Cholecystectomy and truncal vagotomy with pyloroplasty
The effect on duodenogastric reflux

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Summary
An experimental study investigated the effect of truncal vagotomy and pyloroplasty (TV+P) alone or combined with cholecystectomy on bile reflux into the stomach. The amount of bile reflux was estimated by measuring the concentration of bile phospholipids in the gastric contents. During each test, reflux was measured over a continuous period of 6 hours. TV+P alone was not invariably associated with increased reflux. When cholecystectomy was added to the TV+P the amount of bile reflux increased significantly \((P < 0.01)\). TV+P inhibited the production of lysolecithin from lecithin. Pathophysiologically this is important because lysolecithin is considered to be injurious to gastric mucosa.

In a recent experimental controlled study the effect of cholecystectomy on duodenogastric reflux was investigated. In the present study, using the same techniques, a project was designed to investigate the effect of truncal vagotomy plus pyloroplasty (TV+P) alone or combined with cholecystectomy on duodenogastric reflux.

Material and methods
Four mongrel dogs were trained to stand quietly in a Pavlov dog stand. As a first stage all animals had a Thomas gastrostomy cannula inserted and a TV+P. The cannula was inserted 8 cm proximal to the pylorus and close to the greater curvature. The adequacy of surgical vagotomy was checked by a Hollander test. Reflux was assessed on many separate occasions in each dog as follows: the dog was starved of food but not water for 16 hours before any scheduled test; it was then put in a Pavlov stand. As a first stage all animals had a Thomas gastrostomy cannula inserted and a TV+P. The cannula was removed, and the lumen was cleansed of any food remnants. A 10-minute period was allowed and then a urine bag containing ethylenediamine tetra-acetic acid (EDTA) powder 0.1 g was connected to the cannula (EDTA at high concentration \((> 0.1 \text{ mmol})\) prevents the \textit{in vitro} formation of lysolecithin from lecithin by inhibiting the action of phospholipase A). The gastric contents were collected over a period of 6 hours. Two aliquots were taken and stored at \(-20^\circ\text{C}\) until analysis. Each dog was subjected to a minimum of 7 and a maximum of 24 tests. The physical condition of the dogs was monitored throughout the study by weekly weight measurements.

Mucosal biopsies of the greater and lesser curvature of the gastric fundus and antrum were taken at the time of gastrectomy and also at cholecystectomy. At the end of the experiments the whole stomach was examined histologically using the ‘Swiss roll’ method as described by Sten. The amount and distribution of the various histological features were measured by Lawson’s method. The various types of gastritis were defined using Whitehead’s histological criteria.

The collected gastric contents were randomly analysed for lecithin and lysolecithin. These phospholipids were extracted with methanol and chloroform and were separated by means of thin-layer chromatography, and their concentration was estimated by phosphorus determination. The efficiency of the technique was assessed by application and recovery of known quantities of pure lecithin and lysolecithin to both low and high ranges. The mean loss was 11.9 ± 0.9% for lecithin and 9.9 ± 0.8% for lysolecithin. The sum of the concentrations of these two phospholipids was used as an index of the amount of bile reflux into the stomach.

The results were analysed by computer. The \(t\)-test and Mann-Whitney \(U\)-test were used, depending on the normality of distribution of frequencies. The results of this study were also compared with those of a previous study by the same author with exactly the same techniques, where bile reflux was measured in normal dogs and in cholecystectomised dogs.

Results
All 4 dogs remained healthy and in none of them was there significant weight loss. The only complication encountered was minor skin sepsis around the exit of the gastrostomy cannulas.

As a second stage all dogs underwent a cholecystectomy. Gastric contents were collected as before cholecystectomy. The tests were carried out for periods of 5 - 6.5 months after cholecystectomy. Each dog was subjected to a minimum of 13 and a maximum of 24 tests. The physical condition of the dogs was monitored throughout the study by weekly weight measurements.

A total of 103 tests were performed on 4 dogs (30 tests after TV+P and 73 after cholecystectomy had been added to TV+P). The mean concentration of total phospholipids in all 4 dogs was 16,356 ± 10,312 mg/dl before cholecystectomy and 66,712 ± 26,413 mg/dl after cholecystectomy \((P < 0.01)\). Results in individual dogs are shown in Table I. The ratio of lecithin to lysolecithin was 5.156 ± 0.174 after TV+P (30 tests) and 4.797 ± 0.296 after cholecystectomy had been added (73 tests) \((t\)-test; \(P > 0.01)\).

<p>| TABLE I. BILE PHOSPHOLIPIDS IN THE STOMACH BEFORE AND AFTER CHOLECYSTECTOMY IN DOGS WITH TV+P |
|-------------------------------------------------|-------------------------------------------------|</p>
<table>
<thead>
<tr>
<th>Dog</th>
<th>Total phospholipids after TV+P (mg/dl)</th>
<th>Total phospholipids after TV+P and cholecystectomy (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>2,065 ± 0.480 (7)</td>
<td>64,074 ± 10,280 (24)</td>
</tr>
<tr>
<td>8</td>
<td>11,408 ± 2,848 (9)</td>
<td>140,000 ± 13,518 (17)</td>
</tr>
<tr>
<td>9</td>
<td>5,212 ± 0,753 (7)</td>
<td>16,737 ± 4,236 (13)</td>
</tr>
<tr>
<td>10</td>
<td>46,740 ± 10,934 (7)</td>
<td>45,050 ± 11,597 (19)</td>
</tr>
</tbody>
</table>

Figures in parentheses represent number of tests.

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0.05). The volume of gastric collections was 81 ± 11 ml after TV+P (30 tests) and 81 ± 9 ml after cholecystectomy had been added (73 tests) (t-test; P > 0.05). All control biopsy specimens taken at the time of TV+P were normal. Specimens from the same areas of the stomach taken at the time of cholecystectomy were normal in 3 of the 4 dogs. In the fourth dog (dog 10) there were mucosal abnormalities in the antrum, mainly foveolar hyperplasia. At the end of the experiments 2 dogs had chronic antral gastritis, mostly in the lesser curvature (dogs 9 and 10). The most common mucosal abnormality was foveolar hyperplasia with occasional patches of atrophic gastritis.

**Discussion**

The advantages and disadvantages of the techniques used for the estimation of duodenogastric reflux have been extensively discussed previously. In the previous study, using exactly the same techniques, the concentrations of bile phospholipids in the gastric contents of 5 dogs with intact stomachs before cholecystectomy (35 tests) and after cholecystectomy (80 tests) were measured. Results in individual dogs are shown in Table II. The amount of bile reflux in dogs with an intact stomach was not statistically different from that in dogs with TV+P (Mann-Whitney U-test; P > 0.05). Again, the reflux after cholecystectomy in the two groups was not significantly different (P > 0.05). The mean ratio of lecithin to lysolecithin in the dogs with an intact stomach was 3.855 ± 0.519 after cholecystectomy and 3.686 ± 0.121 after cholecystectomy. These ratios were significantly lower than in the dogs with TV+P, in both conditions, before and after cholecystectomy (t-test; P < 0.01).

**TABLE II. BILE PHOSPHOLIPIDS IN THE STOMACH BEFORE AND AFTER CHOLECYSTECTOMY**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Total phospholipids before cholecystectomy (mg/dl)</th>
<th>Total phospholipids after cholecystectomy (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>7.604 ± 0.958 (7)</td>
<td>31.415 ± 10.431 (13)</td>
</tr>
<tr>
<td>3</td>
<td>5.836 ± 1.066 (7)</td>
<td>9.748 ± 2.230 (10)</td>
</tr>
<tr>
<td>4</td>
<td>12.885 ± 3.918 (8)</td>
<td>64.950 ± 9.432 (19)</td>
</tr>
<tr>
<td>5</td>
<td>9.198 ± 1.714 (7)</td>
<td>53.896 ± 8.930 (19)</td>
</tr>
<tr>
<td>6</td>
<td>3.232 ± 0.686 (6)</td>
<td>15.888 ± 2.311 (19)</td>
</tr>
</tbody>
</table>

Figures in parentheses represent number of tests. Total phospholipids = lecithin + lysolecithin.

It is generally accepted that TV+P is associated with increased reflux due to destruction of the pyloric sphincter. However, the findings in the present and previous study (Table II) suggest that TV+P is not invariably associated with increased reflux. Similar reports were made by Kilby, James et al., and Brough et al. When a cholecystectomy was added to the TV+P, bile reflux increased significantly (P < 0.01), but it was not higher (P > 0.05) than in dogs with only a cholecystectomy. Brough et al. reported similar results with technetium-99m-EHIDA, but Taylor et al. found higher reflux in TV+P and cholecystectomy than after cholecystectomy alone. These findings lend support to the suggestion that the pyloric sphincter is not as important in preventing duodenogastric reflux as initially thought. Sonnenberg et al. and Munk and Johnson showed in animals that reflux depends more on the contractile pattern on either side of the pylorus than on the diameter of the pyloric ring itself. Kilby suggested that pyloroplasty destroys the ability of the duodenal cap to contract and as a result the ability of the proximal duodenum to produce reflux is reduced. He also suggested that after truncal vagotomy the mixing ability of the stomach is reduced since gastric retropulsion is impaired and evacuation of the distal stomach is improved. Thus any refluxed material is evacuated rather than mixed with gastric contents.

The ratio of lecithin to lysolecithin in dogs with TV+P was significantly higher than in dogs with an intact stomach. This was so both before and after cholecystectomy. It seems that vagotomy inhibits the production of lysolecithin from lecithin. Pathophysiologically, this is important because lysolecithin is a cytotoxic agent injurious to gastric mucosa. The decreased production of lysolecithin in vagotomised dogs could be due to reduced pancreatic secretion after vagotomy. The pancreatic enzymes phospholipase A and trypsin are very important in the production of lysolecithin. The indirect effect of vagotomy may be of equal importance: vagotomy inhibits gastric acid secretions and this results in decreased release of secretin. Secretin has been shown to promote lysolecithin production.

By the end of the experiments 2 dogs had developed antral gastritis. The predominant mucosal abnormality was foveolar hyperplasia. Many authors reported similar histological findings with bile reflux. It has been suggested that foveolar hyperplasia is a histological marker for bile reflux. The general view that, whenever possible, TV+P should not be combined with cholecystectomy because of the high incidence of bile gastritis is not confirmed in the present study. Cholecystectomy combined with TV+P was not associated with higher bile reflux than cholecystectomy alone. Theoretically, there are a number of reasons why the addition of TV+P to cholecystectomy may decrease or modify the damaging effect of duodenogastric reflux. Firstly, vagotomy would decrease the amount of acid secretion, and it is the presence of H+ diffusing through mucosa the permeability of which has been increased by exposure to bile that is responsible for mucosal damage. Secondly, TV+P results in rapid gastric emptying of liquid refluxed material therefore the mucosal damage should be less because of the shortened contact time of the mucosa with bile. Finally, vagotomy seems to inhibit the production of lysolecithin from lecithin. Lysolecithin has been incriminated in the pathogenesis of gastritis. However, these are experimental findings and their possible clinical implications still have to be shown.

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**REFERENCES**

Gastric juice carcino-embryonic antigen estimation

A useful additional test in the diagnosis of gastric carcinoma?

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Summary

There is a high incidence of gastric carcinoma in the coloured population of the Western Cape. Diagnostic tests other than barium meal examination or gastroscopy were investigated. In this study 50 patients were assessed and grouped according to the gastroscopic and histological findings. Twenty-five patients with gastric carcinoma and 25 with benign gastric ulcer and/or chronic atrophic gastritis and/or intestinal metaplasia were tabulated. The gastric juice and plasma carcino-embryonic antigen (CEA) levels were identified in both groups and compared in the two groups. The gastric juice CEA level was more useful than the plasma CEA level as an aid in diagnosing malignant gastric lesions.

No correlation was evident between CEA values and the extent of the gastric carcinoma and/or histological typing. An elevated gastric juice CEA level was an additional aid in diagnosing gastric carcinoma. Markedly elevated values may also identify the high-risk patient who is prone to develop gastric carcinoma.

The highest incidence of gastric carcinoma in South Africa and the fourth-highest incidence in the world are attributed to colour males living in the Western Cape. These patients present at an advanced stage of the disease and 40 - 60% of cases are not amenable to surgical resection. Earlier diagnosis would be desirable for a surgical cure or longer postoperative survival. Diagnosis of gastric carcinoma could be made earlier by: (i) using tests other than histological examination to distinguish benign from malignant lesions; and (ii) identifying the high-risk patient and subjecting him to regular follow-up studies.

Carcino-embryonic antigen (CEA) has been utilised as an aid in the diagnosis of gastric carcinoma by several workers. CEA is a glycoprotein with antigentic properties. High CEA values are usually evident in the fetal gastro-intestinal tract at 2 - 6 months, and its level is abnormally elevated in adults with malignant gastro-intestinal lesions. CEA is at present utilised not only in the diagnosis of malignant gastro-intestinal disease but also as a test after surgery to detect recurrence.