The Young Diabetic

Panel Discussion

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Moderator

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MODERATOR WHITE: The most important age periods in the management of the juvenile diabetic patient are infancy and adolescence. Some physicians dread the management of diabetes when the patient is under five years of age. The condition sometimes seems difficult to handle and it places extreme strain on the morale of the patients. Dr. Guest, what is your advice in regard to the diabetic infant?

DR. GUEST: In my opinion diabetic infants are not necessarily more difficult to manage than older children. I should say that the age of adolescence is a much more difficult period than that of infancy, but then of course, other problems are involved. As most of you know, I recommend the so-called "free-diet-glycosuric" regime which is a subject of continuing debate. (See editorials in DIABETES: 1:487-89, Nov.-Dec. 1952.) In our clinic we have eighteen diabetic infants with onset of diabetes under the age of two years. Of these, eight were under one year of age when symptoms were first recognized. The youngest started glycosuria at nine days of age. The diagnosis was made by the astute mother because she had another diabetic child then aged one and one-half years. When she noted the new infant was passing a lot of urine, she tested it and found sugar. On admission to the hospital, the baby's blood sugar was 350 mg. per 100 cc. The urinalysis showed 3-plus glycosuria but no ketonuria. During twenty-four hours we determined the blood sugar every two hours and found it fluctuating between 300 and 500. Because there was no ketonuria, we felt that a period of observation before starting insulin would do no harm. After that brief period of observation the baby was given an initial dose of three units of protamine zinc insulin. During the next twenty-four hours the blood sugar fell progressively (determined at two-hour intervals) to 150 and then 100. Again, three units of protamine zinc insulin kept the blood sugar within normal range. (Let me stress the necessity for microchemical methods for following blood chemical changes in infants, whether diabetic or nondiabetic.) The baby was sent home on the fifth day, receiving two units of protamine zinc insulin daily. He was breast fed for ten months, on a demand schedule, with the dosage of protamine zinc varying from one to three units daily and solid foods offered at usual ages. (Please note that breast feeding is the ultimate in "free diet," while it lasts!) That child is now seven years of age and has not suffered any illness that required hospitalization. His urine is rarely free of sugar, but excessive glycosuria with polyuria is likewise rare. Transient ketonuria has occurred occasionally during intercurrent infections, but has always cleared up promptly with the administration of extra doses of quick-acting insulin. The insulin requirement increased slowly with age and increasing body weight, from five units a day at one year of age, to thirty-five units (globin insulin) a day at the present time.

Other practical suggestions may be pertinent here as a guide to facilitate the mother's daily routine of urine tests. Don't forget that if taken quickly a few drops of urine easily sufficient for testing for both sugar and acetone can be squeezed from a wet diaper. Another method we have used is to place a wad of absorbent cotton in a paper or soft plastic cup inside the diaper. The cotton retains a generous amount of urine that can be squeezed out easily. Also, there is a transparent soft plastic triangular diaper now on the market with a

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long tip to catch the urine. To obtain the urine sample the tip is simply cut off with a scissors to allow urine to run into a beaker. It is important to recommend to mothers all possible simple practical aids to facilitate home management of the diabetic infant.

I should like to stress the importance of alertness to avoid the crisis of ketonemic acidosis, insisting on the dictum that severe acidosis and coma should *never* occur if extra doses of insulin are given promptly when needed. Parents who fear insulin reaction are apt to decrease or omit insulin if an infant refuses food or vomits. They must be warned that the insulin requirement increases sharply during infections. Regardless of food intake they should be prepared and alert to give extra doses of insulin promptly if glycosuria increases and is accompanied by acetonuria.

MODERATOR WHITE: Thank you, Dr. Guest. Would you care to discuss the problems of the adolescent, Dr. Kennedy?

DR. KENNEDY: If we could solve the problems of the normal adolescent, we might begin to solve the problems of the diabetic adolescent.

The diabetic child is likely to have been fairly cooperative until he reaches adolescence when he begins to want to behave just like his fellow boys and girls. I think that many of the problems of this situation are best solved by trying to reason with these youngsters and helping them to adjust to a regime that will allow them to be as nearly like their friends as it is possible to be. Perhaps we have to modify our ideal program in handling the adolescent. Perhaps this is a period of life when diet freedom can with good reason be increased just a little, hoping that the need for this is temporary and will not establish a rule that will be carried beyond the adolescent stage.

However, at the same time as the youngster needs a little more freedom, he also begins to cooperate in other ways. He becomes more intelligent and you can reason with him a little more. He can respond to the education about diabetes more effectively. He is beginning to become an adult. You can look forward to a period following adolescence when better control returns and when stabilization of the diabetes becomes easier. Therefore, we can have hopes for the future and this helps us get through what is a very trying period.

Let us not forget, if you as a physician have established a relationship with your young diabetic patient which is ideal—one of trust, one of confidence, one of mutual exchange of ideas and cooperation—you are going to find far less trouble with him or her during the adolescent period than you will have if you are strangers apart and not able to cooperate with each other.

MODERATOR WHITE: A very important question is: How do you make the diagnosis of diabetes in children? Dr. Harwood?

DR. HARWOOD: It is not greatly different from the diagnosis of diabetes in adults. Glycosuria in the child is perhaps less apt to mean diabetes, but the diagnosis in the end will depend, as it does in the adult, on the blood sugar. A pathological blood sugar level in childhood has the same significance as it does in adulthood.

MODERATOR WHITE: We are dodging the issue, what is the diagnostic level for the blood sugar?

DR. HARWOOD: In general, I should say that a fasting blood sugar of 120 or higher, by the Folin-Wu method, is pathologic. A postprandial blood sugar of 200 mg. is also to be considered abnormal.

DR. GUEST: The fasting blood sugar level often may not offer critical help in the diagnosis of juvenile diabetes. A postprandial blood sugar is usually just as informative as a complete glucose tolerance test and nearly always will disclose frank diabetes. During a period of insidious onset of diabetes in children, with mild manifestations, the morning blood sugar level after overnight fasting may be even lower than normal; but it will be high after generous meals.

DR. HARWOOD: I didn't mean to imply that if the blood sugar was under 120 that that excluded the diagnosis of diabetes. In mild diabetes it is extremely common for the fasting blood sugar to be normal; yet the blood sugar after a meal, or a glucose tolerance test, may disclose the presence of diabetes. I think a test taken between an hour and an hour and a half after a hearty carbohydrate meal is to all intents and purposes a sugar tolerance test, and I prefer to get a blood test at that time rather than fasting.

QUESTIONER: How can you be sure about diabetes by a one-hour test? Suppose you have liver disease, or rapid emptying of the stomach, and why not a two-hour test?

DR. HARWOOD: Of course, one has to consider the patient's general condition in interpreting a single blood sugar test. If a patient has a condition known to affect carbohydrate metabolism, such as cirrhosis, thyrotoxicosis, and acute illness, one must be more cautious in diagnosing diabetes from a single abnormal blood sugar.

ROBERT L. JACKSON, M.D., (*Columbia, Missouri*): I should like to ask about the comments of Dr. White with regard to the accelerated needs of insulin in terms of one to three years after the initial regulation of the patient. It has been our experience (my associates and I

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are analyzing data at the moment) that the linear growth is very intimately associated with its acceleration which we are seeing primarily after six weeks, three months, or certainly within the first six months after the initial regulation. As soon as the metabolic stores have been recovered and the patient transitorily has a chance to catch up, he will then start growing in height and concurrent with that his insulin requirement will follow a definite pattern highly correlated with his growth from there on. We have not observed the delay that was mentioned.

MODERATOR WHITE: I think I made the time element a little too specific. It was really approximate and I agree absolutely with Dr. Jackson's remark.

QUESTIONER: I should like to ask two questions: The first one, your definition of potential diabetes as evidenced by blood sugar findings in the glucose tolerance test. The second, the normal values fasting one-half hour, one hour and two hours after the ingestion of 100 gm. of carbohydrate?

MODERATOR WHITE: I think that was addressed to you, Dr. Harwood.

DR. HARWOOD: I try to avoid making a diagnosis of "potential diabetes" from a glucose tolerance test. As to the normal figures for a glucose tolerance test they are: fasting, 80 to 110 (using venous blood by the Folin-Wu method), in one-half hour 140 to 160, falling to normal in two hours, and in three hours the figure is often lower than the fasting level.

DR. KENNEDY: Dr. White, may I insert a practical note here.

MODERATOR WHITE: Please do.

DR. KENNEDY: In my experience the development of diabetes in the juvenile person is usually rapid. If we are seriously in doubt after applying all these scientific tests and can't say definitely the child is either perfectly normal or definitely diabetic, don't you think it might be safe to observe him closely and wait a few weeks? I realize that it is an advantage to find diabetes as early as we can. However, I don't think it is right to take a chance and treat a possibly normal child as though he were a diabetic on the suspicion that he just might possibly develop diabetes.

MODERATOR WHITE: Is there a definite correlation between added insulin requirement and dosage of cortisone, hydrocortisone or corticotropin? Will you answer that question, Dr. Guest?

DR. GUEST: This question regarding corticotropin directs attention to the role of various factors of stress in the diabetic; this certainly merits discussion. Adrenal cortical stimulation may be an important trigger mechanism that influences the onset of diabetes. Perhaps this mechanism is involved when a child suddenly develops frank symptoms of diabetes after infection (for example, streptococcal sore throat). In our hospital we recently observed the development of diabetes in a girl aged two and a half years who had suffered from severe asthma since the age of fourteen months, and who was treated with several courses of cortisone (each giving some relief of asthma) at various times from the age of eighteen months onward. After an unusually severe attack of asthma and another course of cortisone, she suddenly developed polyuria and glycosuria with persistent hyperglycemia. There was a family history of diabetes in a paternal aunt with onset at seventy years of age. We concluded that in this child, potentially diabetic from birth, the stress of asthma plus the administration of cortisone might have acted to precipitate manifestations of frank diabetes. Several investigators have reported that the administration of corticotropin or cortisone in nondiabetic persons leads to elevation of blood sugar, and in the diabetic patient to increased "insulin resistance." This effect disappears when the administration of corticotropin or cortisone is stopped. It is the "potentially" diabetic person (with genetic factors usually disclosed by a family history) that factors of stress may constitute a trigger mechanism.

MODERATOR WHITE: Here is a question we can all answer quickly and briefly. What growth standards do you use?

DR. GUEST: We have used Wetzel's grid, also the standards of Dr. Jackson and Dr. Harold Stewart.

MODERATOR WHITE: Dr. Kennedy, have you found choline to have a favorable effect in regard to insulin requirement?

DR. KENNEDY: I don't think choline has any place in our therapeutic armentarium at the present time.

MODERATOR WHITE: This is a very important question—what does the electroencephalogram show in the young diabetic who has many episodes of hypoglycemia?

We find that there is often an abnormal pattern; under stress slow waves may appear. Such patients may be subject to many questionable insulin reactions. When treated with phenobarbital or Dilantin or other anticonvulsant the episodes may disappear and it may seem easier to control the diabetes. In our experience this therapy usually has to be continued for about a year, perhaps two; then it can often be discontinued.

QUESTIONER: Dr. Kennedy, you have emphasized the advantage of multiple injections. Why are two doses of long-acting insulin necessary in the younger group of diabetics? Is its action more quickly dispelled or is it

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destroyed by anti-insulin factors or some other factor?

DR. KENNEDY: If we give two doses of x units each of a long-acting insulin at twelve-hour intervals, the resultant rate of insulin absorption is much steadier than that obtained from one dose of 2x units each twenty-four hours. With the two-dose schedule, the absorption peak of one injection may coincide with a period of low absorption from the second injection, thus providing insulin to the body at a relatively constant rate. This effect is desirable in certain cases.

MODERATOR WHITE: Dr. Harwood, will you answer a question on diabetic coma? In the case of a girl aged thirteen years, the daily insulin requirement rose from twenty-four to eighty units after coma. Is it customary for the insulin requirement to rise very much after coma? Does the requirement remain high if it does go up?

DR. HARWOOD: It is my impression that there tends to be a slight increase in the insulin requirement following coma, but it is not always so. More regularly, however, there is a period of remarkable instability after severe acidosis. We have all seen the insulin requirement rise markedly and unaccountably after several years of diabetes, with or without coma.

QUESTIONER: Dr. White, did any of your patients who needed less insulin postpartum not have estrogen therapy?

MODERATOR WHITE: Yes, 5 per cent of the patients had no estrogen therapy.

In an unselected sample of our obstetrical diabetic population, if we divide the patients who received female sex endocrine therapy into two groups, with onset of diabetes under the age of fifteen, and with onset above fifteen years, 60 per cent of those whose diabetes started in childhood took less insulin after termination of pregnancy than their usual adult dose of insulin. Fifty per cent of these had more than a 50 per cent drop and 17 per cent of these had more than a 75 per cent drop. In contrast to this, those patients with onset of diabetes above the age of fifteen years had a 50 per cent drop in only 5 per cent of the group.

QUESTIONER: Is there a fixed scale of insulin dosage according to the amount of sugar shown by urine tests—5, 10, 15 or 20 units of insulin when the tests are 1-plus, 2-plus, 3-plus, or 4-plus? Sometimes insulin ordered after operations according to this scale has led to reactions—when 20 units of regular insulin have been given for 4-plus urine.

MODERATOR WHITE: Of course all insulin prescriptions have to be individualized for the patient, taking into account the requirement of the patient in the pre-surgical period, the age of the patient, and the impression of the severity or type of diabetes. There is no such fixed prescription which we use for our patients. The precipitation of hypoglycemia following surgery has been emphasized. After a glucose infusion, the first urinalysis may show sugar; this should be discarded and a second specimen should be used to guide the adjustment of the insulin dosage.

Dr. Harwood, I think you have more questions on diabetic coma.

DR. HARWOOD: How would you manage the patient in diabetic coma of long duration when the blood sugar is approximately 220 to 250 mg., particularly in respect to insulin dosage and earlier administration of glucose? I would use smaller doses of insulin and watch the blood sugar to see whether the smaller dosage was effective in lowering the blood sugar and relieving the ketosis. I suggest a dose of twenty to thirty units for a child, and forty to fifty units for an adult.

Again, in a patient with a blood sugar that low and with severe ketosis, I think it quite reasonable to start the administration of glucose earlier than one in a case in which the blood sugar is very high.

ROBERT L. JACKSON: I should like to make one comment. I think it is most important in children to base the insulin dosage on body weight rather than on a specific figure. I think one may really get in trouble in considering doses of ten, twenty, or forty units without regard to the body weight of the patient which of course varies tremendously from infant to full adult size.

MODERATOR WHITE: Dr. Guest, have you any comment?

DR. GUEST: On this question of insulin dosage, I feel strongly that it is not desirable or possible to arrive at a fixed dosage for long periods of time. The patient who is self-dependent and well trained can adjust the dosage of insulin daily, according to need. I might cite a case in point (Pediatrics, 1953, page 756). A boy, aged fourteen years, admitted to hospital in coma at the onset of the disease, remained in the hospital for seven days, then went home with his indoctrination seemingly complete, to live on a farm. He went home taking 100 units, a mixture of protamine zinc and regular insulin. During the next month he decreased the dosage, being guided by daily urine tests, until he got down to five units a day. He required only five or ten units of insulin a day between February and the end of March when he suddenly got a sore throat. According to the mother, when the family physician came to call and found the boy had lots of sugar and acetone in the urine he said, "Well, I'll treat his sore throat with

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antibiotics, but I don't know anything about diabetes." The boy promptly said, "I do!"

The chart made from the record he kept through this whole period showed that during two days he increased his insulin dosage again up to 100 units. With his sore throat recovered he went back to school still taking 100 units. Again his glycosuria diminished rather rapidly and during the next month he decreased his insulin to ten units. He went through both periods of decreasing insulin requirement without ever having had an insulin reaction.

QUESTIONER: Does the blood lipid or cholesterol content parallel the degree of vascular sclerosis in infants?

DR. KENNEDY: Vascular sclerosis in infants isn't common enough to make us worry about this.

QUESTIONER: Please discuss the role of dietary fat in the prevention of vascular lesions in juvenile diabetes.

MODERATOR WHITE: There has been some excellent work by Kinsell and his associates who have shown that fat of vegetable origin appears to be less harmful than fat of animal origin. More and more we are thinking in terms of oleomargarine, peanut butter, olive oil and so forth.

QUESTIONER: In regard to the decreased insulin requirement of women in the puerperium, how long does it last? Do they continue their improvement? Are multiple pregnancies favorable, and shall we recommend frequent pregnancies and childbearing?

MODERATOR WHITE: Well, literally, we are doing that. The second and third pregnancies appear to be more favorable in lowering the insulin requirement than the first. The longest duration of lowered insulin requirement that we have observed has been ten years and the patients who showed this improvement have not gone back to their former high dose level. Dr. Jackson asked me if we could explain it on extra activity of the patient taking care of children and extra care in the diet because of added responsibility. We have weighed all of these things and do not think that that is the explanation for the altered requirement.

QUESTIONER: Do you recommend the use of salt by mouth in the early stages of acidosis before fluids are needed intravenously?

DR. HARWOOD: That is a good question. Sodium and potassium salts, carbohydrate and water all have an effect of protecting the patient to a certain degree from acidosis. If a patient is still able to eat or to drink, there is often no need for intravenous fluids. Frequent small feedings, with insulin ordered according to test, may be all the treatment needed in early acidosis.

MODERATOR WHITE: Hypoglycemia is a very serious problem in the young diabetic, and a question has been submitted regarding permanent damage. Dr. Guest, will you answer that?

DR. GUEST: It is something we all worry about. There are several cases recorded of children, apparently mentally normal, who showed evidence of cerebral damage and feeble-mindedness following a very severe prolonged hypoglycemic reaction.

MODERATOR WHITE: Dr. Harwood, I think you have a few more questions on diabetic coma.

DR. HARWOOD: Is there an explanation for the extreme restlessness one sometimes encounters in a coma or acidotic patient? I can think of several explanations. Nausea, vomiting, and abdominal pain can make the patient restless. So can peripheral vascular collapse. The discomfort of air hunger may also contribute to his restlessness. I have observed restlessness in patients developing the syndrome of potassium deficiency, and I suppose it may be due in part to weakness of respiratory muscles.

MODERATOR WHITE: A question has been asked regarding the earliest age at which aneurysms in the ocular fundi have been observed. Dr. Guest says he hasn't seen any in children. I must admit that I have but they are extremely exceptional in childhood years. I have seen one at the age of fourteen. This child developed diabetes in 1922 and her past history had been characterized by many bouts of ketoacidosis.

QUESTIONER: We have been told the evils of giving too little insulin over long periods. Is it desirable to give as much insulin as possible without producing hypoglycemic reactions? And, should the insulin dosage be pushed up to tolerance?

DR. KENNEDY: I remember the statement of Dr. Francis Lukens, "The dose of insulin is *enough*." Of course we should give as much insulin as necessary to allow complete utilization of an adequate diet without producing hypoglycemic reactions. In other words, insulin dosage should be pushed up to tolerance assuming *that dietary intake is proper in amount and hypoglycemic* reactions are minimal in number and severity.

QUESTIONER: What is the role of fructose in the treatment of diabetic acidosis?

DR. HARWOOD: I have had no experience with the use of fructose. I have read that a goodly percentage of it, something like 60 to 70 per cent, becomes converted to glucose in the course of its metabolism and, therefore, I should feel that it is perhaps not a good thing to use in the early hours of treatment of diabetic acidosis. On the other hand, fructose does not require

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insulin to be converted to glycogen and in the patient whose acidosis is coming under control it might be quite useful. Have you had any experience regarding this, Dr. Guest?

DR. GUEST: I might elaborate that a little bit. Dr. Best touched on this subject and has said that there is evidence that fructose can be utilized without insulin especially by muscles. There is an additional point with regard to the use of fructose in the acidotic patient. There is some experimental evidence that the utilization of fructose is less inhibited by acidosis (that is, by a low *p*H) than is the utilization of glucose.

MODERATOR WHITE: I have a group of questions: What is the effect of oxytoxics on blood sugar and insulin requirement? We have occasionally used pitressin for severe insulin reactions and the insulin requirement might be increased but I have had no experience.

Have any electroencephalogram changes been observed in cases of labile diabetes? These have been reported but not confirmed.

Dr. Richard Harvey reported the appearance of retinal microaneurysms, after cortisone administration to experimental animals. Are we advised to use cortisone for these lesions despite these findings? I am not quite sure what that question means. Ophthalmologists often use cortisone in solution in the eye and certainly no harmful effects have been produced. When corticotropin first came out, it seemed to me that perhaps corticotropin and cortisone might help in the problem of retinitis proliferans. Some twelve patients were treated with rather large doses of corticotropin, some of it intravenously, for a period of six weeks. Well, we precipitated massive hemorrhages which fortunately later resolved so I, for one, would not recommend it for the management of retinopathy.

Is there any information as to prediabetic determinations especially in the children of diabetic women? We think that the children of diabetic mothers have no greater susceptibility to diabetes than do the children of young diabetic fathers. To answer this problem to our own satisfaction we recalled 204 children of young diabetic parents, all of whom were under the age of twenty. Where both of the parents were identified as diabetic, 33 per cent had clinical diabetes and a total of 62 per cent had either clinical diabetes or an abnormal glucose tolerance curve. Where the mother was a diabetic, 9 per cent had clinical diabetes and 14 per cent had positive glucose tolerance curves. There were 100 of those. Eighty-five children of diabetic fathers were recalled and 9 per cent had clinical diabetes and 12 per cent had positive glucose tolerance curves. Whether the parent was a diabetic father or a diabetic mother, the susceptibility to diabetes appeared to be the same. We were alarmed at this high figure and wondered whether we should carry out eugenic advice further. There is some new work, however, that makes us a little bit less pessimistic about this. Biochemists have become interested in genetic and endocrine diseases and they are finding that carriers have some of the characteristics of the disease. We wonder if our positive tolerance curves may not be the identification of a carrier rather than of a prediabetic; at least we hope so.

QUESTIONER: I'd like to ask Dr. White one other question pertaining to this. Were the children of diabetic parents who showed signs of diabetes mainly in the older age groups?

MODERATOR WHITE: Yes, the cases of clinical diabetes, although one developed it at six.

QUESTIONER: Over twenty years, the incidence may be much higher?

MODERATOR WHITE: Yes, but there was an extraordinarily high incidence for children under the age of twenty. We expect only one child in about 2,500 of the average population to contract diabetes under the age of fifteen. Dr. Guest, do you wish to discuss family history?

DR. GUEST: I should like to sound a warning against accepting a negative family history from the hospital records. Follow up the cases in future years. The longer you follow the family history of a diabetic, the greater the chances are that you will find more cases among the relatives.

MODERATOR WHITE: A question on that important subject of vitamin B_{12}. Do you believe that B_{12} orally or parenterally is of value in the treatment of diabetic retinopathy? I certainly don't think it does any harm, but we have not been able to demonstrate any change in the frequency or the character of the retinopathy. I should like to ask other members of the group who see retinopathy what their experience is.

DR. HARWOOD: Well, I certainly agree with that.

MODERATOR WHITE: How much regular insulin may be mixed with NPH or lente to retain the individual effect of each insulin?

DR. GUEST: I should say that's settled by trial and error.

MODERATOR WHITE: I agree to that. The advantage of lente and NPH insulin over protamine insulin in this respect is that they do not adsorb large quantities of rapidly acting insulin, so that one does not reverse ratios as one does in using mixtures of rapidly acting insulin with protamine insulin.

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