Approach to CLD & ALD

Classification

- Hepatocellular (viral hepatitis)
- Cholestatic (gall stone, malignant obstruction)
- Mixed (drug-induced, viral hepatitis)

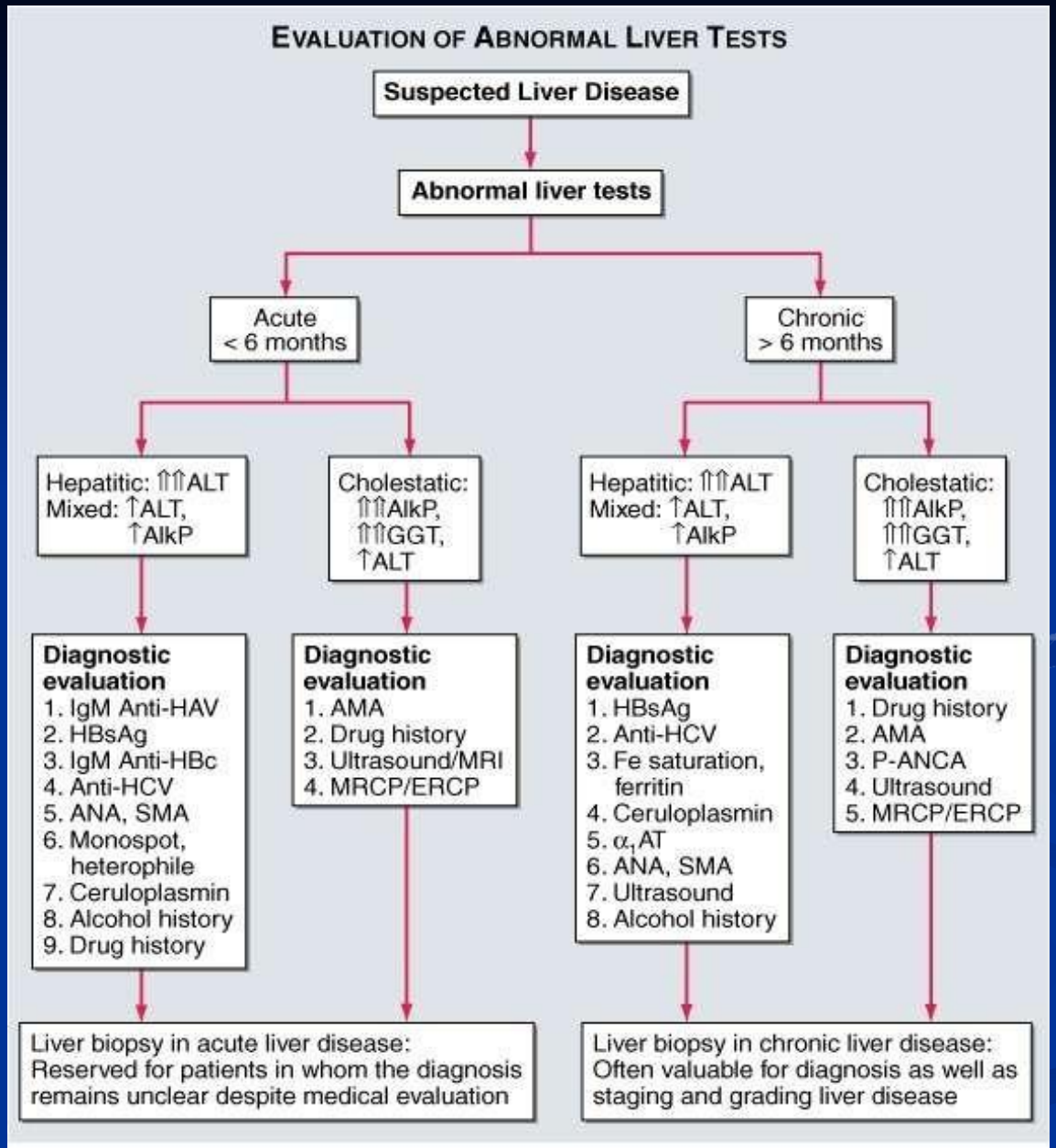
Table 295-1 Liver Diseases

- Inherited hyperbilirubinemia
  - Gilbert syndrome
  - Crigler-Najjar syndrome, types I and II
  - Dubin-Johnson syndrome
  - Rotor syndrome
- Viral hepatitis
  - Hepatitis A
  - Hepatitis B
  - Hepatitis C
  - Hepatitis D
  - Hepatitis E
  - Others (mononucleosis, herpes, adenovirus hepatitis)
  - Cryptogenic hepatitis
- Immune and autoimmune liver diseases
  - Primary biliary cirrhosis
  - Autoimmune hepatitis
  - Sclerosing cholangitis
  - Overlap syndromes
  - Graft-vs-host disease
  - Allograft rejection
- Genetic liver diseases
  - α_1 Antitrypsin deficiency
  - Hemochromatosis
  - Wilson disease
  - Benign recurrent intrahepatic cholestasis (BRIC)
  - Progressive familial intrahepatic cholestasis (PFIC), types I–III
- Liver involvement in systemic diseases
  - Sarcoidosis
  - Amyloidosis
  - Glycogen storage diseases
  - Celiac disease
  - Tuberculosis
  - *Mycobacterium avium intracellulare*
- Cholestatic syndromes
  - Benign postoperative cholestasis
  - Jaundice of sepsis
  - Total parenteral nutrition (TPN)–induced jaundice
  - Cholestasis of pregnancy
  - Cholangitis and cholecystitis
  - Extrahepatic biliary obstruction (stone, stricture, cancer)
  - Biliary atresia
  - Caroli disease
  - Cryptosporidiosis
- Drug-induced liver disease
  - Hepatocellular patterns (isoniazid, acetaminophen)
  - Cholestatic patterns (methyltestosterone)
  - Mixed patterns (sulfonamides, phenytoin)
  - Micro- and macrovesicular steatosis (methotrexate, fialuridine)
- Vascular injury
  - Venoocclusive disease
  - Budd-Chiari syndrome

Others (galactosemia, tyrosinemia, cystic fibrosis, Newman-Pick disease, Gaucher disease)	Ischemic hepatitis
Alcoholic liver disease	Passive congestion
Acute fatty liver	Portal vein thrombosis
Acute alcoholic hepatitis	Nodular regenerative hyperplasia
Laennec cirrhosis	Mass lesions
Nonalcoholic fatty liver	Hepatocellular carcinoma
Steatosis	Cholangiocarcinoma
Steatohepatitis	Adenoma
Acute fatty liver of pregnancy	Focal nodular hyperplasia
	Metastatic tumors
	Abscess
	Cysts
	Hemangioma

Evaluation

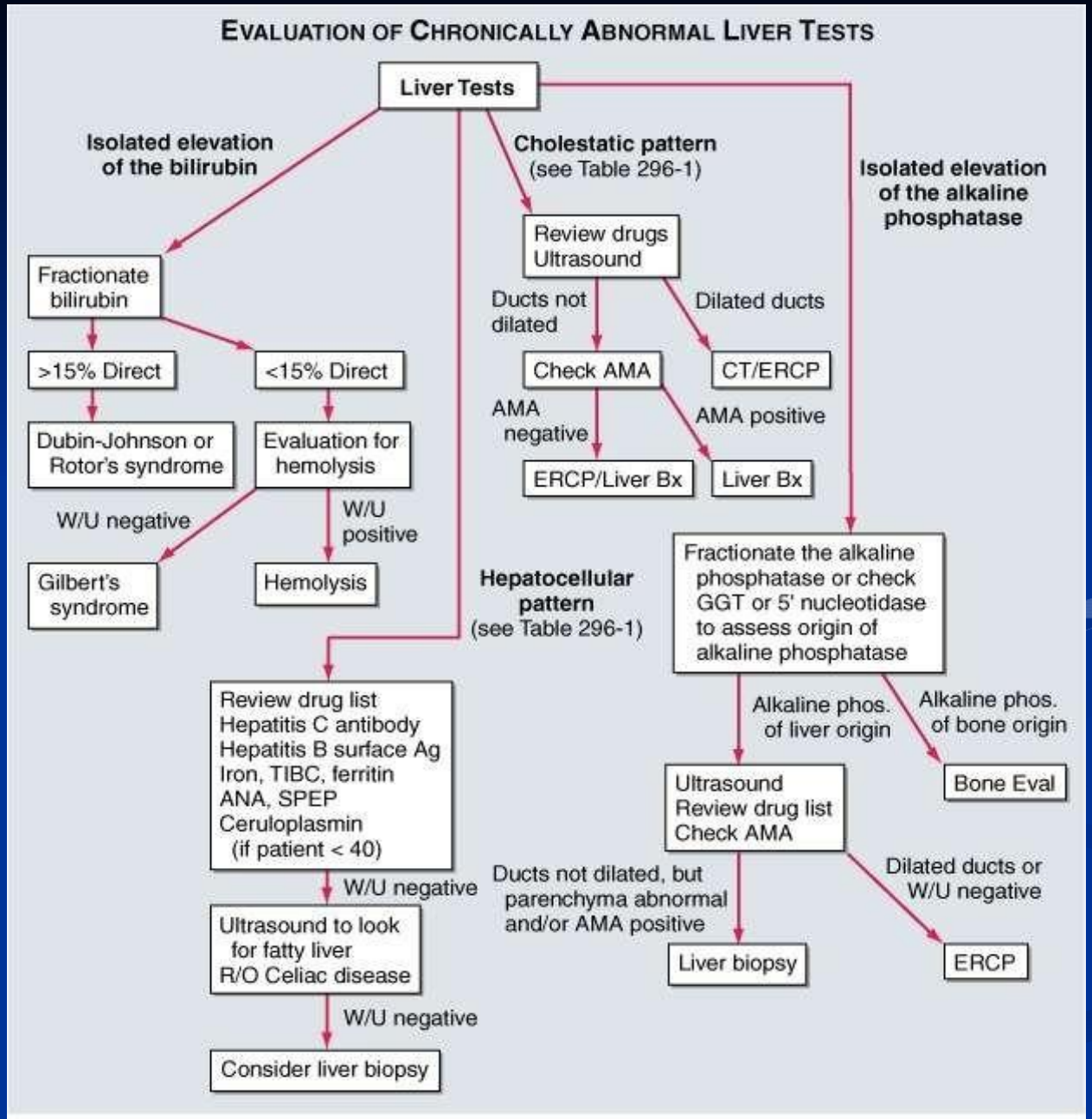
- Establishing the etiologic diagnosis: hepatocellular, cholestatic or mixed
- Estimating the disease severity (grading): active or inactive, mild to severe
- Establishing the disease stage: acute or chronic, pre-cirrhotic, cirrhotic, or end stage



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Clinical Symptomatology

- Jaundice
- Fatigue
- Weakness
- Pruritus
- RUQ pain
- Anorexia
- Dark urine
- Light stools
- Asymptomatic



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Portal hypertension

- Ascites
- Prominent superficial veins
- Edema
- Weight loss

Table 295-3 Important Diagnostic Tests in Common Liver Diseases

Disease	Diagnostic Test
Hepatitis A	Anti-HAV IgM
Hepatitis B	
Acute	HBsAg and anti-HBc IgM
Chronic	HBsAg and HBeAg and/or HBV DNA
Hepatitis C	Anti-HCV and HCV RNA
Hepatitis D (delta)	HBsAg and anti-HDV
Hepatitis E	Anti-HEV
Autoimmune hepatitis	ANA or SMA, elevated IgG levels, and compatible histology
Primary biliary cirrhosis	Mitochondrial antibody, elevated IgM levels, and compatible histology
Primary sclerosing cholangitis	P-ANCA, cholangiography
Drug-induced liver disease	History of drug ingestion
Alcoholic liver disease	History of excessive alcohol intake and compatible histology
Nonalcoholic steatohepatitis	Ultrasound or CT evidence of fatty liver and compatible histology
$_1$ Antitrypsin disease	Reduced $_1$ antitrypsin levels, phenotypes PiZZ or PiSZ
Wilson disease	Decreased serum ceruloplasmin and increased urinary copper; increased hepatic copper level
Hemochromatosis	Elevated iron saturation and serum ferritin; genetic testing for HFE gene mutations
Hepatocellular cancer	Elevated -fetoprotein level >500; ultrasound or CT image of mass

Clinical History

- Prodromal symptoms
- Use of parenteral illicit drugs
- Maternal history of hepatitis
- Exposure to jaundiced patients
- Use of medications (including herbal meds)
- Sexual history (multiple partners, same sex)
- Blood transfusion
- Family history: Wilson's disease, hemochromatosis,

Alcohol abuse

- US: 70% consume alcohol
- Only 5% have more than 2 drinks/day; 11-15g alcohol/drink
- Women: 22-30g alcohol/day
- Men: 33-45g alcohol/day
- Cirrhosis: at least 10 years of alcohol intake

P.E. Findings

- Icterus (Bilirubin > 2.5 mg/dL)
- Hepatomegaly
- Hepatic tenderness
- Spider angiomata
- Palmar erythema
- Splenomegaly
- Ascites
- Edema
- Skin hyperpigmentation

Hepatic Failure (Encephalopathy)

- Altered sleeping patterns
- Mental dullness
- Altered sensorium – disorientation, confusion, stupor, coma
- Fetor hepaticus
- Asterexis

Precipitating Factors

- GI Bleeding
- Over diuresis
- Dehydration
- Electrolyte imbalance
- Infection
- Constipation
- Use of narcotic analgesics

Diagnostic Evaluation

- ALT
- AST
- Alkaline phosphatase
- Serum bilirubin (direct, indirect)
- Albumin
- Prothrombin time
- GGT
- Hepatitis serology
- Autoimmune markers

Diagnostic Imaging

- Ultrasonography
- CT Scan
- MRI/MRCP
- ERCP
- Hepatic Elastography

Liver Biopsy

- Gold standard
- Etiology, Grading, Staging of the disease
- Monitoring response to therapy
- Core biopsy, 1.5 to 2.0 cm specimen length
- Replaced by fibrosis markers, elastography

Diagnosis of Liver Disease

- GRADING
  A. Acute or Chronic
  B. Active or Inactive
  C. Mild, Moderate or Severe

- STAGING
  A. Early or Advanced
  B. PreCirrhotic
  C. Cirrhotic

Table 295-4 Child-Pugh Classification of Cirrhosis				
Factor	Units	1	2	3
Serum bilirubin	mol/L mg/ dL	<34 <2.0	34–51 2.0–3.0	>51 >3.0
Serum albumin	g/L g/dL	>35 >3.5	30–35 3.0–3.5	<30 <3.0
Prothrombin time	seconds prolonged INR	0–4 <1.7	4–6 1.7–2.3	>6 >2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

Table 296-1 Liver Test Patterns in Hepatobiliary Disorders

Type of Disorder	Bilirubin	ALT/AST	Alk Phos	Albumin	Prothrombin Time
Hemolysis/Gilbert's syndrome	Normal to 86 mmol/L (5 mg/dL) 85% due to indirect fractions No bilirubinuria	Normal	Normal	Normal	Normal
Acute hepatocellular necrosis (viral and drug hepatitis, hepatotoxins, acute heart failure)	Both fractions may be elevated Peak usually follows aminotransferases Bilirubinuria	Elevated, often >500 IU ALT >AST	Normal to <3x ULN	Normal	Usually normal. If >5X above control and not corrected by parenteral vitamin K, suggests poor prognosis
Chronic hepatocellular disorders	Both fractions may be elevated Bilirubinuria	Elevated, but usually <300 IU	Normal to <3x ULN	Often decreased	Often prolonged Fails to correct with parenteral vitamin K

Alcoholic hepatitis Cirrhosis	Both fractions may be elevated Bilirubinuria	AST:ALT > 2 suggests alcoholic hepatitis or cirrhosis	Normal to <3x ULN	Often decreased	Often prolonged Fails to correct
Intra- and extra-hepatic cholestasis (Obstructive jaundice)	Both fractions may be elevated Bilirubinuria	Normal to moderate elevation Rarely >500 IU	Elevated, often >4x ULN	Normal, unless chronic	Normal If prolonged, will correct with parenteral vitamin K
Infiltrative diseases (tumor, granulomata); partial bile duct obstruction	Usually normal	Normal to slight elevation	Elevated, often >4x ULN	Normal	Normal