Analysis of Lab Results:

Key Abnormal Parameters and Appropriate Clinical Responses

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Lecture Overview:

- Review 'common' abnormal lab results pertaining to Lithium, Depakote, Tegretol, Clozaril, Electrolytes/Calcium/Vitamin D, Renal, Liver and Thyroid Function, Diabetes, and Lipid Metabolism.
- Discuss steps towards the proper interpretation of results
- Outline appropriate clinical interventions

Philosophy:
A number is not just a number.

- To understand the significance of a lab value, we need to know the story behind it

- Under what conditions was the blood-work obtained: e.g., fasting, length of time following dose, morning or evening. What is the patient's medical history (old, young, diabetic, etc)? What meds is the patient taking? And most importantly, what are the "baseline" labs that we can refer back to.

Lithium

- Overview: Natural element used to treat mania, mood instability, and occasionally depression.

- Classified as a Mood Stabilizer

Lithium

- Forms: Lithium Carbonate (regular release) and Lithobid/Eskalith (long acting). Doses are roughly equivalent. Most adults are stabilized between 1,200-1,500 mg/day. Doses above 1,800 should raise eyebrows. Lower doses required in elderly and/or pts with diminished GFR.

Lithium

- Pertinent Lab Values: Lithium Level, Renal Function (GFR, BUN/Cr), Thyroid Function, and Electrolytes. After initiation, screen every 6 mo. All women of reproductive age should be screened for pregnancy/breast-feeding.
  - Lithium Panel: Li level, Sodium, Bun/Cr, GFR, TSH. (See below for interpretation of Lithium level).
    - Monitor for dehydration: low sodium (values less than 136), BUN/Cr ratios greater than 20:1.
    - Monitor for evidence renal disease: GFR < 60 or Cr greater than 1.2 (in context).
    - Monitor for hypothyroidism: TSH greater than 4.5
  - Where do we draw the line between urgent and emergent: each case on own terms, but in general, sudden rises of Cr or plunges in GFR, or sudden rises in TSH above 10.

Lithium

- Normal Range: levels need to be drawn 10-12 hours after last dose. Regimens given at bedtime will produce levels that are 10-20% higher than those with BID dosing. Five days to steady state on any new dose.
  - Generally, 0.8-1.0 for management of acute mania—but varies with pt. Maintenance doses may be lower. Little clinical benefit for levels less than 0.5 or over 1.0. Most people show adverse side effects by 1.2
  - Trough levels above 1.5 cause serious side effects—nausea, tremor, altered mental state, ataxia. Greatest worry is renal failure, seizures, delirium, coma, and of course death.
  - Abnormal highs: Always follow up with the patient. Check that blood was drawn 10-12 hours post dose and find out how long they've been on current dose. Abnormal high levels will almost certainly be detected in blood drawn only 2-4 hours post dose, but this is not usually dangerous—although it may be clinically significant.

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Lithium

- Risk factors for abnormal highs: too high a dose; use of NSAIDs; sodium depletion as in dehydration, diuretics, renal insufficiency.
- If side effects are present pt. should be sent to ER. If no side effects, but level is above 2.0, would likely send to ER, especially if high confidence in trough. Trough above 3.0 is unequivocally a medical emergency and pt needs to be sent to ER regardless of whether they have side effects.

Depakote

- An anticonvulsant, FDA approved for treatment of mania, and frequently used also for maintenance.

Depakote

- Forms: Valproic Acid, Depakote (Valproic Acid Sodium), Depakote ER, Depakote XL, Depakene (syrup). All Dose equivalent. Most adults stabilized between 1000-2500 mg.

Depakote

- Pertinent Lab Values: VPA level, LFTs, Platelets, Pregnancy tests. After initiation, screen every six months.
  - •VPA levels: 50-100. Draw 10-12 hours post last dose. About 1 week to steady state. Poor correlation between level and efficacy. Levels above 100 are okay if tolerated. Would rarely exceed levels above 150.
  - •Generally, if above 100 would call to check for side effects: nausea, sedation, tremor, ataxia. If above 150, would lower and if severe side effects would send to ER.
  - •LFTs: mild elevations in SGOT and SGPT are common. If levels >2x, would initiate work-up and consider stopping for a time to see what happens. If >3x, would stop.
  - •Platelets: dose-related autoimmune thrombocytopenia is not uncommon. Maintain levels above 50 (below is bleeding risk). Levels between 50-100 are of concern, but can be monitored safely with more frequent testing.
  - •Pregnancy is very serious: 5% risk Neuro Tube Defect. Breastfeeding generally okay.

Tegretol

- An Anticonvulsant, clinically useful for prevention and treatment of mania

Tegretol

- Forms: Just the one form. Generic carbamazepine. Dose range 400-1,200 mg/day, but higher doses often used

Tegretol

- Pertinent Lab Values: CBZ (carbamazepine) level, Sodium, LFTs, CBC. After initiation, screen every six months.
  - CBZ level: 4-12. Draw 10-12 hours post dose. Poor correlation between level and efficacy. Levels above 12 okay if tolerated. Wait 2-4 weeks post initiation to check level due to auto-induced metabolism. For maintenance, check every 6 mo.
  - Generally, if above 12 check for side effects: dizziness, sedation, ataxia.
  - CBC often checked, mainly to screen for low WBC (extremely rare).
  - LFTs: same protocol as Depakote, though incidence is quite rare
  - Sodium: SIADH is not uncommon (Sodium less than 135). Its occurrence is often at the outset of tx.
  - Avoid in both pregnancy and breastfeeding. Very high risk of birth defects.

Clozapine (Clozaril/Fazaclo)

- The most powerful antipsychotic. Used for treatment of refractory patients.

Clozapine (Clozaril/Fazaclo)

- Forms: Generic Clozapine often goes by the trade name Clozaril. Fazaclo is an orally disintegrating tablet (ODT)

Clozapine (Clozaril/Fazaclo)

- Pertinent Labs: CBC. 1% risk of Agranulocytosis (loss of neutrophils).

Clozapine (Clozaril/Fazaclo)

- The entire Monitoring System is **now** changing: www.clozapinerems.com . RNs who input CBC data for providers will need to register into the new nationwide system (Clozapine REMS Program), and be designated as 'designees'. The new system is due to take effect October 12, 2015.
  - Initiation: ANC > 1500 (often expressed in multiples of 1000)
  - Mild Leukopenia: ANC 1000-1499
  - Moderate Leukopenia: ANC 500-999

Electrolytes/Calcium/Vit D

- Sodium: normal range: 135-145

•**Hyponatremia:** sodium <135. Serious symptoms can occur at varying levels depending on state of patient, but usually <125 is considered severe. Elderly and those with CNS impairment, may be more susceptible. Symptoms are mainly neurologic: headache, confusion, stupor, seizures, coma due to cerebral edema. Levels below 115 are a true medical emergency, but some pts show serious symptoms at higher levels. Hyponatremia is better tolerated when it is chronic rather than acute (levels dropping over 48 hours).

•**Hypernatremia:** >146. Symptoms may be very similar to hyponatremia. Serious symptoms usually occur >257, and death > 180. Symptoms more likely in acute rises, and in patients with preexisting CNS impairment.

Electrolytes/Calcium/Vit D

- Potassium: normal range 3.5-5.0. (Most the body's potassium is stored in cells rather than serum).
  - **Hypokalemia:** potassium < 3.5. Symptoms: weakness, fatigue, muscle cramps, constipation. Biggest concern is abnormal heart rhythms. Early EKG changes include T-wave flattening, ST depression, wide PR, and U waves. With critically low potassium, ventricular arrhythmias and cardiac arrest. Hypokalemia can magnify risk for Torsades de Points in patients taking QTc prolonging meds (e.g common antidepressants, antipsychotics and antihistamines). Levels between 3-3.5 probably can be managed with dietary supplementation and alleviation of cause (e.g., excessive diuretic use, vomiting/diarrhea, inadequate PO intake). Low threshold for having them come to clinic for EKG and clinical assessment. Levels below 2.5 generally require IVs and additional lab tests (Magnesium). Below 2.5 is a medical emergency.
  - **Hyperkalemia:** potassium >5.0. Symptoms: malaise, palpitations, muscle weakness. Occasional EKG changes in the early course. Most worrisome is sudden v-fib and sudden death. 5.5-7.0 generally cause symptoms. Above 7 can lead to critical cardiac issues. Greater than 8.5 is fatal.

Electrolytes/Calcium/Vit D

- Calcium: normal range for total serum calcium; 8.5-10.2 mg/dl. Ionized calcium 4.4-5.4. Difference due to binding to albumen. Only the ionized form is bioactive.

  - Hypocalcemia: total serum Ca < 8.5, or ionized Ca <4.6 . In terms of symptoms, we're really only interested in the ionized calcium. Causes: Vitamin D deficiency, CRF, hypoparathyroidism. Symptoms: muscle spasm, tetany, seizures, cardiac problems.

  - Hypercalcemia: total serum Ca >10.2 or ionized Ca >5.4 Ionized calcium levels greater than 10 are critical. Symptoms include loss of appetite, weakness, constipation, conduction blocks in heart.

Electrolytes/Calcium/Vit D

- Vitamin D. Normal role is to encourage intestines to absorb calcium from food and to decrease calcium excretion from kidney. Too little Vitamin D causes low calcium. However, too much vitamin D seldom causes elevated calcium due to the down-regulation of PTH. PTH causes calcium to be mobilized from bone and held onto by kidneys. Note that there are cases where people have high calcium and low Vitamin D—parathyroid tumor. There are a lot of unsubstantiated reports that Vitamin D improves immunity, fights cancer, treats pain, addresses depression, lowers blood pressure.
  - Vitamin D normal levels: 20-50. Below 12 is considered clinically significant.

Renal, Liver and Thyroid Functions

- Renal Function: BUN/Cr, Creatinine. Other labs are creatinine clearance and urine creatinine.

  - Normal range Cr 0.5-1.2. BUN 7-20 (varies with age). GFR normal is 90-120. Below 60 indicates moderate kidney disease.

  - An elevated BUN:Cr ration indicates a problem 'prior' to the kidney (e.g. dehydration, usually because BUN re-absorption by kidneys is increased). A diminished ratio due to increased Cr indicates intrinsic renal disease.

Renal, Liver and Thyroid Functions

- Liver Function Tests: a group of tests that detect inflammation or damage to the liver.
  - Aspartate Aminotransferase (AST)—previousy SGOT, measures liver damage
  - Alanine Aminotransferase (ALT)—previously SGPT, measures liver damange
  - Alkaline Phosphatase and GGT—blockage of bile flow
  - PT/INR: lowered in liver disease
  - Albumin: lowered in liver disease
  - Bilirubin: increased in liver disease, causes jaundice
  - NH3 (ammonia): Elevated in liver disease, can cause encephalopathy.

Renal, Liver and Thyroid Functions

- Thyroid Function Tests: TSH
  - TSH: normal 0.5-4.5. Often elevated in hypothyroidism, low in hyperthyroidism, but not always
    - Pituitary adenomas can overproduce TSH even when thyroid hormones are elevated
    - Low levels of TSH in hypothyroidism can occur in hypothalamus disease
    - Alterations in TSH are often sub-clinical, and often associated with normal T3/T4.
    - Mild Elevation: 4.5-10; Advanced Elevation > 10.
    - Mild Suppression: low but detectable 0.1-0.4; non-detectable < 0.1.

Renal, Liver and Thyroid Functions

- Thyroid Function Tests: Total T4 (Thyroxine), FT4 (Free Thyroxine), T3 (Triiodothyoinine).
  - Total T4 (Thyroxine): elevated in hyperthyroidism, low in hypothyroidism. Rarely measured
  - FT4 (Free Thyroxin): the amount of unbound T4 (biologically active).
  - FT3 (Triiodothyoinine): the amount of unbound T3

Diabetes:

HgA1c, Random Blood Sugar, Fasting Blood Sugar

- Hemoglobin A1C: indicates the average blood sugar for 2-3 months prior to test.
  - <5.7 normal
  - 5.7-6.4 prediabetes
  - 6>6.4 diabetes

Lipid Metabolism

- Fasting versus non-fasting—a raging controversy. Much better to get lipids even when not-fasting than to not get them at all.
  - Total Cholesterol: normal < 200 mg/dL. >240 considered high
    - LDL: 100-129. More is bad, less is good.
    - HDL: 40-59 mg/dL. Less is bad. More is good.
    - Total chol: HDL ratio <5 is good.
    - Triglycerides: <150 is good.