

tests to other data collected from the clinical and administrative control of tuberculosis; (3) that the adrenaline-Pirquet test is harmless, reliable, and easily applied, and gives straightforward results; (4) that B.C.G. vaccination is harmless; it is very rarely attended by complications, and these are on the whole quite benign; (5) that if reliable information is to be obtained the follow-up of those vaccinated should be centralized both clinically and administratively.

(6) *Tuberculosis control* has benefited from the campaign in three main ways. First, it has stimulated in the public a healthy interest in tuberculosis; secondly, the age, sex, and district analyses of the results of tuberculin-testing have given us a fairly clear picture of the way tuberculous infection is affecting the community; finally, through B.C.G. vaccination we have conferred on 40% of our younger generation a degree of protection from tuberculous disease which they could not, with equal safety, have otherwise secured.

It is for the future to show us not only the duration of the immunity we have conferred but also: (1) whether in Malta, by comparing the incidence of tuberculosis before and after the present campaign, further evidence can be obtained that B.C.G. vaccination is in reality the effective preventive measure we now believe it is; and (2) whether, by comparing the incidence of tuberculosis in those vaccinated with B.C.G. and in those unvaccinated, it can be shown that B.C.G. offers efficient protection from tuberculous disease, as we now believe it does.

Summary

Between March and June, 1950, 54,328 persons in Malta were tuberculin-tested and 38,681 were vaccinated with B.C.G. The reasons for this campaign and the methods of its actuation are given.

The tuberculin-testing results are subjected to age, sex, and district analyses; while the results of vaccination, together with the local reactions seen and the complications encountered, are described.

The methods adopted for following up the campaign, such as the retesting of those vaccinated and the x-ray examination of selected groups of initially "positive" reactors, are included.

It would not have been possible to carry out this campaign but for the generosity of the I.T.C. Organization, which, in addition to sending a skilled team, supplied all the necessary equipment, tuberculin, and vaccine, and, together with the Malta Government, bore all the expenses involved. I am indebted to all who took part in the campaign and particularly to the teams so ably led by Dr. A. Weidemann, I.T.C. Chief of Mission, and his Norwegian staff. I wish to thank the Chief Government Medical Officer and his staff for their valuable administrative help; Dr. H. J. Ustvedt for his interest and advice; Miss Nordahl, of W.H.O., for her statistical work; and Miss C. Busuttill and Mr. J. R. C. Agius, of this department, for their help during the campaign and in the preparation of this paper. My thanks are also due to Professor A. C. Briffa, Chief Government Medical Officer, Malta, for permission to publish this paper.

REFERENCE

Ustvedt, H. J., and Aaonson, A. (1948). *Tidsskr. norske Lægeforen.*, 68, 69.

GALL-STONES: A CLINICAL SURVEY

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Gall-stones have been recognized as a clinical entity for several hundred years. Indeed, Robertson (1945), in an exhaustive review of the historical aspect, quotes a publication by Benevenius dated 1506 on gall-stones, very aptly entitled *On the Hidden Causes of Disease*. Although we have progressed some distance since those early days, gall-bladder disease still remains an unsatisfactory chapter, containing far too many loose ends.

Aetiology

Davidson (1944) discusses the aetiology of cholecystitis and cholelithiasis, and states that a considerable diversity of opinion exists about the relative significance of the various possible causative factors. Weiss (1944) suggested that there is probably a hereditary predisposition to cholelithiasis; the anamnesis frequently reveals that members of several generations show the disease or that several siblings suffer from it. The same writer also mentions the patient's mode of life (sedentary habits), tight garments (corsets and belts constricting the abdomen and checking the flow of bile), infectious diseases (typhoid, pneumonia), dietary indiscretions, and pregnancy—the well-known so-called predisposing factors. As an explanation Weiss suggested that there may be a hereditary disturbance of cholesterol metabolism in the gall-stone patient, but Davidson in the same year stated that there is no proof of any general metabolic defect in cholesterol metabolism, but suggested that some other factor, such as infection, is needed to bring about the precipitation of cholesterol or pigments in the form of gall-stones. It seems to be more generally agreed that a sedentary life and an unbalanced diet play an essential part. Commenting on the well-recognized high incidence of gall-stones in the middle-aged and elderly, Davidson suggests that failing function and decreased efficiency in certain essential functions of the liver and gall-bladder are also probable factors.

But more recent work on steroid metabolism tends to support the views of Weiss, that a fundamental disturbance in cholesterol metabolism may be the principal factor in gall-stone production. Hitherto unknown disturbances of steroid metabolism have recently been recognized in another quite distinct disorder, and may well prove to be of great significance in its aetiology: we refer to rheumatoid arthritis. Sommerville *et al.* (1950) demonstrated that rheumatoid arthritics of both sexes excrete an unusually high proportion of intramuscularly injected progesterone in the urine as pregnanediol, a finding supported later by Copeman *et al.* (1950).

Cholesterol is a constituent of every cell in the body; like progesterone it is a steroid, although little is known about its site of origin, function, or metabolism (Davidson, 1944). It is well known that large amounts of cholesterol are present in most gall-stones, and that the highest concentration of the steroid is to be found in the suprarenal glands. There is a known association between pregnancy and cholelithiasis (Weiss, 1944), and we also know that the sex incidence and age incidence of this disease run closely parallel with those of rheumatoid arthritis, in which abnormal steroid metabolism is known to occur. It is not, perhaps, stretching imagination too far if we press the analogy between the two diseases and suggest that abnormal steroid metabolism may be the basic factor in the lithogenous process. A virtue of this

The Canadian National Research Council is supporting investigations for devising artificial hearts, reports the division of medical research. Three workers at the Sick Children's Hospital, Toronto, have built an artificial heart, designed to shunt the blood from the heart of a child suffering from congenital heart disease while the surgeon is repairing the heart. In their preliminary work they have demonstrated that the instrument may safely be used in surgery. The council has made 10 other grants to medical scientists to investigate various phases of cardiac failure.

theory is that it would help to explain the definite clinical association of obesity, sex and age incidence, parity, and hereditary predisposition with cholelithiasis. It would appear that steroid metabolism is more likely to become unbalanced in females as a result of either pregnancy or advancing years.

Symptomatology

Mentzer (1932) observed that the clinical diagnosis of cholecystic disease is far from simple. The predominating impression gained from the average textbook account of symptoms is one of vagueness, in sharp contradistinction to the symptomatology of peptic ulcer. It was the search for a guiding star that led to the present investigation. We felt that gall-stones were being discovered too often accidentally, as the result of an investigation undertaken when everything else was negative. And the converse was only too bitterly true—normal cholecystograms in our imagined "typical history."

Jordan (1948) attempted to clarify the symptomatology by differentiating two groups of patients: (1) those with definite attacks of typical pain and associated symptoms, who remain symptom-free between attacks; and (2) those who are almost constantly disturbed by chronic dyspepsia—constipation, transient attacks of diarrhoea, migratory abdominal cramp-like pains, postprandial distension, and flatulence. These multifarious symptoms are usually grouped as "gall-bladder dyspepsia," and we have adhered to this time-honoured terminology though it is completely misleading. All that such symptoms denote is disordered alimentary function, and it is the all-too-common belief that they directly point the finger of sin at the gall-bladder. When careful investigation proves the innocence of that organ we are disappointed, if not actually annoyed; our proposed victim has eluded us, and another will not be easy to find.

It is impossible to deny that on occasion chronic disease of the gall-bladder can produce alimentary dysfunction by interference presumably with the peristaltic gradient in the stomach and bowel, on the analogy of the severe "dyspepsia" which can undoubtedly be caused by relapsing appendicular disease. But the latter syndrome is not common, and it is our firm belief that true gall-bladder dyspepsia is not common either. Cholecystectomy for gall-bladder dyspepsia is highly unfruitful: the patient loses her gall-bladder but not her symptoms. The unsuccessful results of surgery for dyspepsia without colic do not, of course, prove that the gall-bladder is not at fault, but unfortunately this organ is only a moiety of the biliary system, and some focus for reflex disturbance may well be left. And there is also the unfortunate fact that an organ long habituated to disordered function relinquishes its bad habits most reluctantly. However, our basic tenet here is that relatively few stout middle-aged women with a flatulent dyspepsia have cholecystitis, with or without gall-stones.

In an analysis of over 1,000 cases of cholelithiasis confirmed at operation, Adams and Stranahan (1947) noted that pain was the predominant symptom, being present in 93% of cases. Detailed descriptions of the colic associated with gall-stones have been published by Weiss (1944), Adams and Stranahan (1947), and McKell (1948). The present study embraces 100 cases, and we have found it helpful to define more than one type of pain associated with gall-stones. Many of our patients did not describe attacks of excruciating colic localized to the right upper abdomen and epigastrium with the typical radiation to the inferior angle of the right scapula. In 50% of our series patients described a pain, often sharply localized, in the right hypochondrium, variously described as a severe discomfort or as a particularly unpleasant aching pain. These symptoms occurred in attacks lasting from half an hour to four hours, and were often not accompanied by "gall-bladder dyspepsia," the commonest associated symptom being vomiting. Our impression was that this latter type of attack constituted a fairly precise clinical entity, particularly when seen in the classical type of patient. These people seldom had textbook biliary colic. We endeavoured, therefore, to differentiate

our material into two groups, which we labelled "major colic" and "minor colic," analogous with major and minor epilepsy. We were also impressed with the frequency with which the pain was nocturnal—a fact noted by McKell, who observed that most patients will have been awakened at night: it is not only the duodenal ulcer which awakens at night. In fact, many of our patients experienced pain only in the late evening or during the night, and were symptom-free throughout the day (see below).

Nausea and vomiting are the next most prevalent symptoms, occurring in 65% of the cases analysed by Adams and Stranahan. When faced by a patient with minor colic accompanied by gall-bladder dyspepsia it is the first duty of the clinician to determine so far as is possible whether the general dyspeptic symptoms are part and parcel of the cholecystic disease. Unfortunately, this is usually impossible, though a barium meal is often well worth while to exclude additional pathological conditions, such as peptic ulcer or hiatus hernia. Many patients with flatulent dyspepsia and vague abdominal cramps are fundamentally neurotic and constitutionally inferior, and if this type of make-up is unsuspected surgery will do little except remove gall-bladder colic and prevent complications. The "irritable colon" is a deeply rooted syndrome in these unfortunates, and is notoriously resistant to medical guile. In other words, we must be aware of what surgery can do, and accept with gratitude, and not expectation, if it does anything more.

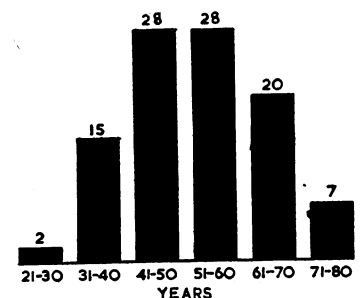
It is an obvious corollary that in the diagnosis of gall-stones little attention should be devoted to such symptoms as belching, flatulent distension, aversion to fatty food, and nausea. It is real pain which should be sought for in the history and made the cornerstone of diagnosis. We stress this because we feel that much current teaching leads the medical student astray and implants ideas which time and experience do not always remove. A good example of wrong stress in diagnosis is the so-called aversion to fatty food. We made a particular point of this in histories, and practically none of our patients had themselves noted that fats upset them; without exception they were avoiding fats, when we saw them, because they had been told to do so by their doctor, but were not noticeably better for the deprivation. Contrast this with the peptic ulcer patient, who without any expert advice rapidly learns what he can and cannot eat—and fried food is usually high on his danger list.

Jaundice occurred in 18.1% of the cases reviewed by Adams and Stranahan. These investigators are of the opinion that jaundice indicates common-duct stones in only 50% of cases; in the remainder they postulate that jaundice, when present, is due to an associated hepatitis or cholangitis.

Analysis of 100 Cases of Cholelithiasis

Our data have been collected from the records and statements of 100 patients with cholelithiasis treated at this hospital between April, 1946, and April, 1951; all were interviewed personally.

Age and Sex Incidence.—It is recognized that gall-stones may occur at any age, even in infancy. Potter (1928) reported a case in a child aged 4½ years, while Dessau (1943), reviewing the higher age groups, stated that after the age of 40 years the incidence rises rapidly. In our series the peak incidence occurred between the ages of 41 and 60 (see Chart), with a secondary peak between the ages of 61 and 70 years. These findings confirm earlier work by Dessau (1943) and Robertson (1945). Marshall and Phillips (1948) noted the close parallelism between the



Age incidence in 100 cases of cholelithiasis.

age incidence of acute cholecystitis and that of cholelithiasis, and stated that 38% of their cases were 60 or over. In our series 27% were over 60 (see Chart). With regard to sex incidence, there is general agreement that this disease shows a marked predilection for the female; our figure (Table I)

TABLE I.—Sex Incidence and Ratio of Female and Male Cases

No. of Cases	Female	Male	Ratio F: M
100	83	17	4.8:1

of nearly 5:1 in favour of the female is supported by Weiss, though it is higher than the figures of Robertson (2:1), Adams and Stranahan (3:1), and Marshall and Phillips (2:1). Over 80% of the female patients in our series gave a past history of one or more pregnancies, the average number of children in the family being three.

Familial Incidence and Diathesis.—Weiss postulates a hereditary predisposition to cholelithiasis. We are impressed by the fact that 20.8% of our cases gave a positive family history of the disease (Table II). Furthermore, in parental

TABLE II.—Analysis of Familial Incidence, Weight, and Parity in 100 Cases of Cholelithiasis

No. of Cases	Familial Incidence	Average Weight		Parous Females
		Female	Male	
100	20.8%	151 lb. (68.5 kg.)	142 lb. (64.4 kg.)	80.7%

disease the same female predilection was noticeable: in no case was there an instance of gall-bladder disease occurring in the father or grandfather of the patients concerned. Marshall (1950) states that there is an increased incidence of gall-stones in the obese. The average weight of the females in our series exceeded the average weight of the males; in health it is generally accepted that the male on the average weighs more than the female. It would thus seem that the male gall-stone patient tends to be thin or of average weight, contrary to the female. The weight of 65% of our female cases was 140 lb. (63.5 kg.) or more.

Symptomatology.—We present our data in Table III; we have compared our findings with those published by Adams and Stranahan (1947). Although the present series is much

TABLE III.—Analysis of Symptomatology of Present Series Compared with Lahey Clinic Findings

Series	No. of Cases	Major Colic	Minor Colic	Nausea or Vomiting	Gall-Bladder Dyspepsia	Jaundice	Symptomless	Nocturnal Attacks
Present	100	46	50	68	56	24	4	38
Lahey Clinic* . .	1,104	93.2%		64.9%		18%	2.3%	—

* Adams and Stranahan (1947).

smaller than that of the Lahey Clinic investigators, the results are essentially similar. Table III shows that pain was the predominant symptom, occurring as major colic in 46% of the cases and as minor colic in 50%. Nausea and vomiting occurred in 68% and gall-bladder dyspepsia in 56%. Jaundice was noted in 24%, and in 4% the stones were apparently silent. The Lahey Clinic series does not mention the frequency of nocturnal pain, though we were impressed with the fact that many of our patients had pain only at night, and only on rare occasions during the day. We cannot suggest any explanation for this.

Discussion

This survey was undertaken because we were dissatisfied with our ability to diagnose cholelithiasis. We were surprised to find how little had been published in England in the last two decades, considering that the disease is so

common. The writings and investigations which have been undertaken mostly derive from America. We have been able to confirm earlier observations on age and sex incidence, and have found the same relationships between pregnancy, obesity, and familial predisposition noted by other observers: admittedly our figures are small. We have drawn attention to certain similarities in the natural history of gall-stones and rheumatoid arthritis, and have offered the suggestion that deranged steroid metabolism may play as important a part in gall-stone formation as it has been shown to do in rheumatoid arthritis.

Our concern, however, was primarily with symptoms, and we have tried, as it were, to build up for ourselves a clinical picture anew, and clear our minds of preconceived notions. We feel satisfied that too much importance is often attached to "windy indigestion" and gall-bladder dyspepsia, so that diagnosis suffers, and have drawn attention to the value of a more careful assessment of the type of pain described by the patient. We have introduced the term "minor colic" to emphasize this; and by that term we mean a right sub-costal pain of considerable severity, occurring with sufficient frequency to be of diagnostic value. There will still, however, be the residue of cases in which the discovery of gall-stones will come as a surprise, and it is concerning this group of patients that we must be most careful to ask ourselves whether the demonstrated stones are indeed causing the symptoms. It is generally accepted, of course, that the discovery of gall-stones is an indication for their removal in the majority of cases, and we agree with this, but it should not blind us to the possibility that some other abdominal disorder altogether may be accounting for the presenting symptoms. Clinical enthusiasm may so easily make us forget that the only concern of the patient is to be freed of his symptoms; and he is entitled to expect this if he undergoes the ordeal of an operation.

Summary

The aetiology of cholelithiasis is reviewed; the possibility of an underlying disturbance of steroid metabolism is postulated as the predisposing factor.

Symptomatology is discussed, and emphasis in diagnosis placed on pain rather than flatulent dyspepsia.

One hundred proved cases of cholelithiasis are analysed from the clinical aspect.

Our thanks are due to the consultant physicians and surgeons at the General Hospital, Birkenhead, who have kindly allowed us access to their cases.

REFERENCES

- Adams, R., and Stranahan, A. (1947). *Surg. Gynec. Obstet.*, 85, 776.
 Copeman, W. S. C., et al. (1950). *British Medical Journal*, 2, 853.
 Davidson, L. S. P. (1944). *Edinb. med. J.*, 51, 184.
 Dessau, F. I. (1943). *New Engl. J. Med.*, 229, 464.
 Jordan, S. M. (1948). *Surg. Clin. N. Amer.*, 28, 613.
 McKell, D. M., jun. (1948). *Ibid.*, 28, 569.
 Marshall, S. F. (1950). *Tex. St. J. Med.*, 46, 12.
 — and Phillips, E. S. (1948). *Surg. Clin. N. Amer.*, 28, 633.
 Mentzer, S. H. (1932). *Surg. Gynec. Obstet.*, 55, 709.
 Potter, A. H. (1928). *Ibid.*, 46, 795.
 Robertson, H. E. (1945). *Gastroenterology*, 5, 345.
 Sommerville, I. F., Marrian, G. F., et al. (1950). *Lancet*, 1, 116.
 Weiss, S. (1944). *Clinical Lectures on the Gallbladder and Bile Ducts*, p. 230. Year Book Publishers, Inc., Chicago.

During 1951 the Ministry of Health lent their three portable exhibition sets on food and drink infections to 29 authorities for showing at clean food, health, and civic weeks throughout the country. The sets have now been entirely renovated and can again be borrowed by local authorities. Each shows by means of pictures and small models how food can become infected by those who handle it, and how a few simple precautions can guard against food-poisoning. A set consists of three units, each occupying approximately 24 sq. ft. There is no charge, but a local authority is expected to pay for transport and be responsible for erection, dismantling, and repacking of the exhibits. This can be done by unskilled labour under proper supervision.