

Approach to Abnormal Liver Test

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Disclosures

- No relevant financial disclosures

Liver Test: Injury vs Function

MARKERS OF LIVER INJURY

AST

ALT

ALP

GGT

MARKERS OF LIVER FUNCTION

Albumin

Bilirubin

PT/INR

Elevated liver enzymes reflect liver injury, not necessarily liver dysfunction.
Conversely, advanced liver disease may present with near-normal aminotransferase levels.

Interpreting a "Normal" ALT

- ▶ Laboratory reference ranges are derived from reference populations, which may include individuals with unrecognized liver disease.
- ▶ The AASLD Practice Guidance recognizes a healthy normal ALT range as **29-33 U/L in men** and **19-25 U/L in women**.
- ▶ Subtle or persistent ALT elevations should be interpreted in the context of metabolic risk factors.

A laboratory "normal" ALT does not necessarily indicate a healthy liver.

Patterns of Liver Test Abnormalities

HEPATOCELLULAR PATTERN

↑ AST

↑ ALT

Disproportionate elevation
of aminotransferases
relative to ALP

CHOLESTATIC PATTERN

↑ Alkaline phosphatase

↑ GGT (Supportive)

Disproportionate elevation of ALP
relative to aminotransferases

MIXED PATTERN: Concurrent elevation of aminotransferases and ALP.

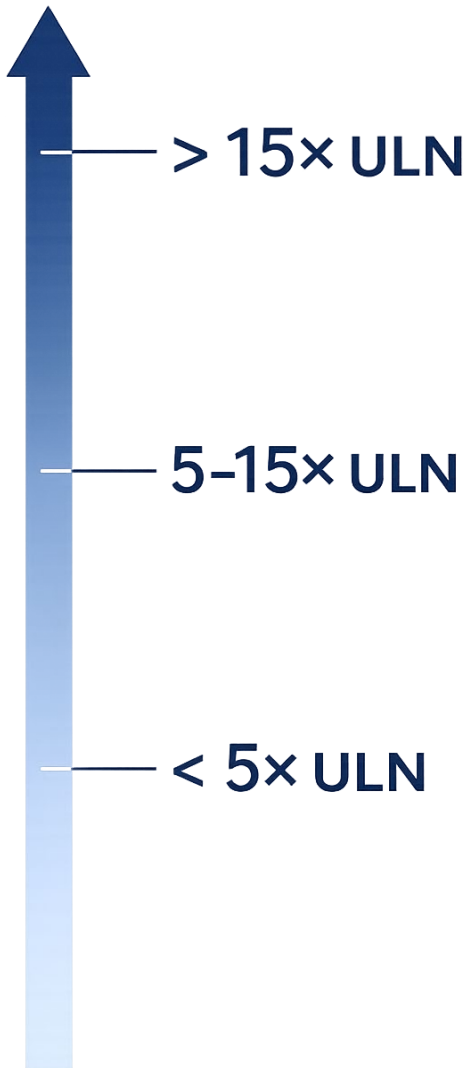
Classifying the biochemical pattern is the first step in narrowing the differential diagnosis.

The R-Factor: Defining the Pattern of Liver Injury

$$R = (\text{ALT} / \text{ULN ALT}) \div (\text{ALP} / \text{ULN ALP})$$



Magnitude of Aminotransferase Elevation



- Ischemic hepatopathy
- Acetaminophen toxicity
- Acute viral hepatitis
- Severe DILI

- Acute viral hepatitis
- Drug-induced liver injury
- Autoimmune hepatitis

- MASLD
- Alcohol-associated liver disease (typically $\text{AST} > \text{ALT}$)
- Medications/supplements

AST:ALT Ratio

ALT > AST

Typical of most hepatocellular disorders

MASLD • Viral hepatitis • DILI • Autoimmune hepatitis

AST:ALT ≥ 2

Suggests alcohol-associated liver disease

Particularly with elevated GGT

AST > ALT

May occur in advanced fibrosis/cirrhosis

Regardless of etiology

Focused History: Narrowing the Differential



Timeline

- Previous abnormal liver tests
- Acute, chronic or acute-on-chronic
- Symptoms



Medical History

- Metabolic risk factors
- Autoimmune disease/IBD
- Cardiac disease
- Prior liver disease



Exposure & Family History

- Country of birth/travel
- Blood or healthcare exposure
- Injection drug use
- Family history of liver disease



Medications & Supplements

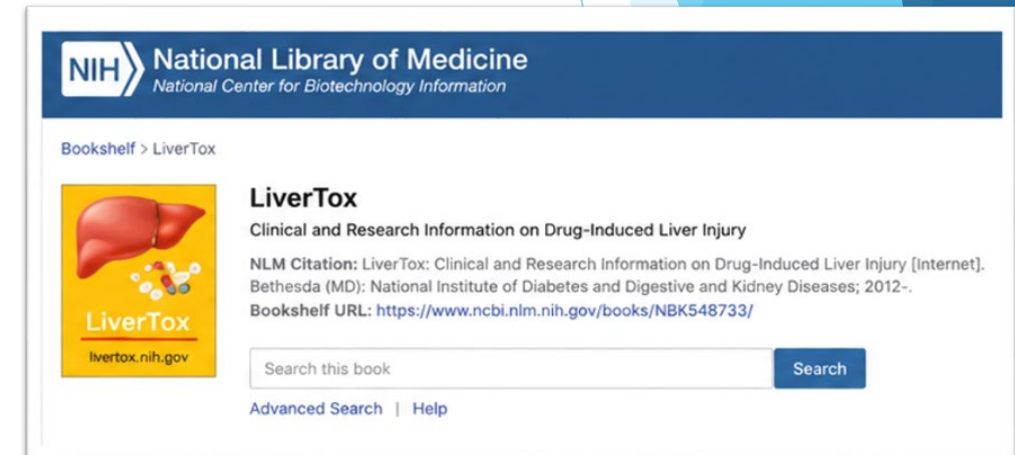


Alcohol History

Medication History: Think Beyond the Medication List

Key Points

- Review all medications.
- Ask specifically about OTCs, herbals, and dietary supplements.
- Confirm the temporal relationship:
 - Start date
 - Dose changes
 - Duration
 - Time to liver injury
- Consult LiverTox:
 - Latency
 - Pattern of injury
 - Likelihood score



Patients often do not consider OTC products or herbal supplements to be "medications" unless asked directly.

Alcohol History: Quantifying Alcohol exposure

What is a standard drink?

12 fl oz of
regular beer



about 5%
alcohol

5 fl oz of
table wine



about 12%
alcohol

1.5 fl oz shot of
80-proof spirits
(whiskey, gin, rum,
vodka, tequila, etc.)



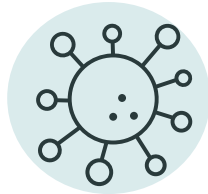
about 40%
alcohol

	MASLD	MetALD	ALD predominant
 WOMEN	≤140 g/week (≤10 drinks/week)	141–350 g/week (~10–25 drinks/week)	>350 g/week (>25 drinks/week)
 MEN	≤210 g/week (≤15 drinks/week)	211–420 g/week (~15–30 drinks/week)	>420 g/week (>30 drinks/week)

Diagnostic Approach to Hepatocellular Liver Injury



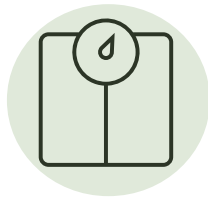
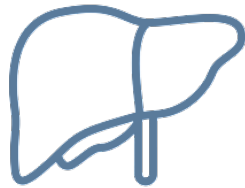
Alcohol



Viral



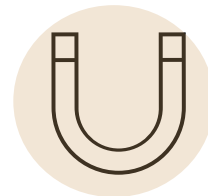
Genetic & Other



Metabolic



Autoimmune



Iron

Viral

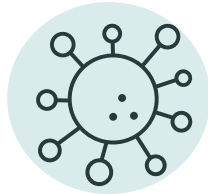
HBsAg
Anti-HBs
Anti-HBc
Anti-HCV
HCV RNA if anti-HCV
positive
HDV Ab if HBV S Ag +

HEV IgM
CMV / EBV / HSV PCR

Diagnostic Approach to Hepatocellular Liver Injury



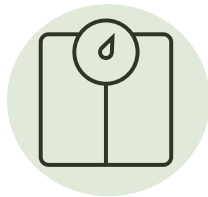
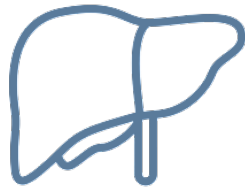
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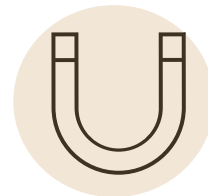
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Autoimmune



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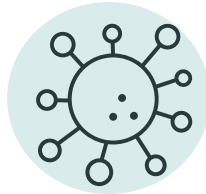
Alcohol

PETH
Ethyl glucuronide
GGT
AST:ALT ratio

Diagnostic Approach to Hepatocellular Liver Injury



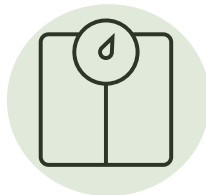
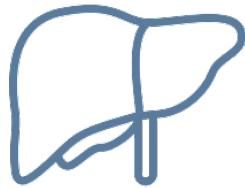
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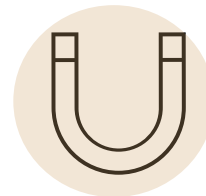
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Metabolic



Autoimmune



Iron

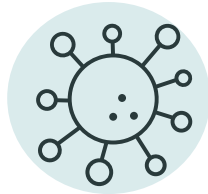
Metabolic

HbA1c
Lipid panel
FIB-4
Elastography if
indicated

Diagnostic Approach to Hepatocellular Liver Injury



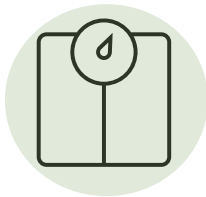
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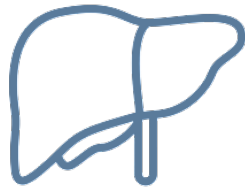
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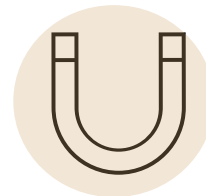
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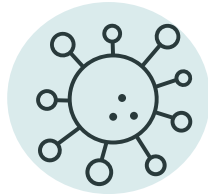
ANA
ASMA
IgG

Anti-LKM / Anti-SLA

Diagnostic Approach to Hepatocellular Liver Injury



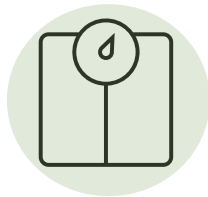
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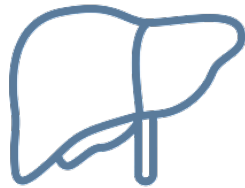
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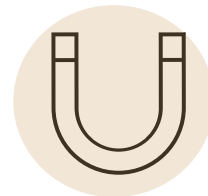
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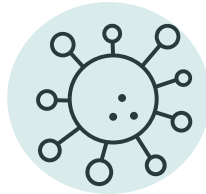
Iron

Ferritin
Transferrin saturation
HFE testing if indicated

Diagnostic Approach to Hepatocellular Liver Injury



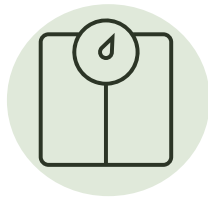
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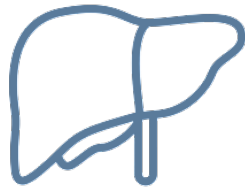
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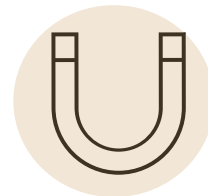
Genetic & Other



Metabolic



Autoimmune



Iron

Genetic & Other

Ceruloplasmin
Alpha-1 antitrypsin
CK
TSH
Celiac serologies

Marked Aminotransferase Elevation ($>15\times$ ULN)

① Assess for Acute Liver Failure

- INR
- Hepatic encephalopathy
- Early transplant center referral (King's College Criteria for prognosis)

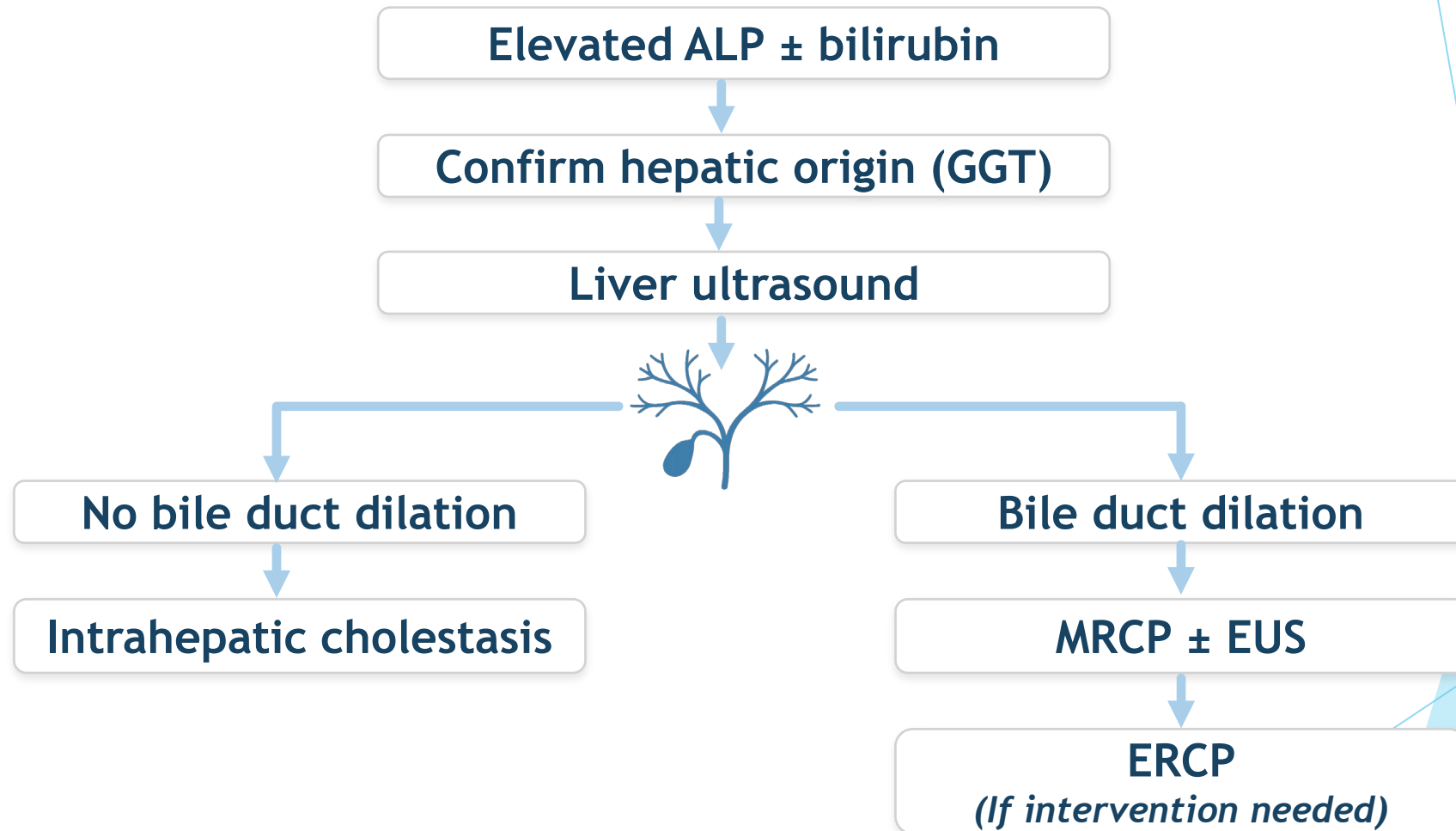
② Initial evaluation

- Acetaminophen level
- Lactate
- Ammonia
- Medication/supplement review
- Acute viral hepatitis panel
- Autoimmune serologies
- History of hypotension/shock

③ Liver Ultrasound with doppler

- Evaluate hepatic and portal vein flow
- Rule out Budd-Chiari

Approach to Cholestatic Liver Tests



Extrahepatic cholestasis

Common etiologies

- ▶ Choledocholithiasis
- ▶ Malignant obstruction
- ▶ Benign biliary stricture
- ▶ Chronic pancreatitis/autoimmune pancreatitis
- ▶ PSC (dominant stricture)



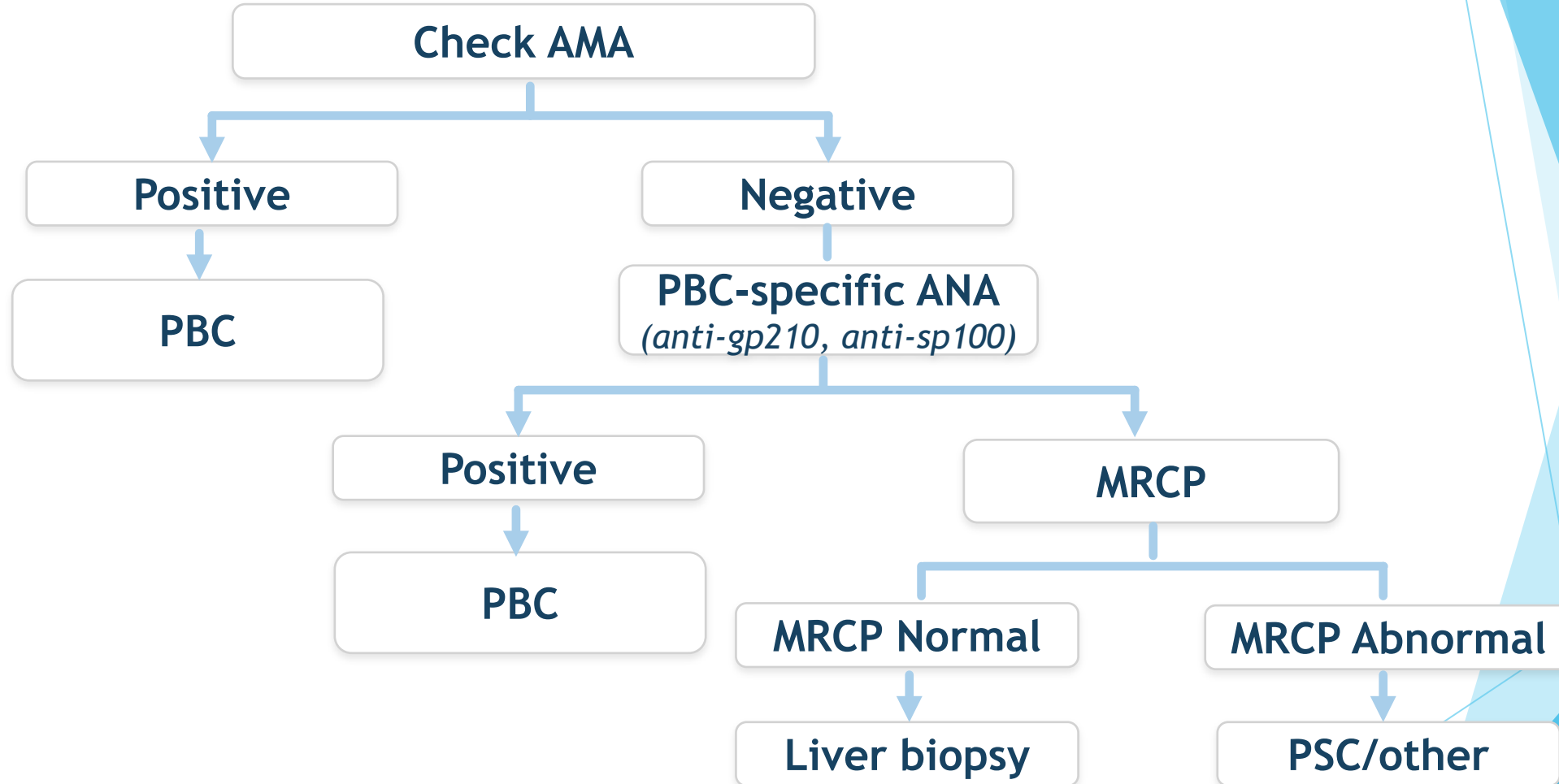
MRCP demonstrating choledocholithiasis.

Intrahepatic cholestasis

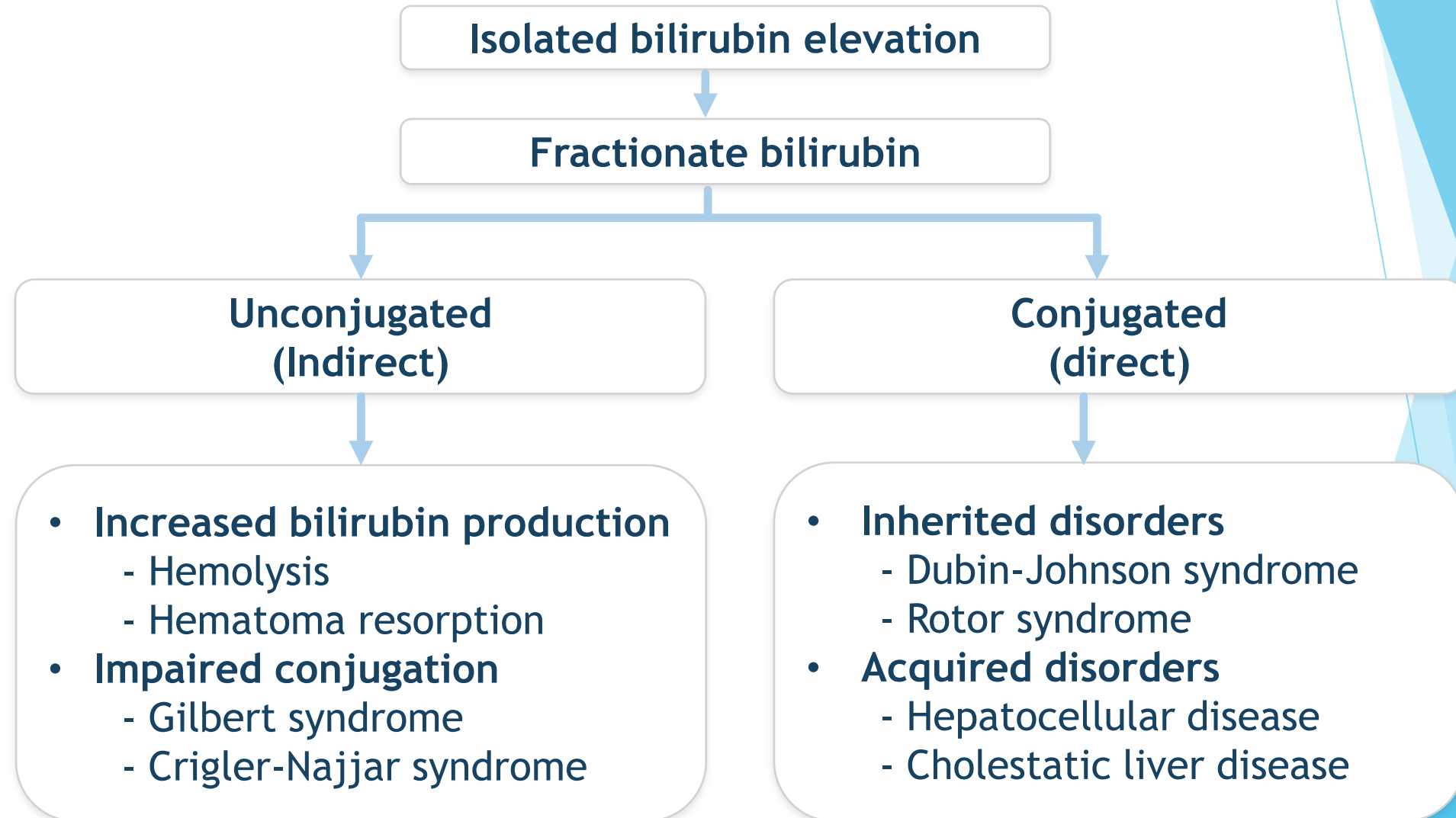
Common etiologies

- ▶ Primary biliary cholangitis (PBC)
- ▶ Primary sclerosing cholangitis (PSC)
- ▶ IgG4-related sclerosing cholangitis
- ▶ Drug-induced liver injury (DILI)
- ▶ Infiltrative diseases (Sarcoidosis, Lymphoma)
- ▶ Sepsis
- ▶ Pregnancy-associated cholestasis
- ▶ Ischemic cholangiopathy

Intrahepatic cholestasis



Isolated hyperbilirubinemia



Key Clinical Pearls

- ▶ Start with the pattern—not the diagnosis.
- ▶ Interpret liver tests in the clinical context —not every positive test represents disease.
- ▶ Liver injury is not the same as liver dysfunction.
- ▶ Always assess for acute liver failure—check INR and mental status.
- ▶ Persistent abnormalities or evidence of advanced liver disease warrant further evaluation/referral.