Interpretation of Clinical Laboratory Tests

- Generally, laboratory tests should be ordered only if the results of the test will affect decisions about the care of the patient.

- The serum, urine, and other bodily fluids can be analyzed routinely.

- A variety of factors can interfere with the accuracy of laboratory tests.

- Patient-related factors (e.g., age, gender, weight, height, time since last meal) can affect the range of normal values for a given test.

- Laboratory-based issues can also influence the accuracy of laboratory values. For example, a specimen can be spoiled because of improper handling or processing (e.g., hyperkalemia due to hydrolysis of a blood specimen); because it was taken at a wrong time (e.g., fasting blood glucose level taken shortly after a meal); because collection was incomplete (e.g., 24-hour urine collection that does not span a full 24-hour period);

Units of Measure:

- The International System of Units (SI) reports clinical laboratory values using the metric system. For example, the basic unit of mass for the SI system, the mole is not influenced by the added weight of salt or ester formulations.

- The mole, therefore, is technically and pharmacologically more meaningful than the gram because each physiological reaction occurs on a molecular level.

Electrolytes and Blood Chemistries

Sodium: Normal: 135–145 mEq/L or mmol/L.

Sodium is the predominant cation of extracellular fluid (ECF). Only a small amount of sodium (~5 mEq/L) is in intracellular fluid (ICF).

Along with chloride, potassium, and water, sodium is important in establishing serum osmolarity and osmotic pressure relationships between ICF and ECF.

Dietary intake of sodium is balanced by renal excretion of sodium, which is regulated by aldosterone (enhances sodium reabsorption), natriuretic hormone (increases excretion of sodium), and antidiuretic hormone (enhances reabsorption of free water).

An increase in the serum sodium concentration could suggest either impaired sodium excretion or volume contraction. Conversely, a decrease in the serum sodium concentration to less-than-normal values could reflect hypervolemia, abnormal sodium losses, or sodium starvation.

- Although healthy individuals are able to maintain sodium homeostasis without difficulty, patients with kidney failure, heart failure, or pulmonary disease often encounter sodium and water imbalance.

- In adults, changes in serum sodium concentrations most often represent water imbalances rather than sodium imbalances.

- Hence, serum sodium concentrations are more reflective of a patient's fluid status rather than sodium balance.

Potassium

Normal: 3.5–5.0 mEq/L or mmol/L:

potassium is the major intracellular cation in the body. The potassium ion in the ECF is filtered freely at the glomerulus of the kidney, reabsorbed in the proximal tubule, and secreted into the distal segments of the nephron.

Because the majority of potassium is sequestered within cells, a serum potassium concentration is not a good measure of total body potassium.

Fortunately, the clinical manifestations of potassium deficiency (e.g., fatigue, drowsiness, dizziness, confusion, electrocardiographic changes, muscle weakness, muscle pain) correlate well with serum concentrations.

The serum potassium concentration is buffered and can be within normal limits despite abnormalities in total body potassium.

- Prolonged intravenous therapy with potassium-free solutions in a patient unable to obtain potassium in foods (e.g., nothing by mouth [NPO] patient) can result in hypokalemia.

- Hypokalemia can also be induced by osmotic diuresis (e.g., mannitol, glucosuria), thiazide or loop diuretics, excessive mineralocorticoid activity, or protracted vomiting.

- The loss of large amounts of colonic fluid through severe diarrhea can cause potassium depletion because fluid in the colon is high in potassium content (i.e., 30–40 mEq/L).

- Insulin and stimulation of β_2-adrenergic receptors can also induce hypokalemia because both increase the movement of potassium into cells from the extracellular fluid.

- Hyperkalemia most commonly results from decreased renal excretion of potassium, excessive exogenous potassium administration (especially when combined with a potassium-sparing diuretic), or excessive cellular breakdown (e.g., hemolysis, burns, crush injuries, surgery, infections).

- Metabolic acidosis also can induce hyperkalemia as hydrogen ions move into cells in exchange for potassium and sodium.

Blood Urea Nitrogen

Normal: 8–18 mg/dL or 2.8–6.4 mmol/L:

Urea nitrogen is an end product of protein metabolism.

It is produced solely by the liver, is transported in the blood, and is excreted by the kidneys.

The serum concentration of urea nitrogen (i.e., BUN) is reflective of renal function because the urea nitrogen in blood is filtered completely at the glomerulus of the kidney, and then reabsorbed and tubularly secreted within nephrons.

Acute or chronic renal failure is the most common cause of an elevated BUN.

Creatinine

Normal: 0.6–1.2 mg/dL or 50–110 µmol/L:

Creatinine is derived from creatine and phosphocreatine, major constituents of muscle.

Its rate of formation for a given individual is remarkably constant and is determined primarily by an individual's muscle mass or lean body weight.

Therefore, the SCr concentration is slightly higher in muscular subjects, but unlike the BUN, it is less directly affected by exogenous factors or liver impairment.

- A doubling of the SCr level roughly corresponds to a 50% reduction in the GFR.

- This general rule of thumb only holds true for steady-state creatinine levels.

Creatinine Clearance

Normal: 75–125 mL/minute or 1.25–2.08 mL/second:

- Because creatinine is cleared almost exclusively through the glomerulus in the kidney, CrCl can be used as a clinically useful measure of a patient's GFR.

- CrCl serves as a valuable clinical parameter because many renally eliminated drugs are dose adjusted based on the patient's renal function.

- To determine actual CrCl, the patient's urine is collected over a 24-hour period, and the concentration of urine creatinine (mg/dL), total volume of urine collected over the 24-hour period (mL/minute), and SCr (mg/dL) are determined.

The Cockcroft-Gault formula

$$\text{Estimated CrCl for males (mL/min)} = \frac{(140 - \text{Age})\,(\text{Body weight in kg})}{(72)\,(\text{SCr}_{(\text{mg/dL})})} \quad \textbf{2-3}$$

the Jelliffe method

$$\text{Estimated CrCl for Males (mL/min/1.73 m}^2) = \frac{98 - [(0.8)\,(\text{Age} - 20)]}{\text{SCr}_{(\text{mg/dL})}} \quad \textbf{2-4}$$

Glycosylated Hemoglobin:

- Glucose molecules irreversibly bind to Hgb which results in glycosylated Hgb (A1c).

- The concentration of Hgb A1c, therefore, reflects a patient's average blood glucose concentration over the life span of circulating RBCs.

- In contrast, fasting glucose serum concentrations can fluctuate acutely based on either meals or insulin use.

- As a result, measurement of Hgb A1c concentrations provides a much better tool for evaluating chronic diabetes therapy.

Calcium

Normal: 8.8 to 10.2 mg/dL or 2.20 to 2.55 mmol/L:

- The total calcium content resides primarily in the bone, with only about 1% freely exchangeable with that in the ECF.

- This reservoir of calcium in bones maintains the concentration of calcium in the plasma constant despite pronounced changes in the external balance of calcium.

- If the homeostatic factors (i.e., parathyroid hormone, vitamin D, calcitonin) that regulate the calcium content of body fluid are intact, a patient can lose 25% to 30% of total body calcium without a change in the concentration of calcium ion in the plasma.

- A reduced calcium concentration usually implies a deficiency in either the production or the response to parathyroid hormone or vitamin D.

- The abnormality in the parathyroid hormone system might result from hypomagnesemia, hypoparathyroidism, or pseudohypoparathyroidism.

- The abnormality in the vitamin D system can be caused by decreased nutritional intake; decreased absorption of vitamin D secondary to gastrectomy, chronic pancreatitis, or small bowel disease; decreased production of 25-hydroxycholecalciferol due to liver disease; increased metabolism of 25-hydroxycholecalciferol because of enzyme-stimulating drugs (e.g., phenobarbital, phenytoin, rifampin); or decreased production of 1,25-dihydroxycholecalciferol due to chronic renal disease.

- Elevated calcium concentrations are commonly associated with malignancy or metastatic diseases.

- Other causes of hypercalcemia include hyperparathyroidism, Paget disease, milk-alkali syndrome, granulomatous disorders, thiazide diuretics, and vitamin D intoxication.

Uric Acid

Normal: 2.0 to 7.0 mg/dL or 0.12 to 0.42 mmol/L:

- Uric acid is an end product of purine metabolism. It serves no biological function, is not metabolized, and must be excreted renally.

- Gout is usually associated with increased serum concentrations of uric acid and deposits of monosodium urate.

- Increased serum uric acid concentrations can result from either a decrease in urate excretion (e.g., renal dysfunction) or excessive urate production (e.g., increased purine metabolism resulting from cytotoxic therapy of neoplastic or myeloproliferative disorders).

- Low serum uric acid concentrations are inconsequential and are usually reflective of drugs that have hypouricemic activity (e.g., high dosages of salicylates).

Proteins:

Prealbumin:

Prealbumin is an effective and useful marker of immediate nutritional status.

Hepatic disease and malnutrition are associated with decreases in both albumin and prealbumin. Hodgkin disease, pregnancy, chronic renal disease, and corticosteroid use can increase prealbumin serum concentrations.

Albumin:

- hypoalbuminemic states are commonly associated with edema and transudation of ECF.

- A lack of essential amino acids from malnutrition or malabsorption, or impaired albumin synthesis by the liver, can result in decreased serum albumin concentrations.

- Most forms of hepatic insufficiency are associated with decreased synthesis of albumin.

- Albumin can be lost directly from the blood because of hemorrhage, burns, or exudates, or it may be lost directly into the urine because of nephrosis.

Enzymes

Creatine Kinase:

Normal: 0 to 150 units/L or 0 to 2.5 µkat/L

- The CK enzyme, formerly known as creatine phosphokinase, catalyzes the transfer of high-energy phosphate groups in tissues that consume large amounts of energy (e.g., skeletal muscle, myocardium, brain).

- The serum concentration of CK can be increased by strenuous exercise, intramuscular injections of drugs that are irritating to tissue (e.g., diazepam, phenytoin), acute psychotic episodes, crush injuries, or myocardial damage.

Troponin

Normal: 0 to 0.03 ng/mL or 0 to 0.03 mcg/L

- Troponins are proteins that mediate the calcium-mediated interaction of actin and myosin within muscles.

- There are two cardiac-specific troponins, cardiac troponin I (cTnI) and cardiac troponin T (cTnT). Whereas cTnT is present in cardiac and skeletal muscle cells, cTnI is present only in cardiac muscle.

Brain Natriuretic Peptide

Normal: 0 to 100 pg/mL or 0 to 100 ng/L

- Brain natriuretic peptide (BNP) is released from the heart when increased demands are placed on the myocardial tissue.

- Elevations in BNP are indicative of patients with congestive heart failure (CHF).

Liver Function Tests:

Aspartate Aminotransferase

Normal: 0 to 35 units/L or 0 to 0.58 µkat/L

The AST enzyme, formerly called “serum glutamic oxaloacetic transaminase,” is abundant in heart and liver tissue and moderately present in skeletal muscle, the kidney, and the pancreas.

In cases of acute cellular injury to the heart or liver, the enzyme is released into the blood from the damaged cells.

In clinical practice, AST determinations have been used to evaluate myocardial injury and to diagnose and assess the prognosis of liver disease resulting from hepatocellular injury.

Alanine Aminotransferase

Normal: 0 to 35 units/L or 0 to 0.58 µkat/L

- The ALT enzyme, formerly called “serum glutamic pyruvic transaminase,” is found in essentially the same tissues that have high concentrations of AST.

- Elevations in serum ALT are more specific for liver-related injuries or diseases.

- Evaluating the ratio of ALT to AST can be potentially useful, particularly in the diagnosis of viral hepatitis.

- The ALT/AST ratio frequently exceeds 1.0 with alcoholic cirrhosis, chronic liver disease, or hepatic cancer. However, ratios <1.0 tend to be observed with viral hepatitis or acute hepatitis, which can be useful when diagnosing liver disease.