perimeters seem to be admirably adapted for the delimitation of scotomata.

Many years ago (1888) Dr. George Mackay, also of Edinburgh, exhibited at the Glasgow meeting of the British Medical Association a large circular perimeter, which perhaps fulfilled to some extent the purposes of a large tangent screen. As has been shown, the ordinary circular perimeters often fail to reveal important defects in the field of vision, which at once become apparent when the more reliable tangent screen method is used. Those who have used screens for the investigation of the centre of the field, say from zero up to 50° , have no doubt of their superiority for that purpose.

In using tangent perimeters, for the reasons above stated, it is desirable to have the patient at a considerable distance from the centre of the screen. At the distance of only half a metre the tangent perimeter does not possess much advantage over a circular perimeter with a radius of curvature of half a metre. If the distance of the patient's eye be a metre from the fixation point on the screen, then for 45° , as the tangent of 45° is unity, the screen must in all directions extend to one metre from the central fixation point. For a distance of two metres a screen would require to measure, for an angular opening of 45° in all directions, at least 200 cm. from the fixation point. That, of course, at once shows the limited use which can be made of tangent screens, because, even with a spacious room, it is impossible to get 70 inches between the fixation point and the floor; moreover, the patient's eye should be as nearly as possible on a level with the fixation spot. For the thorough examination of the centre of the field of vision the tangent perimeter will be found to be most serviceable. In the usual forms supplied for recording perimetric examinations there is the same distance between zero and the circle representing 45° as there is between the circle representing 45° and that representing 90° , also the same distance between zero and

30° as there is between 30° and 60° and as there is between 60° and 90° . So long as the examiner recognizes the fact that he is dealing with polar co-ordinates and can translate their meaning then no great harm will accrue. But one advantage of tangent perimeters, where applicable, is that they give the field of vision without any need of interpretation.

Dr. Sinclair of Edinburgh, and probably other workers, have availed themselves of tangent scales. A tangent scale can be easily prepared for any radius, such as that of a metre or of two metres, or any other measurement that may be required; but I think that nothing more is necessary than to take a note of the field given by a tangent perimeter in ordinary rectangular co-ordinates. The screen perimeter I use is black, and on it are traced in black tape the ordinary x and y co-ordinates. There is nothing to prevent the whole screen being divided up by such pieces of tape into little squares, the length of the side of each little square being two inches or even less, according to the breadth of the tape.

In the first quadrant both the abscissa and the ordinate are positive; in the second the abscissa is negative and the ordinate is positive; in the third quadrant both the abscissa and the ordinate are negative, and in the fourth the abscissa is positive and the ordinate is negative. Now with such a perimeter all that has to be done is to note accurately the values for x and y of every point taken in the boundary of a scotoma. There is no need whatever to transfer it to polar co-ordinates. Of course, should any such need arise, the calculation is of the most simple kind provided the distance at which the patient was placed from the fixation point has been accurately noted.

This simple method seems to avoid a considerable amount of trouble, and has the advantage that no special diagram requires to be made for the recording of the results; ordinary ruled paper, such as is commonly used for graphs, is all that is necessary.

ICTERUS WITHOUT HAEMOGLOBINURIA AFTER QUININE TREATMENT.

BY

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THE part played by quinine in the genesis of haemoglobinuria has received the attention of many investigators, and the opinion has been expressed that in certain cases it can act as the precipitating agent of the attack. Castellani and Chalmers, indeed, in their textbook, consider the relationship so intimate as to warrant quinine haemoglobinuria being defined as a clinical entity apart from true haemoglobinuric fever. There seems, however, no justification for this from the clinical point of view, since the symptoms and course of the disease are essentially the same in both.

Stephens and Stott (1915) have collected a record of 103 cases in which the intimate relationship between the administration of quinine and haemoglobinuria could not be ignored; while Thomson (1924) has more recently published records of two cases in which the correlation was most striking. The consensus of opinion would seem to be that while quinine in many cases does not play a leading part in the genesis of haemoglobinuria, cases do occur in which it seems to act definitely as the immediate cause.

How quinine may bring about haemoglobinuria will not be discussed further than to say that it is generally accepted that the haemoglobinuria is secondary to a haemoglobinaemia brought about by the lysis of erythrocytes in the blood stream. Plehn (1920), mainly on histological grounds, has disputed this theory of intravascular haemolysis in haemoglobinuria, and considers that the haemolysis takes place in the renal tubules. Salvioli (1922) and

Ziemann (1926), however, working on the same lines as Plehn, were unable to confirm his findings.

Barratt and Yorke (1909), on the other hand, have brought forward evidence pointing to the blood stream as the site of lysis. In a series of observations on black-water cases they found that in certain cases the percentage of haemoglobin free in the plasma was considerably higher than in normal controls. In others, however, the figure approximated to that found in health, but they consider that this does not necessarily refute their assumption of intravascular haemolysis, since, owing to the relatively long intervals at which patients may pass urine, it may quite well be that, although the urine does contain haemoglobin, active excretion of it may have ceased. Arkwright and Lepper (1918) and Dudgeon (1920) have reported similar findings.

While direct proof of haemoglobinaemia may be lacking, it is possible to obtain information indirectly that supports this hypothesis. Thus an increased content of substances in the blood stream which are known to be derivatives of haemoglobin would point to an intravascular haemolysis.

It is now generally accepted that haemoglobin is broken down in the cells of the reticulo-endothelial system, particularly, if not wholly, by the Kupffer cells which are found in the liver sinuses, and is converted into bilirubin and haemosiderin. Thus, in conditions in which haemolysis exists, an increased output of bilirubin can be anticipated. That this is the case in malaria, in which blood destruction in excess of normal exists, has been shown by van den Bergh (1924), Hughes (1924), and Kingsbury (1926). Van den Bergh's test is now so widely employed that it requires no description, but it may be emphasized that not only does it afford a measurement of the amount of bilirubin present but it also distinguishes between what might be termed mature and immature bilirubin in the serum. Mature bilirubin is that which has passed through the polygonal cells of the liver and has then been absorbed into the blood stream, and is present in cases of obstructive jaundice. This variety gives the direct reaction. If, however, owing to rapid blood destruction, bilirubin is

produced at so rapid a rate that the polygonal cells are unable to deal with it *in toto*, the excess is absorbed directly into the blood stream from the Kupffer cells, and forms the immature bilirubin which gives the indirect reaction. An indirect reaction should, then, be obtained in those cases where the pathological factor is increased blood destruction, and it is this variety which occurs in pernicious anaemia and malaria. Such a reaction can be accepted as evidence of intravascular haemolysis.

In haemoglobinuric fever, in the initial stages of the disease, the indirect reaction is strongly positive and the number of units of bilirubin present shows a huge increase on the normal amount of 0.2 to 0.5 unit found in normal controls (unpublished results of one of us, G. R. R.). We have thus indirect evidence that haemoglobinuria in haemoglobinuric fever is accompanied by haemoglobinaemia. There can be no doubt that the haemoglobinaemia must precede the haemoglobinuria. Assuming, then, that haemoglobinaemia exists, it can be postulated that two mechanisms at least come into play in the endeavour to rid the body of the haemoglobin dissolved in the plasma. At first there is an increase in the activity of the reticulo-endothelial system, so that as much as possible of the haemoglobin may be disposed of by the normal methods of converting it into bilirubin. This we know does happen. If, however, the amount of haemoglobin is in excess of the maximum with which the reticulo-endothelial system can deal, then excretion by the kidneys occurs, with consequent haemoglobinuria. We can thus assume that there exists a threshold value for haemoglobin; whether that is constant or whether it varies from individual to individual is not as yet clear. It cannot be assumed at present that the reticulo-endothelial system, on the activity of which the threshold value must in part depend, functions equally in every individual. It is, however, known that if the haemolysis be slow and gradual, as in pernicious anaemia, or even sudden but relatively slight, as in malaria, haemoglobin does not appear in the urine.

Turning now to the question of quinine haemolysis *in vivo*, it is conceivable that if quinine can produce haemolysis sufficient to cause the appearance of haemoglobin in the urine, cases might occur in which the degree of haemolysis is so slight that the free haemoglobin can be disposed of entirely by the reticulo-endothelial system without the appearance of haemoglobinuria. References to this possibility are relatively few. Koch (1898) stated that after the administration of quinine an attack of icterus may occur. Blacklock (1923) believes that haemolysis with slight jaundice can occur without haemoglobinuria and that this condition is frequently due to the same cause as blackwater fever.

The following case is reported as an example of haemolytic jaundice after quinine treatment without the development of haemoglobinuria.

A male European, aged 11, was admitted to Salisbury Hospital under the care of one of us (G. H. P.) as a "pre-blackwater case" on March 4th, 1926. A history was obtained of repeated attacks of malaria throughout the previous six months. The patient was pale, sallow, and thin. He exhibited characteristic malarial cachexia with lemon-yellow conjunctivae. There was, however, no clinical jaundice in the true sense of the term. A blood examination on the day of admission gave the following result: Red blood corpuscles 1,300,000 per c.mm., white blood corpuscles 5,700 per c.mm., haemoglobin 39 per cent. The red cells did not exhibit any abnormality except occasional polychromasia. A differential count showed: Polymorphonuclears 56 per cent., lymphocytes 21 per cent., mononuclears 20 per cent., eosinophils 2 per cent., transitionals 1 per cent. No malarial parasites were seen.

Examination for parasites was also negative on March 6th, 7th, and 9th. The spleen was enlarged to two fingerbreadths below the costal margin. The treatment adopted was on general lines, including the exhibition of liquor arsenicalis and sodium bicarbonate with ample quantities of bland fluids. On March 9th, acting on the assumption that antimalarial treatment was indicated, quinine therapy was instituted, starting with extremely small doses in view of the possible onset of haemoglobinuria.

Thus on March 9th 1/32 grain of quinine bishydrochloride was given; on March 12th the dose was increased to 1/32 grain thrice daily, on March 14th to 1/16 grain thrice daily, on March 15th to 1/8 grain thrice daily, on March 18th to 1/4 grain thrice daily, on March 19th to 1/2 grain thrice daily.

On March 20th the patient complained of severe headache, nausea, and splenic pain. The spleen was now four fingerbreadths below the costal margin. There was slight vomiting, and the temperature, which had been rather febrile for about a week,

rose to 100.2°, and on the two succeeding days reached maxima of 100.8° and 100.6°. On the morning of March 21st the patient was obviously jaundiced, and in the course of a few hours became intensely so. Blood counts done on this day gave the following results: Red blood cells 1,250,000 per c.mm., white blood cells 6,000, haemoglobin 35 per cent. Fouchet's test for bile pigment in the serum was positive. The van den Bergh test gave a positive indirect reaction, and the number of units of bilirubin present, as estimated by the Tannhäuser and Andersen technique, was 2.5. Blood smears were examined on March 21st, 22nd, 23rd, and 24th, but the red cells showed no abnormality and malarial parasites were absent.

Quinine was immediately stopped and the icterus completely disappeared in the course of two days. The temperature came down to normal, and the pulse, which in the pre-icteric period had varied between 80 and 90, and which during the icterus varied between 120 and 140, returned to its former level. The stools were normally coloured throughout the icterus. An estimation of bilirubin made on March 24th showed 0.75 unit to be present in the serum, which is slightly in excess of normal.

The patient was given injections of sodium methylarsenate and was kept under observation for a period of fourteen days, during which no untoward symptoms developed. The urine was examined daily, in twenty-four hour specimens, for blood pigment, during the icteric period, by the benzidine test and spectroscopically; the results were invariably negative. Urobilin was never present in a greater dilution than 1 in 10 (Marcussen and Hansen technique).

This case, in our opinion, is an example of an intravascular haemolysis, evidenced by jaundice, but with no accompanying haemoglobinuria. There can be no doubt that the jaundice was haemolytic in type. As regards the relationship of quinine to the intravascular haemolysis, it is true that the icterus did not make its appearance clinically until the twelfth day after the institution of quinine treatment, but it must be remembered that the sallowness of the patient and the lemon-yellow conjunctivae, so characteristic of chronic malaria, prevented the appreciation of slight additional degrees of icterus.

Again, the dosage of quinine was exceedingly small; only 1½ grains were being given daily, and only 5½ grains had been administered altogether when the jaundice became clinically apparent.

The disappearance of the icterus on the stoppage of quinine treatment affords additional support to our belief that the quinine acted as a haemolytic agent.

The interest of the case, however, lies mainly in the fact that, while intravascular haemolysis sufficient to produce marked clinical jaundice had taken place, haemoglobinuria did not develop.

REFERENCES.

- Arkwright, J. A., and Lepper, E. H. (1918): *Trans. Soc. Trop. Med. and Hygiene*, vol. ii, No. 4, p. 127.
Barratt, J. O. W., and Yorke, W. (1909): *Annals of Trop. Med. and Parasitol.*, vol. 3, No. 5, p. 1.
Blacklock, B. (1923): *Ibid.*, vol. 17, No. 1, p. 79.
Dudgeon, L. S. (1920): *Journ. of Hygiene*, vol. 19, No. 2, p. 208.
Hughes, T. A. (1924): *Indian Journ. of Med. Research*, October, vol. xii, No. 2, p. 403.
Kingsbury, A. Neave (1926): *Trans. Roy. Soc. Trop. Med. and Hygiene*, February 18th, vol. xix, No. 8, p. 459.
Koch, R. (1898): *Arbeiten aus dem Kaiserlichen Gesundheitsamte*, No. 14, p. 304.
Plehn, A. (1920): *Arch. f. Schiffs- u. Tropen-Hygiene*, vol. 24, No. 11, p. 321.
Salvioli (1922): *Ibid.*, vol. 26, p. 6.
Stephens, J. W. W., and Stott, W. (1915): *Annals of Trop. Med. and Parasitol.*, vol. 9, No. 1, p. 201.
Thomson, J. Gordon (1924): *London School of Tropical Medicine, Research Memoir Series*, vol. vi, *Researches in Blackwater Fever in Southern Rhodesia*, p. 83.
Van den Bergh, Hijmans (1924): *BRITISH MEDICAL JOURNAL*, September 24th, p. 495.
Ziemann, H. (1926): Discussion of paper by Plehn, *Beihefte, Arch. f. Schiffs- u. Tropen-Hygiene*, vol. 30, No. 1, p. 56.

DETOXICATION IN THE TREATMENT OF BURNS.

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DETOXICATION, as part of the treatment of burns and scalds, has not received the attention it deserves, though burns owe most of their deadliness to toxæmia. In the course of prolonged inquiries in many directions I have come across only one man who had used a dressing with detoxicating properties; this was an application of ichthyol and glycerin, covered over with boric fomentations. None of the younger men had heard of such treatment, which is the more remarkable in view of the great advances made in the treatment of infected wounds during the latter part of the war.