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Upon successful completion of this activity 1 contact hour will be awarded

Successful completion of this continuing education activity includes the following:

- Attending the entire CE activity;
- Completing the online evaluation;
- Submitting an online CE request.

Your certificate will be sent via email

If you have any questions about this CE activity, contact Michelle Daugherty at mdaugherty@cardeaservices.org or (206) 447-9538

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CONFLICT OF INTEREST

Paulina Deming is on an advisory committee for Gilead.

None of the other planners or presenters of this CE activity have any relevant financial relationships with any commercial entities pertaining to this activity.

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HCV ECHO®
WESTERN STATES

Liver Fibrosis Staging

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Original presentation by:
Date prepared:

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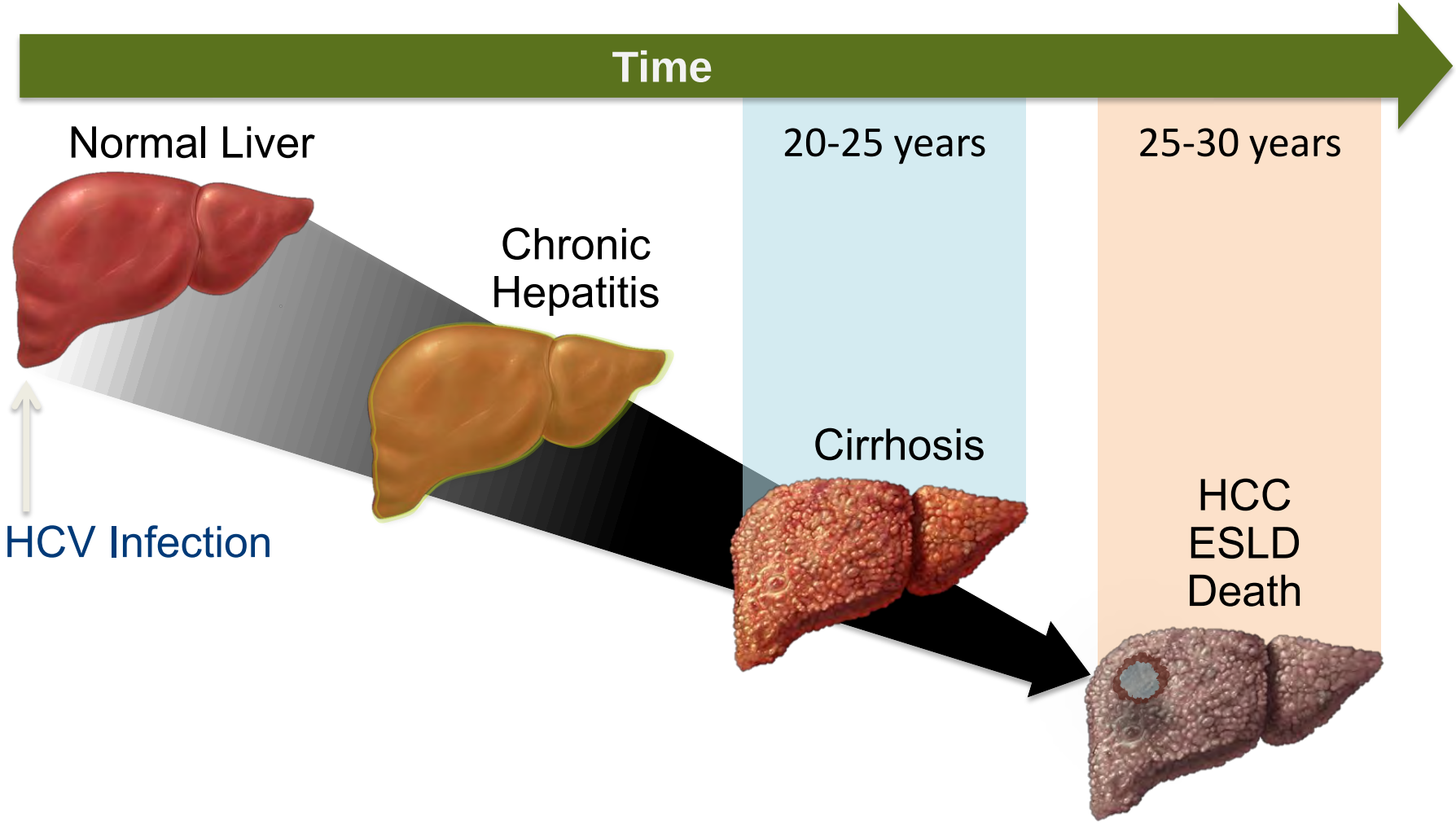
OBJECTIVES

1. Describe the stages of hepatitis C related liver disease;
2. Identify non-invasive liver fibrosis staging methods

Why is it Important to Stage a Patient's Level of Liver Disease?

- Patients with cirrhosis may require a longer duration of HCV treatment and/or addition of ribavirin
- Patients with cirrhosis require additional evaluation and follow up care
  - Endoscopy for evaluation of varices
  - On-going (and indefinite) surveillance for hepatocellular carcinoma

Hepatitis C: Progression of Disease



Hepatitis web study

Laboratories for Recognizing Fibrosis/Cirrhosis

- Alanine aminotransferase (ALT), aspartate aminotransferase (AST)

Recognize level of inflammation and liver injury

- Serum albumin, direct bilirubin, international normalized ratio (INR)

Assess hepatic synthetic function

- Complete blood count with differential

Identify changes consistent with cirrhosis

Why is the CBC Important to Understand Liver Disease Severity?

- Anemia
  - Can indicate complications of cirrhosis
  - Sudden decline in hemoglobin concerning for bleeding
  - Trends in declining hemoglobin concerning for slow bleeding
- Thrombocytopenia (<150 thousand)
  - Due to portal hypertension caused by cirrhosis
  - Portal hypertension causes:
    - Platelets to become “stuck” in spleen
    - More platelets damaged/destroyed
- Neutropenia
  - Cirrhosis can cause bone marrow suppression

Abnormalities in Hepatic Panel

- Elevations in AST or ALT useful for measuring liver cell injury
  - What is normal AST or ALT? 40 IU/mL
  - Studies suggest this is too high and normal should be lower and different for men vs. women
  - **Healthy ALT** is <30 IU/mL for men and <19 IU/mL for women
- Elevations in conjugated bilirubin suggest liver disease
- Loss of liver's ability to synthesize (lack of synthetic function) can be seen with:
  - Low serum albumin
  - Prolonged prothrombin time (elevated INR)
  - Important to look at trends in labs over time

Findings Suggestive of Advanced Fibrosis/ Cirrhosis

- Presence or history of ascites or esophageal varices
- Low platelet count (<150,000 mm^3)
- APRI $\geq$ 1.0
- FIB-4 $\geq$ 3.25
- Fibrosure $\geq$ 0.72
- Imaging with evidence of cirrhosis (nodular contour of liver or evidence of portal hypertension)
- Liver biopsy with F3 or F4 fibrosis
- Transient elastography consistent with advanced fibrosis/cirrhosis

AST to Platelet Ratio Index (APRI) Calculator

This is an AST to Platelet Ratio Index calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most laboratories use 40 IU/L as the value for the AST upper limit of normal.

Use an upper limit of normal of 40

$$\text{APRI} = \frac{\dfrac{\text{AST Level } (IU/L)}{0}}{\dfrac{\text{AST (Upper Limit of Normal) } (IU/L)}{0}} \Big/ \frac{\text{Platelet Count } (10^9/L)}{0} \times 100 =$$

Interpretation:
In a meta-analysis of 40 studies, investigators concluded that an APRI cuttoff of 1.0 had a sensitivity of 76% and specificity of 72% for predicting cirrhosis. Similarly, an APRI cuttoff of 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.

Source: Lin ZH, Xin YN, Dong QJ, et al. Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis. Hepatology. 2011;53:726-36.

https://www.hepatitisc.uw.edu/page/clinical-calculators/apri

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Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT (U/L)}}} =$$

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis. In the patient cohort in which this formula was first validated, at least 70% patients had values <1.45 or >3.25. Authors argued that these individuals could potentially have avoided liver biopsy with an overall accuracy of 86%.

Sources

Sterling RK, Lissen E, Clumeck N, et. al. Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. Hepatology 2006;43:1317-1325.

https://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4

Project ECHO

Child-Pugh Classification of Cirrhosis for Drug Dosing

	1 Point	2 Points	3 Points
Encephalopathy	None	Moderate	Severe
Ascites	Absent	Mild-Moderate	Severe/ Refractory
Bilirubin (mg/dL)	< 2	2 - 3	> 3
Albumin (g/dL)	> 3.5	2.8 - 3.5	< 2.8
INR (PT Prolongation *sec over control)*	<1.7 (0-4)	1.7-2.3 4-6	>2.3 (>6)

Child-Pugh Interpretation of Hepatic Function in a Patient with Cirrhosis

C-P Score (Class)	***Liver Function***
5-6 (A)	Mild Dysfunction
7-9 (B)	Moderate Dysfunction Moderate dose reduction (~25%) for drugs that are mostly hepatically metabolized
> 9 (C)	Severe Dysfunction Significant dose reduction (~50%) for drugs that are mostly hepatically metabolized

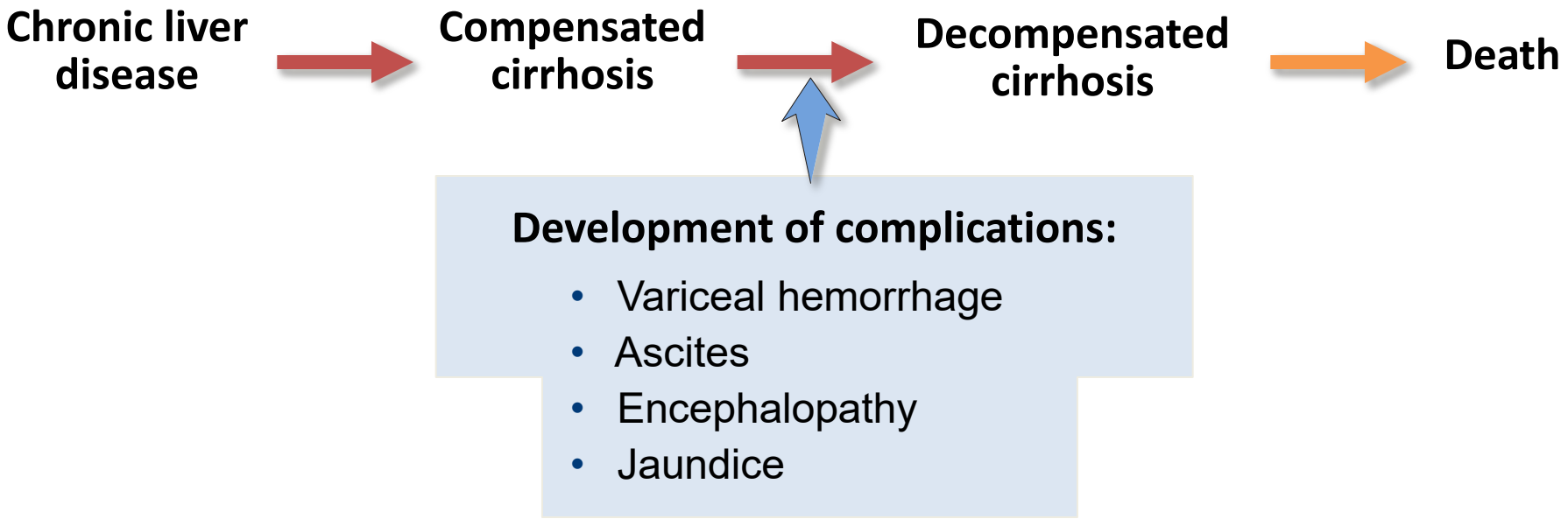
Note: Child Pugh Score is calculated only for patients with cirrhosis

Liver Biopsy is Gold Standard but…

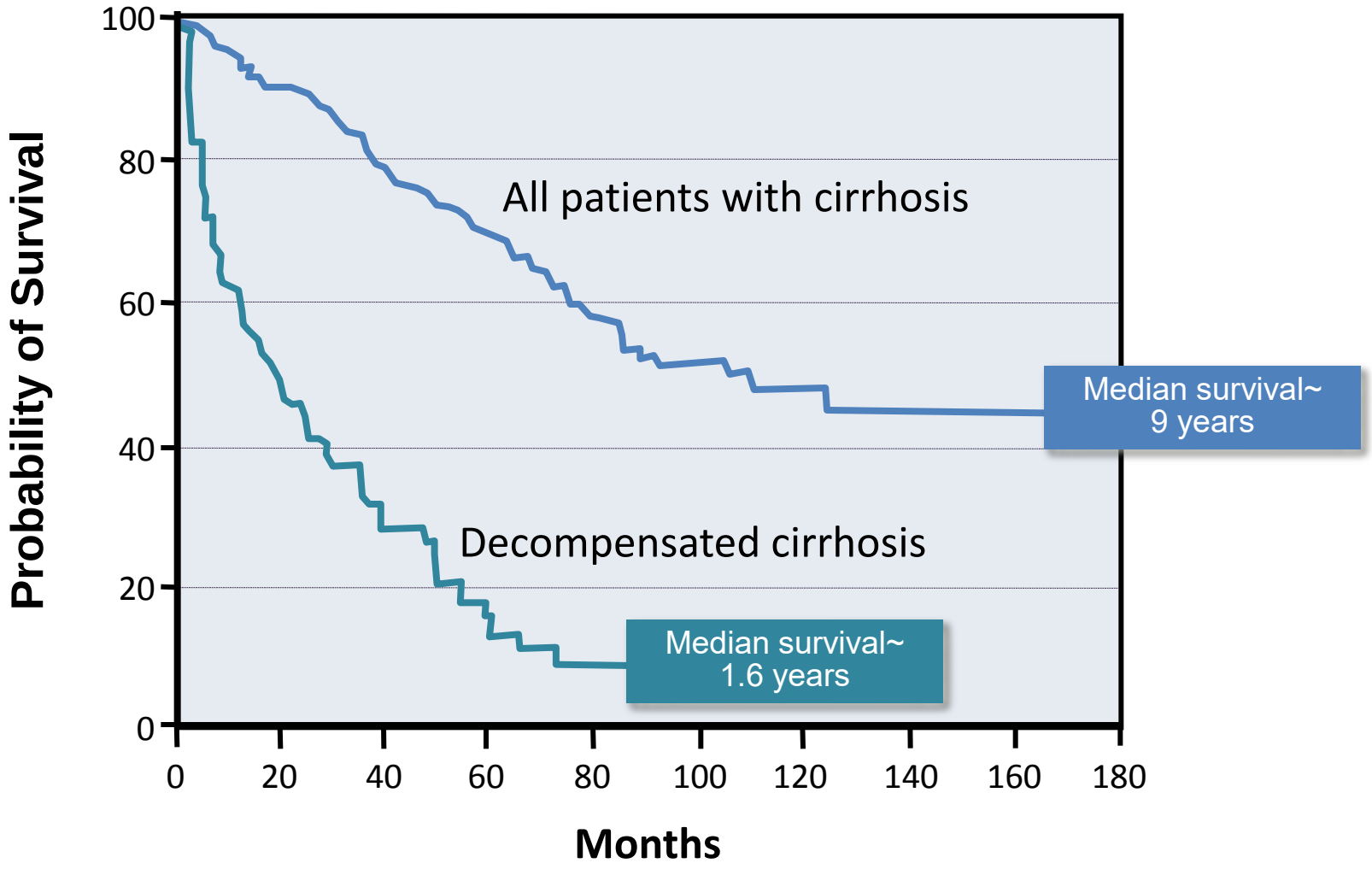
- Liver biopsy is not reliable gold standard
  - Sampling error leads to misinterpretation in 10-15% of cases
  - Can miss the diagnosis of cirrhosis
  - Invasive procedure with complications
  - Expensive
  - Poor patient acceptance
  - Interpretation has significant inter observer variability

Seeff LB, et al. Clin Gastroenterol Hepatol. 2010;8:877–883.
The French METAVIR Cooperative Study Group. Hepatology. 1994;20:15-20

Natural History of Chronic Liver Disease



Patients with Cirrhosis
Decompensation Shortens Survival



Source: Ginés P, et al. Hepatology 1987; 7:122-8.

Summary

- Important to recognize cirrhosis for medical management of HCV and for management of complications associated with chronic liver disease
- Advanced fibrosis/cirrhosis can be identified by
  - Minimally invasive tests including laboratories
  - Scoring systems utilizing laboratories
  - Imaging
  - Transient elastography
- Role of biopsy diminished in identifying cirrhosis

End of Presentation

Questions?