The Normal ("Average") Versus Normal ("Physiologic") Diurnal Blood Glucose Pattern

E. Cheraskin, M.D., D.MD.i

Introduction

There seems to be no question that blood measures carbohydrate metabolism, specifically blood sugar and Wood glucose, are among the most commonly studied biochemical parameters in clinical medicine.

In this connection, there is a plethora of information on the subject of blood sugar and blood glucose under numerous conditions (1-11). What is most surprising is that there is only one report {12) outlining the *diurnal* blood sugar or blood glucose under usual and customary conditions.

The purpose of this report is to investigate the normal ("average") versus the normal ("physiologic") diurnal blood glucose pattern.

Method of Investigation

Nine hundred sixty-nine doctors and their spouses participated in this study. The blood glucose levels were determined by the Autoanalyzer method at 8:30 a.m., 10:30 ajn., 12:30 p.m., 2:30 p.m. and 4:30 p.m. under usual conditions. In other words, the subjects were instructed to carry on their customary and usual activities and to consume their usual food and drink.

Additionally, each subject completed the Cornell Medical Index Health Questionnaire (CMI). The CMI is a self-administered health questionnaire consisting of 195 questions. Each question is answered by circling the word <fyes" or "no". The questions are phrased so that the affirmative answers indicate pathology. The clinical findings in this report are the total number of affirmative CMI responses (CMI score).

Results

First Morning Sarnple (8:30 a.m.): Table 1 (line 1) shows the total sample of 969 subjects who completed the Cornell Medical Index Health Questionnaire. The range of affirmative responses spread from 0 to 125 with a mean clinical score of 15.6. The 8:30 a.m. blood glucose range spread from 45 to 338 mg. percent with a mean and standard deviation of 94±23mg. percent. Since these doctors and their spouses are presumed to be healthy, one would ordinarily conclude that the usual 8:30 a.m. blood glucose for approximately

1. Post Office Box 20287
Vestavia Hills, Alabama 35216-0287 United States of America

two-thirds of the sample (one standard deviation) should be from about 71 mg. to 117 mg. percent.

You will note (line 2) that those subjects with more than 50 clinical symptoms and signs have been eliminated, leaving a sample of 948 subjects. The mean CMI score is 14.9. The 8:30 a.m. blood glucose range remains the same (45-338 mg. percent). As one proceeds downward in Table 1 the group becomes progressively healthier by virtue of the fact that the subjects are characterized by progressively fewer clinical symptoms and signs. Obviously, the sample size drops sharply. It is noteworthy that, under these conditions, the mean blood glucose decreases in perfect order from 94 mg. percent (line 1) to 84 mg. percent (line 11). Also, it will be noted that the standard deviation also shrinks from 23 mg. percent to 9 mg. percent. Table 2 indicates that, as one

Table 1

relationship of reported diurnal blood glucose (8:30 a.m.) and reported total clinical findings (Cornell Medical Index Health Questionnaire) in a presumably healthy male and female sample

line	group	sample size	clinical findings (affirmative CMI responses) range	clinical findings mean & S.D.	diurnal blood glucose (8:30 a.m.) (mg. per cent) range	diurnal blood glucose mean & S.D.
1	entire sample	969	0-125	15.6±11.9	45-338	94+23
2	CMI <50	948	0- 49	14.9±10.0	45-338	94^23
3	CMI <40-	923	0- 39	14.0+ 8.8	45-338	94±22
4	CMI <30	855	0- 29	12.4+ 7.1	45-338	94±22
5	CMI <20	694	0-19	9.8+5.0	45-338	94+23
6	CMI <10	349	0- 9	5.6+ 2.4	45-217	93+21
7	CMI < 5	109	0- 4	2.7+1.2	45-152	92+20
8	CMI < 4	71	0- 3	2.0+1.0	45-152	91+19
9	CMI < 3	45	0 - 2	1.5+ 0.8	45-152	91+20
10	CMI < 2	17	0 - 1	0.6+ 0.5	45-137	88+18
11	CMI 0	7	0	0.0+ 0.0	70- 97	84+ 9

* **Table 2**

statistical significance of the relationship of diurnal blood glucose (8:30 a.m.) and reported clinical findings (CMI)

			significance of the differences of the means P	significance of the differences of the variances P
1	entire sample		969 versus	
2	CMI <10	349	>0.200	<0.025**
3	CMI < 5	109	>0.200	<0.050**
4	CMI < 4	71	>0.200	<0.050**
5	CMI < 3	45	>0.200	>0.100
6	CMI < 2	17	>0.200	>0.100
7	CMI 0	7	<0.010*	<0.010**

♦statistically significant difference of the means

♦♦statistically significant difference of the variances creates the symptomless-signfree group, the lower mean and the narrower range are statistically significant.

Hence, it would appear, that presumably healthy subjects, at 8:30 a.m. on their customary regime, demonstrate a blood glucose range of about 70 to 120 mg. percent. However, in a relatively healthier subsample, the blood glucose range is about 75 to 95 mg. percent.

Second Morning Sample (10:30 a.m.): Table 3 (line 1) shows the total sample of 887 subjects who completed the Cornell Medical Index Health Questionnaire. The range of affirmative responses spread from 0 to 125 with a mean clinical score of 16.3. The 10:30 a.m. blood glucose range spread from 42 to 332 mg. percent with a mean and standard deviation of 97±20. Since these doctors and their spouses are presumed to be healthy, one would therefore conclude that the usual 10:30 a.m. blood glucose for approximately two-thirds of the sample (one standard deviation) should be from about 77 to 117 mg. percent.

As one proceeds downward in Table 3, the group becomes progressively healthier by virtue of the fact that the subjects are characterized by progressively fewer clinical symptoms and signs. It is noteworthy that, under these conditions, the mean blood glucose rises from 97 mg. percent (line 1) to 106 mg. percent (line 11). Also, it will be noted that the standard deviation shrinks from 20 to 13 mg. percent. Table 4 indicates that, as one creates the symptomless-signfree group, the higher mean is not statistically significant. However, the smaller standard deviation is of statistical import.

Therefore, it would appear, that presumably healthy subjects, at 10:30 a.m. on their customary regime demonstrate a blood glucose range from about 75 to 115 mg. percent. However, in a relatively healthier subsample, the blood glucose range is about from 95 to 120 mg. percent.

Table 3

relationship of reported diurnal blood glucose (10:30 a.m.) and reported total clinical findings Cornell Medical Index Health Questionnaire) in a presumably healthy male and female sample

line	group	sample size	clinical findings (affirmative CMI responses) range	clinical findings (affirmative CMI responses) mean & S.D.	diurnal blood glucose (10:30 a.m.) (mg. per cent) range	diurnal blood glucose (10:30 a.m.) (mg. per cent) mean & S.D.
1	entire sample	887	0-125	16.3*12.4	42-332	97±20
2	CMI <50	868	0-49	15.2+10.0	42-332	97+20
3	CMI <40	842	0- 39	14.4+ 8.8	42-332	97+19
4	CMI <30	776	0- 29	12.8+ 7.1	42-332	97+20
5	CMI <20	621	0- 19	10.1+ 4.9	42-332	97+20
6	CMI <10	298	0- 9	5.8+ 2.2	58-223	96+17
7	CMI < 5	83	0- 4	2.9+ 1.1	60-130	95+15
8	CMI < 4	51	0- 3	2.2+ 0.9	60-130	94+15
9	CMI < 3	29	0- 2	1.6+ 0.7	60-130	98+17
10	CMI < 2	10	0- 1	0.7+ 0.5	77-130	103+17
11	CMI 0	3	0	0.0+ 0.0	92-118	106+13

Table 4

statistical significance of the relationship of diurnal blood glucose (10:30 a.m.) and reported clinical findings (CMI)

			means P	significance of the difference of the variances P
1	entire sample	887 versus		
2	CMI <10	298	0.200	<0.005*
3	CMI < 5	83	0.100	<0.005*
4	CMI < 4	51	0.200	<0.010*
5	CMI < 3	29	0.500	>0.100
6	CMI < 2	10	0.200	>0.250
7	CMI 0	3	0.200	<0.050*

***statistically significant difference of the variances**

First Afternoon Sample (12:30 p.m.): Table 5 (line 1) shows the total sample of 891 subjects who completed the Cornell Medical Index Health Questionnaire. Utilizing the techniques previously outlined with the earlier blood samples, it is evident that the 12:30 p.m. blood glucose is 102±26 mg. percent. As one proceeds downward in Table 5, the group becomes progressively healthier by virtue of the fact that the subjects are characterized by progressively fewer clinical symptoms and signs. It is noteworthy that under these conditions, the mean blood glucose declines from 102 to 97 (line 11). Also, it will be observed that the standard deviation shrinks from 26 to 8 mg. percent. Table 6 indicates that, as one creates the symptomless-signfree group, the lower mean is not statistically significant. However, the smaller standard deviation is of statistical significance. *Therefore, it would suggest, that presum-*

Table 5

relationship of reported diurnal blood glucose (12:30 p.m.) and reported.total clinical findings (Cornell Medical Index Health Questionnaire) in a presumably healthy male and female sample

line	**group**	**sample size**	**clinical findings (affirmative CMI responses) range**	**mean & S.D.**	**diurnal blood qlucose (12:30 D.m. (mg. per cent) range**	**mean & S.D.**
1	entire sample	891	0-125	16.3+12.6	41-364	102+26
2	CMI <50	870	0- 49	15.2+10.0	41-364	102+26
3	CMI <40	844	0- 39	14.3+ 8.8	41-352	102+25
4	CMI <30	778	0 - 2 9	12.7+7.1	41-352	102+25
5	CMI <20	625	0- 19	10.0+ 4.9	41-352	101±25
6	CMI <10	302	0 - 9	5.8+2.2	54-229	100+21
7	CMI < 5	86	0- 4	2.9+ 1.1	65-160	101+18
8	CMI < 4	51	0- 3	2.2+ 0.9	65-146	100±19
9	CMI < 3	30	0- 2	1.6+0.7	65-138	97+17
10	CMI < 2	10	0 - 1	0.7+ 0.5	75-117	95+11
11	CMI 0	3	0	0.0+ 0.0	89-105	97+ 8

ably healthy subjects, at 12:30p.m. on their customary regime demonstrate a blood glucose range from about 75 to 125 mg. percent. However, in a relatively healthier subsample, the blood glucose spread is from 90 to 105 mg. percent.

Second Afternoon Sample (2:30 p.m.): Table 7 summarizes the total sample of 881 subjects who completed the Cornell Medical Index Health Questionnaire. Employing the techniques already outlined with the earlier blood samples, it is evident that the 2:30 p.m. blood glucose is 103±24 mg. percent. As one proceeds downward in Table 7, the group becomes progressively healthier by virtue of the fact that the subjects are characterized by progressively fewer clinical symptoms and signs. It is noteworthy that, under these conditions, the mean blood glucose declines from 103 to 93 (line 11). Also, it will be noted that the standard deviation shrinks from 24 to 5 mg. percent. Table 8 indicates that, as one creates the symptomless-signfree group, the lower mean is statistically significant as is the smaller standard deviation.

Table 6

statistical significance of the relationship of diurnal blood glucose (12:30 p.m.) and reported clinical findings (CMI)

			statistical significant difference of the means P	variances P
1	entire sample	891 versus		
2	CMI <10	302	>0.200	<0.0005*
3	CMI < 5	86	>0.400	<0.0005*
4	CMI < 4	51	>0.200	<0.0050*
5	CMI < 3	30	>0.050	<0.0050*
6	CMI < 2	10	>0.050	<0.0005*
7	CMI 0	3	>0.200	<0.0005*

*statistically significant difference of the variances

Table 7

relationship of reported diurnal blood glucose (2:30 p.m.) and reported total clinical findings (Cornell Medical Index Health Questionnaire) in a presumably healthy male and female sample

line	group	sample size	clinical findings (affirmative CMI responses) range	clinical findings mean & S.D.	diurnal blood glucose (2:30 p.m.) (mg. per cent) range	diurnal blood glucose mean & S.D.
1	entire sample	881	0-125	16.4112.9	57-396	103+24
2	CMI <50	860	0 - 4 9	15.2±10.0	57-396	103+24
3	CMI <40	834	0 - 3 9	4.3+ 8.9	57-332	103+22
4	CMI <30	773	0 - 2 9	1 2 . 7 + 7 . 2	60-332	103±22
5	CMI <20	620	0 - 1 9	9 . 7 + 4 . 9	60-332	103+23
6	CMI <10	299	0 - 9	5 . 8 + 2 . 2	60-215	101+20
7	CMI < 5	87	0 - 4	2.9+1.1	60-163	104+21
8	CMI < 4	53	0 - 3	2.2+ 0.9	60-163	103+21
9	CMI < 3	30	0 - 2	1.6± 0.7	60-163	106±22
10	CMI < 2	10	0 - 1	0.7+ 0.5	88-112	98+ 7
11	CM! 0	3	0	0.0± 0.0	88- 98	93+ 5

Hence, it would appear, that presumably healthy subjects, at 2:30 p.m. on their customary regime demonstrate a blood glucose range from about 80 to 125 mg. percent. However, in a relatively healthier subsample, the blood glucose spread is from approximately 88 to 98 mg. percent.

Third Afternoon 'Sample (4:30 p.m.): Table 9 (line 1) shows the total sample of 866 subjects. The average values at 4:30 p.m. are 101±24 mg. percent. As one proceeds downward in Table 9, the mean blood glucose declines from 101 to 91 mg. percent and the standard deviation shrinks from 24 to 8 mg. percent. Table 10 indicates that, as one produces the symptomless-signfree subgroup, both the lower mean and the smaller standard deviation are statistically significant.

Thus, the evidence suggests, that presumably healthy subjects, at 4:30 p.m. on their customary regime demonstrate a blood glucose range from about 75 to 125 mg. percent. However, in a relatively healthier subgroup, the blood glucose spread is from approximately 80 to 100 mg. percent.

Table 8

statistical significance of the relationship of diurnal blood glucose (2:30 p.m.) and reported clinical findings (CMI)

			statistical significant difference of the means P		variances P
1	entire sample	881	versus		
2	CMI <10	299	>0.100		<0.0005*
3	CMI < 5	87	>0.500		>0.0500
4	CMI < 4	53	>0.500		>0.1000
5	CMI < 3	30	>0.500		=0.2500
6	CMI < 2	10	<0.050*	<0.0005*	
7	CMI 0	3	<0.001*	<0.0005*	

*statistically significant difference of the means

**statistically significant difference of the variances

Table 9

relationship of reported diurnal blood glucose (4:30 p.m.) and reported total clinical findings (Cornell Medical Index Health Questionnaire) in a presumably healthy male and female sample

			clinical findings (affirmative CMI sample responses)		diurnal blood glucose (4:30 p.m.) (mg. per cent)	
line	group	size	range	mean & S.D.	range	mean & S.D.
1	entire sample	866	0-125	16.4±12.5	62-416	101±24
2	CMI <50	846	0- 49	15.3+ 9.9	62-416	101±25
3	CMI <40	819	0- 39	14.41+8.7	62-416	100t23
4	CMI <30	756	0- 29	12.8+ 7.0	62-416	101±23
5	CMI <20	610	0-19	10.2+4.8	63-416	101±24
6	CMI <10	288	0- 9	5.6+ 2.2	63-201	100±19
7	CMI < 5	76	0- 4	3.0+1.1	63-157	97±15
8	CMI < 4	43	0- 3	2.2+ 0.9	63-125	96J12
9	CMI < 3	24	0- 2	1.5+0.7	63-123	97±13
10	CMI < 2	9	0 - 1	0.7+0.5	75-103	931 9
11	CMI 0	3	0	0.0+ 0.0	85-100	91+. 8

Table 10

statistical significance of the relationship of diurnal blood glucose (4:30 p.m.) and reported clinical findings (CMI)

			significance of the differences of the means P	significance of the differences of the variances P
1	entire sample	866 versus		
2	CMI <10	288	>0.500	<0.0005**
3	CMI < 5	76	>0.050	<0.0005**
4	CMI < 4	43	<0.050*	<0.0005**
5	CMI < 3	24	>0.200	<0.0005**
6	CMI < 2	9	<0.025*	<0.0050**
7	CMI 0	3	<0.050*	<0.0500**

♦statistically significant difference of the means ♦♦statistically significant difference of the variances

Discussion

The evidence seems clear that, in a relatively symptomless-signfree group, the diurnal range of blood glucose is significantly smaller than in a group of presumably healthy subjects. The question now is whether there is any practical import in this observation. This will be attempted by answering the following five questions:

1. What is the carbohydrate metabolic picture of a presumably healthy person during a routine day?
2. How does carbohydrate metabolism relate to the sugar equivalent of carbohydrate foods in a regular diet?
3. What changes in carbohydrate metabolism follow a decrease in refined carbohydrate (sugar and white flour) ingestion?
4. Is there any relationship between carbohydrate metabolism and the physiologic state (e.g. blood pressure)?
5. Can physiologic state (e.g. blood pressure) be significantly modified by reducing refined-carbohydrate intake?

Seven dental practitioners participated in this program during a two week period. On the Monday through Thursday of the first week, the seven subjects carried out their usual activities while consuming their regular diets. On Thursday, each reported to the clinic at 8:00 a.m. fasting (immediately before an 8:15 a.m. breakfast), 10:00 a.m. (about 30 minutes after the usual 9:30 a.m. coffee-shop visit), 12:00 noon (about 30 minutes prior to the 12:30 p.m. lunch), 2:00 p.m. (about 1 hour before the customary 3:00 p.m. coffee break) and at 4:00 p.m. At each visit, the blood glucose (Somogyi-Nelson method) was ascertained. Also, at each of the sessions, the blood pressure was recorded.

The following Monday through Thursday, the subjects carried out their usual duties. However, as far as possible, refined carbohydrates (sugar and white flour products) were eliminated from the diet. On Thursday, the subjects reported to the clinic for blood glucose and blood pressure measurements as earlier reported for the initial visit.

Question One: Table 11 lists the blood glucose values for the seven subjects at the five different time intervals during the initial visit. The overall individual spread is 115 mg. per cent. It is of paranthetic interest that there are significant differences of the means and the variances between all temporal points except the 10:00 a.m. and noon values. Figure 1 pictorially portrays the mean blood glucose fluctuations in the seven subjects during the experimental day (interrupted line). The spread for the entire group is approximately 46 mg. per cent (73.4 to 119.0 mg. per cent).

Within the limits of these observations and of the reported literature, (13-16) carbohydrate metabolism (as measured by blood glucose) fluctuates significantly during the day and the oscillations differ among the various participants.

Question Two: There are undoubtedly numerous factors which modify the carbohydrate metabolic pattern. Certainly, one of the important variables is the diet. Table 12 is a composite of the sugar equivalent intake (expressed in teaspoonsful) calculated from the dietary record. (17) The sugar intake at any one temporal point varied from zero to 28.9 teaspoonsful. Table 12 underscores the fact that the mean differences were significant in all instances except between 8:15 a.m. mean (breakfast) and the mid-morning coffee break (9:30 a.m.). The variances were statistically significant only between the afternoon meals. Figure 2 graphically shows the mean sugar intake for the experimental days (white columns). The range for the group is approximately 29 teaspoonsful (from 0 to 29). It is reasonable to conclude, from these data, that the sugar intake fluctuates widely and significantly during the day in any one person and also varies considerably among individuals.

Table 11

blood glucose values in seven dentists following a three-day regular diet

subjects	8:00 A.M.	10:00 A.M.	12:00 Noon	2:00 P.M.	4:00 P.M.
RiBl	70	117	60	140	83
BrSp	70	83	72	105	92
ShDu	63	77	72	110	110
YoKa	71	92	83	80	77
ThSh	77	102	87	175	85
WiGr	85	100	90	111	85
HeBr	78	83	100	112	90
mean	73.4	93.4	80.6	119.0	88.9
S.D.	7.1	13.9	13.4	30.2	10.5
range	63-85	77-117	60-100	80-175	77-110
significance of the difference of the means		<0.0500*	>0.1000	<0.0250*	<0.0500*
significance of the difference of the variances		=0.0250*	=0.5000	=0.0050*	=0.0005*

^statistically significant

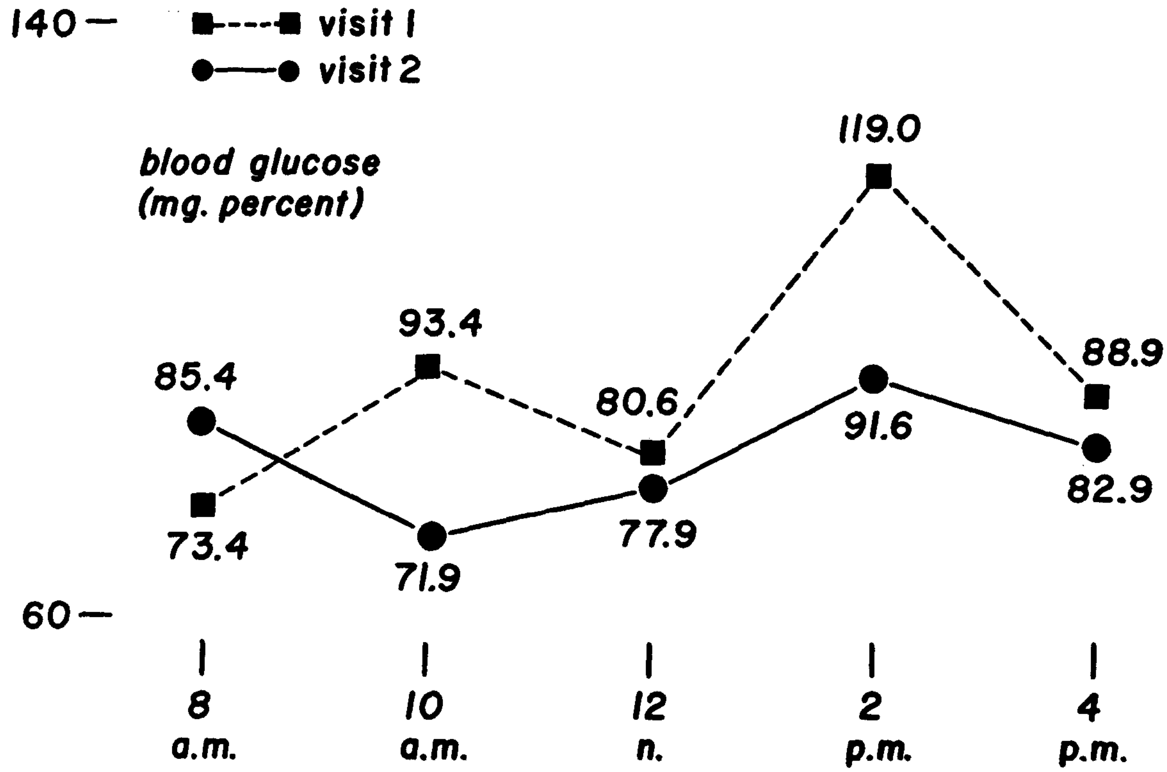


Figure 1. Daily fluctuations in mean blood glucose following a three-day regular diet (visit 1, interrupted line) and after a three-day decrease in refined-carbohydrate foods (visit 2, continuous line).

Table 12

daily dietary sugar equivalent (expressed in teaspoonsful) during a three-day regular diet regime

subjects	8:15 A.M.	9:30 A.M.	12:30 P.M.	3:00 P.M.	6:00 P.M.
RiBl	7.9	5.5	23.4	4.5	24.3
BrSp	17.1	1.5	12.2	2.0	26.4
ShDu	22.3	0.0	16.1	7.5	28.9
YoKa	6.5	0.0	10.6	0.0	17.9
ThSh	6.9	8.5	25.0	1.8	20.5
WiGr	9.4	2.5	11.5	2.7	12.1
HeBr	12.0	5.0	15.9	2.2	17.8
mean	11.7	3.3	16.4	3.0	21.1
S.D.	5.9	3.2	5.8	2.4	5.8
range	6.5-22.3	0.0-8.5	10.6-25.0	0.0-7.5	12.1-28.9
significance of the dif ference of the means	=0.5000	<0.0010*	<0.0010*	<0.0010*	
significance of the difference of the variances	=0.1000	=0.1000	=0.0250*	=0.0250*	

*statistica!ly significant

An analysis of Figure 3 shows the relationship between the ingestion of sugar and white flour foods and the blood glucose levels. It appears from the available data that orderly relationships prevail between the dietary sugar equivalent intake and carbohydrate metabolism. In brief, after sugar intake, the blood glucose rises. Apparently, the glycemic responses are more severe following sucrose ingestion than after isoglucogenic quantities of other carbohydrates or protein. (18)

Question Three: While the observations thus far appear to be of considerable interest, it should be underlined that no cause-and-effect relationships of sugar intake to blood glucose can be established.

Earlier mention was made of the fact that, on Monday through Thursday of the second week, the subjects were instructed to reduce sugar and white flour intake to a minimum. Table 13 summarizes the daily sugar equivalent intake expressed in teaspoonsful. (17) In all instances, there are clearcut significant differences of the means and the variances. The mean sugar equivalent intake for the subjects at the initial (white columns) and the final visit (black columns) is summarized in Figure 2. It is abundantly clear from this chart that the sugar equivalent intake at every temporal point has been sharply curtailed. With this background information in hand, it is now possible to reiterate the question as to what effect this dietary change exerted upon the blood glucose pattern.

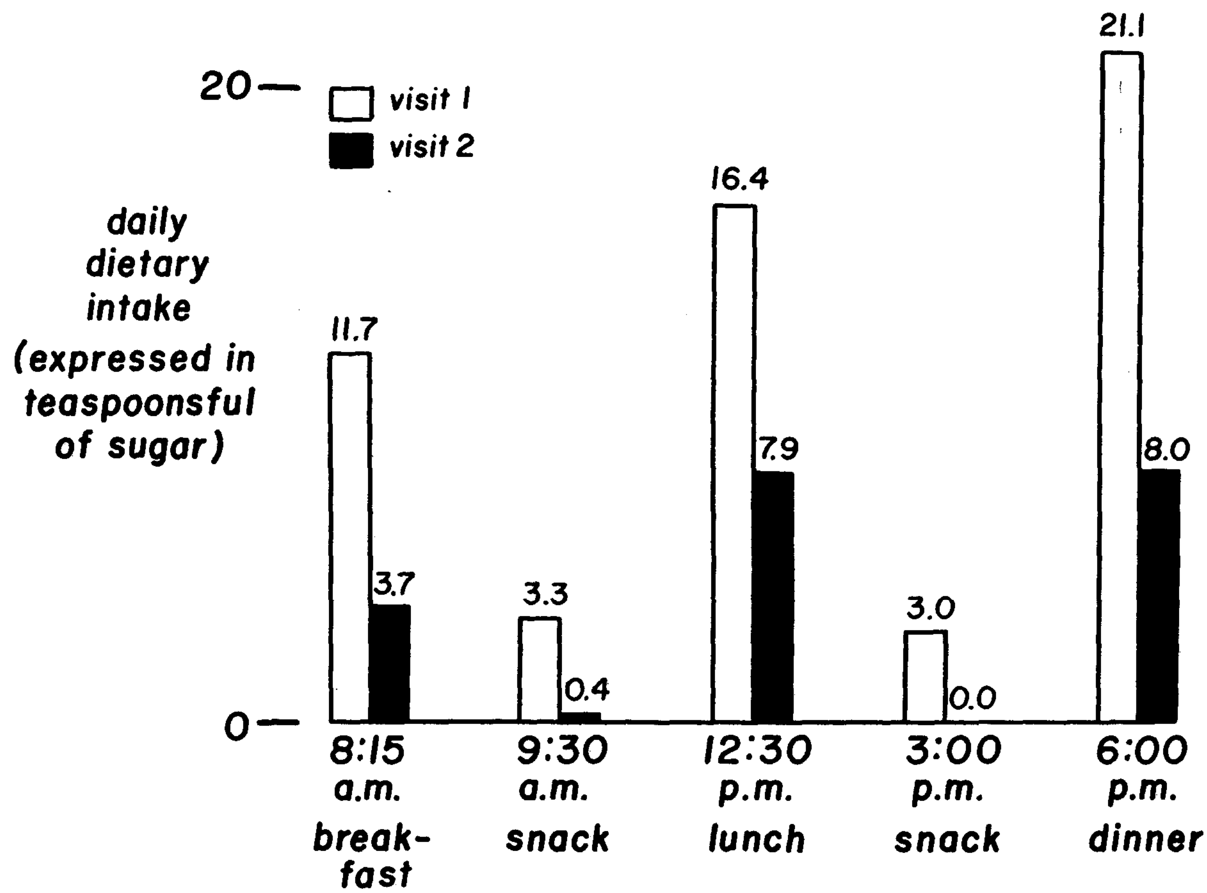


Figure 2. Mean sugar equivalent intake (expressed in teaspoonsful) after a three-day regular diet (visit 1, white columns) and following a three-day reduction in refined-carbohydrate foods (visit 2, dark columns).

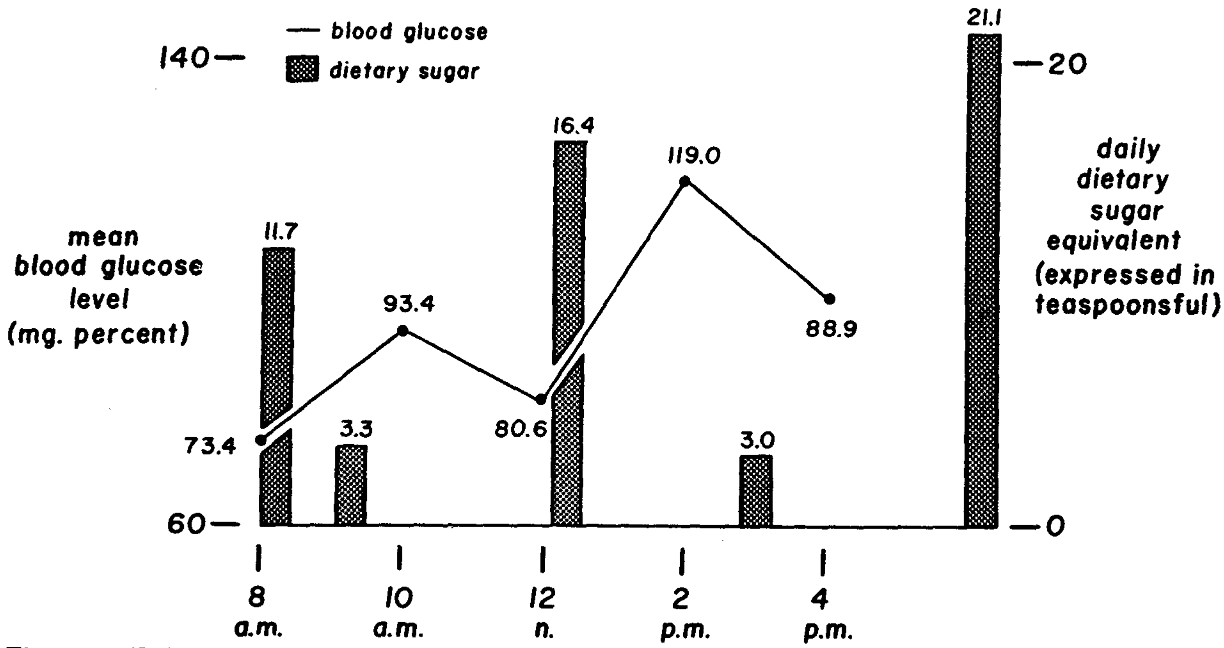


Figure 3. Relationship of the daily fluctuations in mean blood glucose (continuous line) to the mean sugar equivalent intake (expressed in teaspoonsful) of a regular diet (stippled columns).

Table 13

daily dietary sugar equivalent (expressed in teaspoonsful) during a three-day low-refined-carbohydrate dietary regime

subjects	8:15 A.M.	9:30 A.M.	12:30 P.M.	3:00 P.M.	6:00 P.M.
RiBl	1.7	0.0	5.6	0,0	4.6
BrSp	6.2	0.5	8.8	0.0	11.9
ShDu	3.8	0.5	11.7	0.0	8.8
YoKa	3.3	0.0	4.9	0.0	6.6
ThSh	0.0	0.5	7.3	0.0	7.4
WiGr	5.1	0.5	9.2	0.0	10.3
HeBr	5.5	0.5	7.9	0.0	6.4
Mean	3.7	0.4	7.9	0.0	8.0
S.D.	2.3	0.2	2.3	0.0	2.5
range	0.0-6.2	0.0-0.5	4.9-11.7	0.0-0.0	4.6-11.9
significance of the dif ference of the means	≤0.0050*	≤0.0010*	≤0.0010*	≤0.0010*	
significance of the dif ference of the variances	=0.0005*	=0.0005*	=0.0005*	=0.0005*	

*statistically significant

Table 14 is a report of the individual and mean blood glucose values at each temporal point following the revised dietary regimen. The means are only statistically different in the morning hours; the variances are significantly different in the afternoon. Figure 1 shows the mean glucose values initially with a regular diet (interrupted line) versus the scores following a reduction in sugar equivalent intake (continuous line). On a regular diet, the mean spread of values is about 46 mg. per cent. At the second visit, the range is 20 mg. per cent. Hence, the mean spread has been cut more than in half.

It is now possible to answer the third question: what changes in carbohydrate metabolism occur with this dietary alteration? Within the limits of this study, it appears that significant blood glucose changes follow the elimination of refined-carbohydrate foods from the diet. Thus, the relative omission of sugars and white flour products seems to yield a more homeostatic picture of carbohydrate metabolism as evidenced by fewer and less abrupt fluctuations in the blood glucose concentration during the day. This is consistent with published reports. (18,19)

Question Four. The point now at hand is to ascertain whether the demonstrated changes in carbohydrate metabolism are of physiologic import. In other words, is the organism biologically better when there is a more homeostatic carbohydrate metabolic state?

Table 15 summarizes the systolic blood pressure scores in the subjects singly and

Table 14

blood glucose values in seven dentists following a three-day low-refined-carbohydrate diet

subjects	8:00 A.M.	10:00 A.M.	12:00 Noon	2:00 P.M.	4:00 P.M.
RiBl	78	74	70	77	72
BrSp	76	69	77	110	90
ShDu	76	63	72	115	95
YoKa	90	80	80	70	70
ThSh	95	77	87	95	83
WiGr	100	65	87	82	92
HeBr	83	75	72	92	78
mean	85.4	71.9	77.9	91.6	82.9
S.D.	9.7	6.3	7.1"	16.7	9.9
range	76-100	63-80	70-87	70-115	70-95
significance of the difference of the means	<u><0.01O0*</u>	>0.1000	>0.0500	>0.2000	
significance of the difference of the variances	=0.1000	=0.5000	<u>=0.0050*</u>	<u>=0.0500*</u>	

*statistically significant

as a group while subsisting on a regular diet. It will be noted that the overall range is 43 mm. Hg for the systolic pressure. Figure 4 pictorially portrays the mean systolic pressures. It can be seen (interrupted line) that the systolic blood pressure fluctuates during the day in any one individual and that there are variations among the subjects.

Figure 5 provides the opportunity of comparing the daily mean blood glucose and systolic blood pressure changes while subsisting on a regular diet. It is interesting that the systolic pressures at the various temporal points (continuous line) parallel almost precisely the fluctuations in blood glucose (interrupted line).

It is now possible to answer the fourth question: is there any relationship between carbohydrate metabolism and the physiologic state (e.g. blood pressure)? It would appear, from these data and an earlier study (20) that parallelisms do indeed exist. Certainly, in the case of the systolic blood pressure, when the blood glucose rises, the systolic pressure increases; when the blood glucose decreases, the blood pressure drops.

Question Five: Now we may return to the all-important point. Is the organism biologically improved when the carbohydrate metabolic pattern is made more steady?

The systolic blood pressure readings following the dietary change are listed in Table 16. Figure 4 provides the opportunity of comparing the initial blood pressure values (interrupted line) and the mean final scores (continuous line). Mention should be made that, following the dietary change, the mean systolic range decreased from 10 mm. Hg (116.6 to 126.7) to about 1 mm. Hg (116.1 to 117.3).

Table 15

systolic blood pressure scores in seven dentists following a three-day regular dietary regime

subjects	8:00 A.M.	10:00 A.M.	12:00 Noon	2:00 P.M.	4:00 P.M.
RiBl	—	122	114	122	120
BrSp	122	136	116	133	132
ShDu	135	140	130	133	134
YoKa	101	100	101	100	100
ThSh	120	140	134	143	130
WiGr	117	124	108	122	112
HeBr	120	125	118	110	122
mean	119.2	126.7 :	117.3	123.3	121.4
S.D.	.: 10.9	14.1 ;	11.6	14.7	12.2
range	101-135	100-140	101-130	100-143	100-134
significance of the difference of the means	>0.2000	>0.2000	>0.4000	>0.5000	
significance of the difference of the variances	=0.5000	=0.5000	=0.2500	=0.5000	

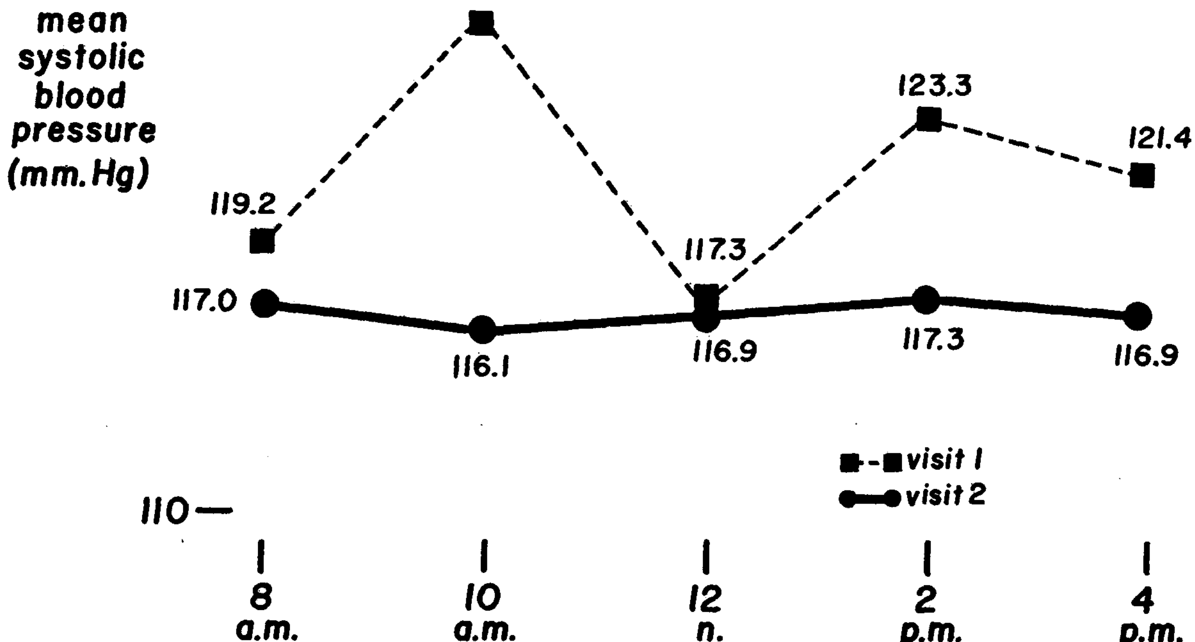


Figure 4. Daily fluctuations in mean systolic blood pressure following a three-day regular diet (visit 1, interrupted line) and after a three-day relatively low-refined-carbohydrate intake (visit 2, continuous line).

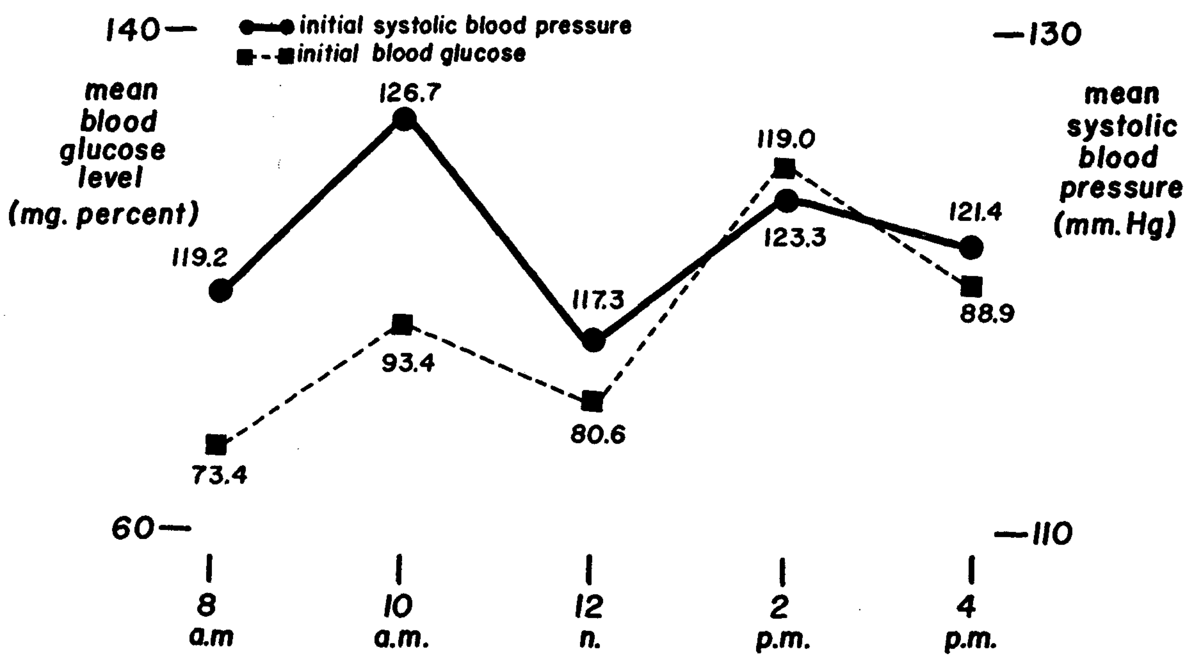


Figure 5. Comparison of the daily variations in the mean blood glucose (interrupted line) and the mean systolic blood pressure (continuous line) after a three-day regular dietary regimen.

/30 —126.7

Table 16

systolic bloodpressure scores in seven dentists following a three-day low-refined-carbohydrate diet

subjects	8:00 A.M.	10:00 A.M.	12:00 Noon	2:00 P.M.	4:00 P.M.
RiBl	112	112	118	110	112
BrSp	122	124	122	126	125
ShDu	123	124	120	125	126
YoKa	108	102	107	104	103
ThSh	122	118	124	122	124
WiGr	114	116	110	114	114
HeBr	118	117	117	120	114
mean	117.0	116.1	116.9	117.3	116.9
S.D.	5.8	7.6	6.2	8.2	8.5
range	108-123	102-124	107-124	104-126	103-126
significance of the difference of the means		=0.5000	=0.5000	=0.5000	=0.5000
significance of the difference of the variances		=0.2500	=0.5000	=0.2500	=0.5000

It is now possible to answer the fifth question: can the physiologic state (e.g. systolic blood pressure) be significantly altered by reducing the intake of sugar and white flour foods? The answer appears to be in the affirmative. (20) With dietary change, the fluctuations in the individual subjects and for the group are fewer and the variations of smaller amplitude.

Much has been written about the mechanisms which control homeostasis (the steady state). Relatively little attention has been accorded the study of how steady is the steady state. Dubos, (21) in his writings about Claude Bernard and homeostasis, made the following statement:

He (Claude Bernard) emphasized that at all levels of biological organization, in plants as well as in animals, survival and fitness are conditioned by the ability of the organism to resist the impact of the outside world and maintain constant *within narrow limits* (italics added) the physico-chemical characteristics of its internal environment.

Surely, during health, body temperature fluctuates slightly during the day (Figure 6). (22) Any sudden rise or abrupt fall is immediately reflected in the clinical state (e.g. sweating and chilling). Likewise, ordinarily, the average man during the usual day has his moments of pleasure and displeasure. When these fluctuations are exaggerated so that the subject is at once manic and moments later catatonic, disease is obvious. It would seem, therefore, that health and disease could be plotted on the basis of the extent of the amplitudes of a constellation of physiologic, biochemical, and clinical parameters. It would appear that carbohydrate metabolism (as reflected in blood glucose) also possesses its physiologic limits. Thus, during the normal day for the healthy man, blood glucose should vary. The question is how much amplitude is physiologically acceptable.

temperature
blood pressure
psychic state
peristalsis blood
sugar

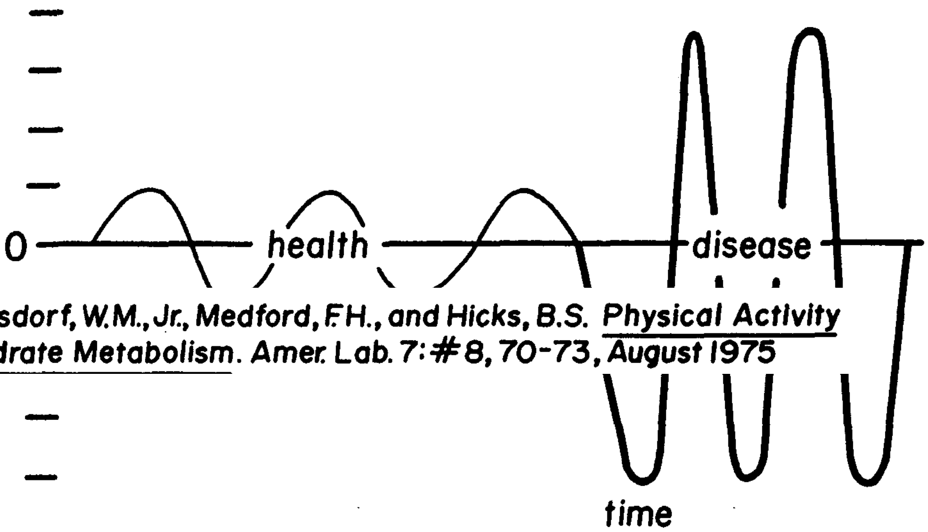


Figure 6. In health, factor* rack as temperature, blood pressure, psychic state, peristalsis, and blood sugar concentration can be represented by small daily fluctuations. In disease, the amplitudes are much greater.

Figure 7 represents an extension of Figure 6 over a period of years. In the very early stages of chronic disease, the amplitudes insidiously increase. With the passage of time, the large undulations become smaller and slowly rise or fall to a plateau, e.g. the course of hyperglycemia in diabetes mellitus and hypertension in heart disease or the converse, hypoglycemia and hypotension. The fact that Figure 7 is not just theoretical is borne out by a study of diurnal blood glucose values in 336 presumably healthy doctors from ages below 30 to in the 70's. It can be noted (Figure 8) that,

with advancing age, the mean values (the bolder center lines) slowly rise and the amplitudes (the range as shown by the thinner lines) become obviously greater and more significant as shown by the statistically significant differences of the means and the variances.

This report shows very clearly that a daily blood glucose variation does indeed exist. This experiment also confirms that the blood glucose concentration parallels dietary habits as shown in the relationship of refined carbohydrate to blood glucose in 7 graduate students. More such infor-

With additional time, the broad undulations become more narrow aad the base line slowly rises (or declines) to a plateasv

temperature blood pressure psychic state blood sugar peristalsis

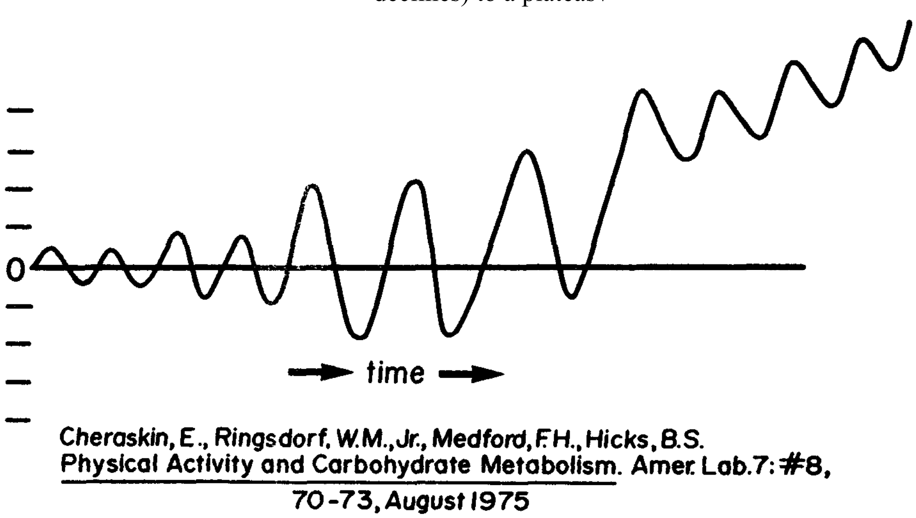
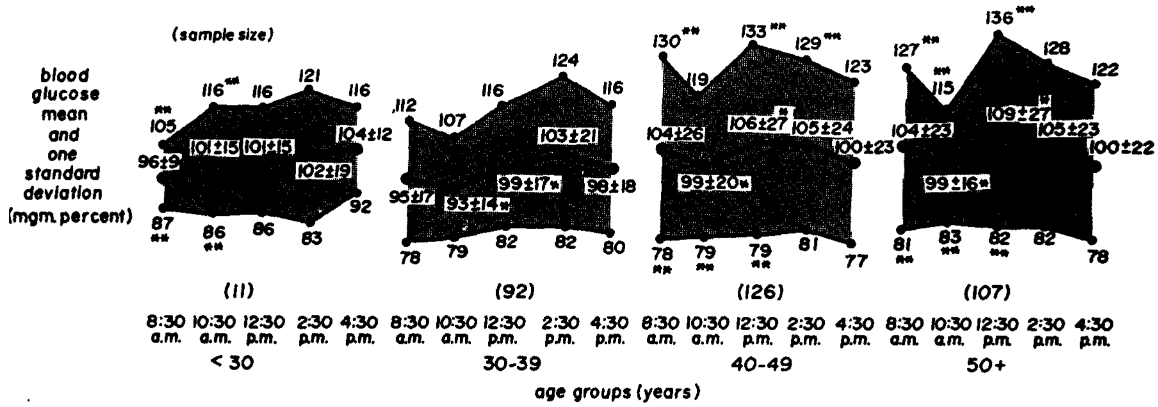


Figure 7. This is aa extension of Figure 6 over a period of years. la the early stages of chronic disease, the amplitudes increase.

diurnal blood glucose levels in presumably *heallhy male* subjects



* statistically significant difference of the means «» statistically significant difference of the variances

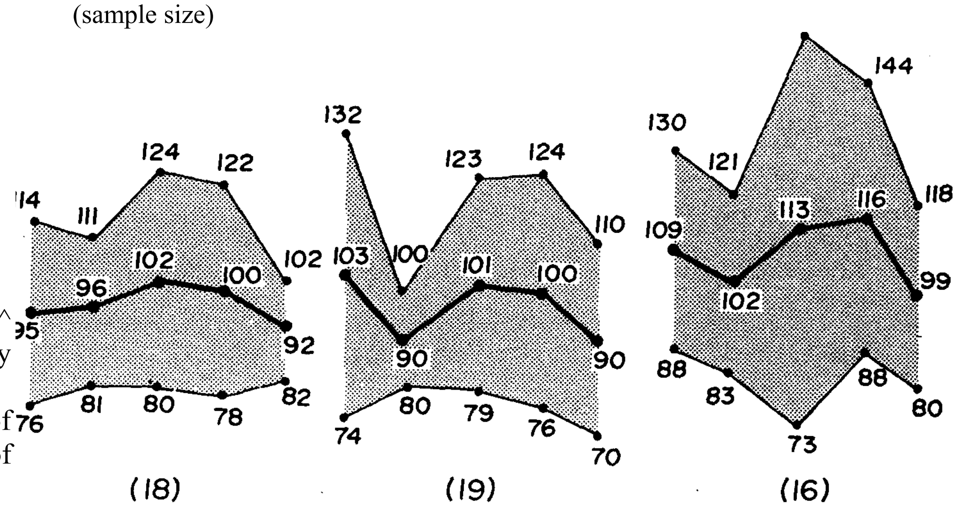
Figure 8. This is an analysis of the diurnal blood glucose valves in 336 presumably healthy doctors at various age groups with 11 subjects below 30 years of age, 92 in their 30's, 126 in the 40's, and 107 50 or more years of age. The center lines represent the mean values and the upper and lower fines outline the limits. It is very clear that, with advancing age, the mean values rise slowly; more importantly, the variance rises abruptly.

relationship *of* diurnal mean blood glucose scores and daily refined carbohydrate consumption in 50+ year old subjects

(sample size)

blood glucose mean and one standard deviation (mgm. percent)

mation is offered^ (Figure 9) in a study of 53 50+year-old subjects in terms of the relationship of daily refined



830 10:30 1230 *2 30* 430 830 10-30 12.30 230 4.30 8.30 1030 12:30 *2-30* 430 *am am* pm pm *pm am am* pm pm pm am am pm pm pm

0-50 5/-8/ *81-164*

daily refined *carbohydrate* consumption (grams)

Figure 9. The relationship of daily refined carbohydrate consumption (grams) versus blood glucose concentration in 53 50+year old subjects. The mean values during the day fluctuate greater with greater intake of sugar products. The variances are markedly greater as daily refined carbohydrate consumption rises.

carbohydrate (in grams) versus blood glucose levels during the day. The illustration indicates very dramatically that, with increased refined carbohydrate intake, there are greater mean fluctuations (the centre line) and even more changes in variance.

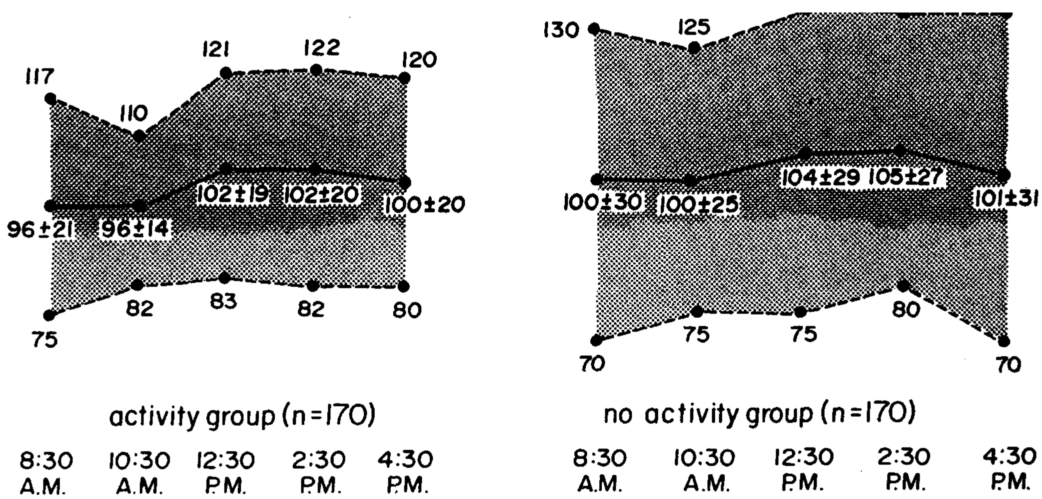
That the undulations in diurnal blood glucose need not necessarily be the result of refined carbohydrate consumption or other dietary factors is clearly borne out (Figure 10) by showing that the undulations during the day are greater in subjects characterized by no physical activity versus those who engage in an activity program such as walking.

That this biochemical phenomenon is not without physiologic benefits has been demonstrated by a study of the cardiovascular system as reflected in blood pressure. Daily fluctuations do indeed occur in the average man. As we have seen, these systolic blood pressure changes correlate with blood glucose levels. The restriction of sugar and white flour products seems to parallel a more steady state in the cardiovascular system as reflected by the blood pressure.

As a matter of fact, this homeostatic phenomenon can be demonstrated in a number of different situations. For example (Figure 11), it is reflected in a study of a group of health practitioners with relatively few clinical symptoms and signs (0-5) versus a large number of clinical symptoms and signs (40+). Figure 11 shows quite graphically that there is less homeostasis (greater fluctuations) in those reporting the greater number of symptoms and signs. This observation not only obtains with nonspecific and very general observations as shown (Figure 11) but also in very specific relationships (Figure 12). For example, there is a statistically significant difference of the variances at 8:30 a.m., 10:30 a.m., 12:30 p.m., and 2:30 p.m. in subjects reporting hemorrhoids versus those with no hemorrhoids. In other words, there is less homeostasis in the symptomatic group.

blood glucose in 40+ year old paired subjects (n=340) 03 i32 132

blood glucose mean and one standard deviation relationship of physical activity and diurnal



statistically significant difference of the variances at (8:30 A.M. t = 0.496 P<0.0005,10:30A.M. t=0.309 P<0.0005, 12:30 PM.f=0.448 P<0.0005, 2:30PM.t=0.513 P<0.0005,4:30PM.f=0.396 P<0.0005)

Figure 10. The diurnal blood glucose part-ems in 170 age and sex paired subjects who performed structured daily activity versus no activity. The range of values is clearly greater in the no activity group as shown by the statistically significant differences at all of the temporal points,

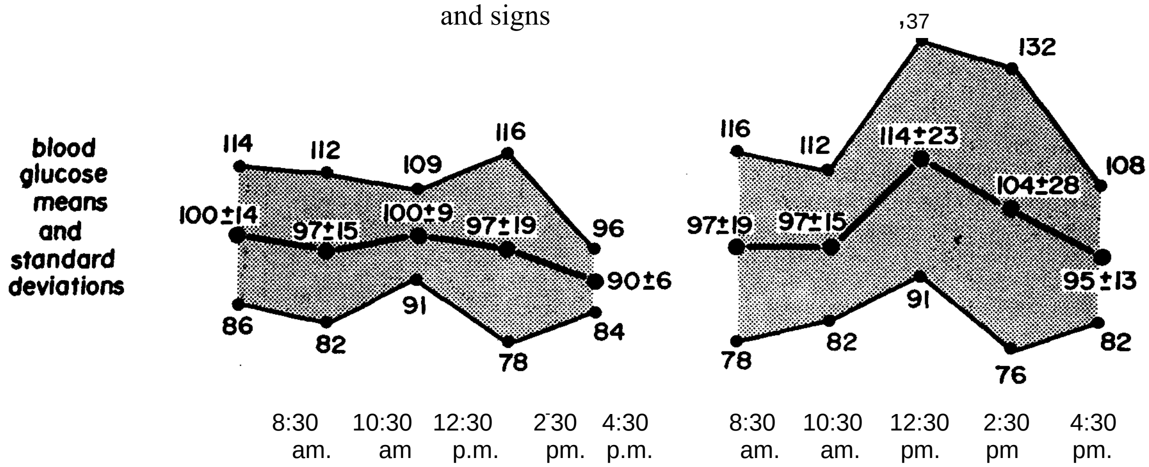
Summary and Conclusions

In the final analysis, life and death are functions of homeostasis. The cells singly and collectively as a total organism survive when host resistance can cope successfully with the many and diverse environmental threats. When the homeostatic machinery collapses, host susceptibility replaces host resistance. The very same environmental, microbial, chemical, physical, and other challenges now overwhelm the system, and disease and then death ensue.

Much as been written about the mechanisms which control homeostasis (the steady state). Relatively little attention has been accorded the study of how steady is the steady state.

The first portion of this report concerned itself with the normal (average) versus normal (physiologic) diurnal blood glucose relationship of diurnai blood glucose scores in 50+year old presumably healthy subjects with relatively few (0-5) and many (40+) clinical symptoms

and signs

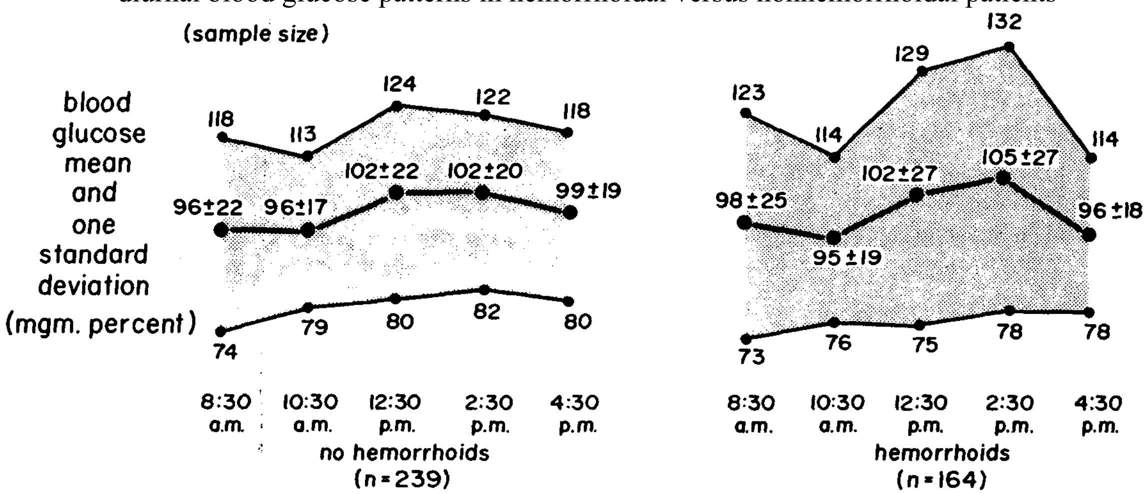


0-5 clinical symptoms and signs 40 + clinical symptoms and signs

Figure 11. The relationships of the diurnal blood glucose patterns in two groups off 50+ year old presumably healthy doctors with relatively few (0-5) versus many (40+) clinical symptoms and signs. The patterns are distinctly different; those with the greater number of problems are less homeostatic,

patterns in 969 health practitioners and their spouses. Within the limits of these observations, it is safe to conclude that in a relatively symptomless and signfree group, the daily fluctuations in blood glucose are much more narrow, suggesting a very steady steady state. This hypothesis was then tested in a group of 7 graduate students which showed a relationship between dietary intake of refined carbo- hydrate foods, diurnal blood glucose, and diurnal systolic blood pressure. With a relative reduction in sugar and other refined food stuffs, both blood glucose and systolic blood pressure became more homeostatic. Finally, the practical import of a normal (average) versus normal (healthy) diurnal blood glucose pattern is underscored by the differences in nonspecific clinical situations as well as precise syndromes.

diurnal blood glucose patterns in hemorrhoidal versus nonhemorrhoidal patients



statistically significant difference of the voriances at 8-'30 am, I0.'30am,l2:30p.m.and2˜30p/n..

Figure 12. The diurnal Mood glucose part-ems in hemorrhoidal versus nonhemorrhoi-dal patients. A comparison of the diurnal blood glucose hi these two groups shows that the variance is statistically significantly different at 8:30 a.m., 10:30 a.m., 12:30 p.m., and 2:30 p.m.

References

1. JONAS, L, MILLER, T.G. and TELLERJ.: All day blood sugar curves in nondiabetic individuals and in diabetic patients with and without insulin. Arch. Int. Med. 35,3,289-314, March 1925.
2. CONN, J.W. and NEWBURGH, L.H.: The glycemic response to isoglucogenic quantities of protein and carbohydrate. J. Clin. Invest. 15, 6, 665-671, November 1936.
3. ROBERTS, H.J.: Afternoon glucose tolerance testing: a key to the pathogenesis, early diagnosis and prognosis of diabetogenic hyperinsulinism. J. Amer. Geriat. Soc. 12,5,423-472, May 1964.
4. BOWEN, A.J. and REEVES, R.L.: Diurnal variation in glucose tolerance. Arch. Int. Med. 119, 3,261-264, March 1967.
5. JARRETT, R.J. and KEEN, H.: Diurnal variation of oral glucose tolerance: a possible pointer to the evolution of diabetes mellitus. Brit. Med. J. 2,5653, 341-345,10 May 1969.
6. JARRETT, R.J. and KEEN, H.: Further observations on the diurnal variation in oral glucose tolerance. Brit. Med. J. 4, 5731, 334-337, 7 November 1970.
7. JARRETT, R.J., BAKER, I.A., KEEN, H. and OAKLEY, N.W.: Diurnal variation in oral glucose tolerance: blood sugar and plasma insulin levels morning, afternoon, and evening. Brit. Med. J. 1, 5794,199-210,22 January 1972.
8. CARROLL, K.F. and NESTEL, P.J.: Diurnal variation in glucose tolerance and in insulin secretion in man. Diabetes 22, 5, 333-348, May 1973.
9. OAKLEY, N.W., MONIER, D. and WYNN, V.: Diurnal variation in oral glucose tolerance: insulin and growth hormone changes with special reference to women taking oral contraceptives. Diabetologia 9,3,235-238, June 1973.
10. ZIMMET, P.A., WALL, J.R., ROME, R., STIMMLER, L. and JARRETT, R.J.: Diurnal variation in glucose tolerance: associated changes in plasma insulin, growth hormone, and non-esterified fatty acids. Brit. Med. J. 1, 5906, 485-488,16 March 1974.
11. WMCHELOW, M.J., STURGE, R.A., KEEN, H., JARRETT, R.J., STIMMLER, L. and GRAINGER, S.: Diurnal variation in response to intravenous glucose. Brit. Med. J. 1, 5906, 488-491, 16 March 1974.
12. CHERASKIN, E. and RINGSDORF, W.M., Jr.: Homeostasis: a study in carbohydrate metabolism. J. Med. Assn. St. Alabama 35, 3, 173-182, September 1965.
13. KRASNYANSKD, L.M.: Variations in the blood sugar concentration in man in the course of the day. Biochem. Z. 205,180-185,1929.
14. MEYER, F.A.: Blood sugar behavior in normal metabolism. I. Blood, sugar, behavior and daily rhythm. Z. ges. exptl. Med. 107, 569, 582, 1940. Abstract Chem. Abst. 36,6221,1942.
15. JONAS, L., MILLER, T.G. and TELLER, I.: All day blood sugar curves in non-diabetic individuals and in diabetic patients with and without insulin. Arch. Int. Med. 35,289-314,1925.
16. ADAMKIEWICZ, V.A.: A new view of the old cold — as sugars go up, hypersensitivity drops. J. A. M. A. 184,4041 (Medical News), 18 May 1963.
17. Council on Dental Health. Philadelphia County Dental Society: A sweet tooth can spoil a sweet smile. Philadelphia, Pennsylvania 1958.
18. CONN. J.W. and NEWBURGH, L.H.: The glycemia response to isoglucogenic quantities of protein and carbohydrate. J. Clin. Invest. 15, 6, 655-671,1936.
19. PAGE, M.E., RINGSDORF, W.M., Jr. and CHERASKIN, E.: The effect of a low-refined-carbohydrate high-protein diet upon nonfasting blood sugar. Odont. Rev. 12,1,1-24,1961.
20. RINGSDORF, W.M., Jr., CHERASKIN, E. and HOLLIS, C.F.: Effect of a low-refined-carbohydrate diet upon nonfasting blood pressure. Ala. Dent. Rev. 9,3,18-30, Spring 1962.
21. DUBOS, R.: Mirage of health. 1959. New York, Harper and Brothers, p. 100.
22. CHERASKIN, E., RINGSDORF, W.M., Jr., MEDFORD, F.H. and HICKS, B.S.: Physical activity and carbohydrate metabolism. Amer. Lab. 7,8, 70-73, August 1975.