

THE PROPER USE OF Laboratory Tests IN THE DIAGNOSIS AND MANAGEMENT OF DIABETES

F. D. W. Lukens, M.D.

ASSOCIATE PROFESSOR OF MEDICINE, UNIVERSITY OF
PENNSYLVANIA SCHOOL OF MEDICINE, PHILADELPHIA

A well-balanced index of suspicion of diabetes is essential to the physician in internal medicine or general practice. As one sees the kaleidoscopic range of disease, the possibility of diabetes should be rapidly, routinely and reflexly considered in dealing with persons in the following categories: all those who have diabetic relatives, the obese, and those with conditions which place a burden on the function of insulin. A suspicion should lead to investigation by laboratory tests.

FACTORS PREDISPOSING TO DIABETES

Examination of the urine for sugar is particularly valuable in the febrile patient. Infection is nature's sugar tolerance test; in many instances fever taxes the function of insulin far more than 100 Gm. of glucose. The alert physician will, therefore, use these occasions to make his routine urinalysis for sugar. If negative, the patient

probably has a good insulin reserve. If positive, one must suspect and usually treat as diabetes, establishing the severity of the disease later by appropriate study.

Part of the mechanism which makes fever antagonistic to insulin is the activation of the adrenal cortex. The proper examination of the urine for sugar during the treatment with ACTH and cortisone may well reveal a number of prediabetics. Endocrine diseases, such as hyperthyroidism, acromegaly, and Cushing's syndrome, have a high incidence of diabetes. Repeated examinations for diabetes are part of the management of such patients.

Finally, whenever one encounters a condition which might be a complication of diabetes, the minimal screening tests are indicated. The following conditions are especially noted—arteriosclerosis of the feet (this may appear before glycosuria and is most common at the age when the incidence of diabetes is high), gallbladder

disease, cataract and retinitis, coronary disease and hypertension. In all these cases, a blood sugar test should be made in addition to routine urinalysis.

If physicians were to watch their patients with a reasonable index of suspicion of diabetes, there would be many fewer cases found by Diabetes Detection Drives and life insurance examinations.

TESTS FOR SUGAR IN THE URINE AND THE BLOOD

With this brief reminder of what may make the physician think of diabetes, the next question that arises is: What laboratory tests should be used for diagnostic screening? For the busy physician these must be simple. The routine urinalysis will suffice in most cases, if the specimen of urine is obtained an hour or more after a meal. If the test is positive, a blood sugar test is required. Where conditions that might be complications of diabetes are found, a blood sugar test, in addition to the urinalysis, should be routine. The blood sugar test should be made one to two hours after a meal.

At this point, a word is in order about false or misleading laboratory tests. If the urine specimen cannot be tested immediately, a preservative should be added, especially in warm weather. I have found 4 plus sugar in testing urine immediately after voiding, although the same sample tested the following day has been reported negative. The morning specimen of a patient with mild diabetes may be negative, although a test made after a meal will show sugar. For routine tests, choose the time when the suspected diabetic is most likely to have glycosuria.

Nondiabetic glycosuria is encountered in a group of rare conditions. For practical purposes, they are eliminated by a blood sugar test; the blood sugar is normal. It must be emphasized that renal glycosuria, pentosuria, and the other meliturias are rare in comparison to diabetes mellitus. It is wise to act on the rule that "glycosuria always means diabetes until proved otherwise." A blood sugar test should be made in order to determine its significance.

The levels of blood sugar deserve comment. The Council of the American Diabetes Association has endorsed the use of the blood sugar values shown in Table 1 in the diagnosis of diabetes. For a flat diagnosis this is fine, but in recent years I have become suspicious of any fasting blood sugar above 100 and of any value above 140 after meals. A single report at such a level does not warrant the diagnosis of diabetes, but it merits repetition within a month or two. As an illustration,

two patients were referred with severe diabetes; two years previously they had had single fasting blood sugar values of 110 and 115, while hospitalized for surgical treatment. These values were textbook normals and nothing more was said or done. How much better one would feel, if these patients had been rechecked in some way. Checking would show an alert attitude to such laboratory reports.

What confirmatory examinations should be made when these initial tests are borderline? These will be indicated by the individual situation. If a decision must be made immediately because of consideration for life insurance or management during pregnancy, or difficult surgery, a sugar tolerance test at once may be in order. In many instances, the repetition of urine and blood sugar tests at times when the patient is to be seen for some other condition may answer the question as well or better. Three or four normal blood sugar tests a year for several years will do more to exclude diabetes than any one test. When the blood sugar is normal, tests should be carried out to identify the type of sugar in the urine, but it is more important to be sure that one is dealing with a nondiabetic glycosuria than to classify the type of nondiabetic melituria.

GLUCOSE TOLERANCE TESTS

In the normal adult given 100 Gm. of glucose by mouth, the venous blood sugar usually rises no higher than 200 and returns to 120 or less in two hours. An elevation of the fasting value or a value above normal at two hours is strong evidence for diabetes. The height or peak of the blood sugar curve at one-half or one hour has limited significance. For this reason, almost everyone has abandoned the one-hour two-dose sugar tolerance test and has returned to the original type of test, in which the blood sugar curve is followed for two or three hours. If the observations are extended for five or six hours, sugar tolerance tests may be of some value in the diagnosis of spontaneous hypoglycemia. The intravenous tolerance test is useful because it excludes changes which might be related to defects in gastrointestinal motility and absorption, but it is still used principally as a research procedure.

The need for preparation of the sugar tolerance test should be emphasized. The patient should have been on a normal type of diet, relatively high in carbohydrate, for three days or more before the test. The test should not be made immediately on any individual who has been treated for diabetes, either with insulin or with restriction of the carbohydrate of the diet. Starvation

or even low-carbohydrate consumption in advance of the test may result in a high blood sugar curve which may even simulate the response of the diabetic.

It is not necessary to perform a sugar tolerance test when the fasting blood sugar is high. This, if confirmed, establishes the diagnosis of diabetes. A sugar tolerance test is a diagnostic aid when other blood sugar values are indecisive. But borderline or bizarre curves are often found in doing tolerance tests. Blood sugar values below the diabetic levels (Table 1), especially normal fasting blood sugar values, do not exclude diabetes. At times a diabetic may have a normal blood sugar both before and after eating, if the diet has been restricted or insulin has been taken before the test. On the other hand, a nondiabetic person may have hyperglycemia and glycosuria after previous starvation.

TABLE 1 Diabetes is present with a high degree of probability when the blood sugar is more than:
(All values in mg. per 100 ml.)

| Source of blood | Folin-Wu Method | | Somogyi Method | |
|-----------------|---------------------------------|-------------|----------------|-------------|
| | Fasting | After meals | Fasting | After meals |
| Venous | 130 | 200 | 110 | 150 |
| Capillary | Folin-Malmros Method 140 240 | | 120 | 200 |

From: Diabetes Guide Book for the Physician, American Diabetes Association, 1950.

Quantitative determination of glucose in a 24 hour specimen of urine is rarely employed in diagnosis. It may be useful when glycosuria is present with normal blood sugar levels. When the glycosuria represents only a few grams in 24 hours while the patient is on an ample diet and when the blood sugar level is normal, it supports the diagnosis of nondiabetic glycosuria.

Until one is familiar with the patient, the presence of sugar in the urine should always lead to a test for ketonuria (the nitroprusside or ferric chloride test). When acetonuria is present, acidosis will be suspected and the carbon dioxide combining power of the serum should be determined to complete the picture. Acetonuria makes one think at once of acidosis, infection and the need for more insulin.

USE OF LABORATORY TESTS IN GUIDING THE TREATMENT OF DIABETES

Chemical tests should be selected according to the needs of the patient and according to the standard of control desired by the physician. The restoration of the diabetic patient to a normal state of metabolism would require that the urine be kept free from sugar and that the

blood sugar be kept normal. Some physicians strive to reach this ideal in all of their cases, others feel satisfied to disregard glycosuria and hyperglycemia, while still others strive for normal tests in certain cases, yet are satisfied with less than perfection in control in other cases. In any case, one factor which influences the choice of laboratory tests is the degree of control reached by the patient at the moment.

Simple laboratory tests help in the estimation of the amount of insulin needed. These include qualitative tests for sugar in the urine, made on fractional specimens of the daily urine output, quantitative urinary sugar examinations on measured specimens, and blood sugar tests. Except in cases of severe diabetes, tests of samples of urine collected four times a day, for example at 7:00 and 11:00 a.m., and 4:00 and 9:00 p.m., provide a satisfactory guide to treatment. The usefulness of this method must not blind one to its limitations. The results may be misleading when there is a wide range of change in the rate of excretion of urine, and in the total volume output. In spite of these objections, the proper use of these serial qualitative tests can give valuable information. They show when qualitative control of glycosuria is being reached, and they also show the time of day when more insulin is needed. Furthermore, if the tests show that for fourteen to eighteen hours of the day there is no glycosuria, one can conclude that control has progressed fairly well.

Quantitative examinations on the excretions of sugar for all or part of the day are useful at times. They reveal the true meaning of qualitative glycosuria which resists the usual methods of control. In juvenile or unstable diabetics, and in diabetics whose diet and insulin have been made irregular because of surgery or complicating disease, it is often helpful to know the amount of carbohydrate utilized. If the estimated intake of sugar exceeds the excretion of sugar in the urine by 100 Gm. or more, the patient can be considered safe, except in unusual circumstances. Further adjustment of the diabetic's regimen can be made after the complication has subsided. When I see a labile diabetic whose daily glycosuria varies from 5 to 80 Gm. on a constant hospital regimen and when the quantitative test shows that on the average enough glucose is utilized to maintain health, I cease to scold the patient for the qualitative glycosuria which is found on office visits.

Blood sugar determinations aid in more accurate control after the urine is largely sugar free. A single blood sugar may be regarded as a one-minute point on a 24 hour curve. In practice, only occasional blood sugars at selected times are required for most diabetics. As a rule,

blood sugars are taken to learn the highest and lowest levels reached during the day. The exact times of interest to the physician will depend upon the particular dose and type of insulin in use.

In the early stages of the management of diabetes, few blood sugar tests are needed while glycosuria persists; glycosuria itself shows that the blood sugar is 200 or more. After glycosuria has been controlled, the blood sugar determination should be checked again. Tests should be made not only in the early-morning fasting, but at various times during the day—for example, the late forenoon and late afternoon.

A word is in order concerning the instruction of patients in the use of laboratory tests. Most well-educated diabetics have learned one of the tests for glycosuria (Benedict's, Clinitest, Galatest, etc.). The physician must direct the use of the test at home. Usually, the urine samples desired by the physician should be tested one day a week. Where there is any question of infection, reaction or other irregularity, special tests may be performed by the patient. However, it is important not to make the diabetic a "laboratory invalid" and, therefore, home testing should be kept at a proper minimum. At present, the test for acetone (Acetone Test powder is available for patients' use) deserves to be used more often. All diabetics ought to make the test at the onset of every intercurrent illness, reporting positive tests to their physicians. It should be pointed out, though, that the nitroprusside reaction is sensitive, and slightly positive tests may have no clinical significance.

If, in spite of large doses of insulin, the 24 hour specimen of urine cannot be kept sugar free, one may be dealing with diabetes of great severity or great instability. There may be peaks of hyperglycemia when glycosuria may be found, while at other times there may be hypoglycemia and insulin reactions. It is obvious that the determination of any single blood sugar will be an uncertain guide to regular treatment. Here the quantitative determination of the urine sugar in a 24 hour specimen is a valuable guide. If the excretion of glucose is small, one can conclude that an adequate amount of carbohydrate is being utilized by the patient. If, for example, a patient is using a diet containing 160 Gm. of glucose and has a total of 20 Gm. of glucose in the urine, this leaves a balance of 140 Gm. of carbohydrate utilized. If the patient's weight and strength are satisfactory, he may safely continue to live with this balance, with confidence that the glucose utilization is adequate to maintain good nutrition. Continued efforts may be made to improve matters by reaching the desired state of freedom from glycosuria.

CONCLUSION

Chemical tests measure silent symptoms which should be interpreted as wisely as other symptoms. The life of the diabetic individual should be improved and not made miserable by these diagnostic and therapeutic guides. Patients must be neither frightened nor neglected, but they must be encouraged to follow the path of discipline which leads to health.

THE INCIDENT OF THE INVOLUNTARY SHOPLIFTER

Medical evidence is not always so readily accepted in a court of law as it was in the case reported in the *Manchester Guardian* of July 20, where a married woman had been charged with shoplifting. It was alleged that she took a "sunsuit" from a rail in a store, put it underneath her coat, and left the shop without paying for it. She later said to the police: "It was a stupid thing to do. I don't know what made me do it. I had money to pay for it."

The defense before the Sheffield magistrates was that the accused had been dieting under doctor's orders and had carried her treatment too far. A medical practitioner stated that, as the result of her blood sugar reaching an abnormally low level after dieting, she was acting automatically and had suffered a lapse of consciousness, similar to that of a man who is kicked on the head during a game of football but continues to play without remembering afterwards what he has done. The magistrates dismissed the charge; if there was no criminal intent there could be no conviction; they obtained from the accused's husband an undertaking that she would discontinue her dieting.

—Lancet, August 4, 1951.