Laboratory Test Considerations for I.V. Therapy

What Tests Are Important
And Why

Recommended Tests

Minimum

- Complete blood count
- Comprehensive metabolic panel
- Lipid panel (CVD concern)
- Vitamin D
- G6PD if giving high dose vitamin C/H_2O_2/Ozone
- Urine dipstick
- Check with your laboratory for values of any lab tests

Supplemental tests to better guide treatment

- Amino acids
- Organic acids
- Plasma vitamin C
- Intracellular minerals
- MTHFR
- NMR Lipoprofile
- Iodine

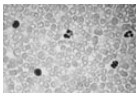
General Test Classification

- Renal function tests help to determine:
  - Allowable fluid load
  - Nutrient or drug dose
  - Infusion rate
- Liver function tests are essential because:
  - What nutrients or drugs are safe
  - What nutrients or drugs are indicated

Complete Blood Count

- White blood cell count
- RBC
- Hgb
- MCV
- Platelet count

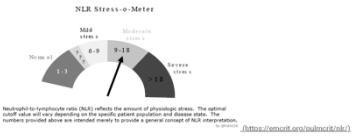
WBC



- Normal 5-10 X 10^3 /mm^3
- Optimal 5-7.5 X 10^3 /mm^3
- Low – immunosuppression, toxic metals, acute or chronic infections
- High - viral (lymphocytes) or bacterial (neutrophils) infection, myeloproliferative (less mature)
- IV Rx: Vit. C, A, Zn, HCl

NL (Neutrophil: Lymphocyte Ratio)

- Normal: Less than or equal to 3:1
- Ideal: Less than or equal to 2:1
- Above 3:1 (indicated immune stress)
  - A *normal* NLR is roughly 1-3.
  - An NLR of 6-9 suggests mild stress (e.g. a patient with uncomplicated appendicitis).
  - Critically ill patients will often have an NLR of ~9 or higher (occasionally reaching values close to 100).

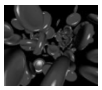


Neutrophil-to-lymphocyte ratio (NLR) reflects the amount of physiologic stress. The optimal cutoff value will vary depending on the specific patient population and disease state. The numbers provided above are intended merely to provide a general concept of NLR interpretation. (https://emcrit.org/pulmcrit/nlr/)

Hgb & RBC

- Normal M 14-18 g/dL , F 12-16 g/dL
- Optimal M 14-15 g/dL, F 13.5-14.5 g/dL
- Low: anemia, need to classify, see MCV. If hemoglobinopathy be careful with vit. C, keep other dosages moderate
- High: Polycythemia: primary, tx similar to Myeloproliferative. Secondary, either chronic lung or environmental.
- Rx: vit. C, antioxidants

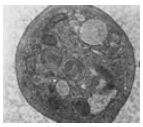
MCV



- Normal 80-95 /mm^3
- Optimal 82-89.9 /mm^3
- Low: iron, B_6 or Cu deficiency. Iron best given deep i.m. Z-trak method. Thalassemia, support with nutrition, DO NOT give iron.
- High: B_{12}/folic acid and SAM-E deficiency, best to treat with these nutrients. If not responding, consider mercury toxicity

Platelet Count

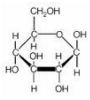
- Normal 150-400 X 10^3, Optimal same
- < 50 or > 700 X 10^3: be aware of possible bleeding/ bruising at infusion site
- Rx Low: glutathione



B12

- Options for B12 assessment:
  - Consider in frank macrocytosis
  - Serum B12
  - Methylmalonic Acid (MMA)
  - "Right Shift" (Hyper segmented neutrophils)

Blood Glucose



- Normal fasting 70-105 mg/dL
- Optimal 80-100 mg/dL
- Low: high dose vit. C can induce hypoglycemia, have patients snack or set up infusion in D5W.
- High: be aware of diabetic complications, sodium effects on hypertension, renal function
- Rx chromium

Albumin

- Normal 4-5.5 g/dL
- Optimal 4-5 g/dL
- Low: liver disease, kidney disease, malnutrition, over hydration, inflammation, hypochlorhydria, oxidative stress, low vitamin C, hormone dysregulation (thyroid, testosterone, estrogen, aldosterone, and insulin)
- Rx: combination amino acids
- High: dehydration

AST

- Normal 5-40 IU/L
- High: MI, cardiac cell injury, liver disease, skeletal muscle disease, pancreatitis
- Low: B6 or Zinc deficiency possible
- IM injections may elevate levels

ALT

- Normal 5-35 IU/L
- Sig. Inc.: hepatitis, hepatic necrosis, ischemia
- Mod. Inc.: cirrhosis, cholestasis, tumor, drugs, obstructive jaundice
- Mild Inc.: myositis, pancreatitis, MI, inf. Mono
- Low: B6 or Zinc deficiency possible
- IM injections may elevate levels

Alkaline Phosphatase

- Children levels: 350 U/L
- Adult level: 25-100 U/L
- Low: zinc deficiency, magnenesium, Vit C/scurvy, B 6 folic acid, hypophosphatemia, celiac disease, malnutrition, hypochlorhydria, hypthryroidism, pernicious anemia, hypoparathyroism, excess vitamin D levels
- High: Oral contraceptives,Obstructive pancreatitis, Hepatitis/Mononucleosis/CMV, CHF, parasites, shingles, low vitamin D, healing fractures, RA, sepsis and GI diseases

GGT

- Normal M or F > 45 years 8-38 U/L
- F < 45 years 5-27 U/L
- Sensitive indicator of hepatobiliary disease.
- Indicator of heavy and chronic alcohol use.
- Increased after MI due to secondary liver insult, increased in EBV infections, infectious mono

BUN

- Normal 7-27 mg/dL
- Optimal 10-16 mg/dL
- Low: may decrease in chronic liver disease or inadequate protein intake
- High: primarily concerned with renal disease and ability to excrete IV metabolites. See creatinine for dosage recommendations.

Creatinine

- Normal 0.5-1.5 mg/dL
- Optimal 0.8-1.1 mg/dL
- Low: low muscle mass, cachexia
- High: primarily concerned with renal disease, some athletes supplementing with creatine will have increase.
- Doubling of creatinine suggests 50% reduction in glomerular filtration rate

Uric Acid

- Normal 2.3-8.2 mg/dL
- Optimal M 3.5-5.9 mg/dL, F 3.0-5.5 mg/dL
- High: Gout, atherosclerosis, oxidative stress, RA, renal disease, leaky gut syndrome, pre-eclampsia
- Low: Deficiency of molybdenum, B12, folic acid, copper; toxic metals, late liver disease
- B5 can help reduce eliminate uric acid from the body

Calcium

- Normal 9.0-10.5 mg/dL
- Vitamin C is a weak chelating agent, so in order to preserve Ca values it is useful to add 1 ml 10% Ca gluconate for each 10 grams vitamin C used
  - Calcium chloride may be used at about 1/3 the dose of calcium gluconate

Electrolytes

Na, K, Cl, CO_2

- Dehydration will usually present with varying degrees of electrolyte imbalance; Lactated Ringers works well for this, 500 ml plain or with some nutrients added.
- Caution in patients with renal disease, especially sodium, potassium.
- More severe electrolyte imbalances need to be corrected with specific electrolytes, guided by HOSPITAL lab measurements, arterial blood gases.

ANION GAP (AG)
INCREASED AG = "MUDPLIERS"

- **M** = Methanol intoxication (via conversion to formic acid)
- **U** = Uremia
- **D** = Diabetic or alcoholic ketoacidosis
- **P** = Paraldehyde
- **L** = Lactic acidosis
- **I** = Isoniazid, Iron overload, Ischemia
- **E** = Ethylene glycol intoxication
- **R** = Rhabdomyolysis
- **S** = Salicylate overdose

- Also consider a decrease in "unmeasured cations" : Mg++, Ca++, K+
- 2 formulas may be used to calculate the AG, so be sure to get an idea of which formula the lab computer is using.
- AG = (Na + K) – (Cl + CO_2) OR AG = Na – (Cl+CO_2)*

Potassium (K)

- Normal 3.5-5.3 mEq/L
- Panic value <2.5 or >7.0 mEq/L
- Optimal 4.0-4.5 mEq/L
- K level 3.5 commonly associated with deficiency
- Most common cause of low K in patients is water or NaCl infusion without adequate K replacement
- Glucose infusion in patients with heart disease can drop K levels as much as 0.4 mEq/L

G6PD

- Normal 2.4-5.1 U/mL of RBC or 8.6-18.6 U/gram hemoglobin
- Low: G6PD deficiency. Vitamin C in sufficient concentration can cause RBC hemolysis
- Normal: May be falsely normal for 6-8 weeks after a hemolytic episode
- Increased: Untreated pernicious anemia, hyperthyroid, viral hepatitis, post MI

G6PD

- Consider prior to H202, over 10 grams IVC, Ozone
- Pre treatment: NAC and Glutathione preserves or improves NADPH availability
  - Because RBC's lack ability to regenerate glutathione in the presence of G6PD deficiency
    - Any increase in H202 will damage cell
  - PO
  - IV
  - http://www.accessbio.net/eng/products/products03.asp

Total Bilirubin

- Normal 0.1-1.5 mg/dL
- Increased: liver may not be able to effectively metabolize high doses of IV constituents, depends on cause: obstruction, cholestasis, hepatitis, cancer.
- Watch dosage of niacin
- Avoid IV vitamin A

Urinalysis- urine dip

- Specific gravity Normal 1.005-1.030, Usually 1.010-1.025
- Low: Renal disease tends to diminish concentration capability, leads to consistent values of around 1.010. Over hydration also shows low values.
- High: dehydration

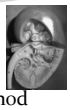
Urinalysis- urine dip

- Glucose
- Normal is negative
- Positive: Indicates that blood glucose is over the renal threshold, about 170 mg/dL. Test blood with glucose meter. Adjust protocol appropriately, e.g amino acids can increase blood glucose. Have patient treat with insulin if needed

Urinalysis- urine dip

- Protein
- Normal is negative
- Positive: Renal disease, acute infection, trauma, hypertension, malignancy, poisoning, toxemia.
- Urine dip protein testing shows many false positives; either retest on a different day or measure 24 hour quantitative protein

Renal Function Testing



- Glomerular filtration rate (GFR) is the best method for determining renal function
- The most accurate method for measuring GFR is the renal clearance of ^{125}I-iothalamate
- 24-hour measured creatinine clearance overestimates GFR by 19%,

Renal Function Testing

- Cockcroft-Gault formula overestimates GFR by 16%.
- Why the overestimates?
  - Elderly patients with normal serum creatinine values and decreased muscle mass may have as much as 30% decrease in GFR despite a normal creatinine clearance
  - Infants and young children exhibit low serum creatinine so GRF estimation by creatinine clearance is difficult and inaccurate

GFR – A better method

- Andrew Levey, et. al. developed an accurate method to predict GFR (Levey, AS et. al. Ann Intern Med 1999;130:461-470)
  - Validated in cohort of patients that differed from the cohort used to derive it
  - Predicts GFR over a wide range
  - Useful for changing the dose of medications excreted by glomerular filtration

GFR – A better method

- Identifies renal insufficiency
- Can detect progression of renal disease
- Detects end-stage renal disease
- Levey's formula uses demographic data and commonly available serum variables

The Levey Formula

- GFR = 170 X $[P_{CR}]^{-0.999}$ X $[Age]^{-0.176}$ X [0.762 if patient is female] X [1.180 if patient is black] X $[BUN]^{-0.170}$ X $[Alb]^{+0.318}$
- Legend: P_{CR} = serum creatinine (mg/dL); BUN = blood urea nitrogen (mg/dL); Alb = serum albumin (g/dL)

GFR Estimation

The Bottom Line

1. GFR = 0.69 X 100/P_{CR}
2. GFR = 0.84 X [Cockcroft-Gault equation]
3. GFR = 0.81 X [Creatinine Clearance]
4. GFR = Levey Equation
5. GFR = >60 or the numerical value given by the reporting lab (using NIH guidelines), may be normal with diminished renal function

Web site for Levy Formula

- www.nephron.com/cgibin/mdrd.cgi

Cystatin-C

1. Biomarker for kidney disease that is NOT dependent on muscle mass.
2. Can be used to indicate kidney dz.
3. Other factors that can impact Cystatin-C: thyroid conditions, glucocorticoids, malignancies.
4. Higher levels are generally associated with increased cardiovascular disease.

Cabarkapa, Velibor. Cystatin-C- More than the marker of the glomerular filtration rate. PMID: 26234025

Amino acids by plasma or blood spot

- Amino acids
  - An increased level of a particular amino acid is a strong sign that there is a problem with the body's ability to metabolize that amino acid
  - Decreased levels of amino acids in the blood may indicate inadequate nutrition or certain medical conditions
  - Plasma amino acids, examples Metametrix Clinical Laboratory Amino Acids 40 Profile – Plasma, Great Plains Laboratory Amino Acids Plasma Test
  - Blood spot profile, example Metametrix Clinical Laboratory, Amino Acids 20 profile – Blood spot

Clinical Applications – Amino Acid Testing

- Amino acid derangements
  - Chronic fatigue, usual treatments not working
  - Frequent headaches
  - Mental, neurological, or learning issues
- Example - Histidine
  - Histadelia – depression that does not respond to drug therapies
  - Histapenia, commonly associated with increased Cu, low Zn. Racing thoughts, hallucinations, paranoia

Organic Acids

- Organic acid molecules are byproducts of cellular metabolism, food digestion, and metabolism of gastrointestinal flora
- Useful for evaluation of intestinal yeast and bacteria health effects
  - Important in neurological, gastrointestinal, and movement disorders
  - Toxic metabolites of microorganisms can cause or worsen behavior & movement disorders, hyperactivity, energy levels, immune function
  - Can indicate increased intestinal permeability
  - ADHD

Vitamin D Tests

- To evaluate vitamin D status order serum 25-OH vitamin D
  - Optimal level in range of 50-80 nmol/L
  - Recent research suggests that PTH levels and calcium absorption are not optimized until serum 25-hydroxyvitamin D levels reach approximately 80 nmol/L (32 ng/mL)
- 1,25-dihydroxyvitamin D
  - Useful if calcium is high or patient has a disease that may produce excess amounts of vitamin D, e.g. sarcoidosis, some forms of lymphoma
  - Low values seen in renal failure

Intracellular Minerals

- Optimal intracellular levels of minerals are required for normal cell function
- Blood mineral levels do not correlate well with intracellular levels
- Sample requirements depend on lab
  - Blood (WBC are tested), SpectraCell Laboratories
  - Epithelial cell scraping from the sublingual area, IntraCellular Diagnostics

MTHFR

- MTHFR is enzyme that converts 5,10-methylenetetrahydrofolate to the product 5-methyltetrahydrofolate
  - May lead to hyperhomocysteinemia and hypohomocysteinemia
- Manage labs
  - MTHFR, sulfur pathway, vitamins, minerals, thyroid (T_3/T_4)
- Increased risk for autism, cardiovascular & cerebral vascular disease, heavy metal toxins, Lyme, thrombosis, methotrexate toxicity, etc…

NMR Lipoprofile

- Cardiovascular disease historically evaulated by measuring LDL-C, HDL-C and triglycerides
- LDL-C has poor correlation with risk for CVD events
- About two-thirds of CVD patients have optimal levels of LDL-C but high Low Density Lipoprotein particle number (LDL-P actual particles of LDL concentration)
- LDL-P lowering useful as primary goal of therapy due to stronger association with cardiovascular risk, i.e., efficacy of treatments can be better evaluated.
- Low risk is < 1000 nmol/L, risk increases linearly to the range of very high risk at > 2000 nmol/L
  - LDL-P size is important, small dense LDL is antherogenic

ApoB:ApoA1 Ratio

- Better tool for accessing coronary artery disease. This ratio is strongly correlated with myocardial infarction and stroke.
- Apo B = atherogenic
- ApoA1 = protective
- Superior to the Framingham Risk Score and Total cholesterol to HDL ratio.

Optimal Ratio: 0 – 0.6 women & 0- 0.7 men

Abnormal: Above 0.7

Lima, Luciana Moreira et al. "Apo B/apo A-I ratio and cardiovascular risk prediction." Arquivos brasileiros de cardiologia vol. 88,6 (2007): e187-90.

Tian, Min et al. "Comparison of Apolipoprotein B/A1 ratio, Framingham risk score and TC/HDL-c for predicting clinical outcomes in patients undergoing percutaneous coronary intervention." Lipids in health and disease vol. 18,1 202. 19 Nov. 2019

Iodine

- Random urine sample is the accepted test (blood may also be used)
  - Iodine value is optimal between 100 and 200 µg/liter. The Journal of Clinical Endocrinology & Metabolism Vol. 92, No. 3 1019-1022
- Iodine loading test as described by Guy Abraham, MD, does not have sufficient scientific basis
- Iodine skin absorption test is not reliable (Lugols')
- Labs: T3-T4 conversion, calcium levels and Vitamin D3 levels for further determination.

Nutrient Evaluation Labs

- Blood Tests
  - Many vitamins, minerals, antioxidants, amino acids.
  - May be useful in customizing or making changes in your infusion.
- Hair
  - Not reliable for internal evaluations
  - Questionable with lead and mercury
  - Frequently tests extraneous sources
- Skin scanners
  - Variability and accuracy still in question

