Interpreting Laboratory Tests

LAB TESTS

1. Why?
   - To aid diagnosis
   - To monitor progress
   - To determine correct dosage

2. Relationship to pharmacy
   - Altered dose in renal failure, liver failure, e.g., digoxin.
   - Drugs may affect lab test results, e.g., urine glucose tests.
   - Monitoring serum drug levels, e.g., tobramycin pre and post levels.
   - Monitoring results of treatment, e.g., effect of antibiotic therapy on WBC in bacterial infection

3. "Normal"
   - Statistical normal, e.g., gaussian curve
   - Depends on equipment and method used; thus may vary between different labs. Use the "normal values" table for appropriate lab.
   - Test may be inaccurate, e.g., hemolyzed RBC and potassium level, failure to refrigerate urine specimens, inaccurate timing - drug post levels.
   - Important to interpret for the patient and disease states involved, e.g., calcium level with hypoproteinemia.

TREAT THE PATIENT, NOT THE LAB DATA.

4. Example of orders that might be written when a patient is admitted to hospital:
   - Admit
   - AAT, DAT
   - Vital signs, routine
   - CBC + diff, platelets, morphology
   - PT/PTT, B12, folate, T4
   - Lytes, BUN, CR, Ca, PO5, Mg
   - AST, LDH, amylase, alk phos, bilirubin (T+D)
   - Serum protein electrophoresis
   - Fasting blood glucose, T/G, cholesterol
   - MSU for C&S
   - 24-hour urine collection for protein and creatinine

ELECTROLYTES

1. Three fluid compartments in the body:
   - Intravascular - inside RBC plus in serum
   - Interstitial fluid
   - Intracellular extravascular
   - Usually it is the **serum concentration** that is measured which usually reflects the concentration in the other compartments, but not always.
   - Concentration depends on water present.

2. Most common measurements:
   - Sodium
     - Major extracellular cation
     - Hyponatremia - often due to edema = relative increase in free body water
       Hypernatremia - often due to dehydration

- Potassium
    - Major intracellular cation
    - Hypokalemia - tied to alkalosis
        - body cells - H+ and K+ exchange
        - renal - H+ and Na+ exchange, Na+ and K+ exchange
        - Hypokalemia plus digitalis toxicity
    - Hyperkalemia - renal failure
- Chloride - major anion
- Note relationship to acid-base balance, renal function.
- Kidney set up to conserve body sodium, excrete potassium and H+
- Calcium - 50% plasma protein may result in abnormally low total serum calcium level, but normal unbound calcium fraction

RENAL FUNCTION

1. Serum creatinine and creatinine clearance

- Creatinine - metabolic product of dephosphorylation of creatine phosphate in muscle
- Relatively constant production hourly and daily
- Excreted by glomerular filtration 70-80% plus tubular secretion
- Relatively sensitive indicator of renal function - creatinine clearance usually parallels GF by +/- 10%
- Factors that may affect test:
    - Depends on muscle mass - lower in females
    - GFR decreases with age
    - Inaccurate at low filtration rates because of the relatively high proportion of secreted fraction
- Creatinine clearance:
    - Normal 1.5 - 2.0 mL/S
    - Requires 24-hour urine collection
    - Or estimate from serum creatinine level:

$$\text{Cockroft-Gault formula: } ClCr = \frac{(140\text{-age}) \times 1.5 \; (\times 0.85 \; ♀)}{SCr \text{ umol/mL}}$$

2. Blood urea nitrogen (BUN)

- Urea - end product of protein metabolism
- Urea is excreted by glomerular filtration plus 40% is reabsorbed.
- Less sensitive index of renal failure because affected by non-renal parameters;
    - protein catabolism rate
    - dietary protein intake
    - hydration
- Clearance most useful in moderate renal failure
- Serum creatinine rises later than BUN

3. Intravenous pyelogram (IVP)

- A radiologic technique: uses contrast material which is secreted by the kidney tubules, then concentrated. Result shows urinary tract outline, revealing obstructions, plus demonstrates ability of kidney to concentrate.

4. Specific gravity

- Ability of kidneys to concentrate is one of the earliest functions lost in renal disease.

URINALYSIS

- Detects renal or non-renal dysfunction.

1. Colour

- Red: Blood, porphyria, phenolphthalein
- Brown: Blood, alkaptonuria, melanin
- Dark orange: Bile, pyridium

2. Protein

- Glomerular membrane normally prevents most large protein molecules from escaping from blood into urine. The small amount that may normally be present in urine is at a low, usually undetectable level.
- Proteinuria indicates dysfunction or specific state: kidney disease, pregnancy, fever, venous congestion, hypertension, multiple myeloma (Bence Jones protein), severe muscle exertion.

3. Glucose

- Normally actively reabsorbed to a maximum threshold (≅ 180 mg/100 mL blood glucose)
- Threshold varies with age, individual.
- Tests use copper reduction or glucose oxidase reactions, which may be affected by concurrent drug administration.
- To diagnose diabetes mellitus, to monitor diabetic control.

4. Sediment

- Normally few cellular elements are excreted.
- Urine sediment examined under microscope.
- RBC
- WBC
- "Casts":
    - muco-protein conglomerates, which may contain RBCs, WBCs, or renal epithelial cells
    - or may be mostly protein - hyaline casts
    - usually cylindrical since they conform to the shape of the renal tubules
    - significance: related to proteinuria, stasis in urinary tract

HEMATOLOGY

- **Complete Blood Count (CBC)**
    - Measure hemoglobin and hematocrit (anemia), RBC count, WBC count, WBC differential, RBC morphology

1. Hemoglobin (Hgb)

- Index of O2 - carrying capacity of blood
- in anemia, hemorrhage

2. Hematocrit (Hct)

- Packed cell volume = % of whole blood volume that is RBC
- Rapidly performed, indicates RBC count
- in anemia, hemorrhage

3. RBC

- Examine number per cubic mm, size, shape, colour, maturation, content
- Affected by posture, extreme exercise, excitement, age, sex, altitude, dehydration
- MCV - Mean Corpuscular Volume = average RBC size
- MCHC - Mean Corpuscular Hemoglobin Concentration

4. Classification of anemias

- Classify in order to pinpoint etiology of the anemia.
- Classify by:
    - RBC size = by MCV - microcytic, normocytic, macrocytic
    - RBC colour = by MCHC - hypochromic = low hemoglobin

e.g., microcytic hypochromic anemia - may be due to iron deficiency
macrocytic normochromic anemia - associated with folic acid deficiency

5. WBC

- defence
- leukocytosis = increased # WBC - suggests invading organism, tissue destruction
- WBC count changes with age, stress, exercise, diurnal rhythm
- WBC differential:
    - Calculate % of each of the 5 types of WBC.
    - lymphocytosis - commonly due to viral infection
    - eosinophilia - associated with allergic conditions, parasites

- immature band neutrophils - appear if prolonged heavy demand for neutrophils results in release of immature cells = "shift to the left" - referring to usual left to right illustration of neutrophil development

6. Reticulocyte count

- Reticulocyte = immature, non-nucleated RBC
- Normal RBC development: nucleated → reticulocyte → non-nucleated mature RBC
- Increased count means increased RBC production, e.g., hemorrhage, hemolysis, recovery from anemia

7. Platelet Count

- Platelets involved in clotting process
- Chemotherapy → bone marrow depression → thrombocytopenia

BLOOD COAGULATION

1. Prothrombin time (PT)

- Tissue thromboplastin + calcium + patient's plasma area combined.
- Indicates defects in Stage III (prothrombin; factors V, VII, X)
- Altered by liver disease, vitamin K disorders, coumadin therapy
- Also affected by heparin therapy
- Used to monitor warfarin anticoagulation - want PT 2-2.5 x control
- Also to diagnose hemorrhagic problems

2. Activated partial thromboplastin time (APTT)

- Combine incomplete thromboplastin reagent (= partial thromboplastin, no factors), + calcium + patient's plasma + activators)
- Sensitive to defects in Stage II, also severe III and IV
- Used to monitor heparin coagulation - want APTT 1½ - 2½ x normal
- Test also affected by warfarin
- Also to diagnose hemorrhagic problems

BLOOD GASES

- Acid-base balance very important: pH outside 6.8-7.8 will not support life.
- Blood pH is determined by the ratio of bicarbonate ion to carbonic acid:

$$pH = pKa + log\ \frac{base}{acid}$$

$$\text{pH} \propto \frac{HCO_3}{H_2CO_3}$$

- HCO_3 concentration regulated by kidney
- H_2CO_3 concentration proportional to partial pressure of carbon dioxide and regulated by lung

1. Total CO_2

- Measures sum of HCO_3, H_2CO_3 and dissolved CO_2
- Mainly HCO_3 → gives the numerator
- Normal value 20-30 mEq/L

2. pCO_2

- Partial pressure of CO_2 ∝ dissolved CO2
- Since most H_2CO_3 is present as dissolved CO_2, this gives the denominator

3. pH

4. Acidosis/Alkalosis

- Classified as to metabolic or respiratory cause

Metabolic HCO_3 (tCO_2)		Respiratory H_2CO_3 (pCO_2)
↑	ALKALOSIS	↓

- For uncomplicated uncompensated cases
- Lungs and kidney try to compensate, but this is not always possible.
- Blood gas measurements used to diagnose or to gauge the severity of the disorder.
- Electrolytes and acid-base - close relationship; e.g.,
  - hypochloremic alkalosis
  - hyperkalemic acidosis
- Anion gap
  - = calculation of unmeasured anions, used to help diagnose types of acidosis, poisoning by salicylates
  - = plasma sodium concentration minus (plasma bicarbonate plus plasma chloride)

LIVER FUNCTION

1. Serum bilirubin

- Hemoglobin broken down by RES to bilirubin → blood stream → liver where it is conjugated with two glucuronide molecules to give bilirubin diglucuronide = conjugated bilirubin. Conjugated bilirubin is excreted in the bile into the duodenum.
- Two tests:
  1. "Direct-acting bilirubin" - conjugated bilirubin is measured
  2. Measures "indirect bilirubin" = unconjugated bilirubin
- Liver cell damage: Increased total Bi, unconj Bi and conj Bi
- Hemolysis of RBC: Increased total Bi, increased unconj Bi, but conj Bi is normal.

2. Urine bilirubin and urobilinogen

- Bile is excreted into the duodenum where conjugated bilirubin is converted by bacteria into urobilinogen. Most urobilinogen is excreted in feces. Some is reabsorbed into the blood, from which it either goes back to the liver to be excreted again into the bile, or is excreted in the urine.
- In complete bile duct obstruction: No urobilinogen is formed. Stool normally gets its colour from urobilinogen, ∴grey-white or clay-coloured stools. The conjugated bilirubin cannot be excreted into bile; therefore it backs up into the blood and spills into the urine. Therefore will measure a high serum level of conjugated (direct) bilirubin and conjugated (direct) bilirubin will be present in urine.

3. Alkaline phosphatase (Alk phos)

- Enzyme produced mainly in liver and bone (but also in kidney, intestine, placenta)
- Excreted by liver into bile, therefore sensitive indicator of biliary obstruction
- Also good indicator of liver space lesions, e.g., carcinoma
- Not specific - level may increase with increased bone osteoblast activity, e.g., hyperparathyroidism
- Five isoenzymes

4. SGOT (AST)

- Serum glutamic - oxaloacetic transaminase
  aspartate transaminase
- Enzyme found mostly in heart and liver (but also skeletal muscle, pancreas, kidney)
- Increase in level proportional to extent of damage to heart or liver cells

5. LDH

- Lactic dehydrogenase
- A group of enzymes found mostly in heart and liver (but actually in all metabolising cells)
- Not very sensitive and not specific
- Can differentiate where cell damage is occurring by examining the isoenzyme pattern

6. SGPT (ALT)

- Serum glutamic pyruric transaminase
- Enzyme found liver, muscle, brain, other tissues

7. Prothrombin Time (PT)

- Prothrombin synthesized in liver
- Only abnormal in very severe liver disease

8. Serum Proteins

- Total protein = albumin + globulins
- Serum albumin - chiefly synthesized in liver
- Serum albumin decreases in most acute and chronic liver disease

HEART

1. SGOT (AST)

- See liver function tests
- Levels rise 8-12 hours after an MI.

2. LDH

- See liver function tests.
- Levels rise 24-48 hours after an MI.
- More sensitive than SGOT

3. CPK

- Creatine phosphokinase = CK = creatine kinase
- Enzyme found in heart muscle, skeletal muscle, brain
- First enzyme level to rise after an acute MI (in 2-6 hours)
- No change with liver damage, but level can increase with strenuous exercise, muscle injury, or often with **intramuscular injection**
- Isoenzymes

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