				Total No. per c.mm.
February 24th.				
Red blood cells 3,240,000	Polymorphs	...	16%	296
Haemoglobin 68 per cent.	Lymphocytes	...	66%	1221
Colour index 1.0	Endothelials	...	16%	296
White blood cells 1,850	Eosinophils	...	1%	
	Mast cells	...	1%	
Size of red cells, 7.81 microns.				
March 3rd.				
Red blood cells 3,910,000	Polymorphs	...	12%	264
Haemoglobin 72 per cent.	Lymphocytes	...	80%	1760
Colour index 0.92	Endothelials	...	8%	
White blood cells 2,200				

Red cells almost normal in appearance and by Eve's halometer 7.48 microns (normal).

It will be seen that throughout there was a very grave anaemia with a high colour index, reaching on January 5th the figure 1.3. The white count in the most serious part of the illness was very low, and the total polymorph count extremely so. The size of the red cells was never enlarged as determined by Eve's halometer, except on one occasion (January 13th), when it was increased and in the pernicious zone. The whole gives a picture of serious interference with the bone marrow, but with some evidence of activity of that tissue. The interpretation of these counts is that the patient suffered from an aplastic type of anaemia (agranulocytic anaemia). The last blood count, though the patient was apparently convalescent, showed a moderate degree of anaemia of this type.

The Cardio-vascular System.

The pulse from the early stage of the illness was fast, and was seldom recorded below 100. When the anaemia was most marked in the early days of December it varied about 120. It appeared to be higher after the first transfusion. On December 11th the pulse was recorded up to 152; on this day the patient appeared to be dying; she was extremely pale, was breathless (respirations 48), and orthopnoeic. Injections of adrenaline chloride 1/1000 of 0.5 c.cm. at three-hourly intervals caused great relief to the breathing and a lowering of the pulse rate. Subsequent to this the injections were repeated thrice daily until December 30th, when they were reduced to two a day. It was reduced to once a day on January 7th and discontinued on February 7th.

Remarks.

The case in one aspect was one of streptococcal septicaemia. The illness began with a sore throat. Fever persisted altogether in the first instance for twenty-nine days at a high level. Though no blood culture was made streptococci were identified as the causal agent of the renal haemorrhage on November 19th. Streptococci were the cause of the thyroidal abscess which was opened on December 24th; the same organism was found in the sloughs passed in the urine on January 24th. The damage so obvious in the kidney and the thyroid appeared also in the bone marrow, as shown by the nature of the anaemia, the rheumatic pains, and the presence of albumose in the urine.

In the matter of therapy only the most important drugs and measures are mentioned. The first blood transfusion appeared to have some effect, but the second following the increased dose of adrenaline appeared to act in a marvellous way. The action of the adrenaline appeared to serve more as a cardiac stimulant than as a haemopoietic, such as appears to be so clear in a previously published case.¹

As convalescence was established the patient returned to her home and ceased to be under our observation. The blood count, it will be seen, was not normal, and as the patient is young there is room for hope that some, if not complete, restoration of function of the bone marrow may ultimately ensue. It may be mentioned, however, that the patient in the case previously described by one of us¹ still retains the blood count of an aplastic anaemia.

Since the above was written the patient, after leading a normal life again, suffered from a severe tonsillitis and died after a short illness.

REFERENCE.

- ¹ Gibson, A. G.: *Lancet*, 1926, ii, 948.

THE DIRECT COMPARATIVE DIFFRACTION METHOD OF DEMONSTRATING MEGALOCYTOSIS.

BY

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Two noteworthy articles by Pijper¹ and Eve² appeared in the literature of the past year describing instruments for the practical application of the diffraction phenomenon to the diagnosis of pernicious anaemia. Both instruments show advance in the direction of simplification of necessary apparatus for convenience in clinical use. Edwards³ has described a modification of Pijper's instrument with a simpler form of illumination.

The "direct comparative diffraction" method is a further simplification. Exhaustive examination of blood films fails to show that it sacrifices efficiency for simplicity. For the practical diagnosis and control of the treatment of pernicious anaemia, I have found that the results compare advantageously with those obtained by either Eve's halometer or Edwards's modification of Pijper's "diffraction micrometer." My personal observations have been controlled and verified by the untutored observation and discrimination of a large number of individuals of varying intelligence, who merely described what they saw in complete ignorance of the significance of their findings.

The only essential apparatus is a normal blood film with which to compare films taken from cases suspected of suffering from the disease. Any source of artificial light may be used, but candle light is probably best on account of its softness. The flame of any small cigarette lighter with an exposed wick gives excellent results and is easily carried.

Principle of the Method.

The method depends on the following facts. If a light is observed through a blood film held close to the eye a diffraction halo is seen which varies in intensity with the thickness of the film and the size, quality, and distance of the light. The halo consists of two zones, the inner of which is a yellow disc surrounded by an orange ring. The outer zone consists of concentric coloured circles of red, orange, yellow, green, blue, indigo, and violet, from without inwards. Interposed between the two zones and actually belonging to the inner one is a red ring, which mingles to a varying degree with the orange and violet. For the test this red ring is taken as the dividing line between the two zones.

If the light is observed through two blood films, one in front of each eye like spectacle lenses, actually only one halo is seen. In reality it consists of the superimposed haloes of the two films. The production of diplopia separates the haloes and presents them side by side for comparison as to size. The haloes for the corresponding films are on the same side as the films. The diplopia can be produced by a voluntary internal squint or by placing a prism, such as is found in refraction test cases, in front of one eye with the base to the inner side.

The inner zone is the one chosen for comparison. By comparison with the halometer and modified micrometer I have found that the central disc varies in size inversely with the average size of the red blood corpuscles. It is possible to note variations of 0.1 degree according to Eve's scale. The greater the degree of megalocytosis the more accurate is the discrimination. Comparatively speaking, the difference in the size of the haloes which would give readings of 4.7 and 4.1 degrees respectively by Eve's scale might be taken as the difference between a halfpenny and a sixpenny piece; 4.3 and 4.1 degrees as the difference between a florin and a halfpenny.

Making of Films.

Wash the slides with soap and water, rinse thoroughly, dry with a towel and polish with a piece of silk. To obtain a drop of blood, pierce the lobe of the ear, which need not be sterilized, with a sterile medium-sized surgical needle. Squeezing the lobe does not affect the test. Take the drop on one end of the slide, allow it to spread along

the edge of another slide, and with the latter push it rapidly towards the other end. This gives a film which tapers off in thickness, a condition ideal for the test.

To obtain a standard film take drops of blood from several known healthy persons and compare the size of the central zones of their diffraction haloes. If no difference in size can be noticed between any of them, any one may be taken as standard.

Technique of Test.

Hold the standard film between the finger and thumb of one hand and the unknown film in the other. Examine the source of light through both separately to find the spot where the halo is seen most clearly. Having done this, hold both films close to the eyes with the upper ends of the slides resting against the eyebrows. Produce diplopia, and compare the size of the central discs of the separated haloes. If a prism is used, fix it to the front of the slide with the finger and thumb, with the base inwards, and examine by the method I have described. Make sure first that the prism will produce diplopia. Whatever method is used the observations should be checked by transposing the slides.

Two fallacies may arise which are easily avoided provided the possibility of their existence is recognized. They only cause confusion when examining slides whose corresponding haloes are practically equal. Prolonged gazing at a bright light may cause a variation in the size of the haloes from irritation of the retina. It may even be found that the smaller halo remains on the same side when the slides are transposed. The remedy is to use a soft light and to carry out the examination as expeditiously as is compatible with accuracy. The soft light of a candle is best, and I always use it in finally deciding doubtful cases.

If the voluntary internal squint is used, too long continuance of it may result in changes in the size of the haloes. This is due to unequal spasm of accommodation, and is most likely to occur if the light is brilliant and the operator unpractised. Only those who can produce diplopia readily should use the squint method. To correct the error rest the eyes for a few moments and examine the film again. If in doubt use candle-light.

Value of the Test.

According to the observations of Price-Jones and Hurst an increase in the size of the red blood corpuscles is a constant feature of pernicious anaemia. The "direct comparative diffraction" method shows this change, if present, by allowing of the comparison of unknown blood films with normal blood films. The accuracy of the test depends on the finding of A. Pijper that the diffraction halo produced by passing a beam of light through a blood film varies in size inversely with the average diameter of the red blood corpuscles.

Application of the Method.

The presence of symptoms suggestive of pernicious anaemia and spinal cord degeneration calls for its use, as also do the symptoms classified under pre-pernicious anaemia described by Eve. Marked positive results are diagnostic. Negative results accompanied by strongly suggestive symptoms of "pre-pernicious anaemia" must be followed by very thorough physical examination, including a test meal for achlorhydria, examination of stools for occult blood, ova, etc. Failure to follow this last rule suggests a compromise between a desire for early diagnosis and a disinclination to follow the desire to a logical conclusion.

Prophylaxis.

The inclusion of "pre-pernicious anaemia" with pernicious anaemia under the heading of "megalocytic anaemia" appears to me confusing. Pre-pernicious anaemia by its very definition is not accompanied by anaemia. Also from the point of view of the pathogenesis of the condition the term as applied by Eve is misleading. Hurst⁴ has shown that the primary condition is achlorhydria, which allows of infection of the duodenum by a haemolytic streptococcus. This appears to be the starting point from which the toxin is produced. Absorption of this toxin eventually results in the changes in the body which are recognized as pernicious anaemia. It would seem to be more helpful to call the interval between

infection and the onset of anaemia the incubation period of pernicious anaemia.

If this view is taken the scope of prophylaxis is extended. A negative result of examination for megalocytosis, if accompanied by achlorhydria, should be followed by removal of all septic foci and treatment by hydrochloric acid. The patient should be told of the possibilities of the condition and instructed to attend every month for blood examination. I am at present treating a patient on these lines with very satisfactory results. I have impressed on her the importance of seeking advice immediately on the reappearance of symptoms. If megalocytosis is found, liver treatment must be given.

Control of Treatment.

Once treatment has been commenced this method may be used as a check on any improvement. Blood films should be taken every fortnight and marked with name and date. Each new blood film should be compared with the standard and as many of the previous films as are necessary to check whether the condition is stationary, improving, or retrogressing. The slides can be safely kept between succeeding folds of white paper.

Comparison with Other Methods.

The disadvantages of this method are more numerous in theory than they are real in actual practice. It might be argued that slight differences in the average diameter of the red blood corpuscles—say 0.05μ —would not produce differences in the size of the haloes easily discernible to the eye. Even if this is literally true, it by no means diminishes the value of the method. On the contrary, it enhances it because the absence of a sharp dividing line between normocytosis and megalocytosis renders such delicate differentiations valueless and misleading in diagnosis.

With regard to delicacy of differentiation in the observation of any increase or decrease in the size of the corpuscles it compares very favourably with Eve's halometer. I have not found that different observers, even with practice, get constant results with the same slides in the use of this instrument. This is due to the fact that as the haloes are approximated the arcs in the red circle cut off by the green circles of the overlapping outer zones become more and more indistinct, making the points of contact, to say the least, arbitrary. This is easily made out by pushing the knob along the slide till the red circles are almost in contact and comparing the clearness of the red at the inner and outer poles.

The modification of Pijper's diffraction micrometer described by Edwards is open to several objections. Very slight faults in construction—for example, errors in alignment of the partition—give erroneous results. The flash-lamp bulbs which may be used for the light may give distorted haloes, so much do they vary in their filaments and in the shape of their glass bulbs. Slight variations in the focusing of the lenses may result in the formation of incomplete semicircles which are useless for differentiation. Films which can easily be differentiated by the "direct comparative diffraction" method, may give results with this instrument the interpretation of which is largely open to questions of opinion.

The method I have described possesses the following advantages. The necessary impedimenta are easily carried. They consist of three glass slides, one with a standard blood film; one glass prism, unnecessary if the user can produce voluntary diplopia easily; one small pocket cigarette lighter, also unnecessary as the candle is ubiquitous; one medium-sized surgical needle; a small piece of cotton-wool to stop bleeding if necessary. All these can be carried in a small cigarette case. Mechanical breakdown is impossible. There are none of the difficulties which are constantly associated with electric lighting.

If it is remembered that (1) variations in size of the haloes which might be considered equivocal constitute a negative result, (2) equivocal observations must be followed by a test meal if the suspicions of pernicious anaemia in any of its stages are strong, this method has nothing to lose by comparison with instrumental methods of measuring megalocytosis.

Conclusion.

Since no fixed boundary line can be determined between normal and abnormal size of the red blood corpuscles for any given individual, I think that the regular comparison of blood films in suspicious cases of pernicious anaemia is of much greater value than attempting to fix a definite point judged by any scale on any instrument. Therefore I submit as worthy of consideration the value of the

"direct comparative diffraction" method of observing the onset and progress of any increase in the size of the red blood corpuscles, which has been shown to be diagnostic of pernicious anaemia and the blood changes of subacute combined degeneration of the spinal cord.

REFERENCES.

¹ *British Medical Journal*, April 6th, 1929, p. 635. ² *Ibid.*, July 13th, 1929, p. 48. ³ *Ibid.*, October 26th, 1929, p. 785. ⁴ *Price's Textbook of the Practice of Medicine*.

MEASUREMENT OF THE DISTRIBUTION OF GAMMA RAYS AROUND A FOUR-GRAM MASS OF RADIUM.

REPORT FROM THE PHYSICS DEPARTMENT, WESTMINSTER HOSPITAL,

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This paper describes an attempt to measure accurately the gamma radiation field, in air, of the radium "bomb" in use at Westminster Hospital Annexe. The bomb is shown, in section only, in Fig. 3; four separate grams of

connected by a long wire to a distant electroscope—led us to believe that many difficulties would be avoided at the outset by combining ionization chamber and electroscope into one small instrument, thereby dispensing with connecting leads altogether. It is, for example, impracticable to use lead screening to prevent ionization losses from the connecting wire on account of the thickness required; the alternative plan of embedding the wire in paraffin wax gives trouble from the static charging-up of the insulation immediately round the wire when exposed to the radiations. The capacity of such a connexion also becomes undesirably large compared with that of the ionization chamber.

Accordingly, a tiny gold leaf electroscope was made up as shown in Fig. 1 (a). The leaf was attached to a brass plate 15 by 6 mm., which was mounted on a sulphur plug, and encased by a thin brass cylinder of radius 10 mm. and length 20 mm., furnished with a transparent circular window back and front. To slow down the movements of the gold leaf to a measurable rate in the intense fields which were being dealt with it was found necessary to add in parallel with the electroscope a small condenser consisting of two co-axial brass cylinders separated by a thin film of sealing-wax (Fig. 1 (b)), whose electrostatic capacity was of the same order as that of the electroscope itself.

To ward off stray beta rays the electroscope and con-

FIG. 1.

radium were placed one at each corner of a 4 inch horizontal square, and so disposed in a lead container* that the issuing radiation was confined to two fairly narrow beams, one above and the other below the container.

An ionization method was chosen for investigating the field. A few preliminary trials with the usual type of apparatus—namely, a small exploring ionization chamber

* For a complete account of the bomb see an article on "Radium Teletherapy" by Francis Rock Carling, in the *British Medical Journal* of February 8th, 1930 (p. 232).

FIG. 2.

denser were assembled one above the other in a cylindrical lead sheath 3 mm. thick (Fig. 1 (c)), which was closed by a circular disc of lead 3 mm. thick; this was located in position by the spike B fixed to the top of the electroscope; the spike also served to indicate the middle of the instrument. The only beta rays which could enter the ionization chamber directly were those which passed in through the narrow diagonal viewing slots S.

In order that scattered radiation from the electroscope supports might be reduced to a minimum, the lead sheath