



Montefiore Montefiore Einstein
Center for Transplantation

The ABCs of Liver Disease

HIV and Hepatitis Management

The New York Course

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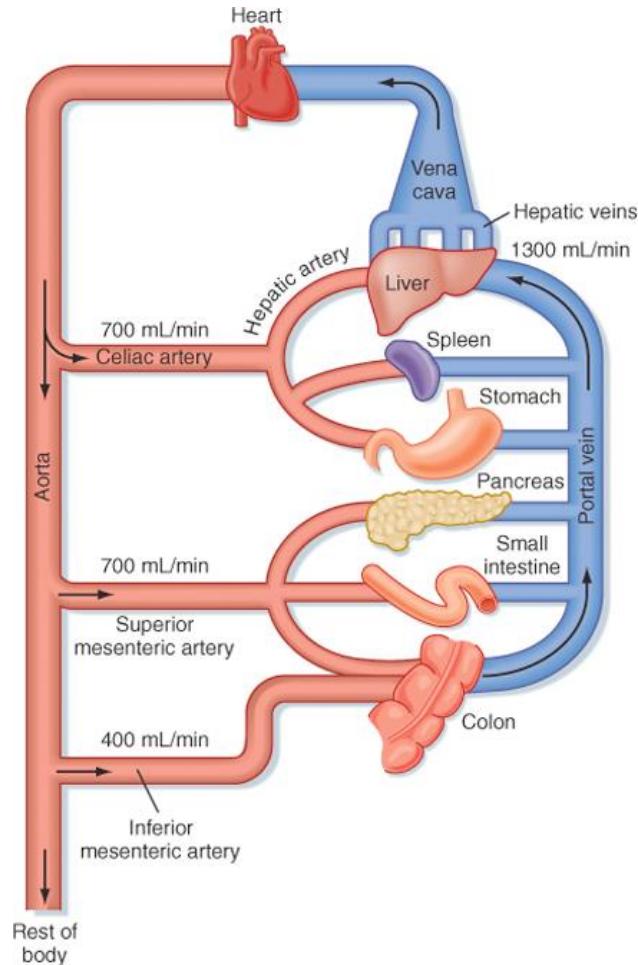
Note on references

References listed in the syllabus are cited by number in the text of slides.

Outline

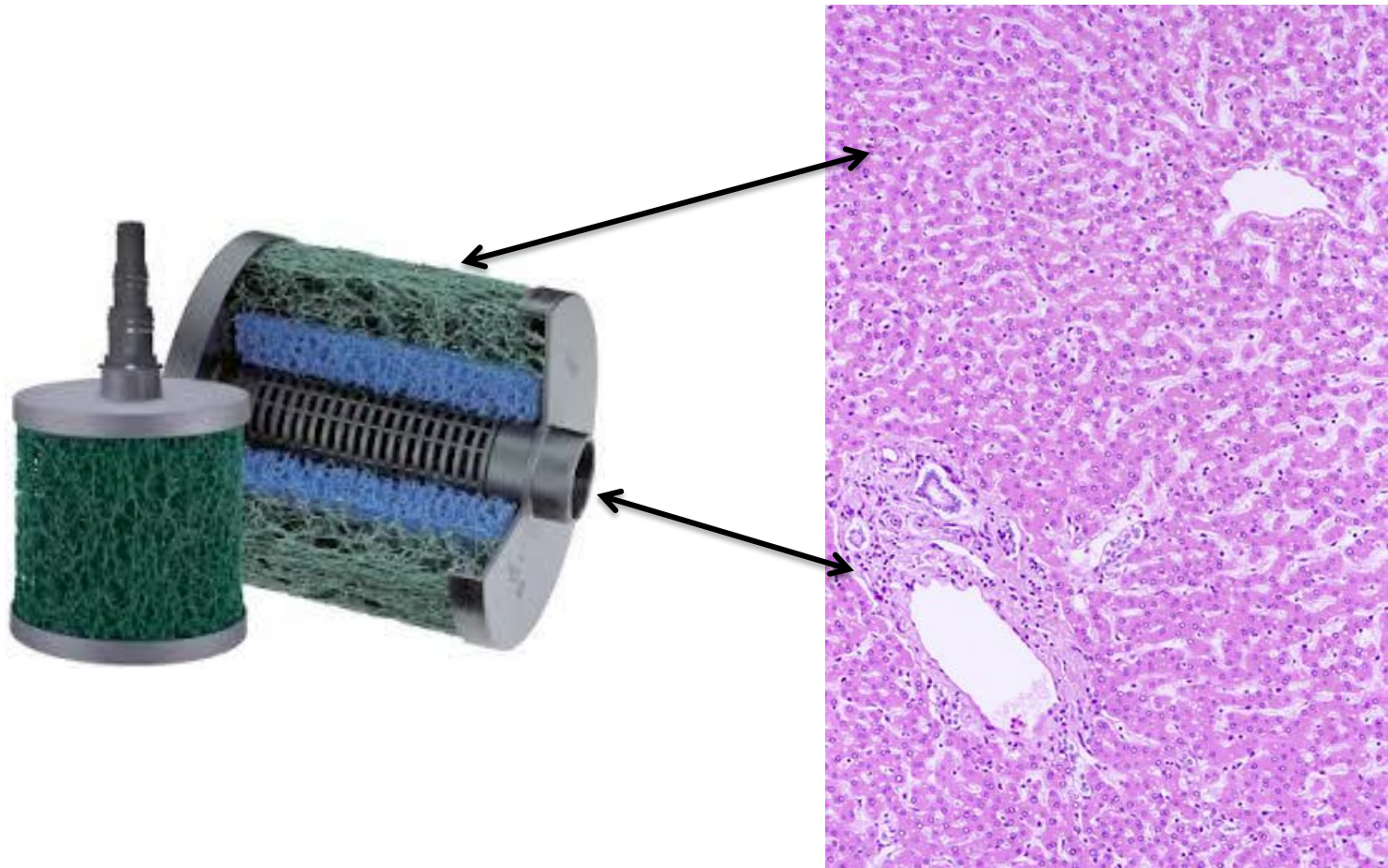
1. Why we need our livers: **LIVER FUNCTION**¹
2. Usual presentations of **LIVER DYSFUNCTION**²
3. Interpretation of **LIVER** ~~function~~ **TESTS**
4. **GARDEN-VARIETY LIVER DISEASE**: what we should expect, what we should fear³
5. The importance of **STAGING** chronic liver disease^{12,13}

Normal liver function



The liver is a metabolically active filter¹

Normal liver microanatomy



Abnormal liver function

Injury	Impaired Filtration	Impaired Metabolism
Acute	O	X
Chronic	X	O
Liver Failure	X	X

Disease discovery: ~~liver function tests~~¹

-
- Cell Integrity:*
- AST
 - ALT

-
- Bile Excretion:*
- Bilirubin
 - Alkaline phosphatase
 - Cholesterol

-
- Metabolic Capacity:*
- Bilirubin
 - Prothrombin time
 - Albumin
 - Cholesterol

-
- Immune Surveillance:*
- Serum globulin
-

Types of liver injury: hepatocellular¹

-
- Cell Integrity:*
- AST
 - ALT

-
- Bile Excretion:*
- Bilirubin
 - Alkaline Phosphatase
 - Cholesterol

-
- Metabolic Capacity:*
- Bilirubin
 - Prothrombin time
 - Albumin
 - Cholesterol

-
- Immune Surveillance:*
- Serum Globulin
-

Types of liver injury: cholestatic¹

-
- Cell Integrity:*
- AST
 - ALT

-
- Bile Excretion:*
- Bilirubin
 - Alkaline Phosphatase
 - Cholesterol

-
- Metabolic Capacity:*
- Bilirubin
 - Prothrombin time
 - Albumin
 - Cholesterol

-
- Immune Surveillance:*
- Serum Globulin
-

Hepatocellular vs cholestatic disease²

$$\frac{\text{ALT}}{\text{Alk Phos}} \quad (\text{expressed as multiples of ULN})$$

Hepatocellular disease: Ratio >5

Cholestatic disease: Ratio <2

Mixed disease: Ratio = 2-5

Etiologic diagnosis

1. The **TYPE** of test abnormality: *cellular, cholestatic, or mixed*
2. The **TIME COURSE** of the test abnormality: *acute, chronic, or acute on chronic (lice & fleas)*
3. The **CONTEXT** of the test abnormality: viral exposure, new medications, alcohol abuse
4. The **PATTERN** of the test abnormality: many etiologies cause characteristic patterns of test results (fingerprints)

Patterns of liver injury

Fatty liver:

- AST & ALT <100
- Often fluctuate
- Normal bilirubin, INR

Hepatic ischemia:

- AST & ALT >1,000
- AST >ALT
- Normal bilirubin, INR
- Progressive resolution

The pattern of the liver-test abnormality is the fingerprint of the perpetrator

Autoimmune:

- AST & ALT >100
- Looks like viral hepatitis
- May have negative markers

What varieties of liver disease are we likely to encounter?³

ACUTE:

Toxic: **DRUGS**; alcohol

Viral: HAV, HBV

Other: immune, **ISCHEMIA**

CHRONIC:

Metabolic: **FAT** (NAFLD; NASH)

Viral: HBV, HCV

Other: immune-mediated

Drug-induced liver injury (DILI)^{4,5,6,7,8}

1. Usually causes primary hepatocellular liver injury (abnormal AST, ALT) but may be cholestatic or mixed
2. Vast majority of episodes are unpredictable, with variable latency (3-365 days)
3. Believed most often to be caused by immuno-allergenic reactions or abnormal metabolism
4. With continued exposure, mild injury often resolves, but severe injury usually worsens
5. Patients with chronic liver disease are generally not more susceptible than others, unless hepatic metabolism impaired
6. Although a clear dose relationship is usually absent, most episodes occur with doses >50 mg/day

Most common causes of adult DILI

Drugs	ALF Study Group⁶ n = 137	DILI Network⁷ n = 519
Antibiotics		
INH	25	28
Sulfa drugs	12	8
Nitrofurantoin	11	23
Azoles	6	12
Amox/clavulanate	0	37
Other	13	115
Anticonvulsants		
Phenytoin	8	7
Others (psychotropics)	10	43
NSAIDS	7	21
Herbal concoctions	14	59

Diagnosis and evaluation of DILI

United States National Library of Medicine
NIDDK NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

LiverTox
Clinical and Research Information on Drug-Induced Liver Injury

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SEARCH THE LIVERTOX DATABASE

Search for a specific medication, herbal or supplement:

Search

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LIVERTOX® provides up-to-date, accurate, and easily accessed information on the diagnosis, cause, frequency, patterns, and management of liver injury attributable to prescription and nonprescription medications, herbals and dietary supplements. LIVERTOX also includes a case registry that will enable scientific analysis and better characterization of the clinical patterns of liver injury. The LIVERTOX website provides a comprehensive resource for physicians and their patients, and for clinical academicians and researchers who specialize in idiosyncratic drug induced hepatotoxicity.

Diagnosis and evaluation of DILI

- Guilt by association
- Other causes (viral; AIH)?
- Encephalopathy?
- Coagulopathy?
- Acidosis?
- Renal failure?

Verizon 3G 2:59 PM

Acute Liver Failure Study Group

Prognostic Score

Predicted transplant free survival at 21 days:

Hepatic Encephalopathy?

Etiology?

Vasopressor Use?

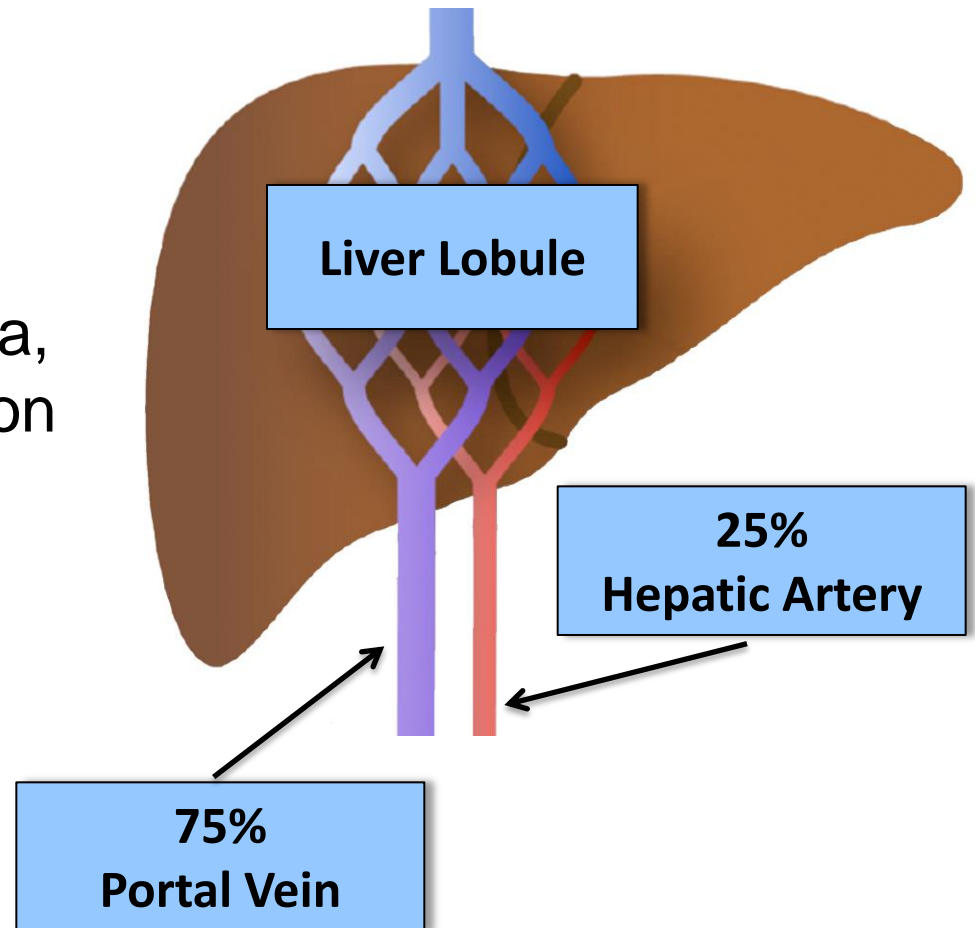
Bilirubin?

INR?

Clear Info

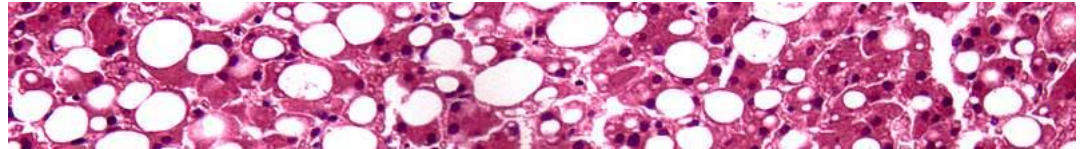
Ischemic liver injury

- Portal flow has low pressure but high volume
- Reduced by diarrhea, vomiting, hypotension
- Aminotransferases 1,000 or greater
- AST > ALT
- Daily improvement



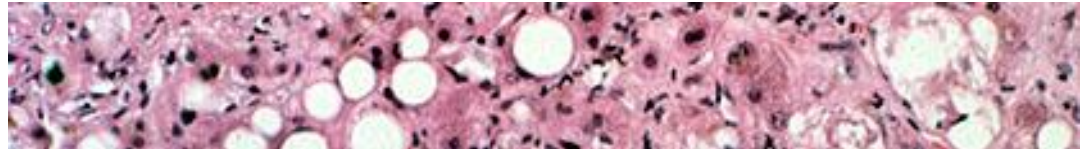
Fatty liver disease (NAFLD)^{9,10,11}

NAFL: 25% of
US population



(99% of the morbidly obese; 3% of lean individuals)

NASH: 30% of
NAFLD



Fibrosis:
50% of NASH



Risk factors for NAFLD^{9,11}

Risk Factor	Prevalence of NAFLD
Truncal obesity	50%-75% (>90% of morbidly obese)
Type-2 diabetes	10%-75%
Hyperlipidemia	30%-50%
None recognized	3%

Diagnosis of fatty liver disease⁹

- A diagnosis of exclusion: with a typical liver-test pattern and no virus or toxin
- Imaging corroborates impression of NAFLD
- Biopsy is necessary to diagnose NASH
- We often assume that NASH is cause in cases of cryptogenic cirrhosis

Reasons for staging in patients with chronic liver disease¹²

- Evidence that chronic injury is causing significant liver damage
- Prognosis of liver disease
- Indication to screen for hepatocellular carcinoma
- Indication to screen for esophageal varices

Staging methods

VALIDATED

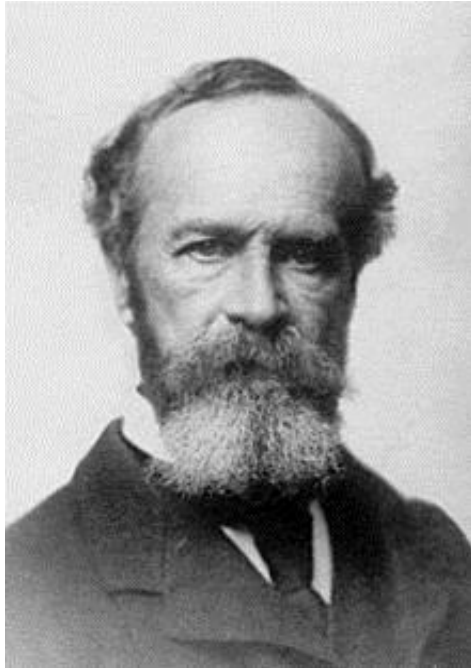
- Liver biopsy
- Serum markers
- Transient elastography
- MR elastography
- Combination of above

NOT FOR STAGING

- Ultrasound
- CT
- Standard MR
- HCV viral load
- Aminotransferase level

The ABCs of liver disease

1. Begin by noting the **PATTERN** and **DURATION** of the liver-test abnormality
2. Does the pattern make sense in terms of the **HISTORY**?
3. **SCREEN** for virus, **SUSPECT** drugs and fat, and **BEWARE** of AIH
4. Always **STAGE** chronic disease
5. **SCREEN FOR HCC** if advanced-stage fibrosis, even after HCV cured or if NASH¹³



Question: Is life worth living?

Answer: It depends upon
the liver!

William James
International Journal of Ethics,
1895

Thank you for your
attention

HIV Management
Hepatitis Management

THE NEW YORK COURSE

