The Prednisolone Glucose Tolerance Test in Pregnancy

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SUMMARY

The response to a prednisolone glucose tolerance test (PGTT) was investigated in 166 pregnant women, divided into control and diabetes-suspect groups. The diabetes-suspect group consisted of pregnant women with a history of a large infant, a family history of diabetes and/or glycosuria during a previous pregnancy. Positive responses by the criteria of Fajans and Conn occurred in 23 per cent of the control group and 44 per cent of the suspect group. After excluding women with abnormal glucose tolerance tests (GTT), the prevalence of positive responses fell to 15 per cent in the control group and 31 per cent in the suspect group. Thirty patients with normal GTT but positive PGTT during pregnancy were studied at varying intervals after delivery. Half of them reverted to normal PGTT. The increased frequency of positive responses to the PGTT in the suspect group suggests that this presumably more rigorous test of islet reserve may permit recognition of suboptimal islet capacity during pregnancy.

There is increasing conviction that abnormal carbohydrate tolerance as demonstrated by the glucose tolerance test is a relatively late development in the course of diabetes. In the search for a means of moving back to that period which precedes an abnormal standard glucose tolerance curve, Conn and Fajans[1-5] introduced the steroid glucose tolerance test. It has been extensively studied by them and others.[6-16] That an abnormal steroid glucose tolerance test probably precedes an abnormal standard glucose tolerance test is suggested by the increased prevalence of abnormal steroid glucose tolerance tests in relatives of diabetics[1-6,8-11,14] and the large number of individuals with abnormal steroid tolerance tests who later developed diabetes.[2-4]

Pregnancy appears to impose a stress on pancreatic islet reserve, and studies of carbohydrate metabolism during pregnancy have revealed an almost uniformly greater frequency of impaired glucose tolerance than in the nonpregnant state.[17] When pregnant women were selected for study on the basis of a diabetic family history, glycosuria during pregnancy, or a history of large babies, the prevalence of abnormal standard oral glucose tolerance tests was high.[17] Although abnormal glucose tolerance may revert to normal during the puerperium, it usually recurs during subsequent pregnancies and permanent diabetes may ensue.[17]

Pregnancy, therefore, affords an opportunity to study carbohydrate tolerance. Conn[4] has referred to the high frequency of positive steroid tolerance tests in some pregnant women but reports no figures. Jackson,[6] Baldi et al.[10] and Rosenwasser and Lissin[11] have reported varying results with tests differing in several respects. We are reporting here our experience with steroid tolerance tests performed in selected groups of pregnant women with the thought that this more sensitive test done during a period of metabolic stress might reveal suboptimal pancreatic reserve.

METHODS

Subjects. Steroid glucose tolerance tests of carbohydrate metabolism were performed in 153 ambulatory pregnant women attending the prenatal clinic of the Hospital of the University of Pennsylvania. Ages varied from eighteen to forty-one years, with the range and mean for the most part the same for each group. They were divided into four groups.

1. *Control group.* Sixty-six pregnant women without a family history of diabetes, glycosuria, a history of delivering an infant weighing more than nine pounds, an abnormal obstetrical history or obesity (contrast groups 2 and 3 below). Obesity is defined as more than twenty-five pounds above ideal weight.

2. *Suspect group.* Sixty-four pregnant women with either one or more of the following: a family history of diabetes (parents and/or siblings), glycosuria on at least one occasion during the current pregnancy, or a history of having had at least one infant weighing more than nine pounds. Patients with symptomatic

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diabetes, fasting hyperglycemia, previously diagnosed diabetes, or with a history of hyperglycemia or glycosuria in a previous pregnancy were excluded.

3. *Obesity—abnormal obstetrical history group.* Twenty-three pregnant women otherwise meeting the criteria for inclusion in the control group, but with a history of either an obstetrical complication during a previous pregnancy (toxemia, intrauterine or neonatal loss, excessive hydramnios) or obesity.

4. *Postpartum group.* Twenty-five women from the three groups above with positive responses to the prednisolone glucose tolerance test during pregnancy, had the test performed again at intervals from a week to several months after delivery.

Qualitative tests for urinary glucose were carried out with a glucose oxidase paper at each prenatal clinic visit.

For the *standard glucose tolerance test (GTT)*, 100 gm. of glucose were ingested in the fasting state. Venous blood samples were obtained at one, two and three hours thereafter and glucose was determined by the Somogyi-Nelson[18] method. We followed the criteria used by Fajans and Conn[1] and regarded curves as diabetic when they fell at or above the following: one hour, 160 mg. per 100 ml.; two hours, 120 mg. per 100 ml. However, we have included in the diabetic curves seven tests in which only the two-hour value was above 120 and, unlike Conn, have included all two-hour blood sugars between 110 and 120 in the normal curves.

The procedure for the *prednisolone glucose tolerance test (PGTT)* was identical to that employed for the GTT except that 10 mg. of prednisolone were administered eight hours and again two hours before the ingestion of 100 mg. of glucose. We, like Fajans and Conn,[1] have used a blood sugar of 140 mg. per 100 ml. at two hours as the critical level for the interpretation of the PGTT. A curve with a two-hour blood sugar level of 140 mg. per 100 ml. or above is regarded as a "positive response," while a curve below this level is a "negative response." There are some differences, however, between the procedure employed by us and that used by them.[1] Whereas Fajans and Conn[1] used cortisone as the priming steroid and gave doses 8.5 hrs. and two hours before the test, with an increased dose in obese patients, we used a uniform dose of prednisolone; Fajans and Conn[1] used 1.75 gm. of glucose per kilogram ideal body weight, we used 100 gm. per subject, and our tolerance tests were not preceded by a period of controlled carbohydrate intake. Dietary histories obtained for the day preceding the tests revealed intakes of 100 gm. or more per day of carbohydrate, except in three subjects (all of whom had normal curves). Since all subjects were apparently healthy, ambulatory young women, we took the position of Wilkerson et al.[19] that adequately nourished ambulatory young individuals need no special high carbohydrate preparation for an oral GTT.

A PGTT was carried out on every subject. Most of those who had "positive responses" also had glucose tolerance tests, but both tests were not performed on all patients. Some subjects of this group had as many as three PGTT during the course of a pregnancy. A negative PGTT in the first or second trimester was usually followed by a repeated PGTT in the second or third trimester. If the PGTT was abnormal, it was followed within two weeks by a GTT and, if that was normal, the GTT was repeated in the next trimester. This approach was employed to reduce to a minimum the possibility of overlooking the development of either an abnormal GTT or abnormal PGTT late in the course of pregnancy. In some instances an initially normal PGTT or GTT became abnormal in a subsequent trimester. Where multiple tests were done, the results were classified as abnormal if any one test was abnormal (see comment under results).

RESULTS

In viewing our results it will be helpful to keep in mind that the first test used in each patient was a PGTT and only in patients with a "positive response" was a GTT performed.

The prevalence of positive and negative responses to the PGTT by the criteria used in the three groups of pregnant women are summarized in figures 1, 2 and 3. The graphic presentation is used for comparison with the studies of others, although the means ± SEM are not ideal for data separated by arbitrary levels of blood glucose, and lacking "normal" distribution and bimodality (see tables 1 and 2).

Comment is needed about the patients who had multiple PGTT as to the consistency of the results, their relation to the progress of pregnancy and to our placing all patients with one positive response among the positive responders. In the control group (figure 1) there were twenty-one patients with repeated tests. In all but five cases there was agreement (positive or negative) between duplicates, i.e., 75 per cent agreement. In three of the five women the positive test

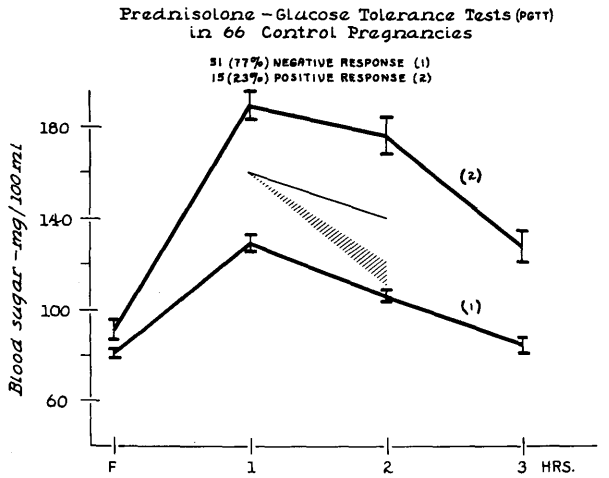

FIG. 1. The curves and vertical lines show the means ± S.E.M. of the negative and positive responses in the control group of sixty-six pregnant women. In this and the subsequent figures, the solid line from 160 to 140 mg. per 100 ml. of blood sugar diagrams the criteria of Fajans and Conn[1] for the steroid glucose tolerance test and the shaded triangle reproduces their criteria for the standard GTT.

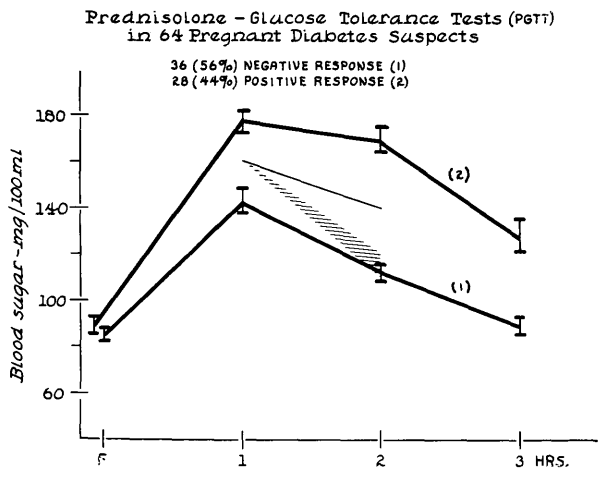

FIGURE 2

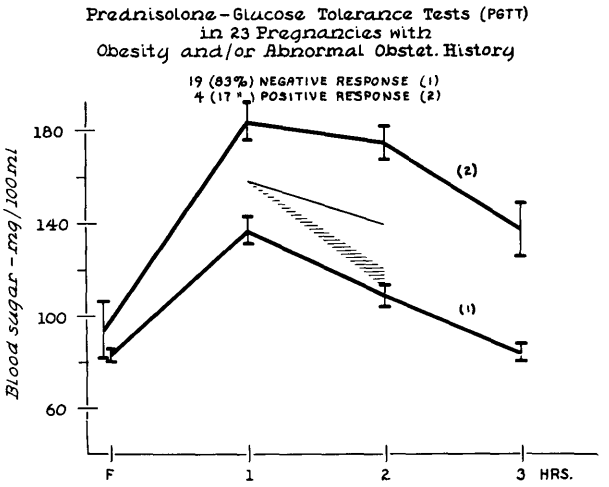

FIGURE 3

TABLE 1

Frequency distribution of blood glucose levels during prednisolone glucose tolerance tests in sixty-six pregnant women: control group

Blood glucose mg. per 100 ml.	Fasting	Hours 1	2	3
60-69	7	—	—	18
70-79	21	—	2	7
80-89	23	5	6	7
90-99	7	—	9	10
100-109	5	6	12	6
110-119	2	9	11	4
120-129	1	6	4	7
130-139	—	3	7	2
140-149	—	10	4	3
150-159	—	9	—	1
160-169	—	6	2	—
170-179	—	2	3	—
180-189	—	4	2	1
190-199	—	1	2	—
200-209	—	1	—	—
210-219	—	2	—	—
220-229	—	—	—	—
230-239	—	2	—	—
240-249	—	—	2	—
Mean	82	143	122	92
±S.E.	1.9	3.8	3.1	3.6
±S.D.	14	27	23	26

was the last one done. Because there is fair agreement that glucose tolerance tests are more likely to be positive later in pregnancy, these seem to be rightly included as "positive." However, in two patients the later tests were normal and these might well be excluded from positive responses and placed with the negative responses. This would alter the prevalence of figure 1 to 80 per cent negative and 20 per cent positive, the latter figure remaining impressively high.

In the suspect group (figure 2) there were fifteen repeated tests with 87 per cent agreement. Only two patients differed, one of whom became positive on a later test. The elimination of this one case would reduce the positive responses of figure 2 to twenty-seven or 42 per cent, which still leaves a strikingly high occurrence of positive responses in this group. For both groups (130 patients) the over-all agreement of duplicate tests in thirty-six women was 80 per cent.

Figure 2 shows the high prevalence (44 per cent) of positive responses in the suspect group compared to 17 and 23 per cent in the other groups (figures 1 and 3). By the chi square test, group 2 is significantly

TABLE 2

Frequency distribution of blood glucose levels during prednisolone glucose tolerance tests in sixty-four pregnant women: suspect group

Blood glucose mg. per 100 ml.	Fasting	Hours 1	2	3
60-69	5	—	—	8
70-79	15	—	3	9
80-89	19	—	1	5
90-99	14	2	6	5
100-109	5	2	1	10
110-119	5	5	11	6
120-129	—	2	9	4
130-139	1	4	5	7
140-149	—	13	8	2
150-159	—	4	5	—
160-169	—	11	3	4
170-179	—	3	2	—
180-189	—	5	2	2
190-199	—	6	1	1
200-209	—	3	4	—
210-219	—	3	—	—
220-229	—	1	2	—
Mean	87	158	137	106
±S.E.	1.8	3.4	2.7	3.4
±S.D.	14	27	22	27

different from the others (P = <.001). The trend to an increased occurrence of positive responses agrees with that found by Fajans and Conn[2-5] and Lambert et al.[14] in the relatives of diabetics and with the experience of others[21] that the production of large babies may foretell maternal diabetes.

The observations on groups 1 and 2 have been summarized in tables 1 and 2 and may be compared with data on a steroid tolerance test reported by Klimt et al.[20] Like them, we find that the distributions are unimodal and positively skewed. It is within these total figures for each group that the difference in prevalence of positive responses between figures 1 and 2 has occurred. (In table 2, the two- and three-hour columns number sixty-three due to loss of a specimen of blood.)

Figure 4 shows the results of the GTT in forty-three patients (from all groups) with positive responses to the PGTT. In subjects so selected the large number of diabetic curves (37 per cent) is not surprising, for patients with abnormal GTT would be expected to have positive responses to the PGTT. The problem arises in our consideration of the twenty-seven women with normal GTT (63 per cent), for though they do not have diabetes as usually defined, they differ from the majority of pregnant women in whom the PGTT is negative. Table 3 shows the distribution of these twenty-seven women among the three clinical groups.

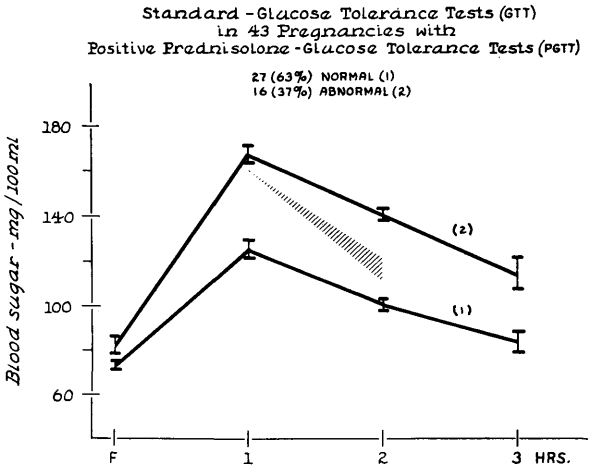

FIGURE 4

Nine, or 15 per cent, of the controls, sixteen, or 31 per cent, of the suspects, and two, or 10 per cent, of the obese-normal obstetrical history group had normal GTT and abnormal PGTT.

The suspect group with positive responses to PGTT was divided into component subgroups (family history, history of large babies and glycosuria during pregnancy) from which women with abnormal GTT were excluded. Table 4 indicates that glycosuria was more often associated with abnormal PGTT than were either a positive family history or history of a large

TABLE 3

Occurrence of positive responses to PGTT in twenty-seven women with normal GTT

Group	Number of patients*	Positive responses to PGTT Number	Per cent
Control	60	9	15
Suspect	52	16	31
Obesity-abnormal	21	2	10

*Total patients of each group who had GTT.

TABLE 4

Occurrence of positive responses to PGTT in women with normal GTT related to specific criteria in the suspect group

Criteria	Number of patients*	Positive responses to PGTT Number	Per cent
Positive family history of diabetes	17	4	24
Large infant	14	4	29
Glycosuria	27	11	42

*Some women met more than one of the criteria and are listed twice.

infant. Only 42 per cent of the women with glycosuria and normal GTT had abnormal PGTT. This seemingly low frequency may be in part the result of including patients in whom glycosuria had occurred only once or twice during pregnancy.

Thirty of the patients with positive PGTT were restudied at some time after delivery. As noted in table 5, about one half reverted to normal. Although the numbers studied are small, the frequency of positive PGTT postpartum seems to be about the same whether the GTT was normal or abnormal during pregnancy. Since the more marked the abnormality of carbohydrate tolerance in pregnancy, the more likely it would be to persist postpartum, this high evidence of reversal may be in part the result of our carefully excluding anyone with symptomatic diabetes, fasting hyperglycemia, previously diagnosed diabetes or with a history of hyperglycemia or glycosuria in a previous pregnancy.

TABLE 5

Postpartum PGTT in twenty-five women with positive responses to PGTT during pregnancy

During pregnancy	Number of patients	Postpartum PGTT Negative Number	Negative Per cent	Positive Number	Positive Per cent
Positive PGTT and normal GTT	18	10	56	8	44
Positive PGTT and abnormal GTT	12	6	50	6	50
Total	30	16	53	14	47

DISCUSSION

Table 6 summarizes some of the results of others who have used various forms of steroid glucose tolerance tests in nonpregnant and pregnant subjects. All have distinguished between subjects with and without a family history of diabetes, although such "prediabetic" features as a history of large infants, a "bad" obstetrical history, obesity, and glycosuria of pregnancy have been variously employed. All cases with an abnormal GTT have been excluded, and the figures refer only to those individuals with positive steroid glucose tolerance tests and normal GTT. The results are not strictly comparable because of technical differences between the test procedures used by different investigators. Thus, Lambert et al.[14] and West[21] followed the method of Fajans and Conn,[1] whereas others have employed some modifications. We have used prednisolone instead of cortisone and we have not altered the dose

TABLE 6

Selected reports of steroid glucose tolerance tests (all patients tabulated had normal GTT)*

Source	Controls† Number	Controls† Positive‡ responses Number	Controls† Positive‡ responses Per cent	Suspects† Number	Suspects† Positive‡ responses Number	Suspects† Positive‡ responses Per cent
A. Nonpregnant						
Fajans and Conn[5]	105	4	4	363	103	26
Lambert et al.[14]	58	4	6	44	10	23
West[21]	22	5	23	17	3	20
Nusimovich[9]	51	1	2	140	39	28
Jackson[6]	36	0	0	Not available		
B. Pregnant						
Jackson[6]	40	11	28	4	4	100
Baldi et al.[10]	31	4	13	13	6	44
Rosenwasser and Lissin[11]	Not available			36	12	33
This report	60	9	15	52	16	31

*The mean ages of the groups reported ranged from twenty-three to forty-five years.

†Controls—subjects with no history of diabetes in family. Suspects—subjects with diabetes in family, or other criteria. See text.

‡Positive response—based on criteria of Fajans and Conn[5] except for results of Lambert et al.[14] and Jackson.[6]

for larger patients. Nusimovich et al.,[9] Baldi et al.,[10] and Rosenwasser and Lissin[11] used prednisolone. We, like the above authors, used 100 gm. of glucose, Fajans and Conn[1,5] used 1.75 gm. per kilogram ideal body weight, and Jackson[6] 50 gm. of glucose. All have used venous blood and true blood sugar methods except Jackson[6] who used capillary sugars and the Hagedorn-Jensen method. The criteria for a positive response were those originally described by Fajans and Conn[1] except for Jackson[6] and Lambert et al.[14] who established their own standards. Despite these differences, the results collected in table 6 are probably comparable since West[21] has shown that in the amounts used the hyperglycemic potency of the several steroids are nearly equivalent.

Except for West[21] the authors cited in table 6 report a low (0 to 6 per cent) prevalence of positive steroid tests in nonpregnant control subjects with a normal GTT. However, West[21] admits that subsequent experience indicates his figures for positive responses to the cortisone-glucose tolerance test may be too high. A much higher and strikingly consistent frequency of positive responses to steroid tolerance tests has been found in nonpregnant diabetes suspects (20 to 28 per cent) with normal GTT.

We, like Baldi et al.,[10] found about 15 per cent positive responses in pregnant control subjects, whereas Jackson[6] reported 28 per cent (table 6). In diabetes suspects,

the occurrence of positive responses is increased and, again, if the patients reported by Jackson[6] are excluded, there is some consistency in the results (31 to 44 per cent). The four out of four positive responses in the pregnant women studied by Jackson[6] are probably the result of selection. They were termed "prediabetic on strong evidence."

Our findings agree in general with those of other investigators; abnormal responses to steroid tolerance tests are more frequent in suspect than in control subjects. When compared to nonpregnant subjects, however, there is a relatively greater increase in positive responses in the control than in the suspect group of pregnant women. There are too few studies to indicate whether more of the control group of pregnant women with positive PGTT will revert to normal PGTT after delivery.

Although the PGTT appears to be more sensitive than the GTT, two comments are in order: (a) The use of 140 mg. per 100 ml. at the two-hour period may not be suitable in pregnancy. Thus, if one takes the two-hour mean ± 2 SD (some would use ± 3 SD), the figure of 168 mg. per 100 ml. becomes the upper normal range in pregnancy. In table 1 there are, above 170 mg. per 100 ml., nine cases, or 13 per cent, a figure which would make the test look less sensitive but no doubt more specific than the 23 per cent of figure 1. (b) The demand for insulin secretion during pregnancy may be great and the PGTT may be positive only during such stress. Thus the islet reserve may never be sufficiently taxed to produce an abnormal GTT. There is some evidence that the greater the number of pregnancies the more likely a woman is to develop diabetes. Pyke[22] noted increasing frequency of diabetes with increased parity. Murphy[23] reported that 50 per cent of a group of women with ten or more children were diabetic.

Conn and Fajans[5] have shown that nonpregnant individuals with positive responses to the steroid-glucose tolerance test are more likely to develop an abnormal GTT. Can we also assume that pregnant women with positive PGTT are more likely to develop an abnormal GTT? It is too soon to say, but pregnant women with positive PGTT should be followed not only during the postpartum period but throughout subsequent pregnancies and other so-called stress situations such as weight gain, infections, etc. Only such studies can determine whether any therapeutic measures are indicated for those who have responses to the prednisolone glucose tolerance test during pregnancy.

SUMMARIO IN INTERLINGUA

Le Test de Tolerantia pro Glucosa a Prednisolona in Subjectos Pregnante

Le responsa a un test del tolerantia pro glucosa post prednisolona esseva investigate in 166 feminas pregnante, dividite in un gruppo de controlo e un gruppo suspecte de diabete. Le gruppo de feminas suspecte de diabete consisteva de feminas con le antecedente de un pesante infante, con antecedentes familial de diabete, e/o con glycosuria durante un previe pregnantia. Positive responsas, secundo le criterios de Fajans e Conn, occurreva in 23 pro cento del feminas in le gruppo de controlo e in 44 pro cento del feminas in le gruppo suspecte. Post excluder feminas con anormal simple tests de tolerantia pro glucosa, le prevalentia de positive responsas declinava a 15 pro cento in le gruppo de controlo e a 31 pro cento in le gruppo suspecte. Trenta patientes con normal simple tests de tolerantia pro glucosa sed positive tests de tolerantia pro glucosa post prednisolona esseva studiate a varie intervallos post le parturition. Un medietate del casos redeveniva normal. Le augmentate frequentia de positivitate in le test de tolerantia pro glucosa post prednisolona in le gruppo suspecte suggere que iste presumitemente plus rigide test del reservas insular permitte possibilemente le recognition de un sub-optimal capacitate insular durante le pregnantia.

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REFERENCES

[1] Fajans, S. S., and Conn, J. W.: An approach to the prediction of diabetes mellitus by modification of the glucose tolerance test with cortisone. Diabetes 3:296-304, 1954.

[2] Fajans, S. S., and Conn, J. W.: Further studies on a test for the "prediction" of diabetes mellitus. Clin. Res. Proc. 3:122, 1955.

[3] Conn, J. W.: The prediabetic state in man. Diabetes 7: 347-57, 1958.

[4] Fajans, S. S., and Conn, J. W.: Comments on the cortisone-glucose tolerance test. Diabetes 10:63-67, 1961.

[5] Conn, J. W., and Fajans, S. S.: The prediabetic state. Amer. J. Med. 31:839-50, 1961.

[6] Jackson, W. P. U.: The cortisone-glucose tolerance test with special reference to the prediction of diabetes. Diabetes 10:33-40, 1961.

[7] Duncan, L. J. P.: Cortisone-induced impairment of glu-

cose tolerance in the detection of the diabetic diathesis. J. Exper. Physiol. *41*:453, 1956.

[8] Nusimovich, B., Sarsotti, C., Spina, L. M., Liscio, I., and Vera, M. A.: The Corticosterone-glucose Test in Prediction of Diabetes. Advance Abstracts of Short Communications. First International Congress of Endocrinology, Copenhagen, Periodica, p. 1261, 1960.

[9] Nusimovich, B., Spina, L. M., Liscio, I., and Ueva, M. A.: Experencia con el test de Conn y Fajans en el prediccion de la diabetes. La Semana Medica *122*:639, 1963.

[10] Baldi, E. M., Nusimovich, B., Mesman, H., Miro, P., Mir, P., y Villafane, A.: El test de Conn y Fajans en el embarazo. Buenos Aires, La Prensa Medica Argentina, 321-29, 1963.

[11] Rosenwasser, E. B., y Lissin, D. J.: Prediabetes: nuestra experencia con el test de Conn y Fajans en el estado gravido-puerperal. La Semana Medica *122*:449-52, 1963.

[12] Kaplan, N. M.: Tolbutamide tolerance test in carbohydrate metabolism evaluation. Ann. Int. Med. *107*:212-24, 1961.

[13] German, J. L.: The glucose tolerance test after cortisone administration in obese and nonobese men. Diabetes 7:261-66, 1958.

[14] Lambert, T. N., Johnson, R. B., and Paul, G. R.: Glucose and cortisone-glucose tolerance in normal and "prediabetic" humans. Ann. Int. Med. *54*:916-23, 1961.

[15] Goto, Y., Kato, J., Takanami, A., and Ohneda, A.: Detection of prediabetes by glucose tolerance test sensitized by prednisolone. Lancet *2*:461, 1960.

[16] Sanders, M. J.: The effect of prednisolone on glucose tolerance in respect to age and family history of diabetes mellitus. Diabetes 10:41-45, 1961.

[17] Kyle, G. C.: Diabetes and pregnancy. Ann. Int. Med., Vol. 59, Supp. 3, 1963.

[18] Nelson, N.: A photometric adaption of the Somogyi method for determination of glucose. J. Biol. Chem. *153*: 375-80, 1954.

[19] Wilkerson, H. L. C., Butler, M. S., and Francis, J. O'S.: The effect of prior carbohydrate intake on the oral tolerance test. Diabetes 9:386-91, 1960.

[20] Klimt, C. R., Wolff, F. W., Silverman, C., and Conant, J.: Calibration of a simplified cortisone glucose tolerance test. Diabetes 10:351-66, 1961.

[21] West, K. M.: Comparison of the hyperglycemic effects of glucocorticoids in human beings. Diabetes 6:168-75, 1957.

[22] Pyke, D. A.: Parity and the incidence of diabetes. Lancet *1*:818, 1956.

[23] Murphy, R.: The hidden diabetic. Conn. Med. 2:306, 1957.

Carbohydrate in Low Protein Diets

(*Continued from page 571*)

on the amount and type of carbohydrate eaten. Weight for weight, sucrose was more effective in promoting fatty livers than was starch. The glucose series showed too much scatter for comparison.

In the sucrose series, the quantity of sterol esters, triglycerides, diglycerides, monoglycerides, and phospholipids increased as sucrose intake increased. The relative proportion of the phospholipid fraction also increased.

Histology revealed fatty livers in rabbits on diets A and hepatic foam cells in animals on diets B and C. Reticulin activity was increased in the livers of rabbits on sucrose diet A but rare in sucrose B diets and starch B and C diets. The effect of sucrose on the reticulin activity of the liver confirmed results reported by others.

Thus, in diets of unbalanced protein to carbohydrate ratios, some of the changes in liver metabolism and structure are attributable to the carbohydrate in the diet. The amount of hepatic lipid was related to the quantity and type of dietary carbohydrate. Sucrose stimulated the greatest increase in the lipid content. Almost all fractions of liver lipid increased as sucrose intake increased. Also, the metabolism of lipid in the liver was altered slightly since the phospholipid fraction increased in its relative proportion. Concomitant with the increase in liver lipid, the animals lost weight. The greatest weight loss was reflected by animals on the highest carbohydrate intake.

Macdonald points out that diets in human beings which lead to kwashiorkor also contain a relative excess of carbohydrate. This factor should be evaluated in its own right, as a cause of some of the manifestations of the disease. The author also notes that changes in bacterial flora may have something to do with the results. In unpublished data, he noted that when chlortetracycline was added to such sucrose diets, the liver showed a tendency towards decreased lipid content. Coccidio-free rabbits also live longer and show no increase in liver lipid when existing on an A diet with sucrose as the carbohydrate source.

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