

THROMBOCYTOPENIC PURPURA IN PREGNANCY

During the past decade this disease has been diagnosed in 40 cases; splenectomy has been performed in 17 of these cases.

Summary

A case of thrombocytopenic purpura complicating pregnancy, treated by splenectomy and cesarean section, has been presented. A macerated fetus was delivered, but complete recovery of the mother occurred. After reviewing the literature it is believed that this is the first reported case in which both splenectomy and cesarean section have been performed.

Bibliography

1. Burnett, C. W. F., and Klass, I.: Review of problem of purpura during pregnancy. *J. Obst. & Gynaec. Brit. Emp.* **50**:393-404 (Dec.) 1943.
2. Finn, W. F.: Thrombocytopenic purpura in pregnancy; review of literature with report of 3 cases. *Am. J. Obst. & Gynec.* **48**: 497-509 (Oct.) 1944.
3. Mosher, G.: Complication of purpura with gestation. *Surg. Gynec. & Obst.* **36**:502-507 (April) 1923.
4. Patterson, W. B.: Thrombocytopenic purpura in pregnancy and in newborn. *J.A.M.A.* **130**:700-702 (March 16) 1946.
5. Polowe, D.: Splenectomy in pregnancy complicated by thrombocytopenic purpura hemorrhagica; report of successful case, with review of literature. *J.A.M.A.*: **124**:771-773 (March 18) 1944.
6. Polowe, D.: Splenectomy in pregnancy complicated by thrombocytopenic purpura hemorrhagica. *J.A.M.A.*: **124**:771-773 (March 18) 1940.
7. Posner, A. C.: Purpura hemorrhagica complicating puerperium. *Am. J. Obst. & Gynec.* **34**:155-158 (July) 1937.
8. Rushmore, S.: Purpura complicating pregnancy. *Am. J. Obst. & Gynec.* **10**:553-560 (Oct. 25) 1925.

PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF DIABETES MELLITUS

EDWARD J. RYAN, M.D., and E. PERRY McCULLAGH, M.D.

Section of Endocrinology and Metabolism

The purpose of this article is to present briefly certain concepts which the writers consider basically important in the management of uncomplicated diabetes mellitus. Most of the program to be discussed agrees in principle with teachings of recognized clinics on diabetes. There are, of course, variations in opinion concerning the details of management among various groups. Since diabetes is a common and chronic disorder of variable severity, and untreated diabetes is often compatible with life for long periods of time, these divergent opinions are understandable. The objectives of treatment remain the same with all groups, that is, maintenance of the patient in a good state of general health, and prevention of the occurrence of complications.

The pathologic physiology of diabetes mellitus is still a controversial subject involving intricate glandular interrelationships and the role of insulin in metabolic processes in body tissues, particularly in the liver and muscles. Brilliant contributions have been made but much remains to be done. From the practical standpoint the responsible disturbing factor may be considered a deficiency in the production of insulin with resultant hyperglycemia, glycosuria, tissue destruction with increased nitrogen excretion, a tendency to ketosis, acidosis, and coma, and a variety of well known symptoms whose number and severity differ with the severity of the disorder.

The diagnosis of diabetes mellitus as a clinical entity should be established with care. Not all examples of glycosuria and not all cases manifesting a decreased tolerance during the glucose tolerance test belong in this classification. Obviously, renal glycosuria may be misleading. A variety of endocrine disturbances and other disorders may be accompanied by a decreased tolerance to glucose, usually of mild degree, and often manifest only by the glucose tolerance curve. True diabetes may sometimes be present in these conditions, and distinction may then be possible only after treatment of the underlying process. Examples of these disorders include hyperthyroidism, Cushing's syndrome, acromegaly, and simple obesity. The finding of a blood glucose level of 130 mg. per cent or higher while fasting or two and one-half hours after a high carbohydrate meal, with or without glycosuria, is presumptive evidence of the presence of diabetes mellitus. However, the final diagnosis should be made only after a careful consideration of the factors just mentioned, since there is no conclusive evidence as yet that true diabetes mellitus is ever completely and permanently cured.

The criteria for adequacy of treatment generally and readily available are four: (1) the symptomatic response of the patient with all that this implies in control of classical symptoms, sense of well-being, growth and development in children, strength and normal nutritional status in adults; (2) the prevention of complications such as neuritis, retinopathy, vascular occlusion, and acidosis; (3) the prevention of glycosuria; (4) the maintenance of normal blood glucose levels. Other studies may be valuable during initial investigations but are not essential in evaluating diabetic control in the uncomplicated case.

It is often possible to maintain the patient in good nutritional balance and completely symptom-free in the presence of persistent hyperglycemia with resultant glycosuria. Since the mechanism of vascular damage in diabetes is not clearly understood, and since reports on the subject are somewhat conflicting, it is not possible to state with certainty that this lack of chemical control results in an earlier appearance of such damage.

However, because our yardsticks for the measurement of adequate treatment are few, yet simple and available to most practitioners, the writers feel that they should be utilized to the fullest possible extent. In other words, not only should the patient be healthy, but the level of glucose in the blood should be normal with a normal postprandial rise and subsequent fall, and glucose should be absent from the urine of those patients with normal renal threshold.

It is obvious that this ideal cannot be reached in all cases. It is, rather, a goal at which to aim, considering the age of the patient, the inherent instability of the diabetes, the frequency and severity of insulin reactions, the intelligent cooperation which may be expected, and other factors which may be apparent in the individual case. The occurrence of frequent insulin reactions would at first appear to be a serious objection to this routine. In actual practice, induced hypoglycemia in most diabetics has been infrequent and has not prevented the attainment of this type of control. It is, of course, far easier to maintain chemical control in older, more stable diabetics than in diabetic children and young adults. In these latter cases, normoglycemia is a goal to be sought, though rarely attained. As an ideal it is a stimulation to careful study and optimum regulation. Due consideration must be given at all times to growth requirements, nutritional requirements, and the avoidance of severe hypoglycemic episodes.

The more detailed summary of diabetic management will be discussed under the following headings: (1) initial study and regulation; (2) instruction of the patient; (3) diet; (4) insulin; (5) progress study.

Initial Study and Regulation

Having established the diagnosis and eliminated complicating factors by careful examination, including chest x-ray, examination of ocular fundi, and renal function tests in older patients, a period of daily observation is initiated for the purpose of diabetic regulation. This period may vary from a few days to two weeks or more, depending on the degree of severity and instability of the disease. During this time hospitalization is considered essential only for the patient whose diabetes is complicated by acidosis, gangrene, or serious systemic disease, or whose diabetes is so severe or unstable that ambulatory status is attended by grave risk. The average diabetic during the initial control period is encouraged in normal physical activity. He is seen once each day by the physician. Estimations of blood glucose levels are made two or three times each day before meals, that is, fasting and four hours and sometimes two hours postprandially. These are correlated with qualitative measurements of glucose in the urine, which is likewise collected before meals. With this routine of management, we find usually

that a single urine specimen before each meal is sufficient. In certain cases of severe and unstable diabetes, it is desirable to collect the urine output each twenty-four hours and to make accurate quantitative glucose determinations on each such sample.

These studies constitute a guide to the adjustment of insulin dosage when it is required or furnish an index to response when dietary management alone is sufficient.

During this time, also, the patient is instructed in measurement and manipulation of his diet, administration of insulin if needed, and all phases of diabetic management which are of importance to him. He is encouraged to devote his time entirely to the study of diabetes. At the expiration of the initial control period, it is expected that the diabetes will be sufficiently well stabilized to permit the patient to pursue his normal daily activities.

Instruction of the Patient

Successful management of diabetes mellitus is dependent as much upon the intelligent cooperation of the patient as upon any other single factor. Such cooperation can only be obtained from the patient who understands the necessity for the restrictions imposed upon him. The foundation of this understanding can be laid during the period of initial regulation. The fundamental alterations in his bodily physiology are simply explained. Potential dangers are stressed to emphasize the need for diabetic regulation, but he is assured that controlled diabetes is entirely compatible with good general health. He is taught to recognize the symptoms of acidosis or hypoglycemia, together with the appropriate steps to be taken in each. The necessity for added caution in the presence of infection or gastrointestinal disturbance is explained. Care of the feet is emphasized. Terms commonly used in discussing diabetes are defined and explained. Normal values for glucose in blood and urine are given. The technic for determination of glucose in the urine, using Benedict's qualitative reagent, is demonstrated. When insulin is necessary, its measurement and administration are explained and injections are given by the patient under supervision. The diet is verbally outlined, a printed list is furnished, and any dietary problems which may arise are discussed and settled. The patient is asked to obtain a diabetic manual and to continue his study of the disorder. Class instruction is indicated for groups of diabetics. Pertinent questions by the physician at the time of daily consultation during initial control will reveal the progress in learning made by the individual patient. The necessity for orderly living, regular habits, and avoidance of all excesses is emphasized. At all times

an effort is made to maintain morale at a high level by assuring the patient that diabetes, although inconvenient, is consistent with normal interests and activities. At the same time the fact is pointed out that he has a chronic disorder with which he must learn to live every day for an indefinite number of years and that the duration of life itself is dependent upon his full cooperation.

Diet

A rigid dietary program is fundamentally important in the successful management of diabetes. The above fact should be emphasized. Dietary instructions are troublesome and time-consuming. Without constant daily caloric and available glucose values, however, diabetic status will fluctuate widely, and consistent smooth regulation will not be obtained. For this reason we favor an exact, quantitative diet, even in the mild case. Accurate weighing of the dietary constituents is ideal and has a desirable psychologic effect. When practical, it should be used during initial dietary familiarization. A majority of patients, however, are well controlled on measured diets. The patient is thoroughly instructed in his diet during the period of initial control. Also during this period it is preferable, though not necessary, that the patient eat his meals in a dining room which is under the supervision of a skilled dietician. Obviously, such an arrangement is appropriate in large diabetic clinics; it is not a necessity, and the intelligent patient can follow a strict dietary program in his home environment during initial regulation.

It is not within the scope of this article to discuss the various types of diets which have been advocated and used in the management of diabetes. For a number of years we have used diets of relatively high carbohydrate, low fat content, with adequate maintenance amounts of protein. The importance of high protein intake should be emphasized. Our trend over a period of years has been to show an increasing quantity of this constituent in dietary prescriptions.

The caloric value of the diet usually depends upon the following considerations: (1) actual weight of the patient in comparison with the ideal weight for height, age, and sex; (2) growth requirements in the case of children; (3) anticipated physical activity. For practical purposes, basal caloric requirements for ideal weight based on height, age, and sex may be quickly determined from a slide rule.* The diet may be maintained below this level to promote weight reduction when such is indicated, or additional calories up to 100 per cent or more above basal caloric requirements may be necessary in the case of malnourished or very active individuals. In our experience, the average adult engaged in a sedentary occupation requires from 30 per cent to 50 per cent above

*The slide rule furnished by Eli Lilly and Co. is convenient and suitable for this purpose.

the basal caloric requirement in order to maintain weight at or slightly below the calculated ideal level. These preliminary calculations constitute a convenient working basis but will be subject to modification as the patient's weight response is noted on subsequent examinations.

The important factor of normal growth requirements enters into the problem in diabetic children; here, the caloric requirements must be calculated on the basis of standard height and weight for age and sex. We have found the Baldwin-Wood charts convenient for obtaining these standards.

When diabetic management is initiated the diet prescription must be fitted to the individual case. For example, the patient of normal weight or less with mild diabetes may be started on his final calculated diet, and his response noted. However, the obese diabetic or any who may require insulin are started on a basic diet containing approximately 100 Gm. of carbohydrate, 62 Gm. of protein, and 50 Gm. of fat, a total of 1098 calories. Subsequent increases, when higher caloric values are indicated, are ordered by number, each numerical increase in carbohydrate and protein being equivalent to one slice of bread, a technic originally formulated by Rabinowitch. Increased caloric requirements are readily met by increasing the fat content of the diet. The carbohydrate to fat ratio in each case is usually kept at approximately 2 + :1. A sample of a portion of the diabetic order sheet will make this clear.

Prescribed Diet**Standard Diets**

1946 Date	Diet No.	C	P	F	CAL.	Diet No.	C	P	F	CAL.
4-28	Basic	100	62	50	1098	Basic	100	62	50	1098
5-2	3+	145	71	70	1494	1	115	65	50	1170
5-5	5+	175	77	80	1728	2	130	68	50	1242
						3	145	71	50	1314
						4	160	74	50	1386
						5	175	77	50	1458
						6	190	80	50	1530
						7	205	83	50	1602
						8	220	86	50	1674
						9	235	89	50	1746

MANAGEMENT OF DIABETES MELLITUS

In the type of case just described, response in blood and urine glucose values to the basic diet is observed for several days, and insulin is started, if considered necessary, before any increase is made in the caloric value of the diet. Subsequent increases are made in several stages as indicated on the order sheet and the diabetic response noted to each before the final value is reached. When insulin is required, the dosage is adjusted and approximate diabetic control is obtained before the diet is increased from one level to the next. It then becomes comparatively simple to increase the insulin dosage to match the increased caloric value of the diet.

A sample menu based on the basic diet we use is as follows:

Weight (Grams)	Household Measurements	Grams CHO	Grams Protein	Grams Fat
	Breakfast			
	1 serving of fruit	10		
	1 egg		6	6
30	1 slice whole wheat bread	15	3	
5	½ square of butter			4.5
100	½ glassful of milk	5	3.3	4
	Coffee or tea as desired			
	Luncheon			
90	3 ounces of meat or substitute		18	7.5
200	1 cupful cooked 5% vegetable	10	2	
100	1 cupful raw 5% vegetable	5	1	
5	½ square of butter			4.5
	1 serving of fruit	10		
200	1 glassful of milk	10	6.6	8
	Dinner			
90	3 ounces of meat or substitute		18	7.5
200	1 cupful cooked 5% vegetable	10	2	
100	½ cupful 10% vegetable	10	1	
5	½ square of butter			4.5
	1 serving of fruit	10		
100	½ glassful of milk	5	3.3	4
	Total	100	64.2	50.5

A few explanatory statements are in order. It is apparent that the quantity of a serving of fruit and the weight of the serving must vary with the carbohydrate content of the fruit in order to furnish 10 Gm. of carbohydrate. For example, a serving of unsweetened applesauce is 6 tablespoons or 75 Gm., while a serving of cooked rhubarb is $1\frac{1}{2}$ cupfuls or 300 Gm. Printed lists of fruits, cereals, 5 per cent, 10 per cent, 15 per cent, and 20 per cent vegetables, various substitutions, and foods of no caloric value are furnished to the patient. These values may be obtained in any standard text on dietetics. It should be apparent that carbohydrate, protein, and fat contents of the same type of food vary from day to day and that an analysis of an aliquot of a day's food would reveal values somewhat different from those given above. The analyses given in various texts also differ in some instances. However, for practical purposes in day by day diabetic management, these values are sufficiently accurate to be readily usable.

The distribution of available glucose in this diet is, in round numbers, 30 per cent at breakfast, 35 per cent at luncheon, and 35 per cent at dinner. Approximately this same distribution is maintained as the caloric value of the diet is increased to meet individual requirements. This distribution is suitable for the diabetic who needs no insulin, or whose requirement of protamine zinc insulin is less than 20 units.

When the requirement of protamine zinc insulin, administered before breakfast, surpasses this value, we have found it convenient to alter the distribution of available glucose to furnish 20 per cent at breakfast, 30 per cent at luncheon, 40 per cent at dinner, and 10 per cent as a bedtime feeding. Obviously, minor alterations in the distribution of available glucose can be made if the need for such is indicated by persistent hyperglycemia at the same time each day. In the case of patients who are subject to frequent insulin reactions associated with physical activity, the use of small feedings between meals is helpful.

The so-called "diabetic foods", except for unsweetened canned fruits and non-caloric gelatin products, are neither prescribed nor recommended.

Insulin

At the present time a detailed discussion of the use of insulin can be an extremely complex subject. A great variety of modified insulins have been used in clinical investigation in the United States and abroad. Promising results have been reported, particularly in the management of severe, and unstable diabetes, where variations in the duration of action of insulin are especially necessary. General use of one or more of these preparations will probably be indicated in the future. For the

present, however, satisfactory regulation can be obtained in the majority of patients who require insulin by the use of insulin, U.S.P., and protamine zinc insulin, U.S.P. Only rarely do we modify the action of each type by administering them simultaneously in the same syringe. It should be stated, however, that some diabetic clinics follow this practice with satisfactory results.

There are no set rules by which one can establish the need for insulin in a given case or determine the probable insulin requirement. Each patient is an individual problem. The age of the patient, the severity of the diabetes, the response to diet regulation, the total caloric requirements, and the relative "sensitivity" to insulin are all important factors which bear on the question. Unless there is judged to be imminent danger of severe acidosis, it is usually advisable to observe the response of blood and urine glucose values to a basic diabetic diet for several days. Unless there is a prompt fall in these levels indicating further reduction to near normal values in the future, insulin is started.

When studies indicate only intermediate severity and fair stability of the diabetes, it is usually satisfactory to initiate insulin management with protamine zinc insulin. An original dose of 15 to 20 units with subsequent modification based on clinical response and caloric requirement is usually suitable. We have routinely administered protamine zinc insulin in a single daily dose before breakfast.

In the individual with severe and/or unstable diabetes, initial regulation is most conveniently initiated with insulin, U.S.P. Because of the relatively short duration of action, dosage can be quickly and readily manipulated.

The original dose given three times daily before meals and at bedtime, is kept small until the degree of responsiveness to insulin can be estimated. The amount is then increased, based on blood and urine glucose findings and increasing quantity of the diet, until satisfactory control is obtained. Protamine zinc insulin is then started, the initial dose being 80 per cent of the total daily requirement of "regular" insulin. The "regular" insulin is reduced in quantity or eliminated beginning with the bedtime dose, and ultimately withdrawn entirely, usually in two to three days. In many cases requiring more than 30 units of insulin per day better regulation of the diabetes is maintained by administering a small dose of "regular" insulin in addition to the daily protamine requirement. As mentioned previously, we do not ordinarily mix these insulins before administration nor give them simultaneously in the same syringe.

The exceptional case of unusual severity and instability may require

radical alterations from the program described.' It is, however, applicable to the majority of diabetics.

Progress Study

It should be emphasized that the period of initial diabetic regulation is a time of daily observation, careful study, frequent blood and urine glucose determinations, and adjustment of diet and manipulation of insulin until satisfactory control is obtained.

At the expiration of this period, the patient is discharged to return to his daily work and routine. He is expected to understand thoroughly the diet, the administration of insulin, and all phases of the diabetic life which will be of practical importance to him. He is directed to keep a daily record of qualitative urine glucose values, at first four times each day (before meals and at bedtime) and to bring this record on return to his physician. He should be seen again at gradually lengthening intervals. On each return visit his progress is evaluated by history, examination, weight, and glucose levels in blood and urine. Alterations in diet and insulin are made when indicated. It is our opinion that each diabetic, after the condition is well stabilized, should be seen by his physician at least once every four months for the remainder of his life.

This brief outline of some phases of diabetic management is presented because it has proved workable in practice, even though it may entail additional trouble at times for both physician and patient. It is believed that the type of control obtained by this routine approaches physiologic normality by the crude measurements now available. There are many variations possible in the complicated problems of diabetic management, and routines and standards naturally vary among different groups and individuals. Diabetes is the subject of extensive laboratory and clinical investigation, and further progress can certainly be anticipated.

It is the conviction of the writers that well controlled and stabilized diabetes tends to improve gradually in status, even though it is never cured, and no amount of work and trouble is too great if this end can be attained.

Summary

Some practical considerations in the management of diabetes mellitus are briefly reviewed. The problem is approached by consideration of the following aspects: (1) initial study and regulation; (2) instruction of the patient; (3) diet; (4) insulin; (5) progress study.

The writers are greatly indebted to Miss Marian Buck for many helpful suggestions in preparing the discussion on dietary management.