CLINICAL DIAGNOSIS AND MANAGEMENT BY LABORATORY METHODS

BIOCHEMICAL PROFILE

Pre-operative chemistry tests

- The American Society of Anesthesiologists recommends preoperative chemistry laboratory tests for Class I and II physical status only if the proposed operative procedure is associated with known significant blood loss.

Pre-operative tests of renal function

- Electrolytes and creatinine or urea nitrogen are the minimum recommended tests in patients with renal disease;
- Or if taking diuretics or digoxin.

- Elderly patients are more likely to have renal impairment.
- Creatinine clearance is a better evaluation of renal status than serum creatinine or urea nitrogen.

Other-preoperative tests

- With steroid use or in patients with diabetes, glucose and electrolytes are the minimum recommended tests.

- Liver enzymes, glucose, electrolytes, creatinine and urea nitrogen are recommended tests in those with liver disease.

Sodium

- Dehydration is suggested by elevated Na^+, urea Nitrogen (BUN), and relatively normal creatinine.
- Na^+ >150 suggests hypothalamic abnormality.

- Na^+ levels of 135 suggest diuretic use
- Normovolemic
- If dilutional (hypervolemic), responds to water restriction.

- Hyperglycemia is often the cause of hypovolemic hyponatremia (elevated serum osmolality noted).

Low sodium

- Na^+ <120 suggests inappropriate ADH secretion.
- Serum osmolality will be low.
- Causes:
- Ectopic ADH production
- Alcohol abuse
- Carbamazepine
- Valproic acid
- Li^+
- Li^+ uncouples receptor for vasopressin from G-protein, producing a nephrogenic diabetes insipidus.

Low sodium

- Responds to sodium restriction and thiazide diuresis.
- Responds to water restriction.
- Central pontine myelinolysis is a complication of too rapid an administration of Na^+ (>0.5mEq/L/hr).

Osmolality

- Calculated plasma osmolality:

  $2xNa^{+}$ + Glucose/18 + BUN/2.8 + alcohol/4.6

  Erroneously low if mannitol, sorbitol, ethylene glycol, methyl alcohol, isopropyl alcohol, excess lactate or ketoacids present

Osmolality

- In the normal patient, urine specific gravity varies directly with osmolality.
- This correlation is lost in the presence of glycosuria.
- A specific gravity of 1.010 is compatible with a urine osmolality of at least 350 mOsm/kg.
- This is the specific gravity of a plasma filtrate.
- Urine osmolality >600mOsm/kg indicates extrarenal water loss.

Potassium

- K^+ <3.5 associated with cardiac arrhythmia.
- Usually reflects diuretic use.
- Monitor with lead II if replacement >20mEq/L/hr.
- Low $K^{\pm}$ in the absence of diuretic use and in the presence of normal glomerular filtration rate suggests hyperaldosteronism or Cushing's syndrome.
- May also be hypertensive.
- Urinary K^+ >30mEq/L indicates renal losses.
- May also be Magnesium deficient.

Potassium

- If K^+ is low and the patient is normotensive, a blood pH<7.4 suggests renal tubular acidosis.
- If hyperglycemic, diabetic ketoacidosis
- If K^+ is low and the patient is normotensive, a blood pH>7.4 suggests diuretics or vomiting as cause.
- Elevated K^+ is seen in renal failure or patients on ACE inhibitors and spironolactone.
- Elevated K^+, LDH, and PO_4^{2-} (reported as phosphorous) suggest hemolyzed specimen used for testing.
- A change of pH by 0.10 alters K^+ levels by 0.5meq/L.

Chloride, Bicarbonate, Phosphate

- Cl^- levels low in chronic vomiting.
- HCO_3^- levels low in metabolic acidosis.
- HCO_3^- levels high in respiratory acidosis associated with chronic lung disease
- OR in metabolic alkalosis secondary to diuretic use.
- PO_4^{2-} levels (reported as phosphorous) are elevated in renal disease, myeloma, sarcoid.

Chloride, Bicarbonate, Phosphate

- Chloride/phosphorous ratio >30 in the fasting patient suggests hyperparathyroid disease.
- PTH decreases renal resorption of bicarbonate, increasing renal resorption of chloride, and phosphorus.

Renal function

- Specific gravity of first morning urine specimen best estimate of renal function.
- Concentrating ability is first function lost.
- Estimated GFR calculations are not accurate if GFR >60 ml/min or <25ml/min.
- Are useful to determine which patients require GFR determinations.
- Estimated GFR in a patient with stable creatinine: [(140 –age) x lean body weight in kg] / (Serum creatinine x 72).

Renal function

- Elevated Cystatin C identifies a preclinical state of kidney dysfunction that is not detected with serum creatinine or estimated glomerular filtration rate.
- More accurate than calculated e-GFR, particularly in those of West African ancestry

Creatinine

- Elevated creatinine is an indicator of renal impairment in patients with normal muscle mass.
- Creatinine is the end product of creatine metabolism
- Trimethoprim and cimetidine interfere with secretion of creatinine.
- Creatinine supplements are also associated with elevated levels of serum creatinine in the absence of renal impairment.

Creatinine

- Creatinine is filtered by the glomerulus and is not absorbed in the tubules.
- Timed creatinine clearance is a good estimate of renal function though with somewhat lower accuracy in the elderly.

Urea Nitrogen

- Urea, measured as Nitrogen, may be elevated in renal failure, gastrointestinal hemorrhage, or dehydration.
- The test is performed on serum but is reported as blood urea Nitrogen (BUN)
- Urea production removes ammonia generated by amino acid, pyrimidine, and purine catabolism in liver.
- Filtered by glomerulus and reabsorbed in proximal tubules when water is resorbed

Urea Nitrogen

- In the absence of acute renal failure, a BUN/creatinine ratio >20:1 suggests pre-renal disease.
- Hypovolemia
- Cardiac or liver failure
- Hemolysis or hemorrhage
- A normal ratio does not exclude acute tubular necrosis.

Urea Nitrogen

- A ratio <5:1 suggests intra-renal disease.
- Ischemia
- Nephrotoxic agents such as aminoglycosides
- Radiocontrast materials
- Myoglobin deposition
- Oxalate deposition (ethylene glycol ingestion)
- Low BUN in patient with renal failure is harbinger of hepato-renal syndrome.

Uric acid

- Completely filtered at the glomerulus.
- Accumulates in renal interstitium
- From which it is excreted as water is lost.
- No tubular reabsorption of uric acid.
- Elevated in patients with
- Gout
- Renal impairment
- Reflecting impaired clearance
- Malignancy
- Reflecting both production and impaired clearance

Uric acid

- Uric acid precipitation in tissue reflects saturation and is pH and temperature dependent.
- Alkalinizing the urine may accelerate excretion.

Calcium

- High Ca^{2+} levels probably reflect chronic vitamin D ingestion.
- PTH is not elevated.
- If that is excluded, a work-up for parathyroid disease is necessary.
- Symptomatic hypercalcemia is likely a result of malignancy, not parathyroid disease.
- Serum Ca^{2+} >11 mg/dl requires therapy whether patient symptomatic or not as 20-40% will become symptomatic in a period of years.
- Hypercalcemia may represent a medical emergency.

Calcium

- Low Ca^{2+} levels are associated with malabsorption syndrome.
- The non-protein bound iCa^{2+} (ionized calcium) is the active form and is not routinely measured, as it adds little to diagnosis or therapy, particularly if total Ca^{2+} is >8mg/dl.
- Hypomagnesemia induces resistance to PTH and may lead to functional hypoparathyroidism.

Calcium

- Renal disease may prevent vitamin D hydroxylation and, thus, intestinal absorption of Calcium.
- Serum Ca^{2+} and PTH are low.
- Serum PO_4^{2-} (phosphorous) will be increased.
- Little urinary loss of Ca^{2+}.
- QT interval prolonged on EKG

Osteoprososis

- DXA only test with clinical correlation.
- Screen white, Asian women if >65years of age.
- Medicare permits repeat every 2 years.
- Screen earlier if postmenopausal AND with nutritional disorder
- OR steroid use for more than 60 days.
- Fractures rare in men and black women.
- There are no data to suggest screening (and intervention to correct bone density) affects fracture rate.
- DXA scan does not change significantly with therapy.
- Do not repeat more frequently than every 2 years while on therapy.

Magnesium

- Low Mg^{+} levels are seen in patients on diuretics as well as in those who abuse alcohol.
- Seizures are a risk.
- High Mg^{+} levels may be associated with depressed neuromuscular function.

Screening for diabetes mellitus type II

- Early detection may not alter survival.
- Begin as early as 18yo if family history or obesity.
- Screen at any age if coronary disease, polycystic ovaries, or gestational diabetes present.
- Screen every 3 years with fasting glucose.

Glucose

- Low glucose levels may be factitious.
- In the presence of classic symptomatology, any random determination of glucose >200 is diagnostic of diabetes mellitus.
- Two consecutive fasting glucose levels >125 are diagnostic as well.
- Repeated fasting glucose levels >90 but in the normal range suggest need for glucose determination after a glucose load to exclude diabetes mellitus as those “normal” patients in this upper quartile have 40% greater risk of cardiovascular disease than do “normal” patients with lower fasting glucose levels.

Hemoglobin A_{1c}

- At 6.5% there are 40 retinopathy events per 100 patient years.
- At 9.0% there are 100 retinopathy events per 100 patient years.
- Nephropathy events begin to rise at 8.5%; At 12.0%, there are 100 nephropathy events per 100 patient years.
- Retinopathy occurs at lower HbA_{1c} levels in blacks.
- Levels above 15% suggest abnormal hemoglobin. Fructosamine as better marker in those cases.

Bilirubin

- Total bilirubin 1.0-2.0 suggest Rotor or Gilbert disease and requires no therapy.
- Elevated bilirubin (indirect or unconjugated) may be seen in hemolytic disease.
- Elevated bilirubin in parenchymal liver disease may reflect poor handling of heme breakdown products or duct obstruction.
- Elevated direct bilirubin (conjugated) is seen in parenchymal liver disease.
- When albumin binding is saturated, bilirubin is deposited in basal ganglia.

Liver enzymes

- Enzyme upper limits of normal may be 25-40% higher in those patients of large body mass.
- ALT elevation is associated with mitochondrial damage.
- First enzyme to rise in liver injury.
- ALT elevation associated with cytoplasmic destruction.
- AST elevation with triglyceride elevation suggestive of metabolic syndrome.
- ALT/AST ratio >2:1 parenchymal not cholestatic disease.

Liver enzymes

- γGT elevation in the non-pregnant patient often an indicator of occult alcohol abuse.
- Alkaline phosphatase elevation if isolated may reflect space occupying lesion in liver.
- Isolated elevations in children reflect bone activity.
- Alkaline phosphatase elevation in patients with malignancy reflects osteoblastic activity.
- Alkaline phosphatase elevation with elevation of γGT is compatible with duct obstruction
- With or without parenchymal liver damage.

Liver enzymes

- Alkaline phosphatase/ALT >1.5 is suggestive of autoimmune hepatitis
- Alkaline phosphatase/ total bilirubin <4.0 with AST/ALT > 2.2 is diagnostic of Wilson's disease (in liver failure)
- Isolated LDH elevation is seen with intravascular hemolysis (as in pernicious anemia) and in P. Jarecki infection.

Cardiac enzymes

- Time to elevation is 3-12 hrs
- CK-MB and cTnI peak at 24 hours
- CK-MB returns to normal in 48-72 hrs, cTnI in 5-10 days,
- cTnT in 5 to 14 days
- LDH (isozymes 1-3) is also elevated with injury
- Elevated B-natriuretic peptide (BNP) predictive of mortality at one year in patients presenting with dyspnea.

Troponin

- Normal troponin I 8 hours after symptomatology effectively excludes myocardial infarction.
- Non ST elevated chest pain patients with negative troponin I should have a stress echocardiogram.
- If negative, no myocardial infarction.
- Elevated with renal impairment.
- Enzyme levels reflect extent of injury.
- The size of the infarct may be estimated from the size of the CKMB isoform.

Creatine kinase

- Elevated CK in ambulatory population without chest pain likely reflects injury to skeletal muscle.
- Elevated CK (and aldolase) in children suggestive of muscular dystrophy.

Screening for cardiovascular disease

- Begin blood pressure screening at 3 years of age.
- Abdominal Ultrasound in men who have used tobacco and are >65 years of age to detect abdominal aortic aneurysm.
- If negative, do not repeat.
- Thallium stress exercise testing after age 40 in women to evaluate chest pain
- All others, after age 50
- Major adverse cardiac events can be predicted by response to reactive hyperemia (endothelial peripheral arterial tonometry).

Screening for dyslipidemia

- Begin screening men older than 35 and women older than 45 years of age if no heritable lipid disorder or known cardiovascular disease;
- If heritable lipid disorder, begin screening at 25 years of age.
- Total cholesterol, HDL best tests
- Repeat every 5 years or with lifestyle change

Lipids

- Total Cholesterol/HDL ratio is the best predictor of cardiovascular risk.
- Patients with angiographically demonstrated coronary stenosis have dyslipidemias other than those associated with an elevated LDL.
- It is the rare laboratory that measures LDL.
- Reported LDL values are calculated values.
- They are inaccurate if triglycerides >400 mg/dL.

Lipids

- A statin may be the best choice for therapy if LDL (calculated) >190mg/dl and cardiovascular disease exists.
- For those with type I or II diabetes mellitus, a statin is suggested for LDL>70mg/dl.
- Statins are associated with long term muscle damage.
- Niacin also lowers LDL and raises HDL.
- Slows catabolism of HDL

Lipids

- Markedly elevated triglyceride levels after 16 hour fast (in the absence of alcohol abuse) suggest metabolic syndrome.
- Lipoprotein α >30 mg/dl associated with increased risk of cardiovascular events. Measure in refractory patients.
- Homocysteine >11.4 µmol/dl (10.4, women) associated with increased risk of cardiovascular events.
- Abnormal in diabetics and in hyperthyroid patients.