²¹ may here be literally quoted, as they seem to me to be very appropriate: "It would appear from the criticisms made on Koch by many writers that they have not taken the trouble to acquaint themselves at first hand with his writings, for views are constantly attributed to him which certainly are not to be found in his writings."

As a matter of fact, R. Koch has in nowise altered his views. Now as formerly he believes that in the majority of cases blackwater fever is the result of quinine poisoning in malaria patients. But, at the same time, he holds that by means of an appropriate quinine prophylaxis malaria, and with it, in the vast majority of cases, blackwater fever, can be stamped out. An imperfect quinine prophylaxis which does not entirely protect against malaria, on the other hand predisposes to blackwater fever, for in such a case plasmodia and quinine unite to act harmfully on the organism.

NOTES AND REFERENCES.

¹ R. Koch, *Reiseberichte*, Berlin, 1898. ² Quoted from Laveran, *Extrait du Bulletin de l'Académie de Médecine*, Séance du 4 Décembre, 1900. See also Foustanos, *La Grèce Médicale*, No. 4. ³ Laveran, *loc. cit.* ⁴ S. Tomasselli, *La Intossicazione Chinica e l'Infezione Melanica*, terza edizione, Catania, 1897. ⁵ F. Plehn, *Ueber das Schwarzwasserfieber an der afrikanischen Westküste*, *Deut. med. Wochenschrift*, 1895, No. 25 et seq. ⁶ Cardamatis, *De la Fièvre Hémoglobinoïdique*, *La Grèce Médicale*, 1900, No. 4. ⁷ G. Laveran, *Traité du Paludisme*, Paris, 1898, p. 197. ⁸ *Loc. cit.* and v. Jaksch, *Klinische Diagnostik*, Berlin and Vienna, 1901. ⁹ Moffat, *Blackwater Fever and Hæmoglobinuria*, *BRITISH MEDICAL JOURNAL*, September 24th, 1898, p. 926. ¹⁰ Harford Battersby, *BRITISH MEDICAL JOURNAL*, October 15th, 1898, p. 1200. ¹¹ Epidemiological Society, *BRITISH MEDICAL JOURNAL*, March 25th, 1899, p. 721. ¹² R. Koch, *Ueber Schwarzwasserfieber (Hæmoglobinurie)*, *Zeitschrift für Hygiene*, etc., 1899, vol. xxx. ¹³ In the history of the patient given under No. 12 the blackwater fever was associated with a quartan ague. ¹⁴ Malaria of course excepted. In Cases 11 and 12 the first blackwater fever attack came on in Germany. ¹⁵ *Loc. cit.* ¹⁶ See Case 14. ¹⁷ *Rapport sur les Travaux du Laboratoire Médical de Léopoldville*, Bruxelles, 1901, p. 96. ¹⁸ Stephens, *Blackwater Fever*, reprinted from the *Lancet*, March 23rd, 1901. ¹⁹ Royal Society, *Reports to the Malaria Committee*, fifth series, London, 1901. ²⁰ *Rapport sur les Travaux du Laboratoire Médical de Léopoldville*, Bruxelles, 1901. ²¹ *Loc. cit.*, p. 21.

THE INFLUENCE OF COLOUR UPON ANOPHELES.

By GEORGE H. F. NUTTALL, M.A., M.D., Ph.D.,
University Lecturer in Bacteriology and Preventive Medicine,
Cambridge.

In pursuing our Studies in Relation to Malaria, which are appearing in the *Journal of Hygiene*, my colleague, Mr. A. E. Shipley, and myself thought 'it desirable, amongst other things, to study the influence of colour upon *Anopheles maculipennis*. From what is known of the behaviour of other insects to colour, and occasional hints we have obtained from observing the behaviour of *Anopheles*, we had concluded that we might, as the result of our experiments, obtain results having a definite practical bearing.

It seemed to us to be a matter of considerable practical utility to determine what influence, if any, colour exerted upon a known malaria-bearing species of mosquito; and we deem our results sufficiently striking to make it worth the while for those who are engaged in similar studies abroad to take the matter up systematically. Our experiments certainly indicate that *Anopheles maculipennis* is attracted by some colours and repelled by others, a matter which would have its practical application in the choice of the colour of clothing and the interior of rooms in malarious districts.

The preference of *Anopheles* for dark and shady places, whither they retreat during the daytime, has been noticed by a number of observers. The behaviour of the insects towards various colours has not as yet received sufficient attention. Whilst engaged upon our experiments we came upon a few data cited in the recent literature.

Austin¹ writes: "If the walls of the room be whitewashed, with a dark dado, it is interesting to note that the insects will always be found upon the dark strips, and never on the white portions of the wall." Buchanan² in India noted that "the men who collect the living *Anopheles* say that the *Anopheles* hide in a black coat, but avoid a white coat, so they hang up one or two black coats in the hospital ward" when they desire to catch the imago. Neither Austin nor Buchanan say anything about the influence of colour. The first, as far

as we know, to refer directly to the influence of colour is Joly, who made observations on mosquitos in Madagascar. He states, without saying what genus, that "mosquitos" there were more attracted to black than to red soil or to white sand. Persons wearing black shoes and socks were more bitten than when these articles of apparel were white. Brown clothes protected less than those of white or blue. He states that the natives of Madagascar know the attraction black offers to mosquitos, and for this reason hang up a black cloth on the rafters of the room for the insects to collect upon. Joly observed that a yellow-haired dog was very much less bitten than a black one. For the same reason the natives are more bitten than the whites, although they suffer less from the after-effects.

Our experiments were made in a large gauze tent, which had been erected within a disused photographic establishment, the one end of the tent ending against large windows, into which the sunlight poured on bright days. Large stone basins were placed on the floor for the *Anopheles* to breed in, the stock being renewed from time to time.

It was noticed at the beginning that when one entered the tent in dark grey clothes the imagos frequently flew up and settled on the dark cloth, but that they never did this when the person entering the tent was clothed in white flannels. To test the influence of colour, a number of pasteboard boxes were taken which measured 20 cm. by 16 cm. and had a depth of 10 cm. The boxes were lined with cloth, having a slightly roughened surface, to which the insects could comfortably cling. All of the fabrics had a dull surface, and each box was lined with a cloth of different colour. The boxes were placed in rows upon the floor and upon each other in tiers, the order being changed each day after the observations had been made. The interior of the boxes was moderately illuminated by light reflected from the surface of the white tent. On seventeen days during a month, beginning with the middle of June, we counted the number of flies which had accumulated in the boxes. Counts were actually made on seventeen sunny and cloudy days, and with the following result:

Colour of Box.		Number of <i>Anopheles maculipennis</i> Counted in each Box during Seventeen Days.	
Navy blue	...	...	108
Dark red	...	...	90
Brown (reddish)	...	...	81
Scarlet	...	...	59
Black	...	...	49
Slate grey	...	...	31
Dark green (olive)	...	...	24
Violet	...	...	18
Leaf green	...	...	17
Blue	...	...	14
Pearl grey	...	...	9
Pale green	...	...	4
Light blue (Forget-me-not)	...	...	3
Ochre	...	...	2
White	...	...	2
Orange	...	...	1
Yellow	...	...	0

We see from the above table that dark blue was most attractive, the other colours being less and less attractive in the order of numbers given. A marked fall in the number of insects resting in the boxes begins with the "blue" box; the colour in this case was a rich full blue. Pale green, light blue, ochre, orange, and yellow, especially the last two colours, seemed to repel the insects.

The khaki uniform at present in vogue should therefore offer advantages besides being invisible to the human enemy. It is of course true that the *Anopheles* bite more frequently during twilight and at night, but the choice of clothing having a repellent colour should afford a measure of protection against the insects which may bite during the daytime. In any case, the number of insects congregating in dwellings might very well be lessened by the choice of colours of a suitable character applied to the walls. It has also occurred to me that some sort of trap might readily be devised, lined with a suitable colour, such as dark blue, within which the insects would congregate and easily be destroyed in considerable numbers. Our experiments with boxes have been so striking that such a plan immediately suggested itself. Unfortunately for the experiment we are not living in a country where *Anopheles* are numerous, so we will hope that those who are placed in more