Failure to attain complete interruption of secretory function by vagotomy is ascribed to two reasons: (1) atypical anatomical distribution of the vagus nerve fibres. Walters *et al.* (1947) find that 10 per cent of their 100 dissections showed such distribution of vagus nerve fibres that it was impossible to get complete vagotomy; (2) the existence of non-vagal pathways whereby cholinergic impulses travel to the gastric mucosa must also be considered. Though this is shown in experimental animals sufficient work has not been produced on man.

According to Hollander (1948), after vagal operation, insulin 'positive' response indicates the persistence of some secretory nerves—either truly vagal or vago-mimetic of spinal origin. A positive response only shows that acid secretion is induced by some pathways not necessarily of vagal origin, and not necessarily that the surgeon failed to interrupt the gastric vagi completely. In the four cases studied after vagal operation in the present series one was found to give insulin 'positive' response, one showed absence of free acidity, and two gave 'equivocal' response. Thus our results confirm the hypothesis that there are some extra-vagal paths for inducing acidity in the stomach.

Summary

1. Results of 8 cases of insulin test are presented.

2. Results of 4 cases of insulin test after operations of vagotomy and gastroenterostomy are presented.

3. Results of insulin test are compared with gastric analysis by fraction method.

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INTRAVENOUS GLUCOSE TOLERANCE TEST IN NORMAL PERSONS

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Introduction

Though it is the usual practice to administer glucose orally to investigate the carbohydrate tolerance, the utility of intravenous glucose test as a supplement to the oral method has been pointed out by many workers. Moreover, the possibility of error in the result of oral method due to diminished absorption has been shown by Beeler, Bryan, Cathcart and Fitz (1922). The flat blood sugar curve obtained by Thaysen (1929) after the oral administration of glucose, as has been shown by the author, is due to the diminished absorption of glucose. We have observed in some of our investigations that oral administration of glucose even up to 100 gm. may have little or no effect on the blood sugar curve for a period of 2 hours. Nausea, sometimes caused by oral administration of glucose, alters the result of the test as has been shown by Hale-White and Payne (1926).

In view of the above facts we decided to study our cases by the intravenous method of glucose tolerance test. Literature shows that the technique adopted by different workers was different and no unanimity regarding dose, etc., was observed amongst the various workers. Some employed fixed dose irrespective of body weight (Davidson and Allen, 1925; Pijoan and Gibson, 1938; Tunbridge and Allibone, 1940), while others have varied the dose with the body weight (Opitz, 1922; Lennox and Bellinger, 1927; McKean, Myers and von der Heide, 1935). The latest work on this subject was that of Tunbridge and Allibone (*loc. cit.*). They used 92 cc. of 30 per cent solution of dextrose but in our experience most of our subjects complained of difficulties and uneasiness towards the latter part of injections, so the whole amount could not be injected. In a few of the cases where we were successful in administering the whole amount of glucose without any inconvenience, the blood sugar did not reach the preglucose level within the

expected period of 60 minutes. This technique did not appear to be suitable to us. We, therefore, considered it desirable to reinvestigate the method on normal Indians.

Experiment and results

(*a*) *Animals.*—In order to gain a preliminary idea regarding the dose and concentration of glucose which may be administered without causing any trouble to the patient and yield uniform results within the shortest possible time, we first carried out experiments on animals. The experimental animals were 12 healthy male rabbits weighing from $2\frac{1}{2}$ to $3\frac{1}{2}$ lb. obtained fresh from the market. No special attention was paid to the strain and species. The animals were kept on usual diet for 3 to 4 weeks under observation and the weight checked weekly. The animals were kept without food from the evening previous to the day of experiment. Glucose was administered through the marginal ear vein of the same ear from which the fasting sample of blood was collected. Subsequent samples were collected from the vein of the other ear. The easiest way of obtaining a free flow of blood was to engorge the vein by mildly massaging the ear with a little ether and make a small longitudinal incision in the engorged vein. After collection of the necessary quantity of blood the wound was sealed with tincture benzoin. It was easy to get subsequent sample through the same incision simply by removing the benzoin seal and massaging lightly with ether. The repeated puncturing of the vein, which may excite the animal, was avoided. First sample of blood after glucose injection was collected within 3 to 5 minutes of the completion of injection and then at an interval of every 10 minutes up to 90 minutes.

After several trials with different doses and concentrations of glucose we found that when 0.2 gm. per kilo of body weight in 50 per cent solution of glucose was given almost all the blood sugar curves were uniform and more or less identical. The results are given in table I.

It is evident from the results that the maximum rise of blood sugar (200 to 245 mg. per cent) took place within 3 to 5 minutes after injection. The blood sugar began to fall rapidly for the first 30 minutes, the fall thereafter was slowed down and the preglucose level (100 to 110 mg. per cent) was reached within 50 to 60 minutes of glucose administration. Urine, whenever passed within 6 hours after injection, was examined for sugar. It was present in traces only in the urine of 5 animals. The urine of rest of 7 animals was sugar-free.

(*b*) *Human beings.*—Thus getting a clue from the animal experiments we extended our observations on human beings. We selected cases from among the healthy persons of ages varying from 25 to 45 years and living on average Indian diet. Some of our experimental subjects were laboratory people who very kindly volunteered to undergo the tests. The rest of the subjects were selected from the general and skin out-patients department of our institute. A detailed history was taken and a thorough physical examination was made of all our experimental subjects. In selecting our material every care was taken as far as practicable to eliminate factors which may disturb the carbohydrate metabolism, such as endocrine dysfunctions and liver diseases. The weight of our normal subjects varied from 121 to 154 lb. The test was performed at about 9 o'clock in the morning before the subject took any food.

TABLE I

Blood sugar values in 12 *rabbits before and after intravenous injection of* 0.2 *gm. of glucose per kilo of body weight in* 50 *per cent solution*

Average of the blood sugar values of every 4 rabbits

Rabbit number	Blood sugar before glucose	Blood sugar after glucose									
		3 to 5 minutes	10 minutes	20 minutes	30 minutes	40 minutes	50 minutes	60 minutes	70 minutes	80 minutes	90 minutes
I–IV ..	108	202	189	170	143	137	117	104	107	106	99
V–VIII ..	109	223	203	166	136	122	113	103	106	102	102
IX–XII ..	113	228	204	177	147	122	116	104	101	106	103
		Maximum, minimum and average values of 12 rabbits									
Maximum	120	245	220	189	158	140	121	110	110	110	110
Minimum	100	200	180	150	130	120	108	100	100	94	90
Average ..	110	222	200	169	144	130	114	105	105	102	100

Fasting sample of blood was drawn from the medium basilic vein and glucose was injected through the same needle. The duration of injection was from 2 to 3 minutes. Subsequent samples were collected from the vein of other arm. Urine was collected as frequently as the subject could pass it and examined for sugar with Benedict's solution. Blood sugar was estimated by Hagedorn-Jensen method. No difficulty or undesirable effect was encountered in any of the subjects during or after the injection. First sample of blood after glucose was collected within 5 minutes of completion of injection. To begin with, samples were collected in some cases at every 10 minutes' interval up to 60 minutes, then at the end of 90 minutes, but this frequent puncture of the vein was found unnecessary as the nature of the blood sugar thus obtained did not show any material alterations in details from the one obtained from samples of blood collected at longer intervals. The results are given in table II.

TABLE II

Blood sugar values in 5 *persons after intravenous injection of* 0.25 *gm. per kilo of body weight in* 50 *per cent solution*

A

Blood collected 3 to 5 minutes after injection then at an interval every 10 minutes up to 60 minutes

	3 to 5 minutes	10 minutes	20 minutes	30 minutes	40 minutes	50 minutes	60 minutes
	250	220	160	140	125	118	100
	240	198	135	139	123	115	102
	223	202	153	140	128	120	110
	262	200	165	145	121	110	98
	200	180	160	130	120	119	100
Average	235	180	158	138	123	112	102

B

Blood collected 2 to 3 minutes after injection then at the end of 15 minutes, 30 minutes and 60 minutes

	2 to 3 minutes	15 minutes	30 minutes	60 minutes
	230	189	142	107
	240	180	145	100
	260	200	140	109
	200	179	142	102
	255	190	135	100
Average	237	187	140	103

We therefore adopted the practice of collecting blood within 5 minutes of injection and then at 15 minutes, 30 minutes, 60 minutes and 90 minutes after the injection of glucose.

Initial (fasting) blood sugar level in all our subjects varied from 80 to 110 mg. per cent. This has not been shown in the table.

A preliminary observation was made by injecting 0.2 gm., 0.25 gm. and 0.3 gm. of glucose per kilo of body weight on 12 persons divided into 3 groups of 4 persons in each. The tests were repeated after an interval of three weeks on the same subjects but the doses were interchanged. The results are given in table III.

TABLE III

Blood sugar values in 12 *healthy persons after intravenous injection of* 0.2 *gm.,* 0.25 *gm. and* 0.3 *gm. of glucose per kilo of body weight in* 50 *per cent solution*

A

Blood sugar values after intravenous injection of 0.2 gm. of glucose per kilo of body weight

Average result of each group has been shown

	3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
Group 1 ..	200	164	120	105	101
„ 2 ..	163	146	103	105	103
„ 3 ..	192	140	98	100	101
Maximum	205	168	123	105	105
Minimum ..	150	130	99	95	90
Average ..	178	143	113	102	102

B

Blood sugar values after intravenous injection of 0.25 gm. of glucose per kilo of body weight

Average result of each group has been shown

	3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
Group 1 ..	237	180	141	102	100
„ 2 ..	238	193	147	102	99
„ 3 ..	241	198	140	100	101
Maximum	252	201	151	110	103
Minimum ..	230	168	130	98	99
Average ..	239	190	143	102	100

C

Blood sugar values after intravenous injection of 0.3 gm. of glucose per kilo of body weight

Average result of each group has been shown

	3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
Group 1 ..	289	258	233	182	141
„ 2 ..	270	257	221	170	154
„ 3 ..	249	239	205	144	136
Maximum	300	262	240	190	144
Minimum ..	245	230	197	167	130
Average ..	275	247	220	165	137

From the three types of blood sugar curve thus obtained in each group of cases, close similarity and uniformity was observed between the results obtained from each group of cases when 0.25 gm. per kilo was used.

Further it has been found that by administering 0.25 gm. per kilo of body weight the total amount of glucose injected in our cases varied from 12.5 to 18.5 gm. Thus, with the idea whether it was possible to find out a fixed amount of glucose which would give uniform results and could be conveniently injected in all adult cases, within normal variations in weight, we gave 15 gm. of glucose in 50 per cent (*i.e.* 30 cc. of 50 per cent) solution to 7 persons. The test was repeated on the same persons after three weeks by injecting 0.25 gm. per kilo of body weight. The results are given in table IV.

TABLE IV

Blood sugar in 7 persons

A

After intravenous injection of 0.25 gm. of glucose per kilo of body weight in 50 per cent solution

3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
205	180	150	100	105
263	202	130	110	102
270	172	125	100	95
232	200	127	102	102
225	210	130	98	102
230	205	152	100	106
200	222	140	103	110
Average 232	198	136	101	103

B

After intravenous injection of 30 cc. (15 gm.) of 50 per cent solution on the same persons

3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
220	170	162	105	99
250	200	135	98	90
280	160	130	100	98
290	200	129	99	97
250	210	120	100	102
275	205	155	104	101
267	222	137	105	100
Average 261	195	139	101	96

The most striking feature of the comparative results, thus obtained, was that they were very closely similar and in some cases almost identical. The only difference in some cases was a slight variation in the peak values. For our final study we therefore injected 30 cc. of 50 per cent solution (15 gm.) in 20 healthy persons irrespective of variations in weight (weight varying from 121 to 154 lb.). The results are given in table V.

TABLE V

Blood sugar values in 20 healthy persons after intravenous injection of 30 cc. (15 gm.) of 50 per cent glucose

Average values of every 5 cases

3 to 5 minutes	15 minutes	30 minutes	60 minutes	90 minutes
229	189	143	101	99
239	180	135	99	99
221	182	144	102	99
224	176	133	102	99
Maximum 260	210	156	110	100
Minimum .. 200	100	130	96	95
Average .. 225	182	138	101	99

From the results it will be observed that the maximum rise of blood sugar, which varied from 200 mg. to 260 mg. per cent, takes place within 5 minutes of injection. The fall of blood sugar thereafter is very sharp and rapid during the first 30 minutes and the major portion of added sugar is removed from the circulation by this time. During the next 30 minutes, that is from 30 to 60 minutes after injection, the fall of blood sugar is somewhat slow and gradual but the preglucose level is reached in all the cases within 50 to 60 minutes. During the last 30

minutes, that is from 60 to 90 minutes, blood sugar may either remain stationary or show a very slight fall.

From the examination of urine collected as frequently as the subject could pass we found that glycosuria was present in 5 cases only, when urine sugar varied from traces to 0.5 per cent. Another fact observed was that glycosuria has no relation to the height of the blood sugar level, because urine sugar was present in some of our cases when the maximum rise of blood sugar was 0.200 per cent or below whereas no sugar was detected in the urine of cases having a maximum rise of 0.260 per cent.

Comments

A method of intravenous glucose tolerance test has been described which has yielded uniform results when performed on Indian adult male subjects.

In our experiments we have observed that carbohydrate tolerance is not materially altered with the normal variations in weight; so we have found it unnecessary to vary the amount of dextrose with the weight of the subject and the remark of Törning (1932) 'a fat person is a thin one with a sack on his back' is justified. For practical purpose a standard dose of 30 cc. of 50 per cent solution (15 gm.) was found to be suitable for judging the carbohydrate tolerance in persons of weight varying from 121 to 154 lb.

In the interpretation of the results the maximum rise of blood sugar has been considered as a criterion of the test by some previous authors (Ross and Tonks, 1938; Jörgensen, 1926). But in our experiments we have observed that when the test is repeated on the same individual under identical experimental condition though the fluctuation in the peak value occurred in some cases to an appreciable degree, practically no difference was observed in other details. And the most striking feature of the curves was that the time taken for the blood sugar to react the preglucose level was almost identical in all cases. We therefore consider that the time taken for the blood sugar to reach the fasting level should be the criterion for judging the sugar tolerance.

Renal threshold for sugar as found by Campbell, Osgood and Haskins (1932) varied from 99 to 228 mg. per cent in different individuals. We also observed that glycosuria does not bear any relation to hyperglycæmia; so glycosuria as an index for carbohydrate tolerance is considered unreliable.

We have observed that the major portion of the injected glucose disappears from the circulation very rapidly during the first 30 minutes of injection and then the removal is slowed down till the blood sugar reaches the fasting level. Thus it appears that the removal of the injected sugar from the circulation takes place in two stages. During the first stage, for a period of first 30 minutes from the time of injection, the removal is very rapid whereas during the second stage for the period of next 30 minutes the rate of removal is slow and sustained till the blood sugar level reaches the preglucose fasting level. No complete explanation of this two-stage removal of sugar is possible for us at present. It may be that as an effect of stimulus due to injection of glucose the entire mechanism controlling carbohydrate metabolism comes into play at the beginning of the test period. Towards the latter part, however, some mechanisms may be still active while others may have waned in their activity. Increased insulin activity soon after the injection of glucose may be one of the causes of the two-stage removal but the rapid liberation of insulin from the pancreas after sugar injection is still a matter of conjecture. Further work on the different aspects of intravenous glucose tolerance test is being continued.

Summary and conclusion

A method of intravenous glucose tolerance test has been described :—

1. Intravenous glucose tolerance test was performed on 20 healthy Indians, ages varying from 25 to 45 years and weights varying from 121 to 154 lb.

2. Thirty cc. of 50 per cent glucose were injected in fasting condition, duration of injection being 3 to 5 minutes.

3. The maximum rise of blood sugar takes place within 5 minutes of injection. The fall of blood sugar thereafter appears to take place in two stages : (*a*) a rapid fall during the first 25 minutes when the major portion of the injected glucose is removed from the circulation, and (*b*) a slow and sustained fall during the next 30 minutes. The preglucose fasting level is reached within 50 to 60 minutes of injection.

4. The maximum height of blood sugar was found to be variable but the time taken for the blood sugar to return to preglucose level was found to be constant in all cases.

5. Glycosuria was found to bear no relation to the height of blood sugar level.

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A Mirror of Hospital Practice

TUBERCULOMA OF THE MYOCARDIUM

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Review of the literature on tuberculosis of the myocardium brings out the infrequency of involvement of heart in generalized tuberculosis. In two extensive reviews by Horn and Saphir (1935) and Auerbach and Guggenheim (1937), the incidence of myocardial involvement in cases of generalized tuberculosis was reported as 0.24 per cent and 0.28 per cent respectively. The cases reported include the miliary form, the nodular form and the diffuse infiltrative type.

Cases of the nodular tuberculosis of the myocardium or tuberculoma are so infrequent as to justify the report of a single case. Auerbach and Guggenheim (1937) were able to collect only 95 cases of nodular myocardial tuberculosis including two of their own. Since then only six other cases have been reported by the writers in English, the last being in 1948 by Rosenbaum and Linn (1948).

The following case is an example of nodular form of myocardial tuberculosis (tuberculoma) and is of special interest not only because of its rarity but because tuberculosis was never diagnosed during life and the patient was admitted and treated in the S. N. Hospital, Agra, as a case of congestive heart failure.

Case report

This 45-year-old Hindu female was admitted to the S. N. Hospital on 11th December, 1950, with the complaints of cough with expectoration and dyspnœa for one month, and generalized œdema over the body for twelve days. She gave a history of vague illness and slow fever for 4 months prior to her admission.

Physical examination revealed an ill-nourished, pale and weak patient. There was no jaundice, cyanosis or glandular enlargement. The neck veins were engorged. The blood pressure was 100/50, and the pulse 110 per minute. Temperature was 100°F. and respiration 24 per minute. There was free fluid in abdomen, and liver was enlarged and tender. Heart was slightly enlarged and the sounds were feeble. No murmurs were heard. Blood counts, urinalysis and blood chemistry were all within normal limits.

The patient remained in the hospital for seven days and at no time was tuberculosis suspected. She gradually went downhill and expired on 18th December, 1950. Clinical diagnosis was congestive heart failure.

Autopsy findings.—The body was that of an undernourished Hindu female of small frame and 45 years of age. On opening the peritoneal cavity, the peritoneum was found studded with minute tubercles, and there were about 1,500 cc. of yellow coloured fluid. The pleural spaces on both sides were obliterated by marked adhesions. The pericardium was adherent to the left pleura. There was no fluid in the pericardial cavity, and no tubercles were seen.

The heart weighed 260 gm. The coronary arteries and the valves were normal, and the myocardium was pale reddish brown. The aorta was smooth. Inside the cavity of the right auricle there was an irregular pale yellowish white mass measuring 6.5 × 5.0 cm., occupying its anterior wall as well as the interauricular septum (plate XXXVIII, figure 1). It was firm in consistency. On section the nodule contained greyish yellow moderately firm caseous material.

Pleuræ covering both the lungs were thickened and adherent. The right lung weighed 487 gm. and the left 350 gm. Emphysematous blebs were seen in both lungs which were normal, greyish pink on section, except for a few shotty tubercles. The spleen weighed 97 gm. Surface was normal and the cut section showed parenchyma markedly congested and smooth. No tubercles were seen. The liver weighed 1,110 gm. The surface was smooth and free from tuberculous lesions. Cut section revealed marked congestion. The gall-bladder showed strawberry mucous membrane.

The œsophagus and stomach were normal. The serosa of the entire bowel was studded with tubercles. The mesenteric nodes were large and caseous. The pancreas was normal.

The combined weight of the kidneys was 127. No tubercles were noted. The uterus and ovaries were normal. The broad ligament was studded with miliary tubercles.