Evaluation of Abnormal Liver tests

- Kwo et al. ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. The American Journal of Gastroenterology. Advance online publication, 20 December 2016.
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Liver chemistries

* Liver chemistries that are commonly ordered in comprehensive metabolic profiles as routine practice are indirect markers of hepatobiliary disease.
* Liver chemistries are markers of liver injury, not liver function.
* They are best referred to as liver chemistries or liver tests, and should not be referred to as liver function tests.
* To date, there are no controlled trials that have been performed to determine the optimal approach to evaluate abnormal liver chemistries.

AST & ALT

* Aminotransferases (transaminases)= AST and ALT
* AST is present in the liver, cardiac muscle, skeletal muscle, kidney, and brain.
* ALT is present primarily in the liver (a more specific marker of hep. Injury).
* ↑AST without↑in ALT is suggestive of cardiac or muscle disease.
* There is a linear relationship between ALT level; those with higher BMIs may have higher ALT levels.
* Some have suggested that an ALT correction for being overweight should be considered.

AST & ALT

* True healthy normal ALT level in prospectively studied populations without identifiable risk factors for liver disease ranges 29-33 for males and 19-25 IU/l for females, and levels above this should be assessed.
* A normal ALT level may not exclude significant liver disease.
* One report found that 9% of HCV patients with normal ALT or near-normal ALT had bridging fibrosis and 11% had cirrhosis.
* Another study treated hepatitis C patients with ALT levels <30 IU/l and noted further reduction in ALT levels by up to 10 IU/l.
* Elevated ALT or AST above ULN in a population without identifiable risk factors is associated with increased liver-related mortality.

AST & ALT

Table 3. ALT and AST levels and liver related mortality

Author /year	Proposed ALT/AST cutoff level	ALT/AST level for increased mortality	Comments
Arndt *et al.* (27)	AST 18	AST>18	3X increase in all cause mortality
Kim *et al.* (28)	ALT<20	ALT 30-39	RR of liver mortality 2.9 (2.4–3.5) and 9.5 (7.9–11.5) in men, 3.8 (1.9–7.7) and 6.6 (1.5–25.6) in women
Lee *et al.* (29)	ALT (ULN 45 IU/l for M, 29 for F	ALT 45-90 M 29-58 for F	SMR risk 1.32 for 1–2X ULN, and 1.78 for >2X ULN
Ruhl and Everhart (30)	ALT 30 IU/l M, 19 IU/L for F	ALT>30 for M ALT >19 for F	liver-related mortality (11.2X) diabetes-related mortality (3.3X)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; F, female; RR, relative risk; M, male; ULN, upper limit of normal.

* Some have argued against lowering of the ALT ULN due to major clinical and financial implications including:
  * Increased health care costs and unnecessary evaluations
  * Increased mental anguish and anxiety
  * Reducing the blood donation pool

Alkaline phosphatase (ALP)

* ALP is part of a family of enzymes that catalyze the hydrolysis of phosphate esters at an alkaline pH.
* This enzyme is found in hepatocytes, not the bile duct cell. ALP is also found in bone, placenta, intestine, and kidney.
* Serum ALP elevated:
  * may be after a fatty meal due to ↑intestinal ALP (In blood type O and B)
  * may be during pregnancy due to placental synthesis of ALP .
  * In children and the elderly especially females > 50, in part due to bone turnover
  * obstruction of the bile ducts (even if is minor), due to increased synthesis
* To confirm hepatic origin of ALP , the gamma- glutamyl transferase (GGT) may be measured.
* ↑ GGT suggests that ↑ALP is of hepatic origin.

Bilirubin

* Bilirubin predominantly circulates in its unconjugated form (indirect bilirubin, ~70% of the total serum bilirubin).
* Conjugation by uridine 5'-diphospho (UDP)-glucuronosyltransferase makes bilirubin water-soluble
* This allows bilirubin to be excreted in bile where it is converted by bacteria in the colon to urobilinogen, which is subsequently excreted in the urine and stool.
* The total serum bilirubin is usually <1.1 mg/dl and an elevated direct (conjugated) bilirubin indicates hepatocellular dysfunction or cholestasis.
* If the total bilirubin is elevated and the majority of the elevation is unconjugated bilirubin, hepatocellular disease is unlikely to be the explanation.

Albumin

* Albumin is exclusively synthesized by the liver with a circulating half-life of 3 weeks.
* A reduction in albumin (normal ≥3.5 g/dl) usually indicates liver disease of more than 3 weeks duration.
* Although any significant illness can decrease albumin levels due to cytokine effects.

Prothrombin time (PT)

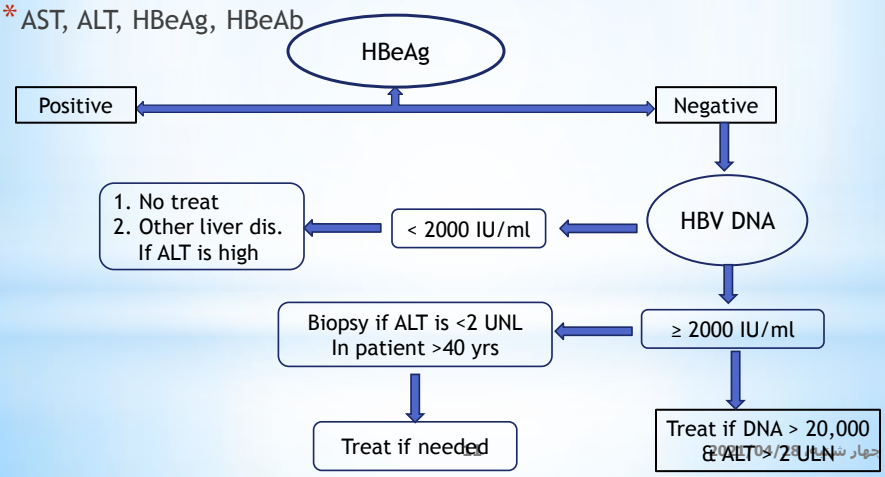
* PT measures the extrinsic pathway of coagulation (factors 1, 2, 5, 7, 9, and 10).
* PT is a far more sensitive measure of liver function than albumin because may be prolonged in patients with severe liver disease of <24h duration.
* Elevated PT:
  * the presence of cholestasis, where vitamin K is not absorbed
  * significant hepatocellular dysfunction (This does not typically occur until concentrations of clotting factors fall below 10% of normal).
  * warfarin, heparin bolus, DIC, and hypothermia.
* As a general rule, in the absence of liver disease, a prolonged PT is due to vitamin K deficiency and/or steatorrhea.

Specific diseases of the liver

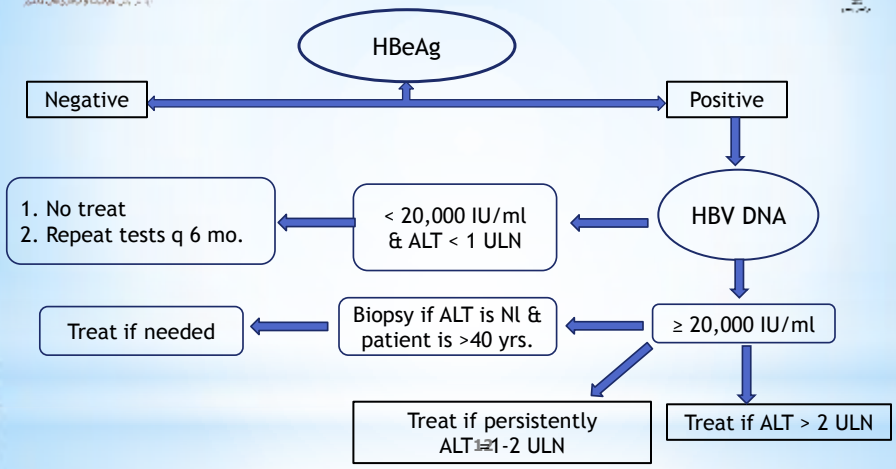
* ***Hepatitis B & C***
* ***NAFLD & NASH***
* ***Alcoholic liver disease***
* ***Autoimmune liver disease***
* ***Metabolic / genetic disorders***
  * ***Hemochromatosis***
  * ***Wilson's disease***
  * ***Alpha-1 anti-trypsin deficiency***
* ***Drug-induced liver injury***
* ***Celiac disease***

Specific diseases of the liver: Hepatitis B

* Testing for HBV should be performed in all patients with persistently elevated AST/ALT levels.
* AST, ALT, HBeAg, HBeAb



Specific diseases of the liver: Hepatitis B



Specific diseases of the liver: Hepatitis C

* Prevalence of HCV infection is estimated as:
  * 2.2% in the world
  * 4.6% in EMRO
  * <0.5% (186500 individuals) in Iranian general population
* Positive predictive value (PPV) of HCV antibody test is:
  * highest among individuals with risk factors; false positives may be 5%
  * but FP may be as high as 30% in individuals without reported risk factors.
* Confirmation of chronic infection is established by PCR assay.

Specific diseases of the liver: NAFLD

* NAFLD is a highly prevalent condition associated with the metabolic syndrome (obesity, D.M., dyslipidemia, and hypertension).
* It should be strongly considered in individuals with mild elevations of AST/ALT levels.
* There is no unique pattern of elevation for ALT and AST levels, although in general, ALT is > AST, and levels are rarely above 300 IU/l.
* It frequently represents a diagnosis of exclusion in which a series of diagnostic labs are obtained to first rule out alternative etiologies.
* Many individuals with NAFLD may have normal liver tests, however, the presence of abnormal tests signals a higher likelihood for NASH with or without fibrosis and therefore warrants clinical evaluation.
* FibroScan was recently approved by FDA, and may be a useful non-invasive tool to determine who might have more advanced fibrosis.

Specific diseases of the liver: Alcoholic liver disease (ALD)

* Alcohol consumption is a common cause for liver injury, independently or as a contributor in patients with other chronic liver diseases such as HCV infection.
* Radiographically and histologically, the pattern of liver injury is similar to that of NAFLD.
* values of AST or ALT rarely exceeding 300 IU/l.
* ~90% of patients with ALD have AST>ALT, and >70% have an AST/ALT ratio>2 (relatively lower activity of ALT driven by pyridoxine deficiency).
* A higher ratio of AST/ALT >3↑further the likelihood of ALD.
* AST>ALT can also be seen in patients with cirrhosis of any etiology, although the AST:ALT ratio is typically not >2.
* Alcohol consumption should be queried in all patients with abnormal liver tests; complete cessation should be recommended in all patients.

Specific diseases of the liver: Autoimmune liver disease

* Autoimmune hepatitis (AIH) represents an important cause of chronic liver disease which is associated with persistently elevated liver chemistries.
* More common in women than men.
* It may occur in the presence of other autoimmune disorders (hypo-thyroidism, ulcerative colitis, synovitis, Sjogren's, RA, and psoriasis).
* It is identified by the presence of characteristic serologic markers, including ANA, ASMA, and less commonly anti-liver kidney microsomal antibody or anti-soluble liver antigen antibody.
* The presence of hypergammaglobulinemia (IgG) is suggestive although not diagnostic.
* A diagnosis of AIH requires histologic confirmation on liver biopsy.

Specific diseases of the liver: Metabolic / genetic disorders

* Hereditary hemochromatosis
* homozygous mutation C282Y (Cys282Tyr)
* A positive family history, or medical history/ physical exam features of end-organ involvement of iron overload within the liver, pancreas, skin, joints, or heart, may all signal a probable diagnosis
* Screening should be considered in all patients with abnormal AST/ALT levels.
* If the transferrin saturation is 45% or higher, or the serum ferritin is elevated consideration should be given for HFE gene mutation analysis.
* An elevated ferritin in the setting of an acute hepatitis likely does not indicate iron overload.
* In patients with homozygous C282Y who have elevated AST/ALT levels or ferritin >1,000 μ g/l, or non-HFE hemochromatosis, liver biopsy should be considered.

Specific diseases of the liver: Metabolic / genetic disorders

* Wilson's disease (WD)
* A rare autosomal recessive disorder of biliary copper excretion due to a defective copper transporter protein (>32 different ATP7B mutations).
* It can present at any age, most commonly diagnosed in young males.
* WD can present with hepatic, neurologic, psychiatric manifestations.
* The liver presentation may include hepatosplenomegaly, abnormal liver enzymes, cirrhosis, and acute liver failure.
* Screening should be considered in all patients with persistently elevated AST/ALT levels, and consists of serum ceruloplasmin testing.
* If ceruloplasmin is low, 24-h urine copper ± serum copper, eye exam (Kayser-Fleischer rings) and possible liver biopsy should be done.
* Molecular genetic analyses can be pursued in cases of diagnostic

Specific diseases of the liver: Metabolic / genetic disorders

* Alpha-1 anti-trypsin deficiency (α1AT def.)
* α1AT def. is a rare genetic disease in adults, although it represents the most common genetic cause of liver disease in children.
* both emphysema and chronic obstructive pulmonary disease, progressive liver disease, liver cirrhosis, and hepatocellular carcinoma.
* Screening should be considered in all patients with persistently abnormal liver AST/ALT levels, and consists of testing for levels of α1AT and genotype testing for the PiZZ mutation.
* Those with heterozygote phenotype (PiMZ) may also be at risk for liver disease, particularly in the presence of concomitant steatosis or viral hepatitis.

Specific diseases of the liver: Drug-induced liver injury

* Prescribed and over-the-counter medications, as well as nonprescribed complimentary alternative medicines or dietary supplements, represent a common source for acute and chronic liver injury.
* Nearly all medications are associated with at least a small risk of elevation of ALT/AST/ alkaline phosphatase or bilirubin with or without hepatotoxicity.
* Common drugs include antibiotics, antiepileptics, NSAIDs, statins, anti-TB drugs, anti- HIVs, biologic agents such as anti-TNF drugs, and some chemotherapeutic agents.
* In those with high ALT levels (>1,000 IU/l) an accurate history of acetaminophen use is essential.
* Attributing liver injury to a specific agent frequently requires empiric trials of drug discontinuation (± drug alternatives) to observe full recovery of liver chemistries.

Specific diseases of the liver: Drug-induced liver injury

* Common herbal supplements associated with hepatotoxicity include chaparral, ephedra, ji bu huan, germander, green tea extract, and shark cartilage.
* A helpful resource to ascertain whether a drug or supplement may be hepatotoxic is the website livertox.nih.gov.
* In cases of acute or severe fulminant hepatitis, liver biopsy may be required to confirm severity of liver injury and establish a diagnosis of offending agent.

Specific diseases of the liver: Celiac disease

* Celiac disease is a common disorder of gluten sensitivity which may be associated with modest elevations of liver transaminases.
* Screening should be considered in patients with persistently elevated liver chemistries and consists of tissue transglutaminase (TTG) IgA and serum IgA level or TTG IgA and anti-deamidated gliadin peptide IgG.

Clinical assessment of the patient with abnormal liver tests

* Clinical assessment of the patient with elevated liver tests should begin with a thorough history and physical examination.
* History should include risk factors for underlying liver disease, associated diseases, associated medical conditions, use of alcohol, and use of medications and herbal supplements.
* Physical examination should assess for stigmata of chronic liver disease, as well as signs or symptoms pointing to a specific liver disease etiology.
* Repeat the lab panel and/or perform a clarifying test to confirm that the test is actually abnormal.

Patterns of liver tests elevations

* Hepatocellular injury is defined as disproportionate elevation of AST/ ALT levels as compared with ALP level.
* Cholestatic injury is defined as disproportionate elevation in ALP as compared with AST/ALT.
* Mixed pattern of injury is defined as elevation of both ALP and AST/ALT levels.
* Isolated hyperbilirubinemia is defined as elevation of bilirubin with normal ALP and AST/ALT.
* Bilirubin levels also may be elevated in any of the first 3 categories.
* The R ratio is calculated as (ALT/ ALT ULN) ÷ (ALP/ ALP ULN)
  * *R* of >5 defined as hepatocellular injury
  * *R* <2 cholestatic injury
  * *R* = 2-5 mixed pattern

Evaluation of AST/ ALT elevation

* The magnitude of AST and ALT elevation varies depending on the cause of hepatocellular injury.
* AST/ ALT elevation:
  * Borderline= <2X ULN
  * Mild= 2-5X ULN
  * Moderate= 5-15X ULN
  * Severe= >15X ULN
  * Massive= >10,000 IU/l

Evaluation of AST/ ALT elevation

Causes of elevated AST and ALT		
Hepatic (generally ALT>AST)		
NAFLD (Steatosis, NASH)	Wilson's disease	Diffuse infiltration with cancer
Chronic viral hepatitis	α-1-antitrypsin defic.	HELLP syndrome
Acute viral hepatitis	Hemophagocytic lymphohistiocytosis	Liver trauma
Drug-induced injury (medications, Herbal)	Acute bile duct obstruction	Sepsis
Toxic hepatitis (amanita exposure)	Acute fatty liver of pregnancy	Celiac disease
Autoimmune hepatitis	Post-liver surgery	
Hemochromatosis	Veno-occlusive disease/ sinusoidal obstruction syn.	

Evaluation of AST/ ALT elevation

Causes of elevated AST and ALT	
Hepatic (generally AST>ALT)	
Alcoholic liver	Acute Budd-Chiari Syn.
Cirrhosis (any etiology)	Hepatic artery damage
Ischemic hepatitis	TPN
Congestive hepatopathy	
Non-hepatic	
Skeletal muscle damage/ rhabdomyolysis	Strenous exercise
Cardiac muscle damage	Heat stroke
Thyroid disease (hypo & hyper thyroidism)	Hemolysis
Macro-AST	Adrenal insufficiency

Evaluation of AST/ ALT elevation

* Patients with ALT/ AST >5X ULN (moderate to massive elevations) require immediate evaluation.
* Such patients should be evaluated for:
  * acute hepatitis including acute hepatitis A, B, C, D, or E
  * acute reactivation of chronic hepatitis B
  * Acute hepatitis from non-hepatotropic viruses including HSV, EBV, CMV
  * Acute autoimmune liver disease
  * idiosyncratic drug reactions or direct hepatotoxin exposure (acetaminophen)
  * ischemic hepatopathy
  * toxin exposure such as Amanita phalloides
* Massive evaluation of ALT/ AST:
  * shock liver/ischemic hepatopathy, or drug-induced/toxic hepatitis, rhabdomyolysis, heat stroke

Evaluation of AST/ ALT elevation

Mild elevation 2-5x ULN | **Borderline elevation <2x ULN**

History and physical exam
Discontinue hepatotoxic meds
Discontinue alcohol consumption
Assess for risk factors for fatty liver and viral hepatitis

CBC/platelet count, AST/ALT, Alk Phos, TB, albumin, PT/INR
HBsAg, HBcAb, HBsAb, HCV Ab with PCR confirmation if +, iron panel, abdominal ultrasound

If negative, consider observation for 3-6 months with repeat AST/ALT, Alk Phos, TB or ...

If persistently elevated, continue investigation: ANA, ASMA, gamma-globulin, ceruloplasmin, alpha-1 antitrypsin phenotype and may consider additional tests based on history (e.g., celiac sprue, tick-borne disease, thyroid disease, and muscle disorders)

If normal, further testing at discretion of clinician or refer to hepatologist for consideration of liver biopsy

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Evaluation of AST/ ALT elevation

Moderate elevation 5-15x ULN

History and physical exam
Discontinue hepatotoxic meds and alcohol
Evaluate for signs of acute liver failure

CBC/platelet count, AST/ALT, Alk Phos, TB, albumin, PT/INR, HAV Ig M, HAV IgG, HBsAg, HBcAb IgM, HBcAb IgG, HBsAb, HCV Ab with PCR confirmation if +, iron panel, ceruloplasmin, ANA, SMA, and gamma-globulin
Abdominal ultrasound

If signs of acute liver failure --> urgent liver consultation with consideration of referral to a liver transplant center

If diagnostic evaluation negative --> consideration for diagnostic liver biopsy if medically stable

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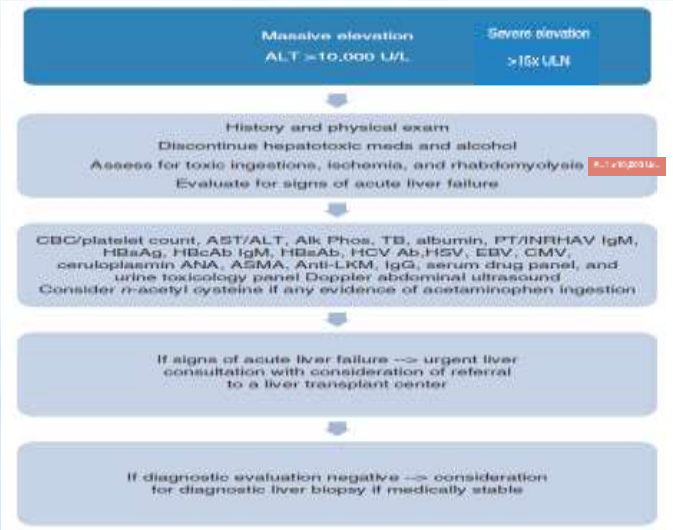
Evaluation of AST/ ALT elevation



Evaluation of ALP elevation

* Cholestatic liver diseases are associated with ↑ALP, ±↑bilirubin.
* They can be categorized as:
  * extra-hepatic (obstructions to bile flow)
  * intra-hepatic cholestasis (functional impairments of bile formation by the hepatocytes).
* Determining the specific etiology of an elevated ALP can generally be accomplished without the need for liver biopsy.
* If ALP is elevated in the presence of other elevated liver chemistries, confirmation of hepatic origin is not required.
* With isolated ALP elevation, confirmation with GGT can be used to help differentiate liver from non-liver sources.
* However, GGT elevation is not specific for cholestatic liver disease, and can be elevated in >50% of alcoholic patients without ALD.

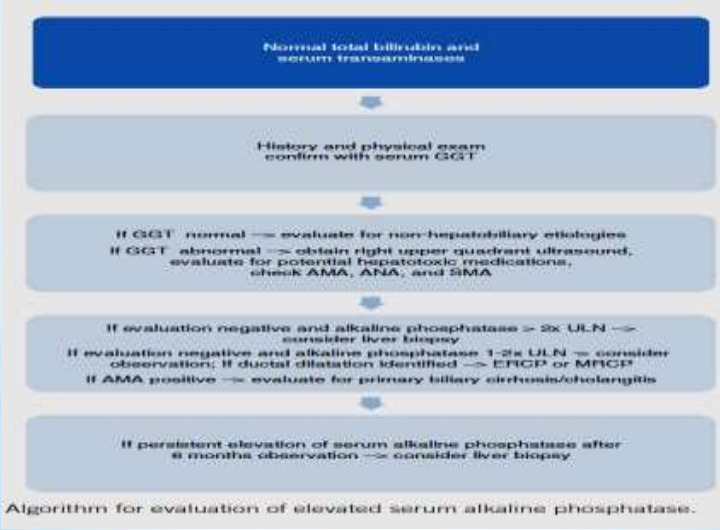
Evaluation of ALP elevation

Causes of elevated ALP		
Hepatobiliary		
Bile duct obstruction	Sarcoid	Alcoholic liver disease
Choledocholithiasis	Granulomatous hepatitis	Intrahepatic cholestasis of pregnancy
Malignant obstruction	Tuberculosis	Benign post-operative jaundice
Bile duct flukes	Amyloid	ICU jaundice or multifactorial jaundice
Bile duct stricture	Metastatic cancer	TPN
Ductopenia	Lymphoma	Liver allograft rejection
AIDS cholangiopathy	Viral hepatitis	Acute alcoholic hepatitis
Cholestatic liver diseases (PBC, PSC)	Cirrhosis	Sickle cell liver crisis
Drug-induced liver injury	Vanishing bile duct syndrome	Sepsis
Liver Infiltrative diseases	Ischemic cholangiopathy	Congestive heart failure
Hepatic abscess	Benign recurrent cholestasis	Hemophagocytic lymphohistiocytosis
Hepatocellular carcinoma	Sarcoidosis	

Evaluation of ALP elevation

Causes of elevated ALP	
Non-hepatic	
Bone disease	Congestive heart failure
Osteomalacia	Childhood growth
Paget's disease	Infection
Primary bony malignancy	Inflammation
Bony metastases	Influx of ALP after a fatty meal
Hyperthyroidism	Blood type O and B
Hyeprparathyroidism	Myeloid metaplasia
Pregnancy (third trimester)	Peritonitis
Chronic renal failure	Diabetes mellitus
Lymphoma	Gastric ulcer
Extra-hepatic malignancy	Increasing age, especially women

Evaluation of ALP elevation



Algorithm for evaluation of elevated serum alkaline phosphatase.

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Evaluation of ALP elevation

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Evaluation of Bilirubin elevation

* Elevated unconjugated bilirubin is due to:
  * over-production of bilirubin (such as hemolysis)
  * decreased hepatic uptake
  * decreased hepatic conjugation (Gilbert's syndrome)
* Hemolysis infrequently causes a bilirubin level >5 mg/dl, unless co-existent renal disease, liver disease, or severe acute hemolysis is present.
* In Gilbert's syndrome, total bilirubin levels almost never exceed 6 mg/dl and are usually <3 mg/dl.
* Fasting or significant illness can increase the unconjugated bilirubin by 2- to 3-fold.

Evaluation of Bilirubin elevation

* In general, in asymptomatic healthy individuals who have mild unconjugated hyper-bilirubinemia (<4 mg/dl), evaluation should:
  * exclude medications that cause hyper-bilirubinemia
  * exclude evidence of hemolysis
  * confirm normal serum transaminases and ALP levels.
* If these are found, then a presumptive diagnosis of Gilbert's syndrome can be made and additional evaluation is not routinely necessary.
* Conjugated (direct) hyperbilirubinemia generally implies the presence of parenchymal liver damage or biliary obstruction.
* Total serum bilirubin levels may exceed 30 mg/dl in cases of severe liver damage, including alcoholic hepatitis with cirrhosis, and may be seen in advanced cirrhosis patients with sepsis and/or renal failure.
* isolated hyper-bilirubinemia may be seen after major surgery and typically resolves.

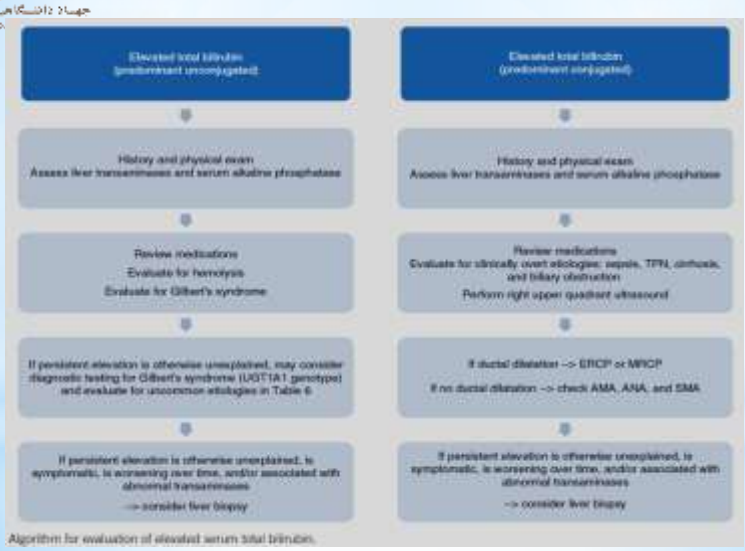
Evaluation of Bilirubin elevation

Causes of elevated Bilirubin		
Elevated unconjugated bilirubin		
Gilbert's syndrome	Ineffective erythropoiesis	Hyperthyroidism
Crigler-Najjar syndrome	Resorption of large hematomas	Medications
Hemolysis	Neonatal jaundice	Post-blood transfusion
Elevated unconjugated bilirubin		
Bile duct obstruction	Toxic hepatitis	Infiltrative diseases of the liver
Choledocholithiasis	Drug-induced liver injury	Sarcoid
Malignant obstruction	Acute alcoholic hepatitis	Granulomatous hepatitis
Bile duct fl ukes	Ischemic hepatitis	Tuberculosis
Bile duct stricture	Cirrhosis	Metastatic cancer
AIDS cholangiopathy	Primary biliary cirrhosis	Lymphoma
Viral hepatitis	primary sclerosing cholangitis	Hepatocellular carcinoma

Evaluation of Bilirubin elevation

Causes of elevated Bilirubin		
Elevated unconjugated bilirubin (count.)		
Wilson disease	Intrahepatic cholestasis of pregnancy	Ductopenia
Autoimmune hepatitis	Benign post-operative jaundice	Dubin-Johnson syndrome
Ischemic hepatitis	ICU or multifactorial jaundice	Rotor syndrome
Congestive hepatopathy	Benign recurrent cholestasis	Sickle cell liver crisis
Sepsis	Vanishing bile duct syndrome	Hemophagocytic lymphohistiocytosis
TPN		

Evaluation of Bilirubin elevation



Algorithm for evaluation of elevated serum total bilirubin.

Summary of recommendations

1. Before initiation of evaluation of abnormal liver chemistries, one should repeat the lab panel and/or perform a clarifying test to confirm that the liver chemistry is actually abnormal.
2. Testing for chronic hepatitis B is conducted with HBsAg testing. Testing for acute hepatitis B is with HBsAg and IgM anti-HBc.
3. Testing for chronic hepatitis C is conducted with anti-HCV and confirmation is performed with HCV-RNA by PCR.
4. Testing for acute Hepatitis A (IgM HAV) should occur in patients presenting with acute hepatitis and possible fecal-oral exposure.
5. Testing for acute hepatitis E (IgM HEV) should also be considered in those whose tests for acute hepatitis A, B, and C are negative.
6. People consuming alcohol with AST>ALT are at risk for alcoholic liver disease and should be counseled for alcohol cessation.

Summary of recommendations

7. Patients with features of metabolic syndrome including D.M., over-weight or obesity, hyperlipidemia, or hypertension with mild elevations of ALT should undergo screening for NAFLD with ultrasound.

8. All patients with abnormal liver chemistries in the absence of acute hepatitis should undergo testing for hereditary hemochromatosis with an iron level, transferrin saturation, and serum ferritin.

   * HFE gene mutation analysis should be performed in patients with transferrin saturation ≥45% and/or elevated serum ferritin.

9. Patients with abnormal AST and ALT, particularly patients with other autoimmune conditions, should undergo testing for autoimmune liver disease including ANA, ASMA, and globulin level.

10. Patients with persistently elevated AST or ALT should undergo screening for α1AT deficiency.

Summary of recommendations

11. Patients especially <55 with persistently elevated AST and ALT, should undergo screening for Wilson's with ceruloplasmin testing.

    * In the setting of low serum ceruloplasmin, 24-h urinary copper and slit-lamp eye examination (Kayser–Fleischer rings) should occur.

12. Physicians should ask patients with abnormal liver chemistries about prescribed and over-the-counter medications, non-prescribed complementary or alternative medicines, and dietary or herbal supp-lements which may be associated with drug-induced liver injury.

13. A liver biopsy may be considered when serologic testing and imaging fails to elucidate a diagnosis, to stage a condition, or when multiple diagnoses are possible.

14. An elevation of ALP should be confirmed with an elevation in GGT

    * GGT should not be used as a screening test for underlying liver disease in the absence of other abnormal liver chemistries.

Summary of recommendations

15. Patients with ALP elevation ± elevation of bilirubin should undergo testing for:

* primary biliary cholangitis (primary biliary cirrhosis) with testing for anti-mitochondrial antibody
* primary sclerosing cholangitis with MR cholangiography or ERCP in conjunction with IgG4

16. If ALT and/or AST levels <5X ULN:

* To assess for hepatitis B and C, alcoholic and NAFLD, hemochromatosis, Wilson's, α1AT deficiency, autoimmune hepatitis, drugs related injury.

17. If ALT and/or AST levels 5–15X ULN:

* To assess also for acute viral hepatitis.

18. If ALT and/or AST levels >15X ULN, or elevation ALT of >10,000 IU/l:

* To assess also for acetaminophen toxicity and ischemic hepatopathy (shock liver).