# Epidemiologic Findings on the Relationship of Time of Day and Time Since Last Meal to Glucose Tolerance

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SUMMARY

**Data from 10,559 men and women, age 30-64, participating in the morning and afternoon in a Chicago Health Department multiphasic screening project, were used to determine the effects of time of day and time since last meal on the values for plasma glucose one and two hours following oral challenge with 100 gm. of glucose.**

**Mean plasma glucose values and rates of suspect glucose intolerance (based on several cutpoints) were sizeably higher in the afternoon than in the morning. In addition, plasma glucose values increased with time elapsed since the last meal, up to 10 hours postprandially. Thereafter, both one- and two-hour plasma glucose values tended to exhibit a decline. Analysis of covariance confirmed that fluctuations in glucose tolerance were related to time of day and time since last meal, but the effects of each parameter were exerted independently. DIABETES *25*:936-43, October, 1976.**

At present, mass screening procedures are being widely employed for the early detection of asymptomatic individuals with predisposition to certain diseases, e.g., clinical diabetes mellitus and premature coronary heart disease. Large-scale surveys often require that populations be screened throughout the day, with little or no possibility of standardizing either time of day or time since last meal. This study was undertaken to determine the relationship of these two time-related parameters to glucose tolerance.

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## MATERIALS AND METHODS

### *Population*

The 10,559 men and women aged 30-64 reported on in this paper were participants from 1965 to 1971 in a Chicago Health Department multiphasic screening project to detect subclinical chronic diseases and risk factors for these diseases. Among the 13,469 persons surveyed in this project, the 10,559 include all individuals with complete data including time of day and time since last meal when the measurements were taken.[1] The effort was based in two Chicago Housing Authority public housing projects for low-income persons, Dearborn and Lathrop homes, the former on Chicago's near south side with a predominantly black population, and the latter on the near northwest side, with a largely white occupancy. In its initial phase, the screening project intensively encouraged participation by all persons aged 30-64 residing in these two public housing facilities. Subsequently its services were extended to all individuals of this age in the general community of the projects. Persons were excluded from this study who were diagnosed diabetics currently on prescribed antidiabetic medication.

### *Screening Tests and Biochemical Methods*

Persons were scheduled for screening by appointment on a weekday (between 8:30 a.m. and 2:00 p.m.) at times of the morning or afternoon most convenient for them. No instructions were given with regard to dietary preparation.

The battery of standardized screening tests, administered by specially trained teams of nurses and technicians, included an interview to collect demographic data and a brief medical history and the measurement of height and weight. To test glucose tolerance, subjects were given a 100-gm. oral glucose load and venous blood samples were collected in fluoridated tubes one and two hours thereafter.

Plasma was separated within two hours, and analysis was done by the AutoAnalyzer method adapted from Hoffman.[2] All chemical analyses were performed in the special research laboratory of the Chicago Health Department and Chicago Health Research Foundation, under the direction of Morton B. Epstein, Ph.D., and Howard Adler, Ph.D., at the Chicago Civic Center.

### *Statistical Methods*

All data collected on standardized forms were transferred to computer tapes, tested, and edited for errors prior to computer analyses.

Since the possibility existed that the group of people screened at different times of day might differ significantly in composition in a manner biasing the relationship of time of day and time since last meal to the clinical variables, distributions by age-sex-race and relative weight were used to examine this matter. The principal statistical methods for assessing the relation between time and the clinical variables were analysis of variance and chi-square.[3] An analysis of covariance was used to determine whether the relationships of time of day and time since last meal to postload plasma glucose were independent of each other.

## RESULTS

### *Evaluation of Possible Bias*

Data designed to determine whether the composition of the groups of people screened at various times of day and various times since last meal differed markedly from each other in respects, possibly introducing bias into the analyses, are presented in tables 1 and 2. As shown in table 1, the several groups stratified by time of day of screening and time since last meal were not grossly different in their age-sex-race composition. Correspondingly, they were not markedly different in mean age and relative weight (table 2).

### *Glucose Tolerance by Time of Day and Time Since Last Meal*

After the 100-gm. oral glucose load, both one-hour and two-hour mean plasma glucose levels were significantly higher in the afternoon than in the corresponding morning values (table 3 and figure 1). The one-hour mean plasma glucose levels increased with time since last meal in both the morning and afternoon groups, up to 10 hours postprandially; the values for the ≥600-minute groups were lower than the

TABLE 1

Age-sex-race composition of those screened stratified by time of day (morning and afternoon) and time since last meal of ingestion of 100-gm. oral glucose load, Chicago Health Department Community Screening Programs, 1965-1971

| Glucose ingestion—Time of day (a.m. and p.m.) and time since last meal—minutes | No. of people | Age-sex-race composition—per cent of row total | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | White male 30-44 | White female 30-44 | Black male 30-44 | Black female 30-44 | White male 45-64 | White female 45-64 | Black male 45-64 | Black female 45-64 | All |
| A.M. | | | | | | | | | | |
| <120 | 573 | 7.0 | 15.4 | 5.6 | 20.0 | 6.1 | 26.3 | 6.5 | 13.1 | 100.0 |
| 120-179 | 1,303 | 6.8 | 17.8 | 4.9 | 15.7 | 10.1 | 21.9 | 5.8 | 17.0 | 100.0 |
| 180-239 | 1,228 | 5.1 | 20.0 | 3.3 | 15.4 | 8.4 | 27.9 | 4.8 | 15.1 | 100.0 |
| 240-299 | 461 | 3.7 | 16.9 | 5.9 | 18.0 | 7.8 | 22.1 | 6.7 | 18.9 | 100.0 |
| 300-419 | 171 | 5.8 | 18.7 | 7.0 | 18.7 | 7.6 | 15.8 | 8.2 | 18.2 | 100.0 |
| 420-599 | 213 | 7.5 | 14.6 | 9.9 | 24.4 | 7.0 | 11.7 | 8.0 | 16.9 | 100.0 |
| ≥600 | 1,673 | 5.3 | 19.2 | 5.4 | 24.4 | 6.9 | 16.4 | 5.6 | 16.8 | 100.0 |
| Total morning | 5,622 | 5.7 | 18.3 | 5.3 | 19.3 | 8.2 | 20.8 | 5.8 | 16.6 | 100.0 |
| P.M. | | | | | | | | | | |
| <120 | 535 | 7.8 | 14.3 | 4.3 | 23.9 | 8.4 | 24.1 | 5.2 | 12.0 | 100.0 |
| 120-179 | 1,223 | 7.3 | 17.6 | 3.6 | 19.0 | 9.2 | 24.0 | 4.3 | 15.0 | 100.0 |
| 180-239 | 1,112 | 4.9 | 15.9 | 3.7 | 19.6 | 7.6 | 23.8 | 5.6 | 18.9 | 100.0 |
| 240-299 | 851 | 5.6 | 16.6 | 4.6 | 19.5 | 8.1 | 22.8 | 4.5 | 18.3 | 100.0 |
| 300-419 | 818 | 4.6 | 15.6 | 4.0 | 19.9 | 7.1 | 24.7 | 4.2 | 19.9 | 100.0 |
| 420-599 | 163 | 3.7 | 14.1 | 5.5 | 20.9 | 6.7 | 24.5 | 9.2 | 15.4 | 100.0 |
| ≥600 | 235 | 7.2 | 11.9 | 8.1 | 24.7 | 9.4 | 20.4 | 3.0 | 15.3 | 100.0 |
| Total afternoon | 4,937 | 5.9 | 16.0 | 4.2 | 20.2 | 7.9 | 23.6 | 4.7 | 17.5 | 100.0 |
| Total population | 10,559 | 5.8 | 17.2 | 4.8 | 19.7 | 8.1 | 22.1 | 5.3 | 17.0 | 100.0 |

TABLE 2

Mean age and relative weight of those screened stratified by time of day (morning and afternoon) and time since last meal of ingestion of 100-gm. oral glucose load, Chicago Health Department Community Screening Programs 1965-1971

| Glucose ingestion— time of day (a.m. or p.m.) and time since last meal (min.) | No. of people | Mean age —years | Mean relative weight* |
|---|---|---|---|
| A.M. | | | |
| <120 | 573 | 45.4 | 1.139 |
| 120-179 | 1,303 | 46.4 | 1.154 |
| 180-239 | 1,228 | 46.8 | 1.153 |
| 240-299 | 461 | 46.2 | 1.177 |
| 300-419 | 171 | 45.0 | 1.178 |
| 420-599 | 213 | 43.7 | 1.181 |
| ≥600 | 1,673 | 44.4 | 1.168 |
| Total morning | 5,622 | 45.6 | 1.160 |
| P.M. | | | |
| <120 | 535 | 45.1 | 1.160 |
| 120-179 | 1,223 | 46.0 | 1.152 |
| 180-239 | 1,112 | 46.5 | 1.157 |
| 240-299 | 851 | 45.9 | 1.168 |
| 300-419 | 818 | 46.6 | 1.182 |
| 420-599 | 163 | 46.7 | 1.200 |
| ≥600 | 235 | 44.3 | 1.181 |
| Total afternoon | 4,937 | 46.0 | 1.165 |
| Total population | 10,559 | 45.8 | 1.162 |

*Relative weight is the ratio of observed weight to desirable weight for sex and height, as obtained from actuarial tables.[4]

preceding 420-599-minute groups, but still elevated in comparison to levels secured closer to the time of the preceding meal.

The two-hour mean plasma glucose levels exhibited a similar increase with time since last meal (table 3 and figure 1). For the morning strata, the highest meal value was again recorded in the 420-599-minute group. For the afternoon strata, the peak value was in the 300-419-minute group.

All two-hour mean plasma glucose values were lower than those of the corresponding one-hour levels (table 3 and figure 1). Analysis of covariance confirmed that postload plasma glucose values were related to both the time of day and the time since last meal but that these two variables exerted their influence on plasma glucose independently.

Results consistent with the foregoing were obtained when the data were analyzed to determine relationship of rate of suspect glucose intolerance to time of day (a.m. vs. p.m.) and time since last meal (table 4). For this purpose, use was made of fixed cut points (>200 and >140 mg./dl. for the one-hour and two-hour postload plasma glucose, respectively), and quantile cut points (upper 5 per cent, 10 per cent, 20 per cent of both the one-hour and two-hour postload distribu-

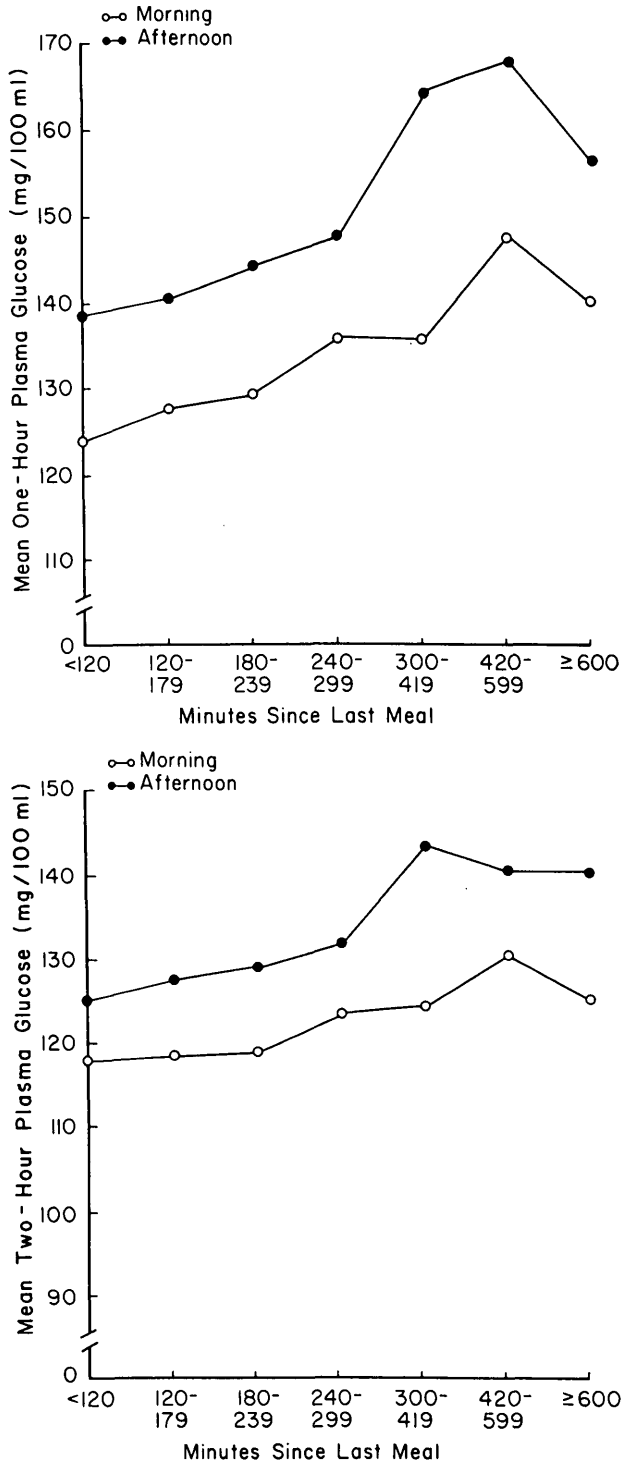


FIG. 1. Relationship of time of day and time since last meal to one-hour (upper graph) and two-hour (lower graph) postload (100 gm.) plasma glucose.

tions); the levels in mg./dl. for the quantile cut points are given in table 4. As judged by conventional criteria measuring glucose intolerance,[5-7] the preva-

TABLE 3

Relationship of mean postload plasma glucose to time of day and time since last meal of ingestion of 100-gm. oral glucose load, Chicago Health Department Community Surveys, 1965-1971

| | Glucose ingestion—time of day and time since last meal—minutes | Number of persons | 1-Hour plasma glucose—mean and standard deviation | 2-Hour plasma glucose—mean and standard deviation |
|---|---|---|---|---|
| Morning | | | | |
| | < 60 | 60 | 118.9 ± 33.2 | 110.4 ± 23.9 |
| | 60-119 | 513 | 124.6 ± 53.9 | 118.8 ± 52.0 |
| | 120-179 | 1,303 | 127.3 ± 58.6 | 118.5 ± 57.0 |
| | 180-239 | 1,228 | 129.4 ± 52.5 | 119.2 ± 47.9 |
| | 240-299 | 461 | 135.7 ± 56.1 | 123.9 ± 51.4 |
| | 300-419 | 171 | 135.6 ± 61.9 | 124.7 ± 61.1 |
| | 420-599 | 213 | 147.5 ± 73.5 | 130.2 ± 77.9 |
| | ≥600 | 1,673 | 140.1 ± 63.9 | 125.1 ± 63.4 |
| | Total morning | 5,622 | 132.9 ± 59.2 | 121.6 ± 57.2 |
| Afternoon | | | | |
| | < 60 | 44 | 126.5 ± 31.8 | 109.7 ± 22.7 |
| | 60-119 | 491 | 138.8 ± 56.1 | 125.7 ± 52.5 |
| | 120-179 | 1,223 | 141.6 ± 58.8 | 127.5 ± 55.4 |
| | 180-239 | 1,112 | 144.1 ± 63.2 | 129.2 ± 57.0 |
| | 240-299 | 851 | 147.6 ± 56.3 | 132.0 ± 52.2 |
| | 300-419 | 818 | 164.1 ± 61.8 | 143.4 ± 60.2 |
| | 420-599 | 163 | 167.7 ± 58.9 | 140.6 ± 59.3 |
| | ≥600 | 235 | 156.3 ± 67.9 | 140.2 ± 71.0 |
| | Total afternoon | 4,937 | 148.1 ± 60.6 | 132.0 ± 56.9 |
| All | | | | |
| | < 60 | 104 | 122.1 ± 32.6 | 110.1 ± 23.3 |
| | 60-119 | 1,004 | 131.5 ± 55.4 | 122.2 ± 52.3 |
| | 120-179 | 2,526 | 134.2 ± 59.1 | 122.9 ± 56.4 |
| | 180-239 | 2,340 | 136.4 ± 58.3 | 123.9 ± 52.6 |
| | 240-299 | 1,312 | 143.4 ± 56.5 | 129.2 ± 52.1 |
| | 300-419 | 989 | 159.2 ± 62.7 | 140.2 ± 60.7 |
| | 420-599 | 376 | 156.2 ± 68.2 | 134.7 ± 70.6 |
| | ≥600 | 1,908 | 142.1 ± 64.6 | 127.0 ± 64.6 |
| | Total population | 10,559 | 140.0 ± 60.3 | 126.5 ± 57.3 |

lence rate was sizably and significantly higher in the afternoon than in the morning for both the one-hour and two-hour values. For seven of eight morning analyses and all eight afternoon analyses, the trend toward higher rates with increasing time since last meal was statistically significant ($p \leq 0.05$); in 11 of these 16 analyses, p was $\leq 0.001$. Further in accord with the findings for the mean postload plasma glucose values, prevalence rates for suspect glucose intolerance were highest at 300-419 or 420-599 minutes after last meal in five of eight morning analyses and all eight afternoon analyses (six of these latter eight being for the interval 300-419 minutes); for three of the eight morning analyses, this rate was highest for the interval ≥ 600 minutes since the last meal (table 4).

## DISCUSSION

Oral ingestion of simple sugars followed by the monitoring of subsequent blood levels has been employed as a diagnostic tool in the elucidation of perturbations in carbohydrate metabolism for over half a century.[8] The test has been under much critical scrutiny over the years, as several variables have been determined to be sources of bias that could undermine the diagnostic value of the technique,[9] and corrective measures have been suggested.[6] The present studies were designed to measure the effects of time of day and time since last meal on blood sugar response to standard oral glucose challenge in an epidemiologic context.

With a test population of 10,559 subjects, we have found that (a) a significantly greater proportion of "abnormal" blood sugar elevations occur during screening in the afternoon than in the morning; and (b) the proportion of "abnormal" responses at either time of day is lowest when oral glucose is given shortly after a meal and highest when the challenge occurs 5-10 hours following prior alimentation.

TABLE 4

Relationship of suspect glucose intolerance (based on several criteria)[5-7] to time of day and time since last meal of ingestion of 100 gm. oral glucose, Chicago Health Department Community Surveys, 1965-1971

| Glucose ingestion—time of day (a.m. and p.m.) and time since last meal—minutes | No. of people | 1-Hour plasma glucose >200 mg./dl. cut point | 1-Hour plasma glucose Upper 5% cut point (>240 mg./dl.) | 1-Hour plasma glucose Upper 10% cut point (>205 mg./dl.) | 1-Hour plasma glucose Upper 20% cut point (>172 mg./dl.) | 2-Hour plasma glucose >140 mg/dl. cut point | 2-Hour plasma glucose Upper 5% cut point (>202 mg./dl.) | 2-Hour plasma glucose Upper 10% cut point (>169 mg./dl.) | 2-Hour plasma glucose Upper 20% cut point (>143 mg./dl.) |
|---|---|---|---|---|---|---|---|---|---|
| A.M. | | | ‡ | * | ‡ | ‡ | | * | † |
| < 60 | 60 | 0§ 0.0¶ | 0 0.0 | 0 0.0 | 5 8.3 | 6 10.0 | 0 0.0 | 1 1.7 | 6 10.0 |
| 60-119 | 513 | 31 6.0 | 17 3.3 | 28 5.5 | 55 10.7 | 74 14.4 | 20 3.9 | 33 6.4 | 67 13.1 |
| 120-179 | 1,303 | 84 6.4 | 50 3.8 | 78 6.0 | 160 12.3 | 190 14.6 | 49 3.8 | 87 6.7 | 179 13.7 |
| 180-239 | 1,228 | 99 8.1 | 39 3.2 | 80 6.5 | 179 14.6 | 219 17.8 | 38 3.1 | 83 6.8 | 195 15.9 |
| 240-299 | 461 | 46 10.0 | 18 3.9 | 40 8.7 | 84 18.2 | 92 20.0 | 15 3.3 | 38 8.2 | 83 18.0 |
| 300-419 | 171 | 19 11.1 | 8 4.7 | 18 10.5 | 29 17.0 | 33 19.3 | 7 4.1 | 17 9.9 | 30 17.5 |
| 420-599 | 213 | 24 11.3 | 11 5.2 | 22 10.3 | 46 21.6 | 42 19.7 | 13 6.1 | 24 11.3 | 38 17.8 |
| ≥600 | 1,673 | 186 11.1 | 97 5.8 | 169 10.1 | 331 19.8 | 335 20.0 | 81 4.8 | 152 9.1 | 305 18.2 |
| Total morning | 5,622 | 489 8.7 | 240 4.3 | 435 7.7 | 889 15.8 | 991 17.6 | 223 4.0 | 435 7.7 | 903 16.1 |
| P.M. | | | ‡ | ‡ | ‡ | ‡ | ‡ | ‡ | ‡ |
| < 60 | 44 | 2 4.5 | 0 0.0 | 2 4.5 | 4 9.1 | 4 9.1 | 0 0.0 | 2 4.5 | 3 6.8 |
| 60-119 | 491 | 50 10.2 | 21 4.3 | 43 8.8 | 91 18.5 | 96 19.6 | 21 4.3 | 43 8.8 | 88 17.9 |
| 120-179 | 1,223 | 131 10.7 | 55 4.5 | 120 9.8 | 254 20.8 | 251 20.5 | 65 5.3 | 121 9.9 | 235 19.2 |
| 180-239 | 1,112 | 133 12.0 | 61 5.5 | 123 11.1 | 248 22.3 | 269 24.2 | 55 4.9 | 120 10.8 | 253 22.8 |
| 240-299 | 851 | 126 14.8 | 47 5.5 | 117 13.7 | 223 26.2 | 239 28.1 | 52 6.1 | 117 13.7 | 229 26.9 |
| 300-419 | 818 | 175 21.4 | 83 10.1 | 162 19.8 | 307 37.5 | 317 38.8 | 83 10.1 | 172 21.0 | 299 36.6 |
| 420-599 | 163 | 35 21.5 | 10 6.1 | 32 19.6 | 62 38.0 | 54 33.1 | 15 9.2 | 28 17.2 | 49 30.1 |
| ≥600 | 235 | 44 18.7 | 19 8.1 | 38 16.2 | 68 28.9 | 68 28.9 | 21 8.9 | 36 15.3 | 64 27.2 |
| Total afternoon | 4,937 | 696 14.1 | 296 6.0 | 637 12.9 | 1,257 25.5 | 1,298 26.3 | 312 6.3 | 639 12.9 | 1,220 24.7 |
| All | | | | | | | | | |
| < 60 | 104 | 2 1.9 | 0 0.0 | 2 1.9 | 9 8.7 | 10 9.6 | 0 0.0 | 3 2.9 | 9 8.7 |
| 60-119 | 1,004 | 81 8.1 | 38 3.8 | 71 7.1 | 146 14.5 | 170 16.9 | 41 4.1 | 76 7.6 | 155 15.4 |
| 120-179 | 2,526 | 215 8.5 | 105 4.2 | 198 7.8 | 414 16.4 | 441 17.5 | 114 4.5 | 208 8.2 | 414 16.4 |
| 180-239 | 2,340 | 232 9.9 | 100 4.3 | 203 8.7 | 427 18.2 | 488 20.9 | 93 4.0 | 203 8.7 | 448 19.1 |
| 240-299 | 1,312 | 172 13.1 | 65 5.0 | 157 12.0 | 307 23.4 | 331 25.2 | 67 5.1 | 155 11.8 | 312 23.8 |
| 300-419 | 989 | 194 19.6 | 91 9.2 | 180 18.2 | 336 34.0 | 350 35.4 | 90 9.1 | 189 19.1 | 329 33.3 |
| 420-599 | 376 | 59 15.7 | 21 5.6 | 54 14.4 | 108 28.7 | 96 25.5 | 28 7.4 | 52 13.8 | 87 23.1 |
| ≥600 | 1,908 | 230 12.1 | 116 6.1 | 207 10.8 | 399 20.9 | 403 21.1 | 102 5.3 | 188 9.9 | 369 19.3 |
| Total population | 10,559 | 1,185 11.2 | 536 5.1 | 1,072 10.2 | 2,146 20.3 | 2,289 21.7 | 535 5.1 | 1,074 10.2 | 2,123 20.1 |

The symbols at the head of the column for the A.M. and P.M. values indicate whether the differences in rate of suspect glucose intolerance (based on the specified criterion) are statistically significant. The chi-square statistic was used for this test; since in six of 16 instances no persons were suspected of glucose intolerance in the small groups of persons tested at <60 min. after last meal, these groups (60 and 44 persons, respectively) were combined with the next group (515 and 491 persons, respectively) for the chi-square tests.

*$p \leq 0.05$

†$p \leq 0.01$

‡$p \leq 0.001$

§No. of people.

¶Rate per 100.

With regard to the first observation, some evidence for a decrease of glucose tolerance in the afternoon and evening has been noted in smaller series during previous assessments of circadian trends in carbohydrate metabolism.[10-18] The phenomenon has been seen with both oral[10,11,13-18] and intravenous[12,16] administration of the glucose load, so that factors involving intestinal absorption or secretagogues do not seem to play a key role. Dietary changes also do not appear to be critical, since subjects fed identical meals at different times of the day exhibited decreased glucose tolerance between morning and afternoon tests.[12,14] Finally, several studies have found higher levels of plasma immunoreactive insulin in the morning than in the afternoon,[14,16,19] and such cyclicity has even been noted in fasting subjects.[19] Thus, these fluctuations must be construed to be a product of an endogenous pattern, responsive to, but independent of, dietary input. Whether the cyclicity is mediated by diurnal changes in the interactions between insulin and insulin antagonists in the periphery or by alterations in beta cell responsiveness to glycemic stimuli[17,20] or both[19] cannot be resolved from existing data. Indeed, as yet the effects of wakefulness per se have not been examined critically.[19] For the moment, however, the unequivocal a.m. versus p.m. differences highlight the necessity to consider time of day in any epidemiologic monitoring of carbohydrate function.

Our second observation—that the interval between prior eating and glucose challenge may affect the magnitude of blood sugar responses—has been noted by others[15,21-27] but not previously recognized as fully independent of the influence of time of day. This finding is not unexpected when viewed in the light of certain theoretical considerations.[28] Immediately following alimentation, insulin release is triggered, anabolism is initiated, and circulating contrainsulin factors such as glucagon[29] and growth hormone[30] are reduced. Administration of a second glucose load at this time should effect facilitated glucose disposition, since islet responsiveness to additional secretagogues should be enhanced by nutrient priming[31] and tissue sensitivity to insulin should be optimal.[32] Earlier observations are consistent with these expectations.[21-24] Thus, Bang,[21] Hamman and Hirschman,[22] and subsequently Staub[23] and Traugott[24] noted that blood sugar rises less when a second dose of oral glucose is given within four hours of the first (the "Staub-Traugott effect"). The same phenomenon has been noted following repetitive administrations of intravenous glucose, and the enhanced glucose disposition under these circumstances does not necessitate commensurate increases in the rate of insulin secretion.[26] Indeed, the ability to sustain tissue "insulinization" independent of exogenous renewal has been demonstrated in an in-vitro model with lipogenesis as the metabolic parameter.[33] On the other hand, coincidentally with the late disposition of exogenous nutrients, counterregulatory hormones would be called into play.[28] Their capacity to offset the effectiveness of insulin action has been fully demonstrated for growth hormone [30,34] and may be equally applicable to hormones such as glucagon, which also rise following disposition of dietary carbohydrates.[29] Moreover, tissue metabolism would be geared to lipid products (of dietary as well as endogenous origin) so that the acute disposition of newly introduced glucose might be compromised.[35] The temporal characteristics of the sequence would be conditioned by the precise mixture of nutrients in the antecedent meal.[36-38] Within the above formulation, one might predict that tolerance to a given glucose challenge should be (a) optimal shortly following a meal, (b) compromised during the counterregulation to previous alimentation (i.e., 5-10 hours, depending on the exogenous substrate mixture), and (c) restored to basal (consistent with the time of day) when disposition of all exogenous nutrients has been completed. Our present finding that glucose tolerance is not fully restored until more than seven hours have elapsed is consistent with the above speculative sequence. Clearly, however, definitive interpretation will have to await more careful correlations with concurrent plasma levels of insulin and contrainsulin hormones, as well as with the exact composition of the antecedent meal.

Regardless of the theoretical implications, these observations on relationship of glucose tolerance to time of day and time since last meal need to be evaluated in terms of their relevance to public health practice. As part of the current emphasis on early detection of symptomatic individuals at risk for the development of various diseases, mass screening is increasingly regarded as an efficacious technique. By its very nature, mass screening is usually incompatible with standardization of time of day or time since last meal. To reach large target populations efficiently in the community or the work place, screening often must be done over a wide range of hours and without alteration of people's daily routine. In view of the present findings, the question therefore arises: would it be useful to apply

varying cut points for suspect hyperglycemia at primary screening based on time of day and/or time since last meal? If a single cut point is used, based on experience with a fasted population given an oral load and tested in the morning, there is the possibility of reporting an inordinate number of false positives when screening in the afternoon.[14,16] This could result in a more than reasonable share of expenditures for complete glucose tolerance testing for these putative "hyperglycemics," as well as a more than reasonable burden of concern for health status. If a single cut point is set high enough to avoid this problem, persons truly at risk may not be detected during morning screening. On the other hand, challenge in the afternoon and/or five to seven hours after meals in which the usual criteria for "normal" and "abnormal" responses are retained[5-7] may be useful for unmasking the vulnerable—analagous, for example, to the cortisone-glucose tolerance test.[39] Without long-term follow-up studies to determine the prognostic significance of various responses, this issue does not appear to be readily resolvable.

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