

Gallstones in Young Women *

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GALLSTONES occur frequently in young women. Their symptomatology in young subjects is varied and sometimes misleading. Difficulties in diagnosis may be aggravated by reluctance to suspect gallstones prior to middle age. Recognition of their presence in early adult life permits the performance of cholecystectomy under the most favorable circumstances for reduction in surgical mortality and morbidity.

The incidence of gallstones increases with each decade of life. The principal factors contributing to fatality in biliary tract surgery are acute and complicated forms of gallbladder disease, old age, and associated cardiovascular, pulmonary, renal, or systemic disease. It is generally agreed that further significant reduction in the mortality of biliary tract surgery will be dependent upon earlier recognition of the disease and earlier extirpation of the gallbladder. In later decades the incidence in men approaches that in women, but in early adult life gallstones are preponderantly a disease of females.

To some extent, the concept of gallstones as a disease of middle or advanced age still prevails, despite the insistence of many writers that gallstone formation is common in early adult life.^{14, 15, 17, 21, 25, 34, 38, 42, 48, 54, 55} This concept is embodied in the descriptive phrase, "fair, fat and forty," which has been attributed to Deaver. While it is true that Deaver employed this phrase,¹³ it is clear that specifically he intended it to describe an advanced or later stage of the

disease, since he was also the author of the following statement:¹⁴ "It is our opinion that the great majority of gallstones are formed during early adult life, between the ages of 20 and 40." Elsewhere in the same text, he adds: "If the time of onset of the present illness were taken as the time of formation of the gallstones, it would be clearly demonstrated that cholelithiasis is a disease of early adult life and not of advanced age; and if it be remembered that even these first symptoms may not appear until years after the formation of the stone, this supposition is strengthened."

While Deaver's idea that most gallstone formation occurs prior to the age of 40 is not tenable, his emphasis on the frequency of this condition in young women is important. In his personal series of 603 cholecystectomies (1914), no less than 14.5 per cent of the group underwent operation in the third decade. Recent statistical studies of large series show a relatively small incidence of cholecystectomies in the third decade, the highest incidence occurring in the fifth and sixth decades (Table I).^{**} The principal emphasis in reports of the current era has been directed to the advanced and complicated forms of cholelithiasis which account for the bulk of the surgical mortality and morbidity. By comparison, the earliest clinical forms of the disease have received little attention. Some

^{**} Greater longevity, expanded scope of surgery in the aged, and the rarity of typhoid fever are factors which now influence the age distribution of cholecystectomy patients toward the older decades, and are partly responsible for a lower incidence of operations in the third decade in current reports.

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TABLE I. *Incidence of Cholecystectomy in Third Decade**

Author	Source	Period	Total Cases	Per Cent in 3rd Decade	Decade in Which Operation Most Frequently Performed
Deaver ¹⁴	German Hosp., Philadelphia	prior to 1914	603	14.5%	4th
Blalock ⁶	J. Hopkins, Baltimore	1889-1924	589*	12.4%	5th
Gaster ¹⁹	Cedars of Leb., Los Angeles	1940-1945	509*	4.8%	5th & 6th
Colcock & McManus ⁹	Lahey Clin., Boston	1950-1953	1356	5.2%	6th
Meagher & Campbell ²⁶	Boston City Hospital	1951-1953	296	11.5%	6th

* All series tabulated include both sexes. If figures were available for females only, the percentages of operations in the younger decades would probably be somewhat higher, since males generally undergo gallbladder operations later in life than females. The total number of patients in the series reported by Blalock has been corrected to exclude patients not having gallstones. Gaster's series was corrected to exclude patients undergoing operations for stricture, postcholecystectomy syndrome, etc.

early manifestations of gallstones are doubtless overlooked or misinterpreted, while in other instances known gallstones are left untreated because the subject is young or is experiencing little difficulty from them. Appreciation of the clinical behavior of gallstones in young women will aid in earlier diagnosis and avoidance of late complications.

In a recent series of 100 consecutive private female patients undergoing operations for cholelithiasis by the author, the incidence of cholelithiasis in the third decade was higher than in any other comparable age group. Twenty-three of 100 patients were between the ages of 21 and 30 at the time of operation (Figure 1). While this series is too small to be statistically significant, it serves to emphasize the frequency of gallstones in young women. Moreover, the members of this group exhibited clinical manifestations differing at times from the traditional concepts, leading in some instances to errors in diagnosis or delays in treatment. These 23 patients are the subject of this review.

CLINICAL DATA

Material for study comprises 100 consecutive female patients subjected to operation for cholecystic disease associated with gallstones. All operations were performed by the author on private patients. Extremes of age ranged from 22 to 85 years. There was no fatality in the series. Age at time of operation, distributed according to decades, is shown in Figure 1. The largest number of cases (23) occurred in the third decade. The next largest group was in the sixth decade. The incidence of operations by decades did not differ greatly from the third through the sixth decade, but the curve falls off sharply after age 60. It was apparent in this series, as in those of other authors, that many patients underwent cholecystectomy several years after the origin of their symptoms. Had all such patients undergone operation in the first years of their symptoms, the incidence curve for the various decades would have been displaced considerably into the younger age groups.

100 CONSECUTIVE OPERATIONS - GALLSTONES IN WOMEN Age At Operation (By Decades)

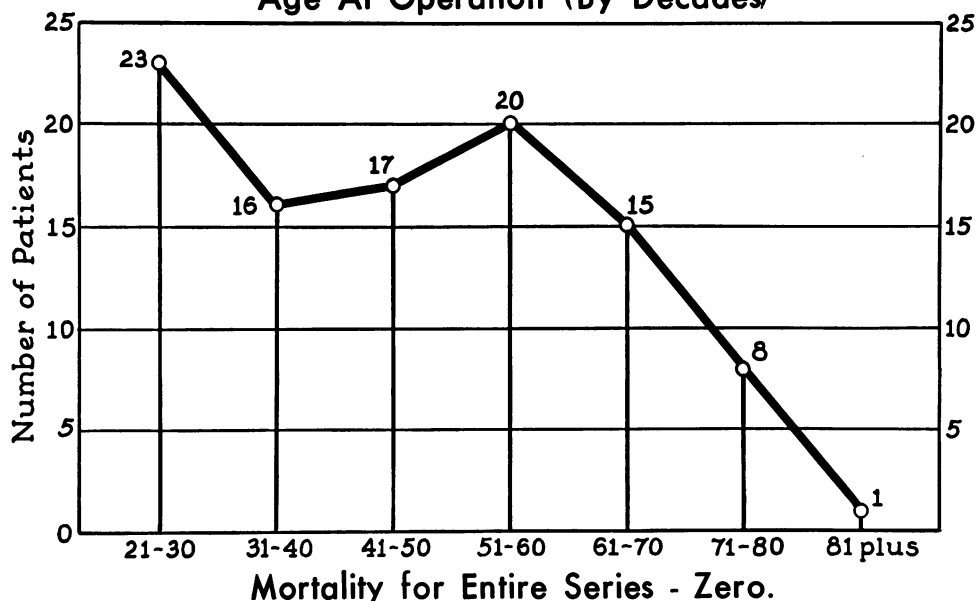


FIG. 1.

Twenty-three patients ranging in age from 22 to 30 are reviewed. One patient, age 25, underwent operation for silent stone which had not produced symptoms at any time. In the remaining 22, the average age at onset of symptoms was 25.3 years, while the average age at operation was 26.8 years. Only six of 23 patients were overweight, while nine were quite slender or extremely so. Eight were of medium or slender-medium build. Seven were of blond or red-blond complexion, seven medium, and nine dark or very dark.

Each of the 23 patients had been pregnant on at least one occasion. Twenty-two of the group had completed term pregnancies; the twenty-third had undergone operation for bilateral tubal pregnancies, with no subsequent pregnancy. Five had one child, 13 had two children, and four had three or more children.

In nine patients the development of attacks was attributed to ingestion of food or to certain foods, while in 11 patients a his-

tory of relationship between food and attacks was entirely lacking. Two additional patients denied relation of early attacks to food, but became aware of such an association in later episodes. Attacks of pain were often attributed to factors other than food. In seven patients attacks characteristically occurred during hours of sleep. Two patients associated their attacks of pain with condition of stress, fatigue, or anxiety.

Attacks of pain usually were severe and of brief duration. In 12 patients the reference of pain followed the classical distribution, being located in the right upper abdomen with or without radiation to the epigastrium and to the back. In ten patients, however, the pain was entirely epigastric with no radiation to the right upper abdomen, but often with radiation straight through to the back. Two of these ten developed right upper abdominal localization in later attacks.

Four patients dated the onset of symptoms to some time during the first preg-

nancy, and three of the four also suffered severe attacks in the corresponding puerperium. Three additional patients suffered their first attacks in the puerperium following the first pregnancy without having experienced any difficulty during the pregnancy. Thus, there were seven patients in whom the first symptoms appeared during the first pregnancy or very shortly thereafter. One additional patient first experienced pain during the second pregnancy, while another suffered her first attack while in the hospital following cesarian section for her third child.

Initial errors in diagnosis were relatively common. These seemed to be due to several factors, as follows: location of pain in the epigastrium rather than in the right upper abdomen; brevity of attacks of pain, which had frequently subsided by the time the patient was seen by a physician; reluctance on the part of the physician to consider gallstone disease as a likely possibility in a young slender woman with no dyspepsia. Therapy for duodenal ulcer was instituted in three, without relief of symptoms. Appendectomy was performed on one, and removal of a stone from the right renal pelvis in another, without relief of symptoms in either. Provisional diagnosis of muscle spasm, functional gastroenteritis, and virus enteritis were made in three others. Four additional patients were treated principally by sedation for one or more years; in two of them gallstones were known to be present, but no operation recommended.

Cholecystectomy was performed in each patient. Two operations were performed during an acute attack, two during the recovery phase from such an attack, and one in a patient in whom the gallbladder had been distended and palpable for several days (hydrops). The remaining 18 procedures were undertaken during an interval of quiescence. The common duct was explored in only one patient, without recovery of stones. Operative cholangiography without common duct exploration was per-

formed in one patient. In all others the procedure was limited to cholecystectomy with or without incidental appendectomy. No patient underwent operation during pregnancy.

All calculi were radiolucent. Single stones were recovered from three patients. Four patients had less than a dozen stones, while 16 had large numbers of stones, generally of very small size. In a few instances two different populations of stones according to size could be recognized. Four patients each had more than 100 stones. In all but two instances the stones appeared to consist principally of cholesterol and were roughly spherical in shape. At operation small stones were often found in the cystic duct between the folds of the valves of Heister.

The average period of hospitalization following operation was six days. One patient developed a small subcutaneous hematoma in the incision; another drained bile from the second to the sixth postoperative day; a third exhibited very faint jaundice on the second and third days after operation, and experienced an attack of pain on the third day similar to those suffered prior to operation (see Case 1). Recovery in these three patients was without further incident. In all others recovery was uncomplicated. Pain has been relieved in all. No patient has complained of subsequent dyspepsia.

DISCUSSION

General Symptomatology. The location of pain in gallstone colic is subject to great variation. In a series reported by Cole,¹⁰ pain was located in the epigastrium in only 27.2 per cent of patients. In the present series of young women, 45 per cent experienced pain which was confined to the epigastrium, with or without radiation to the back. Two of these patients subsequently developed localization in the right upper abdomen. Limitation of pain to the epigastrium often led to confusion in diagnosis.

In half the patients in this series attacks

of pain seemed to bear no relationship to meals or to particular foods. Thirty per cent suffered attacks which characteristically awakened them from sleep, usually in the early hours of the morning. The frequency of nocturnal attacks in young women has been mentioned by Ravdin.⁴² The development of gallstone colic during the hours of sleep may be related to the tendency of gallstones to settle to dependent portions of the gallbladder. With the patient in the recumbent position, small stones may settle in the cystic duct, leading to obstruction of the duct and subsequent colic.

The attacks of pain experienced by several patients in this series were often so brief that they were over before the physician had an opportunity to examine the patient. This was particularly true in the earlier episodes. Brevity of pain in gallstone colic has been emphasized by Cole.¹⁰

The idea that the female harboring gallstones is usually overweight is firmly entrenched in the minds of many physicians. While this may be true in the patients of middle age, it is not the case in young women suffering from gallstones. In an analysis of 1,032 instances of gallstones, Robertson⁴³ found that 578 (56%) occurred in individuals estimated to be of normal or subnormal weight. Ravdin⁴² stated that "contrary to frequent teaching, the patient need not be 'fair, fat and forty'; thin young women in their twenties, particularly those who have borne children, may present symptoms of cholelithiasis." In Gerwig's series²¹ of ten patients, seven were of normal build, while three were thin. In the present series, the subjects were more frequently thin than obese, and more frequently brunette than blond.

Relationship of Pregnancy to Stone Formation and Symptomatology. It has often been suggested that gallstones may be formed in a very brief period of time during some critical period when circumstances are favorable to the precipitation of cholesterol.^{1, 2, 14, 37, 43, 46, 47} This idea is supported

by the observation that the stones in a given patient are frequently all of the same size and shape, suggesting simultaneous formation. In addition, two or more distinct populations of stones are often found, suggesting that the patient has experienced more than one critical period conducive to stone formation. There is considerable clinical and experimental evidence to suggest that the metabolic and functional changes incident to pregnancy give rise to circumstances favorable to the precipitation of cholesterol gallstones.

Hermann and Neumann²⁷ (1912) first showed that blood cholesterol levels are elevated during pregnancy. Mann and Higgins³⁸ (1926), employing experimental animals, found that the gallbladder emptied slowly and poorly in pregnant subjects, and that the impairment of function increased with the duration of pregnancy. They suggested that failure of the gallbladder of pregnant animals to empty following the ingestion of food might bear some relation to the high incidence of gallstones following pregnancy in the human.

Cholecystography in pregnant women was attempted by Crossen and Moore¹¹ (1928). Thirteen patients without history of cholecystic disease were studied; satisfactory visualization was obtained in only five. In the same year, Levyn, Beck, and Aaron³¹ studied 17 primiparas, with failure of visualization in seven. They later reported an additional series totalling 39 studies,³² with failure of visualization in 20. Both Crossen and Levyn reported successful visualization in the same subjects in studies performed after the conclusion of pregnancy. In a comparable study, Fogelson¹⁸ (1920) failed to obtain visualization of the gallbladder in 43 of 59 pregnant women studied, and was uniformly unsuccessful in 14 studies undertaken subsequent to 7½ months gestation. All the foregoing were in agreement that visualization becomes less likely as the duration of pregnancy increases.

Potter³⁹ (1936) made direct observations of the gallbladder in the course of 390 cesarean sections in normal pregnant women at term. In 75 per cent the gallbladder was found to be greatly distended and atonic. Bile was aspirated from the gallbladder of each patient; analysis disclosed a high content of cholesterol and a low concentration of bile salts in each instance. The aspirated bile was described as being thick, tarry, and viscid.

Gerdes and Boyden²⁰ (1938), employing intravenous cholecystographic agents, were able to obtain some degree of visualization of the gallbladder in 19 of 21 pregnant women, but observed that emptying of the gallbladder was markedly retarded during the second and third trimesters of pregnancy. In reviewing their own work and that of their predecessors they concluded that "the stage is set in pregnancy for the precipitation of cholesterol."

In a comprehensive review and statistical analysis published in 1944, Robertson and Dochat⁴⁴ concluded that there is no reliable evidence to show that gallstones are more frequent in women who have borne children than in those who have not done so. While this may be correct if one considers the full life span of woman, it appears certain that gallstones develop or become clinically apparent at a much earlier age in women who have borne children, and, further, that a woman who has experienced a pregnancy becomes a candidate for the development of gallstones, regardless of her age.

Association of gallstone attacks with pregnancy or the puerperium was noted by some of the earliest writers on gallbladder disease. According to Hoppe-Seyler, Etmuller¹⁶ (1708) stated that gallstone colic and icterus were sometimes seen after childbirth. Willemin⁵⁶ (1862) described two patients, one of whom had an attack after each of four labors and the other after two labors, neither of them having experienced attacks at any other time. Huchard²⁹ (1882)

presented histories of several patients thought by him to represent instances of gallstone or renal colic, all occurring during pregnancy or the puerperium. Cyr¹² (1883), Naunyn³⁷ (1891), Rambert⁴⁰ (1889), and other nineteenth century writers made similar observations. By the beginning of the twentieth century the liability of women to gallstone attacks during pregnancy or the puerperium had become well recognized. Since that time it has been commented upon by many authors.^{14, 15, 17, 21, 28, 34, 38, 42, 45, 48, 54, 55}

Eliason and Ferguson¹⁵ described one patient who suffered attacks of gallstone colic following each of four deliveries and stated that a large majority of their cases in women in the third decade occurred during or immediately following the first or second pregnancy. Gerwig and Thistlethwaite²¹ recently reported their experience with ten women under 30 years of age, all of whom underwent cholecystectomy within a period of six months; in all cases symptoms began during or following a pregnancy.

In reviewing the material of the various writers on this subject, it appears that the postpartum period is a time of greater susceptibility to gallstone attacks than the period of gestation itself, and that the attacks of the puerperium are generally more severe than those of pregnancy. While cholecystectomy has been performed with some frequency in the early period following pregnancy, reports of cholecystectomy during pregnancy itself are relatively uncommon. This is undoubtedly due in part to reluctance to subject the pregnant woman to a procedure as extensive as cholecystectomy under anything short of urgent circumstances. There is some basis, however, for the supposition that severe unremitting attacks of cholecystitis are not prone to occur in pregnancy. If one examines the reports of various writers on the subject of surgical complications in pregnancy, it is found that cholecystectomy is one of the uncommon operations to be performed

TABLE II. *Incidence of Cholecystectomy During Pregnancy*

Authors	Place and Date	Pregnant Admissions	Laparotomies	Gallbladder Operations	Data on Gallbladder Operations
Child & Douglas ⁸	N. Y. Hosp. 1932-43	40,000	55	4	3 in 1st trimester; 1 in 4th month. Two were acute.
Smith & Bartlett ^{51, 52}	Boston Lying-in 1916-38	66,431	61	3	Operations at 5, 7, and 8 months. One had common duct stones.
Hamlin, Bartlett & Smith ²⁶	Boston Lying-in 1939-48	26,341	49	0	4 cases acute cholecystitis; all subsided and progressed uneventfully to term.
Stedje & Wilson ^{53, 57}	R. Packer Hosp. 1927-45	10,000	43	1	No data available *
Scott ^{49, 50}	Toronto Gen. Hosp. 1937-45	9,897	57	0	—
McLean ³⁵	Parkland Hosp. Dallas 1944-49	7,945	19	0	—
Randall & Baetz ⁴¹	Buffalo Gen. Hosp. 1937-52	16,000	74	3	No data available*
Total		176,614	358	11	

Summary: 3 operations in 1st trimester; 2 in 2nd; 2 in 3rd; no data available in 4. Only one known exploration of common duct in the entire group.

* Personal correspondence with authors; data relative to patients undergoing cholecystectomy no longer available.

upon pregnant women. Seven such reports have been reviewed, and are presented in Table II.^{3, 7, 8, 26, 35, 41, 49, 50-53, 57} The composite yields a total of hospital admissions of pregnant women exceeding 176,000, among whom only 11 cholecystectomies were performed. Only one of these 11 patients is known to have undergone exploration of the common duct, with recovery of stones. It has often been stated that pregnancy is favorable to the clinical course of duodenal ulcer. A similar protective influence against the development of the more severe forms of cholecystitis in pregnancy may be postulated, in response to the same factors which bring about the known dilatation and impairment of function of the gallbladder in the late months of pregnancy.

Common Duct Stones in Young Women. In patients of all ages undergoing cholecystectomy, the incidence of stones recov-

ered from the common duct is related to the duration of symptoms, the number and severity of attacks of colic, and the age of the patient. Common duct stones are generally considered to be uncommon in young women who have suffered relatively few attacks. In the series reported by Gerwig,²¹ no common duct involvement was observed.

No stones were recovered from the common duct in any patient in this series. However, in three patients there was evidence to suggest that passage of stones through the common duct had occurred on one or more occasions. Moreover, the character of pain experienced by other patients in this series (epigastrium boring into the back) was compatible with the expulsion of stones through the duodenal ampulla.

If we consider the very small size of the stones which are so frequently recovered from the gallbladders of young women, and

observe that such stones are often found within the cystic duct itself, it seems logical to assume that such stones make their way into the common duct. It is the author's hypothesis that this occurs frequently in young women, but that the stones are subsequently extruded into the duodenum, and are therefore not recovered at operation. As time elapses, the stones which remain in the gallbladder probably enlarge or coalesce, thus making it more difficult for them to gain access to the common duct.

CASE REPORTS

Case 1. Mrs. S. J., age 22, height 5' 4" (162 cm.), weight 116 lbs. (52.7 Kg.); one child. First attack of pain was experienced 5 months after termination of pregnancy. Onset occurred at 2 a.m. with excruciating pain in back extending around both costal margins. Pain lasted 10 minutes, without nausea. Within a month 3 such attacks had occurred; diagnosis of muscle spasm was made by 2 physicians. Four months later similar attacks recurred, with the addition of nausea and right upper abdominal tenderness. Oral cholecystogram disclosed multiple small radiolucencies in a functioning gallbladder. All attacks occurred in early morning without relation to food.

At operation the gallbladder contained a tenacious coagulum of bile, in which were suspended many tiny stones, the largest measuring 3 mm. in diameter. It was difficult to extricate these stones from the dark viscid bile in which they were suspended. The cystic duct appeared slightly enlarged, but the common duct was small. The procedure was limited to removal of the gallbladder, with incidental appendectomy.

On the second and third days faint but definite jaundice was observed in the sclerae; on the third day she experienced a brief severe attack of pain in the back identical with her earliest attacks. By the following day jaundice was no longer apparent. There has been no further pain or jaundice, and she remains well 2½ years after operation.

It is probable that some of the attacks of pain experienced by this patient represented the passage of stones through the duodenal ampulla rather than blockage of the cystic duct. The one episode of pain and jaundice subsequent to operation is presumably indicative of a retained stone in the common duct which passed sponta-

neously. It is notable that stones of this size which are suspended in thick bile cannot be detected by palpation through the intact wall of the gallbladder. In young women any estimate of stone incidence based on palpation of the gallbladder³⁹ will be lower than the actual incidence because of the frequency with which the small stones cannot be felt.

Case 2. Mrs. O. F. T., age 24, height 5'2" (157 cm.), weight 108 lbs. (49 Kg.); one child. Mild attacks of epigastric pain were first experienced 2 to 3 months following pregnancy, developing around 5 a.m. and usually relieved by food. Attacks became more severe and frequent, with associated vomiting, but 18 months elapsed before she consulted a physician. Following roentgenography of the stomach she was told that she had a "nervous stomach." Three weeks later she was hospitalized briefly because of a more severe attack. Jaundice was observed at that time, and had been noticed in one previous attack. By this time attacks were attributed to rich food. She consulted a different physician, who performed cholecystograms for the first time. On the first attempt the gallbladder failed to visualize; on the second test numerous small spherical radiolucencies were demonstrated in a functioning gallbladder. Shortly thereafter she was hospitalized for elective cholecystectomy. On the night before operation she suffered another characteristic attack. At operation the gallbladder contained thick viscid bile, through which some 30 small spherical stones were dispersed. The largest of these measured 3 mm. in diameter. The cystic duct was dilated to a caliber adequate to allow passage of these stones. The common duct was of normal size, but was explored. No stones were recovered. A subsequent cholangiogram was normal. Convalescence was uncomplicated and the patient remains well 2½ years after cholecystectomy.

Case 3. Mrs. L. L., age 28, height 5'7" (170 cm.), weight 165 lbs. (74.9 Kg.); two children. Five months after termination of her second pregnancy she first experienced nocturnal attacks of pain characteristic of biliary colic but unrelated to food. She was hospitalized during such an attack; definite jaundice was observed; concomitantly the stools were light and the urine contained bile. Studies of liver function were normal. The gallbladder failed to visualize on the first attempt, but on the second several small radiolucencies were demonstrated in a functioning gallbladder. Operation was recommended at this time, but was declined pending arrangement for care of the patient's children. Jaundice subsided promptly.

At operation 2 months later the cystic duct and common duct were of normal size, while the gallbladder contained multiple small stones. The gallbladder was removed. Operative cholangiogram through the stump of the cystic duct appeared normal. The common duct was not explored. She remains well 3 years after operation.

It seems highly probable that stones gained access to the common duct of each of the above patients on one or more occasions, with spontaneous passage into the duodenum. Agents for intravenous cholangiography were not available when these patients were seen. Subsequently the employment of Cholografin® has provided information which has aided greatly in preoperative selection of patients requiring common duct exploration.

Importance of Diagnosis and Treatment at an Early Age. Mortality statistics of recent series of cholecystectomies show clearly that the older age groups account for the majority of fatalities. In a study of 3,439 patients with non-malignant disease of the biliary tract, Glenn²³ (1952) found that 76 per cent of all deaths occurred in patients over 50 years of age. Colcock and McManus⁹ (1955), in an analysis of 1,356 cases of cholecystitis and cholelithiasis, had no death in patients under 50, with 16 deaths in patients over this age. In 2,243 operations for chronic cholecystitis, Bartlett and Quinby⁴ (1956) reported 15 deaths in patients over 50 and two deaths in patients under that age. The mortality rate in Gaster's series¹⁹ was approximately ten times greater after 50 than before that age. These authors are unanimous in their agreement that the principal hope for further reduction of mortality and morbidity lies in earlier recognition of cholecystic disease and extirpation of the gallbladder before complications ensue. In discussing acute cholecystitis, Glenn²² states, "The fact that we have not had a death in our group under 40 years of age for a period of 17 years, save for one child with acute typhoid cholecystitis, is significant and lends support to the

contention that interruption of biliary tract disease can best be accomplished soon after its onset." Cole¹⁰ expresses a similar view in his statement that "in patients having symptoms of gallbladder disease without complications, there is a certain amount of urgency in removal of the gallbladder before complications develop." Bartlett⁵ urges "elective surgery at a younger age and earlier in the course of the disease . . . as a means of reducing the number of deaths from acute cholecystitis."

The patients described in this report represent gallstone disease in its earliest recognizable clinical form. This is the stage of cholecystitis when the lowest operative mortality and morbidity may be anticipated. Recognition of the early manifestations of gallstones by obstetricians and internists and willingness on their part to recommend operation at this time have contributed greatly to the high incidence of patients in the third decade in the author's report, and are essential to the early surgical treatment of cholecystitis.

Prevention of Gallstone Formation During Pregnancy. Speculative opinions have been expressed concerning the prophylaxis of gallstones in pregnancy. On the assumption that hypercholesterolemia in pregnancy is a factor in causation of gallstones, one group¹⁷ feels that an attempt should be made to reduce the cholesterol content of blood and bile by restriction of diet. Others^{24, 30, 38} advocate inclusion of fat in the diet to augment evacuation of the sluggish gallbladder of pregnancy. These two ideas are divergent, and neither can be substantiated by clinical or experimental data. Further study of these factors is desirable.

Resumé of Clinical Characteristics of Gallstones in Young Women. On the basis of the experience gained with this series of patients, as well as that reported by other authors, the composite manifestations of gallstones in the average young woman may be outlined as follows:

1. She has usually had one or more children; subsequent to her first pregnancy she is a candidate for gallstone formation, regardless of her age.

2. While she may experience symptoms referable to the gallbladder during pregnancy, she is unlikely to undergo an operation of necessity for acute cholecystitis during this time. She is more likely to suffer severe attacks during the early weeks or months following pregnancy than during the pregnancy itself.

3. She may be of any physical stature or complexion; she is as often slender as obese, and as often brunette as blonde.

4. Her attacks of pain tend to be brief and severe. Their relationship to food is inconstant, and is as often lacking as present. Her pain frequently awakens her from sleep, or may develop during periods of fatigue or anxiety. It is as likely to be in the epigastrium as in the right upper abdomen.

5. She is often observed in several attacks or treated for months before the correct diagnosis is established. She is frequently suspected of having duodenal ulcer or gastro-enteritis.

6. Her stones are usually multiple, small (4 mm. or less), round, radiolucent, and composed largely of cholesterol. At operation they are often encountered in the cystic duct between the folds of the valves of Heister. In later years her stones probably grow larger.

7. Stones are rarely recovered from her common duct. The author believes that such stones gain access to the common duct more frequently than has been supposed, but that, since they are small, they are usually expelled through the duodenal ampulla.

8. When she undergoes cholecystectomy, the operation is ordinarily accomplished under highly favorable circumstances with gratifyingly low mortality and morbidity.

9. Following operation she is unlikely to suffer from any subsequent dyspepsia attributable to loss of the gallbladder.

SUMMARY

In 100 consecutive cholecystectomies performed in women for cholelithiasis, 23 patients were in the third decade. Many patients in the older age groups dated the origin of their symptoms back to this decade. Experiences with these 23 patients are reviewed.

Gallstones are common in women in the third decade. Their development at this time of life is probably more closely related to pregnancy than to any other single factor. In the woman who has borne children, the development of gallstones at any age should not be considered unusual. No classical physical type is apparent in young subjects with cholelithiasis. The attacks of gallstone colic which make their appearance during or shortly after pregnancy represent the earliest common clinical form of the disease.

The manifestations of gallstones in the third decade may differ significantly from the symptoms of later years. As a consequence errors in diagnosis are not uncommon in the early attacks.

Since the mortality and morbidity of biliary tract surgery increase with the age of the subject and the duration of symptoms, the young patient is the ideal candidate for cholecystectomy. Hope for further reduction in mortality and morbidity of surgical disease of the biliary tract lies in earlier recognition and treatment.

REFERENCES

1. Aschoff, L.: Die Gallensteine. *Med. Klin., Beihefte*, 27 (3): 1, 1931.
2. Aschoff, L. and A. Bacmeister: *Die Cholelithiasis*. Jena: 1909, Gustav Fischer.
3. Baetz, R. W.: Personal Communication.
4. Bartlett, M. K. and W. C. Quinby, Jr.: *Surgery of the Biliary Tract: I. Chronic Cholecystitis*. *New Eng. J. Med.*, 254: 154, 1956.
5. Bartlett, M. K., W. C. Quinby, Jr. and G. A. Donaldson: *Surgery of the Biliary Tract: II. Acute Cholecystitis*. *New Eng. J. Med.* 254: 200, 1956.

6. Blalock, A.: Statistical Study of Eight Hundred and Eighty-eight Cases of Biliary Tract Disease. *Johns Hopkins Hosp. Bull.*, **35**: 391, 1924.
7. Campbell, A. J. A.: Personal Communication.
8. Child, C. G., III and R. G. Douglas: Surgical Problems Arising During Pregnancy. *Am. J. Obst. & Gynec.*, **47**: 213, 1944.
9. Colcock, B. P. and J. E. McManus: Experiences with 1,356 Cases of Cholecystitis and Cholelithiasis. *Surg., Gynec. & Obst.*, **101**: 161, 1955.
10. Cole, W. H.: Recent Trends in Gallbladder Surgery. *J. A. M. A.*, **150**: 631, 1952.
11. Crossen, R. J. and S. Moore: Cholecystographic Studies in Pregnancy. *Am. J. Obst. & Gynec.*, **16**: 840, 1928.
12. Cyr, J.: quoted by Rambert. See reference no. 40.
13. Deaver, J. B.: Sequelae of Biliary Tract Infection. *J. A. M. A.*, **95**: 1644, 1930.
14. Deaver, J. B. and A. P. C. Ashhurst: Surgery of the Upper Abdomen, Vol. II: Gall-bladder, Liver, Pancreas and Spleen, p. 87. P. Blakiston's Son & Co., Philadelphia, 1914.
15. Eliason, E. L. and L. K. Ferguson: Some Results of Surgery of the Biliary Tract. *Ann. Surg.*, **85**: 565, 1927.
16. Etmuller: quoted by Hoppe-Seyler. See reference no. 28.
17. Ferguson, L. K. and J. T. Priestley: Relation of Gallbladder Disease to Pregnancy, with Special Relation to Factor of Hypercholesterolemia. *Am. J. Obst. & Gynec.*, **16**: 82, 1928.
18. Fogelson, S. E.: Cholecystography as Aid in Determining Gallbladder Stasis in Pregnancy. *Am. J. Obst. & Gynec.*, **17**: 613, 1929.
19. Gaster, J.: Surgery of the Biliary Tract. *Arch. Surg.*, **60**: 21, 1950.
20. Gerdes, M. M. and E. A. Boyden: Rate of Emptying of Human Gall Bladder in Pregnancy. *Surg., Gynec. & Obst.*, **66**: 145, 1938.
21. Gerwig, W. H., Jr. and J. R. Thistlethwaite: Cholecystitis and Cholelithiasis in Young Women Following Pregnancy. *Surgery*, **28**: 983, 1950.
22. Glenn, Frank: Surgical Treatment of Acute Cholecystitis. *Surg., Gynec. & Obst.*, **90**: 643, 1950.
23. Glenn, Frank: Causes of Death Following Biliary Tract Surgery for Nonmalignant Disease. *Surg., Gynec. & Obst.*, **94**: 283, 1952.
24. Goldstine, M. T.: in discussion of Fogelson, S. F.: Cholecystography as an Aid in Determining Gall Bladder Stasis in Pregnancy. *Am. J. Obst. & Gynec.*, **17**: 731, 1929.
25. Griffin, G. D. J. and L. A. Smith: Gallbladder Disease in Adolescence and Young Adults. *J. A. M. A.*, **154**: 731, 1954.
26. Hamlin, E., Jr., M. K. Bartlett and J. A. Smith: Acute Surgical Emergencies of Abdomen in Pregnancy. *New Eng. J. Med.*, **244**: 128, 1951.
27. Hermann, E. and J. Neuman: Lipoids of Pregnancy and Their Excretion After Delivery. *Wien. klin. Wchnschr.*, **25**: 1157, 1912.
28. Hoppe-Seyler, G.: Diseases of the Liver, Pancreas, and Suprarenal Glands. *Nothnagel's Encyclopedia of Practical Medicine*, p. 525. American Edition; W. B. Saunders & Co., Philadelphia, 1905.
29. Huchard, H.: Coliques hépatiques et coliques néphrétiques de la grossesse et de l'accouchement. *Union Med.*, Paris, 3rd. ser., **33**: 616, 1882.
30. Ivy, A. C. and G. S. Bergh: Applied Physiology of the Extrahepatic Biliary Tract. *J. A. M. A.*, **103**: 1500, 1954.
31. Levyn, L., E. C. Beck and A. H. Aaron: Cholecystography in Late Months of Pregnancy. *Radiol.*, **11**: 48, 1928.
32. Levyn, L., E. C. Beck and A. H. Aaron: Further Cholecystographic Studies in Late Months of Pregnancy. *Am. J. Roent. & Rad. Ther.*, **30**: 774, 1933.
33. Mann, F. C. and G. M. Higgins: Effect of Pregnancy Upon Emptying of Gallbladder. *Proc. Soc. Exp. Biol. & Med.*, **24**: 930, 1926.
34. Mayo, W. J.: "Innocent" Gallstones, A Myth. *J. A. M. A.*, **56**: 1021, 1911.
35. McLean, W. F.: Pregnancy and Coincidental Surgical Operation. *Texas State J. Med.*, **46**: 164, 1950.
36. Meagher, S. W. and A. J. A. Campbell: Acute and Chronic Cholecystitis. *New Eng. J. Med.*, **252**: 615, 1955.
37. Naunyn, B.: A Treatise on Cholelithiasis. English Translation by A. E. Garrod. London, The New Sydenham Society; Jas. Truscott & Son, 1896.
38. Peterson, R.: Gallstones During Pregnancy and Puerperium. *Surg., Gynec. & Obst.*, **11**: 1, 1910.
39. Potter, M. G.: Observations of Gallbladder and Bile During Pregnancy at Term. *J. A. M. A.*, **106**: 1070, 1936.
40. Rambert, P. E. J. M. F.: Contribution à l'étude des relations de la lithiase biliare avec la grossesse, l'accouchement et les suites de couches; 135 pp. no. 404. Paris, 1899.
41. Randall, C. L. and R. W. Baetz: Surgery During Pregnancy. *Obst. & Gynec.*, **3**: 100, 1954.

42. Ravdin, I. S. and W. H. Hagan: Diseases of the Biliary System. *Med. Clin. N. Amer.*, **35**: 6, 1951.
43. Robertson, H. E.: Preponderance of Gallstones in Women. *Int. Abst. Surg.*, **80**: 1, 1945.
44. Robertson, H. E. and G. R. Dochat: Pregnancy and Gallstones; Collective Review. *Int. Abst. Surg.*, **78**: 193, 1944.
45. Rolleston, H. D.: Disease of Liver, Gall-bladder and Bile-ducts, p. 709. W. B. Saunders & Co., Phil.-N. Y.-London, 1905.
46. Rous, Peyton and P. D. McMaster: Observations on Some Causes of Gallstone Formation. *J. Exp. Med.*, **39**: 77, 1924.
47. Rovsing, T.: Pathogenese der Gallenstein-krankheit. *Acta Chir. Scand.*, **56**: 103, 1923.
48. Schrage, V. L.: Clinical Observations on Etiology of Gall Stones in Women. *Surg., Gynec. & Obstr.*, **38**: 344, 1924.
49. Scott, W. A.: Surgical Complications During Pregnancy and Labor. *Am. J. Obst. & Gynec.*, **49**: 494, 1945.
50. Scott, W. A.: Personal Communication.
51. Smith, J. A. and M. K. Bartlett: Acute Surgical Emergencies of the Abdomen in Pregnancy. *New Eng. J. Med.*, **223**: 529, 1940.
52. Smith, J. A.: Personal Communication.
53. Stedje, R. L. and J. F. Wilson: Surgical Emergencies of the Abdomen Complicating Pregnancy. *Guthrie Clin. Bull.*, **15**: 59, 1945.
54. Vineberg, H. N.: Acute Cholecystitis in the Puerperium. *Med. Record*, **67**: 532, 1905.
55. Whipple, Allen O.: Surgery of the Biliary Tract. *Nelson Loose-Leaf Surgery*, Vol. 5, Chapter 9, p. 449. Thomas Nelson & Sons, New York. Copyright 1927-1940.
56. Willemin: quoted by Vineberg. See reference no. 54.
57. Wilson, J. F.: Personal Communication.

