associations between environment and childhood chest illness are highly suggestive of a cause and effect relation at those ages.[7] This coupled with evidence from another study of young children, in which initial ventilatory function in those who subsequently suffered chest illnesses was similar to that of children spared such illness, lends support to the model of acquired lung damage predisposing to adult disease.[16]

If this conclusion is correct it has relevance for the future prevention of childhood chest illness and limiting subsequent adult chest disease by reducing or avoiding exposure to certain environmental influences. Currently, indoor air pollution by cigarette smoke is probably the only important factor that can readily be altered.

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Migration of gall stones

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Abstract

The factors influencing the migration of gall stones are ill understood. Altogether 331 patients undergoing cholecystectomy were studied prospectively. The diameters of the cystic and common bile ducts and of stones in the gall bladder and bile ducts were measured. Increasing pressure was applied to the freshly excised gall bladder in an attempt to evacuate stones through the cystic duct. Stones passed in 33 (60·0%) of patients with choledocholithiasis, 45 (67·2%) of patients with pancreatitis, and 7 (3·2%) of patients without either pancreatitis or choledocholithiasis. Stones migrated in 6 (3·0%) who had a normal cystic duct diameter (≤4 mm) and in 46 (32·5%) with a duct over 4 mm diameter. Common bile duct stones were often larger than the diameter of the cystic duct and when reintroduced into the gall bladder would not migrate. The passage of debris (≤1 mm) through the cystic duct bore no relation to the presence or absence of choledocholithiasis or a dilated cystic duct.

Small stones (1-4 mm diameter) must migrate to initiate and facilitate further migration; some must increase in size in the common bile duct. Increased biliary pressure consequently dilates the duct system retrogradely, allowing larger stones to follow. Patients at risk of stone migration and thereby pancreatitis and jaundice have large ducts that can be detected by ultrasound assessment.

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Introduction

Although cholecystectomy is the most commonly performed abdominal operation—over half a million are performed each year in the United States—there is a fundamental lack of understanding of the mechanism by which gall stones either leave the gall bladder or develop in the common bile duct. Such knowledge is essential in comprehending the clinical course of gall stones and their complications, choledocholithiasis, pancreatitis, and jaundice. Patients with microlithiasis (stones ≤3 mm) are more prone to develop pancreatitis, while those with medium and large gall stones are more susceptible to acute cholecystitis.[1]

Several groups of workers have shown unequivocally that gall stones may migrate and thereby cause pancreatitis,[2-8] but argument still exists about whether stones form in the common bile duct de novo[9] and nothing is known of the growth pattern of a gall stone within the common bile duct. Small stones that pass into the bile duct are clearly capable of passing through the ampulla[2 3]; this must also be true of "gravel." But what of large stones in the common bile duct? Do these pass as large stones from the gall bladder? Do they grow in the duct? Or do they reduce in size in the medium of less lithogenic bile in the duct? This study attempted to answer these questions.

Patients and methods

In a prospective study of 331 patients who were undergoing cholecystectomy for cholelithiasis at two centres the potential for stones to migrate through the cystic duct was assessed. The first 201 formed a consecutive series, the second 130 were selected to increase the number of patients with gall stone pancreatitis and choledocholithiasis. Pressure was applied digitally by squeezing the intact gall bladder immediately after excision to evacuate the contents through the cystic duct. Every attempt was made to coax stones through the duct by digital manipulation of the gall bladder, Hartmann's pouch, and duct so that any feasible migration would be recorded. Solid material >1 mm in diameter passing through the cystic duct was regarded as

stone migration; solid particles within the bile, visible to the naked eye but of diameter >1 mm, were recorded as debris. The number of stones in the gall bladder and bile duct was counted and their minimum diameters measured. The internal diameter of the cystic duct was measured at the narrowest point along the freshly excised length. Operative cholangiography was performed in all patients, three radiographs being taken at each examination after the injection of 3, 8, and 16 ml dye.

Of the 331 patients, 55 had stones in the common bile duct at the time of operation and 67 had a history of gall stone pancreatitis. When the stones were seen within the common bile duct on cholangiography exploration was performed and the stones removed. These stones were then put into the empty excised gall bladder, the fundus of which had been opened, and an attempt made to manipulate them through the intact gall bladder outlet and cystic duct.

Results

Of the consecutive series of 201 patients stone migration through the cystic duct occurred in 33 (16·5%). Of the 55 patients with stones in the common bile duct 33 (60%) had stones that migrated along the length of and through the cystic duct. Among the 67 patients with gall stone pancreatitis stones passed through the cystic duct in 45 (67%). Among the 209 patients with neither common bile duct stones nor pancreatitis stones passed through in only seven (3%) ($\chi^2=155·3$, $p<0·00001$, 2 df). Stones migrated in six patients (3%) in whom the diameter of the cystic duct was normal (≤4 mm) compared with 46 patients (32·5%) in whom diameter was over 4 mm ($\chi^2=26·7$, $p<0·0001$, 1 df). In no patient would a stone with a diameter greater than that of the cystic duct migrate, and it was never possible to increase the diameter of the cystic duct by forwards compression; this tended to result in rupture rather than stretching of the duct.

Debris (≤1 mm diameter) passed through the cystic duct in 42 (17%) of patients with stones that did not migrate and in 16 (19%) of those with stones that did. Debris passed irrespective of whether the patients had bile duct stones, pancreatitis, or dilatation of the cystic duct; this makes the importance of its migration questionable.

Common bile duct stones often had a diameter greater than that of the cystic duct, and on reintroduction into the gall bladder, only 46 (32%) migrated: the mean diameter of the cystic duct was 6·1 (SD 1·9) mm (median 6·0 mm, range 4-13 mm) whereas that of the common bile duct stones was 7·4 (SD 4·7) mm (median 6·0 mm, range 3-20 mm). The common bile duct stones were often softer in consistency than the gall bladder stones and fragmented more easily. Seven patients had stones in the cystic duct at operation; these were always smaller than or equal in size to the diameter of the cystic duct, which was never seen to be grossly dilated behind an obstructing stone.

Discussion

After removal of the gall bladder few patients develop choledocholithiasis again, indicating that in general the gall bladder or gall bladder bile is essential for the early stages of gall stone formation.[10] Supersaturation of bile with cholesterol and the subsequent process of nucleation, necessary for stones to develop, must therefore occur in the gall bladders of the many thousands of patients developing gall stones each year.[11] But what of common bile duct stones? To reach the common bile duct they must be smaller than the diameter of the cystic duct, which is generally less than 4 mm and usually less than 3 mm. Biliary debris of less than 1 mm diameter was equally common in the bile of patients with and without bile duct stones, which suggests that it is not important in their development. It has been suggested that the presence of cholesterol crystals in duodenal aspirate might be used to predict migrating stones; this premise is, however, controversial.[12-14] The irrelevance of migrating crystals to the development of choledocholithiasis may be because they pass through the ampulla of Vater.

True stones migrated in only 3% of patients with neither pancreatitis nor common bile duct stones and 3% of those in whom the diameter of the cystic duct was normal. No stone larger than the cystic duct ever migrated. Among patients with pancreatitis or choledocholithiasis, however, stones migrated through the cystic duct in 67% and 60%, respectively. In these patients the duct was appreciably larger but would not dilate in response to short term impaction of a stone and subsequent manipulation: the duct merely tore rather than dilated when pressure was increased around the stone. Dilatation of the cystic duct then might either be congenital or result from longer term retrograde increased pressure from the common bile duct. Increased pressure is almost certainly the case; this hypothesis is supported by the unimportance of migrating debris. The common bile duct is increased in size in patients with gall stone pancreatitis who do not have choledocholithiasis at operation. It is well known that in these patients stones have migrated through the common bile duct and that these stones, though usually small, can reach a diameter of 7 mm or greater.[2,3] Thus the common bile ducts of these patients probably increase in size as a result of temporary obstruction at their lower ends producing an increase in biliary pressure. Retrograde biliary hypertension exerted equally along the duct system in all directions would be more likely to produce dilatation than forwards pressure on a stone in the origin of the duct: this is likely to be the differentiating factor.

Small stones must therefore migrate initially, perhaps gradually increasing the size of the cystic duct as they obstruct the sphincter of Oddi. This would allow slightly larger stones to follow. This course of events would account for the presence in the common bile duct of stones initially up to 4 mm and later up to 6 mm in diameter. But what of larger stones? Most stones in the common bile duct were larger than the diameter of the cystic duct; when reintroduced into the gall bladder they would not migrate, and their consistency was softer than that of gall bladder stones. They must therefore have grown in the common bile duct though they did not originate there.

Once the nucleation of stones has occurred bile that is supersaturated with cholesterol will propagate stone growth.[15,16] Contraction of the gall bladder will place the common bile duct stone in "gall bladder bile" rather than "liver bile." As the gall bladder contracts and evacuates bile so this concentrated bile will remain in the common bile duct on completion of the contraction and the gall bladder will then preferentially refill with bile passing down the common hepatic duct.[17,18] Although intermittent emptying of the common bile duct can be seen to occur between contractions of the gall bladder, stones in the lower common bile duct must, for some of the time, be in gall bladder bile supersaturated in cholesterol. This environment, like that of the gall bladder, will be conducive to stone growth until such time as the gall bladder is removed. The softer consistency of bile duct stones is probably due to the absence of the pressure effects produced in the gall bladder by its contraction. Such repeated contractions give rise to the characteristic smoothness and faceting of gall bladder stones. In addition, the hepatic bile in patients with gall stones contains excessive cholesterol in relation to bile acids and lecithin[19,20]; thus once nucleation has occurred in the gall bladder this bile may in itself be conducive to stone growth.

An alternative, much simpler explanation for the migration of large stones is that the cystic duct slowly dilates around a large stone, ultimately transmitting it and extruding it into the common bile duct. Evidence against this is, firstly, the lack of migration of any stone bigger than the cystic duct in the present study. Secondly, in none of our 331 patients did the cystic duct itself, beyond Hartmann's pouch, contain a stone of much larger diameter than the remaining duct. Small stones were sometimes present in the valvular system of the cystic duct, but we did not see any patient with a large migrating stone in the middle of the duct with a collapsed duct in front and a dilated duct behind. In three cases of acute cholecystitis, however, in which the cystic duct was so short as to be almost absent, a large stone obstructed the junction of the cystic and common bile ducts.

In conclusion, migration of gall stones along the cystic duct occurs in only 16·5% of patients and in only 3% with a normal sized cystic duct. Small gall stones migrate through the cystic ducts of patients with choledocholithiasis and grow in the bile ducts. Some of these small stones become temporarily arrested at the lower end of the common bile duct, causing a transient increase in biliary pressure, which produces dilatation of the duct and subsequently relief of the obstruction. Although the gall bladder is necessary for the nucleation of cholesterol crystals in bile, which is supersaturated

with cholesterol, factors are present within the common bile duct that are conducive to further stone growth. Patients at risk of stone migration and thereby pancreatitis and jaundice have large cystic and common bile ducts that can be detected by ultrasound assessment. Those with dilated ducts should undergo early surgical treatment to prevent these complications. In the short term migration is likely to occur in only 3% of patients with normal sized ducts.

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SHORT REPORTS

Probable amniotic fluid embolism precipitated by amniocentesis and treated by exchange transfusion

Amniotic fluid embolism is a serious complication of pregnancy with a high mortality. We report a case which occurred after amniocentesis for relief of polyhydramnios and which was successfully treated by exchange transfusion. ABO incompatibility appeared to play a part in the pathogenesis of the condition.

Case report

A 17 year old pregnant girl presented at 28 weeks' gestation with a volume of liquor that appeared excessive on clinical examination; this was confirmed by ultrasound examination. No fetal abnormalities were noted. At 32 weeks' gestation an ultrasound scan showed a double bubble affecting the fetal stomach, which suggested duodenal atresia. The uterus at this stage was tense. Amniocentesis was performed to relieve the abdominal tension and to obtain fluid for chromosome analysis. A total of 200 ml of clear liquor was drained into a closed draining system before the catheter fell out. She then vomited and complained of pain in the shoulder tip; 10 mg of a combination of morphine tartrate and cyclizine tartrate (Cyclimorph) was given intramuscularly. Ninety minutes later she developed dyspnoea, central cyanosis, and a pulse rate of 140 beats/min. Blood samples were taken for blood gas analysis and coagulation studies (table). Bleeding was persistent from the venepuncture sites, and results of the coagulation studies confirmed a diagnosis of disseminated intravascular coagulation. She was treated with three units of fresh frozen plasma, heparin (500 units every hour), methylprednisolone 1 g eight hourly, cefuroxime 750 mg eight hourly, 10 mg vitamin K, frusemide 20 mg, and an infusion of dopamine (2 μg/kg/min). A central venous pressure line was inserted via an antecubital fossa vein. A sample of peripheral blood taken before delivery failed to show fetal squames or mucus.

Fifteen hours after the acute episode no fetal heart beat could be heard. Four units of blood were exchanged during the next 90 minutes using packed red cells and fresh frozen plasma; clotting indices improved slightly. A second exchange transfusion with a similar volume of blood was followed by a more dramatic improvement in clotting function. Forty hours after the acute episode the platelet count was 48×10^9/l; four units of platelets were given. At 41 hours she was delivered of a stillborn female infant weighing 2140 g. Blood loss was 100 ml. The amniotic fluid had shown chromosomes from an apparently normal female karyotype. The baby's blood group was B rhesus positive. Necropsy showed that the baby died of asphyxia, and duodenal atresia was not confirmed.

A crossmatch sample of blood taken before amniocentesis appeared normal. Cells grouped as A rhesus positive and the serum contained anti-B agglutinin to a titre of 1/512. The samples taken after the patient collapsed were grossly haemolysed, failed to clot, and lacked anti-B agglutinins. A sample of amniotic fluid collected at amniocentesis contained group B substance in high concentration.

Comment

Amniotic fluid embolism occurs in between one in 8000 and one in 80 000 deliveries.[1] In the confidential inquiries 1975-8 it was responsible for

Results of investigations

	Before amniocentesis	90 Minutes after amniotic fluid embolism	Before first exchange transfusion (20 h after embolism)	Before second exchange transfusion (30 h after embolism)	Before delivery (41 h after embolism)
Pulse rate (beats/minute)		140	100	120	80
Temperature (°C)		38·2	37·0	38·0	36·7
Respiration rate (breaths/minute)		40	32	32	20
Urine output (ml/h)		40	45	0	0
Blood gas analysis:					
Partial pressure of carbon dioxide (kPa)		3·1	4·4	3·9	—
Partial pressure of oxygen (kPa)		3·6	9·2	5·3	—
Bicarbonate concentration (mmol/l)		15·4	20·0	16·3	—
Base excess (mmol/l)		−6·1	−3·3 (with oxygen)	−7·3	—
Haematology:					
Clotting time (minutes)		>15	>15	—	6
Platelet count ($\times10^9$/l)		130	84	Adequate	48
Haemoglobin concentration (g/dl)	82 (iron deficiency anaemia)	80	71	110	101
White cell count ($\times10^9$/l)		16·7	23·5	14·0	18
Fibrin degradation products (mg/ml)		>1280	>1280	640	160
Prothrombin time/control (seconds)		25/12	40/10	14/13	12·5/13
Kaolin cephalin time/control (seconds)		120/43	56/42	56/44	35/42
Fibrinogen titre		<1/2	<1/2	1/8	1/128
Blood urea concentration (mmol/l)		7·4	12·8	16·4	28·6