Clinical Interpretation of Plasma Glucose Values

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SUMMARY

The use of plasma instead of whole blood for glucose determinations has become increasingly frequent. Since the values obtained differ significantly, it is necessary to establish new standards for the interpretation of plasma glucose levels.

Both whole blood and plasma glucose concentrations were determined simultaneously on 480 blood samples from 120 glucose tolerance tests. From these determinations, a mathematical formula for the interconversion of plasma and whole blood glucose values was established: Whole blood glucose equals .0925 + .8543 plasma glucose. From this formula, normal upper limits were derived for the interpretation of the oral glucose tolerance test using plasma glucose values: 185 mg. per 100 ml. at one hour and 140 mg. per 100 ml. at two hours. Applying these levels, interpretations from simultaneous plasma and whole blood glucose values of the 120 glucose tolerance tests were compared and the results agreed well. DIABETES *15*:775-77, November, 1966.

The use of plasma, rather than whole blood, has been advocated for the laboratory analysis of glucose concentrations. As set forth by Zalme and Knowles,[1] there are several reasons why such a change is desirable. With increased laboratory automation, as with the Technicon AutoAnalyzer, plasma is technically more satisfactory. Either anemia or polycythemia will cause significant variation of whole blood sugar values,[1,4] while plasma sugar remains constant. Since it is the concentration of glucose in extracellular fluid that is important in the consideration of carbohydrate metabolism, it seems desirable to measure the plasma sugar content which closely approaches the extracellular level.

Previously established criteria for the interpretation of glucose concentration have been expressed in terms of whole blood levels. In order to make plasma glucose results clinically meaningful, it is necessary either to compile large numbers of plasma glucose determinations and statistically establish standard values or to derive a simple formula for the conversion of these established whole blood glucose values to equivalent plasma levels. The latter alternative would be preferable, provided a constant relationship between the two measurements could be documented. A conversion factor would furnish a simple aid to the physician until he acquired the ability to apply plasma glucose results directly to clinical situations and it would help to avoid much of the confusion and uncertainty which has been associated with the changing of other laboratory methods in the past.

The establishment of dependable diagnostic criteria is perhaps the most exacting demand in changing any laboratory procedure. This is especially true of glucose determinations, since at the moment the diagnosis of diabetes mellitus rests with this laboratory measurement. Therefore, if plasma glucose measurement is to be used, new criteria must be established to relate closely with the values of whole blood now used in the interpretation of the oral glucose tolerance test and the two-hour postprandial glucose level.

METHODS

To obtain a simple mathematical relationship adequate for clinical purposes, whole blood and plasma glucose were simultaneously determined on 480 blood samples from 120 glucose tolerance tests. The glucose load was 75 gm. of glucose from hydrolyzed cornstarch.* All the determinations were done on the Technicon AutoAnalyzer apparatus, using the alkaline potassium ferricyanide method of analysis.

The regression equation calculated by the sum of the least squares reveals the mean relationship between plasma glucose (X) and whole blood glucose (Y) to be $Y = 0.0925 + 0.8543X$. (figure 1). The standard deviation of Y at average X is $\pm$ 4.37. Added errors from variations of the mean value of Y and of the regression slope are so small that the standard deviation of Y at average X may be used for values up to 500 mg. per 100 ml. of blood glucose.

RESULTS

Although there is disagreement, the whole blood sugar levels necessary to establish a diagnosis of diabetes mellitus from the glucose tolerance test generally fall within a narrow range. Listed in table 1 are the whole blood glucose concentrations that we judge necessary

*Glucola, Ames Company, Elkhart, Indiana.

for the diagnosis of diabetes mellitus from the three-hour glucose tolerance test. These values are based on data published by Fajans and Conn.[3] Solving the equation $Y = .0925 + .8543X$ for X, $(X = 1.1705Y - 0.1083)$ corresponding plasma glucose levels have been derived as listed in table 1. These values were rounded to the nearest multiple of five.

TABLE 1

Comparable blood and plasma glucose levels for the diagnosis of diabetes mellitus from the oral glucose tolerance test

Time	Whole blood glucose (mg./100 ml.)	Plasma glucose (mg./100 ml.)
Fasting	100	115
1 hour	160	185
2 hours	120	140
3 hours	100	115

To test the validity of our mathematical conversion in actual practice, the results of the 120 oral glucose tolerance tests were classified separately by whole blood and plasma glucose concentrations. If both the one-hour and two-hour glucose values exceeded those in table 1, the test was judged indicative of diabetes. If either the one or two-hour value, but not both, exceeded these limits, the test was called borderline. If all determinations fell below these levels, the response was listed as normal.

Of the 120 glucose tolerance tests done, thirty-two showed unequivocal diabetes by both methods. One test was classified as diabetic using plasma glucose values, but borderline using blood glucose values. Three tests were borderline from the plasma sugars but normal by whole blood level. Four tests were borderline by whole blood, but normal by plasma. Ten tests were borderline by both methods. Sixty-eight tests were normal by both methods. All samples tested had hematocrits between 35 and 45 per cent. All tests showing a disparity between the plasma and whole blood glucose results are listed in table 2.

For most clinical purposes, the equation $Y = 0.9X$ will be adequate for converting plasma glucose levels to the comparable whole blood sugar. This approximation, however, is not sufficiently accurate to be used in interpreting the glucose tolerance test or in giving diagnostic significance to modestly elevated two-hour postprandial sugars. It should also be noticed that this simplified approach becomes relatively more inaccurate with high levels of blood glucose (figure 1—dotted line).

DISCUSSION

The advantages of plasma glucose measurement, which are technical desirability, consistency, and accuracy, are significant and clearly recommend its use over that of whole blood glucose determination. The major deterrent thus far to adopting the plasma glucose method has been the lack of well-defined criteria to use in the clinical interpretation of plasma glucose results. The development of the conversion factor derived from comparing a large number of simultaneous plasma and whole blood glucose samples offers a satisfactory means of resolving this problem. Using data published by Fajans and Conn[3]

TABLE 2

All glucose tolerance tests exhibiting a disparity between interpretation of glucose tolerance tests by plasma and whole blood sugar methods

Interpretation	Initials		Blood sugar mg. per 100 ml. Fasting	1-hr.	2-hr.	3-hr.
Borderline—plasma	A.P.	Plasma	98	192	135	148
		Whole blood	85	160	114	125
Normal—whole blood	F.E.	Plasma	105	204	125	88
		Whole blood	85	157	105	70
	G.S.	Plasma	127	196	140	84
		Whole blood	70	124	109	65
Borderline—whole blood	P.L.	Plasma	88	170	135	100
		Whole blood	70	145	123	85
Normal—plasma	V.C.	Plasma	86	178	124	76
		Whole blood	70	163	107	63
	E.W.	Plasma	104	163	124	94
		Whole blood	83	143	124	81
	C.M.	Plasma	87	147	124	78
		Whole blood	103	164	117	73
Diabetic—plasma	G.H.	Plasma	108	205	148	80
Borderline—whole blood		Whole blood	85	145	142	65

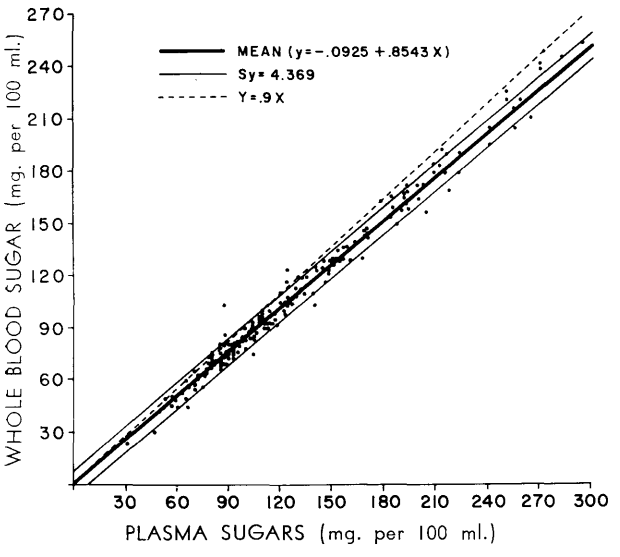

FIG. 1. Comparison of 480 simultaneous whole blood and plasma sugar determinations. See text.

for the interpretation of the glucose tolerance test, equivalent plasma glucose levels were calculated using a conversion factor. A comparison of the whole blood and plasma glucose interpretations from a large number of oral three-hour glucose tolerance tests shows excellent correlation. In those few cases where a disparity occurred, the plasma glucose levels were relatively higher and more suggestive of diabetes. These results establish the validity of using plasma glucose values of 185 mg. per 100 ml. at one hour and 140 mg. per 100 ml. at two hours as the upper limits of normal in the oral glucose tolerance test in place of the corresponding whole blood glucose values of 160 mg. per 100 ml. and 120 mg. per 100 ml.

In the aged, during pregnancy, and with the cortisone glucose tolerance test, the generally accepted upper limit for the two-hour (whole blood sugar) value is 140 mg. per 100 ml. In these situations, a plasma glucose level of 165 mg. per 100 ml. is comparable.

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Trace Compounds in Expired Air

The sensitive technics of gas liquid chromatography have allowed the simultaneous recognition and quantitation of trace compounds in many biologic media. Recently, volatile organic compounds responsible for the odor of perfumes have been under intensive investigation by such technics. It is thus not surprising that attention is currently being directed to odoriferous and other trace compounds in expired air. Eleven different organic compounds and four unidentified peaks have been detected in the expired air of man and this number can be further increased by gaseous contaminants from the environment.

In studying trace compounds in expired air, S. Levey and O. J. Balchum (*J. Lab. Clin. Med.* 62:247, 1963) first analyzed the methane in rebreathed purified oxygen from a six-liter bag forty times. Although it is well known that methane is produced in the intestinal tract by the decay of vegetable material and appears in cecal gases in concentrations as high as 90 per cent, it has not been previously reported in gases recovered from the stomach or in expired air. These authors found that methane could be detected in normal subjects in concentrations varying widely from 1 to 99 p.p.m. in the rebreathed gas.

Perhaps because of this wide variability among normal subjects, they were disappointed in a search for some relationship of this gas with a particular disease process or unusual diet. Abnormally high levels of expired methane were not found in patients with constipation, fecal impaction, or postoperative ileus, and changes in diet, even including the cessation of the oral intake of food in patients on parenteral alimentation. In fact, it appeared that the increase in volume of intestinal gas was ordinarily associated with rather low levels of methane in the expired gas. This confirmed earlier speculations that the excess gases retained in the intestinal tract are usually other gases (carbon dioxide and air) which might be expected to dilute any methane formed there.

In a later investigation (Levey, Balchum, V. Medrano, and R. Jung (*J. Lab. Clin. Med.* 63:574, 1964) the

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