work of revision should be allowed an opportunity of expressing his opinion before the book is published and before the official formulæ and processes are rendered unalterable for the time being." Just think, gentlemen, of trying to harmonise the opinions of everyone who thinks himself competent to give an opinion on the subject! And to quote further from the same article: "There appears to be a growing feeling amongst pharmacists that unless such recognition is forthcoming they ought to decline to have anything to do with future revisions of the *Pharmacopœia*, and if in addition they proceed to prove by deeds rather than words that they alone are competent to deal with a certain section of the work it may be that long before another new *Pharmacopœia* is called for pharmacy will have attained its proper position in the matter."

If we consider the way in which trade interests are affected by the *Pharmacopœia*, if we consider that the volume deals with things bought and sold, it is impossible not to realise the risks of trade competition, of trade influence, and the constant danger of introducing a standard which might create a monopoly. I would ask you whether, with this in view, it is not better that the compilation should be in the hands of those whose motives cannot be assailed, that the final responsibility should rest with those whose interests are not at stake?

THE ESSENTIAL TOXIC SYMPTOMS OF DIPHTHERIA.

By JOHN BIERNACKI, M.D.,

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IN the widest sense the total symptoms of an acute microbic disease may be regarded as the outcome of specific intoxication; but the directly toxic element in the complex morbid condition is generally masked by secondarily-induced phenomena. Among the latter there stands out the train of symptoms accompanying pyrexia—no doubt itself toxic in origin. In light of this consideration diphtheria appears to be a suitable disease for analysis since, in addition to the fact that data are available on the experimental side, there is at its acme a frequent absence of febrile symptoms.

It is obvious that fatal cases, in which the toxic symptoms are extreme, afford the best material for observation, care being taken to exclude a large proportion in which the issue has been wholly or in part determined by such adventitious factors as laryngeal obstruction, hæmorrhage, or pneumonia. Between the residual cases thus selected a notable resemblance will be found to exist. Briefly, for a time the only symptoms present are those ascribable to sore throat and fever, the first specific signs being undue pallor, moderate compressibility of the pulse, and lassitude. The significance of the latter signs is such that they frequently suggest the examination of the pharynx in children too young to complain of sore throat. There is little further change in the case until three or four days have passed. Then the pallor becomes increasingly intense and the pulse more compressible, but the pyrexia less. Later the pulse is irregular, the urine diminishes in quantity, and the extremities tend to become cold. Frequently there is oppressive pain referred to the cardiac region or epigastrium. Towards the end the surface of the body is blanched and cold, the temperature is subnormal, and the radial pulse disappears. Other symptoms are jactitation and dimness of vision. The patient's mind remains clear until the end.

Some years ago I was struck by the resemblance between the above symptoms and those which accompany fatal hæmorrhage in cases of enteric fever, the inference being that a common cause existed, namely, a fall in blood pressure. Dr. Brodie¹ has shown that an injection of diphtheria toxin produces in cats a rapid fall in blood pressure followed by a slower recovery. This depression Dr. Brodie traces to relaxation of the blood vessels. In fatal cases it is accompanied by a fall in temperature. As a result of hearing Dr. Brodie lecture on these researches it occurred to me that blood-pressure records obtained by means of a sphygmometer in cases of diphtheria might prove instructive. For this purpose I employed the pocket form of the Hill-Barnard instrument. In the result, successive observations in the same

case are accepted as accurate, although, owing to all the patients being children, certain considerations suggest a higher absolute pressure than that registered. Six cases ending in death, and twenty in recovery, have been studied. The results obtained in the former cases, which are at present alone under consideration, prove sufficiently consistent to permit the selection of a type, variations from which can be subsequently noted.

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, the pulse-rate, and the number of respirations. 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.

HISTORY OF A CASE.

K. M., aged 3 years, was admitted on the afternoon of the fourth day of an attack of diphtheria. She was a well-nourished child, with an excellent past history. Although somewhat pale she was bright and intelligent. The vital organs were healthy. Typical membrane (from which the medium bacillus was cultivated) covered both tonsils, and extended on the left side over a small part of the soft palate. The cervical lymphatic glands on the same side were slightly inflamed. There was no discharge from the nose. The patient's temperature was 100 F. The respirations numbered 26, and the pulse 124, the latter being slightly compressible. Half an ounce of chlorine solution internally was ordered every four hours, the pharynx being syringed at similar intervals with a saturated solution of boric acid. The diet consisted of 4 ounces of milk given two-hourly, with 1 drachm of whisky added. At 11.30 P.M. 15,000 units of antitoxin were injected. On the following day—the fifth of the attack—there was little change in the case beyond increased swelling of the neck, and the appearance of a very faint trace of albumen in the urine. It may be noted here that the albumen increased in subsequent specimens, until—in the last obtainable—the proportion was about 30 per cent. On the sixth day the general condition remained unchanged. Late in the evening a second dose of 21,000 units of antitoxin was given, as the membrane persisted and the cervical inflammation was increasing. On the seventh day it was reported that the patient had been sick during the night, when the pulse was weaker for a time. The whisky was now doubled, as it was difficult to give the patient her full quantity of milk. Fragments of membrane were washed away each time the pharynx was syringed. Towards evening the extremities were cold. On the ninth day much of the membrane had disappeared, the remainder being diffident. The pulse was more compressible. Sickness beginning in the night continued, and the patient was ordered whisky and water only by mouth, enemata of over-zymised milk being given. The difficulty in keeping the patient warm increased, and the skin was of a waxen hue. On the tenth day champagne replaced the whisky, and zymised meat suppositories the enemata. The pulse was slightly irregular. On the eleventh day the sickness was persistent, the urine almost suppressed, and the pulse progressively weaker and more irregular in force and rhythm. On the twelfth day the child had passed a very restless night, tossing about in her cot. The radial pulse was difficult to count. No urine was passed. On the thirteenth day the child was throwing herself about so that it was difficult to keep her covered. From time to time she gave the peculiar cry which, in the case of older patients, is accounted for by distressing cardiac pain. Although she was apathetic her mind remained unclouded. Finally the radial pulse disappeared, and death occurred shortly after midnight.

REMARKS.—The striking fall in the blood pressure will be followed on the chart. A point not mentioned, but also shown, is the fairly consistent fall in temperature. The slight rise on the fifth day is explained by an inflammatory reaction at the seat of the first injection of antitoxin. The progressive diminution in the urine is noteworthy, as it is seldom possible to measure the urine throughout the course of a fatal case.

In all six cases the fall in blood pressure was slight at the outset, but it suddenly became more marked, and was then maintained until the end. In the two most severe cases this

final drop only occupied forty-eight hours. On the other hand it was, in one case, prolonged to six days.

One significant fact may be added. The symptoms which have been suggested as essentially toxic were in some degree a constant feature, and their incidence and subsequent intensity bore an evident relation to the fall in blood pressure.

REFERENCE.

1 BRITISH MEDICAL JOURNAL, November 4th, 1899, p. 1282.

THE TREATMENT OF DIPHTHERIA.*

By A. JEFFERIS TURNER, M.D.LOND.,
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In the year 1891 a new era in the treatment of diphtheria was introduced by a remarkable series of investigations published by Professor Behring, now of Marburg University. Although, as Behring remarks, all the essential points in the antitoxin treatment of diphtheria had been by that time fully worked out in the laboratory, the subject did not at first attract very much attention. It was not until 1894, when the acquisition of serum from large animals, particularly horses, permitted the extension of the methods discovered in the pathological laboratory to the treatment of human beings that general interest was aroused. The treatment rapidly spread, and by the commencement of 1895 was on its trial throughout the whole civilised world. In the five years that have since elapsed the diminution in the hospital mortality of diphtheria has been nothing short of marvellous to all but the few who had made themselves acquainted with the thorough and unimpeachable experimental basis on which the new treatment had been established. The records of hospital experience have in this instance been in complete accord with the conclusions of the laboratory. In private practice also, in Australia at least, antitoxin has been very widely used with very gratifying results in the reduction of the mortality from this disease. Nevertheless, its use is not yet universal, and it is every now and then our sad experience to see children admitted into hospital dying from diphtheria, to whom an injection of serum has never been administered, although they have been under medical treatment. In England this appears to be the case to a larger extent. One reads with astonishment¹ that the reduction of the diphtheria mortality in London is almost entirely confined to cases treated in hospital, and that it appears very doubtful whether antitoxin is much used in general practice. Though the contrary statement is true in these colonies, I believe that the remedy, even by practitioners of repute, is not always administered in sufficient doses. In mild and early cases a small dose of 600 to 1,000 units is sufficient, but in advanced and desperate conditions many practitioners are satisfied with injecting 1,000 or 1,500 units, when 4,000, 6,000, or even 8,000 or more units are really needed. The treatment of diphtheria appears to be, therefore, still a proper subject for discussion, and I shall endeavour in the first place to lay before you as briefly as possible the facts on which my opinions are based.

The records of the Brisbane Children's Hospital have been very carefully kept for the past ten years, and the majority of the diphtheria cases during that time have come under my personal observation. I am, therefore, in a position to guarantee the similarity and continuity of the statistical material.

During the preantitoxin period of five and a half years the diagnosis was based solely on clinical observation. Doubtless a few cases not really diphtherial were included, and these would make the mortality appear lower than it really was. I do not think they made much difference in the totals.

The antitoxin period is divided into five sections, of which the results of the two first have been already published.² In them we have included no cases but such as were verified by bacteriological examination. The new treatment being on its trial, such a course seemed advisable. During the next two sections we have included only cases which were verified bacteriologically, or which on clinical grounds could be recognised as diphtheria beyond any reasonable doubt. In the last period we have had to rely on clinical evidence alone,³ but

this has been interpreted with great strictness, much greater than in the preantitoxin period. In the absence of bacteriological examination the diagnosis of early and mild cases must often be doubtful, but in the severer cases, including the laryngeal cases, I am convinced that no appreciable fallacy has been introduced. All cases of possibly catarrhal laryngitis have been excluded.

The first division of the antitoxin period may be regarded as to some extent transitional. We used a serum of unknown but certainly very low antitoxin strength, of which 23 c.cm. was usually injected. In the second division the same serum was mainly used in doses up to 100 c.cm., and much better results were obtained. Since then we have used a serum of known antitoxin strength, and severe cases have usually received 4,000 units. Latterly, we have increased this dose in some cases to 6,000, 8,000, or even 12,000 units, and we believe that the lowered mortality of the last division is partly attributable to this increase.

The following table gives the total mortality for both preantitoxin and antitoxin periods:

Cases of Diphtheria treated in the Children's Hospital, Brisbane.

Preantitoxin Period.	Admissions.	Deaths.	Mortality.
July, 1889, to June, 1891 (2 years)	73	34	Per Cent. 46.6
July, 1891, to June, 1893 (2 years)	114	48	42.1
July, 1893, to January, 1895 (18 months)	116	46	39.7
Total	303	128	42.2

Antitoxin Period.	Admissions.	Deaths.	Mortality.
Small doses : January, 1895, to November, 1895 (11 months)...	40	10	Per Cent. 25.0
Large doses : November, 1895, to September, 1896 (10 months)	43	5	11.6
September, 1896, to December, 1897 (15 months)	83	8	9.8
January to December, 1898 (12 months)	45	7	15.6
January to August, 1899 (8 months)	106	10	9.4
Total	317	40	12.6

In presenting these statistics, I must not omit to acknowledge my indebtedness to the hospital residents, L. N. Ashworth, M.B., B.S.Melb., T. E. Green, M.B., B.S.Melb., Hugh Bell, F.R.C.S.Eng., and P. Dixon, M.B. Ch.M.Sydney, to whose assiduous care the good results are greatly attributable, and but for whose careful records I should be unable to write the present paper.

Although the whole number of cases is small as compared with other statistics that have been published, they have the advantage of having been treated in the same institution and under the same personal observation. Their lesson appears clear enough, but it is necessary, in order to exclude any possible doubt, to consider objections that have been raised by various critics to other similar statistics.

It has been objected that the introduction of a new treatment is accompanied by greater attention to the cases, and more care on the part of the residents and nursing staff. As far as our Hospital is concerned, I can testify that the greatest possible pains were taken over these cases during the preantitoxin period. It will be shown presently that nearly half of the cases were so severe as to necessitate intubation or tracheotomy, and, allowing for this, the results obtained compared favourably with other institutions at the same date.

Again it has been urged that the introduction of bacteriological methods of diagnosis has led to the inclusion of mild cases which would not formerly have been recognised as diphtheria, and so caused an apparent reduction of mortality. This certainly does not apply to our present figures. Cases not recognisable clinically as diphtheria, but in which diphtheria bacilli are present, have occurred with us very rarely: we have only record of three such cases (which came

* Read in the Section of Medicine of the Intercolonial Medical Congress, held in Brisbane.