A SERIES OF 80 CASES TREATED WITH DIPHTHERIA ANTITOXIN,

WITH

OBSERVATIONS ON THEIR BACTERIOLOGY.

Being an Abstract of a Paper read before the Clinical Society of London.

BY

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THE serum was supplied by the British Institute of Preventive Medicine, was prepared by Dr. Ruffer, and was used at the Eastern Hospital.

BACTERIOLOGICAL EXAMINATION.

A bacteriological examination was made in all the cases; care was taken that the colonies should be evenly distributed over the surface of the blood serum in the tube, and should be separate. Cover-glass preparations were made from the exudation, and in about a third of the cases a diagnosis could be made from this alone.

The tubes were examined carefully after about twenty hours' incubation, and on several occasions for the next two or three days. Special attention was paid to the character and number of colonies other than diphtheria that developed, on account of the importance that has been attached to the association of other bacteria with the diphtheria bacillus with regard to the severity of the disease.

DIAGNOSTIC VALUE OF BACTERIOLOGICAL EXAMINATION.

After twenty hours the majority of the diphtheria colonies were characteristic, and were likely to be mistaken only for the Brisou coccus, from which they were distinguished by their opacity and microscopical appearances.

Atypical diphtheria colonies often developed in addition to the typical ones. In 8 out of the 61 cases of true diphtheria none of the diphtheria colonies presented the characteristic appearances. Eighty cases certified to be suffering from diphtheria were examined, and in only 61 were diphtheria bacilli found. With one exception, all the cases in which diphtheria bacilli were found were also diagnosed from the clinical point of view as diphtheria. This exceptional case was one that had the clinical aspect of follicular tonsillitis. Of the 19 cases in which diphtheria bacilli were absent, 8 would have been considered not to have been diphtheria had a bacteriological examination not been made. The other 11 cases were, on admission, clinically diphtheria, but the further progress of the cases fully bore out the bacteriological evidence. One of the cases died, but was complicated with bronchitis, to which death was attributed. A careful consideration of these cases fully confirms the belief of the writers in the extreme value of a bacteriological examination.

PROGNOSTIC VALUE OF BACTERIOLOGICAL EXAMINATION IN TRUE DIPHTHERIA.

A careful analysis was made of all the cases, both from the clinical and from the bacteriological point of view, in order to determine the prognostic value of the bacteriological examination.

MICROSCOPICAL EXAMINATION OF THE EXUDATION.

The following results were obtained: In the majority of cases a large number of bacteria were found. In 6 cases the exudation was remarkably free from bacteria; and of these cases 4 were mild and 2 of moderate severity. In 10 cases the exudation was comparatively free; half of these cases were mild, and only one severe; none of them were fatal. From these figures the writers concluded that the fewer bacteria in the exudation the less severe is the case likely to be.

As to the character of the bacteria found in the exudation: they were of various kinds, and included straight bacilli of different sizes, comma-shaped bacilli, fine spirilla, diplococci, streptococci, and other micrococci. Diplococci were almost always abundant, and were often grouped in large masses, especially on the surface of epithelial cells. In only 7 cases were they absent.

In 12 cases fine spirilla were present, and sometimes in large numbers. In 22 cases comma-shaped bacilli were present, and at times in abundance. In about half the cases straight bacilli of various sizes were present. No prognostic value could be attached to the absence, or presence, or to the number, of the diplococci, spirilla, straight or comma-shaped bacilli.

Particular attention was paid to the streptococci. In more than half the cases some were found in the exudation. In 7 cases many were found, and of these 4 were mild cases, 2 severe, and 1 moderately severe. Careful analysis of these, as well as of the cases in which a smaller number of streptococci were found, showed that they were neither more nor less severe than the average of the cases.

In about a third of the cases characteristic diphtheria bacilli could be distinguished in the exudation with sufficient certainty to make a diagnosis of the disease. Very few of these cases were mild, and more than a third of them died; so that the finding of any quantity of the characteristic bacilli in the exudation is of unfavourable import.

EXAMINATION OF THE CULTIVATIONS.

1. *Cases in which only Diphtheria Colonies Developed.*—In 13 cases no other colonies than those of diphtheria developed in the tubes, even after three days' incubation. The majority of these cases were of a severe type, and a third of them died.

2. *Cases where only a Small Number of Diphtheria Colonies Developed.*—In 17 cases only a comparatively small number of diphtheria colonies developed in the tubes; 11 of these cases were mild, and only 4 were severe.

3. *Cases where the Diphtheria Colonies were Atypical.*—In 8 cases the diphtheria colonies were atypical. Of these cases, 5 were mild, 2 severe, and 1 moderately severe.

It would thus appear that when only diphtheria colonies develop in the tubes the case is likely to be severe; but that when the diphtheria colonies are few in number or atypical in character the case is likely to be mild.

4. *Cases where the Diphtheria Colonies were Associated with Streptococci.*—In 45 cases colonies of streptococci developed in addition to those of diphtheria; but in only 18 were they present in large numbers. Of the 18 cases, 10 were mild, and 4 were severe; only 3 died; 17 of these cases showed the long variety of bacillus. In the series of 61 cases of true diphtheria there were 3 cases which were remarkable for containing a very large number of streptococci both in the cover-glass preparations of the exudation and in the cultivations. Two of these cases were mild. The other was severe and ended fatally, but was complicated with scarlet fever. In one of these two mild cases many diphtheria colonies of the long variety developed, and in the other a moderate number, also of the long variety.

It will be noted that these observations show that the association with streptococci, as evidenced by a single bacteriological examination, is not of unfavourable import, but rather the contrary, a conclusion which differs from that of other observers.

5. *Cases where the Diphtheria Colonies were Associated with those of the Brisou Coccus.*—Three cases were associated with the Brisou coccus; 2 were mild, and the other moderately severe.

6. *Cases where the Diphtheria Colonies were Associated with the Staphylococcus Aureus.*—Two cases were associated with the staphylococcus aureus; both were mild.

7. *The Variety of the Diphtheria Bacillus.*—In 3 cases only the short variety of the diphtheria bacillus was found; all were mild. In 10 cases the medium variety was found; half of the cases were mild. In the rest of the cases the bacilli were of the ordinary long variety. It would thus appear that the short variety is the least virulent, and that the medium variety is less virulent than the long.

Bacteriological Examination of Non-diphtherial Cases.—In the 19 cases where no diphtheria bacilli were found, the colonies which developed were those of streptococci and of the Brisou coccus. In 1 case streptococci alone developed,

in 1 the Brisou coccus alone, and in the rest both in varying proportions.

CLINICAL OBSERVATIONS.

Mode of Injection.—The injection was made into the flank with strict aseptic precautions. The quantity injected varied from 5 to 30 c.cm. at one dose, the total quantity during the course of any one case varying from 5 to 90 c.cm. With a well-made syringe no difficulty is experienced in injecting as much as 20 c.cm. at a time; 182 separate injections were made, and in none of them was there the slightest sign of any local inflammation.

Results and Statistics.— Eighty patients under 15, certified to be suffering from diphtheria, were treated; 8 were excluded from the statistics because they were clinically as well as bacteriologically not cases of diphtheria. The remaining 72 cases would have clinically been considered diphtheria, and can thus be compared with previous cases. The following table shows the results obtained:

Case Mortality of Diphtheria in Children under 15 at the Eastern Hospital.

	Cases.	Deaths.	Mortality per Cent.
1893	397	166	41.8
January 1st, 1894 to October 22nd, 1894	400	144	36.0
January 1st, 1893 to October 22nd, 1894	797	310	38.8
September 14th, 1894 to October 22nd, 1894 (39 days).			
Not treated with serum	72	28	38.8
October 23rd, 1894 to November 27th, 1894 (36 days).			
Cases treated with serum	72	14	19.4

It will be seen that the mortality has been diminished by one half. The diagnosis of all diphtheria cases at the Eastern Hospital since 1892 has been personally supervised by one of the authors (E. W. G.). It is the opinion of this observer that the cases treated with the serum were rather above than below the average severity. Not much stress was laid on comparisons with other hospitals on account of the varying standards of diagnosis. During the period of antitoxin treatment at the Eastern Hospital, the mortality at the Western, South-Western, Fountain, and South-Eastern Hospitals was 33.3, 32.2, 30.5, and 23.6 per cent. respectively. At the last named hospital the number of cases was too small for accurate comparison.

Of the 72 cases in the series only 61 showed diphtheria bacilli; of these 61 cases 13 died, a mortality of 21.3 per cent., considerably lower than that (38.8) of the previous series of 72 cases clinically diphtheria. An account was given of the cause of death in the fatal cases. In 10 death ued from the poisoning of diphtheria, and in the rest m complications. In one case death occurred within eight urs and in another thirty-two hours after admission.

Tracheotomy.—There were 9 cases of tracheotomy, and 6 recovered. In 13 previous series of 9 tracheotomies the number of recoveries varied between 0 and 4, and the average number of recoveries was 1.75.

For the sake of comparison with M. Roux's cases, the authors analysed their cases of true diphtheria, and divided them into the following categories: Anginas, Croups not operated on, Tracheotomies.

Angina Pure (that is, without association with other bacteria): 30 cases with 8 deaths, 26 6 per cent.

Angina associated with Streptococci; 11 cases with 1 death, 9 per cent.

Angina associated with Brisou Coccus: 3 cases, no death.

Angina associated with Streptococci and Staphylococcus Aureus: 2 cases, no death.

Croups not operated upon: 6 cases with 2 deaths. True diphtheria: 4 with 2 deaths. Associated with Brisou: 1 with no death. Associated with streptococci: 1 with no death.

Tracheotomies: 9 cases with 3 deaths. True diphtheria: 5 with 1 death. Associated with streptococcus: 3 with 2 deaths. Associated with streptococcus and staphylococcus aureus: 1 case, no death.

In comparing these with M. Roux's statistics remarkable differences were found. Of pure diphtherial angina there were in his series 120 cases, with 9 deaths, a mortality of 7.5 per cent. Of angina associated with streptococci, 35 cases, with 12 deaths, a mortality of 34.2 per cent.

It will thus be seen that pure angina cases at the Eastern Hospital showed a much higher mortality, and those associated with streptococci a much lower mortality than M. Roux's; in fact, the mortalities were almost reversed.

On the other hand, the cases associated with the Brisou coccus agree with his in being mild. The number of tracheotomies and croups is too small to draw any conclusions in reference to this point.

The clinical course of the cases under treatment fully bore out the evidence given by the above statistics. An account was given of the effect of antitoxin in diminishing the exudation, reducing the pulse rate, and in improving the general condition of the patient. In severe cases the effects were not observed till after two or three days.

Mention was made of the fact that 20 out of the 61 cases were on admission suffering from the toxic effects of diphtheria, and an unfavourable prognosis was made; 8 of these cases recovered. There is no evidence that the antitoxin diminished the incidence of albuminuria. It is still too early to speak of the effect on the incidence of paralysis, but so far 6 cases have occurred.

Apart from the curative action, two other effects were noticed—a rash, and the onset of joint pains. The rash occurred in 25 per cent. of cases, and appeared from seven to nineteen days after the first injection. It was of an erythematous character, and was sometimes accompanied by pyrexia. Except for itching it gave rise to no further inconvenience. In 6 of the cases there were joint pains, which appeared about the same time as the rash, and lasted at most three days.

The hips were most frequently attacked; there was pyrexia, no cardiac affection, and the condition of the patient was never serious. It was noticed that the incidence of rash and joint pains was greater in the cases treated with the serum from the first of two horses from which it was obtained, than in those treated with serum from the second. The latter serum was much stronger than the first, and was used in smaller doses. With the exception of the antitoxin no other treatment was adopted, except that complications were treated *secundum artem.*

Dosage.— The authors recommended the following doses of the serum of which 0.0001 c.cm. neutralises a dose of the diphtheria toxin otherwise fatal to guinea-pigs. In severe cases 20 c.cm, when the patient is first seen, followed by 10 c.cm. in from 18 to 24 hours, and again another 5 or 10 c.cm. in another 18 to 24 hours; for a moderately severe case a first dose of 10 c.cm., followed by one of 5 c.cm. the next day, and perhaps another 5 c.cm. the day after that; for a mild or doubtful case one dose of 5 c.cm., should there be any reason to suspect that the case is likely to become worse.

Because in any given case the larynx is involved the writers did not necessarily consider the case a severe one; for by severe they meant one in which the toxic symptoms of diphtheria were present. But seeing with what rapidity membrane will spread along the air passages, they recommended that from 5 to 10 c.cm. of serum should be given in every case of diphtherial croup without toxic symptoms, to be followed by another 5 c.cm. the next day if the symptoms showed no improvement.

This series of cases showed that if in a severe case there was no improvement by the fourth day of the treatment, none was likely to ensue. But where improvement is observed by that time it is well to give another injection of 5 c.cm. on the fifth and sixth day.

The authors recommended the amount of the dose to be regulated not by the age or weight of the patient but by the severity of the attack.

A clinical account was given of the 19 cases that were shown bacteriologically not to be diphtheria. These cases were admitted into the diphtheria wards, yet did not contract the disease; but this was not attributed by the authors to the action of the antitoxin, the previous experience at the Eastern Hospital showing that there is little fear of the disease attacking such cases if proper precautions be taken.

In conclusion, the authors expressed their thanks to the Council of the British Institute of Preventive Medicine, and especially to Sir Joseph Lister and Dr. Ruffer. Thanks were also recorded to Dr. Richards, of the Eastern Hospital, for his assistance in carrying out the treatment and in recording of notes.

SIXTY-SECOND ANNUAL MEETING

OF THE

BRITISH MEDICAL ASSOCIATION.

Held in BRISTOL July 31st, and August 1st, 2nd, 3rd.

PROCEEDINGS OF SECTIONS.

SECTION OF OBSTETRIC MEDICINE AND GYNÆCOLOGY.

J. G. SWAYNE, M.D., President.

AN INTRODUCTION TO A DISCUSSION ON THE INDUCTION OF LABOUR.

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THE induction of labour under just indications marks the progress of medical science, and it is one of the most brilliant examples of conservative surgery. These characters must also command the earnest attention of the obstetric surgeon. And hardly less forcibly do they challenge the attention of all physicians on account of the light which they throw upon general pathology.

The application of the proceeding is one leading expression of the state of obstetric science; therefore as science advances the necessity for revising the conditions under which this proceeding should be resorted to is ever recurring. This consideration proves the wisdom of those who have selected this topic for discussion at this meeting. When seeking to determine the indications for bringing pregnancy to an end, the first source of light will rightly be sought in the observation of the conditions under which Nature herself seeks relief by adopting this course, and the evils incurred if this mode of escape or relief be missed. *Natura ostendit viam.*

Our search for guidance towards the solution of the problem before us must therefore be determined by the steady observation of the physiology of gestation, and of the pathological accidents emanating from or associated with it.

The history of reproduction is marked by four distinct epochs: (1) Gestation, (2) Parturition, (3) Puerpery, (4) Lactation. The strict scope of our inquiry is comprised within the first three epochs. The question of shortening the duration of pregnancy can rarely arise in the cases of women who have simply proved unequal to the task of lactation. But when women, who through some fault of structure or constitutional defect have struggled through parturition and puerpery with serious difficulty threatening life, become pregnant again, the question whether it be possible to lessen the dangers attending these processes at the natural term by terminating the gestation at a chosen time, is a fair subject for consideration.

The question, indeed, sometimes forces itself whether it would not be more prudent to avoid pregnancy altogether. But evasion of the difficulty by prohibition is rarely feasible. Preventive medicine has not yet achieved adequate authority. We cannot, however, evade the call to act upon the indications so frequently given by the observation of the accidents arising during pregnancy and puerpery. The indications spring from the study of the conditions which imperil the mother, the embryo, or both. In accordance with the law generally accepted, the safety of the mother is the first claim, that of the child is a secondary consideration. Sometimes, indeed, frequently the two interests run together, they do not conflict. The course best calculated to preserve one is also the best for, or is at least compatible with, the preservation of the other. And with the advance of science, the occasions on which the necessity of condemning one or the other arises have become less frequent. Thus the advance of science brings us more and more in accord with the law of Nature.

It would be difficult to state a problem in practical medicine more widely interesting than this of demonstrating the conditions which indicate the propriety of inducing labour. The physiological and pathological factors which have to be studied and weighed in the search for a solution are many; and there yet lingers a prejudice of mistaken morality which, ignoring the law that true medicine is based upon the right appreciation of physiology and pathology, further complicates the question. The obvious duty of the physician when he sees a pregnant woman in difficulty is to consider and determine how to secure the safety of both mother and child. There is no parallel problem in the range of medicine. The ordinary physician has to deal with one subject. Whether it be due to this circumstance or to his defective understanding of the physiology of gestation, he is apt to concentrate his attention upon the mother. He fails to recognise the interdependence and correlation of the two beings. So, for example, in the case of a woman suffering from albuminuria, his attention is engrossed by this symptom, and he directs his treatment accordingly. His conduct is ruled by the specious and ignorant dictum: "Treat the symptoms and let the cause continue to act." It is needless to point out to those who study the physiology of pregnancy that this course imperils both mother and embryo.

Our theme does not embrace the cases in which interference with the course of gestation is indicated by mechanical obstructions to the process of labour. But one remark pertinent to this subject is not inappropriate. In case of mechanical difficulty the question for decision may lie between embryotomy and the Cæsarean section or the sacrifice of the embryo by inducing labour before the term of viability is reached. This question is one of growing interest, as the advance of abdominal surgery is rapidly tending to minimise the resort to sacrificial operations. Here, then, we have further confirmation of the law that obstetric practice becomes every day more conservative—the day is at hand when Cæsarean section will greatly, if not quite, supplant embryotomy.

We may, therefore, pass on to the study of those constitutions which so overtax the powers of the systems as to threaten life directly or to lay the foundation of organic change of structure which may lead to permanent disease.

The theme so stated leads us to follow up the survey of the conditions which threaten death or disease by the study of the means resorted to with the view of averting these calamities and their relative efficacy. These means may be classed under the three heads: (1) General; (2) medical; (3) surgical.

The solution of the problem depends primarily upon a right appreciation of the forces brought into action under the influence of pregnancy. Then we must observe the disturbing factors—watch how Nature succeeds or fails in the struggle to preserve the physiological balance—and then by combined physiological observation and clinical experience we may arrive at certain definite indications for medical and surgical intervention.

Let us, then, in the first place, observe the phenomena evoked by pregnancy. The most remarkable are the marvellous exaltation of nervous and vascular tension, and attending alterations in the qualities and quantity of the blood.

From the moment that the embryo takes possession of the woman every drop of blood, every fibre, every organ is affected, the entire system is working under high pressure. It is our business to watch narrowly to see how far she is able to bear the strain and to be prepared with means to help her in preserving or in restoring the just equilibrium. Failing in that we endeavour to relieve the overstrained organism by removing the cause of the disturbance, that is to remove the embryo by the induction of labour.

At the outset of the discussion we must recognise the fact that the struggle is at first strictly physiological. So long as we can help Nature to preserve the physiological predominance we may pursue a policy of expectancy. Keeping a vigilant watch over the patient, testing the capacity of each