Liver – Functions, Disorders and Diagnostic Tests

Objectives

SLO BI 6.13.1 Enumerate functions of liver

SLO BI 6.14.1 Discuss the biochemical tests which are done to assess the function of liver

SLO BI 11.17.5 Enumerate and explain the biochemical basis of Liver Function tests

SLO BI 6.15.1 Discuss the biochemical alterations in patients with jaundice

Liver

- Largest solid organ, right upper quadrant
- Large reserve capacity
- Capable of regeneration
- Functions:

✓ Metabolism: Fat, carbohydrates, protein, xenobiotics, hormones

✓ Synthesis: Albumin, α and β globulins, coagulation factors

✓ Storage: fluids, vitamins, minerals

Some examples of Liver dysfunction

- Hepatocellular diseases (viral hepatitis, ALD)
- Cholestastic disease (intra and extra hepatic obstruction)
- Cirrhosis
- Cancer (secondary or primary)
- Fatty Liver
- Genetic Disorders
- ✓ Hemochromatosis (iron storage)
- ✓ Wilsons disease

Liver dysfunction diagnosis

- The diagnosis of liver disease depends on a combination of patient history, physical examination, **laboratory testing**, biopsy and imaging studies such as ultrasound/ CT /MRI scans

Liver Function Test Used to ……

- detect the presence of liver disease
- distinguish among different types of liver disorders
- gauge the extent of known liver damage
- follow the response to treatment

Liver Function Test Shortcomings

- can be normal in a patient with serious liver disease and abnormal in a patient with diseases that do not affect the liver
- rarely suggest a specific diagnosis rather suggest a general category of liver disease → further directs the evaluation

Liver Function Test point to be noted…….

- Liver – thousands of biochemical functions – most cannot be measured
- Enzymes – do not measure liver function at all – detect damage or interference with the bile flow
- Interpretation must be performed within the context of the patient's risk factors, symptoms, concomitant conditions, medications, and physical findings
- Differing laboratories → Differing normal values

Liver Function Test point to be noted…….

- No one test enables the clinician to accurately assess the liver's total functional capacity
- to increase the sensitivity and specificity use them as a battery
- when one test provide abnormal finding or persistently abnormal on serial determination – probability of liver disease is high
- when all results are normal – probability of missing occult liver disease is low
- Commonly employed tests: Bilirubin, Aminotransferases, Alkaline phasphatase, Albimin and Prothrombin time

Liver Function Test
Sample collection

- Serum or plasma
- Avoid hemolytic and lipemic sample
- Sample transport/storage
- Precautions (viral hepatitis B and C)

Liver Function Test Categorization

- Test based on detoxification and excretory function
- Test for enzymes that reflect damage to hepatocytes
- Test for enzymes that reflect cholestasis
- Test that measure synthetic function

Liver Function Test

Test based on detoxification and excretory function:

Van den Bergh assay: determination of total, conjugated (direct) and unconjugated bilirubin (indirect)

- ✓ Normal value of total < 1-1.5mg/dl
- ✓ Normal value of direct: up to 15% of the total (upper limit = 0.3mg/dl)

Liver Function Test

Test based on detoxification and excretory function:

- ✓ Isolated elevation of UCB – bilirubin elevated but < 15% direct - W/U for hemolysis – if absent – Gilbert disease
- ✓ Conjugated hyperbilirubinemia – liver or biliary tract disease
- ✓ In most liver diseases both fractions are increased

Liver Function Test

Test based on detoxification and excretory function:

Urine Bilirubin:

- ✓ any bilirubin found in urine is conjugated bilirubin
- ✓ bilirubinuria implies the presence of liver disease

Blood ammonia:

- ✓ Was used for detecting encephalopathy or for monitoring hepatic synthetic function (poor corelation)

Liver Function Test

Test for enzymes that reflect damage to hepatocytes

Aminnotransferases (ALT and AST):

- **AST**: Liver, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes, and RBC - (Normal serum level)
- **ALT**: Liver - (Normal serum level)
- Liver cell damage – increased permeability – increase serum levels
- **BUT poor correlation b/w liver cell damage and level of AST and ALT**
- Up to 300 U/L – non specific/ any type of liver disorder

Liver Function Test

Test for enzymes that reflect damage to hepatocytes

Aminnotransferases (ALT and AST):

- ✓ Levels > 1000 U/L extensive hepatocellular injury (viral hepatitis, Ischemic Liver disease, Drug or Toxin induced)
- ✓ In most acute hepatocellular damage ALT > AST
- ✓ AST:ALT > 2:1 (suggestive) & > 3:1 (highly suggestive) of (Alcoholic Liver Disease) ALD
- ✓ Aminotransferases are usually not greatly elevated in obstructive jaundice

Liver Function Test

Test for enzymes that reflect cholestasis:

- ALP, 5'NT, GGT
- GGT – more diffuse localization – less specific than ALP and 5'NT
- Use of GGT to identify patient with occult alcohol use – questionable
- ALP: non pathological causes of increased levels
- Normal levels

Liver Function Test

Test for enzymes that reflect cholestasis:

ALP:

- < 3 fold increase: not specific for cholestasis (seen in almost any type of liver disease)
- >4 fold increase: cholestatic liver disorder, infilterative liver disease (Cancer), bone conditions with rapid turnover of bone (Pagets disease)
- ALP is NOT useful to distinguish b/w intra and extra hepatic obstruction

Liver Function Test

Test that measure biosynthetic function of the Liver

Serum albumin:

- ✓ Synthesized exclusively by hepatocytes
- ✓ T1/2: 15-20 days
- ✓ NOT a good indicator of acute/mild hepatic dysfunction
- ✓ Minimum change in Viral hepatitis/drug induced hepatitis/ Obs. Jaundice
- ✓ In hepatitis Alb levels less than 3gm/dl – chronic liver disease

Liver Function Test

Test that measure biosynthetic function of the Liver

Serum albumin:

- ✓ Other causes of decrease: Protein malnutrition/ Protein losing enteropathies / Nephrotic syndrome/ Chronic infections

Liver Function Tests

Test that measure biosynthetic function of the Liver

Coagulation factors:

- ✓ Except for factor VIII, blood clotting factors are exclusively synthesized in hepatocytes
- ✓ T1/2 of factor VII- 6 hrs / Fibrinogen – 5days (shorter than albumin)
- ✓ Rapid turnover – thus measurement of clotting factors is the single best acute measure of hapatic synthetic function (in the diagnosis and assessment of liver function in acute parenchymal liver disease)

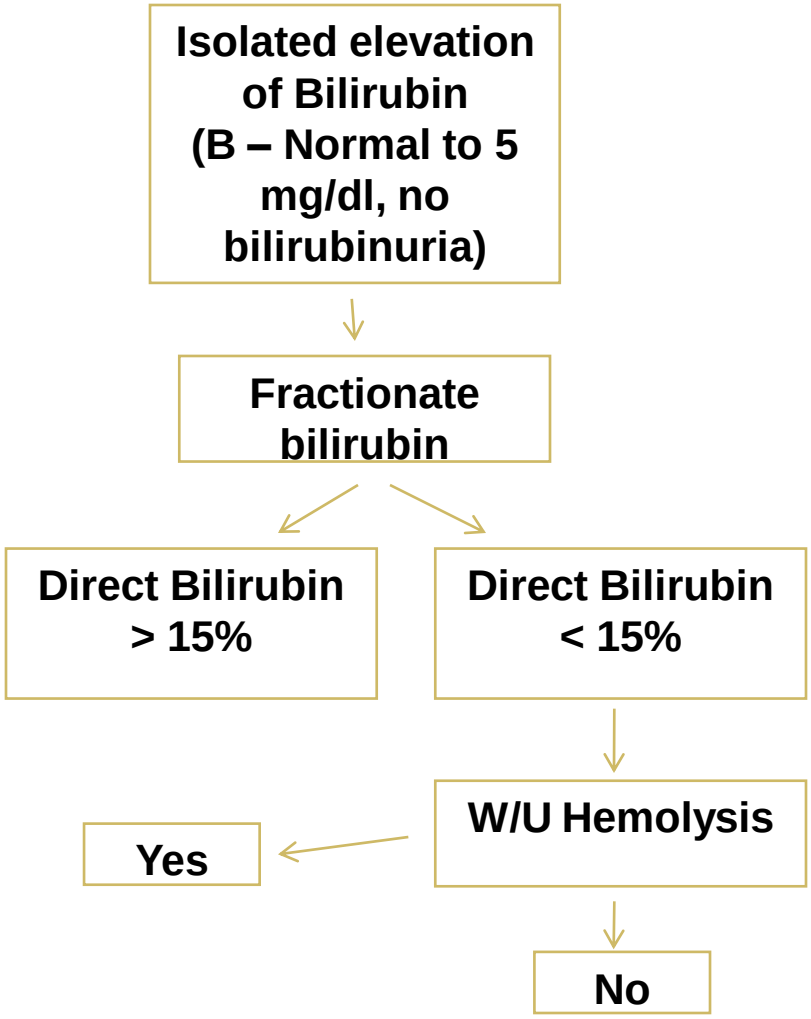
Liver Function Tests

Test that measure biosynthetic function of the Liver

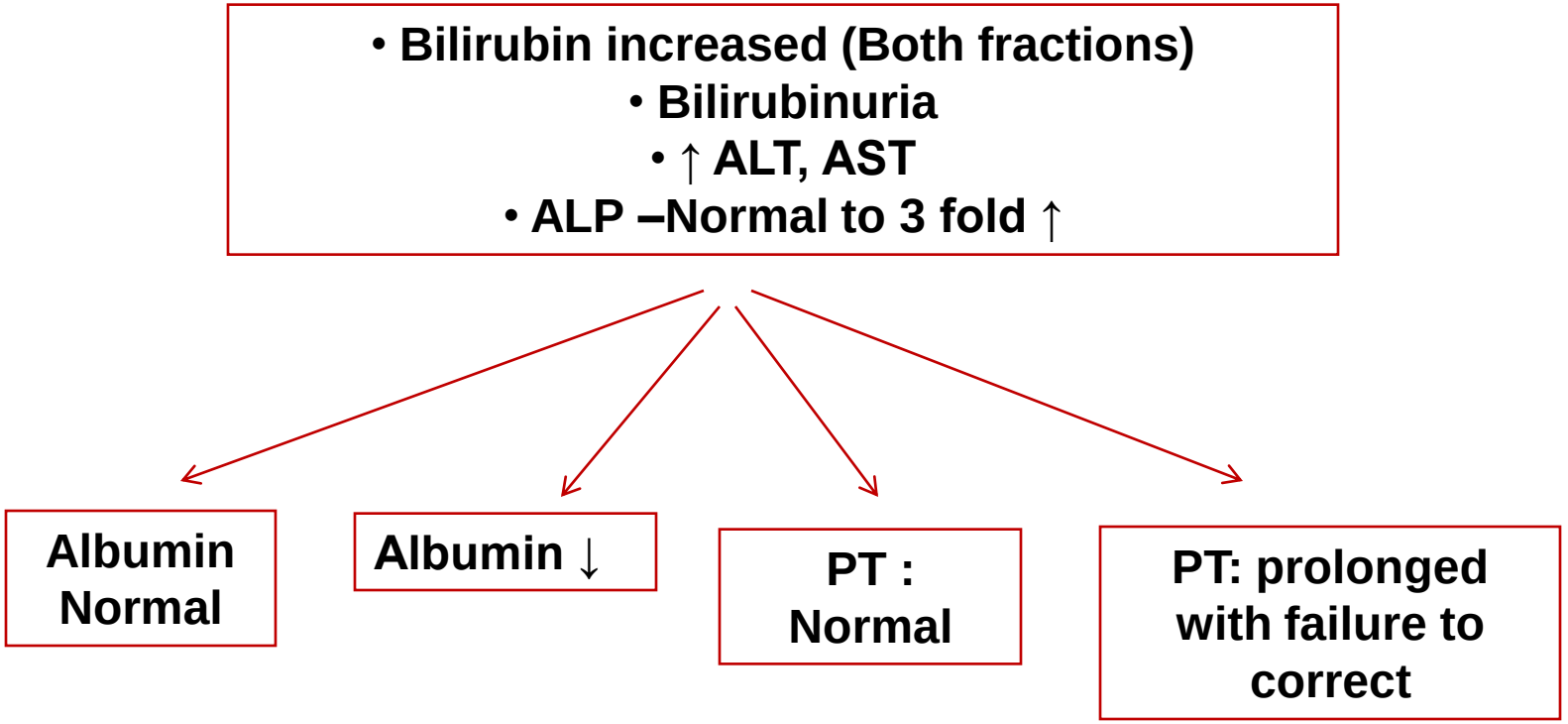
Coagulation factors:

- What is measured **Prothrombin Time (PT)** - collectively measures II/V/VII/X
- Biosynthesis of factors II/VII/IX/X depends on Vit. K
- PT may be elevated in hepatitis, cirrhosis and disorders that result in Vit. K deficiency (eg obstructive jaundice)
- Markedly prolonged PT (>5 secs above control), not corrected by Vit. K is a poor prognostic sign in acute viral hepatitis and other acute and chronic liver diseases

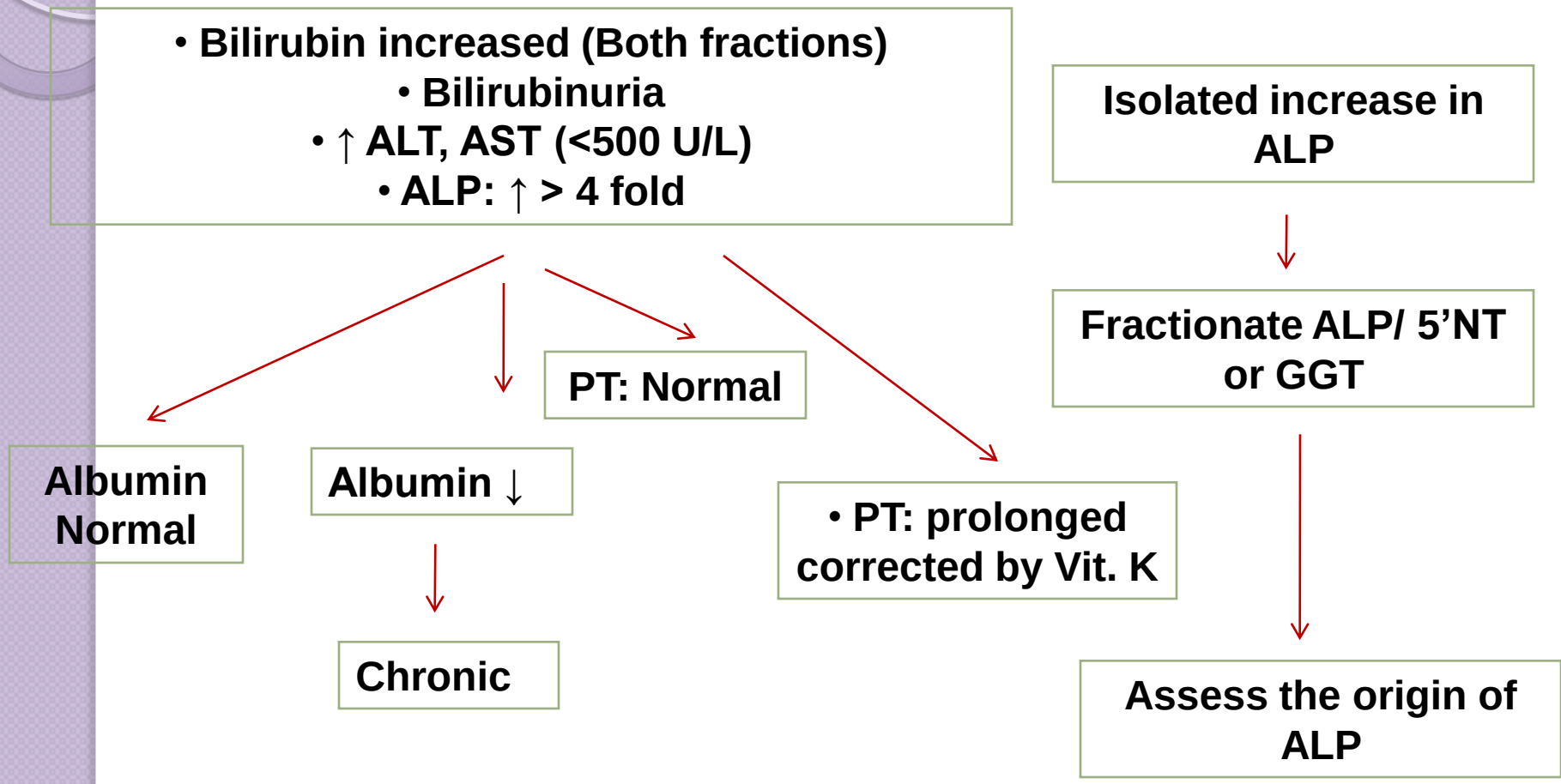
Hemolytic or Pre Hepatic Jaundice



Hepatocellular or Hepatic Jaundice



Obstructive or Post Hepatic Jaundice



Summary

Liver Function test	Clinical implication of abnormality
ALT	Hepatocellular damage
AST	Hepatocellular damage
Bilirubin	Cholestasis, impair conjugation, or biliary obstruction
ALP	Cholestasis, infiltrative disease, or biliary obstruction
PT	Synthetic function
Albumin	Synthetic function
GGT	Cholestasis or biliary obstruction
5`-nucleotidase	Cholestasis or biliary obstruction