LIVER DISEASE

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Overview
Chronic liver disease continues to be a major health concern in Canada. The spectrum of liver disease extends from acute and chronic hepatitis (caused primarily by alcohol or viral infection) to cirrhosis, liver failure, and liver cancer (resulting from viral hepatitis, alcoholic liver disease, or toxins). At present, there are 500,000 to 600,000 people in Canada infected with HBV or HCV.

Patterns of liver disease:

<table>
<thead>
<tr>
<th>Disease Examples</th>
<th>Hepatocellular disease</th>
<th>Cholestatic diseases</th>
<th>Mixed pattern</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>E.g. viral hepatitis or alcoholic liver disease</td>
<td>E.g. gallstone or malignant obstruction, primary biliary cirrhosis, drug-induced liver disease</td>
<td>Mixed presentation</td>
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<tr>
<td>Pathophysiology</td>
<td>Liver injury, inflammation, &amp; necrosis predominate</td>
<td>Inhibition of bile flow predominate</td>
<td>Mixed pathology</td>
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<tr>
<td>Lab Findings</td>
<td>↑↑ aminotransferases &gt;&gt; alkaline phosphatase</td>
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<td>↑↑LFTs</td>
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Evaluation of patients with liver disease:

1. Establishing the etiologic diagnosis
2. Estimating the disease severity (grading): active or inactive, and mild, moderate, or severe
3. Estimating the disease stage (staging): acute or chronic; early or late; pre-cirrhotic, cirrhotic, or end-stage

A complete medical history is the most important part of the evaluation:

- Fatigue (most characteristic symptom)
- Nausea (more severe liver disease)
- Poor appetite with weight loss (common in acute, rare in chronic disease)
- Diarrhea (with severe jaundice)
- Jaundice
- Dark urine
- Light stools (severe cholestasis)
- Injection drug use
- Recent surgery
- Remote or recent transfusion
- Occupation
- Accidental exposure to blood or needlestick
- Familial history of liver disease

Physical examination

Typical physical findings:

- icterus
- hepatomegaly
- hepatic tenderness
- splenomegaly
- spider angioma
- palmar erythema
- excoriation

Signs of advanced disease:

- muscle wasting
- ascites
- edema
- dilated abdominal veins
- hepatic feto
- asterixis
- loss of male-pattern hair distribution
- enlarged Virchow's or Sister Mary Joseph's nodes
- JVD or Rt pleural effusion
- mental confusion
- stupor/ coma
- gynecomastia
- testicular atrophy

Laboratory Studies

As a general rule:

1. Serum bilirubin: a measure of hepatic conjugation and excretion
   - Jaundice without dark urine indicates unconjugated hyperbilirubinemia, seen in hemolytic anemia and genetic disorders of bilirubin conjugation (benign form Gilbert's syndrome, severe form Crigler-Najjar syndrome)
2. Serum albumin: measure of protein synthesis
   - Low albumin suggests chronic process such as cirrhosis or cancer; normal albumin suggests acute process such as viral hepatitis or choledocholithiasis
3. Prothrombin time: a measure of protein synthesis
   - Elevated prothrombin time indicates vitamin K deficiency due to prolonged jaundice and malabsorption or significant hepatocellular dysfunction
   - The failure to correct with IV vitamin K indicates severe hepatocellular injury
Diagnostic Approach

- **Routine history & physical**
- **Initial investigations:**
  - Albumin, Bili, ALT, AST, GGT, AlkP
- **If Acute disease (<6 months) with hepatocellular pattern:**
  - Dx: Hep A/B/C, autoimmune hepatitis, mononucleosis associated hepatitis, Wilson’s disease, ETOH/drug use
  - Evaluation:
    - IgM Anti-HAV, HBsAg, IgM AntiHBC, AntiHCV, ANA, SMA, monospot, ceruloplasm
    - Liver bx reserved for patients in whom dx remains unclear
- **If Acute disease (<6 months) with cholestatic pattern:**
  - Dx: Primary biliary cirrhosis, Drug Abuse, gallstone, biliary duct dilation, fatty liver, masses, ampullary lesions, primary sclerosing cholangitis
  - Evaluation:
    - AMA, drug history, ERCP/MRCP, U/S, MRI
    - Liver bx reserved for patients in whom the dx remains unclear
- **If Chronic disease with hepatocellular pattern:**
  - Dx: Hepatitis B and C, hemochromatosis, Wilson’s disease, autoimmune hepatitis, Alcohol abuse
  - Evaluation:
    - HBsAg, anti-HCV, Fe saturation, ferritin, ceruloplasm, alpha-1 antitrypsin ab, ANA, SMA, U/s, alcohol hx
    - Liver bx often useful to help clarify diagnosis, as well as for staging/grading
- **If Chronic disease with cholestatic pattern:**
  - Dx: Drug abuse, Primary Biliary cirrhosis, Primary sclerosing cholangitis
  - Evaluation:
    - Drug hx, AMA, P-ANCA, u/s, MRCP/ERCP
    - Liver bx often useful to help clarify diagnosis, as well as for staging/grading

Imaging studies

<table>
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<th>CT</th>
<th>U/S</th>
<th>MRI</th>
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<td>Most commonly employed and are complementary to each other</td>
<td>Assess hepatic vasculature and hemodynamics and to monitor surgically or radiologically placed vascular shunts</td>
<td>Evaluation of hepatic masses, staging of liver tumors, and preoperative assessment</td>
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<td>May be useful to detect different degrees of hepatic fibrosis and to obviate the need for liver biopsy in assessing disease stage</td>
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<th>MRCP</th>
<th>ERCP</th>
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<td>Procedures of choice for visualization of the biliary tree</td>
<td>More valuable in evaluating ampullary lesions and primary sclerosing cholangitis</td>
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<tr>
<td>No need for contrast media or ionizing radiation</td>
<td>Offers therapeutic options</td>
</tr>
<tr>
<td>Faster</td>
<td>Less operator dependent</td>
</tr>
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<td>Offers for biopsy, direct visualization of the ampulla and common bile duct, and intraductal ultrasonography</td>
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The two most common schemes for grading liver function are:
1. The Model for End-Stage Liver Disease: provides a more objective measure of disease severity and is currently used to establish priority for liver transplant (MELD score = 3.78[Ln serum bilirubin (mg/dL)] + 11.2[Ln INR] + 9.57[Ln serum creatinine (mg/dL)] + 6.43)
2. The modified Child-Turcotte-Pugh (CTP) score: estimates the likelihood of survival and complications of cirrhosis; it is also used to determine candidacy for liver transplant

Management

Differs based on presentation, diagnosis, and severity. An overall approach should include:
- Abstinence from alcohol
- Hepatitis A & B vaccination
- Influenza and pneumococcal vaccination
- Be careful using any medications, check for effects on liver and liver metabolism
- Upper endoscopy for varices if cirrhosis; chronic therapy with beta blockers or endoscopic obliteration if large varices found
- With cirrhosis: screening and surveillance for hepatocellular carcinoma
  - One appropriate approach is US of the liver q6-12 months

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm