



The Management of Diabetes in Children

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I think the time will come when we will all agree that diabetes mellitus is indeed the most common endocrinopathy, and that if we live long enough, at least 25% of the people in this room will develop diabetes. I believe that diabetes has manifestations both as a homozygous and heterozygous state, and that the heterozygous state or so-called carrier state becomes clinically manifest as we get older. Now I am not sure that such diabetes has the same significance as diabetes coming on earlier in life. It may be a benign type of diabetes, but at any rate, it is common.

The problem of diabetes of childhood onset is of tremendous importance because here we see diabetes in its most florid state, and here we see most clearly its devastating end results in certain patients. Here, at this moment, we stand by helplessly watching the evolution of some of the problems.

INCIDENCE AND DIAGNOSIS

It has been estimated that 5% to 10% of the total diabetic population has the onset of diabetes during childhood. I do not know how accurate these figures are since we do not know how common diabetes is. Diabetes in children, in contrast to adults, is characterized by the presence of symptoms. Adults, as you know, can go for years and not know they have diabetes because it is asymptomatic and often demonstrable only by glucose tolerance tests. This is not true in children.

In looking over the records of several hundred children with diabetes, one finds that polyuria, polydipsia, weight loss, polyphagia and fatigue are present in 90% or more of the children. These are the classical symptoms that we ordinarily associate with diabetes, although they are not present in the majority of adults. About 20% of childhood diabetics are first diagnosed when admitted to the hospital with diabetic acidosis. Often the diagnosis of diabetes is not suspected early and is actually made in retrospect. Practically everything else may be done in the case of a youngster who is having anorexia, nausea, and vomiting, including a gastrointestinal series, but not a blood sugar determination or a urinalysis. The recurrence of bed-wetting in a previously trained child pointed to the presence of diabetes in 13% of these patients.

More than half the children with diabetes are diagnosed in the first 30 days. That is because the disease is symptomatic. However, there are some who apparently go on for periods of months or perhaps for as long as a year or two without diagnosis. January is the month in which diabetes is diagnosed most frequently and one wonders why this is so. Of course in the North one can say that it is the time of year when respiratory infections are present and this would make diabetes worse. There are those of us who might feel that overindulgence, particularly at Christmas-time, has something to do with it.

There is a fairly symmetrical distribution curve of the age of onset

of diabetes in childhood. The youngest diabetic on record is one diagnosed by urine test within an hour or two of birth. The youngster did have permanent diabetes and still has it, but is doing well now some 10 or 12 years later.

Diabetes occurs in families. Particularly one finds that the grandmothers of a diabetic on both the maternal and paternal side have diabetes. This does not necessarily mean that there is such a striking difference between grandmothers and grandfathers, but it probably reflects the fact that grandmothers live longer than do grandfathers. At the time the diabetes is diagnosed, one can obtain a history of known diabetes in some relative in approximately 20% of the patients. If one waits a period of five years and surveys the group again, this percentage increases to 60%. What happens is probably that other members of the family are tested, or with the passage of time, diabetes appears in the others.

THERAPY

Diet

Once the diabetes is diagnosed, one is faced with the problem of therapy. There are many choices open to us. With regard to diet, in general we take the attitude that children will eat, and that if children are properly brought up, they will eat the same kind of diet that we would prescribe. Indeed this is the custom that we follow. We begin with an approximation based on calories per kg, starting at birth

with 125 calories per kg, and decreasing to 40 to 45 calories per kg when the body weight reaches 60 kg or 130 lbs. One can use this approximation as a starting point. If the youngster says he is hungry, we give him more food. If he cannot eat it all, we give him less. When we get through, actually the youngster is selecting his diet. Not everyone practices this approach, and indeed we do not try to do this with every patient. There are some patients or families who derive tremendous reassurance from a program based on careful measurement of food intake. But by and large, most patients over the long pull object to a precise regimen. This represents not necessarily a yielding to their wishes, but rather an attempt to "custom-tailor" the program to meet the needs of the majority of children with diabetes.

The diets outlined by the American Dietetic Association provide a large number of calories from fat, as high as 45% to 50% of the total calories. We think that all Americans eat too many calories, too much fat, and too much saturated fat. A better diet for us, diabetic or non-diabetic, would be one that restricted calories, restricted the amount of fat to some figure around 30%, and increased the proportion of unsaturated fat. This may or may not have any relationship to the problem of atherosclerosis, but it would seem reasonable to adjust our diets in this direction.

Insulin

Virtually all children require in-

sulin, in contrast to adults. The reason, of course, is that they require insulin not only for energy purposes, activity and so on, but also for growth. The mean dosage of insulin is approximately 1 unit per kg body weight, but this is just an average dose, and does not apply to every patient with diabetes. You must give a quantity of insulin sufficient to meet the need. There is no rule of thumb that we can give to the house officers as much as they love the one plus, 5 units; two plus, 10 units, and so on. This is not a rational way of treating diabetes at any age, and certainly not in the case of children.

When diabetes begins, it is possible to demonstrate in approximately two out of seven patients a responsiveness to the sulfonylurea oral drugs. But at the end of a year or two, virtually all of them are no longer responsive. In other words, it is most unusual to find a child with diabetes who does not need insulin, and who can be maintained on diet alone or diet and oral hypoglycemic agents. I do not say that there may not be a place for phenformin (DBI) in the treatment of some diabetic children. This drug, used in conjunction with insulin, will often smooth out the lability which so characterizes juvenile-onset diabetes.

PROBLEMS IN REGULATION

The problem of "brittle" diabetes is often a vexing one in juvenile diabetics. Many patients are sent to us who swing between hyperglycemia or ketosis and hypoglycemia.

When I see these patients, the first thing I look for is a "brittle doctor." Often the physician has the idea that children with diabetes should be so perfectly regulated that all urine sugars are negative and the blood sugar normal at all times. This goal is perfectly reasonable in many adult diabetics, but you cannot do this with children. If you try, you are forcing a square peg into a round hole. The child will inevitably have hypoglycemic reactions, with rebound hyperglycemia and often acetonuria afterwards, and his diabetes will really be "brittle." You will most often have to let the child spill some sugar to avoid hypoglycemia at other times.

The next consideration with the "brittle" diabetic is the patient himself, or his family. Are they so obsessed with the goal of sugar-free urine tests as to bring on hypoglycemic reactions with the same consequences.

Then we look for inadvertent overinsulinization. This can sometimes be demonstrated by taking the patient who is receiving 90 or 100 units per day and reducing the dose to 30 units. Sometimes you find that he does just as well, or just as badly, and sometimes you find that he does a great deal better. Repeated insulin shocks, sometimes unrecognized, may be making the diabetes worse, and this can be corrected by lowering rather than increasing the dose.

And we also look for liver disease which is occasionally a cause of brittleness, because the liver cannot adequately store glycogen to buffer the blood sugar level.

By the time we have considered all these possibilities, the brittleness has usually disappeared. If you remember that even precise regulation of diabetes does not guarantee freedom from vascular disease, you can begin thinking of your patient not as a diabetic, but as an individual, with the same problems as anyone else, of growing up and becoming a useful citizen. Please understand that I am not promulgating the idea that you should ignore the blood sugar or the glycosuria, or that you should not regulate the diabetes as well as you can. I am saying that when you strive for perfection in this regulation, you may defeat your own purpose. The price you pay may be too great for the product you get. Indeed, you may get nothing at all.

A true physician does not really alter many things. Often his role is that of an observer, a confidant, a philosopher. If you admit this to yourself, and can approach the problem of regulation of diabetes in a child without preconception or emotional involvement, it is sometimes amazing to see how the tension is relieved in a household, and how much better a youngster does when you get away from urging him to a goal he cannot reach.

GROWTH AND DEVELOPMENT OF THE JUVENILE DIABETIC

Once the patient is started on diet, insulin, and urine testing, we have to consider growth and development. When the diabetes is diagnosed you will note that the diabetic patients are generally just about as tall or sometimes a little shorter than their non-diabetic peers. This is interesting because it used to be said that children are taller when they develop diabetes than their non-diabetic peers.

After treatment for a period of 5 or 10 years, we find that the diabetics are shorter than their peers even though they start off approximately the same. This is not a new observation. Prior to the advent of PZI insulin in 1936, diabetes in

children was the commonest cause of dwarfism. With the use of PZI insulin and more adequate programs of regulation, frank dwarfism disappeared. Apparently this tendency to be shorter than the population as a whole is still left. Whether this is nutritional or genetic I am not sure.

In contrast to adults, diabetic children seldom present the problem of obesity. Usually the children are of average or below average size, and they continue to maintain this position relative to non-diabetic children.

An interesting finding is that if you obtain gastrointestinal x-rays on 100 youngsters with diabetes, you will find abnormal patterns in the duodenum in approximately 18. Twelve of these will represent duodenal deformities that appear to be inactive and six of them will represent an active ulcer. This is a surprising finding, although pediatricians are finding more peptic disease in children generally than was formerly suspected. It has some importance because when a diabetic child begins to have nausea and vomiting, we think of diabetic acidosis, but rarely think of an acute ulcer.

EMOTIONAL IMPACT OF DIABETES IN THE CHILD

Another aspect of therapy which is exceedingly important has to do with the emotional patterns of these diabetic children. Any family that has a diabetic child, or indeed any child who is in any way less than perfect, experiences a sense of guilt. Now this sense of guilt may be manifest by projection upon the professional people around them. These are the people we find difficult to deal with, but we can succeed in winning them over. The mother and father may become overprotective about the child. They will team up with a pad and pencil and they will mark down every single event in the life of this child. When they take the child to the doctor, both parents are often pres-

ent and are anxious to do exactly the right thing.

The youngster has one of several choices. One choice is to comply; this is perfectly acceptable up to the time of adolescence. But adolescence normally includes a period of rebellion which is a normal manifestation of growing up. The child has to disavow his family so that he can set himself up as an individual. He can come back into the family circle afterwards, but if he is overprotected and does not rebel, he does not mature. Experience indicates that diabetic children, as a group, are emotionally immature. You have to be very careful because you can be confused into thinking that they are well-organized and mature, because they are asked to assume responsibilities such as urine testing and abiding by diets and administering their own insulin. Teachers and everyone around them think they are maturing very well. They may be maturing physically, but not emotionally. This is manifest later on in life by poor scholastic records, by poor employment records, and by poor marital records. This is one pattern that evolves.

Another pattern is one of undue rebellion on the part of the youngster, because there is no more effective weapon than an insulin hypoglycemic convulsion or a diabetic keto-acidosis to extract practically anything that one wishes from parents and those about him. This is the type of youngster who is best handled by removing him in every way except environmentally from parental supervision. The physician should deal with him on a kind of man-to-man basis, pointing out that this attitude could mean self-destruction. This kind of behavior may also be present in adults who did not develop diabetes in childhood.

SPECIAL COMPLICATIONS

I should like to turn to some of the incidental events that occur in the lives of these children. Let us

consider diabetic keto-acidosis and coma. In our experience these youngsters develop coma once in five years. Now this does not mean that they have to. Some patients never develop it, and we have had some that have coma every month for 12 months in a row. There should be a low mortality associated with keto-acidosis and coma in a child that is known to have diabetes. The deaths that have occurred have invariably occurred in previously undiagnosed diabetic children, who, as I have indicated, are often admitted to a hospital and studied for all types of entities other than diabetes. When the diabetes has reached the point of no return, the diagnosis is made and they are transferred to a medical center, but it is too late then. Another difficulty is that they sometimes get into hospitals where the staff is not experienced in dealing with keto-acidosis in general, especially in children, and mortality ensues. There are about 200 deaths a year from diabetic keto-acidosis in children in the whole country.

The big problem we are left with is that these youngsters are heir to small blood vessel lesions which involve the kidneys and the eyes, and possibly the blood supply to the nervous system. This microangiopathy, or tri-angiopathy, consisting of retinopathy, glomerulosclerosis, and neuropathy, is present in every single child that has had diabetes for any period of time. One of these, glomerulosclerosis, is present at the time diabetes is diagnosed. In these patients, there is a thickening of the capillary basement membrane, which we recognize as diffuse glomerulosclerosis, and it is present at the time the diabetes appears. Indeed it can antedate the carbohydrate disturbance. Studies demonstrate very clearly that in identical twins, one of whom has already developed diabetes and the other still has a normal glucose tolerance test, such changes in the basement membrane of the glomeruli are already present in the non-diabetic twin.

We cannot, therefore, speak of prophylaxis when something is there before we know that the patient has diabetes. Fortunately, this is not meaningful in terms of survival in the majority of the youngsters. However, it is true that after 15 years of diabetes, some 40% of them have proteinuria. The commonest cause for this is glomerulosclerosis. But the damaging statistic is that after 25 years, 25% of them have died from uremia on the basis of the Kimmelstiel-Wilson syndrome.

The other problem, that of retinopathy, is equally devastating, but only in a minority of the youngsters. After 7 or 8 years there is tortuosity and dilatation of the retinal veins, and after 9 or 10 years microaneurysms may appear. After 15 years, the incidence of microaneurysms is 80%, and after 25 years, it is 100%. Microaneurysms are nothing to worry about; they can come and go and they need not concern us. The dilatation of the retinal veins is unimportant. What we are concerned about is the appearance of neovascularization (new blood vessel formation), and of retinitis proliferans, with resultant scarring. Finally there occur preretinal hemorrhages, and hemorrhages into the vitreous, resulting from the neovascularization and the retinitis proliferans. The end-result is blindness. I cannot give you any specific figures as to how many diabetic youngsters ultimately develop blindness, but it is well known that diabetic retinopathy is the most common cause of blindness of recent onset in young adults in the United States today.

The third member of the triad of small blood vessel lesions is neuropathy. We think that this may have a vascular basis also. A large percentage of the youngsters will ultimately have evidence of neuropathy at some time, but there are usually no clinical manifestations. You can show changes in vibration perception, or absence of the ankle reflex in some, but these have no meaning.

We cannot promise any of these patients that if they abide by an optimal regimen they will be freed from these hazards. I would not want to say that their chances of avoiding these hazards are not improved by a strict regimen, but we cannot be sure of this. Statistics supposedly bearing on this question are very difficult to interpret.

The last point I want to make has to do with atherosclerosis. With the survival of these children into young adulthood and into middle age, we are faced with the early onset of atherosclerosis, and its more extensive presence, with the hazards of myocardial infarction, peripheral vascular disease, and perhaps strokes. These complications may occur when the juvenile diabetic reaches young adulthood, or later. If we are on the right track with regard to atherosclerosis in the population as a whole, perhaps changing the diet given to these youngsters or to diabetics in general will make a difference, as we hope it will in the non-diabetic population.

As time goes on it becomes more and more apparent that there is a merging of atherosclerosis and diabetes. There is increasing evidence that the patient who comes in with a myocardial infarction has often been an unsuspected diabetic. In tackling the problem of diabetes in both adults and in children, you are not only dealing with a devastating illness, a metabolic disturbance, which affects a minority, but at the same time you are working with a problem which will ultimately afflict the majority of any population group.