

and there appears to be no clear distinction, either in the severity or in the duration of the attacks, which indicates the precise cause of the pain. Probably the pain may arise from one or more of several causes in a variety of sites in the biliary tract.

Judging from the data from 50 case histories of renal colic, the pattern of pain is often similar, but it is also common to have severe background pain, upon which bouts of even greater intensity are superimposed. In renal colic, infection can usually be excluded as a factor by examination of the urine. It is probable, therefore, that high pressure in the renal tract or smooth-muscle spasm, or a combination of these two, is responsible for the pain. That obstruction is present is strongly suggested by the fact that an I.V.P. during the attacks shows increased density of the kidney on the affected side with delay in the pyelogram. Evidence that a high pressure occurs proximal to the obstruction is provided by a recent experience. A man aged 49 developed typical right renal colic: an intravenous pyelogram was made about 45 minutes after the onset, when the pain was at its height. The first films showed a normal left pyelogram, an increase in the density of the right kidney, with a small stone at the lower end of the ureter, and later a delayed normal right pyelogram. A radiograph taken a few minutes later showed that the dye had burst out of the renal pelvis as a large cloud in the peripelvic tissues. Thirty-six hours after this there was

right shoulder-tip pain, made worse by breathing, which persisted for 24 hours and then subsided without further incident. Retrograde pyelography a few days after the onset showed a normal renal pelvis, and the stone passed uneventfully.

Summary

A clinical study is made of the time/intensity pattern of pain in biliary and in renal colic. In biliary colic the pain rises to a plateau and does not usually show fluctuations in severity. Renal colic often has a similar pattern, but nearly half the patients noted some fluctuations in severity during an attack. Possible causes of these pains are discussed. Intermittent pain such as is implied by the word "colic" is rare.

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GALL-BLADDER DYSPEPSIA

BY

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The purpose of this inquiry was to examine the relationship between dyspepsia and gall-bladder disease. Patients who suffer from biliary colic or acute cholecystitis frequently deny a previous history of indigestion (Colp *et al.*, 1935). Moreover, it is unfortunately the experience of many practitioners that patients are often not relieved of various types of chronic dyspepsia by cholecystectomy. Yet gaseous eructation, flatulence, heaviness, epigastric pains of varying intensity, and heartburn were described by Moynihan (1908) as "the inaugural symptoms of gall-bladder disease." This view was shared by many well-known medical men, including Mayo Robson, Bland-Sutton, and Mayo, and it is expressed in numerous textbooks. However, the literature contains conflicting opinions on the significance of so-called "gall-bladder dyspepsia." For instance, Bockus and Dozzi (1946) state: "We have become more and more convinced that dyspeptic symptoms occurring day after day are rarely due to uncomplicated cholelithiasis." Alvarez (1943) and Ivy *et al.* (1950) believe that such symptoms are due usually to functional disease of the gastro-intestinal tract, and are not connected with the gall-bladder.

The scheme of this investigation was to record the histories from a group of women who were then submitted to routine cholecystography. It was thought that in this way the relationship between various types of dyspepsia and the presence of gall-stones could be examined without bias.

Choice of Subjects

The inquiry was conducted within a general practice of about 3,000 patients in a densely populated urban area of whom approximately half were women. The survey was restricted to women aged 50-70. The reasons for this

choice were: (1) it was desirable to include within the survey a reasonable proportion of subjects with gall-stones; (2) gall-stones are known to be commoner in women than in men in the proportion of 3:2 (Bockus); and (3) the frequency of gall-stones rises with advancing years: over the age of 50 about one woman in five in this country has gall-stones (Bockus).

At the outset it was decided to exclude: (1) Eight women who, because of illness, were unable to attend the hospital for x-ray examination. Four of these were in mental hospitals; one was blind, deaf, and dumb; one had inoperable carcinoma; and two were crippled by rheumatoid arthritis. (2) Five women upon whom cholecystectomy had been performed. These were excluded as it would not be possible to obtain an unbiased history, but they were later interviewed to determine as far as was possible the reason for operation and the effect it had had on pre-operative symptoms.

With these exceptions, all the women aged 50-70 were circularized by letter asking if they would co-operate in an investigation into indigestion. A second letter was sent three months later to those who did not reply. If there was still no response the address was visited. Information extracted from the N.H.S. card included: (1) Name, age, and address; (2) distance of the home from the surgery; (3) average annual surgery attendance for the previous three years; and (4) previous complaint of dyspepsia.

Among the 204 women who were circularized 142 (70%) were interviewed and x-rayed, while the other 62 (30%) refused to co-operate. No difference was demonstrated between these two groups when compared by age, previous complaint of dyspepsia to the practitioner, and distance from the home to the surgery (Table I). Annual surgery

attendances were, however, significantly greater among the women who agreed to take part.

TABLE I.—Analysis of Sample Selected for Survey. Comparison of Group Interviewed and X-rayed With Those That Refused to Co-operate Shows a Significant Difference in the Annual Surgery Attendance

	Total Population		Interviewed and X-rayed		Refusals		Value for P
	No.	%	No.	%	No.	%	
Total	204	100	142	100	62	100	
Age in years:							
50-54	57	28	41	29	16	26	$\chi^2 = 0.89$
55-59	66	32	43	30	23	37	
60-64	41	20	29	20.5	12	19	
65-69	40	20	29	20.5	11	18	
Distance from surgery:							
Less than 1/2 mile	148	72	98	69	50	80	$\chi^2 = 2.73$
1/2-1 mile	28	14	25	18	3	5.5	
Greater than 1 mile	28	14	19	13	9	14.5	
Annual surgery attendances:							
0-4	134	65.5	86	60.5	48		$\chi^2 = 10.2$
5-10	50	24.5	36	25.5	14	77	
More than 10	14	7	14	10	0	23	
Unknown	6	3	6	4	0		
Previous complaints of dyspepsia:	30	14.8	21	14.8	9	14.5	

Interview

Those who were interviewed were asked a standardized form and sequence of questions. These covered:

Personal Data.—Marital status, number of children, and occupation of the head of the household.

Food Intolerance.—Nature and duration of symptoms. Care was taken to distinguish between food intolerance and avoidance of particular food on medical or other advice. Symptoms of intolerance could not be analysed for rhythm or periodicity since they were usually avoided by omitting the particular item from the diet. Severity was also not assessed.

Dyspepsia.—The subject's account was prompted when necessary in order to obtain information about abdominal pain, fullness or discomfort, flatulence, nausea and vomiting, heartburn, acid regurgitation, and waterbrash. Except when these symptoms could be attributed to a particular item in the diet, they were analysed for the time they had been present, the length of remission, the duration and severity of attacks, the time of occurrence, and factors influencing the symptoms. Pain was analysed further in respect of site, extent, radiation, character, mode of onset, and constancy.

Symptoms were allotted to one of three grades of severity according to the following criteria: *mild*—the doctor had not been consulted and no remedy had been tried; *moderate*—some action had been taken, but the symptom had not prevented normal activities; *severe*—the symptom had interfered with work.

Cholecystography

Each interviewed subject was later x-rayed. Iopanoic acid ("telepaque") in a dose of six 0.5-g. tablets had been taken orally 12 hours earlier and three hours after the last meal.

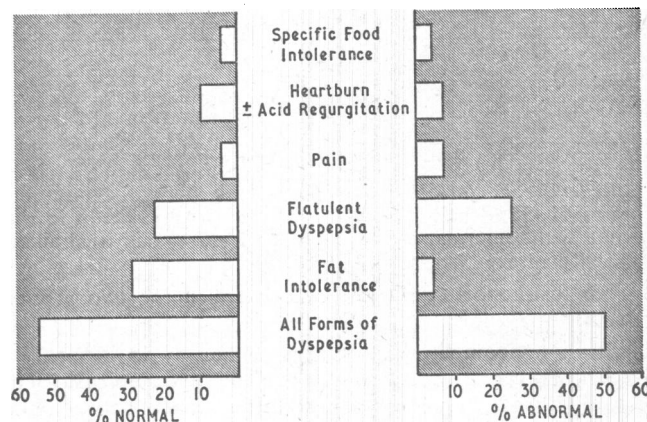
Eighteen women were shown to have gall-stones and in two of these concentration of dye was very poor. In another six women concentration of iopanoic acid in the gall-bladder did not occur or was very poor, but opaque medium in the large gut proved that the dye had been taken. No gall-stones could be seen. Of 31 patients with similar cholecystograms reported by Gordon (1953) 26 (84%) were

found at operation to have gall-stones. In the present series, therefore, these six women were added to the 18 with definite evidence of gall-stones to make a total of 24 for comparison with the 118 women who had normal cholecystograms. In each subject radiographs had been taken in the lying position. In only 15 cases were additional films taken in the erect position. None of these showed stones. Greater accuracy might have been achieved if erect films had always been taken (Akerlund, 1938).

Comparison of Subjects with Normal and Abnormal Cholecystograms

Personal Data.—In respect of age, social grading (Registrar-General's classification), marital status, and number of children there was no significant difference between the two groups.

Dyspepsia.—Dyspepsia was noted in 63 (53%) of those with normal cholecystograms and in 12 (50%) of those with abnormal cholecystograms. In the Chart it can be seen that the distribution of several dyspeptic symptoms is fairly even among women with normal or diseased gall-bladders. Particular mention is made of fat-intolerance and flatulence because these two symptoms in particular have often been supposed to be characteristic of gall-bladder disease.



Frequency of symptoms in subjects with normal and abnormal cholecystograms.

Intolerance to Fat.—Without exception women with intolerance to fat specified greasy food and fried food. There was no intolerance to other forms of fat. Symptoms which could be provoked or aggravated in this way were mentioned by 33 (28%) in the group with normal cholecystograms compared with 1 (4%) in the abnormal x-ray group. Among the former, four had avoided fat on medical advice, but had previously noticed intolerance.

Flatulent Dyspepsia.—This consisted of abdominal discomfort or a sensation of fullness associated with belching. It occurred in 26 (22%) of those with normal cholecystograms and in 6 (25%) of the abnormal group.

The further analysis of symptoms is given below:

Length of History.—Among those with normal cholecystograms who suffered symptoms the great majority had complained for more than three years and only 4 (16%) had had symptoms for less than a year. Among those with abnormal cholecystograms who also had symptoms all had suffered for three or more years.

Recurrence of Symptoms.—On the basis of the frequency with which symptoms occurred it was possible to recognize two groups. One group had experienced dyspepsia daily without remission, and comprised 27 (23%) of those with normal compared with 2 (8%) of those with abnormal cholecystograms.

The other group had short attacks with remissions of a few weeks or sometimes months and comprised 36 (30.5%) and 10 (42%) of the two groups respectively (Table II). The frequency with which symptoms were provoked by greasy food depended upon how rigidly such food was omitted from the diet. They were in all cases intermittent.

TABLE II.—Frequency of Symptoms in Subjects of Normal and Abnormal Groups. They Are More Commonly Intermittent in the Abnormal Cholecystogram Group, but the Difference is Not Significant at the 2% Level

Recurrence of Symptoms	Whole Sample	Women with Normal Cholecystograms	Women with Abnormal Cholecystograms	Value for P
Daily	29 (21%)	27 (23.0%)	2 (8%)	<0.05 ($\chi^2=3.75$)
Intermittent	46 (32.5%)	36 (30.5%)	10 (42%)	

Duration of Attacks of Dyspepsia.—Attacks of dyspepsia were prolonged for more than half an hour in 21 (18%) of the normal group compared with 5 (21%) of the abnormal. The remainder in both groups described their attacks as brief.

Severity of Symptoms.—Table III shows that the severity of symptoms is greater in those with normal cholecystograms. The difference is not significant at the 2% level.

TABLE III.—Severity of Symptoms, Other Than Those Induced by Fat, in Both Groups and in Whole Sample. Severe Symptoms Occurred Only in the Normal Cholecystogram Group

	Severity of All but Fat-induced Symptoms			Value for P
	Mild	Moderate	Severe	
Women with abnormal cholecystograms (24)	11 (46%)	1 (4%)	0	<0.05 ($\chi^2=6.0$)
Women with normal cholecystograms (108)*	29 (27%)	20 (19%)	3 (3%)	
Whole sample*	40 (30.5%)	21 (16%)	2 (3%)	

* Excluding 10 subjects who had fat-induced symptoms alone.

Relieving Factors.—Of the group with normal cholecystograms 41 (35%) had tried alkali, 39 (33%) with relief. In the group with abnormal cholecystograms 6 (25%) had tried alkali and all had experienced relief of symptoms.

No distinction could be made between the two groups on this analysis.

Pain.—A complaint of pain was made by 13 women, of whom two had gall-stones. The site was epigastric in seven, retrosternal in four, and in the back between the scapulae in two. Two were investigated and shown to have duodenal ulcers, and in seven, including the two with gall-stones, the accounts suggested peptic ulcer. In another four, epigastric pain was attributed to eating and was relieved by alkali, but there was no rhythm or periodicity.

Women Previously Treated by Cholecystectomy

Of the five women whose gall-bladders had been removed three had been operated upon because of biliary colic and obstructive jaundice. Two had never experienced dyspepsia; the third had developed severe heartburn after operation and was later found to have a para-oesophageal hernia. The fourth woman had been operated upon 32 years earlier and could not recall the reason for operation. For several years up to the present time she had complained of flatulent dyspepsia. In the remaining patient cholecystectomy had been carried out for chronic dyspepsia, including flatulence and intolerance to greasy food. These symptoms persisted post-operatively and she was later shown to have a hiatus hernia and duodenal ulcer.

Discussion

The survey described in this paper was planned in such a way that neither the patient nor the doctor could know of the presence or absence of stones when the history of

dyspepsia was obtained. It was believed that in this way there would be no bias which might favour the recollection of symptoms by the patient or which might influence the interviewer in extracting the history. The information would not differ greatly, therefore, from that obtained in the course of the usual history-taking.

The results of this investigation do not suggest that chronic dyspepsia can be attributed to gall-stones. Thus: (1) The frequency of indigestion in women with radiologically normal gall-bladders was the same as in women in whom the gall-bladders showed stones or poor concentration of dye. (2) Half of those with stones had no symptoms. (3) Those with symptoms who also had gall-stones were not distinguishable by any particular form or by the severity of their dyspepsia. (Symptoms were more commonly intermittent in those with abnormal cholecystograms, but because of the small numbers with stones this difference could be ascribed to chance.)

On the contrary, therefore, the evidence indicates that the association of dyspepsia and gall-stones is purely fortuitous.

An association between gall-stones and dyspeptic symptoms has long been disputed. Whereas Moynihan (1908) denied the occurrence of symptomless stones, Kehr (1901) estimated that only 5% of 433 patients found to have gall-stones at laparotomy had complained of symptoms. Similarly, Barker (1920) found that 90% of gall-stones discovered at necropsy had been unsuspected during life. He attributed this to failure by doctors to recognize that "certain digestive disturbances, often lasting many years," are due to gall-stones. In another necropsy study based on 1,027 cases reported to have gall-stones Robertson (1945) found no record of symptoms in 61%. Colp *et al.* (1935, 1936) estimated that 25% of patients with acute cholecystitis had been symptom-free prior to the attack. In 50 women described by Truesdell (1944) gall-stones had been unsuspected before their discovery at laparotomy. When, however, the histories of the patients were "supplemented" post-operatively only two could with certainty be established as symptomless. No control series was described. Mayo (1911) believed likewise that symptoms of gall-bladder disease may be unrecognized and that after stones have been discovered symptoms can be elicited. Many of these series are retrospective and do not take into account the frequency of these symptoms in the general population. No series could be found in the literature in which a careful inquiry had been made before the gall-stones were sought.

The incidence of chronic dyspepsia in 63 (53%) out of 118 of the women with normal cholecystograms in this series tallies with that of 47.5% found by Rivers and Ferreira (1938) in 3,000 patients in the same age-group, but of both sexes. It is probable that this high incidence of dyspepsia occurs also among patients with gall-stones, as was found in the small series described here. Although it is possible that the higher surgery-attendance rate of the interviewed group influenced the results in the present survey, it was noted that the frequency with which the complaint of dyspepsia was entered on the N.H.S. card was no greater than in the un-interviewed group.

In practice, therefore, a history of chronic dyspepsia in women of this age-group should not be taken to indicate gall-bladder disease or to suggest the presence of gall-stones. It would clearly be unreasonable to ascribe such symptoms to gall-stones, even if these are demonstrated, and unjustifiable to regard chronic dyspepsia as an indication for cholecystectomy.

Summary

An attempt has been made to determine what association, if any, exists between chronic dyspepsia and the presence of gall-stones, determined radiologically in women aged 50–70 years.

The survey was conducted in a general practice to avoid the selection inevitable in a hospital population.

The women were interviewed before being x-rayed, so that their histories were not biased by any knowledge of whether gall-stones were present or not.

A history of dyspepsia was obtained from 12 (50%) out of 24 subjects with gall-bladder disease. Of those with normal cholecystograms 63 (53%) out of 118 had similar symptoms.

The dyspepsia suffered by those with gall-stones was not distinguishable from that experienced by those with normal gall-bladders.

It is concluded that among women aged between 50 and 70 the occurrence of chronic dyspepsia and gall-bladder disease is coincidental. These symptoms cannot assist in diagnosis of gall-bladder disease and should not influence its treatment.

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INCIDENCE OF HYPOMAGNESAEMIA IN INTESTINAL MALABSORPTION

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Electrolyte deficiencies are a common complication of intestinal malabsorption. However, although subnormal serum levels of sodium, potassium, and calcium frequently occur, magnesium deficiency has been described only on rare occasions until recently. Single cases with subnormal serum magnesium levels have been reported by several groups of workers (Card and Marks, 1958; Fletcher, Henly, Sammons, and Squire, 1960; Hanna, Harrison, MacIntyre, and Fraser, 1960; Vallee, Wacker, and Ulmer, 1960; MacIntyre, Hanna, Booth, and Read, 1961; Goldman, Van Fossan, and Baird, 1962), but the incidence of magnesium deficiency in patients with intestinal malabsorption and its clinical significance have not been studied hitherto.

In this paper we report the serum magnesium concentrations in 42 patients suffering from intestinal malabsorption due to a variety of causes. The incidence of subnormal serum magnesium levels and their relation to the concentrations of other electrolytes and to faecal fat excretion are described. Balance studies and responses to treatment are also given.

Materials and Methods

Chemical Estimations.—Magnesium was measured by the method described by Alcock, MacIntyre, and Radde (1960), calcium by the method of MacIntyre (1961), and sodium and potassium as described by King and Wootton (1956). Faecal fat was estimated by the method of Van der Kamer (1958).

Balance Studies.—Balance studies were carried out in a metabolic unit and were usually made during successive

three-day periods after an initial equilibration period of five days. Chromium sesquioxide in oral doses of 0.5 g. thrice daily was used as a marker (Whitby and Lang, 1960). The chromium content of stools was estimated by flame spectrophotometer after extraction of the chromium into 4-methyl-2-pentanone (H. Anstell and J. Daley, unpublished observations).

Patients Studied.—Observations were made on 24 patients suffering from idiopathic steatorrhoea, on seven with steatorrhoea following partial gastrectomy, and on seven who had undergone partial resection of the small intestine or who had intestinal blind loops. There were also four other patients with steatorrhoea associated with intestinal lymphectasia (1), Whipple's disease (1), or chronic biliary obstruction (2).

Serum Magnesium Levels and Concentrations of Ca⁺⁺, Na⁺, and K⁺

The results of the serum magnesium estimations together with the concentrations of calcium, sodium, and potassium are shown in Fig. 1.

Idiopathic Steatorrhoea.—Ten of the 24 patients with idiopathic steatorrhoea had serum magnesium levels of less than 1.5 mEq/l., the lower limit of the normal range. In only two of these patients was the level lower than 1 mEq/l. Both of these latter patients had levels of 0.7 mEq/l. and they had strikingly low serum calcium levels in addition (3.4 and 3.9 mEq/l.). The serum calcium levels were also low in five of the other eight patients whose serum magnesium levels were subnormal; one of these, whose serum magnesium level was 1.3 mEq/l., had a serum calcium of only 2.6 mEq/l. However, subnormal serum calcium levels were also recorded in four of the remaining

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