A British Medical Association Lecture

ON THE

UNDERLYING DISTURBANCES OF METABOLISM OF THE NERVOUS CHILD.

DELIVERED BEFORE THE WEST SUFFOLK DIVISION

BY

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THE metabolic processes of all children, just because they are children, are less stable than they become in later life. It is in this instability that we find the explanation of the greater frequency in childhood of many disorders due to biochemical derangement—as, for example, eczema, tetany, convulsions, urticaria, or asthma. The peculiar liability of the nervous child to these derangements of metabolism, especially to that common condition known as acidosis, is not only a direct result of his undue sensitiveness to emotional excitement or to physical fatigue, but the state of disordered metabolism so produced is of itself provocative of that restlessness, irritability, or nervousness for which our advice is sought. The nervous child is prone to acidosis, but whenever the symptoms of acidosis are recognizable there is apt to be a simultaneous exacerbation of all the symptoms of nervousness.

The Liability of the Nervous Child to Cyclical Disturbances.

We may look on the nervous child from one point of view as a problem in management, quick to respond to all influences for good, but quick also to react violently even to small mistakes in our management of him. Or, again, we may lay stress upon the physical defects which are so often characteristic of him—the faulty posture, the lax and toneless muscles, the drooping, sagging stance, and the neuro-muscular inco-ordination—all of which are the outward and visible signs of the tired, restless, and irritable brain. But from another point of view we must attempt to probe even more deeply into the problem. We must seek to determine the nature of these recurring waves of disturbed metabolism, which account for the peculiar instability both of physical health and of conduct characteristic of the nervous child, and which are manifested in the “bouts” or “attacks” or “turns” of which, in one form or another, complaint is almost always made. The symptoms which together make up the well-recognized and familiar attack are not the same in different children—in one vomiting, in another nervous diarrhoea; in one drowsiness and prostration, in another restlessness and irritability.

What is the underlying cause of this recurring state of collapse, physical and mental, so characteristic of the nervous child? Why does he so often suddenly fall from a state of comparative well-being to a deplorable condition of weakness, accompanied by loss of weight and loss of colour—with circumoral pallor and dark-rimmed eyes; loss of muscular tone and loss of co-ordination—so that at the worst his walk deteriorates to a mere shuffle and the frequency of his falls becomes a common complaint; loss of energy, so that he lags behind on his daily walks abroad, or, at their conclusion, throws himself down with many significant yawnings and sighings; loss of control, so that clamour, opposition, and tears may become unceasing; and loss of concentration, so that his work at school sensibly deteriorates? And with all these distressing backslidings there are often, almost usually, other complaints—rapid, excitable overaction of the heart, which sometimes leads to a diagnosis of dilatation of the heart; a continuous irregularity of the temperature which cannot but rouse fears of latent tuberculosis; transitory aches and pains in the lax and toneless muscles of the limbs after any exertion, apt to cause confusion with the subacute arthritis of rheumatic

fever; and recurrent bouts of abdominal pain of short duration and always accompanied by a striking vasomotor pallor, which must arouse the fear of the presence of appendicitis. The tongue is almost always white, the breath, especially in the early morning, is apt to be charged with the faint odour of acetone, while sleep, always disturbed and restless, is often broken by night terrors or sleep-walking. It may be that vomiting is by far the most prominent feature of the attack, as in the classical picture of so-called cyclical vomiting. More often vomiting is only occasional, or it may be altogether absent. Sometimes nausea and dizziness may be complained of, especially in the early morning; sometimes there may be no complaints of gastric symptoms at all. Lastly, it is when the child falls into this state of pallor and prostration that all nervous symptoms tend to undergo an exacerbation. It will often be found that, coincidentally with the state described above, the particular disturbance to which any child is prone—masturbation, enuresis, tics and habitual movements of all sorts, squintings, stammerings, and the rest—spring to life again, and proceed with renewed force.

Glycopenia.

Our food is the source of the energy expended in all the activities of life, physical and mental. Our food contains fat, carbohydrate, and protein in suitable proportions. In general it may be said that comparatively little of the protein is utilized as fuel. The protein is too valuable to be employed merely to provide energy for the machine, and is used mainly for structural repair and replacement. The carbohydrate may be said to be the petrol of choice, that on which our machine is run in the first instance. But we have only a meagre store of carbohydrate in our bodies. In an adult male perhaps about 8 ounces may be stored away in the form of glycogen in the liver and in the muscles. These slender reserves of carbohydrate are readily exhausted, especially by physical exertion, by emotional excitement, and by pyrexia. When so exhausted we may, perhaps, speak of a state of glycopenia. The actual percentage of sugar in the blood varies within well-defined limits. After a meal of starch or sugar the blood sugar rises rapidly to 0.18 per cent., to fall within a few hours to the fasting level of 0.07 per cent. We speak, therefore, of a blood sugar curve. Without the frequent administration of carbohydrate the blood sugar remains constantly at the fasting level. Certain diseased states are characterized by a definite hypoglycaemia, a definitely low blood sugar. In Addison's disease, for example, in which the suprarenal glands are destroyed by caseation, there is often hypoglycaemia accompanied by great vasomotor weakness and pallor, a low blood pressure, a rapid pulse, extreme amyotonia and muscular weakness, prostration and loss of energy, and attacks of nausea and vomiting.

We know that the suprarenal glands are exhausted and that their function becomes impaired under the stress of great exertion, of great emotional excitement, or of persistent infection. These are the same conditions which lead to the exhaustion of the carbohydrate reserves and the fall of the blood sugar to the lowest level, and they are the same conditions which in practice we are forced to regard as productive of the “bouts” or “attacks” of pallor, prostration, and vomiting of the nervous child. If speculation is permitted where certainty is not yet, we may surmise that in Addison's disease we are observing the effects of the gross destruction of the suprarenal tissue; in an attack of cyclical vomiting we are encountering the temporary exhaustion and functional impairment of the same gland. The failure to mobilize by means of the suprarenal glands sufficient carbohydrate to achieve the complete metabolism of the absorbed fat is in all probability the explanation of all these “bouts” or “turns,” so variable in their individual symptoms. That in most cases the mobilization of the necessary carbohydrate is in the end successfully achieved spontaneously and somewhat suddenly, after an interval in which the child may suffer extreme distress, is in keeping with the hypothesis that the suprarenals have become temporarily exhausted. In many cases of severe cyclical vomiting, without any treatment at all,

the symptoms, which, up to a point, have been progressive and threatening, suddenly subside. There has been delay in the necessary mechanism for carbohydrate mobilization.

Ketonaemia.

Without sufficient carbohydrate the metabolism of fat is unable to proceed smoothly. Fat is, as it were, the reserve fuel, of which, unlike carbohydrate, there is plentiful storage. But fat can only serve as a satisfactory fuel, can only be metabolized completely, in the presence of a sufficient amount of carbohydrate. Without sufficient carbohydrate the process of reduction to oxygen and water is not completed, but certain intermediate products of combustion, the so-called ketone bodies, accumulate in the blood and are excreted for the most part by the lungs, but also, especially when present in great amounts, in the urine. The condition, commonly called acidosis, is therefore more strictly a ketosis, because although ketosis is a form of acidosis, yet it is only one of many varieties of acidosis.

The presence of ketone bodies in the blood produces further chemical reactions. When we speak of acidosis we do not by any means imply that the reaction of the blood has definitely moved to the acid side. We mean only that we are able to detect the shifts that the body is put to in its successful effort to prevent any significant alteration in the reaction of the blood. We recognize, in other words, that the reserves have been called into action. Only in states of great danger, in the presence of death itself, when these reserve mechanisms fail or become exhausted, is there an actual shift of the reaction of the blood to the acid side. The acid base balance is preserved by many and complicated devices, but that which plays perhaps the greatest part is the regulating power of the respiratory centre acting under the stimulus of the excess of carbonic acid in the blood. The acid ketone bodies combine with the sodium bicarbonate in the blood, setting free an equivalent amount of carbonic acid, which is then removed from the blood by the stimulation of the respiratory centre and the consequent increase of pulmonary ventilation. Hence in the condition known clinically as acidosis, besides a state of glyopenia with a blood sugar at a low fasting level, or even occasionally a definite hypoglycaemia, and besides a significant ketonaemia, there is found a diminution in the alkaline reserves of the blood, compensated for to some extent by an increased formation of ammonia.

In the need for increased pulmonary ventilation we have the explanation of the common complaint of the mother that the child is constantly yawning, sighing, or taking deep breaths. When the smouldering state of acidosis erupts into a definite bout of cyclical vomiting the onset is usually heralded in this way by much yawning and sighing. If we pursue this attempt to find some explanation of these common symptoms of physical and mental prostration we may perhaps attribute especially to the ketonaemia the extreme muscular relaxation, both of the skeletal muscles which shows in the flat-foot, the winged scapulae, and the lordosis with the too prominent abdomen, and of the vasomotor muscles which results in such striking pallor. The effect of the accumulation in the blood of these imperfectly oxidized fatty acids is in many ways comparable to the effect of chloroform anaesthesia, not only in derangement of the function of the liver, but equally strikingly in the profound muscular relaxation and vasomotor paresis. Through the toneless abdominal muscles of a child suffering severely from acidosis I have seen an intussusception reduced by manipulation with the greatest ease. Muscular relaxation more perfect for the purpose could not have been produced by profound chloroform anaesthesia. The muscular aches and pains, and the tendency to fall too readily, are secondary results of the amyotonia. It is, perhaps, not to be wondered at that the child with a persistent acidosis, with quick, rapid, and uncontrolled movements and toneless musculature, is more liable to suffer from greenstick fractures than are other children, not because the bones are softer or more brittle, but because the muscular support is poor and the child is incapable of making that sudden movement necessary to restore the balance, or at any rate to mitigate the severity of the fall. In "night terrors," in the comatose sleep of enuresis, and in the tendency to

nausea and bilious vomiting we have further symptoms which bring to mind the similarity between the effects of chloroform and the effects of the ketone bodies in acidosis. The behaviour of a child struggling under light anaesthesia and of a child with night terrors are strikingly alike.

The Part Played by Infection.

Very often this state of prostration and of pallor is directly caused or greatly increased by some infection, and the removal of some persistent source of infection—as, for example, by tonsillectomy—becomes a necessary part of the treatment, not only of the state of acidosis but of the plentiful crop of nervous symptoms of one sort or another which thrive in this particular soil of acidosis. Infection is a potent and frequent cause of acidosis. Yet it is also true that acidosis, even in its mildest degree or in its incipient stages, powerfully predisposes to infection. The proneness of many of these pallid and lax children to trivial catarrhal infections adds greatly to the difficulties of their management, because, although the infection in itself may be of the slightest, the further disturbance of metabolism to which it gives rise is apt to be severe and persistent. In the total illness a trivial infective component may be altogether submerged in the metabolic component.

Acidosis and Asthma.

Nor is it enough to realize that acidosis predisposes to infection, and that infection produces a great exacerbation in the acidosis. An examination of a large number of children of this type will show many in whom it is clear that the disturbance of metabolism is itself capable of producing irritation and a catarrhal reaction in the mucous membranes lining both the bronchi and the bowel. In certain children mucous diarrhoea takes the place of vomiting as the most prominent symptom of the cyclical disturbance. In others, again, the main symptom is that of recurring attacks of bronchial asthma. We are reminded of a similar association in the so-called uraemic colitis and uraemic asthma. The part played by acidosis in the production of the asthma of childhood, or at least, if production is too strong a word, in the determination of the moment when an attack comes on, has not been sufficiently emphasized. A large number of children with asthma suffer at the same time from cyclical vomiting in greater or lesser degree. That there are other factors concerned in the production of the liability to asthma is clear, but it may well be that the danger point for an attack of asthma is reached, in the child so predisposed, when the blood sugar is at its lowest. Over-exertion, over-excitement, and infection are the main exciting causes in the cycle both of asthma and acetonaemic vomiting. In the part played by glyopenia we have, perhaps, the explanation of the tendency, common to both disorders, to nocturnal exacerbation. Asthma is apt to become worse at night; cyclical vomiting almost always begins at night. Such children stand even the physiological starvation of the night badly, and in the absence of a frequent intake of sugar the nocturnal metabolism is relatively unstable. The frequent combination of asthma with cyclical vomiting, or with some other manifestation of acidosis, is perhaps to be accounted for by the circumstance that both disorders occur almost entirely in excitable eager children who in action mobilize all their reserves of energy and suffer a corresponding exhaustion in reaction. In practice it is often found that successful control of the acidosis brings with it cessation of the asthmatic attacks, or at least a diminution of their number.

In the pale, exhausted, irritable, and nervous child suffering from, or about to suffer from, a "bout" or "attack," with or without vomiting, biochemical examination shows as a rule a blood sugar at a low level, if not a definite hypoglycaemia, ketonaemia, and a diminution of the alkaline reserves of the blood. In some children the attacks are very slight, in some very severe, but a study of the children and of their health from day to day and from month to month can leave no doubt of the essential identity of all the attacks, major and minor. In the same child not all the attacks culminate in vomiting. Many are, as it were, abortive. Nor do I think that there can be

any doubt as to the success of therapy based upon those biochemical findings—a reduction of the intake of fat to within the limits of the tolerance of the individual child, a freer intake of easily absorbed carbohydrate, and the provision of a daily depot of alkali.

Reduction of the Intake of Fat.

The reduction of the intake of fat need not, as a rule, be very drastic. There is, however, a natural tendency on the part of parents, made anxious by the extreme thinness of the child, to endeavour to improve matters by adding very considerably to the intake of fat. Cream or top milk and cod-liver oil are apt to be given freely, with the result that the trouble is increased and perpetuated. This is especially apt to occur when the fear of tuberculosis has been aroused. The propaganda in favour of a diet rich in fat receives support largely from observations upon the children of the poor, who, in general, are fed on much carbohydrate and little fat. The cost of sugar and starch per calorie is low, of fat high. Among the poor the ill effects upon this disorder of a diet too rich in fat are seldom apparent. Among the better-to-do they may be very evident. The omission of cream and cod-liver oil, the removal from a very rich milk of some part of the cream, the restriction of the intake of eggs and butter, perhaps to three eggs and a quarter of a pound of butter a week, may be necessary in households where the provision of milk, cream, butter, and eggs in large amounts has been considered the first essential for health and strength. Chocolate contains a high proportion of a fat which these children appear to tolerate especially badly, and should be omitted, as should all forms of sweets which are rich in fat. Radiostol or ostelin may perhaps usefully be prescribed to children whose intake of fat is restricted for the time being in this way. With improvement in weight and in colour the restrictions may be gradually removed. It is very evident that we have especially to consider the state of the child at the moment when the meal rich in fat is taken. When tired or pale, after exertion or excitement, or in convalescence from infection—when, as we may imagine, there is a state of glycopenia—fat metabolism may be especially unstable. One observant schoolgirl, having fallen prey to one of her attacks of sickness, wrote home to her mother that it was not the rehearsal for the school play which was responsible for her sad state, nor was it the dripping of which she had partaken freely; “it was eating the dripping after the play.”

The Provision of Carbohydrate.

For children in the state described the provision of a free intake of easily assimilated carbohydrate is very necessary. Moreover, experience shows that if the nervous child is apt at times and in certain states to have a low tolerance for fat, there is, as a rule, a high tolerance as well as a high need for carbohydrate. Only by constant replenishment of the carbohydrate reserves can we prevent that wasteful and imperfect oxidation of the meagre store of body fat which manifests itself in the bout of acidosis with the sudden and extreme loss of weight. The digestion of carbohydrate is usually well accomplished. If we encounter difficulties they are concerned usually not with digestion, but with the dislike for sweet things. The natural desire for sugar, which is part of healthy childhood, is apt to be absent in these infant intellectuals, who may prefer the savoury to the sweet. On the other hand, many constantly make demands for sugar, demands which some parents, influenced by the propaganda against sugar, sternly repress.

Propaganda on health matters is apt to suffer from the disadvantage that in the process of the simplification necessary for popular understanding most of the truth is apt to disappear. A diagrammatic presentment without light and shade, and with no place for the exceptions to the general rule, is all that can be attempted. The child with an inborn tendency to acidosis is, in this respect, the exception, and an indiscriminate propaganda in favour of a diet with much milk and cream, and with little or no sugar, has worked steadily against him.

Meat, fish, green vegetables, and fruit may be given as usual. On one side we must supervise, and may have

to restrict the intake of fat. On the other side we must raise proportionately the intake of sugars and starches. All cereal foods, wholemeal bread, rusks, oatcake, wheat-meal biscuits, sugar, jams, jelly, honey, and golden syrup may be given more freely than usual. Suet pudding consists of so much flour and so little suet that it is permissible. A reasonable amount of barley sugar, maple sugar, sugar candy, or boiled sweets may be given daily at meal-times.

The prescription of glucose in the form of a drink flavoured with fruit juice has been of real service. Glucose has several advantages over cane sugar as a means of replenishing the carbohydrate reserves. It is only about one-half as sweet as cane sugar; it is absorbed very rapidly into the blood stream from the upper alimentary tract, and has not the same tendency to cause a fermentative diarrhoea. Its use, too, seems less likely to be followed by the appearance of urticaria, a troublesome result in some children of the free administration of cane sugar. Given between meals it does not disturb appetite, and has something of the effect of a glass of wine in the resulting improvement in colour and sense of well-being.

In insulin hypoglycaemia, mental states of excitement, apprehension, and confusion, as well as muscular weakness, are controlled with astonishing rapidity by means of a few lumps of sugar. In these nervous children something of the same sort can be achieved, if less strikingly and in less degree.

The daily prescription of a small dose of alkali is often helpful. It is common to advise the intake daily of a teaspoonful of sodium bicarbonate. If, as is often the case, there is constipation, to the morning dose of glucose there may be added a little Vichy water or other laxative saline.

By dietetic regulation along these lines, and by the free administration of glucose and of a small amount of alkali, good results can sometimes be achieved. Often a very rapid increase in weight, and improvement in colour and energy, follow the subsidence of the state of acidosis. Sometimes the whole character of the child seems to alter for the better, so that ceaseless opposition and resistance, or timidity, or tearfulness disappear. There may be unmistakable improvement in such symptoms as night terrors, asthma, enuresis, train sickness, even stammering, as the general health improves and self-confidence returns. Almost always the more direct symptoms of the acidosis, the tendency to bouts or attacks of vomiting or diarrhoea, or pyrexia, are manifestly controlled. When no such fortunate result occurs, but the symptoms continue unabated, the explanation lies sometimes in the presence of some focal infection, and sometimes in a persistent failure of the management. Encouragement, rest, freedom from infection, and a high intake of sugar—these seem the special needs of the nervous child.

DIAGNOSIS OF CANCER OF THE COLON.

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CANCER occurs more commonly in the colon than in any other part of the alimentary tract, with the exception of the stomach. Colonic cancer is, however, of the less virulent type—that is to say, its rate of growth is comparatively slow, invasion of the lymphatic vessels and glands is relatively late, while remote secondary deposits, such as liver metastases, are, save in advanced and exceptional cases, distinctly rare. *A priori*, therefore, we have here a favourable field for surgical intervention, a fact which carries with it a correspondingly serious responsibility. If we are to meet this responsibility fairly all our resources must be thrown into the effort to detect the cancerous lesion at the earliest moment.

THE DEVELOPMENT OF COLONIC CANCER.

It will perhaps make for clearness of description if we regard cancer of the large intestine as exhibiting, from the clinico-pathological aspect, three distinct phases.