30 Mar 2025

Berlin

Mahidol University
Faculty of Medicine
Siriraj Hospital

Common Hepatic Diseases

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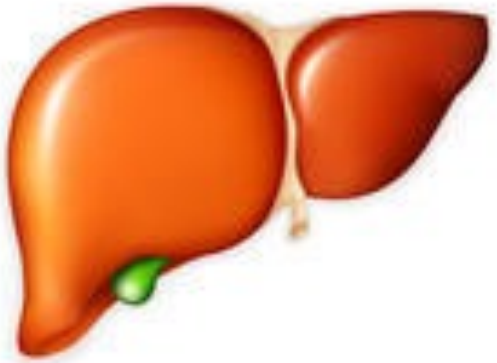
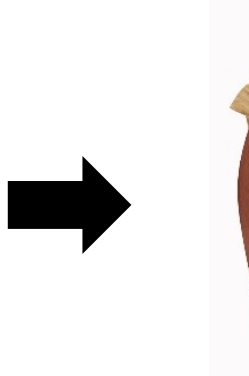
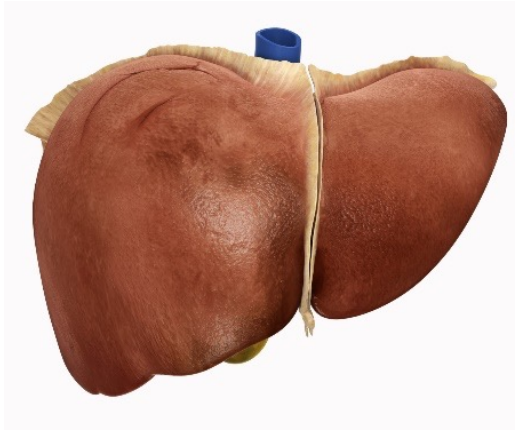
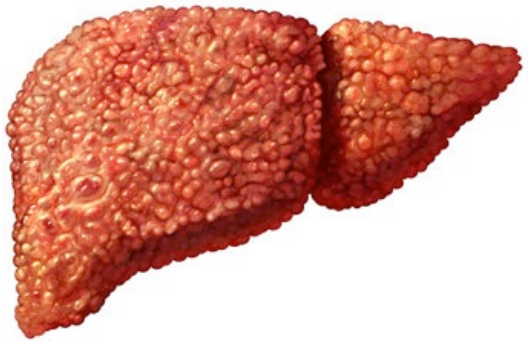
Siriraj Hospital, **Mahidol** University

Agenda









Acute Hepatitis

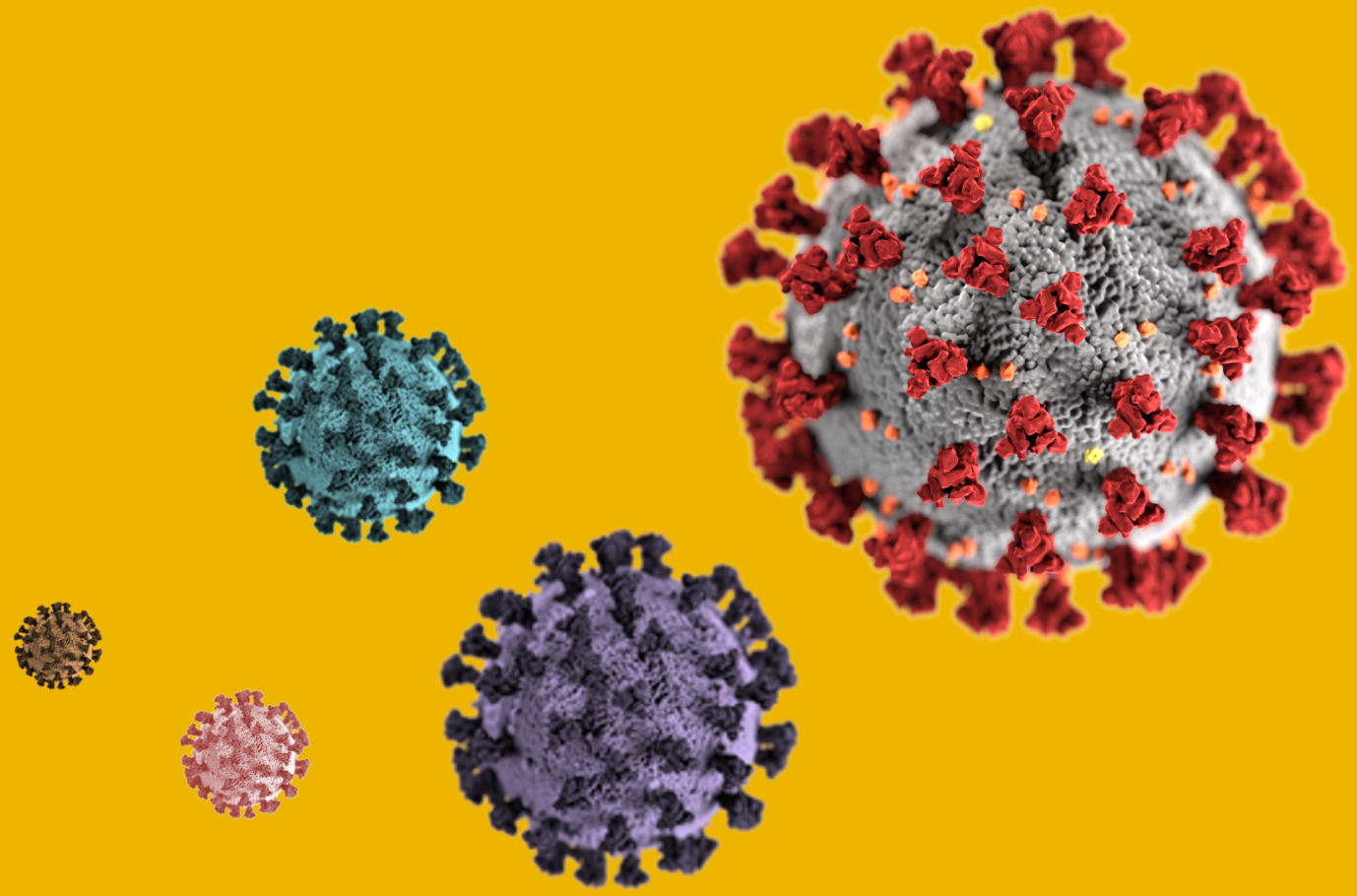
- Virus
- AIH
- DILI
- Wilson disease
- Vascular diseases

Chronic Hepatitis

- Virus
- Alcohol, MASLD
- Autoimmune
- WD, HH
- BCS

Cirrhosis

- Esophageal varices
- Ascites, SBP
- HRS
- Hepatic encephalopathy
- HCC



1

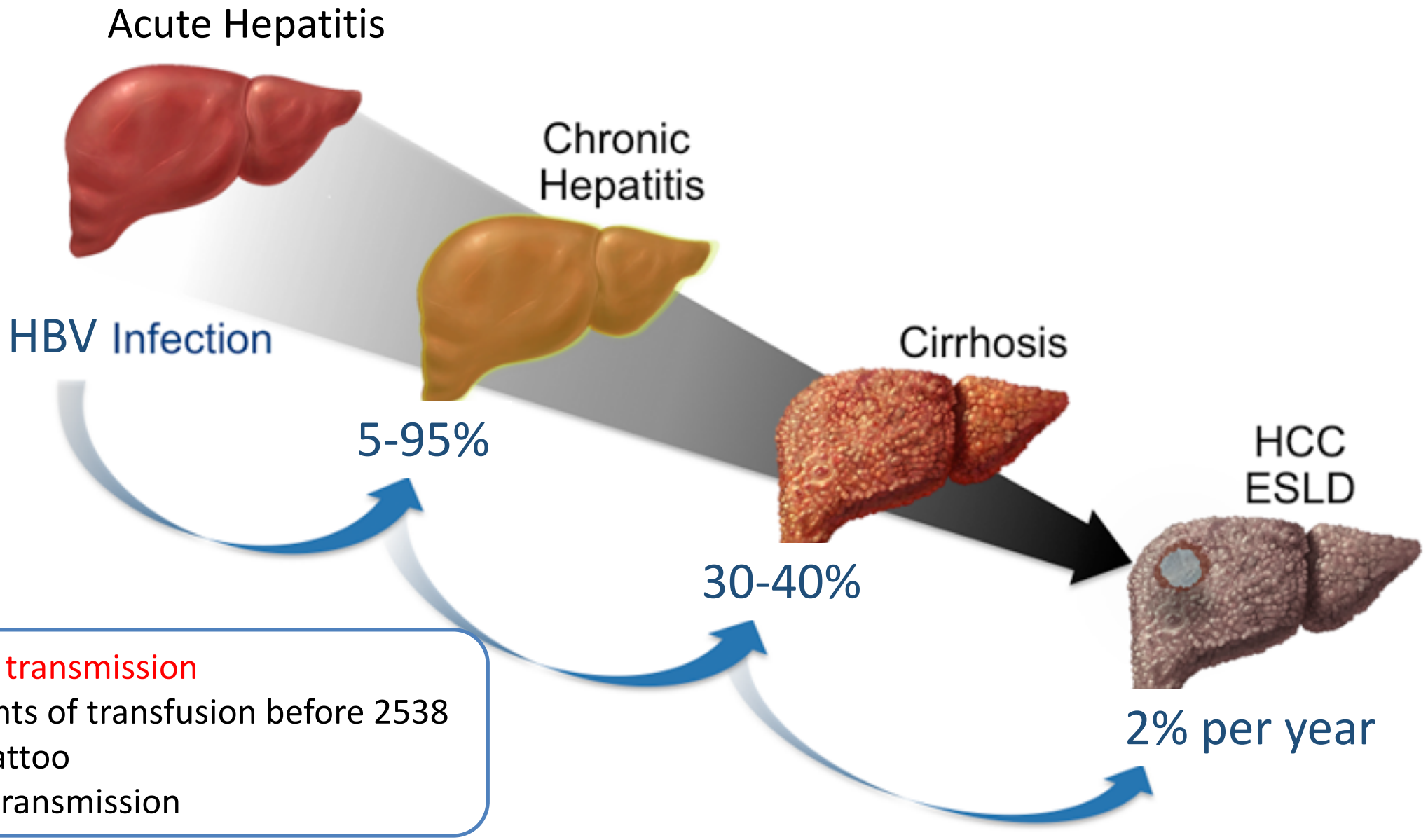
Viral hepatitis

Summary of viral hepatitis

	HAV	HEV	HBV	HDV	HCV
Transmission	Feco-oral	Zoonosis	Blood, Sexual Vertical	HBsAg-dependent	Blood
Presentation	Acute	Acute (Chronic*)	Acute Chronic	Acute Chronic	(Acute) Chronic
Risk factors	Contaminated food, MSM	Uncooked pork	IVDU, tattoo, blood Tx, unsafe sex, family Hx	IVDU	IVDU, tattoo, blood Tx, MSM
Diagnosis	Anti-HAV IgM	Anti-HEV IgM & IgG PCR for HEV	Anti-HBc IgM HBsAg	Anti-HDV IgG HDV PCR	Anti-HCV HCV RNA, core Ag
Treatment	Supportive	Ribavirin in chronic infection	ETV, TDF, TAF	IFN	SOF/VEL ± RBV
Prevention	Vaccine 0,6 mo.		Vaccine 0,1,6 HBIG		

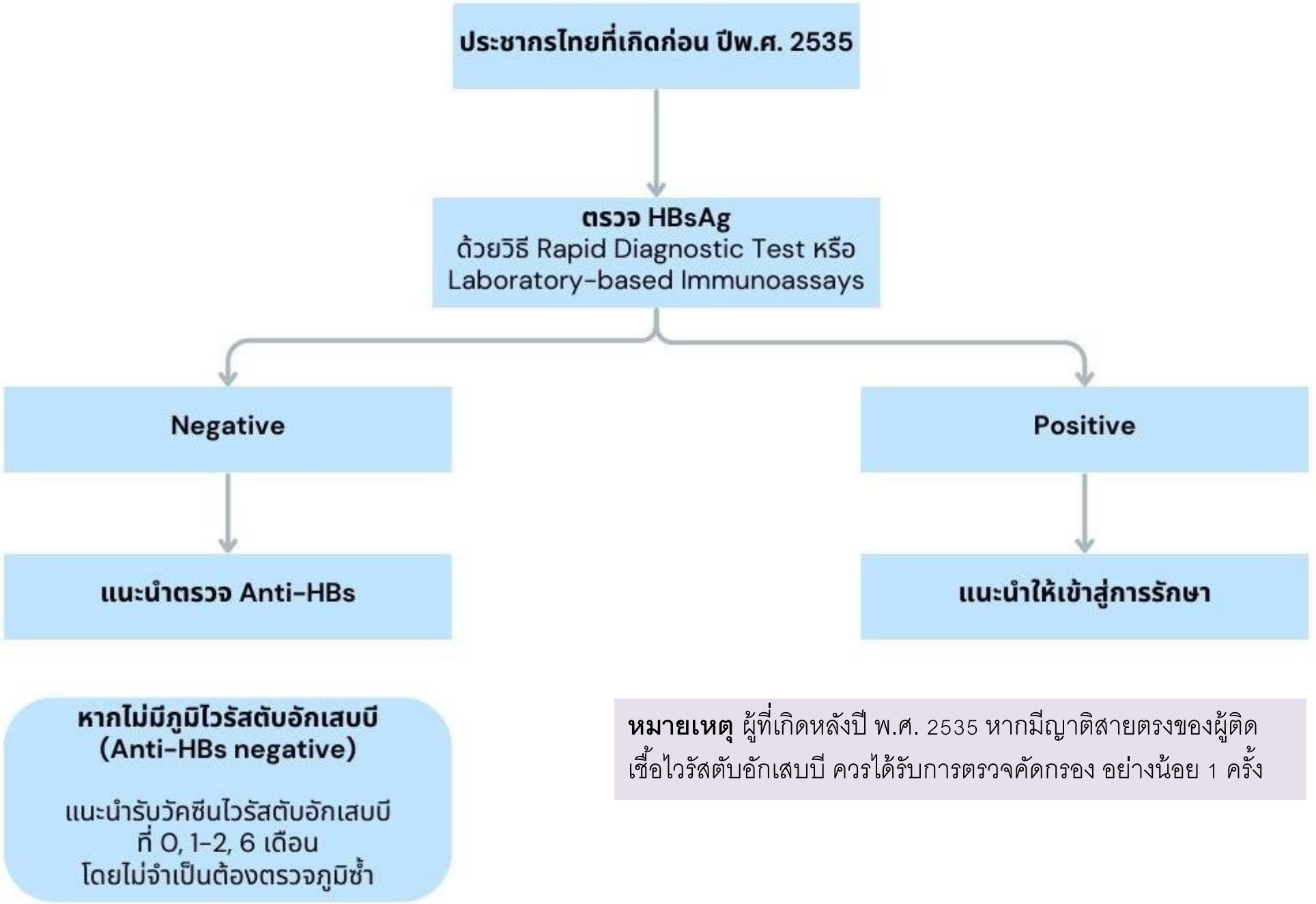
*AIDS, post organ transplantation, immunosuppression

Natural course of HBV infection



- Vertical transmission
- Recipients of transfusion before 2538
- IVDU, tattoo
- Sexual transmission

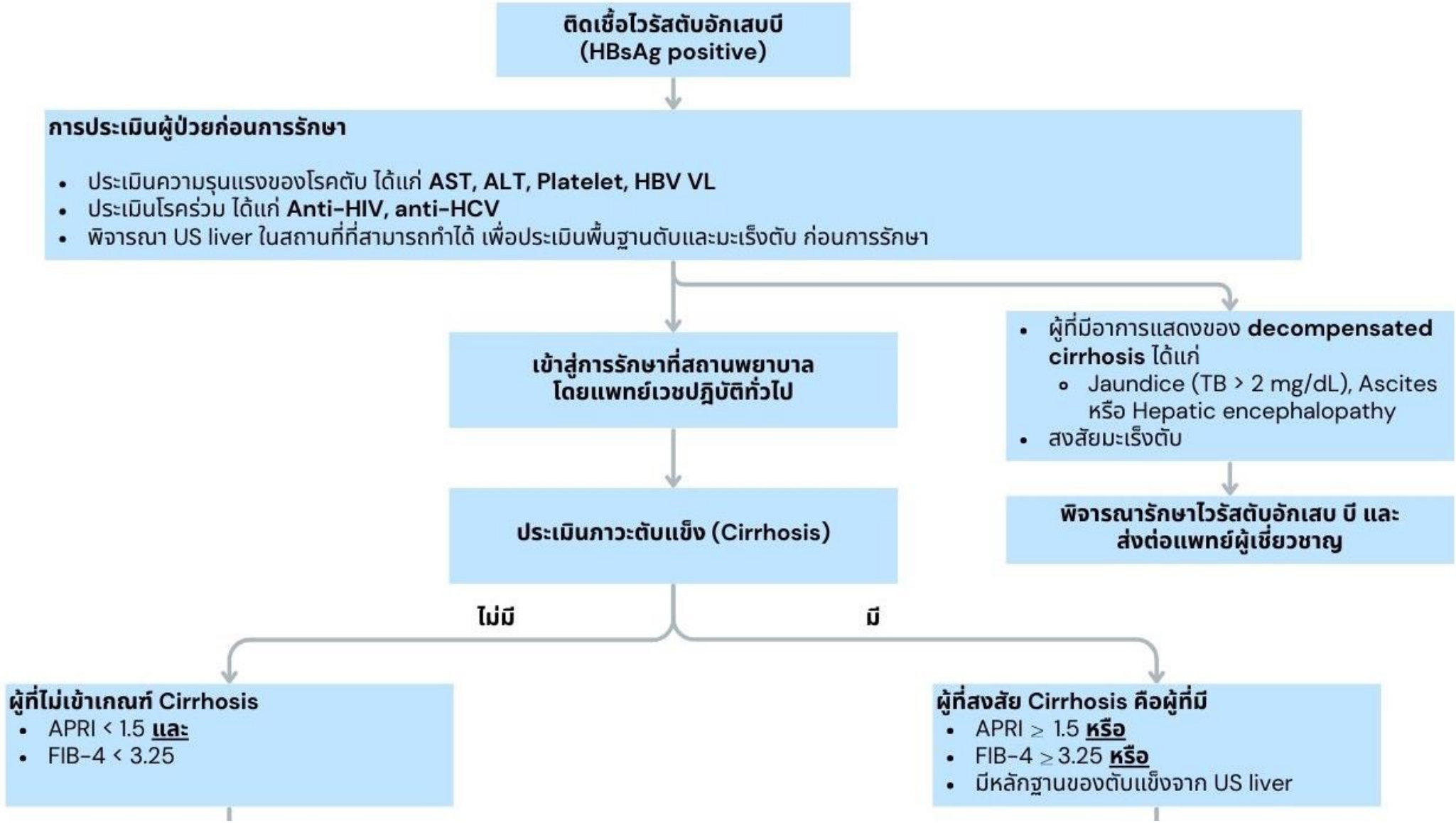
แนวทางการตรวจคัดกรองผู้ป่วยไวรัสตับอักเสบบี พ.ศ.2567



หมายเหตุ ผู้ที่เกิดหลังปี พ.ศ. 2535 หากมีญาติสายตรงของผู้ติดเชื้อไวรัสตับอักเสบบี ควรได้รับการตรวจคัดกรอง อย่างน้อย 1 ครั้ง

กรมควบคุมโรค กระทรวงสาธารณสุข

แนวทางการติดตามและรักษาผู้ป่วยไวรัสตับอักเสบบี พ.ศ.2567



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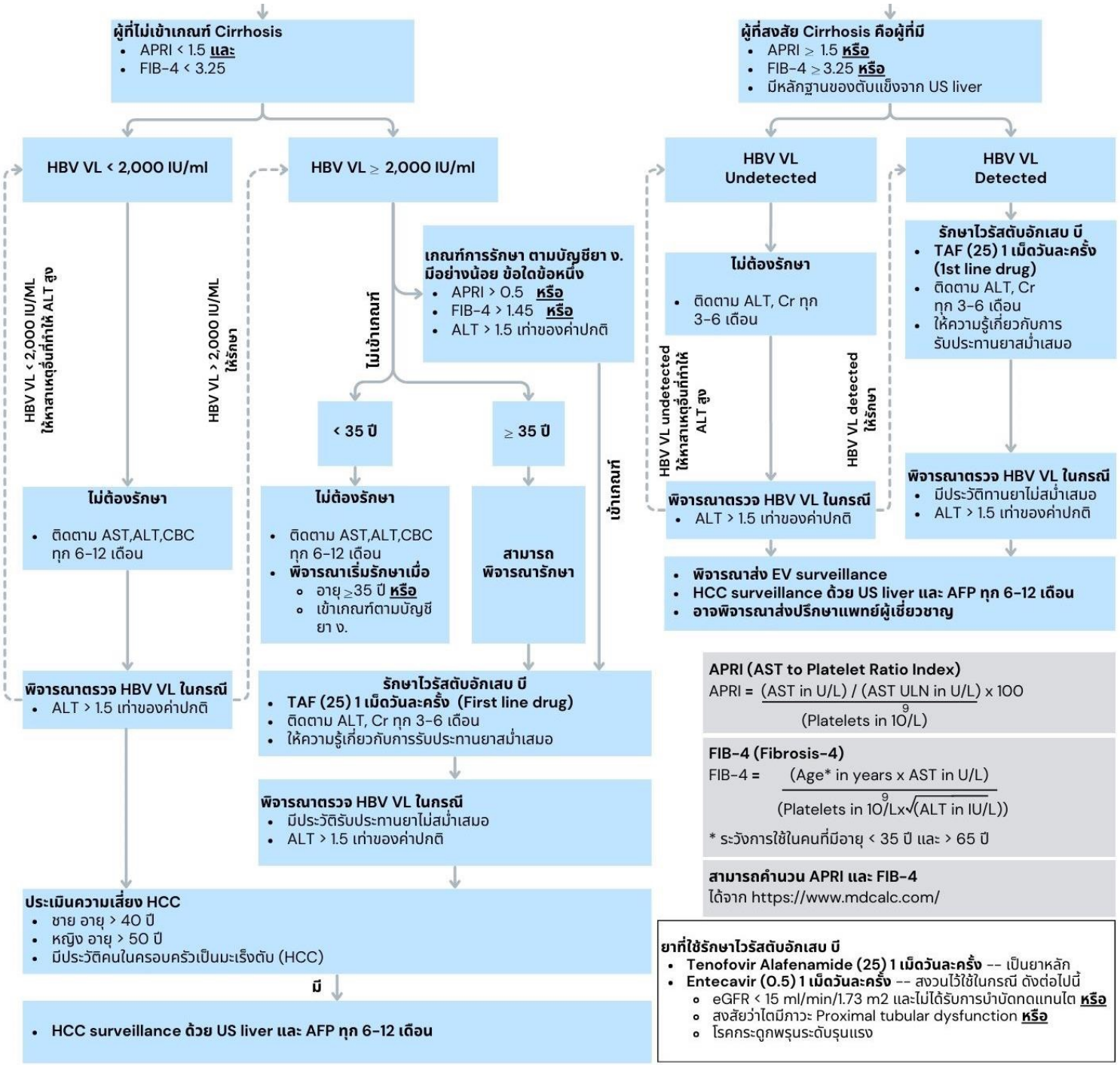

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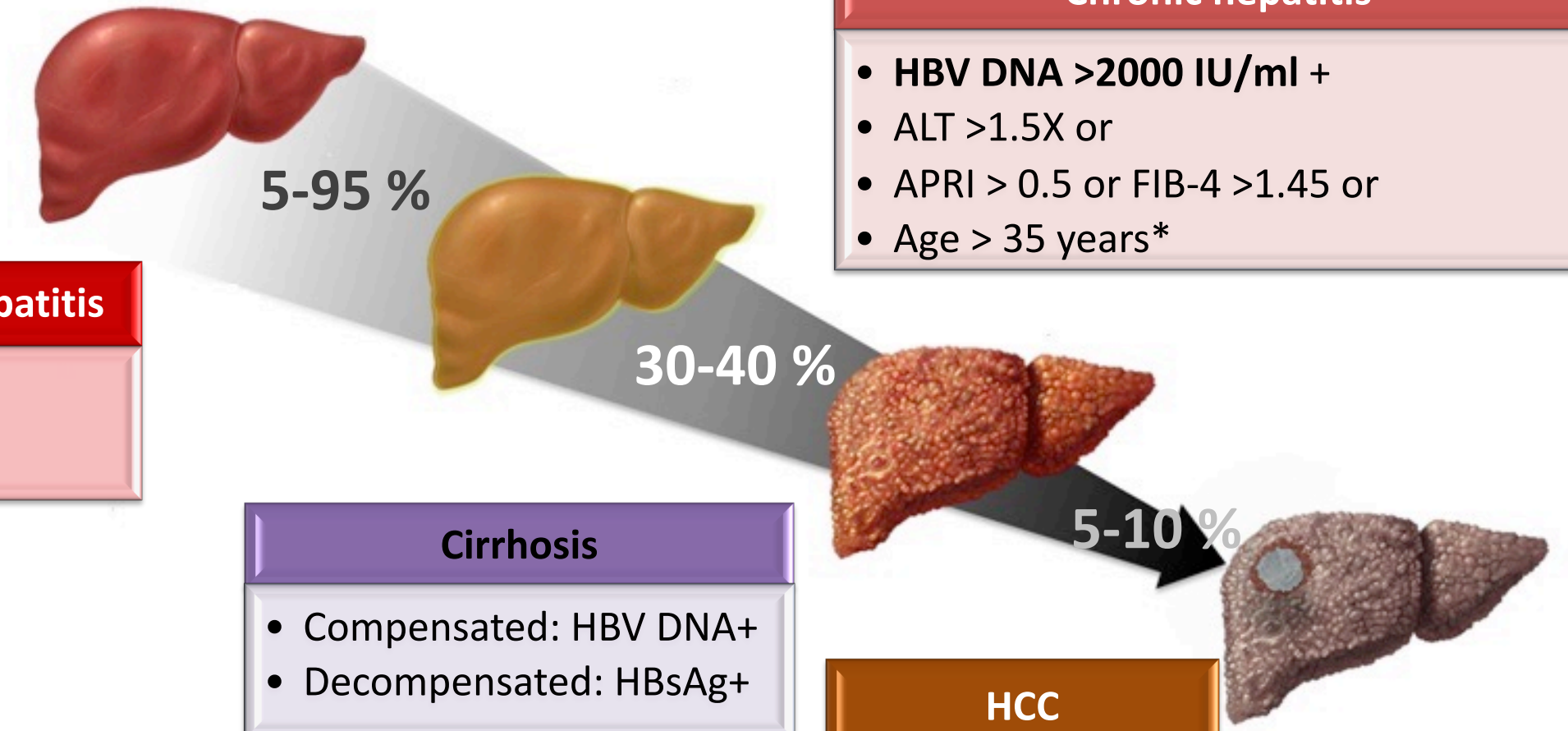
Indication for HBV treatment



Chronic hepatitis

- **HBV DNA >2000 IU/ml** +
- ALT >1.5X or
- APRI > 0.5 or FIB-4 >1.45 or
- Age > 35 years*

Acute hepatitis

- ALF
- ACLF

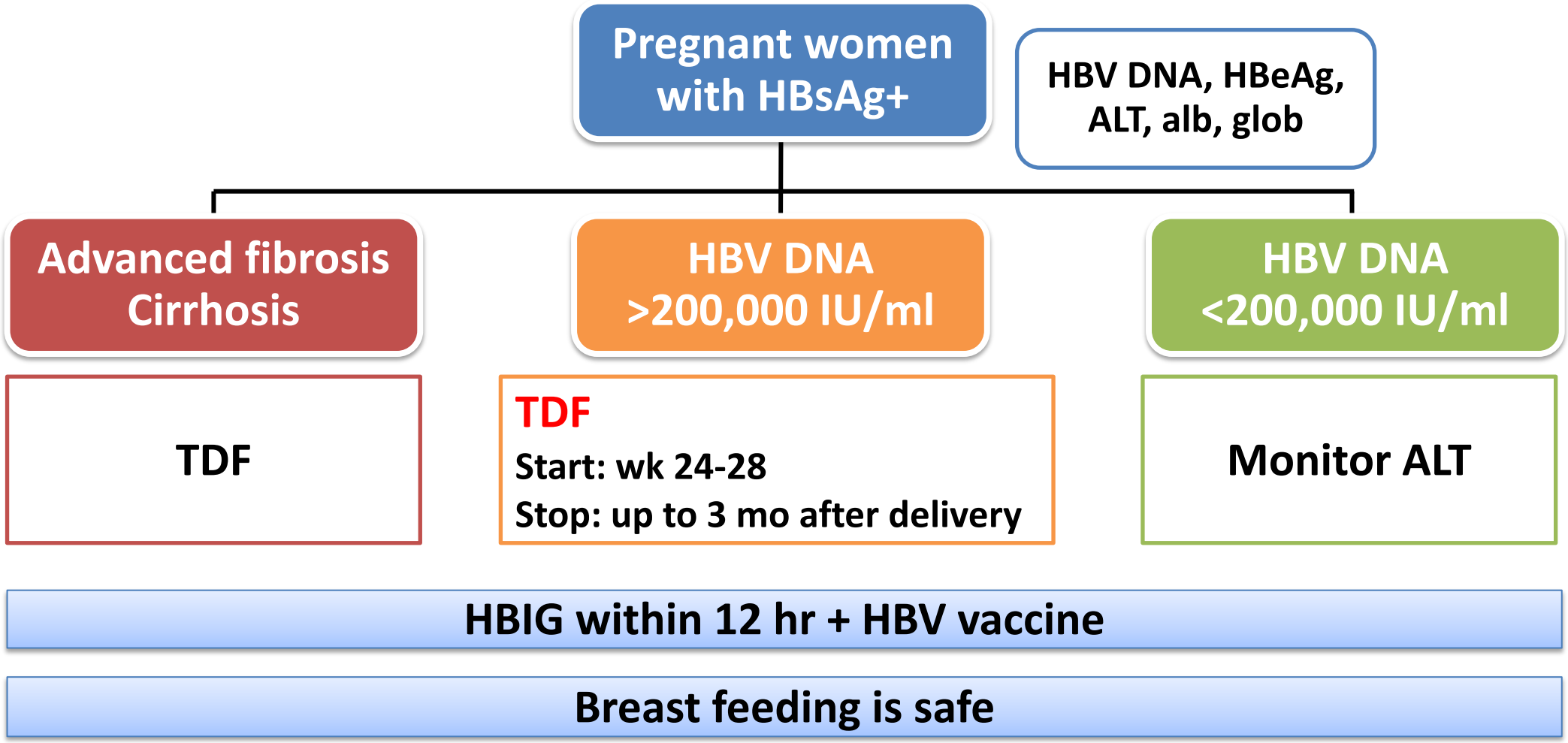
Cirrhosis

- Compensated: HBV DNA+
- Decompensated: HBsAg+

HCC

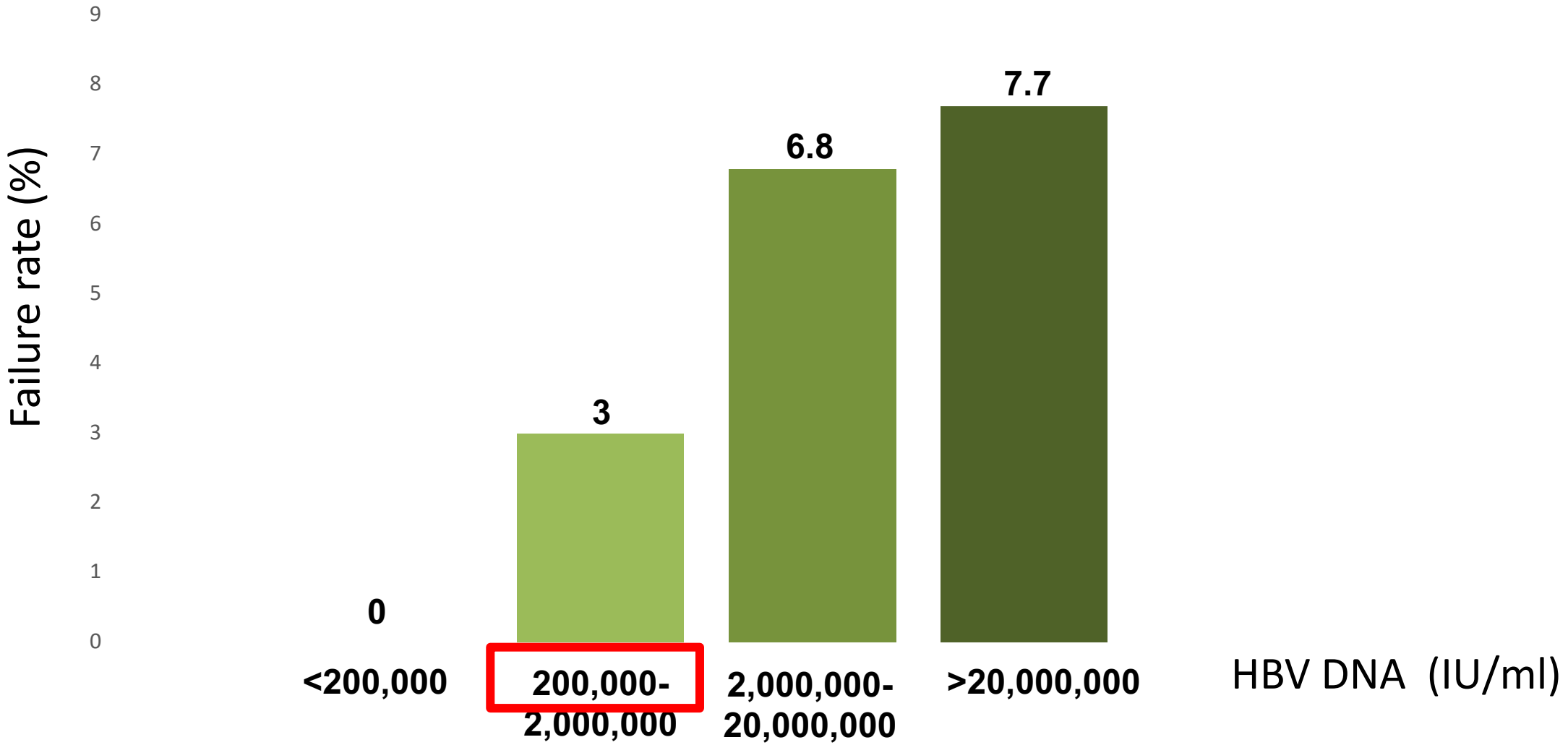
- ⬇ Recurrence after curative Rx

Algorithm for HBV management in pregnancy



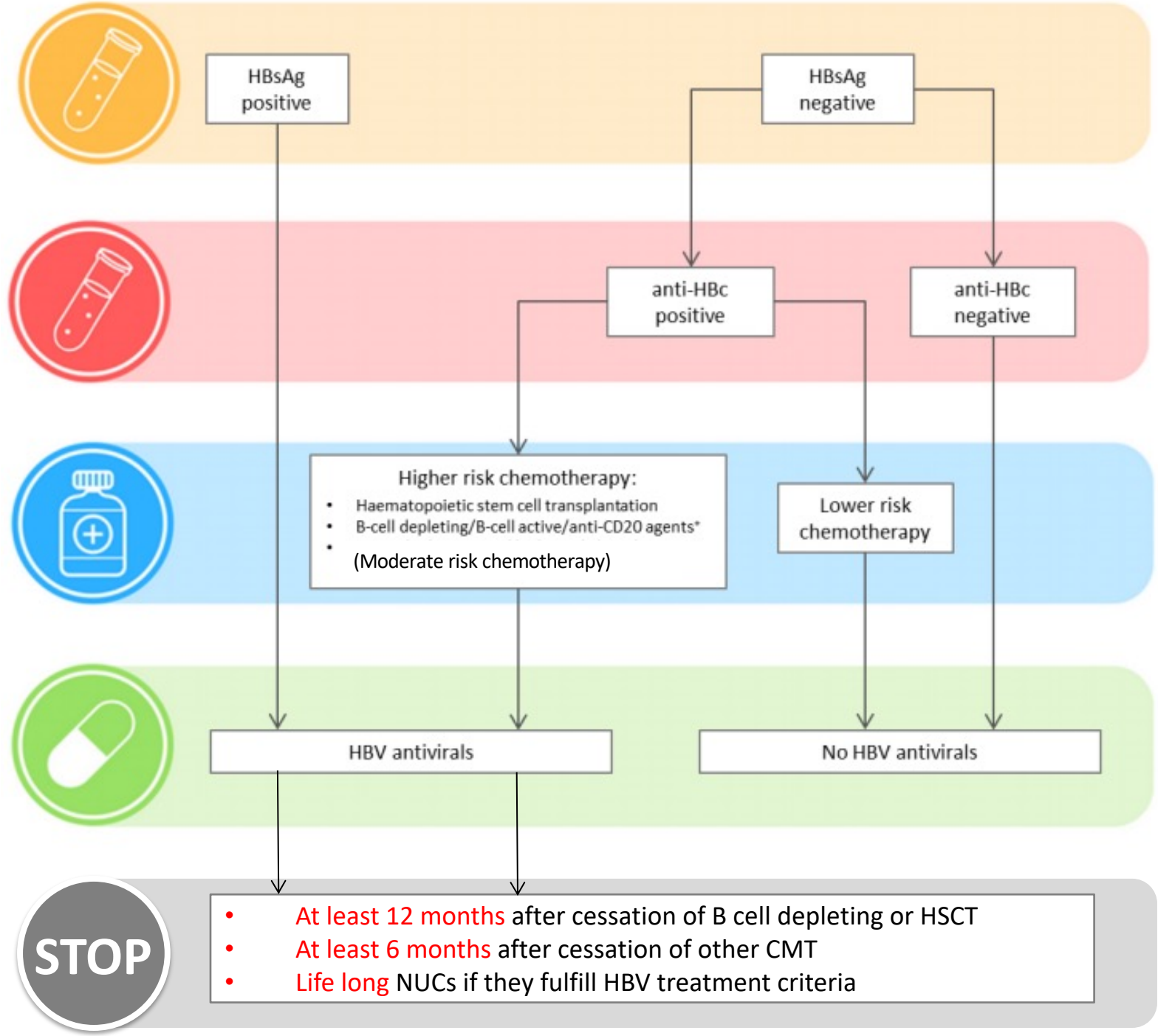
EASL guideline 2017

HBV immunoprophylaxis failure rate



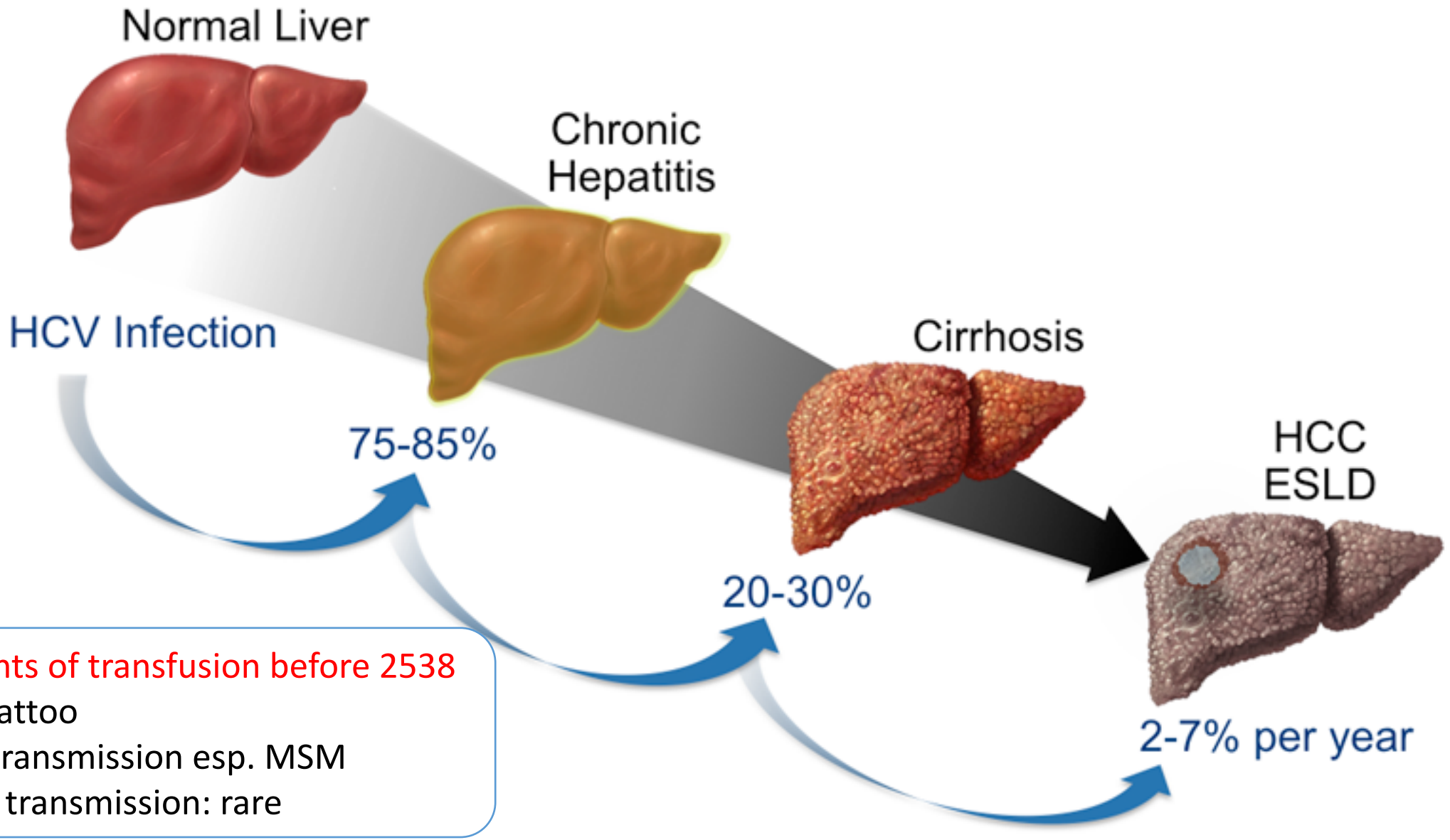
Patton H and Tran TT. Nat Rev Gastroenterol Hepatol 2014

HBV prophylaxis



*i.e. Rituximab
Ofatumumab

Natural course of HCV infection



- Recipients of transfusion before 2538
- PWID, tattoo
- Sexual transmission esp. MSM
- Vertical transmission: rare

HCV serology

Anti HCV	HCV Ag or HCV RNA	Interpretation
+	+	Chronic hepatitis C
+	-	False positive SVR (post Rx, spontaneous clearance)
-	+	Acute hepatitis C Immunocompromised host
-	-	No HCV infection

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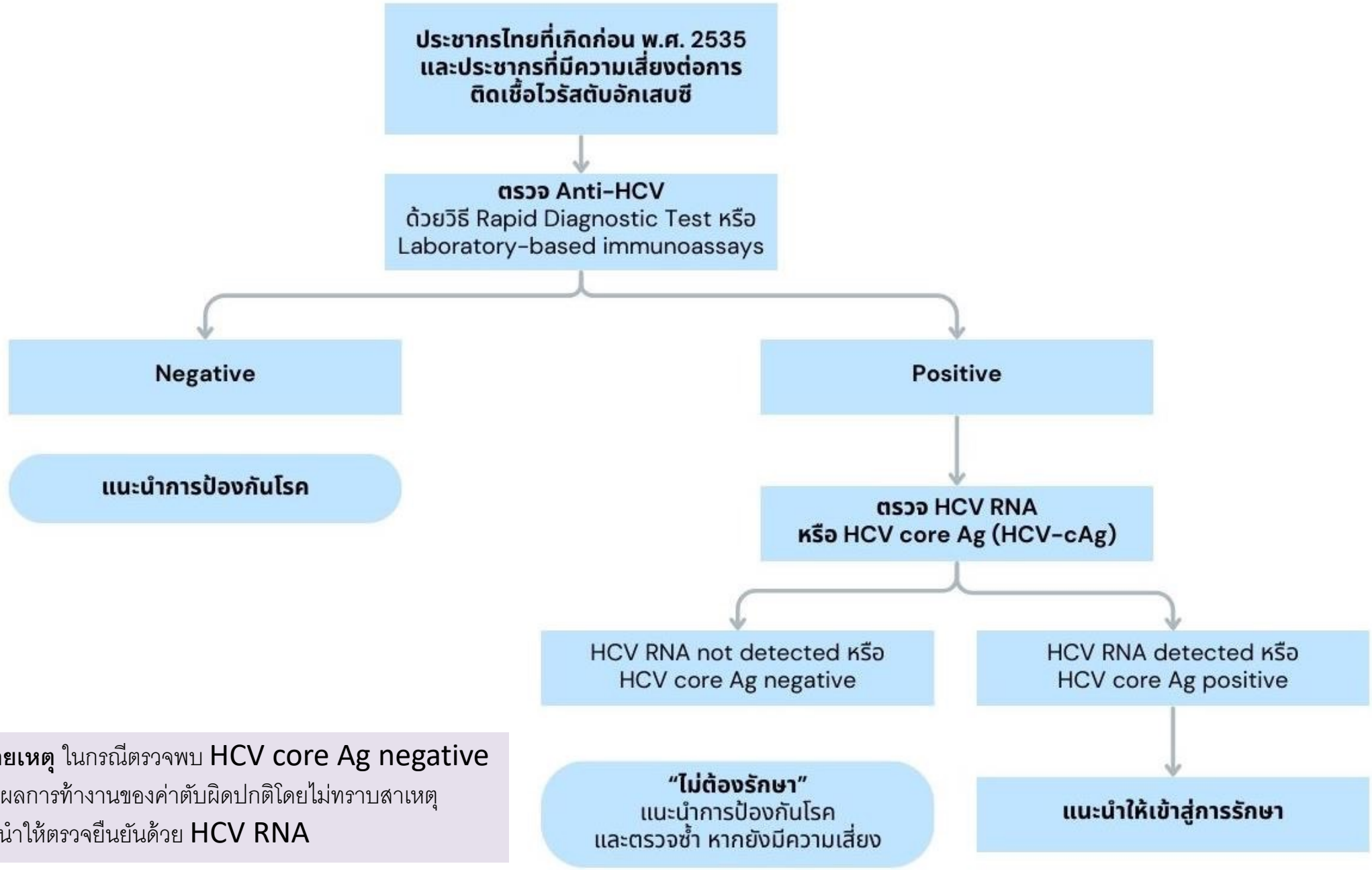

หมายเหตุ ในกรณีตรวจพบ HCV core Ag negative แต่มีผลการท้างานของค่าตับผิดปกติโดยไม่ทราบสาเหตุ แนะนำให้ตรวจยืนยันด้วย HCV RNA

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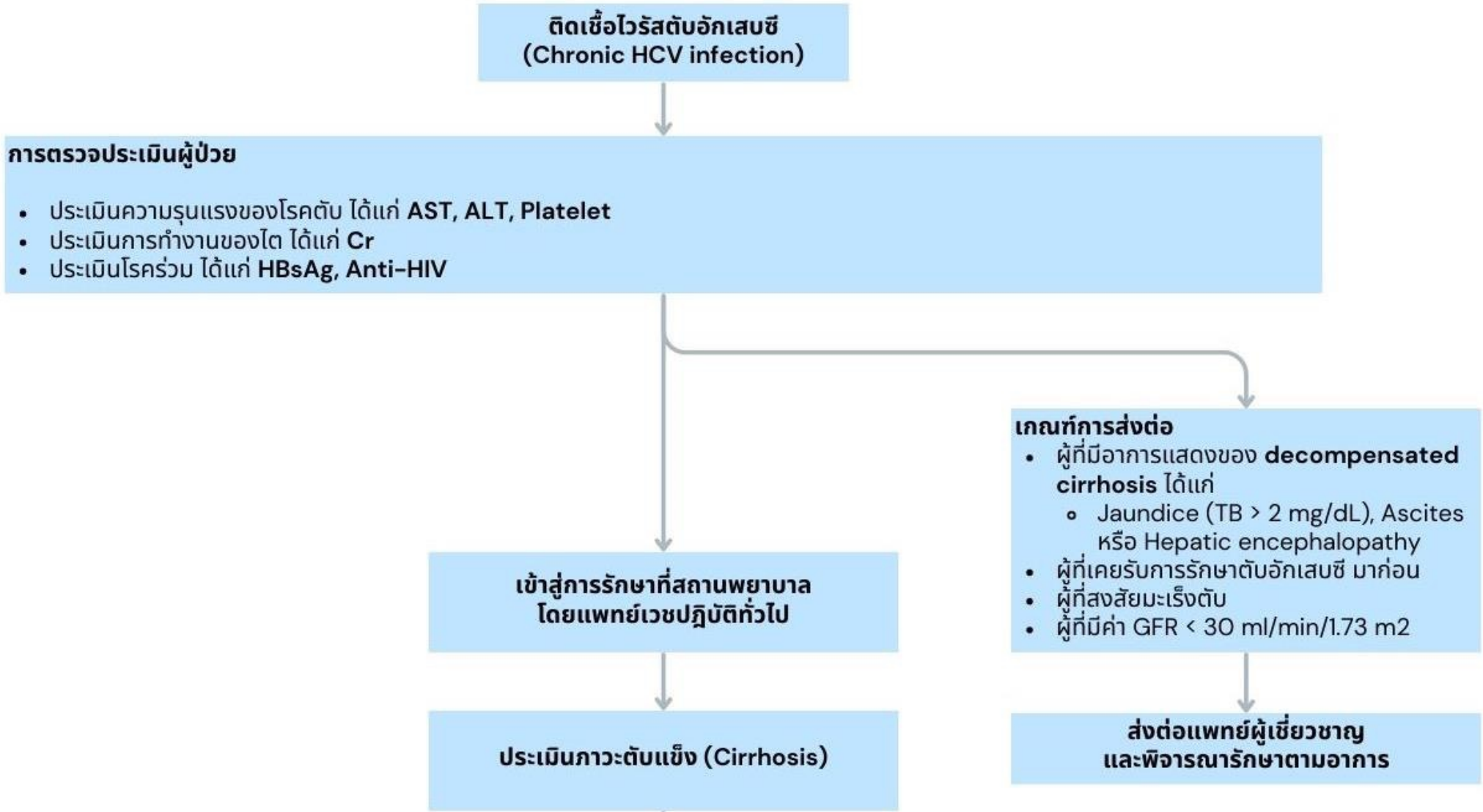

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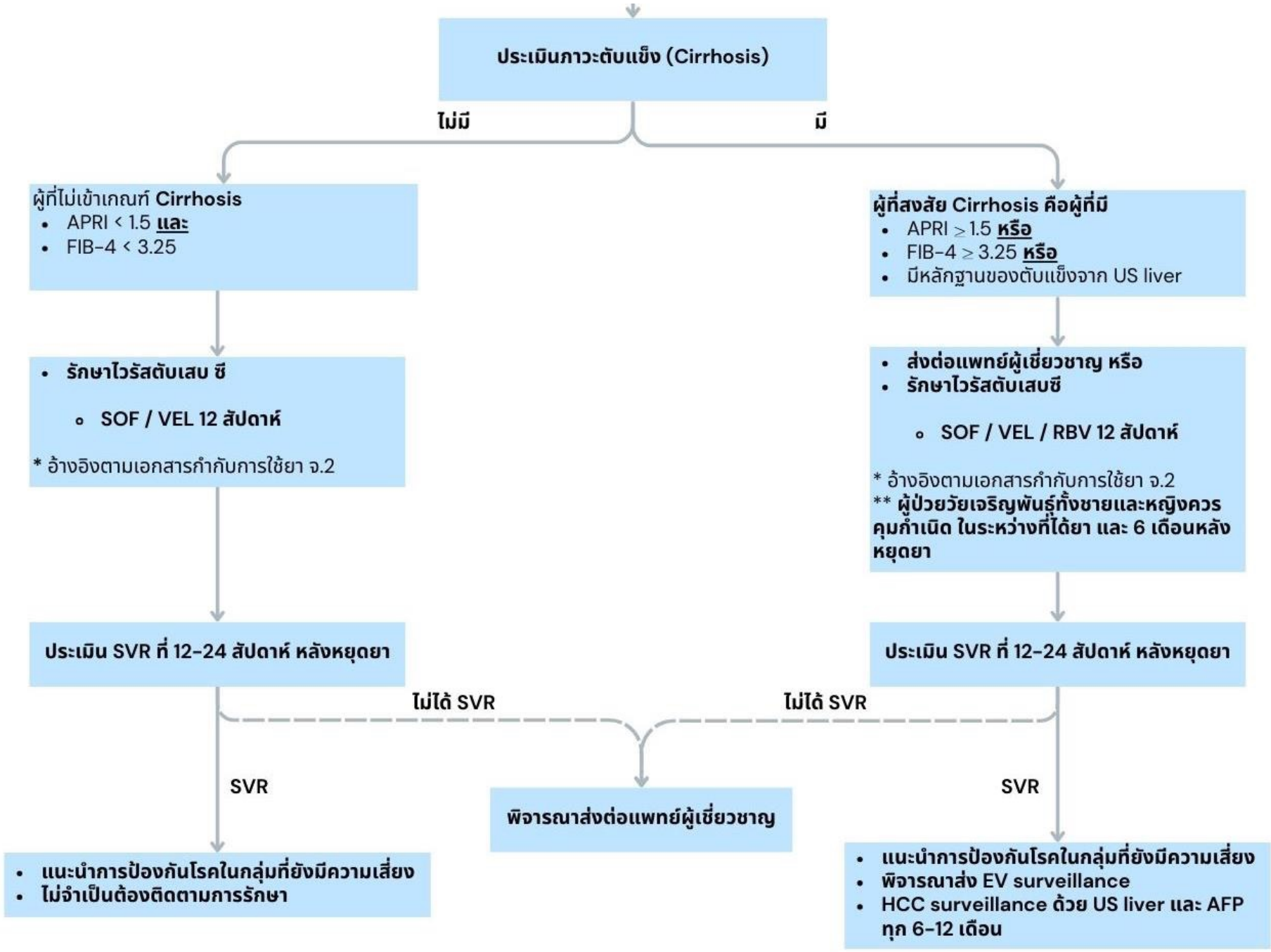

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แนวทางการดูแลรักษาผู้ป่วยโรคไวรัสตับอักเสบ ซี เรื้อรัง ในประเทศไทย 2566

	No cirrhosis	Cirrhosis
Genotype Any	**Sofosbuvir + Velpatasvir** 12 wk	**Sofosbuvir + Velpatasvir + Ribavirin** 12 wk

Drug interaction

ยา	Contraindication	Potential interaction (Require dose adjustment and monitoring)
ยาต้านไวรัสเอชไอวี	Efavirenz, Nevirapine, Lopinavir	Rilpivirine, Atazanavir, Ritonavir, Darunavir
ยาลดกรด	PPIs (ยกเว้น Omeprazole 20 mg)	Omeprazole 20 mg* H2RA**, Antacids***
ยากันชัก	Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	
ยาหลอดเลือดหัวใจและยาลดไขมัน	Amiodarone	Statins Digoxin, Dabigatran, Ticagrelor, Carvedilol, Diltiazem

* หากจำเป็น ควรให้ SOF/VEL พร้อมอาหาร ที่เวลา 4 ชั่วโมงก่อน PPI และไม่ใช้ Omeprazole ขนาดสูงกว่า 20 mg/d

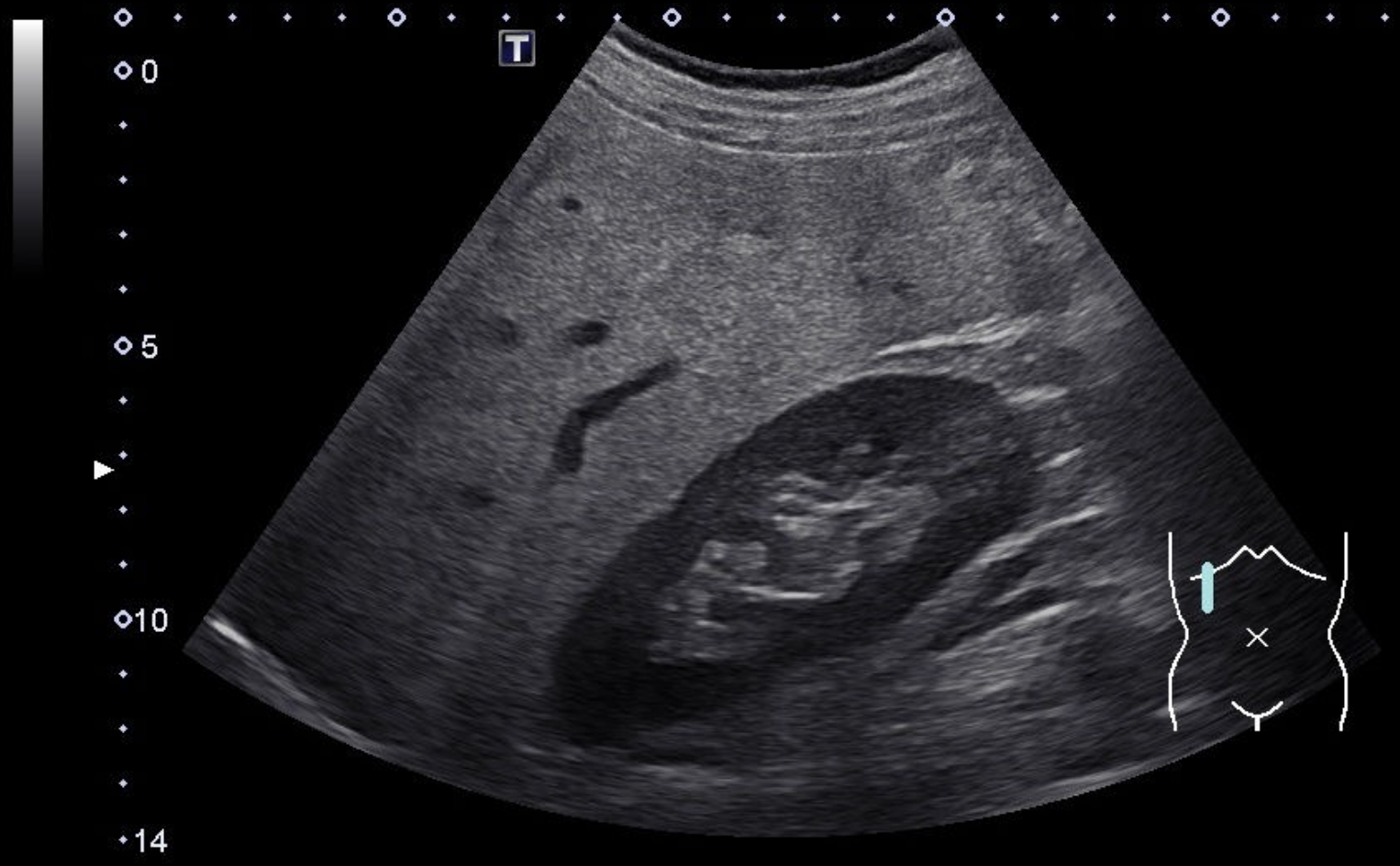
** หากจำเป็น ควรให้ SOF/VEL พร้อมกับ H2RA หรือห่างกับ H2RA อย่างน้อย 12 ชั่วโมง และไม่ใช้ H2RA ขนาดสูงกว่าขนาดที่เทียบเท่ากับ Famotidine 40 mg BID

***ควรให้ SOF/VEL ห่างจากยา Antacids อย่างน้อย 4 ชั่วโมง

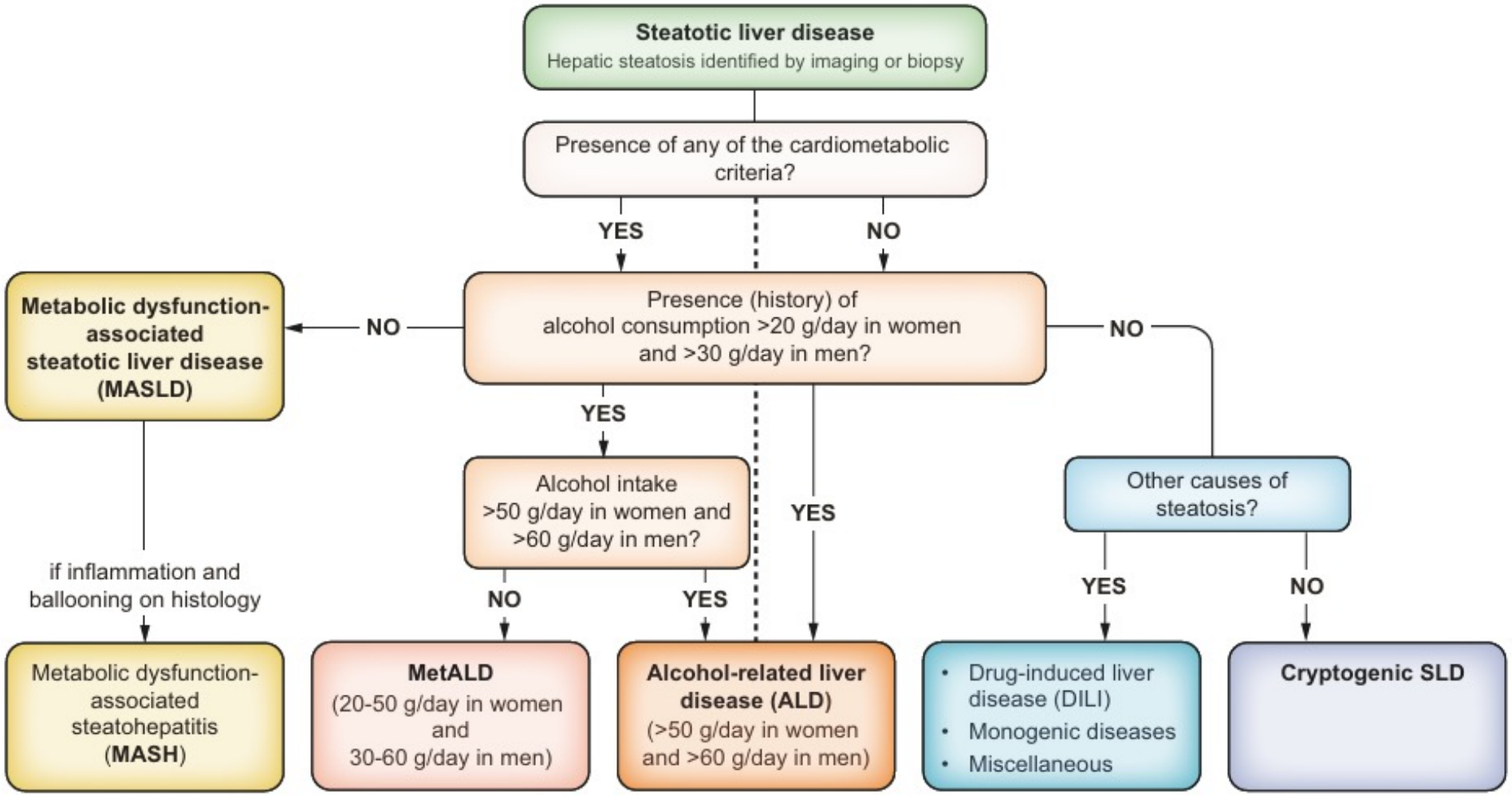
2

Steatotic liver diseases

Fatty liver



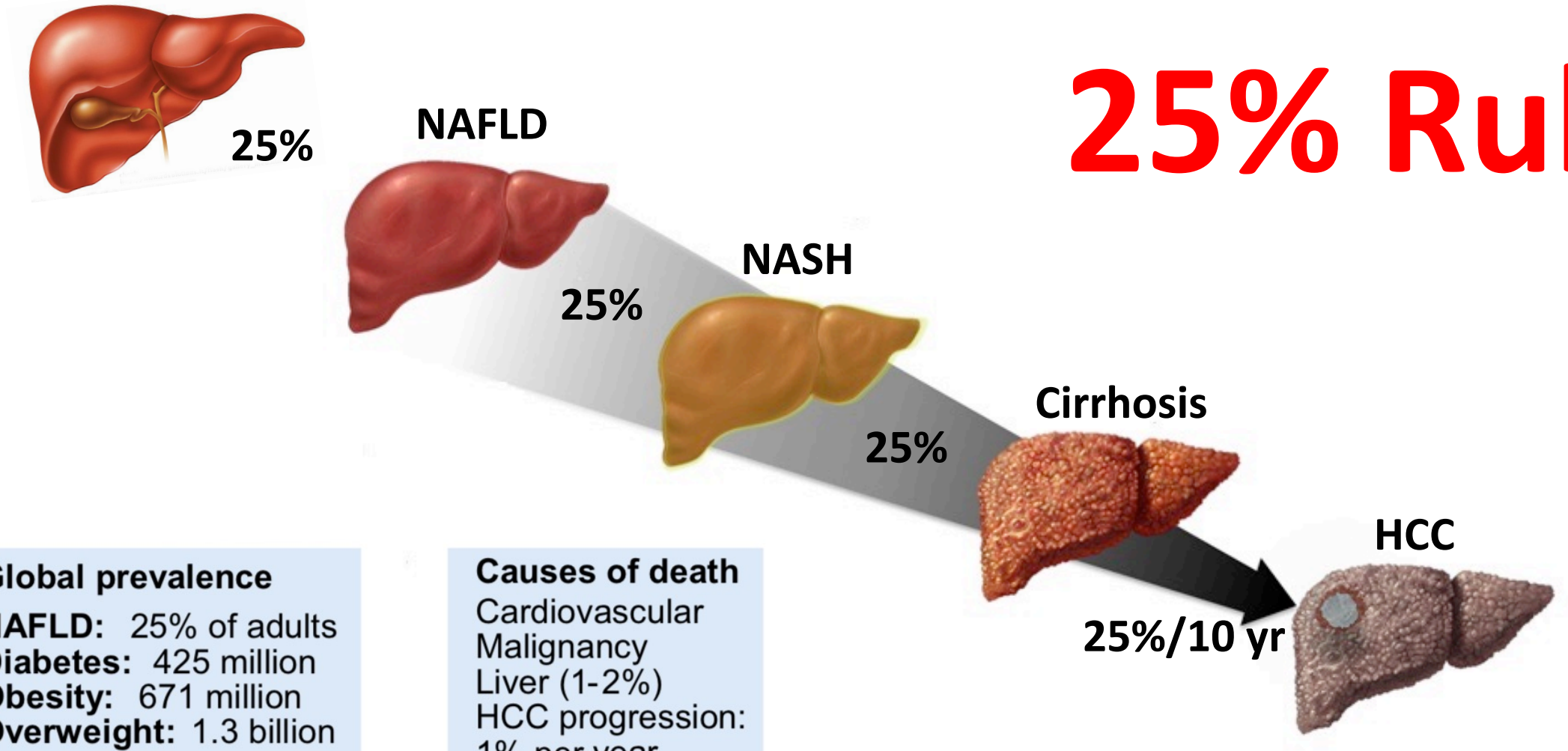
New classification of steatotic liver disease (SLD)



EASL–EASD–EASO Clinical Practice Guidelines, J Hep 2024

Natural history of NAFLD

25% Rule



Global prevalence

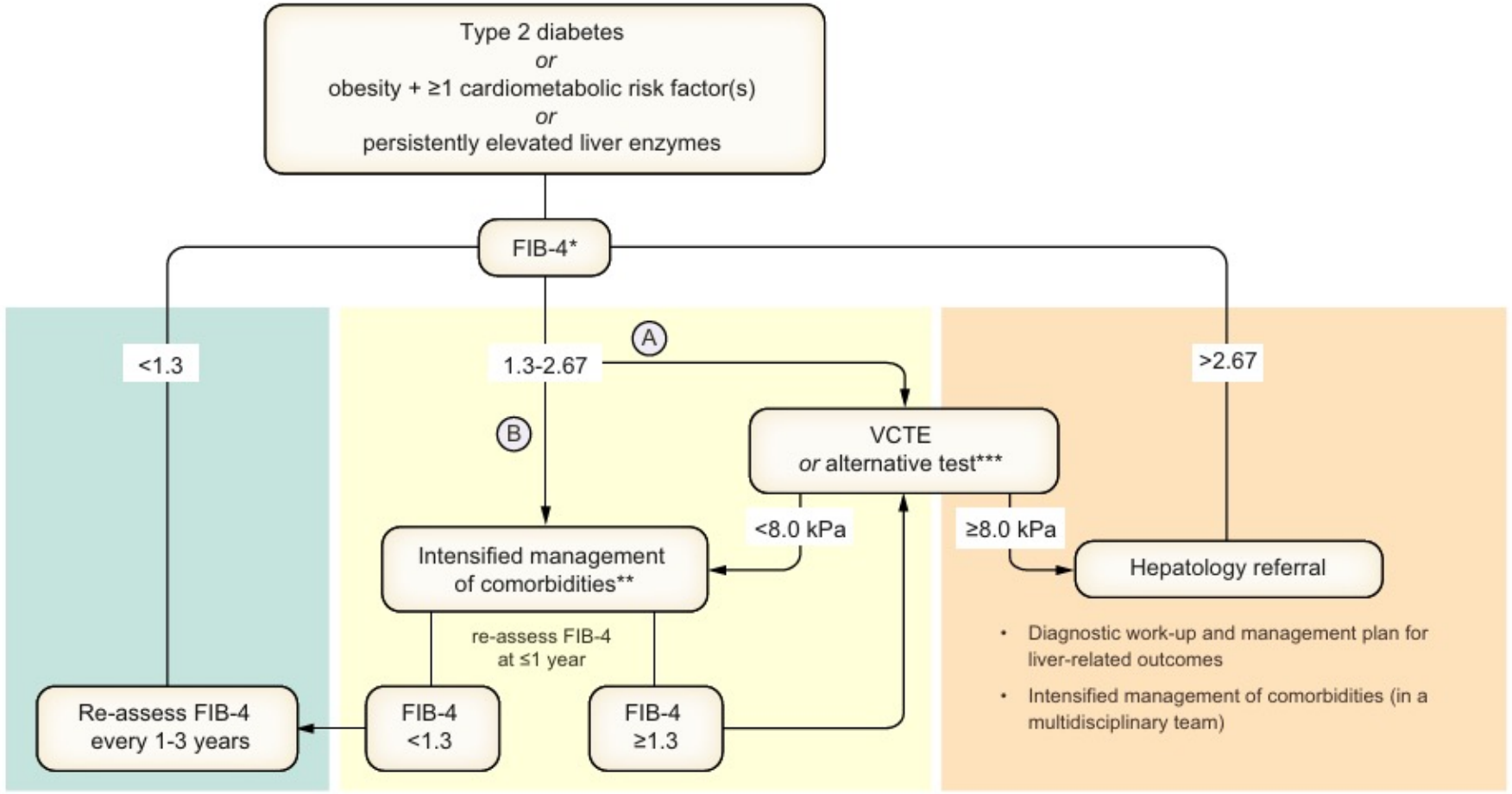
NAFLD: 25% of adults
Diabetes: 425 million
Obesity: 671 million
Overweight: 1.3 billion

Causes of death

Cardiovascular
Malignancy
Liver (1-2%)
HCC progression:
1% per year

Asrani S. J Hepatol 2019.

Stratification of patients with MASLD



* FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cut-off is 2.0)
** *e.g.* lifestyle intervention, treatment of comorbidities (*e.g.* GLP1RA), bariatric procedures
*** *e.g.* MRE, SWE, ELF, with adapted thresholds
Ⓐ and Ⓑ are options, depending on medical history, clinical context and local resources

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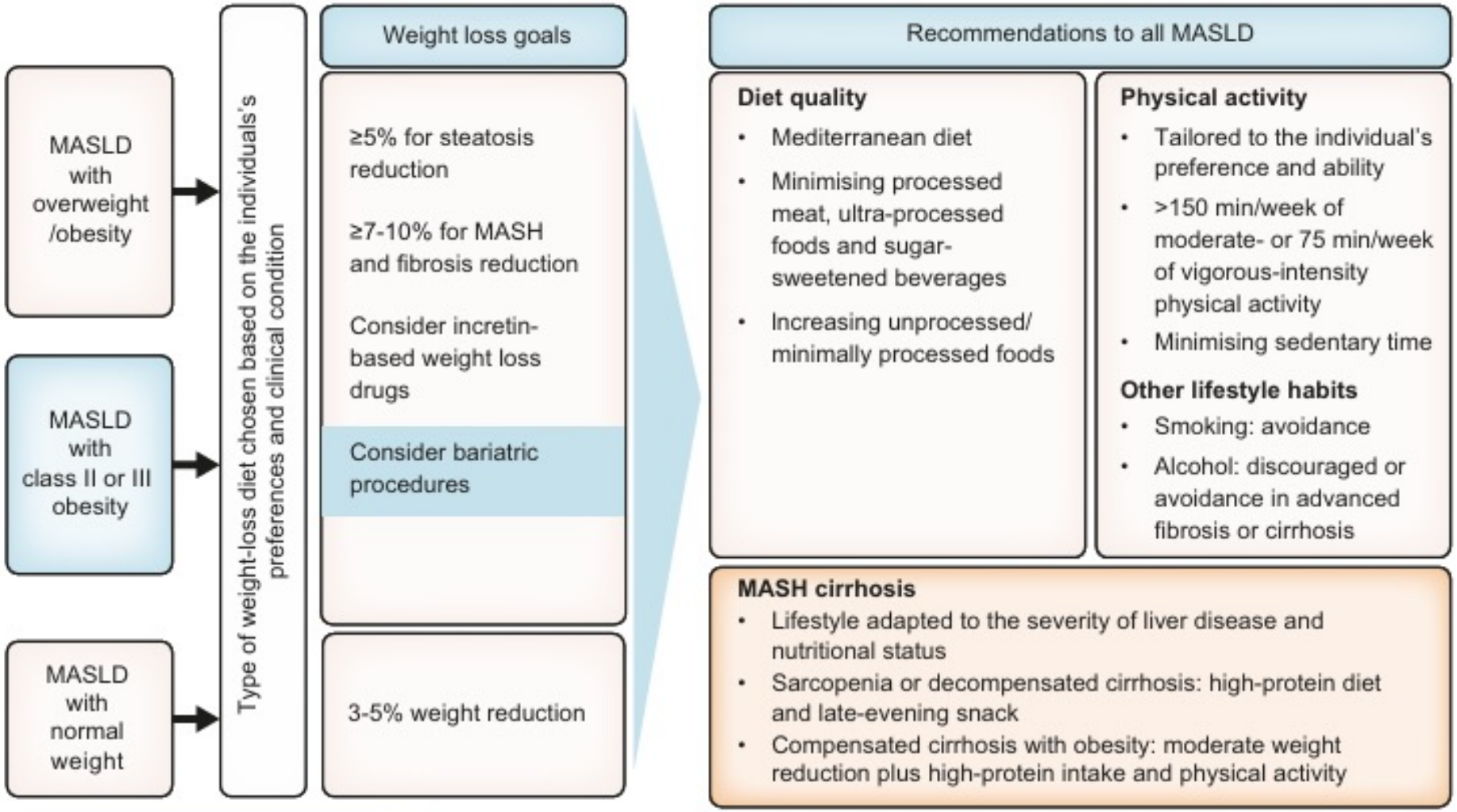
Lifestyle modification



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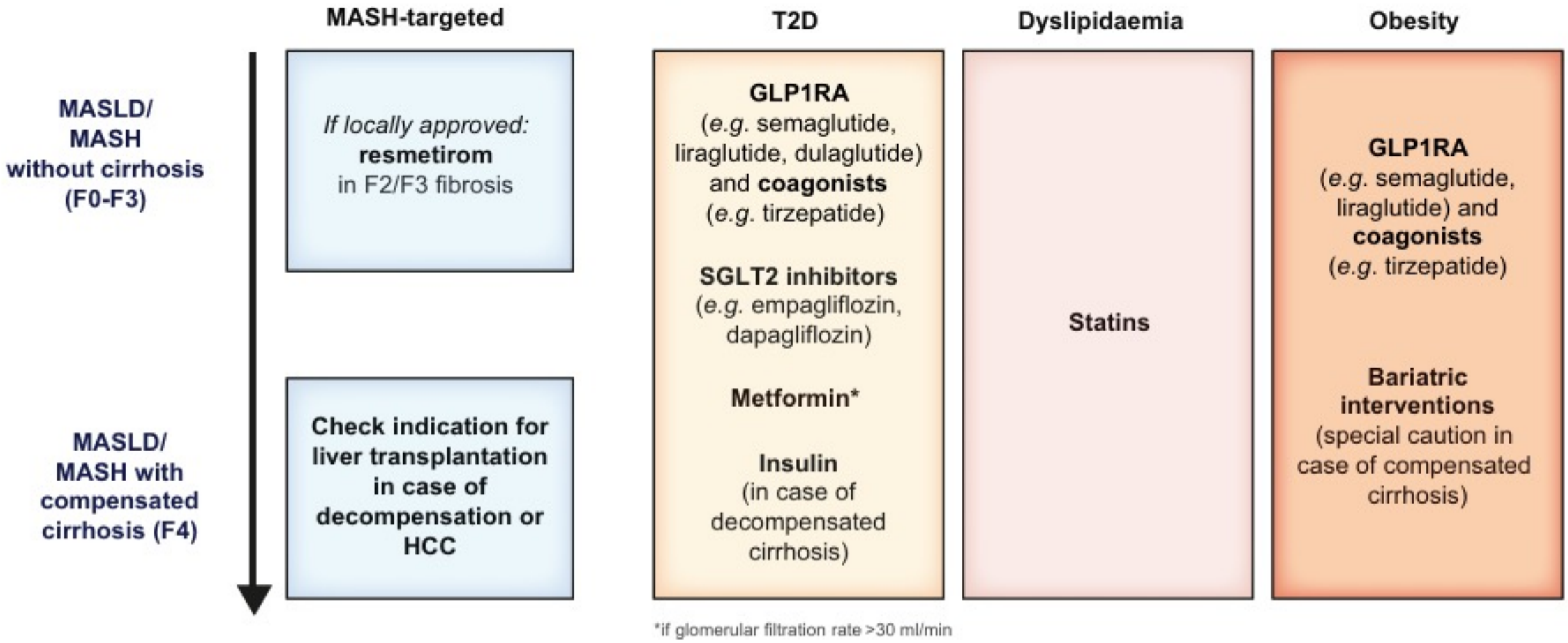
Pharmacological treatment of MASLD



EASL–EASD–EASO Clinical Practice Guidelines, J Hep 2024

The standard drink: 12-14 gram of alcohol

12 fl oz of regular beer = **8–9 fl oz of malt liquor** (shown in a 12 oz glass) = **5 fl oz of table wine** = **1.5 fl oz shot of distilled spirits** (gin, rum, tequila, vodka, whiskey, etc.)

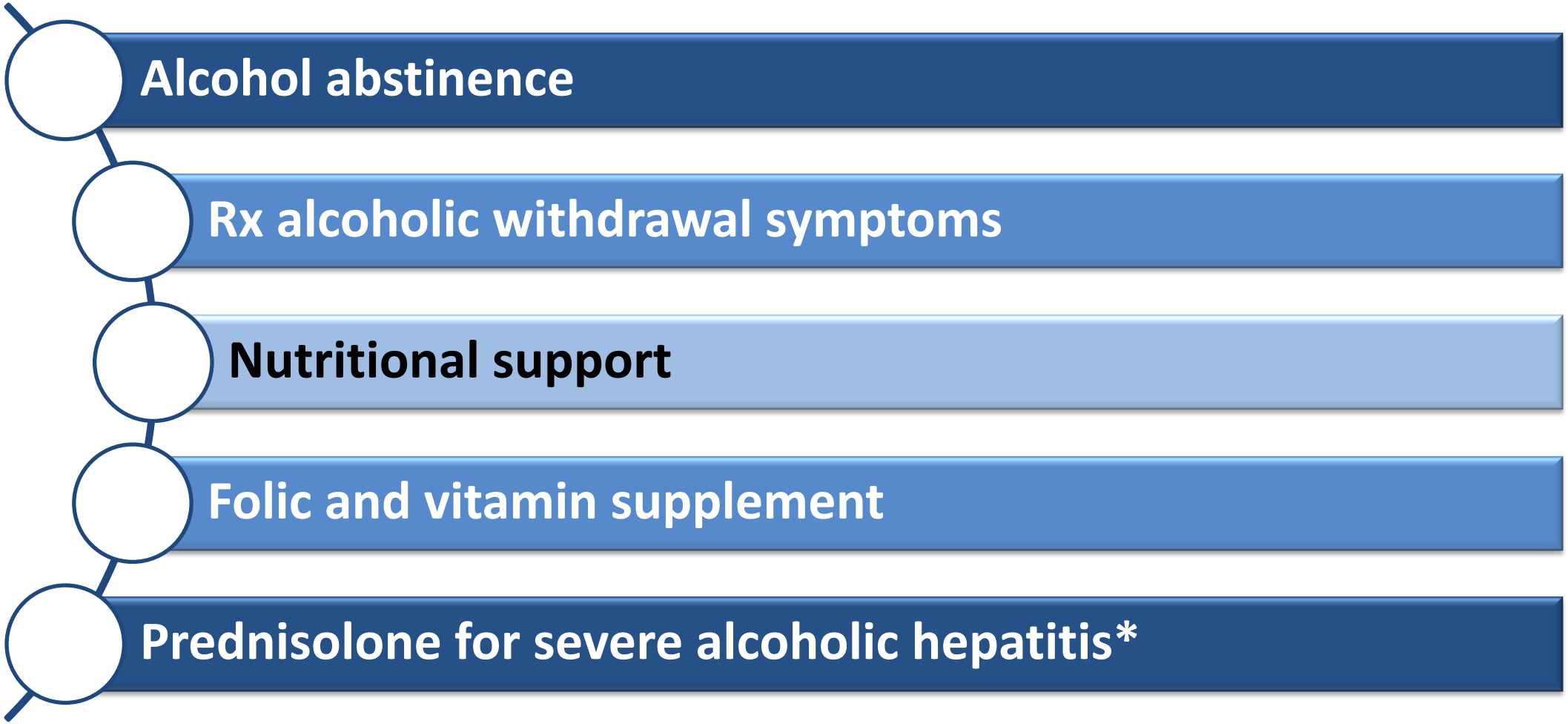
about 5% alcohol

about 7% alcohol

about 12% alcohol

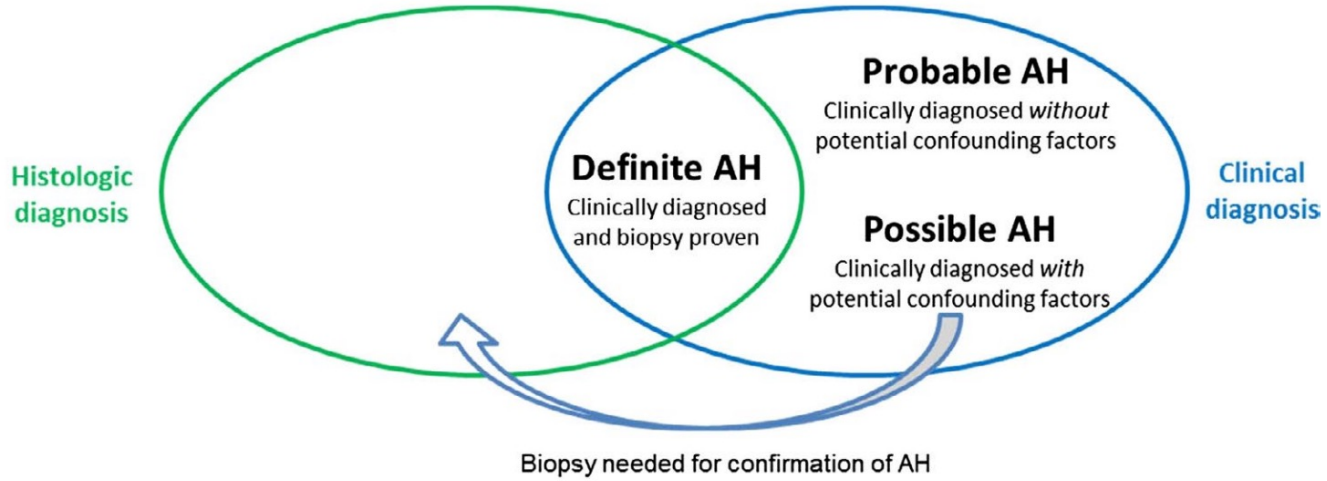
about 40% alcohol

Management of alcohol-related liver disease



*mDF, Maddrey's discriminant function = 4.6 x (PT*patient* – PT*control*) + Total bilirubin

Consensus definitions for alcoholic hepatitis



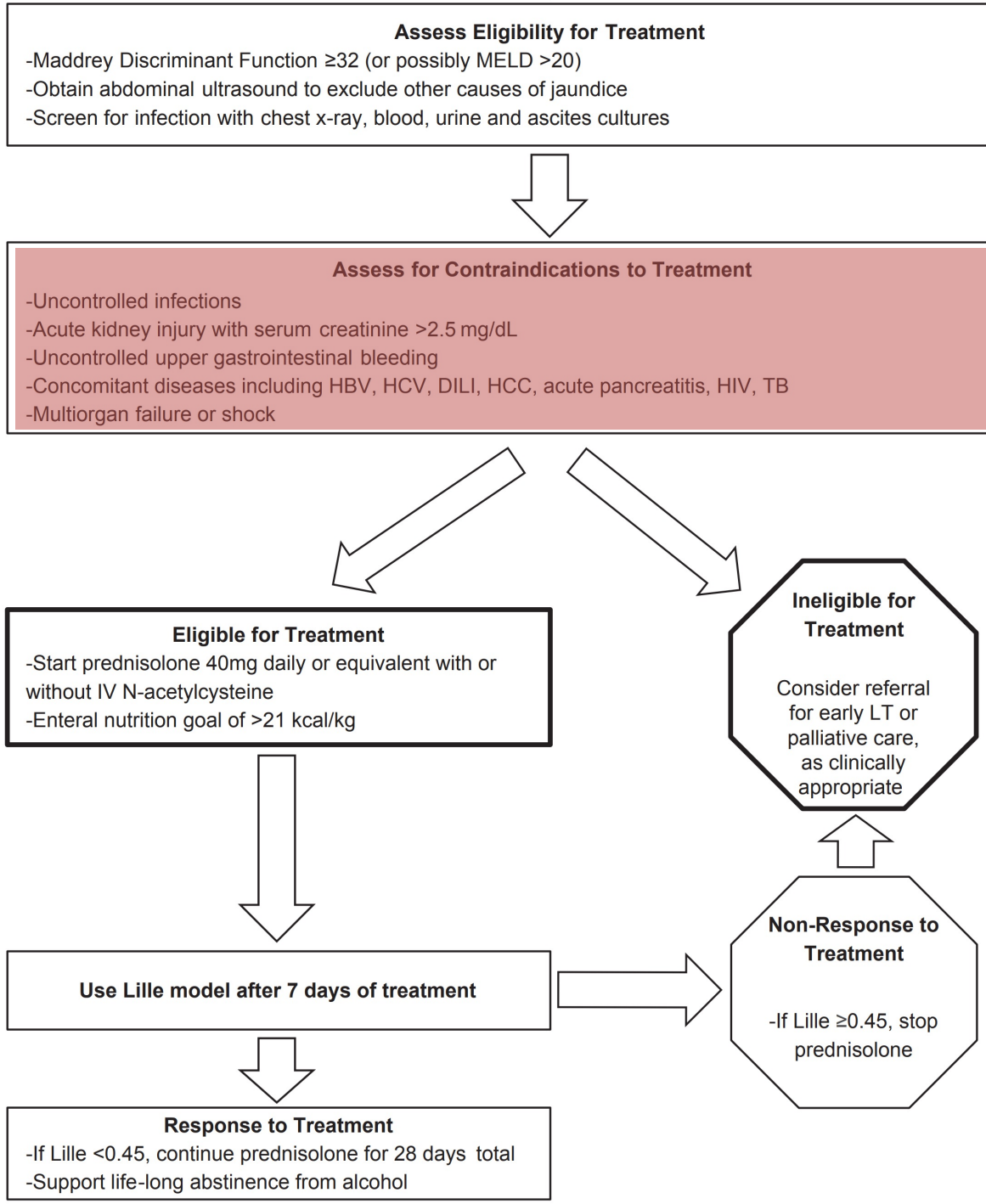
Clinical diagnosis of AH

- Onset of jaundice within prior 8 weeks
- Ongoing consumption of >40 (female) or 60 (male) g alcohol/day for ≥6 months, with <60 days of abstinence before the onset of jaundice
- AST >50, AST/ALT >1.5, and both values <400 IU/L
- Serum total bilirubin >3.0 mg/dL

Potential confounding factors

- Possible ischemic hepatitis (e.g., severe upper gastrointestinal bleed, hypotension, or cocaine use within 7 days) or metabolic liver disease (Wilson disease, alpha 1 antitrypsin deficiency)
- Possible drug-induced liver disease (suspect drug within 30 days of onset of jaundice)
- Uncertain alcohol use assessment (e.g., patient denies excessive alcohol use)
- Presence of atypical laboratory tests (e.g., AST <50 or >400 IU/L, AST/ALT <1.5), ANA >1:160 or SMA >1:80.

Crabb DW. Hepatology 2020.



Crabb DW. Hepatology 2020.

SLD due to other etiologies

Condition	Clinical/lab/histological findings	Diagnostic criteria
Hepatitis C virus-associated steatotic liver (genotype 3)	Low triglycerides, HCV genotype 3	HCV antibody with reflex testing HCV RNA and HCV genotype
Drug-induced liver disease (DILI)	Mostly microvescicular SLD	Investigate for drug intake: • Corticosteroids • Tamoxifen • Amiodarone • Irinotecan • Methotrexate • Lomitapide • Valproate • 5-Fluorouracil Liver biopsy for confirmation
Hypobetalipoproteinaemia	Low triglycerides and cholesterol, fat malabsorption, vitamin A deficiency	ApoB level, genetic testing (*APOB, MTTP, PCSK-9*, targeted panel sequencing)
Lipodystrophy	Accumulation of fat in the visceral area and in the muscle (generically inherited or induced by HAART therapy)	CT scan or MRI, targeted panel sequencing for congenital lipodystrophies, MRI
LAL deficiency (Wolman disease, cholesteryl ester storage disease-CESD)	Elevated LDL-C and triglycerides, low HDL-C, hypersplenism, advanced fibrosis in young age, predominately microvesicular steatosis	Enzyme assay, genetic testing (LIPA)
Pregnancy associated	HELLP syndrome Acute onset	Elevated liver enzymes and low platelets, haemolysis, SLD at abdominal ultrasound
Wilson disease	Younger age, neuropsychiatric symptoms, low ceruloplasmin	24-h urine copper excretion; quantitative copper on liver biopsy, genetic testing (*ATP7B*)
Nutrient deficiency/malnutrition	Parenteral nutrition, bypass surgeries, bariatric surgery, anorexia	Nutrient levels
Celiac disease	Diarrhoea, iron deficiency, vitamins deficiency	Tissue transglutaminase IgA, duodenal biopsy
Endocrine diseases	Hypothyroidism, PCOS, growth hormone (GH) deficiency, panhypopituitarism (primary or secondary)	TSH, fT4, fT3, endocrine testing
Other inherited metabolic conditions	Early age and severe onset, absence of triggering factors, systemic involvement, positive history of advanced disease in first degree relatives	Targeted panel sequencing, whole exome sequencing (WES)

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3

Autoimmune liver diseases

Autoimmune hepatitis (AIH)

Risk factors

- Female (all age groups); F:M = 9:1
- Autoimmune diseases: thyroiditis, Sjogren, scleroderma

	Younger	Older
Presentation	Acute hepatitis	Acute on chronic hepatitis Cirrhosis
Type	Type I (ANA, SMA) Type II (anti LKM-1) *SLA, LC: both types	Type I

Simplified scoring system

Features	Score
ANA or SMA 1:40 ANA or SMA ≥1:80 or anti LKM-1 ≥1:40 or SLA +	1 2
IgG >UNL IgG >1.1 UNL	1 2
Viral hepatitis: absence	2
Histology: compatible with AIH typical AIH	1 2

Probable AIH: 6 points
Definite AIH: 7-8 points

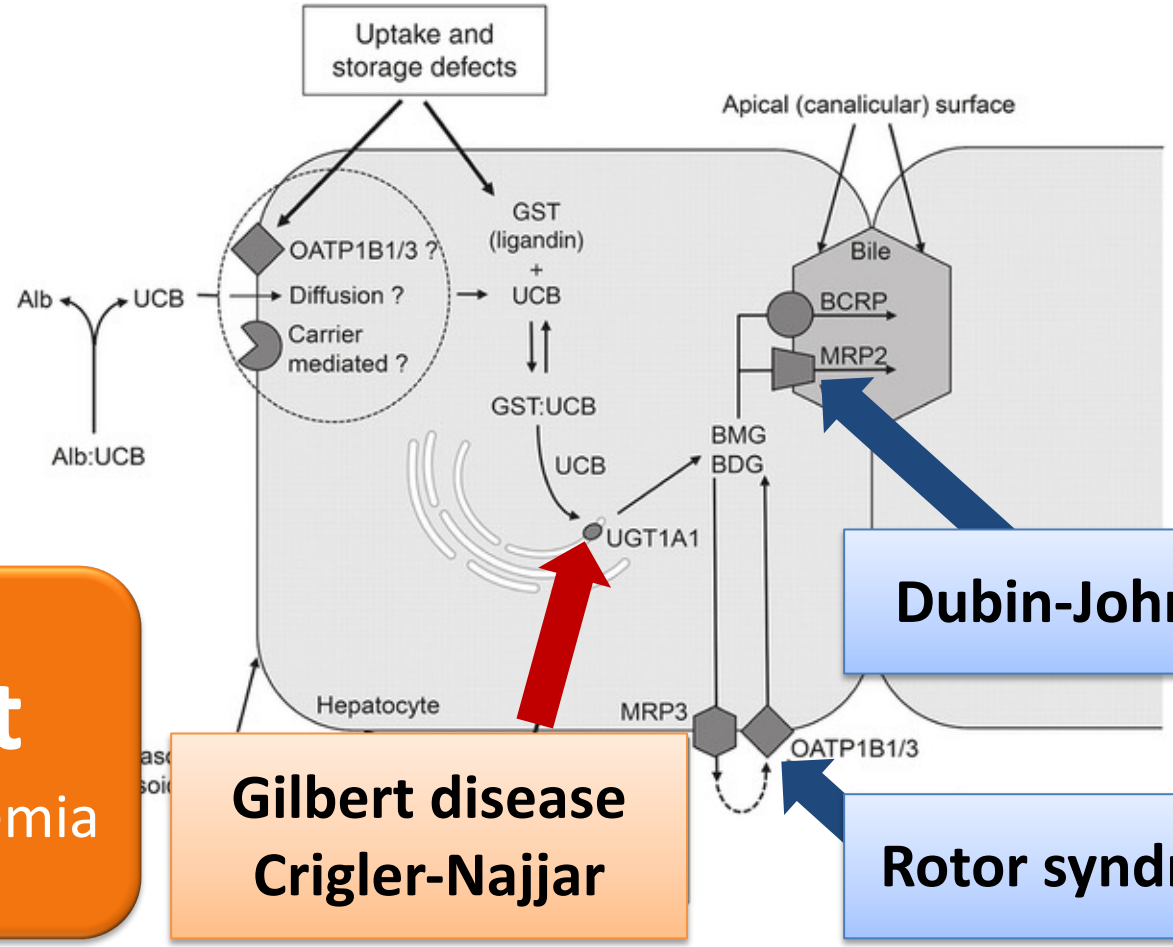
PBC vs PSC

Features	PBC	PSC
Site	Small IHD	Large IHD, EHD
Sex	F	M
Presentation	Elevated ALP Pruritus, fatigue Jaundice (late stage)	Jaundice
Associated diseases	Sicca, RA, scleroderma, autoimmune thyroiditis	IBD (UC > CD)
Autoantibody	AMA	-
Cholangiogram	Normal	Bead-like appearance
Histology	Florid duct lesion	Onion skin fibrosis
Treatment	UDCA	Dilation of dominant stricture

4

Hereditary liver diseases

Inherited disorders of bilirubin



Indirect
hyperbilirubinemia

Gilbert disease
Crigler-Najjar

Dubin-Johnson

Rotor syndrome

Direct
hyperbilirubinemia

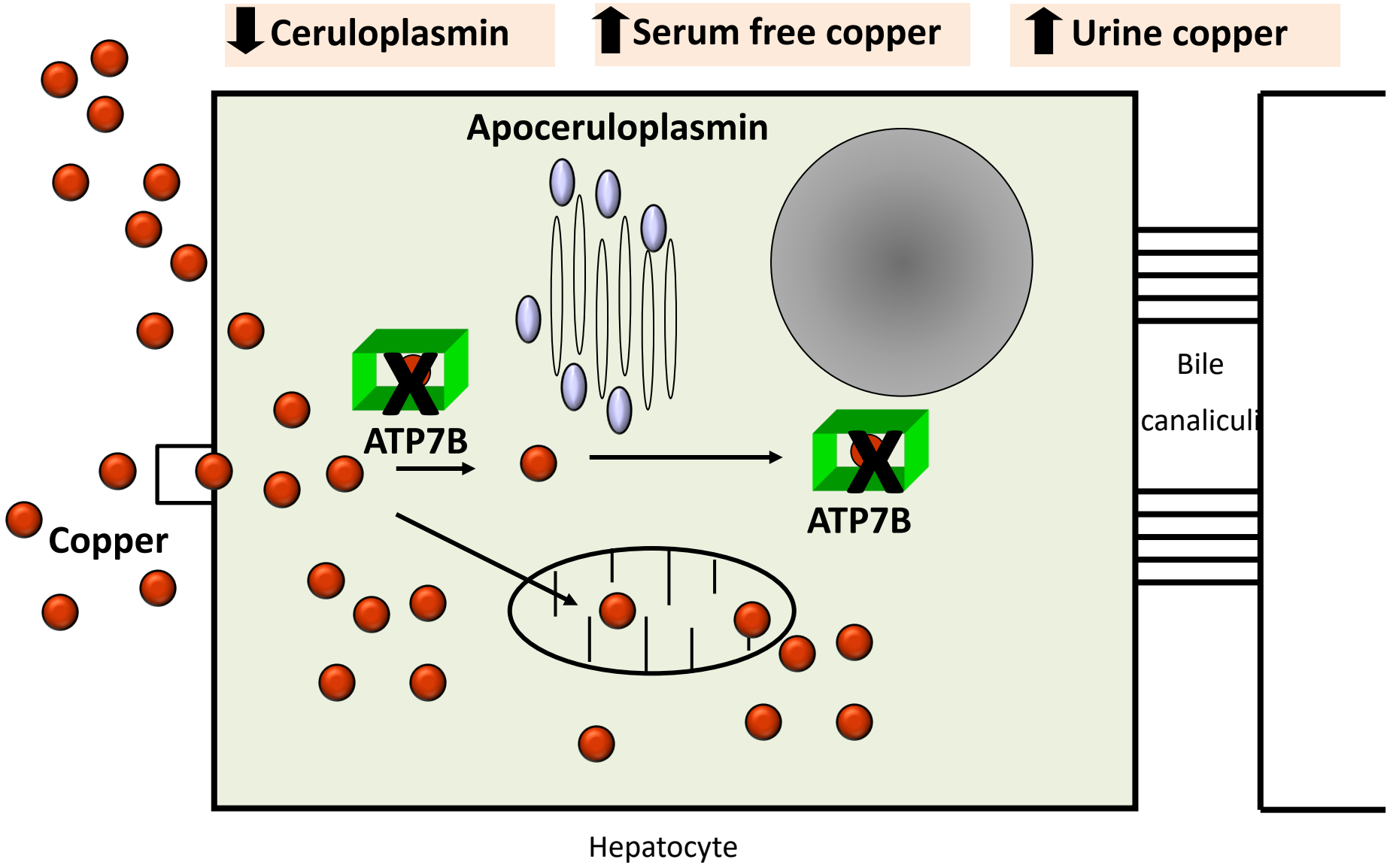
Wilson disease (WD)

Clinical clues

- Onset <30-40 yr
- Cirrhosis in young patients
- Family Hx (AR)
- KF ring (50-95%)
- Neurological involvement

  : Parkinsonism, neuropsychiatric

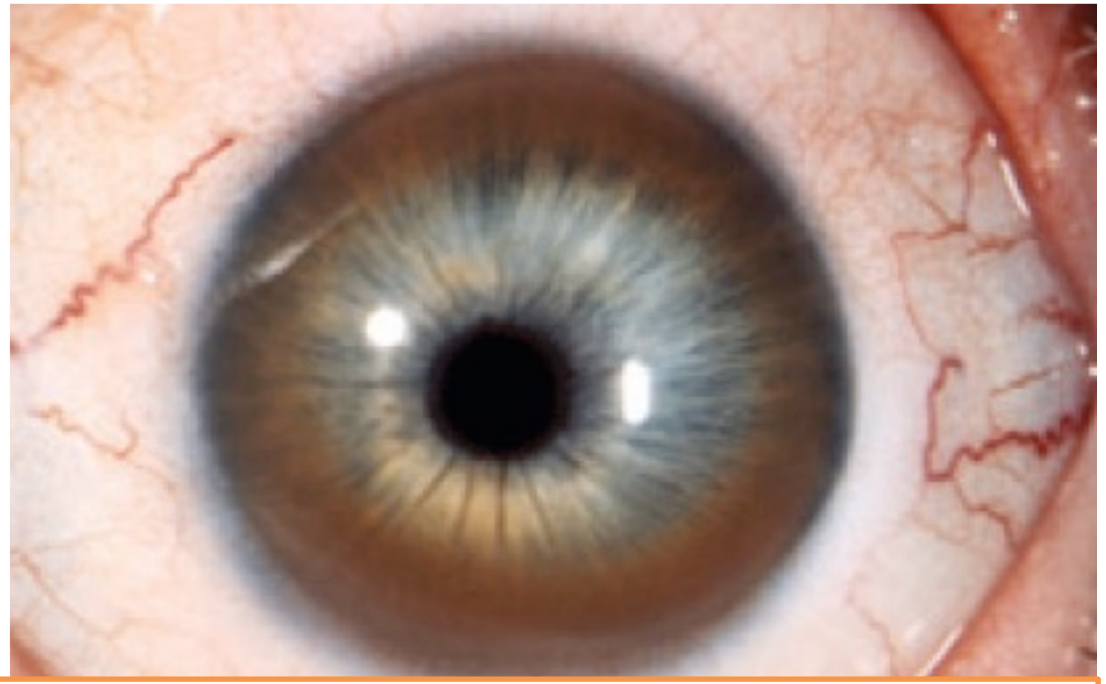
Pathophysiology



Diagnostic tests of WD

Tests	Normal	WD	False positive	False negative
Ceruloplasmin	>20 mg/dl	<20 mg/dl (S >90%) <5 mg/dl (high Sp)	• Infant, childhood • End-stage cirrhosis • NS / PLE • Copper deficiency • Menkes disease • Aceruloplasminemia • Heterozygote (20%) • General population (1%)	• Acute inflammation • Severe liver injury • Hyperestrogenemia : pregnancy, pills
24-hr urine copper	<40 μg	>100 μg (S 77-84%)	• Chronic liver diseases • Heterozygote (40-70 μg)	• Renal failure

Kayser-Fleischer (KF) ring



Required slit-lamp examination by experienced ophthalmologist

- **20-30%** in asymptomatic WD
- **50%** in WD with hepatic disease
- **95%** in WD with neurological disease

- Primary biliary cholangitis
- Multiple myeloma
- Long term estrogen use

EA Roberts, Michael LS. Hepatology 2008

WD with acute liver failure

- **Coombs-negative hemolytic anemia: 5-15%**
- **⬆ AST&ALT (<2000 IU/L), AST > ALT**
- **Normal or low ALP**

Tools	Sens (%)	Spec (%)
ALP:bilirubin <4	94	96
AST:ALT >2.2	94	86
Both	100	100

Hereditary hemochromatosis (HH)

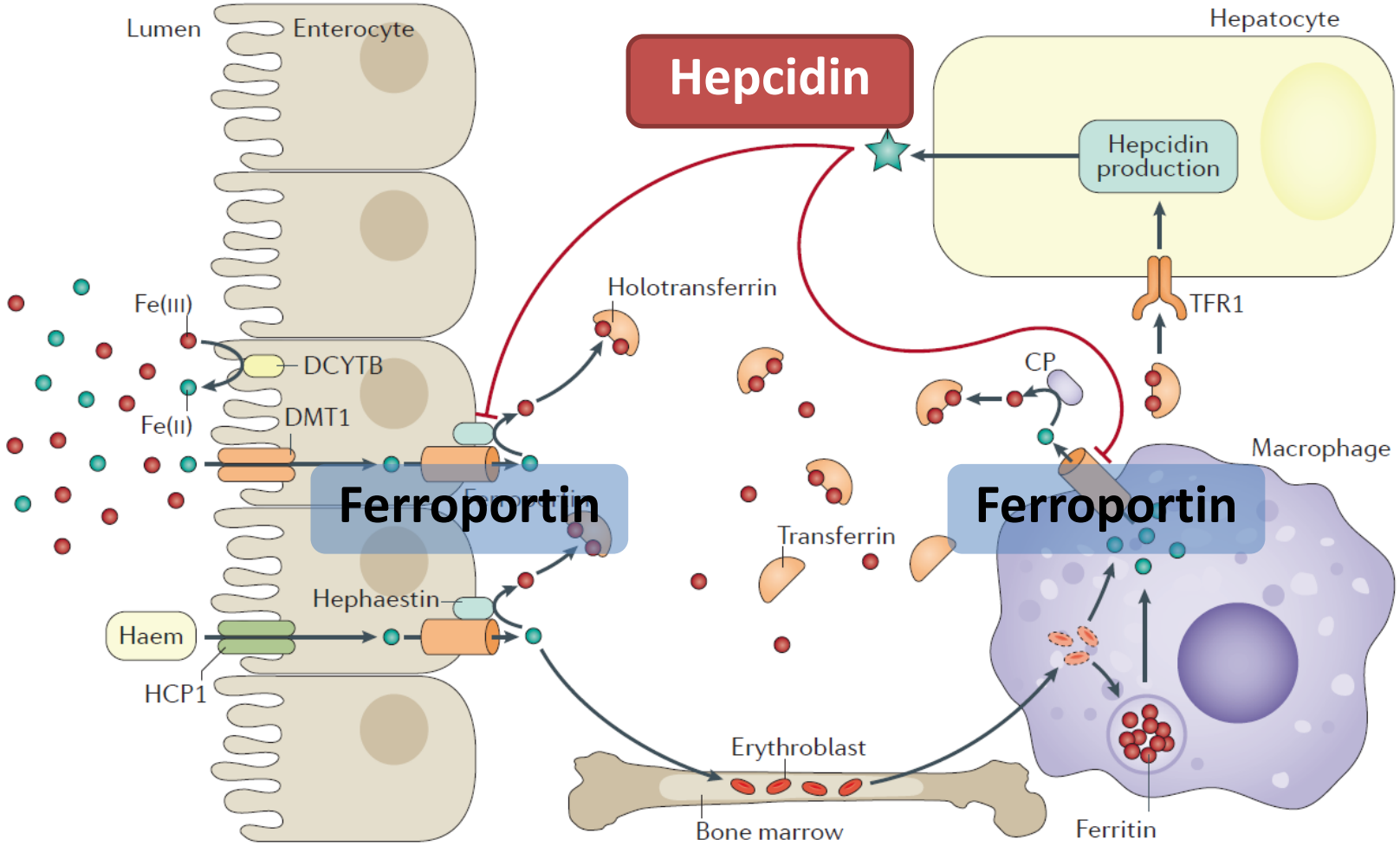
Clinical clues

- Onset: M >40, F >50
- Family Hx (AR, AD)
- Hepatomegaly
- Arthropathy (2nd, 3rd MCP) diabetes, restrictive cardiomyopathy

Diagnosis

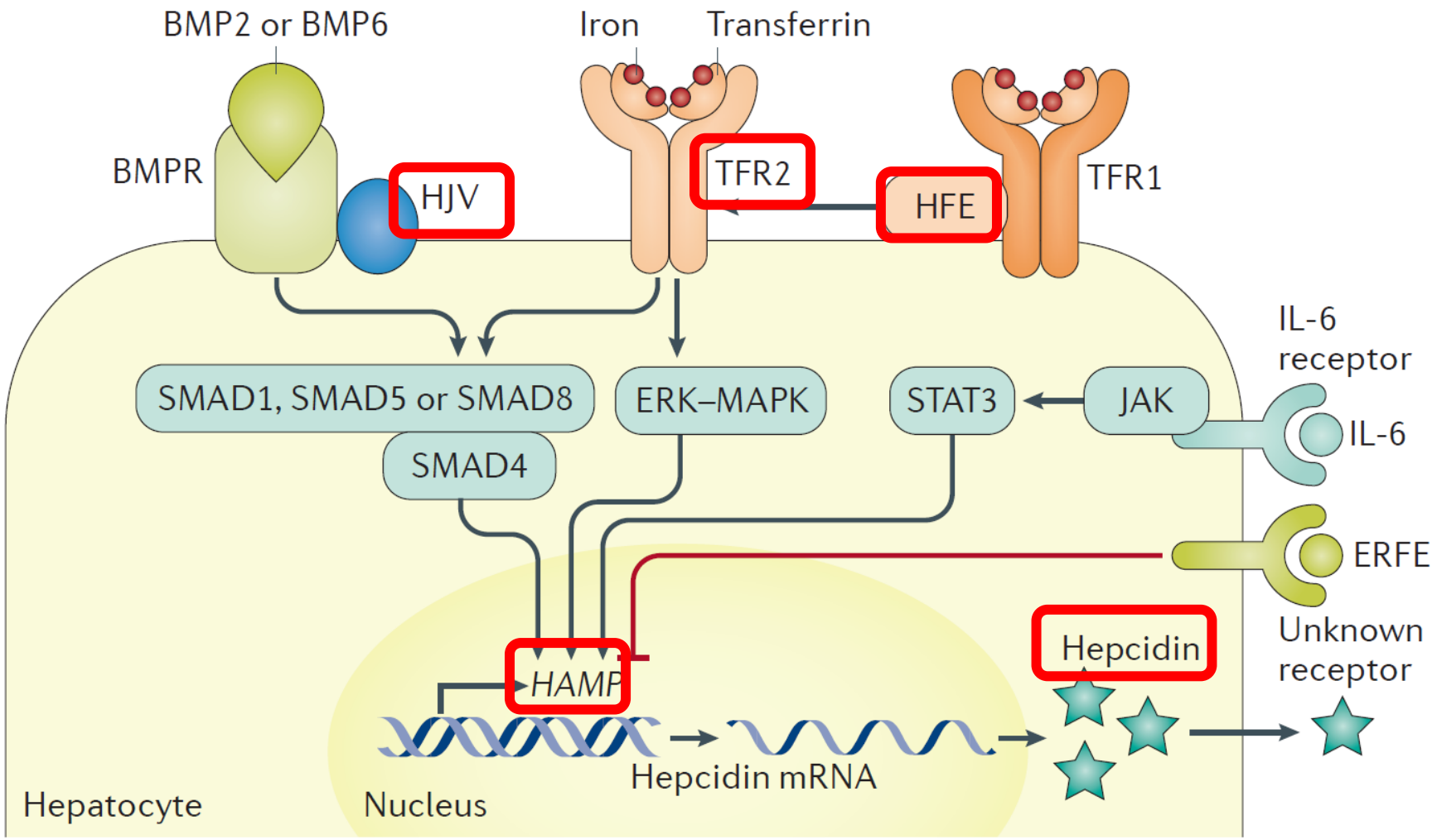
- Tissue/organ iron overload
  - Iron study: TSAT >45%, high serum ferritin
  - Liver biopsy/ MRI liver
- Exclude 2^{o} hemochromatosis
- Genetic testing

Iron homeostasis



Brissot P. Nat Rev Dis Primers 2018.

Hepcidin regulation in hepatocyte

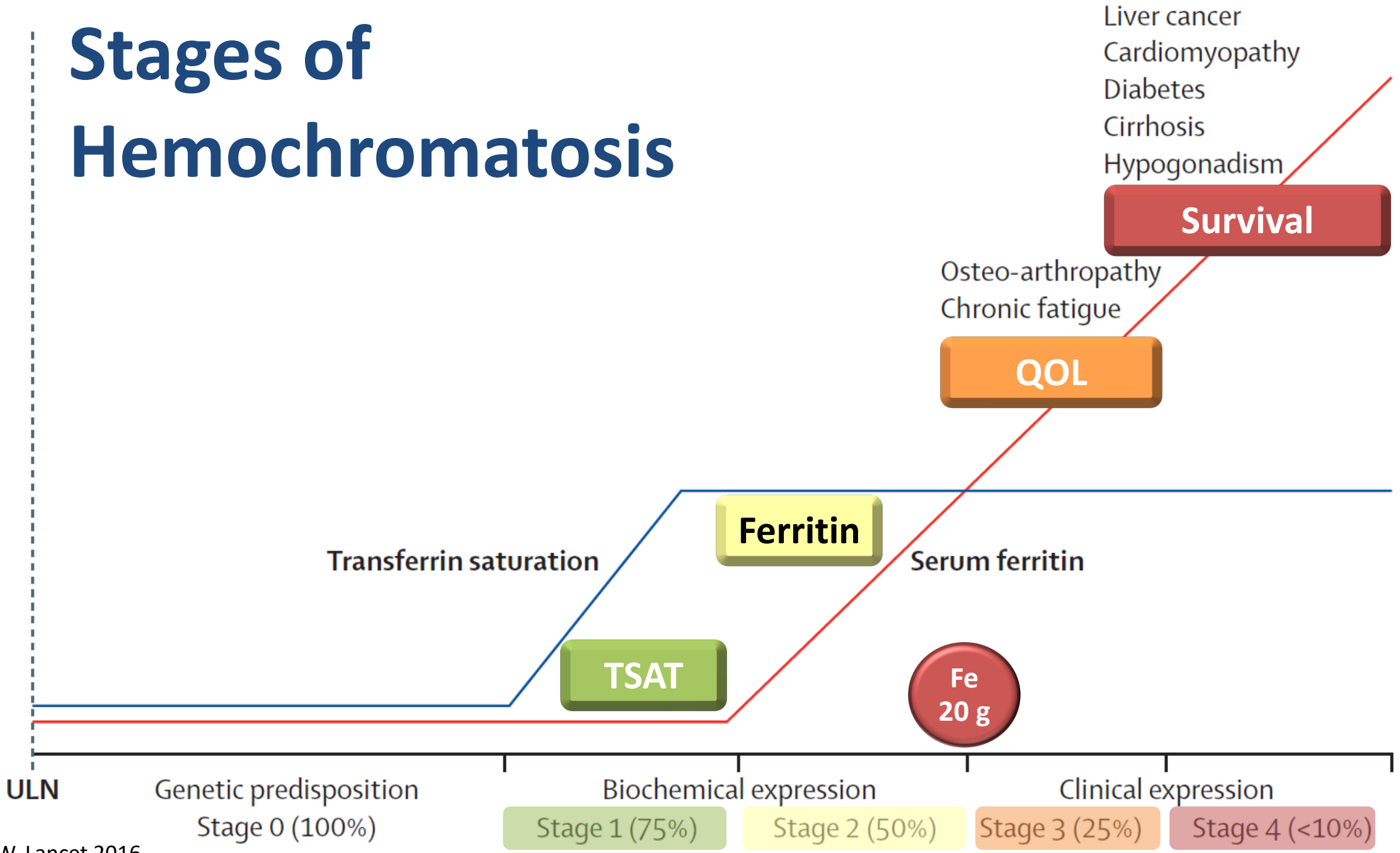


Brissot P. Nat Rev Dis Primers 2018.

Clinical features of various types of HH

Type	Gene	Protein	Inheritance	Clinical features
Type 1 HFE-related HH	HFE	HFE	AR	Classic HH
Type 2A Juvenile HH	HJV	Hemojuvelin	AR	Younger age More severe Cardiac complication Hypogonadism
Type 2B Juvenile HH	HAMP	Hepcidin	AR	
Type 3 TfR2-related HH	TfR2	Transferrin receptor2	AR	Similar to type 1 HH
Type 4 Ferroportin disease	SCL40A1	Ferroportin	AD	Less severe TSAT may be normal

Stages of Hemochromatosis



Powell LW. Lancet 2016.

Iron study

Transferrin saturation = Serum iron/ TIBC

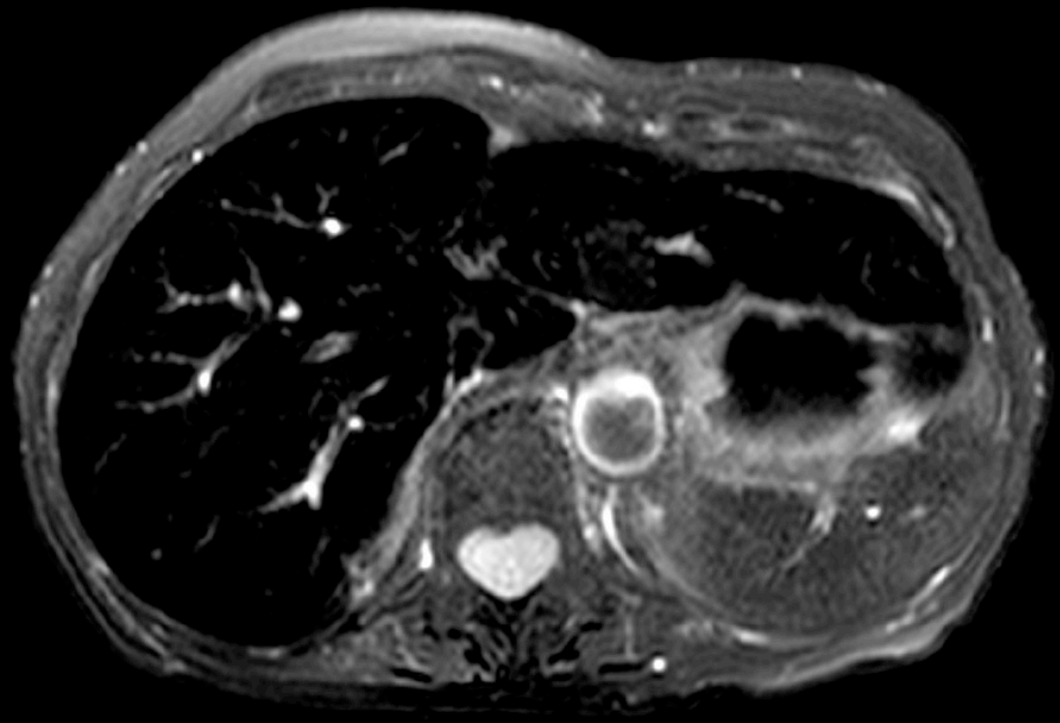
- Diagnosis: TS >45% (Sens 98%, NPV 93%)
- False positive
  - 22% of heterozygote
  - Secondary iron overload
- May be normal in Ferroportin disease type 4A (up to 75%)

Serum ferritin

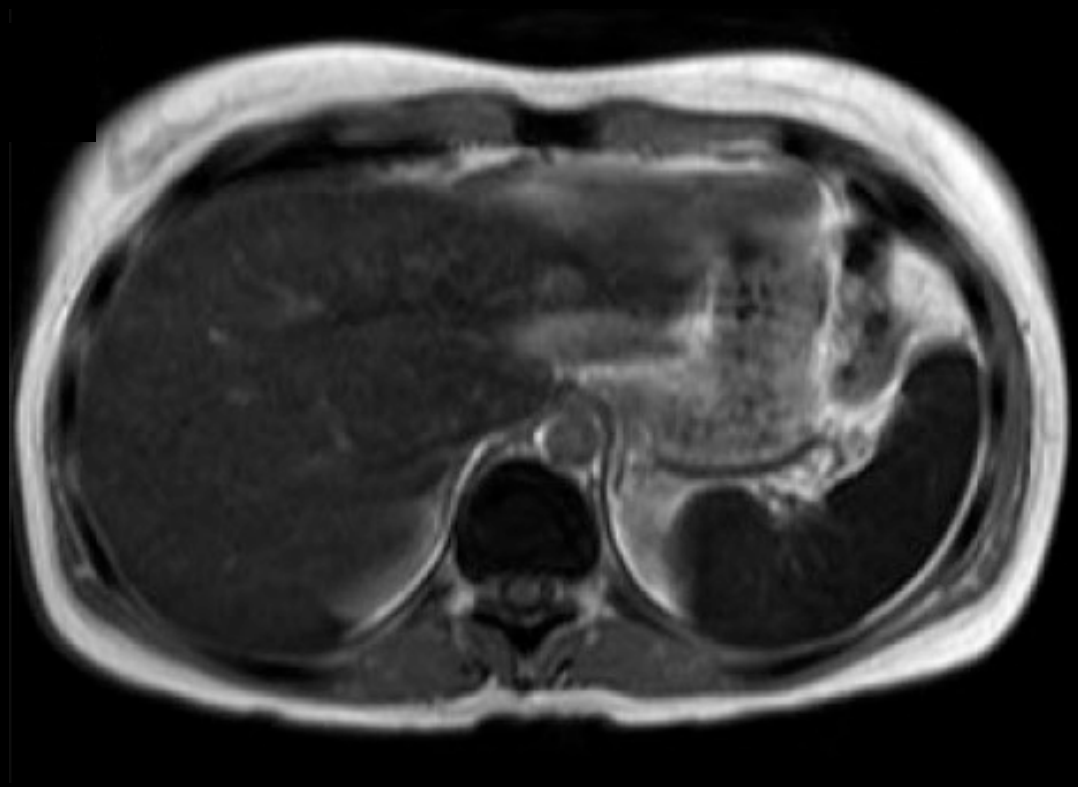
- Diagnosis: high Sens, low Spec
- Marker of fibrosis (>1000 mcg/L)
- Monitor treatment

Guyader D, et al. Gastroenterology 1998

MRI liver



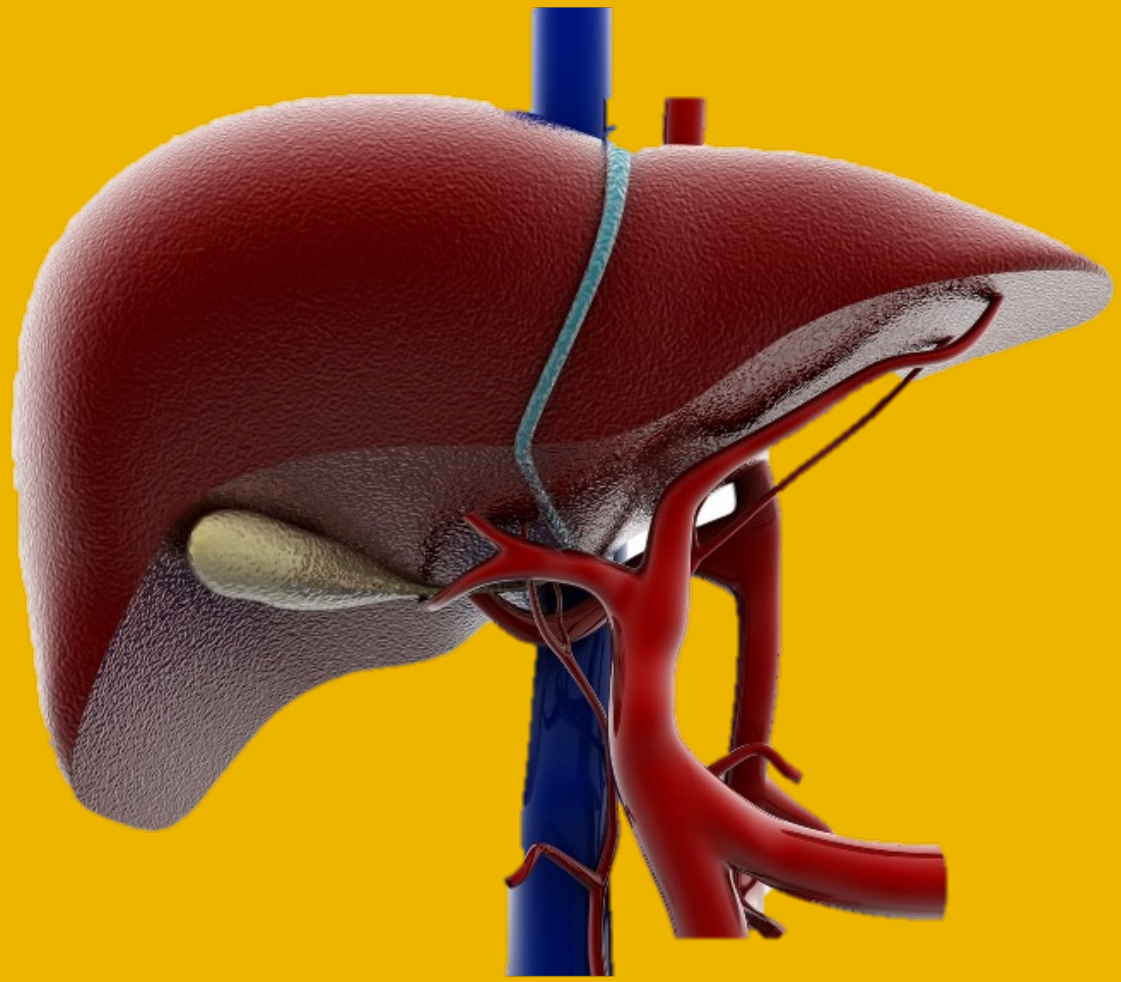
HH



Thalassemia or
Ferroportin disease type 4A

WD vs HH

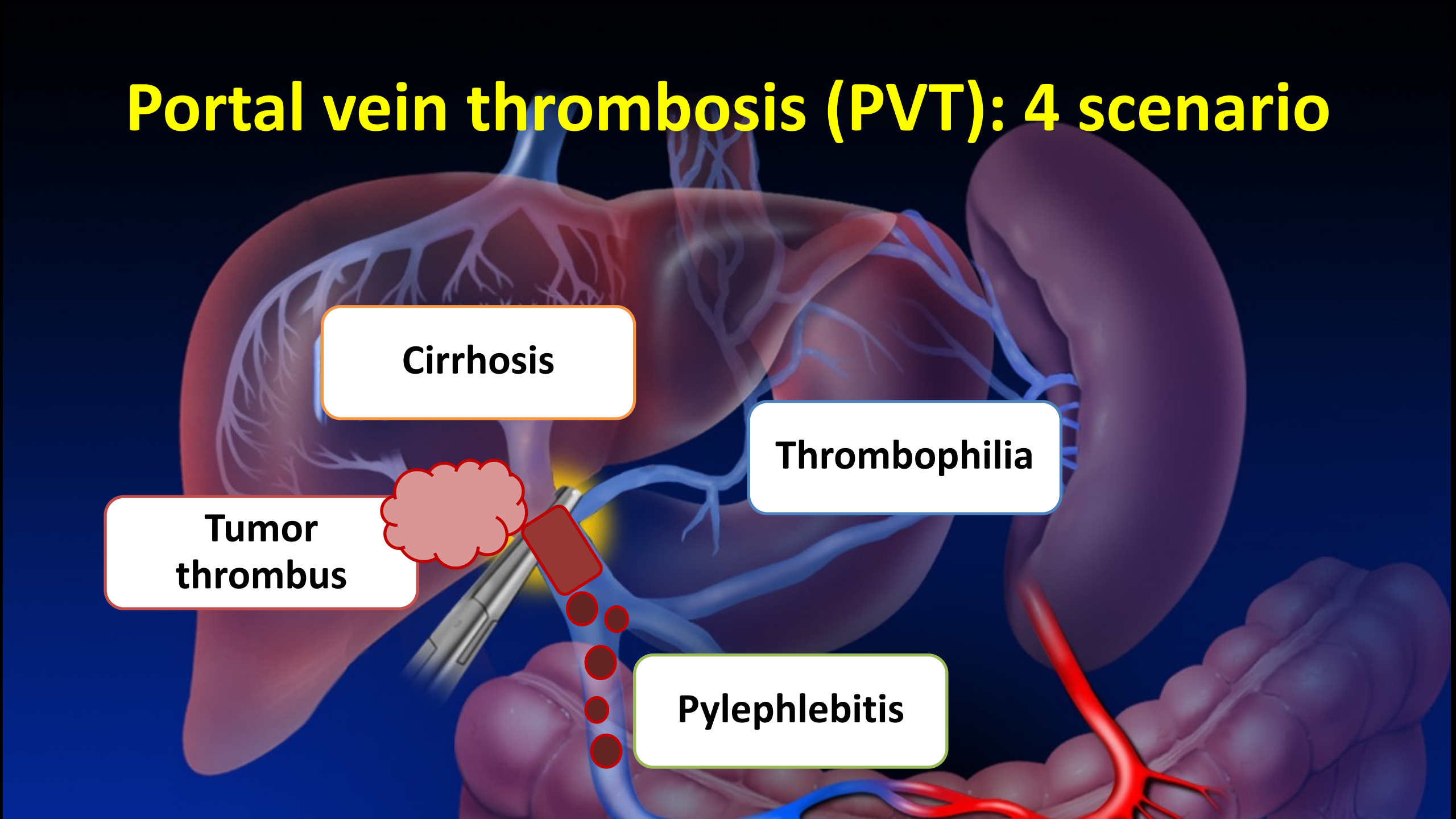
Features	WD	HH
Mutation	ATP7B	HFE & non-HFE
Inheritance	AR	AR, AD (type 4)
Penetrance	Complete	Incomplete
Onset	Before 35-40	M 30-40, F 40-50
Hepatic manifestations	Acute on chronic hepatitis Cirrhosis, ALF	Chronic hepatitis Cirrhosis, HCC
Other organs involvement	Brain, eye	Pancreas, heart, joints
Treatment	D-Penicillamine, Zinc	Phlebotomy
5-yr survival after OLT	Better (75%)	Poorer (34%)



5

Vascular liver diseases

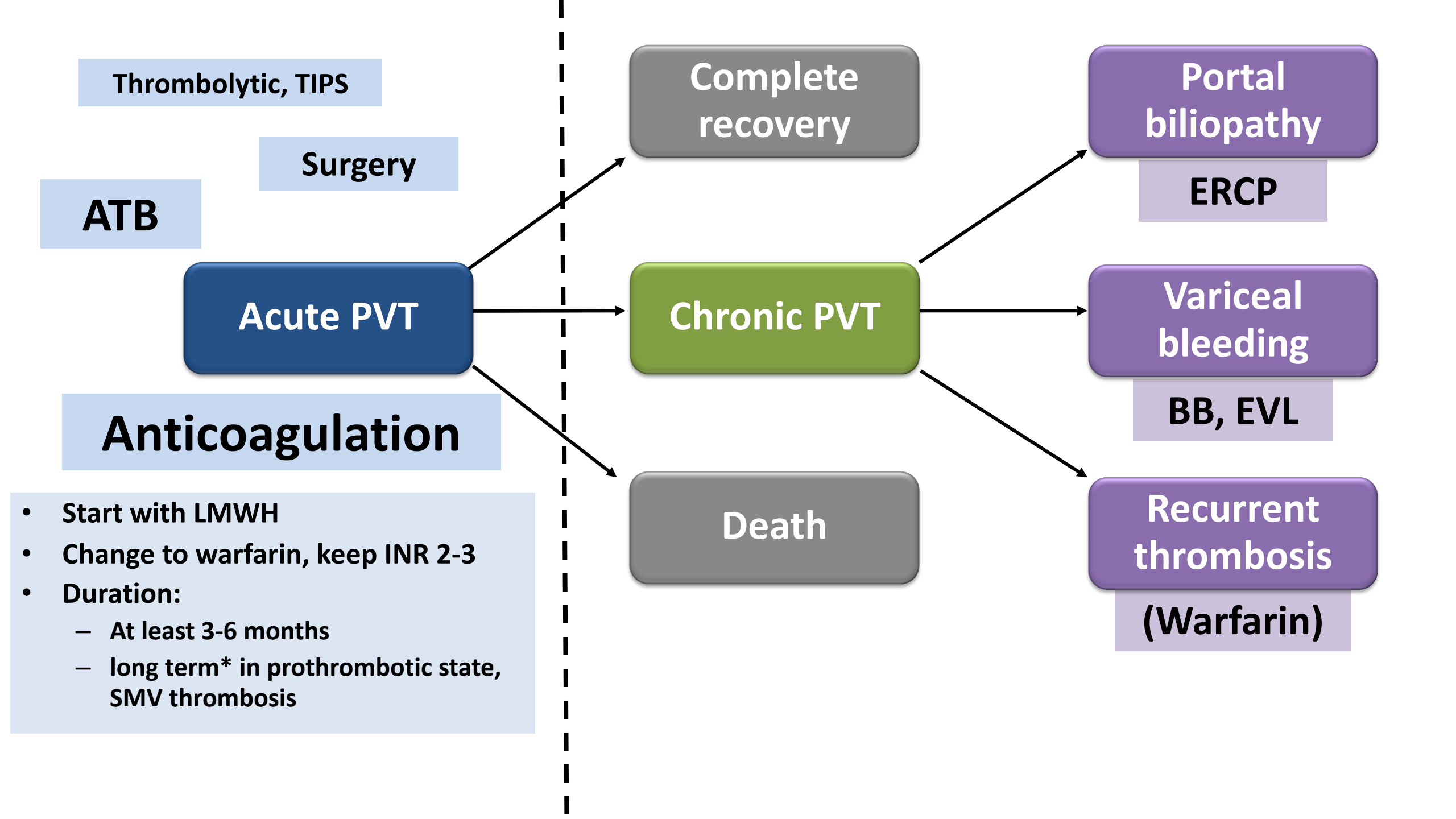
Portal vein thrombosis (PVT): 4 scenario



I. PVT due to thrombophilia

Prothrombotic states	Investigations
MPN	V617F JAK2 mutation (80% in PV, 50% in ET and PMF), BM biopsy (even normal CBC)
PNH	CD55- & CD59-deficient clone at flow cytometry
Behcet's disease	Conventional criteria
Antiphospholipid syndrome	Anticardiolipin Ab or LA or antiβ2 glycoprotein 1 Ab
Antithrombin deficiency	Antithrombin level
Protein C deficiency	Protein C level
Protein S deficiency	Protein S level

*Pills, pregnancy; co-factors


Thrombolytic, TIPS
Surgery
ATB
Acute PVT
Anticoagulation
Start with LMWH
Change to warfarin, keep INR 2-3
Duration:
At least 3-6 months
long term* in prothrombotic state, SMV thrombosis
Complete recovery
Chronic PVT
Death
Portal biliopathy
ERCP
Variceal bleeding
BB, EVL
Recurrent thrombosis
(Warfarin)

II. Cirrhosis with PVT

- Thrombocytopenia
- Platelets dysfunction
- ↓ coagulation factors
- Hyperfibrinolysis

- Stasis of blood flow
- ↓ natural anticoagulants
  - Protein C
  - Protein S
  - Antithrombin

Bleeding

Clot

Cirrhosis with PVT

- May be asymptomatic
- Spontaneous resolution 40%

Indication for anticoagulant

- Cirrhosis Child C, on waiting list for LT
- Symptomatic i.e. acute decompensation, worsening PHT
- Progression of thrombus
- Risk for intestinal ischemia

Drugs ???

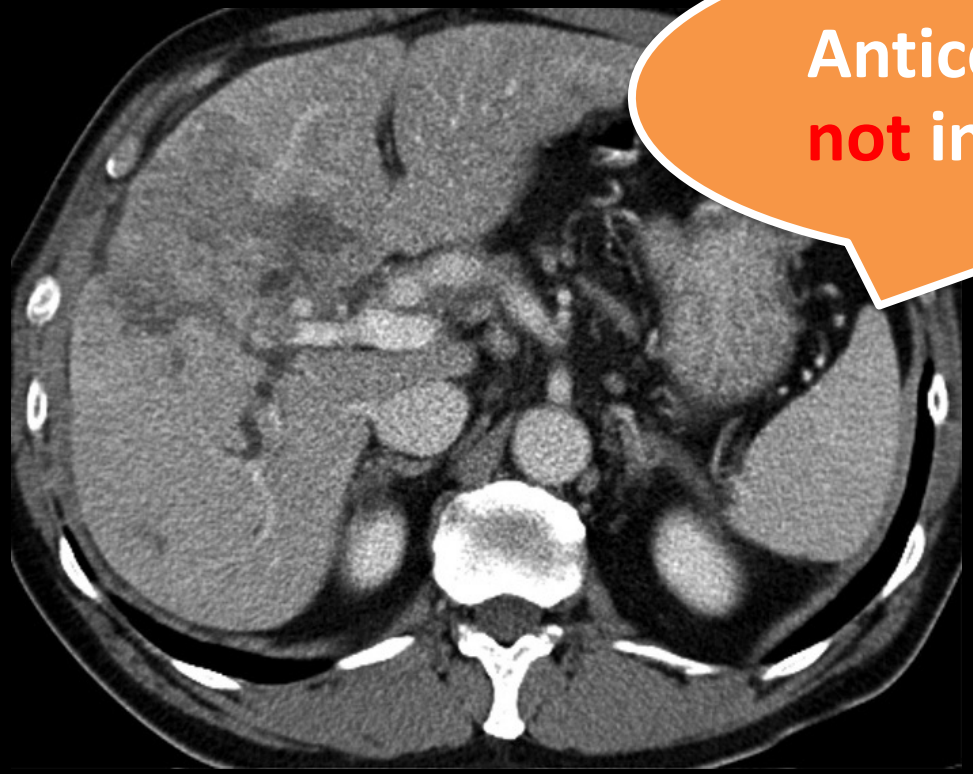
- Warfarin, heparin, LMWH
- Low dose rivaroxaban

Duration ???

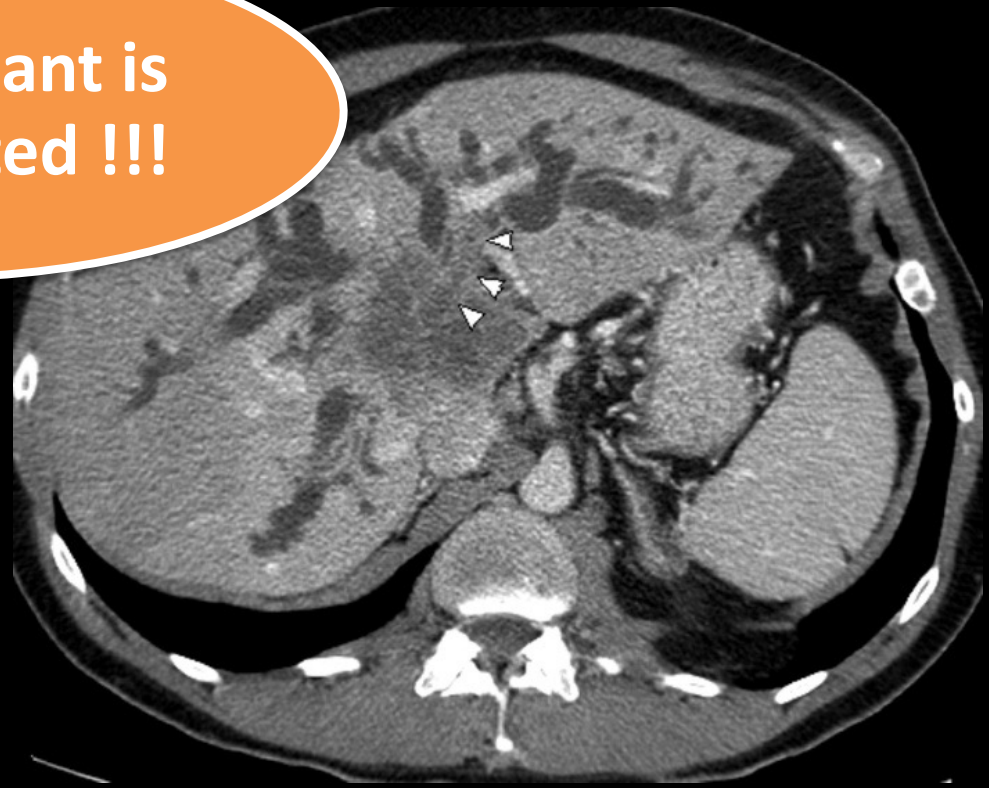
- At least 6 months *or*
- Long term use in patients on waiting list for LT, hypercoagulable state

Intagliata NM, et al. Gastroenterology 2019

III. Malignant PVT



Anticoagulant is **not** indicated !!!



HCC

Cholangiocarcinoma

IV. Pylephlebitis

Septic thrombophlebitis

Common causes

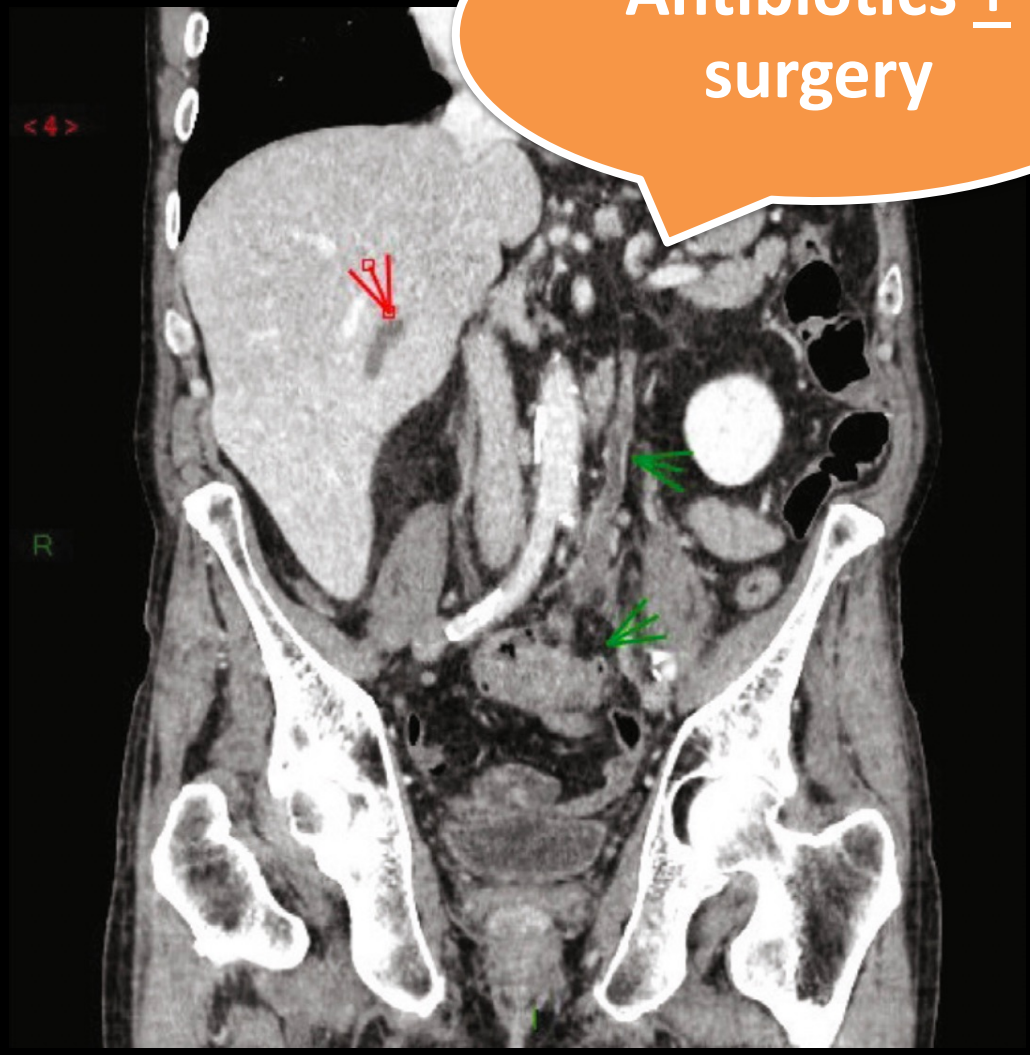
- **Diverticulitis**
- **Appendicitis**

Common pathogen

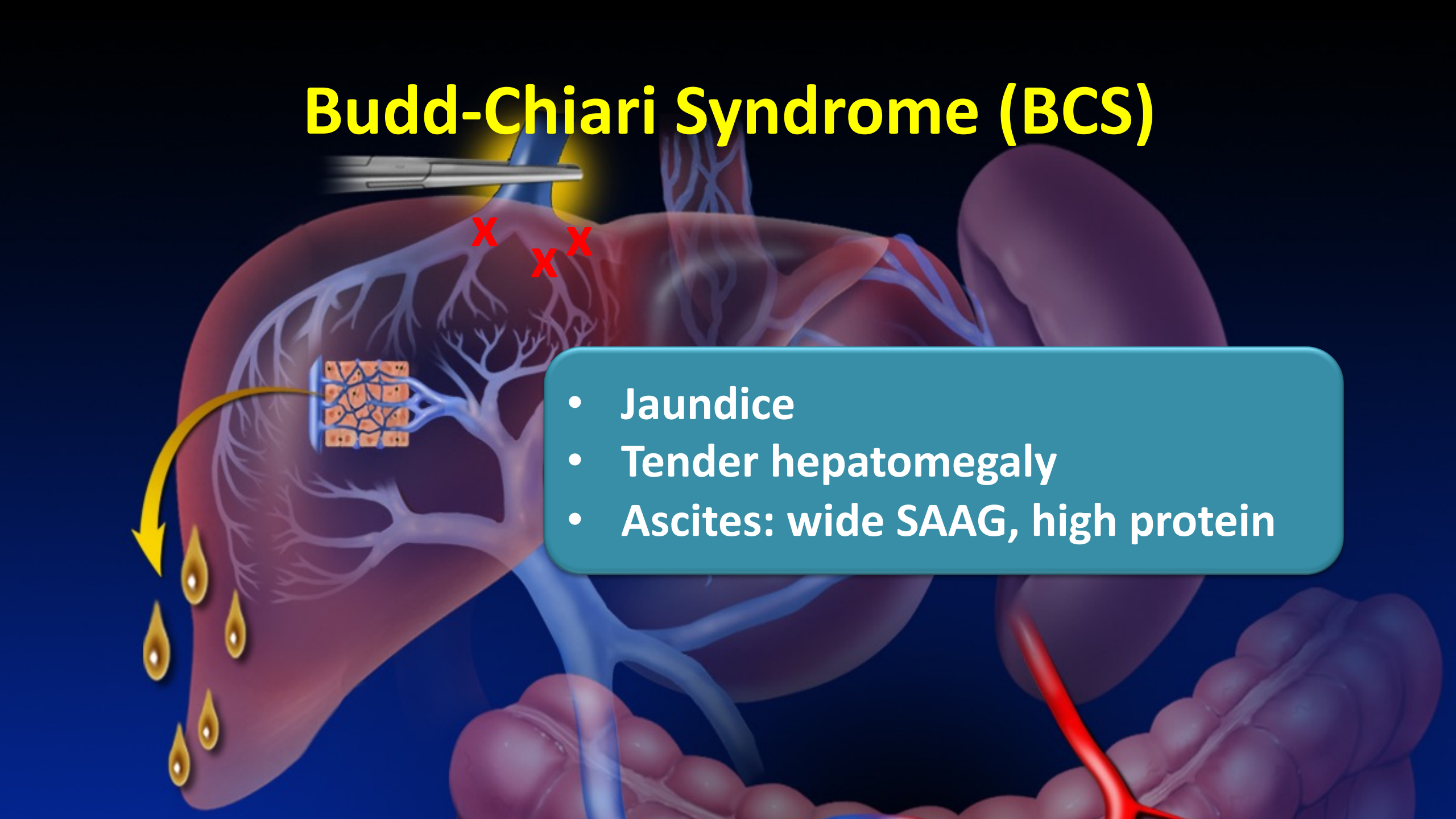
- ***Bacteroides fragilis***

Symptoms

- **Fever**
- **Abdominal pain**

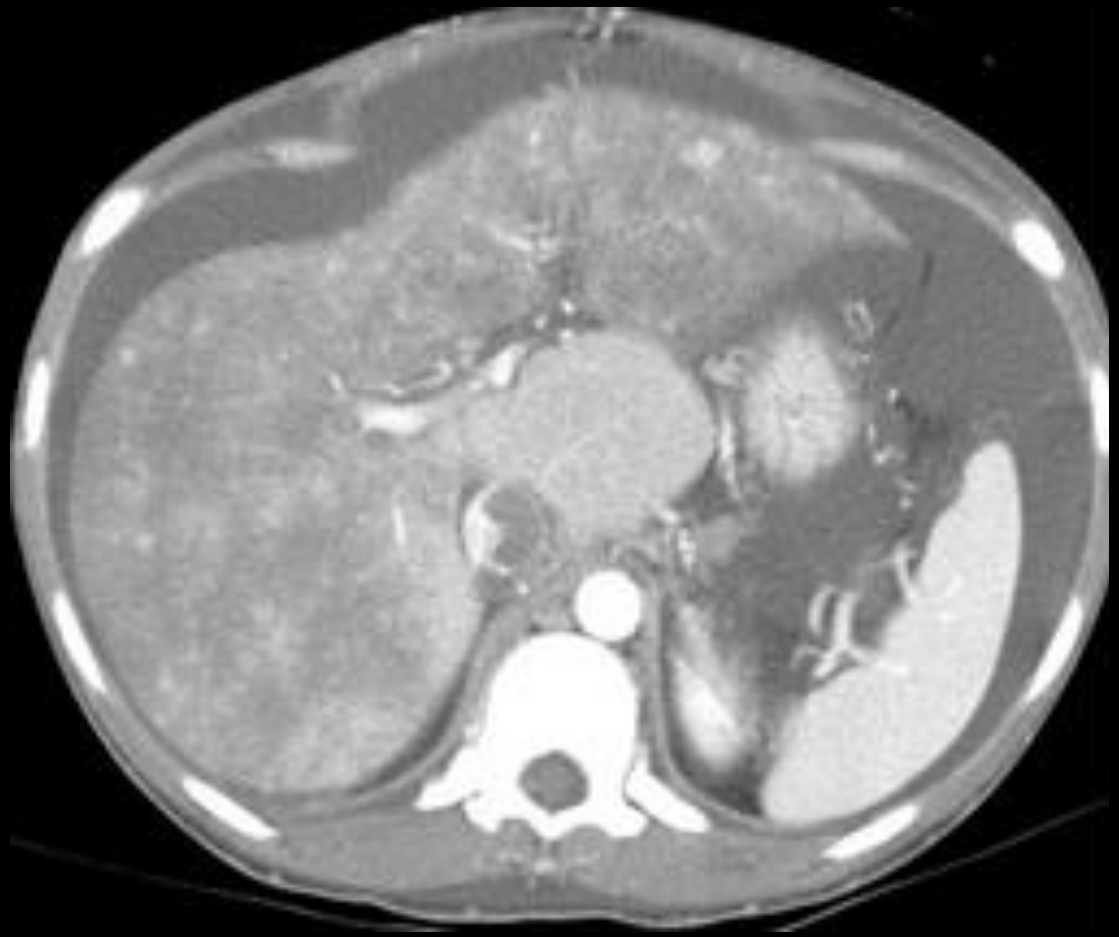


Budd-Chiari Syndrome (BCS)



- Jaundice
- Tender hepatomegaly
- Ascites: wide SAAG, high protein

CT scan



Heterogeneous enhancement***

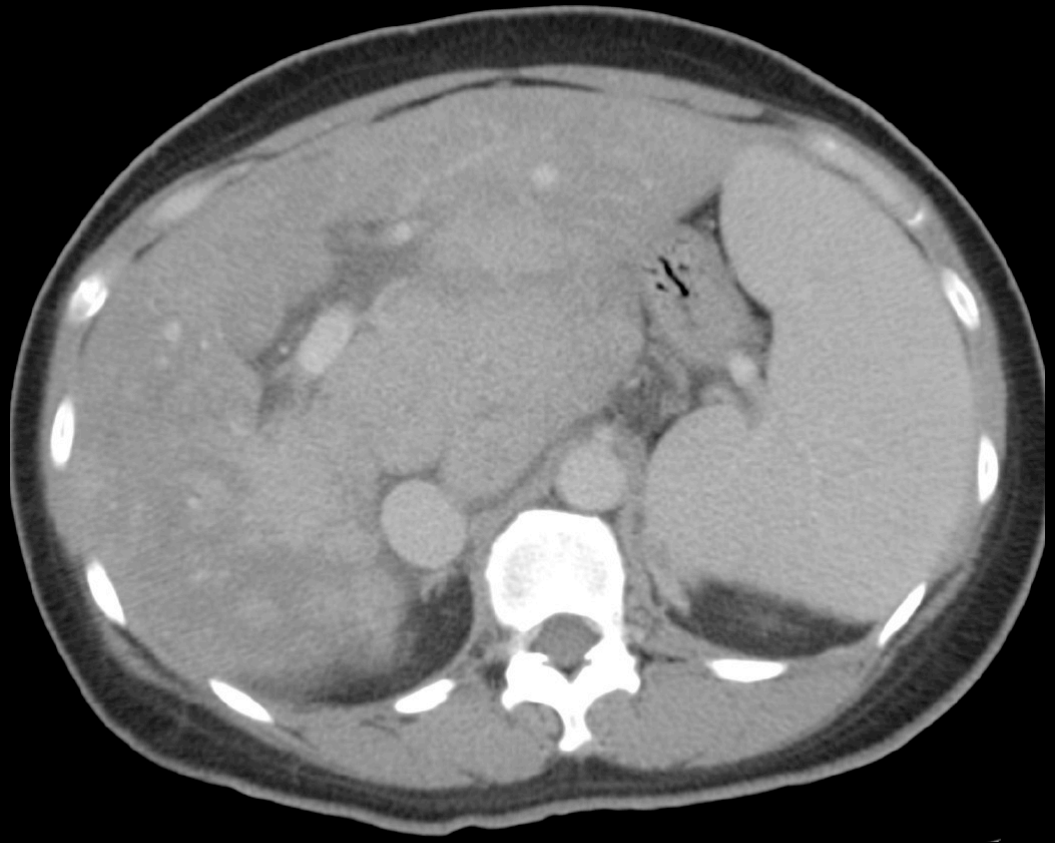
Caudate lobe hypertrophy

Thrombus in IVC

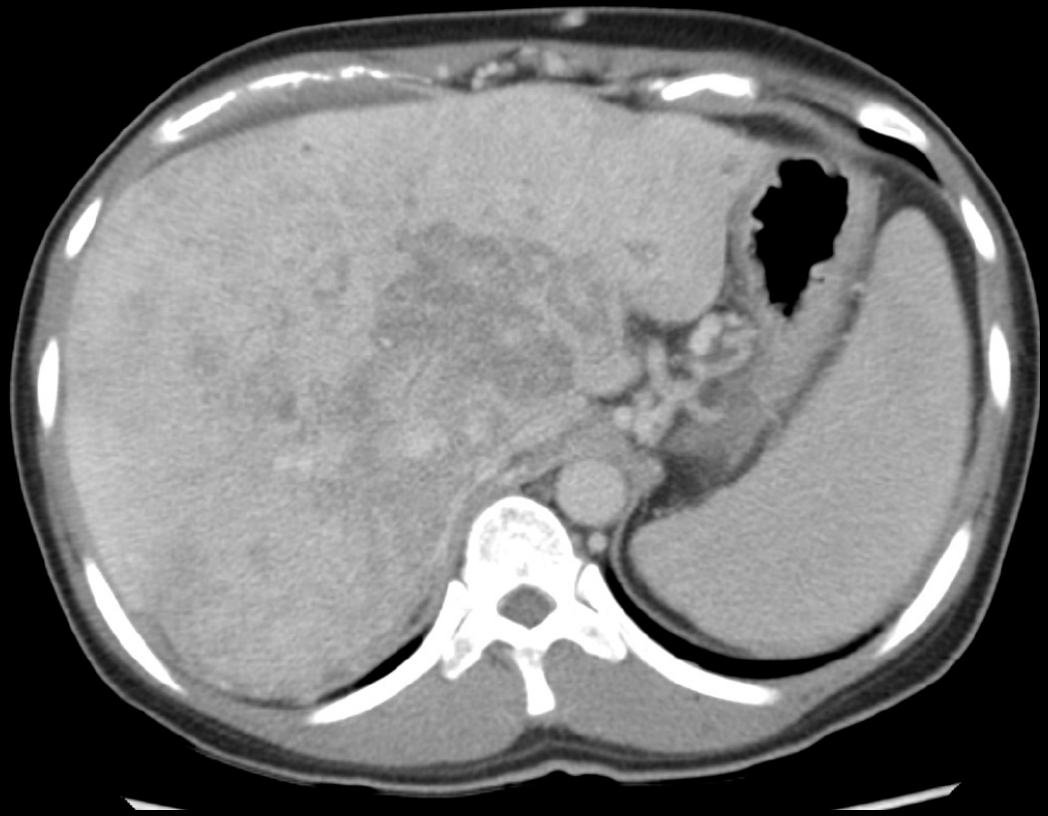
Splenomegaly

Ascites

Flip flop phenomenon



Early central enhancement



Delayed peripheral enhancement

Causes of BCS

Rare

Local factors

IVC web

Malignancies

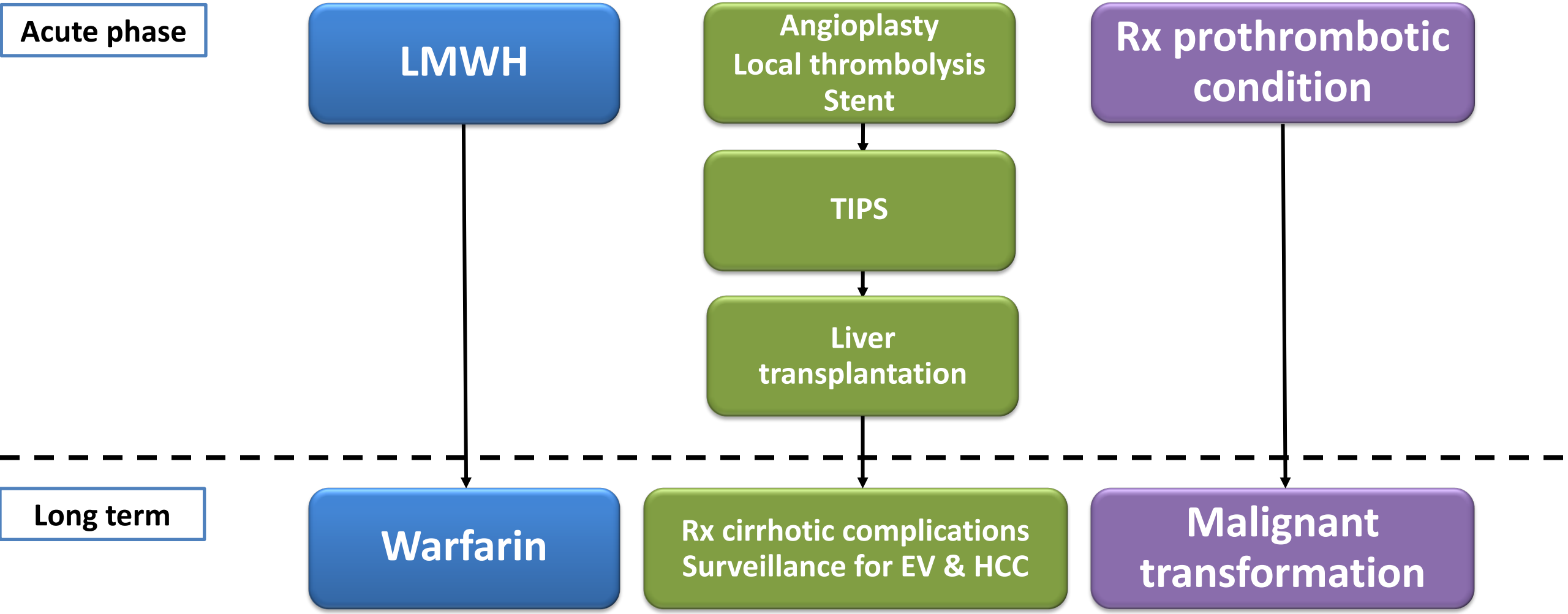
- HCC
- RCC
- Adrenal carcinoma

Common

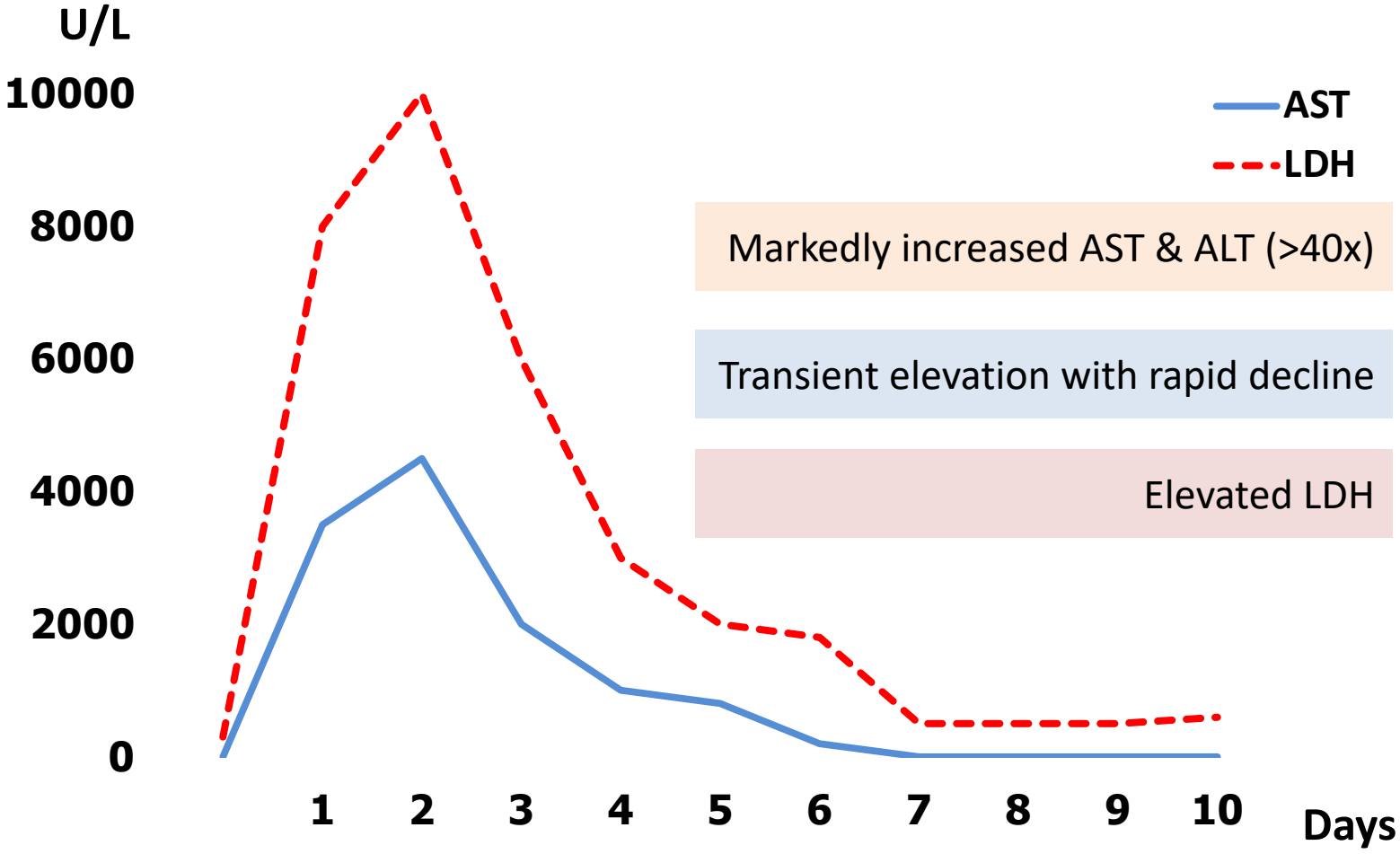
Prothrombotic disorders	%
Myeloproliferative diseases	40-50
Antiphospholipid syndrome	4-25
PNH	0-4
Behcet's disease	0-33
Factor V Leiden mutation	6-32
Factor II mutation	5-7
Protein C deficiency	10-30
Protein S deficiency	7-20
Anti-thrombin III deficiency	0-23
Plasminogen deficiency	0-4
Pregnancy	6-12
Oral contraceptive use	6-60
Hyperhomocysteinemia	37
TT677 MTHFR genotype	12-22

DeLeve LD, et al. Hepatology 2009

Treatment of BCS



Ischemic hepatitis

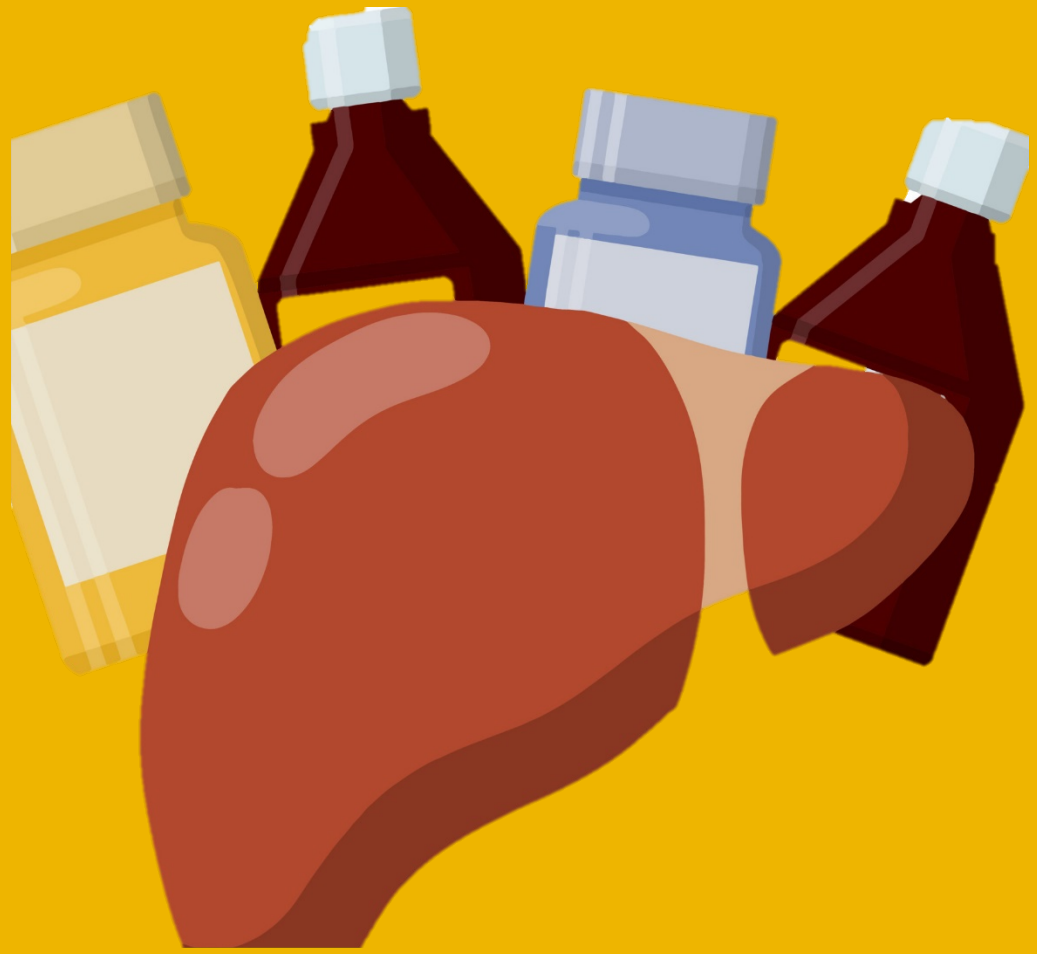


Predisposing factors

Acute cardiac event 80%

Hypotension 50%

Tapper EB, et al. Am J Med 2015



6

Drug induced liver injury

Drug-induced liver injury (DILI)

Diagnosis

1. Temporal relationship
2. Biochemical injury pattern
   - Signature drug
   - Prior reports / cases
3. De-challenge
4. Re-challenge
5. Exclude other causes

Management

1. Severity assessment
2. Stop culprit drug
3. Specific antidote:
   - Acetaminophen: NAC
   - Amanitin: silymarin
   - ICIs: prednisolone

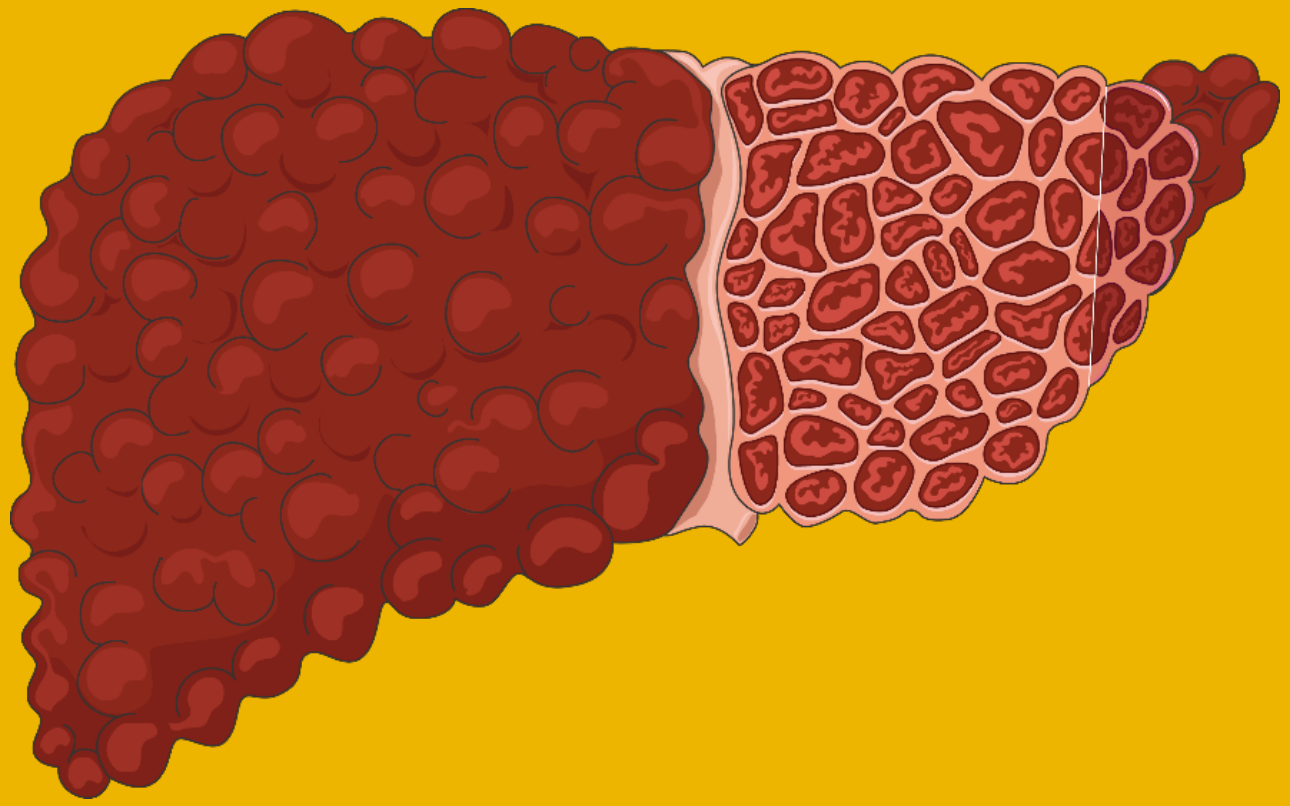
Toxic mushroom in Thailand

Amanita virosa

Amanita verna

Amanita exitialis

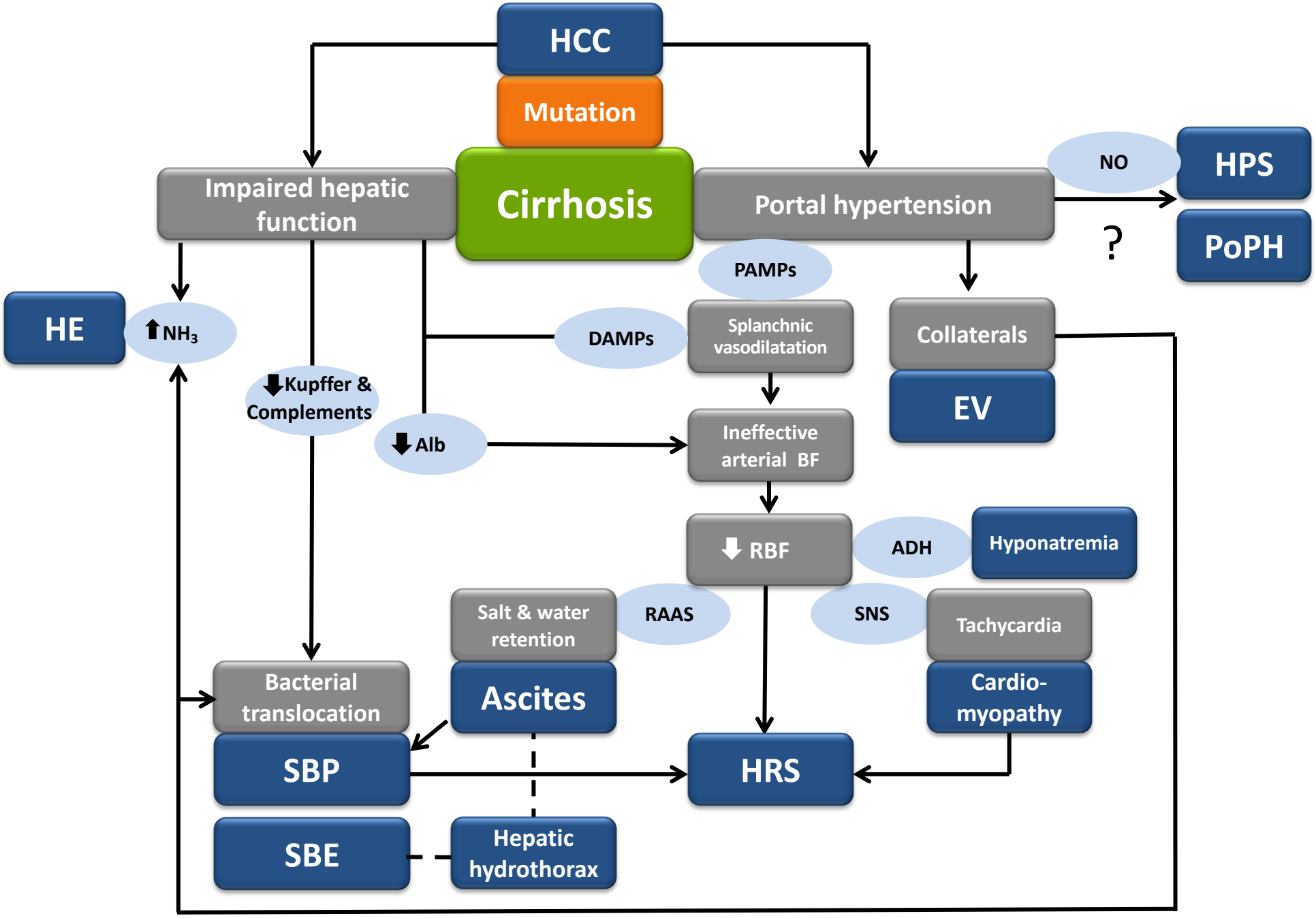
“เห็ดไข่ตายซาก หรือ เห็ดระโงกหิน”



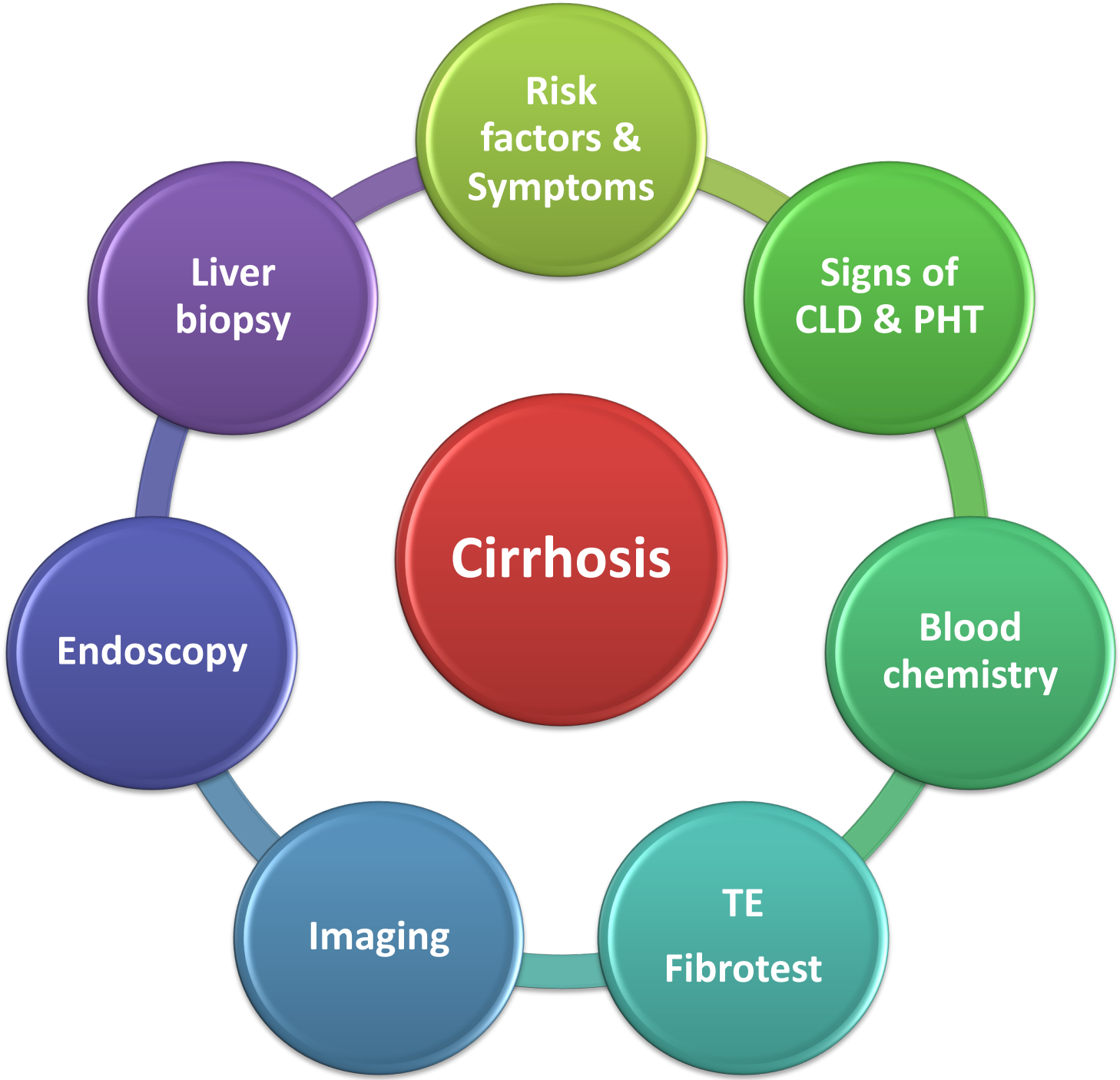
7

Cirrhosis

Pathophysiology of cirrhosis



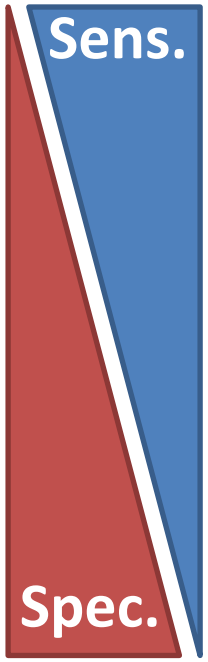
Diagnosis of cirrhosis



Signs of chronic liver disease

Signs	Mechanism	Frequent association
Spider nevi	Estrogen excess	Alcohol
Palmar erythema	Estrogen excess	
Digital clubbing	Pulmonary shunt	HPS, cystic fibrosis
Dupuytren's contracture	Thickened palmar fascia	Alcohol
Gynaecomastia	Estrogen excess	Alcohol, spironolactone
Testicular atrophy	Estrogen excess	Alcohol, hemochromatosis

Ultrasonographic findings of cirrhosis

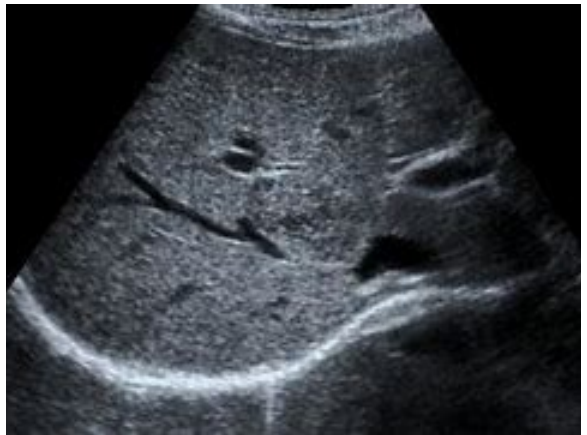


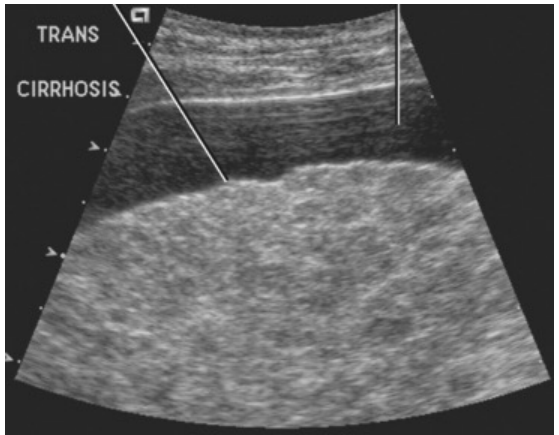
Liver architecture

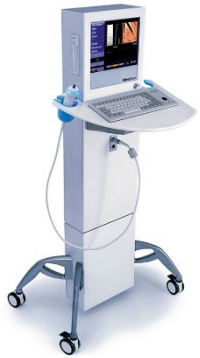
- Heterogenous echogenicity
- Left lobe & caudate lobe hypertrophy
- Regenerative nodules
- Nodular surface

Portal hypertension

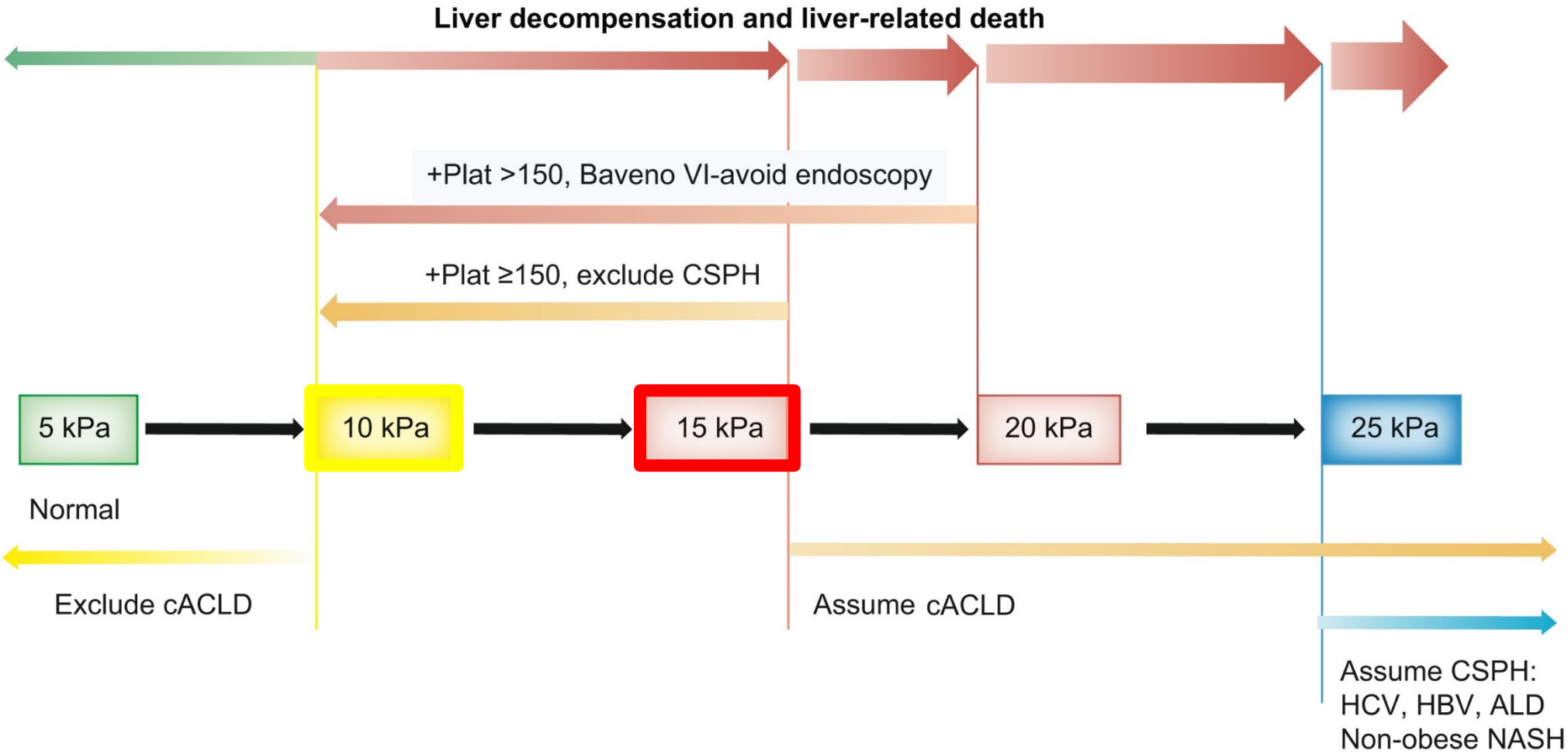
- Enlarged portal vein (>13 mm)
- Splenomegaly
- Ascites
- Portosystemic collaterals







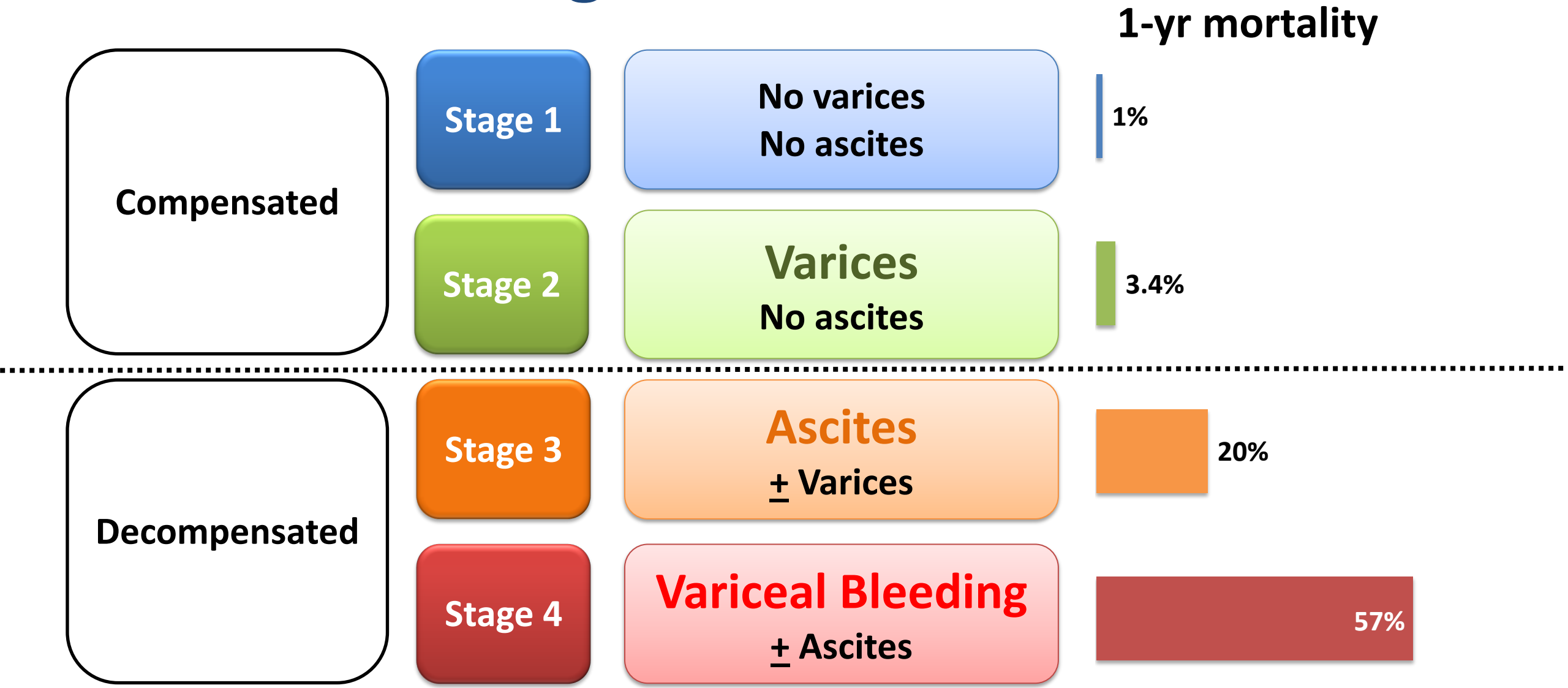
TE plus platelets: the rule of five



cACLD; compensated advanced chronic liver disease
CSPH; clinical significant portal hypertension

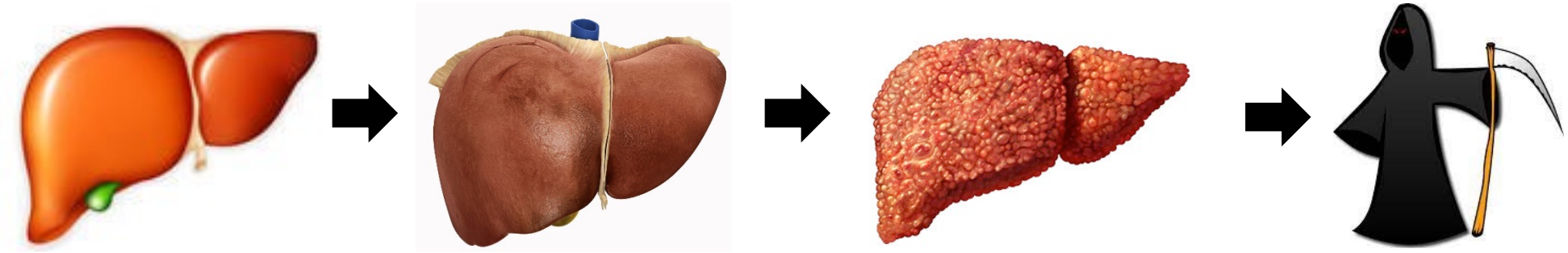
BAVENO VII

Stage of cirrhosis



D' Amico G, J Hepatol 2006

Management of cirrhosis



Compensated cirrhosis → Compensated cirrhosis with CSPH → Decompensated cirrhosis → Death

Specific treatment →

General care →

Complications

- Prevent first decompensation
- Treat complications

Specific treatment of cirrhosis

Etiologies	Specific treatment
HBV	NUCs: **TAF, TDF, ETV**
HCV	DAAs: **SOF/VEL/RBV**
Alcohol	Alcohol abstinence
MAFLD	Weight reduction
AIH	Immunosuppressive agents
PBC	UDCA
PSC	Dilation of dominant stricture
Wilson disease	D-penicillamine, Zn
Hemochromatosis	Iron chelation
Chronic BCS	Anticoagulant

General management of cirrhosis

- **Diet;** adequate calories, high protein, low salt*, avoid raw food
- **Avoid** hepatotoxic drugs, alcohol and obesity
- **Vaccination;** HAV, HBV, influenza, pneumococcal
- **Exercise;** regular and appropriate

Nutritional interventions for cirrhotic patients

Nutritional interventions	Level of recommendations
Daily **energy**: 35-40 Kcal/kg ideal BW	IA
Daily **protein** intake: 1.2-1.5 g/kg	IA
Small meals throughout the day & **late-night snack** of complex carbohydrate	IA
Oral BCAA in patients who are intolerant of dietary protein	IIB

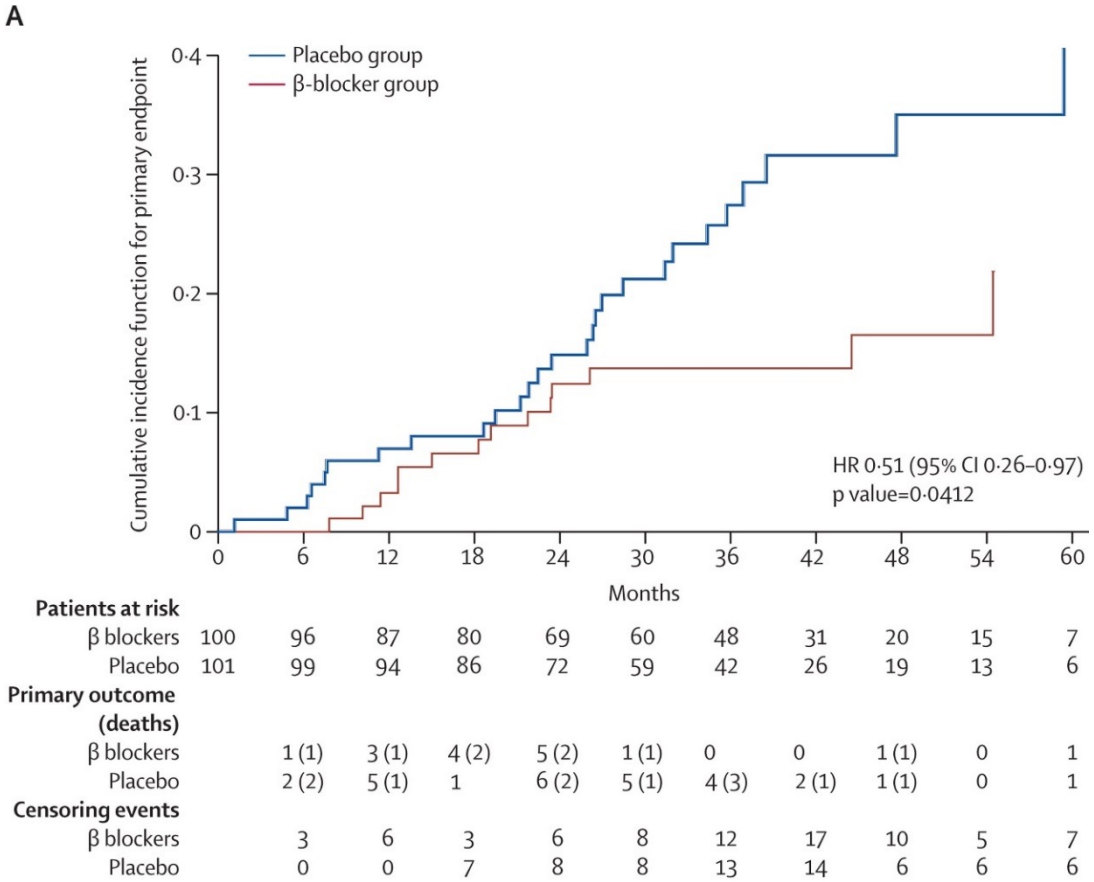
ISHEN Practice Guidelines. Hepatology 2013

PREDESCI: non-selective beta blocker to prevent decompensation of cirrhosis in patients with CSPH

- RCT, N=201
- Compensated cirrhosis with CSPH with no/small EV
- NSBB =100 (propranolol 67, carvedilol 33) vs Placebo =101

Primary endpoint: **incidence of decompensation** (ascites, bleeding, or overt HE) or death

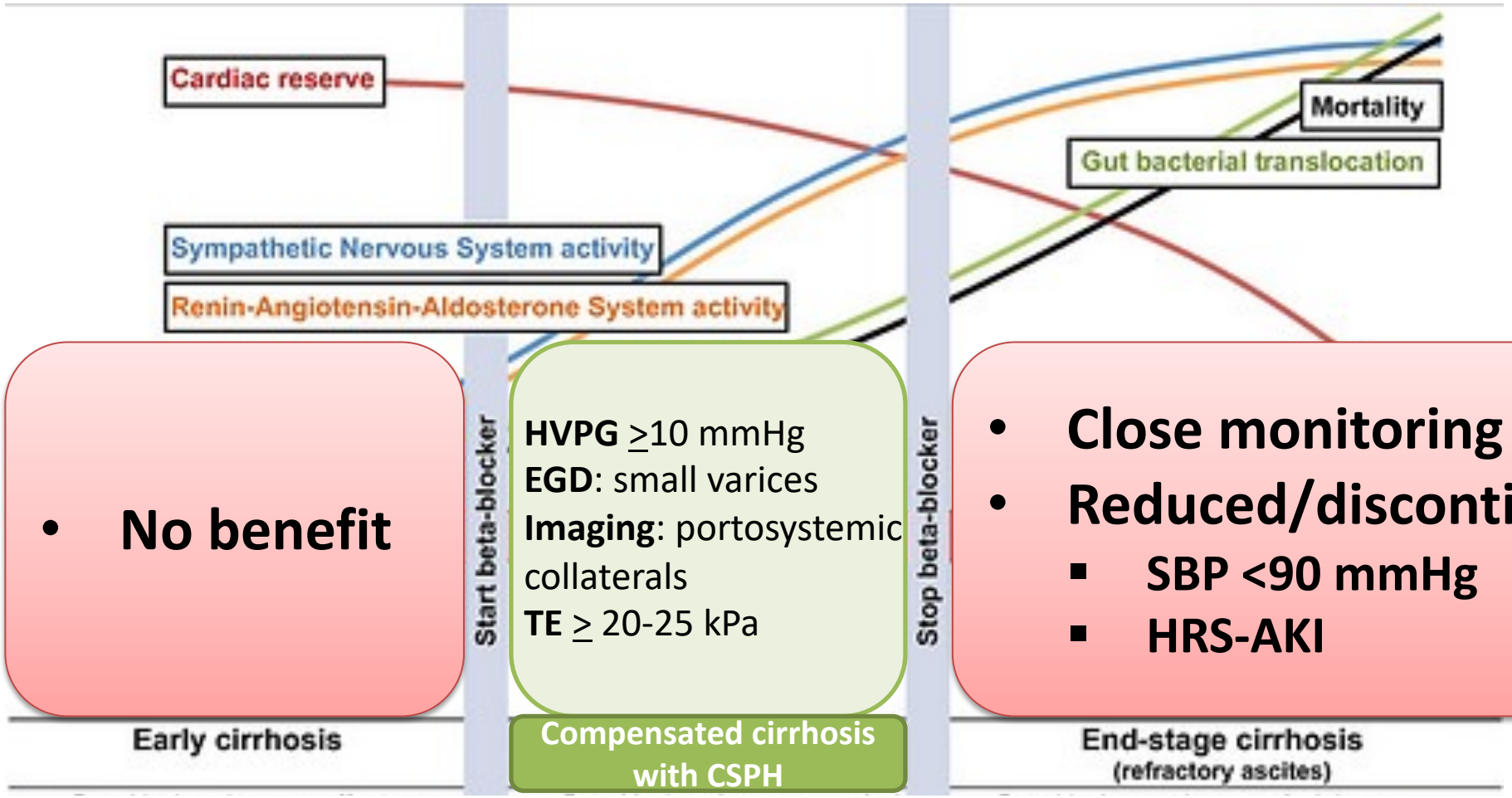
- 16% of BB vs 27% of placebo group (HR 0·51, 95% CI 0·26–0·97, p=0·041)
- The difference was due to a reduced incidence of ascites (HR 0·42, 95% CI 0·19–0·92, p=0·03)
- Adverse events was similar in both groups



Patients at risk											
β blockers	100	96	87	80	69	60	48	31	20	15	7
Placebo	101	99	94	86	72	59	42	26	19	13	6
Primary outcome (deaths)											
β blockers		1 (1)	3 (1)	4 (2)	5 (2)	1 (1)	0	0	1 (1)	0	1
Placebo		2 (2)	5 (1)	1	6 (2)	5 (1)	4 (3)	2 (1)	1 (1)	0	1
Censoring events											
β blockers		3	6	3	6	8	12	17	10	5	7
Placebo		0	0	7	8	8	13	14	6	6	6

Villanueva. Lancet 2019

When to start NSBB ?



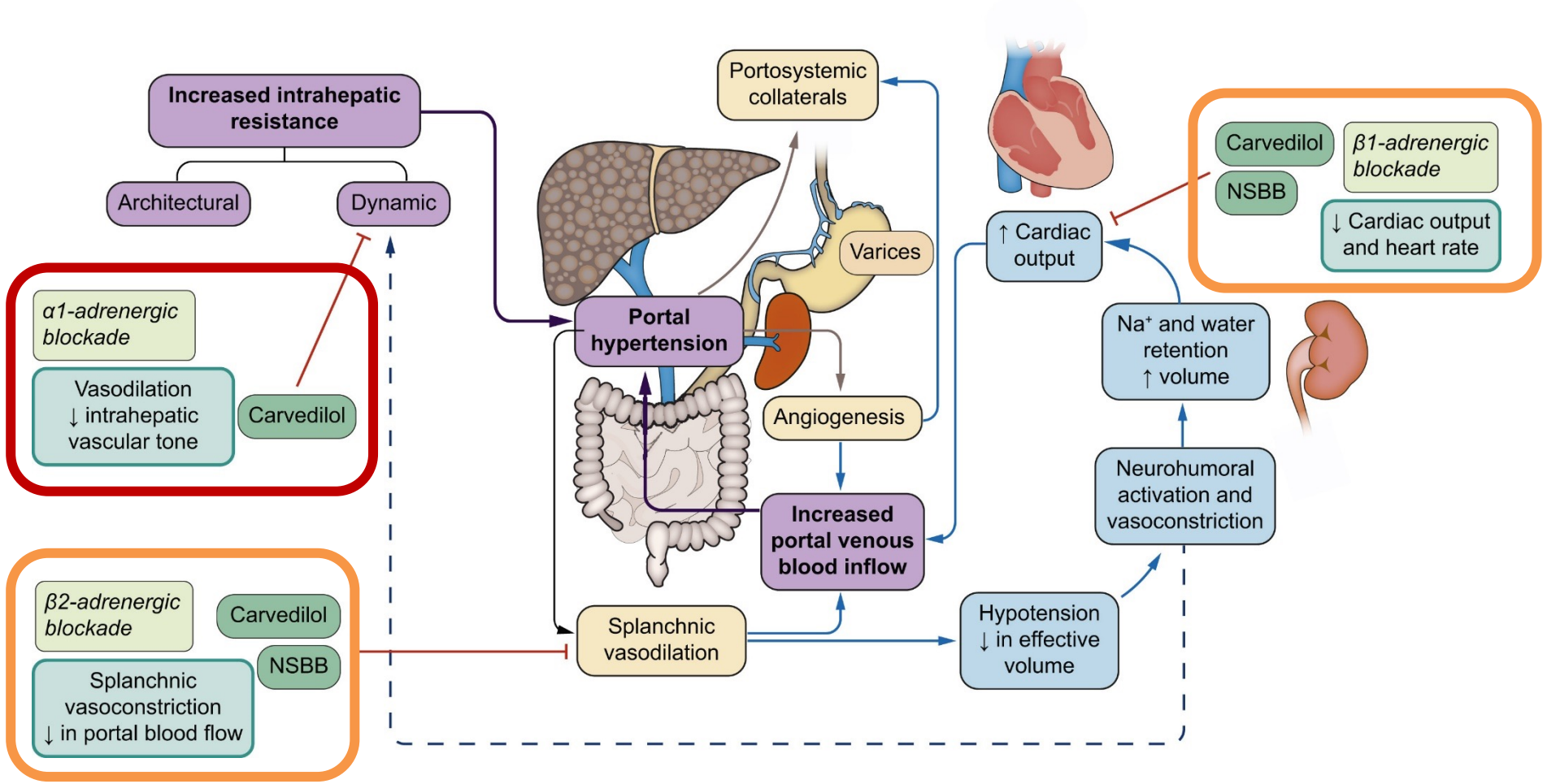
- **No benefit**

HVPG ≥10 mmHg
EGD: small varices
Imaging: portosystemic collaterals
TE ≥ 20-25 kPa

- **Close monitoring**
- **Reduced/discontinued if**
  - **SBP <90 mmHg**
  - **HRS-AKI**

Baveno VII

Action of NSBB in CSPH



Portal pressure = Resistance x Blood flow

Rodrigues, JHEP Report 2020

Management of variceal bleeding

Pre-endoscopy

- Vasoactive agents
- Restrictive fluid Rx
- Ceftriaxone 1 g iv

Endoscopy (within 12 hr)

Post-endoscopy

- Vasoactive agents (2-3 d)
- Blood transfusion (Hb 7-8 g/dl)
- Norfloxacin (until 7 d)
- Assessment of ACLF
- 2^{o} prophylaxis
  - EVL + NSBB
  - TIPS

Franchis. J Hepatol 2022

Fluid therapy

Restrictive fluid therapy

Goal

- Restore & maintain hemodynamic stability
- Target Hb 7-8 g/dl*

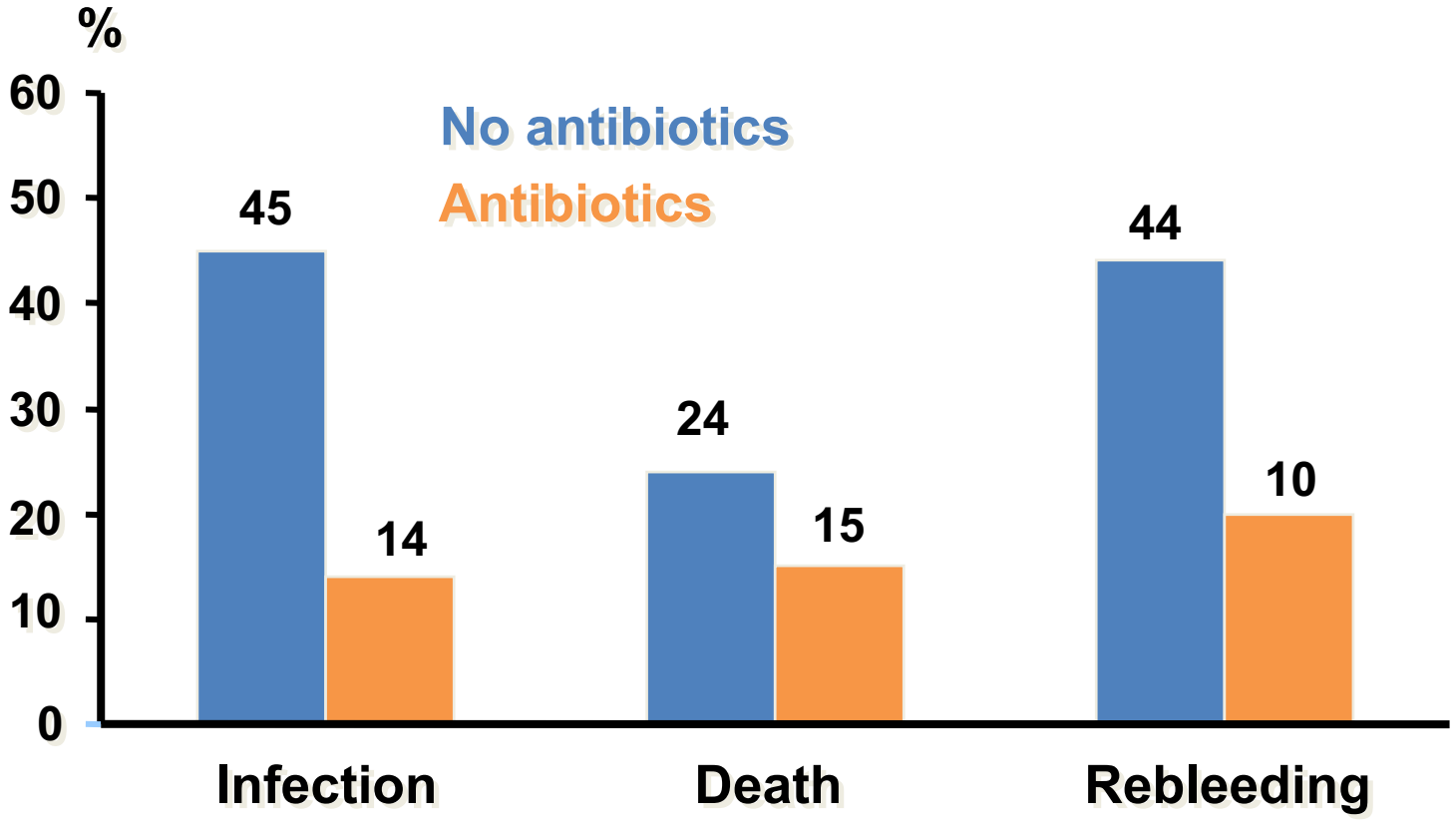
*individualized to cardiovascular disorders, age, hemodynamic status and ongoing bleeding

Franchis. J Hepatol 2022

Vasoactive drugs

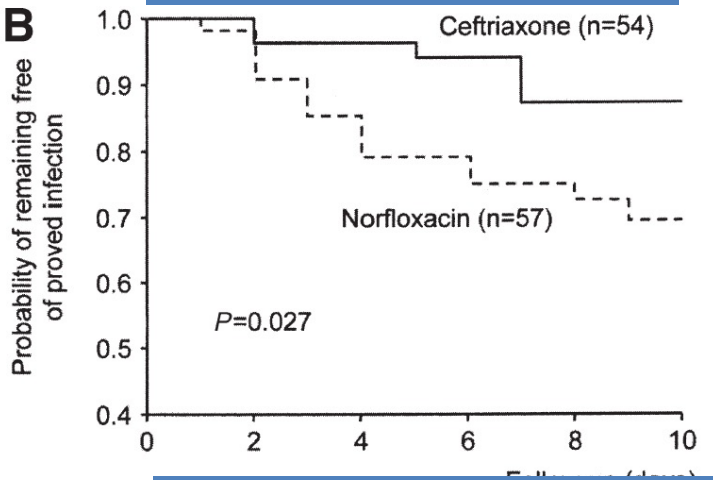
	Somatostatin	Octreotide	Terlipressin
Dose	250 µg iv bolus then 250 µg/hr	50 µg iv bolus then 50 µg/hr	0.5-2 mg iv q 4 hr
Half life	1-3 min	1.7-1.9 hr	6 hr
Tachyphylaxis	+	+	-
Side effects	rare	rare	Caution in CAD, PVD

Prophylactic antibiotics

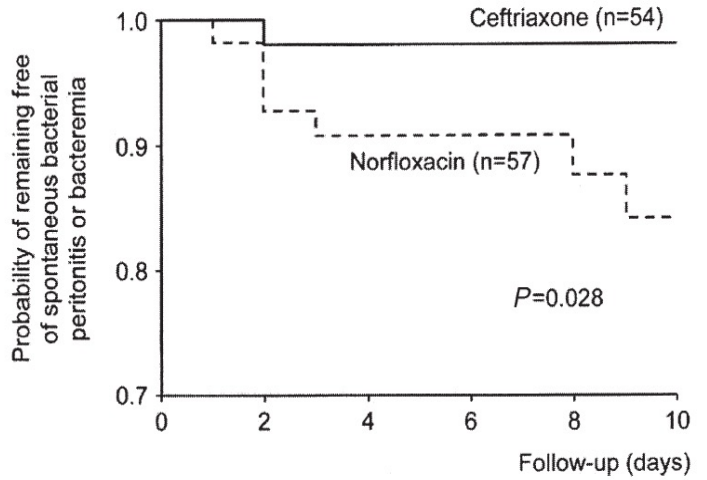


Ceftriaxone 1 g IV OD

Infection



SBP or bacteremia



Fernandez J. Gastroenetrology 2006

Rebalanced homeostasis in cirrhosis

- Thrombocytopenia
- Platelets dysfunction
- ⬇ coagulation factors
- Hyperfibrinolysis

- Stasis of blood flow
- ⬇ natural anticoagulants
  - Protein C
  - Protein S
  - Antithrombin

Bleeding **Clot**

BAVENO VII recommendation

PT, aPTT	• Not reflect the hemostatic status
FFP	• Not recommended • May lead to volume overload & worsening PHT
Platelets Fibrinogen level	• Should be considered on a case-by-case basis
Recombinant factor VIIa Tranexamic acid	• Not recommended

Franchis. J Hepatol 2022

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Endoscopy (within 12 hr)

Post-endoscopy

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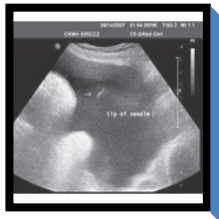
- Blood transfusion (Hb 7-8 g/dl)
- Norfloxacin (until 7 d)
- Assessment of ACLF
- 2^{o} prophylaxis
  - EVL + NSBB
  - TIPS

Franchis. J Hepatol 2022

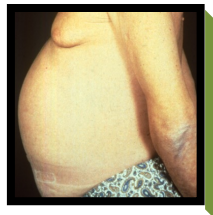
Treatment of ascites



Mild

- No treatment

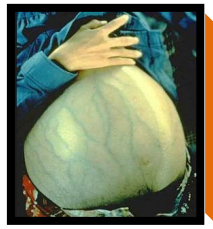
+



Moderate

- Salt restriction
- Spironolactone ± furosemide

+



Severe

- Large volume paracentesis (LVP)
- Albumin 8 g/L of released ascites

+

Refractory

- TIPS, liver transplantation

Treatment of SBP

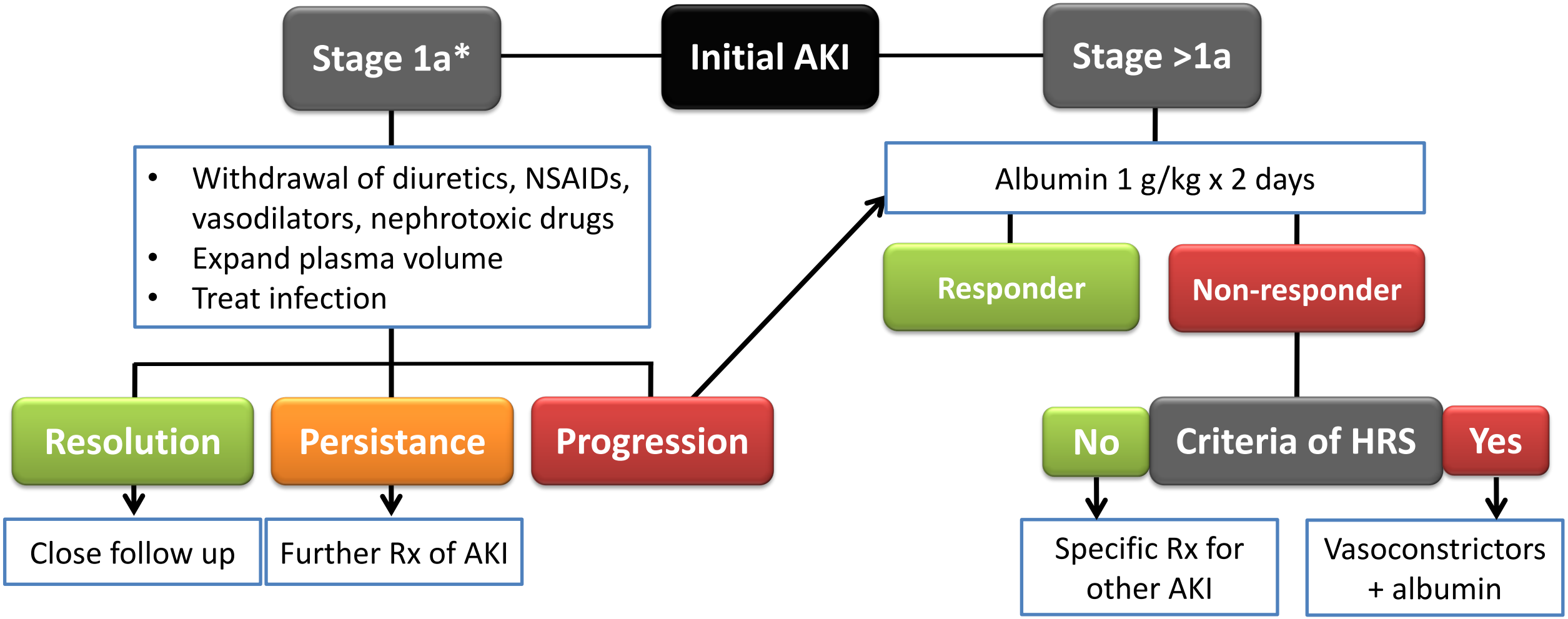
Antibiotics

- Cefotaxime 1-2 g iv q 6 hr x 5-10 days
- Amoxicillin/clavulanic acid, ciprofloxacin
- Ofloxacin 400 mg twice daily x 8 days in uncomplicated SBP (no GI bleeding/ shock/ HE/ renal failure)
- Aminoglycosides should not be used

Albumin

- 1.5 g/kg within 6 hr and 1 g/kg on day 3
- Decrease type I HRS (30%->10%)
- Decrease mortality rate (29%->10%)
- Indicated in patients
  - Cr >1 mg/dL
  - BUN >30 mg/dL
  - TB >4 mg/dL

Management of AKI in cirrhotic patients



*Increased sCr ≥0.3mg/dl or 1.5-2X from baseline with sCr <1.5 mg/dl

Wong F. J Hepatol 2016

New diagnostic criteria of HRS-AKI

(ICA-ADQI 2024)

- Cirrhosis with ascites
- Increase in serum creatinine ≥0.3 mg/dl (26.5 μmol/L) within 48 hours or ≥50% from baseline value known or presumed to have occurred within the prior 7 days and/or urinary output ≤0.5 ml/kg for ≥6 hours
- Absence of improvement in serum creatinine and/or urine output within 24 hours following adequate volume resuscitation (when clinically indicated)
- Absence of strong evidence for an alternative explanation as the primary cause of AKI

Presence of underlying kidney disease does not exclude a diagnosis of superimposed HRS-AKI and HRS-AKI may coexist with other causes of AKI. Examples of alternative causes of AKI include septic shock requiring vasopressors, drug-induced AKI, obstruction, or acute glomerular injury. Patients who meet HRS criteria are considered to have HRS-AKI, HRS-AKD or HRS-CKD based on timing and duration of kidney dysfunction. ADQI, Acute Disease Quality Initiative; AKD, acute kidney disease; AKI, acute kidney injury; CKD, chronic kidney disease; HRS, hepatorenal syndrome; ICA, International Club of Ascites.

Nadim. J Hepatol 2024

Vasoconstrictors in HRS-AKI

Criteria for discontinuation
• SCr within 0.3 mg/dl of baseline
• No improvement in SCr after 48-72 h with maximal tolerated doses
• Serious adverse reaction
• Initiation of RRT
• Liver transplantation
• Total duration of 14 days
Dose titration
• Terlipressin dose should be increased by at least 2 mg/day every 24 h for those on continuous infusion up to a maximum of 12 mg/day and increased from 1 to 2 mg every 6 h for i.v. bolus, if SCr has not improved by 25%.
• Norepinephrine dose is increased every 4 h in steps of 0.5 mg/h, up to the maximum dose of 3 mg/h if no increase in MAP >10 mmHg or UO 50 ml/h x 4 h
• Daily 20-25% albumin (20-40 g/day) is recommended, however, amount and dose should be adjusted daily based on patients' volume status. Albumin should be withheld if evidence of fluid overload and/or pulmonary oedema

All vasoconstrictors are given in combination with albumin.

ICU, intensive care unit; MAP, mean arterial pressure; RRT, renal replacement therapy; SCr, serum creatinine; UO, urine output.

*Continuous infusion of terlipressin may be associated with a lower incidence of side effects compared to i.v. bolus, most likely due to lower cumulative daily dose.[178].

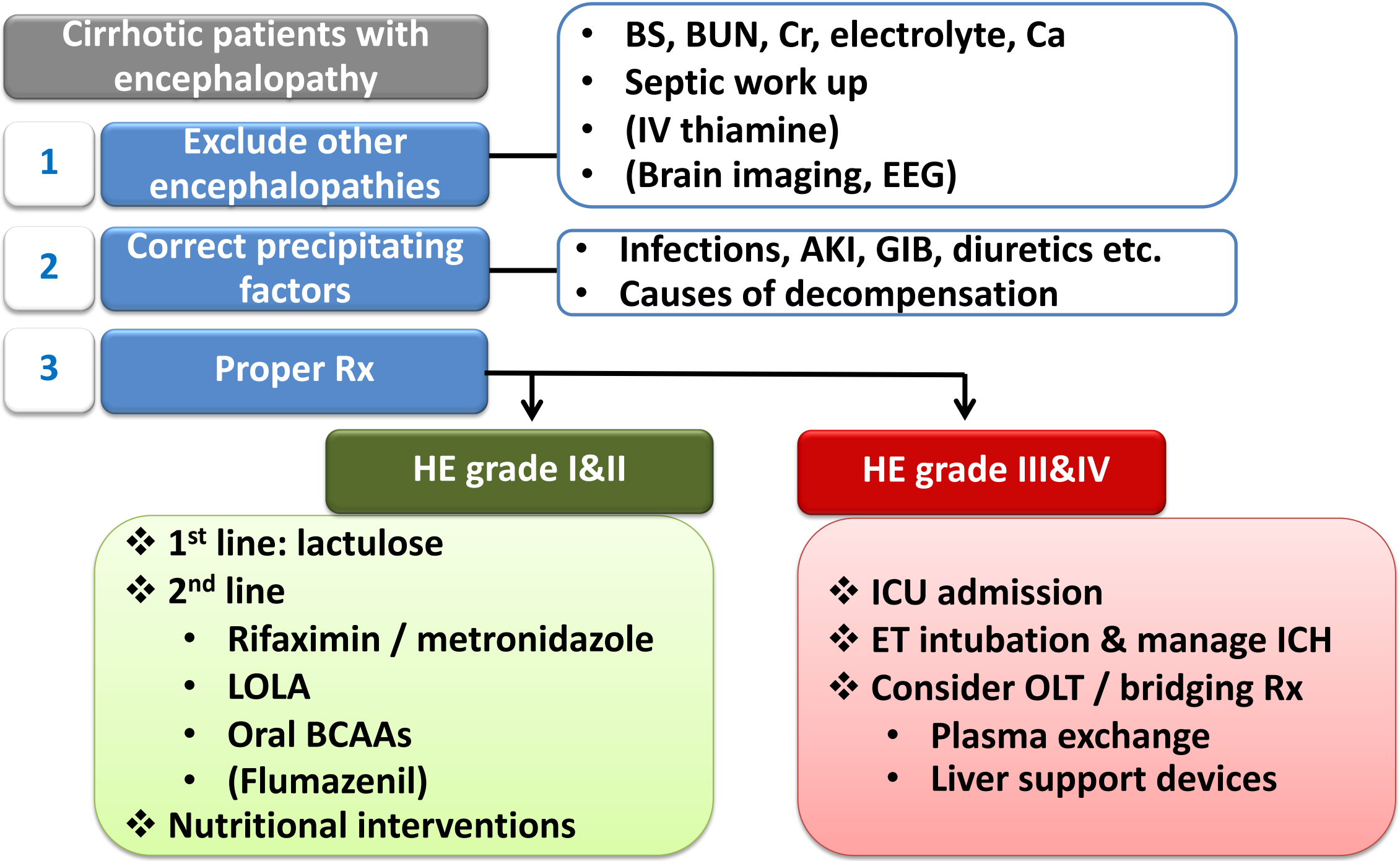
**1 vial = 0.85 mg terlipressin (North American FDA label) = 1 mg terlipressin acetate.

Nadim. J Hepatol 2024

Albumin for cirrhotic patients

1. Prevention of PCD	
• Large volume paracentesis	• 6-8 g/L of released ascites
2. HRS	
• Prevention: High risk SBP*	• 1.5 g/kg in D1, 1 g/kg in D3
• Diagnosis	• 1 g/kg in D1-(2)
• Treatment	• 1 g/kg in D1, then 40 g/d
3. Decompensated cirrhosis	
• Improved survival	• 20-40 g weekly?

*Cr >1mg/dl, BUN >30 mg/dl, TB >4mg/dl


Cirrhotic patients with encephalopathy
1
Exclude other encephalopathies
• BS, BUN, Cr, electrolyte, Ca
• Septic work up
• (IV thiamine)
• (Brain imaging, EEG)
2
Correct precipitating factors
• Infections, AKI, GIB, diuretics etc.
• Causes of decompensation
3
Proper Rx
HE grade I&II
❖ 1st line: lactulose
❖ 2nd line
• Rifaximin / metronidazole
• LOLA
• Oral BCAAs
• (Flumazenil)
❖ Nutritional interventions
HE grade III&IV
❖ ICU admission
❖ ET intubation & manage ICH
❖ Consider OLT / bridging Rx
• Plasma exchange
• Liver support devices

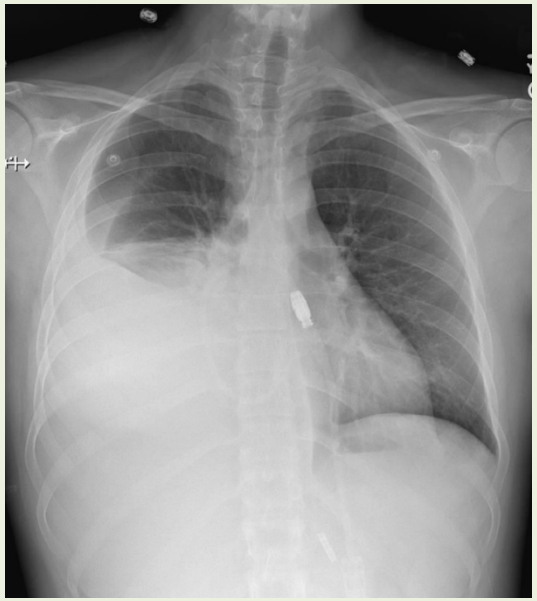
Hepatic hydrothorax

Diagnosis

- Right 73%, left 17%, bilateral 10%; with or without ascites (9%)
- Pleural fluid analysis: transudate, SPAG >1.1, TP <2.5 g/dl
- May develop spontaneous bacterial empyema (ANC >250 cells/mm^3)

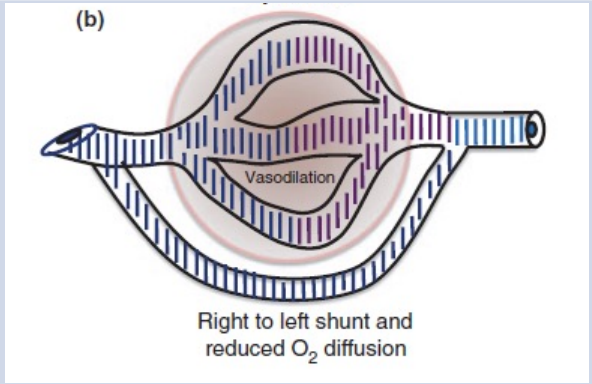
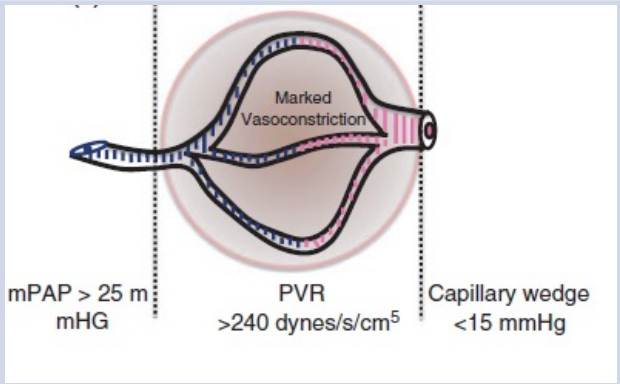
Treatment

- 1º line: salt restriction + diuretics
- Refractory: TIPS, liver transplantation, (pleurodesis)
- Other options:
  - Thoracentesis in patients with dyspnea
  - Mesh repair of diaphragmatic defects in selected cases
  - Antibiotics in spontaneous bacterial empyema
  - ICD - **NOT** recommended



Badillo R. Medicine 2014.

HPS & PPHT

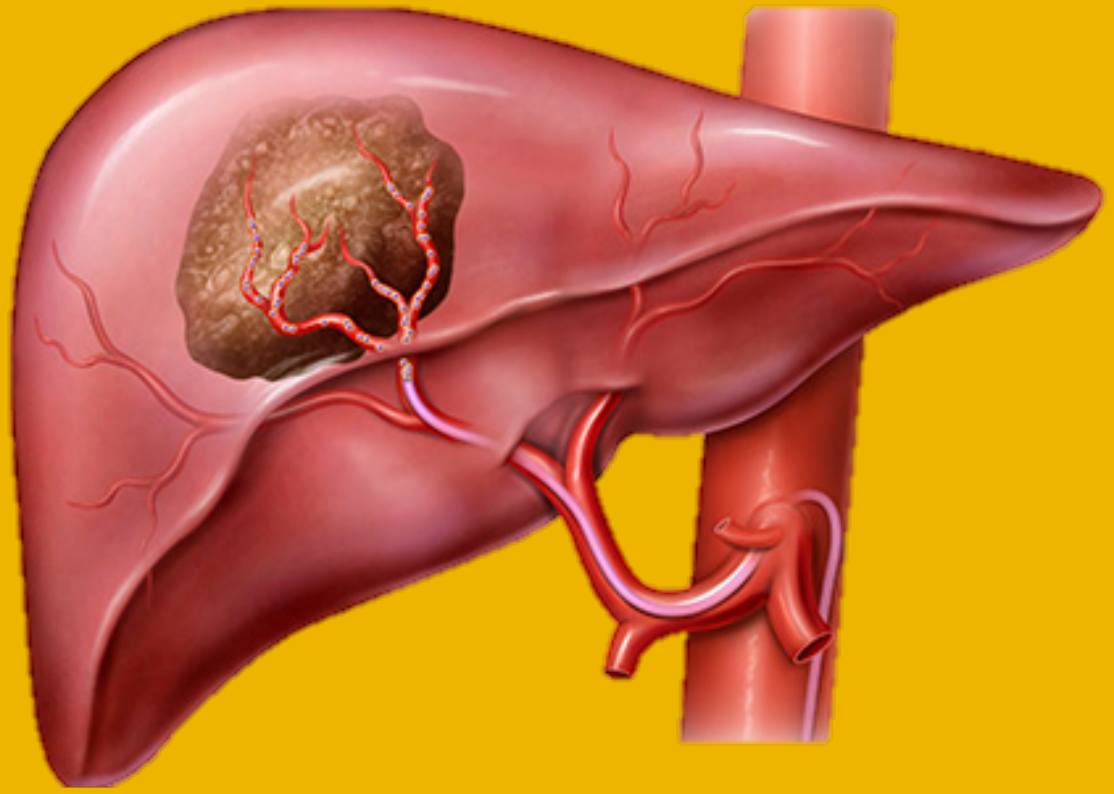
	HPS	PPHT
Pathogenesis		
Prevalence	30%	0.7%
Symptoms & signs	Platypnea, orthodeoxia, cyanosis, digital clubbing, spider nevi	Dyspnea, loud P2, RV heaving, TR murmur, elevated JVP, edema
CXR	Normal	Prominent PA, RAE, RVH
Screening test	ABG; PaO_2 <80, widening $P(A\text{-}a)O_2$	Doppler echocardiography
Diagnostic test	Contrast echo, MAA scan	Right heart catheterization
Treatment	Long-term oxygen therapy Liver transplantation	Medical treatment (LT is contradicted if mPAP >45 mmHg)

Diagnosis — **Cirrhosis**

Staging

- **Compensated**
  - No CSPH
  - CSPH
- **Decompensated:**
  - Ascites
  - Variceal bleeding
  - Overt HE

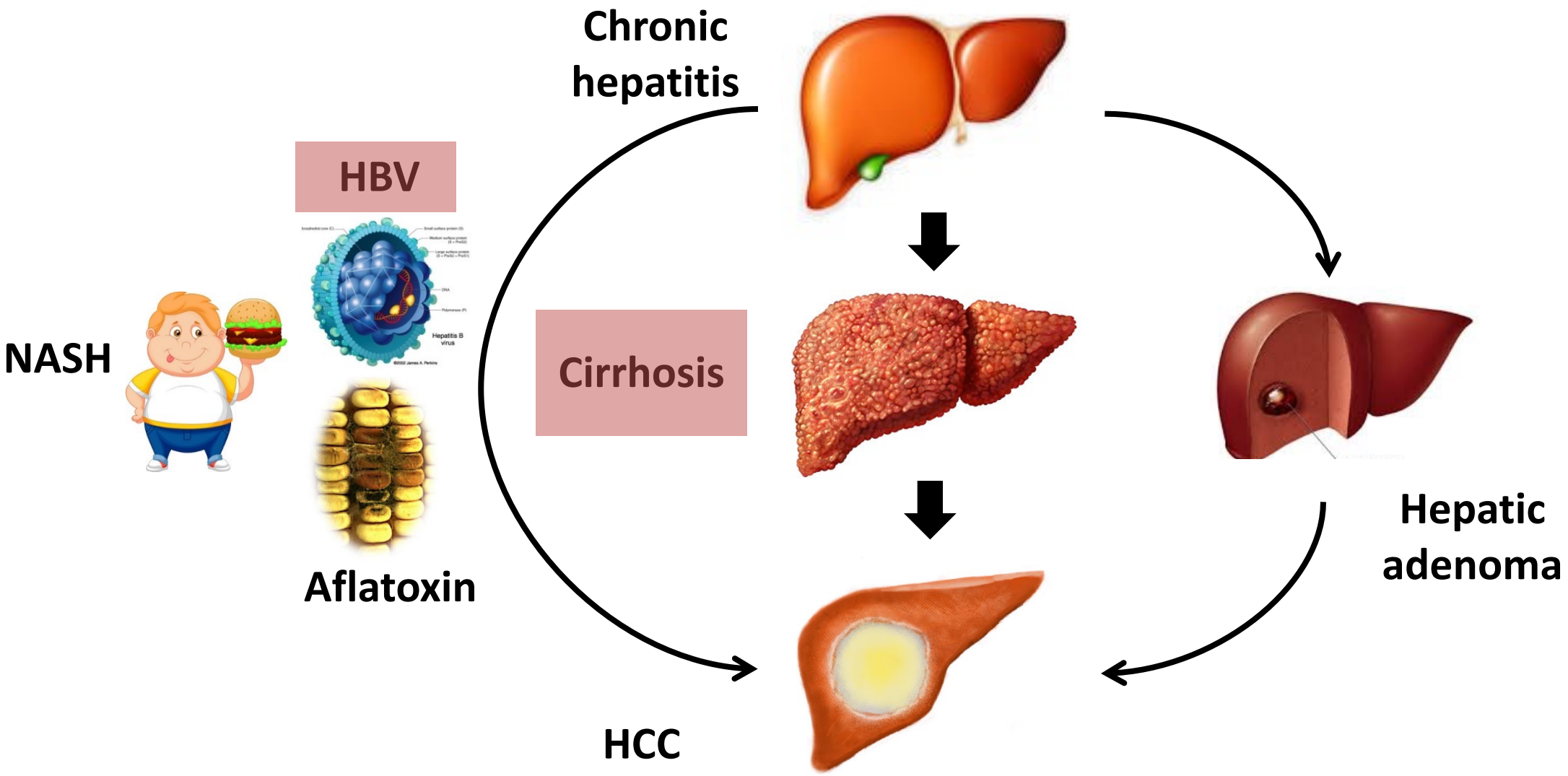
Management			
Specific treatment	→	→	→
General care	→	→	→
Surveillance - HCC - EV	→	→	List for LT
Prevent decompensation : NSBB		→	
Treat complications			→



8

HCC

Pathogenesis of HCC



HCC Surveillance

High risk group
Cirrhotic patients • Child-Pugh A and B • Child-Pugh C awaiting LT
HBV • Age; M>40, F>50 • Family history of HCC
Any etiologies • F3 fibrosis

US + AFP

Sens 60%
Spec 97%

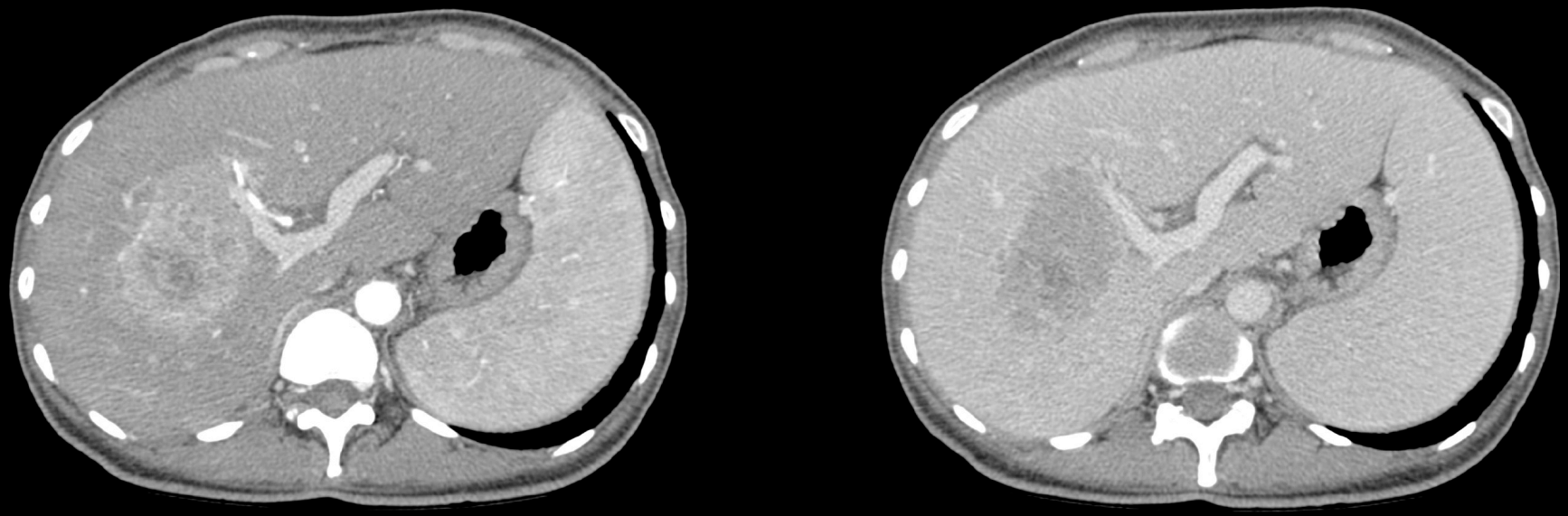
Add-on benefit 18%

Every 6 months

EASL guidelines 2018

Bruix J, Sherman M. Hepatology 2010

Diagnosis of HCC



Imaging (dynamic CT or MRI)

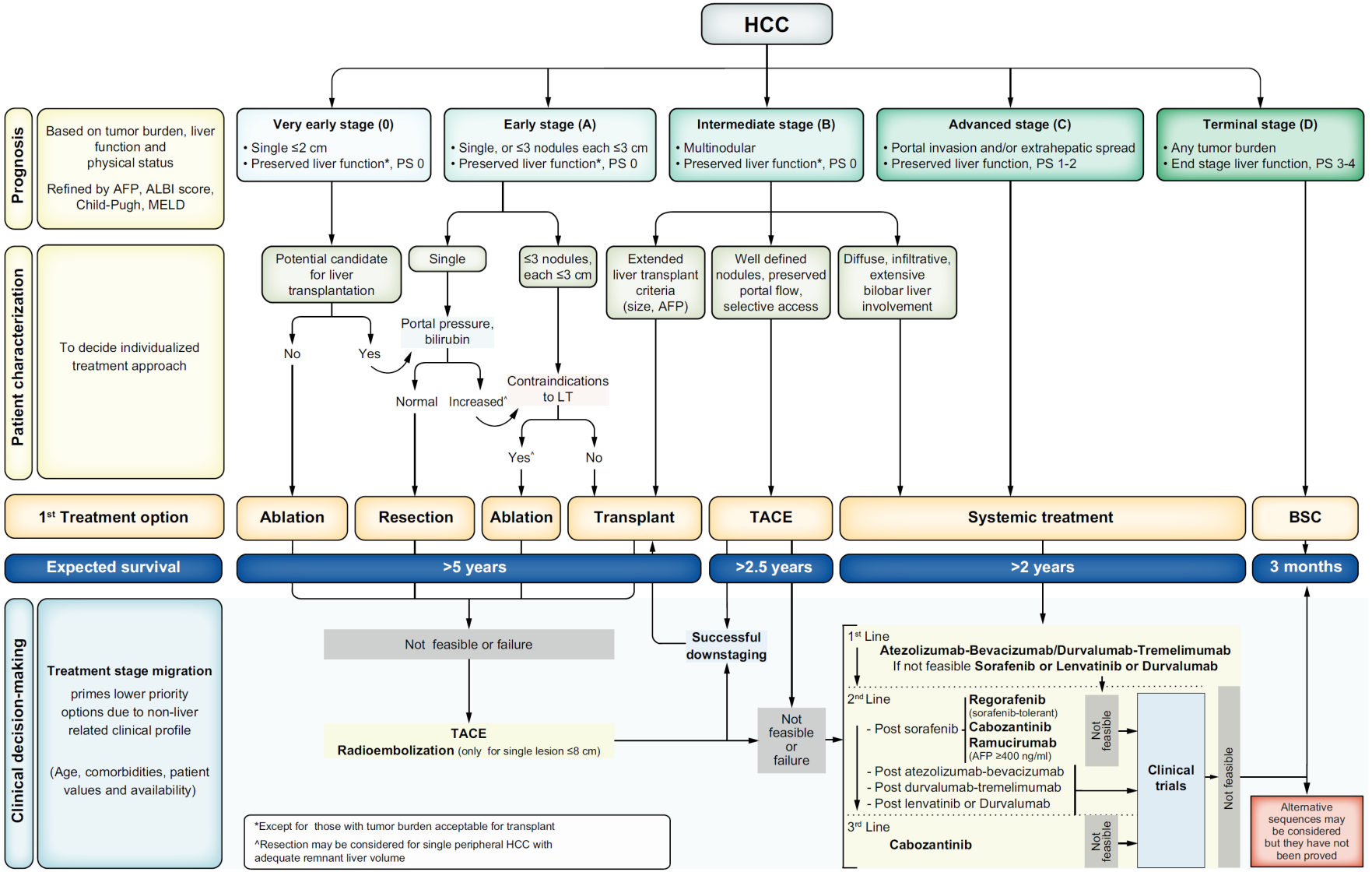
: Liver mass (>1 cm) with arterial enhancement + wash out in PV phase

- Cirrhosis
- Non-cirrhosis: positive HBsAg + AFP >200 ng/ml

Pathology

: H&E staining or Immunohistochemistry

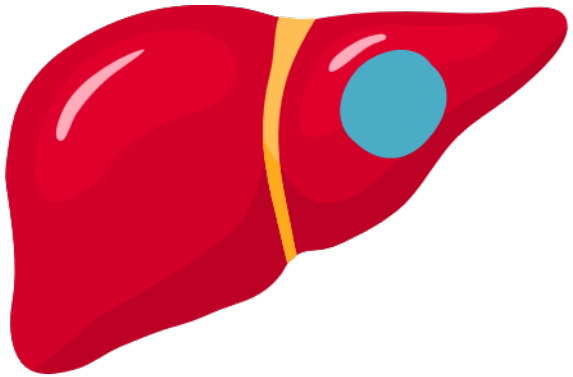
BCLC staging system 2022



Reig M, et al. J Hepatol 2022

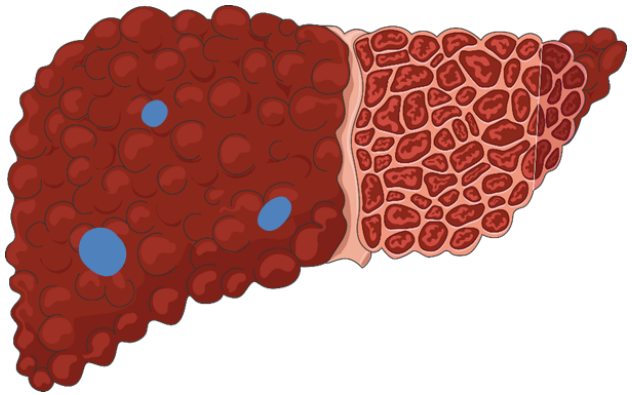
Early HCC

Resection



Tumor: single, size?
CTP A, PS 0, no C/I for surgery
No PHT (EV, splenomegaly, plt <100,000)

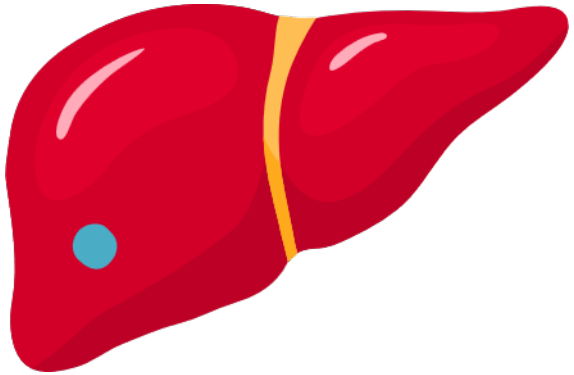
Transplant



Milan criteria:

- Single tumor <5 cm *or*
- Three tumors <3 cm *or*
- Total <7 cm

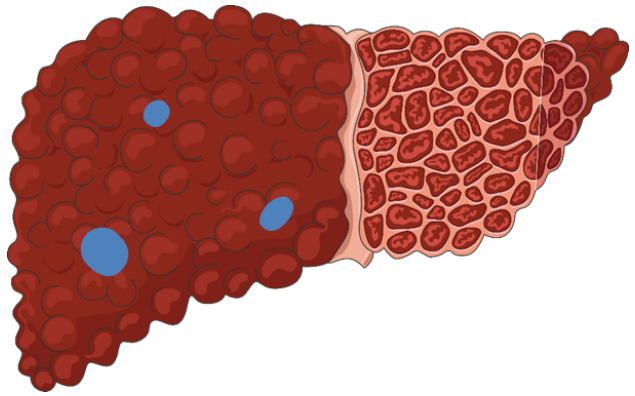
Ablation



Tumor: n=1-2, size <3 cm
Site: accessible, safe
CTP A

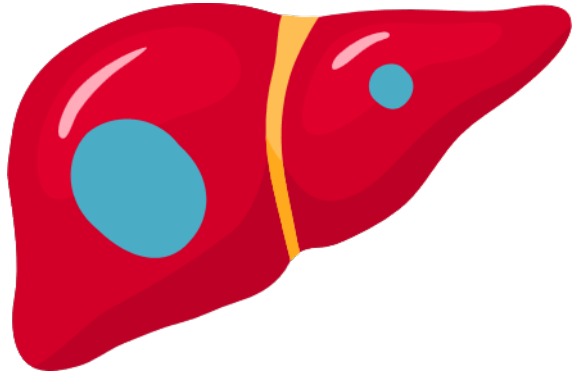
Intermediate HCC

Transplant



Within **extended criteria (size, AFP)**

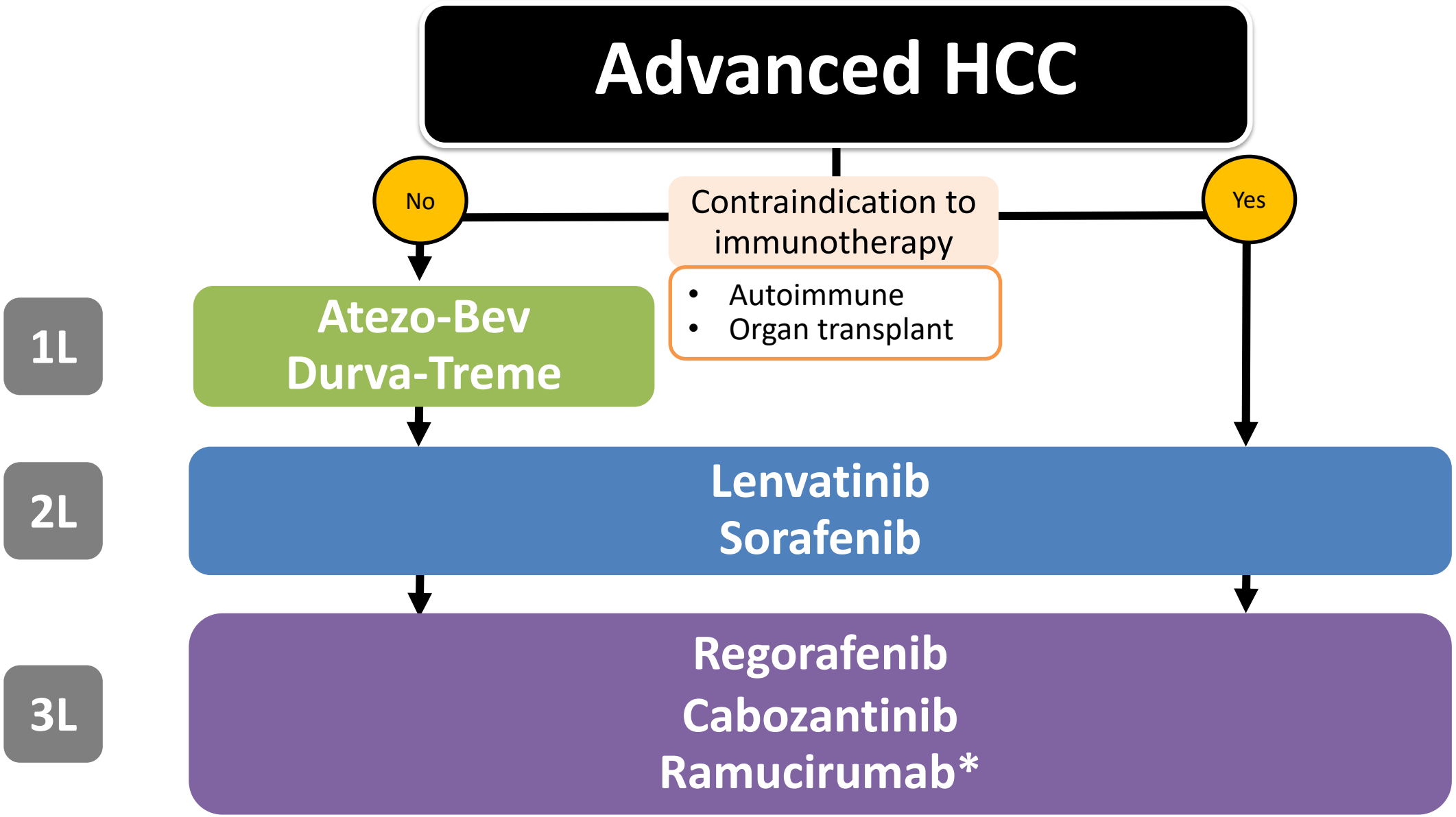
TACE



Tumor volume **<10 cm or <50% of liver**
CTP A-B8, no vascular invasion

Systemic Rx

Diffuse, infiltrative, extensive bilobar involvement
CTP A



*If AFP >400 ng/ml

Adapted from ESMO guideline 2023


Good Luck !