THE SCIENTIFIC BASIS FOR THE ARTIFICIAL FEEDING OF INFANTS *

JOHN HOWLAND, M.D.

BALTIMORE

The inability of many women to nurse their infants is usually regarded as an evil of modern growth and development. This is probably not the case, if one may judge from occasional references to the subject in the Bible, in the writings of Tacitus and elsewhere. But any particular mention in old literature of children is almost lacking, and they were not apparently matters of much concern to people in general until the few last centuries. The references to children before that time are almost entirely of a sentimental nature or by some moralist urging reform and regeneration, and inveighing against the wickedness of modern days. While we are informed that many mothers did not nurse their children, we cannot learn from the general diatribes whether it was because they could not or would not do so.

But whatever the reason why a woman did not nurse her infant, two methods have always been possible by which to supply him sustenance — the employment of a wet-nurse or some form of artificial food, in almost all instances the milk of a domesticated animal. Until the nineteenth century, the former of these was the only method of general application. For, if the prevalent superstitions, that a child might acquire from animal's milk some of the physical characteristics of that animal in the shape of a stray beard or horns, were disregarded, any slight experience with artificial feeding showed the direful consequences to the infant. It was a misnomer to call it "bringing up by hand" because in this way children were not brought up. Apart from lack of information as to the quantity and quality of food, there was a total ignorance in regard to cleanliness. It seems strange, but not unlikely, that any form of artificial feeding would have failed in those days on account of the lack of proper utensils. Horns for bottles with sponges and pieces of perforated leather for nipples, hardly meet what we look on now as necessary requirements.

Artificial feeding was then, as now, chiefly necessary in cities, and the milk-supply of cities was absolutely bad. The unfortunate and diseased animals that furnished the milk were kept in the filthiest of buildings, often with no light or ventilation, were covered with sores

*A lecture delivered before the Harvey Society of New York, March 29, 1913.

and had usually for their only food the fluid refuse from breweries. But the evils of wet-nursing were so appreciable that a substitute for it was constantly sought and attempts were made with artificial mixtures of various kinds. Gradually, in a purely empirical way, the most unsuccessful of these were eliminated. But it was not until after the middle of the last century that artificial feeding was largely used. But anything more than empiricism has been of very recent date, and it is really only in the last twenty years that much that can be dignified by the word scientific, has been learned about the nutrition of infants.

It would not be too much to say that the majority of artificial feeding has been done and still is done empirically by rule of thumb, and with excellent results. Empiricism here has frequently shown the way before there has been satisfactory explanation of the *modus operandi* of some procedure, while, oftentimes, the explanation generally accepted, has required revision though the fact established by observation has remained. Nevertheless, empiricism has also been responsible for the prevalence of many false ideas that have been rooted out only with great difficulty. Probably the reason for this is that the healthy infant has a great margin of safety. The flame of life, though small, burns fiercely within him. He will thrive at times under the most adverse circumstances and will withstand a great amount of well-meant but misdirected attention. The distinction is not sharp between what may allow of satisfactory development and what produces it.

There is only one safe criterion of the proper food for an infant. It must so further his nutrition that he will leave the period of infancy and enter into that of childhood with an entirely normal mental and bodily development. If a decision as to the value of a diet were reached in this way, after long observation and with sharp criticism as to any deviation from the normal, there would not be so much difference of opinion as to proper methods. By clinical observation and not by physiological or chemical determinations must the superiority or inferiority of a diet or of a method of feeding eventually be established, and the acuteness of observers varies and their conclusions may be widely divergent.

When artificial feeding is begun, one of the first problems that presents itself, is the total quantity of food that should be given to a normal infant, sufficient to supply his maintenance requirements and his requirements for growth. With the majority of breast-fed infants this does not have to be considered. The infant nurses until his appetite is satisfied, and the appetite and the quantity of milk are in most cases so nicely regulated that the demands of one are supplied by the other. But with the bottle-fed infant, the danger of overfeeding or underfeeding is real. The child's appetite, though still a guide, is not so much to

be relied on, and what might be regarded as hunger is often discomfort from too much food.

How then are we to judge of his requirements?

The answer to this question has been sought in three ways: by metabolism experiments, by the determination of the energy exchange and by the so-called "statistical method," or the balancing of the intake over long periods of time with the calculated output obtained by the occasional estimation of the excreta.

Metabolism experiments do not offer a satisfactory solution of the question for the chief reason that they can be of only short duration compared with the whole period of infancy. This would mean the application of the conclusions of a few days to a period many times that length, the continuance of what might temporarily be borne to a point of intolerance and the multiplication of any false conclusion or trifling error to a substantial amount.

Metabolism experiments show excellently whether a food is distinctly deficient; they are not designed to show that an excess is given unless this excess is very great, and they are not at all well adapted to determine the food requirements.

Partly with the idea of determining food requirements, Rubner and Heubner first studied the energy exchange of infants with a Petenkofer-Voit apparatus. In order to judge whether their results are to be taken as universally applicable, it is necessary to remember that the observations cannot be continuous. They must be interrupted every four hours in order that the infant may be fed, and once a day for a longer period. It is, therefore, impossible to make the determinations during more than twenty hours out of the twenty-four, and these four lost hours differ very greatly from the others in the activities that go on in them. The infant is much more active outside of his restraining frame than when in it. With the Petenkofer-Voit apparatus the metabolism of quiet and active periods could not be separately measured, consequently it was assumed that there was not much difference between them and that the muscular activity of an infant had a negligible influence on the total metabolism.

Working with Dr. Lusk's calorimeter of the Atwater-Rosa-Benedict type, which was especially built for use with infants, I have shown that activity has an unexpectedly great influence; that crying increased the heat elimination of one infant 18 per cent., and that of another 39 per cent. It is very apparent, therefore, that if the determination of active periods is lost, the error may be a large one and it is also apparent that the metabolism may vary greatly from day to day, according to whether the infant is especially quiet or especially active. It is quite obvious that experiments necessarily conducted in this manner, cannot furnish the

information that is required as to the heat elimination of infants under normal conditions, and so the amount of potential energy that they require.

Determinations of the energy exchange may be made during sleep with a high degree of accuracy, using the modified Atwater calorimeter. I have made many such determinations and have obtained concordant results, provided the conditions were the same as to diet and that the infants were asleep. Any deviation from these conditions allows of no comparison between different infants or between different periods with the same one. With this method then, we may obtain valuable information as to the effect of different kinds of food, of different environment and perhaps of different pathological conditions, but we cannot learn the total amount of energy that should be furnished the normal growing child.

The statistical methods consist in determining by actual weighing the daily intake of infants over long periods of time. A small number of observations have been made in this way by physicians, chiefly on their own children. Occasionally, the urine and feces have also been examined. But while the weighing is accurate, the variations in the composition of breast milk make it practically impossible to draw conclusions as to the total food value of the amount ingested, even if frequent samples are taken for analysis. The composition of breast milk is different to a marked degree at the beginning and end of each nursing period, and may be different at each period. If we rely on this method for information as to the total energy that should be furnished to an infant in his food, it makes a great deal of difference whether we consider, as Heubner did, that the caloric value of a liter of breast milk is 650 calories, or with Schlossman, that it is 782 calories.

The statistical observations have been almost without exception on breast-fed infants. It seems to me that there is a distinct opportunity offered to make the same observations much more easily and accurately on the bottle-fed, especially if the feedings are made up in a milk laboratory and the various ingredients carefully measured. It would then only require that the children should gain sufficiently and regularly. They will not do it for a prolonged period of time in hospitals, and such observations are impossible there. Here is the chance for the practicing physician to furnish information that may be of great practical use.

With all its sources of error this statistical method, which is really a refined empiricism, offers a better means of determining the average requirements of infants than do the others, and it is only the average that can be determined. No two infants even of the same size and weight have the same requirements. I have found that a healthy infant when asleep has a heat production of 1,094 calories a day, calculated in

terms of square meter of body surface. But when infants are awake, a variable factor is introduced; for their activities are never the same, and these cannot be controlled and cannot be measured. For this reason it is never possible to say with certainty how much food any one particular infant will require. The problem of determining accurately the requirements of infants has not remained unsolved for lack of trying. The trouble lies in the inherent difficulty of the problem itself.

Before discussing the influence of various foods on digestion and metabolism, I should like to say that it is obviously impossible to give even a sketch of the whole field. I shall, therefore, confine myself to a consideration of those aspects that chiefly have claimed and do claim at present the attention of pediatricists. And I shall not attempt systematically to outline the uses of the food-stuffs or the transformations that they undergo, but rather to point out in what way it is believed they may be harmful and the proof that is brought that they are.

In the study of infant feeding it is to the several components of the milk that attention has especially been directed. The endeavor has been from the beginning to find out why it is that children fed on human milk thrive almost without exception in a satisfactory manner, while those that receive cow's milk may, oftentimes, do so badly that either extensive modification is necessary or a change to some other form of food. Ten years ago the answer to this seemed perfectly plain. Chemical analysis showed as the most striking difference in the composition of the two milks that the protein of cow's milk was present in three times greater quantity than in human milk and that the proportion of casein to lactalbumin, was much greater in the former. It appeared logical to suspect the casein as the substance most difficult of digestion and when Biedert, by means of reactions which cannot now be looked on as conclusive, determined what he considered to be undigested casein in the stools, it was generally assumed that the excess of protein in cow's milk was the explanation of the failure of cow's milk as a food for infants. In spite of the objections that were raised to this opinion, it was the prevalent one for many years, and has been given up reluctantly. For to a certain extent the belief seemed supported by the theory of Hamburger that "*Artfremdes Eiweiss*" is an irritant to the especially sensitive cells of the infant's alimentary tract and that the necessity of breaking down the protein molecule to such simple substances that they could not be injurious after absorption, threw an added burden on the digestion, and one which was unnecessary with milk of the same species.

Support was also offered by some of the experiments of von Behring on the permeability of the gastro-intestinal tract of the young for bacteria and his insistence that finely divided casein could pass through the coarse filter of the intestinal wall. But the experiments of Bährdt and

Langstein on newly-born children have proven Hamburger at fault, for they have shown that the gastro-intestinal tract of the young does not treat in a different way "*artfremdes*" and "*arteigenes Eiweiss*"; it breaks both down to albumose in the stomach and to amino acids in the small intestine. Von Behring's views are also not possible of acceptance. If unaltered cow's casein were regularly absorbed, it would cause the production of an antiserum to cow's casein with the regularity that the parenteral injection of this substance does in experimental animals. Only in a few instances have precipitins for cow's milk been found in the blood of marantic children, by Moro and Brauer; but it is a very unusual finding compared with what one would expect if the absorption of the unchanged casein were of frequent occurrence. And a certain degree of increased permeability in the very ill or moribund is not to be wondered at. Uffenheimer has emphasized the very perfect provision of the body against such an occurrence as the absorption of foreign protein by the prompt and complete precipitation of the casein by rennet in the stomach and of the protein substances out of the gastric contents, when they reach the intestine, by the cholates of the bile.

But it has been shown also that the observations of Biedert were false. The small white or yellowish masses which he considered to be undigested casein have been determined to be the insoluble soaps of the fatty acids, and indeed are much more frequently found with breast than with artificial feeding. Adler has shown that the precipitate, the result of the addition of acetic acid in the cold, was not composed of casein, as Biedert and Albu and Calvo had insisted. The nucleoprotein of the intestinal secretion and the nuclealbumin of the bile react in a like manner. He also showed that fasting stools contained a similar substance and that the minute quantities of albumin, albumoses and amino acids that were present were common to the stools of breast-fed and artificially-fed children alike. Numberless metabolism experiments have demonstrated in addition, that the nitrogen of cow's milk is absorbed and retained, within the limits of experimental error, as satisfactorily as that of breast milk. The assumption, therefore, that cow's casein is difficult of digestion, appears in the stools as such and composes a "*Schädlicher Nahrungsrest*" is unsupported.

It should be mentioned, however, that casein does at times appear in the stools. The pretty experiments of Talbot have determined this. Occasionally when children are fed on raw milk, large bean-shaped, firm masses are found in the stools. These are largely composed of protein containing in its meshes neutral fat. The proportion of protein in these curds is so large as to make it impossible that it could come from the intestinal secretions, and Talbot was able to demonstrate that the protein was casein by precipitin tests in which the dissolved protein was pre-

precipitated by anticow-casein serum, in the same way that pure cow's casein was precipitated, while no precipitate was obtained with other stools. Uffenheimer, later, also showed their biological character by anaphylactic tests, so that it may now be regarded as certain that cow's casein may appear practically unchanged in the stools. But that it has a limited if any pathological importance, but rather depends on physical conditions in the gastro-intestinal tract, may be assumed from the fact that these curds can be caused to disappear by boiling the milk, as a consequence of which the precipitation of casein by the rennet occurs in much finer flakes, and that infants passing even a large number of such curds present usually no evidences of discomfort or other derangements of digestion.

From numerous metabolism experiments it appears undoubted that, with this exception, the nitrogenous constituents of the food even when that food is cow's milk are completely absorbed and that the nitrogen of the feces comes almost entirely from the intestinal secretions, and from bacteria. The nitrogen in 100 grams of the dried feces of the breast-fed infant is practically as great as that in the feces of the artificially-fed, when allowance is made for the slight differences that occur from time to time with any feeding and with any child. Indeed, when equal amounts of protein are given, the amount of nitrogen may be greater with the breast-fed child, as a result of the excess of fat in breast milk, which causes an increase in the intestinal secretions.

From an examination of the stools, therefore, we obtain no clear indication that the protein of cow's milk is more poorly digested or absorbed than is that of breast milk.

But the chief interest attaches to the retention of the nitrogen. One of the most striking facts in this connection is the extraordinary eagerness with which all infants retain nitrogen. Growth is as normal and necessary a process for them as is the maintenance of equilibrium for an adult. The child's attempts to grow cease only with life itself. For this reason, he retains nitrogen and the other substances necessary to form his protein material, if it is any way possible, and continues to do it under the most discouraging circumstances. Even when receiving a food the caloric content of which is insufficient for his requirements, he retains nitrogen and a not inconsiderable quantity of this, and burns his stored-up glycogen and fat to compensate for the lack of energy supplied in his food. Instead of utilizing all the food ingested to furnish energy as would the adult, he continues to use some nitrogen for growth and sacrifices other tissues of his body for this purpose. In other words he grows at the expense of his general nutrition.

This statement has been repeatedly proved by metabolism experiments, but clinically the fact is also appreciable, for children, not gain-

ing or even losing weight, may continue to grow, at a diminished rate to be sure, but nevertheless, to an extent that can be measured.

The protein food that is taken serves three purposes: first, it replaces that which has been used in the performance of the ordinary functions of the body and lost as desquamated cells, and as secretions; second, a small part is burned to furnish energy, and third, a distinct amount is retained for growth, often 50 per cent., and even more.

It has been impossible up to the present time to contrive any experiments that will determine the amount used in the wear and tear of the body and that part destroyed for the production of energy. It is clear, however, that if the diet contains other ingredients in proper quantity and quality the amount of protein destroyed for these purposes is not large. The total amount of protein which is requisite, requisite and no more, is similarly undetermined. There is very reason to believe that the amount furnished to a healthy nursing infant represents at least a sufficient quantity and cannot be much in excess. As I have said before, it seems assured that cow's protein is not only digested as easily as human, but that the nitrogen of it is retained as readily, and it, therefore, appears not unlikely that other things being equal, less nitrogen might be required with cow's milk for the reason that nearly all of the nitrogen of cow's milk is available for use, while only about 80 per cent. of the nitrogen of human milk is available. The other 20 per cent. is in the form of urea and extractives that can only be at once excreted in the infant's urine. I said other things being equal, for it is not beyond the bounds of possibility that it is advantageous to furnish an artificially fed infant some energy in the form of protein which may be at once used for the production of heat when the gastro-intestinal tract is especially liable to injury from the amount of fat and sugar necessary to produce the heat, with no help from the protein. Except for such a purpose, the protein requisite is strikingly small, and if we may accept the evidence furnished by breast milk, the protein does not require to be greatly increased after the first few months of life until toward the end of the first year. The chief demands for protein are to compensate for wear and tear, and to provide for growth and as the one of these increases the other diminishes. Growth which is most rapid in the early months becomes less and less so, while as the body assumes a larger size, the wear and tear is greater. Thus it comes about that these two demands nearly balance one another throughout a large part of the first year.

The nitrogen retention of the normal infant is dependent to a great degree on the amount of protein food. After partial or complete deprivation of this, he retains a large amount for some time, when it is again offered, as if to make up for that which he had lost. If the protein continues to be given in excess, however, after a few days of very great

retention, the retained nitrogen gradually diminishes day by day to an amount equal to that which would have been held, provided the infant had received the optimum quantity and no more.

But all of the other food-stuffs have an important influence on the retention of nitrogen. With a normal infant receiving enough food to meet his requirements the addition of fat to the diet in any form has no great influence. The addition of sugar or carbohydrates causes a much greater retention. The effect of a disturbance of digestion caused by either fats or carbohydrates is striking, especially when fat is the offending element. A negative nitrogen balance is the result. The loss of nitrogen occurs not only in the feces due to the greater amount of intestinal secretion, but in the urine as well, and to a larger extent. This loss of nitrogen is the result of changes in salt metabolism, for on the unfavorable influence of this the elimination of nitrogen chiefly depends.

But the retention of nitrogen is also largely dependent on mineral metabolism. The retained nitrogen cannot circulate in the blood nor be loosely held by the tissues for any considerable length of time. It must be built up into living protein material and to do this salts must be available. Unless they are available the nitrogen is excreted again. Thus there must be a certain parallelism between the amount of nitrogen and the amount of total ash retained, and this has been found to be so. For every gram of nitrogen about 1.7 grams of ash are retained, not always at exactly the same time, but if the experiments are of long enough duration, these figures hold nearly true. A close parallelism between the retention of nitrogen and that of the individual bases cannot at present be shown, probably chiefly on account of the technical difficulties of the experiments, but also on account of the formation at different times of nitrogenous compounds now richer in one element and now in another.

I have already stated that it is the general belief that the protein of cow's milk is as readily utilized as is that of human milk. Is there then any possibility that it is injurious to the infant in the quantity in which it is given, usually two, three or four times as much as the breast-fed infant receives of human casein? Does this put an excessive strain on the organs transforming the products into eliminable form and those excreting these products? The only answer to this can be that no such injurious effect has ever been noticed.

There is a possibility, however, that a great excess of protein may, under certain circumstances, be harmful. Two calorimetric experiments that I have made indicate this. The heat production of one infant was raised 10 per cent. by an increase of protein in his food and that of another 26 per cent. Moreover, it could be calculated in the case of the second child that all of the extra heat and carbon dioxid could not come

from the protein alone, but that this protein, or more probably its decomposition products, acted as a stimulus to the metabolism of all the food-stuffs. This extra heat produced must be eliminated. Under ordinary circumstances, this is undoubtedly accomplished without difficulty. But if to excessive atmospheric temperature and humidity, factors preventing the elimination of heat, there is added the incurred burden of disposing of an excessive and unnecessary amount of heat, the possibility of nutritional disturbance may be increased.

Two other possibilities have been mentioned as factors causing failure in artificial feeding, one the formation of toxic decomposition products of protein and the other anaphylactic phenomena. The great size of the protein molecule allows of the formation of an enormous number of products, many of which are undoubtedly poisonous, provided the natural defenses of the body are inadequate. But nature has guarded against injury by them in a most thorough manner and though the possibility remains, proof that injury is caused is lacking. Moreover, Ernst Magnus has shown that, after all kinds of feeding, the intestinal contents obtained from an intestinal fistula may be toxic, except on a diet of milk, and then the toxicity is absent.

That anaphylactic phenomena are at all common with cow's milk feeding is much to be doubted. But that they occur as rarities seems likely. The only infant of which I have personal knowledge presenting such symptoms had regularly, severe vomiting after the ingestion of less than one ounce of cow's milk, with an intense urticarial eruption and collapse, and this was repeated as often as the cow's milk was given. No tests were used with this child, nor so far as I am aware have they ever been used to show a hypersusceptibility to casein in the same way that they were by Schloss to show a hypersusceptibility to white of egg. Hypersusceptibility in the biological sense cannot be used to explain the ordinary failures with artificial feeding.

Recently a series of interesting observations has been made by Drs. Holt and Levene and their coworkers on infants that had received a "synthetic" food very rich in casein. After a period of from four to six days on this diet, fever resulted and this continued until the food was stopped, when it immediately subsided. Interesting speculations are at once raised by these results, but they have little bearing on the question of artificial feeding, first on account of the artificial character of the food with its high sodium hydroxid content, and second, on account of the great quantity of casein given, greater by far than could be taken even in undiluted milk.

There is one other possibility that I should like to consider, and that is, that a large amount of protein may play a not inconsiderable part in the production of the symptoms of what Czerny has called "*Milchnähr-*

schaden," and which will be later discussed. It seems not improbable that some of the benefit to be derived from a change to a carbohydrate rich diet in this condition may be due no less to the limitation of protein, and thus of the putrefaction, than it is to the diminution of fats; at least some experiments that I have been conducting point that way. But when all is said, actual and possible, against the protein and especially the casein of cow's milk, it must be granted that it has so far lived down its evil reputation that it is generally regarded as a factor of but little if any importance in the general production of disorders of nutrition.

The differences of opinion that have been entertained in regard to the fat of the food, have been all as to the dangers of it and the disturbances that it might cause. There is unanimity in the belief that fat is beneficial for infants, and that those who, because of nutritional disturbances, cannot take a reasonable amount of it do not thrive so satisfactorily as do those who can. The very large proportion of fat in human milk indicates the amount of energy that advantageously may be provided by fat for the healthy infant. But the difficulty comes in furnishing this to the artificially-fed child without danger. It is necessary to emphasize "without danger" for the reason that the tolerance of infants for cow's milk fat varies to an astounding degree. One will take even more than is found in human milk without a symptom and over a long period of time. This tolerance belongs especially to the older infant though the very young may also exhibit it. Thus R. A. Cooke and I, in the course of some experiments, gave a boy of 10 months 76 grams of fat a day for several weeks. He had no evidence of disturbance, his nitrogen partition was normal, with no increase of ammonia, he gained weight with rapidity and was comfortable.

But another infant, especially a young one, cannot take even a small amount without evidences of its harmful effects. Generally these evidences do not appear at once and perhaps only after a period of apparent benefit. Hence it has come about that there are widely divergent views as to the amount of fat that may be given with safety. To stay within safe limits is eminently the wise thing to do. For an intolerance to fat once established persists longer than an intolerance to any other food ingredient and compels the reduction of the fat to such a low point as to throw the burden of furnishing energy almost completely on the carbohydrates, and carbohydrates in excess are an insecure support for the young infant.

The digestion of fat and the effect of fat on the digestion of infants have been studied with great care by Tobler, Uffenheimer and others. Fats so retard the emptying of the stomach that stagnation may occur, and when the quantity is large, selective retention of the fat takes place. In marked instances of this, at the end of the day, it may be possible to

obtain by the stomach tube almost all of the fat. But given such admirable opportunity for it, vomiting usually takes place. The strong odor of butyric acid suggests that the lower fatty acids are increased. Huldshinsky failed to obtain proof of this in persistently vomiting infants.

Though the presence of a fat-splitting enzyme in the stomach was definitely determined by Sedgwick, it probably plays a very small part, and the splitting of fats is accomplished chiefly in the intestine, and so completely, that under normal circumstances, not more than 1 per cent. of the fat escapes this action. The further fate of the fats is not sufficiently understood. It would be of great assistance to know the form in which they are absorbed. Are they absorbed chiefly as fatty acids or as soaps, and if as the latter, as the soluble soaps of sodium and potassium or the insoluble ones of calcium and magnesium? Are the insoluble soaps the chief and most important means for the absorption of calcium and magnesium, or are they substances incapable of utilization? Are sodium and potassium driven out of combination with the acids, as has been suggested, and replaced by calcium and magnesium in the colon?

Much in regard to the form of fat even in the stools is denied us on account of the difficulty of separately determining neutral fat, fatty acids and soaps. So many methods have been employed each in itself more or less inadequate that a comparison of results obtained by different experimenters is hardly of value. The one good present method, Inaba's modification of the method of Kumagawa and Suto, allows the determination of only total fat. It may be said that approximately 40 per cent. of the stool of the normal infant is fat, and of this, 10 per cent. is neutral fat; about 10 per cent. is soluble soaps and the rest fatty acids and insoluble soaps. The amount and relative proportion of each of these may be greatly influenced by circumstances and the absorption of fat may be similarly influenced. For example, while more than 90 per cent. of the fat is absorbed under normal conditions, less than 50 per cent. may be absorbed with severe diarrhea of gastro-intestinal origin, and the neutral fat instead of being well split and forming only 10 per cent. of the stools may form 40 per cent. or more.

Fat was for a long time disregarded as a cause of harm to the infant. Biedert was one of the first to insist on the part that it might play in the production of diarrhea, but it was Czerny's and Keller's experiments and writings and those of their coworkers that showed unmistakably that fat was a power for harm.

The most discussed and most studied of the conditions ascribed to fat is that called by Czerny, "*Milchnährschaden*," which he says is synonymous with "*Fettnährschaden*." According to his view, the element responsible for this condition is the fat of the food. Increasing this fat

makes the condition worse, and diminishing it makes it better. Infants with this condition are pale, and while perhaps fat, are pasty. Their appetite is poor, they gain in weight slowly, and finally not at all. The most striking thing, however, is the character of their stools. They are constipated. The stools are large, dry, light colored and foul, the so-called "*Seifenstühle*." The condition is amenable to treatment, and infants with this disorder usually respond rapidly to a diminution in milk and the addition of cereal and sugar especially in the form of one of the malt-soups, a combination of dextrins and maltose.

There are certain definite chemical changes with these "*Seifenstühle*." The nitrogen is somewhat increased, but the general retention of it is in no wise interfered with. The carbohydrates of the feces are very much decreased, or rather, as Usuki has shown, these soap stools only occur when there is less than half of the carbohydrate in the stools that is ordinarily found. The fat is absorbed to a surprisingly good extent. It was held by Freund and others that the absorption was even better than under normal conditions, but the poor methods of analysis allowed this faulty conclusion. We know now that absorption suffers somewhat, but only to a slight extent, so slight, that a lack of sufficient nutritive material cannot account in any way for the clinical picture.

The positive evidence of harm is shown by the study of the mineral metabolism. It is the earthy alkalies that suffer most. Rothberg and Birk first pointed out this fact, the former for calcium and the latter for magnesium, and it has been shown since then, over and over again. Why so much of these earthy bases is excreted is not clear. Bahrdt has calculated that much more calcium is passed in the stools than could be accounted for by the binding power of the fatty acids, but he was not able to determine the form in which this excess of calcium was lost. The fact remains, however, that the calcium and magnesium are not retained. Whether this, the most constant and striking of the findings, is the only explanation of the poor condition of the infant and the failure to gain is not quite clear.

Stolte has pointed out that fat and calcium must be present in the food in considerable concentration in order that soap stools and constipation can result. But putrefaction is also necessary for the production of these stools as opposed to fermentation. Meyer and others have shown that the addition of casein may cause soap stools with evidences of putrefaction. But this excess of putrefaction only takes place when there is an insufficient quantity of carbohydrate in the food. If fermentation is active, putrefaction cannot take place, and without this putrefaction soap stools cannot be formed. Usuki, in studying the partition of fat in the stools, found that when carbohydrate is present in the stool in any quantity, that is, when there is a substance that can ferment, soap stools

are absent. If, however, the carbohydrate is in such quantity or of such quality that it is rapidly absorbed and therefore does not ferment, soap stools may be present.

There are three requisites for the production of these stools; at least a moderate amount of fat, casein and calcium in considerable quantity and the absence of sufficient carbohydrate. This is an excellent example to show how complicated are the conditions in nutritional disturbances and how the food-stuffs interact, and how difficult and indeed unwise it is to consider one alone as the cause of any disturbance. The condition is usually considered a "*Fettnährschaden*." One could with nearly as good reason uphold the proposition that it is an "*Eiweissnährschaden*," while it is presumably more dependent on insufficient or improper carbohydrate than anything else. For the condition can be cured without reducing the fat and protein if the proper amount of suitable carbohydrates is added.

The diarrhea caused by fat is quite a different condition. It is almost always acute and brings about chemical changes quite distinct from those just described. The endeavor was made by Salge to prove an association between a bacillus, the acidophilus, with this condition, but without sufficient evidence. Racinski has shown in the breast-fed, and Langstein and Meyer in artificially-fed infants, an excess of lower fatty acids in the diarrheal stools. These, by their irritating effect, undoubtedly play an important part in the production of the diarrhea. For a long time the cause of the high ammonia content of the urine could not be explained. Keller unavailingly sought for abnormal acids in the urine. Eventually, Steinitz demonstrated that there is a great loss of alkali, especially of sodium, by the bowel. The body is thereby so deprived of bases with which to neutralize the acids of intermediary metabolism, that ammonia must be furnished to take their place. The condition is therefore a relative acidosis. Though this increased ammonia was originally supposed to be due to the excess of fat, it is really quite independent of it, and occurs with diarrhea due to any cause. Even with a severe diarrhea the calcium and magnesium may be well absorbed and retained. So with these two disturbances that may be due to fat we have quite different chemical changes. One may run its course with a positive sodium and potassium balance, but with a loss of calcium and magnesium, the other with a positive calcium and magnesium balance, but with a loss of sodium and potassium. From their relative importance in the organism we would expect the condition in which calcium and magnesium loss occurred to be better and more persistently borne, and such is true of the clinical course.

The stormy condition sometimes met with as the result of feeding excessive quantities of fat, with sudden onset, high fever, repeated convulsions, persistent lack of appetite, vomiting and diarrhea has found no adequate explanation. It is for lack of a better name often spoken of as "acute acidosis" without evidence that the accompanying acidosis plays more than a secondary and subordinate rôle. Despite the lack of information in regard to it, the condition is a very serious and oftentimes fatal one.

In controversy, the battle usually rages thickest and hottest around some definite point. So it has always been with the question of artificial feeding and so it is now. Proteins and fats are temporarily disregarded and the carbohydrates and salts are the objects of chief attack. With new knowledge and new hypotheses the assault is made from different quarters. The questions at present at issue are not at all those of ten or even five years ago.

Opportunity is given for a great difference of opinion in regard to the sugars and carbohydrates, because their fate in the organism is so little understood and the various intermediary products of their metabolism from the time of their absorption to their complete disintegration to carbon dioxide and water are quite unknown. It is thus not possible to follow these substances to the same extent that it is the proteins and the salts.

For the same reason opinions reached in regard to the carbohydrates must be largely the result of clinical observations. Now, while it is contended that clinical observations may have the same value as laboratory experiments, it can only be so when they are planned with the same care, conducted with the same adherence to technic and with the same avoidance of interfering, extraneous influences, and finally viewed with the same critical skepticism that the trained laboratory worker would employ. Usually these conditions have not been fulfilled, and for this reason from clinical observations absolutely contrary opinions in regard to almost any aspect of the question are obtained. To cite a few examples: It is claimed that lactose is absorbed from the intestinal tract very slowly and is therefore dangerous on account of the rare opportunity that it gives for fermentation. Again, it is asserted that it is dangerous because it is absorbed so rapidly that lactose does not have an opportunity to break it down, and that, after its absorption as such, it acts as a poisonous and pyrogenic substance. Sainmont believes that he has demonstrated by observations on puppies that lactose is a much safer sugar than saccharose or glucose, while Heim came to a totally different conclusion. And in spite of the proof that could be brought against him, Weigert denies that milk-sugar has a nutritional value and insists that as good results can be obtained with milk and cereal mixtures as with

these plus milk-sugar. If one should rely entirely on published opinions, he would be left in a sad state of perplexity.

I do not wish to review matters concerning which there is complete unanimity of opinion, but I should like to emphasize, as so many others have done, the great dependence of the infant on the carbohydrates. He normally, and for his best advantage, obtains a large proportion of his energy from them. For a time he may disadvantageously exist with a minimum of carbohydrate food, but a lack of it very soon threatens life. So long as the infant with a nutritional disturbance retains a certain tolerance for carbohydrates, recovery may take place; but an entire loss of tolerance takes away the possibility of this. Especially in artificial feeding are the carbohydrates of importance; for the infant cannot take, or it is not wise to give him, the amount of fat that the breast-fed infant receives. The deficiency of energy must therefore be supplied largely by the carbohydrates.

There has been, and still is, much discussion as to the form of sugar which is to be preferred for infants. What one is most satisfactory as regards (1) tolerance, (2) influence on gain in weight, (3) influence on the absorption and retention of other substances, (4) influence as a corrective when nutritional disturbances exist and (5) as regards safety.

The disaccharids are the only sugars ordinarily employed in infant feeding, the monosaccharids and polysaccharids have been used only for experimental purposes and need not concern us here. Of the disaccharids, lactose and saccharose are alone employed. Maltose is barred by its considerable cost. An especial place must be accorded to maltose in combination with other substances in the preparations known as dextrimaltoses, *nährzuckers*, malt-soups and various proprietary foods; but it must be recognized that maltose plays only a partial, perhaps an insubordinate, rôle in them. These mixtures contain a multitude of substances, known and unknown, maltose, salts, nitrogen-containing compounds and a great variety of dextrans and substances closely allied to them. And the beneficial results following their use cannot be ascribed to any one particular substance.

It may be said in general that the limit of tolerance for sugars before mellituria takes place is very high in the normal infant. The sick infant, the feeble and premature and the eczematous may excrete sugar in the urine with a very small intake, but this sugar, so far as has been demonstrated, is almost always lactose or galactose, rarely saccharose and never glucose, unless diabetes is present.

This tolerance is so high — Grosz, Nobécourt, Finizio, Aschenheim and others have shown this — as to put the danger of alimentary mellituria for normal children, with a reasonable intake, out of the necessity for consideration. This is the conclusion that one must reach even

though different concentrations have been used and these have yielded different results. But these experiments give us no indication that either lactose or saccharose is superior. The limit of tolerance is about the same for both. That for maltose is twice as high, probably because maltose can be burned after passing the intestinal wall. Lactose and saccharose cannot be burned by the body cells, except apparently in very small quantity and after repeated injections, as Leopold has demonstrated for lactose. The tolerance for the maltose combinations has not been determined.

Under ordinary circumstances, all sugars act satisfactorily enough so far as gain in weight and a favorable influence on the retention of other substances is concerned. There is no convincing proof clinically or experimentally that one is superior to the other. They apparently furnish utilizable energy in the same proportion and their favorable influence on the retention of nitrogen seems to be the same, though experimental evidence for saccharose is almost lacking. After the first few months additional carbohydrates in other forms have a distinctly beneficial effect. Here the malt preparations may find application; but there is no proof that the normal infant may not thrive entirely satisfactorily without them, with the ordinary cereals.

It is, however, in the correction of nutritional disturbances that a great difference between the sugars is seen. The disturbance described by Czerny and Keller as "*milchnährschaden*," responds promptly to the malt preparations, especially when combined with cereals in considerable quantity, and this more or less irrespective of whether the amount of milk is reduced or not. To increase the lactose or saccharose unless they have been present in very small amount, is a dangerous method to bring about a similar result, because it may cause an excessive fermentation with severe diarrhea. Maltose alone has no advantage over lactose or saccharose in correcting this disturbance as Usuki and Gerstenberger have demonstrated. It is equally if not more dangerous. It is the malt preparations combined with large amounts of cereals that are the most efficacious. Exactly why, no one knows. Usuki found after their use three or four times as much carbohydrate in the stools as when maltose alone was given, so that it might be said that the substance least utilized gave the best results. He believed that the beneficial effect was due to the slow, continuous and never rapid fermentation. On the other hand, DuBois and Stolte maintain that it is the potassium carbonate contained in the malt-soup that is of value, especially in preventing the excretion of calcium. It will take further experiments especially planned to decide this.

It is not so easy to determine what is the safest sugar. The difference of opinion here is very great. There is a tendency at the present time,

even for many who were formerly warm in its praise, to accuse milk-sugar of being a dangerous substance even for normal infants, and of being the cause of most of the nutritional disturbances to which the infant is heir. The complaint is overdrawn. The satisfactory results with thousands in the past and at present prove this. Those who entertain these extreme views in regard to milk-sugar reach them as the result of hospital experiences in which hardly a normal child is ever seen. They forget the good results with healthy infants. Those who would deny milk-sugar any place in the dietary of infants must take the stand that it is dangerous only on account of its combination with cow's milk. For the milk-sugar of all animals is identical and nutritional disturbances are most promptly and permanently cured by breast milk in which milk-sugar is in greater proportion than is found in any artificial mixture. It is, I think, a conservative conclusion that for the normal infant, lactose and saccharose, within reasonable limits, are by no means dangerous; indeed, they are probably safer in the very early months than malt preparations would be. When nutritional disturbances do arise, these sugars must be reduced or temporarily entirely withdrawn, and if introduced again into the food must be introduced only with caution.

There is ample evidence that the sugars can initiate trouble, especially in the feeble and those who have previously suffered from nutritional disturbances. Exactly how they do so is not clearly understood. The process is usually spoken of as fermentation, but the irritative and poisonous products of this have not been isolated. Von Bokay, Escherich and others, have incriminated the lower fatty acids formed from the carbohydrates. Certainly the lower fatty acids are in excess in the diarrheal stools, but whether they come from the sugars or the fats cannot be determined. Whether the effect is direct from products of sugar disintegration or indirect perhaps by action on bacterial growth, the result is the same. The food substances, especially the fat, are poorly absorbed, there is a loss of sodium and potassium salts as a result of the excessive intestinal secretions, so that a negative balance of these substances results and there is an excessive ammonia content in the urine.

I should like to postpone consideration of some of the other effects, including the pyrogenic effect, of the sugars, especially lactose, until the salts are discussed, because of their close association together in whey, which has been in the last few years accorded a prominent place in the production of nutritional disturbances of infancy. Mention, however, should be made of the carbohydrates other than the sugars because of their general employment during the latter part of the first year and of their beneficial effect even in early infancy. Of their *modus operandi*, little accurate is known. That they act to a degree like sugars is undoubtedly true, but clinical, and to a certain extent chemical, testi-

mony is to the effect that they have another influence. An infant may maintain his weight, neither gaining nor losing for many days or weeks, when only diluted milk and sugar are given to him. If then a small amount of cereal is added, improvement in general condition and in weight may take place at once. On a milk and milk-sugar mixture an infant may be losing calcium and magnesium. If a cereal is added, the negative balance becomes a positive one and may continue positive even if the sugar be entirely withdrawn. The beneficial influence is perhaps to be found in the constant slight fermentation and acid formation that results. Klotz has shown that a small amount of lactic acid by mouth had clearly an influence in improving the absorption and utilization of organic and inorganic compounds.

There is the thought that perhaps cereals made from the whole grain may have an additional value, but while this is suggested by the influence of polished rice on the production of beri-beri, it is a suggestion only.

As to the injurious effects of an excess of properly cooked cereal, we know very little in this country. The obscure condition known to the Germans as "*Mehlnährschaden*," with its disastrous outcome, is a clinical picture unknown to us. It is undoubtedly in part the result of hunger and nitrogenous and salt starvation, but whether the excess of cereal may also have a share in its production, is quite unknown.

The mineral metabolism of infants has been studied first to observe the effect of the increase or decrease of the mineral constituents, and second, as the means of determining the beneficial or harmful influence exerted by an alteration in the quantity or quality of the food. For in the ultimate analysis it is by the response of the mineral metabolism that we judge of the value of a food. It is the most sensitive indicator that we possess, and as such it is universally employed. There is, however, the very great disadvantage that under normal circumstances its behavior is very little known. There can be no doubt that normally, some of each of the mineral constituents is retained; yet in the literature can be found less than a half dozen experiments on breast-fed infants with complete, positive balances, and an equally small number on those artificially fed. In the great majority of metabolism experiments, on supposedly normal infants that have been published, one or more of the minerals has been excreted in greater amount than it was ingested. And, even when the balance of one mineral in a series of observations has been positive, the actual amount of it retained has been found to vary within extremely wide limits. The quantity that one considers should be retained is a question of personal belief and not one of demonstrated fact. For many decisions I believe that one period is not sufficient, but that two consecutive periods closely agreeing should be employed, and this, so far as I am aware, has practically never been done. Nor has it

been shown, except very rarely, that two periods may closely agree. Perhaps it is true that the minerals are not continuously or regularly retained. It is much more probable that our experiments are not planned so that we can demonstrate this. For there are a good many possible sources of error. The infants are rarely normal infants, and the conditions under which the experiments are made are not normal. The observations have, in many instances, been too short, and the periods of collection of excreta not sharply differentiated. The urine may always be sharply separated. The stools seldom are, and there is the chance that too little or too much may be included in collecting. In the case of substances that are largely excreted by the intestines this fact may alter the meaning of the whole experiment. Furthermore, the change from one diet to another is often made too abruptly and the experiment begun immediately on the change without opportunity for the infant to become adjusted to the new conditions. A subsequent experiment on the same diet might give a very different picture. Thus, with a great increase in the nitrogen or of the mineral constituents of the food, there may be an excessive retention of these for several days, the retained amount, however, becoming less and less until a point is reached, not much if any, above what it was on a much lower diet. Conversely, on a change to an insufficient diet there may be a great loss of nitrogen and salts; but as L. F. Meyer has demonstrated, this may be only for a time. The infant accustoms himself to a much lower level of metabolism and may even retain, in small quantity, nitrogen and salts, when losing weight. An early determination of his chemical balance would have given a totally erroneous impression of what the ultimate result would be, and one would have thought that he could go on losing minerals *ad infinitum*. It has been common to obtain one or two sets of figures and draw far-reaching conclusions from these which more careful observation would show to be quite unjustified. The literature is full of such conclusions. To explain some of these apparent contradictions it has been assumed that the infant possesses depots or stores of minerals that he may draw on during the first year at time of need, and that his body is therefore richer in some elements than it will subsequently be. This has not been proven except for iron, which, it is well known, his liver holds in excess. With this exception, from the time of birth until old age, the body becomes poorer and poorer in water and contains more and more salts.

The mineral metabolism of the artificially-fed differs greatly from that of the breast-fed infant. A comparison between the two is, therefore, well nigh impossible. The infant receiving cow's milk with its greater salt content, lives on a higher plane of mineral metabolism than does the one receiving breast milk. He absorbs 60 per cent. of the total

ash and retains only about 15 per cent., while the breast-fed child utilizes to the full his opportunities and absorbs 80 per cent. of the ash and retains 40 to 50 per cent. In the majority of instances this excessive salt intake undoubtedly does no harm; the surplus is not absorbed or is merely eliminated.

It is to the earthy alkalies and the alkaline bases that attention has chiefly been directed during the last few years. I have previously indicated the influence that the various foods may have on them. Sodium and potassium are usually well retained, unless severe diarrhea is present, due to any cause, and excess of fat or an excess of sugar. Under such circumstances they are lost, and the loss is badly borne and cannot indefinitely be continued. When all available alkalies have been drawn on, the infant breaks down his own tissue to furnish more of these substances, which is an explanation, for a part at least, of the excessive nitrogen excretion under such conditions. When diarrhea ceases and the intake is sufficient, a positive balance is rapidly instituted.

The metabolism of calcium has been largely studied on account of its close relationship to rickets and tetany. Calcium is so largely excreted by the bowel that it is impossible to say how much is absorbed, plays a part in the organism and is then excreted by the intestine, either because it is in excess or because, as in the case of rickets, the body cannot utilize it. This is also true of magnesium and to a much less extent of sodium and potassium. I have considered in detail the factors causing a retention and loss of calcium and the part played by protein, fat and carbohydrate. But in the study of the metabolism of rickets, these have rarely, if ever, been heeded. To cite a specific instance: In one study an infant on milk and cereal water was considered rachitic because he had a loss of calcium, and another fed on milk and malt-soup was considered non-rachitic because he retained calcium. In view of the work of Usuki and Stolte especially, the metabolism of rickets and tetany must be rewritten.

It was Finkelstein who first developed the conception that the sugar and salts of cow's milk, in the proportion in which they exist in cow's whey, were productive of much harm to the artificially fed infant, and were the cause of many, if not most, of the disturbances of nutrition. He emphasized that foods rich in whey were those on which infants developed their unfavorable symptoms, and that they were only cured by a diet in which cow's whey composed a minimum or from which it was excluded altogether. Finkelstein's contention seemed supported by Meyers' "*Austauschversuch*," in which he fed to the same infant human whey and cow's fat and casein, and later cow's whey and human fat and casein. When the human whey was given, the infant's digestion was normal and he gained weight. When cow's whey was given, he lost

weight and had marked diarrhea. This experiment was claimed to prove the unfavorable influence of cow's whey. Stolte has criticized the conclusions drawn from it. He pointed out that the proportion of fat, protein and calcium was improper for the production of formed stools when cow's whey was given, while when human whey was given, there was ingested at the same time fat and calcium from the curd, in exactly the right proportion to produce formed stools.

It has been a fact generally known for many years that infants with acute nutritional disturbances excrete sugar in the urine when receiving milk of any kind. This is usually lactose. Such infants have more or less fever at the same time. From clinical observations Finkelstein and Meyer came to the conclusion that the sugar and salts that were allowed to reach the tissues of the body unchanged by reason of the diseased intestinal wall had a toxic and distinctly pyrogenic action. Contrary as was this belief to the general conception of the causation of fever, it obtained support from the experiments of Schaps. Schaps injected dilute solutions of lactose and sodium chlorid subcutaneously and obtained a perfectly definite and more or less characteristic temperature rise, beginning four to six hours after the injection, reaching the maximum in eight to twelve hours and becoming normal again in twenty-four.

Since these results were published in 1906 a considerable literature, containing the results of a great number of experiments by different observers, chiefly in Germany, has grown up around the subject of sugar fever and salt fever. Febrile reactions have been obtained many times in different ways and a number of ingenious hypotheses have been proposed to explain the method of production of the fever.

In order to judge whether the results obtained are applicable to the question of infant-feeding and prove the dependence of fever and other untoward symptoms on sugars and salts taken in the cow's milk, let us consider how these experiments have been conducted. The sugars and salts have been given by mouth and by subcutaneous injection to normal infants and those with nutritional disturbances. When normal infants have taken by mouth at one time as much as 30 grams of sugar or even more, no fever results. At least this is the consensus of opinion of most of those who have experimented with them; and even when the huge doses were employed for the determination of tolerance, no mention was made of fever by Grosz, Nobécourt, Terrien, Keller and others.

With sick infants it is different. They will react, but by no means regularly; less than 50 per cent. will do it. The temperature rise is not usually high; indeed, it is usually only slight, and it is somewhat delayed. The fever is found as often after large doses of glucose and saccharose, as after lactose and nearly as often after maltose. The

quantity that produces this reaction is, moreover, very large, 30 grams at one time, as much as the infant would otherwise take in the whole day.

It is difficult to see how such experiments can be expected to have any bearing on the question of infant-feeding or to prove the pyrogenic effect of lactose in the proportion in which it is found in cow's milk. They show unmistakably that concentrated sugar solutions have a bad effect on sick infants and this has long been known. More than this they cannot do.

Similarly with the various salts with which most of the experiments have been performed. Normal children do not usually respond with fever. Those who have been or are ill do so. But to produce fever, even with the sick, an amount is necessary that would at once indicate the impossibility of drawing any practical conclusions so far as nutritional disturbances are concerned. Indeed, doubt, and a very substantial doubt, is at once thrown on the part that these substances are claimed to play in such conditions. Thus infants of $3\frac{1}{2}$ kilos and less have been given in a day $5\frac{1}{2}$ grams of sodium chlorid, or 12 grams of sodium phosphate, 5 grams of sodium bromid, 10 grams of calcium lactate, 10 grams of calcium acetate and other substances in like proportion. The quantity at one dose has been 3 grams and sometimes more. It is only fair to ask, as Salge has done, what such experiments are designed to investigate and prove, even if fever, collapse, vomiting, diarrhea, hyperglycemia, mellituria and great loss of weight are produced. These studies are toxicological studies and have no bearing on the nutrition of infants. It is no wonder that febrile reaction occurs after giving at one dose in concentrated solution, six, eight or ten times as much of a substance as would be ingested under ordinary circumstances in a day and in a very dilute form. It is not at all improbable that similar or perhaps more disastrous results would follow the ingestion of a similar proportion of the other food ingredients provided they could be given at one time.

Injection experiments have seemed to offer more suggestive results. Schaps obtained fever regularly with minute quantities of sugar and salt in healthy and sick infants when given hypodermatically. Gofferjé, Möllhausen, Rietschel, Meyer and Schloss and many others had the same results. Weiland and Tjulpin were not able to produce fever and Friberger produced it in only one-third of his experiments. But the negative results were disregarded on account of the preponderance of the positive ones. The subject has been studied with great zeal, and the greater activity of sodium in combination with the halogens and the inhibiting effect of the divalent bases on the influence of the monovalent bases presumably established. But carefully conducted animal experiments lend no support to these views. Helmholtz and Schultz in this

country, independently, investigated the effect of sugar and salt solutions on rabbits. Helmholtz could show no pyrogenic influence for salts nor could Schlutz for sugars.

The studies of Wechselmann with salvarsan injections by which he showed that a febrile reaction frequently followed the use of distilled water if not immediately sterilized, and that the febrile reaction was absent if sterilization closely followed distillation, offered another field for inquiry. So also did the studies of the Lister Institute of Preventive Medicine in London, where it was demonstrated that salt solution or water is not free from pyrogenic properties even after all organisms have been destroyed by heat. Samelson, therefore, made a series of experiments with children less than 3 months of age, when they are supposed to be most likely to react. He used 20 to 80 c.c. of an 0.8 per cent. sodium chlorid solution freshly distilled and freshly sterilized, in all, seventeen times. No fever was ever produced and none of the other symptoms usually following injections. Fever was frequently produced when ordinary distilled and sterilized water was employed. The results that Bendix obtained were even more instructive. He injected seventeen infants with 50 c.c. of a 0.75 per cent. solution of salt and produced fever fifteen times. He then found that the water that had been used had been distilled the evening before and not been sterilized until twelve hours later. He therefore repeated his experiments, using freshly distilled and freshly sterilized water, and produced no fever and no symptoms in any single case. It appears, therefore, that there is no satisfactory proof that sugar or salt hypodermatically has a pyrogenic effect, and that experimental evidence that would show that the sugars and salts of the whey are responsible for fever and the chain of constitutional symptoms associated with it, is lacking. It may be that they act indirectly in injuring the cells of the intestinal tract so that other substances, perhaps bacterial, are absorbed. It may be that they act in a variety of other ways, but their own direct and damaging influence has not been proved, and has been, undoubtedly, greatly overemphasized.

The reasons for the difficulties or the failures with artificial feeding are at times sufficiently apparent. At others no fault, so far as one's experience goes, can be found, and yet the result may be far from satisfactory. This is more apt to be true of methods designed to correct some existing disturbance than it is of those employed with the normal infant. What is the explanation of failure with these?

Biological reasons have been offered and the influence of the prevalent views of workers in biological laboratories is reflected in these reasons. I have already referred to Hamburger's views on "*arteigenes*" and "*artfremdes Eiweiss*," and the effect that the latter might exert on the immature organism. This was when the distinction was drawn between

homologous and heterologous compounds. In recent years the idea of anaphylaxis has crept into the discussion. This has been equally incapable of shedding light on the ordinary problems of nutrition. The diatheses have, therefore, been called on. Here we enter a very large and indefinite field.

The conception of diatheses first arose in an endeavor to explain the different degree of susceptibility and the different resistance manifested toward infection. Now they are used in questions of nutrition to explain what cannot be accounted for on a purely chemical basis. These diatheses are not sharply defined. The "scrophulous diathesis" has gradually disappeared, its place to be taken, in the non-tuberculous cases, by the "exudative diathesis" of Czerny. A lymphatic diathesis has been described, a thymico-lymphatic, an arthritic and a neuropsychopathic. The French have a different classification from the Germans and no two authors agree. If a conception to one seems too narrow it is broadened by combining two diatheses, as in the neurolymphatic; and finally all possible constitutional abnormalities and predispositions have been massed together and called "*Oxyopathie*" by Stoeltzner.

The only diathesis, except for the pathological status thymico-lymphaticus, that rests on a tangible basis is the "exudative diathesis" of Czerny. It has been shown that infants exhibiting symptoms of this usually utilize their ingested fats less well than the average and that their symptoms are increased by fat; that they have frequently hyperglycemia and alimentary mellituria, even with a small carbohydrate intake, and that they show a marked tendency to retain salt and water in their tissues. It is a question, however, how much light this conception of diatheses has brought to the subject that now interests us; probably not much. It has certainly tended to confuse.

We are thus left without an adequate explanation for many difficulties and many failures. This gives an incentive for future work.

20 East Eager Street.