

## CARBOHYDRATE METABOLISM IN DYSFUNCTIONAL UTERINE BLEEDING

by

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Several investigators have found that the incidence of diabetes mellitus and impaired glucose tolerance is high in cases of carcinoma of the body of the uterus. Way in 1954 reported that 29% of such patients had frank diabetes mellitus and a further 43% showed a prediabetic type of glucose tolerance curve. Many others — Garnet (1958) Noble and Atwood (1958) have reported similar findings but none so striking as Way.

Endometrial cancer is essentially a post-menopausal disease. The association of endometrial hyperplasia, especially postmenopausal, and carcinoma of the endometrium has been emphasised by Novak and Yui (1936) Novak and Richardson (1941), Hertig and Sommers (1949) Way (1954) Turnbull (1956) and many others. Benjamin (1960) reported a very

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*Paper read at the 12th All-India Obstetric and Gynaecological Congress at Ahmedabad in December 1963.*

high incidence of abnormal glucose tolerance curves in dysfunctional bleeding and has established by glucose tolerance studies the association of impaired glucose tolerance and cancer of the endometrium.

In the Government Hospital for Women and Children, the incidence of dysfunctional uterine bleeding in all age groups was 14.1% of all gynaecological admissions during a 2 years period 1960 and 1961. (1540 cases of dysfunctional uterine bleeding among 10,974 admissions). If only those occurring after the age of 35 years are taken into account there were 479 cases among these 1540, thus constituting 13.1% of such cases. During the same two-year period the number of cases of carcinoma of the endometrium was only 17 as against 1892 cases of carcinoma of the cervix. It is rather puzzling and intriguing to find that despite the large incidence of dysfunctional uterine bleeding, the incidence of carcinoma of the endometrium is very very low indeed. Benjamin (1960) pointed out that in his series of similar cases of hyperplasia of the endometrium in women over the age of 45 years there was abnormal glucose tolerance curve

(diabetic and prediabetic) in nearly 84%. This finding prompted us to carry out studies on carbohydrate metabolism by glucose tolerance test in as many cases of dysfunctional bleeding as possible.

#### Method of Study

1. Only women over 35 years of age, proved to be suffering from dysfunctional uterine bleeding by ruling out after careful investigation and examination any organic cause, were taken up for study.

2. Patients satisfying the requirements for admission to the study were submitted to glucose tolerance test. Cortisone-stressed glucose tolerance test was preferred as it is stated to expose a latent defect in carbohydrate metabolism more surely and more accurately than an ordinary glucose tolerance test.

3. The test is done as follows:—

10 mgms. of Prednisolone was given orally at 8 P.M. and 10 mgms. at 6 A.M. The patients were not permitted to take anything after 8 P.M. The fasting blood sugar and glucose tolerance tests were done at 10 A.M. the next morning in the usual manner.

The blood sugar curve so obtained was interpreted as:

(a) Normal — fasting blood sugar level below 120 mgm. per 100 ml. Within  $\frac{1}{2}$  to 1 hour blood sugar rises sharply to reach a maximum of 40-50 mgms. above the fasting level and blood sugar falls to normal fasting

level within  $1\frac{1}{2}$ -2 hours. At times at the end of 2 hours there may be a slight fall reaching slight subfasting levels but which reaches fasting levels in 3-4 hours.

(b) Diabetic curve — fasting level usually above 120 mgm%. Maximum rise reaches above 160 mgm% and usually after one hour. At the end of 2 hours blood sugar level is still elevated.

(c) Abnormal or pre-diabetic curve — fasting level below 120 mgm%. Peak rise may reach upto 200 mgm. in half to one hour. At the end of 2 hours the blood sugar level is above 140 mgm. or 40% above the fasting blood sugar level.

3. All patients were submitted to a thorough curettage and histology of the endometrium studied.

4. As controls women whose periods were quite normal and regular and over the age of 35 years were investigated with cortisone-stressed glucose tolerance test. These were mostly patients admitted into hospital for various other complaints like pelvic infection, prolapse, leucorrhoea.

#### Results and Observations

Two hundred and twenty patients suffering from dysfunctional uterine bleeding were studied as above. As controls 100 patients were studied. The age distribution of the study group and control group is shown in Table I below.

TABLE I  
Age Distribution

Age in years	35-45	46-55	56-63	Total
No. of cases — study group	116	94	10	220
No. of cases controls	55	45	—	100

Table II shows the results of groups the incidence of abnormal cortisone-stressed glucose tolerance test (C.G.T.T.) in the study group and control group. While in a control group of 100 patients the incidence was as high as 30.9% glucose tolerance curves was 30.9%.

TABLE II  
Results of C. G. T. T.

	Normal curve	Abnormal or prediabetic curve
Study group .. ..	152	69 (30.9%)
Controls .. ..	75	25 (25%)

Table III below shows the number of cases with the histological features of the endometrium. This difference on statistical analysis has been reported as not significant. It was considered desirable to look into the incidence of such abnormal curves in age groups because it is well known that aberrations in carbohydrate metabolism are more likely to increase with advancing age.

TABLE III  
Histological Study of the Endometrium

Histology	Proliferative	Secretory	Hyperplasia	C. G. H.	Atrophic
No. of cases	85 (38.6%)	32 14.4%	51 23.2%	40 18.1%	12 5.5%

41.3% showed evidence of hyperestrinism as demonstrated by hyperplasia and cystic glandular hyperplasia (C.G.H.) in the endometrium.

In Table IV is shown the correlation between the histological patterns of the endometrium and cortisone-stressed glucose tolerance test.

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Table V below shows the incidence

TABLE IV  
Histology and C. G. T.

Histology	Proliferative	Secretory	Hyperplasia	C. G. H.	Atrophic
	(85)	(32)	(51)	(40)	(12)
Normal curve	62	24	32	23	1
Prediabetic curve	23 (27%)	8 (25%)	19 (37.3%)	17 (42.5%)	11 (8.3%)

It is observed from the foregoing statements that in dysfunctional uterine bleeding including all age groups according to age. of abnormal glucose tolerance curves in the study and control groups according to age.

TABLE V

*Incidence of Abnormal Glucose Tolerance Curve in Study and Control Groups*

Age group	Prediabetic curves	
	Study group	Control group
35-45 .. ..	(116) 24-20.6%	(55) 10-18.1%
46-55 .. ..	(94) 40-42.5%	(45) 15-33.3%
56-63 .. ..	(10) 4-40%	

Figures in brackets give the total number of cases.

In the age group after 45 the incidence of abnormal glucose tolerance curves is 42.5% in the study group as against 33.3% in the controls. Again the difference in the incidence noticed in each age group was reported as not significant on statistical analysis. Hyperplasia and cystic glandular hyperplasia were found in the study among 41.1%. In this group the incidence of abnormal glucose tolerance curves was 39.5% as against 25% in controls. Statistically this is significant. This type of endometrium was seen in dysfunctional bleeding in women over 45, in 48.1% of cases i.e. in 52 out of 104 patients over 45 years. And in this group the incidence of abnormal glucose tolerance curve was again only 40.4% (21 abnormal curves out of 52 cases).

Six patients with dysfunctional bleeding had frank diabetes mellitus. They have not been included in the study.

#### Discussion

From the study it is observed that in general the incidence of abnormal glucose tolerance curves indicating a

possible derangement of carbohydrate metabolism was evident in 30.9% of patients with dysfunctional bleeding while in a control study of 100 patients such incidence was 25%. The difference between the two groups is not significant statistically.

An attempt has been made to correlate the histological pattern of the endometrium with the incidence of abnormal glucose tolerance curves. If it is accepted that hyperoestrinism is usually manifest in the endometrium in the form of marked hyperplasia and cystic glandular hyperplasia, in the group of 220 patients there were 91 (41.4%) with such endometrium.

In 36 or 39.5% abnormal carbohydrate metabolism was demonstrated by the glucose tolerance test. This incidence when compared with controls (25%) is significant. In 117 patients with normal endometrium the incidence of prediabetic curve was 31 or 26.5%. In the age group over 45, the incidence of abnormal glucose tolerance curves with dysfunctional bleeding was 42.5% as compared to 33.3% in the controls of the same group. These variations are not statistically significant. With hyperplasia and cystic glandular

hyperplasia of the endometrium incidence of abnormal curves after 45 years was found to be statistically not significant.

These findings are thus not in agreement with those of Benjamin who found abnormal curves in 64%, excluding frank diabetes in women with hyperplasia after the age of 45 years.

It is therefore to be assumed that in the cases met with here, there does not seem to be a significantly high incidence of abnormal carbohydrate metabolism.

The hereditary and familial predisposition to diabetes is well known. If an enquiry had been made into the family history of diabetes in the controls and study group some such factor might or might not have been evident. It is regretted that it was not possible to obtain reliable data on these lines.

The aim of this work — which was meant only as pilot study — was only

to find out whether there was really an abnormally high incidence of abnormalities in carbohydrate metabolism in women suffering from dysfunctional bleeding.

We are lead to conclude that there is little significant aberration but not to the extent as made out by Benjamin even taking the group over 45 years with hyperplasia.

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