

# Triamcinolone Provocative Test in Offspring of Two Diabetic Parents

Victoriano N. Navarrete, M.D., and Isabel H. Torres, M.D., Mexico City

## SUMMARY

In fifty-five subjects, with two diabetic parents, and who had a previous normal glucose tolerance test, 67.2 per cent showed abnormalities when tested by a triamcinolone glucose tolerance test (54.5 per cent abnormal and 12.7 per cent suspicious). This result contrasted with an incidence of 1.6 per cent abnormal tests and an additional 1.6 per cent suspicious tests in a control group matched for age and sex.

It is suggested that the triamcinolone provocative test be further employed in the search for diabetic tendencies in suspicious or likely subjects. *DIABETES* 16:57-60, January, 1967.

There is universal recognition of a high frequency of diabetes among the relatives of diabetics, and a higher incidence in those with both parents with diabetes.<sup>1</sup> Thus any method that seeks to anticipate the development of the recognizable disease should be tested in this group. A high index of abnormal results by any testing method on such subjects would offer a valuable approach to identify the future diabetic.

Recently we described the triamcinolone test<sup>2</sup> on patients "clinically prediabetic" (chosen as such by obstetrical complications and some of them with two diabetic parents) and found it to be highly sensitive for the possible recognition of the early states of the disease. The main purpose of the present work is to present the results of a study of subjects whose parents are both diabetics and who yielded a normal standard glucose tolerance test when retested with the triamcinolone test.

## MATERIAL AND METHODS

One-hundred and sixteen subjects were divided in two groups.

*Group I.* Over a two-year period we were able to gather sixty-one subjects from twenty-five different fam-

INCIDENCE OF ABNORMAL TRIAMCINOLONE GLUCOSE TOLERANCE TEST IN SUBJECTS WITH BOTH DIABETIC PARENTS

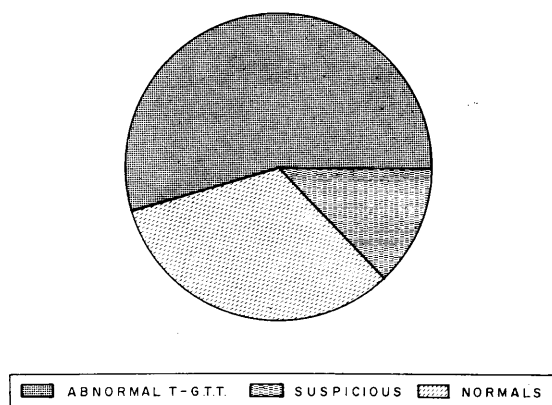


FIGURE 1

INCIDENCE OF ABNORMAL TGTT AT DIFFERENT AGES IN CHILDREN OF BOTH PARENTS WITH DIABETES

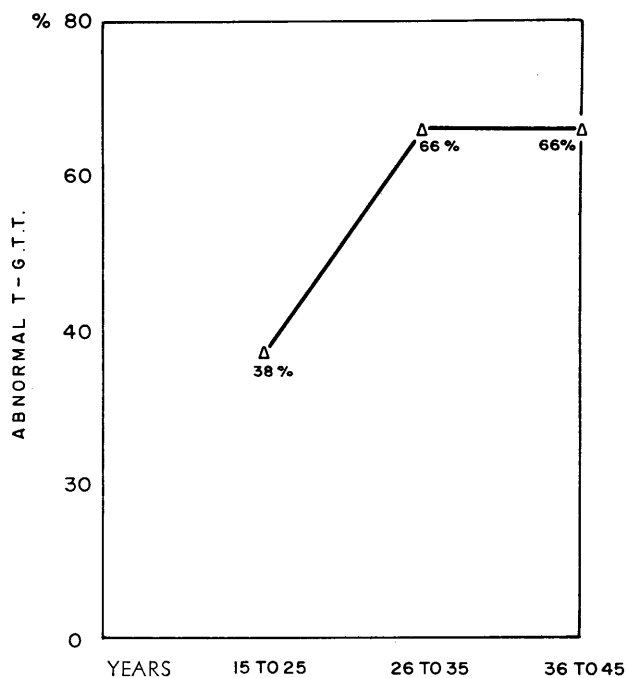


FIGURE 2

From The Internal Medicine Department, Hospital de Gineco-Obstetricia No. 1, "I.M.S.S.," Mexico City, México.

TRIAMCINOLONE PROVOCATIVE TEST IN OFFSPRING OF TWO DIABETIC PARENTS

TABLE 1

Subjects with both parents with diabetes  
(Tramit signifies subject not yet registered by number.)

Control group

FILE NUMBER	AGE	CORTISONE				INTERPRETATION	TRIAMCINOLONE				INTERPRETATION	AGE	TRIAMCINOLONE				
		0	1	2	3		0	1	2	3			0	1	2	3	
164-44-4827	35	87	120	83	90	—	125	160	153	140	+	32	91	104	104	80	
TRAMIT	24	100	124	100	83	—	125	110	140	105	+	24	71	130	112	64	
49-62-0191	32	87	133	87	80	—	110	183	135	115	+	32	104	142	128	106	
49-64-37-1024	21	94	108	94	87	—	110	130	140	105	+	21	70	114	104	50	
146-19-356	43	140	200	135	120	+	95	223	140	130	+	43	75	154	112	95	
144-17-3732	31	87	132	115	108	—	100	199	146	162	+	29	42	104	68	62	
156-35-2519	29	88	132	83	83	—	112	159	143	122	+	28	73	144	92	42	
TRAMIT	30	71	149	103	75	—	108	200	168	116	+	30	82	132	128	109	
164-24-1028	17	92	159	127	127	—	88	138	147	132	+	22	91	165	124	100	
164-24-1028	20	74	88	74	74	—	88	112	83	79	—	20	71	91	75	71	
164-24-1028	15	102	117	117	112	—	74	102	79	74	—	16	96	138	114	112	
652-18-43	17	68	138	109	64	—	83	112	92	83	—	23	100	138	113	105	
162-24-1028	19	88	143	159	88	+	96	188	194	103	+	19	73	107	99	90	
TRAMIT	18	102	220	189	122	+	98	250	195	127	+	24	71	130	112	64	
154-29-1506	28	79	149	112	64	—	92	202	153	132	+	28	68	153	92	43	
164-18-581	23	108	102	79	74	—	102	132	138	109	+	25	100	157	116	96	
164-18-581	21	98	153	74	68	—	112	182	165	102	+	25	86	130	110	72	
164-18-581	15	88	92	98	92	—	98	68	74	64	—	16	52	138	64	48	
162-24-1028	15	64	50	60	43	—	98	160	110	80	—	21	79	112	91	115	
AGE												AGE					
MEAN 23.8 YEARS		NORMALS 84.3 %					NORMALS 26.8 %					MEAN 25 YEARS					

ilies both of whose parents presented overt diabetes. Of the sixty-one subjects, six showed an "abnormal" standard glucose tolerance test (GTT), and were excluded from the study. The remaining fifty-five cases with strictly "normal" GTT comprised Group I; sixteen were men and thirty-nine were women; thirty ranged between fifteen and twenty-five years of age, eighteen between twenty-six and thirty-five years, and seven between thirty-six and forty-five years of age.

*Group II.* A control group of sixty subjects was matched for age and sex and without antecedents of diabetes in the family or clinical "prediabetic state."<sup>2</sup> Both groups took a high carbohydrate diet for at least three days, then were given 8 mg. of triamcinolone eleven hours and one hour prior to an oral glucose tolerance test (12 mg. per dose if the weight exceeded 66 kg.). The glucose load in the standard cortisone and triamcinolone tests was 1.75 gm. per kilogram as established previously.<sup>2</sup>

A cortisone glucose tolerance test, following the Fajans and Conn<sup>3</sup> method and interpretation was also performed in nineteen cases.

*Criteria:*

*The standard glucose tolerance test (GTT)*

(a) Normal—None of the figures reached 100, 150, 110 and 105 mg. at 0, 1, 2 and 3 hrs., respectively. (b) Abnormal—Two figures at or above the normal.<sup>2</sup>

*The cortisone glucose tolerance test (CGTT)*

Positive—The two-hour figure at or above 140 mg.<sup>3</sup>

*The triamcinolone glucose tolerance test (TGTT)*

Abnormal—Two figures at or above 115, 170, 135 and 120 mg. at 0, 1, 2 and 3 hrs., respectively. Suspicious—Only one altered figure.<sup>2</sup>

In both groups a TGTT was performed. In only nineteen cases was it possible to perform a comparative study of cortisone versus triamcinolone tests. In this comparative group all but three cases weighed below

T - G.T.T.:	
●	ABNORMAL
◐	SUSPICIOUS
○	NORMAL
●	OVERT DIABETES

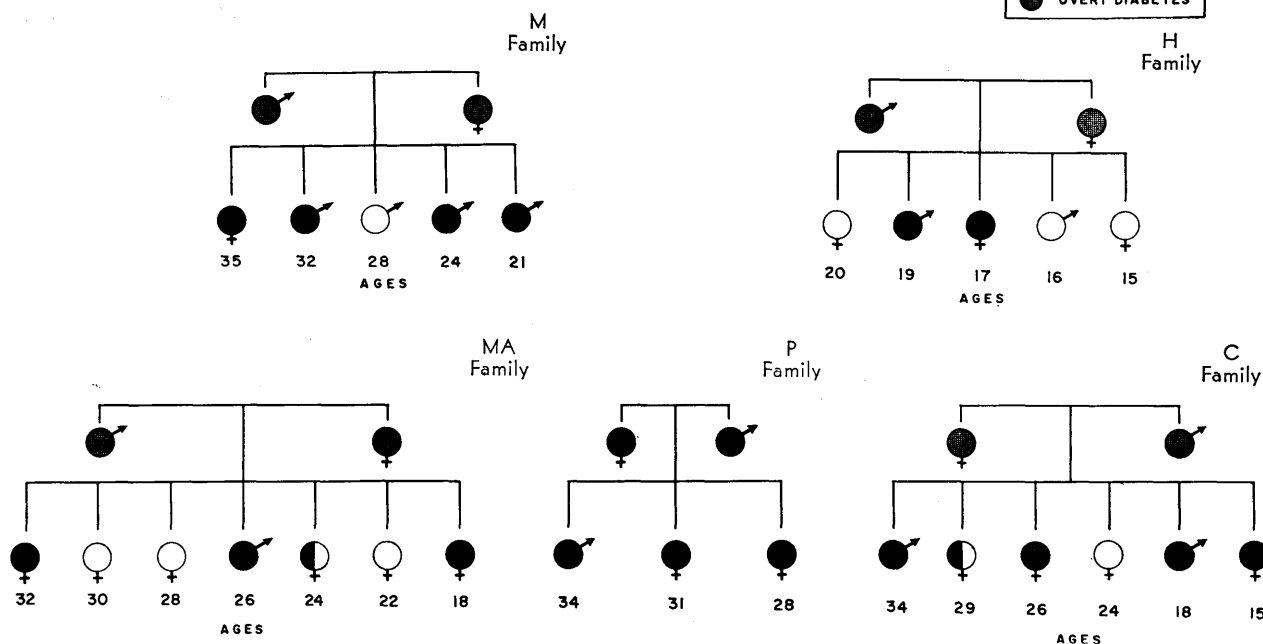


FIG. 3. Illustrative currents of abnormal triamcinolone-glucose tolerance tests in five families with both parents diabetic

66 kg. In the comparison 100 mg. of cortisone and 16 mg. of triamcinolone were administered.

#### RESULTS

(1) Of the fifty-five cases from Group I, 67.2 per cent yielded an altered triamcinolone test; 54.5 per cent presented frankly abnormal test (two altered figures); and 12.7 per cent were "suspicious" (only one altered figure) figure 1.

(2) The frequency of abnormal triamcinolone test appeared differently at different ages; among subjects between fifteen and twenty-five years of age: 38 per cent of abnormal TGTT were found, 66 per cent between twenty-six and thirty-five years and 66 per cent between thirty-six to forty-five years of age (figure 2). These data contrast with those observed in the control group where only one case in sixty gave an abnormal triamcinolone test and one suspicious case.

(3) Of the nineteen cases where both a TGTT and a CGTT were carried out, 15 per cent gave "positive" cortisone test contrasting with 63 per cent abnormal triamcinolone tests (table 1).\*

\*Case 5 was classified as cortisone-positive in spite of presenting 135 mg. at two hours, due to its frankly altered curve.

(4) The pedigrees of five different illustrative families are shown in figure 3.

#### DISCUSSION

Although it is universally accepted that diabetes is a hereditary disease the mode of inheritance is not clearly established.<sup>4</sup> Actually we lack an effective genetic marker which may permit with a reasonable degree of confidence the designation of the inheritance on diabetes. Genetic studies have been based on an abnormal glucose tolerance test or on the detection of the overt disease. Yet many subjects with the diabetic stigma may never develop an abnormal GTT.<sup>4</sup> It is quite possible that with more sensitive diagnostic procedures the genetic problem of the disease could have a more accurate approach.

It is difficult and we do not pretend to do an exhaustive evaluation of the three diagnostic procedures on the basis of a single tolerance test. First, there is the lack of reproducibility of the standard glucose tolerance test;<sup>5</sup> second, there are employed different criteria and methods for establishing normal values in the cortisone and triamcinolone tests. Nevertheless, the latter shows a high incidence of abnormal results in the

offspring of two diabetic parents, an incidence not shown by the cortisone test.<sup>6</sup> Might the varying dosages of cortisone and of triamcinolone make a great deal of difference in the results? We hardly believe that this could be a good explanation, as sixteen out of nineteen of the cases compared weighed below 66 kg. and the dose of 100 mg. of cortisone is roughly "equivalent" to the 16 mg. of triamcinolone employed in these cases. Only three cases, numbers 7, 9 and 13 (table 1), were 15 per cent above their "ideal" weight and they were given 125 mg. of cortisone.

As the frequency of overt diabetes is higher in the fourth and fifth decade of life, we expected a higher incidence of abnormal TGTT as the age increased. This occurrence was really observed on those from fifteen up to thirty-five years, but the curve showed a plateau after this age. Perhaps that would mean that if a subject with two diabetic parents does not show an ab-

normal TGTT in the third decade of life, would he be safe of overt disease? These and other questions need many years of observations and extensive genetic search.

REFERENCES

<sup>1</sup> Steinberg, A. G.: The genetics of diabetes: a review. *Ann. N.Y. Acad. Sci.* 82:197-207, 1959.  
<sup>2</sup> Navarrete, V. N., and Torres, I. H.: A triamcinolone-glucose tolerance test in the early diagnosis of diabetes. *Diabetes* 14:481, 1965.  
<sup>3</sup> Fajans, S. S., and Conn, J. W.: An approach to the prediction of diabetes mellitus by modifications of the glucose tolerance test with cortisone. *Diabetes* 3:296, 1954.  
<sup>4</sup> Vallance-Owen, J.: Synalbumin Insulin Antagonism and Diabetes: Ciba Colloquia of Endocrinology 15, 1964.  
<sup>5</sup> McDonald, G. W., Fisher, G. F., and Burnham, C.: Reproducibility of the oral glucose tolerance test. *Diabetes* 14:473, 1965.  
<sup>6</sup> West, K. M.: Response to cortisone in prediabetes. Glucose and steroid-glucose tolerance in subjects whose parents are both diabetic. *Diabetes* 9:379, 1960.

BRIEF NOTES AND COMMENTS

Use of Chlorpropamide in the Treatment of Diabetes in Pregnancy

C. P. Douglas, B.A., M.B., and R. Richards, M.B., Kingston, Jamaica

SUMMARY

In an underdeveloped community there are many logistic difficulties in the control and management of diabetes mellitus. Because it often was impossible to carry out insulin therapy at home, one of us (R.R.) made early use of oral hypoglycemic drugs in the diabetic clinic at the University of the West Indies in Kingston. Since 1961 sulfonylureas have been used in pregnant diabetic patients. The present report describes the results of chlorpropamide treatment in 34 pregnant diabetic women. *DIABETES* 16:60-61, January, 1967.

METHODS

One hundred and six patients were observed during 128 pregnancies in the Department of Obstetrics in the seven years prior to June, 1965. During this time it was our practice to

consider together diabetes and early diabetes as diabetic pregnancy, since the fetal hazard is high in prediabetes as well as in diabetes.<sup>1</sup> The early diabetic patients, nineteen in number, were those in whom the results of a cortisone-modified glucose tolerance test<sup>2</sup> were abnormal and in whom criteria suggested by Wilkerson<sup>3</sup> were fulfilled. These criteria include repeated glucosuria, and, in some patients, the recurrence of a stillbirth or delivery of a large child which died neonatally and at autopsy showed changes associated with diabetes in pregnancy such as hyperplasia of the islets of Langerhans and infiltration with eosinophils.<sup>4</sup>

From 1961 on, pregnant diabetic patients who were over the age of thirty were considered for chlorpropamide therapy. These amounted to thirty-four, of whom five were on treatment when they became pregnant, nineteen were first treated between the fourteenth and twenty-eighth weeks, and ten were given treatment after the twenty-eighth week. Forty-one of the remaining patients were treated with diet alone, and forty-two were given insulin (twenty had need of between fifty and 100 units daily, and five had need of more than 100 units daily). Eleven patients had no treatment, eight being admitted in labor unbooked and three diagnosed only postpartum.

Medical and obstetric management was based, in all patients, on the same principles of antenatal care and of method

From the Departments of Obstetrics and Gynaecology, and Medicine, University of the West Indies, Kingston, Jamaica. Present address: Royal Free Hospital, Liverpool Road, London, N1, England.