

in jaundice or allied cholæmic conditions or by any toxic results such as cholæmic affections are usually credited with. Whether there be any analogy between the disappearance of the tachycardia of exophthalmic goitre and the brachycardia of cholæmia I would not venture to say, or between the antithetic conditions of the two diseases as seen in the nervous, hæmopoietic, vaso-motor, and other systems, producing manifestations so strongly in contrast in the two diseases. But of one thing I am satisfied—that instead of any untoward symptoms being produced there were, on the contrary, a general improvement and a feeling of well-being in the nervous, circulatory, and digestive systems.

Such is a rough description of a suggested method of treatment of what is at best a most intractable and fatal disease, but one which frequently partakes of considerable amelioration in time without any active treatment whatever and is in that respect comparable to what is found in many infective processes from whatever cause arising.

On August 7th, 1899, I examined this patient, whom I had not seen for six months. She looked well and she said that she felt well; there was no palpitation, and the pulse-rate was 86. There were no tremors. The thyroid gland was still somewhat enlarged. She had an attack of diarrhœa in the previous week for which medicine was sent, one dose only being required. She volunteered the information that the thyroid had enlarged somewhat since the occurrence of the diarrhœa and that she did not notice any enlargement before the attack. The gland consisted of tough fibrous tissue.

A woman, aged 45 years, married, and with two children, "caught cold" six months previously to my seeing her. She was said to be suffering from "change of life," although her periods were still regular. She complained of nervousness, palpitation, and debility, that the bowels had become relaxed without any apparent cause or from slight causes, and that she was afraid to sleep. She looked frightened. The patient was pale and sallow and so nervous that she could not articulate properly. There was no exophthalmos but there was slight enlargement of the thyroid, noticeable only on examination. The pulse-rate at first counted 140 per minute and 129 when recounted at the end of the visit. There were tremors of the upper limbs, flexors without interossei, and weakness of the legs. She passed an abundance of pale urine but with no albumin. The diarrhœa was paroxysmal, copious, and pale. Bile equivalent to 240 grains was administered every four hours by the mouth and in three days it appeared in the urine and the dejecta. Owing to an apparent relaxing effect (not paroxysmal) the amount was modified to eight grains thrice daily. Hypodermic injections were given at the beginning of the second week. There were injected in all—one injection being given daily for 10 days—3000 grains. Thyroid so small that only one injection of 120 grains into its substance was given. The administration of four grains night and morning was continued for two months. At the end of that time, though slight nervousness still existed, the tremors were almost gone and the heart was quite steady. The patient had occasionally had relaxed bowels, especially during thunderstorms. She eats and sleeps well and has gained six pounds in weight. The distance at which she lives from my house prevented detailed notes of the case.

Longton, Staffs.

HÆMATURIA, AN EARLY SYMPTOM IN TUBERCULOSIS OF THE KIDNEY; AND RENAL "PHTHISIS AB HÆMOPTOË";

WITH ILLUSTRATIVE CASES.

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THE purpose of this paper is to draw attention to two points of importance, one having reference to the etiology and the other to the early diagnosis of tuberculous disease of the kidney.

In studying the relationship of hæmaturia to tuberculous disease it may be observed that bleedings occur—(1) from injury, independent of any pre-existing tuberculous lesion, the effused blood or injured tissues forming a nidus for

tuberculous infection; (2) as early hæmaturiæ, a premonitory symptom of tuberculous disease long antecedent to the development of a gross renal lesion; and (3) as late hæmaturiæ, from destructive tuberculous processes in the pelvis or renal parenchyma.

RENAL "PHTHISIS AB HÆMOPTOË" FOLLOWING TRAUMATIC HÆMORRHAGE.

Hæmoptyses have long been regarded as occupying an important relationship to pulmonary phthisis from the circumstance that they often precede the more evident symptoms and physical signs of the disease. Since early times pathologists have differed in their opinions respecting the etiological importance of such bleedings. One class of observers have regarded the effusion of blood as the origin of the tuberculosis and distinguished it by the old term "phthisis ab hæmoptoë." Others have supposed this explanation to be based upon inadequate foundations and have held to the idea that the hæmorrhages were evidence of the existence of an initial tuberculous lesion, but at the same time they willingly admitted that the occurrence of hæmorrhage may by providing a suitable nidus accelerate the progress of the disease. These two conceptions as to the relationship of hæmorrhages to tuberculosis are probably both correct and certainly are reconcileable with our present knowledge of the etiology and life history of tuberculous disease. No one, however, can now argue, as was formerly contended, that mere blood infiltration can of itself cause tuberculosis; but, on the other hand, it is now fully admitted that injury is an important influence in determining not only the localisation but even the occurrence of tuberculous disease. Probably the best example of this is found in the disease as it attacks bones and joints. The trauma causes extravasation of blood or of serum, and at the same time weakens the resisting power of the tissues of the part. Even in slight injuries where there is no perceptible extravasation the deposit and multiplication of tubercle bacilli may be favoured by the simple disturbance of the circulation associated with the processes of repair. Indeed, the onset of the malady is seldom attributed to severe blows on bones or strains of joints but rather to very slight injuries, which in the first instance attract little attention. It is probable that these slight traumatisms, by depressing the resisting power of the tissues, not only provide a suitable nidus for the implantation of the bacilli, but also supply a pabulum in which they multiply. It is also well known that the employment of force, in rectifying the deformities of bones or of the joints, may lead to a fresh outburst of the disease.

Two conditions are necessary to the establishment of tuberculous disease in the kidney—the presence of a suitable nidus there and the conveyance of the specific organisms to the part. The healthy kidney tissue, being very vascular, has a remarkable power of destroying tuberculous organisms introduced into its substance or of eliminating them from the system. To discuss how this is brought about is beyond the scope of the present inquiry. But an important clinical fact must here be referred to—viz., that tubercle bacilli which are carried by the blood from distant parts may be eliminated without any morbid change in structure being produced in evidence of their sojourn through the kidney. For example, tubercle bacilli may be found in the urine of patients suffering from tuberculous disease of the bones, of the lungs, or of other organs. Their presence in the urine is therefore not pathognomonic of tuberculosis of the urinary tract, and although the observation of these organisms furnishes positive proof that the patient is tuberculous the precise seat of the lesion remains to be determined. In cases where the kidney eliminates these bacilli without itself being involved in the tuberculous process, as an explanation it must be assumed either that the quantity which is carried to the organ at a given time is too small, or that the virulence of the microbes is insufficient to overcome the normal preventive power of the renal tissue and produce a specific pathological effect. The natural power of the renal tissue in destroying micro-organisms may be rendered less powerful by malformations of the organ or by disease. Hence we find that Bright's disease, cystic degeneration, amyloid degeneration, displacements, or congenital malformations all tend to make the kidney more liable to septic and tuberculous diseases, and, as in other organs, so also in the kidney injury or hæmorrhage may be an exciting cause of tuberculosis. In order that tuberculous bacilli may grow and multiply in the kidney it is necessary that they be conveyed

by the blood-stream to a part where there is a favourable soil for their growth and where they are not liable to be washed away by the current of blood or the flow of urine. Suppose that tubercle bacilli are present in the blood when a blow is sustained by the kidney, then the effused blood, with thrombosis of capillaries and the injury of the tissues, provide the conditions required. The following cases are illustrations of tuberculous disease of the kidney following injuries sufficiently severe to produce hæmaturia.

CASE 1. *History of a fall of 26 feet; severe pain in the left renal region; hæmaturia and effusion of blood around the left kidney; apparent complete recovery from injury; two and a half years afterwards suffering from advanced tuberculous disease of the left kidney.*—A man, aged 30 years, was admitted into the Glasgow Royal Infirmary on May 11th, 1893. The patient was working on the deck of a steamer when he accidentally fell into the hold, a distance of 26 feet. He was rendered unconscious and when admitted to the hospital was suffering from severe shock. Besides other injuries he complained of severe pain in the left lumbar region and the first urine passed after admission contained a considerable quantity of blood. On examination a distinct fulness and increased resistance were made out in the left flank and over this area the percussion was dull. The patient made a slow but steady recovery, but he was detained in hospital until August 17th on account of the other injuries, the kidney condition having apparently been recovered from within a fortnight. The hæmaturia disappeared 10 days after admission. The man was again seen on Nov. 27th, 1895—two and a half years after the accident—by Dr. D. McKellar Dewar, who recommended him to go into the hospital, but this he refused to do, preferring to be under the care of his private medical attendant, with whom Dr. Newman saw him in consultation. The patient stated that he remained well and was able to follow his occupation until the end of May, 1895, when he complained for the first time of a recurrence of the pain in the left lumbar region, and although on palpation a distinct fulness could be made out no fluctuation was detected. The urine was free from any deposit, blood, or albumin. Tubercle bacilli were not looked for. In November the urine contained an abundant muco-purulent deposit, six specimens of which were examined for tubercle bacilli, and in two of these bacilli were found. From May to November the patient's general health rapidly deteriorated, his appetite was impaired, and he lost 16 lb. in weight. The evening temperature was elevated irregularly and he complained of night-sweats, but there was no vesical irritation. By the end of December a distinct fluid accumulation was discovered in the left kidney and the patient was advised to have a nephrotomy performed when the kidney was found to be occupied by a typical tuberculous pyonephrosis.

CASE 2. *History of a blow causing ecchymosis in the right lumbar region; hæmaturia of five days' duration with one recurrence on the eleventh day; severe pain and some swelling in the right renal region; six months after the injury the urine became muco-purulent and bloody; symptoms and physical signs of renal phthisis.*—A woman, aged 47 years, was admitted into the Glasgow Royal Infirmary on August 2nd, 1895. On inquiry it appeared that in January the patient fell from "house steps," a distance of eight feet, and on falling struck her "right side" against the back of a chair. The blow was received on the right lumbar region and it caused considerable ecchymosis between the lower ribs and the crest of the ilium. On recovering from the immediate shock of the injury she suffered from severe deep pain in the region and the urine which was first passed after the accident contained blood. The hæmaturia continued for five days after the injury and recurred once only on the eleventh (?) day. There was some swelling in the region of the kidney, but how long it lasted the patient did not know. Since the fall the "side" had always felt weak, but the pain was not severe till seven weeks previously to admission to the infirmary, and about the same time she observed the urine to be dark in colour and that it contained blood together with a white deposit. On admission the patient complained of a swelling in the right lumbar region. She had always been rather spare in body and lacking in colour, but she said that she had fallen off considerably of late. About a month previously to admission she had pain in the lumbar region whenever she moved about and about the same time the urine presented the abnormal appearance above mentioned. On examination the whole space between the liver and the crest of the ilium was

dull and fluctuant and presented the characteristic features of a large pyonephrosis, but there was no sudden discharge of purulent urine at any time. The specific gravity of the urine was 1012, it was strongly alkaline and contained a considerable quantity of pus, some blood, and crystals or oxalate of lime; tubercle bacilli were also numerous. On August 17th the kidney was incised, when a large quantity of pus, urine, and tuberculous debris was evacuated, and a large cavity was scraped out with a Volkmann's spoon. Later in the history of the case the lungs became involved, there being dullness and abundant moist râles at the bases of both lungs behind, but at the apices there was no evidence of consolidation.

In each of these cases it was clearly shown by the history that the patients enjoyed perfect health until the occasion of the injury and it may be safely presumed in both instances that the traumatism was the only cause of the hæmorrhage. In cases where slight indirect violence has been followed by the appearance of blood for the first time the question may be legitimately raised as to the presence of pre-existing disease, which may not, up to the time of the accident, have shown itself by hæmaturia. But in these cases the blows were severe and direct and sufficient to injure the kidney. The most reasonable explanation seems to be that the injury reduced the resisting power of the organ, and at the same time caused an effusion of blood into its substance; that tuberculous bacilli were present in the effused blood or were conveyed to the neighbourhood of the effusion later, took root and multiplied and formed the centre of infection and thus produced what may be called a renal "phthisis ab hæmoptoë."

EARLY HÆMATURIA A PREMONITORY SYMPTOM OF TUBERCULOUS DISEASE LONG ANTECEDENT TO THE DEVELOPMENT OF A GROSS RENAL LESION.

It is by no means uncommon to meet with cases of profuse and frequent hæmoptyses long prior to the development of any recognisable physical signs of pulmonary phthisis; so also in renal tuberculosis, hæmaturia may be present as a premonitory symptom of the disease. Those who have had much experience in the post-mortem room must have seen cases of chronic phthisis pulmonalis where shortly before death hæmorrhages have occurred and blood has escaped into the parenchyma of one kidney or into the pelvis, and where on minute examination the renal tissue or even the effused blood was found to be occupied by tubercle bacilli; yet on microscopic examination the histological structure of the kidney was little altered, and, beyond the blood infiltration, presented the same microscopic appearance as its fellow on the opposite side. In such cases numerous tubercle bacilli may be found in the thrombosed vessels of the Malpighian tufts without any inflammatory changes having taken place.

But while hæmoptysis has been looked upon as a valuable danger signal of phthisis pulmonalis, even when unaccompanied by other physical signs, hæmaturia has not been regarded in the same light, although doubtless in some instances it carries with it the same warning of trouble to come. Hæmaturia is often the first indication of danger and induces the patient to seek advice, and in many instances, unless repeated and most minute examinations are made, the medical adviser may find it difficult to arrive at a satisfactory explanation of the symptoms. In tuberculous disease the urine presents very marked variations in the different stages of the malady; in the initial phases of the affection the presence of the virus induces a congested condition of the organ and hæmorrhages occur which are analogous to the early hæmoptyses of pulmonary tuberculosis and are probably due to a local interference with the circulation arising directly from the intimate relationship of the tuberculous deposit with the vascular supply.

CASE 3. *Profuse hæmaturia with slight pain in the left kidney recurring thrice; no other deposit in the urine and no swelling in the lumbar region; apparent recovery for two years followed by a relapse of the symptoms and a swelling in the left lumbar region; muco-purulent deposit in the urine and tubercle bacilli; no vesical irritation.*—A young woman, aged 18 years, consulted me in September, 1893, on account of a profuse hæmaturia which had occurred a fortnight previously. No reason could be assigned for the onset of the bleeding and it was unaccompanied by any pain over and above a sense of fulness and weight in the left renal region. A careful examination of the urine failed to reveal any abnormal constituents beyond

a small trace of blood, but the hæmaturia had practically disappeared at the time I saw the patient. Three months after this first hæmorrhage a second attack, not so profuse or so prolonged as the first, occurred and two months thereafter a third attack, all without any concomitant symptoms. On account of the difficulty in forming a diagnosis an examination of the bladder was made during the last attack and blood was seen issuing from the left ureter in a distinct cloud. It was therefore evident that the hæmorrhage was of renal origin, but as there were no symptoms pointing to the nature of the malady complete rest in bed was enjoined and the patient made what was regarded at the time as a complete recovery. Two years after the first hæmorrhage a fourth hæmorrhage occurred; this was associated with considerable pain in the left lumbar region and a distinct swelling could be made out by palpation. Examination of the urine two weeks after the hæmorrhage occurred showed it to contain a deposit of muco-purulent material as well as blood corpuscles and on microscopic examination tubercle bacilli were discovered. Still there were no symptoms present indicating any irritation of the bladder. The temperature was now elevated for the first time and the patient suffered from night-sweats, but there was no emaciation, loss of appetite, or serious constitutional disturbance.

CASE 4. *Hæmaturia 13 years previously to admission and again nine years after the first bleeding; large tuberculous pyonephrosis.*—A man, aged 39 years, was admitted to the Glasgow Royal Infirmary on April 28th, 1896, complaining of pain in the region of the right kidney. The patient's first trouble in connexion with the urine dated back to 13 years previously, when he had a slight attack of hæmaturia accompanied by pain over the right kidney, but these symptoms passed off in a few days. The patient had been in the infirmary in February, 1896, with hæmaturia. He first noticed blood regularly present in his urine in November, 1895. He, however, was able to continue at work until the end of January, 1896, when he came into the hospital; at that time the hæmaturia was very considerable. He said that it was only three weeks previously to admission that he noticed anything like severe pain in the right side and since the pain came on he had not noticed any blood in the urine. On examination a very distinct fulness was found in the right lumbar region. The whole space between the liver and the crest of the ilium was dull on percussion and on pressure considerable tenderness was produced. The thoracic organs and the other abdominal organs were normal, so also was the bladder. The urine contained a considerable quantity of pus and some blood and tubercle bacilli were present. The left kidney was healthy. On operation a large tuberculous kidney was discovered on the right side; it was scraped and evacuated.

In early hæmaturia the urine contains blood but is free from tuberculous deposits such as can be recognised by the naked eye or even by the microscope. Cultivation observations and inoculation experiments may, however, detect the presence of tuberculous bacilli.

LATE HÆMATURIA, FROM DESTRUCTIVE TUBERCULOUS PROCESSES IN THE PELVIS AND RENAL PARENCHYMA.

When the kidney parenchyma and the calyces become more seriously involved the characteristics of the urine are more distinct, but this is not always the case. The physical characters of the urine are in some instances such that one can with certainty state that the urinary tract is the seat of a tuberculous lesion, while in other cases the excretion may be to no appreciable extent altered from the normal. Before destructive processes commence within the renal pelvis or substance traces of albumin and small quantities of blood may be detected, but when the tuberculous deposit has commenced to break down and to evacuate into the ureter the quantity of albumin is increased, the urine is liable after a time to become alkaline, and along with greater or less quantities of débris of renal tissue pus appears in considerable quantity. The albuminuria differs from that of Bright's disease in that the urine is not clear, but contains much mucus; it is viscid, cloudy, and opaque, and it does not contain tube-casts. The deposit contains small caseous masses mixed with renal débris and on standing, although a considerable amount of pus may be precipitated, a certain quantity remains suspended and imparts a cloudy appearance to the fluid.

It is only in rare instances that profuse hæmaturia occurs in renal tuberculosis. Trautenroth¹ records the case of a

woman, aged 24 years, who was the subject of pulmonary tuberculosis in its early stage, out who also suffered from profuse hæmorrhage from a tuberculous kidney which necessitated nephrectomy. The pelvis of the kidney was filled with coagulated blood and upon one of the papilli a considerable ulcer was discovered. The parenchyma of the kidney was the seat of a diffuse tuberculosis. The urine before the operation was found to contain tubercle bacilli. The patient made a good recovery. Routier² records a somewhat similar case where the right kidney was the seat of a large tuberculous ulceration. Severe hæmorrhage occurred and continued during 17 days, associated with renal colic. On making pressure over the right kidney blood was seen to escape from the right ureter by the cystoscope. The kidney was removed and the patient made a good recovery.

CASE 5.—The only case worthy of note where severe hæmaturia occurred in advanced tuberculous disease was in that of a man, aged 37 years, who was admitted to the Glasgow Royal Infirmary on June 16th, 1895. The patient was under treatment for a long period for tuberculous disease of the right kidney, and whilst occasional slight hæmaturia were observed from time to time, it was not until March, 1897, that a large amount of blood escaped and at that time a very considerable hæmorrhage, amounting as the patient thought "to about a pint of blood and blood-clot" escaped, but as far as is known no recurrence of bleeding of such dimensions occurred.

As the disease advances the odour of the urine as a rule becomes more and more offensive; the fluid deposits large quantities of mucus and triple phosphates and on examination it is found to be highly albuminous. Occasionally while the urine is pale and of low specific gravity there may be evidences of retention on the diseased side, as shown by increase in the renal swelling, with perhaps indistinct fluctuation and pain accompanied by general constitutional disturbance, or there may be complete suppression, death being ushered in by uræmic symptoms.

In addition to the diagnostic points already indicated the detection of the tubercle bacillus in the urinary débris is of great value. It is when tuberculous lesions begin to break down that tubercle bacilli are most abundant and sometimes their number is very large. Several examinations are required before it can be concluded from negative results that the case is not tuberculous. It is more difficult to obtain the bacilli from urine than from sputum, they are less numerous in proportion to the medium in which they lie, decomposition destroys them more rapidly, and smegma bacilli are apt to be mistaken for them. The method is as follows. Allow a quantity of urine to stand in a conical glass in a cold place for not more than six hours and from the deposit select a small quantity of débris, place it in a glass of $\frac{3}{4}$ per cent. salt solution. It is more rapid and more reliable, however, to obtain their separation by the employment of the centrifuge. This method should always be resorted to when the numbers are small or when the urine contains much mucus or blood. When large quantities of mucus are present it may be necessary to render the urine slightly alkaline before using the centrifuge. Having placed a small fragment of the débris on a clean cover-glass it should be spread out into a thin layer by pressing another cover-glass against it between the finger and thumb. On separating the cover-glasses a thin film of débris will be found adhering to each. The glasses must be air-dried and then the films may be more firmly fixed by drying over a spirit-lamp or in front of a fire. The cover-glasses are then placed in or, still better, floated upon (with film side downwards) a solution of aniline magenta or a staining fluid of gentian violet. When the film has become sufficiently stained the colour may be abstracted from all structures other than the tubercle bacilli by passing the cover-glass through a 25 per cent. solution of nitric acid. The action of the acid may be arrested by carefully washing the specimen in pure water. When examining the urinary débris for tubercle bacilli it is necessary in most cases to prepare at least half a dozen specimens. Should bacilli be present they will be recognised by a magnifying power of 750 diameters as minute rod-shaped bodies, coloured according to the nature of the staining fluid employed. They are from three to seven micro-millimetres long, they may be straight, but are more frequently curved or bent upon themselves at an obtuse angle, they are frequently beaded, and they occur in bundles or singly. From the urine

¹ Centralblatt für Chirurgie, 1896, No. 16.

² Bulletin et Mémoire de la Société de Chirurgie de Paris, vol. xxi., p. 148.

the micro-organisms are not easily cultivated, as putrefactive bacteria contaminate the culture and destroy the specific bacilli. Koch, however, states that he has succeeded in cultivating tubercle bacilli from cases of tuberculous pyelitis.

In some instances the bacilli in the urine are so few in number that it is difficult or almost impossible to discover them simply by the microscope; in such instances inoculation experiments may help to clear up the diagnosis. Tuberculosis can be communicated artificially to animals in many different ways, in fact, through any of the channels of access to the body—by inhalation, by feeding animals on tuberculous products, by injection into the serous cavities beneath the skin, into the anterior chamber of the eye, or into veins. When tuberculous urine is injected subcutaneously into guinea-pigs or into rabbits it produces a typical tuberculosis within 10 or 12 days. The local swelling may break down, caseate, and ulcerate, while the lymphatic glands related to the part become enlarged and firm and after a time may also caseate, and the disease passes on to another group. When injected into the peritoneal cavity it produces an extensive tuberculous infiltration of the omentum and acute tuberculous peritonitis. Normal urine when aseptic becomes absorbed without producing any evil effect or when septic it may produce a suppurative peritonitis. If, however, the experiment is performed with care healthy urine produces a negative result, but if the urine contains tubercle bacilli or their spores, acute miliary tuberculosis is developed in the course of a few weeks when the injection is made into the peritoneum, or if the urine is placed underneath the skin a hard tuberculous nodule is formed.

Besides the detection of the tubercle bacillus it is necessary to determine whether the disease is on one or on both sides. I have several times had occasion to examine by ureteral catheterisation cases of tuberculous pyelitis in which it was considered of importance to determine the extent to which the disease had involved one or both kidneys. Catheterisation can only determine the organ to which the tuberculous disease is limited; it cannot indicate the extent of the tuberculous lesion in the affected organ, but to make sure that one kidney is free from disease is a point of importance. The first time the writer succeeded in doing this was in 1886, when a case was examined and it was clearly shown that the tuberculous lesion was limited to one kidney.

Glasgow.

DIPHTHERITIC PARALYSIS IN CASES

TREATED WITH ANTITOXIN.

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THE use of antitoxic serum in the treatment of diphtheria has up to the present time in the London fever hospitals had two main results—the death-rate has fallen while the paralysis rate has risen. In the hospitals of the Metropolitan Asylums Board the former has been reduced from 29 per cent. to 15·3 per cent., while the latter has risen from 13 per cent. to as high as 21 per cent. in 1896. This increase of paralysis is chiefly due to the fact that many more patients now recover from the primary disease and live long enough for paralysis to show itself. During the last two years, however, the occurrence of paralysis has begun to diminish in frequency. From a review of the past few years it appears probable, as I shall endeavour to show, that this is due to the more efficient use of antitoxin. Table I. comprises cases treated at the Eastern Fever Hospital, the figures being chiefly obtained from the Metropolitan Asylums Board reports.

Of the nine fatal cases of paralysis during 1895 only four had previously received antitoxin, while in the following years all the 22 fatal cases had been injected. Examination of Table I. shows that in 1895, the first year in which antitoxin was largely used, its life-saving influence began to make itself felt, but at the same time paralysis became more frequent. In 1896 the average dose of antitoxin was increased and a larger proportion of patients received the treatment. The death-rate fell considerably and the paralysis rate rose. In 1897 the former remained about the same but there was a marked decrease of paralysis, a decrease more than maintained in the following year. The cause of this is

worth investigation. Apparently it was not due to a change in the type of disease, for the death-rate remained about the same. Nor was it due to the fact that the patients remained under observation for a shorter time than before, or that their age grouping had altered, or that there was an increase in the number of so-called “bacteriological” cases of diphtheria. I have examined these points in some detail and I find that little or no change has occurred. On the whole, however, the cases came somewhat earlier under treatment in 1897 than in 1896, but the absence of a definite fall in the mortality shows that this factor was not of much

TABLE I.—Cases of Diphtheria at the Eastern Fever Hospital.

Years.	All completed cases.	Cases treated with anti-toxin.	All paralysis cases.	Percentage of paralysis.	Deaths from paralysis.	Percentage of deaths from paralysis.	Total mortality per cent.
1892, 1893, } and 1894 }	1523	—	174	11·4	19	1·24	33·8
1895	641	276	103	16·0	9	1·40	25·5
1896	633	475	136	21·5	9	1·42	17·3
1897*	1060	980	161	15·1	6	0·56	17·2
1898	1301	1280	164	12·6	7	0·53	15·9

* The increase in numbers during the year was due to the fact that more accommodation was provided for cases of diphtheria.

importance. Two points remain for consideration—(1) the proportion of cases treated with antitoxin and (2) the dose of antitoxin. It will be noticed from Table 1 that a far larger proportion of patients received the serum treatment in 1897 than in 1896. This alone, though possibly of some influence, will not account for the decrease of paralysis. Of the 158 non-antitoxin cases in 1896 only 17, or 10·7 per cent., became paralysed, so that even if antitoxin had prevented paralysis in every one of these cases the total rate would still be 18·8 per cent.—i.e., considerably higher than in the following year. Finally, the dose of antitoxin must be considered.

Towards the end of 1896 and in the succeeding years antitoxin was administered in larger doses than before. The effect of this would become apparent in the 1897 group of cases—i.e., the cases of patients who left the hospital in that year. It is true that large doses had frequently been given before, but small ones—e.g., 1500 or 2000 units—were common. The change of which I speak was a systematic increase in the minimum dose. In the early part of 1897 the minimum dose was 3000 units; later it rose to 4000 units, at which it still remains. However mild the case this was the dose, no attempt being made to reduce it because the symptoms of diphtheria appeared to be slight. Severe cases, of course, as previously, received larger doses. It is to this systematic use of a comparatively large dose that, I believe, the fall in the paralysis rate is to be chiefly attributed. The one coincided so exactly with the other that in the absence of proof to the contrary it seems reasonable to regard them as standing in the relation of cause and effect. In 1898 the minimum dose was always 4000 units and practically all patients were injected, and in this year there was (see Table I.) still less paralysis. Whether a further increase of the dose be advisable it is difficult to say. When speaking of “dose” I mean the initial dose, as this is by far the most important one. It should be mentioned, however, that during 1897 and 1898 secondary doses were larger and quite as common as formerly.

There is no doubt that differences of opinion may exist in the diagnosis of loss of power following diphtheria or that many of the slighter forms of paralysis may escape notice unless carefully looked for. This source of error, however, is eliminated if we consider only the fatal cases. A reference to Table I. shows that during 1897 the mortality directly due to paralysis was less than half of that which it had previously been. Thus during the large-dose period paralysis was less fatal as well as less frequent. The above conclusions are based entirely on results obtained at the Eastern Fever Hospital. In some hospitals the paralysis rate still remains high, although on the whole in the Metropolitan Asylums Board hospitals it has shown a tendency to fall. The dosage, the proportion of cases treated with antitoxin, and other factors vary so much in different hospitals