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The effect of cholecystectomy on duodenogastric reflux : an experimental study

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presence of phospholipase A in the lysosomes of the gall bladder epithelium, implying local formation of lysolecithin, and they suggested that the lysolecithin produced here was normally degraded by a local lysophospholipase. Philips (172) detected traces of lysolecithin in normal hepatic bile.

3.5.2 Clinical significance of lysolecithin

Lysolecithin, which has detergent properties, damages biological and artificial membranes by means of surface activity (173,174). In recent years it has been incriminated in the pathogenesis of acute cholecystitis, acute pancreatitis and acute and chronic gastric ulceration (169 173,174) Johnson (28) found significantly higher concentrations of lysolecithin in the stomach of patients with gastric ulcer, than in normal controls. Similar results were reported by others (24,25,27,175). Davenport (26) found that concentrations of lysolecithin between 20 and 160 mg% disrupted the canine gastric mucosal barrier.

3.6 Physiology of secretin

Secretin is a hormone secreted by the mucosal villus epithelial cells, mainly in the duodenum and to a lesser extent the jejunum and ileum (176). Hydrochloric acid and the products of fat and protein hydrolysis stimulate the release of the hormone (81). Synthetic and natural secretin have the same properties (177). The response to pharmacological doses of secretin, on different

parts of the human and canine gastrointestinal tract, are listed below:

a) Stomach - inhibition of acid secretion (79,82,83) and gastric motility (178,179), inhibition of gastrin release (79). Decrease of intragastric pressure (78) and increase of the pyloric sphincter pressure (33,67,179,180). Stimulation of pepsin secretion (79). Fisher (37) reported that during endogenous release or exogenous administration of secretin, the pyloric pressure increased in normal subjects, but failed to do so in patients with gastric ulcer.

b) Duodenum - decrease in intraluminal pressure (78) and inhibition of motility (181).

c) Liver - increase of bile flow (182-184) and electrolyte output (67,79). No change in the composition of bile (182).

d) Gall bladder - no effect when given alone, but enhanced contractions caused by cholocystokinin (36,185).

e) Pancreatic secretion - increase in volume and electrolytic output (79) and trypsin secretion (81).

Chey et al (186) reported that truncal vagotomy had no effect on plasma secretin levels. The pancreatic response to secretin does not change after truncal vagotomy (160).

3.7 Defence mechanisms of the gastric mucosa

The architecture and physiological properties of the apical membranes of the epithelial cells of the gastric mucosa, create a barrier which prevents water and water soluble substances entering the cells. This is very important in the defence of the mucosa against potentially damaging factors. The barrier may be disrupted by bile salts, urea, aspirin and synthetic detergents (187-189). These substances act on the surface epithelium and as a result H^+ and other ions penetrate and damage the cells (187).

Some authors suggested that exposure of the gastric mucosa to mild cytotoxic agents increases mucosal resistance. Code (190) proposed three possible mechanisms for this 'cytoprotection':

a) molecular re-arrangement in the apical membrane which results in decreased permeability of the mucosa to H^+ and damaging factors;

b) increased production of HCO_3^- ;

c) increased mucus secretion. Mucus may help wash away or bind the damaging factors.

Clemencon et al (24) showed that in rats small doses of lysolecithin exerted cytoprotection against the effect of bile acids. Ivey(191), experimenting on healthy humans, found that bile salts instilled into the stomach, caused H^+ irflux into the mucosa. However, after repeated instillations, the amount of back diffusion of H^+ was progressively decreased. The author considered

this phenomenon to be evidence of development of cytoprotection against bile. Scheurer et al (192) reported that bile diversion into the stomach by means of a cholecysto-gastrostomy and ligation of the common bile duct, increased the resistance of the gastric mucosal barrier: control dogs had gastric bleeding after exposure to high concentrations of bile, while dogs with cholecystogastrostomy did not.

Robert (193) suggested that prostaglandins exerted cytoprotection. The author further postulated that endogenous formation of prostaglandins could be stimulated by mild irritants. Müller-Lissner et al (194) reported contradictory results.

3.8 Post-cholecystectomy syndrome

Not all patients with gall stone disease become asymptomatic after cholecystectomy. The incidence of the so-called 'post-cholecystectomy syndrome' has been estimated to be between 10 and 40% (42,132,195). Many hypotheses have been advanced to explain this syndrome. Some authors attributed the symptoms to organic causes, such as common bile duct stones, pancreatic disease, long cystic duct remnant, etc. Others have incriminated functional causes mediated by hypertonic biliary dyskinesia due to increased vagal tone, or atonic diskinesia due to sympathetic predominance (132). Bodrall (196) suggested a genetically influenced disturbance of cholesterol and bile salt metabolism. Collins (195) made the suggestion that the increased levels of

cholecystokinin, which follow cholecystectomy, may cause spasm of the common bile duct and thus pain. Some recent retrospective clinical studies suggested that after cholecystectomy the incidence of D/G reflux was higher than in normal subjects (37,41, 44). Other studies (47-49) reported no correlation between cholecystectomy and bile reflux gastritis. This finding will be discussed further in 4.5.

3.9 Assessment of adequacy of surgical vagotomy

The completeness of vagotomy can be assessed intra-operatively and post-operatively. Intra-operative tests include electrical stimulation of the proximal stump of the vagus, leucomethylene blue or Congo red tests, and gastric pH-metering. These tests are not widely used because they are difficult to carry out and their accuracy is questionable. Post-operative insulin, pentagastrin, or histamine tests may be done. The insulin test , as introduced by Hollander (197) has gained general acceptance. In this test, basal gastric secretion is collected during four consecutive 15-minute periods. Insulin (0,3 i.u. per Kilogram weight) is administered intravenously, and gastric secretions are collected over eight 15-minute periods. The result is considered positive when the gastric acidity increases by more than 20 mmol/l, above the basal level in any of the collections after insulin injection. If the basal acidity is zero, a 10 mmol increase is considered a positive result. A blood sugar below 45 mg/100 ml (2,5 mmol/l) is necessary.

Ross et Kay (198) suggested that a positive test in the first 45 minutes should be considered as evidence of inadequate vagotomy, and that positive tests after the first 45 minutes should be considered as evidence of incomplete but adequate vagotomy. Johnston (199) put the critical time at 60 minutes.

3.10 Confirmation of the preservation of antral innervation after HSV.

It has been found that there is an omnipresent rhythm of electrical waves in the distal stomach. They are known as pacesetter potentials, and originate in a pacemaker located in the midcorpus of the stomach, in the greater curvature (200,201). The pacesetter potential has a frequency of approximately 3 cycles per minute in humans and 5 cycles per minute in dogs (94,200,202,203). Motor activity when present is associated with action potentials which are superimposed on the basic pacesetter potential.

The electrical activity of the stomach can be recorded either from the serosal or mucosal surface of the stomach (203). The electrical potential can be suppressed or modified by excessive handling of the stomach during an operation or by barbiturate anaesthesia (204,205). General anaesthesia induced by urethane or chloralose has no adverse effect on the electrical potential of the stomach (206). Intravenous insulin injection (1,5 to 2 units per Kg weight) in dogs with intact vagal innervation of the antrum, triggers the onset of action potentials (94,203). When

the antrum is denervated, insulin no longer stimulates the appearance of action potentials (94,202,203). Stoddard et al (203) showed that in humans the normal triphasic waveform of the pacesetter potential changed to a sinusoidal rhythm after vagal denervation of the antrum.

Anatomical and functional integrity of the vagal innervation of the antrum after HSV can be assessed by monitoring the waveform of the pacesetter potential or by injecting insulin intravenously and looking for the appearance of action potentials. If the innervation of the antrum has been damaged the pacesetter potential should have a sinusoidal rhythm (203) and injection of insulin should not be associated with action potentials.

3.11 Gastric mucosa histology

3.11.1 Normal stomach

The stomach is divided into 3 histologically distinct areas, using conventional light microscopy: the cardia, the fundus and the pyloric region. The cardia is a small area distal to the cardio-oesophageal junction. The pyloric region is a roughly triangular area in the distal third of the stomach. The fundus occupies the area between the cardia and the pyloric region. The mucosal junction between the three areas may be abrupt or across a transitional zone.

The normal histology of the gastric mucosa of the dog was described by Harvey (207) in 1906, and later by Bensley (208).

The fundal mucosa is characterized by shallow gastric pits, into each of which open about 4 gastric glands. The glands are tightly packed together and occupy three quarters of the thickness of the mucosa. They contain the 3 following types of cells: the mucous neck cells which are found at the junction of the glands with the pits; the parietal cells, which are polyhedral in shape and contain eosinophilic cytoplasm with a central nucleus. They are situated in the upper part of the glands. The chief cells occupy the lower half of the glands. These are elongated cells, have a basal nucleus and a basophilic granular cytoplasm. The lamina propria of the mucosa contains a small number of plasma cells, lymphocytes, eosinophils and histiocytes (209).

The pyloric mucosa is characterized by deep gastric pits, which extend halfway through the mucosal thickness. The glands are shorter and fewer in number than in the fundus, and they contain mucous secreting cells (209).

The cardiac mucosa is essentially similar to the pyloric mucosa, except that the glands are fewer (209).

The transitional mucosa contains both fundal and pyloric type glands. The gastric pits occupy about half of the thickness of the mucosa (209).

Mitotic activity is normally limited to the area of the mucous neck cells.

3.11.2 Chronic gastritis

The histology in chronic gastritis was studied by Schindler (210) and later by Whitehead et al (209). It is important to note that macroscopically normal stomach may have extensive gastritis microscopically (33,211).

3.11.2.1 Classification of chronic gastritis

There are various classifications based on the grade of chronic gastritis, the activity of gastritis and the presence of metaplasia (209). Most authors advocate two major subdivisions, namely superficial and atrophic gastritis. In superficial gastritis inflammatory and reactive changes occur only in the superficial epithelium, the gastric pits and the related lamina propria. Changes may include epithelial proliferation and increased mitotic activity. In atrophic gastritis, changes affect the glandular layer, with cyst formation in the lamina propria, corkscrew appearance of the glands and increased mitotic activity. Atrophic gastritis is classified into mild, moderate and severe types, according to the extent of glandular damage. In mild gastritis, only one or two groups of tubules have disappeared. In severe gastritis all normal tubules are lost or only one or two groups remain. Moderate gastritis includes all appearances between the two extremes.

Chronic gastritis could also be classified as active or inactive, according to whether there is polymorphonuclear infiltration or not of the gastric mucosa.

Two types of metaplasia may occur (212). Intestinal metaplasia usually occurs on a background of atrophic gastritis. It is rarely seen with bile reflux gastritis, but occurs more frequently with gastric cancer. Pseudopyloric metaplasia is of doubtful significance and it is usually limited to the fundus.

3.11.2.2 Clinical significance of histological chronic gastritis.

It is generally accepted that chronic gastritis predisposes to gastric ulceration. Cruveilhier (213) was the first to notice that gastric ulcers develop in areas of atrophic gastritis. Lawson (214) showed that, in dogs when an area of atrophic gastritis was exposed to gastric secretion, ulceration occurred. He suggested that acid and pepsin are necessary for the ulceration. Other authors found similar results (9,10,215).

Most authors agree that there is no correlation between symptoms and the presence of histological chronic gastritis (216,217). Hoare et al (216) found that active gastritis in the proximal stomach was usually symptomatic, while active antral gastritis or inactive proximal gastritis was usually asymptomatic.

3.11.3 Vagotomy and gastric mucosa

Gastric mucosal changes after vagotomy might be due to denervation, stasis or reflux (218).

3.11.3.1 Truncal vagotomy and gastric mucosa

There are many differences of opinion regarding the effect of TV on the gastric mucosa.

Lawson (218), in a controlled study in dogs, reported mild atrophic gastritis in the antrum after TV and Finney pyloroplasty. When a TV was performed without a drainage procedure, mucosal changes depended on whether gastric stasis was present or not. Animals with clinical signs of stasis developed superficial antral ulceration, whereas animals with no signs of stasis had no mucosal changes.

Sander (219) and Ellis et al (220) in controlled studies in rats, found no change in the number of parietal cells per area of mucosal surface, after TV. Melrose et al (221) found no increase in the frequency of histological gastritis, in a follow-up of 46 patients, 1 to 10 years after TV and a drainage procedure. The patients were assessed histologically post-operatively only.

Asher (222) suggested that TV alone caused gastritis. However, the study comprised a small number of patients with pre-operative gastric ulcer. The gastritis may well have existed before TV. Macleod et al (223) reported patchy gastritis after TV with

pyloroplasty. The patients had no pre-operative biopsies, therefore pre-existing gastritis was not excluded. Liavag et al (224) reported reduction of mucosal thickness and decreased proliferative activity on the gastric mucosa after TV with pyloroplasty.

3.11.3.2 Highly selective vagotomy and gastric mucosa

Roland et al (225), in a controlled study in humans, found a significant increase in chronic gastritis after HSV. The increase in gastritis was due to an increased infiltration of inflammatory cells and not to actual glandular atrophy. Holle et al (226) found a decrease in the number of parietal cells after HSV with a drainage procedure. This might be the result of increased reflux due to the drainage procedure. Romeo et al (227), in a controlled study in patients with duodenal ulcer, found that after HSV the number of parietal cells did not change. However, cells showed structural cytoplasmic changes. These changes were temporary, and in 2 to 3 months the cells had resumed their preoperative appearance. Lawson (218),in a controlled study in dogs, observed a change in chief cells after HSV, described as the 'disappearing chief cell phenomenon'. He considered this phenomenon a normal occurrence and not a sign of atrophic gastritis.

4. A CRITICAL ASSESSMENT OF ASPECTS OF THE RELEVANT LITERATURE

4.1 Significance of D/G reflux

Although it is generally accepted that D/G reflux is injurious to gastric mucosa (6-22), some authors have challenged this concept.

Byers and Johnson (228) transplanted full thickness grafts of gastric mucosa into the gall bladder. No graft damage was found one year after operation. However, there are two considerations in regard to this experiment. Firstly, the gastric mucosa was not exposed to the acid-pepsin contents of the stomach, and secondly, the authors did not distinguish between fundal and antral epithelium. Lawson (11) produced antral gastritis by performing cholecysto-gastrostomy with common bile duct ligation. Similar results were reported by Mosiman et al (229) and Menguy et al (16). Scheurer et al (192) recorded no gastritis after the same procedure. However, their histological follow up was only 4 weeks, perhaps too short a period for changes to occur. It seems that bile without acid is not injurious to gastric mucosa. Lawson (23) reported gastritis but not ulceration, after diversion of pure bile, pure pancreatic secretion, and total duodenal contents into the stomach of dogs. The author suggested that the lack of ulceration could be explained by the fact that dogs are not interdigestive secretors of acid.

Russell et al (230) reported that in rats no mucosal damage occurred when pure bile was instilled into the stomach. When acid or aspirin were added, mucosal erosions occurred. Ritchie (231) showed that in dogs the topical application of pure bile to normal gastric mucosa was not acutely ulcerogenic, but that the combination of bile, acid, and mucosal ischemia, led to acute ulceration. Any two of these factors alone did not produce obvious mucosal injury. In the later two experiments the gastric mucosa was exposed to the effect of high concentrations of bile in acute experiments. With chronic low exposures, the reaction of the gastric mucosa might be different. Many authors suggested that exposure of the stomach to low concentrations of bile increased the resistance of the mucosa to higher concentrations of bile (24,190,191,193).

Sonnenberg et al (232) questioned the importance of D/G reflux as a cause of gastric pathology. They found that the cytotoxic activity in the gastric juice of patients with antral gastritis or gastric ulcer, was the same as that in subjects whose stomachs were normal at endoscopy. There are three considerations, however, with regard to this study. Firstly, the authors used subjects who were normal endoscopically as controls. Normal endoscopy does not exclude histological gastritis. It has been shown that macroscopically normal mucosa may be associated with severe microscopic gastritis (33,211). Secondly, cytotoxic activity was assessed by observing the effect of gastric content

on red cells. It may well be that gastric mucosal cells and red blood cells react differently to the same stimulus. Thirdly, cytotoxic activity is not necessarily the result of bile reflux. It could be due to bacterial toxins present in the stomach. Most of their patients with increased cytotoxic activity had a high pH, which favours bacterial growth. Hinder et al (233), using data from the work of Schumpelick et al (234) challenged the significance of D/G reflux in gastric pathology. The amount of reflux was compared in 2 groups of patients: those with gastric ulcer and those with duodenal ulcer. No normal subjects were used as controls. Furthermore, these groups lacked homogenicity as they comprised untreated patients, patients under treatment, and patients with varying duration of ulcer symptoms.

Mosimann et al (235) considered D/G reflux of minor pathological significance. Of 202 patients with truncal vagotomy and pyloroplasty, they found only 3% with symptoms related to reflux. A point to be considered with regard to their method is that they assumed that all patients with truncal vagotomy and pyloroplasty had increased D/G reflux. However, many investigators have reported no increase in D/G reflux after truncal vagotomy and pyloroplasty.

4.2 Methods used for D/G reflux measurement

Various methods have been used to detect D/G reflux. They can be classified into 3 groups: (a) detection in the stomach of a

non-abosrbable marker, previously infused into the duodenum; (b) detection of duodenal contents in the stomach; (c) radiological methods.

4.2.1 Detection in the stomach of a non-absorbable marker, previously infused into the duodenum.

Various non-absorbable markers have been used, the most common being polyethylene glycol and phenol red (35,237). The marker is infused into the duodenum by means of a transpyloric tube, and the concentration of the dye which refluxes into the stomach is estimated from gastric aspirates. There are some important disadvantages with this method. Firstly, gastric intubation, irrespective of how gently it is performed, may cause motility disturbances and promote reflux. Secondly, this method does not give any information about the emptying time of the refluxed material, a factor which in terms of pathophysiology is of considerable importance. Thirdly, it does not give any information about the cytotoxic agents in the refluxed contents.

4.2.2 Detection of duodenal contents in the stomach

Bile was the first component to be used as an indicator of D/G reflux. Initially, assessment was inaccurate and subjective, and was based on the gross appearance of bile in gastric aspirates or evidence of bile on endoscopy (238). Later, more accurate quantitative measurements of bile acids in gastric aspirates

were performed by means of paper chromatography (239). Other duodenal components, such as trypsin, bilirubin and lysolecithin were used for the assessment of reflux (24,27,35,136,169). The disadvantages of these techniques include lack of information about the emptying rate of the refluxed material, the complicated chromatographic or biochemical techniques required, and the necessity for gastric intubation. Furthermore, the refluxed material may not contain any bile products, if at the time of reflux no bile has been discharged into the duodenum (35). Despite the above disadvantages, these methods may give information about the concentration of cytotoxic substances, such as bile acids and lysolecithin, in the refluxed material. Pathophysiologically, it is more important to know the concentration of the cytotoxic agents, than the amount of duodenal reflux.

4.2.3 Radiological methods

The first radiological technique used for D/G reflux studies was intraduodenal infusion of barium suspension. Reflux was assessed by means of continuous screening (42,240). However, this method is subjective and therefore inaccurate. Furthermore, the use of a transpyloric tube may provoke reflux, and finally, screening cannot be prolonged due to the danger of irradiation. In another radiological method, using a T-tube in the common bile duct, sodium diatrozate is infused into the tube, and its presence in the stomach is detected by cineradiography (241). With this

method there is still the radiation problem and the inability to measure the actual amount of bile reflux.

More recent techniques using isotopes have solved many problems. Various hepatobiliary markers, such as ^{14}C-chenodeoxycholic acid and $^{99}Tc^{m}$-EHIDA, have been used (45,242,243). The radioactive tracer is injected intravenously and its distribution in the biliary system and the upper gastrointestinal tract is detected with a gamma camera. The recording can be performed continuously or at intervals. With this technique there is no necessity for gastroduodenal intubation, and information about the gastric emptying time of the refluxed material can be obtained. However, there are also several problems regarding this technique. Firstly, small amounts of reflux are difficult to detect. Secondly, superimposition of jejunal loops on the stomach may give false positive results. Thirdly, there is always some retention of the tracer in the gall bladder. Cholecystokinin injection to eliminate the sequestrated tracer is not advisable since it affects gastroduodenal motility. Finally, it again does not give any information about the concentration of cytotoxic substances.

4.3 The effect of secretin on duodenogastric reflux

Very few studies investigating the effect of secretin on duodenogastric reflux have been published. Wormsley (35) recorded

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little or no reflux in normal subjects or subjects with duodenal ulcer, during secretin infusion (GIH Laboratory). There are some problems regarding this study. Firstly, the author used asymptomatic subjects as normal controls, without obtaining gastric biopsies. It is well known that subjects with histological gastritis may be asymptomatic. Secondly, the reflux was measured only after secretin infusion and not before. Had this been done, each patient could have acted as his/her own control, and this would have added to the value of the study.

Fisher and Cohen (37) and Geller and Petrenko (78), using manometric and electrical activity studies, suggested that secretin prevented reflux in normal and duodenal ulcer subjects. They reached this conclusion after finding that the pyloric ring pressure increased during secretin stimulation. However, during secretin stimulation there is a concomitant decrease in the intraluminal pressure of the stomach and duodenum (78). It has been shown that reflux depended more on the pressure gradient on either side of the pylorus, than on the diameter of the pyloric ring itself (73,74).

Ferreira (244), using isotopic techniques, found an increased reflux in normal dogs after secretin (Boots) infusions.

4.4 The effect of vagotomy on duodenogastric reflux

4.4.1 TV with pyloroplasty and reflux

It is widely accepted that TV with pyloroplasty is associated with increased reflux, due to destruction of the pyloric sphincter (34,43,65,69,245), but not all authors are in agreement. Hollinger et al (246), using ^{99}Tc-hepatobida found no characteristic reflux pattern after TV with pyloroplasty. The small number of cases reported by these authors, must be taken into account when considering their results.

Kilby (72) reported that TV with pyloroplasty was not associated with increased reflux. He went so far as to suggest that the operation may actually prevent reflux in two ways. He postulated that the pyloroplasty destroyed the pumping effect of the duodenal cap which was responsible for the reflux (3.1.1), and that the vagotomy caused rapid emptying of any refluxed fluid material. James et al (236) used the same methods and reported similar results. There is a serious criticism regarding the techniques used in the last two studies. The reflux was estimated by intubation of the duodenum and introduction of contrast media. The problem of the reliability of the transpyloric tube has been discussed, and the value of the assessment of the amount of reflux by simply observing refluxing barium is open to question.

Keighley et al (267), in an uncontrolled clinical study, found that many patients with TV and pyloroplasty had no increased reflux.

4.4.2 HSV and reflux

It is generally accepted that HSV is not associated with increased reflux (69,245,247). Dewar et al (245,247) reported that HSV decreased reflux in patients with gastric or duodenal ulcer. The explanation given was that HSV caused an increase in intragastric pressure and a faster emptying of liquids. These changes may prevent reflux or promote fast empyting of any refluxed material. An alternative explanation may simply be that HSV allowed the ulcer to heal without interfering with antral innervation, so that a normal physiological state was restored. It would have been of additional value to know that tests to establish the completeness of the HSV had been carried out, as well as tests to establish that the antrum was in fact normally innervated.

4.5 Cholecystectomy and bile reflux

Very little work has been done in this field. The existing studies are mainly clinical and uncontrolled, and the conclusions are conflicting. To the best of the author's knowledge, no experimental controlled studies have been reported.

Kalima and Sjöberg (41), using retrospective clinical data, found that patients who had undergone cholecystectomy or had a non-functioning gall bladder, had a higher incidence of bile reflux gastritis. It was not a controlled study and no measure-

ments of bile reflux were made. The combination of bile stained fluid in the stomach during endoscopy and histological gastritis was considered to be diagnostic of bile gastritis.

Warshaw (44) performed endoscopy and biopsies on 10 patients with symptoms of chronic gastritis, which appeared at various periods after cholecystectomy. He found histological gastritis in all patients. The author suggested that this might be the result of increased bile reflux. However, the study was made on a small number of selected patients, no measurement of bile reflux was performed, and there was no histological assessment of the stomach before cholecystectomy.

Mackie et al (45), using $^{99}Tc^{m}$-EHIDA, measured bile reflux in 22 patients who had previously undergone a cholecystectomy or had a non-functioning gall bladder. They found increased reflux in half of their patients, and suggested that these two conditions were factors that predisposed to bile reflux. A serious consideration in regard to this study is the lack of information about bile reflux before cholecystectomy, or before the gall bladder became non-functioning.

Buxbaum (248) found that 51% of 107 cases with bile gastritis had had a previous cholecystectomy, while only 14% had had no previous biliary or gastric surgery. The author estimated that 17% of the patients with upper gastrointestinal symptoms and previous cholecystectomy, had severe bile reflux. However, the

subjective endoscopic method used for the diagnosis of bile gastritis (bile stained mucosa) must be taken into account when considering these results.

The findings of Capper et al (46) in an uncontrolled study suggested that the presence of gall stones predisposed to an increased bile reflux.

As indicated previously, Earlam (47) suggested that increased bile reflux associated with gall bladder disease, usually reverted to normal after a cholecystectomy. In another study (48), the same author concluded that a non-functioning gall bladder was associated with decreased reflux. The author went on to postulate that in the presence of a non-functioning gall bladder or after-cholecystectomy, bile flowed slowly into the duodenum in a dilute non-concentrated form, therefore bile reflux was less. The study was clinical, uncontrolled and the diagnosis of reflux was based on clinical symptoms, with no objective measurement of reflux.

Lee (49) suggested that cholecystectomy did not increase the incidence of bile gastritis. The author's conclusions were based on a study where the frequency of cholecystectomy was not found to be higher in patients with gastric ulcer or gastritis when compared with subjects with a normal stomach. The diagnosis of gastritis was mainly done endoscopically with no histological assessment. It is well known that macroscopically normal stomach may have extensive histological gastritis (32,211).

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Taylor et al (43,249), using uncontrolled clinical data, suggested that the combination of TV, pyloroplasty and cholecystectomy, was associated with a higher incidence of gastritis than TV with pyloroplasty alone.

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