Electrocardiographic Changes after Glucose Ingestion

By Leon D. Ostrander, Jr., M.D., and Belson Jack Weinstein, M.D.

Health appraisals involving multiple laboratory studies are becoming increasingly common both in private practice and in surveys conducted by industry, public health groups, and epidemiologists. Electrocardiograms and tests of glucose tolerance are usually included. These tests vary in the amount of glucose and the time interval at which the blood specimen is drawn, but usually either 50 or 100 Gm. of glucose are administered and the specimen is taken after 60 or 120 minutes.

Since there is a period of an hour or more between glucose administration and the withdrawal of the blood specimen, this interval could be used for other parts of the examination such as the electrocardiogram. This has been the practice in at least one large survey.1

The literature,2-10 however, suggests that electrocardiograms are altered sufficiently by food or glucose to make postprandial tracings deceptive. Most investigators, utilizing either a standard test meal or a measured quantity of glucose, report postprandial changes in heart rate, ST-segment levels, and T-wave amplitudes.2-9 While very slight depression of ST segments and decreases in T waves have been noted in the electrocardiograms of most normal subjects, their postprandial tracings remained in the broad range of normality.3,8 On the other hand, subjects with coronary heart disease but normal fasting electrocardiograms sometimes developed sufficiently marked postprandial changes to be classified as "abnormal."4, 6, 7-9 Indeed, some workers have recommended postprandial electrocardiograms as a diagnostic tool in the detection of occult coronary heart disease.6, 8, 9 Such glucose or food induced electrocardiographic changes have also been described as misleading and of no significance.10

In previous studies, excepting those of Simonson and co-workers employing the test meal,5, 5, 6 postprandial electrocardiographic changes have not been expressed in quantitative terms and in none have the electrocardiograms been classified by a standard coding system.

Table 1

Minnesota Code for ST-Segment and T-Wave Changes

| IV S-T junction and segment (measured from preceding PR segment at onset of QRS) |
| Depression: |
| 1. S-T-J depression 1 mm. or more | I, II, aVL, aVF, V1-V6 |
| 2. S-T-J depression 0.5-0.9 mm. and ST segment horizontal or downward sloping | I, II, aVL, aVF, V1-V6 |
| 3. No S-T-J depression as much as 0.5 mm. but ST segment sloping down and reaching 0.5 mm. or more below PR segment | I, II, aVL, aVF, V1-V6 |

| V T-wave items |
| 1. T amplitude = minus 5 mm. or more | I, II, V2-V6 |
| when R amplitude = 5 mm. or more | aVL, aVF |
| when QRS mainly upright | aVF |
| 2. T amplitude = minus 1-5 mm. | I, II, V2-V6 |
| when R amplitude = 5 mm. or more | aVL, aVF |
| when QRS mainly upright | aVF |
| 3. T wave flat or small diphasic (negative phase) less than 1 mm. | I, II, V3-V6 |
| when R amplitude = 5 mm. or more | aVL, aVF |

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Table 2

ST-Segment and T-Wave Changes * after Glucose Ingestion

<table>
<thead>
<tr>
<th>Number with</th>
<th>Subjects without coronary heart disease; N = 30</th>
<th>Subjects with coronary heart disease receiving digitalis; N = 11</th>
<th>Subjects with coronary heart disease not receiving digitalis; N = 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST-segment changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ST segment change, t</td>
<td>-1.1 ± 1.1</td>
<td>-1.2 ± 1.7</td>
<td>-0.5 ± 1.3</td>
</tr>
<tr>
<td>Range of ST-segment changes (mm.)</td>
<td>+1.5 to -3.5</td>
<td>+1.5 to -3.5</td>
<td>+1.0 to -2.5</td>
</tr>
<tr>
<td>Number with T-wave changes</td>
<td>30</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Mean T wave change</td>
<td>-9.7 ± 5.5</td>
<td>-3.1 ± 4.0</td>
<td>-6.7 ± 2.8</td>
</tr>
<tr>
<td>Range of T-wave change (mm.)</td>
<td>-3.5 to -28.5</td>
<td>+3.0 to -10.5</td>
<td>-4.0 to -9.5</td>
</tr>
</tbody>
</table>

* These changes represent the means of the algebraic sums of the individual changes observed in leads I, II, aVL, aVF, and V_{2}-V_{6}.

† ST-segment changes do not include isolated junctional changes.

Table 3

Heart Rate Change after the Oral Administration of Glucose

<table>
<thead>
<tr>
<th>Number of subjects</th>
<th>Rate during fasting state (beats/min.)</th>
<th>Number with slower rate after glucose (beats/min.)</th>
<th>Number with faster rate after glucose (beats/min.)</th>
<th>Mean increase in rate (beats/min.) after glucose ingestion 60 min.</th>
<th>Mean increase in rate (beats/min.) after glucose ingestion 90 min.</th>
<th>Mean increase in rate (beats/min.) after glucose ingestion 120 min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without heart disease; N = 30</td>
<td>69.5</td>
<td>56-88</td>
<td>6</td>
<td>24</td>
<td>5.1</td>
<td>2.5</td>
</tr>
<tr>
<td>With coronary heart disease; N = 23</td>
<td>78.1</td>
<td>57-100</td>
<td>7</td>
<td>16</td>
<td>4.5</td>
<td>3.3</td>
</tr>
</tbody>
</table>

The purpose of this investigation is to quantitate the ST-segment and T-wave changes after oral glucose in hospitalized patients with and without manifest coronary heart disease and to code the electrocardiograms in a uniform manner.

Methods

Fifty-three ambulatory male medical inpatients at the Ann Arbor Veterans Administration Hospital were studied; all but one were white. Thirty men, age 22 to 66 years (mean age 46 years) had no evidence of heart disease by history, physical examination, electrocardiogram, or chest x-ray, but were hospitalized for other conditions. Twenty-three men, age 39 to 86 years (mean age 61 years), had coronary heart disease as evidenced by angina pectoris, myocardial infarction, or previous congestive heart failure without other apparent cause; 11 of these patients were receiving digitalis.

Subjects were prohibited from eating, drinking, or smoking after midnight before the test. In the morning, a fasting blood specimen and electrocardiogram were taken, and 100 Gm. of glucose in 240 ml. of cool water were administered. Blood samples and electrocardiograms were then taken at 30, 60, 90, and 120 minutes after glucose ingestion. During this period the patients were allowed to lie or sit quietly or go to the bathroom but were not allowed to eat, drink, or smoke.

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Table 4

Relation between Variations in Heart Rate and Changes in ST-Segment Elevation, T-Wave Amplitudes and Classification by “Minnesota Code”

<table>
<thead>
<tr>
<th>Subjects without apparent heart disease</th>
<th>Subjects with coronary heart disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean rank-ST*</td>
<td>Mean rank-T wave†</td>
</tr>
<tr>
<td>A</td>
<td>10.0</td>
</tr>
<tr>
<td>B</td>
<td>15.7</td>
</tr>
<tr>
<td>C</td>
<td>20.8</td>
</tr>
</tbody>
</table>

A Tertile with greatest increase in heart rate after glucose ingestion.
B Tertile with medium increase in heart rate after glucose ingestion.
C Tertile with least increase in heart rate after glucose ingestion.
* Mean rank in degree of ST-segment depression for each tertile, the subjects with the greatest ST depression having the highest rank and thus the lowest number.
† Mean rank in degree of T-wave amplitude.
‡ Number of changes in “Minnesota” classification of ST-segment or T-wave items.

Table 5

Changes in Class IV and V Items of “Minnesota Code” after Glucose Ingestion

<table>
<thead>
<tr>
<th>Subjects without apparent heart disease</th>
<th>ST-segment and T-wave changes</th>
<th>Other coded items*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject without apparent heart disease; N = 3</td>
<td>Fasting</td>
<td>After glucose</td>
</tr>
<tr>
<td>0</td>
<td>IV-3</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>V-3</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>V-3</td>
<td>0</td>
</tr>
<tr>
<td>Subjects with coronary heart</td>
<td>IV-2</td>
<td>IV-3, V-3</td>
</tr>
<tr>
<td>disease receiving</td>
<td>IV-3</td>
<td>IV-2</td>
</tr>
<tr>
<td>digitalis; N = 5</td>
<td>IV-3</td>
<td>IV-2</td>
</tr>
<tr>
<td>IV-3</td>
<td>IV-2, V-2</td>
<td>0</td>
</tr>
<tr>
<td>Subjects with coronary heart</td>
<td>IV-2, V-3</td>
<td>IV-2, V-2</td>
</tr>
<tr>
<td>disease not receiving</td>
<td>IV-2, V-2</td>
<td>IV-1, V-2</td>
</tr>
<tr>
<td>digitalis; N = 3</td>
<td>V-3</td>
<td>V-2</td>
</tr>
</tbody>
</table>

* See Blackburn and associates.11

The electrocardiograms were recorded on a direct-writing instrument at a paper speed of 25 mm. per second. The “Minnesota Code” of Blackburn and associates11 (table 1) was used to classify the ST-segment and T-wave characteristics of each electrocardiogram. In addition, ST-segment deviations from the PR segment at the onset of QRS were measured to the nearest 0.5 mm. in leads I, II, aV1, aVF, and V5-V6, and the algebraic sum of these deviations was calculated for each electrocardiogram. T-wave amplitudes were measured from the same baseline and added together in a like manner. The summed ST-segment deviations and T-wave amplitudes were used for comparing fasting electrocardiograms with those taken at successive 30-minute intervals after glucose ingestion. Since the changes in a given subject were in the same direction in all leads, the sum of such changes for each electrocardiogram simplified comparisons; Simonson and McKinley employed a similar method.6

Glucose was determined from whole blood by an automated procedure with use of a modification of the Hoffman12 technic.

Three subjects with coronary heart disease and four without heart disease were re-examined with saccharine in water instead of glucose.

Results

ST-segment and T-wave Changes after Oral Glucose Administration

Definite ST-segment shifts occurred in 28 of 30 subjects without heart disease, 24 showing depression and four elevation (table 2). ST-segment shifts were observed in 21 of 23 subjects with coronary heart disease, 14

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showing depression and seven elevation. The mean depression was greater for the 11 subjects receiving digitalis.

A decrease in T-wave amplitude followed glucose ingestion in all 30 subjects without heart disease. The greatest absolute changes generally occurred in the subjects with the highest fasting T-wave amplitudes. T-wave amplitudes decreased after glucose ingestion in 19 of 23 subjects with coronary heart disease, two did not change, and two showed slight increases.

The seven subjects re-examined with saccharine in water showed only trivial differences between tracings. Blood glucose levels changed little after the placebo.

Changes in Heart Rate after Glucose Administration

The subjects without heart disease had a mean fasting heart rate of 70, while those with coronary heart disease had a rate of 78. Both groups showed a mean increase in rate after glucose ingestion but the response was variable resulting in a slower rate in some subjects and increases up to 25 beats per minute in a few (table 3).

Figure 1

A “borderline” electrocardiogram recorded 90 minutes after the ingestion of 100 Gm. of glucose shows diphasic T waves in chest leads V3-V4, coded V-3. This subject had a normal fasting electrocardiogram and no evidence of heart disease.
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Men with the greater increases in heart rate tended to have more marked ST-segment depression and a majority of the ST-segment and T-wave changes coded by the Minnesota system. There did not appear to be any clear relation between absolute decreases in T-wave amplitude and increases in heart rate (table 4).

**ST-segment and T-wave Changes Coded According to the Minnesota Criteria**

*Subjects without Heart Disease*

One man developed slight ST-segment depression in lead aVF, coded IV-3, and two developed diphasic T waves in the midchest leads after glucose ingestion, coded V-3 (table 5, fig. 1). When one of these subjects was re-examined with use of a placebo, his electrocardiogram remained normal throughout the test.

*Subjects with Coronary Heart Disease*

Most subjects with coronary heart disease had abnormal fasting electrocardiograms, and many tracings included coded

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An abnormal electrocardiogram recorded 90 minutes after the ingestion of 100 Gm. of glucose shows slight T-wave inversion in leads V₅-V₆, coded V-3. This subject had angina pectoris but his fasting electrocardiogram was normal.
ST-segment and T-wave abnormalities prior to glucose ingestion.

Eight subjects were re-coded after glucose administration because of ST-segment or T wave changes; five of these subjects were receiving digitalis (table 5, fig. 2). Glucose ingestion accentuated the ST-segment depression in most digitalized subjects, regardless of classification (fig. 3).

In general, postprandial ST-segment and T-wave changes were less marked at the end of the 2-hour test but some were still present.

Blood Glucose Levels in Subjects with Coronary Heart Disease and Those without Heart Disease

Although subjects with known diabetes were excluded from the study, blood glucose analysis of the two groups revealed higher mean blood glucose levels at each time interval in the subjects with coronary heart disease (table 6). The differences were statistically significant at the 60-, 90-, and 120-minute intervals after glucose.

Discussion

The administration of oral glucose was fol-

Figure 3A

An abnormal electrocardiogram from a fasting digitalized subject, showing AV nodal rhythm and ST depression due to digitalis. This tracing was coded IV-1 and VIII-6.
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Figure 3B

An electrocardiogram from the same subject as in figure 3A 30 minutes after the ingestion of glucose shows more pronounced ST-segment depression and continued AV nodal rhythm. The code was unchanged.

allowed by changes in ST-segment elevations, T-wave amplitudes, and heart rates in all subjects. Slight depression of ST segments occurred in most subjects who were not taking digitalis, while the ST-segment depression resulting from digitalis was accentuated in the digitalized subjects. While the mean postprandial ST-segment changes for each group were slight, a few individuals developed clinically important changes after glucose ingestion.

T-wave amplitudes decreased in most subjects, the greatest quantitative changes occurring in those with the most positive T-wave deflections in the fasting electrocardiogram.

The mean heart rates increased slightly after glucose in both groups, although responses were quite variable. The degree of ST-segment depression roughly paralleled the increases in heart rate, but the absolute decrease in T-wave amplitudes was unrelated to change in heart rate.

The various changes could not be attributed to gastric filling, since the placebo did not reproduce them in the seven subjects...
who were retested. Potassium depletion may explain the decrease in T-wave amplitudes and the accentuation of digitalis effect on the ST segments, but some of the changes were not typical of hypokalemia. The terminal T-wave inversion observed in several subjects suggested some other nonspecific change in the myocardium.

When ST-segment and T-wave changes in each electrocardiogram were classified according to the "Minnesota Code," three of 30 subjects without heart disease developed postprandial changes, consisting of diphasic T waves in two and slight ST-segment depression in the third.

Eight of the 23 subjects with coronary heart disease developed new or more marked ST-segment or T-wave changes after glucose ingestion, although only one had a normal fasting electrocardiogram. Five subjects were receiving digitalis and in two the principal change was deepening of the digitalis induced ST-segment depression.

Since oral glucose administration produced at least borderline ST-segment or T-wave changes in 10 per cent of the apparently normal subjects and failed to cause or accentuate such changes in 65 per cent of subjects with manifest coronary heart disease, electrocardiograms after glucose are not likely to be a useful method for the detection of occult coronary heart disease. Previous reports advocating such tests have not presented results in quantitative terms nor have the interpretations of the electrocardiograms been based on clearly defined criteria.

On the other hand, the quantitative ST-segment and T-wave changes that generally follow glucose ingestion may be of clinical importance in the electrocardiograms of at least a few subjects without other signs of heart disease.

Because of the uncertain significance of such changes, any ST-segment or T-wave abnormalities occurring after glucose ingestion must be interpreted cautiously. Although such changes may suggest underlying heart disease, a diagnosis should not be based on this evidence alone. Preferably glucose should not be administered for several hours before recording routine clinical electrocardiograms.

The higher mean blood glucose levels in the coronary heart disease subjects may be interpreted in several ways. Chronic hepatic congestion can alter liver function sufficiently to reduce glucose tolerance, but none of the subjects studied was in definite congestive heart failure at the time of the test. Aging is also said to reduce glucose tolerance and the subjects with coronary heart disease had a mean age 15 years older than the subjects without heart disease. Several reports in recent years have suggested that abnormalities in glucose metabolism are frequent in atherosclerotic individuals. Although the effects of age and possible hepatic impairment cannot be ignored, there may well be significant differences in glucose metabolism between subjects with coronary heart disease and those without heart disease.
Summary

In order to determine the effect of glucose ingestion on the electrocardiogram, 23 men with coronary heart disease and 30 without known heart disease had electrocardiograms in the fasting state and serial tracings at 30-minute intervals after the administration of 100 Gm. of oral glucose. In both groups the mean changes after glucose ingestion were slight ST-segment depression, a moderate decrease in T-wave amplitude, and a slight increase in heart rate, although individual variability was great. When the electrocardiograms were classified by a uniform coding system, new ST-segment or T-wave classifications were recorded for eight of 23 subjects with coronary heart disease and three of 30 men without known heart disease.

Since ST-segment and T-wave changes regularly follow glucose ingestion and are sometimes of sufficient degree to suggest heart disease in apparently normal individuals, electrocardiograms recorded within several hours after glucose administration must be interpreted with caution. Because of the uncertain significance of postprandial ST-segment and T-wave changes, electrocardiograms after glucose ingestion do not appear to be a very useful method for the detection of occult heart disease. Glucose ingestion should be avoided before routine clinical tracings.

Acknowledgment

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References

Fabricius and Discovery of Valves in Veins

“April 10, 1565. Owing to the vacancy of the chair of surgery in our University of Padua, created by the death of the eminent Fallopia, and since such a chair is very useful and necessary for certain sciences, we have agreed to appoint the appropriate individual in the person of the excellent Hyeronimo Fabrizio de Acquapendente, who has a good grasp of the aptitude for science and particularly in view of his recent successes in the field of anatomy. And the said excellent Messer Hyeronimo, in addition to his lectures upon surgery, will also undertake the necessary dissections during the four years of his appointment, for which work we offer him a salary of 100 florins per annum with the agreement of the Signoria.”

It was towards the end of the 1570’s that he began to note peculiar formations on the veins while dissecting: In places small flaps hung down into the inside of the veins. They were like small sacks (usually two opposite one another) and they resembled the valves of the heart. He was very pleased, not remembering ever having read about them.

Finally in 1601 (he was now 63 years old) he decided to publish a small book about them, for he felt he had arrived at the solution of the problem.

The little sacks stood out into the inside of the veins with their openings uppermost. They obstructed the downward flow of blood, for when they were swollen the blood could proceed no further. What was the purpose of this arrangement? It could only be that as the blood coursed towards the feet and the lower extremities as well as towards the fingers, it would burst open the walls of the veins with its weight if the small sacks did not prevent this from happening. Filled with blood, the free ends of the two sacks lying opposite one another fit together and prevented the further progress of the blood.

He made exact drawings of opened veins and pointed out that when the arm is bound these valves become visible even from the outside in the form of small protuberances.

Fabricius showed the pictures to his students, among them an Englishman named Harvey who attentively examined the diagrams and listened to what his teacher had to say.—Tibor Doby, M.D. Discoverers of Blood Circulation. From Aristotle to the Times of Da Vinci and Harvey. New York, Abelard-Schuman, 1963, p. 182.
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