Intrahepatic Stones:
A Clinical Study

CHUNG-CHIEH WEN, M.D., HSIN-CHAO LEE, M.D.

From the General Surgical Service, Triservice General Hospital, and the Department of Surgery, National Defense Medical Center, Taipei, Taiwan, Republic of China

THE pathogenesis of stone formation in the biliary tract is not completely understood. It has been attributed to metabolic disturbances, stasis or infection. The predominant opinion expressed in textbooks is that gallstones are formed primarily in the gallbladder; those found in the common duct presumably have passed from the gallbladder either during contraction or manipulation during operation.

However, for centuries both surgeons and pathologists have noticed another type of stone in the intrahepatic biliary ducts. The location, consistency, number and behavior of such stones were found to be entirely different from choledocholithiasis of gallbladder origin. *Liver stones* or *intrahepatic stones* were the names designated for this condition. According to Rufanov,[15] such isolated cases were described in the literature of the sixteenth and seventeenth centuries. The largest collective review done by Courvoisier up to 1890,[1] consisted of 50 cases, and the excellent thesis of Rufanov in the analysis of 57 such cases from various sources contained only five patients of his own. As a whole the incidence of intrahepatic stones in the Western countries has been very low and the reports are scanty; it is understandable that the general medical profession of the West has not been familiar with the problem.

After Waltman Walters had visited the surgical clinics in Japan and Hong Kong in 1959 and 1960, he expressed, in an editorial in *JAMA*, 1961,[18] his acquaintance with and conviction in the distinct clinical entity of intrahepatic stones. Glenn [6] in the same year reported four cases of intrahepatic stones from New York Hospital. His opinion was: "That there have been so few reports from America and Europe probably indicates that it is not rare but it escapes recognition by both clinician and pathologist."

In contrast, in Southeast Asia this condition of intrahepatic stones has been encountered very frequently. As early as 1913, Miyake found 20 cases of intrahepatic stones and 257 cases of cholelithiasis in 8,406 routine autopsies collected from three pathology laboratories in Japan. This gave a 7.7% incidence of intrahepatic stones.[1, 15] The clinical syndrome of intrahepatic stones was first described by Digby [5] in 1931 in Hong Kong. Subsequently surgeons of that locality and those of other Southeast Asian countries added further descriptions of the same problem. The incidence has been so common in Hong Kong that it was reported to be the third commonest abdominal surgical emergency at the Queen Mary Hospital.[17]

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Taiwan is one of the places where the incidence of intrahepatic stones is very high. From 1957 to 1969 we have collected 150 cases from the Triservice General Hospital and the Veterans General Hospital, both of which are the teaching hospitals of National Defense Medical Center. This paper reports the clinical study of the 150 cases. Those cases prior to 1957 are not included because of insufficient data.

Clinical Features

Sex Ratio

One hundred sixteen men and 34 women had intrahepatic stones. Since both of these hospitals are mainly for men patients, as the names indicate, these figures can not be interpreted as a male predominance in this particular disease. The estimate of the ratio of the number of patients compared to the number of beds of each sex and informations of others,[4, 8, 10 15, 16] would indicate that both men and women are equally affected.

Age Incidence

The age of our patients with intrahepatic stones ranged from 17 to 76, but the highest incidence, or 36.6%, fell in the 21–30 age group (Fig. 1). One hundred twenty-nine of the patients, or 86%, were between 21–50 years old. This coincides with the statistical figures of Hong Kong,[4, 17] Singapore [8] and Japan.[10]

Socio-economic Condition

All of the patients were ward patients and the list contained no high-ranking officials nor members of rich families. Most patients were undernourished and none was obese. Only one patient with intrahepatic stones was admitted to our private patient section in the past 20 years. He underwent the first choledochostomy in Hong Kong and came to us for further treatment.

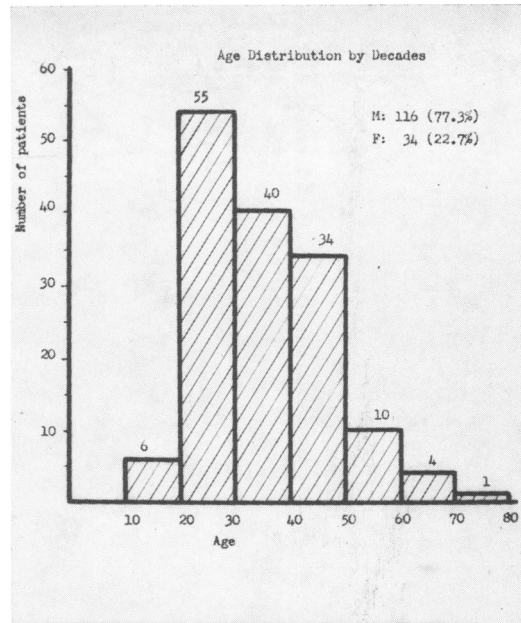

FIG. 1. Age distribution by decades.

Clinical Manifestations

The attack generally indicated cholangitis (Table 1). More often than not, all three features of Charcot's triad of fever, right upper abdominal pain and jaundice were present. At times one of the symptoms was less severe. A typical attack began with chills and fever, with concomitant right upper quadrant abdominal pain. The jaundice appeared one or two days later. The fever usually varied, but could reach 39° C.–40° C. and lasted for 2 and at most 4 days. The pain intensified and the jaundice deepened. Usually it took 1 to 2 weeks for a moderate attack and longer for a more severe attack to subside spontaneously. Many of these patients had very severe toxic symptoms. When the attack reached its severest form, the patients had symptoms of shock and collapsed from toxemia. Death would be imminent unless

TABLE 1. *Main Symptoms of 150 Intrahepatic Stone Patients*

Symptoms	No. of Patients	%
1. Epigastric or R.U.Q. abdominal pain	149	99.3%
Colic pain	77	51.3%
Severe pain	43	28.8%
Dull pain	29	19.3%
2. Fever:	110	73.3%
Low grade	37	24.7%
Moderate	31	20.7%
High grade	42	28.0%
3. Chill or rigor	100	66.7%
4. Nausea and vomiting	93	62.0%
5. Radiating pain to back and/or to shoulder	75	50.0%
6. Itching of skin	14	9.3%
7. Clay colored stool	11	7.3%

operation could be performed before the condition became too advanced. The interval between the attacks varied from once a week to once in more than a year (Table 2). The longest history was 30 years.

Physical Findings

In addition to the usual signs of cholangitis, it is interesting to note that 19.3% of our patients had variable hepatic enlargement and 9.3% had palpable gallbladder (Table 3).

Laboratory Results

The laboratory tests usually did not offer much important additional diagnostic information and served mainly to indicate the severity of the infection and the degree of biliary obstruction (Table 4).

Radiological Examinations

As a whole the surgeons here have been highly aware of and familiar with the condition of intrahepatic stones; thus the diagnosis was readily and accurately made in almost every case. Since all the stones were radiolucent, plain x-ray examination of the abdomen was not helpful. Almost all patients were jaundiced during the acute attack, and both oral and intravenous cholangiography failed to yield useful information. Even during remission, 70% of conventional cholangiographic studies showed non-visualization of the biliary tract. However from 1966–1969, percutaneous transhepatic cholangiography (PTC) has been of tremendous help, and was successful in 28 attempts. In those cholangiograms the amount and distribution of stones at various levels in the biliary tree were clearly demonstrated and the site and the degree of obstruction, including the strictures in the hepatic ducts and their radicals, were beautifully delineated. Examples are shown in Figures 2, 3 and 4. Besides diagnosis, the information also gave us guidance in the technical approach during operation. However, in two patients with biliary obstruction, bile leakage following the procedure required emergency operative intervention. Since then our roentgenologists

TABLE 2. *Interval between Attacks*

Interval of Attacks	No. of Cases	%
Frequent attacks	43	28.7%
Once a month	6	4.0%
Once in 2 months	15	10.0%
Once in 6 months	22	14.7%
Once a year	27	18.0%
Once in more than a year	28	18.7%
Not stated	9	6.0%
Total	150	100.0%

TABLE 3. *Important Physical Findings in 150 Intrahepatic Stone Patients*

Sign	No. of Patients	%
1. Epigastric or R.U.Q. Tenderness; with	135	90.0%
Spasm	57	38.0%
Rigidity	13	8.7%
2. Jaundice	111	74.0%
3. Enlargement of liver	29	19.3%
4. Enlargement of spleen	15	10.0%
5. Palpable gallbladder	14	9.3%

have followed our advice to leave the Teflon tube in place after completion of transhepatic cholangiography, for decompression of the distended biliary system. Bile was allowed to drain from the exernal opening of the Teflon tube. The decompression not only prevented bile leakage but also improved the patient's condition before operation. This process occasionally lasted several hours and required attendance and patience, but it has been rewarding.

Operative Findings

Upon opening the peritoneal cavity the most significant abnormalities were congestion of the liver and a greatly enlarged gallbladder. In general the gallbladder was edematous, thickened and dilated without much adhesion to the adjacent structures. Most impressive in this series of 150 cases has been the fact that only one third of the gallbladder contained stones. Of course, invariably the common duct was thickened, distended and dilated. In some instances it reached the size of the small intestine. The main hepatic ducts were also dilated and often admitted an index finger, but occasionally there were strictures in the intrahepatic portion.

The narrow aperture obstructed by stone or sludge contributed to abscess formation. In 11 such cases the obstruction produced a cistern with huge dilatation of the hepatic duct and thinning out of the overlying liver parenchyma, enabling the operator to detect the presence of stones in the abscess by palpation.

The stones of intrahepatic origin were mostly made up of bile pigments. The color was black, green, brown or yellow. Although they could be multichromic, mostly they appeared in various shades of brown. They also could be of different colors at different levels in the biliary tract. Their shape was sometimes formed or even faceted, but invariably they were very friable. Usually the black and green ones were formed and the brown and yellow precipitates were amorphous and muddy. The former were only occasionally found high up in the intrahepatic segments (Figs. 5, 6) while the latter group was the usual type found throughout the whole biliary tract. The amorphous precipitates felt sticky and greasy, like mud, and would smear on the inner surface of the biliary ducts.

TABLE 4. *Laboratory Findings in 150 Intrahepatic Stone Cases*

Findings	No. of Patients	%
1. Hyperbilirubinemia	111	74.0%
Slight (1–3 mg./100 ml)	49	32.7%
Moderate (3–5 mg./100 ml.)	19	12.7%
Severe (above 5 mg./100 ml.)	43	28.7%
2. Neutrophilia	90	60.0%
3. Leucocytosis	81	54.0%
4. Hypoproteinemia (below 6 mg./100 ml.)	41	27.3%
Without A/G reversion	18	20.0%
With A/G reversion	23	15.3%

Methods of Removing the Stones

When the common bile duct was incised there was always a gushing of a mixture

FIG. 2. PTC of patient L. T. Y. showing stones in common and right hepatic ducts; stone in left hepatic duct with stricture and dilatation.

FIG. 3 (left). PTC of patient C. F. Y. showing big stones in common duct and stones in the hepatic ducts producing dilatation.

FIG. 4 (right). PTC of patient L. S. L. showing stones in the common duct, non-visualization of right hepatic duct due to stone obstruction, and a huge gallbladder without stones.

of purulent bile and muddy debris which was removed by suction. The stones in the common duct were removed with stone forceps in the conventional manner. However, big and long cylindrical sausage-shaped stones had to be removed in sections due to their friability and size. The muddy remnants which stuck on the ductal wall were removed by saline irrigation and gentle gauze swabbing. Difficulty with stone obstruction at the sphincteric portion of the ampulla of Vater was never encountered because the sphincter of Oddi was always loose and patulous.

Although the hepatic ducts were also dilated, the removal of stones from these ducts was very difficult because the stone had to be grasped blindly with the forceps following digital exploration. The extremely friable stones could not stand the holding force of the forceps and thus more often than not would break into small fragments during the process of extraction. Whenever an incarcerated stone or a long segment of compact sludge filled the entire hepatic duct, it was broken up and removed in pieces. This made the lithotomy procedure tedious and time consuming. Consequently from experience we devised a method of removing the stone fragments and sludge by *flushing*. A big Dakin syringe filled with sterile normal saline was inserted into the lumen of the stone-containing hepatic duct. The shaft of the Dakin syringe would obstruct the opening of the hepatic duct, into which saline was instilled under pressure. The saline would distend the hepatic duct and its radicals and separate the stones from the ductal wall. When the pressure was suddenly released by quickly removing the syringe, the returning forceful back flush of saline would carry small stones, fragments, sludge and pus down into the common duct to be removed. Often it would take more than 2 hours of flushing to completely clear both of the hepatic ducts. But in cases of stricture of the hepatic duct, the problem became even more complicated. The narrow aperture prevented the stones from being extracted by forceps or *back flushing* with saline. At times, when a cistern had formed and could be located by palpation, the

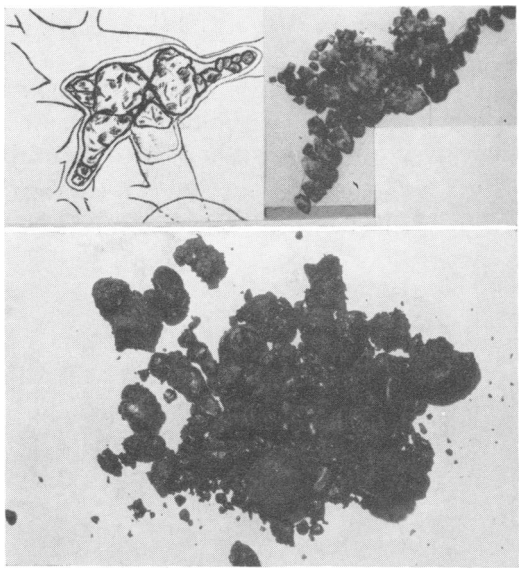

FIG. 5 (top). Reconstruction of the blockage at liver hilum and intrahepatic ducts by stones (40 gm.) in patient T. P. S.

FIG. 6 (bottom). Stones removed from left hepatic duct and its main branches after left hemihepatectomy in patient T. S. S.

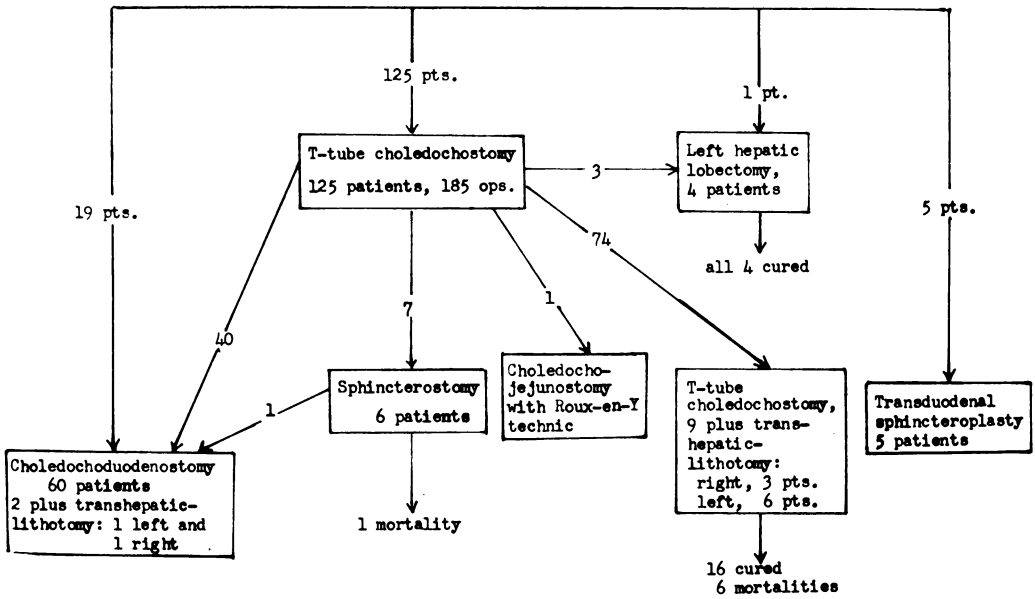

FIG. 7. Summary of surgical treatment of 150 patients with intrahepatic stones. (All surgical procedures were done after the removal of accessible intrahepatic stones.)

stones could be removed and the abscess drained by cutting into the dilated hepatic duct through the thin layer of overlying atrophic liver tissue (transhepatic lithotomy). In rare occasions when preoperative percutaneous transhepatic cholangiography or T-tube cholangiography demonstrated only the unilateral occurrence of stones in one of the hepatic ducts, particularly in the left lobe, hemihepatectomy was contemplated to remove all the stones completely.

Surgical Procedures

The surgical procedures which were performed are outlined in Figure 7. In general, operation was done during remission in symptoms and after careful preoperative preparations. If the patient had severe toxemia and impending hepatic failure due to biliary obstruction and suppurative cholangitis, it was imperative that simple decompression choledocholithotomy and a T-tube drainage, with minimal manipulation, he carried out as a life-saving procedure.

Except in an emergency drainage operation for the purpose of decompression, cholecystectomy was performed in every patient, whether stones were present or not, because it is desirable to remove a diseased gallbladder. Furthermore the gallbladder would not be needed if any subsequent surgical procedure in case of recurrence. Actually a huge gallbladder would interfere with the procedure of choledocho-

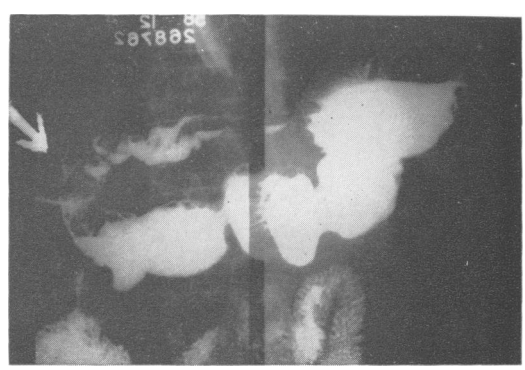

FIG. 8. Upper GI series of patient C. F. Y. after side-to-side choledochoduodenostomy. Arrow pointing to recurrence of stones in the common duct.

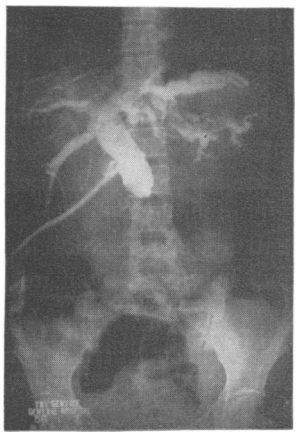

FIG. 9. Postoperative T-tube cholangiography of patient W. T. H. showing recurrence and mainly left unilateral involvement.

duodenostomy. Cook and Digby [4] held a different view.

In the earlier days every patient was treated with a T-tube choledochostomy after removal of the accessible stones. But invariably every postoperative T-tube cholangiography 2 weeks later revealed refilling of the common duct with radiolucent stones. Reoperation would usually be followed by another refilling. In one of the very early cases before 1957, excluded from the present study, such series of events were repeated six times in the course of 2 years and the patient eventually died of bleeding from esophageal varices. Of 125 patients of the present series who had received T-tube choledochostomy following choledolithotomy, 60 subsequently received another similar operation before being discharged from the hospital. All received some benefit but none was cured of the disease.

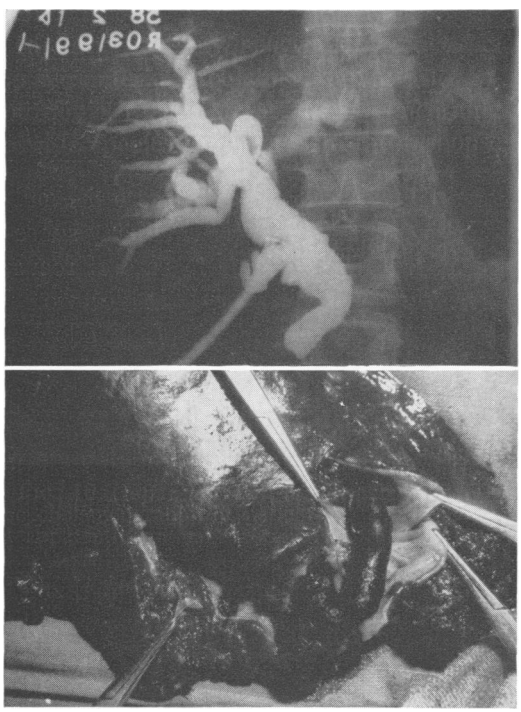

FIG. 10 (top). Post left-hemihepatectomy T-tube cholangiography of patient W. T. H. showing apparently normal right hepatic duct and its radicals.

FIG. 11 (bottom). Resected left lobe of liver of patient W. T. H., showing stones obstructing left hepatic duct and branches.

The same procedure was performed again on 76 of the 125 patients at second admission. Nine had a concurrent transhepatic lithotomy during operation. In this group, 16 (two had concurrent transhepatic lithotomies), or 21.6%, had no more stones on follow-up, T-tube cholangiography. They never returned and were considered cured.

Due to the high percentage of failure by the above method, side-to-side choledochoduodenostomy was therefore performed on some patients after all of the accessible intrahepatic stones had been apparently removed. The idea was to provide an extra exit for bile flow to reduce the chance of complete biliary obstruction in case of recurrence. Altogether there were 60 patients in this group; 41 had undergone previous operation unsuccessfully and 19 had undergone the operation as a primary procedure. Transhepatic lithotomy was added to two of the 60 upon indication during operation. Following this type of operation a number of the patients also returned with symptoms of Charcot's triad, which were related to recurrence of stone obstruction (Fig. 8).

One patient in the 125 readmissions received a Roux-en-T choledochojejunostomy. This patient was found to have marked cir-

rhosis of the liver during operation and was discharged to the medical service of another hospital. The result was unknown. From 1957 to 1959 sphincterotomy was attempted on seven patients with recurrent stones, but this method was soon abandoned because of ineffectiveness.

The development of hemihepatectomy was a recent event (Figs. 9, 10 and 11). It was first performed on a patient in whom percutaneous transhepatic cholangiography had shown only a unilateral left-sided lesion. This success encouraged the performance of the same procedure on three other patients in the group of 125 choledocholithotomy failures. These four patients had no further recurrence although a unilateral lesion has been so very rare.

In 1969 transduodenal sphincteroplasty [9] was performed in five patients, but the number is too small and the follow-up period is too short for evaluation.

Postoperative Complication

The postoperative complications are listed in Table 5. The chief causative offenders were suppurative cholangitis, which initiated infection, and jaundice which promoted bleeding.

Mortality

There were seven (4.6%) operative mortalities (Table 6). The chief cause was hepatic failure, while infection was a contributing factor. One patient who died of suppurative cholangitis due to stone obstruction of the stoma of the choledochoduodenostomy 1 year after operation was considered a late death and thus was not included. There were also other patients who died of cirrhosis of the liver either with or without bleeding from esophageal varices long after operation.

Associated Problems

Bile which was cultured in 59 cases during the operation, grew colon group mainly and other bacterial flora (Table 7).

TABLE 5. *Operative Complications of 150 Cases of Intrahepatic Stones*

Complication	No. of Cases
Wound infection	14
Intra-abdominal bleeding	3
Duodenal fistula	3
Pelvic abscess	2*
Postoperative cholangitis	2
Intestinal obstruction	2*
Intra-abdominal abscess and rupture of esophageal varices	1*
Duodenal obstruction	1
Postoperative bleeding from the choledodocho-duodenostomy	1
Retroperitoneal abscess	1
Partial collapse of left lower lobe of lung	1
* Mortality case	31(20.6%)

The analysis of the chemical composition of the intrahepatic stones will be included in the chemical study of the problem in a separate report.

Although the incidence of primary carcinoma of the liver is very high in Taiwan, We have found no association of this disease with intrahepatic stones. One patient was encountered who had undergone a T-tube choledochostomy and failed to return for further treatment. In the course of 2 years he tried herb drugs and "stone-dissolving" medicines at home. Eventually he returned after deep jaundice had de-

TABLE 6. *Mortality*

Cause of Death	No. of Patients
Cholangitis and hepatic failure	2
Cholangitis, intra-hepatic abscess and hepatic failure	2
Cholangitis and hepatic failure following the complication of duodenal leakage	1
Cholangitis and hepatic failure following the complication of intestinal obstruction and pelvic abscess	1
Cholangitis, retroperitoneal abscess and hepatic failure	1
Total	7

TABLE 7. *Result of Bile Culture*

	No. of Patients
E. coli:	29 (2 mortalities)
Aerobacter cloacae	12
Pseudomonas aeruginosa	5
Paracolon group	2
Coliform bacilli	2
Staphylococcus coagulase negative	2
E. coli and paracolon group	1
Salmonella (group A)	1
Alk. fecales	1
Proteus and *Staphylococcus aureus*	1
L-hemolytic streptococcus	1
Pseudomonas aeruginosa and L-hemolytic streptococcus	1 (1 mortality)
Proteus vulgaris	1
Total	59

veloped. Exploration revealed the common and hepatic ducts to be filled with tumor growth, pathologic section showed carcinoma of the gallbladder. Glenn [6] also reported that one of four patients had carcinoma of the biliary duct.

Discussion

Intrahepatic Stone: a Distinct Disease Entity

Subsequent to our review of surgical and pathologic reports on biliary calculi and clinical manifestations of our patients suffering from biliary stones, we fully support and agree with the concept that there are two types of common duct stones; one of the gallbladder origin and the other of intrahepatic biliary duct origin. Since the latter condition is rare in the United States and European countries, it is appropriate to enumerate the points of differentiation between these two conditions. For simplicity *choledocholithiasis* shall refer to common duct stones of gallbladder origin and *intrahepatic stones* shall refer to those of biliary duct origin.

1. **Age Incidence.** The first item to be considered is the age incidence. According to Glenn [7] the incidence of gallstones in the common duct increases with age. Choledocholithiasis is infrequent in patients with cholelithiasis under 40 years of of age (less than 6%) and thereafter the incidence gradually increases. After 80 years of age one half of the patients with cholelithiasis may be expected to have choledocholithiasis. From our experience with cases of intrahepatic stones, the incidence is highest among the young and middle age groups. In our series the 21–30 age group included 36.6% and the 21–50 age groups 86% of the total. Stock [16] also emphasized the number of his patients in 20–40 age groups. Cobo [3] found that in five of his 22 young patients with intrahepatic stones the initial symptoms had occurred by the age of ten. Cook [4] had very young patients and the age distribution was similar to ours.

2. **Financial Status of the Patients.** Cholelithiasis, which always precedes the development of choledocholithiasis, affects the general population with probably more preference to obese and overfed individuals. All of our patients with intrahepatic stones belonged to low income brackets and appeared more or less undernourished. The same condition was reported in Hong Kong [4, 16] in which intrahepatic stones occurred only among the local Chinese; Europeans there appeared exempted. Although there is an apparent racial difference, the financial disparity between the above mentioned two groups of people in Hong Kong is probably more important. Chiam of Singapore [2] also believed that socio-economic conditions appeared to be related to the site of stone formation. Although he did not separate common duct stones according to their different origins as we have done, he found that 34% of patients with gallstones were paying patients while only 6% of those with common duct stones were fee-paying. Maki [10] noted similar differences.

3. **Clinical Features.** Choledocholithiasis, when causing obstruction, can lead to cholangitis with the triad of fever, jaundice and right upper abdominal pain. Unless the stone is impacted at the lower end of the common duct the obstruction is usually relieved by the ball-valve mechanism. Patients with intrahepatic stones, besides exhibiting the triad symptoms, more often look very prostrated and have symptoms of toxemia. In an extreme case the attack is fulminating with shock-like reactions due to extensive suppurative cholangitis which results from longstanding obstruction.

According to the law of Courvoisier the gallbladder should not be palpable in a case of choledocholithiasis because it has lost its pliability and distensibility due to chronic infection. In patients with intrahepatic stones the gallbladder is frequently uninvolved, and Stock [17] and we have often found a palpable, enlarged gallbladder. Our figure is 9.3%. Twenty of Cook's 66 surgical patients also had palpable gallbladders.[4] From the frequent findings of a very enlarged gallbladder during operation; we believe that had it not been due to the rigidity of the overlying abdominal muscles, experienced hands would be able to elicit a much higher percentage of enlarged gallbladders during physical examination.

4. **Operative Findings.** The cardinal differences between choledocholithiasis and intrahepatic stones are demonstrated by surgical operation. Primarily, as described previously, the form, consistency and distribution in the biliary tract of these two types of stones are different. Secondly in choledocholithiasis, rarely are stones found also in the gallbladder. In cases of intrahepatic stones, only one third of our patients retained muddy or formed bilirubinate stones in the gallbladder, which was usually huge, very edematous and never contracted nor was fibrotic. Thirdly, unless a stone has passed through the lower end of the common duct, the sphincter of Oddi in a case of choledocholithiasis is usually a little resistant to the passage of a medium sized dilator. But the sphincter of Oddi in the case of intrahepatic stones is invariably patulous and loose; a No. 11 or 12 Baker dilator can pass through without any difficulty.

5. **Postoperative Course.** In a case of choledocholithiasis, after cholecystectomy and a complete choledocholithotomy, without leaving any residual stone behind, the patient is cured. Postoperative recurrence is the rule with cases of intrahepatic stones.

6. **Chemical Composition of the Stone.** The chemical composition of intrahepatic stones is entirely different from that of choledocholithiasis. The intrahepatic stone consists chiefly of bilirubinates, and the stone of gallbladder origin contains mainly cholesterol and often high calcium. The low calcium content in the intrahepatic stone indicates its non-association with the gallbladder, which has been found to be the main contributor of calcium to the stone.

Although surgical procedure can relieve symptoms, prolong life and render cure in a small number of favorable instances of intrahepatic stones, it is not definitive treatment for the large majority of cases, particularly when the stones are at the periphery of the biliary tree or held back by strictures. The cure rate in the present series is only 13.3% (20 cases). Efforts to elucidate the cause of intrahepatic stones and to prevent their formation in vulnerable individuals will be the most appropriate and direct solution to this problem. But what are the possible etiological factors?

Surgeons in Hong Kong [4, 16] attributed the cause of intrahepatic stones to liver fluke *Clonorchis sinensis*) infestation. But clonorchiasis is not known in Taiwan. Some Japanese workers [10, 12] and Cobo of Colombia [7] thought ascaris was the offender. If so, the condition should be a world-wide

affair, or at least the condition should be more prevalent in the countries in which the public health administration is less efficient than that in the above mentioned Southeast Asian countries. In the microscopic examination of 49 stone specimens of our patients, only four contained ascaris ova. One dead ascaris was found mingling with the intrahepatic stones of one of our patients. Cook could only isolate ascaris ova from the feces of 15% of his patients.

In 1962 Harrison-Levy [8] reported the cause to be due to narrowing of the sphincteric portion of the common bile duct and formation of stone was the result of obstruction. Maki [10] mentioned papillitis and obstruction of the common duct as a possible cause of intrahepatic stones. However, we always found the sphincter of Oddi loose and patulous, and could pass a large-sized dilator through the lower end of the common duct of our patients. Stock [16] also mentioned that a bougie passed distally in to the common bile duct slipped easily into the duodenum.

The difficulties with these theories made us, for a time, suspect malaria, which was then prevalent in Taiwan, as a cause of excessive hemolysis which would predispose to precipitation of bilirubinate stones in the biliary tract. However, persistent questioning of our patients only obtained 25 positive histories of malaria (16.7%). Consequently, our attention was soon drawn to the constant close relationship of intrahepatic stones with the poor nutritional status and low socio-economic condition of our patients. In particular we noticed that none of the well-nourished well-to-do class came to us for the same trouble. Therefore we have strongly suspected the cause of intrahepatic stones to be due to metabolic derangement, particularly dietary deficiency. In 1961 Maki [10] reported the diminishing incidence of pigment stones in Japan after the Second War, and he attributed the change to a higher dietary intake in connection with the improvement in living standard. In his subsequent report [11] he also mentioned the possible relationship of a functional disturbance of the liver to the etiology of intrahepatic stones.

In 1969 we encountered two reports [13, 14] by Palmer on the production of stones in the livers of rats by feeding them lithocholic acid. He reported the protective effect after addition of protein to the animals' diet which increased our interest and enthusiasm. We hope that investigations on the metabolic disturbances in intrahepatic stones will lead to an understanding of the pathogenesis and a rational approach to the prevention and treatment of this condition.

Summary

Intrahepatic stones is a common problem in Southeast Asia. This report describes our experience with 150 patients over the past 12 years. There are several features that clearly distinguish this syndrome from the more familiar variety of choledocholithiasis due to gallbladder stones. First, the peak incidence occurs in the third decade and declines thereafter. This is in sharp contrast to the incidence of cholesterol lithiasis, which increases with age. Second, the disease is characteristically found in patients from lower socio-economic groups. Third, the stones differ in composition, form, color, consistency and location. The intrahepatic location favors infection and stricture formation in the ducts, whereas the gallbladder is usually not involved, and is not uncommonly palpable during an acute attack. Fourth, the sphincter of Oddi is usually patulous, with no evidence of obstruction at that site. Fifth, intrahepatic stones tend to recur intractably despite various operative procedures. In our experience, the most satisfactory results have been derived from par-

tial hepatectomy and removal of the involved bile ducts in the few patients in whom this has been possible. An effective solution to the problem will probably require a better understanding of the pathogenesis, and intervention at the metabolic or biochemical level.

Acknowledgment

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References

1. Best, R. R.: The Incidence of Liver Stones Associated with Cholelithiasis and Its Clinical Significance. Surg. Gynecol. Obstet., **78**:425, 1944.
2. Chiam, H. K., Unni, P. N. and Hwang, W. S.: Cholelithiasis in Singapore. Part II. A Clinical Study. Gut, **11**:148, 1970.
3. Cobo, A., Hall, R. C., Torres, E. and Cuello, C. J.: Intrahepatic Calculi. Arch. Surg., **89**:936, 1964.
4. Cook, J., Hou, P. C., Ho, H. C. and McFadzean, A. J. S.: Recurrent Pyogenic Cholangitis. Brit. J. Surg., **42**:188, 1954.
5. Digby, K. H.: Common Duct Stones of Liver Origin. Brit. J. Surg., **17**:578, 1930.
6. Glenn, F. and Moody, F. G.: Intrahepatic Calculi. Ann. Surg., **153**:711, 1961.
7. Glenn, F.: Christopher's Textbook of Surgery (Ed. 7). Philadelphia, W. B. Saunders, 1960, 778.
8. Harrison-Levy, A.: The Biliary Obstruction Syndrome of the Chinese. Brit. J. Surg., **49**:674, 1962.
9. Jones, S. A., Steedman, R. A., Keller, T. B. and Smith, L. L.: Transduodenal Sphincteroplasty (Not Sphincterotomy) for Biliary and Pancreatic Disease. Amer. J. Surg., **118**:292, 1969.
10. Maki, T.: Cholelithiasis in the Japanese. Arch. Surg., **82**:599, 1961.
11. Maki, T., Sato, T., Yamaguchi, I. and Sato, T.: Treatment of Intrahepatic Gallstones. Arch. Surg., **88**:260, 1964.
12. Miyake, H.: Gallstone in Kyushu, Japan. Arch. Surg., **85**:425, 1962.
13. Palmer, R. H.: Gallstones Produced Experimentally by Litho-cholic Acid in Rats. Science, **148**:1339, 1965.
14. Palmer, R. H.: Production of Bile Duct Hyperplasia and Gallstones by Lithocholic Acid. J. Clin. Invest., **45**:1255, 1966.
15. Rufanov, I. G.: Liver Stones. Ann. Surg., **103**:321, 580, 1936.
16. Stock, P. E. and Tinckler, L. F.: Choledochoduodenostomy in the Treatment of Cholangiohepatitis. Surg. Gynecol. Obstet., **101**: 599, 1955.
17. Stock, F. E. and Fung, J. H. Y.: Oriental Cholangiohepatitis. Surgery, **84**:409, 1962.
18. Walters, W.: Cholangiohepatitis or Recurrent Pyogenic Cholangitis with Intrahepatic and Extrahepatic Bile-pigment Stones. Editorial, JAMA, **178**:934, 1961.