

HEPATITIS C CURRICULUM

Referral for Liver Transplantation Evaluation

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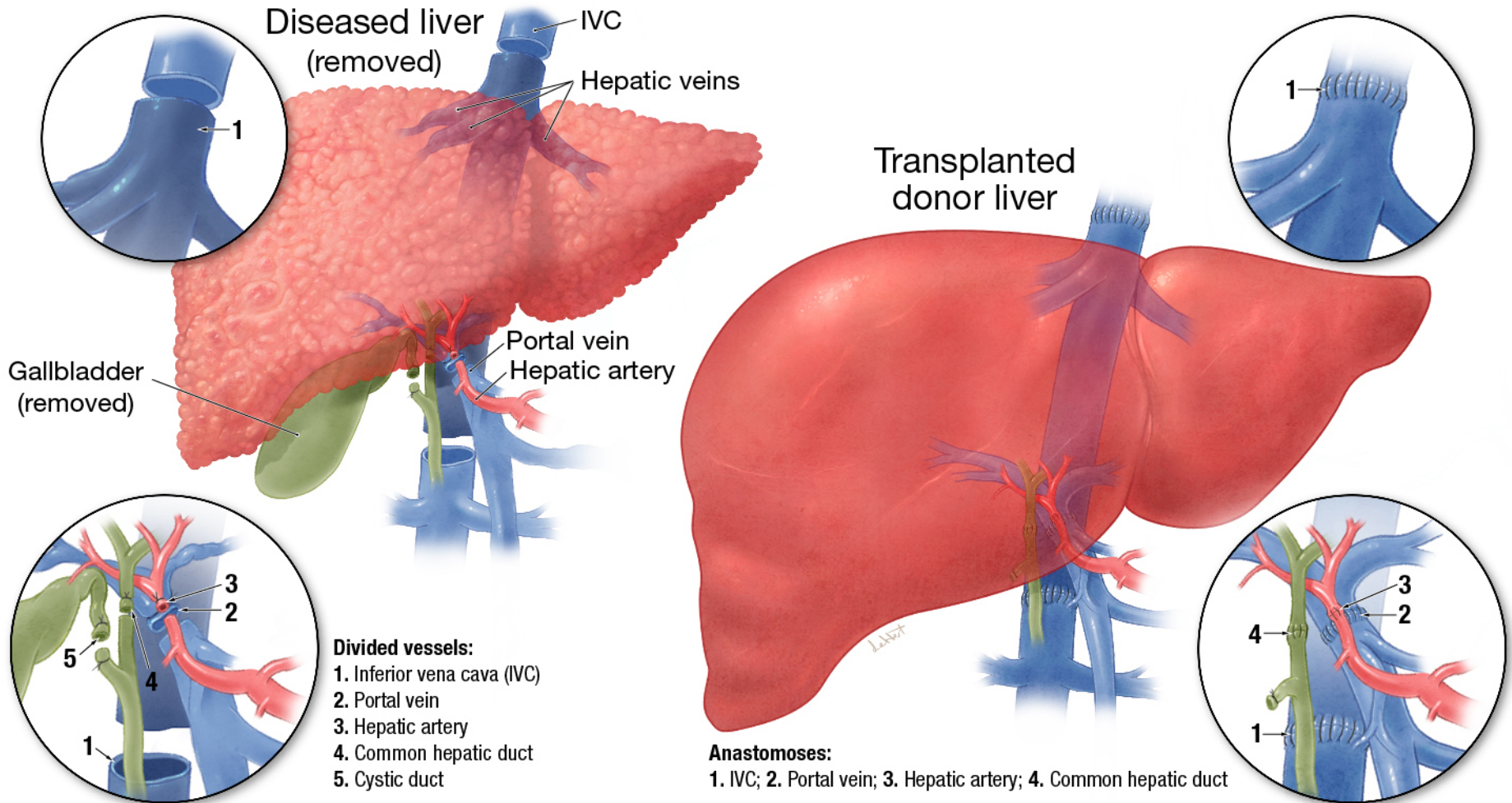
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Disclosures

- **Research Support**
 - AbbVie, BMS, Genfit, Gilead, Idenix, Ikaria, Janssen, Lumena, Merck, Roche/Genentech, Salix, Sundise, Vertex, Vital Therapies
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 - Roche/Genentech, Salix, Vertex
- **Consultant**
 - Genentech, Gilead, Kadmon, Janssen

Dr. Box was a Recipient of a Liver Transplant, October 2002

Liver Transplantation



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Referral for Liver Transplantation

- Background and goals
- Common indications
- Cirrhosis and liver transplantation
- Timing for referral
- Evaluation and patient selection

Background and Goals

Liver transplantation: Background

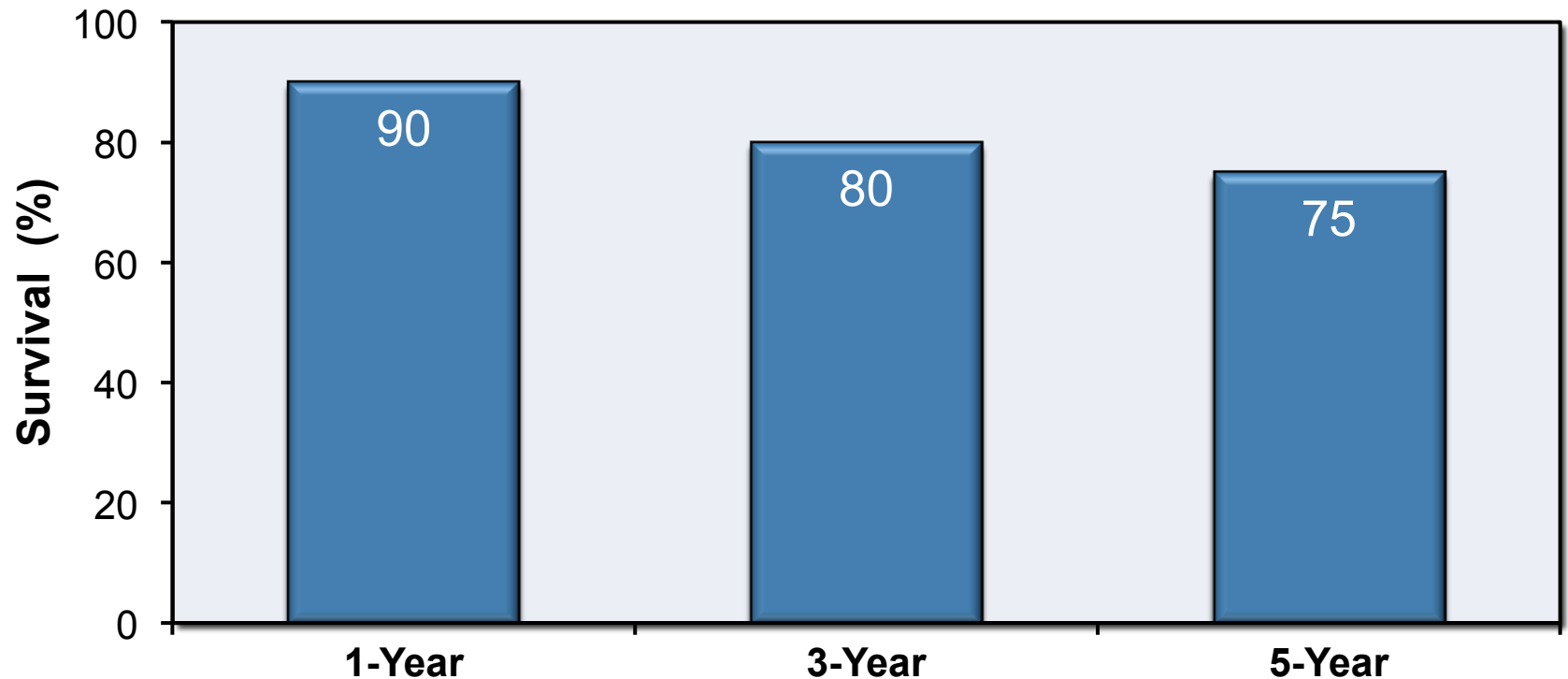
- ~19,000 patients listed for LT in the US
- ~6,000 LT performed annually in US
- 137 LT centers in US (37 States/DC)

Goals of Liver Transplantation

- Provides maximum benefit to patients with liver failure who have no other medical or surgical alternative for survival
- Likely prolongs life at least 5 years
- Restores patient to normal or near normal functional status

Liver Transplant Survival

Overall Patient Survival after Liver Transplant



MELD ≥ 15 break-point where LT has survival benefit

Common Indications for LT

Common Indications for Liver Transplantation

- Acute liver failure
- Chronic liver disease with cirrhosis
- Hepatocellular cancer
- Metabolic derangements

Cirrhosis and Liver Transplantation

- The most common indication for liver transplantation is end-stage chronic liver disease consequent to HCV and cirrhosis.
- Patients with end-stage chronic liver disease consequent to cirrhosis account for approximately 80-85% of all patients transplanted.

Cirrhosis and LT

Liver Transplants

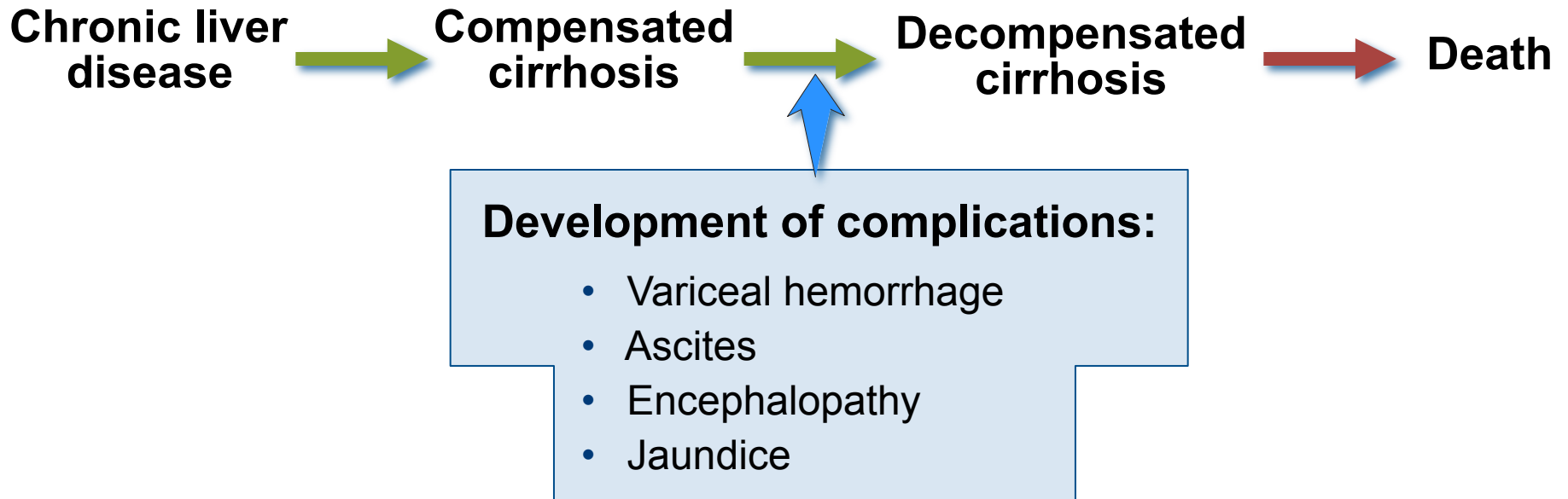
- Hepatitis C is the leading cause of cirrhosis and hepatocellular cancer in the United States ⁽²⁾
- 30-50% with chronic HCV will progress to cirrhosis and/or liver cancer ⁽¹⁾
- Hepatitis C accounts for 30% of adults on liver transplant waiting list and is leading indication for liver transplant ⁽²⁾

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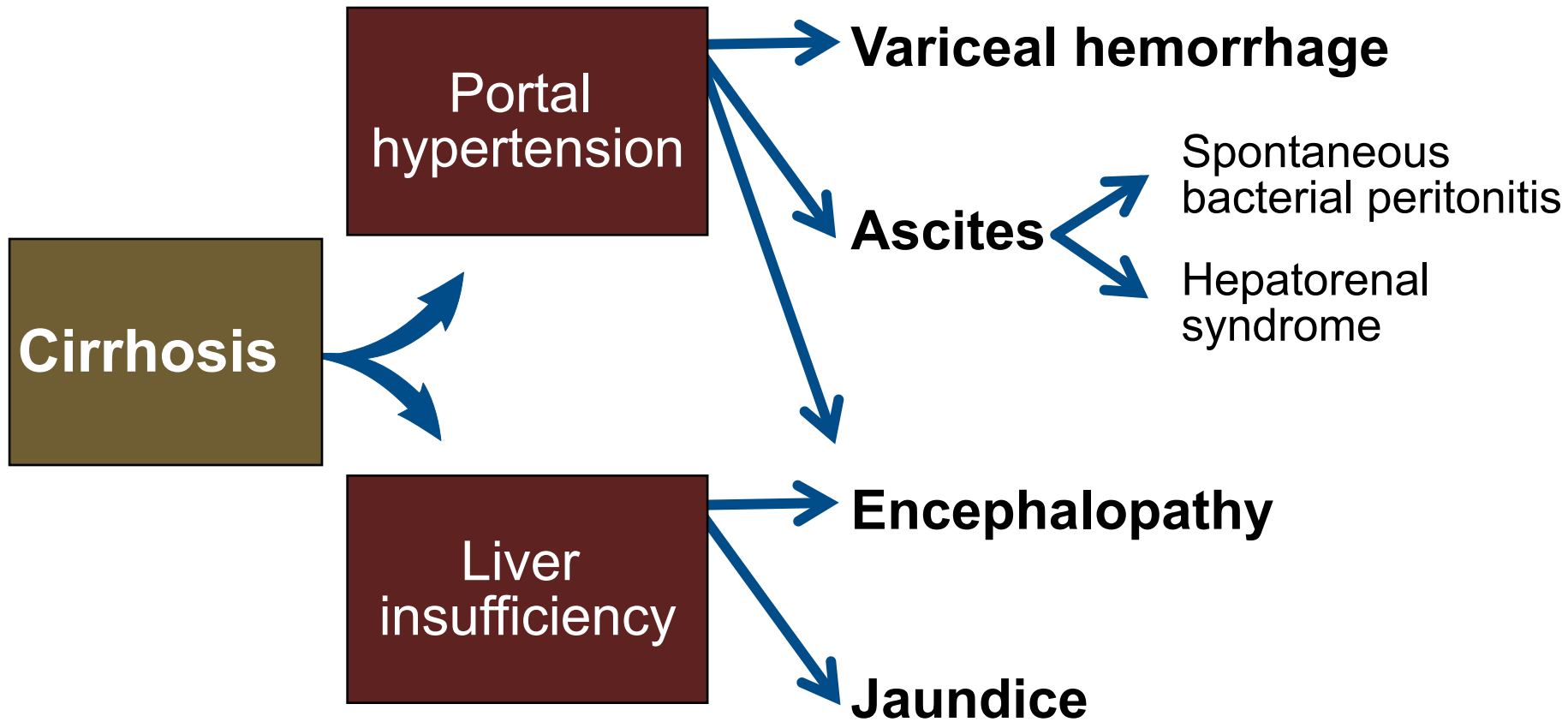
Cirrhosis: Definitions

- End stage of any chronic liver disease
- Characterized histologically by regenerative nodules surrounded by fibrous tissue
- Clinically there are two types of cirrhosis:
 - Compensated
 - Decompensated

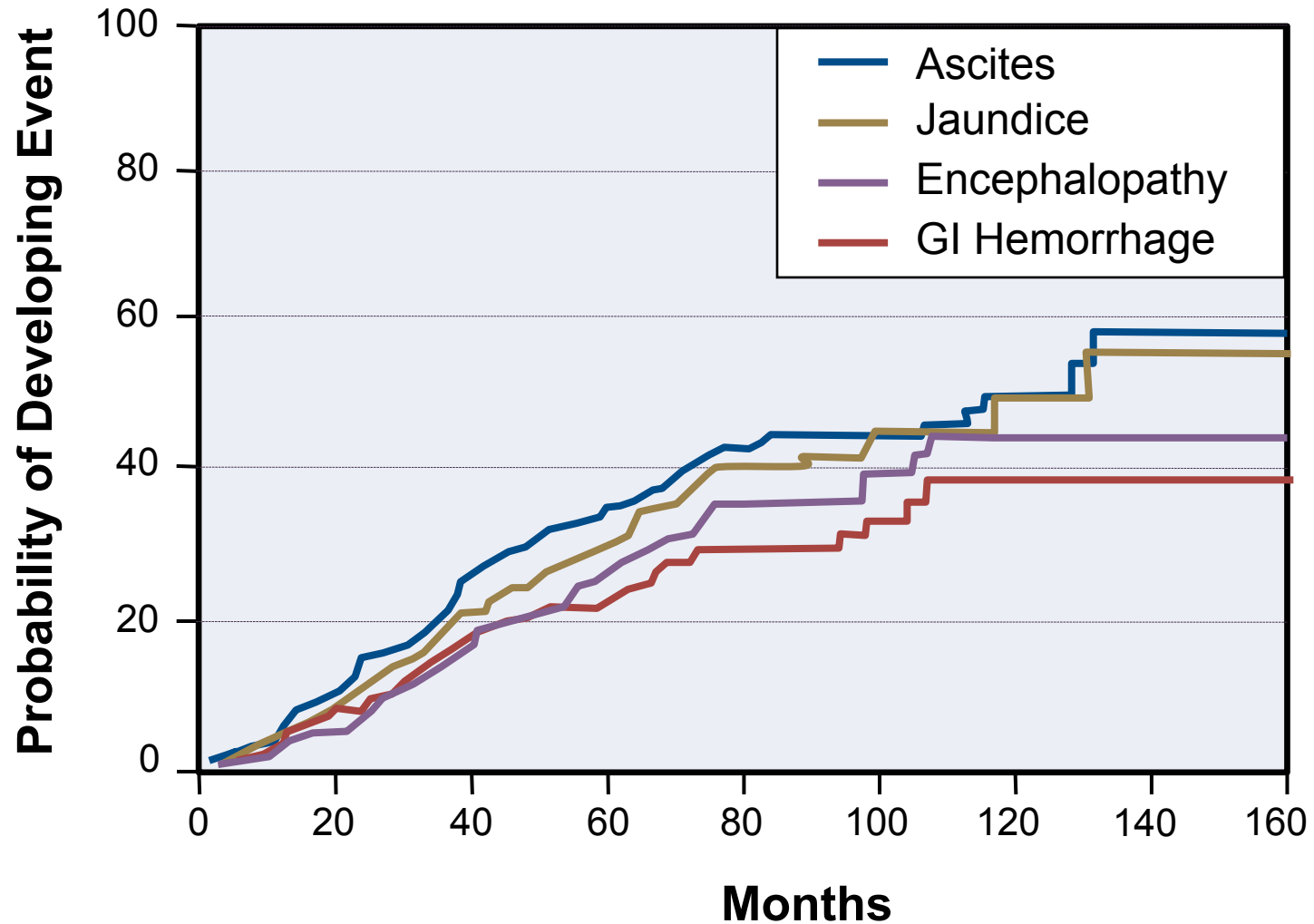
Natural History of Chronic Liver Disease



Complications of Cirrhosis Result from Portal Hypertension or Liver Insufficiency

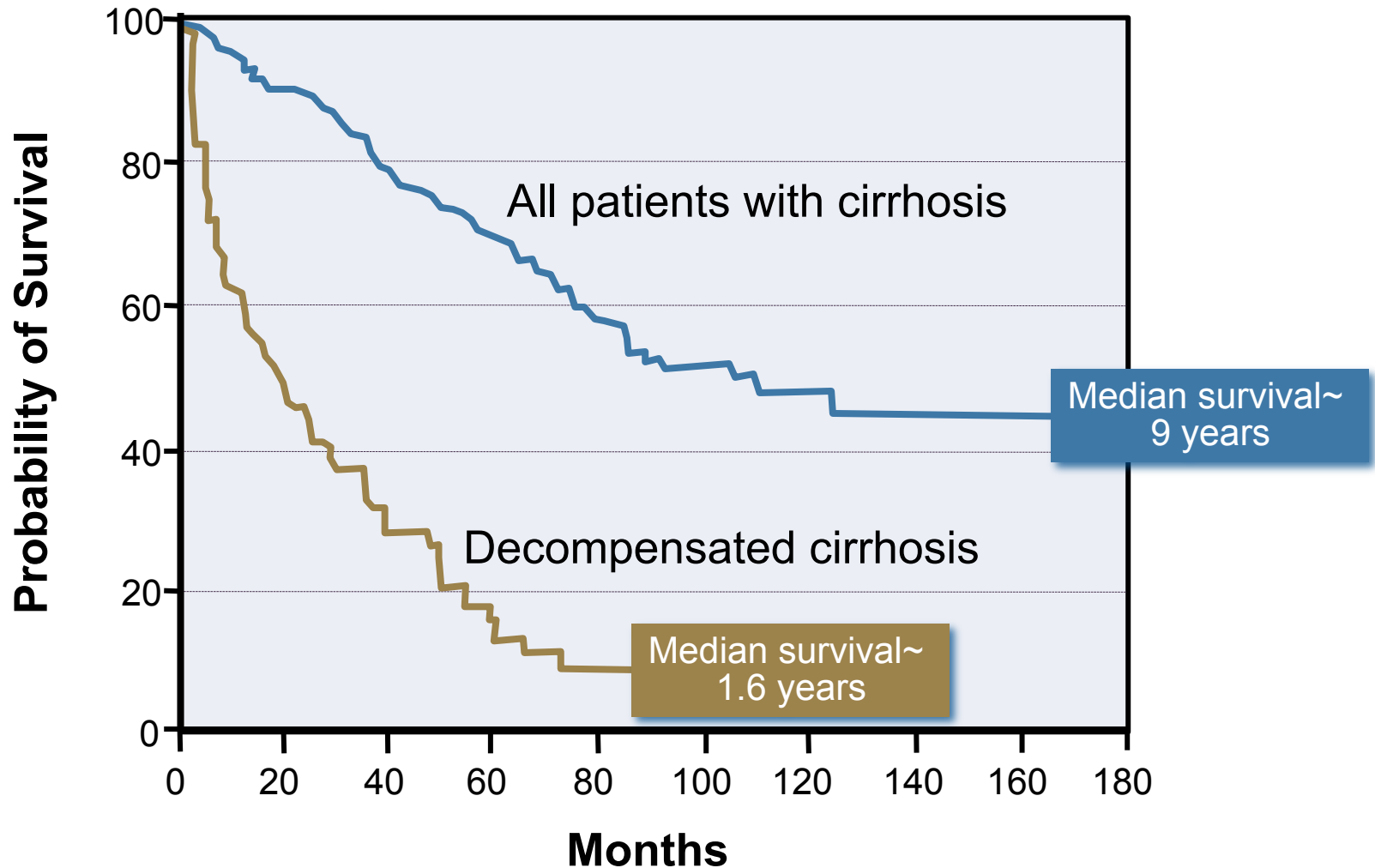


Patients with Compensated Cirrhosis Development of Complications



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

Patients with Cirrhosis Decompensation Shortens Survival

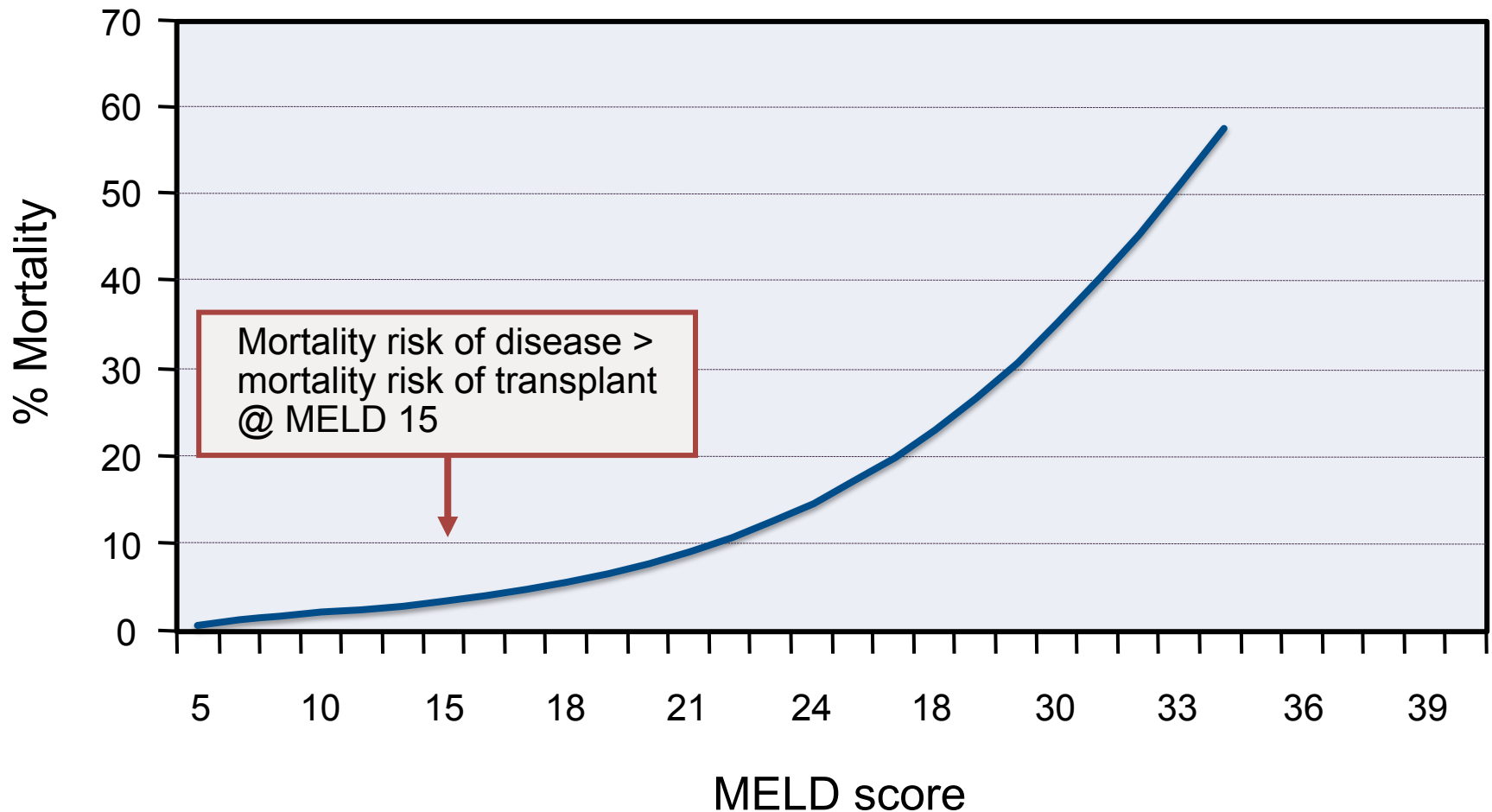


Timing for Referral

UNOS Model for End-stage Liver Disease (MELD) Score As a Predictor of Mortality

- MELD score based on Creatinine, Bilirubin, and INR
- Range = 6 (lowest risk) to 40 (highest risk)
- Predicts survival
- Also used in organ allocation process

Predicted 3-Month Mortality by MELD Score



CTP Class and Survival without Transplant

- Class A (5-6 points) 90% 5-year survival
- Class B (7-9 points) 80% 5-year survival
- Class C (≥ 10 points) 35% 1-year mortality

Timing for Referral for Liver Transplantation Evaluation

- EARLY REFERRAL IS BEST (donor shortage)
- Fulminant Liver Failure: immediate
 - Acute liver failure (encephalopathy with coagulopathy) in patient without known chronic liver disease
- Liver Cirrhosis:
 - Decompensation (ascites, encephalopathy, varices)
 - MELD \geq 10 or CPT \geq 7 (measures of severity)
- HCC (Milan criteria)
- Type 1 HRS

Progressive Disease without Effective Alternative Treatment

Evaluation and Patient Selection

General Clinical and Biochemical Indications for Liver Transplantation

- Patients with chronic hepatocellular diseases
 - > Serum albumin <3.5 g/dL
 - > Prothrombin time >3 seconds above control or INR >1.3
 - > Encephalopathy
 - > Ascites
 - > Bilirubin >2 mg/dL

Patient Selection Criteria for Liver Transplantation

- Severe fatigue
- Unacceptable quality of life
- Recurrent variceal bleeding
- Intractable ascites
- Recurrent or severe hepatic encephalopathy
- Spontaneous bacterial peritonitis
- Hepatorenal syndrome
- Small hepatocellular carcinoma on hepatic imaging

Potential for Successful Liver Transplantation

- Can patient survive surgery/postoperative period?
- Can patient comply/adhere to complex medical regimen after transplantation?
- Comorbid conditions that can compromise patient/graft survival and make transplantation futile?

Special Circumstances for Acceptance

- **Alcoholic cirrhosis:**
Only for patients having psychosocial factors predicting long-term sobriety
 - Previous social stability
 - Employment record
 - Psychiatric status
 - Length of sobriety
 - Participation in alcohol recovery awaiting transplantation
- **Patients over age 60:**
 - Particular attention to silent coronary or vascular disease
 - Typically approved if no other major organ disease & expected to live >5 years
- **Patients with hepatocellular carcinoma**
Undergo special scrutiny and adjunctive therapy
 - Thorough evaluation for identifiable malignancy outside of the liver
 - Adjuvant therapy in the form of chemo-embolization or chemotherapy to control the spread of cancer cells or unrecognized micrometastases

Absolute Contraindications to Transplant

- Irreversible brain damage
- Multi-system failure not correctable by liver transplantation
- Malignancy outside the liver (not skin cancer)
- Infection outside the hepatobiliary system
- Active alcohol or substance abuse
- Advanced cardiopulmonary or other systemic disease
- Psychosocial concerns

Relative Contraindications to Transplant

- **Comorbid Conditions**
 - Advanced age
 - Advanced chronic renal failure
 - Cholangiocarcinoma
 - Hypoxemia from intrapulmonary shunts
 - Severe malnutrition
 - HIV positivity
- **Anatomic Considerations**
 - Portal vein thrombosis
 - Prior portosystemic shunt surgery
 - Prior biliary tract surgery

Liver Transplant Evaluation

What can patients do?

- Get involved in chemical dependency treatment program if indicated and DOCUMENT attendance
- Lose weight if needed (BMI<35 recommended)
- Quit smoking NOW
- Avoid narcotic use if possible
- Methadone should NOT be a barrier to transplantation

Selection Committee

- Review of history and physical
- Review of psychosocial interview
- Review of laboratory studies
- Determination of medical need & psychosocial clearance
- May be accepted, rejected, or provisional

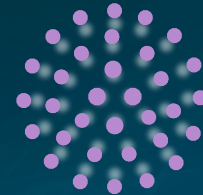
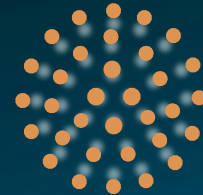
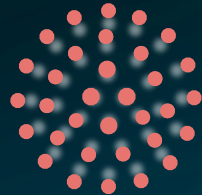


Liver Transplantation Evaluation Summary

- Liver transplantation restores health to the terminally ill.
- As percentage of those waiting, the annual number of liver transplants is declining.
- Identification of the complications of cirrhosis is critical to timely referral to transplant center.
- Patients with advanced liver disease strongly advised to adopt healthy liver lifestyle.
- Sign up to be an organ and tissue donor-

Donate Life

End



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