ABNORMAL LAB RESULTS: Deciphering the Mysteries

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LGM 2023

Non-Declaration Statement: I have no relevant relationships with ineligible companies to disclose within the past 24 months. (Note: Ineligible companies are defined as those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.)

LEARNING OBJECTIVES

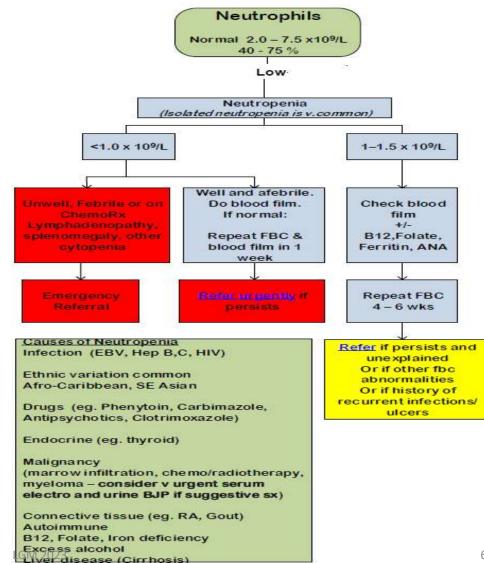
- 1) Identify the most common abnormal lab and their etiology for a complete blood count (CBC)
- 2) Identify the most common abnormal lab results and their etiology for a basic metabolic panel (BMP)
- 3) Identify the most common abnormal lab results and their etiology for a urinalysis (UA)

Leukopenia

- WBC < 4*10⁹ /L High susceptibility to infections Pancytopenia causes:
- bone marrow tumor
- aplastic state of bone marrow
 - ionizing radiation
 - chemotherapy of tumors (cytostatics)
 - intoxication with benzene, myelotoxic drugs (levomycetine, NSAIDs)
- B12 deficiency
- overactive spleen.

Neutropenia

- Benign ethnic neutropenia
- Familial neutropenia
- Congenital neutropenia
- Infection
- **Medications**
- Nutritional deficiencies (vitamin B12, folate, copper)
- Hematologic malignancies
- Rheumatologic disorders
- Autoimmune neutropenia
- Aplastic anemia
- Chronic idiopathic neutropenia



Case 1

History:

54-year-old male
Over the year noted
increasing fatigue, sinus
infections and bronchitis
20 lb unintended weight loss,
diarrhea

Physical Exam:

Thrush,

• WBC: 1.4 x 10³/uL (4.5-10.5)

• Neutrophils: 24 % (65-75)

• Bands: 5% (0-1)

• Lymphocytes: 69 % (35-45)

• Eosinophils: 2 % (0-5)

• Basophils: 0 % (0-1)

• Monocytes: 0 % (0-7)

• Platelets: 74 x 10³/uL (150-400)

RBC: 4.55 x 10⁶/uL (4.2-5.4)

HGB: 13.4 g/dL (14-18)

HCT: 40.1 % (38-48)

MCV: 90.5 fL (80-100)

MCH: 30.5 pg (26-34)

MCHC: 35.6 g/dL (31-37)

RDW: 12.9 % (<14)

LEUKOCYTOSIS

Table 4. Selected Conditions Associated with Elevations in Certain White Blood Cell Types

White blood cell line	Conditions that typically cause elevations
Basophils	Allergic conditions, leukemias
Eosinophils	Allergic conditions, dermatologic conditions, eosinophilic esophagitis, idiopathic hypereosinophilic syndrome, malignancies, medication reactions, parasitic infections
Lymphocytes	Acute or chronic leukemia, hypersensitivity reaction, infections (viral, pertussis)
Monocytes	Autoimmune disease, infections (Epstein-Barr virus, fungal, protozoan, rickettsial, tuberculosis), splenectomy
Neutrophils	Bone marrow stimulation, chronic inflammation, congenital, infection, medication induced, reactive, splenectomy

Table 3. Nonn	nalignant Causes of Neutrophilia	
Cause	Distinguishing features	Evaluation
Patient characteristics	Pregnancy, obesity, race, age	Reference appropriate WBC count by age or pregnancy trimester Compare WBC count to recent baseline (if available)
Infection	Fever, system-specific symptoms Physical examination findings	Obtain system-specific cultures and imaging (e.g., sputum cultures, chest radiography) Consider empiric antibiotics Consider use of other biomarkers, such as CRP and procalcitonin
Reactive neutrophilia	Exercise, physical stress (e.g., postsurgical, febrile seizures), emotional stress (e.g., panic attacks), smoking	Confirm with history
Chronic inflammation	Rheumatic disease, inflammatory bowel disease, granulomatous disease, vasculitides, chronic hepatitis	Obtain personal and family medical history Consider erythrocyte sedimentation rate and CRP levels, specific rheumatology laboratories Consider subspecialist consultation (e.g., rheumatology, gastroenterology)
Medication induced	Corticosteroids, beta agonists, lithium, epinephrine, colony-stimulating factors	Confirm with history; consider discontinuation of medication, if warranted
Bone marrow stimulation	Hemolytic anemia, immune thrombocytopenia, bone marrow suppression recovery, colonystimulating factors	Complete blood count differential; compare with baseline values (if available) Examine peripheral smear Consider reticulocyte and lactate dehydrogenase levels Consider flow cytometry, bone marrow examination, hematology/oncology consultation
Splenectomy	History of trauma or sickle cell disease	Confirm with history
Congenital	Hereditary/chronic idiopathic neutrophilia, Down syndrome, leukocyte adhesion deficiency	Obtain family, developmental history Consider hematology/oncology, genetics, and immunology consultations

NOTE: After patient characteristics, causes are listed in approximate order of frequency.

 $\mathit{CRP} = \mathit{C-reactive protein; WBC} = \mathit{white blood cell.}$

Information from references 1 through 7, 9, and 10.

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CASE 2

History:

23-year-old male

Over the past week noted increasing fatigue, sore throat, earaches, headaches, and episodic fever and chills

Unable to run his customary 20 miles per week

Physical Exam:

Erythematous throat and tonsils

Swollen cervical lymph nodes

No other organomegaly

WBC: $14.4 \times 10^3 / \text{uL}$ (4.5-10.5)

Neutrophils: 24 % (65-75)

RBC: 5.25 x 10⁶/uL (4.2-5.4)

Lymphocytes: 73 % (35-45) HGB: 15.4 g/dL (14-18)

HCT: 46.1 % (38-48)

MCV: 87.9 fL (80-100)

MCH: 29.3 pg (26-34)

MCHC: 33.4 g/dL (31-37)

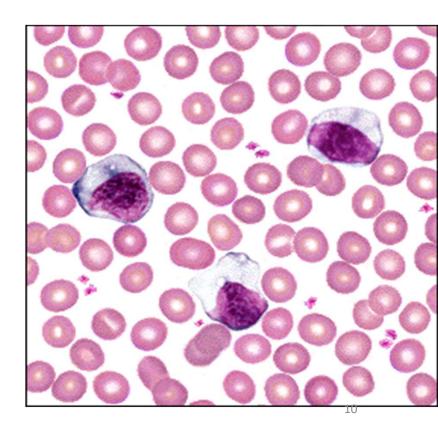
RDW: 12.2 % (<14)

Monocytes: 0 % (0-7)

Eosinophils: 3 % (0-5)

Basophils: 0 % (0-1)

Platelets: 333 x 10³/uL⁴ 150² 400)



Normal: < 1%

Clincially significant: > 10%

Band neutrophils are slightly less mature than segmented neutrophils and have indented, unsegmented "C" or "S" shaped nuclei.

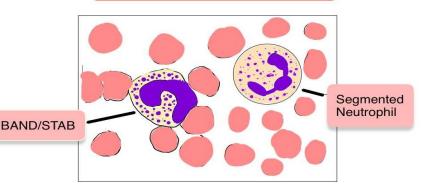
Band neutrophils normally account for approximately 5-10% of peripheral blood leukocytes.

LEFT SHIFT:

- -Cell population has "shifted towards immature precursors "
- -Stab cell- nucleus looked like a Shepard's crook (Stab in German) -neutrophils counted left to right with bands being on the left



BANDEMIA



Differential Diagnosis:

- -Seizures
- -Toxic ingestions
- -metabolic abnormalities
- -inflammatory processes
- -Tissue damage
- -leukemia
- -Corticosteroid use
- -autoimmune diseases
- -chemotherapy













Myeloblast. Promyelocyte Myelocyte Metamyelocyte

LEFT SHIFT-acute infection



Segmented Neutrophil



Even with normal WBC.

Pts with moderate and high BANDEMIA on admission had significantly increased odds of having positive cultures, including blood cultures and of in hospital mortality

https://www.amjmed.com/article/S0002-9343(12)00450-0/abstract

BANDEMIA is highly predictive of a serious infection, suggesting that clinicians who do not appreciate the value of band counts may delay diagnosis or overlook severe infections.

Degree of bandemia, especially in the setting of concurrent tachycardia or fever, is associated with greater likelihood of negative clinical outcomes.

https://www.sciencedirect.com/science/article/abs/pii/ 50735675715001795

Bandemia is a superior indicator of infection relative to both WBC and Temp.

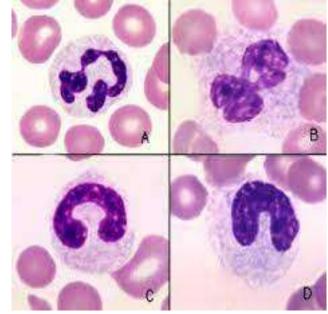
- -Abnormal temperature (hypo/hyperthermia) had a sensitivity of 67% for culture proven bacteremia
- -Abnormal WBC count had a sensitivity of 48% for culture proven bacteremia
- -Bandemia had a sensitivity of 82% for culture proven bacteremia
- -In patients with bacteremia and hypotension or septic shock, 33% had normal temperature and 21% had normal WBC count on initial evaluation

https://doi.org/10.1016/j.jemermed.2010.05.038

CASE 3

HISTORY:

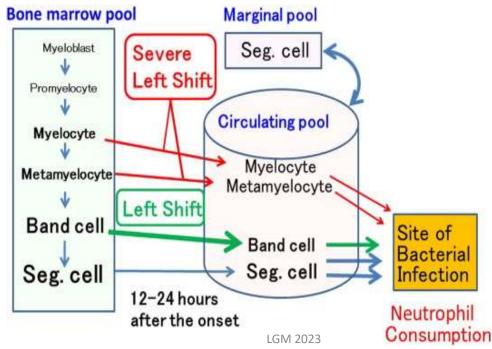
32-year-old male with no significant past medical history presents to the emergency department with abdominal pain. He states the pain began a few days ago in the right lower quadrant of the abdomen, and now feels as though it is spreading to the midabdomen.



CBC

WBC 18.4 x 10 /mcl 61% neutrophils 11% lymphocytes 6% monocytes 2% eosinophils, 20% bands

HGB/HCT 14.6/44.6 g/dl PLT 356 x 10 /mcl

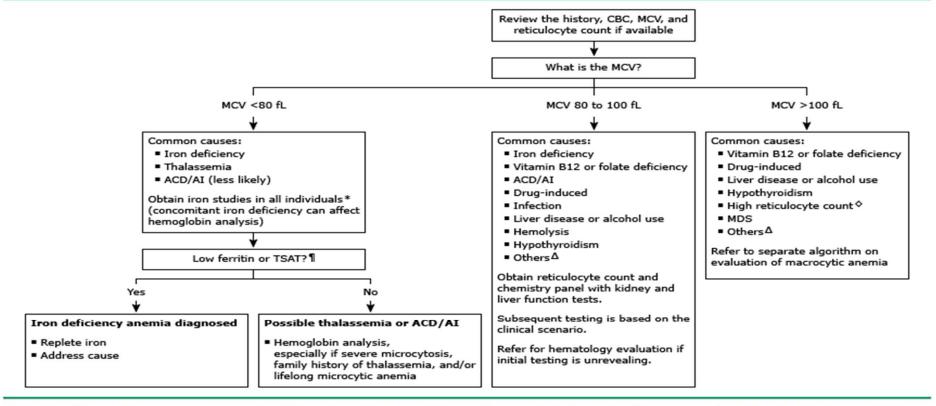


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Anemia

- Reduction in one or more of the major RBC measurements: Hgb, Hct or RBC count
- A low hemoglobin concentration and/or low hematocrit are the parameters most widely used to diagnose anemia.
- Caveats for normal:
 - Causes of lower values: intense physical activity, pregnancy, older age
 - Causes of higher values: smoking, hemoconcentration (hypovolemia), high altitude

Anemia evaluation in outpatients (nonpregnant adults)



This algorithm addresses anemia in healthy outpatients, which is often an incidental finding or may be identified when a CBC is performed to evaluate mild symptoms such as fatigue. It is not appropriate for individuals who are acutely ill with fever, bleeding, neurologic symptoms, or any severe cytopenia (hemoglobin <7 to 8 g/dL; platelet count <50,000/microL, absolute neutrophil count [ANC] <1000/microL). Consider the history, CBC, MCV, and reticulocyte count (if available) simultaneously. Refer to UpToDate for details of testing for specific causes of anemia.

CASE 4

History:

70 year old female.

Symptoms of dyspnea on exertion, easy fatigability, and lassitude for past 2 to 3 months. Denied hemoptysis, GI, or vaginal bleeding. Claimed diet was good, but appetite varied.

Physical Exam:

Other than pallor, no significant physical findings were noted. Occult blood was negative.

CBC

(with microscopic differential)

RBC 3.71 x 10¹²/L HGB 5.9 g/dL HCT 20.9 % L 13 MCV 56.2 fL M 1 MCH 15.9 pg

MCHC 28.3 g/dL

RDW 20.2

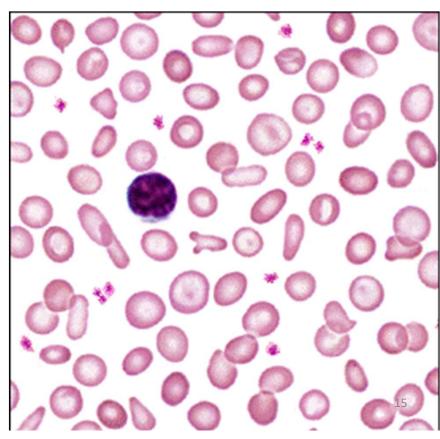
WBC $5.9 \times 10^9/L$

N 82 %

E 4

B 0

PLT 383 x 10⁹/L



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CASE 5

HISTORY:

37 year old male.

Lifelong history of a seizure disorder, treated since age two.

At a routine check with his neurologist, he complained of fatigue, exertional dyspnea, and lightheadedness over the past 2-3 months.

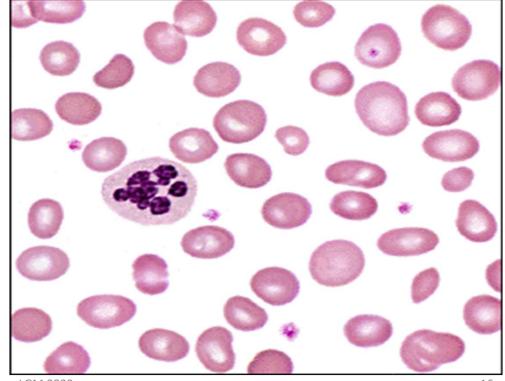
He appeared pale, but otherwise his physical exam was within normal limits. He was found to have a decreased

hemoglobin, and was referred to Hematology Clinic.

CBC

RDW 18.1

(with microscopic differential)	•
	N 73 %
RBC 1.26 x 10 ¹² /L	L 21
HGB 5.7 g/dL	M 1
HCT 16.3 %	E 4
MCV 130 fL	B 1
MCH 45.2 pg	PLT 219 x 10 ⁹ /L
MCHC 34.9 g/dI	



THROMBOCYTOPENIA

- Norm platelet count >150,000 per μl
- Thrombocytopenia <50,000 has 个 risk of major hemorrhage
- Causes: bone marrow depression, immune diseases and/or infections (particularly viral infections)
- Petechiae are often noted with a platelet count < 50,000
- Decrease in # of platelets

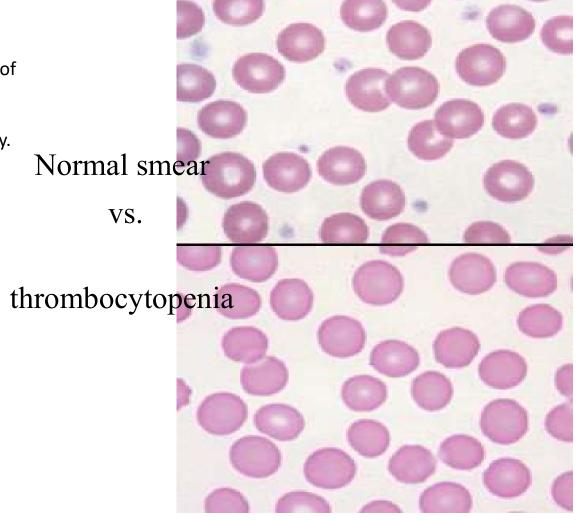
- Most common cause of abnormal bleeding
- Causes:
 - Bone marrow damage (RT, chemo)
 - Idiopathic
 - Chemicals (benzene, insecticides)
 - Complication of viral diseases
 - Myelodysplastic syndrome
 - Drugs (thiazide diuretics, alcohol)
 - Malignancy (marrow infiltration)
 - Multiple myeloma
 - Acute leukemias
 - Lymphomas
 - Myeloproliferative disorders

CASE 6

21 yr old with no significant medical history complains of hematuria, bleeding gums while brushing his teeth.

On Physical exam, petechiae are noted in the oral cavity.

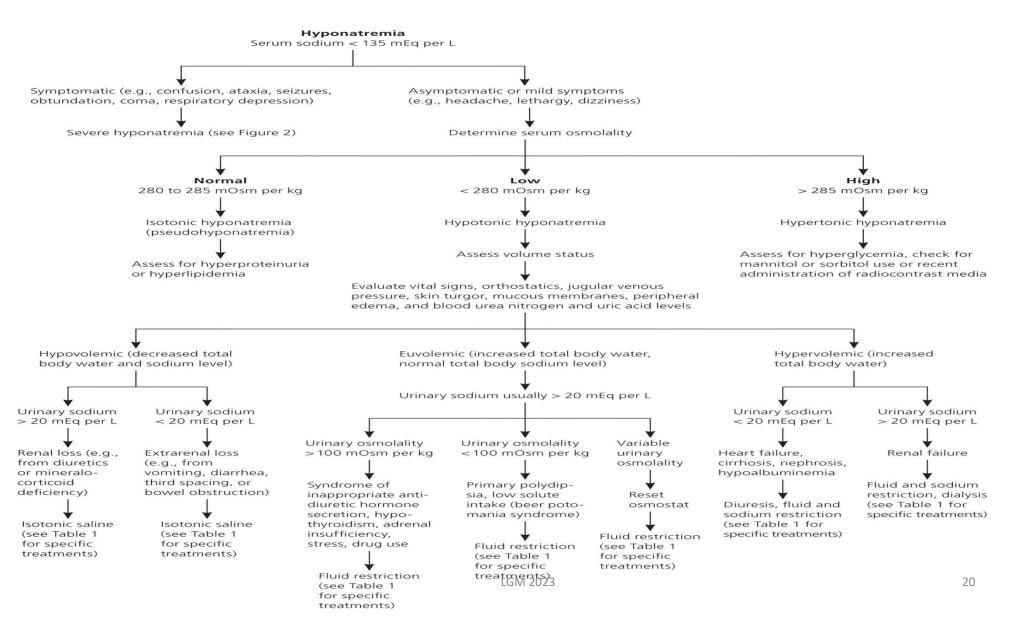
WBC 8,000 /mm3 Hematocrit 35% Platelet count 13,000 PT 13 s PTT 28 s



Hyponatremia

- Na < 120 mEq per L
- Most common electrolyte abnormality seen in medical practice
- Classified based on volume status
- In adults, the most common causes of hyponatremia are thiazide diuretic use, postoperative state with infusion of IV fluids, syndrome of inappropriate antidiuretic hormone secretion (SIADH), psychogenic polydipsia, exercise-associated hyponatremia, and unintentional water intoxication.

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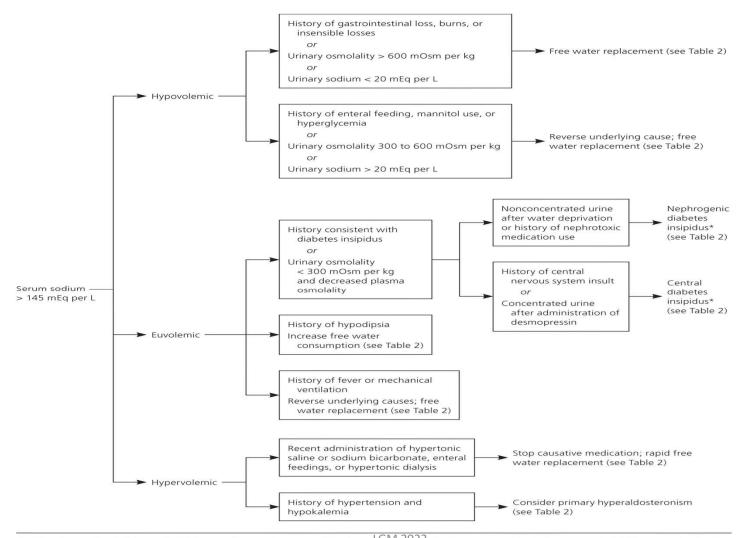
Case 7

- 70 year old female with moderate dementia presents c/o increased lethargy and confusion
- Her caregiver reports increased thirst throughout the day
- Meds: Donepezil, Lisinopril/HCTZ, Famotidine

Serum Na-	128	(135-145) mEq/L
Serum OSM	275	(280-285/kg)
Urine Na	25	(>20 mEq/L)
Urine Osm	20	(50-1200 mmol/kg)

Hypernatremia

- Na > 145 mEq per L
- Associated w/ increased m&m in inpatient setting
- Caused by net water loss
- Risk factors: impaired thirst mechanism, restricted access to water, AMS, intubated patients, infant, elderly



^{*—}The diagnosis of diabetes insipidus usually requires a combination of water deprivation and a trial of desmopressin. With water deprivation, patients with diabetes insipidus will have increased plasma osmolality but not urinary osmolality. In patients with central diabetes insipidus, urinary osmolality will increase by approximately 200 mOsm per kg after receiving desmopressin.35

Condition	Diagnosis	Treatment
Hypovolemic hypernatremia		
Body fluid loss (e.g., burns, sweating)	Clinical	Free water replacement
Diuretic use	Clinical	Stop diuretic
Gastrointestinal loss (e.g., vomiting, diarrhea, fistulas)	Clinical	Free water replacement
Heat injury	Elevated temperature, myoglobinuria, elevated creatinine level	Intravenous fluids, supportive care
Osmotic diuresis (e.g., hyperosmolar nonketotic coma, mannitol use, enteral feeding)	Elevated glucose level; sodium level often elevated after correction	Correct glucose level, stop causative agent
Post-obstruction	Clinical	Supportive care
Euvolemic hypernatremia Central diabetes insipidus	Clinical history of central nervous system insult; urinary concentration after administration of desmopressin	Treatment is rarely required unless thirst is impaired
Fever	Clinical	Treat underlying cause
Hyperventilation/mechanical ventilation	Clinical	Adjust ventilation
Hypodipsia	Clinical	Increase free water consumptio
Medications (e.g., amphotericin, amino- glycosides, lithium, phenytoin [Dilantin])	Medication review	Stop causative medication
Nephrogenic diabetes insipidus	History of nephrotoxic medication use (amphotericin, demeclocycline [Declomycin], foscarnet, lithium, methoxyflurane), failure to concentrate urine after administration of desmopressin	Stop causative medication
Sickle cell disease	Hemoglobin electrophoresis	Treat underlying disease
Suprasellar and infrasellar tumors	Magnetic resonance imaging	Treat underlying disease
Hypervolemic hypernatremia Cushing syndrome	24-hour urinary cortisol and adrenocorticotropic hormone levels, dexamethasone suppression test	Treat underlying disease
Hemodialysis	Clinical history	Treat underlying disease
Hyperaldosteronism	History of hypertension and hypokalemia, plasma aldosterone-to-renin ratio, ³ history of hypertension and hypokalemia	Treatment usually not needed for hypernatremia
latrogenic (e.g., salt tablet or salt water ingestion, saline infusions, saline enemas, intravenous bicarbonate, enteral feedings)	Recent administration of hypertonic saline, enteral feedings, sodium bicarbonate infusion, or hypertonic dialysis	Stop causative medication, rapid free water replacement
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Hypokalemia

- < 3.6 mmol/L
- Can results from decreased intake, increased translocation into cell, or most often due to increased losses due to GI tract or urine

Major causes of hypokalemia

Decreased potassium intake
Increased entry into cells
An elevation in extracellular pH
Increased availability of insulin
Elevated β -adrenergic activity - stress or administration of beta agonists
Hypokalemic periodic paralysis
Marked increase in blood cell production
Hypothermia
Chloroquine intoxication
Increased gastrointestinal losses
Vomiting
Diarrhea
Tube drainage
Laxative abuse
Increased urinary losses
Diuretics
Primary mineralocorticoid excess
Loss of gastric secretions
Nonreabsorbable anions
Renal tubular acidosis
Hypomagnesemia
Amphotericin B
Salt-wasting nephropathies - including Bartter's or Gitelman's syndrome
Polyuria
Increased sweat losses
Dialysis
Plasmapheresis

Hyperkalemia

- >5.2 mmol/L
- Commonly triggered by medications affecting K+ homeostasis, illness or dehydration
- The presence of ECG changes or rapid rise is potentially life-threatening
- IV calcium will stabilize cardiac membrane
- Insulin, bicarb will allow for intracellular shift of K+
- Kayexalate, dialysis allow for removal of K+

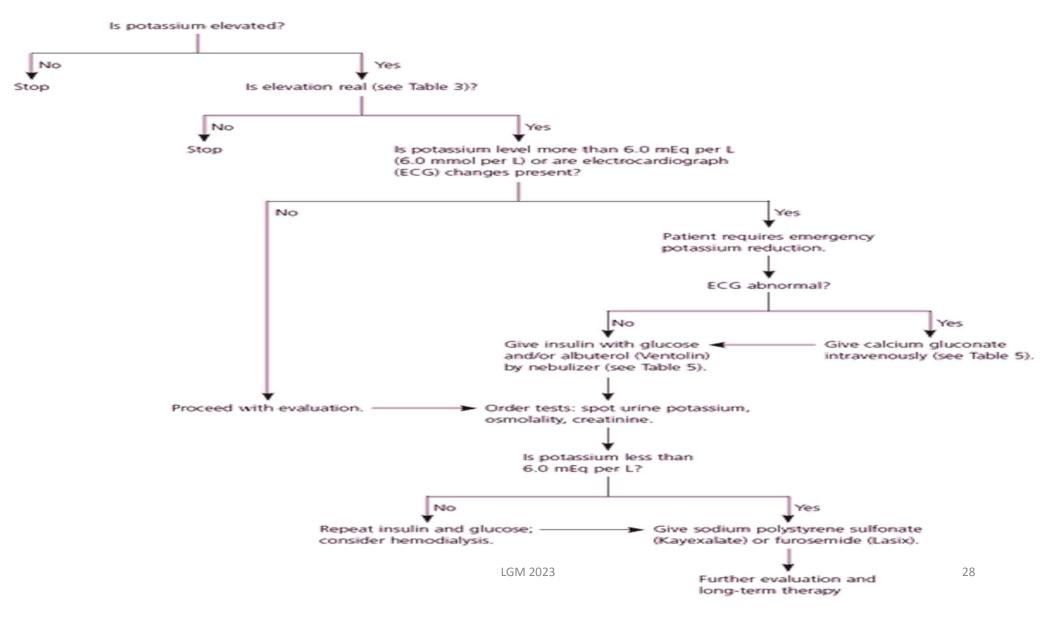
Major causes of hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality
Increased tissue catabolism
Beta blockers
Exercise
Hyperkalemic periodic paralysis
Other
Overdose of digitalis or related digitalis glycosides
Red cell transfusion
Succinylcholine
Arginine hydrochloride
Activators of ATP-dependent potassium channels (eg, calcineurin inhibitors, diazoxide, minoxidil, and some volatile anesthetics)
Reduced urinary potassium excretion
Reduced aldosterone secretion
Reduced response to aldosterone
Reduced distal sodium and water delivery
Effective arterial blood volume depletion
Acute and chronic kidney disease
Other
Selective impairment in potassium secretion
Gordon's syndrome
Ureterojejunostomy LGM 2023 UpToData

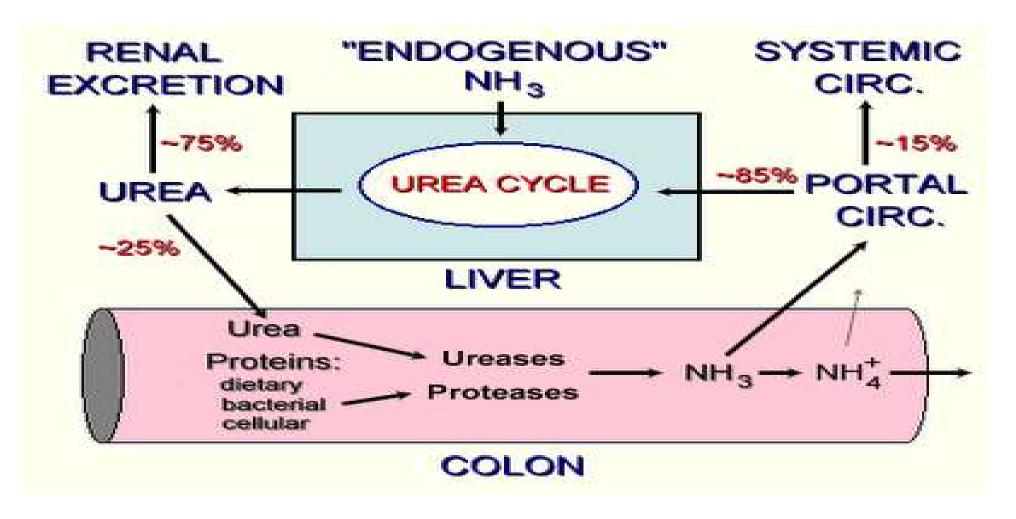
Case 8

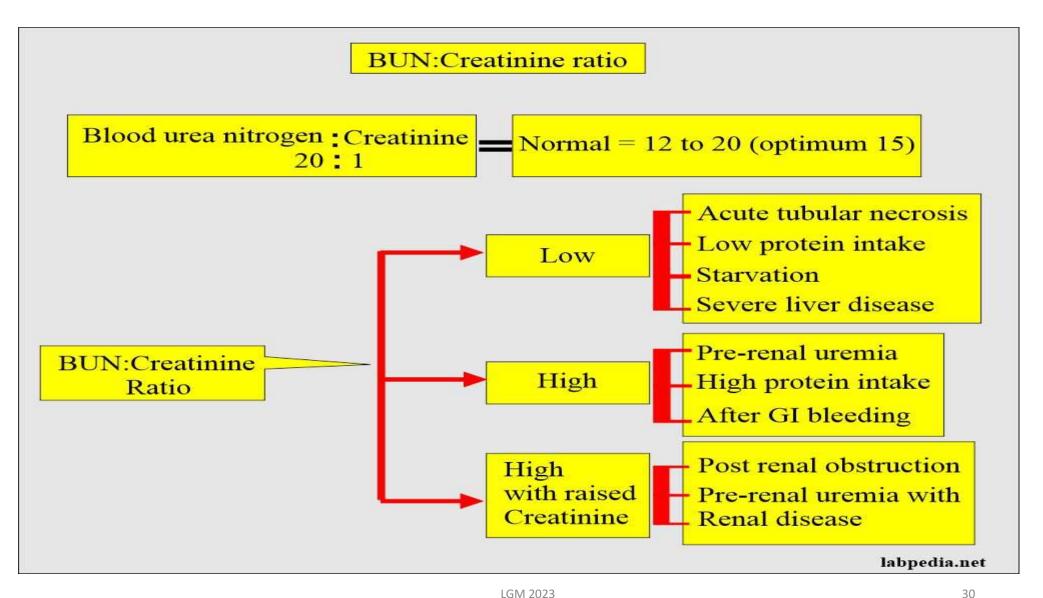
- 64 yr old female c/o progressive weakness, nausea and palpitations.
- Meds: Digoxin, Lisinopril, Synthroid, Citalopram
- BMI-32.2

	Results	Normal Values
Plasma Na	130 mEq/L	
K	8.5 mEq/L	
Chloride	98 mEq/L	
HCO3	17 mEq/L	
Creatinine	2.7 mEq/L	
pH	7.32	
Capillary blood glucose	400 mmol/L	
Serum acetone	+	



BUN and Creatinine





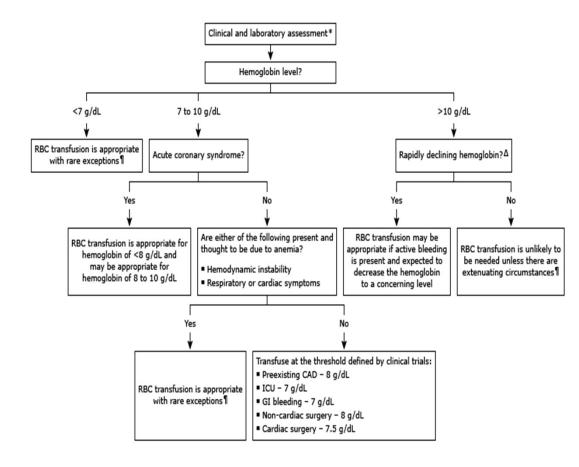
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Case 9

A 40 year old male presents c/o "coughing up blood"

H/H - 8.0 g/25% BUN - 42Creatinine 1.0 BUN/Cr ratio = 42:1

CBC: MCV 112 fL, RDW 20



UPTODATE, 2023

URINALYSIS GROSS EXAMINATION: urine colors

PINK OR RED & CLOUDY	RBCs
PINK OR RED & CLEAR	Hemoglobin or myoglobin Porphyrins
DARK AMBER	Presence of conjugated bilirubin
BLACK	Melanin (metastatic malignant melanoma)
DARK YELLOW / VARIATIONS OF YELLOW	Hydration status
DARK ORANGE	Pyridium Rifampin

URINALYSIS GROSS EXAMINATION: turbidity

• Can be seen in presence of infection or contamination

• Lipids

• RBCs

URINALYSIS GROSS EXAMINATION: Urine odor

- Most commonly a result of production of ammonia by bacteria
- Presence of ketones can cause sweet or fruity odor
- Certain rare disorders can cause others:
 - Maple syrup urine disease- maple syrup odor
 - PKU- musty or mousy odor
- Foods: i.e. asparagus

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URINALYSIS DIPSTICK / CHEMICAL ANAYLSIS

CHARACTERISTIC	NORMAL	ABNORMAL	INTERPRETATION
SPECIFIC GRAVITY	1.005- 1.030		Low: hypovolemia, diabetes insipidus, High: hypervolemia, glucosuria, proteinuria, contrast, mannitol
рН	5.0-7.0		Aids in identification of acid-base disorders
HEME	(-)	(+)	RBCs, abnormal intravascular hemolysis, extensive burns, rhabdomyolysis, MI, Ascorbic acid (Vitamin C) can yield false-negative
LEUKOCYTE ESTERASE	(-)	(+)	Marker for presence of WBCs due to infection/inflammation Concentrated urine, proteinuria or glucosuria may produce false-negative
NITRITES	(-)	(+)	Bacteria
PROTEIN	(-)	(+)	Rhabdomyolysis, pregnancy, pre-eclampsia, eclampsia, multiple myeloma (Bence-jones proteins), Kidney disease, drugs/toxins,
GLUCOSE	(-)	(+)	Diabetes, pregnancy, renal glycosuria
KETONES	(-)	(+)	Inadequate carbohydrate intake, frequent vomiting/diarrhea, DKA, GM 2023 36

URINALYSIS: MICROSCOPIC EVALUATION

RBCS Normal: 0-2/hpf	UTI, stones, benign or malignant urinary tract neoplasms, trauma, prostatitis, glomerular or tubular disease, pyelonephritis, toxins, multisystem diseases i.e. SLE, blood dyscrasias i.e. Sickle cell disease, Rhabdomyolysis, menstrual contamination
	Infection or inflammation of genitourinary system
WBCS Normal: 0-3/hpf	Pyelonephritis- Present with moderate/heavy proteinuria, pyuria, WBC casts, and hematuria Cystitis- Present with pyuria, hematuria, and smaller amounts of protein. No casts
EPITHELIAL CELLS	Squamous Epithelial Cells- most frequently seen, clinically least significant Transitional Epithelial Cells- large numbers typically after instrument procedures, suspect pathology if no h/o instrumentation i.e. catherization
Clean: < 5/hpf	Renal Tubular Epithelial Cells- increased number indicates tubular necrosis or damage LGM 2023 38

ТҮРЕ	INTERPRETATION
RBC CASTS	Proliferative glomerulonephritis
WBC CASTS	Kidney infection, inflammation, or trauma
RENAL TUBULAR EPITHELIAL CASTS	Intrinsic renal tubular disease: ATN, acute interstitial nephritis, proliferative glomerulonephritis
GRANULAR CASTS	ATN, patients w/ischemic or toxic injury to tubular epithelial cells
HYALINE CASTS	Non-pathologic- strenuous exercise, dehydration, fever, emotional stress, diuretic therapy Pathologic- acute glomerulonephritis, pyelonephritis, chronic renal disease
WAXY CASTS	Severe urine stasis in renal tubules; often present in chronic renal failure
BROAD CASTS	Advanced CKD, ESRF

Microscopic examination: crystals

- Calcium oxalate or calcium phosphate- form in alkaline urine, usually benign. Can be seen in ethylene glycol poisoning
- Magnesium ammonium phosphate- constituents of struvite stones.
 Occurs with increased ammonia production and elevated urine pH in the setting of UTI with a urease- producing organism i.e. Proteus or Klebsiella
- Uric acid- seen in diseases causing hyperuricemia (gout)
- Cystine- seen in cystinuria, an amino acid disorder

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Microscopic examination: microorganisms

• Bacteria- UTI, bacterial contamination

Yeast

• Parasites- most common *Trichomonas vaginalis*

CASE 10

History: 24 F with no significant PMHx presents w/chief complaint of dysuria. She admits fever, vomiting, & flank pain.

Vitals: BP: 120/85 mmHg, HR: 115 bpm, RR: 22, Temperature: 103 F

PE: Non-toxic appearing, (+) R CVA tenderness, Abdomen is soft, non-tender and non-rigid without peritoneal signs.

CBC: Elevated WBCs, otherwise WNL

CMP: WNL

Urinalysis: (+) Nitrites, (+) LE, (+) WBCs > 10/hpf, (+) RBCs

Urine Pregnancy: (-)

Questions?

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