cane-sugar (saccharose) required digestion both in animals and plants before it could be utilised in nutrition. The cane-sugar stored up in beet-root and in the sugar-cane is changed by ferment-action into invert sugar before it is permitted to circulate in the sap, and take part in the nutritive operations of the plant. He found also that an analogous transformation was requisite before cane-sugar could be assimilated by animals. He states that, when cane-sugar is injected into the blood, it circulates therein as an inert body, and is in no degree used as nutriment by the tissues, but is eventually entirely removed unchanged with the urine. Cane-sugar is, however, an important article of food, and is consumed by us in large quantities every day; and we know that, when thus consumed, it does not behave like an inert matter, circulating awhile in the blood, and then being eliminated by the kidneys as a waste product. It is evidently absorbed and assimilated, and must, therefore, somewhere or other, be transformed or digested in animals as it is in plants. Reasoning this way, Bernard sought for an inversive ferment for cane-sugar in the alimentary tract; and after searching in the saliva, in the stomach, and in the pancreas in vain, he at length discovered it in the small intestine. In the small intestine, he found that cane-sugar was transformed into invert-sugar, and by a similar ferment with that destined for analogous purposes in yeast, in beet-root, and in the sugar-cane.

The transformation of cane-sugar into invert-sugar is represented by a very simple equation:—

The inversive ferment was detected by Bernard in the small intestine of dogs, rabbits, birds, and frogs. Balbiani found it in the intestine of the silkworm. It was recognised by myself in the small intestine of the pig, the fowl, and the hare. It does not exist in the large intestine.

But although my observations on this subject coincided in the main with those of Bernard, I noted two points which I think merit further attention. The first was, that, while a piece of small intestine infused in water yielded a mixture which was capable of inverting cane-sugar, the same infusion when filtered through paper until it was perfectly clear had no such power. It seemed as if the inversive ferment did not pass freely, if at all, into true solution, but remained attached to some of the formed elements contained in the intestine. The second point which I noted was the extreme slowness of the action. When cane-sugar was added to the unfiltered infusion of intestine, and the mixture maintained at blood-heat, it generally took a couple of hours before a reducing effect with the copper test could be obtained. Both these circumstances reminded one of the action of formed ferments, and I could not help thinking that there was here something which required clearing up at some future time.

TOXIC ACTION OF OXALIC ACID.—Drs. Kobert and Kiessner describe in Virchow's *Archiv*, Band 78, the result of experiments made by them on nearly sixty animals, mostly dogs, cats, and rabbits, and in rare instances porpoises, hamsters, rats, and hedgehogs. They state that the symptoms of poisoning by oxalic acid have in many points a strong resemblance to those of poisoning by fungi, and suggest the possibility of a part of the phenomena of the latter being due to oxalic acid contained in the fungi. The authors thus sum up the results of their researches. Oxalic acid is not a cardiac poison, but its action is in the first place on the nervous system. In this way are explained the lowering of the blood-pressure, the loss of rhythm and the retardation of the pulse, and also the slow breathing. Further indications of the same effect are phenomena of irritation and of depression (the latter predominating) in the motor, sensory, and reflex nerves. These phenomena are most distinctly marked in rapidly acute poisoning, but are by no means wanting in subacute or even in chronic cases. Their mode of onset, and the manner in which the symptoms are combined, are not constant, and therefore not pathognomonic. There are, however, other signs which are typical of poisoning with oxalic acid. These are the changes in the urine during life, and those found in the kidneys after death. These changes are the only characteristic phenomena produced; they are present both in acute and in chronic poisoning, and only gradually disappear. The principal sign—one which has hitherto been quite unrecognised—is the appearance in the urine of a powerful reducing substance, the nature of which cannot as yet be described. The urine also almost always contains albumen; and microscopic examination reveals, besides numerous cylinders and a few blood-corpuscles, crystals of oxalate in very various forms. These crystals are found—and this is the special characteristic phenomenon—in the uriniferous tubules; sometimes only in the convoluted, occasionally also in the straight tubes.

THE CROONIAN LECTURES

SOME POINTS IN THE PATHOLOGY AND TREATMENT OF TYPHOID FEVER.

Delivered before the Royal College of Physicians of London.

By WILLIAM CAYLEY, M.D., F.R.C.P.,

Physician to the Middlesex Hospital and to the London Fever Hospital; Lecturer on Medicine to the Middlesex Hospital Medical College.

LECTURE II.*

WE have next to consider what is the relation which these different processes bear to one another and to the symptoms of the disease. According to the views of many pathologists, the phenomena of typhoid fever are produced in the following manner. The poison is swallowed, and enters the system through the lymph-follicles of the ileum, on which it produces its primary effects; it then passes into the mesenteric glands, where it goes through a stage of latency or incubation, and at last enters the circulation and is deposited in other lymphatic organs and the spleen, and causes a rapid hyperplasia of their cells, and so produces the characteristic local lesions. The poison also acts on the heat-regulating centres, and produces the febrile temperature. The high temperature, in its turn, causes all the other morbid phenomena: the albuminous infiltration and softening of the heart and other organs, the vitreous degeneration of the muscles, the acceleration of the circulation and respiration, the febrile consumption of the body, and especially the disturbances of the nervous system, the delirium and stupor of the typhoid condition. The correctness or not of this view is, I need hardly say, of the utmost importance in the treatment of the disease. It is, therefore, very necessary that we should examine the arguments by which it is supported.

In the first place, it is urged that these phenomena occur in many febrile diseases which have nothing in common but the high temperature. Secondly, it is possible to produce many of them by artificially raising the temperature. Thus, the experiments of Dr. Wickham Legg show that, by raising the temperature of animals to 112° Fahr., albuminous infiltration of the liver and other organs is produced. Max Schultze, by means of his microscopic warming apparatus, directly demonstrated the injurious effects of high temperatures on living cells. We have, too, distinct evidence that raising the temperature of the body increases metabolism. By means of a vapour-bath, it is quite easy to raise the temperature many degrees, as the evaporation from the skin, and so the compensatory dispersion of heat, is prevented. Bärtsels found that sufficiently prolonged vapour-baths raised the temperature, accelerated the pulse and respiration, increased the discharge of urea 16 per cent., and diminished the weight of the body. It is interesting to observe that the discharge of urea was greater in the second twenty-four hours after the bath, when the temperature was again normal, than during the time the temperature was raised. This is analogous to the epicritical discharge of urea which takes place in those fevers which terminate by crisis. In both cases, it is probably due to its partial retention and accumulation during the febrile period, in consequence of the unfavourable conditions for its elimination during this time. Similar results were obtained by Naunyn in experimenting on dogs.

Lastly, in support of this view, may be adduced the effects of treatment. If a patient in the typhoid state—i.e., in a condition of delirium or stupor, with a dry brown tongue, tremulous muscles, greatly accelerated pulse, and other symptoms which are liable to occur in severe fever—be placed in a cold bath and the temperature reduced to below 100°, a remarkable improvement usually takes place in his symptoms: the stupor passes off, the delirium ceases, the tongue becomes moister, the pulse less frequent, and commonly he falls into a quiet sleep; the symptoms recurring in the course of a few hours, when the temperature has again risen to its former height. The effects of a cold bath in cases of hyperpyrexia, as in rheumatic fever, are still more striking, and are well known to all who have employed this mode of treatment. Hence there can be little doubt that the pathological changes and injurious effects of fever are largely due to the high temperature. But, notwithstanding these and other arguments which may

* Concluded from page 507 of last number.

be adduced to show that almost all the phenomena of fever are due to the high temperature, other facts, I think, prove decisively that this view is only in part correct, and that many of them may occur independently.

In the first place, there are strong reasons for believing that the increased metabolism, as shown by increase in the discharge of urea is, in part at least, due to the direct action of the fever-poison, and not solely to the high temperature. Thus, in the artificial septic fever of the lower animals produced by the injection of pyrogenetic substances, it is found that the increased excretion of urea precedes the rise of temperature. Dr. Ringer has shown that this also takes place in intermittent fever, and other observers have proved the same for relapsing fever. In typhoid fever, we are unable to produce similar proofs, as the attack cannot be predicted; but there can be no doubt that the same law holds good in this fever also.

We have next to consider how far the albuminous infiltration and softening of the heart and other organs are solely caused by the temperature. Against this view, it may be urged that these degenerations occur in conditions not attended by fever, as after severe burns, before any febrile reaction has had time to take place; the immediate effect of a burn, as of all stimulations of the sensory nerves, being to depress the temperature. A case has been recorded where death took place six hours after a burn affecting nearly the whole surface of the body, and, on *post mortem* examination, the kidneys and heart were found in an extreme state of granular infiltration. These degenerations have, moreover, been met with in cases of typhoid fever where the temperature has been but little raised; so that, on the whole, we must conclude that they may be in part produced by the direct action of the poison, though it cannot be doubted but that a prolonged high temperature not only greatly conduces to them, but is capable itself of their production. The vitreous degeneration of the striped muscles is probably entirely due to the high temperature.

The next question is, how far the characteristic symptoms of fever are due to the temperature, especially the nerve-symptoms, the restlessness, delirium, and stupor. I think we must answer that these symptoms, especially the delirium and stupor, are not necessarily dependent on the temperature, though they are largely influenced by it. Dr. Murchison regarded them as caused by the accumulation in the blood of the urea and other products of the disintegration of the albuminous tissues. The occurrence of cases of afebrile typhoid shows that they occur independently; and, moreover, we often see very high temperatures, as in relapsing fever, without any marked disturbance of the nervous system. But although it seems clear from these examples that many of the phenomena of fever which are ascribed by Brand and Liebermeister solely to the temperature may occur independently, yet it is quite certain that the high temperature exercises a most injurious influence, inasmuch as it increases the frequency of the pulse and respiration, augments the metabolism of the albumen, and consequently the febrile consumption of the body, adds an additional factor to the albuminous infiltration and softening of the heart, muscles, and glandular organs, and injuriously affects the nervous system, both indirectly by favouring the accumulation in the blood of the products of the disintegration of the tissues, and directly, when it reaches a certain degree, by causing delirium, stupor, and coma.

Another point of great practical importance in the pathology of fever is the effect produced on the digestion. Usually, though not invariably, when the temperature rises above 102° Fahr., the appetite becomes very much impaired, and, when the tongue becomes dry, it is entirely lost; and it has generally been assumed, though on imperfect data, that a state of fever more or less completely stops the secretion of the gastric juice, and so arrests the digestive function. Modern observations, however, show that this is by no means always the case. Dr. Pavy, in this country, and Hoppe-Seyler, in Germany, have proved that an active digestive fluid can be prepared from the stomachs of animals in a state of fever. And Manassëin has shown that, though in dogs affected with septicæmic fever the natural digestive fluid, procured by introducing sponges into the stomach, had a much inferior power to that of healthy animals, nevertheless, if hydrochloric acid were added, then the digestive power was equal to that in health. Hence it is probable that the impaired digestion in fever is rather due to a diminished secretion of acid than of pepsine; and this perhaps explains the beneficial effects often seen to attend the administration of hydrochloric acid. The disinclination, and even complete inability, to take food, are doubtless largely due to the partial or complete arrest of the secretion of the saliva, and the dryness of the mouth; and these symptoms, perhaps more than any others, are dependent on the temperature. No doubt in fever the stomach frequently rejects food, but the vomited matters are often a decisive proof that the gastric juice is still being secreted. How active the digestive power may be in typhoid, is shown

by a case where Dr. Huebner fed a patient through a severe attack on beef-steaks, without any injurious consequences. On the whole, I think we need not be deterred from giving fever-patients sufficient food, with proper precautions, from fear that it is incapable of being assimilated. But although in fever the gastric juice may be formed in sufficient quantity, there are strong reasons for believing that the secretion of the saliva and pancreatic fluid is greatly impaired; hence starchy foods are not digested so well as albuminous foods; and I am of opinion that any considerable quantity of starch, given in the form of arrow-root, cornflour, and sago, is injurious, and tends to cause intestinal irritation.

I now propose to consider some of the phenomena peculiar to typhoid, among the most important of which are the type and duration of the fever.

The latter appears at first sight to be extremely irregular, and to differ remarkably from the much more regular course of the other zymotic diseases. The causes of this irregularity are, in the main, two. First, we have, in an ordinary attack of typhoid, two distinct fevers—a primary, due to the infection of the system by the typhoid poison; and a secondary, caused by gangrene and ulceration of the intestine, and consequent septicæmia. The first of these two processes has, I believe, as definite a course as the other zymotic fevers; the second, or septicæmic fever, is much more irregular. The second cause is the frequency of relapses.

The fact that we have, in typhoid, two forms of fever to deal with, is of considerable importance, both in the pathology and treatment of the disease, and it is one which, I think, is sometimes neglected. Many other fevers, of course, present an exact analogy in this respect to typhoid; thus, in small-pox, we have a primary fever caused by the direct action of the small-pox poison, lasting usually about three days, then a period of remission, which is followed by a septicæmic fever due to suppuration. In scarlatina, we have in uncomplicated cases a primary fever, lasting five or six days; but where there is ulceration of the fauces or implication of the glands, a septicæmic fever of indefinite duration, which usually comes on before the primary fever has subsided, but sometimes after a period of remission. In typhus, there is usually no secondary fever, and the primary fever subsides by crisis about the fourteenth day. Now, typhoid resembles typhus in the long duration of the primary fever, and scarlatina in the fact that the secondary or septicæmic fever supervenes before the subsidence of the primary, the two processes overlapping, so that there is no intervening remission. The change, however, shows itself by an alteration in the type of the fever, which, from being continuous in character with only slight diurnal fluctuations, becomes remittent with marked diurnal variations. This is at once seen on the temperature chart of a case of typhoid, where the fever has been allowed to run its course unchecked. This change in the type of the fever usually takes place during the third week, sometimes even as early as the fourteenth day. Generally, it is a gradual change, but not unfrequently it takes place very suddenly, and at the same time there is a perturbation of temperature—often an evening rise exceeding that of the previous days, and followed by a considerable morning fall. This resembles the critical perturbations of those fevers which terminate by crisis, and probably indicates a kind of crisis of the primary fever. Not unfrequently profuse perspirations now appear, and an eruption of sudamina; while, in the majority of cases, the roseola of typhoid ceases to appear after the middle of the third week. The phenomena of the disease are now made up of three factors; first, the local lesions; secondly, the septicæmia; thirdly, the high temperature. Sometimes one of these predominates, sometimes another.

The great resemblance which other forms of internal gangrene may bear to the later stages of typhoid fever was strongly impressed upon me by a case of gangrene of the lung, which was under my care in the Middlesex Hospital in 1876. The patient was delirious, very prostrate, with a dry tongue, diarrhoea, great enlargement of the spleen, a temperature varying from 105° to 101°, sordes on the teeth, and well marked *tache*. There were the physical signs of capillary bronchitis of both lungs posteriorly, with patches of bronchial breathing. These signs were attributed to hypostatic congestion and lobular pneumonia. In this case, all the signs of typhoid fever except the roseola were well marked, and for some days the diagnosis from this disease could not be made. The case was ultimately regarded as one of acute tuberculosis. After death, several circumscribed patches of gangrene were found in both lungs, evidently caused by embolisms blocking branches of the pulmonary artery, these embolisms being derived from thrombi of the prostatic veins. The ordinary signs of pulmonary gangrene—fœtor of the breath and expectoration—were absent throughout the whole course of the disease.

This question has some bearing upon treatment. First, with

regard to the use of alcoholic stimulants during the first stage of the disease, when the patient is suffering from the effects of the specific typhoid poison, some difference of opinion prevails as to the advantage of stimulants. Some authorities are of opinion that alcoholic stimulants in all severe febrile diseases have a beneficial effect, by serving as a kind of food, and diminishing the febrile consumption of the tissues, and so tending to counteract the degeneration and consequent failure of the heart and central nervous system. Others, again, disbelieve in these effects, and only administer alcohol as a true stimulant when the heart actually begins to fail. But, in the later stages of the disease, when we have to deal with a septicæmia due to gangrene and ulceration, if we follow the established principles of surgery, we can have no doubt as to the utility of alcohol. I believe all surgeons, without exception, treat external gangrene, accompanied by symptoms of septicæmia and depression, by free stimulation; and the fact that the gangrene is internal, instead of external, cannot make any difference in the treatment.

So, too, with regard to the use of certain drugs, especially opium. Some physicians regard opium as contraindicated, on the ground that it produces constipation, and so tends to retain the decomposing fæces in the intestinal canal. Others, on the contrary, regard it as beneficial by checking the peristaltic movements, and so favouring the healing of the ulcers, and diminishing the risk of perforation. But, apart from its local action on the intestinal canal, it is evident that, according to the principles of surgery, its use in the second stage of typhoid fever is often indicated. External gangrene and phagedæna are unquestionably benefited by opium, which renders the system more tolerant of their injurious effects; and there can be no reason for treating internal gangrene on different principles.

The duration of the primary fever due to the direct action of the typhoid poison is probably between two and three weeks, occasionally about fourteen days, *i. e.*, the same length as typhus, but most commonly a few days longer. This is shown by the perturbations of temperature not unfrequently occurring at this time, and by the change of type of the fever from a continuous to a remittent form. Moreover, not unfrequently we see cases of what are known as abortive typhoid, in which the early stages of the fever are severe, the temperature very high, the onset sudden, and the febrile condition strongly marked; then, about the fourteenth day, defervescence rapidly takes place. The explanation of these cases is, no doubt, that, though the poison has powerfully acted on the general system, for some reason or another—possibly some idiosyncrasy on the part of the patient—the local intestinal lesions have been slight, the infiltration of the glands only moderate, and the deposit has become absorbed instead of sloughing. These cases are exactly analogous to a very common form of modified small-pox, in which we have the primary fever due to the effect of the small-pox poison on the system of great severity; but, in consequence of the slight local affection of the skin, the secondary or suppurative fever is absent.

In typhoid, as in small-pox, the intensity of the primary fever is not always a certain indication of the amount of the local mischief and consequent severity of the secondary fever; and, as in these abortive cases, the former may be severe and the latter slight, though usually a severe primary fever is accompanied by extensive infiltration and subsequent sloughing of the intestinal glands. The converse condition is much more common, in which we have a slight primary fever and mild constitutional symptoms early in the disease, with very severe intestinal lesions and consequent gravity of the later stages. Hence the well-known difficulty of forming a correct prognosis in the early stages of the disease, and the importance of treating the milder cases with the same precautions as the severe ones.

There can, I think, be little doubt that cases of typhoid which are from time to time described as having been cut short by special remedies—as by emetics or calomel—are really of this character, the observer ascribing to the remedy what is, in fact, one of the natural phenomena of the disease.

Another point of interest in the history of typhoid fever is the mode in which defervescence takes place. In most of the zymotic fevers, defervescence takes place either by crisis or a very rapid lysis. Thus, typhus, relapsing fever, uncomplicated measles, the primary fever of small-pox, usually terminate by crisis; scarlatina, when uncomplicated, usually by a rapid lysis. Crisis, therefore, or rapid lysis, would seem to be the natural mode in which zymotic fevers terminate. Typhoid presents an apparent exception to this rule. But here, too, I think we have indications that the primary fever tends to terminate in the same way; and the usual prolonged lysis is a phenomenon of the secondary or septicæmic fever. This is indicated by the perturbation of temperature often present about the middle of the third week, and the rapid defervescence of the abortive cases.

The second cause of the variable duration of typhoid fever is the

frequent occurrence of relapses. Now, relapses in typhoid take place much oftener than is usually supposed. They may occur at any time to as late as three or four weeks after complete defervescence, the longest apyretic interval being, I believe, thirty-one days. Most commonly, it varies from one or two to fourteen or fifteen days. The frequency with which these relapses occur after an apyretic interval has been very variously estimated. At the London Fever Hospital, during a period of seven years, they occurred in about 3 per cent. of the cases; in the hospital at Basle, 8.6 per cent. Other authorities give numbers varying from 1.4 to 11 per cent. This great difference depends, perhaps, in part on a different estimation of what constitutes a relapse; but there can, I think, be no doubt but that the frequency of relapses is much influenced by treatment. If the fever be allowed to run its course unchecked, relapses are much less frequent than when the temperature is systematically kept down by cold baths and antipyretic medicines. Thus, at Basle, under the expectant treatment, about 8.6 per cent. of the cases relapsed. Since the introduction of the treatment by cold bathing, this proportion has been nearly doubled. About 10 per cent. of the cases treated by me in the same manner have relapsed.

It is of course necessary to distinguish between a true and a false relapse. In typhoid fever, long after defervescence has taken place, the temperature remains labile, and the vasomotor system very unstable, as shown by the continuance of the *tache*. I have long looked on the persistence of this latter phenomenon as a valuable guide, and as indicating that the intestinal ulcers have not yet healed, and that therefore the patient is still liable to the sequelæ of the disease. As long as the patient continues in this condition of labile temperature and instability of the vasomotor system, very slight causes, as errors of diet—nay, the mere resumption of solid food—mental emotions, slight exertion, will send up the temperature; so any extension of the local mischief will cause a fresh febrile paroxysm. These cases must be distinguished from true relapses, where there are a fresh infection of the blood with the typhoid poison, fresh deposit in the glands, and commonly a fresh eruption of the roseola.

But besides these relapses which take place after a distinct apyretic interval, and about which there can be no question, it is very common for the relapse to take place much earlier, during the secondary or septicæmic fever. These early relapses are often called recrudescences, to distinguish them from the later ones; but there can, I think, be no doubt that they are of exactly the same nature. They are indicated by an exacerbation of the fever, and usually by the appearance of a fresh crop of rose spots, which commonly cease to come out after the middle of the third week. It is well known that the later relapses may be repeated twice, or even thrice; and the same thing also occurs with the earlier ones or recrudescences. Hence we may have an attack of typhoid of an indefinite duration without any distinct remission.

The most prolonged case which has come under my own notice was one in which the temperature was maintained at febrile heights, without any distinct intermission, for nearly eighty days. The patient was a gentleman of middle age, who had a very severe attack with prolonged delirium and great prostration, and in the third week pretty free intestinal hæmorrhage; he then had pneumonia of the right base, which did not clear up for several weeks; then there was a distinct relapse, with a recurrence of the hæmorrhage. This was succeeded by thrombosis of the veins of the lower extremities, on which some serious cardiac lesion supervened, the nature of which was not quite clear, but which I attributed to thrombosis of the right cavities. This caused alarming dyspnoea and a tendency to syncope, and was followed by general dropsy, which lasted many months, but the temperature became normal about the eightieth day, and did not again rise. This patient ultimately recovered, but he could not be considered as convalescent for nearly twelve months; and when I saw him two years later, there were still some indications of obstruction to the return of blood from the head and upper extremities.

We may then, I think, regard those cases in which the fever lasts for many weeks without intermission as due to early relapse or recrudescence.

We have now to consider the pathology and causation of these relapses. There can, I think, be little doubt that in relapse there is a fresh infection of the blood by the typhoid poison; and the opinion has been entertained that this takes place from without, either from emanations from other cases in hospital practice, or from the patient's own dejections, where cleanliness is neglected or the sanitary conditions are defective. Relapses, however, not unfrequently occur among isolated cases, and where every sanitary precaution has been strictly observed. Hence there can be little doubt that the reinfection is usually an internal one, though an external affection is of course quite conceivable.

The opinion is widely prevalent that relapses may be caused by errors of diet, and doubtless they often follow such errors; but I believe this

to be an accidental coincidence. In the first place, relapses or recrudescences are very common before the fever has subsided and the appetite returned; secondly, they occur later in cases where it is quite certain that the proper regimen has been strictly observed; lastly, errors of diet during convalescence from typhoid are, I believe, the rule, and not the exception—certainly this is the case among the uneducated classes, who are seldom willing to put any restraint upon their appetites. Even in hospital practice, where care is taken to exclude improper articles of food, every one must be aware how often this regulation is evaded, and all kinds of indigestible viands are smuggled in. When the poor are treated at their own homes, as a rule, directly the appetite returns they begin to gratify it with whatever most takes their fancy; yet it is very doubtful whether relapses are more frequent under these circumstances.

Some time ago, I had under my care, in the Middlesex Hospital, a boy about fourteen years of age, who passed through a very severe attack of typhoid, and whose appetite returned before the temperature became normal. He continued, of course, to be restricted to liquid food. He complained to his mother, who remonstrated with me. I endeavoured to explain to her the danger of beginning solid food too soon. She replied that she would rather see her boy die of fever than of starvation. She accordingly took him home, stuffed him with solid food, and he recovered rapidly—much sooner, I have no doubt, than if he had remained in the hospital on a restricted diet.

In fact, this error of diet, *i.e.*, the early resumption of solid food, is in most cases beneficial. After an attack of typhoid, a large amount of tissue has to be built up. The return of the appetite shows that the digestive and assimilating powers are again active; and, the more food the patient eats, the sooner will this be effected. Hence, by continuing to restrict the diet, we retard convalescence. We are, of course, unable to act upon this view; as we know that, in a certain number of cases, the intestinal ulcers are in such a state that the passage over them of any irritating particles might easily produce an extension of the ulceration, and so cause perforation; and, as we have no certain means of distinguishing between those cases where the ulcers are granulating and not likely to be injuriously affected by solid food, and those where they are in an irritable or an atonic state, we are compelled to restrict the diet of all cases for a time, the evil of somewhat retarding convalescence being of trifling importance when compared with the risk of causing perforation. I believe, then, that errors of diet, though they may cause a spurious relapse by increasing the local mischief, are incapable of re-infecting the blood with the typhoid poison, and so producing a true relapse.

Assuming the causes of the relapse to be the reinfection of the blood by a fresh absorption of the typhoid poison, there is every reason to believe that this takes place from the mesenteric glands and the glands of the ileum, in which there can be little doubt but that the poison is deposited. This reabsorption probably takes place in all cases; but generally the system is protected by having just gone through an attack. In some cases, however, it is probable that the zymotic process has not been complete, and then a relapse takes place; and it is remarkable that, when the fever is prevented from running its usual course by persistently reducing the temperature, the frequency of relapses is nearly doubled.

In scarlatina we have an exact parallel to the relapses of typhoid, though they occur much less frequently. During the past year, four cases of relapse in scarlatina occurred in the London Fever Hospital, at varying times, from five or six days to a fortnight, from the commencement of the primary attack, sometimes after an apyretic interval, sometimes before defervescence had taken place; and, as occasionally takes place in typhoid, the second rash has been more intense than the primary. As in typhoid, it is of course necessary to distinguish these true relapses with a recurrence of the eruption from the very frequent spurious relapses due to absorption of septic poisons from the throat or glands. In scarlatina, as in typhoid, there is very commonly infiltration of the lymphatic glands; and in all probability the relapse here also is due to reabsorption of the poison contained in them.

Syphilis also presents a close analogy. Here also we have reason to believe that the poison remains deposited in the lymphatic glands, and relapses are due to reabsorption from these; the great difference from the acute infectious fevers consisting in the fact that in syphilis the glands remain chronically enlarged, and hence relapses may occur after long intervals; whereas in typhoid and scarlatina the process runs a rapid course, and after the lapse of a few weeks the glands return to their normal condition, and the poison is entirely eliminated from the system. In those fevers, as typhus, where there is no affection of the glands, relapses are hardly ever met with.

Dr. R. S. HUDSON of Redruth has been admitted, after examination, a Fellow of the Royal College of Surgeons of Ireland.

THE GULSTONIAN LECTURES ON EPILEPSY.

Delivered before the Royal College of Physicians of London.

By W. R. GOWERS, M.D., F.R.C.P.,

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LECTURE III.*

THE treatment of epilepsy is a subject on which numerical analysis gives little help. A large number of cases are under observation too short a time to enable the effect of remedies to be fairly estimated; and, of the cases in which benefit is derived, we have no means of ascertaining how many relapse when treatment is discontinued. My notes of the result of treatment in this series of cases extend to 562 cases only. In the remainder, either the period of observation was too short for a just conclusion to be drawn, or, in the press of out-patient work, the influence of remedies was not noted with sufficient precision. The effect of treatment is more likely to be recorded when it is distinct and considerable, than when it is slight. Hence the following figures have no relative value. Of the 562 cases, the attacks ceased while the treatment was maintained in 241; doubtless many of these relapsed when treatment was discontinued, but in a few I have been able to ascertain that the patients remained free from fits even for years after they ceased to take medicine. In 266 cases, improvement short of arrest was obtained; the fits being reduced in many to $\frac{1}{2}$, $\frac{1}{4}$, $\frac{1}{8}$, and even $\frac{1}{16}$ of their former frequency. In 55 cases, little improvement was obtained by any method of treatment.

Time forbids me to enter at any length on the details of treatment, and I can do little more than mention the remedies which in this series of cases were of most distinct service. The subject of possible modes of action it is better to leave almost untouched. It may be doubted whether a rational therapeutics of epilepsy is yet possible. At any rate, up to the present time, remedies used empirically have been of most service.

Although the results show that we must not only rely exclusively upon bromides in our treatment of epilepsy, they show also, as might be expected, that on these our chief trust must still be placed. Of the arrests of fits, 66 per cent., and of the improvements short of arrest, 62 per cent., were due to bromides given alone. Of the three alkaline salts of bromine, that of potassium deserves, I think, as it has popularly received, the first place. I have made a careful comparison between the salts of sodium and of potassium in a series of about fifty cases, substituting the one for the other. In a few cases, the sodic salt appeared to do better; in the great majority, it was distinctly less useful. Bromide of ammonium possesses slightly more power than bromide of potassium; but this is not greater than the larger quantity of bromine which it contains will account for.

The period after its administration at which the maximum effect of a dose of a bromide is obtained varies, I believe, with the dose. The larger the dose, the longer is the maximum effect deferred; the smaller the dose, the sooner does it occur, and the sooner is its action over. When small doses are employed in cases in which attacks occur at regular times, they should not therefore be given more than two or three hours before the attack is expected. This is contrary to some opinions which have been expressed; but I have several times known attacks arrested, when a dose was given about two or three hours before the fit was expected, which were not arrested when the same dose was given twelve hours earlier.

The effect of bromide upon fits appears to be for a time cumulative, just as is, indeed, its action in causing bromism. Attacks may continue under its administration for a time, and yet ultimately cease without any increase in the dose. On the other hand, still later, tolerance or rather indifference may be established, and attacks which have been for a time arrested may ultimately recur.

Drugs which increase reflex action, such as strychnia, are now believed to do so by lessening the resistance in the nerve-centres involved. Bromide diminishes reflex action, antagonises strychnia, and it is probable that it does so by increasing the resistance in the centres. If the view above expressed be correct, that the morbid state in epilepsy is essentially an instability of the resistance in the cells, it is also

* Concluded from page 504 of last number.