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 III.

IN estimating the value of any particular mode of treatment, we base our judgment on two classes of facts. First, by the observation of individual cases, we see whether it appears to relieve the symptoms and exercise a favourable influence on the course of the disease. Secondly, we apply the test of statistics, and, by collecting a great number of instances, we ascertain the effect on the general rate of mortality. Now, both these methods are open to many fallacies. In the first place, if the observer be not familiar with the natural course of the disease, and the various deviations which are liable to occur, he is apt to ascribe to his remedies what is really the unaided effect of nature; secondly, he may confound temporary amelioration with permanent benefit, and may thus incur the danger of relieving urgent symptoms at the expense of diminishing the chances of ultimate recovery.

Both these mistakes have frequently been committed in the treatment of typhoid fever. Thus the early recovery of the abortive forms has repeatedly been ascribed to the effects of remedies, as calomel or emetics. Again, the great relief which bleeding often gives to the urgent symptoms of this, as of other acute febrile diseases, has in former times caused it to be extensively practised, with the effect of greatly increasing the mortality.

The second method is still more open to fallacy, so that it is often said in opprobrium that anything may be proved by statistics. But, nevertheless, they form the final test by which all modes of treatment must at last be decided. The fallacies of statistics depend on two main errors—first, an insufficient collection of facts; secondly, the comparing together of unlike instances. We must, therefore, in applying this test, take care to compare together only like instances, and, if possible, accumulate such an overwhelming number as ultimately to reduce all sources of error to the vanishing point.

Before, then, we are in a position to estimate the value of any particular mode of treating typhoid fever, we must be acquainted, not only with the natural course of the disease, but also with the usual rate of mortality, which of late years has, I think, been but little affected by treatment apart from nursing and feeding—the treatment generally practised being what may be termed the expectant, or, as some would prefer to term it, the rational method. This consists in not treating the disease at all. We begin by confessing that we are quite unable to arrest its progress or materially to modify its course, and all we aim at is to put the patient in the most favourable condition to support its effects. We see that he is carefully nursed and properly fed, that all injurious influences are as far as possible removed, and urgent symptoms are combated as they may arise. Thus, if there be severe diarrhoea, we probably give him astringents; if hæmorrhage, styptics; if he cannot sleep, we administer narcotics; if there be delirium, calmatives; and when his strength begins to fail, stimulants; if there be congestion of the lungs, we perhaps venture on a mustard poultice or a turpentine stupor; or if there be severe headache, an ice-cap. But we leave the fever itself to run its course unchecked.

We have now to consider what are the results obtained by this mode of treatment. The most trustworthy statistics are those afforded by hospitals, but in them the rate of mortality is no doubt higher than in private practice. This is partly owing to the previous condition of the patients, partly to the fact that the more severe cases seek admission into hospitals, and partly because they commonly do not come under treatment till late in the disease; and nothing so much increases the mortality of typhoid fever as delay in the commencement of treatment.

If we take the results afforded by the London Fever Hospital, we may divide them into two periods—1. A period of twenty-one years, during which the hospital received all the pauper patients of the metropolis; 2. A period of nine years, during which the pauper cases have

been excluded, and the patients have consisted of artisans, domestic servants, policemen, *employés* in shops and houses of business, together with persons in a higher position, who have occupied private rooms. During the first period, 8,000 cases were admitted, and 1,519 died, giving a mortality of 18.9 per cent. During the second period, 590 cases have been admitted, and 80 died, giving a mortality of 15.9 per cent. These figures include a considerable number of cases which were admitted moribund, and died within twenty-four or forty-eight hours.

The Pauper Hospital at Homerton: cases, 1,509; deaths, 255; rate of mortality, 16.8 per cent.

The Stockwell Pauper Hospital: cases, 1,223; deaths, 301; rate, 22.6 per cent.

The principal general hospitals of London, taking the last ten or twelve years, give the following results. St. George's, cases, 387; deaths, 76; rate of mortality, 19.6. Guy's: cases, 295; deaths, 57; rate, 19.3. University College: cases, 163; deaths, 29; rate, 17.7. St. Bartholomew's: cases, 635; deaths, 104; rate, 16.3. St. Thomas's: cases, 445; deaths, 70; rate, 15.7. Middlesex: cases, 461; deaths, 72; rate, 15.6. King's College: cases, 318; deaths, 39; rate, 12.2. Total for the hospitals of London: cases, 14,125; deaths, 2,522; rate, 17.8 per cent. These figures no doubt include a considerable number of cases treated specifically.

If we take foreign statistics, we find that, in France, Jaccoud, with a collection of 60,000 cases, gives a mortality of about 20 per cent. The General Hospital of Vienna, with 17,000 cases, has a mortality of 22.5 per cent. The Hospital at Basle, with 1,718 cases, a mortality of 27.3; and generally, in the principal continental hospitals, a rate of mortality varying from 16 to 25 per cent.

The English Army gives the following results for a period of six years ending 1877: On home service, cases 545, deaths 131; rate of mortality 24 per cent.: On foreign service, cases 1,383, deaths 564; rate 40.7 per cent. The foreign returns are not, however, complete. In the Royal Navy, during a period of six years ending 1878, cases 414, deaths 110; rate 26.5 per cent.

Such, then, are the results of the expectant treatment of typhoid fever, with which, I think, we have little reason to be satisfied.

It does not fall within the scope of these lectures to give a description of the various methods which have been from time to time introduced for the specific treatment of typhoid fever; they have most of them again, sooner or later, fallen into disuse, till at last a complete scepticism on the effects of treatment in this disease has been proclaimed by many of the highest authorities. Thus, Skoda says it makes no difference whether we do or do not administer remedies; and the same opinion has been expressed by many others. Of late years, however, a plan of treatment has been revived, which aims at controlling the fever and preventing its injurious effects on the organism, by keeping the temperature throughout the whole course of the disease under a moderate febrile heat.

Typhoid fever can hardly be looked upon as a malignant disease; upwards of 80 per cent. of the cases, if properly nursed and fed, will recover; and those who die are rarely struck down at once, overwhelmed by the virulence of the poison, but usually succumb after a protracted struggle. Hence it seems only reasonable to suppose that, if we can succeed in striking out one of the factors adverse to the patient, even if it be not the most important, this will generally suffice. So evenly is the balance poised in most cases between life and death, that the removal of the smallest weight from the opposite scale will give the preponderance to the side of recovery.

Now, the factor in typhoid fever which is most under our control is the febrile heat: it lies in our power to prevent the temperature throughout the whole course of the disease from rising above a very moderate height; and hence we may obviate those injurious effects which are directly or indirectly caused by the febrile state as such. The great acceleration of the pulse and breathing, the febrile oppression and malaise, the dry brown tongue, the thirst, the headache, the delirium, the stupor—may all be controlled. Nay, not only can we prevent the accession of these symptoms, but sometimes we can remove them after they have supervened. And, as a result, the granular degeneration and softening of the various organs and tissues, and the febrile consumption itself, may be in part checked.

Therefore, from Hippocrates downwards, to reduce the temperature has at all times been regarded as one of the most important indications of the treatment of fever. It would seem, then, that all we have to consider is how far we are able to effect this, and whether the means which we employ are in themselves devoid of danger; and I think a sufficient amount of evidence has been now accumulated to answer both these questions. With regard to the first, it can be experimentally shown that, by the repeated application of cold to the surface of the

body—chiefly by means of cold water on the one hand, and on the other by the administration of certain drugs which have the property of reducing temperature, the most important being quinine, salicylate of soda, and digitalis—the febrile heat can almost always be controlled. Such being the case, the second and more important question arises: Is it always, or even generally, a safe and expedient proceeding? We must accordingly apply to it the two tests I have mentioned above—first, whether it seems to relieve the symptoms and exercise a favourable influence on the course of the disease; and, secondly, whether it diminishes the general rate of mortality.

The history of the introduction of what is now called the antipyretic treatment of fever is a very interesting and instructive one. The first person who treated febrile disease by systematically reducing the temperature by cold affusions was the celebrated Dr. James Currie; and he seems to have been induced to try this method by the account published by Dr. Wright of an outbreak of typhus on board-ship. Dr. Wright himself caught the disease, and, finding that the cold air of the deck relieved the febrile oppression, caused himself to be treated by cold affusions, and with such good results that he applied the same method to a passenger at his own request.

Dr. Currie, as is well known, systematically treated by cold affusions, and sometimes by cold baths, a great variety of febrile diseases, especially typhus, typhoid, and scarlatina, making careful thermometric observations; and he laid down rules by which we may still guide ourselves. It is interesting to see how soon he discovered that although, when applied late in the disease, this method would occasionally rescue the patient from a condition apparently desperate, nevertheless, to ensure success, it was absolutely necessary to have recourse to it at the very onset, before the fever had, as it were, got the upper hand. Although he does not expressly remark the lability of the temperature in fever, he was nevertheless quite aware how easily it may be raised or depressed by external agencies; and he describes a striking instance of a case of typhus where he caused a patient, who in his delirium had thrown off all his bedclothes, to be stripped to his shirt and exposed, in a state of nudity, to a current of cold air from an open window. The effect was to reduce his temperature from 104° to 101° , to calm the delirium, and to throw him into a quiet sleep.

Dr. Currie soon had numerous followers, both in this country and on the Continent. Thus Dr. Gregory applied it with great success in small-pox; Desgenettes, in Egypt, during an epidemic of plague, having witnessed the unexpected recovery of a patient who, in his delirium, threw himself into the Nile, was led to apply the cold bathing treatment with great success in this disease. Giannini, in 1805, became an ardent advocate of Currie's method. In 1813, after the retreat from Russia, a fearful epidemic of fever broke out among the troops and spread among the civil populations. At Berlin, it raged almost with the virulence of the plague; and, in the hope of doing something to check its ravages, Dr. Horn, the Director of the Charité Hospital, determined to follow the plan of treatment recommended by Currie. The results were most satisfactory, and fully confirmed Dr. Currie's experience. Since this time, the treatment, though very imperfectly applied, has never quite died out in the Charité at Berlin.

In 1821, the celebrated Priessnitz of Graefenberg founded what is commonly known as the cold-water cure. He was a man who had all the qualifications necessary for a successful empiric. He was entirely ignorant of science and medicine, of great common sense, self-confident, and a firm believer in his own system. In consequence, he soon became the fashion, and all the celebrities of Germany crowded to Graefenberg to be cured of all manner of diseases. Now, there can be no doubt that Priessnitz met with the most remarkable success in the treatment of acute febrile diseases, especially pneumonia. His plan was to immerse the patients in a shallow bath, and keep them in it sometimes for several hours; the effect being, of course, to subdue the febrile heat, and so relieve the most urgent symptoms. When we remember that the orthodox mode of treating pneumonia at this time was free bleeding, tartar emetic, and calomel, we must confess that the empiric was far in advance of his time.

Chomel practised the treatment in typhoid fever; Graves and Trousseau in scarlatina.

In 1850, Dr. Armitage, a member of this College, after visiting Graefenberg, with the consent of Professor Schoenlein and in conjunction with Dr. Traube, treated a large number of cases of acute disease, especially typhoid fever, in the Charité Hospital at Berlin, again with the most remarkable success; and, on his return to England, he published the results in a small work called *Hydropathy in Acute Disease*. It is impossible to read this book without at once seeing the great advantages of this method. Nevertheless, it failed to obtain the recognition of the profession, and the treatment of Currie may be said to have died out in the land of its birth. The reasons for this are not far

to seek. In the first place, it conflicted with popular and professional prejudices; and, in the second, it is somewhat difficult to carry out.

Now, when facts conflict with prevailing theories, they are pretty sure to be ignored; and the prejudice that patients with fever are injuriously affected by cold is perhaps more deeply ingrained in human nature than almost any other. This theory or prejudice is by no means confined to the vulgar; it is largely shared—often, no doubt, unconsciously—by the profession. I expect most practitioners would be horrified at the idea of exposing a patient, prostrate and delirious from typhus, to a cold draught from an open window, in a state of nudity; and yet by this means Dr. Currie at once relieved the threatening symptoms, and the patient made a good recovery. Usually, when we are called to a case of fever, we find the patient warm in bed, covered by several blankets; a good fire in the room; all draughts carefully excluded, and everybody anxious lest he should catch cold. I have seen a case of typhoid where the temperature was 105° , and there were five blankets on the bed. Now, in health, it makes little or no difference to the internal temperature of the body whether there are five blankets or none; but in the labile temperature of typhoid fever it not unfrequently means a difference of 2° .

The revival of the antipyretic treatment must be ascribed to Dr. Brand of Stettin, whose method, variously modified, has now been adopted by most of the leading physicians in Germany, Austria, and Switzerland; and the number of cases thus treated is now so large that the results may be fairly estimated. Dr. Brand, in the last edition of his work, has collected upwards of eight thousand. From Germany, the treatment was introduced into France in a remarkable manner. Among the French prisoners in the late war who were confined at Stettin was Dr. Glénard, a clinical assistant at Lyons. An epidemic of typhoid broke out among the prisoners (twenty-three thousand in number), and ninety-three French soldiers were attacked. They were all treated by Dr. Brand according to his method, Dr. Glénard (certainly no partial witness) assisting, and they all recovered. Considering the very high rate of mortality of typhoid fever in times of war amongst troops depressed by hardships and dispirited by defeat and imprisonment, such a result naturally filled Dr. Glénard with enthusiasm; and on his return to Lyons, he introduced this mode of treatment into the Lyons Hospital, again with the effect of greatly reducing the rate of mortality; and it has since been extensively tried by many of the leading French physicians.

In England, since Dr. Wilson Fox published instances of hyperpyrexia treated by the cold bath, its utility in this affection has been generally acknowledged; but the systematic treatment of fever from its commencement in this manner seems at present only to have been tried tentatively in this country. Where it has been so tried, the results have been most satisfactory. I may refer to the series of cases reported by Dr. Ord in the *St. Thomas's Hospital Reports*. Though the treatment, according to Dr. Brand's view, was only partially carried out, the mortality was decidedly diminished.

Dr. Edes of Boston introduced the treatment into America, and he also speaks most highly of it.

Such, then, is a short and imperfect sketch of the history of this method of treatment. I now propose briefly to describe the manner of applying it, and the results obtained by it.

The principle underlying the treatment is to keep the temperature throughout the whole course of the disease, from its very commencement to its termination, under a moderate fever-heat; and the means employed to effect this are, in the main, abstraction of heat by the application of cold water, supplemented by the use of the drugs I have mentioned, though Dr. Brand is of opinion that, the more we confine ourselves to the former and the less we use the latter, the more favourable are the results obtained.

The modes of applying cold water are the cold bath, cold affusion, cold packing, cold compresses, and the graduated bath, which consists in placing the patient in a warm bath and gradually cooling it down. Each of these methods is adapted to special cases, but for general use the cold bath is by far the best and the least troublesome to apply, and the rule for its use is this: whenever the patient's temperature exceeds 102.2° , he should be put into a bath. It must be remembered that Dr. Brand always takes the temperature in the rectum. If we measure in the axilla, a somewhat lower height must be taken. He insists very strongly on the great advantages of rectum over axillary measurements, and there can be no doubt but that he is right; but I am so convinced of the impossibility of taking rectum temperatures six or eight times a-day in this country, even in hospital practice, that, except under special circumstances, I never attempt to do so. Next, with regard to the temperature of the bath; this must be regulated according to the patient's condition and the effect we wish to produce. As a rule, it should not exceed 70° Fahr., and may often be advantageously much

lower; 65° to 70° may be taken as the average limits. The duration of the bath must also be regulated by the patient's condition and the effect it produces. We ought to cause a reduction of at least two or three degrees, and if this be not obtained, the next bath must be colder or longer. It must be remembered that the temperature usually continues to fall for some time after removal from the bath; it is therefore not necessary to take the temperature in the bath itself, but it should be done about half-an-hour after. The bath should be prolonged for some little time after distinct shivering has begun, watching, of course, the effect on the circulation. Usually the bath will be well borne for from ten to twenty minutes. The patient should then be put to bed, wiped dry, and covered with a blanket. In many cases, it is advisable to give some brandy or other stimulant before or during the bath.

In severe cases, the cooling effect of the bath often only lasts about three hours; therefore the temperature should be taken every three hours by day and night, and whenever the temperature rises to 102° , the bath should be repeated. The number of baths required will vary with the severity of the case. The rapidity with which the temperature rises after the bath is one of the best indications which we possess of the impression which the fever has produced on the nervous system. It would be a great mistake to suppose that the only or even the principal effect of the bath is to abstract a certain amount of heat from the body. It exercises a most powerful influence on the central nervous system, especially on the vaso-motor centres, and stimulates them to a resumption of their heat-regulating functions. This is shown by a well known experiment. Heidenhain found that stimulation of the sciatic nerve of a dog under curare caused a fall of nearly 2° Fahr. in the temperature of the internal organs, but that this fall did not take place if the animal were febrile; if, however, when in this state it were first cooled by being placed in a cold bath, the usual fall took place.

When, as is not very unfrequent, we meet with cases of typhoid in which there are stupor and great nervous depression, subsultus tendinum, and meteorismus, with only a moderate elevation of the temperature, the stimulating effect of the bath on the nerve-centres is of more importance than its refrigerating effect; and in such cases a cold bath of short duration, or cold affusion, is indicated. In other cases, a more prolonged bath of higher temperature is required for the more complete abstraction of heat. As soon as the immediate effect has passed off, the patient should be lightly covered with a sheet and thin counterpane, and perhaps a blanket over the feet, but all general woollen coverings should be strictly forbidden. During the past cold winter, I never allowed even a single blanket to a patient with typhoid fever in the Fever Hospital, as long as the temperature was raised. In other respects, the ordinary regimen should be observed. Abundance of cold drinks should be given; if there be headache, an ice-cap may be applied; if meteorismus or abdominal pain, a cold compress to the belly. Dr. Brand strongly recommends the use of cold compresses between the baths in all cases.

The other methods of abstracting heat are inferior in their effects, and are indicated in those cases where, from any reason, the cold baths are inadmissible. The graduated baths are useful in persons advanced in life, in cases of extreme prostration, where there is organic disease of the heart or lungs, where there is a tendency to syncope, or where, which is not often the case, the patient has an invincible repugnance to the cold baths. As an exclusive mode of treatment, they would be found impracticable, especially in private houses. Six or eight hot baths daily would be found to overtax the resources of most middle and lower class establishments; whereas the cold bath may be kept ready in the room, and the water need only be changed once or twice daily, a little warm water being added each time before it is used, or in hot weather some ice. Cold sponging and cold affusion are especially adapted to the milder cases, and the former together with iced compresses when, from hemorrhage or peritonitis, we are afraid to move the patients. Cold packing is very inferior to bathing as a means of reducing temperature, and very troublesome to apply, but is sometimes more readily submitted to.

Liebermeister, Jurgensen, and most of the physicians who practise the antipyretic treatment, supplement the cold baths by the administration of those drugs which have the effect of lowering the temperature, especially quinine, salicylate of soda, and digitalis. Brand, however, deprecates their use, and only employs them where bathing is inadmissible. The great advantage they afford is that of diminishing the frequency of the baths; but they do not produce so favourable an effect on the nervous system, and sometimes themselves cause unpleasant symptoms. Their great use, then, is as adjuncts to the bath; but they cannot be employed generally as substitutes.

The most important of these remedies is quinine. It probably reduces temperature by diminishing oxidation, its effect being to impair

the oxygen-carrying powers of the red blood-corpuscles. Quinine is very rapidly eliminated by the kidneys; and, in order to obtain the antipyretic effect, it is necessary that the blood should be highly charged with it. For this purpose, then, it is useless to give small doses at considerable intervals. One large dose should be given at once, or in divided portions within half an hour. To produce a decided fall of temperature in an adult, from thirty to forty grains are usually required. I generally give ten grains in suspension every ten minutes, till the required amount has been taken. This will often depress the temperature three or four degrees, and this depression is often prolonged for many hours. It is best given at night-time, when the evening exacerbation is subsiding, or after the temperature has been lowered by a bath, as it exercises a greater effect on a falling than on a rising temperature. Given in doses of thirty or forty grains in typhoid, quinine often causes some of the disagreeable symptoms of cinchonism, as deafness and singing in the ears. These, however, are of little consequence; a far more serious effect is vomiting, which sometimes follows its use. This may be sometimes prevented by combining it with opium, and administering ice.

Salicylate of soda, given in large doses, has a more powerful effect in depressing temperature even than quinine, and acts more rapidly. It has very largely replaced quinine in the treatment of typhoid fever in Germany; but, after a pretty extensive trial of it, it appears to me to possess all the disadvantages of quinine, and in addition it often has a very depressing effect; so that I now never give it where there are symptoms of prostration or failure of the circulation.

The only other of these antipyretic drugs of which I have any experience is digitalis, and it appears to be universally well spoken of. Dr. Murchison, who had very little faith in the advantages of quinine, says that digitalis is far too much neglected. The antipyretic property of digitalis is probably due to its action on the vaso-motor system. The primary effect is to stimulate the vagus nerve, and so to retard the heart's action; in larger doses, it accelerates the heart by paralysing the vagus; and in still larger doses it brings the organ to a standstill by directly paralysing its muscular fibres. With these effects, it causes contraction of the small arteries, and so increases the blood-pressure in them and diminishes that in the veins. This effect appears not to be due to its action on the vaso-motor centres, but to its direct stimulation of the peripheral nerves. Now, this contraction affects the internal arteries, especially those of the mesenteric system, much more than it does the superficial vessels; hence the blood is diverted from the heat-producing to the heat-dissipating organs, and consequently the temperature falls.

Considerable care is required in giving digitalis as an antipyretic in fever. We must administer full doses, or no effect is produced on the temperature; but we must be very careful not to go beyond the first degree of its action on the heart. When so given, it diminishes the frequency and improves the tone of the pulse, and tends to counteract that general arterial relaxation which is so marked in severe fever, and at the same time it lowers the temperature. It is, however, a dangerous remedy where the heart is softened by acute granular degeneration, and therefore ill adapted for use in the later periods of fever, when the protracted high temperature has already caused more or less of the change to have taken place in the heart.

Such, then, are the principal means at our disposal for keeping the temperature down during the course of typhoid fever. We have now to consider what are the effects on the symptoms and course of the disease.

[To be continued.]

ASTON MANOR.—In this rapidly progressing district, which is now more than three times as populous as in 1861, and eight times as populous as in 1851, sanitary work appears to be well sustained. The death-rate for last year (17.1 per 1,000) was 1.7 lower than the average of the last eight years, and the lowest yet recorded. Moreover, the infantile death-rate is diminishing, being last year 1.4 below the average; and only two deaths were registered from typhoid fever. The very low temperature at the beginning and end of the year caused a large increase in the deaths from diseases of the respiratory organs, which in fact numbered a quarter of the total deaths. On the other hand, diarrhoea greatly decreased, the deaths falling from 64 in 1878 to 17 in 1879, and the number during the third quarter from 48 to 5. The zymotic death-rate was 3.3 per 1,000, the actual number of deaths being 149, against 256 in 1878. Scarletina caused 47 deaths, and was, according to Mr. May, largely spread by attendance at public elementary schools. Whooping-cough was very fatal, causing 107 deaths. Measles was fatal in 15 and diphtheria and croup in 27 instances. A disinfecting chamber has been provided by the authority, but an infectious hospital seems to be much wanted.