By subtracting Equation 1 from Equation 3 we obtain the difference in length between the two arcs ED and AD:

$$z \text{ difference in length} = \frac{x^3 (r^2 - r_1^2)}{6 r^2 r_1^3} + \text{etc.} \dots (3)$$

Equation 3 therefore represents the increased length of the fibre after the centre of the membrane has been driven in. This produces a corresponding increase of the tension of the fibre, and hence an increased intensity of the sound conducted by the fibre.

Suppose the centre of the membrane to be now fixed by the locking of the malleus against the incus so that an increase of the pressure of the air in the meatus tends to flatten the arch formed by the fibre. The resistance of the circular fibres will be overcome and the radial fibre will become straightened; hence the arc AD now becomes the cord AD; thus: $AD^2 = AK^2 + KD^2 - 2AK \cdot KD \cdot \cos \theta_1$ (where $\theta_1 = \angle AKD = 2r_1^2$).

$$\therefore \text{chord AD} = r_1 \sqrt{2(1 - \cos \theta_1)}.$$

Replacing $\cos \theta_1$ by its equivalent $\frac{\sqrt{r_1^2 - x^2}}{r_1}$,

expanding and simplifying we obtain:

$$\text{chord AD} = x + \frac{x^3}{8r_1^3} - \text{etc.} \dots (4)$$

Subtracting Equation 4 from Equation 2:

$$u \text{ (difference in length)} = \frac{x^3}{24r_1^3} + \text{etc.} \dots (5)$$

Equation 5 therefore represents the shortening of the fibre which occurs when the centre of the membrane is arrested in its inward movement and the fibre becomes straightened. This produces a diminution in the tension of the fibre, and hence a diminution in the intensity of the sound on reaching the handle of the hammer. This accounts for the fact that when the finger is pushed tightly into the meatus the sound is heard with less intensity than if it is only applied lightly.

These changes in length are of course very small, but it must be remembered that the number of radial fibres is considerable. The close proximity also to the inner ear makes differences in loudness which would be insignificant at some distance, quite noticeable.

For the sake of simplicity a horizontal section through the membrane has been taken. This gives us an arc whose tangent at the margin is sufficiently nearly perpendicular to the direction of movement. A vertical section would give us a different figure; but, without going into the mathematical detail, it may be stated that the results would be similar, indeed the changes in length and tension would be rather greater.

It is to be noted in this connection that when the air in the meatus is condensed by placing the finger in the meatus the effect upon the membrane is the same as that produced by inserting a tube into the meatus and blowing into it. In both cases there is a preliminary increase in the tension of the radial fibres and then a diminution in this tension. In the case of inserting a finger into the meatus, however, another factor is introduced, because the sound waves which would otherwise escape are prevented from doing so, with the result that the duration of the sound conducted by the bones is still further increased. This explanation was given originally by Mach,⁵ and there is no doubt that it is correct in the particular case, though of course it does not explain the increased duration of bone conduction of sound in other cases, whether they are pathological or experimental.

In the opposite condition to those described—that is, in rarefaction of air in the meatus the explanation is more simple. In this case the handle of the hammer swings outwards, and though the membrane does not become quite flat the circular fibres prevent any outward bending of the radial ones sufficient to make up for the shortening produced by the outward swing of the handle of the hammer.

The practical application of the investigation to the testing of the hearing by bone conduction in the deaf will be described in a later publication.

Besides the matter described above, experiments were made with the view of investigating the part played by the tympanic membrane in the generation of differential tones. The results of this investigation, however, will also be published later.

REFERENCES.

¹ Helmholtz: *Tonempfindung*, 3rd edition, translated by Ellis, p. 200. ² See a paper by the writer in the *Journal of Anatomy and Physiology*, 1897, on *The Principles of Auscultation*. ³ Helmholtz, *loc. cit.* ⁴ Politzer: *Diseases of Ear*, 1894, p. 80. ⁵ Mach, *Sitz d. Wien. Akad. d. Wissensch.*, 1864, t. 3, 2.

A FAMILY WITH ADDISON'S DISEASE.

BY
ROBERT A. FLEMING, and JAMES MILLER,
M.D., F.R.C.P. Edin., MB., Ch.B.,

Lecturer on the Practice of Medicine, School of Medicine of the Royal Colleges, Edinburgh; Pathologist to the Royal Infirmary, Edinburgh; Senior Physician to the Western Dispensary, Edinburgh; etc.

Resident Physician, Royal Infirmary, Edinburgh.

The following record of the occurrence of what appears to be Addison's disease in a mother and her four children seems to be worthy of record:

The Mother.

Mrs. H., aged 28, came to the Western Dispensary complaining of weakness, diarrhoea, and pain in the region of the heart.

Family History.—Her father and mother are alive and healthy. One brother died of pleurisy and typhoid fever. One sister died in infancy, and the only surviving sister is healthy. Her mother's mother and an aunt on the mother's side died of cancer.

Personal History.—The patient's work has been very hard since she was 13 years of age. She has had five children, one of whom died in infancy of "inflammation of the bowels." Her home is comfortable, although her husband is a working man in receipt of a small wage. Previous illnesses call for little comment; she has had the usual ailments of childhood, scarlet fever, measles, and whooping-cough, and she has been delicate from childhood upwards, and especially liable to bilious attacks.

Present Illness.—Her present illness may be dated from her first pregnancy, at which time she became darker in colour. She suffered during her pregnancy from great weakness, and every one noted the change in her complexion, which was put down to her condition. After her confinement she suffered from a mammary abscess. With each successive pregnancy she has experienced an increasing degree of debility, and especially was this so with her last pregnancy. She was treated in the Royal Infirmary, in Professor Simpson's wards, during the winter of 1897 for retroflexion of the uterus, and the uterus was curetted early in 1898.

Condition when First Seen.—Mrs. H. came under our notice first at the Western Dispensary in July of 1898. Her skin was extremely dark, the nipples being deeply pigmented, and there were a number of small dark, almost black, spots scattered over the whole body. These had only appeared comparatively recently, and many of them the patient had not previously noticed. She complained of great weakness and prostration, and said that she had many times suffered from attacks of giddiness and faintness, and apparently causeless and severe diarrhoea and vomiting. She complained of pains in the back shooting up to the shoulder. She was a slightly built woman of medium height, with dark hair and a sad, wearied-looking face. When she was first seen there was no pigmentation on the mucosa of the mouth or gums, although the teeth were very bad; the tongue showed no abnormal colour. Within the past few months, however, the mucous membrane of the mouth had become very markedly pigmented. Nausea and fullness after food were frequent, and the repeated causeless attacks of vomiting and diarrhoea, sometimes together, often separate, were specially complained of. Giddiness and faintness were often present, frequently with the attacks of vomiting and diarrhoea. Palpitation and pain over the heart and constant breathlessness on exertion were troublesome. The pulse was weak and dicrotic. There was no obvious cardiac bruit. The respiratory system appeared to be normal. The pigmentation of the skin was darker in summer than in winter but had gradually become deeper with each pregnancy, and the nipples and external genitalia were very deeply bronzed. The moles were of black colour, varied in size from a millet seed to a lentil, and were scattered over the face, back, and abdomen in greatest numbers. They increased in number during the period of observation of the patient, but not rapidly. The urinary system was normal. She suffered from severe dysmenorrhoea and leucorrhoea, with the usual accompanying pain in the "small of the back." Headaches were frequent and severe, usually frontal, and general inability for mental effort was always present.

The Children.

1. Girl, aged 7. The skin was noticed to be specially dark four years ago, after an attack of gastritis; she has been getting much darker lately. The nipples are very dark, and there are black spots or moles all over the body. She has complained of frequent attacks of causeless sickness and diarrhoea for some time past. Headaches are frequent, and sometimes for a week at a time, from no apparent reason, she is quite unable to go to school or to endure any exertion bodily or mental.

2. Girl, aged 4. Her skin began to darken one year ago after a slight attack of eczema, and she has become much darker lately. There are numerous black spots all over the body. She is very subject to diarrhoea, with occasional attacks of sickness unconnected with taking food.

3. Boy, aged 3½. He has always been a dark child. Black spots scattered all over the body appeared first six months ago. He complains of frequent attacks of sickness, specially at night, and sometimes diarrhoea.

4. Girl, aged 2½. A fair child, but she has been getting distinctly darker during the last four or five months. Two black spots have appeared, one on the abdomen and another on the thigh. Occasional attacks of diarrhoea are present.

The question may be asked whether these five individuals, all members of the same family, are in reality all true cases of Addison's disease. If they are, then the family have the most undesirable distinction of being, so far as we can find out, the first recorded instance of the kind, and the prognosis must be considered grave in the extreme. The mother shows

all the typical clinical features, including pigmentation of the mucous membrane of the mouth and lips, while the children, in order of age, demonstrate the same phenomena in decreasing severity and distinctness. The moles, placed so prominently in the list of important clinical features by Addison, Greenhowe, and others, are specially characteristic of this family group. If less significance is attached to them, then the correctness of our diagnosis is much more open to question.

The cases were shown at a meeting of the Medico-Chirurgical Society of Edinburgh on February 1st, 1900.

Why should it not be conceivable that a tuberculous lesion so often hereditary might not exist in the same family in every child? But why is it that in so many recorded cases of Addison's disease, amounting now to several hundreds, so seldom is any reference made to plurality of cases in one family?

The future will clear up the mystery as far as this family is concerned, and the record is published in the hope that by directing attention to investigation into family history, more carefully than has been done in the past, similar instances may be met with.

PRELIMINARY NOTE ON A NEW QUANTITATIVE METHOD FOR SERUM DIAGNOSIS.

BY

RICHARD T. HEWLETT, and SYDNEY ROWLAND,
M.D., M.A.,

Bacteriologists to the Jenner Institute of Preventive Medicine.
[From the Jenner Institute of Preventive Medicine.]

For the successful application of the agglutination test ("Widal" method) in the diagnosis of disease, it is universally admitted that some dilution of the blood is desirable, a dilution which should be approximately known, and which varies in practice between 1 in 10 and 1 in 100, while for the investigation and comparison of the specific agglutinating power of the blood in different cases or diseases, and under varying conditions, an accurate quantitative method for carrying out the dilutions is a necessity.

Of the various methods employed for diluting, the following may be mentioned:

1. Dilution by means of a platinum loop (McWeeney, Delépine, and others). This at the best can be but approximate.
2. Dilution by means of a capillary pipette (Wright). This is more suitable for serum than for the whole blood.
3. The dry-blood method (Johnson). This is subject to many inaccuracies: for example, variability in the amount of solids in the blood and in the dryness of the film, and the difficulty of weighing out so small a quantity as 1 milligram.
4. The hæmoglobinometric method, the blood being diluted to a given standard colorimetrically by its contained hæmoglobin, a very variable factor.
5. The capillary-tube method (McFarland). Independently of McFarland, we carried out experiments with the capillary-tube method, and early abandoned it, for we found it impossible to obtain capillary tubes of even approximately the same internal diameter, while accurate calibration by capillarity is attended with great difficulties.

We do not mean to imply that the above methods are useless, all of them give satisfactory results for rapid clinical diagnosis or in those cases where an approximation suffices, but we believe that the capillary pipette method (No. 2 above) is the only one which has any claims to accuracy. We have, therefore, devised the following quantitative method, which is suitable not only for serum but also for the whole blood, and is capable of the greatest accuracy.

Ordinary vaccine tubes are taken, the large, the very small, and any irregular ones being discarded. We prefer those varying in diameter from about 0.9-1.2 mm., they are boiled in strong nitric acid, thoroughly rinsed in tap, and then in distilled water and dried; a large number can thus be treated at one operation. The selected tubes are charged with the blood to be examined, being preferably one-half to two-thirds filled, and are carefully sealed by melting their ends in a flame in the ordinary way. In the laboratory the length of the column of blood between the bases of the two menisci is first measured by means of a scale graduated to half millimetres assisted by a lens mounted to avoid parallax. The end of the tube is then cut off by means of a fine file or writing diamond, and its internal diameter is measured. This, the most important of all the manipulations, is carried out in the following manner:—

The tube is supported in the axis of the microscope by means of two iris diaphragms carried respectively by the stage and by the substage. These close concentrically and support the tube, at the same time cutting off all light reflected from the mirror. The opaque blood in the interior of the tube in the same way cuts off all light that might pass through the lumen of the tube. The only light that thus reaches the optical system is that transmitted by the glass walls of the tube. In the field of vision the lumen of the tube now appears as a black circle surrounded by a brilliantly-illuminated annulus. Owing to the extreme sharpness of the image the measurement of the diameter of the tube can be carried out with great accuracy by means of an eye-piece micrometer arranged to give readings to the one-thousandth of a millimetre. From the formula

$$V = D^2 \times L \times 0.7854,$$

Where V = volume of the cylinder,

D = diameter of the cylinder,

And L = the length of the cylinder,

the volume of the blood is calculated. If many measurements have to be made, a Fuller's slide-rule greatly expedites the calculations. It is of the utmost importance that the diameter of the tube be accurately measured, and therefore the adjustment of the eye-piece micrometer must be carried out with great care, and the scale by which it is set should be one the accuracy of which is undoubted. For, considering the formula ($V = D^2 \times L \times 0.7854$), it will be seen that any error in the measurement of D will be increased in a geometrical ratio in the final result, hence the comparative inefficiency of a capillary-tube method in which D is measured indirectly and with less accuracy.

We have controlled the accuracy of the method by filling tubes with distilled water, ascertaining the amount of water by direct weighing, and afterwards calculating the weight of the water by the formula given above; it is easy to obtain results which are within 0.5 per cent. of the true weight. Having ascertained the volume of blood, it remains to carry out the dilutions; this is accomplished as follows:

The capillary tube is placed in a vertical thick-walled glass tube of slightly larger bore, the lower end of which is submerged in the required amount of the diluting medium (measured out by a graduated pipette) contained in a hollowed-out block of glass, such as is used in histological and microscopical work. The capillary tube with its contained blood is then crushed *en masse* by means of a soft iron plunger, and the interior of the containing tube is washed out several times by drawing up the diluting medium into its lumen, either with the mouth or by means of an india-rubber teat. The powdered glass quickly falls to the bottom, and the mixture may be employed for conducting the serum reaction either by the microscopic or by the macroscopic method.

On a future occasion we propose giving further data and details, but we may say in conclusion that this method has been tested at the Jenner Institute of Preventive Medicine, and has proved to be easily carried out, and to give satisfactory results, while the time consumed in the whole of the manipulations (5 to 10 minutes) is comparatively short.

ON THE VALUE OF THE AGGLUTINATION TEST AS A MEANS OF DIAGNOSIS OF THE B. TYPHOSUS FROM COLIFORM ORGANISMS.

By W. H. HORROCKS, M.B., B.Sc.LOND.,
Assistant Professor of Hygiene, Army Medical School, Netley; Major
R.A.M.C.

THE difficulties which surround the correct interpretation of the agglutination test are well shown by the following bacteriological examination of a drinking water derived from a polluted upland surface. The water was sent for analysis as there had been several cases of enteric fever amongst the consumers, though no real epidemic, such as might be attributed to a polluted water supply, had occurred. On arrival at the laboratory the water was found to contain a large number of micro-organisms, so the usual plan of concentrating the sample by pumping one or two litres through a Berkefeld bougie had to be abandoned. Consequently 1 c.cm. of the water was added to each of twelve broth tubes containing 0.05 per cent. of carbolic acid; all the tubes were then incubated at 37° C. At the end of twenty-four hours some of the tubes were hazy in the upper half and some in the lower half, and three tubes were turbid throughout. These three tubes were then plated out in gelatine containing 0.05 per cent. carbolic acid. After seventy-two hours' incubation at 22° C. the plates made from two of the tubes showed almost pure cultures of coliform colonies, whilst the plates made from the third tube showed numerous colonies of *B. megaterium*. Nearly all the coliform colonies were fished and their cultural characteristics studied. It was then found that the coliform organisms could be arranged in three groups.