would not produce this result. Here also there was summation, but no evidence of any specific action.

These results, in which more than one agent is brought to bear on a pathological condition, at any rate suggest that the summated action of several agents may be a better form of treatment than the pushing of a single agent to near the limit of the patient's tolerance.

REFERENCE.

¹ Mottram, J. C.: *British Medical Journal*, January 28th, 1928, p. 132.

"DEBILITY" IN CHILDREN AND CYCLICAL VOMITING.*

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ALL physicians are familiar with the large group of children who are brought for advice regarding the most varied symptoms, for which no adequate cause can be found, and yet which do not seem to be directly due to some antecedent illness such as scarlet fever, measles, or tonsillitis. Such children are for the most part labelled "debility," and are either given tonics or sent away to the country or seaside, the unlucky ones having their tonsils removed first. It is this group which forms the bulk of all the cases attending any out-patient department for diseases of children.

The object of the present communication is to show that, although the symptoms for which these children attend are varied, yet the common underlying set of causes are of the same nature as those found in the cyclical vomiting of children; in other words, that the "debility" and cyclical vomiting to be described hereafter may be regarded as the minor and major manifestations of one disorder, bearing to each other much the same relation as petit mal and grand mal in epilepsy. Further, it is desired to emphasize the frequency with which cyclical vomiting occurs in children of all classes, and not only among the well-to-do, as is commonly taught. Finally, it is hoped to show that both the minor and the major forms of this disorder are easily preventable by the same treatment.

In September, 1923, a group of 30 children suffering from attacks of cyclical vomiting was collected, observed, treated, and followed up for the following three years. It was then believed that this disorder was rare in children of the hospital class, but it soon became evident that this was not the case. On two separate occasions a census of such cases was taken in the out-patient departments of two London hospitals, and it was found that approximately 30 per cent. of all children over 2 years of age gave a history of typical attacks. Since then it has become apparent that cyclical vomiting in children of the social class that makes use of hospital out-patient departments is so frequent that it is regarded by the parents as a normal accompaniment of childhood. They regard it as a "bilious attack" attributable to indiscretions of diet, and do not as a rule consider it sufficiently important to require medical attention. Probably for these reasons, and because attacks rarely occur in children already in institutions, it has been regarded by the profession as an infrequent condition in hospital class children.

Early in the investigation an attempt was made to study the conditions in the blood and urine before, during, and after the attacks. At first several cases were admitted to hospital, but in none of them did attacks supervene. It therefore became obvious that in-patient observations of this disorder were impracticable, and the cases under observation attended as out-patients at fortnightly intervals. After some months it was noticed that, though new cases of cyclical vomiting were seen, none of those already under observation had further attacks, though no special treatment had been undertaken. In order to secure regular attendance malt extract had been given to all the cases as a placebo; but on further investigation it was found that it was the malt which was preventing the occurrence of

attacks, and that sugar in other forms had a similar result. Thereafter all children with this complaint were given extra sugar as a routine, with the result that in the great majority of over 200 cases treated the attacks have been entirely prevented.

It is now well known that the whole subject of cyclical vomiting is intimately related to that of ketosis. Frew¹ in 1911 showed that acetonuria was present in 61.2 per cent. of 662 children admitted to hospital for various reasons. It was first shown by Marfan² that attacks of cyclical vomiting were regularly accompanied by excess of ketone bodies in the urine. Gamble, Ross, and Tisdall³ state that the amount of acidosis present (reduction of serum bicarbonate of blood) is fully accounted for by the excess of ketone bodies in the blood. Ross and Josephs in 1924⁴ produced attacks of cyclical vomiting in children by starvation, and from a study of the blood sugar under these conditions suggested that hypoglycaemia was probably an essential feature of the attacks. Brown and Graham⁵ in 1926 also studied the blood sugar, plasma bicarbonate, and ketone bodies in the blood and urine of children given a ketogenic (high fat and low carbohydrate) and an anti-ketogenic (high carbohydrate and low fat) diet, and also the effects of treating the resulting ketosis with sugar, alkalis, and alkalis plus sugar. They concluded that sugar was the most useful method of treatment. Investigations on the children forming the subject of this paper show that, at least in many cases, there is not a progressive fall of blood sugar culminating in an attack. On the contrary, the blood sugar often remains normal right up to and during the early stages of the attack, though later it may fall quite suddenly to a very low figure, though not necessarily with any increase in the symptoms present. These facts, together with the knowledge that the prophylactic administration of sugar usually prevents attacks, suggests that the underlying defect is a too rapid depletion of the glycogen reserves of the liver in the circumstances existing at the time. To understand how this glycogen depletion is brought about it will first be necessary to consider the symptomatology of the condition, and then the predisposing and exciting causes.

The cardinal signs and symptoms of cyclical vomiting are extraordinarily constant. They are lassitude, drowsiness, headache, pyrexia, vomiting, and marked muscular prostration. Abdominal pain is frequently complained of, even before vomiting sets in, and constipation is generally present, though diarrhoea accompanies the vomiting in some cases. Pyrexia is invariably present at the outset, and often reaches 103° F. on the first day. In the complete absence of pyrexia cyclical vomiting is unlikely to be the correct diagnosis. The muscular prostration may be extreme, with transient squints, loss of knee-jerks, and carination of the abdomen. In such a case drowsiness may give place to actual coma, and not infrequently there is a mild jaundice with pale-coloured stools. The urine is as a rule acid, scanty, high-coloured, and contains an excess of acetone bodies. Often the attacks are preceded by a prodromal stage lasting from a few hours to a day, with lassitude, anorexia, and headache. Sometimes a sense of chilliness or actual shivering precedes the attack. The vomiting is persistent, and is brought on by the mere sight of food. The vomited material is usually acid, and is often highly coloured with bile. The attacks generally last two or three days and then gradually and spontaneously remit, leaving the child after a few days in normal health. Attacks usually begin at about 3 or 4 years of age, and continue at regular or irregular intervals until 12 or 13 years of age, when they tend to become less frequent and less severe, and by the time of puberty they have generally ceased altogether. Sometimes at puberty the attacks are replaced by symptoms of migraine. In some instances cyclical vomiting commences in infancy, though usually in an atypical form.

It is well recognized that cyclical vomiting only occurs in children with an inherited or acquired nervous instability. On examining the causes which excite the actual attacks it is found that they fall into three main groups, of which the first is by far the most important. They are: (1) mental excitement, such as occurs when attending parties, during examinations, and so forth; (2) infection accompanied by

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pyrexia, as at the onset of scarlet fever, tonsillitis, and "colds"; (3) muscular over-exertion, as after vigorous games in which there is a competitive element. Hilliger⁶ has suggested that all these causes act by the over-production of adrenaline through sympathetic stimulation. The signs and symptoms, the nature of the predisposing and exciting causes, and the readiness with which the attacks can be prevented by the addition of extra sugar to the diet, can all be satisfactorily explained by such an hypothesis. It is common knowledge that most healthy children prefer sugar and "sweets" and dislike fats. This may be readily understood when it is remembered that the child always works on the "all-out" principle, while the adult, with greater cerebral inhibition, has learnt to conserve energy by the highly co-ordinated use of a few muscle groups. The child's need for relatively larger supplies of a readily combustible and assimilable food such as sugar is therefore much greater. The monosaccharides and disaccharides are necessary for sudden demands when glycogen stores are getting low. There can be no doubt that the child's desire for sugar and "sweets" subserves a valuable physiological function, and should be gratified.

Treatment.

The amount of sugar to be given varies in every case and in different circumstances. Thus a child who remains free from attacks on a certain allowance of sugar will require an extra supply before attending a party, or going for a ride, or being subjected to any other stimulus known to cause attacks. The following rules have been successful in a large number of cases, and may be of value as a rough guide. Apparently one form of sugar is as effective as another. At least two level teaspoonfuls of sugar are given in a cup of weak tea for breakfast and tea. For dinner, lemonade sweetened with sugar is given. Sandwiches of bread-and-butter and Demerara sugar are taken at each meal, and in some cases an extra sandwich for supper. Milk is allowed in the tea, and in milk puddings, but is not recommended as a beverage, though if desired it may be taken after being skimmed. Glucose powder, 2 or 3 drachms, is given in lemonade three times a day between meals, or, when this is not possible, the child is allowed and even encouraged to eat sweets (boiled sweets are excellent) instead. The extra glass of milk often provided in the mornings is forbidden, and often the school authorities are informed that the child should be allowed to eat sweets in school. As a result of such measures no untoward results have been encountered at any time during the past five years. Glycosuria has never been found in any of these patients. Occasionally during the first fortnight of such a diet urticaria has been complained of, but without exception it has proved quite transitory, and cleared up without any modification of the treatment. Giving sugar and sweets between meals does not impair the appetite in the majority of cases.

"DEBILITY" AND SUGAR SHORTAGE.

The term "debility" covers that large group of children who, though not suffering from any recognizable disease, are nevertheless persistently or temporarily in a subnormal state of health. They may seek advice for headache, constipation, listlessness, anaemia (pallor), backwardness, incipient tuberculosis, failure to put on weight, loss of appetite, growing pains, pyrexia, recurrent diarrhoea or colitis, "nervousness," night terrors, nocturnal enuresis, asthma, and cough. This group of symptoms, when not obviously associated with or due to some definite and well-recognized disease, occurs almost exclusively in highly strung nervous children. Acetone bodies are frequently found in the urine of many of these children. Their plasma bicarbonate is subject to much wider variations from the normal than that of children with a stable nervous system, and many of them suffer from persistent acidosis (decreased plasma bicarbonate), of which the exact cause has not yet been determined. The blood sugar, on the average, is not lower than in normal children, and is again subject to greater fluctuations. The conclusion appears to be justified that this great group of children, commonly called debilitated, is really suffering from relative or absolute insufficiency of sugar—that, in fact, it is suffering from a minor form of the disorder called cyclical vomiting. It is not suggested

that the symptoms named are necessarily due to shortage of sugar. That they are frequently due to such shortage, however, is shown by the fact that very often they can be cured and prevented by the simple expedient of adding sugar to the diet. Broadly speaking, these minor symptoms are more frequently the manifestations of sugar shortage in younger children; as age increases the symptoms tend to become aggregated into definite major attacks with normal health in the intervening periods. At a later age, again, the major attacks become less frequent, and less severe, and ultimately cease altogether. The predisposing nervous instability may persist throughout life, but during the adult period increased cerebral inhibition exerts some measure of control over the biochemical responses to outside influence. In this connexion it is significant that with increasing age fluctuations in the amounts of many of the normal chemical constituents of the blood become progressively less marked.

Some Common Symptoms.

A detailed consideration of a few common symptoms may serve to illustrate some of the points already made, and perhaps throw some light on the nature of certain complaints frequently met with in paediatric practice.

Sugar shortage, in the sense already considered, would appear to be by far the most common cause of headache and constipation in children, both symptoms, in the majority of cases, yielding readily to extra allowances of sugar. The constipation is probably only an expression of defective tone of the intestinal musculature.

Abdominal pain, with and without obvious constipation, often clears up with sugar treatment. Major attacks of cyclical vomiting are also generally accompanied by abdominal pain, often in the right iliac fossa, and occasionally with tenderness and rigidity. Not infrequently children are seen who have undergone appendicectomy for such symptoms, but with attacks persisting until prophylactic treatment with sugar is instituted. In many cases the differential diagnosis between recurrent appendicitis and cyclical vomiting is quite impossible. Sometimes sugar given by the mouth, or as a 5 per cent. solution of glucose per rectum, produces such rapid amelioration of symptoms as to render postponement of operation reasonably safe. In recurrent cases of abdominal pain simulating appendicitis extra sugar in the diet should always be tried before resorting to operation. The point is of great importance, because the child subject to cyclical vomiting is especially liable to delayed chloroform poisoning.

The common symptoms of early tuberculous infection in children are lassitude, failure to put on weight, pallor, and anorexia. Large numbers of children are diagnosed as tuberculous on these criteria and without evidence of any local lesion. A considerable number of these children never develop active tuberculeosis, and not infrequently all the symptoms subside when extra sugar is given.

"Growing pains" are commonly regarded as having a rheumatic origin, or as indicating a predisposition to acute rheumatism. But in many instances these pains may be due to abnormal stresses resulting from the faulty attitudes adopted by children with poor muscle tone. Quite often these pains disappear when the muscle tone is improved by means of an increased allowance of sugar. "Growing pains," it would appear, are more often related to poor muscle tone than to acute or subacute rheumatism, though this view is contrary to that of Goodhart and Still.

The only other single symptom which calls for detailed discussion is unexplained continued pyrexia. Quite commonly children retain a considerable degree of pyrexia, often without other symptoms, long after the apparent subsidence of an acute illness. Sugar treatment may be followed by an immediate and permanent return of normal temperature. The pyrexia in these cases may represent a continued variety of the pyrexia of shorter duration which invariably accompanies major attacks of cyclical vomiting. More than one child has been confined to bed for several months at a time for this reason alone. The following case will illustrate this point.

A boy, aged 7, was admitted to hospital on July 27th, 1927, for unexplained pyrexia, possibly due to tuberculosis. It was not known for how long pyrexia had been present, but it was discovered three weeks previously by his doctor. There was a history

of lassitude, headaches, and constipation for about two months. There was no family history of tuberculosis, and no signs or symptoms of this disease could be discovered in the child. A radiograph of the lungs showed nothing abnormal. He had never suffered from "bilious attacks," and was an only child. As will be seen from the accompanying chart, the temperature became

Chart showing subsidence of prolonged unexplained pyrexia on administration of sugar.

normal almost immediately after giving extra sugar (3 drachms of glucose powder in lemonade three times a day). It will be seen also that he at once began to gain in weight. Since then he has attended as an out-patient at intervals, and now (October, 1928) he is apparently in normal health, having had no further symptoms. During the whole of this period he has continued to take glucose.

The following conclusions would appear to be justified.

1. Cyclical vomiting is an extremely common affection in children of all classes.
2. It is due to depletion of the glycogen reserves of the liver.
3. It occurs mainly in "nervous" children, attacks usually being precipitated by mental stress.
4. It can generally be prevented by giving extra sugar in the diet.
5. The child's desire for sweets subserves a physiological function, and should be gratified.
6. A large proportion of cases of "debility" is due also to sugar shortage.
7. Such debility can generally be cured and prevented by increasing the allowance of sugar in the diet.
8. Sugar shortage is the most common cause of headaches, constipation, abdominal pains, and "growing pains" in children.

POSTSCRIPT.

Since writing the above I have read a paper on "The pre-rheumatic child," by Professor C. W. Vining of Leeds (Bath Conference on Rheumatic Disorders, 1928). In it he shows that a very large proportion of frankly rheumatic children give a preceding history of various symptoms of minor ill health, lasting for months or years. He groups these symptoms under the heading of "toxic debility," and shows that their incidence is very much less in normal children. This state of "toxic debility," Professor Vining suggests, is intimately and causally related to the incidence of acute rheumatic fever, and he concludes that "the success of our efforts to prevent and control rheumatism (acute) will be in proportion to the amount of recognition we give to the pre-rheumatic health defect, and I would suggest on the evidence brought forward in this paper that prevention lies first and foremost in the provision of a well-balanced diet from infancy onwards." The symptoms Professor Vining includes under the title of the "pre-rheumatic" state are identical with those I have suggested as being due to a relative insufficiency of sugar in the diet. As, moreover, they may be readily cured and prevented in the majority of cases by the addition of sugar to the diet, it is possible that this dietetic modification affords a means of preventing acute rheumatism, or at least of diminishing its frequency.

REFERENCES.

- ¹ Frew, R. S.: *Lancet*, 1911, ii, 1264. ² Marfan: *Arch. de Méd. d'Enf.*, xxiv, January, 1921. ³ Gamble, Ross, and Tisdall: *Transactions Thirty-fourth Annual Meeting American Pediatric Society*. ⁴ Ross, S. G., and Josephs, H. W.: *Amer. Journ. Dis. Child.*, xxviii, 447, 1924. ⁵ Brown, M. J., and Graham, G.: *Arch. Dis. Child.*, i, 302, 1926. ⁶ Hilliger: *Jahrb. f. Kinderheilk.*, lxxx, 1, 1914.

SUDDEN DEATH FROM PNEUMONIA WITHOUT APPARENT SYMPTOMS.

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SUDDEN deaths in marasmic infants in the first year of life are not uncommon, especially in the presence of severe anhydraemia. Heart failure, respiratory failure, or what appears to be a sort of general nervous collapse, sometimes brought on by an unsuitable meal, may extinguish suddenly the flickering little life. When the child seems to be doing well and death occurs without any warning symptoms the matter becomes very puzzling. Such deaths are commonly certified as being due to "marasmus," a term which is inadequate, if not actually inaccurate. The following case of this nature, therefore, seems to us of some importance and interest.

A female infant, born on November 13th, 1927, was admitted to the Burnside Infant Welfare Home, Aberdeen, on December 1st, 1927, weighing 6 lb. 9 oz. She was put on the routine feed for infants of her age—namely, lactic acid milk sweetened with dextri-maltose—but did not gain weight satisfactorily. Little could be made out clinically, except that after a few weeks a pustular eruption developed on the chin. This cleared up fairly readily with a coal-tar and zinc paste. There was no albuminuria. Progress, however, remained unsatisfactory, the gain being only 26 ounces in fifteen weeks. At this point one unit of insulin daily was given subcutaneously, followed by a drachm of glucose by the mouth, a method of treatment which has given some happy results in our hands. In the first week of this treatment the child gained 11 ounces, and in the next 3 ounces, and in every way appeared to be much improved. At 2.20 a.m. on March 25th she was found in her cot just dying. During the week prior to death the temperature, taken morning and evening, varied between 97° and 98.2° F., the pulse between 124 and 130, and the respirations between 22 and 28. The 10 p.m. feed on March 24th was finished as usual; at 1.45 a.m. on March 25th her napkins were changed, and there was no suspicion that anything was amiss. The last dose of insulin was given at 3 p.m. the previous day, nearly twelve hours before death.

At the *post-mortem* examination the lower lobes of both lungs were found to be solid and in the red hepatization stage of lobar pneumonia, microscopical sections showing the alveoli to be filled with red cells and leucocytes. A pure culture of pneumococci was grown from the affected lung substance. In the upper lobes were found scattered patches of broncho-pneumonia. The only other abnormality was a large thymus. The thyroid did not appear to be abnormal in any way. Unfortunately, these glands were not weighed.

Discussion.

The point of immediate interest in connexion with this case is that a sudden, unexpected, and apparently inexplicable death in an infant in the first year of life may be due to pneumonia. Dr. Simonds, in *Abt's Pediatrics* (vol. 8, p. 630), indeed, states that broncho-pneumonia is the most common cause of sudden death in the first year of life. Lobar pneumonia is not mentioned in this connexion. While lobar pneumonia is much less frequent in children under 1 year, and is held by some not to occur at all, our experience, confirmed by clinical, radiological, bacteriological, and pathological findings, is that it does occur, and in the case here recorded the pathological and bacteriological findings were as stated above. Discussing the mechanism of death in these cases, Simonds considers that the fatal result is brought about by toxic absorption from the focus, and, probably chiefly, by asphyxia induced by the great reduction in alveoli, which are small in infancy, available for blood exchange. In our case, if asphyxia were the chief cause of death, it would be necessary to postulate its very sudden onset, for it is difficult to see how a child with any degree of respiratory embarrassment could, without showing some recognizable signs of distress, take a feed of several ounces as this child did four hours before death, at which time the pneumonia must almost certainly have been fairly well established. An overwhelming toxæmia seems to be the more probable explanation. In reviewing the case from birth to necropsy four points stand out—namely, (a) the failure to gain weight normally on an adequate diet, arguing a faulty metabolism; (b) increase in weight in response to insulin;