

# Hepatology for the Nonhepatologist

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IAS-USA

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## Learning Objectives

After attending this presentation, learners will be able to:

- Describe the progression of liver fibrosis and methods to stage it
- Describe the features of decompensated liver disease
- Know when to send patients to a transplant center

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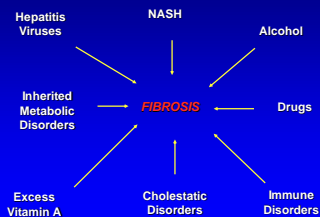
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## Hepatic Fibrosis is the Liver's Wound Healing Response to Many Chronic Injuries



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### CLASSIFICATION OF INJURY PATTERNS

Hepatocellular	Cholestatic	Mixed
ALT	Bilirubin	All with Similar Abnormalities
AST	Alkaline Phosphatase	
	GGT	

R score: ALT/Alk Phos expressed as multiple of upper limit of normal range  
 R>5= Hepatocellular; R= 2-4.99= Mixed; R<2= Cholestatic

Danan et al. *J CLIN EPI*, 1993

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### ACUTE VS. CHRONIC

- Acute
  - Resolved within 6 months of onset or
  - Resolved following drug discontinuation
- Chronic
  - Persists beyond 6 months

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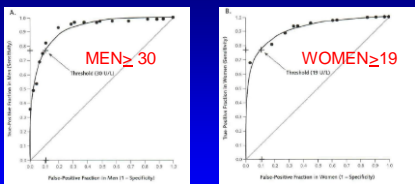
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### Updated ALT Ranges



Newly calculated healthy limits are indicated in each panel. A) Male participants. B) Female participants. To convert the alanine aminotransferase thresholds to  $\mu\text{kat/L}$ , multiply by 16,667.

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Prati, et al. 2002, *Ann of Int Med*

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## ASSESSMENT OF HEPATIC FIBROSIS and STEATOSIS/STEATOHEPATITIS

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### Hepatic Fibrosis

- Type of injury determines pattern
- For most diseases, distribution is homogenous
- Inflammation is transient, fibrosis is plastic but the process of change is glacial
- Cirrhosis is a histological diagnosis, not a clinical diagnosis but in the U.S. decompensated disease=cirrhosis

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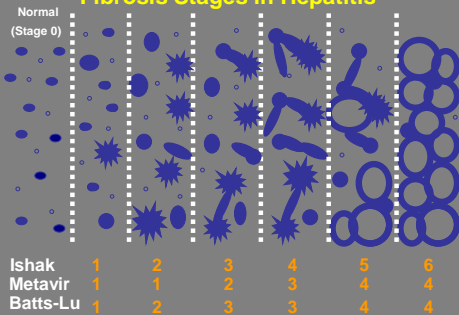
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### Fibrosis Stages in Hepatitis



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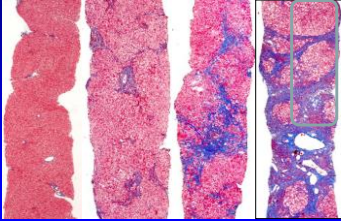
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## Fibrosis/Cirrhosis



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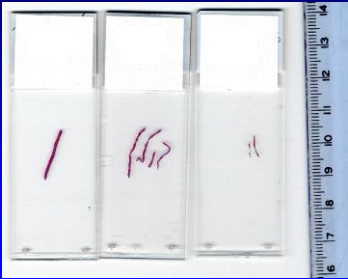
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## Transient Elastography



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## TRANSIENT ELASTOGRAPHY Readout



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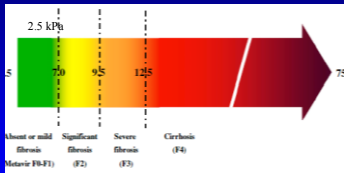
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## Elastography: HCV



Affected by weight, access of probe (2 cm), ascites, inflammation, iron and other factors

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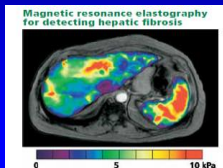
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## MRI Elastography

- Similar to transient elastography but can demonstrate the liver stiffness in the WHOLE organ and is colour coded
- Can distinguish Child-Pugh grade A cirrhosis from other grades to be 93% sensitive and 82% specific



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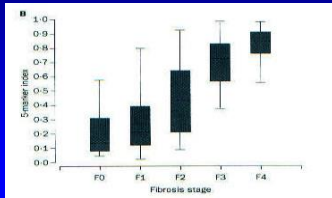
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## FIBROSIS MARKERS Predictive Model



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Imbert-Bismut, LANCET, 2001

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## FIBROTEST/FIBROSURE Interpretation

Fibrotest® score	Estimate of fibrosis stage
0,00-0,21	F0
0,22-0,27	F0-F1
0,28-0,31	F1
0,32-0,48	F1-F2
0,49-0,58	F2
0,59-0,72	F3
0,73-0,74	F3-F4
0,75-1,00	F4

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## FIB-4

- Uses easily acquired information

- Age
- Platelet Count
- AST
- ALT

- Formula

$$\frac{\text{AGE} \times \text{AST}}{\text{PLT} \times \sqrt{\text{ALT}}}$$

Interpretation: <1.45 is F0/1 or >3.25 is F3/4 with 65% Positive Predictive value

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Sterling RK et al, HEPATOLOGY 2006

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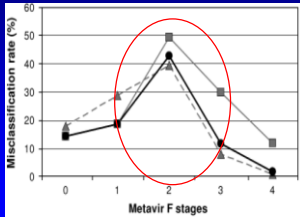
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## MISCLASSIFICATION RATE Non-Invasive Tests



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Boursier J et al. LIVER INT, 2009

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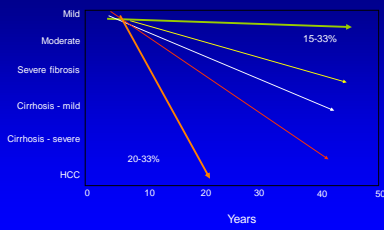
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## FIBROTIC PROGRESSION



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adapted from Akthal, Sem Liver Disease, 2004

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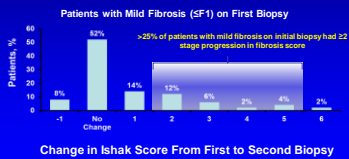
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## Rapid Progression of Liver Disease in HIV/HCV-Coinfected Patients

- Prospective study of fibrosis progression in 67 coinfectd patients
- 2 biopsies; median time between biopsies was 2.84 years



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Sulkowski M et al. AIDS, 2007 and Konerman MA et al. HEPATOLOGY 2014

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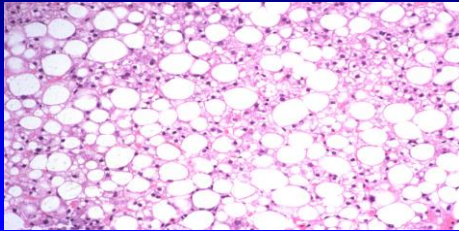
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## FATTY LIVER



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## CAP Interpretation

### NAS (Brunt) Steatosis Grade

- Stage 0 <5% <240
- Stage 1 6-33% 241-300
- Stage 2 34-66% 300-350
- Stage 3 67-100% >350

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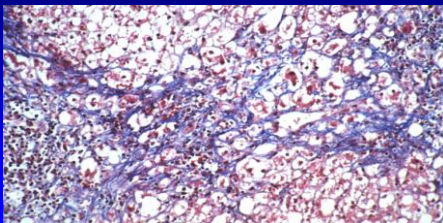
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## STEATOHEPATITIS WITH PERICELLULAR FIBROSIS



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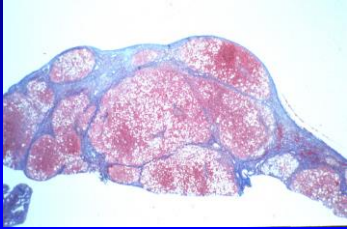
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## NASH CIRRHOSIS



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## NASH CRN Scoring System

NASH activity grade: grade = total score: S + L + B (range 0-8)

Steatosis	S score	Lobular inflammation	L score	Hepatocyte ballooning	B score
< 5%	0	None	0	None	0
5-33%	1	< 2	1	Few ballooned cells	1
34-66%	2	2-4	2	Many ballooned cells	2
> 66%	3	> 4	3		

NASH fibrosis stage	Stage
None	0
Mild, zone 3 perisinusoidal fibrosis	1a
Moderate, zone 3 perisinusoidal fibrosis	1b
Portal/perportal fibrosis only	1c
Zone 3 perisinusoidal and portal/perportal fibrosis	2
Bridging fibrosis	3
Cirrhosis	4

NASH = 5 or Greater

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Kleiner et al. HEPATOLOGY, 2005

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## COMPLICATIONS OF CIRRHOSIS

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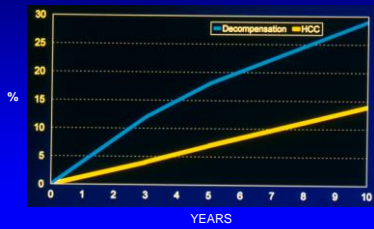
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### HCV in Cirrhotic Patients Risk of Decompensation and HCC



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Fattovich et al., Gastroenterology 1997; 112:463

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### HEPATIC DECOMPENSATION

- Ascites
  - Hepato-Renal Syndrome (HRS)
  - Hepatic Hydrothorax
  - SBP
- Encephalopathy
- Bleeding Varices
- Coagulopathy (PT >3 seconds>control)

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### Clinical Staging of Cirrhosis: Child-Turcotte-Pugh Score

Score	Bilirubin (mg/dL)	Albumin (g/dL)	PT (INR)	Hepatic Encephal	Ascites (grade)
1	<2	>3.5	<1.7	None	None
2	2-3	2.8-3.5	1.8-2.3	1-2	Mild
3	>3	<2.8	>2.3	3-4	Severe
<b>Child Class</b>		<b>A</b>	<b>5-6</b>		
		<b>B</b>	<b>7-9</b>		
		<b>C</b>	<b>&gt;9</b>		

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Pugh RNH et al. *Brit J Surg.* 1973; 60:464-69.

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## MELD

- MODEL FOR END-STAGE LIVER DISEASE
  - Bilirubin
  - Creatinine
  - INR
- Used to predict mortality and time for OTL Tx
  - Example: Creatinine 1.6; Bili 1.4; INR 1.6
  - MELD=17
  - Estimated 3 month mortality: 18%

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## LIVER TRANSPLANTATION When to Refer

- Any hepatic decompensation
  - Ascites
  - Encephalopathy
  - Variceal bleeding
- MELD >10
- HCC

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## HCC SURVEILLANCE

- Ultrasound
  - Every 6 months
  - Subjective, experience matters
- AFP and related markers
  - Not recommended by AASLD
  - Used by most hepatologists

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## SUMMARY

- HCV is ALSO a Liver Disease
  - Ask Whether Advanced Fibrosis is Present
  - If Yes, Start Surveillance for
    - Varices (EGD)
    - Ascites (US)
    - HCC (US)
- CONTACT HEPATOLOGIST EARLY WHEN ANY SIGN OF DECOMPENSATION IS PRESENT

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## Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!

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