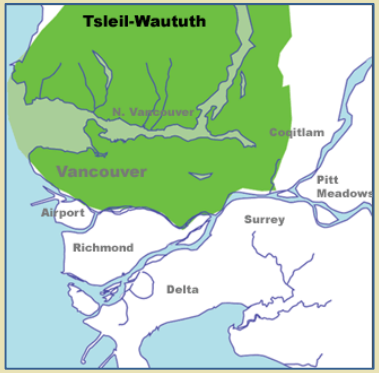
Investigating the Patient with Liver Disease

Eric M. Yoshida
MD, MHSc, FRCPC
Division of Gastroenterology
University of British Columbia

Acknowledgement

With humility, we acknowledge that the sites occupied by the Vancouver General Hospital, GF Strong Centre and UBC Hospital, are on the traditional, ancestral and unceded lands of the Coast Salish community that includes the territories of the Musqueam, Squamish and Tsleil-Waututh Nations



Disclosures
Dr. Eric Yoshida

- Disclosures:
  - Clinical Trials: Pfizer, Vertex Inc, Gilead Sciences, Madrigal, Allergan, Intercept, Genfit, Celgene, Novodisc
  - Unrestricted Research Grants: Paladin Labs

Objectives

- Be aware of the spectrum of liver disease
- Be aware of ‘liver tests’ and their role in the investigation of a patient with liver disease


liver
50 years
1 in 4 Canadians may be affected by liver disease.
Help us, help them.
DONATE NOW

Introduction

- Clinical Context:
  - Acute vs. Chronic Liver Disease
  - Etiology of Liver Disease:
    - viral hepatitis
    - alcoholic/toxin-induced liver disease
    - autoimmune liver disease
    - metabolic liver disease
    - liver cancer
    - multi-factorial

History & Physical Exam

- History:
  - Demographic Information:
    - age
    - gender
    - demographic background
    - place of birth
  - Relevance: etiology, treatment tolerance & likelihood of success

History & Physical Exam

Symptomatic or Asymptomatic:

- decompensated liver disease:
  - GI bleeding (varices)
  - abdominal distention, edema (ascites)
  - day-night reversal, confusion, cognitive problems (encephalopathy)
  - jaundice, pruritis

History & Physical Exam

- Symptomatic Liver Disease
  - Constitutional Symptoms:
    - weight-loss, fever, sweats
  - Viral Extra-hepatic Symptoms:
    - arthritis, arthralgia
    - skin rashes
  - Non-specific: fatigue, " brain fog", RUQ discomfort

History & Physical Exam

- Risk Factors for Viral Infection:
- " Where and When"
  - transfusion of ANY blood products (rbc, plasma, cryoprecipitate, immune globulin)
  - street drug use: injection, intra-nasal, with partners
  - sexual history
  - medical/dental/health procedures

History & Physical Exam

- Risk Factors:
  - occupational history
  - history of physical injury (e.g. assault)
- Alcohol Use: quantity and duration

History & Physical Exam

- Past Medical History & Concurrent Health Problems:
  - previous treatment for viral hepatitis
  - conditions associated with chronic liver disease

    eg. diabetes mellitus (hemochromatosis, HCV), osteoarthritis (hemochromatosis), chronic renal disease (HBV, HCV), obesity (NASH) etc.
  - potential contra-indications for therapy
  - HIV co-infection

History & Physical Exam

- Medications (current and recent)
  - extremely important in acute liver failure (eg. acetaminophen and alcohol, INH, potentially any drug including herbal meds)
  - HAART in HIV, chemotherapy (especially check point inhibitors)
  - Basically any and every drug has been reported to have liver toxicity in someone in the world

History and Physical Exam

- Social History
  - employment history: level of recent functioning, need for disability
  - social support system (implications for therapy)
  - addiction history (implications for therapy)
  - medical compliance assessment
  - dietary and exercise history

History & Physical Exam

- Physical Exam:
  - General Physical Exam (all systems)
  - Note: cognitive state (encephalopathy), muscle wasting (decreased in ESLD), skin rashes (HCV-assoc vasculitic lesions) including excoriations (pruritis in cholestasis), BMI

History & Physical Exam

- Note any specific signs of Liver Disease;
  - hepatic fetor (sweet clover smell)
  - jaundice (scleral icterus)
  - palmer erythema
  - spider nevi
  - abdominal distention (ascites) & peripheral edema

History & Physical Exam

- Liver span and texture (soft, firm, nodular, hard)
- Splenomegaly (presence of portal hypertension)
- Asterixis (liver flap – encephalopathy)

Laboratory Assessment

- General assessment:
  - anemia
  - MCV (increased in liver disease, decreased in iron deficiency)
  - leukopenia (possible splenomegaly)
  - thrombocytopenia (always decreased in splenomegaly)

Laboratory Assessment

- Liver Enzymes:
  - AST, ALT: also found in skeletal muscle damage (eg. traumatic injury, polymyositis)
  - alkaline phosphatase: also found in bone (eg. compression fractures, bone mets)
  - GGT (induced by drugs especially alcohol)

Laboratory Assessment

- Pattern of Liver Enzymes Important
  - Hepatocellular: AST, ALT eg. viral hepatitis, autoimmune hepatitis
  - Cholestatic: alkaline phosphatase, GGT eg. biliary obstruction, cholestatic liver disease (PBC, PSC)

Laboratory Assessment

- Pattern of Liver Enzymes:
  - Mixed: AST, ALT, alk phos, GGT all increased
- Liver Enzyme abnormalities: etiologically non-specific!

Laboratory Assessment

- Liver Function Tests:
  - synthetic function: serum albumin, coagulation factors (ie. INR)
  - abnormality implies severe liver dysfunction
  - liver excretion: total bilirubin (increased in end-stage disease or biliary obstruction)
  - serum creatinine is a liver function test! (renal function deteriorates in liver disease)

Laboratory Assessment

- Specific Diagnostic Tests
- Hepatitis A:
  - HAV-IgM (acute infection)
  - HAV-IgG (previous infection/vaccination)

Laboratory Assessment

- Hepatitis B
  - HBsAg (on-going infection)
  - anti-HBs (previous infection/vaccination)
  - anti-HBc (previous infection: either on-going or cleared)
  - HBeAg (active replication – active infection)
  - anti-HBe (no active replication, chronic carrier)

Laboratory Assessment

- Hepatitis B
  - HBV-DNA: gold standard of active replication
  - problem with pre-core mutants (limits usefulness of HBe/antiHBe significance)

Laboratory Assessment

- Hepatitis D
  - frequent co-infection with HBV
- Hepatitis C
  - anti-HCV serology: previous infection, 75-80% chronic infection
  - HCV-RNA: qualitative vs. quantitative (can get genotype, less sensitive)

Laboratory Assessment

- Metabolic Liver Disease
  - hemochromatosis: ferritin, serum iron, TIBC & % iron binding, genetic markers (C282Y, H63D)
  - Wilson's Disease; serum ceruloplasmin, serum copper, 24 hour urinary copper
  - Alpha 1 anti-trypsin level (A1T deficiency)

Laboratory Assessment

- Autoimmune Liver Disease
  - Autoimmune Hepatitis: ANA (anti-nuclear antibody), anti-smooth muscle antibody
  - Primary Biliary Cirrhosis: AMA (anti-mitochondrial antibody)

Laboratory Assessment

- Hepatocellular Carcinoma (Hepatoma)
  - alphafetoprotein (AFP): mild-moderate elevation in chronic hepatitis, can be normal despite large HCC
- Cholangiocarcinoma:
  - CA 19-9: also marked elevation in pancreatic cancer

Diagnostic Imaging

- Abdominal Ultrasound:
  - screen for portal hypertension (splenomegaly, ascites, hilar varices)
  - screen for hepatocellular carcinoma
  - dilated biliary ducts: implies obstruction (eg. stones, stricture, tumour)
  - can detect hepatic steatosis

Diagnostic Imaging

- Triphasic CT Scan/MRI:
  - confirm benign mass (hemanigoma), maligancies

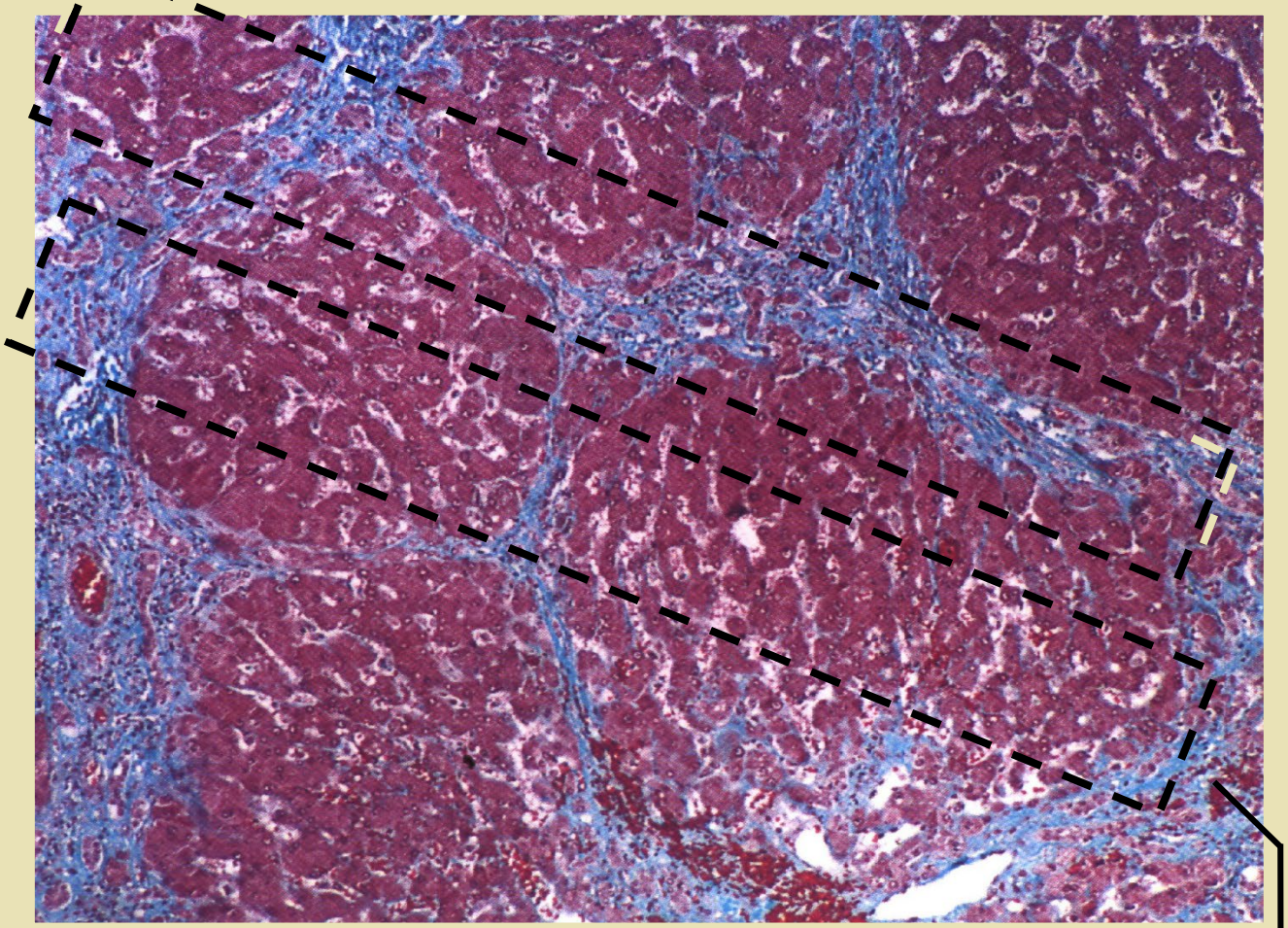
Diagnostic Imaging

- Biliary Imaging:
  - cholangiogram: ERCP vs MRCP
  - direct visualisation of intra-extra hepatic ducts: primary sclerosing cholangitis, cholangiocarcinoma, extra-hepatic obstruction (eg. pancreatic ca), biliary stones

Histopathology

- Liver Biopsy;
  - degree of chronic hepatitis
  - grade of fibrosis (including cirrhosis)
  - iron deposition
  - Tumour (cancer cells can seed outside liver)

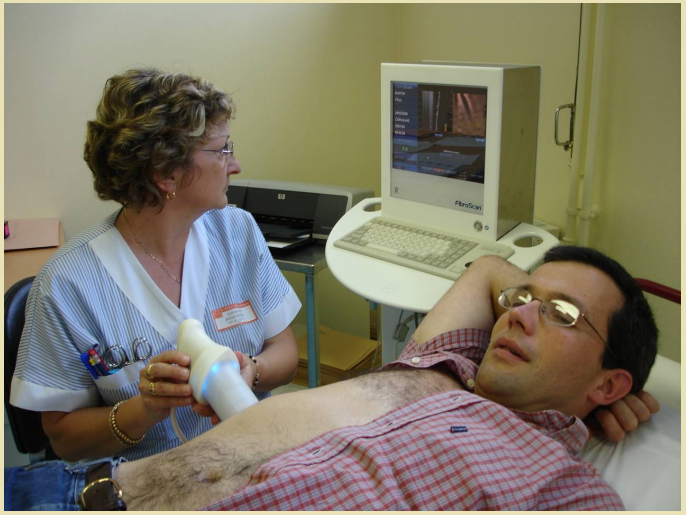
Sampling Error of Liver Biopsy



Courtesy of M. Pinzani, Florence

FibroScan

- Non-invasive
- Examination time < 5 minutes
- Median value of 10 successful acquisitions
- Sampling volume
  - Biopsy – 1/50,000
  - Fibroscan – 1/500



Global Liver Assessment

- Child-Pugh Score:
  - composite score: ascites, encephalopathy, total bilirubin, serum albumin, INR
  - each category: scored 1-3 based on severity
  - global score: 5 (normal) to 15
  - Child's A (5-6), B (7-8), C (9+)

MELD Score

- Adopted by United Network for Organ Sharing (USA) for classification of disease severity
- Formula Includes Natural Log of Total Bilirubin, S. Creatinine, INR

Investigation of Liver Disease

- " What are the end-points of investigation?"
  - etiology of liver disease
  - public health considerations
  - assessment of disease severity (including consideration of referral)
  - consideration of therapy (including liver transplant candidacy)
  - monitoring of therapy and outcome of therapy

In Memorium: Dr. Pieter Swart