a second immersion in absolute alcohol. The alcohol having been removed by washing in water, they are stained by the modified Ziehl-Neelson method previously described. Unless the fat is removed by ether or some similar solvent, it will be found almost impossible to decolorise the specimens without danger of decolorising the tubercle bacilli. The prepared slides should now be examined carefully and thoroughly under the microscope, care being taken that all the slide is examined. (I do not think that this can be satisfactorily done without some form of mechanical stage). When the slides are examined several things may be seen: 1. Tubercle bacilli may be present. 2. No tubercle bacilli may be found, but (a) a fairly large number of some other bacterium; or (b) a great excess of leucocytes, often amounting to pus; or (c) a considerable amount of vegetable matter and debris. 3. Nothing but a few leucocytes may be seen.

1. *Tubercle Bacilli may be Found.*—If these are found there can be no doubt the milk is totally unfit for human consumption.

2. *Tubercle Bacilli cannot be Found.*—As a rule the milks one has to examine are mixed, and may be derived from several cows, of which perhaps only one is diseased. When this is the case it will be evident that in our examination we shall have only included a very small portion of the milk of this diseased cow, and although we may find some evidence of a lesion in the form of an excessive number of leucocytes, we may not be able to find any tubercle bacilli.

(a) *Another Organism may have produced the Lesion.*—I believe that quite a considerable proportion of cattle suffer from a form of simple (that is, non-tuberculous) mastitis. In a great number of these the streptococcus of bovine mastitis can be found, which has not been shown to be pathogenic to man, and therefore it may be argued that the milk would not be harmful. To this two things may be urged in objection: First, several cases of streptococcal enteritis, occurring in children, have been recorded, and the simplest explanation certainly would be that the milk has been the cause; secondly, the condition of the udder, which gives abundant streptococci and pus, is an acute mastitis, and surely the secretion from an acutely diseased gland is totally unfit for consumption, especially by children.

(b) *An Excess of Leucocytes may be found.*—Normal milk contains leucocytes, as does every normal secretion. The number of these cells in the centrifugised deposit of normal milk is small. In the field of a one-sixth objective one or two may be seen, sometimes none. When there is a considerable excess—for instance, twenty or thirty—in the field of the one-sixth, the milk, in my opinion, becomes very suspicious. This increase of leucocytes, and even the presence of pus, may occur even when it is impossible to find either tubercle bacilli or any such excess of a particular organism (as the streptococcus) which would suggest it as the cause. This condition is a more chronic form, and it may be either tuberculous or simple. It is well known how difficult it is to demonstrate the presence of tubercle bacilli in the pus from a discharging tuberculous sinus, and I think that one would be justified in condemning any sample of milk which contained pus on the ground that it was possibly tuberculous. Even if it were a chronic simple mastitis the milk came from a diseased udder, and should therefore be condemned.

(c) *The Sediment may contain much Vegetable Matter and Debris.*—In itself it is of little import, but in connection with the spread of disease, such as enteric fever, it is of some importance in pointing to carelessness in the handling and collection of the milk.

3. *Nothing but a few Leucocytes may be found.*—This may occur when the milk is normal, or where it has been impossible to centrifugalise the milk. It is impossible to examine milk which has clotted with satisfaction. One would therefore never trouble to examine a sample which had obviously clotted. But before this takes place there is a preliminary stage which I should designate as microscopic clotting. The milk is apparently quite fluid, but when it is examined after having been centrifugalised, it is found that the three layers—that is, cream, skim milk, and sediment, are wanting, and that the contents of the tube are in a sense jelly-like. If under these circumstances what remains at the bottom of the tube after the contents have been quickly poured out be examined, often nothing more than a few leucocytes can be seen. In order to be able to say that the milk appears to be normal,

therefore, one must be careful to eliminate this microscopic clotting; it follows that if it is present none of the previous conditions can be diagnosed.

B. Typhi Abdominalis.—In searching for this organism the procedure described in the section on water is to be adopted, but the enormous number of bacteria present in milk makes the examination extremely laborious, and one is generally doomed to disappointment.

The Klebs-Loeffler bacillus has been found in milk by taking advantage of its rapid growth on good inspissated blood serum. The sediment from the centrifugal tubes as well as the cream is inoculated on to the serum in series. A loopful of the sediment or cream is rubbed all over the surface of the serum in one test tube, and without reinoculation rubbed over another tube, and also over the third tube of serum. Every portion of the surface of the serum should be covered with the loop in order to separate the colonies as much as possible. Six or eight of these sets should be inoculated from the sediment, and a like number from the cream. The tubes are then incubated at 37° C. for from eight to twelve hours, and inspected. Any colonies which can be seen with the naked eye should be examined microscopically, and subcultures made. The tubes are then returned to the incubator for further incubation, and examined at the expiry of eighteen and twenty-four hours.

Every endeavour should be made to obtain a pure culture, and its pathogenicity should be determined.

If this organism be isolated, there can be no doubt as to the harmfulness of the milk, and it should be condemned. Unfortunately, the milk will have been consumed long before the bacillus is isolated, but it will probably enable the medical officer of health to localise the source of the infection. Owing to the difficulties attending this examination, a negative result is no evidence of the absence of the organism from the milk.

REFERENCES.

¹ *Journal of Experimental Medicine*, vol. iii, p. 451. ² *Berl. klin. Woch.*, 1898, p. 809. ³ *Ibid.*, 1898, p. 880. ⁴ *Arbeiten aus dem path.-anat. Inst. zu Tübingen*, N. V. Baumgarten. ⁵ *Id.*, 1896, Heft 2, p. 317. ⁶ *Lancet*, May 29th, 1897. ⁷ Part of the expenses of the research in connection with this method was defrayed by a grant from the British Medical Association.

THE CONTINUITY OF THE TOXIC PROCESS IN FATAL CASES OF DIPHTHERIA.

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In a previous paper¹ I have stated that the symptoms of uncomplicated fatal diphtheria are sufficiently constant to justify a general definition. Among such symptoms are pallor, progressive weakness and irregularity of the pulse, coldness of the surface of the body, oliguria probably leading to suppression, oppressive cardiac pain, a subnormal temperature, sickness, and jactitation. Attention has also been called to the fact that the mind remains clear until the end.

That the effects of diphtheria toxin, as experimentally evidenced, resemble those observed in the human subject is generally admitted, and it is sufficient to mention the changes in the tissues, including the blood; but the dilatation of the blood vessels, noted some years ago by Roux and Yersin² after subcutaneous injections of the toxin, is of special interest at present owing to the researches of Dr. T. G. Brodie.³ He injected a broth solution of the toxin into the external jugular vein of cats, the result being an immediate relaxation of the blood vessels, with a consequent fall in pressure. A slower recovery followed, and, in cases dying within forty-eight hours, the blood pressure was almost at the normal level, when a second relaxation led to death. In these cases the heart was not involved, and continued to beat strongly until the end.

These facts suggested to me the study of the blood-pressure curve in cases of diphtheria. For this purpose the pocket form of the Hill-Barnard sphygmometer was employed. Although preferable when objections exist to the repeated constriction of a limb, it gives a less definite record than the aneroid instrument. The curves obtained from successive records are therefore to be regarded as only approximate, and minor gradations accepted with caution, two observers working together when possible. As all the fatal cases examined were

under 10 years of age, it may be noted that, while the normal blood pressure as recorded in adults by the Hill-Barnard sphygmometers is about 110 mm., I have frequently found that the pocket instrument registers a somewhat lower point in children, even when applied to the femoral artery.

With a larger number of blood-pressure curves available, a greater diversity is manifested than was anticipated from the resemblance existing between the first six, upon which a previous report was based. Nevertheless, they are all roughly divisible into three parts. In the first stage the pressure is maintained at or near the normal level; then follows a period during which there is a slight decline; while the last stage is marked by a rapid fall, beginning more or less abruptly and persisting until death. The absolute and relative periods occupied by these three stages varies widely. In protracted cases it is the second stage which is generally most prolonged, and there may then be a partial recovery preceding the final depression. If the third stage is exceptionally lengthy the fall usually becomes gradually less until a condition of equilibrium at a low level is apparently maintained until the approach of death. Certain considerations, however, suggest that the fall is continuous, and might be registered by another form of instrument.

The excursion of the oscillating fluid in the graduated tube of the sphygmometer shows no change in the first stage, and in the second only a doubtful diminution, but in the third it becomes less in proportion to the fall in pressure, until it is a mere flicker, and finally disappears. This is significant if the maximum obtainable excursion, although obviously affected by other factors, is accepted as some indication of the heart's output during successive beats, since the maintenance of the blood pressure depends not only on the contraction of the blood vessels, but on the output of the heart.⁴ It is a reasonable inference, amply confirmed by clinical examination, that, while the lowered pressure in the second stage is due to relaxation of the blood vessels, in the third heart failure is added as a more potent factor. Whether early death is ever associated with a rapid and extreme secondary relaxation of the vessels, without the heart being affected, as might be anticipated from Dr. Brodie's experiments, remains to be proved. When heart failure occurs, it is no doubt caused by the direct action of the toxin upon the muscular tissue. Possibly the altered blood, also, has a prejudicial effect.⁵

The symptoms ascribed at the outset to lowered blood pressure are absent in the first stage, and few of them are well marked until the second is advanced. With the incidence of the third stage they undergo a marked aggravation. In prolonged cases they are more fully developed, and, as they become prominent towards the end, when the pressure is lowest, are interpretable as the expression of some secondary toxic condition. That such a condition—namely, uræmia—appears in a modified form as an intercurrent element may be admitted; but its supervention is not apparently necessary to the evolution of the symptoms described as essential. For if such symptoms are secondary in origin, they should differ in kind as well as degree from those manifested in rapidly fatal cases. The latter form of the disease is uncommon in hospital practice, and so far I have only been able to secure the blood pressure curve in a single instance. It shows the same pressure curve and symptoms as the longer type of case.

Morning and evening chart of case. In the uppermost transverse column is shown the duration of the disease in days. In similar columns below are given the urine in ounces and the pulse-rate. The thinner line in the body of the chart indicates the temperature in accordance with the Fahrenheit scale on the left, and the thicker one the blood pressure in mm. of mercury, as shown by the figures on the right.

H. F., aged 6, was admitted on the afternoon of the third day of an attack of diphtheria. The vital organs were healthy, and the urine—tested next day—contained no albumen. Typical thick membrane covered both tonsils, the uvula, and the sides of the pharynx. There was a profuse, slightly blood-stained discharge from the nose, and both sides of the neck were considerably swollen. The usual local treatment was adopted. At 11.40 P.M., 18,000 units of antitoxin were injected. At this time sickness was reported. The patient was restless during the night and obtained very little sleep. In the early morning he passed 4 ounces of urine. During the day he was much quieter and the sickness ceased. At 1 P.M. a second dose of 18,000 units was given. During the night sickness became persistent, jactitation was marked, and the patient could not be kept warm. He passed half an ounce of urine in the early morning. The pulse, which had steadily weakened from the time of admission, could not be counted towards the end, and the sphygmometer only showed an occasional flicker. The patient was conscious until death, which occurred at 10.30 A.M.

In maintaining that the symptoms of fatal diphtheria, as the outcome of a fall in blood pressure, do not vary radically with the duration of the disease, no exception need be made of the cases in which they are masked by the extreme cardiac distress. Even if it be admitted that paralysis is sometimes the chief cause of late heart failure, the fall in blood pressure, when not too rapid, is followed by the appearance of the related symptoms. Marked dyspnoea is common in this type of case, especially when the cardiac distress is paroxysmal, but is less obvious, although frequently present, in the ordinary type. The form of dyspnoea resulting from paralysis of the respiratory muscles may be regarded as an extrinsic cause of death, and the same statement applied to sudden syncope, which I believe to be adventitious and always the result of exertion or change of position. Reference to the pulse-rate has been omitted because it is very variable, and, although generally rapid in the earlier stages, may become abnormally slow before death.

The gravity of diphtheria may be in part explained by the diverse action of its toxin, which, in the first place, causes a fall in blood pressure, and, in the second, a change in certain tissues, of which the cardiac and renal are most important in the present regard. One result of the lowered blood pressure is a diminution in the quantity of urine passed. As the urine contains the toxin,² the latter accumulates in the blood, and determines a further fall in pressure, aggravated by heart failure. An active part in this process may be taken by sickness and diarrhoea. The latter, stated to be frequently associated with sickness,⁶ is, however, extremely rare in my wards. No doubt the toxic change in the renal tissue in some degree prejudices excretion, but it is apparently not a main factor in the development of anuria. In this relation it is noteworthy that albuminuria is not always present in fatal cases. Reference has already been made to the question whether uræmia may not appear as an intercurrent lethal factor. I believe that, even when the duration of a fatal case is short, oliguria supervenes and is followed by suppression. When, however, the patient is within a few hours of death the latter condition can have but little effect if the fact that a healthy subject does not show symptoms of uræmia until suppression has existed for at least two days is accepted as a criterion.⁷ In prolonged cases, however, with a final period of suppression lasting for several days, the presence in the blood of uræmic poisons in sufficient quantity to produce secondary symptoms appears inevitable. One of these symptoms—namely, myosis, is almost invariably present under such conditions. It is possible that the final aggravation of sickness has in part a similar source. On the other hand, there is a striking absence of headache, stupor, coma, and convulsions. Admitting that the uræmic poison is complex, it is probable that the specific toxin counteracts the effect of some of the elements, and thus maintains the continuity of the primary symptoms.

REFERENCES.

- ¹ BRITISH MEDICAL JOURNAL, December 30th, 1899, p. 1787. ² *Annales de l'Institut Pasteur*, June, 1889. ³ BRITISH MEDICAL JOURNAL, November 4th, 1899, p. 1282. ⁴ *Lancet*, June 10th, 1899, p. 1552. ⁵ BRITISH MEDICAL JOURNAL, April 2nd, 1892, p. 698. ⁶ *Tirard's Diphtheria and Antitoxin*, p. 19. ⁷ Oliver's translation of Bouchard's *Auto-intoxication in Disease*, p. 113.

BRADFORD AND DISTRICT MEDICO-ETHICAL SOCIETY.—The annual general meeting of this Society was held on January 17th, when Dr. J. H. Bell was elected President for the ensuing year; Dr. D. Goyder, Vice-President; Dr. F. K. March, Honorary Treasurer; and Dr. W. Horrocks and Dr. A. Manknell, Honorary Secretaries. Certain alterations were made in the rules of the Society.