Liver and Biliary Tract Disease in Children

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Foreword

For serious students of liver and biliary tract disease in children the Clinique de Pédiatrie of Professor Alagille at the Hôpital de Bicêtre, Université Paris Sud represents a valuable resource. Those who have visited the unit are impressed by the vigor and enthusiasm with which the members of this group join in the investigation and treatment of hepatic disorders in childhood. One is struck by the richness of the case material, the care and attention devoted to every detail of clinical management, and the research activities which have provided important insights into pediatric liver disease.

Toward his American colleagues, Professor Alagille has been extremely generous in sharing clinical expertise and in providing preliminary communications for review and discussion. With the preparation of this volume, the experience gathered over the years in Bicêtre can be shared by all. This work is a very personal view of pediatric hepatology, detailing disorders both common and rare. For those who will not have the opportunity to visit Bicêtre, the book will serve as a source of valuable information and unique experience.

Richard J. Grand, M.D.

Boston, Massachusetts
November 1, 1978

Preface

The plan to write this book was conceived more than fifteen years ago. However, the rapid accumulation of new knowledge always drove us to postpone the project, as every new medical discovery destroyed what we thought to be established fact. Thus, continued revision of our own concepts of liver disease in children kept us from recording our experience. For example, new advances in enzymology forced revision in older classifications of metabolic disorders. The possibility of cultivating hepatotropic viruses and the development of specific serologic tests permitted positive identification of teratogenic infections. The characterization of the hepatitis B virus antigenic system changed what we thought we knew of the placental transmission of hepatitis-causing viruses. Disorders considered to be congenital defects and prenatal in origin seemed, upon reconsideration, to be caused by peri- or post-natal injury or infection. The concept of idiopathic neonatal hepatitis was an example of the controversy which arose from our attempts to separate abnormalities dependent upon infection from those dependent upon heredity. Indeed, not all of the confusion surrounding the classification of liver disease in childhood has been settled.

During this stimulating and exciting period, our team has encountered a great number of pathological situations in which the liver and biliary tract of children were the main or the only target of disease processes. What we were learning at the bedside, contrasted with the available literature, made us more and more critical. Our doubts were growing at the same rate as the wealth of our experience.

It was then with some apprehension that we finally decided to write this book. We have tried to report here what we have experienced. Thus, our references to other works do not pretend to be an exhaustive bibliography. They are limited to publications related to our own experience. In some areas where our experience is lacking, we have summarized pertinent research and clinical work from other groups.

The fragile and transient character of all the material assembled in this book must be underlined. We are already convinced that, in future editions, many notions we have formulated hesitatingly will need to be completely revised.

We wish to express our gratitude to the families whose children have been placed in our care and who are not shaken by our feelings of ignorance; to our colleagues who helped us: nurses, whose devotion was sometimes interrupted by liver disease contracted while taking care of patients (and from which one of them died); clinical collaborators whose stay in our unit brings the irreplaceable

stimulation of youth and controversy; researchers and technicians in our Institut National de la Santé et de la Recherche Médicale research unit whose work is almost entirely defined by the unsolved problems of pediatric liver disease and whose efforts directly or indirectly benefit our patients. Finally, the whole team wishes to pay tribute to Marie-Christine Lalanne for her exceptional degree of excellence and her unfailing devotion; and to Dr. Micheline T. Ste-Marie, who provided inestimable help not only in the translation, but also in the content of this work. We wish also to thank Dr. Richard J. Grand for his review and comments of the English edition.

Daniel Alagille, M.D.

Contents

1 Methods of Investigation

GENERAL CONSIDERATIONS

Clinical and laboratory assessment of liver function must cover three essential and complementary areas:

- macro- and microscopic structural investigation, in order to evaluate the liver as a whole as well as its constituents (parenchyma, stroma, bile ducts, blood vessels);
- functional investigation of the blood supply to study the dynamics of intra- and extrahepatic flow;
- metabolic investigation to study the biological activities of the liver, including synthesis, transformation or detoxification of endogenous or exogenous substances, some of which are returned to the systemic circulation while others are excreted into bile.

Since metabolic functions of the liver correlate very well with structural findings, clinical assessment of one area will usually provide valuable information about the others. Investigation should not be limited to the liver itself: frequently liver disease is but one manifestation of a more generalized disorder (infectious or inflammatory, toxic, metabolic), of regional pathology (digestive, cardiac) or of associated multiple malformation syndromes. In most cases then, investigation should include assessment of other involved organs or systems.

Methods of Investigation and Their Limits in Pediatrics

Biological Investigation

In spite of micromethod techniques now available, thorough biological investigation of the liver requires large amounts of blood. In the small infant, priorities must be established according to the diagnostic importance of the test or its prognostic value. Results should be interpreted in relation to developmental criteria based on known values according to age and sex or to control data obtained simultaneously.

Structural and Circulatory Investigations

Endoscopy, biopsy or techniques using x-rays, isotopes and ultrasound have increasing value in pediatrics, and their full potential has not yet been realized. In

children, measures of hepatic blood flow are performed infrequently due to technical difficulties, while measurements of portal vein, or hepatic vein pressure are more readily carried out. In spite of recent progress, some investigative techniques are nearly impossible to attempt and may be harmful to the child: in the small infant, laparoscopy and selective angiography should be done only by expert personnel and retrograde cannulation of the bile ducts is not yet possible. Children should not be exposed to excessive doses of radiation only to gather perfect radiological documents. Finally, the psychological impact of invasive procedures must be remembered: some tests should be done under general anesthesia (see Chapter 10, section on "Anesthesia"), but the risks of anesthesia must be balanced against the psychological or physical risks expected without use of anesthesia (general anesthesia does facilitate the investigator's movements). Major procedures attempted under general anesthesia include endoscopy, splenoportography, selective angiography and percutaneous transhepatic cholangiography. As many tests as possible should be done at the same time keeping in mind relative contraindications. For example, liver biopsy and splenoportography should not be attempted during the same session since major bleeding complications can occur in both procedures. Finally, sufficient time for recuperation should be allowed between invasive procedures whether done under general anesthesia or not.

PHYSICAL EXAMINATION

The Liver

Clinical examination of the liver gives information on the localization and actual size of the liver. The lower anterior margin should not be felt below the costal margin, except in infancy when 2 to 3 cm distance between the costal margin and the liver margin is normal. However, liver palpated left of the midline is abnormal. Liver span measured by percussion at the right midclavicular line may be less reliable in infants than in older children (19).

- In respiratory distress syndromes and thoracic dystrophies when the liver and the spleen are displaced downward under loops of bowel, liver dullness may be absent. In these conditions the domes of the diaphragm are lowered and the liver, attached to the diaphragm by a nondistensible ligament, follows (ptosis is a misnomer).
- In diaphragmatic hernias the liver may be elevated into the chest.

Sometimes, voluminous choledochus cysts and retro- or intraperitoneal masses growing anteriorly cannot be differentiated from the liver on palpation; conversely, in the young infant, liver tumor or hypertrophy of the right lobe can give a false impression of hepatomegaly. A large gallbladder may be difficult to differentiate from an indistinct liver edge.

The consistency of the liver may be variable: firm, hard or soft. A firm liver on palpation might be histologically normal or show steatosis, but a soft liver will rarely contain appreciable fibrosis. Some livers are so soft that they cannot be distinguished from other abdominal viscera; they can escape detection even if they are enormous (as in cases of glycogen storage diseases).

The smoothness and the regularity of the hepatic surface and its lower margin are best appreciated by comparison between the right and the left lobes.

Hypertrophy of one lobe is usually secondary to atrophy of the other as in congenital lobar atrophy; more often, it is due to large regenerative nodules as in cirrhosis. Some tumors arising from the left lobe are palpated so far left of the midline they seem almost dissociated from the liver mass.

Accentuation of liver tenderness is usually a feature of rapid enlargement of the liver with stretching of the capsule. This may occur in many settings, for example right-sided heart failure, acute hepatitis, or cholangitis.

Auscultation is mandatory in the presence of a palpable mass; it may reveal the presence of an angioma, malignant tumor or arterio-venous fistula. Repeated examinations are imperative; the liver and spleen sizes should be reproduced on serial tracings in order to evaluate changes.

Clinical Aspects of Liver Dysfunction

Impaired secretion of bile typically is associated with jaundice, dark urine, acholic stools and pruritus. Palpation should be oriented towards finding a sub-hepatic mass (gallbladder or choledochus cyst).

Severe hepatic failure may be associated with diffuse bleeding, generalized edema, and peculiar breath (fetor hepaticus). Changes in mental status, neurological signs of extrapyramidal and pyramidal impairment and flapping tremor (asterixis) characterize hepatic encephalopathy. Sometimes, patients may present with psychiatric disorders or generalized seizures.

Findings of splenomegaly, gastro-intestinal hemorrhage, ascites and an increased abdominal wall collateral circulation are suggestive of portal hypertension.

Modifications of the microcirculation seen in cirrhosis include facial telangiectasias, spider angiomas, liver palms and digital clubbing associated with pulmonary arterio-venous anastomoses. Telangiectasias should be looked for inside the mouth as Rendu-Osler-Weber disease may produce pseudo-cirrhosis. Finally hepatomegaly may be the presenting sign of some forms of chronic pericarditis (see Chapter 16, "Congestive Liver Disease"). Complete cardiovascular evaluation is therefore extremely valuable.

Failure to thrive is rarely a presenting feature of chronic liver disease but is commonly found in chronic cholestatic disorders of infancy. Growth and endocrine functions, notably sexual maturation, will be impaired only when disease is severe or involves other organs, especially the digestive tract.

In summary, liver disease can be diagnosed either when overt clinical signs of impaired liver function are associated with positive findings on clinical examination or when there is isolated hepatic enlargement.

LABORATORY TESTS

The two main avenues of laboratory investigation of liver functions are a selective approach to study liver involvement in the metabolism of various substrates (lipids, carbohydrates, proteins, pigments, vitamins, hormones, drugs, etc.), as in

inborn errors of metabolism, and a more inclusive investigation of liver functions regrouping tests reflecting the particular area of liver function affected in various clinical syndromes. The discussion in this section is oriented towards the latter approach and for more selective tests the reader is referred to related chapters.

Tests Evaluating Bile Secretion

Unconjugated bilirubin bound to albumin is normally found in plasma. It is derived from heme catabolism. Normal concentrations vary from 0.5 to 0.9 mg%. Bilirubin is taken up by the hepatocyte, transported by proteins to intracellular sites where conjugation takes place. Conjugated bilirubin is then secreted across the canalicular membrane into biliary ductules and excreted into the duodenum by intra- and extrahepatic ducts. Unconjugated hyperbilirubinemia may result from overproduction of bile pigment (hemolysis), impaired uptake or conjugation (congenital or transient in the newborn) (25, 27). Conjugated hyperbilirubinemia results from impaired excretion of bilirubin or bile duct obstruction. Mixed hyperbilirubinemia without hemolysis can reflect complex perturbations in the hepatocyte but unconjugated hyperbilirubinemia is present in "pure" biliary underexcretion (e.g. massive hemolysis) because of saturated transport and conjugation mechanisms in the hepatocytes (16, 30, 31). Conversely, serum bilirubin can be abnormally low (< 0.5 mg%) in patients taking drugs which act as inducers of transport or conjugation of bilirubin, or in patients with an increased functional hepatic mass or blood flow.

Lipids: except in rare instances (Chapter 10), cholestasis is associated with hyperlipidemia which can be characterized as follows: increased serum beta-lipoproteins and cholesterol levels and to a lesser degree triglycerides; the mechanisms involved include biliary underexcretion and increased synthesis by the hepatocytes (10); serum cholesterol levels are often higher in intrahepatic biliary obstruction syndromes than in extrahepatic ones; and the presence of an abnormal low density lipoprotein (lipoprotein X) in the serum of patients with cholestasis. Although its increase in intrahepatic cholestasis is reported to be statistically significant, it is also found in extrahepatic biliary obstruction and hence is of limited usefulness in differentiating between these two conditions (20, 26, 35).

Bile acids can be measured in blood, bile and urine. In cholestasis, their blood level increases greatly over a normal level of a few milligrams percent. However, total serum bile acids or cholic to chenodeoxycholic acid ratio will not differentiate between intrahepatic and extrahepatic cholestasis (17).

Alkaline phosphatases hydrolyse organic phosphate esters at an alkaline pH. Their increase in cholestasis corresponds to an overproduction by the liver. In children, high levels may be due to alkaline phosphatase originating from bone (rickets, periods of rapid growth). If confusion exists, iso-enzymes can be obtained or alkaline phosphatase levels should be compared to those of *5′ nucleotidases,* specific hepatic enzymes.

Sulfobromophthalein (BSP) is an artificial dye handled by the liver in a manner similar to that of bilirubin; however, it is conjugated with glutathione and not with glucuronic acid. After intravenous injection of a test dose of 150 mg/m^2, its

disappearance curve from plasma is studied; it provides information in follow-up studies of liver disease, in demonstrating cholestasis without apparent jaundice, or in the study of specific abnormalities in bilirubin metabolism (see Chapter 2, section on "Neonatal Conjugated Hyperbilirubinemia"). Removal of BSP from blood is impaired when hepatic blood flow is decreased (heart failure, cavernomatous transformation of the portal vein) (see Chapter 15, "Portal Hypertension"). The test gives misleading results in the first three weeks of life because of immature excretory pathways.

Concentrations are measured in plasma at various times after BSP injection (cf. annex: Micromethods), or the fractional clearance of BSP is evaluated. Tm and fractionation of various metabolites can be studied: these tests are of limited interest and their results can only be applied to the study of extremely rare inborn errors of bilirubin metabolism.

^{131}I *Rose Bengal test.* After saturation of the thyroid gland with iodine, the dye is injected intravenously and is taken up by the hepatocytes, excreted through the bile into the intestinal tract and eliminated in the stools. In cholestasis, part of the dye is degraded in the liver; freed radioactive iodine leaks back into the blood and is excreted into the urine. The test is useful in differentiating between bile duct obstruction (extrahepatic biliary atresia) when less than 10% of the injected dose is recovered from the 72 hours stool collection and partial bile duct obstruction (intrahepatic cholestasis in the neonatal period) when more than 20% of the injected dose is recovered in the feces (11, 28). Scanning the liver and the small intestine can provide additional valuable information: concentration of the isotope in an abnormal area below the liver together with delayed appearance of radioactivity in the intestine is suggestive of a choledochus cyst (34).

Tests of Hepatocellular Injury

Transaminases. Hepatic cells contain numerous enzymes which are released into the systemic circulation as a result of injury. Of these, the transaminases are used extensively in current practice. Glutamic-oxalacetic transaminases (SGOT) are usually below 22 IU/l when measured by an enzymatic method. Normal levels of glutamic-pyruvic transaminases (SGPT) are equivalent to 31 IU/l or less. SGPT are more specific to the liver than SGOT. Levels correlate well with cellular injury; highest values are found in severe acute hepatitis, toxic or viral. A moderate increase is regularly seen in cholestasis, indicating poor cellular tolerance to bile stasis. Transaminases are increased in several other entities and apart from their diagnostic value in hepatitis, they are useful during the follow-up of hepatocellular diseases.

Other enzymes, although specific to the liver, do not provide further information. Their quantitative determination is more difficult and their increase parallels that of the transaminases; they include sorbitol dehydrogenase, ornithine carbamyl transferase, and hepatic LDH. Gamma glutamyl transpeptidase is not very useful even if extremely sensitive because it would lack organ-specificity and its increase would be of doubtful significance in liver diseases (12). In all forms of hepatocellular injury other cell constituents can be released in the blood: iron, copper, vitamin B_{12}, etc.

Functional Exploration of Hepatocellular Metabolism

Decrease in synthesis and impaired uptake and/or biotransformation of substrates evaluate the degree of hepatic insufficiency.

Synthesis

Protein electrophoresis on cellulose acetate will evaluate quantitatively the synthesis of serum proteins:

- *Serum albumin* (normal: equal or above 3.5 g%). Lower levels are found in hemodilution (edema, ascites) or in protein-losing enteropathy. Decreased hepatic synthesis of albumin reflects severe liver disease of long term duration;
- *Alpha-1-globulins* (normal: 0.2 to 0.4 g%). A minimal peak is suggestive of congenital alpha-1-antitrypsin deficiency which is confirmed by quantitative analysis (immuno-diffusion) and phenotyping (see Chapter 12, "Inborn Errors of Metabolism");
- *Alpha-2-globulins* (normal: 0.4 to 0.8 g%) include ceruloplasmin (normal: 20 to 50 mg%) and globulins active in hemostasis. Low levels of ceruloplasmin are found in severe hepatic failure and gastrointestinal protein loss, although extremely low values are specific of Wilson's disease. Conversely, ceruloplasmin increases in cholestasis, inflammatory processes and hyper-estrogenic states;
- *Many other globulins* can be measured but interpretation of the results is difficult because levels vary with decreased hepatic synthesis, inflammation, cholestasis or hemolysis: normal serum concentration of haptoglobin (alpha-2-globulin) is 50 to 150 mg%, of transferrin (beta-1-globulin) 0.2 to 0.4 g%; fibrinolysis, consumption coagulopathy and other disorders of hemostasis will also influence fibrinogen levels (normal 0.35 g%).

Activity index of serum proteins is assessed by studying the *globulins of hemostasis.* The Quick prothrombin time (normal: 80-100%) reflects the activity of four coagulation factors synthesized by the liver. Individual determinations are necessary to provide adequate interpretation of the test (2, 33): factors II (prothrombin), VII (proconvertin) and X (Stuart-Prower factor) are dependent on vitamin K for synthesis. A dietary deficiency or impaired absorption of vitamin K can influence synthesis. Control determinations should be done after parenteral administration of vitamin K. Factor V (proaccelerin), vitamin-K independent, is not decreased as much as other factors in hepatic failure; however, a level lower than 30% suggests a poor prognosis. Factor IX (plasma thromboplastin compound [PTC], Christmas factor), is synthesized by the liver in the presence of vitamin K; depressed synthesis will be reflected in a prolonged PTT. The site of synthesis of factor VIII (antihemophilic factor) has not been definitely determined; in acute hepatic necrosis, its level may be markedly increased and correlates positively with the degree of hepatic failure. Abnormal hemostasis may result from decreased synthesis of coagulation factors by the liver cells and/or consumption coagulopathy: disseminated intravascular coagulation is frequent in acute hepatic necrosis (24) and is sometimes seen in chronic hepatitis (see Chapter 7, section on "Chronic Active Hepatitis"). Determination of fibrin

degradation products gives reliable information only if a positive result is obtained (24).

Levels of serum *complement* in liver disease confirm the major role of the liver in the synthesis and catabolism of complement components, although until now a precise role for this protein has not been demonstrated in the genesis of hepatic disease. Complement studies in viral hepatitis (13) have demonstrated the effective pathogenic role of HBs Ag-anti HBs Ab complexes. Finally, total complement, C_3 and particularly C_4 components can provide a sensitive index of disease activity in long term follow up of patients with chronic hepatitis.

Lipid synthesis can be modified by either cholestasis or hepatocellular insufficiency in chronic or acute liver diseases (10). An hepatic acylase as well as a plasma lecithin cholesterol acyltransferase intervene in cholesterol esterification. Sensitivity of this particular test is low since serum esterified cholesterol levels drop only when there is severe hepatocellular dysfunction. Likewise, *hypoglycemia,* outside of specific conditions related to disorders of carbohydrate metabolism, appears when massive hepatic failure is evident.

Tests of Substrate Uptake and Biotransformation

In the liver, *aminoacids* coming from the digestion of alimentary proteins or endogenous metabolism are either catabolized into urea or reutilized for protein synthesis. Likewise, ammonia is carried from the digestive tract to the liver by the portal vein and is incorporated into the urea cycle. Major hepatic insufficiency is accompanied by hyperammonia, increase in plasma aminoacids, particularly of methionine, phenylalanine, tyrosine and a decrease in urea production. Determinations of these substrates may provide some information on the degree of severity of hepatocellular dysfunction, keeping in mind that several other factors may influence the results (dietary contribution, increased nitrogen catabolism, gastrointestinal hemorrhage, porta-caval shunts). Thus an abnormal elevation of postprandial *ammonia* is related to deficient hepatic metabolism associated with spontaneous portacaval shunts secondary to portal hypertension.

Biotransformation of various physiological or artificial substances assesses the functional capacity of the hepatocyte. Even if theoretically the choice is unlimited, few substances are actually used in pediatric clinical investigation. The disappearance curve of plasma *galactose* after a single intravenous injection dose of 500 mg/kg is a good indicator of hepatocyte function (32). It is not influenced by biliary dysfunction but must be corrected in terms of renal galactose clearance. This test is rarely performed in children.

Measurement of expired $^{14}CO_2$ after oral administration of labelled ^{14}C aminopyrine reflects drug demethylation by the liver and assesses the microsomal function of the liver cells (14). Such elegant methods of investigation will probably attract more interest in the future; as a matter of fact, studies on biotransformation of drugs have been very helpful in the comprehension of several toxic hepatic syndromes (see Chapter 10, "Toxic Liver Disease in Children").

Tests of Hepatic Regeneration

Not one available test can appreciate the importance and the dynamic biological evolution of hepatic regeneration. After severe hepatic necrosis, the best indica-

tion of hepatic regeneration remains a serial determination of the hepatic globulins involved in hemostasis. *Alpha-fetoprotein* (AFP) is secreted by the liver during fetal life and cannot be detected in serum after the first 2 to 3 months of life (by radioimmunoassay, serum levels of 0.01 mg/ml are detectable in normal individuals until adulthood). Demonstrable levels of AFP can be observed in massive cytolytic hepatitis and hepatectomy (3); its presence indicates liver cell synthesis at an early stage of cellular differentiation and thus reflects active parenchymal regeneration (see Chapter 7, "Hepatitis in Children"). Levels should be interpreted according to age: in the neonatal period, AFP is increased in several hepatic disorders including hepatitis (4, 36), but highest levels (> 20 mg/ml) are found in hepatoblastoma and hereditary tyrosinemia (21), when their determination becomes a valuable diagnostic tool.

Tests of Inflammation and Liver Immunopathology

Liver disease is frequently associated with a non-specific inflammatory response as shown by elevated serum gammaglobulins. Serum immunoglobulins can be measured by several immunochemical methods; IgG, IgA and IgM levels vary with age. Very few flocculation tests are used today. The McLagan thymol turbidity test may be of some interest. Likewise, the sedimentation rate, because of its availability, remains a valuable test. Inflammatory reactions reflect complex immunologic processes which are discussed in detail in Chapter 7.

RADIOLOGY AND OTHER METHODS OF INVESTIGATION

Biliary Tract

The bile ducts and gallbladder can be investigated radiologically by:

- Oral cholecystography;
- Intravenous cholangiography;
- Percutaneous hepatic cholangiography;
- Endoscopic retrograde pancreato-cholangiography.

Indications for *oral cholecystography* in pediatrics are limited even if the test can be done in very young infants. It is the procedure of choice for the study of gallbladder morphology, stones or gallbladder dyskinesia, but it does not give any information on intrahepatic bile ducts. In our institution, calcium iopodate (Solubiloptine^{R}, Oragrafin^{R} Calcium) is administered 7 hours before the examination in small infants and 14 hours before in older children.

Intravenous cholangiography is a more complete examination because the intrahepatic bile ducts are visualized; opacification of the gallbladder is possible as in oral cholecystography (7, 8). Because the dye is injected intravenously, dosage is more precise; it is the procedure of choice when intestinal malabsorption is present. Iodipamide is diluted to a 50% solution and is then either injected in a single dose of 1 ml/kg body weight or infused over a period of one hour (usual cholangiography). Intrahepatic bile ducts are visualized and the gallbladder is partially seen at the end of the examination. Successful cholangiography corre-

lates with the serum bilirubin concentration. Longer perfusions are used when levels of serum bilirubin are moderately elevated: the infusion is given slowly over a period of 12 hours (long-term cholangiography) and an intravenous cholecystogram is then obtained. Visualization is excellent when total serum bilirubin does not exceed 1.5 mg%, generally good if bilirubin is lower than 4 mg%, but the contrast material is poorly concentrated and the bile ducts are hardly visualized. Results are poor when serum bilirubin exceeds 4 mg% and negative when serum bilirubin levels are higher than 5 mg%.

Intrahepatic bile ducts, the common bile duct and the gallbladder are commonly seen in older children when serum bilirubin levels are normal or moderately elevated. In the young infant, because of the small caliber of the bile ducts, only the gallbladder is opacified. Sometimes, when the gallbladder is not visualized, opacification of small intestinal loops will confirm the biliary excretion of the dye. For these reasons, the long-term perfusion is the method of choice in this age group.

Indications for associated tomography are few in children; gentle hepatic compression will usually be sufficient to obtain good visualization of the biliary tree.

Percutaneous transhepatic cholangiography. The major indication for this procedure is severe cholestasis when good visualization of the biliary system is essential to confirm the presence of a congenital malformation or obstruction of bile ducts. The examination is performed immediately before surgery in order to avoid bile peritonitis or cholangitis. In children, depending upon age, the examination may need to be done under general anesthesia. Fluoroscopic control is required. A Chiba needle (23G) is introduced into the right lobe of the liver, at the midpoint of maximum dullness between the right anterior and mid-axillary lines. The needle is directed towards the xiphoid and then the metallic shaft is taken out. Opacification is carried out with a small teflon catheter (22).

The left side of the liver can be studied if the needle is positioned anteriorly or the left lobe itself is punctured. Success of the procedure depends on the degree of dilatation of the bile ducts.

Endoscopic retrograde pancreato-cholangiography. Because of inadequate fiberoptic instruments, the cannulation of the ampulla of Vater is rarely done in children younger than 4 years of age. Infectious complications can occur and, for this reason, percutaneous cholangiography is preferred. This procedure provides structural information concerning the biliary system, but sparse data as to its function. Gallbladder contraction and evacuation after a fatty meal or a milk bottle in infants is partly a functional test but it helps visualize the common bile duct.

Plain films of the abdomen and barium studies of the gastro-intestinal tract are important adjuncts of biliary tract investigation. Radioopaque stones, not infrequent in children, can be seen on plain films of the abdomen (see Chapter 11, "Cholestasis in Children"). The presence of upper abdominal masses can be suspected on such films; their shape and size will be further delineated by upper gastro-intestinal barium studies and angiography. Echotomography may show dilatation of the bile ducts when their diameter exceeds 4 mm. It is even more helpful in the diagnosis of choledochus cysts (Chapter 11).