Importance of the Hematocrit in Interpretation of Blood Sugar

Richard S. Dillon, M.D., Bryn Mawr

SUMMARY

1. The glucose concentration in whole blood may be calculated with reasonable accuracy from the plasma sugar level and the hematocrit by the following formula: WBS = PS (1-0.30 hct.).

2. Anemia must be recognized as a factor contributing to an apparent decreased glucose tolerance seen in chronic diseases. DIABETES *14*:672-74, October 1965.

The erythrocyte sugar concentration is less than that of plasma. As a result, whole blood sugar concentration will lie somewhere between those of erythrocyte and plasma and will be affected inversely by changes in hematocrit.[1,2] It is the purpose of this report to illustrate how anemia can raise the blood sugar from normal to pathological concentrations and to provide a means by which plasma sugar levels, if determined, may be converted to those of whole blood sugar for evaluation by whole blood standards.

METHODS

Glucose tolerance tests were performed in five patients who had previously ingested the three-day 300 gm. of carbohydrate daily as recommended by Conn.[3] Venous samples were drawn in the fasting state and at one, one and one-half, two, three, and on two occasions, four hours after the ingestion of 1.5 gm. glucose per kilogram of body weight. The blood samples were drawn in 10 ml. commercial Vacutainer tubes* containing 20 mg. of potassium oxalate and 25 mg. of sodium fluoride. Each sample, as soon as it was obtained, was taken at once to the laboratory where the hematocrit was determined and aliquots of plasma and whole blood immediately frozen. Sugar was determined by the AutoAnalyzer with the Hoffman ferricyanide method. The standard deviation of the method as determined with ten replicate samples with a mean of 108.2 mg. per 100 ml. was 1.03 mg. per 100 ml. The hematocrits were determined by the micromethod of Strumia, the standard deviation of the method being ±0.21 hematocrit points.[5]

If the assumption is made that sugar exists in equivalent concentrations in red cell and plasma water, the effect of hematocrit may be calculated. The water contents of red cells and plasma are respectively approximately 65 and 93 per cent.[4] In 100 ml. of blood the plasma water volume is 93 (1-hct.) and the red cell water volume is 65 (hct.). Specific gravities are disregarded in the calculation. As the sugar is contained

TABLE 1

Plasma and whole blood sugar concentration

	1 Hematocrit (ml. per 100 ml.)	2 Plasma sugar (mg. per 100 ml.)	3 Blood sugar (mg. per 100 ml.)	4 Calculated blood sugar (mg. per 100 ml.)	5 3-4/3x100 (per cent)
Patient					
C.D.	44.8	242	211	209	+0.9
	45.2	248	210	214	−1.9
	46.0	232	194	200	−3.1
	46.3	154	128	133	−3.9
	46.6	52	51	45	+12.0
J.F.	40.2	90	81	79	+2.5
	—	208	176	183	—
	—	186	160	163	—
	39.9	176	151	155	−2.6
	38.6	94	84	83	+1.2
	—	72	63	64	—
P.B.	14.0	82	80	78	+2.5
	14.0	191	180	183	−1.7
	14.0	196	188	188	0.0
	13.8	172	164	165	−0.6
	15.1	84	78	80	−2.5
	15.1	98	92	93	−1.1
P.B.	22.1	83	75	77	−2.7
	22.6	184	166	171	−3.0
	22.5	184	167	171	−2.4
	21.1	158	150	149	+0.7
	24.4	108	100	100	0.0
	21.7	77	70	72	−2.8
N.C.	—	94	90	84	—
	35.7	182	166	163	+1.8
	—	200	180	179	—
	—	226	200	202	—
	—	156	138	139	—
	22.7	164	156	153	+1.9

From the Bryn Mawr Hospital, Bryn Mawr, Pennsylvania. Dr. Dillon is currently Captain, USAF, MC, Plattsburgh Air Force Base, Plattsburgh, New York.

*Vacutainer tube #3204PS supplied by Becton, Dickinson and Co., Rutherford, N.J.

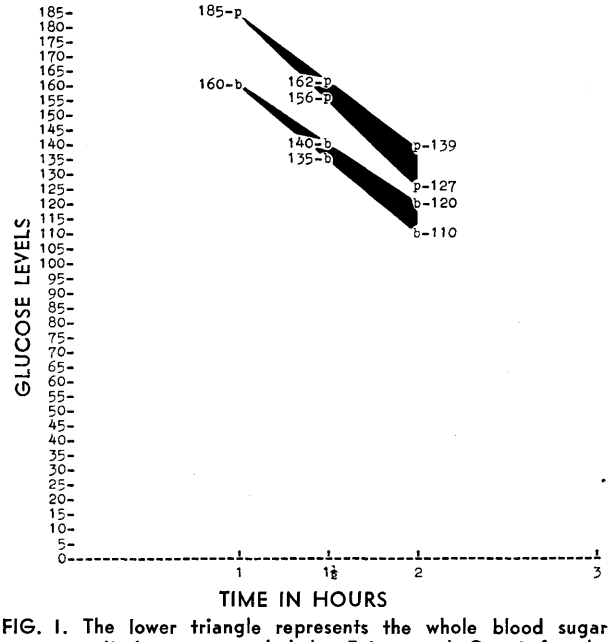

FIG. 1. The lower triangle represents the whole blood sugar criteria recommended by Fajans and Conn[6] for the diagnosis of diabetes mellitus. If all of the points in a glucose tolerance test are above the 160-140-120-line, the test is diagnostic of diabetes. If a curve falls in the shaded area (i.e., a one-hour value over 160, a one-and-a-half-hour value over 135, and a two-hour value between 110 and 120), the patient is a "probable diabetic." If only the one-hour value is high, the patient is a "diabetic suspect." The upper triangle represents the plasma sugars that may be calculated to correspond with these values at a hematocrit of 45.0. The plasma values of the triangle rounded off to the nearest five would be 185-160-140 and 185-155-125.

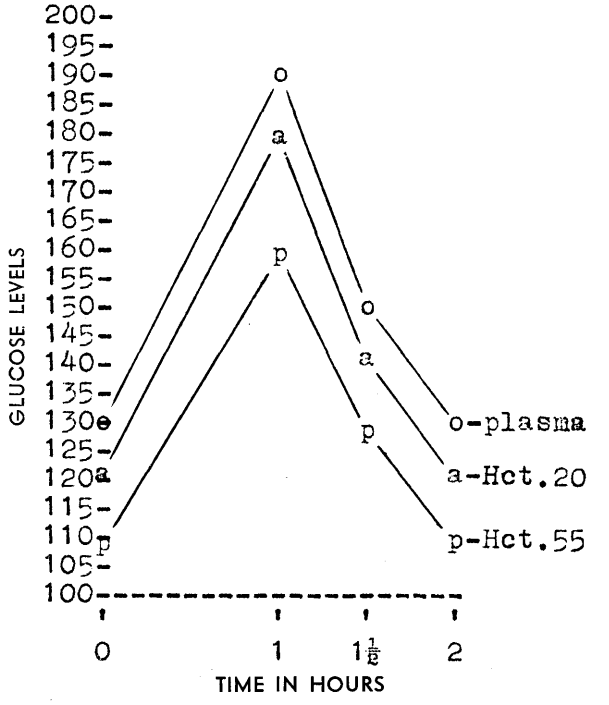

FIG. 2. Calculated whole blood glucose tolerance curves are shown for two patients who have the same plasma levels (the "o" points) but widely different hematocrits. Using the criteria of Fajans and Conn, one would label the anemic patient diabetic and the polycythemic patient normal.

in the 93 per cent of the plasma that is water, the plasma water sugar concentration must equal 100/93 times the whole plasma sugar. Therefore, the sugar concentration in whole blood may be expressed:

Whole blood sugar = (Plasma water sugar) (Plasma water volume + red cell water volume)

Whole blood sugar = (100/93 PS) (93-93 hct. + 65 hct.)

Whole blood sugar = PS (1-0.30 hct.)

where PS is the plasma sugar concentration.

This formula may be rearranged to give the ratio between the sugar concentrations in whole blood and plasma:

Whole blood sugar/plasma sugar = 1-0.30 hct.

It is seen that the difference between the sugar levels in whole blood and plasma is not constant but increases as the glucose level rises.

RESULTS AND DISCUSSION

In table 1 are shown the plasma sugar values, and those of whole blood obtained by analysis and by calculation from the values of plasma sugar and hematocrit. It can be seen that the differences between plasma and blood sugar found when the hematocrit is normal (patient C.D.) diminish as the hematocrit decreases (patient P.B.). It is apparent also that the calculated blood values agree closely with those of direct analysis. The fifth sample of C.D. which only had a difference of 6 mg. per 100 ml. had a 12 per cent error, however. Larger percentage errors are to be expected with low values. If this last variation is omitted, the standard deviation of the percentage difference between the calculated whole blood sugar and the measured whole blood sugar was only 2.0 per cent. Accordingly, the formula would seem to provide valid results.

The determination of sugar in plasma instead of blood has many advantages. The plasma sugar concentration is more appropriate physiologically since it approaches the concentration in extracellular fluid bathing cells. Second, the modifying effect of a variable hematocrit is eliminated. Third, it is more suitable for Auto-Analyzer analysis to employ plasma rather than blood.

In figure 1 are shown blood sugar values advocated by Fajans and Conn for the diagnosis of diabetes.[6] Shown also are the calculated plasma values of the same samples given a hematocrit of 45 per cent. In figure 2 are contrasted the values of blood sugar in two patients

with the same plasma concentrations but of whom one is anemic and the other polycythemic. If the criteria of Fajans and Conn are used, the anemic patient would have a diabetic glucose tolerance test and the polycythemic patient a normal test. As a result, information concerning glucose tolerance in patients with chronic illness and anemia must be interpreted in light of a decreasing hematocrit spuriously elevating the blood sugar.

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BOOK REVIEW

ETIOLOGY OF DIABETES MELLITUS AND ITS COMPLICATIONS. *Ciba Foundation Colloquia on Endocrinology, volume XV. Editors, Cameron and O'Connor. $12.50, 405 pp. Little, Brown and Co., Boston, 1964.*

This volume contains the proceedings of a colloquium on diabetes, held in October 1963 in London, under the chairmanship of Professor Tunbridge. Dr. Charles Best was guest of honor. The following five topics are discussed: natural history of diabetes, the endocrine pancreas, plasma insulin, insulin antagonism and vascular lesions. Each paper is followed by a bibliography and the transcript of the ensuing discussion. Contrary to some symposia, the chapters in this book are uniformly of high quality. This is a most useful volume for anyone seriously interested in current trends in diabetes research. There is essentially no discussion of treatment of diabetes.

Natural history of diabetes: Walker showed data of a diabetes survey performed first in 1957 and repeated in 1962 in a village (Ibstock) of approximately 5,000 inhabitants. During the first survey, 81 per cent of the population over five years of age underwent urine testing and 5 per cent had an oral glucose tolerance test. Four per cent were discovered to be new glycosurics, in addition to 0.8 per cent known diabetics. Five years later an additional 1.4 per cent new glycosurics were detected. Factors associated with diabetes were familial incidence, advancing age with a peak incidence in the fifty-five to sixty-four decade, obesity and multiparity. Yerganian presented an excellent review of spontaneous diabetes in the Chinese hamster and then made special reference to genetic aspects. Earlier suggestions that diabetes was due either to a single recessive or incomplete dominant gene proved to be too simple. At the moment the inheritance pattern appears to be extremely complex, as the diabetic gene even though homozygous may remain dormant for up to three generations. This suggests additional mechanisms for the expression of diabetes such as modifying genes which would activate the diabetic gene.

Endocrine pancreas: The following two papers deal with the morphology of the pancreatic islets, employing either light or electron microscopy. Ogilvie summarized light microscopy of the islets in health, established diabetes, developing diabetes and prediabetes. He defined prediabetes by bodyweight, as "obesity is a common antecedent to diabetes." In established diabetes the classical lesions are reviewed (hyalinization, fibrosis, glycogen infiltration, lymphocytic infiltration, atrophy, hypertrophy and iron deposition). The belief is expressed that even with the light microscope every pancreas from a subject with established diabetes will exhibit detectable changes of one order or another. In young acute diabetics and in obese (prediabetic) adults, enlargement of the islets of Langerhans was noted. Lacy described his experience with the electron microscope. Unfortunately, very little is known about the ultrastructure of the *human* islet. In animals, the appearance of the beta granule varies with the species, possibly related to the difference in amino-acid sequence of the insulin molecule within each granule. Secretion of beta granules occurs in response to hyperglycemia or to tolbutamide; the mechanism at least by morphological criteria appears to be identical. This contrasts with the clinical observation that patients with maturity-onset diabetes may respond well to tolbutamide but not to an increased blood glucose level. Synthesis of beta granules occurs within the ergastoplasm. The hyaline material present in some diabetics and in functioning islet cell tumors has the ultrastructural features of amyloid. Following this, there was a panel discussion on biosynthesis and secretion of insulin. Taylor presented data obtained by in vitro studies with rat and ox pancreas, employing tritium labeled leucine, and Renold reported briefly on similar studies with the giant islets of the toadfish. Fajans reviewed the mechanism of leucine induced hypoglycemia. He concluded that the primary mechanism is pancreatic insulin release which is triggered by leucine itself. Randle described in detail an in vitro technic employing pieces of rabbit pancreas for study of insulin release. It appears that insulin release is enhanced by glucose, mannose and tolbutamide, inhibited by epinephrine and mannoheptulose. The latter probably acts by inhibiting