Application of the Intravenous and Oral Glucose Tolerance Tests in Pregnancy

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SUMMARY

Using recently available pregnancy criteria a direct comparison of both the intravenous GTT and the oral GTTs was undertaken in 149 pregnant women. In suspects, intravenous testing gave a higher yield (16 per cent) than oral testing (8 per cent). Nonpregnant oral criteria gave the lowest yield in suspects (7 per cent) and a number of nondiagnostic responses (30 per cent) which did not parallel the degree of clinical risk and appeared normal by other nonpregnant criteria.

The advantage of a one-hour test expressed in a convenient numerical index of tolerance, combined with favorable sensitivity in suspects should favor the use of the intravenous glucose tolerance test in pregnancy. DIABETES *20*:476-84, July, 1971.

Overt diabetes may be aggravated during pregnancy and previously unsuspected or undetected diabetes may become apparent for the first time.[1] Furthermore, obstetric stigmata such as heavy newborns and perinatal deaths occur even without manifest diabetes and may presage clinical diabetes in the future. These circumstances together with the improvement in perinatal survival afforded by appropriate treatment[2] have stimulated the search for diabetes by the application of diagnostic tests during pregnancy in women suspected of having a greater risk for the disease.

The widely used oral glucose tolerance test (oral GTT) continues to be evaluated in pregnancy by criteria derived from nonpregnant populations.[3-5] Such interpretations may at times be misleading in evaluation of the pregnant subject, since the oral glucose tolerance curve in pregnancy has been demonstrated to be higher than in the nonpregnant state.[6-8] Pregnancy criteria are available for the intravenous glucose tolerance test (i.v. GTT).[9] This method is less well known, however, and has been regarded as less sensitive[10] than the oral test by those not accepting a gestational decrease in oral tolerance with normal pregnancy. Since O'Sullivan and Mahan have published criteria[8] for modifying the interpretation of the oral GTT in pregnancy, a direct comparison of the intravenous and oral methods by pregnancy criteria is now possible.

This study compares the intravenous and oral GTTs performed as paired tests in pregnant subjects with different degrees of risk for diabetes using pregnancy criteria for both tests. In addition, the intravenous tolerance test was studied in relation to a numerical index of oral tolerance derived from the sum of the oral tolerance test values. This allowed comparisons independent of arbitrary criteria of normality. The widely known oral GTT criteria of Fajans and Conn[3] were applied to compare the use of nonpregnancy criteria. Although not originally proposed for pregnancy, their criteria with various modifications are in wide use for this purpose.

MATERIALS AND METHODS

Pregnant women attending the obstetric clinic of the Maimonides Medical Center of Brooklyn were referred for testing because of family, obstetric or laboratory evidence suggesting diabetes mellitus. Only subjects who were ambulatory, on a diet containing at least 2,000 calories daily for no less than one week before testing and whose weight had been constant for two weeks were selected for screening by a detailed history, physical examination and urinalysis. Exclusion was based on (a) a previous fasting blood sugar in excess of 100 mg./100 ml. or a history of diabetes, (b) alcoholism or liver disease, (c) thyroid or other endocrine disease, (d) cardiac decompensation or edema, (e) gastrointestinal disturbances, (f) steroid or diuretic therapy (all other drugs were omitted for twenty-four hours

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before testing) and (g) infection, fever, or trauma within one week of the test. There were 136 successful screenees who were classified in three groups of descending clinical risk of diabetes. (1) The label of "significant suspects" was applied to sixty women with a diabetic parent or sibling, an unexplained stillbirth or a newborn weighing 10 lbs. or more, or with laboratory evidence of glycosuria when not pregnant or a history of an abnormal glucose tolerance test. (2) "Remote suspects" comprised thirty-six women with diabetes in a grandparent, aunt or cousin, or with a child weighing between 9 and 10 lbs. at birth. (3) "Glycosuria in pregnancy": there were forty women with glycosuria restricted to pregnancy and without evidence of impaired carbohydrate metabolism. After similar screening an additional thirteen pregnant patients with negative family, obstetric and laboratory backgrounds were selected to serve as a "nondiabetic" group.

An oral and an intravenous GTT were performed on each subject. The order of these tests was random. The mean interval between tests was two weeks. Under basal conditions an indwelling modified Lindemann needle was placed in an antecubital vein to obtain venous blood samples and a fasting blood specimen was drawn. For the intravenous GTT, 50 ml. of a 50 per cent glucose solution were injected within two minutes into an antecubital vein of the opposite arm. Blood samples were then obtained at ten-minute intervals for one hour after the beginning of the glucose injection. In the oral GTT a flavored drink containing 100 gm. of glucose was given and blood samples were drawn at 1, 1½, 2 and 3-hr. intervals. All blood samples were placed at once in heparin-fluoride tubes and analyzed within six hours for glucose by the Nelson-Somogyi method.

The index of tolerance, k, for the intravenous GTT was derived from the visually fitted slope of the blood glucose concentrations from ten to sixty minutes plotted on a semilogarithmic graph. The value of k was calculated from the difference between the natural logs of two points on the slope divided by the intervening time in minutes. Multiplied by 100 this quotient expresses k as per cent blood sugar fall per minute. The lower limits of normal k[9] applied in this study were: first trimester of pregnancy, 1.37; second trimester, 1.18; third trimester, 1.13.

The oral test was evaluated by pregnancy[8] and nonpregnancy[3] criteria. By pregnancy criteria the upper limits were taken as: fasting—90 mg./100 ml., 1 hr.—165 mg., 2 hrs.—145 mg. and 3 hrs.—125 mg.; elevation of any two values was considered an abnormal response. Under nonpregnancy criteria for the oral GTT the upper limits were: fasting—100 mg./100 ml., 1 hr.—less than 160 mg., 1.5 hrs.—less than 135 mg. (doubtful at 135 to 140), 2 hrs.—less than 110 mg. (doubtful at 110 to 120 mg.). The four ways in which this test is evaluated are shown in table 1, which summarizes the criteria for the intravenous and both oral GTT methods. None of our subjects had a "probably abnormal" response.

Certain numerical indices of oral glucose tolerance were also studied: a four-point score obtained by adding the fasting, 1 hr., 2 hr. and 3-hr. blood glucose concentrations[11] and a three-point score obtained similarly, but omitting the fasting blood glucose value. (The

TABLE 1

Criteria of glucose tolerance applied to pregnancy

Intravenous glucose tolerance, Silverstone et al.[9] Lower limits of k, the index of tolerance:			
1st trimester	2nd trimester	3rd trimester	
1.37	1.18	1.13	
Nonpregnancy oral glucose tolerance, Fajans and Conn[3] True blood sugar, mg./100 ml.			
Interpretation	1 hr.	1.5 hrs.	2 hrs.
Normal	less than 160, and	less than 135, and	less than 110
Abnormal	160 or more, and	140 or more, and	120 or more
Probably abnormal	160 or more, and	135 to 140	110 to 120
Unclassified		All other combinations	
Pregnancy oral glucose tolerance, O'Sullivan and Mahan[8] Upper limits of normal, true blood sugar, mg./100 ml.			
Fasting	1 hr.	2 hrs.	3 hrs.
90	165	145	125
Abnormal if any two values are elevated.			

TABLE 2

Oral and intravenous glucose tolerance in pregnancy
(Subject characteristics)

Group	No.	First test Weight, lbs. Mean	Weight, lbs. Range	Height, ins. Mean	Height, ins. Range	Differences, test I-II Weight, lbs. Mean	Weight, lbs. Range	Time, wks. Mean	Time, wks. Range
Nondiabetics	13	152	92-219	63	55-69	+1	−2 to + 3	2	2/7 to 6
Significant suspects	60	156	100-267	63	57-69	+1.5	−7 to + 8	2	2/7 to 4
Remote suspects	36	160	115-282	64	61-70	+1	−2 to + 6	2	2/7 to 7
Glycosuria of pregnancy	40	142	97-213	63	55-68	+2	−3 to + 8	2	1 to 4
All subjects	149	153	92-282	63	55-70	+1.5	−7 to + 8	2	2/7 to 7

latter is unrelated to the glucose load and has no counterpart in the intravenous test index, k.)

Subject characteristics: The heights and weights of subjects and the differences in time and weight between the intravenous and oral GTTs are given in table 2. There was a tendency to a small gain in weight between tests attributable to the advancement of pregnancy. The maximum interval between tests was seven weeks and the maximum weight change was a gain of 8 lbs.

RESULTS

Abnormal responses: Table 3 lists the test results for each group and some combined groups. In the thirteen nondiabetics there were no abnormal responses by pregnancy standards. One "unclassified" response was recorded by nonpregnancy criteria. The yield of abnormal responses in ninety-six combined significant and remote suspects was 16 per cent by the intravenous GTT, 8 per cent by pregnancy oral criteria and 7 per cent by unmodified oral criteria. Lower yields were obtained in the glycosuria of pregnancy group.

Agreements and conflicts: Twelve of the thirteen nondiabetic subjects (92 per cent) showed normal responses by all criteria. Agreement was considerably less in the other subjects (table 4). Of the whole group of 149 pregnant women, ninety-three (62 per cent) were normal by intravenous as well as pregnancy and nonpregnancy oral standards and four (3 per cent) were abnormal by all three standards. The fifty-two (35 per cent) remaining subjects had conflicting results as tabulated in table 5. An unclassified response by nonpregnancy oral criteria occurred in forty-five subjects and

TABLE 3

Comparison of intravenous and oral glucose tolerance tests in pregnancy
(Responses to oral test judged by two different sets of criteria)

	All subjects Total	Normal No.	Normal (%)	Abnormal No.	Abnormal (%)	Unclass. No.	Unclass. (%)	Significant and remote suspects Total	Normal No.	Normal (%)	Abnormal No.	Abnormal (%)	Unclass. No.	Unclass. (%)
I.V. test (a)	149	131	(88)	18	(12)			96	81	(84)	15	(16)		
Oral test, pregnancy criteria (b)	149	139	(93)	10	(7)			96	88	(92)	8	(8)		
Oral test, nonpregnancy criteria (c)	149	96	(65)	8	(5)	45	(30)	96	60	(63)	7	(7)	29	(30)
	Nondiabetic subjects Total	Normal		Abnormal		Unclass.		Significant suspects Total	Normal		Abnormal		Unclass.	
I.V. test	13	13	(100)	0	(0)			60	49	(82)	11	(18)		
Oral test, pregnancy criteria	13	13	(100)	0	(0)			60	54	(90)	6	(10)		
Oral test, nonpregnancy criteria	13	12	(92)	0	(0)	1	(8)	60	37	(61)	4	(7)	19	(32)
	Glycosuria only Total	Normal		Abnormal		Unclass.		Remote suspects Total	Normal		Abnormal		Unclass.	
I.V. test	40	37	(92)	3	(8)			36	32	(89)	4	(11)		
Oral test, pregnancy criteria	40	38	(95)	2	(5)			36	34	(94)	2	(6)		
Oral test, nonpregnancy criteria	40	24	(60)	1	(2)	15	(38)	36	23	(64)	3	(8)	10	(28)

(a) Criteria of Silverstone et al.; (b) criteria of O'Sullivan and Mahan; (c) criteria of Fajans and Conn.

TABLE 4

Intravenous and oral glucose tolerance in pregnancy
Agreements by all criteria
(Pregnancy intravenous, pregnancy and nonpregnancy oral)

	Nondiabetics	Significant suspects	Remote suspects	Glycosuria of pregnancy	All subjects
Total subjects	13	60	36	40	149
Subjects found normal by all 3 criteria	12	34	23	24	93
Subjects found abnormal by all 3 criteria	0	2	1	1	4
Subjects exhibiting agreement of all 3 criteria	12 (92%)	36 (60%)	24 (67%)	25 (63%)	97 (65%)

was the sole source of conflict in thirty-nine instances. Among the conflicts in the other thirteen subjects, twelve arose from disagreement between the pregnancy calibrated oral GTT and the intravenous test. In only one subject did an abnormal response by nonpregnancy criteria stand alone.

Pregnancy criteria: The proportion of agreements between criteria was considerably increased when comparison was restricted to the pregnancy calibrated standards (table 6). Over-all agreement for both normal and abnormal outcomes reached 92 per cent, ranging from 88 per cent in significant suspects to 100 per cent in nondiabetics. Ten of the twelve observed conflicts concerned subjects with abnormal intravenous as opposed to normal oral tests; six of these were in significant suspects, three were in remote suspects and one was in a subject with glycosuria. Of the remaining conflicts between normal intravenous and abnormal oral tolerance one occurred in a significant suspect and one in a remote suspect.

With the use of O'Sullivan's pregnancy criteria for evaluating the oral test, test results on all 149 subjects are tabled once more as follows:

		Oral GTT pregnancy criteria: Normal	Abnormal	
Intravenous GTT	Normal	129	2	131
	Abnormal	10	8	18
		139	10	149

A positive association between the two GTTs was found present and showed extremely high statistical significance ($P < .000, 01$) by Fisher's exact one-sided test.[12] The McNemar test[13] with Yates correction showed that the intravenous GTT labeled a significantly ($P < .04$) larger number of individuals as abnormal than did the oral GTT.

When O'Sullivan's pregnancy criteria were replaced by Fajans and Conn's nonpregnancy criteria it became necessary to exclude from analysis forty-five subjects labeled as "unclassified" by the latter standards. This led to the following table:

		Oral GTT nonpregnancy criteria: Normal	Abnormal	
Intravenous GTT	Normal	94	3	97
	Abnormal	3	4	7
		97	7	104

TABLE 5

Intravenous and oral glucose tolerance in pregnancy
Conflicts by all criteria
(Pregnancy intravenous, pregnancy and nonpregnancy oral)

Type of conflict			Type of subject				No. of conflicts
Intravenous	Nonpregnancy oral	Pregnancy oral	Non-diabetics	Significant suspects	Remote suspects	Glycosuria of pregnancy	
Normal	Unclassified	Normal	1	13	8	13	35
Abnormal	Unclassified	Abnormal		3		1	4
Abnormal	Unclassified	Normal		3	2	1	6
Abnormal	Normal	Normal		3			3
Normal	Abnormal	Abnormal		1	1		2
Normal	Abnormal	Normal		1			1
Abnormal	Abnormal	Normal			1		1
Totals			1	24	12	15	52

TABLE 6

Comparison of intravenous and oral glucose tolerance using pregnancy criteria

	Non-diabetics		Significant suspects		Remote suspects		Glycosuria of pregnancy		All subjects	
Total	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Subjects	13	(100)	60	(100)	36	(100)	40	(100)	149	(100)
Subjects found normal by both criteria	13	(100)	48	(80)	31	(86)	37	(92.5)	129	(87)
Subjects found abnormal by both criteria	0		5	(8)	1	(3)	2	(5)	8	(5)
Subjects exhibiting agreements of both criteria	13	(100)	53	(88)	32	(89)	39	(97.5)	137	(92)
			Conflict in test results							
Subjects found normal by i.v. and abnormal by oral	0		1	(2)	1	(3)	0	(0)	2	(1)
Subjects found abnormal by i.v. and normal by oral	0		6	(10)	3	(8)	1	(2.5)	10	(7)
Subjects exhibiting conflicting results of tests	0		7	(12)	4	(11)	1	(2.5)	12	(8)

Again, the positive association between the GTT results was found highly significant ($P < .000{,}03$). There were six disagreements between tests, three in each direction.

Regarding the association of the intravenous GTT index k with either of the two score indices derived from the oral GTT curve, such association was apparently absent among the subjects labeled "nondiabetic" and "glycosuria in pregnancy." By contrast, among the "significant suspects" and "remote suspects," a negative association between k and either the four-point score or the three-point score was found to exist at a high significance level ($P < .001$). Figures 1a and 1b show spot graphs for significant and remote suspects separately of the three-point score plotted against k, together with the fitted least squares lines. Fitting of a quadratic rather than linear regression function results in a slightly improved fit, in the sense that the apparent curvature suggested in the graphs can be shown not to be a random effect caused by the sample in hand ($P < .025$ for significance of the quadratic term). Although these associations undoubtedly exist, the regressions do not seem very useful for predicting the three-point scores or the four-point scores by means of k. The use of a linear regression achieves a reduction of about 25 per cent, and the use of a quadratic regression a reduction of about 30 per cent in the standard deviation of either type of score.

Outcome of pregnancy: There were no stillbirths among the 144 subjects whose outcome of pregnancy was known. Three newborns weighed 10 lbs. or more. The mother of one had glycosuria of pregnancy with all tests abnormal; another was a significant suspect with normal intravenous and pregnancy oral GTTs and an unclassified response to the unmodified oral test. The third mother, also a significant suspect had abnormal responses by all test criteria. A remote suspect bore a child with an anomaly, pectus excavatum. Her tests were normal by all criteria. Slightly higher birth weights were noted in subjects with abnormal tests, attributable to the three infants exceeding 10 lbs.

DISCUSSION

Several factors may account for the discrepancies observed when comparing diagnostic tests for diabetes. These include differences in the populations under study which vary in their composition of diabetes-prone individuals as well as in age and pregnancy status, variations in test procedure and criteria, and differences in the metabolic mechanisms expressed by the tests. Unfortunately validation of test results by long-term clinical studies is difficult and confirmation by a sensitive and specific parameter independent of blood sugar is not available. That the outcome of pregnancy might itself provide a short-term clinical proving ground cannot be ascertained from the data available in our relatively small sample of women with abnormal tolerance by any criteria. The uncertainty regarding the degree of obstetric risk in minimal diabetes adds to the dilemma. Consequently, the merits of tolerance tests are frequently judged solely by the incidence of positive responses; the test with the highest yield is more likely to be preferred, often with insufficient regard to the responses in nondiabetic control subjects or to the association with

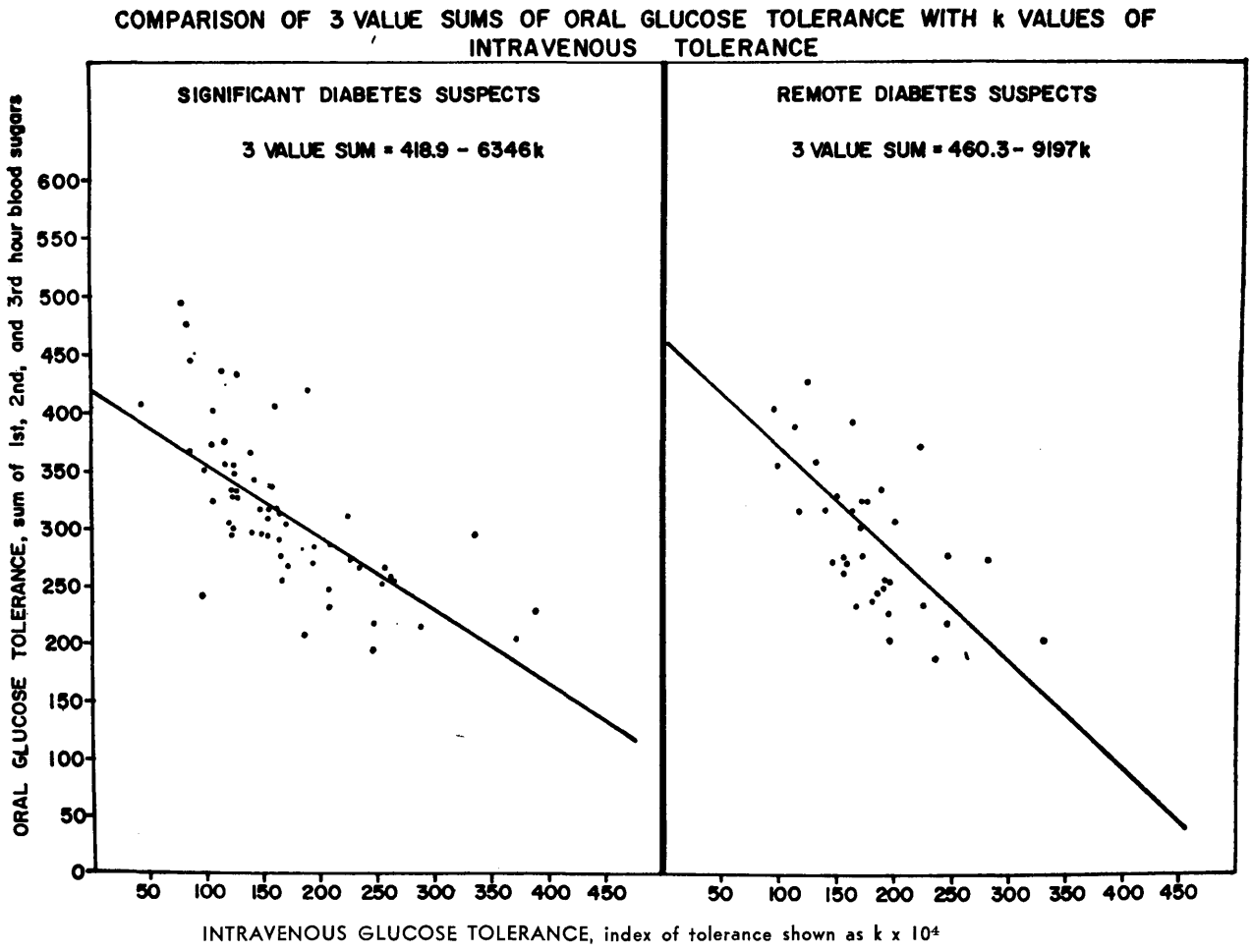

FIGURE 1

the clinical likelihood of diabetes.

Investigators who have calibrated their test criteria against nondiabetic subjects have been able to demonstrate progressive degrees of impaired tolerance with either the oral or i.v. GTT which parallel the severity of diabetes[5,14] and the genetic likelihood for diabetes.[3,9] Tests so calibrated also reveal altered responses to other influences such as age and drugs.[15] By this approach the most promising diagnostic method would be the one retaining specificity for controls, exhibiting a high order of impaired response to minor degrees of the diabetic state and showing progressive impairment paralleling the state of the disease.

In table 3 pregnancy criteria applied to the intravenous and oral GTTs resulted in graded yields paralleling the degree of diabetic risk represented by the subject groups. All nondiabetic subjects were negative. Although this group was small, the criteria under study have been calibrated in larger groups and the present results were merely confirmatory. With the i.v. GTT, significant suspects presented the highest yield of 18 per cent, remote suspects were intermediate at 11 per cent and the glycosuria of pregnancy group was lowest at 8 per cent. The oral test yields were smaller but followed the same progression. The lower oral yields suggest that the criteria of O'Sullivan and Mahan (table 1) based on a mixed population are probably not as stringent as the intravenous test criteria, derived from nondiabetic controls. The yield with nonpregnancy criteria for the oral test did not conform to clinical risk and showed a loss of usefulness because of 30 per cent unclassified responses. Yannone and Goldfein[16] observed a comparable incidence of unclassified responses in pregnant subjects. Similarly Pote and Poucher have reported 20 per cent unclassified responses in 175 men and nonpregnant women.[17] From table 5 it was apparent that

thirty-five of the entire fifty-two conflicts were due to unclassified oral tests in subjects with normal responses by pregnancy criteria. While this raises the possibility that unclassified responses are borderline abnormalities indicating a high order of test sensitivity, this point is weakened by the failure to correlate with the degree of clinical risk in suspect groups (table 3). Unclassified responses showed little distinction between significant and remote suspects and occurred even more frequently in the glycosuria only group. Glycosuria restricted to pregnancy is often attributable to alterations in renal function and as such represents a lower diabetes risk.[9]

In all forty-five subjects with unclassified responses by the nonpregnant oral GTT, the basis of this interpretation rested on a normal one-hour glucose level (less than 160 mg./100 ml.) in the face of elevated levels at 1.5 or 2 hrs. or at both these intervals. The two-hour concentration was elevated in forty-three subjects while in fourteen both the 1.5 and 2-hr. values were raised. Elevation at only 1.5 hrs. occurred in two subjects. Thus the tolerance curve of pregnancy in this group appeared to follow the same configuration apparent in O'Sullivan's pregnancy criteria, table 1, namely a delay in the fall of the oral tolerance curve accompanied by little or no elevation at one hour. One subject with an unclassified response had a slightly elevated fasting blood sugar of 102 mg./100 ml.; both her i.v. GTT and pregnancy oral interpretations were abnormal. The i.v. GTT was abnormal in ten other subjects with unclassified responses, four of which also had abnormal results by O'Sullivan's pregnancy standards. These findings do not support the view that unclassified responses are borderline abnormalities associated with a test of superior sensitivity. Conceivably the relationship found between intravenous and oral test results might be altered by the application of a different set of nonpregnancy oral criteria incorporating a three-hour blood sugar response. In this connection criteria[4] as proposed by a panel of consultants to the U.S. Public Health Service were applied. Following 100 gm. of glucose orally, this tolerance test is abnormal if any three or more of the following values, or the fasting and three-hour combination, are met or exceeded: fasting—110 mg./100 ml., 1 hr.—170 mg., 2 hrs.—120 mg., 3 hrs.—110 mg. Since there were no unclassified response subjects whose fasting sugar levels reached 110 mg./100 ml. nor whose one-hour values reached 170 mg., all unclassified responses became normal by these criteria. Furthermore these criteria did not affect subjects with normal Fajans and Conn responses and when applied to the eight subjects with abnormal Fajans and Conn responses only one remained abnormal. Consequently the application of another nonpregnancy interpretation did away with the unclassified category but at the cost of a marked over-all loss of test sensitivity. It is realized that other criteria are in use[10] which could result in an increased yield. However, they lack sufficient validation from studies of pregnant populations to justify their application in this pregnancy study on any other basis than yield. It has already been noted that an alternate method of evaluation independent of blood sugar response is not available.

An illustration of the difficulties encountered in applying nonpregnancy criteria is seen in the report of Ocampo et al.[18] Their twenty-two pregnant nondiabetic screenees were negative by the i.v. GTT. The infants were born with normal weights and none of the mothers developed diabetes during a nine to sixteen months follow-up period. However they had twelve abnormal responses (55 per cent) using nonpregnancy criteria for the oral test after 100 gm. of glucose. Their criteria for impaired tolerance required two or more values equaling or exceeding the following: 110 mg./100 ml. for fasting blood sugar, 160 mg. at 1 hr., 140 mg. at 1.5 hrs., 120 mg. at 2 hrs., 110 mg. at 3 hrs. A reinterpretation of their data by the Fajans and Conn criteria converted four abnormalities to unclassified responses. Even after applying the pregnancy criteria of O'Sullivan there were eight abnormalities though in different subjects. This persistent residue of abnormal responses directed attention to their mean sugar values which were found to be distinctly higher than O'Sullivan's. This degree of blood sugar elevation was the more unusual since O'Sullivan had studied a mixed population which included diabetes suspects. Thus laboratory variations in blood sugar may account for the poor specificity reported by Ocampo with the oral test and serve to emphasize the need for calibration of individual laboratory results in appropriate control subjects. The intravenous test offers the advantage of expressing tolerance as a rate relatively unaffected by variations in absolute glucose concentrations among laboratories as long as the serial blood determinations remain proportionally correct.

Benjamin and Casper,[10] examining pregnant suspects, found 34 per cent of 350 diabetes suspects and women with glycosuria of pregnancy to have impaired intravenous glucose tolerance. Using nonpregnancy criteria, the oral test with 100 gm. glucose yielded 72 per cent abnormal responses. They regarded oral tolerance curves as normal if the fasting blood sugar was below 100 mg./100 ml., the peak value below 160 mg. and the

two-hour value below 120 mg. Despite the extraordinary size of their oral test yield in a mixed suspect population the authors favored the application of nonpregnancy criteria in pregnancy.

The oral glucose loading dose used in our study was 100 gm. instead of 1.75 gm./kg. of ideal body weight as used by Fajans and Conn.[3] Castro et al. studied dose differences of 100 gm. and 1.75 gm./kg. and reported similar tolerance test results up to two-and-one-half hours after the glucose load.[19]

Discussion of k vs. oral sums: Summation of oral tolerance in a single numerical index might be expected to simplify interpretations as well as comparative studies, advantages inherent in the intravenous test index, k. However there are problems raised by this approach. Equal weighting of all points in the sum fails to recognize physiologic or clinical factors which may exert selective effects. The fasting blood sugar reflects a basal state whereas postglucose load values are in response to provocation. In our study omission of the fasting value by the use of the three-point sum mattered little, since these values were in the normal range and fairly closely clustered. On the other hand pregnancy itself appears to exert a greater influence on the later values of the oral curve. Even if these considerations were of no consequence, the sum index remains dependent on absolute blood sugar concentrations and thereby subject to laboratory variations. Additional data, in and out of pregnancy, are necessary to determine the further usefulness of this technic.

While oral tolerance in general is impaired in pregnancy, intravenous tolerance is sustained or slightly improved in nondiabetics. In suspects k deteriorates concordantly with oral tolerance. These circumstances may underlie the lack of association noted in the study between the oral and intravenous indices in nondiabetics as well as the presence of an association in suspects. The glycosurias of pregnancy may be regarded as a mixed group whose test outcome is influenced by the mechanism of the glycosuria in the involved individuals.

The absence of neonatal deaths or unexplained stillbirths from the present series of 144 pregnancies for which such data were available is attributable to the size of the sample. There were three infants exceeding 10 lbs. in the suspects and glycosuria groups. Two of the involved mothers had abnormal tolerance tests.

Increased plasma insulin levels have been found in pregnancy.[20] This may account for the preservation or enhancement of intravenous glucose tolerance in nondiabetic women.[9] The deterioration in oral tolerance manifested by increased blood sugar levels after oral glucose is puzzling. Recent studies[21,22] indicate that plasma insulin levels are greater following oral than after intravenous glucose loading in nonpregnant subjects. The greater insulinogenic response has been attributed to the release of polypeptides or glucagon during the absorption of glucose. This mechanism has not been studied in pregnancy and may offer an explanation of the differential response between the intravenous and oral tolerance tests. Observations in our laboratory[15] of the "pseudo-pregnant" state induced by estrogen-progestin drugs used for contraception revealed impaired intravenous tolerance concordant with the impaired oral glucose tolerance reported by others.

Differences with regard to the routes of glucose administration underlie the criticism that the i.v. GTT is "unphysiologic." Uncertainties based on these differences should not obscure the advantages of the intravenous method. A well defined, approximately equal stimulus is presented, namely the elevation of the blood sugar. The test results are conveniently expressed as a single numerical index of tolerance and are relatively independent of laboratory variations in absolute glucose concentration scales.

Advantages to the subject are the short duration of the test and the removal of nausea and vomiting provoked by oral glucose. The use of a short indwelling cannula, the Lindemann needle, eliminates multiple venipunctures for successive blood samples. These technical advantages of the i.v. GTT, the availability of pregnancy criteria and a sensitivity at least comparable to the oral test should promote a wider use of the procedure in pregnant women.

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