exciting causes. Scrupulous cleanliness, the removal of adenoid vegetations, the treatment of anaemia, and the importance of air and exercise, must receive proper attention. In boys, circumcision is sometimes advisable, and if threadworms are present, special measures must be used to get rid of them, ordinarily an easy task.

The question of drugs is important. The number that have been employed is enormous, and many of these have been praised as efficacious. I have used a large variety, but have found three only of much service, and of these three belladonna or atropine is by far the most successful. It may be used in the form of the extract, or the tincture, or as liquor atropinae, and each has its advocates. I do not regard the point as essential, though personally I always employ the tincture. What is essential is that the dose shoul l be sufficient to produce evidence of its action, and that it be used over a long period. I usually give 10 minims of the tincture three times a day as the initial dose, and raise the dose week by week up to a drachm three times a day. With these doses in a large number of cases immediate benefit is obtained, and usually as time goes on the frequency of the enuresis sensibly diminishes, and finally disappears. At this period it is essential not to abandon the drug, but to slowly diminish the dose until it can safely be dispensed with. A period of three to six months will usually be required for the permanent relief of the complaint, but occasionally there are cases where that time must be considerably prolonged.

The danger of poisoning is slight. Of the many cases I have treated in this manner only one has had delirium, though loss of accommodation is nearly always present in the beginning. This, however, soon passes off, and it is not an indication for relaxing the use of the drug. Dryness of the throat and mouth and a smarting sensation in the pharynx are also complained of sometimes, but these also are temporary discomforts. I employ the belladonna in conjunction with potassium citrate in the majority of cases, and in a few instances where I have had reason to believe that hyperacidity of the urine was the chief cause I have found potassium citrate alone to be efficacious. The third drug which has proved successful is urotropin, and this is especially indicated in cases of bacteriuria. It must be given well diluted, for in concentrated solutions it has been known to produce haematuria, and painful micturition. I used it on a series of thirty consecutive cases, with good results in nine instances.

Of other drugs my experience has been disappointing; I have never succeeded in obtaining good results with ergot, antipyrin, rhus aromatica, lycopodium, or any of the other drugs which others have found useful. In excitable children, who are the subjects of night terrors, a small dose of potassium bromide at bedtime is beneficial, and in ill-nourished, anaemic children, iron and strychnine are good tonics.

Electrical treatment, with one pole in the urethra, or over the pubes, and one on the lumbar region, is said to succeed where other measures fail, but it also fails frequently, and I cannot ascertain that the cases in which medicinal treatment fails are cured by the employment of the electric current. It is true that all treatment in this complaint is empirical, but in my experience comparatively few cases resist, if the treatment indicated is perseveringly carried out. When, however, failure still attends one's efforts at the end of six months and there is no sign of improvement, the patient should be removed entirely from his or her surroundings, and placed in bed under supervision. What have been apparently hopeless cases often derive striking benefit from such a course, and, the force of habit thus attenuated, the final results are usually good. I believe that the prospects of treatment are better than is usually supposed. I estimate that between 70 and 80 per cent. of my cases get well in about four months, that 10 to 16 per cent. recover in about eight months, and that from 1 to 2 per cent. remain almost as bad as before. Of these last, however, I do not despair; some of them are improved; all are capable of improvement, but subject to relapses. The only point remaining to notice is that I find boys more amenable to treatment than girls, and that the most hopeless cases are those in which mental development is below the average. Of cases occurring in young adults I have little experience, but I believe that the majority are in girls, and that they are usually cases where treatment in earlier years has been spasmodic or even wholly neglected.

THE CAUSES AND TREATMENT OF ENURESIS.*

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This is a subject in which I have long taken great interest, and in 1899 I published in the *King's College Hospital Reports* my ideas on the matter, which followed a number of cases successfully treated by an antidiabetic diet. Since then many failures by this treatment, together with more work at the subject, have induced me to alter my views, or rather to enlarge them.

I will now endeavour to offer an explanation of the conditions which brings all the varieties of this malady into line, and of the reasons for the success or failure of the various treatments in common use.

Causes.

Nocturnal enuresis is a symptom the causes of which are believed to be various. Dr. Goodhart, in his work on *Diseases of Children*, says:

> There are few conditions which require more careful study than this, and few in which such a variety of circumstances conspire to bring it about. Whoever will treat enuresis with success must be prepared for a preliminary inquiry of a somewhat complicated nature.

This opinion becomes confirmed on reading the views of various writers on the subject, for it is found that hardly any two are in agreement as to the causes of this distressing malady. It may be that as the causes are admittedly various there is some truth in all. It will be our endeavour, then, to extract from this mass of contradictory material some general ideas which may bring these dicta into harmony, and so formulate a broad basis for treatment.

Condition of the Urine.

All writers agree that the urine shows variations from the normal. Owen noted that the urine might be acid or alkaline. At times it is extremely acid, loaded with urates and of high specific gravity. In these cases it is held by some that, being abnormally irritating, the urine excites the reflex act of emptying the bladder without the intervention of the consciousness. The more common variation, however, is a condition of low specific gravity, neutral or alkaline urine with triple phosphates or oxalates, a few pus cells, and a trace of albumen. Then it must be the amount of the urine which excites the reflex, for the quantity passed in twenty-four hours, and especially at night, is thrice or even more times than the normal. There is, in fact, a condition of polyuria. It is quite common to find a bed deluged with urine an hour or so after a child has been taken up and made to pass water.

Typical examples of urine from enuresis cases are as follow:

(*a*) Specific gravity 1030, highly acid reaction. Total quantity in 24 hours, 20 oz. Colour, mahogany. Urea, 6 per cent. Deposit, uric acid crystals in abundance. No albumen or sugar.

(*b*) Specific gravity 1005. Alkaline reaction. Total quantity in 24 hours, 3 pints. Colour, very pale straw colour. Urea, 0.3 per cent. Deposit, triple phosphates with a few pus cells. Trace of albumen. No sugar.

Condition of the Patient.

But if the urine is admitted to be abnormal, there is an equal agreement that the subjects of the complaint are also abnormal. The varieties of this abnormality have by different writers been made to include a very large number of the disorders to which the flesh of childhood is heir. Rachford found anaemia in 80 per cent. of his cases, and it is always present in the alkaline class. Trousseau says enuresis is essentially a neurosis, and often found in families prone to epilepsy. Some have considered it a mild form of nocturnal epilepsy. Goodhart says the tone of the nervous system is at fault. Some authorities have described the sufferers as mainly of a neurotic type, whilst others as flabby, anaemic, and lymphatic. A vasomotor neurosis of the renal vessels has been suggested as an explanation. Whitla finds enuresis very common in the neglected children sent into the industrial and charity schools, where it is often associated in its worst forms with a low standard of intellectual development. Ashby

* Read at a meeting of the Folkestone Division of the British Medical Association.

and Wright consider that mere delicacy of health may give rise to enuresis. It is usually affirmed to be more common in boys than in girls, but this is not the writer's experience. Of 38 cases, Goodhart found 20 in girls and 18 in boys. Eustace Smith says the worst forms are found in girls, and West and Whitla confirm this. Many observers have noted the occurrence of enuresis in the subjects of rickets, rheumatism, adenoids, and constipation. Slow carbonic acid poisoning has been given as a cause. Thus, G. W. Major and Zeim explain the incontinence of mouth-breathing children. Some local condition of the urethra or bladder or their neighbourhood has also been blamed as a cause. To mention only a few of these will be sufficient—namely, long prepuce, worms, hip-joint disease, polypus of the rectum, pinhole meatus, and urethral caruncle. Nocturnal enuresis has been noted as an early symptom in nephritis, renal calculus, diabetes, and in tuberculosis of the urinary organs.

Condition of the Nervous System.

It is held by some that in these cases the nervous system is either generally or locally at fault. By others it is attributed to a retrogression to, or a continuation of, the infantile condition, to laziness, or to defective training. That there must be a debility of the whole nervous system is apparent from the large number of these sufferers amongst the insane, and also, as Whitla noticed, in the children of the charity schools. There can be no doubt that the habit of enuresis often remains long after the cause has been removed. It is owing to this that many methods get the reputation of curing when they have only broken a habit. In this category we may place nearly all those cases which are cured by operative procedures, and by the various forms of local treatment. Thus is explained the frequent failure of each method, and the fact that some methods, such for instance as circumcision, have been followed by enuresis in subjects who had not previously suffered from it. The contention is that such an impression is made on the nervous system by the surgical or other method of procedure, that the attention is forcibly directed to the new source of discomfort, and the habit of emptying the bladder during sleep is broken. The tendency to spontaneous cure is well known. Sachs is of the opinion that profoundness of sleep alone is sufficient to cause the phenomenon. Goodhart and others have noticed that in enuresis sleep is too profound, and it is a matter of common observation that when taking such a patient up at night, he hardly ever quite awakes, and that he relapses again into slumber directly he is put back into bed. Such cures as are brought about by corporeal punishment, or the cure by the American method of vigorously spanking the nates, may operate by causing sleep to be less profound and so breaking into the vicious circle. But corporeal punishment sometimes acts in a way not intended. The writer knows of boys who attempted to keep awake all night in order to avoid a thrashing, of others who tied pieces of string round the prepuce, and of one case where sloughing of the penis resulted from the application of a brass ring for the same purpose.

Condition of the Digestive System.

But behind the admitted weakness of the nervous system there is always a digestive disturbance. In the writer's opinion this is the key to the situation. Owen and several writers have noted the great importance of diet in treatment. But Owen admits that all treatment is empirical. A. Jacobi says that whenever the urine is abnormal the digestive system must receive attention, and that treatment is useless until the normal action of the digestive organs is restored. Goodhart recommends abstinence from meat, and this undoubtedly does good where the urine is too acid. Whitla noted the frequent bad effect of a too starchy diet. This is most noticeable where the urine is neutral or alkaline. The curative effect of a non-farinaceous diet is often immediate. The fact that the alkaline variation of the urine is the more common, accounts for the large measure of success which this treatment has effected. The researches of Luff, Chalmers Watson, and others, on intestinal fermentations and bacterial processes in the digestive organs, make it certain that the formation of a toxin as a result of their action is a very important element in the condition under review. In fact, it is held that this is another condition which is in a large measure the consequence of intestinal sepsis. Dr. S. J. Wright, in the *New York Medical Record* for July, 1897, records a case of a lady of 34, where the trouble had existed from childhood. She was cured by taking naphthol (an intestinal antiseptic) internally. It is now admitted that the highly acid urine of gout is due to bacterial action in the intestine. In the alkaline variety of enuresis the polyuria is probably due to a toxin acting on the renal vessels and causing their dilatation, or, even more possibly, to its effect on the general blood pressure.

In the BRITISH MEDICAL JOURNAL for February 17th Dr. Bushnell describes a condition of bacilluria, in which large quantities of living bacilli of various sorts are eliminated by the kidneys. This he says is a not infrequent cause of nocturnal incontinence in children.

One cannot but be struck by the ease with which this view that intestinal sepsis is an essential part of the condition explains the facts of enuresis. Enuresis with acid urine is the result of putrefactive decomposition of the albuminous constituents of the food. Enuresis with neutral or alkaline urine is the result of putrefactive decomposition of the farinaceous constituents.

Intestinal sepsis occurs most easily in those whose vitality is depressed from any cause, and hence all the various conditions which have been named as causes are brought into line by this hypothesis. Intestinal sepsis is much influenced by the state of the general health, which accounts for the curative effects of tonics, for spontaneous cure, for recurrence, for the effects of regular diet, for the cures which so often follow on the improved health consequent on the removal of adenoids or other morbid conditions, and for the failure of altering the position during sleep or tilting the end of the bed, as noted by Crawford.

This fact of intestinal sepsis, combined with a nervous system (and consequently the local nervous mechanism of micturition) temporarily weak, together with what has been said as to the formation of a habit of enuresis, offers, indeed, an explanation of the success or failure of all the methods of treatment in vogue, and forms concord amongst the many apparently diverse explanations of the cause of enuresis which have obtained in the past. Hence is made plain the occurrence of the condition occasionally in adults, and its much greater frequency in children. The effects of intestinal sepsis are more manifest, and the results tend to remain longer as a habit in children owing to the little assistance which the breaking of the habit receives from the will. It is often necessary with them to make an impression on the mind, by surgical or other measures as before mentioned. There are no commonly-used treatments which cannot have their success or failure explained on the theory of intestinal sepsis, with a weakened nervous system as an essential element, at some time or other in all cases.

TREATMENT.

General Considerations.

When undertaking the treatment of a case of enuresis it is first necessary to consider:

1. Whether the case is simply one of general want of tone.
2. Whether intestinal sepsis is now a prominent feature, and if so, is the urine passed at night abnormally acid, and of diminished quantity, or is it of low specific gravity, alkaline or neutral, and of increased quantity?
3. Or whether the case is simply one of habit remaining after the cause has been removed, or after improvement in the general health has become such that enuresis need not occur.

As a rule it is quite easy to determine this point, but one must own that it is not always possible to be quite sure. In practice it is found that failure on one line of treatment will soon be followed by success by substituting one of the other two. At all events, viewing the matter in this way, we have a knowledge which enables us to judge with accuracy how long persistence in one line of treatment should be allowed.

Tonics.

In the first of these classes are those cases which different writers describe by saying that the children do not look ill, and also those in which anaemia is present without much evidence of intestinal sepsis, and mostly also those who have not suffered long. These are the cases which Ashby and Wright allude to as due to

delicacy alone. Almost any good tonic will effect a cure. Many physicians have a preference for phosphate of iron in its popular form, or perchloride of iron as strongly advocated by West, or strychnine as advised by Ringer. Included in this method are all measures which tend to improve the health, such as cold douches, massage, "running wild" in the country, change of air, or any of the many things which we are in the habit of prescribing to improve the general health and tone of our patients. The practice of taking the patient up several times at night is a convenient method of protecting the bed, but it is in no sense a means of cure.

Treatment of the Digestion.

In the second class, evidences of indigestion are to be found more or less prominent, and all the causes which produce intestinal sepsis are to be looked for, and, if possible, removed. These are the cases which are often so easily cured by diet. In the acid form the cutting off of meat alone may be followed by success, and in the alkaline form the use of a non-farinaceous diet is often immediate in its good results. The failure of either diet is due to such method alone not being sufficient by itself to stay the course of an intestinal sepsis once begun. There are, of course, a number of ways of combating intestinal sepsis. A good routine treatment consists in securing a good daily evacuation of the bowels by giving ¼ gr. of calomel every night and a mild saline aperient in the morning. In addition one may give one or more of the many drugs which aid intestinal asepsis. Further assistance may be obtained from any of the health-improving methods before mentioned, which can be selected at the discretion of the physician. He must also decide each case on its merits, as to whether medicinal tonics can be used at the same time that the septic condition of the digestive organs is being combated.

ILLUSTRATIVE CASES.

1. Enuresis had existed for a long time in the son, aged 7 years, of a lodging-house keeper. He was at once cured by being taken into hospital and kept on the ordinary hospital diet without any other treatment.

2. A girl, aged 21 years, the servant at another lodging house, was cured as rapidly by the same method.

The obvious cause in each instance was intestinal sepsis from irregular and injudicious feeding.

3. A girl, aged 10, had had enuresis for three months. She had immediate freedom from this symptom while taking a non-farinaceous diet, but for the first six weeks relapse followed the slightest consumption of starchy food.

4. A boy at school with enuresis and highly acid urine showed no improvement when taken off meat. He was, however, rapidly cured by a course of ¼ gr. calomel every night, and 5 gr. of salicylate of soda thrice daily.

Breaking the Habit.

In the third class one may look for sources of irritation which might require treatment—for example, worms, fissure *in ano*, adherent prepuce, etc. This is more especially the case as one may, so to speak, "kill two birds with one stone." That is to say, the operative treatment necessary to cure the local condition, acting strongly on the mind, or by making sleep less profound, frequently breaks the habit of enuresis. And this it may do in spite of the fact that the local condition had nothing whatever to do with the formation of the habit. Other surgical methods, such as blistering the sacrum, blistering the penis, freely cauterizing the urethra, the passing of large metal bougies, and the various ways of using electricity—all act in one or other of these two ways. Equally efficacious and far more rational is it to talk seriously before the patient of the possibility of one or other of these measures having to be adopted if improvement does not immediately occur. This is the class of case which the schoolmaster, much to his satisfaction if the physician has failed, succeeds in curing by corporeal punishment. As, however, he cannot be expected to diagnose as to which of the three classes the case belongs, the odds are against his success, and, as previously pointed out, worse evils than enuresis may result.

Former Treatments.

Of other treatments, one need mention a few which have not been previously dealt with. The success or failure of all others is easily explained if the view herein advocated be adopted.

The limitation of the amount of fluid drunk never gained much reputation—in fact, it rather tends to aggravate than relieve the symptom, by adding to the digestive disturbance.

Belladonna in small doses acts as a tonic to the nervous system, and may, as other tonics, succeed in the first class of cases. When given in semipoisonous doses it acts on the mind, and is then successful by diverting the attention. Professor Fonnsagrives thinks it acts by making sleep less profound, so that control of the sphincter muscles is not lost. This is interesting in connexion with Macalister's opinion that belladonna acts better when combined with strychnine. A. Jacobi says belladonna is only useful when there is vesical catarrh.

Sedatives such as chloral and bromide may succeed for a time by blunting the nervous mechanism of micturition, but they do not touch the cause, and their use is consequently unscientific.

CONCLUSION.

In conclusion I would contend that nocturnal enuresis is capable of the simple explanation here given, that order is by this explanation introduced into the chaos of conflicting views and opinions, that reasons are now obvious for the success or failure of the various methods of treatment formerly in use, and that treatment can now be carried out on rational and scientific lines instead of by the empirical and haphazard methods of the past.

BIBLIOGRAPHY.

Ringer, *Textbook of Therapeutics.* Holmes, *System of Surgery.* Ashby and Wright, *Diseases of Children.* Goodhart. *Diseases of Children.* West, *Diseases of Infancy and Childhood.* Eustace Smith, *Disease in Children.* Whitla, *Dictionary of Treatment.* Sachs, *Nervous Diseases of Children,* Trousseau, *Medicine.* Lauder Brunton, *Therapeutics and Materia Medica.* Strümpell, *Textbook of Medicine.* Owen, *Surgical Diseases of Children. Medical Annual,* 1896. *Year Book of Treatment,* 1889. Crawford, *King's College Hospital Reports,* 1896. Lewis, ibid, 1899.

UPON THE PROPERTIES OF AN ANTITYPHOID SERUM OBTAINED FROM THE GOAT.*

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IN this communication I propose to give a brief account of the results obtained by the immunization of the goat with the cell juices of the *Bacillus typhosus.* The experiments are a continuation of those already published, which had as their main object the production of an antibody for the endotoxin of the typhoid bacillus.[1] The difficulties to be overcome proved numerous, and served to retard the progress of the work. It will be sufficient for the present to say that the goat was found to be a more suitable animal than the horse for arriving at a solution of the theoretical and practical considerations involved. The experiments on the goat having fulfilled their purpose may now be recorded. That purpose was to determine the best method of producing with the material employed an anti-endotoxin, and of increasing to an adequate degree the antitoxic value of the treated animals' serum. It was the latter point that presented the chief difficulty in the initial stages of the investigation. It is, however, one of fundamental importance in the preparation of any serum which it is proposed to test for therapeutic possibilities. I therefore felt justified in devoting considerable time to the experiments on the goat, in order to arrive at a method that would give the desired result.

During the progress of the experiments two papers have been published by Besredka upon an antibody for the typhoid endotoxin and to these I will in the first instance make reference.[2] Besredka gives an account of the immunization of a horse with dead and living cultures of the *B. typhosus.* The intravenous injections of the bacilli extended over a period of two years. The horse's serum was then tested against (1) killed and dried cultures of the typhoid bacillus, of which 0.01 gram killed a guinea-pig on intraperitoneal injection; (2) a soluble endotoxin extracted from the dead and dried bacilli, of which ⅛ c.cm. killed the guinea-pig. The main results were as follows: 10 cg. of the dried horse serum (about 1 c.cm. before drying) neutralized 10 lethal doses of the killed typhoid

* The results of this investigation were communicated on March 8th, 1906, to the Royal Society, with the exception of the subcutaneous experiments, and those upon guinea-pigs, which have since been completed.