

Prevention of cholelithiasis: intervention based on risk factors

Cholesterol gallstone disease is encountered by every doctor in practice. Can we do anything in the 1980s to reduce the prevalence?

C Noel Williams, Reshat Memiche

The main factor that seems to predispose an individual to cholesterol-saturated bile is excess weight.

In the past decade there has been a tremendous surge of new knowledge concerning the pathogenesis of cholesterol gallstones. The current theory is that cholesterol saturation of bile occurs prior to cholesterol gallstone formation. To illustrate this, the risk factors for the two conditions are presented separately below.

Risk factors for cholesterol-saturated bile

Many factors cause a predisposition to cholesterol-saturated bile (Table 1).

Cultural predisposition: certain ethnic groups are susceptible; for example, the women of the Micmac Indian population of Nova Scotia who do not have gallstones have a high prevalence of cholesterol-saturated bile (54.3%; Table 2).

Puberty: there is an increased incidence of cholesterol-saturated bile among females at puberty.

Familial: 50% of sisters of patients with cholesterol gallstones have been found to have cholesterol-saturated bile.

Obesity: the main factor that seems to predispose an individual to cholesterol-saturated bile is excess weight. This is exemplified in the condition of morbid obesity in which, typically, the average molar percent cholesterol is 13 compared to the normal value of 6.6 (all with cholesterol-saturated bile of the labile type). This predisposition is also prevalent in individuals who are only 20–50% above ideal body weight. In normal-weight women, relative obesity, represented by the body mass index, correlates significantly with the ranked lithogenic index.

Fasting is known to be associated with increased cholesterol saturation of bile. There is a sex difference in this regard; healthy women appear to tolerate 16 hours of fasting more poorly than men, with a significantly greater proportion manifesting lithogenic bile at this time (54.5% versus 36.8%).

C Noel Williams FRCP(C) FACP FACG is a Professor of Medicine and Head of the Division of Gastroenterology at Dalhousie University. He qualified from the University of Leeds, UK, and trained in internal medicine at Leeds University and Dalhousie with specialty training in gastroenterology at the University of Pennsylvania, Philadelphia. His research interests include cholesterol gallstones and liver diseases.

Reshat Memiche MD FRCP(C) is a final-year gastrointestinal resident at Dalhousie University. He qualified from the University of Istanbul, Turkey and trained in internal medicine at Dalhousie University, Halifax, Nova Scotia.

Surgical intervention in pancreatic disease

Any patient with an atypical presentation of peptic ulcer disease should probably have a peripheral fasting gastrin level measured.

gastrinemic range with secretin in true gastrinomas.

Treatment: there is a complete lack of agreement as to the best treatment of a gastrinoma once it has been diagnosed. Some suggest that an apparently single primary tumor should be excised surgically and the patient followed for recurrence of high gastrin levels. If multiple tumors or metastases are present, some advise attempting to remove functioning endocrine tissue by debulking. Others suggest the use of one of the very potent newer agents which can switch off gastric acid secretion, such as high doses of an H₂ blocker, or omeprazole which interferes with the primary proton pump in the parietal cell. These agents control the symptoms of peptic ulcer disease, and some patients so treated have survived in relative comfort for many years.

A third approach favored by some involves resection of the target organ, i.e. total gastrectomy. The high circulating gastrin levels therefore continue, but have minimal clinical effects. Although this procedure has been relatively successful in the past, it appears to be losing favor.

Newer therapeutic approaches include use of somatostatin analogs which hold great promise for controlling the hyperacidity and perhaps even tumor growth. Chemotherapy also has a palliative role.

Transplantation

Exocrine secretions of the pancreas can be totally replaced by oral pancreatic enzyme preparations; thus, requirement

for exocrine secretory function does not serve as an indication for pancreatic transplantation.

Lack of endocrine secretions from the pancreatic islets are the primary reason for attempting pancreatic transplantation in man. So far, results from transplantation of islets alone has not been particularly encouraging.

Transplantation of the whole pancreas has been attempted, most commonly in severe diabetics who require renal transplantation. Simultaneous transplantation of the whole pancreas or a segment of the gland has resulted in reduced or no requirements for insulin. However, long-term follow-up of these patients is needed. □

MEDICINE North America cross references

Acute and chronic pancreatitis: 3rd series 20, Render KC, Van Rosendaal GMA.

Further reading

- Bornman PC, Harries-Jones EP, Tobia R, *et al.* Prospective controlled trial of transhepatic biliary endoprosthesis versus bypass surgery for incurable carcinoma of head of pancreas. *Lancet* 1986; i:69-71.
- Carter DC. Pancreatic endocrine tumours. *Br Med J* 1987; 294:593-94.
- Corry RJ, Nghiem DD, Schulak JA, *et al.* Surgical treatment of diabetic nephropathy with simultaneous pancreatic duodenal and renal transplantation. *Surg Gyn Obstet* 1986; 162:547-55.
- Delhaye M, Engelholm L, Cremer M. Pancreas divisum: congenital anatomic variant or anomaly? *Gastroenterology* 1985; 89:951-8.
- Mayer AD, McMahon MJ, Corfield AP, *et al.* Controlled clinical trial of peritoneal lavage for the treatment of severe acute pancreatitis. *New Engl J Med* 1985; 312:399-404.
- Stone HH, Fabian TC, Sattiani B, *et al.* Experiences in the management of pancreatic trauma. *J Trauma* 1981; 21:257-261.

Prevention of cholelithiasis: intervention based on risk factors



Figure 1a This oral cholecystogram from a patient with recent gastric bypass operation shows multiple radiolucent gallstones which 'float'. A cholecystogram prior to surgery was normal.



Figure 1b The gallstones have dissolved after 3 months of chenodeoxycholic acid treatment.

Table 3 — Diet for hastening gallstone dissolution and possible prevention

- Reduce weight to ideal body weight
- Maintain at ideal body weight
- Regular meals and late-night snack with sufficient protein or fat to contract the gallbladder
- Reduce duration of overnight fast
- More protein, (20 – 25% of total)
- Less carbohydrate, (50% of total)
- Less refined carbohydrate, (30% of total)
- More dietary fiber to 30 grams

In contrast, patients with prior cholecystectomy and both symptomatic and asymptomatic individuals have different reported factors, as would be expected. These include:

- obesity
- relatives with cholecystectomy
- reduced intake of protein (or calcium)
- duration of oral contraceptive use.

When assessed prospectively, a diet with higher protein intake (22%) than normal (15%) is associated with a lower cholesterol content in bile. In contrast, a diet containing a high proportion of both carbohydrate and refined carbohydrate increases bile cholesterol content up to

saturation and beyond. Virtually every study has noted obesity, relative obesity and morbid obesity as the most significant risk factors for the formation of cholesterol-saturated bile and then gallstones. Fasting promotes the formation of cholesterol-saturated bile.

Using these facts, it is possible to define a diet which minimizes bile cholesterol and which does indeed hasten gallstone dissolution (Table 3).

The diet has been used in patients with cholesterol gallstones who were taking oral medication to dissolve their gallstones (chenodeoxycholic acid) and, in contrast with a similar group eating

Prevention of cholelithiasis

Table 4 — Effect of diet and chenodeoxycholic acid on gallstone dissolution

Groups*	A*	B*
● Randomized number	28	26
● Withdrawals	4	5
● Number remaining	19F 5M	17F 4M
● Complete dissolution	5F 4M	12F 2M
● % dissolved	37.5	66.7
● Time to mean dissolution (months)	16	9

F = female, M = male

*Group A maintained their regular diet, and Group B the modified diet, described in Table 3. The dose of chenodeoxycholic acid was 15 mg/kg body wt/day taken at bedtime.

their regular diet, the first group's gallstones were dissolved more quickly and at a greater frequency (Table 4).

The question now remains as to whether this diet, when continued, can prevent gallstones from recurring. (The current rate is 50% recurrence after five years.)

Ursodeoxycholic acid may be a useful preventative in high-risk circumstances such as after jejunio-ileal bypass.

Preventative measures

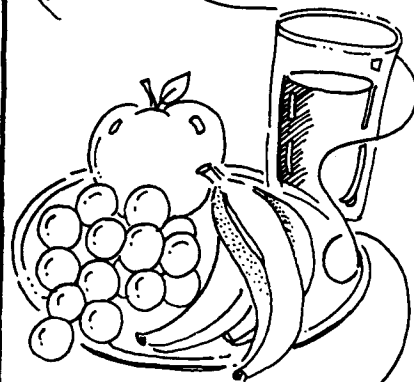
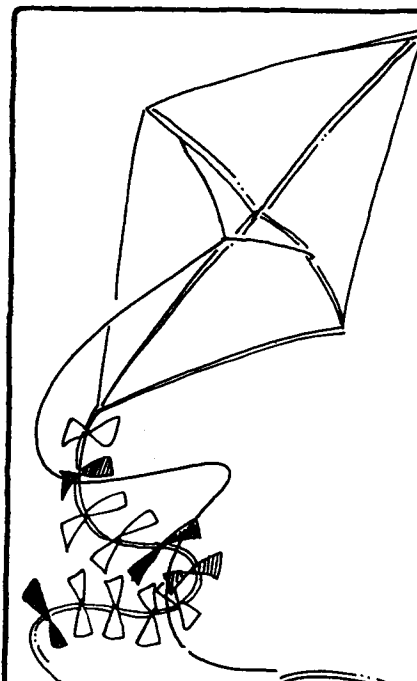
Several general measures can be taken:

- reduction and maintenance of ideal body weight
- avoidance of repetitive, prolonged fasting
- use of an oral contraceptive of low estrogen content or an alternate method of birth control
- reduction of bile cholesterol saturation by changes in diet.

Diet

Diet alone may be useful in:

- individuals at medium and high risk
- patients whose gallstones have been dissolved by medication (especially if weight reduction has occurred and is being maintained)



Oh what a feeling!

PARTICIPATION 