CLINICAL LABORATORY TESTING:

BLOOD CHEMISTRY & CBC ANALYSIS

FROM A FUNCTIONAL MEDICINE PERSPECTIVE

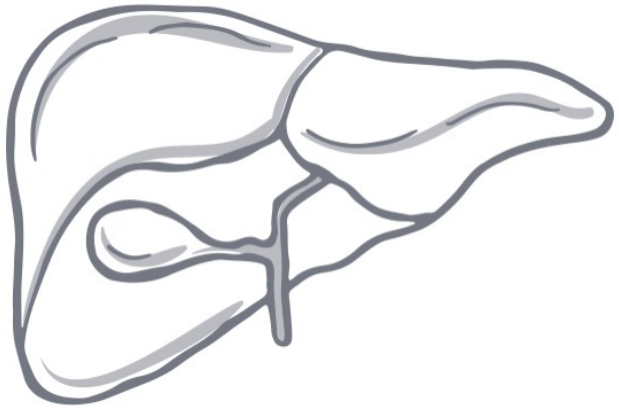
Part 3 of 8

Liver, Gallbladder, and Pancreas

Dr. Wayne Sodano, DC, DABCI, DACBN, CIHP, BCTN
Director of Clinical Support & Education, Evexia Diagnostics, Inc.

EVEXIA DIAGNOSTICS™

8 PART SERIES



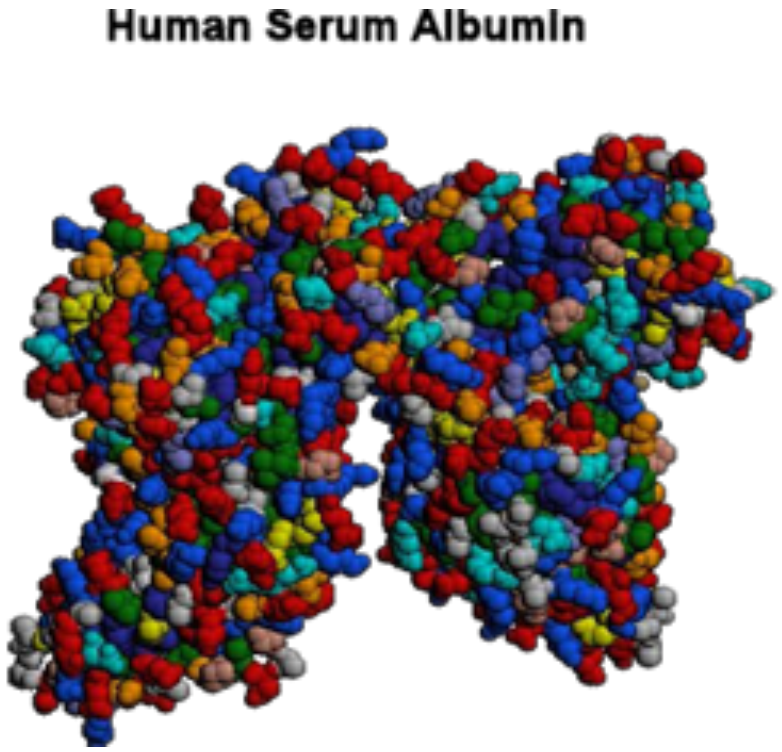
The liver is the largest organ in the body, contributing about 2% of the total body weight, or about 1.5 kg in the average adult human.

The main functions of the liver include:

- Filtration and storage of blood
- Metabolism of carbohydrates, proteins, fats, and hormone
- Detoxification of endogenous and exogenous substances
- Formation of bile
- Storage of vitamins and iron
- Formation of coagulation factors

Most of the plasma proteins are synthesized in the liver, which includes albumin and globulin. The **globulin** fraction includes hundreds of serum proteins including carrier proteins, enzymes, complement, and immunoglobulins (synthesized by plasma cells).

Albumin is the major protein component of serum.



EVEXIA DIAGNOSTICS™

Liver studies (function) are roughly divided by the particular functions of the liver:

- Synthetic liver function
- Excretory liver function and gallbladder function
- Hepatocellular injury
- Detoxification

Liver Function Assessment	Analyte Testing Considerations
Protein synthesis	Albumin Prealbumin PT/INR (Not sensitive to low level of liver damage)
Excretion into bile duct	Gamma-Glutamyl Transpeptidase Bilirubin Alkaline Phosphatase 5’ - Nucleotidase
Hepatocellular injury	Aspartate Aminotransferase Alanine Aminotransferase

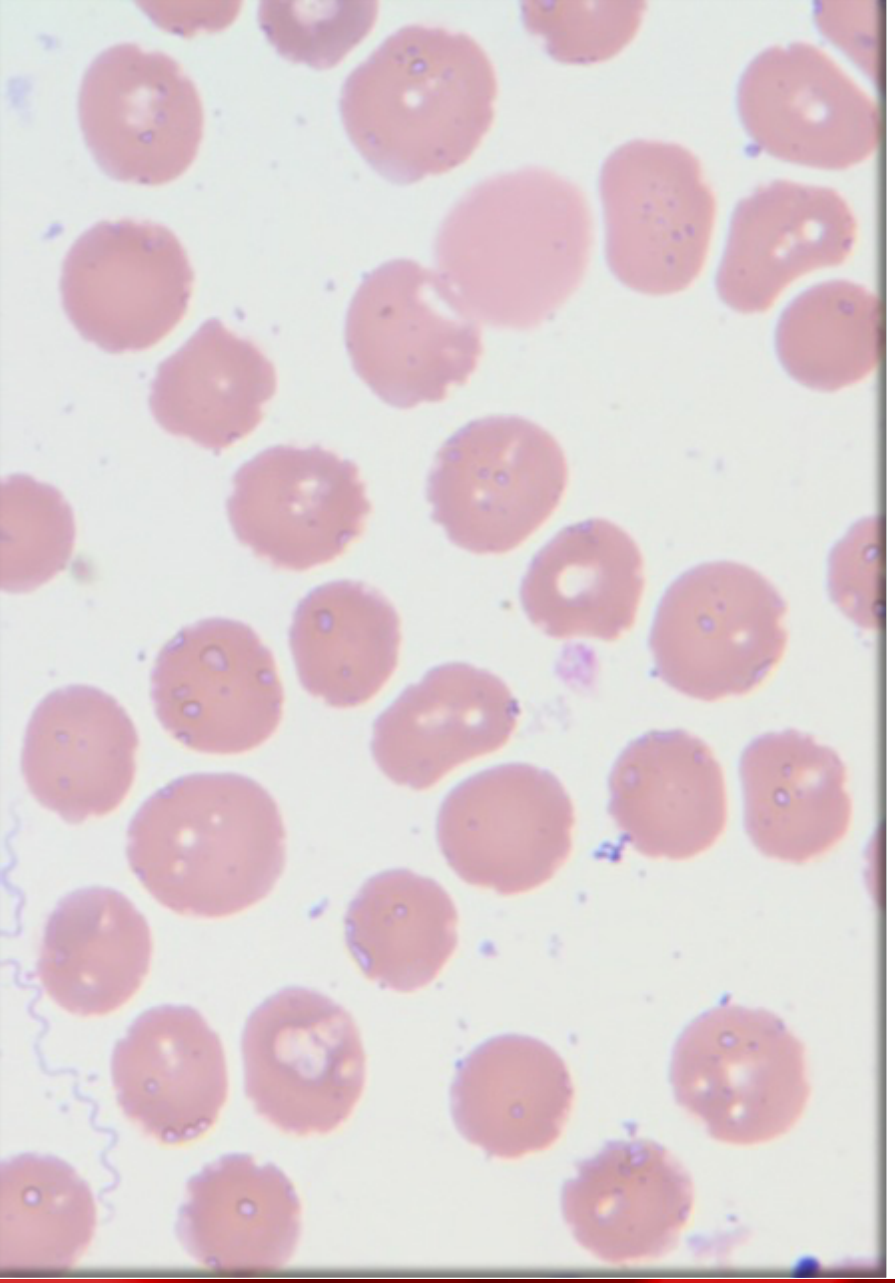
Total serum protein = albumin, prealbumin, and globulins.

Albumin makes up about 60% of the total serum protein and has a half-life of 12 to 18 days.

Albumin maintains colloidal osmotic pressure in the blood and acts as a transport carrier for hormones, enzymes and drugs

Prealbumin involved in the binding and transport of various solutes (e.g. thyroxin and retinol)

Globulins are used in the synthesis of antibodies. The sub-fractions of globulins include the alpha, beta, and gamma.



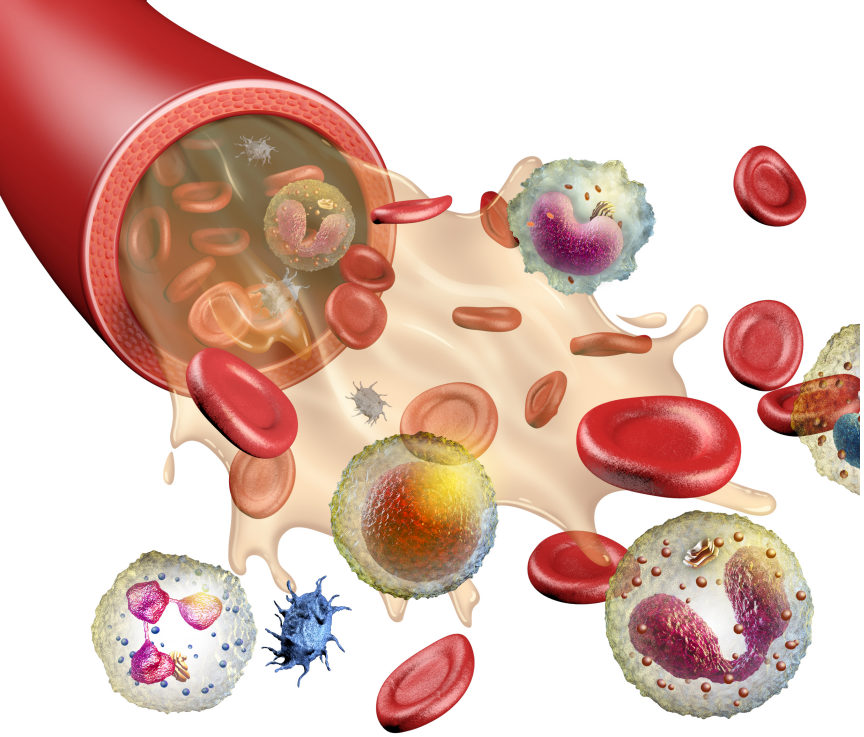
The liver is required for the synthesis of most clotting factors and serves as a large reservoir for these factors.

Only substantial liver damage (> 80% loss of synthesis) will result in abnormal INR, albumin and prealbumin values

EVEXIA DIAGNOSTICS™

Total Serum Protein, Albumin, Globulin, A/G Ratio

Analyte	Age	Reference Range g/dL (except prealbumin)	SI Units g/L (except prealbumin)	Optimal Range g/dL
Total Protein	Adult	6 – 8.5	60 – 85	6.9 – 7.4
Albumin	Adult	4.0 – 5.0	40 – 50	4 – 5
Total Globulins	Adult	2.3 – 3.4	23 – 34	2.0 – 3.5
		Chris Please delete the blank cells		
A/G Ratio	Adult	1.4 – 2.6	1.4 – 2.6	1.5 – 2.0



Total serum protein is a combination of pre-albumin, albumin, and globulins.

Total serum protein that is in the normal reference range does not mean that the quantity of each analyte "is within" the normal reference range. **The analytes must be viewed individually.**

Increased: Dehydration, digestive dysfunction may cause an increase in total serum globulin

Decreased: Protein malnutrition/need for digestive support (need for amino acids), digestive inflammation (i.e. enteropathies)

EVEXIA DIAGNOSTICS™

Pre-Albumin

Regarded as the best lab test of protein malnutrition.

Prealbumin can bind thyroxine, however it is secondary to thyroid-binding globulin in transportation of T3 and T4. It also plays a role in transport and metabolism of vitamin A.

Increased: Hodgkin's disease, pregnancy

Decreased: malnutrition, liver damage, burns, and inflammation (negative acute-phase reactant)

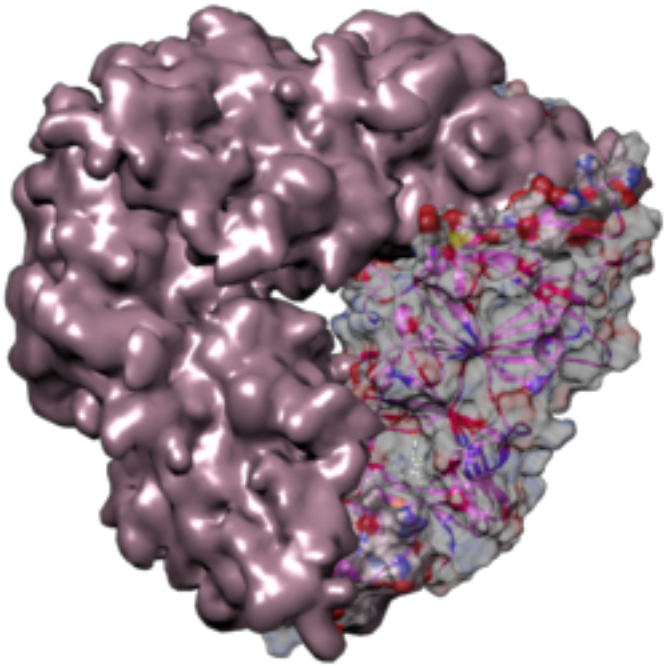
Albumin

Increased : Dehydration

Decreased : Chronic cachectic or wasting disease, chronic infections, inflammatory diseases, malnutrition, protein-losing enteropathies (e.g. Crohn disease), and digestive inflammation/malabsorption. **Albumin can serve as a negative acute-phase reactant.**

Total Globulins

The distribution of the globulin fractions must be taken into consideration when assessing an abnormal total globulin value. Total globulin is useful with other tests for assessing degenerative, inflammatory, infectious processes and a need for digestive support.



EVEXIA DIAGNOSTICS™

Albumin/Globulin Ratio

The value of the A/G ratio is limited due to the countless number of protein variables.

Increased: Generally of no clinical value.

Decreased: Indication of a rise in globulin, which can be attributed to a variety of causes such as cancer, inflammation, infection, and systemic diseases.

Excretion into the Bile Duct

- Gamma-Glutamyl Transpeptidase (GGT)
- Bilirubin (indirect and direct = total)
- Alkaline Phosphatase (ALP)
- 5’ - Nucleotidase

Analyte	Age	Reference Range	SI Units	Optimal Range
GGT	Adult	9- 58 units/L	Same	0- 30
Total Bilirubin	Adult	0.3 – 1.3 mg/dL	5.13 – 22.23 umol/L	0.1 – 1.2 mg/dL
Unconjugated (Indirect, insoluble) Bilirubin	Adult	0.2 – 0.9 mg/dL	3.42 – 15.39 umol/L	-----
Conjugated (Direct, water soluble) Bilirubin	Adult	0.1 – 0.4 mg/dL	1.71 – 6.84 umol/L	------
Alkaline Phosphatase	Adult	33 – 96 units/L	Same	70 - 96
5' - nucleotidase	Adult	0.0 – 1.6 units at 37° C	Same	------

Bile

- Cells of the liver produce bile (about 600 to 1000 mg/day), which passes through ducts within the liver to the gallbladder.
- Bile aids in digestion of fat and fat-soluble vitamin.
- Bile also serves to export toxins.
- Cholestasis is defined as a decrease in bile flow due to impaired secretion by hepatocytes or to obstruction of bile flow through intra- or extra-hepatic bile ducts.
- The effects of cholestasis are profound and widespread leading to worsening liver disease and systemic illness. The clinical presentation of cholestasis may include: scleral icterus, high level of conjugated bilirubin, cutaneous jaundice, pruritus, and xanthomas.

Gamma-Glutamyl Transpeptidase (GGT)

Transfer of amino acids and peptides across cellular membranes is responsible for extracellular metabolism of glutathione, the main antioxidant in cells.

The highest concentration found in the liver and biliary tract. Used to diagnose and monitor hepatobiliary disease.

Elevated GGT helps to identify a higher demand for glutathione due to excessive exposure to toxins or lifelong accumulation of toxicants.

Research has shown that patients who are obese with higher levels of GGT (between 40 – 60) may be experiencing an increased toxic burden, resulting in an elevated demand placed on glutathione production. Obese patients with elevated normal ranges of GGT levels have a higher association with diabetic risk. Elevated GGT is also a risk factor for myocardial infarction and stroke. GGT activity can catalyze the oxidation of low-density lipoprotein, a process involved in the pathogenesis of arthrosclerosis

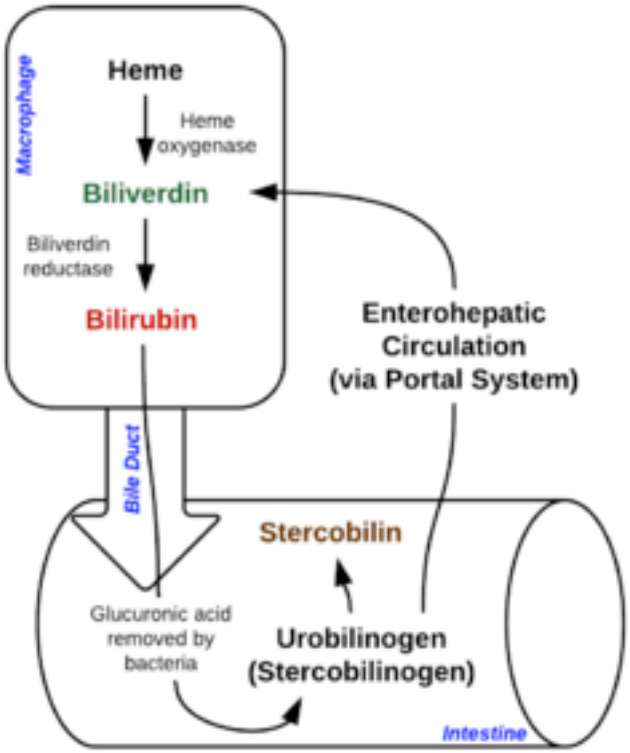
Increased GGT: Liver disease, alcohol abuse, primary biliary cirrhosis, fatty liver, cholestasis, pancreatitis, diabetes mellitus, hyperthyroidism, environmental toxin exposure and/or toxic body burden, oxidative stress, chronic inflammation, EBV, severe COPD, certain cancers, and RA

Decreased GGT: hypothyroidism

Bilirubin (Total = Direct + Indirect)

Bilirubin is formed from the hemoglobin that is released after the breakdown of RBCs via the reticuloendothelial system (mainly in the spleen).

The heme portion is catabolized to form biliverdin and subsequently transformed to unconjugated (indirect/insoluble) bilirubin. The unconjugated bilirubin enters the liver where it is conjugated (made water soluble) by a glucuronide, resulting in the formation of conjugated (direct) bilirubin.

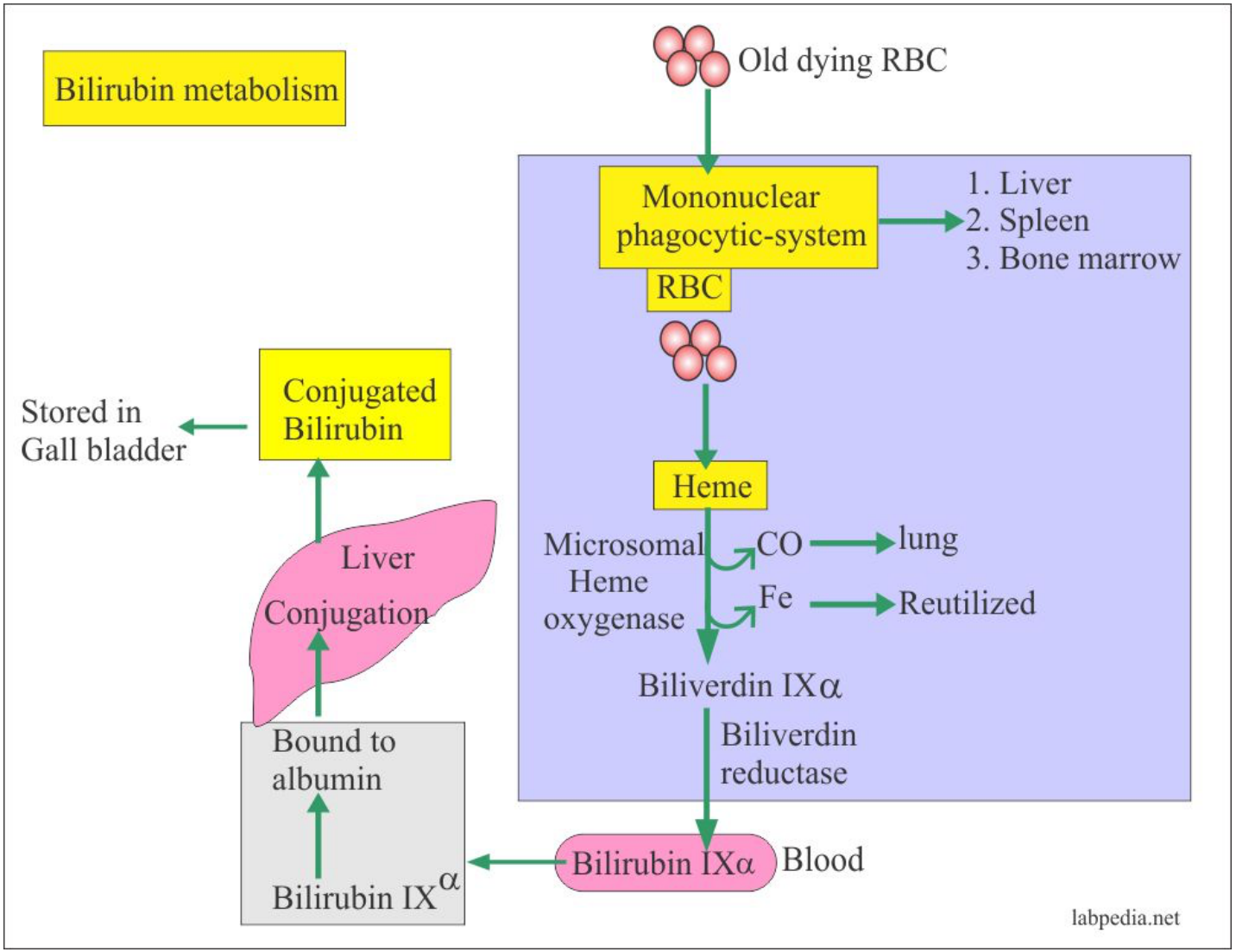


EVEXIA DIAGNOSTICS™

Bilirubin (total = direct + indirect)

(direct = conjugated → water soluble)

(indirect = unconjugated → water insoluble



EVEXIA DIAGNOSTICS™

Bilirubin (Total = Direct + Indirect)

Increased Total Bilirubin: Liver/biliary dysfunction

Increased Conjugated (direct, water soluble) bilirubin: gallstones, extra-hepatic duct obstruction (e.g. tumor, inflammation, scarring), drug induced cholestasis

Increased Unconjugated (indirect, insoluble) bilirubin: sickle cell anemia, hemolytic anemia, hepatitis, pernicious anemia, erythroblastosis fetalis, transfusion reaction, Gilbert syndrome.

Gilbert syndrome is an inherited, benign trait present in 3 to 5 % of the population. It's caused by the reduced production of hepatic glucuronyl transferase enzymes, resulting in intermittent mild elevation of unconjugated (indirect) bilirubin.

Alkaline Phosphatase

Alkaline phosphatase (ALP) refers to a group of isoenzymes that are found mainly in the **liver**, **bone**, small intestines, kidneys, placenta, and leukocytes.

Serum ALP is of interest in the diagnosis of two main groups of conditions: **hepatobiliary diseases** and **bone diseases** associated with increased osteoblastic activity (e.g. Paget's disease, malignant tumors, fractures and osteomalacia).

Moderate elevation in ALP is also seen in ulcerative colitis, regional enteritis, congestive heart failure, and Hodgkin's disease.

A cofactor for these enzymes is zinc; therefore a **zinc deficiency can cause low serum ALP**.

Elevation of ALP due to liver disease does not distinguish between intra- and extra-hepatic diseases; therefore it must be interpreted in concert with other analytes.

Increased ALP: liver disease (primary or metastatic), diabetes mellitus, bone disease (healing fractures, osteomalacia, Paget disease, hyperparathyroidism, sarcoidosis, **pregnancy about the 16th to 20th week**), hyperthyroidism, and renal disease

Decreased ALP: hypothyroidism, vitamin B12 deficiency, **excessive vitamin D ingestion**, vitamin C, zinc, and magnesium deficiency, **celiac disease**, scurvy, and hypophosphatemia

5’ – Nucleotidase (5’ – NT)

An intrinsic membrane glucoprotein that catalyzes hydrolysis of 5 – nucleotides to their corresponding nucleosides.

5’ – NT was described in heart and skeletal muscle about 60 years ago

Clinically useful for the differential diagnosis of hepatobiliary and osseous diseases; **the enzyme activity being increased only in hepatobiliary disease**.

Precise marker for early hepatic primary or secondary tumors

Hyder MA, Hasan M, Mohieledien. Comparative study of 5’-Nucleotidase Test in Various Liver Disease. J Clin Diagn Res. Feb 2016; 10(2): BC01 – BC03.

5’ – nucleotidase is an enzyme that is most often elevated in individuals with liver disease**. The presence of an elevated ALP with a normal 5’ – nucleotidase value suggests that ALP is elevated secondary to non-hepatic causes**. In other word, if the 5’ – nucleotidase is normal in the face of an elevated ALP, the pathologic source is outside the liver (e.g. bone, kidney, or spleen).

Increased 5’ – nucleotidase: bile duct obstruction, cholestasis, hepatitis, hepatic necrosis, ischemia, and tumor, hepatotoxic drugs.

Hepatocellular Injury Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT)

Analyte	Age	Reference Range Units/L	SI Units	Optimal Range
ALT	Adult	7-41	Same	6 - 29
AST	Adult	12 - 38	Same	10 - 35

Transaminases: metabolic links between carbohydrate and protein metabolism.

ALT is involved in the glucose-alanine cycle, and interchanges alanine and pyruvate; regenerate glucose consumed by the muscle.

AST is even more vital for aerobic glycolysis by allowing the NADH that is generated in the cytoplasm to be effectively relocated within the mitochondria through the shuffling of malate (as well as α-ketoglutarate, aspartate, and glutamate).

Both of these enzymes require the cofactor pyridoxal phosphate (B6) for activity. Therefore **a low serum level of both of these enzymes may be due to a B6 deficiency.**

It should also be kept in mind that most labs only measure the **active form** of these enzymes (i.e. only those with the B6 cofactor), meaning that if the patient is B6 deficient as is common in alcoholics, the levels of the enzymes may be falsely low.

ALT and AST analysis for hepatocellular damage

ALT is found mainly in the **hepatocytes**, with lesser quantities found in the kidneys, heart, and skeletal muscle.

AST is found in very high concentration within highly metabolic tissue, such as the heart, liver cells, skeletal muscle, and to a lesser degree in the kidneys, pancreas, and RBCs.

Damage to the hepatocytes causes the release of these enzymes even with minor levels of liver damage.

Both AST and ALT have half-lives of 17 and 47 hours respectively, so they reflect active hepatocyte damage

Liver abnormality is one of the associated extra-intestinal manifestations with celiac disease.

Modest elevation on serum aminotransferase levels is common in untreated celiac disease.

Celiac disease is a multi-systemic disease and abnormal unexplained elevated liver enzymes are common in individuals with celiac disease.

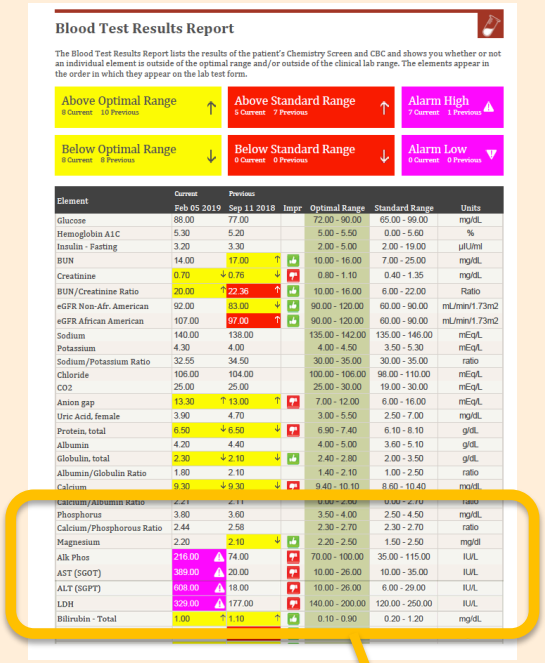
Patients with unexplained elevations of liver enzymes should be screened for celiac disease, as nine percent of patients with abnormal liver chemistries are diagnosed with celiac disease.

Increased AST: liver diseases, skeletal muscle diseases, acute hemolysis anemia, acute pancreatitis, celiac disease, and heart disease

Decreased AST: renal disease and vitamin B6 deficiency

Increased ALT: liver disease (high – hepatitis/ moderate – cirrhosis, cholestasis, obstructive jaundice, hepatotoxic drugs, hepatic tumor/ mild – pancreatitis, infectious mononucleosis)

Decreased ALT: vitamin B6 deficiency



Blood Test Results Report

The Blood Test Results Report lists the results of the patient's Chemistry Screen and CBC and shows you whether or not an individual element is outside of the optimal range and/or outside of the clinical lab range. The elements appear in the order in which they appear on the lab test form.

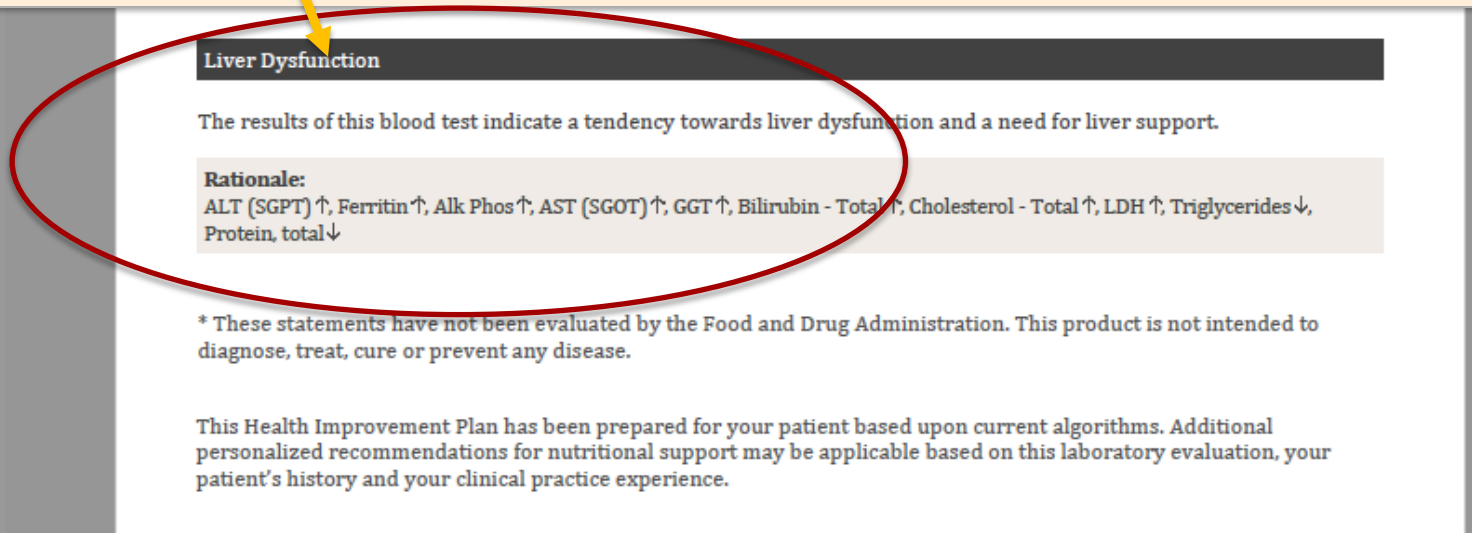
Above Optimal Range — 8 Current 10 Previous
Above Standard Range — 5 Current 7 Previous
Alarm High — 7 Current 1 Previous
Below Optimal Range — 8 Current 8 Previous
Below Standard Range — 0 Current 0 Previous
Alarm Low — 0 Current 0 Previous

Element	Current Feb 05 2019	Previous Sep 11 2018	Impr	Optimal Range	Standard Range	Units
Glucose	88.00	77.00		72.00 - 90.00	65.00 - 99.00	mg/dL
Hemoglobin A1C	5.30	5.20		5.00 - 5.50	0.00 - 5.60	%
Insulin - Fasting	3.20	3.30		2.00 - 5.00	2.00 - 19.00	µIU/ml
BUN	14.00	17.00 ↑		10.00 - 16.00	7.00 - 25.00	mg/dL
Creatinine	0.70	↓ 0.76		0.80 - 1.10	0.40 - 1.35	mg/dL
BUN/Creatinine Ratio	20.00	↑ 22.36 ↑		10.00 - 16.00	6.00 - 22.00	Ratio
eGFR Non-Afr. American	92.00	83.00		90.00 - 120.00	60.00 - 90.00	mL/min/1.73m2
eGFR African American	107.00	97.00 ↑		90.00 - 120.00	60.00 - 90.00	mL/min/1.73m2
Sodium	140.00	138.00		135.00 - 142.00	135.00 - 146.00	mEq/L
Potassium	4.30	4.00		4.00 - 4.50	3.50 - 5.30	mEq/L
Sodium/Potassium Ratio	32.55	34.50		30.00 - 35.00	30.00 - 35.00	ratio
Chloride	106.00	104.00		100.00 - 106.00	98.00 - 110.00	mEq/L
CO2	25.00	25.00		25.00 - 30.00	19.00 - 30.00	mEq/L
Anion gap	13.30	↑ 13.00 ↑		7.00 - 12.00	6.00 - 16.00	mEq/L
Uric Acid, female	3.90	4.70		3.00 - 5.50	2.50 - 7.00	mg/dL
Protein, total	6.50	↓ 6.50 ↓		6.90 - 7.40	6.10 - 8.10	g/dL
Albumin	4.20	4.40		4.00 - 5.00	3.60 - 5.10	g/dL
Globulin, total	2.30	↓ 2.10 ↓		2.40 - 2.80	2.00 - 3.50	g/dL
Albumin/Globulin Ratio	1.80	2.10		1.40 - 2.10	1.00 - 2.50	ratio
Calcium	9.30	↓ 9.30 ↓		9.40 - 10.10	8.60 - 10.40	mg/dL
Calcium/Albumin Ratio	2.21	2.11		0.00 - 2.60	0.00 - 2.70	ratio
Phosphorus	3.80	3.60		3.50 - 4.00	2.50 - 4.50	mg/dL
Calcium/Phosphorous Ratio	2.44	2.58		2.30 - 2.70	2.30 - 2.70	ratio
Magnesium	2.20	2.10 ↓		2.20 - 2.50	1.50 - 2.50	mg/dl
Alk Phos	216.00 !	74.00		70.00 - 100.00	35.00 - 115.00	IU/L
AST (SGOT)	389.00 !	20.00		10.00 - 26.00	10.00 - 35.00	IU/L
ALT (SGPT)	608.00 !	18.00		10.00 - 26.00	6.00 - 29.00	IU/L
LDH	329.00 !	177.00		140.00 - 200.00	120.00 - 250.00	IU/L
Bilirubin - Total	1.00	↑ 1.10 ↑		0.10 - 0.90	0.20 - 1.20	mg/dL

FHR shows ELEVATED AST & ALT

The Functional Health Report highlights out-of-range analytes and then provides a summary of possible health conditions related to the results in multiple summary areas like, Health Improvement Plan, Functional Index Report and Clinical Dysfunctions Report.

Here is an example of the summary, from a report with Alarmingly High ALT and AST levels, provided in the **Health Improvement Plan** section of the FHR.



Liver Dysfunction

The results of this blood test indicate a tendency towards liver dysfunction and a need for liver support.

Rationale:
ALT (SGPT) ↑, Ferritin ↑, Alk Phos ↑, AST (SGOT) ↑, GGT ↑, Bilirubin - Total ↑, Cholesterol - Total ↑, LDH ↑, Triglycerides ↓, Protein, total ↓

* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

This Health Improvement Plan has been prepared for your patient based upon current algorithms. Additional personalized recommendations for nutritional support may be applicable based on this laboratory evaluation, your patient's history and your clinical practice experience.

Guide for Interpreting Liver Enzymes

ALP	GGT, 5'-Nucleotidase	ALT and AST	Differential Diagnosis
Mildly elevated	WNL	WNL	Pregnancy, non-hepatic causes
Moderately elevated	Markedly elevated	WNL of slightly elevated	Cholestatic syndrome
Mildly elevated	Mildly elevated	Markedly elevated	Hepatocellular disease

If the patient is taking medication, consider drug-induced toxic liver damage as a cause of elevated enzymes

Isolated Abnormalities in Liver Function Test Results

Test	Non-Hepatic Source
Bilirubin	Red blood cells (e.g. hemolysis, intra-abdominal bleeding, hematoma)
AST	Skeletal muscle, cardiac muscle, and red blood cells
ALT	Skeletal muscle, cardiac muscle, and kidneys
LDH*	Heart, red blood cells (e.g. hemolysis)
ALP	Bone, first trimester placenta, kidneys,
GGT	Environmental toxin exposure and/or toxic body burden, oxidative stress, drugs, alcohol, chronic inflammation, EBV, severe COPD, certain cancers, and RA
Bilirubin	Gilbert's syndrome (total and/or unconjugated)

Modest elevation on serum aminotransferase levels is common in untreated celiac disease.

Pancreatic Enzymes

Analyte	Age	Reference Range units/L	SI Units	Optimal Range
Amylase	Adult	5 - 125	Same	Same
Lipase	Adult	0 - 50	Same	Same

Amylase and Lipase

Amylases are a group of enzymes that breakdown (i.e. digests) starch into glucose. Most circulating amylase originates from the **pancreas and salivary glands** accounting for 40 to 60 % of the total serum amylase.

The kidneys are responsible to clearing about 25% of the amylase from the blood; therefore kidney dysfunction can cause an elevation in serum amylase.

The main diagnostic use of serum amylase is to diagnose and monitor pancreatitis. However; this analyte has a low sensitivity, with about 20% of patients with acute pancreatitis having normal levels

Increased Serum Lipase: Pancreatic disease, biliary disease, renal failure, intestinal diseases (e.g. infarction, bowel obstruction), drugs, salivary gland inflammation

Lipase is an enzyme secreted by the pancreas into the duodenum to breakdown triglycerides into fatty acids and glycerol.

Most of the serum lipase is of pancreatic origin, which makes it more specific than amylase for pancreatic disease .

The most common cause of elevated serum lipase is acute pancreatitis.

Increased Serum Lipase: Pancreatic disease, biliary disease, renal failure, intestinal diseases (e.g. infarction, bowel obstruction), drugs, salivary gland inflammation.

Lactic Dehydrogenase (Isoenzymes)

Analyte	Reference Range units/L	SI Units	Optimal Range units/L
LD (total)	110-240	Same	120 - 190

Lactic dehydrogenase is an intracellular enzyme that occurs exists in the cytoplasm of all cells, and represents a group of enzymes (isoenzymes) involved in **carbohydrate metabolism**.

Catalyzes the inter-conversion of lactate and pyruvate.

Highest concentrations of LD are found in the heart, liver, RBCs, skeletal muscle, and kidneys, with lesser concentrations in the brain, lung, and smooth muscle.

Total serum LD can be elevated for a variety of pathological reasons. An isoenzyme study can help isolate the potential cause of the elevation.

Percentage of Activity of LD Isoenzymes in Tissue

Organ	LD-1	LD-2	LD-3	LD-4	LD-5
Heart	60	30	5	3	2
Liver	0.2	0.8	1	4	94
Kidney	28	34	21	11	6
Cerebrum	28	32	19	16	5
Skeletal muscle	3	4	8	9	76
Lung	10	18	28	23	21
Spleen	5	15	31	31	18
RBCs	40	30	15	10	5
Skin	0	0	4	17	79

LD Isoenzyme Patterns in Selected Conditions

Condition	Increased LD Isoenzyme(s)
Acute myocardial infarction	LD-1 more than LD-2
Sickle cell crisis	LD-1 and LD-2
Early hepatitis	LD-5 (may become normal, even when ALT is still rising)
Malignant lymphoma	LD-3 and LD-4 (LD-2 may also increase)
Carcinoma of the prostate	LD5; LD-5 to LD-1 ratio is greater than 1
Dermatomyositis	LD-5
SLE	LD-3 and LD-4
Collagen disorders	LD-2, LD-3 and LD-4
Congestive heart failure	LD-2, LD-3 and LD-4
Viral infections	LD-2, LD-3 and LD-4
Various neoplasms	LD-2, LD-3 and LD-4
Strenuous physical exercise	LD-4 and LD-5
Benign prostatic hypertrophy Uterine hypertrophy	LD-4
Pancreatitis	LD-4
Asthma	LD3 and LD5
Infectious mononucleosis	LD-1, LD-2, LD3 and LD-5

Ask the Doctor

A **FREE** service available to all Evexia clients, accessed via your Evexia Clinician Portal. Dr. Wayne Sodano, will **review test results, clinical conditions, further test recommendations or answer any other questions you may have via email**. In addition our clients have the option of scheduling either a **telephone or video conference for a fee.**

To learn more about Evexia Diagnostics

www.evexiadiagnostics.com

(888) 852-2723

Live chat is available at
www.evexiadiagnostics.com

info@evexiadiagnostics.com

18 Titus Road / PO Box 1272
Washington, CT 06793

Office Hours
Monday - Friday, 8am - 8pm ET

Dr. Wayne L. Sodano
DC, DABCI, DACBN, CFMP, CIHP, BCTN

Next lesson: Part 4 of 8
Electrolytes, Minerals and Acid-Base