Differences in Glucose Determinations Obtained From Plasma or Whole Blood

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Glucose determinations obtained on the AutoAnalyzer from plasma are consistently higher than those obtained from whole blood. These differences are large enough to require the adjustment of critical values for screening and diagnostic tests. These differences should be considered also in various research efforts. The data presented here indicate the relationship of whole blood to plasma and suggest equivalent values for screening levels and diagnostic levels as specified for standard oral glucose tolerance tests. The relationships also indicate the adequacy of research results obtained by interpretation of values from either whole blood or plasma.

THE INCREASED availability of automated equipment for obtaining quantitative glucose readings has affected diabetes screening and research programs which require the processing of many blood samples. While automated equipment permits the processing of many samples in less time at lower cost, its characteristics have made it desirable, in some instances, to process plasma rather than whole blood samples. This has precipitated a problem in the interpretation of results.

The data in this paper describe the relationship between glucose determinations obtained from whole blood and from plasma. These data were obtained in a study in which a large group of nondiabetic male prisoners were given repeated standard oral glucose tolerance tests.

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Glucose determinations were obtained on both whole blood and plasma prepared from the same blood sample. Quality control procedures in the laboratory were precise and rigidly maintained. All blood samples were obtained and processed as uniformly as possible. Glucose determinations were obtained on the Technicon AutoAnalyzer by the methodology recommended by the manufacturer at the time of the study, 1962–63.

A description of the AutoAnalyzer and essentially the same glucose methodology used has been given by Johnson (*1*). Samples were processed at a rate of 40 per hour. Standard solutions were run after each set of 12 unknown blood samples in order to increase the precision of the method (*2*).

Venous blood samples were drawn from two men each day, using Becton Dickinson vacutainers, No. 3204, 7 cc., containing 50 mg. of sodium fluoride as a preservative and EDTA as an anticoagulant. Plasma was prepared from a portion of each sample, and both plasma and whole blood were processed in duplicate. Most of the determinations were recorded within 2 hours after the blood specimens were drawn. Results presented in this paper are based on the average value of each pair.

The men studied were principally 20 to 50 years of age. They were not known to have diabetes or any physical condition which would affect their glucose tolerance. For the most part, the glucose determinations obtained fell within normal ranges as related to the time since glucose intake. For a small portion of the group, critical values were exceeded on some readings; however, values which greatly

exceeded normal range at 1 hour after glucose intake were infrequent.

We recognize that there are several distinct needs for comparative data on plasma and whole blood glucose values as obtained on the AutoAnalyzer. The precision required for estimated equivalents varies according to the specific need. Therefore, the data are presented with reference to particular needs. Errors in estimates as well as the statistical methods employed are discussed in the last two sections of the paper.

Specifically, the study had the following three objectives.

1. To provide equivalent values for critical glucose levels used frequently in diabetes screening programs. Values often used are 160, 150, 140, and 130 mg. per 100 ml.

2. To provide equivalent values for critical glucose levels in interpreting results of the standard oral glucose tolerance test. Critical levels recommended by a consultant committee of the Public Health Service for interpretation of this test when based on whole blood are 110 mg. per 100 ml. at fasting, 170 mg. at 1 hour after glucose, 120 mg. at 2 hours, and 110 mg. at 3 hours. (Point values often are used in interpretation with 1 point assigned for values of 110 or more at fasting and 3 hours and one-half point for values at or exceeding the stated levels at 1 and 2 hours. A total of 2 points usually is regarded as diagnostic.) In addition to giving equivalent values for the four recommended levels, the data in this paper permit the determination of equivalent values for other established critical levels of glucose tolerance tests.

3. To provide information on the adequacy of the results of research based on glucose determinations obtained from whole blood or plasma and, in addition, to present data which will aid the researcher in approximating whole blood glucose determinations from plasma readings of individual samples when required.

Objective 1

Critical levels often used in diabetes screening with venous blood tests are 160, 150, 140, and 130 mg. per 100 ml. Increasingly, lower critical levels are recommended and used because it

is feasible to process larger quantities of blood samples and conduct adequate retesting programs. The combination of a relatively low critical level for the screening test and a definitive retest for positive screenees succeeds in identifying more persons who are later diagnosed as diabetic by their physicians than do programs using higher critical levels without retest procedures. At the same time, the private physician is not burdened with excessive referrals. Therefore, we have also given equivalents at levels of 120 and 115 mg. per 100 ml.

The following table contains plasma values which are comparable to the stated whole blood values. The equivalent values for plasma were estimated and then rounded to the nearest 5 mg. for ease in application. Following are suggested equivalent values for glucose determinations, obtained on the AutoAnalyzer from plasma and whole blood, at levels frequently used in diabetes screening activities.

Whole blood mg./100 ml.	Plasma mg./100 ml.
160	190
150	180
140	170
130	155
120	145
115	140

Objective 2

Results of the oral glucose tolerance test are sometimes interpreted from glucose determinations obtained from plasma. It is necessary in such instances to adjust the critical levels used in interpreting results.

Results of glucose tolerance tests can be and are interpreted in a variety of ways with varying levels regarded as critical. For convenience, equivalent values for plasma are presented for the criteria recommended to the Public Health Service and discussed in the booklet, "Diabetes Program Guide" (3). These criteria were described previously. Again, the estimated values for plasma have been rounded to the nearest 5 mg. for ease in application.

Following are suggested equivalent values for glucose determinations, obtained from plasma and whole blood at levels used in interpreting the oral glucose tolerance test.

Interval	Whole blood mg./100 ml.	Plasma mg./100 ml.
Fasting_____	110	135
1 hour_____	170	205
2 hours_____	120	145
3 hours_____	110	135

Figure 1 shows the linear regression line observed in our data. This line may be used to convert either plasma to whole blood or whole blood to plasma equivalents. It may also be used to obtain equivalents for critical levels other than those included in the text table.
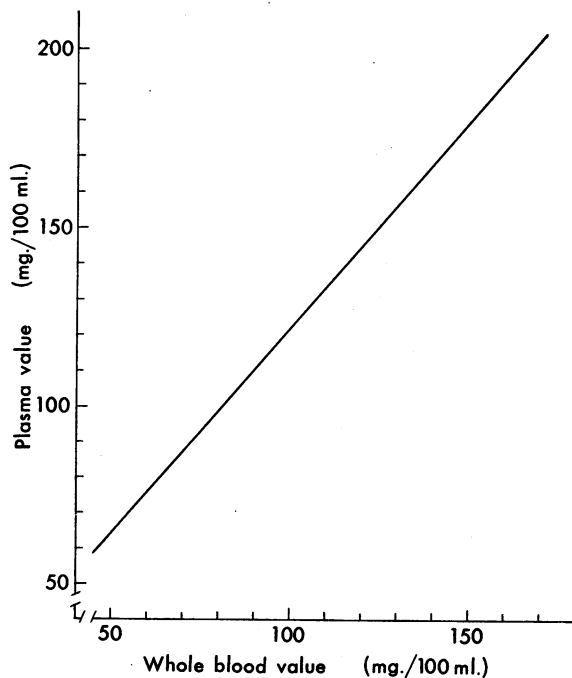
Objective 3

The analysis of data obtained from this and other projects using the AutoAnalyzer has provided information about the relationship of glucose determinations obtained from whole blood to those obtained from plasma. Some general statements can be made, based on analysis of these data.

1. Glucose determinations obtained from plasma are always higher than those obtained from whole blood.

2. The difference between determinations obtained from plasma and whole blood is not absolute but tends to increase as the level of glucose increases.

3. There is a high degree of relationship between plasma and whole blood glucose determinations obtained from the same samples.

4. Because of the close relationship, it is possible to predict plasma values from whole blood values or whole blood values from plasma values with a relatively high degree of precision. This is true for individual samples as well as for average values.

5. Therefore, it is possible to set critical levels for plasma and whole blood values which correspond. When adjustments are made in critical levels, essentially the same persons would be regarded as positive to a screening or diagnostic test, whether this interpretation was based on levels obtained from whole blood or plasma.

6. Interpretation of data based on either whole blood or plasma is equally valid as long as adjustments are made in critical levels. Individual values may be converted for purposes of comparison.

Data supporting these general statements, which are the basis for the suggested equivalent values in the earlier text tables, are presented in table 1. Administration of the oral glucose tolerance test to a group of male prisoners on three occasions yielded the values given for the four readings. There was approximately a 2-month interval between tests for each study member. Sixty-two men were included in the first test, 86 in the second, and 82 in the third. The majority of the men participated in all three series.

Examination of the mean whole blood and the mean plasma values indicates the magnitude of the differences between the two. It is apparent that there is not a consistent absolute difference. The difference tends to increase as the value of the glucose determination increases. Therefore, the differences seen are highest for the 1-hour reading of the test.

The correlation coefficients in table 1 are of particular interest. The coefficients are consistently 0.98 or 0.99 for all tests and readings, with the exception of tests 1 and 2 for fasting. For these readings they are also high; 0.95 and 0.88. Since a correlation coefficient of ±1.00

Figure 1. Linear regression line showing observed relationship between whole blood and plasma glucose determinations obtained on the AutoAnalyzer

describes a perfectly predictable relationship, these coefficients indicate that the relationship between plasma and whole blood glucose determinations is sufficiently precise to permit conversion of the values with relatively accurate results. It is possible, therefore, to predict plasma values from whole blood values or whole blood from plasma with a high degree of accuracy, even for individual samples.

Predicting Plasma Levels From Whole Blood

Linear regression estimating equations (Y on X) provide the most precise method of predicting plasma glucose values when whole blood levels are known. The equations shown in table 2 by time after glucose load and test number were obtained by the method of least squares. The application of these equations for whole blood levels of 110, 120, and 170 mg./100 ml. are shown in table 2 along with their respective standard errors of estimate. Since the fasting and 3-hour sets of data did not contain whole blood values above 110 mg./100 ml., their plasma estimates in table 2 were obtained by extrapolation.

It is apparent that the differences in values obtained from the various predicting equations are not large. For convenience in application, a single equation must be selected which yields good plasma estimates.

Since our objectives are (a) the prediction of critical plasma levels and (b) the conversion of individual whole blood values to their plasma equivalents, we have selected the data taken 1 hour after the glucose load as being the most consistent with our aims (table 3). These data have the advantage of a whole blood range from 60–170 mg./100 ml. with a few values over 170 mg./100 ml. To express the plasma-whole blood relationship in terms of one linear equation, it was decided to use the second test (1 hour after glucose) data which contained the largest number of subjects (n), 86, and the smallest standard error of estimate (2.48 mg./100 ml.). The resulting equation ($\hat{Y}=6.61+1.153X$) was the basis of the suggested equivalents given earlier. Using this regression line, we are 95 percent confident that the true parameter will be within the interval of the expected value ($\hat{Y}$)±5 mg./100 ml. when considering individual conversions.

This error was computed at 50 units from the mean ($\bar{X}$); $2S'_{\hat{y}}=2S_\epsilon\sqrt{1+\frac{1}{n}+\frac{(X-\bar{X})^2}{\sum x^2}}$

$=2(2.48)(1.024)\doteq 2(2.48)$ or 4.96 mg./100 ml.

Because $\sqrt{1+\frac{1}{n}+\frac{(X-\bar{X})^2}{\sum x^2}}$, the factor by which the error due [1] to the regression modifies the standard error of estimate, is approxi-

Table 1. Comparison of whole blood and plasma glucose determinations on the same blood samples, by time after 100 gm. oral glucose load and test number

Glucose tolerance reading and test number	Number of samples	Mean whole blood mg./100 ml. $\bar{X}$	Mean plasma mg./100 ml. $\bar{Y}$	Correlation coefficient r	Mean differences mg./100 ml. $\bar{Y}-\bar{X}$	Ratio of means $\bar{Y}\div\bar{X}$
Fasting:						
First test	62	76. 8	93. 5	0. 945	16. 7	1. 22
Second test	86	76. 0	93. 5	. 876	17. 5	1. 23
Third test	82	76. 3	93. 7	. 980	17. 4	1. 23
1 hour:						
First test	62	105. 2	127. 0	. 995	21. 8	1. 21
Second test	86	103. 9	126. 4	. 997	22. 5	1. 22
Third test	[1] 81	105. 7	128. 1	. 996	22. 4	1. 21
2 hours:						
First test	62	85. 4	103. 8	. 991	18. 4	1. 22
Second test	86	84. 3	102. 9	. 992	18. 6	1. 22
Third test	82	90. 2	110. 3	. 994	20. 1	1. 22
3 hours:						
First test	62	69. 9	86. 4	. 984	16. 5	1. 24
Second test	86	67. 2	83. 2	. 991	16. 0	1. 24
Third test	82	65. 9	83. 0	. 993	17. 1	1. 26

[1] One sample excluded owing to laboratory error.

mately 1, the confidence interval given by $(\hat{Y})\pm 5$ mg./100 ml. at 50 mg./100 ml. from the mean $(\overline{X})$ is approximately twice the standard error of estimate and for practical purposes does not represent an increase over the confidence interval computed at the mean $(\overline{X})$. Therefore it can be assumed to be a constant as reported.

Several other statistics in table 3 could be used to predict plasma values from whole blood val-

ues. The absolute differences between mean values could be used. However, for general application such differences would have to be obtained at other glucose levels, since the absolute difference varies with the amount of glucose.

The ratio of $\overline{Y}$ (mean plasma) to $\overline{X}$ (mean whole blood) could also be used. These figures indicate that an increase of 22 percent is required for the prediction of plasma values at these levels. If a simple conversion system is

Table 2. Simple linear regression equations and estimated plasma levels for specified whole blood glucose levels, by time after 100 gm. oral glucose load and test number

Glucose tolerance reading and test number	Linear regression equations of Y on X $\hat{Y}=b_0+b_1 X$	Estimated plasma levels $\hat{Y}$ when whole blood X equals—			Standard error of estimate mg./100 ml. $S_e=\sqrt{\dfrac{\Sigma(Y-\hat{Y})^2}{n-2}}$
		110 mg./ 100 ml.	120 mg./ 100 ml.	170 mg./ 100 ml.	
Fasting:					
First test	$\hat{Y}=5.49+1.146X$	131. 6	143. 0	200. 3	2. 03
Second test	$\hat{Y}=13.22+1.057X$	129. 5	140. 1	192. 9	2. 72
Third test	$\hat{Y}=-2.33+1.259X$	136. 2	148. 8	211. 7	1. 15
1 hour:					
First test	$\hat{Y}=5.70+1.153X$	132. 5	144. 1	201. 7	3. 56
Second test	$\hat{Y}=6.61+1.153X$	133. 4	145. 0	202. 6	2. 48
Third test	$\hat{Y}=7.14+1.144X$	133. 0	144. 4	201. 6	3. 46
2 hours:					
First test	$\hat{Y}=3.49+1.175X$	132. 7	144. 5	203. 2	3. 17
Second test	$\hat{Y}=4.69+1.165X$	132. 8	144. 5	202. 7	3. 37
Third test	$\hat{Y}=5.87+1.158X$	133. 2	144. 8	202. 7	3. 30
3 hours:					
First test	$\hat{Y}=9.40+1.102X$	130. 6	141. 6	196. 7	3. 37
Second test	$\hat{Y}=9.55+1.096X$	130. 1	141. 1	195. 9	2. 95
Third test	$\hat{Y}=9.95+1.109X$	131. 9	143. 0	198. 5	2. 53

Table 3. Comparison of whole blood and plasma glucose determinations 1 hour after 100 gm. oral glucose load, by test number

Test number	Number of samples	Mean whole blood mg./100 ml. $\overline{X}$	Mean plasma mg./100 ml. $\overline{Y}$	Correlation coefficient r	Mean differences mg./100 ml. $\overline{Y}-\overline{X}$	Ratio of means $\overline{Y}\div\overline{X}$	Linear regression equations $\hat{Y}=b_0+b_1 X$	Standard error of estimate mg./100 ml.
First	62	105. 2	127. 0	0. 995	21. 8	1. 21	$\hat{Y}=5.70+1.153X$	3. 56
Second	86	103. 9	126. 4	. 997	22. 5	1. 22	$\hat{Y}=6.61+1.153X$	2. 48
Third	[1] 81	105. 7	128. 1	. 996	22. 4	1. 21	$\hat{Y}=7.14+1.144X$	3. 46

[1] One sample excluded owing to laboratory error.

required and precision of predicting is not of extreme importance, such a method of converting values would be practical.

Figure 2 is the scatter diagram of the glucose determinations obtained from plasma and whole blood for the 86 samples taken 1 hour after glucose during the second tolerance test. The superimposed lines show the estimated plasma values obtained using (*a*) the linear regression estimating equation ($\hat{Y}=6.61+1.153X$), (*b*) the mean ratio ($\hat{Y}=1.22X$), and (*c*) the absolute mean difference ($\hat{Y}=22.5+X$). This chart indicates the relative lack of precision of the two lines representing the mean ratio and the absolute mean difference.

Predicting Whole Blood Levels From Plasma

The linear regression equation of Y on X was found to be $\hat{Y}=6.61+1.153X$, where X was the observed whole blood level from which we wished to estimate the associated plasma level ($\hat{Y}$). If we solve this equation for X, we obtain $\hat{X}=-5.73+0.867Y$, where Y is the observed plasma level from which we wish to estimate the associated whole blood level ($\hat{X}$) (*4*). The 95 percent confidence limits for a given individual estimate of whole blood obtained in this manner is $\hat{X}\pm5$ mg./100 ml., reported as a constant.

Again, a less precise method of converting would be to define the association by the ratio of $\overline{X}$ (mean whole blood) to $\overline{Y}$ (mean plasma). Our data indicate that if this method is applied, the whole blood value would be equal to 0.82 (82 percent) times the observed plasma values.

Unpublished data from other sources have been compiled and reviewed by the Diabetes and Arthritis Branch to determine if the observed relationships are consistent. The correlation between plasma and whole blood values obtained on the AutoAnalyzer is consistently high in data which have been reviewed. Regressions of plasma and whole blood do not differ significantly for male and female populations. Data were obtained from a clinical setting on 11 diabetics whose fasting mean whole blood glucose level was 154 mg./100 ml. The regression of plasma and whole blood glucose values for these 11 persons does not appear to be different from

Figure 2. Scatter diagram of plasma and whole blood glucose determinations obtained from same blood sample 1 hour after glucose load in second test
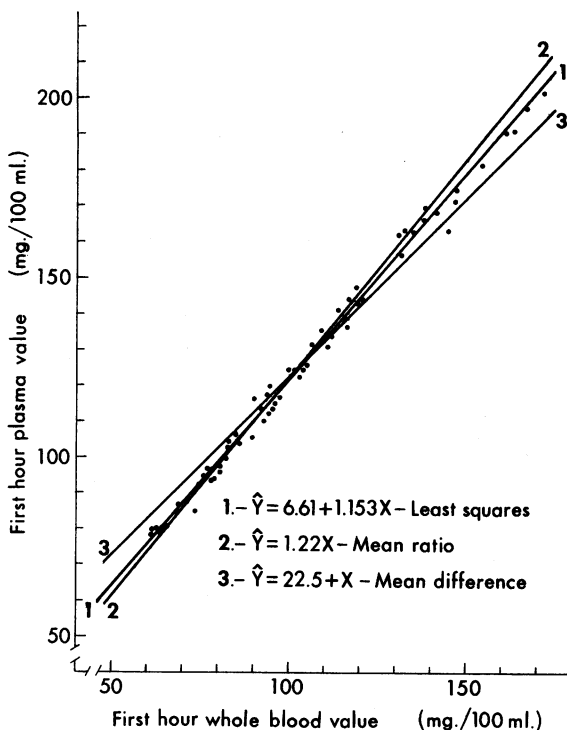
those given here. Since the prison study group provides a large number of samples processed under well-controlled circumstances, it seems appropriate to use the resulting data until such time as more information is available.

Summary

Glucose determinations obtained on the Auto-Analyzer from plasma are consistently higher than those obtained from whole blood. The difference is not absolute but tends to increase as the level of glucose increases. Since there is a close relationship between plasma and whole blood glucose values obtained from the same samples, it is possible to set critical levels which correspond. Such levels are presented for values used frequently in diabetes screening programs or in the interpretation of the standard 100 gm. oral glucose tolerance test. The relationship of glucose values obtained from whole blood and plasma is sufficiently precise that interpretation of data based on whole blood

or based on plasma is equally valid as long as adjustments for differences in levels are made. Data are presented which permit the estimation of equivalent values for levels other than those presented.

REFERENCES

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Sharing Project and Activity Information

A mimeographed list of current or recent public health projects and activities in Georgia, compiled and distributed quarterly by the Georgia Department of Public Health, alerts staff throughout the State to useful ideas developed anywhere in the State.

On forms sent regularly to potential contributors (division, branch, service, section, and program directors of the department and district health directors), the department collects, bimonthly, project information for the 4- to 5-page report. The form asks only for: title of project or activity, time limitations, whether continuing or periodic, specific dates (where possible), a single short descriptive sentence telling what the project deals with, and the name of the key person or persons from whom to seek additional information.

The time required in preparation of the list is negligible. As the information is collected, it is recorded under the heading of the service reporting the item. From the third issue of the report, an alert senior stenographer has been able to handle efficiently the entire mechanics of the project.

Health department service directors distribute the composite mimeographed lists to department personnel. Beginning with the second year of publication, district health directors across the entire State were also added, at their request, to the distribution list.

The number of items contributed for the publication remains uniformly high, and there are frequent requests for additional copies of the list. The device contributes to better routing of requests for information and more prompt replies to inquiries. It also enhances the status of fieldworkers, sinces it enables them to supply requested information in areas other than that of their specialization.

In many large organizations there is an inherent tendency for activities to develop that seem to be more or less independent of other components of the organization. These groups gradually tend to communicate less and less with fellow groups, so that eventually little is known of their special contributions or potential for contributing to the total organizational effort. Our plan for sharing activity and project information was developed in 1962 because such a situation, we believed, existed to some degree in the Georgia Department of Public Health and contributed to the inability of staff, especially those engaged in statewide counseling, to serve to full capacity.— GEORGE W. WATSON, *health educator, currently serving the health departments in Guernsey and Muskingum Counties and Zanesville, Ohio.*