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Carbohydrate metabolism and cervical (uterine) carcinoma

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The classical glucose tolerance test was performed on 26 ambulatory, nonhospitalized, biopsy-proved squamous cell cervical carcinoma patients and compared with similar testing of 26 age- and sex-paired individuals without cancer. Three items deserve special mention. First, the frequency of glycosuria in the cancer group is approximately fourfold that observed in the noncancer persons. Second, the frequency of elevated blood glucose levels in the cancer group is approximately twofold that in the noncancer group. Third, the mean blood glucose values at every temporal point are statistically higher in the oncologic group versus those without cancer.

THE PAST 80 years have yielded well over one hundred reports with regard to the relationship of carcinomatosis and carbohydrate metabolism. The consensus appears to be that a significant correlation does prevail.[1] However, the frequency of this relationship remains controversial. We submit that, in part, the discrepancy stems from a lack of recognition of two important facts: (1) a disturbance in carbohydrate metabolism and diabetes mellitus are not synonymous; and (2) the biochemical criteria for diabetes mellitus may be questioned.

Accordingly, this report will concern itself with a consideration of the relationship of blood glucose (rather than diabetes mellitus) and cervical (uterine) carcinoma.

Method of investigation

Twenty-six ambulatory, nonhospitalized, biopsy-proved, squamous cell carcinoma patients were subjected to the classical glucose tolerance test.[2] Venous blood samples fasting, 30 minutes, 1, 2, and 3 hours (Somogyi-Nelson method[3-5]) were performed with parallel urinalyses for glucose and acetone. Twenty-six sex- and age-paired dental patients served as the control group.

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Results

Table I provides the original data showing the case numbers, age, and glucose tolerance patterns for the 52 individuals. Glycosuria is indicated by dagger. An analysis of the means and standard deviations for the ages (Table IV) shows no statistically significant difference of the means ($P > 0.500$) or variance ($P > 0.250$).

Table II summarizes the frequency of glycosuria in the two groups. For example, 2 of the 26 individuals (8 per cent) demonstrated glycosuria under fasting conditions; in contrast, none of the noncancer group had sugar in the urine. Several points warrant special mention. First, at every temporal point, the frequency of glycosuria in the cancer group is much higher than noted among the noncancer individuals. Second,

Table I. Classical glucose tolerance patterns in cancer and noncancer patients

		*Cancer group**				
Case No.	*Age*	*Fasting*	*30 min.*	*1 hr.*	*2 hr.*	*3 hr.*
12	33	*102*	*224*	*205†*	*115†*	53
16	34	97†	*165†*	*210†*	*102†*	90†
24	38	97	150	147	*132*	*127*
08	40	*147*	*175*	*223*	*210*	*160*
23	41	92	*160*	*185*	*170†*	*138†*
11	43	95	130	95	*102*	*102*
07	45	*107*	*160*	130	*103*	80
17	47	*102*	*207*	*207*	*155*	80
10	48	*110*	140	*204*	*210†*	*127*
14	48	77	115	120	*120*	*110*
15	52	90	*180*	*210†*	*185†*	100†
05	53	85	150	*184*	*160*	*123*
03	55	77	120	110	77	63
09	56	82	115	110	72	82
13	57	97	150	*185*	*110*	*120*
22	57	59	100	102	*103*	80
04	57	82	*195*	*210†*	*200†*	*127*
19	58	*117*	*160*	*165*	*200*	*170*
20	58	*130*	*242*	*320*	*330†*	*260*
21	59	85	—	*170*	*210*	*155*
01	61	*270†*	*330†*	*406†*	*364†*	*360†*
06	62	95	150	*184*	*155*	*120*
18	63	72	118	140	*110*	63
02	65	93	110	*166*	*240†*	*170†*
25	60	95	137	*155*	*142*	92
26	72	95	145	*210*	*175†*	*155*

*Italics indicate elevated blood glucose levels.
†Glycosuria.

Table II. Frequency of glycosuria

	Cancer group		*Noncancer group*	
Time	*No.*	*%*	*No.*	*%*
Fasting	2/26	8	0/26	0
Thirty minutes	2/25	8	0/26	0
One hour	5/26	19	1/26	4
Two hours	10/26	38	4/26	15
Three hours	5/26	19	2/26	8
Total	24/129	19	7/130	5

Table III. Frequency of elevated blood glucose levels

	Cancer group		*Noncancer group*	
Time	*No.*	*%*	*No.*	*%*
Fasting	8/26	31	2/26	8
Thirty minutes	11/25	44	7/26	27
One hour	18/26	69	7/26	27
Two hours	24/26	92	13/26	50
Three hours	16/26	62	6/26	23
Total	77/129	60	35/130	27

the greatest frequency of glycosuria in both groups is at 2 hours. Third, even at this point, glycosuria occurs approximately two and one-half times more frequently in the cancer versus the noncancer group. Last, over-all, the incidence of glycosuria in the cancer group is almost fourfold (19 per cent) versus that observed in the noncancer group (5 per cent). Chi square analysis for the entire group is statistically significant (10.7399 and $P < 0.001$).

In Table I elevated blood glucose levels are shown by underline. For example, it is generally recognized that a fasting blood glucose level according to the Somogyi-Nelson technique should not exceed 100 mg. per cent. In Case No. 12, the fasting determination is 102 mg. per cent. This value is accordingly underscored. The consensus is that the peak should not exceed 150 mg. per cent. Case No. 12 shows a 30 minute determination of 224 mg. per cent. This score is therefore underlined. Finally, it is

		Noncancer group*				
Case No.	*Age*	*Fasting*	*30 min.*	*1 hr.*	*2 hr.*	*3 hr.*
504	33	*110*	150	*175*	*104†*	90
528	34	74	120	55	51	48
529	38	65	143	97	63	67
511	40	99	150	134	*132*	82
586	41	91	133	140	97	81
519	43	75	120	120	74	74
559	45	70	95	79	88	88
590	48	*180*	*234*	*306†*	*340†*	*306†*
517	49	68	95	57	90	55
527	49	80	*178*	*155*	*139*	51
523	52	75	*155*	*175*	*117†*	57
553	53	90	*157*	*155*	*117*	82
503	55	80	135	150	*133*	*107*
560	56	85	135	138	100	82
607	50	74	115	*165*	*107*	85
608	64	85	135	153	*175†*	*153†*
598	55	74	104	104	95	81
606	70	65	95	68	56	50
565	58	75	107	135	*132*	100
571	59	70	125	107	76	44
563	61	75	140	133	90	95
513	62	85	*157*	*155*	*155*	*110*
494	60	85	*157*	125	*155*	*115*
591	65	81	125	81	79	83
497	54	86	*153*	125	80	90
537	52	82	133	130	*130*	*104*

Table IV. Statistical analyses of blood glucose values in cancer versus noncancer groups

	Cancer group	*Noncancer group*	*Significance of the differences*	
			Means	*Variances*
Sample size	26	26		
Age (mean and S.D.)	52.4 ± 10.0	51.8 ± 9.6	$P > 0.500$	$P > 0.250$
Fasting blood glucose (mean and S.D.)	101.9 ± 38.6	83.8 ± 22.1	$P < 0.050$*	$P < 0.005$*
30 Minute blood glucose† (mean and S.D.)	161.1 ± 49.9	136.4 ± 29.6	$P < 0.050$*	$P < 0.010$*
1 Hour blood glucose (mean and S.D.)	182.8 ± 66.6	131.4 ± 49.6	$P < 0.005$*	$P > 0.050$
2 Hour blood glucose (mean and S.D.)	163.5 ± 71.0	114.4 ± 55.9	$P < 0.010$*	$P > 0.100$
3 Hour blood glucose (mean and S.D.)	127.2 ± 64.8	91.5 ± 50.1	$P < 0.050$*	$P > 0.100$

*Statistically significant.

†The sample size for the cancer group is 25 (see Table I).

generally recognized that the 2 and 3 hour samples should not be above 100 mg. per cent. Case No. 12 has a 2 hour determination of 115 mg. per cent. These values are also emphasized.

Table III summarizes the frequency of elevated blood glucose levels. For example, under fasting conditions, 8 of the 26 patients (31 per cent) of the cancer group had blood glucose levels above 100 mg. per cent. In contrast, only 2 of those in the noncancer group exceeded 100 mg. per cent (8 per cent). It will be observed that, at every temporal point, the frequency of elevated levels is distinctly higher in the cancer group. It is noteworthy that, at 2 hours, 92 per cent of the individuals in the cancer category showed blood glucose levels in excess of 100 mg. per cent in contrast to a frequency of 50 per cent in the noncancer

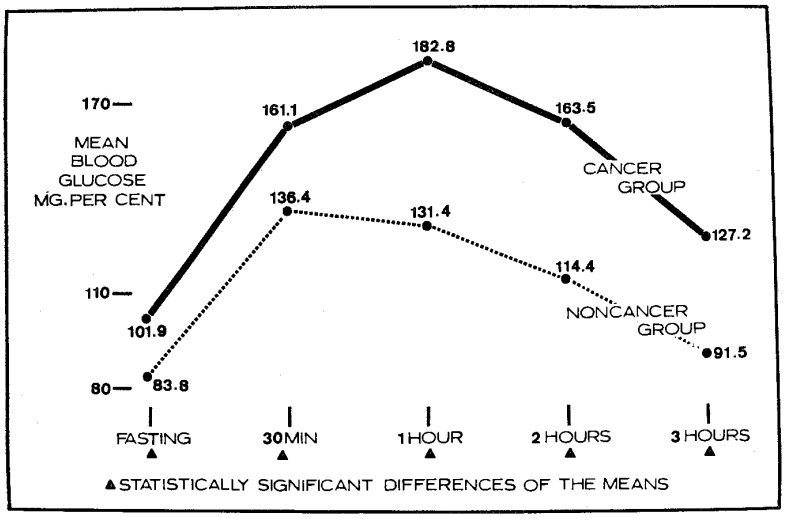

Fig. 1. A comparison of the classical glucose tolerance test patterns in a group of 26 patients with biopsy-proved squamous cell carcinoma of the cervix uteri versus the pattern for an age- and sex-paired noncancer group. At every temporal point, the mean blood glucose values for the cancer group are statistically significantly higher.

group. The frequency of elevated blood glucose levels over-all is more than double in the cancer versus the noncancer patients. The statistical significance is emphasized by a chi square of 26.2180 ($P < 0.001$).

The literature is replete with reports indicating that the upper physiologic limits for blood glucose during the glucose tolerance test are still open to question. Even less attention has been given to the physiologic lower limits. In order to obviate these objections, Table IV and Fig. 1 are a summary of the means, standard deviations, significance of the differences of the means, and significance of the difference of the variances for the two groups. It is noteworthy that the means for all of the blood glucose determinations are significantly different at the 5 per cent level or less. Also, mention should be made of the fact that there are also statistically significant differences of the variances at the fasting and 30 minute levels.

Comment

The data from this study add some validity to the observation of a significant correlation between carbohydrate metabolism and carcinomatosis. This is evident when one examines the relationship by traditional means such as glycosuria and the frequency of elevated blood glucose levels. The correlation appears to be even more striking when one ignores standard parameters and simply equates the blood glucose levels of an age-paired cancer versus noncancer group.

Since the prevalence of cancer in various populations is well-established, it would be interesting to observe the rate of development and frequency in a select group of individuals with a very efficient carbohydrate metabolism versus a hyperglycemic group treated to maintain very stable blood sugar levels.

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