Failure to Gain Weight

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THE INFANT or young child who fails to gain weight properly without any obvious disturbance of digestion presents an interesting and a puzzling clinical problem. Where does the food go? We put in a normal quantity of a normal food. The excreta do not seem to be in any way abnormal and yet gain in weight is either stationary or minimal. Sometimes this situation is encountered after an acute illness, sometimes it follows some chronic disorder; in still other cases it cannot be related to any antecedent or precipitating disease and is evident in very early infancy. In New York City we encounter this problem not very infrequently among immigrants from Puerto Rico, whose diet and living conditions have been substandard, but it is by no means confined to this group. We correct the diet, and rid these children of such parasites as they may have. Yet often for many months they do not gain weight and grow properly. Where does the energy go?

The few experiments of Siwe[1] in which bomb calorimetry of excreta were carried out failed to reveal unusually large losses by these routes. Observations by Levine and others[2] showed a somewhat greater basal heat production in these infants per unit of body weight, but not enough to account for their failure to thrive. It is difficult to reconcile these observations with the first law of thermodynamics.

There are, however, several possible explanations of this apparent paradox, and it is the purpose of this communication to call attention to several that we have encountered. An appreciation of their nature may help, in some instances at least, to better therapy.

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In many instances, failure to gain weight is caused by unappreciated losses of nutrients in the excreta. One of the first of these conditions to come to my attention was that of *masked steatorrhea*. An excess of fat may be lost in the stools, although the gross and often the microscopic appearance remains quite normal. I became aware of this condition some years ago in Baltimore when we were running fat balance studies on normal babies fed different kinds of fat.[3] From time to time one of our subjects would pick up an infection and develop diarrhea, necessitating an interruption of the study. We would wait for this to subside, allowing a few days in addition for good measure before resuming the study, but almost invariably the findings of the first period after the infection had to be discarded because of an unsuspected steatorrhea. The water and electrolyte losses had ceased and the stools were no longer loose, but fat absorption had not yet returned to normal. The time required for the assimilation of fat to return to normal varies greatly in individual infants. It may be very prompt, requiring only a few days or it may last for a longer time. If it is sufficiently delayed and the fact is recognized, we label the child a celiac. One of the most striking examples of latent steatorrhea is the steatorrhea of the premature infant. The stools in these infants appear normal even though as much as 50 per cent of the ingested fat is being lost. Here, too, a microscopic study of the stool reveals no abnormality.

A simple remedy for steatorrhea is to make up for the loss of calories by an increased caloric intake. This can be done perfectly well by adding carbohydrate or protein. We have shown, however, that it can also be done in all the forms of steatorrhea that we have studied[4–7] by giving additional fat. When more fat is added the proportion of absorbed fat remains unchanged. More is excreted in

the stool, to be sure, but more is absorbed, and we have found no evidence that unabsorbed fat is in any way harmful or causes losses of other nutrients as has been feared by some.

Are there conditions in which there is masked loss in the stools of nutrients other than fat? Loss of nitrogen is rarely obvious to the eye. But it is well recognized that when the digestive secretions are impaired considerable unsplit protein may escape digestion. The most familiar example of this condition is cystic fibrosis of the pancreas in which we attempt to overcome this defect by giving more protein. Lesions of the pancreas differing somewhat from cystic fibrosis have been observed in states of severe chronic protein deficiency known as malignant malnutrition, *kwashiorkor*, and by various other names. That serious fecal loss of nitrogen may occur in this condition is well known. This, too, has often been attributed to insufficiency of the digestive enzymes, but other factors also play a part. There is a depletion not merely of the digestive enzymes, but of body enzymes in general. The processes of assimilation of food as well as of digestion are affected and tissue synthesis throughout the body is impaired. Of the limited amount of nitrogen absorbed a substantial fraction cannot be used and spills out in the urine. Excessive nitrogen may thus be lost both in the urine and the stools.

We encounter occasional examples of kwashiorkor among Puerto Rican children who come to New York. We have also been fortunate in being able to collaborate with Dr. Federico Gomeź and his group in Mexico City in a study of that condition. The accompanying Table (Table I) shows one such patient in whom nitrogen balance studies were carried out at intervals. There is considerable variation in individual cases in the extent of the fecal and the urinary losses, but in this patient there were substantial losses by both routes. When first studied, immediately on admission, only 32 per cent of the nitrogen intake was being absorbed, the normal proportion being 80 to 90 per cent. One week later the figure had risen to 60 per cent, but it required two and one-half months before normal absorption figures were obtained. The urinary nitrogen loss of 0.82 g a day, a substantial loss for an intake of only 1.42 g, was decreasing on an identical intake a week later. The final high figure for urinary nitrogen is not relevant, since it reflects an exceptionally high nitrogen intake given just before the third period of study.

Further light upon the anabolic defect in these patients is shown in Table II which illustrates the result of a tryptophan load test carried out on admission and during the early and later recovery phase. Ingested L-tryptophan may be used for tissue synthesis or it may be degraded in various ways, one of the latter being the degradation through kynurenine to N-methyl nicotinamide (NMN), a compound

TABLE I

Nitrogen Balance in Kwashiorkor
Patient R.—12 months old

Period	I	II	III
Date	4/20–4/24	4/27–5/1	7/13–7/17
Diet	Tortilla and beans	Tortilla and beans Whole milk	Whole milk
Weight, av	5.0 kg	5.1 kg	6.2 kg
N intake, g/day	1.832	1.914	3.330
Stool N, g/day	1.240	0.760	0.487
Urine N, g/day	0.837	0.704	2.83
N absorbed, g/day	0.592	1.159	2.843
% intake absorbed	32.3	60.4	85.4
N retained, g/day	−0.244	0.456	−0.033

TABLE II

Tryptophan Load Test in Kwashiorkor
(Excretion of N methyl nicotinamide (mg) After Ingestion of 1 g L-tryptophan)
Patient R.

Period	I	II	III
Day 1	0.81	0.55	1.97
Day 2	1.76	0.78	3.06
Day 3	5.18	0.75	1.98
Day 4	5.90	0.81	1.53

readily measured in the urine by its fluorescence. When first observed on admission this patient showed a marked and clear-cut excretion of NMN after the tryptophan load, the increased excretion lasting for several days. It was obvious from this that the kynurenine metabolic pathway was in good working order. From the second test, carried out a week later, one might be tempted to conclude that this pathway had failed since the test was completely negative, no increase in NMN being found. A more reasonable interpretation, however, in the light of the nitrogen balance study shown above, is that with the resumption of tissue anabolic processes, as indicated by the improved nitrogen retention, no surplus of tryptophan remained for degradation of NMN. Such degradation took place in the initial period only because the anabolic processes were not functioning properly. In the final period, two and one-half months later, when the anabolic needs had been to a considerable extent taken care of there is evidence of a return of the NMN excretion after the tryptophan load.

The management of the protein-starvation syndrome as usually stated is to give protein and to give it generously. This appears to make sense, but requires a certain amount of qualification. When food of any kind is withheld the adaptive enzymes responsible for metabolizing it suffer and the tolerance for that particular food is to some extent lost. This phenomenon has been known for a long time. In the case of carbohydrate it is known as Hofmeister's diabetes or "starvation diabetes." The individual who has been deprived of carbohydrate reacts for a few days like a diabetic when carbohydrate is freely supplied to him. In the case of fat a similar transitory loss of tolerance from disuse was described by Ivar Bang of Sweden,[8] a phenomenon which we ourselves observed in Baltimore. The situation in the case of protein deprivation is similar, but more serious than in the case of fat and carbohydrate in that adaptation appears to be less rapid, if one may judge from animal studies. The animal presented with an additional load of protein requires more liver tissue to deaminate it and more renal tissue to secrete the additional urea load. Hypertrophy of these two organs follows an elevation of the protein intake with great regularity.[9,10] When the protein load is introduced by the oral route the consequences are not too serious because of the impaired nitrogen absorption which I have illustrated above, which limits the uptake, but when hydrolyzed protein or amino acids are introduced intravenously fatal consequences may follow, as was discovered in the case of concentration-camp victims. Even with oral feeding of patients with kwashiorkor Dean and Schwartz[11] have reported that the nonprotein nitrogen of the blood rises to pathologic levels for some days which suggests a measure of caution in introducing protein food and the desirability of using both carbohydrate and fat at this time, since adaptation to these two foodstuffs is more quickly achieved.

Impairment of nitrogen retention results from failure of anabolic enzyme systems. The cause of such failure may be congenital or acquired. The conditions responsible for such failure differ in different parts of the world and are changing with us here. In underdeveloped countries inadequate food and infection, both products of ignorance and a low standard of living, are responsible for this. With us these obvious extrinsic causes are disappearing and we are learning to search for some intrinsic cause, some *silent metabolic anomaly* of which an ever-increasing number are coming to light. Some of these are transitory, of longer or shorter duration, and others are permanent. Metabolic anomalies interfere with gain in weight in two ways: (1) by causing impaired appetite, and (2) by causing masked caloric losses in the excreta.

The list of metabolic anomalies is a long one and is increasing every year. These entities are all rare, but the chance of encountering one of them is not so rare. Some metabolic anomalies although interfering with growth produce other more conspicuous symptoms which attract attention. Diabetes mellitus and nephrosis often involve serious caloric losses in the urine. Frequently recurring infections, such as may occur in agammaglobulinemia may cause serious losses in the stools as well as in the urine. We also have to consider a large and increasingly recognized group of "silent"

metabolic anomalies where the symptoms are insidious, perhaps confined to anorexia with a little vomiting and chiefly characterized by failure to thrive. Several of these syndromes are discussed in the present symposium: *idiopathic hypochloremic renal acidosis*, *idiopathic hypercalcemia and galactosemia*. The various forms of renal glycosuria, including the Debré-deToni—Fanconi syndrome should be mentioned among the conditions in which unusual caloric losses in the excreta take place.

A number of metabolic anomalies, some congenital and some acquired, are associated with aminoaciduria. They include vitamin D-deficient rickets, vitamin D-resistant rickets, the Fanconi syndrome, the Hartnup syndrome, galactosemia, phenylketonuria, cystinosis, cystinuria, Wilson's disease, and various other forms of liver disease, the aminoaciduria of the neonatal period and that caused by various poisons, notably lead. The loss of amino acids in some of these conditions may be as much as ten times the normal figure. However the absolute quantity of amino acids so lost remains small and does not *per se* cause a serious caloric deficit. Only in those conditions where there is an accompanying loss of sugar or some other caloric nutriment is there likely to be a caloric deficit. The metabolic anomaly exerts its effect largely by impairment of appetite.

There is, however, a different group of conditions associated with unexplained failure to gain weight, a group even more common than those referred to above. The following is a typical example:

Case Report: N.C. (#17594-55) was admitted to Bellevue Hospital at the age of 19 months because of failure to gain any appreciable amount of weight for the past year. His family history and the history of the pregnancy were in no way remarkable. His birth weight was 6 lb, 15 oz. He was breast fed for a few weeks only, being then put on an evaporated milk formula, solids and vitamins being added during the fourth month. He failed to thrive almost from the start and during his first eight months of life he added only 3 lb to his birth weight. From then on his weight remained stationary. At the age of eight months he had been admitted to another hospital for study because of his failure to gain weight, where he remained for the succeeding 11 months (Fig. 1). He was the subject of considerable interest on the part of the hospital staff and was studied in considerable detail.

Physical examination failed to reveal any definite cause for his malnutrition and failure to thrive. His appetite was not good, but with persistence a reason-

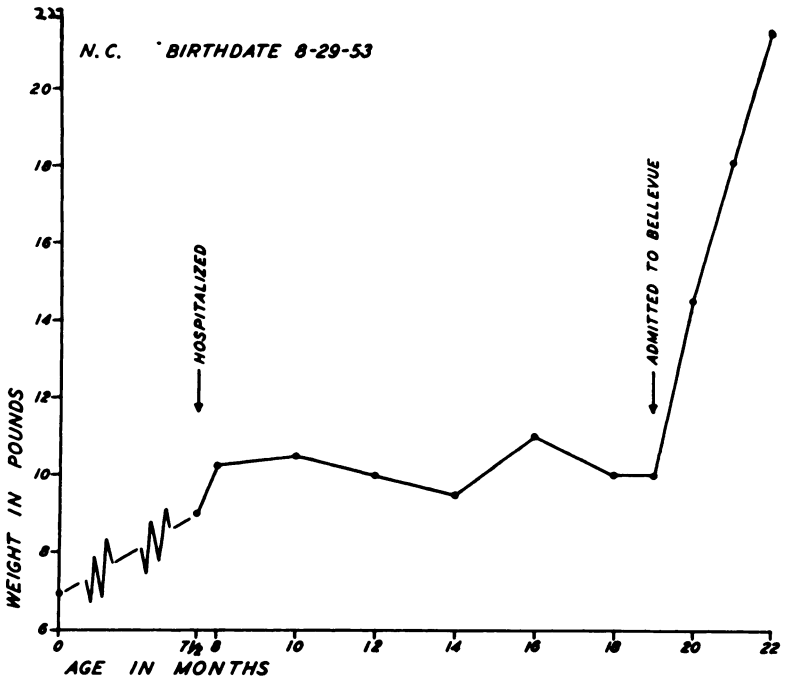

Fig. 1.

able amount of mixed diet was consumed. The bowels were quite normal. From time to time regurgitation of food was noted and some epigastric peristaltic waves travelling from left to right were seen. Barium swallow on one occasion revealed slight dilatation of the esophagus and reflux of barium from the stomach. A laparotomy was performed at the age of 17 months because of the suspicion that some malformation of the gastrointestinal tract was present but no such condition was discovered. An intercurrent respiratory infection, possibly related to aspiration was associated with fever for a time, but this did not persist.

Many laboratory studies were undertaken which failed to reveal anything abnormal. Therapy consisted in altering the diet to tempt the child's appetite, gavage when an insufficient quantity of food was taken; a variety of drugs were also tried including antispasmodics, thyroid extract, Thorazine®, and cortisone. None of these measures resulted in any gain in weight.

At the age of 19 months the possibility of some unusual metabolic anomaly was considered and the child was transferred to Bellevue Hospital for study. He then weighed 10 lb and presented a pathetic picture of extreme emaciation and apathy. Again physical examination and laboratory studies revealed no evidence of disease that would account for the picture. The food was reasonably well taken, but some regurgitation was noted. On close observation by the nursing staff it was found that the child was a persistent ruminator. This condition was treated by a concerted effort on the part of the nurses and house staff to divert the child after meals and whenever he started to ruminate. He was picked up, carried around, and given a great deal of personal attention. The therapy was successful and within a few days rumination ceased. Gain in weight began some 10 days after admission and continued without interruption. In the course of the next three months his weight doubled. He was discharged at the age of 22 months weighing 21½ lb (Fig. 2).

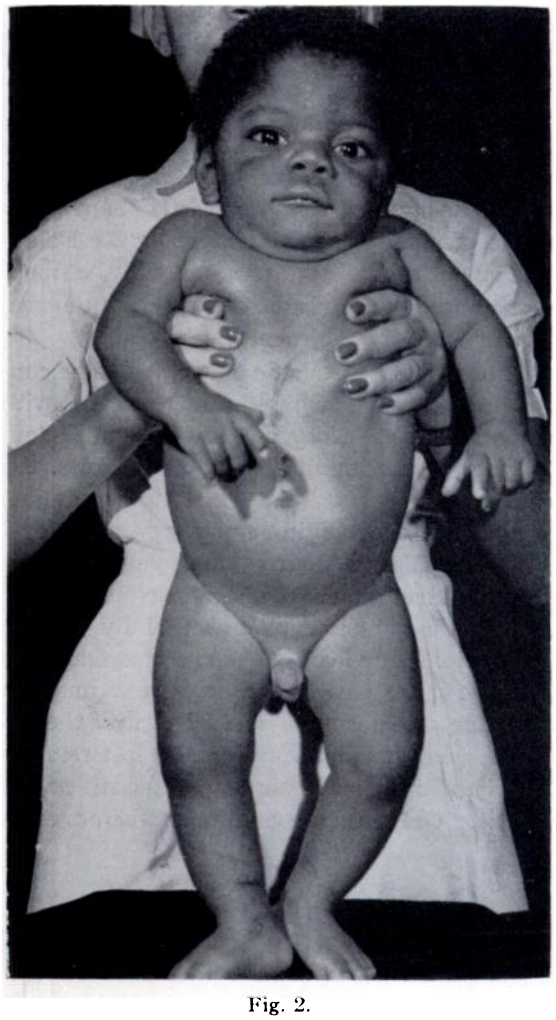

Fig. 2.

It is not our intent to give the impression that rumination is a frequent cause of failure to gain weight. The situation described is certainly an exceptional one. But it is by no means rare to find a discrepancy between the amount of food a child is thought to be taking and the amount he actually receives. When accurate records are not kept the impressions about quantities ingested may be very faulty. And when there is regurgitation it is extremely difficult to estimate with any degree of accuracy the caloric loss. A meticulous examination of the intake will often provide the explanation for the calories that have apparently vanished.

In conclusion, it may be noted that the paradoxical situation is not infrequently encountered of a child who although apparently receiving adequate calories and with no apparent excessive caloric loss in the excreta fails to gain weight and grow. Examination of a number of such situations has revealed that excreta of quite normal appearance may conceal marked caloric losses. Other instances are explained by failure to ingest the calories actually thought to be ingested or to estimate accurately losses sustained by regurgitation.

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