

condition is rarely, in the absence of symptoms, suspected for the first two or three weeks, the tumour is not found because it is not looked for. As the child emaciates the detection of the tumour becomes easier, but this is no evidence of any rapid increase of the pyloric tumour. The more widely the affection becomes known the earlier will the pyloric thickening be detected.

Our knowledge of the nervous mechanism of the stomach is as yet so imperfect that it seems premature to found any hypothesis as to the causation on a theory of lack of coördination.²⁶

The results of operative treatment throw but little light on the question. The success that has attended the various surgical measures is consistent with any of the explanations of the causation hitherto advanced. Forcible dilatation of the pylorus or pyloroplasty would overcome spasm or would restore the lumen of a passage that had been compressed by an excessive muscular development. At first sight it would seem natural to suppose that after a time the muscle would recover and that the spasm would return, and this might be held to favour the view that pyloric spasm is not the real factor. The sphincter ani, for example, recovers its power after forcible stretching. We can hardly imagine that forcible dilatation could bring about proper coördination, which depends on the innervation of the gastric muscles. Practically, the mechanical obstruction is relieved by the mechanical stretching or even more efficiently by pyloroplasty. Though it is premature at present to say that recovery is permanent, as far as experience goes the good effects may at least be prolonged for months or years. The fact that gastro-enterostomy may bring about recovery from all the symptoms may be held to favour the theory of spasm. Possibly the pyloric sphincter after this operation may revert gradually to its normal extent and functional efficiency, but there is no evidence as yet that it does so. After a successful gastro-enterostomy for a non-malignant condition of the pylorus the nutrition may become perfectly normal though the pyloric passage remains closed, and this benefit is even more likely to come about in a child than an adult.

On the whole, we are disposed to think that the balance of evidence is in favour of the hyperplasia being primary. The solution of the problem probably lies in the hands of the morphologist. Very little is known about the development of the upper part of the alimentary canal that lies in the abdominal cavity.

The thickness of the normal pyloric sphincter (Fig. 2) varies greatly as specimens prepared from the stomachs of children less than 12 months old will show. Our best thanks are due to Dr. W. J. Fenton for preparing the specimens, and to Dr. H. R. D. Spitta for the excellent micro-photographs made from them.

A full bibliography will be published in the next volume of the Transactions of the Royal Medical and Chirurgical Society.

ON THE TREATMENT OF DIPHTHERIA BY THE INTRAVENOUS ADMINISTRATION OF ANTI-DIPHTHERITIC SERUM.

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THE use of antitoxin in the treatment of diphtheria may fairly be said to have passed its period of probation and to have become the commonly recognised method of treatment and there is now a consensus of opinion regarding the striking reduction in the mortality from this disease, especially in the earlier years of life, which has followed upon the adoption of the serum treatment.

Anti-sera differ from most powerful therapeutic remedies in that while the proportion of the anti-bodies present in different sera is inconstant, yet for therapeutic purposes this

does not interfere in any way with the exhibition of even very large doses as there is no evidence to show that any deleterious consequences result from the administration of large doses—from 20,000 to 80,000 units—beyond the temporary inconvenience caused by rheumatoid pains in the joints and muscles and by occasional cutaneous eruptions of an urticarial or erythematous kind. In fact, it would seem to be difficult, if not impossible, to give a fatal overdose of antitoxic serum. In illustration of the benign action of the serum it may be pointed out here that notwithstanding the large doses employed the amount of albumin present in the urine was not increased. On the contrary, in those cases in which large doses of serum were employed less albuminuria was found usually than in those in which smaller doses were given. This seems to strengthen the conclusion that the serum itself does not possess any toxic properties.

The marked reduction in the case-mortality in diphtheria effected since the introduction of the diphtheria antitoxin is now admitted by everyone, but great as this reduction has been the experience gained in the treatment of this disease in the City of Glasgow Fever Hospital, Belvidere, suggests that even a further fall in the case-mortality may be hoped for. The lines along which this improvement may be effected are twofold—(1) by the exhibition of larger doses than those commonly recommended and (2) in certain cases by the intravenous use of the remedy. The employment of larger doses of serum has been already advocated by several observers, but so far as I am aware no one has recommended the intravenous use of the remedy. In a paper dealing with the serum treatment of bubonic plague published in THE LANCET¹ I have advocated the intravenous use of Yersin's serum as a most useful adjunct to the subcutaneous injection of the remedy, and the encouraging results obtained in apparently hopeless cases of this disease suggested the employment of the same method of administration in the treatment of severe cases of diphtheria. Both diseases are due to the reception at a particular part of the body of a specific micro-organism which must be considered as the essential cause of the local lesion, whilst the general symptoms of the disease are brought about by the absorption into the system of a definite chemical poison or toxin which is formed by the life processes of the organism at the seat of inoculation. In plague² the subcutaneous injection of Yersin's serum is followed not only by a marked antitoxic effect, as evidenced by improvement in general symptoms, but when introduced into the lymphatic drain towards the bubo a directly bactericidal effect can be demonstrated, the organisms contained in the bubo showing evidence of degeneration very soon after the administration of the serum. When given subcutaneously, even in large doses, however, the effect of the serum appears to be chiefly a local one, degeneration occurring only in those organisms which lie within the area of injection. By the intravenous method the maximum influence of the serum on the tissues, and also on the organisms, is obtained with greater rapidity than when the serum is used subcutaneously and those bacilli which have overflowed from the primary focus of infection into the general circulation can be reached directly and similar degenerative changes be produced, whilst at the same time the circulating toxin is most effectively dealt with. The fact that the administration of even large doses of serum subcutaneously is not followed by a commensurate improvement suggests that the serum in its passage through the lymphatic vessels and glands undergoes a qualitative change whereby its power of neutralising toxin is considerably diminished. This may be due to (1) a selective action exercised by the lymphatic glands in filtering out the active constituent of the serum, or (2) to the fact that, as Ehrlich has shown, there are a definite chemical action and reaction between toxin and antitoxin, neutralisation going on more quickly and more effectively in concentrated solutions than in diluted ones. In the case of plague the local action of the subcutaneous injection of serum is probably directed in the first instance to the neutralisation of the toxin locally present in the bubo and its vicinity and also to inducing bacillary degeneration in the comparatively large numbers of organisms present in the primary lesion. Any surplus of antitoxic bodies which reaches the general circulation after passing through the lymphatic channels will probably be present in the blood in such a state of dilution as to be comparatively ineffective, especially in septicæmic cases of plague. By immediate introduction of

²⁶ Among the most recent views on the innervation of the stomach and pylorus are those of Openchowski who states: "*Pylorus and antrum*.—Central centres which cause constriction lie in the corpora quadrigemina; the fibres run almost entirely in the vagi. In the corpora quadrigemina are also centres for causing the pyloric sphincter to gape; apparently the path is down the cord and by the splanchnic nerves. It is of importance to know that the opening of the cardiac end in point of time coincides with contraction of the pylorus." Quoted by Tiegerstedt, *Physiologie des Menschen*, vol. i., p. 269, 1897.

¹ THE LANCET, June 22nd, 1901, p. 1746.

² Loc. cit.

the serum into the general circulation, however, those bacilli which have found their way to the deeper organs may be destroyed and the circulating toxin neutralised by the comparatively concentrated solution of antitoxins.

Diphtheria presents a distinct analogy to plague inasmuch as the bacilli appear to be confined at first to the seat of primary infection, the symptoms being generally ascribed to the effect of the toxin absorbed into the circulation. In plague, on the other hand, there is a very marked tendency to dissemination of the organisms and the disease may finally manifest itself as a plague septicæmia. In diphtheria this tendency until recently has been overlooked, but there is now every reason to believe that in certain exceptional cases the specific bacilli enter the circulation and so invade the deeper organs. A most valuable addition to our knowledge of the pathology and bacteriology of diphtheria is the excellent monograph on the subject published recently by Councilman, Mallory, and Pierce. These observers investigated the pathology and bacteriology of 220 fatal cases and the general result of their bacteriological examinations is so significant that it may be of value to quote here some of their results and observations. Cultures were taken from the heart's blood and from the liver, the spleen, and the kidney in 153 cases of diphtheria. In the blood the specific organism was found seven times, in the liver 30 times, in the spleen 19 times, and in the kidney 27 times. In one case of diphtheria complicated by scarlet fever diphtheria bacilli, together with cocci, were found in vegetations on the mitral valve. That diphtheria may become a generalised bacterial infection and is not merely a local disease is the conclusion to which these workers have been led. The same conclusion had been previously arrived at by Kanthack and others. In a series of 12 consecutive post-mortem examinations Kanthack discovered that an escape of the organisms to the general circulation had occurred in nine of the cases. In this respect, therefore, diphtheria is brought more into line with bubonic plague, and this fact encouraged the hope that the intravenous injection of serum, which had been found so efficacious in the latter disease, might be equally useful in the former.

Attention has already been called to the tendency in diphtheria, especially in fatal cases, to a general irruption of the bacillus from the local lesion into the circulation and to the presence of the organism in situations not in direct continuity with the primary focus. In this connexion it must be remembered that infection of the lungs usually takes place by direct extension along the air passages from the primary seat of infection. When this occurs a diphtheritic broncho-pneumonia, which has rightly been regarded as one of the most fatal complications of this disease, results. The pneumonic process in such cases was formerly regarded as due to a streptococcal infection, but recent observations go to prove that in nearly all such cases there is a true diphtheritic infection of the lung and that only exceptionally do we fail to find the Klebs-Loeffler bacillus in the fibrinous exudate lining the finer bronchioles and alveoli. 88 cases of pneumonia secondary to diphtheria were examined bacteriologically by the observers already mentioned and the specific organism was found in 82, whilst Kanthack states that "in almost all fatal cases of broncho-pneumonia, especially if the process be laryngeal or if tracheotomy has been performed, the Klebs-Loeffler bacillus can be found in the lung."

This extension of the diphtheritic process to the bronchioles and alveoli is of such great importance as completely to overshadow the effects of the disease at its primary seat in the fauces or larynx. Not only is the extent of surface involved and therefore the amount of toxin absorbed enormously increased, but the great vascularity of the lungs and the extreme thinness of the supra-vascular tissues of the bronchioles and alveoli combine to favour the rapid absorption of toxin into the circulation. The amount of toxin circulating in the blood in such circumstances must be very considerable and if the cure of diphtheria depends upon the neutralisation of this toxin by the anti-bodies in the serum, the necessity for the immediate introduction into the circulation of large quantities of serum is self-evident.

This specific bronchitis or broncho-pneumonia is perhaps the most frequent cause of death after tracheotomy and when the condition is at all well marked the number of such cases which recover, even in the most favourable circumstances, is comparatively small. If present at the time of operation its diagnosis by ordinary methods of physical examination is difficult and uncertain. On account of the

extremely urgent condition of the patient it is hardly possible to carry out an exact physical examination of the chest, particularly when the dyspnoea is severe and all the accessory muscles of inspiration are convulsed. Even when an examination is attempted the information so derived—apart from the occurrence of actual dulness to percussion, which is comparatively seldom found—is not of much value on account of the obstacle which the loud laryngeal sounds present to auscultation. The presence of this dangerous complication, however, may generally be correctly inferred if the breathing is unusually rapid and shallow: while its presence is certain if, after tracheotomy, the dyspnoea continues unabated, the lividity in place of disappearing steadily increases, the pulse continues to rise in frequency, and a discoloured muco-purulent secretion lodges in the lumen of the tube. It is in such cases that tracheotomy signally fails to alleviate the sufferings of the patient, and too frequently the only effect of the operation is to substitute pulmonary for laryngeal dyspnoea. It was in this type of case where the outlook was apparently hopeless that the intravenous injection of serum was first tried with encouraging results. In illustration of this type of case a few summarised clinical reports of cases of patients in whom pulmonary symptoms were prominent and to whom serum was administered intravenously are of interest.

CASE 1.—The patient, a girl, aged two years, was admitted on the fifth day of illness with a history of severe dyspnoea and stridor lasting for 36 hours prior to admission. When admitted she was pulseless and apparently moribund, the extremities as well as the surface of the body generally being cold and livid. The lips were swollen and cyanotic, the face was puffy and greyish-white in colour, and the child presented all the symptoms of a profound toxæmia. On auscultation it was found that the heart was beating at the rate of from 185 to 195 per minute. The laryngeal obstruction was almost complete and retraction of all the yielding parts of the thorax was present to an exaggerated degree. Inspiratory stridor was not pronounced, partly no doubt on account of the rapidity and shallowness of the respirations (from 50 to 60 per minute), but chiefly as a result of an extreme laryngeal stenosis. Tracheotomy was at once performed, and on the trachea being opened a large quantity of dark, chocolate-coloured, muco-purulent secretion, along with several pieces of membrane, was ejected from the wound. After insertion of the tube the child breathed easily but more rapidly than before (from 70 to 174 per minute). The lividity, however, was not appreciably diminished by the operation, and as there was now undoubted evidence of a widespread broncho-pneumonia involving both lungs, 26,000 units of serum were injected into the right median basilic vein. The patient slept soundly for several hours after operation, and the pulse, though still running between 170 and 180, could now be readily counted at the wrist. During the night the child was exceedingly restless and next morning the respirations had increased to 90 per minute and the pulse to 190, and occasionally even to 200, per minute. At this stage the hypodermic injection every six hours of two grains of caffeine and three minims of liquor strychninæ had a most beneficial influence on the pulse. The urine now collected for the first time was loaded with albumin and became almost solid on boiling. The patient had again a very restless night, but on the following morning very decided signs of improvement were present as indicated by a total disappearance of the poisoned look, by a diminution in the lividity, and by a slowing and steadying of the pulse. These signs of improvement were coincident with the establishment of a copious muco-purulent discharge from the tube. From this point onwards the patient steadily and rapidly improved, the temperature falling by a steady lysis to normal and being accompanied by corresponding reductions in both the pulse- and respiration-rate. The tube was removed on the eighth day after admission, but the discharge through the wound continued abundant for about a week longer. The appetite quickly returned, and with the exception of some pyrexial disturbance due to the serum administered convalescence was uninterrupted. The urine, which at first was highly albuminous, quickly cleared up.

CASE 2.—The patient, a male, aged two years, was admitted on the fifth day of illness with a history of severe dyspnoea and stridor for two days before admission. The face was pale yet cyanosed and the lips and finger-nails were almost black. The pulse was flickering and hardly perceptible at the wrist, while the cardiac action was se

rapid that its rate could not be counted accurately. The child was very rickety, with marked enlargement of the epiphyses and great rachitic deformity of the chest. Tracheotomy was immediately performed but the child ceased to breathe immediately after making the skin incision. The trachea was then rapidly opened and a large membranous cast was extracted with a feather. After prolonged artificial respiration the patient began to breathe spontaneously and rallied slowly under the influence of subcutaneous injections of ether and of brandy administered by the rectum. In view of the intense degree of poisoning and the evident malignant character of the case it was not considered likely that recovery could take place, yet it was resolved to try what a large dose of serum administered intravenously would effect. On account of the extreme feebleness of the circulation no veins could be seen in any of the limbs and attempts to find the larger superficial vessels of the arm by transverse incision at the bend of the elbow failed on both sides. There was, in fact, no bleeding of any consequence. The external jugular was then defined and opened and 30,000 units of serum were injected intravenously. The wound was closed with collodion. No anæsthetic was employed. The patient slept soundly for several hours after the operation, and the pulse, which at the time the serum was administered was running between 180 and 200 per minute, rapidly fell till it reached 150 nine hours later. The respirations, though easy, were very rapid, numbering between 60 and 70 per minute, and the secretion from the tube was copious and muco-purulent in character. On the third day the respirations fell to 40 and the pulse to 140 per minute. During the second week the pulse and respiration fell to normal. The tube was removed on the seventh day and from this point onwards convalescence was rapid and uneventful. The urine contained only a faint haze of albumin for a few days after admission.

CASE 3.—The patient, a girl, aged three years, was admitted on the eighth day of illness suffering from dyspnoea due to advanced laryngeal obstruction. A large patch of membrane, in appearance typically diphtheritic, was present on the right tonsil. The pulse was rapid and irregular and the respirations numbered between 30 and 40 per minute. The patient had a profoundly toxæmic appearance. 10,000 units of serum were injected subcutaneously and she was placed in a steam tent. Several hours after admission she was seized with a violent spasm of dyspnoea and became so excited that only with difficulty was she prevented from jumping out of bed. The face rapidly became cyanosed and after three or four abortive attempts at inspiration she suddenly fell back on the pillow apparently dead. As no effort at voluntary breathing followed, artificial respiration was at once performed by the nurse and apparently with benefit till assistance could be procured. The trachea was opened as soon as possible and a large piece of membrane was extracted. A further dose of 21,000 units was now given intravenously. Within 24 hours the pulse fell from 160 to 120, the toxæmic appearance had completely passed off, and the mucous membranes now assumed their normal rosy colour. Convalescence was protracted on account of an extensive broncho-pneumonia which was present on admission and also by the occurrence of a severe nephritis. The latter complication was of exceptional severity, the urine on several occasions becoming solid on boiling. From both complications the patient made a good recovery and was dismissed well on the fifty-third day of her illness.

CASE 4.—The patient, a girl, aged four years, was admitted *in extremis* suffering from almost complete laryngeal obstruction. The lips were almost black and the skin of the body generally was covered with dark cyanosed areas. The pulse was hardly perceptible at the wrist and could not be counted. The respirations numbered 36 per minute. Tracheotomy was immediately performed and a large piece of membrane was removed from the trachea. At the same time 34,000 units of serum were injected intravenously. The patient was very restless after operation and the respirations steadily increased from 36 to 66 the same evening, when it became apparent that the child was suffering from a severe broncho-pneumonia. She had a violent paroxysmal cough which determined an emphysema of the neck and upper part of the chest; and the tube in spite of constant spraying continued dry till the following evening, when a profuse secretion, at first mucous in character and later muco-purulent, began to flow from the tube. From this point improvement was continuous and steady, and

the temperature fell by a steady lysis from 103° to 97·6° F. which was reached on the fifth day after admission, and that during the same period the respirations declined from 64 to 22. The urine contained only a faint haze of albumin for a few days after admission and convalescence was uneventful.

The four cases just cited illustrate the influence of the intravenous administration of serum where broncho-pneumonia was present when the patients first came under observation. The following case in which broncho-pneumonia supervened after the administration of serum subcutaneously, this complication rapidly disappearing under the influence of a subsequent intravenous injection of serum, is of even greater interest.

CASE 5.—The patient, a girl, aged five years, was admitted on the sixth day of her illness suffering from laryngeal diphtheria with dyspnoea and associated retraction of the soft parts of the chest. The dyspnoea, however, was not of such urgency as to warrant immediate tracheotomy. The pulse was small and rapid, from 150 to 160 per minute, very irregular at times, and of low tension. The respirations varied between 32 and 38 per minute. The face was slightly cyanosed, but this was more marked in the lips and nails. 18,000 units of serum were injected subcutaneously and the child was placed in a steam tent. A temporary improvement, lasting about 36 hours, followed upon this treatment, but on the third day after admission the dyspnoea recurred with increased severity, and an incessant hard barking cough, unaccompanied by any expectoration, exhausted the patient's strength by preventing rest and sleep. On the following day the temperature was 102° F. and both pulse and respiration continued steadily to increase in frequency. The retraction of the chest was now so extreme, the lividity, not only of the face and extremities, but also of the body generally, was so pronounced, and the restlessness, cachectic look, and anxiety of countenance were so urgent as to necessitate immediate tracheotomy. Shortly before operation the pulse, which had been running between 170 and 180, rose so that its rate could not be determined at the wrist. The respirations likewise increased in frequency till they reached from 50 to 60 per minute, and as the physical signs now indicated a widespread infection of the lungs 22,000 units of serum were injected into the right median basilic vein immediately after tracheotomy had been performed. With the introduction of the tracheotomy tube the paroxysms of coughing ceased and the patient slept soundly for several hours, though the mucous membranes still showed some lividity. A few hours after operation a small membranous cast was coughed up, but as yet no secretion escaped from the tube. 24 hours after the intravenous injection the toxæmic appearance had completely vanished and a profuse muco-purulent secretion having a very foetid odour commenced to flow from the tube. From this point onwards the patient steadily improved, the temperature falling by a steady lysis to 97°, which was reached on the fourth day after the intravenous injection and was accompanied by a very striking reduction in the pulse- and respiration-rate, the former falling from 195 to 102 and the latter from 60 to 30 per minute. During this fall the pulse was very unsteady and irregular, showing at times a tendency to failure, but this was combated by the hypodermic injection of two grains of caffeine and three minims of liquor strychninæ administered every six hours. On account of the abundance of the secretion it was found impossible finally to remove the tube till the eighth day. With the appearance of a serum rash a slight but temporary recurrence of the dyspnoea, associated with a degree of lividity, took place, due possibly to a similar involvement of the mucous membrane lining the air passages. This, however, quickly subsided and from this point onwards convalescence was uninterrupted.

Another class of case which seemed to call for this method of treatment was what may be termed the "malignant type," of which the following two cases are examples.

CASE 6.—The patient, a female, aged eight years, was admitted on the fifth day of her illness with a history of sore-throat and swollen glands of four days' duration. The face was pale and the skin of the body generally was blanched. The eyes were heavy and listless and the expression was languid yet apprehensive. The clinical features of the case indicated a complete saturation of the tissues with the toxic products of diphtheria. The breathing was somewhat obstructed and entirely oral, due to great tumefaction of the

tonsils and soft palate. The breath had a gangrenous odour and the teeth and gums were covered with sordes and tough mucus. The tongue was heavily coated with a thick brown fur overlaid with foul-smelling secretion, on removal of which a dry parched surface was exposed. The condition of the fauces could not be determined till after the removal of a quantity of decomposing secretion and gangrenous tissue. On removal of this it was found that both tonsils were greatly enlarged and covered with thick felty layers of decomposing greyish-black membrane which extended inwards and forwards so as to cover the whole of the soft, and the greater part of the hard, palate. The left tonsil was already showing signs of disintegration, whilst from the free edge of the soft palate the membrane hung in ragged fringes. The uvula was completely encased in a glove-like process of membrane continuous with that covering the soft palate which was very cedematous and projected forwards into the mouth. The membrane was firmly adherent to the subjacent tissues. The submaxillary and cervical glands on both sides were enormously enlarged and most acutely painful. They formed a large hard mass which completely filled out the hollow of the neck, but on account of the extent of the surrounding cellular infiltration and induration the individual glands could not be defined. The nasal fossæ appeared to be also involved, as there was a thin serous discharge from both nostrils which caused considerable excoriation of the upper lip. The pulse was not rapid (from 120 to 130) but markedly irregular in force. On account of the extreme degree of poisoning and of the exceptionally malignant type of the disease 30,000 units of serum were injected into the left median basilic vein. No anæsthetic was employed on account of the critical condition of the patient. During the night she was exceedingly restless and next morning she looked very ill. The further extension of the membrane, however, had been checked and the glands were decidedly less painful though not reduced in size. 12 hours later, however—i.e., 36 hours after admission—there were undoubted signs of improvement as manifested by a great diminution in the restlessness, by a lessening in the cellular tumefaction in the neck, by a lowering and steadying of the pulse-rate, and by a remarkable amelioration of the patient's general condition. These satisfactory results were quickly followed by a moistening and cleaning of the tongue, by an improvement in the complexion due apparently to the disappearance of the toxæmia, and also by a remarkable subsidence in the glandular swelling which could now be freely manipulated without pain. By the fourth day the nasal discharge had ceased, the membrane had disappeared from the throat, the normal contour of the neck had been restored, and the glandular enlargement had so completely subsided that swelling of the neck was no longer evident. Further evidence of the severity of the infection is afforded by the fact that a portion of the soft palate and left tonsil became gangrenous, the slough separating about a week after admission. The urine, which contained a considerable quantity of albumin for the first four or five days after admission, rapidly cleared up. Convalescence was quickly established, but for several weeks the heart showed great instability and irregularity of action. Paralytic sequelæ were entirely absent.

CASE 7.—The patient was a boy, aged six years. When admitted he seemed to be moribund, although the illness was only of 24 hours' duration. Early on the morning of admission he was seized with severe dyspnoea and though he was removed to hospital without delay his general condition on admission was such as to promise little prospect of recovery. The pulse could not be felt at the wrist, the body was almost cold, and the colour of the skin was dark purple. The lips were swollen and of a deep violet hue, the eyes were congested and staring, and the muscles of the neck stood out with every spasmodic attempt at inspiration. The laryngeal obstruction was almost complete. The cervical and submaxillary glands on both sides were enormously enlarged and acutely tender, the surrounding cellular tissue being extensively infiltrated, simulating the "collar-neck" of scarlet fever. There was a profuse sanious discharge from both nostrils. Tracheotomy was immediately performed, a large quantity of muco-purulent secretion with a few fragments of membrane being expelled from the wound. The respirations continuing as rapid after the operation as before (40 per minute) it was feared that the diphtheritic process had extended to the finer bronchioles and 25,000 units of serum were therefore given intravenously. The child

was much collapsed but rallied quickly, and 20 minutes later the pulse had returned to the wrist and was beating at the rate of from 150 to 160 per minute. Four hours after operation the rate had fallen to 128 and the tension had greatly improved. The skin was now acting freely and the body generally was warm. On the following evening a striking diminution in the glandular enlargement had taken place, whilst the tenderness had completely disappeared. By the fourth day all glandular swelling had subsided and the nasal discharge had ceased. The tube was removed on the fourth day but the secretion from the trachea continued very abundant and muco-purulent in character during the first week. Though the physical signs of pneumonia were not obtained yet the greatly increased respiration-rate taken in association with the very abundant expectoration seemed to point to some pulmonary affection. A steady decline of the pulse-rate from 180 to 86 took place during the first week of illness. The urine contained only a haze of albumin on two occasions after the operation and the patient made a rapid and satisfactory recovery.

That the intravenous use of serum is capable of producing therapeutic results not obtainable by the subcutaneous method of administration will be apparent from a study of the clinical histories already given. The effect of such injections on the course of the disease, and particularly on the temperature and the pulse- and respiration-rate, will be evident from an examination of the charts, but there are several points which have been intentionally omitted from the reports and which call for special remark. Some of the most obvious results of the intravenous method of treatment are the following: (1) the strikingly rapid disappearance of the signs of toxæmia already referred to; (2) the surprisingly rapid disappearance—sometimes in the course of three or four days—of the great glandular enlargement in malignant cases; and (3) in pneumonic cases the marked diminution of the restlessness which is so distressing a feature of such cases. The dyspnoea in the latter type of case is frequently most painful to witness, and even when laryngeal dyspnoea has been relieved by operation the patient only too frequently gains little or no relief. The almost immediate improvement after the intravenous injection of serum in such cases is as striking in its results as it is difficult of explanation. Soon after the injection the patient falls into a quiet sleep and though the breathing may continue rapid and shallow yet there is an entire absence of the pulmonary distress previously noted. Further, it is a matter of frequent observation that patients suffering from pulmonary diphtheria are exceedingly difficult and troublesome to manage, resenting all the attentions of the nurse, no matter how kindly and carefully these are performed. After intravenous administration of serum such patients soon become more amenable and since its regular employment in the wards of this hospital the beneficial results following upon its use have been independently noticed and commented upon by those more immediately concerned in the care of the patients. The nurses state that as the patients are quieter than when treated by other methods they require much less individual attention and the invincible vomiting and loathing of food, so frequently seen in severe types of the disease, are seldom met with. The appetite quickly improves and, as a rule, convalescence is rapidly established. Although in the treatment of severe cases of diphtheria the intravenous injection of serum has been chiefly relied upon, the ordinary adjuvant measures were not neglected. Local disinfection of the throat was systematically carried out and, as a rule, laryngeal cases were kept in a moist warm atmosphere for 48 hours or longer.

The preceding clinical histories formed part of a series of 50 consecutive cases, and from the fact that in no less than 20 of these the intravenous method was used it will be readily inferred that the type of diphtheria dealt with was fairly severe. This severity is further evidenced by the comparatively large proportion of laryngeal cases, of which there were 31. 15 of these were complicated by broncho-pneumonia of greater or less severity and in 17 tracheotomy was performed. In accordance with the ordinary hospital custom patients who were admitted moribund and died within 24 hours of admission have been excluded from the following tables as not offering any scope for effective treatment. It is to be understood that in doubtful cases the diagnosis was established by bacteriological methods, but that when membrane presenting typically diphtheritic features was present on the fauces or was dislodged by coughing from the trachea, and where the clinical appearances generally left little room

for doubt a detailed bacteriological examination was not undertaken.

TABLE I.—*Giving Particulars of 50 Cases of Diphtheria in 20 of which Serum was injected Intravenously.*

Varieties of infection.	Number of cases.	Details as to tracheotomy in the 50 cases.	1900-1901.
Pharyngeal ...	19	Number of tracheotomies, 17. Number of deaths, 1	—
Laryngeal... ..	14	Percentage of tracheotomies to total number of cases, 34.	25%
Pharyngeal and laryngeal ... }	17	Percentage mortality of tracheotomy, 5·8.	34·7%
Nasal... ..	*		

* Of the above a nasal infection was present in seven.
The total number of deaths in the 50 cases was three, being a mortality of 6 per cent.

TABLE II.—*Showing the Age Incidence of Cases.*

Age in years.	Number of cases.	Number of deaths.
Under 1	3	—
„ 2	9	1
„ 3	8	—
„ 4	3	—
„ 5	7	—
5-10	17	1
10-15	2	—
15-20	1	1

The case-mortality, as will be seen from the accompanying table, was 6 per cent., compared with 10·7 per cent. for the previous year, and that in spite of the fact that the cases were of a more than usually severe type. The three deaths which occurred were respectively due (1) to malignant diphtheria; (2) to paralysis complicated by chorea in the sixth week of illness; and (3) to double broncho-pneumonia in a marasmic child, aged two years. It will be observed that while the percentage of tracheotomies is greater than that of the previous year—34 per cent. as compared with 25 per cent.—the mortality after the operation shows a striking reduction—viz., 5·8 per cent. in place of 34·7 per cent. Of the cases of tracheotomy no less than 12 were complicated with broncho-pneumonia and this makes the case-recovery all the more remarkable. This high rate of recovery is probably to be ascribed to the influence of the serum administered intravenously.

Serum rash.—The occurrence of these rashes apparently depends to some extent upon, and seems to vary with, the source of the serum employed, and it may be mentioned that the following remarks refer to the results obtained with serum supplied by Messrs. Parke, Davies, and Co. A serum rash was present in 70 per cent. of the cases. It generally appeared about the ninth day after injection and lasted, as a rule, about three days. The earliest date of its appearance was the third day after injection and the latest the thirteenth. No appreciable difference in the date of its appearance, its severity, or duration could be ascribed to the method of administration. The rash was rather more frequently met with when the intravenous method was employed, but in other respects the results were the same as those obtained when the serum was administered subcutaneously.

Dose.—The dose employed subcutaneously varied from 4000 to 20,000 units, and intravenously from 20,000 to 35,000 units. The largest amount injected was 82,000 units in three separate doses. Despite the large quantities employed no untoward results beyond the usual serum rash, pyrexia, &c., were observed. At no time could the presence of albumin in the urine be ascribed to the use of the serum, for many of the patients who received the largest doses had little or no albuminuria, and a consideration of this along with all the points which have gone before shows that there need be no hesitation in pushing the intravenous administration of the serum.

As already mentioned the intravenous method of treatment was at first employed only in those cases which were apparently hopeless at the time of admission and later in cases which, though very severe, promised some hope of

recovery, yet so far it has not been employed in this hospital in the treatment of the milder forms of the disease. The general indications for its use were considered to be the following: (1) malignant forms of the disease—i.e., those characterised by hæmorrhage from the nose or into the skin, by great glandular enlargement with marked cellular infiltration, and by extreme blanching of the skin; (2) any marked involvement of the lungs, either at the time of admission or subsequently; (3) a moribund condition of the patient on admission; and (4) profoundly toxæmic condition of the patient. In all such cases an initial dose of from 20,000 to 25,000 units is perhaps not excessive, and if in 24 hours the patient fails to respond to the treatment, as indicated by persistence of the signs of toxæmia, by continued rise of temperature and increased frequency of pulse- and respiration-rate, and by an extension of the membrane, the dose may be safely repeated. From a consideration of the cases already detailed it may be readily inferred that antitoxic serum when given intravenously in comparatively large doses is a remedy which will yield highly successful results even in those cases which appear from the first to be quite hopeless. It is frankly admitted that the number of cases dealt with is small, but as they are strictly consecutive cases and not selected ones the results obtained may be deemed sufficiently satisfactory to encourage a more extended trial of this method in the treatment of diphtheria.

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SOME FACTS BEARING ON THE VACCINATION CONTROVERSY DRAWN FROM THE RECENT EPIDEMIC OF SMALL-POX IN SOUTH-WEST ESSEX.

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THE present moment is not inopportune for glancing at some of the more outstanding facts bearing on the relations of small-pox and vaccination as observed in the recent epidemic in South-West Essex. The opportunity for making an exhaustive analysis of the available material has been wanting, so that the present survey is a restricted one—firstly, in point of time (the report dealing only with cases admitted to hospital up to July 31st); and, secondly, in the matter of the cases selected for comparison. For reasons that are purely personal it has been found impracticable to consider the revaccinated group. Further, over 100 cases have been excluded for such reasons as that the records were found to be questionable or that the patient had been vaccinated during the incubation period. The classification into unvaccinated and vaccinated—the latter consisting of persons who have been vaccinated once—has been adopted, the numbers being respectively 271 and 857. Notwithstanding the fact that the scope of the inquiry is limited in the directions indicated, this report may fairly claim to be a small contribution to the growing mass of evidence in favour of the practice of vaccination.

It is necessary at the outset to define the terms employed in the classification of the cases from the clinical standpoint since their application is bound to be more or less arbitrary. In *mild* cases the eruption consists of a score of spots, more or less; the constitutional symptoms are slight and evanescent and rarely extend to the eruptive period. In the *discrete* type the pocks are more numerous but never touch. Any degree of coalescence brings the case within the *confluent* group, in which for convenience *hæmorrhagic* cases are included.

The following comparison of vaccinated and unvaccinated is noteworthy:—

	Vaccinated.	Unvaccinated.
Mild	36 per cent.	8 per cent.
Discrete	45 „	45 „
Confluent	19 „	47 „

It will be seen that the proportion of mild cases is more than four times greater among the vaccinated than among the unvaccinated, while, on the other hand, the proportion of confluent cases in the same group is two and a half times less. The even distribution of discrete cases must, of course,