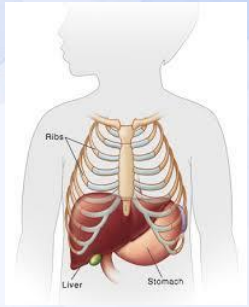
In the Name of God

Abnormal LFT in children



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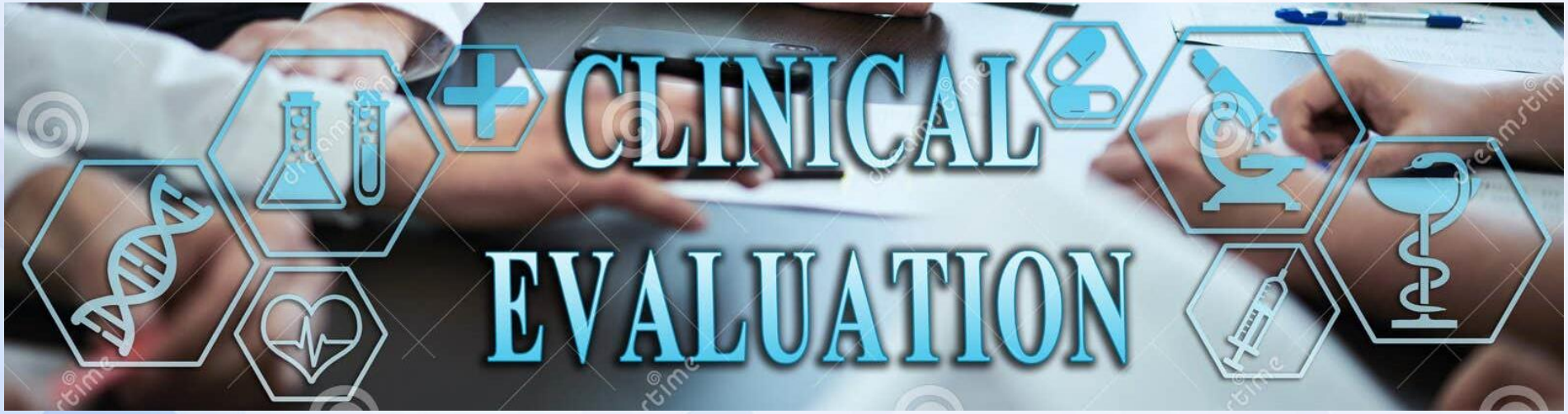
معرفی بیمار:

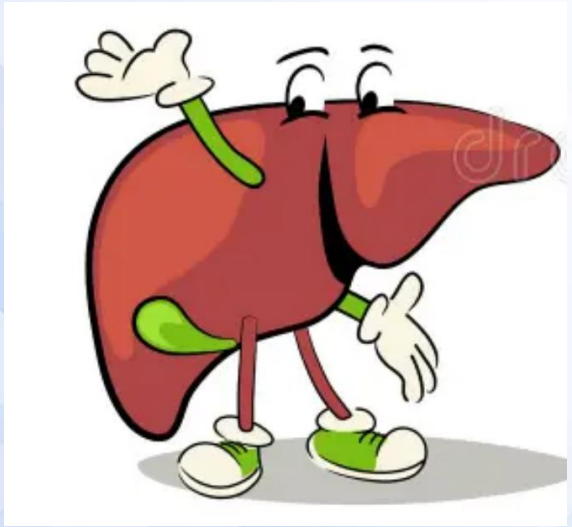
- در آزمایش روتین کودک ۳ ساله ای، آلکالین فسفاتاز سرم ۵۶۵۰ واحد گزارش شده است. دو هفته بعد مجددا چک شده و همچنان خیلی بالاست. والدین شدیدا نگران هستند. بیمار به شما ارجاع شده است. کودک سابقه بیماری خاصی نداشته و در معاینه نیز یافته قابل توجهی ندارد.
- در رابطه با این بیمار چگونه تصمیم گیری می کنید؟

EVALUATION:

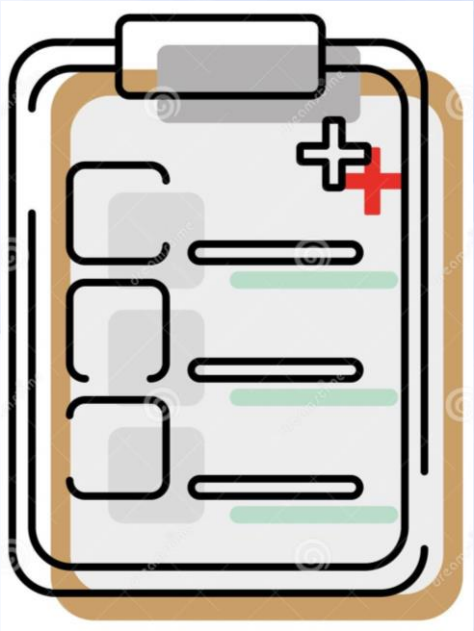
- Careful history
- Physical examination
- Laboratory evaluation
- Consider liver and bone diseases



ALP is present in:



History:



- Assessment of risk factors for nutritional rickets:
  - Infants: at least 400 IU daily of vitamin D.
  - In children ≥ 1 yr/o: vitamin D intake: 600 IU daily.
- Features suggesting bone dx
- Symptoms suggesting liver dx or cholestasis
- History of kidney dx or suggestive symptoms (polyuria, poor growth).
  - renal osteodystrophy.
- Nonspecific: anorexia, poor growth, wt loss, fever: systemic disease

Physical examination:

- Signs suggesting bone dx:
  - Bone deformities or tenderness
  - Skeletal abnormalities associated with rickets:
    - beading at the costochondral junction
    - bowing of long bones
    - delayed closure of the fontanelles in infants.
- Signs suggesting liver dx:
  - Hepatomegaly
  - Splenomegaly
  - liver tenderness
  - Jaundice
  - stigmata of chronic liver disease

Laboratory testing:

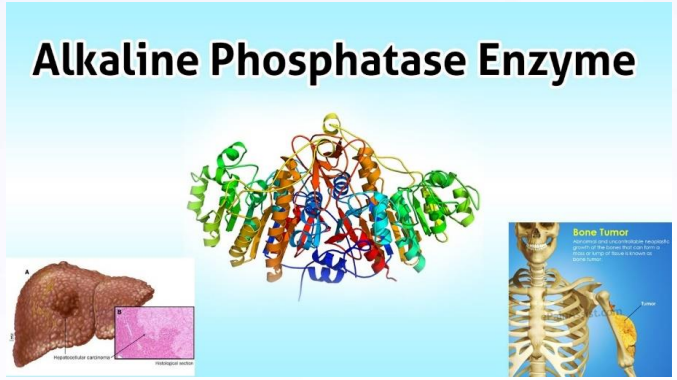
- Screen for primary liver disease, rickets, and renal osteodystrophy.
- Initial lab:
  - AST, ALT
  - T & D bili
  - GGT
  - calcium, phosphorus, 25-hydroxyvitamin D, PTH
  - BUN, and creatinine

DIFFERENTIAL DIAGNOSIS:

- **Normal bone growth:**
- Serum ALK ph is generally higher in children than in adults
- **Liver disease:**
- Hepatocellular injury: ↑ALT and AST: viral hepatitis, metabolic dx, and drug toxicity.
- Cholestatic injury: ↑ Alk ph and GGT, out of proportion to elevation of ALT and AST.

DIFFERENTIAL DIAGNOSIS:

- **Bone disease:**
- Rickets: ↓ serum 25-OH vit D with ↓ serum calcium and/or phosphorus, ↑ levels of PTH, a history of risk factors for vit D deficiency or typical skeletal abnormalities.
  - Any of these findings: prompt further evaluation for rickets with radiographs of long bones.
- Renal osteodystrophy: ↑ creatinine
- Other primary bone disorders: tumor, fracture, or juvenile Paget disease
- Limb pain: orthopedic, infectious, rheumatic, and neoplastic disorders



Isolated ↑ ALP: not indicate liver or biliary dx

↑ALP in the absence of liver & bone dx:

- Pregnancy
- Familial inheritance
- Chronic renal failure
- Blood groups B or O
- Transient hyperphosphatasemia

low ALP:

- Zinc deficiency
- Wilson's disease.

- Vitamin D: 47
- Ca: 9.2
- P: 4.1
- AST: 25
- ALT: 22
- GGT: 38
- 5'-nuclotidase???
- Cr: 0.6
- Sono: normal

With ↑ ALP: the best indicator of hepatobiliary dx: concomitant ↑ of GGT and 5' nucleotidase

Transient hyperphosphatasemia of infancy and early childhood:

- TH should be suspected in a child < 5 yrs of age presenting with isolated ↑ in ALK ph 4-10 times ULN
- A provisional diagnosis: history, physical examination, and laboratory testing: no evidence of underlying liver or bone disease.
- The confirmed diagnosis: if Alk ph returns to the normal range within 4 months

MANAGEMENT:

- Adequate intake of vitamin D and calcium.
  - to avoid confounding from coincidental vitamin D insufficiency.
- Repeat alk ph measurement within 6-8 weeks
- Follow-up: return of serum Alk ph levels to normal: critical for confirmation
- Gradually returns to normal within 2-3 months→ as long as 6 months
- No clinical sequelae were noted up to 4 years after the episode of TH
- Sustained Alk ph elevation lasting > 4 months: reconsideration and evaluation

Tests that evaluate liver: 5 categories:

1) liver injury (liver enzymes: ALT & AST).

2) ↓ bile flow or cholestasis (ALP, GGT & 5'-nuncleotidase).

3) ↓ liver synthetic functions (albumin, PT, INR, factor VII & V).

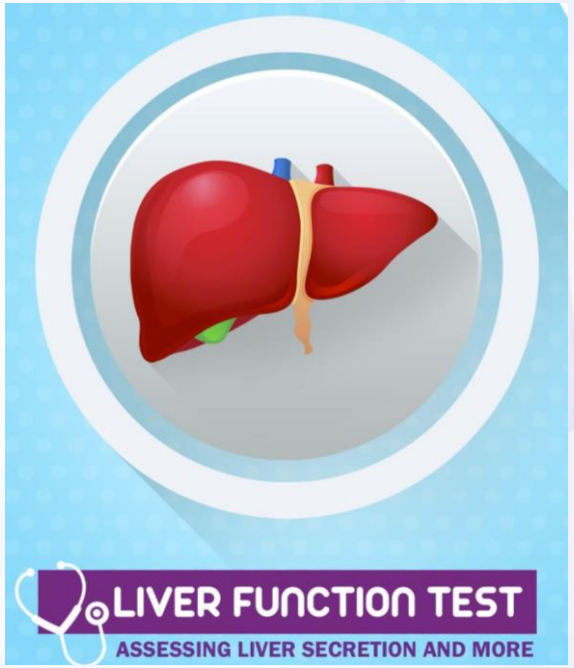
4) ↓ hepatic excretory functions (bilirubin, bile acids).

5) hepatic metabolic functions: detoxification and clearance of endogenous metabolites: ammonia.

Which tests are done in a routine LFT?

- AST
- AST
- ALP
- T. & D. Bili
- Total prot
- Alb

Misnomer



What is the upper limit of NL of ALT?

Adults :

Males = 29 IU/L , Females = 22 IU/L

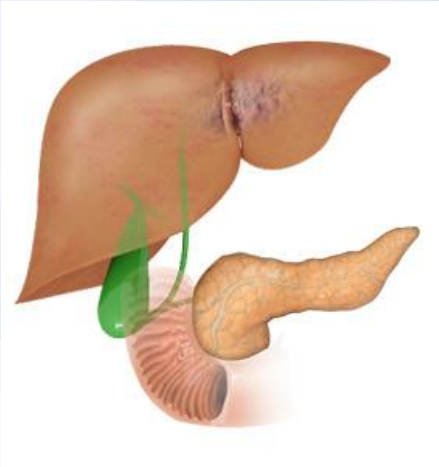
Children:

Boys = 25 IU/L , Girls = 22 IU/L

The causes of isolated AST & ALT elevation:

- Hepatic
- Extra hepatic

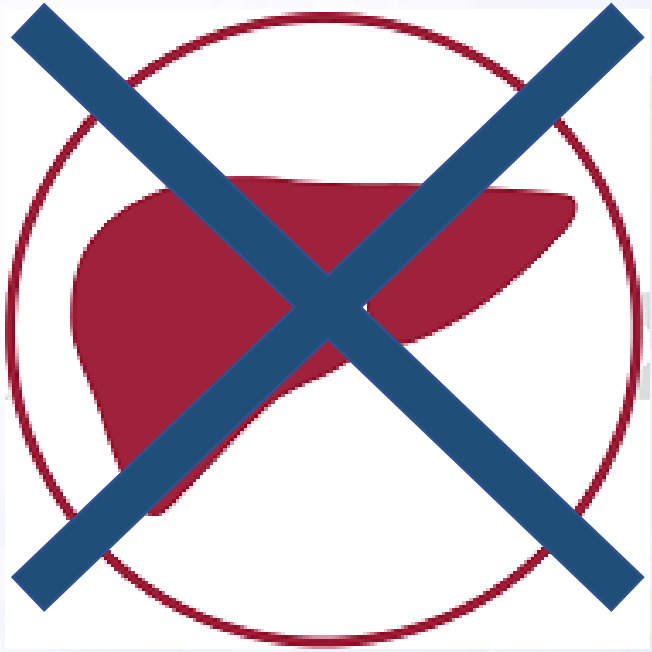
Causes of hepatobiliary dx:



1) Viral hepatitis
2) Medications: any medication: a careful history
   - NSAIDs; anti-TB; antibiotics; anticonvulsants and statins.
   - Herbal medications
   - Alcohol abuse: common in adults
3) Hepatic steatosis & steatohepatitis
4) Autoimmune hepatitis
5) Wilson's disease
6) Glycogen storage disease: usually > 6 months of age.
7) Hemochromatosis: a common genetic disorder: usually in adults
8) Alpha-1 ATD: the most common metabolic liver dx in children
9) Biliary dx

Extrahepatic Causes of Liver Enzyme Elevation:

- Muscle dx: myopathies, myositis
- Cardiac problem
- Thyroid disease: mainly hypothyroidism
- Celiac
- Adrenal insufficiency
- Anorexia nervosa



with LFT:

1) Nl LFT: not ensure that the pt is free of liver dx (compensated cirrhosis).

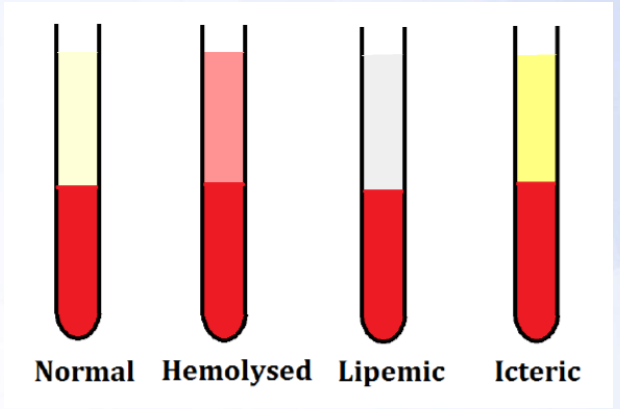
2) Not specific for liver function and can ↑in other conditions (non hepatic).

3) Not usually provide a specific etiology, but indicative of a liver disorder.

- Clinical significance of abnl LFT: must be interpreted individually
- AST & ALT: the most commonly ordered tests for liver function: do not show liver function, only show liver damage.

AST and ALT are neither specific nor sensitive for liver

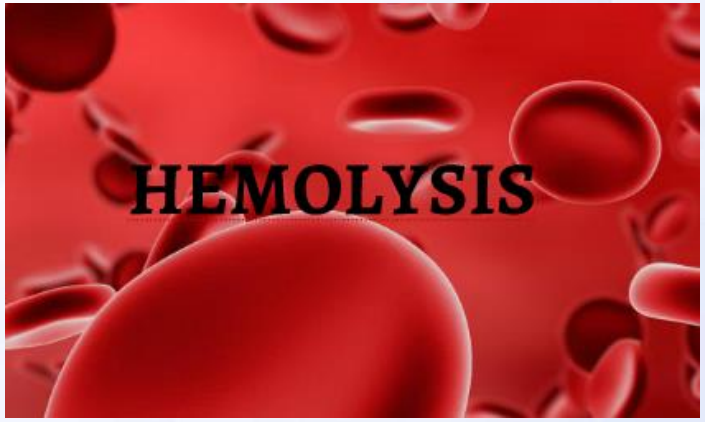
Conjugated + Unconjugated Bilirubin



- Conj. hyperbili. (> 20% of T. Bili): hepatobiliary dx: always pathologic.
- Usually accompanied by bilirubinuria (deep yellow urine)
  - urine dipstick.
  - may appear before overt clinical jaundice.
- Anicteric acute liver dx: no possibility for FHF
  - The chance of hepatic failure increases with rising bilirubin levels.
- Serum bilirubin: an indicator of prognosis in patients with ALF

Unconjugated hyperbilirubinemia:

- Hemolysis
- Crigler–Najjar Sx
- Gilbert Sx: benign: occurring in up to 5% of the normal population.
- Physiologic jaundice
- Breast feeding & breast milk jaundice



Which component is specific for liver?

Work up to rule out these differential diagnosis:

1) HAV IgM, HCV Ab, Hbs Ag
2) Auto Ab: ANA, ASMA, ALKM, total IgG
3) Serum ceruloplasmin, 24 h urine copper
4) Alpha-1 AT mutation
5) Ferritin
6) Metabolic and genetic evaluation

Imaging:

- Abd Sonography
- MRCP

Any case with unexplained ↑ liver enzymes:

- CPK
- LDH
- TSH, T4
- Total IgA, anti TTG IgA ab
- Muscle injury and ↑ transaminase: ↑CPK & LDH.

FINALLY!

- Any case with persistent AST, ALT levels > 2 times ULN, if the above mentioned tests are ambiguous, a **liver biopsy** is recommended
- Persistent: > 3 month