6.2.11 Volumes of gastric contents during secretin stimulation before and after cholecystectomy

The volumes of collected gastric contents during secretin stimulation in cholecystectomized dogs were higher than in dogs with an intact gall bladder (p<0.01 for DD\(8\), DD\(10\) and DD\(14\); p<0.05 for DD\(12\), overall p<0.05). Details are shown in Table 21.

Raw data is available in Appendices F and G.

TABLE 21: VOLUMES OF GASTRIC CONTENTS DURING SECRETIN STIMULATION BEFORE AND AFTER CHOLECYSTECTOMY

<table>
<thead>
<tr>
<th>Dog</th>
<th>(\bar{x}_V) ± SEM(_V) (mls) (TV+P+secretin)</th>
<th>(\bar{x}) ± SEM(_V) (mls) (TV+P+cholecystectomy+secretin)</th>
<th>Statistical significance (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD(8)</td>
<td>45.3 ± 6.8 (7)</td>
<td>112.5 ± 18.0 (8)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD(10)</td>
<td>25.4 ± 5.6 (9)</td>
<td>55.7 ± 7.3 (7)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD(12)</td>
<td>33.4 ± 2.4 (7)</td>
<td>47.6 ± 9.4 (7)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>DD(14)</td>
<td>29.7 ± 4.3</td>
<td>59.9 ± 5.4 (7)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

\(\bar{x}_V\) = mean value of the volumes
SEM\(_V\) = standard error of the mean of the volumes
() = numbers in parentheses represent the number of tests
In 3 of the 4 dogs used in this part of the study, there was no significant change in the pH after cholecystectomy when compared with the pH before cholecystectomy (t-test, \(p > 0.05\) for DD\(_8\), DD\(_{12}\) and DD\(_{14}\)). However, in DD\(_{10}\) there was a significant increase in the pH after cholecystectomy (\(p < 0.01\), overall in the 4 dogs \(p > 0.05\)). A possible explanation for the varying results in the 4 dogs is given in the section which includes the Discussion (section 6.3). Table 22 shows the results in individual dogs. Raw data is given in Appendix E.

### Table 22: pH of Gastric Contents Before and After Cholecystectomy in Dogs with TV+P

<table>
<thead>
<tr>
<th>Dog</th>
<th>(\bar{x}_{\text{pH}} \pm \text{SEM}) (TV+P)</th>
<th>(\bar{x}_{\text{pH}} \pm \text{SEM}) (TV+P+cholecystectomy)</th>
<th>Statistical significance (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD(_8)</td>
<td>6.191 ± 0.195 (7)</td>
<td>6.175 ± 0.103 (24)</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>DD(_{10})</td>
<td>3.568 ± 0.237 (9)</td>
<td>4.730 ± 0.127 (17)</td>
<td>(p &lt; 0.01)</td>
</tr>
<tr>
<td>DD(_{12})</td>
<td>3.625 ± 0.122 (7)</td>
<td>3.940 ± 0.283 (13)</td>
<td>(p &gt; 0.05)</td>
</tr>
<tr>
<td>DD(_{14})</td>
<td>4.043 ± 0.149 (7)</td>
<td>4.234 ± 0.368 (19)</td>
<td>(p &gt; 0.05)</td>
</tr>
</tbody>
</table>

\(\bar{x}_{\text{pH}}\) = mean value of pH

\(\text{SEM}_{\text{pH}}\) = standard error of the mean

() = numbers in parentheses represent the number of tests
6.2.13  pH of gastric contents during secretin stimulation

6.2.13.1  Before cholecystectomy

Secretin stimulation in dogs with TV+P and an intact gall bladder significantly increased the pH (t-test, p < 0.01 for DD_10, DD_12, DD_14 and p < 0.05 for DD_3, overall p < 0.01). Details are shown in table 23. Raw data is given in Appendix F.

**TABLE 23 : pH OF GASTRIC CONTENTS BEFORE AND AFTER SECRETIN STIMULATION, IN DOGS WITH TV+P AND AN INTACT GALL BLADDER**

<table>
<thead>
<tr>
<th>Dog</th>
<th>$X_{\text{pH}} \pm \text{SEM}$ (basal conditions)</th>
<th>$X_{\text{pH}} \pm \text{SEM}$ secretin stimulation</th>
<th>Statistical significance (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD_3</td>
<td>6.191 ± 0.195 (7)</td>
<td>6.953 ± 0.285 (7)</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>DD_10</td>
<td>3.568 ± 0.237 (9)</td>
<td>6.300 ± 0.262 (9)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD_12</td>
<td>3.625 ± 0.122 (7)</td>
<td>6.195 ± 0.313 (7)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD_14</td>
<td>4.043 ± 0.149 (7)</td>
<td>6.237 ± 0.236 (7)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

$x_{\text{pH}}$ = mean value of pH  
SEM = standard error of the mean  
() = numbers in parentheses represent the number of tests
6.2.13.2 After cholecystectomy

Secretin stimulation in dogs with TV+P and a cholecystectomy significantly increased the pH when compared with the pH under basal fasting conditions (t-test, p < 0.01 in all 4 dogs). Table 24 gives details in individual dogs. Raw data is given in Appendix G.

**TABLE 24**: pH OF GASTRIC CONTENTS BEFORE AND AFTER SECRETIN STIMULATION IN DOGS WITH TV+P AND CHOLECYSTECTOMY

<table>
<thead>
<tr>
<th>Dog</th>
<th>$\bar{\text{pH}} \pm \text{SEM}$ (basal conditions)</th>
<th>$\bar{\text{pH}} \pm \text{SEM}$ (secretin stimulation)</th>
<th>Statistical Significance (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD_8</td>
<td>6.175 ± 0.103 (24)</td>
<td>7.090 ± 0.031 (8)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD_10</td>
<td>4.730 ± 0.127 (17)</td>
<td>6.860 ± 0.230 (7)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD_12</td>
<td>3.940 ± 0.283 (13)</td>
<td>6.661 ± 0.243 (7)</td>
<td>p &lt; 0.01</td>
</tr>
<tr>
<td>DD_14</td>
<td>4.234 ± 0.368 (19)</td>
<td>6.647 ± 0.237 (7)</td>
<td>p &lt; 0.01</td>
</tr>
</tbody>
</table>

$\bar{\text{pH}}$ = mean value of pH
SEM = standard error of the means
() = numbers in parentheses represent the number of tests
6.2.13.3 Secretin infusion before cholecystectomy compared with infusion after cholecystectomy

The pH of gastric contents collected during secretin stimulation in dogs with TV+P and an intact gall bladder was not statistically different from the pH during secretin stimulation in dogs with TV+P and cholecystectomy (Table 25).

**TABLE 25: pH OF GASTRIC CONTENTS COLLECTED DURING SECRETIN STIMULATION BEFORE AND AFTER CHOLECYSTECTOMY**

<table>
<thead>
<tr>
<th>Dog</th>
<th>$\bar{x}_{pH} \pm SEM$ (TV+P+secretin)</th>
<th>$\bar{x}_{pH} \pm SEM$ (TV+P+cholecystectomy + secretin)</th>
<th>Statistical significance (t-test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD8</td>
<td>6.953 ± 0.285 (7)</td>
<td>7.090 ± 0.031 (8)</td>
<td>$p &gt; 0.05$</td>
</tr>
<tr>
<td>DD10</td>
<td>6.300 ± 0.262 (9)</td>
<td>6.860 ± 0.230 (7)</td>
<td>$p &gt; 0.05$</td>
</tr>
<tr>
<td>DD12</td>
<td>6.195 ± 0.313 (7)</td>
<td>6.661 ± 0.243 (7)</td>
<td>$p &gt; 0.05$</td>
</tr>
<tr>
<td>DD14</td>
<td>6.237 ± 0.236 (7)</td>
<td>6.647 ± 0.237 (7)</td>
<td>$p &gt; 0.05$</td>
</tr>
</tbody>
</table>

$\bar{x}_{pH}$ = mean value of pH
SEM = standard error of the mean
() = numbers in parentheses represent the number of tests
5.2.14 Post-mortem findings

5.2.14.1 Macroscopic findings

Post-mortem examinations were carried out in all 4 dogs, at the end of the experiments. Minor skin sepsis around the exit of the gastrostomy cannula was present in all 4 animals. No intra-peritoneal sepsis was found. Beside adhesions in the upper abdomen, no other abnormality was found. No macroscopic lesions were seen on the gastric mucosa.

5.2.14.2 Histological findings

Control mucosal biopsies were taken at the time of the gastrostomy and TV+P, from the fundus and antrum of the stomach, and were normal in all 4 dogs (Table 26). Biopsies from the same areas of the stomach, taken later, at the time of cholecystectomy, were normal in 3 of the dogs, namely in those dogs where TV+P had not been associated with increased reflux (DD_8, DD_10, DD_12). However, in DD_14 in which TV+P had been associated with increased bile reflux (section 6.2.5) there were epithelial changes in the antral mucosa, while the fundus was normal. Of a total of 18 mm of antral mucosa examined histologically, 4 mm were abnormal. The mucosal change consisted of foveolar hyperplasia and it had a patchy distribution.

After the animals had been sacrificed, the gastric mucosa was examined using the 'Swiss roll' method (section 5.1.7). Two of the dogs (DD_8 and DD_10) had normal fundal and antral mucosa,
except for 4 mm of foveolar hyperplasia in the lesser curvature of the antrum of DD_8. However, in the remaining 2 dogs (DD_12 and DD_14) there was gastritis. A detailed analysis of the histological findings in these 2 dogs follows.

Bar diagrams showing the amount and distribution of gastritis in the 4 different areas of the stomach (section 5.1.7) were prepared. The method of interpretation of the bar diagrams has been shown in section 5.2.14.2.

TABLE 26: THE AMOUNT OF GASTRIC MUCOSA ASSESSED HISTOLOGICALLY IN INDIVIDUAL DOGS

<table>
<thead>
<tr>
<th>Dog</th>
<th>GA (mm)</th>
<th>GF (mm)</th>
<th>CA (mm)</th>
<th>CF (mm)</th>
<th>A (mm)</th>
<th>F (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD_8</td>
<td>59</td>
<td>34</td>
<td>20</td>
<td>36</td>
<td>233</td>
<td>498</td>
</tr>
<tr>
<td>DD_10</td>
<td>14</td>
<td>20</td>
<td>16</td>
<td>25</td>
<td>199</td>
<td>476</td>
</tr>
<tr>
<td>DD_12</td>
<td>18</td>
<td>24</td>
<td>26</td>
<td>24</td>
<td>172</td>
<td>498</td>
</tr>
<tr>
<td>DD_14</td>
<td>26</td>
<td>21</td>
<td>18</td>
<td>32</td>
<td>262</td>
<td>486</td>
</tr>
</tbody>
</table>

GA: antral biopsies at the time of gastrostomy + TV+P
GF: fundal biopsies at the time of gastrostomy + TV+P
CA: antral biopsies at the time of cholecystectomy
CF: fundal biopsies at the time of cholecystectomy
A: total length of 5 strips from the antrum at the end of the experiments
F: total length of 5 strips from the fundus at the end of the experiments
Dog DD\textsubscript{12} was sacrificed 5 months after cholecystectomy. A total length of 498 mm of gastric fundus (from 5 'Swiss rolls' was examined histologically (Table 26), and no mucosal abnormality was found. However, in the antrum gastritis occurred. Of a total of 172 mm (5 'Swiss rolls') of antrum assessed histologically, 74 mm were affected by gastritis of various types (Figures 42 a, b, c, d, e). This was statistically significant ($x^2$ test, $p < 0.01$) when compared with the 18 mm and 26 mm of normal biopsies taken at the time of TV+P and cholecystectomy respectively (Table 26).

The distribution of gastritis was patchy. The amount of gastritis in the distal half of the antrum was not significantly different from that in the proximal half ($p > 0.05$). The most common mucosal abnormality was foveolar hyperplasia which was found in 62 mm out of a total of 74 mm of abnormal mucosa ($p < 0.01$).

Occasionally foveolar hyperplasia co-existed with atrophic gastritis (Figure 43).
Figure 42a. Dog DD_{12}. The histological changes along the anterior part of the greater curvature of the antrum.

Figure 42b. Dog DD_{12}. The histological changes along the posterior wall of the antrum.
Figure 42c. Dog DD\textsubscript{12}. The histological changes along the lesser curvature of the antrum.

Figure 42d. Dog DD\textsubscript{12}. The histological changes along the posterior wall of the antrum.
Figure 42e. Dog DD$_{12}$. The histological changes along the posterior wall of the greater curvature of the antrum.

Figure 43. Antral mucosa with epithelial proliferation and atrophic gastritis.
Dog DD\textsubscript{14} was sacrificed 6 months after cholecystectomy. A total of 486 mm of fundal mucosa (5 'Swiss rolls') was examined and gastritis was found in the distal 14 mm of the anterior part of the greater curvature, in the distal 6 mm of the anterior wall, in the distal 6 mm of the lesser curvature and in the distal 10 mm of the posterior part of the greater curvature. In these areas foveolar hyperplasia was found. The amount of fundal gastritis was statistically significant (p < 0.01) when compared with the normal fundus at the time of TV+P (21 mm) and at the time of cholecystectomy (32 mm). A total length of 262 mm of antral mucosa was assessed and 204 mm were found to be abnormal. This was statistically significant (x\textsuperscript{2} test, p < 0.01) when compared with the 26 mm of normal biopsies taken at the time of TV+P, an' when compared with the biopsies taken at the time of cholecystectomy (4 mm of abnormal mucosa out of 18 mm of assessed mucosa). As with dog DD\textsubscript{12}, the predominant mucosal abnormality was foveolar hyperplasia (200 mm) followed by moderate atrophic gastritis (52 mm). The distribution of gastritis was patchy. The amount of gastritis in the distal half of the antrum was not significantly different from that in the proximal half (p > 0.05). The lesser curvature appeared to have more gastritis than the remainder of the antrum, although this was not statistically significant (p > 0.05). Figure 44 (a,b,c,d,e) shows the mucosal changes in the antrum of DD\textsubscript{14}. 

Dox.
Figure 44a. Dog DD₁₄. The histological changes along the anterior part of the greater curvature of the antrum.

Figure 44b. Dog DD₁₄. The histological changes along the posterior wall of the antrum.
Figure 44c. Dog DD4-c. The histological changes along the lesser curvature of the antrum.

Figure 44d. Dog DD4-d. The histological changes along the posterior wall of the antrum.
Figure 44c. Dog DD14. The histological changes along the lesser curvature of the antrum.

Figure 44d. Dog DD14. The histological changes along the posterior wall of the antrum.
Figure 44e. Dog DD14. The histological changes along the posterior part of the greater curvature of the antrum.
6.2.15 Dogs with TV+P compared with dogs with an intact stomach

6.2.15.1 D/G reflux under fasting conditions

The amount of bile reflux (the sum of the concentrations of lecithin and lysolecithin) in 5 dogs (35 tests) with an intact pylorus and intact vagi (group A, section 5.2.5) was compared with the reflux in 4 dogs (30 tests) with TV+P (group B, section 6.2.5). There was no significant difference between the 2 groups (Mann-Whitney, p > 0.15).

After cholecystectomy was carried out on all dogs in group A and group B, bile reflux in the 5 dogs of group A (71 tests) was compared with the reflux in the 4 dogs of group B (73 tests) and it was found that there was no significant difference between the 2 groups (Mann-Whitney, p > 0.05). In 2 of the dogs of group A (DD_2 and DD_3) post-cholecystectomy bile reflux was increased for only a few weeks and then returned to pre-cholecystectomy levels (section 5.2.6). Only tests during the period of increased bile reflux were included in the above comparison. It is concluded that if the post-cholecystectomy reflux in dogs with an intact pylorus and intact vagi is increased, it does not differ significantly from the post-cholecystectomy reflux in dogs with TV+P.

6.2.15.2 Bile reflux during secretin stimulation

The effect of secretin on the amount of bile reflux in the 5 dogs (35 tests) with an intact pylorus and intact vagi (group A) was
compared with the 4 dogs (30 tests) with TV+P (group B). The amount of reflux in the group with TV+P was significantly greater than in the dogs of group A (Mann-Whitney, p<0.05).

When cholecystectomy was added to both groups of dogs, the amount of reflux during secretin stimulation was again significantly greater in group B (p<0.01, 44 tests in the 5 dogs of group A and 29 tests on the 4 dogs of group B).

6.2.15.3 Ratio of lecithin to lysolecithin
6.2.15.3.1 Under basal fasting conditions

The ratios of lecithin to lysolecithin in the 5 dogs (35 tests) with an intact pylorus and intact vagi (group A) were compared with the ratios in the 4 dogs (30 tests) with TV+P (group B).

In dogs with TV+P the values of these ratios were significantly higher than in dogs of group A (t-test, p<0.01).

The post-cholecystectomy ratios of lecithin to lysolecithin in the 5 dogs of group A (80 tests) were compared with the ratios in the 4 dogs of group B (73 tests). Again in dogs with TV+P these ratios were significantly higher than in group A (p<0.01). The above findings suggest that TV+P inhibit the production of lysolecithin from lecithin. A detailed discussion is presented in section 6.3.1.
6.2.15.3.2  During secretin stimulation

The ratios of lecithin to lysolecithin in the gastric contents collected during secretin stimulation in the 5 dogs (35 tests) of group A before cholecystectomy were compared with the ratios in the 4 dogs (30 tests) of group B before cholecystectomy and during secretin infusion. There was no significant difference (t-test, p>0.05). When cholecystectomy was added to both groups, again there was no significant difference (43 tests in group A vs 29 tests in group B, p>0.05).

6.2.15.4  Volumes of gastric contents
6.2.15.4.1  Under basal fasting conditions

The pre-cholecystectomy volumes of gastric collections under basal fasting conditions in the 5 dogs (35 tests) of group A were compared with the pre-cholecystectomy volumes in the 4 dogs (30 tests) of group B. The volumes in group B (TV+P) were significantly smaller than in group A (t-test, p<0.01). After cholecystectomy was added to this group the volumes in the dogs with TV+P (73 tests) were again significantly smaller than in group A (80 tests, p<0.01).

6.2.15.4.2  During secretin stimulation

The pre-cholecystectomy volumes of gastric collections during secretin stimulation were compared in the 5 dogs (36 tests) in group A and in the 4 dogs (30 tests) in group B. The volumes
in the dogs of group B (TV+P) were significantly smaller in the
dogs of group A (intact pylorus and intact vagi) \((p < 0.01)\).
However, after cholecystectomy there was no significant difference
(45 tests in group A vs 29 tests in group B, \(p > 0.05\)).

6.2.15.5  pH of gastric contents

6.2.15.5.1  Under basal fasting conditions

The pH of gastric contents in the 5 dogs (35 tests) of group A
was compared with the pH in the 4 dogs (30 tests) of group B.
The dogs of group B (TV+P) had a significantly higher pH than
the dogs of group A \((t\)-test, \(p < 0.01)\). This difference remained
significant when cholecystectomy was added to both groups (80
tests in group A vs 73 tests in group B, \(p < 0.01)\).

6.2.15.5.2  During secretin stimulation

The pH of gastric contents in the 4 dogs with TV+P (30 tests)
was significantly higher \((p < 0.01)\) than the pH in the 5 dogs of
group A (35 tests). This difference remained after cholecystec-
tomy (43 tests in group A compared with 29 tests in group B, \(p < 0.01)\).

6.2.15.6  Histological findings

Two of the 5 dogs with intact vagi and an intact pylorus, and 2
of the 4 dogs with TV+P had developed gastritis by the end of
the experiments. A detailed discussion is presented in section
6.3.2.
6.3 DISCUSSION

6.3.1 Discussion of biochemical results

In 3 of the 4 dogs with TV+P there was always evidence of a small amount of bile reflux, but this reflux was not higher than in dogs with an intact stomach. In the remaining dog (DD_14) of the group with TV+P bile reflux was higher than in the rest of this group and higher than in the dogs with an intact stomach (section 6.2.5). However, overall there was no significant difference in the amount of bile reflux between the 2 groups of dogs (sections 6.2.5 and 6.2.15.1).

It is generally accepted that TV+P is associated with increased reflux due to destruction of the pyloric sphincter (34, 43, 65, 69, 245). However the findings in the present study suggest that TV+P is not invariably associated with increased reflux. This is in agreement with some other reports: Kilby (72) reported that TV+P was not associated with increased reflux. Similar reports were made by James et al (236). A detailed discussion of these reports has been given in section 4.4.1. Keighley (267) reported that in many cases humans with TV+P did not have increased reflux. Some authors suggested that the pyloric sphincter was not as important as initially thought in preventing reflux. Sonnenburg (73) and Munk (74) showed in animals that reflux depended more on the contractile pattern on either side of the pylorus, than on the diameter of the pyloric ring itself. Kilby (72) 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. A detailed discussion of the significance of the pylorus in preventing reflux has been given in section 3.1.1. Another factor which may account for the absence of increased reflux after TV+P might be the effect of the vagotomy; Kilby (72) suggested that after truncal vagotomy the mixing ability of the stomach was reduced since gastric retropulsion was impaired. Evacuation of the distal stomach was improved. Thus any refluxed material was evacuated rather than mixed with gastric contents.

It is interesting to note that in dog DD₁₂, which had a mild 'dumping syndrome' (fast gastric and intestinal emptying - section 6.2.2), TV+P was not associated with increased reflux. This is not in agreement with the observations of Donovan et al (265) who reported that dumping and reflux usually co-exist. However, firm conclusions cannot be made from the single observation made in the present study.

When cholecystectomy was added to the TV+P, bile reflux increased in 3 dogs (section 6.2.6). In the remaining dog (DD₁₄), which had been shown to have an increased amount of bile reflux after TV+P, cholecystectomy did not appear to alter the amount of reflux. Since the volumes of gastric collections were the same before and after cholecystectomy, it is unlikely that the amount of duodenal contents refluxing into the stomach increased after cholecystectomy. The most likely mechanism for
the increased concentrations of duodenal contents in the stomach would seem to be the permanent presence of bile in the duodenum which follows cholecystectomy. This theory has been discussed in section 5.3.2.

The amount of post-cholecystectomy bile reflux in 3 of the 4 dogs with TV+P did not vary significantly from the post-cholecystectomy reflux in the 5 dogs with intact vagi and an intact pylorus (section 6.2.15.1). This supports the view that the pylorus may not play an important role in the prevention of D/G reflux. If the pylorus did in fact play an important role in preventing reflux as suggested by many authors, the post-cholecystectomy reflux in dogs with an intact pylorus could reasonably be expected to be less than the reflux which occurs in dogs with a pyloroplasty. On the other hand, if pyloroplasty prevented reflux, as suggested by Kilby (72) (Section 4.4.1) the post-cholecystectomy reflux would be expected to be less than in dogs with an intact pylorus. However, there is some reservation about these conclusions because vagotomy could be a complicating factor as it could interfere with the normal antroduodenal motility. In conclusion, the results concerning the amount of bile reflux obtained in 3 dogs with TV+P and in all 4 dogs with TV+P and cholecystectomy when compared with the results in dogs with intact vagi and an intact pylorus (section 6.2.15.1), suggest that the pylorus does not play a major role in preventing reflux.
Again, as in dogs with intact vagi and an intact pylorus, the amount of reflux in dogs with TV+P varied markedly from time to time in the same dog. The findings in the present study reconfirmed the periodic pattern of reflux and the importance of measuring reflux many times and over long periods of time in order to get a reliable picture of reflux. This has been discussed in detail in sections 5.1.11.1 and 5.3.1.

The ratio of lecithin to lysolecithin in dogs with TV+P was significantly more in favour of lecithin when compared with the dogs with an intact pylorus and intact vagi (section 6.2.15.3). The effect of truncal vagotomy on the biliary system has been discussed in section 3.3 and it seems that it does not affect the production of lysolecithin. The decreased production of lysolecithin in vagotomised dogs could be the result of a direct or indirect effect of vagotomy on the pancreas: truncal vagotomy does directly reduce pancreatic secretion (159,160) which is important in the production of lysolecithin (section 3.5.1).

The indirect effects of truncal vagotomy may be of equal importance: vagotomy inhibits gastric acid secretion and this results in a decreased release of secretin. In the present study secretin has been shown to favour lysolecithin production (section 5.3.2). When secretin was administered exogenously, the ratio of lecithin to lysolecithin changed significantly in favour of lysolecithin (section 6.2.7) and this was not different from the ratios obtained during secretin stimulation in dogs with intact vagi (section 6.2.15.3.2).
Secretin stimulation in dogs with TV+P resulted in significantly higher reflux than in dogs with intact vagi and an intact pylorus, both before and after cholecystectomy (section 6.2.15.2). A possible explanation is that the alteration in the pressure gradient across the pylorus induced by secretin (38,67,78,179, 180) in dogs with TV+P is more conducive to reflux than that in dogs with an intact pylorus and intact vagi. Further studies are needed in this field.

Two of the dogs in the group with an intact stomach showed increased post-cholecystectomy bile reflux for about 2 months only, thereafter returning to pre-cholecystectomy levels. A possible explanation was that in dogs the common bile duct (CBD) dilates after cholecystectomy and perhaps takes over part of the gall bladder reservoir function (section 5.3.2). In contrast to this all 4 dogs with TV+P showed consistently increased reflux after cholecystectomy. In all of them reflux remained increased for about 6 months after cholecystectomy till the end of the present study when they were sacrificed. Although the number of dogs in the two groups was too small to draw firm conclusions, it is possible that a vagally denervated CBD may not be able to re-adjust after cholecystectomy and, as a result, the reflux remained consistently increased. Again, further studies are needed to clarify this point.

The volumes of gastric contents collected under basal fasting conditions in dogs with TV+P were significantly smaller than in
dogs with an intact stomach, both before and after cholecystectomy (section 6.2.15.4.1). This might be the result of decreased rate of gastric secretion or increased rate of gastric emptying of liquids which follow a TV+P. Similar results were found during secretin tests before cholecystectomy. However, the volumes during secretin tests in cholecystectomized dogs did not vary significantly in the two groups (section 6.2.15.4.2). It is difficult to offer a satisfactory explanation for this observation.

6.3.2 Discussion of histological findings

Of the 4 dogs with TV+P and cholecystectomy, only 2 (DD12 and DD14) had developed histological gastritis by the end of the experiments despite the increased bile reflux in all of them. The incidence of gastritis was not higher than that in cholecystectomized dogs with an intact pylorus and intact vagi.

Dog DD14 was the only animal in which TV+P alone was associated with increased reflux (section 6.2.5). As a result, the gastric mucosa was exposed to high concentrations of duodenal contents for a longer period of time than the remainder of the group. The period of increased reflux in DD14 was 8 months - 2 months longer than the other dogs in the same group. A 6 month period seems to be sufficient time to allow gastritis to develop, as gastritis was seen in the dogs with an intact pylorus and intact vagi (section 5.2.14.2). A possible explanation as to why dogs DD8
and DD$_{10}$ did not develop gastritis despite the increased reflux, is that the decreased acid secretion which follows vagotomy, makes bile less damaging to the gastric mucosa (23,230,231). Perhaps longer periods of observation after cholecystectomy were needed. Another possible explanation is the rapid gastric emptying of fluids which follows TV+P. This results in a shortened contact time between bile and gastric mucosa, a factor which influences the injurious effect of bile. No explanation can be offered as to why dog DD$_{12}$ developed gastritis in spite of a smaller amount of bile reflux than that occurring in dogs DD$_8$ and DD$_{10}$, which had normal mucosa. Individual sensitivity of the gastric mucosa to bile may be a factor.

The predominant mucosal abnormality in the 2 dogs with gastritis was foveolar hyperplasia, and the distribution of gastritis was patchy. The significance of these findings has been discussed in section 5.3.3.

6.3.3 Clinical significance of the results of the present study

The dangers of extrapolation from the experimental to the human situation are well recognized, but the results of this study suggest that in the dog TV+P with cholecystectomy is associated with more reflux than is TV+P alone. This is in agreement with other reports (43,249). However, the combination of TV+P and cholecystectomy was not associated with a higher incidence of