

## ASSESSMENT OF VAGOTOMY BY THE INSULIN TEST

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### SYNOPSIS

The insulin test for vagal innervation was done in 21 patients, who had vagotomy for peptic ulceration. Assessment of the results by multiple criteria showed that about 95% of the cases, excluding 2 invalid tests, had a positive response. Incomplete vagotomy, based on 3 or more criteria, was found in 11 cases (about 58%). The incidence of incomplete vagotomy in the present study is thus higher than that of all western reports.

### INTRODUCTION

Since its original introduction by Lester Dragstedt, in 1945, vagotomy with drainage has become an accepted form of treatment for chronic duodenal ulceration (Goligher *et al*, 1968a and 1968b; Cox, 1968; Pulvertaft and Cox, 1969). One of the greatest advantages of vagotomy with drainage over partial gastrectomy, in the treatment of duodenal ulcer, has been its lower mortality rate of under 1% (Holt and Robinson, 1955; Hindmarsh, 1957; Weinberg *et al*, 1956), as compared to the higher mortality of around 3 to 4% in partial gastrectomy (Hosford, 1949; McKeown, 1962; Priestley *et al*, 1954; Harvey, 1961; Goligher and Riley, 1952; Amdrug *et al*, 1969). The main attraction of vagotomy with drainage, for the average surgeon, is thus probably its lower mortality rate (B.M.J. leader, 1970). Unfortunately, recurrent ulceration after vagotomy with drainage has been reported to be higher than after partial gastrectomy (B.M.J. leader, 1970). Such recurrence is, however, not a direct complication of vagotomy but usually associated with an incomplete section of the vagal nerves. Most surgeons have an incomplete vagotomy rate, based on Hollander's insulin test, of around 20% (Fawcett *et al*, 1969). It was with these facts in mind that the present study was initiated. This report concerns an assessment of the completeness of 21 vagotomies, by the insulin test. This is the first report of such a study in Singapore, although vagotomy has been practised here for many years.

### METHOD

The insulin test for the presence of intact nerve fibers, after vagal operations for peptic ulcer, was first described by Hollander in 1946.

Since then, the test has been widely used for the assessment of the completeness of vagotomy.

The insulin test was performed as follows: The patient was fasted overnight. In the morning, a Salem double-lumen nasogastric tube was inserted and the patient rested on his left side. The intragastric position of the tube was confirmed by a recovery test as described by Hassan and Hobsley, 1970. All the night secretion was aspirated and discarded, after which, gastric juice was obtained by continuous suction with an electric suction pump. Gastric juice was collected for 1 hour, giving the basal acid secretion. After this, insulin was injected intravenously at a dose of 0.2 units/kg. body weight, but within 10 to 16 units. Following this, gastric juice was aspirated for 2 hours, giving the first post-insulin hour and the second post-insulin hour specimens. A blood sugar was done between the first and second post-insulin hours.

Aliquots of the gastric juice collections were titrated with N/20 NaOH, using an automatic titrator with pH meter (Radiometer, Copenhagen), to an end-point of pH 7.4. The volume, pH, acid concentration, and acid output of each sample were measured. The results obtained were expressed as the basal acid output (mEq./hour), post-insulin output (mEq./hour)—1st hour and 2nd hour; and post-insulin concentration (mEq./L)—1st hour and 2nd hour.

### Assessment of Insulin Test by Multiple Criteria

Although the insulin test has been used to assess completeness of vagotomy for more than 20 years, controversy still exists as to which criterion is best for interpretation. The original criterion of Hollander (1948) was an arbitrary one and still widely used. Hollander proposed that a positive response is indicated by an increase in acid concentration of more than 20 mEq./L over the basal pre-insulin level, or an increase of more than 10 mEq./L if the basal acid secretion is anacid. Following Hollander's proposal, several

workers have suggested other criteria. Bank *et al*, in 1967, then suggested that the use of multiple criteria may give a more accurate assessment of the completeness of vagotomy than any single criterion alone. This was later supported by Gillespie *et al*, 1968.

In the present study, the results of the insulin tests were assessed according to the following criteria as used previously by Bank *et al* (1967) and Gillespie *et al* (1968):—

1. An increase in the volume of gastric secretion after insulin stimulation (Waddell, 1957).
2. A basal acid output more than 2 mEq./hour as proposed by Bachrach, 1962.
3. An increase in acid concentration of more than 20 mEq./L over the basal level, or an increase of more than 10 mEq./L if there is basal anacidity (Hollander, 1948).
4. An "early" rise in acid concentration following the insulin injection; that is, the same criteria as Hollander (3) but occurring during the first post-insulin hour. This

criterion was proposed by Ross and Kay, 1964.

5. A total acid output more than 2.0 mEq. in any post-insulin hour, as proposed by Bank *et al*, 1967.

## RESULTS

The results of the insulin test in 21 patients, who underwent vagotomy, are shown in Tables I to III. Of 21 cases investigated, 18 had a positive response to insulin. The remaining 3 cases had a negative response to insulin. In 2 of these 3 cases, however, the test was considered invalid since the blood sugar was above 50 mg.%. Of the 18 cases with a positive response, 2 had 5 positive criteria, 2 had 4 positive criteria, 7 had 3 positive criteria, 5 had 2 positive criteria and 2 had a single positive criterion.

As the percentage reduction in the augmented histamine test has been reported to show no significant difference between patients with 2 or less positive criteria and patients who were insulin

TABLE I  
DIAGNOSIS AND TYPE OF OPERATION DONE

Case No.	Age (Years)	Sex	Race	Diagnosis	Operation
1	40	M	Ch.	Duodenal Ulcer	T.V. + ANT.
2	36	M	Eur.	Hypertrophic Gastritis	T.V. + G.J.
3	23	M	Ch.	Bleeding Peptic Ulcer	T.V. + Pyl.
4	19	M	Ch.	D.U. + Pyloric Stenosis	T.V. + G.J.
5	26	M	Ch.	Chronic Duodenal Ulcer	T.V. + G.J.
6	42	M	Ch.	Chronic Duodenal Ulcer	T.V. + Pyl.
7	20	F	Ch.	D.U. + Pyloric Stenosis	T.V. + Pyl.
8	38	M	Ch.	Duodenal Ulcer	T.V. + Pyl.
9	32	M	Mal.	Chronic Duodenal Ulcer	T.V. + Pyl.
10	39	M	Ch.	Pyloric Stenosis	T.V. + Pyl.
11	52	M	Ch.	Perforated G.U.	T.V. + P. Gast.
12	29	M	Ch.	Chronic Duodenal Ulcer	T.V. + Pyl.
13	26	M	Ch.	Duodenal Ulcer	T.V. + Pyl.
14	21	M	Ch.	Duodenal Ulcer	T.V. + Pyl.
15	23	M	Ch.	Duodenal Ulcer	T.V. + Pyl.
16	61	M	Ch.	Perforated D.U.	T.V. + Pyl.
17	35	M	Ind.	Chronic Duodenal Ulcer	S.V. + Pyl.
18	40	M	Ch.	Bleeding Duodenal Ulcer	S.V. + Pyl.
19	33	M	Ch.	D.U. + Pyloric Stenosis	S.V. + ANT.
20	16	M	Ch.	Perforated D.U.	S.V. + ANT.
21	19	M	Ch.	Duodenal Ulcer	T.V. + Pyl.

M = Male

Eur. = Eurasian

T.V. = Truncal Vagotomy

Pyl. = Pyloroplasty

F = Female

Ind. = Indian

S.V. = Selective Vagotomy

G.J. = Gastro-Jejunostomy

Ch. = Chinese

Mal. = Malay

ANT. = Antrectomy

P. Gast. = Partial Gastrectomy

TABLE II  
RESULTS OF INSULIN TEST

Case No.	Interval Between Operation and Insulin Test (Months)	Insulin Test			Acid Concentration (mEq./L)		
		BAO (mEq./Hr.)	Post-Insulin		Basal	Post-Insulin	
			1st Hr. (mEq./Hr.)	2nd Hr. (mEq./Hr.)		1st Hr.	2nd Hr.
1	3	0.1	0.3	2.2	7	20	53
2	3½	0.0	2.0	0.6	0	36	33
3	3	1.7	2.1	2.5	56	52	41
4	7	1.5	0.0	6.7	30	0	63
5	3	4.7	18.4	22.5	52	76	112
6	3	0.5	0.0	0.9	12	0	30
7	1	10.9	5.4	8.5	54	108	42
8	24	0.1	0.8	3.3	10	20	80
9	16	0.0	0.0	0.1	0	0	5
10	3	1.7	0.6	2.1	14	14	16
11	1	2.7	0.9	2.1	68	68	70
12	36	0.8	0.0	7.4	11	0	74
13	12	1.2	0.1	0.1	17	3	10
14	3	0.7	1.5	5.3	23	75	90
15	3	5.8	4.3	4.2	52	54	50
16	6	0.3	1.8	—	15	40	—
17	3	2.5	0.6	0.8	12	5	16
18	24	1.2	2.1	10.5	40	42	74
19	3	11.3	3.5	3.9	75	88	70
20	6	0.0	0.0	0.0	10	0	0
21	4	2.6	1.9	4.3	43	39	61

BAO = Basal Acid Output

negative (Gillespie *et al*, 1968), cases with 3 or more positive criteria may be considered to have incomplete vagotomy, while those with 2 or less positive criteria may be considered to have doubtful completeness of their vagotomies. In the present study, if the 2 invalid tests are excluded, 11 cases (57.9%) had 3 or more positive criteria (incomplete vagotomy), 7 cases (36.8%) had 2 or less positive criteria (doubtful incomplete vagotomy), and only 1 case had a negative response to insulin (complete vagotomy). On the whole, therefore, about 95% of the cases had a positive response to insulin, of which about 58% had firm evidence of incomplete vagotomy, as shown by the presence of 3 or more positive criteria.

## DISCUSSION

Vagotomy is one of the commonest operations for chronic duodenal ulceration. The completeness of vagotomy may be assessed by the widely used insulin test, which was originally introduced by Hollander (1946 and 1948). Based on the insulin test, the incidence of incomplete vagotomy has

been reported from many centres: 14% by Woodward *et al* (1949), 43% by Weinstein *et al* (1950), 30% by Davies (1956), 12% by Lythgoe (1961), 27% by Ross (1964), and recently 50% by Gillespie *et al* (1970). It has been estimated that about 20% of cases with vagotomy will have incomplete vagotomy on insulin testing, about 12% will have a poor clinical result, and about 7% will develop recurrent ulceration (Fawcett *et al*, 1969). Since an incomplete vagotomy is a bad operation, some test of vagal innervation should be done in every case operated upon (Baron, 1970). The vagal centres maybe stimulated by hypoglycaemia, which may be induced in one of 3 ways: (1) by intravenous injection of insulin (Hollander, 1946, 1948); (2) by endogenous insulin (tolbutamide-stimulated); and (3) by inducing an intracellular glycopenia with 2-deoxy-D-glucose (2DG) or 3-O-methyl glucose (Duke *et al*, 1965; Thomas *et al*, 1968). Because of a wide variety of serious-side effects from 2DG, such as hypokalaemic atrial fibrillation, hypothermia and hepatotoxicity (Duke *et al*, 1965; Thomas *et al*, 1968; Himsworth

TABLE III  
INTERPRETATION OF THE INSULIN TESTS

Case No.	MULTIPLE CRITERIA					Conclusion
	Increase in Volume	BAO >2.0 (mEq./hr.)	PIC-BC >20.0 (mEq./L)	Early Rise (1st hr.)	PIO (1 hr.) >2.0 (mEq./hr.)	
	Waddell	Bachrach	Hollander	Ross and Kay	Bank et al	
1	+	0	+	0	+	Incomplete
2	+	0	+	+	+	Incomplete
3	+	0	0	0	+	? Incomplete
4	+	0	+	0	+	Incomplete
5	+	+	+	+	+	Incomplete
6	0	0	0	0	0	Invalid (75)
7	+	+	+	+	+	Incomplete
8	+	0	+	0	+	Incomplete
9	0	0	0	0	0	Complete
10	+	0	0	0	+	? Incomplete
11	0	+	0	0	+	? Incomplete
12	+	0	+	0	+	Incomplete
13	0	0	0	0	0	Invalid (71)
14	+	0	+	+	+	Incomplete
15	0	+	0	0	+	? Incomplete
16	+	0	+	+	0	Incomplete
17	0	+	0	0	0	? Incomplete
18	+	0	+	0	+	Incomplete
19	0	+	0	0	+	? Incomplete
20	+	0	0	0	0	? Incomplete
21	+	+	0	0	+	Incomplete

BAO = Basal Acid Output  
 PIC = Post-Insulin Concentration  
 BC = Basal Concentration  
 PIO = Post-Insulin Output  
 ? Incomplete = Doubtful Incomplete Vagotomy

*et al*, 1969), the insulin test remains the best standard clinical test for vagal innervation (Baron, 1970).

The insulin test should not be done immediately after vagotomy, since it has been shown that insulin testing in the second week after vagotomy will result in an underestimation of the incidence of positive responses (Mason and Giles, 1968 and 1969; Gillespie *et al*, 1970). In a recent study by Gillespie *et al* (1970), about 50% of patients with a negative insulin test done in the 2nd week after vagotomy, were found to have positive responses when re-tested 3 months to 4 years later.

The most striking feature of the present study is the very high incidence of positive response to insulin (about 95%). Using multiple criteria, the incidence of incomplete vagotomy, as defined by

3 or more positive criteria, was about 58%, which is much higher than the average incidence of 20% (Fawcett *et al*, 1969) previously reported in the western literature. The high incidence of incomplete vagotomy, in the present study, is similar to a recent report by Gillespie *et al* (1970), who found that about 50% of their cases had some degree of incomplete vagotomy, based on the insulin test. If the results are interpreted according to Hollander's criterion alone, the incidence of incomplete vagotomy is 52.6%. This is very close to the 58% incomplete vagotomy, based on 3 or more positive criteria. There was, thus, good correlation between assessment by multiple criteria and assessment by Hollander's criterion, in this study. Although a positive response to multiple criteria has been shown to give a better assessment of the completeness of

vagotomy than any single criterion alone (Bank *et al*, 1967; Gillespie *et al*, 1968), none of the individual criteria has been found to be superior to the original criterion of Hollander (Gillespie *et al*, 1968). In the present study, 7 cases had doubtful completeness of vagotomy as defined by 1 or 2 positive criteria. Decker (1969) failed to find any superiority of the multiple criteria over the original Hollander criterion.

A positive response to insulin indicates the presence of intact secretomotor vagal fibers to the stomach. This may be due to incomplete section of the vagal nerves at operation or to a regeneration of vagal fibers. Although incomplete vagotomy as shown by the insulin test does not necessarily mean recurrence of ulceration, it does indicate that the vagotomy was unsatisfactory. Every case considered for vagotomy should have a pentagastrin test prior to operation and this should be repeated together with an insulin test about 6 months after operation.

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