Laboratory Diagnosis Review

Hematology

Definition: The study of the three cellular elements of blood: Red Blood Cells (RBCs), White Blood Cells (WBCs), and Platelets

Hemoglobin (Hgb or Hb): The oxygen carrying compound in RBCs

Reference Range: Men 14-18 g/dL, Women 12-16 g/dL, Boy and girl levels are equal till age 11
Smoking increases, Pregnancy decreases, Capillary levels in newborns are higher than venous levels, Race, Position, and Time of day have minor effects, High WBCs may falsely raise Hgb.
Below normal Hgb = anemia

Red Blood Cell Count

Reference Range: Men 4l5-6 million / cubic ml, Women4.0-5.5 million / ml^3.

Hematocrit (Hct): The ratio of RBCs to plasma

Reference Range, Men 40%-54%, Women 37%-47%, Depends mostly on the number of RBCs but is slightly effected by the average RBC size, Not measured directly, but is calculated from the RBC count and the mean corpuscular volume (MCV).
Increased by smoking, Decrease = anemia

Useful Relationships:

Hb X 3 = Hct
RBCs (millions) X 3 = Hgb
RBCs (millions) X 9 = Hct

Wintrobe Indices: These indices are only significant if the RBCs, Hgb, and/or Hct. is abnormal

MCV: Mean Corpuscular Volume
MCH: Mean Corpuscular Hemoglobin
MCHC: Mean Corpuscular Hemoglobin Concentration
RDW: Red blood cell Distribution Width

MCV: Reference Ranges: Men 80-95 fl (femtoliters), Women 81-99 fl (femto = 1 quadrillionth)
Increased MCV = Macrocytosis, Decreased = Microcytosis
MCV is <u>increased</u> by smoking, by B_{12} and/or folic acid deficiency, chronic liver disease, chronic alcoholism, Cardiorespiratory problems… Some macrocytic patients will not have macrocytosis
MCV is <u>decreased</u> by iron deficiency, thalassemia, and anemia of chronic disease

MCH: Reference Range 27-31 pg
MCH is <u>increased</u> by Macrocytic anemias. <u>Decreased</u> by Microcytic and hypochromic anemias

MCHC: Reference Range 32-36 g/dl or 32%-36%
MCHC is <u>increased</u> by Spherocytosis or Intravascular hemolysis. It is <u>decreased</u> by Iron def. anemia and Thalassemia

RDW: Reference Range 11-14%, RDW <u>increases</u> when there are different sized red blood cells, so both microcytosis and macrocytosis will increase RDW. A <u>decreased</u> RDW is not significant
The state of having different sized RBCs is called anisocytosis.

<u>NOTE</u>: I doubt that you will be asked any reference ranges for the Wintrobe indices, but have provided them for your convenience if you chose to learn them.

Peripheral Blood Smear:

Stained with Wright stain to allow examination of RBC abnormalities.

Red blood cell abnormalities: <u>Hypochromia</u> = iron deficiency. <u>Oval macrocytes</u> can indicate folic acid or B_{12} deficiency or myelodysplasia. <u>Round macrocytes</u> can indicate alcoholism, cirrhosis, hypothyroidism… Other RBC abnormalities include: Spherocytes, Reticulocytes, Schistocytes, Acanthocytes, Echinocytes (crenated), Bite cells (degmacytes), Sickle cells, Elliptocytes, Target cells, Teardrop cells, Stomatocytes, and Rouleaux. RBC inclusions include Basophilic stippling, Howell-Jolly bodies, Heinz bodies, and Pappenheimer bodies.

<u>NOTE</u>: **<u>If you do not know what these RBC abnormalities look like or what they signify, refer to the appropriate section of your Laboratory Diagnosis lecture notes.</u>**

White Blood Cells: Reference Range 4,500-11,000 / mm^3.

Differential Values

Neutrophils (Segs, Polys)	50%-70%
Lymphocytes	20%-40%
Monocytes	0% - 7%
Eosinophils	0% - 5%
Basophils	0% - 1%

WBC abnormalities: Pelger-Huet: The most important WBC abnormality. Many of the nuclei hyposegment into a dumbbell or eyeglass shape. It can be congenital, but most often seen in myeloproliferative disorders, myeloid leukemia, metastasis to bone marrow or some cases of drug toxicity.

Increased neutrophils (neutrophilic leukocytosis) can be caused by Inflammation (the most common cause), bacterial infection, some viral infections, tissue destruction, metabolic toxicity, drug and chemical toxicity, and cigarette smoking

Increased Lymphocytes (lymphocytosis) may be due to viral infection, Addison's disease, viral hepatitis, mononucleosis.

Monocytosis may be due to Sub-acute bacterial endocarditis, Disseminated tuberculosis, Malignant lymphomas and carcinomas, Rheumatoid collagen diseases…

Eosinophilia can be caused by Parasites, Allergies, Chronic skin diseases, Scarlet Fever…

Basophilia can be due to Chronic myelogenous leukemia, Myeloproliferative diseases, and some non-malignant conditions.

Neutropenia (<4,000 / mm3) can be due to megaloblastic anemia, Aplastic anemia, Leukemia, Systemic Lupus, overwhelming bacterial infections…

Leukoerythroblastosis: (the presence of immature WBCs and nucleated RBCs in the peripheral blood) is seen with Metastatic bone marrow tumors, Leukemia, Hemolytic anemia, Acute hemorrhage…

Chemistry / Serology

Glucose (fasting): Reference range 70-105 mg/dl. **Increased –** Diabetes, Acute stress response, Cushing's syndrome, Chronic renal failure… **Decreased –** Hypothyroidism, Insulinoma, Addison's disease, Insulin overdose…

Glucose Tolerance Test (GTT):

Reference ranges: Fasting: 70-105 mg/dl

30 min:	<200
1 hour:	<200
2 hours:	<140
3 hours:	70-105
4 hours:	70-105

Contraindications: Current infection, endocrine disorders, patient vomits all or part of the glucose meal. **Potential complications:** Dizziness, anxiety, sweating, fainting, tremors…

Interfering Factors: Smoking or exercise during the test, aspirin, beta blockers, furosemide, oral contraceptives, steroids, psychotropic drugs…

Glycosylated Hemoglobin (AKA: Glycohemoglobin, Hemoglobin $A_{1C,}$)

Reference ranges:	Normal adult:	2.2%-4.8%
	Good Diabetic Control:	2.5%-5.9%

Indicates the average blood glucose over the past 100-120 days. Can be fasting or non-fasting,

Interfering factors: Anything that lengthens or shortens the RBC life span, **Increased** can indicate a newly diagnosed or poorly controlled diabetic patient. Levels can **decrease** due to hemolytic anemia, chronic blood loss or chronic renal failure.

Blood Urea Nitrogen (BUN): Reference Range 10-20 mg/dl. It is made in the liver and is excreted through the kidneys so it evaluates both organs. **Increased** indicates kidney pathology, CHF…**Decreased** indicates liver pathology, nephrotic syndrome. Elevated BUN is called azotemia. **Interfering Factors:** Low or High-protein diets, Advanced pregnancy, Over or under hydration, Medications. **Increased BUN**: Kidney disease, Hypovolemia, CHF, MI… **Decreased Bun:** Liver failure, Overhydration, Early pregnancy.

Creatinine: Used to diagnose impaired renal function, Made from creatine phosphate which is used in muscle contraction, Reference ranges: Female 0.5-1.1 mg/dl, Male 0.6-1.2 mg/dl, **Critical Value: >4 mg/dl**, Can increase slightly with meals containing meat, **Increased:** Kidney disease, Rhabdomyolysis, Acromegaly, **Decreased:** Decreased muscle mass (debilitation, Muscular Dystrophy, Myasthenia gravis…

Uric Acid: The final breakdown product of purine, Used to evaluate gout or urinary calculi, Soft-tissue deposits of uric acid are called tophi. Reference Ranges Male: 4.0-8.5 mg/dl, Female, 2.7-7.3, **Critical Value: >12 mg/dl**, **Interfering Factors:** increased by stress, high-protein infusion, some drugs, decreased by x-ray contrast agents and some drugs, **Increased due to increased production:** increase purine consumption (organ meat, red meat, anchovies), Rhabdomyolysis, Cancer, Hemolysis. **Increased due to decreased excretion:** Idiopathic – the most common cause of increase, chronic renal disease… **Decreased:** Wilson's disease, Falconi's syndrome, Lead poisoning.

Sodium: Reference Range 136-145 mEq/L, **Critical value:** <120, >160, Monitors fluid and electrolyte balance, **Increased:** Excess salt intake, Cushing's, Loss of water, **Decreased:** Insufficient intake, Addison's, Vomiting, Diarrhea, Increased water (CHF…)

Potassium: Reference Range 3.5-5.0 mEq/L, Critical value <2.5 or >8 mEq/L, Important for heart rate and Contractility, **Interfering factors:** Making a fist with the tourniquet on, hemolysis, drugs… **Increased:** Excess intake, renal failure, Addison's… **Decreased:** Deficient intake, burns, diuretics, Cushing's…

Chloride: Reference Range 98-106 mEq/L, **Critical Value:** <80 or >115, Helps evaluate acid/base balance and hydration, **Increased:** Dehydration, metabolic acidosis, kidney dysfunction, **Decreased:** Overhydration, Congestive Heart Failure, vomiting…

Phosphorus: Reference Range 3.0-4.5 mg/dl, **Critical Value:** <1 mg/dl, Used to investigate parathyroid and calcium abnormalities. **Increased:** Excess intake, Hypoparathyroidism, renal failure, bone metastasis, acromegaly, **Decreased:** Inadequate intake, Hyperparathyroidism, chronic antacid intake, chronic alcoholism, Vitamin D deficiency …

Calcium: Reference Range for Total Calcium 9.0-10.5, **Critical Value:** <6 or >13, Evaluates parathyroid function and calcium metabolism, **Interfering factors:** Vitamin D intoxication, Excessive milk consumption, **Increased:** Hyperparathyroidism, Metastatic bone tumor, Paget's, Hyperthyroidism, **Decreased:** Hypoparathyroidism, renal failure, Rickets, Vitamin D deficiency

Protein Electrophoresis: Reference Ranges: **Total Protein** 6.4-8.3 g/dl, **Albumin:** 3.5-5.0 g/dl, Globulin 2.3-3.4 g/dl, **Albumin/Globulin Ratio: >1**Used to diagnose and monitor patients with cancer, protein wasting states, immune disorders, liver disease…, Gamma Globulins are antibodies, **Increased Albumin:** Dehydration, **Decreased Albumin:** Liver disease, malnutrition, pregnancy, **Increased Globulin:** Malignancy, Multiple Myeloma, Cirrhosis, **Decreased Globulin:** Immune deficiency, An A/G ratio below 1 is called an inverted or reversed A/G ration and is a sign of serious illness.

Bilirubin: Reference Ranges **Total Bilirubin** 0.3-1.0 mg/dl, **Indirect (unconjugated) Bilirubin** 0.2-0.8 mg/dl, **Direct (conjugated) Bilirubin** 0.1-0.3 mg/dl, **Critical Value** >12, Used to evaluate liver function, **Increased direct bilirubin:** Obstruction due to gallstones, tumor, trauma, inflammation, liver metastasis, **Increased indirect bilirubin:** Hemolysis**,** Erythroblastosis fetalis, Transfusion reaction, hepatitis, cirrhosis…

Alkaline Phosphatase (ALP): Reference Range 30-120 U/L, Used to detect and monitor diseases of the liver and bone, **Interfering factors:** Recent meal, children with rapid bone growth, drugs, **Increased:** Primary cirrhosis, Biliary obstruction, Liver cancer, Late pregnancy, Bone tumor, Healing fracture, Paget's, RA… **Decreased:** Malnutrition, Pernicious anemia, scurvy…

Aspartate Aminotransferase (AST aka SGOT): Reference Range 0.0-3.5 U/L, Concentrated in heart muscle, skeletal muscle, and liver cells, Evaluates suspected coronary artery occlusion or liver disease, **Interfering factors:** Pregnancy decreases AST, Exercise may increase AST, drugs, **Increased:** M.I. or other injury to the myocardium, Hepatitis, cirrhosis, or other liver injury, Skeletal muscle injury, Muscular Dystrophy, **Decreased:** Acute renal disease, Diabetic ketoacidosis, Beriberi

Alanine Aminotransferase (ALT aka SGPT): Reference Range 4-36 U/L, Identifies and monitors liver disease, **Interfering factors:** I.M. injections, Drugs, **Significantly Increased:** Hepatitis, hepatic necrosis, hepatic ischemia, **Moderately Increased:** Cirrhosis, Cholestasis, Hepatic tumor, **Mildly Increased:** Myositis, pancreatitis, M.I. Mononucleosis, Shock

Lactic Dehydrogenase (LDH): Reference Range 100-190 U/L, Indicates cell damage – heart, liver, RBC, kidneys, skeletal muscle, brain, lungs, LDH isoenzymes can indicate which tissue is damaged, **Interfering factors:** Hemolysis, Strenuous exercise, Medications, **Increased:** M.I. and RBC disease (LDH-1), Pulmonary disease (LDH – 2 & 3), Hepatic and skeletal muscle disease (LDH-5), Cancer, diffuse disease or injury,

Creatine Phosphokinase (CPK or CK): Reference Range Male: 55-170 U/L, Female: 30-135 U/L, Indicates injury to the myocardium, skeletal muscle, or neurological tissue, **Interfering factors:** I.M. injections, strenuous exercise, early pregnancy – CPK is related to muscle mass. **Increased Total CPK:** Injury to the heart, skeletal muscle, brain, **Increase CPK-BB:** CNS disease, Pulmonary infarction, Breast or lung cancer, **Increased CPK-MB:** Cardiac damage, **Increased CPK-MM:** Damage to muscle – muscular dystrophy, surgery…

Gamma-Glutamyl Transpeptidase (GGTP aka GGT): Reference Ranges < age 45 8-38 U/L, > age 54 5-27 U/L, a sensitive indicator of hepatobiliary disease and an indicator of chronic and heavy alcohol use, Elevated GGTP and elevated alkaline phosphatase suggest liver disease. Normal GGTP with elevated alkaline phosphatase indicate bone disease, **Interfering factors:** Late pregnancy, drugs, **Increased:** Liver disease, M.I., Alcohol ingestion, EB virus…

Serum Iron: Reference Range: Male 80-180 mcg/dl, Female 60-160 mcg/dl, **Increased:** Iron poisoning, Hemochromatosis or hemosiderosis, **Decreased:** Dietary iron deficiency, malabsorption, Chronic blood loss…

Triglyceride: Reference ranges: Male 40-160 mg/dl, Female 35-135 mg/dl, Indicates cardiovascular risk and lipid metabolism disorders, **Interfering factors:** Eating a high fat meal, Alcohol ingestion, Pregnancy… **Increased:** Hyperlipidemia, High carbohydrate diet, Poorly controlled diabetes, chronic renal failure… **Decreased:** Malabsorption, Malnutrition, Hyperthyroid…

Cholesterol: Reference Range <200 mg/dl, Used to assess the risk of coronary heart disease, Must be considered with other factors such as LDL, HDL, Homocysteine, LP(a), and others, **Risk Factor =** Total cholesterol / HDL, Elevated cholesterol should be verified by repeating the test, Test preparation requires a 12-14 hour fast after eating a low-fat meal, **Increased:** High-cholesterol diet, Diabetes, Hyperlipidemia, **Decreased:** Malabsorption, Malnutrition, Advanced cancer, Liver disease, Hyperthyroidism

HDL: Reference Range Male >45m Female >55, Made in the liver and intestines, removes cholesterol from the tissues and transports it to the liver for excretion, <35 mg/dl increases cardiovascular risk, >60 is considered to be cardioprotective

LDL: Reference Range 60-180 mg/dl, Deposits cholesterol in the peripheral tissues, LDL=total cholesterol-(HDL+triglycerides/5)

Lipoproteins: Alcohol, bad diet, liver disease, and smoking lower HDL and raise LDL. A good diet and exercise can raise HDL and lower LDL

Acid Phosphatase aka Prostatic Acid Phosphatase (PAP): Reference Range 0.13-0.63 U/L, Used primarily to diagnose and stage prostate cancer, High levels generally indicate that prostate cancer has spread – usually to bone, **Interfering factors:** Prostate manipulation (exam) can cause levels to rise 25-50% for up to 48 hours. Conditions that raise ALP may also raise PAP. **Increased:** Prostatic carcinoma, BPH, Multiple Myeloma…

Prostate Specific Antigen (PSA): Reference Range <4 ng/ml, Used to screen for prostate cancer. Combined with a rectal exam, almost 90% of significant cancers can be detected. PSA is more sensitive than other prostatic tumor markers, **Interfering factors:** May be elevated by prostate exam, Elevated significantly by a prostate biopsy, Elevated for 24 hours by ejaculation, Recent UTI or prostatitis can elevate as much as 5X baseline for up to 6 weeks. **Increased:** Prostate cancer, BPH, prostatitis.

Amylase: Reference Range 60-120 Somogyi units/dl, Used to diagnose and monitor pancreatitis, ordered for patients experiencing severe abdominal pain, **Increased:** Pancreatitis, Acute cholecystitis, renal failure, intestinal disease…

Lipase: Reference Range 0-160 U/L, Used to evaluate the pancreas, Acute pancreatitis is the most common cause of elevation, **Increased:** Same as amylase

Carbon Dioxide Content: Reference Range 23-30 mEq/dl, Used to evaluate pH status, **Interfering factors:** Underfilling the collection tube, Medication, **Increased:** Severe vomiting, COPD, Metabolic alkalosis, **Decreased:** Chronic diarrhea, renal failure, diabetic ketoacidosis, Starvation

Cortisol: Reference Ranges 8:00 AM: 5-23 mcg,/ 4:00 PM: 3-13 mcg/dl, Used to evaluate adrenal gland function, **Interfering factors:** Physical and emotional stress can elevate cortisol levels, **Increased:** Stress, Cushing's, Hyperthyroidism… **Decreased:** Addison's, Hypothyroidism

C-Peptide aka Connecting Peptide: Reference Ranges Fasting: 0.78-1.89 ng/ml, 1 hour after glucose load: 5-12 ng/dl, Used to monitor diabetic patients who may be secretly taking insulin and for monitoring patients with an insulinoma, **Interfering factors,** Kidney failure can cause elevation, **Increased:** Insulinoma, Kidney failure, **Decreased,** Diabetes, exogenous insulin

C-Reactive Protein: Reference Range <1.0, Used to indicate an acute inflammatory condition, More sensitive than ESR, **Increased:** Acute Inflammatory reaction, bacterial infection, Malignant disease,

Erythrocyte Sedimentation Rat (ESR): Reference Ranges: Male – up to 15 mm/hr, Female – up to 20 mm/hr, Used to detect acute and chronic inflammation, **Interfering factors:** Non-vertical tube, Pregnancy, Menstruation… **Increased:** Acute or chronic inflammation, Chronic renal failure, Malignant disease…

Creatinine Clearance: Reference Ranges: Male – 107-139 mm/min, Female – 87-107 mm/min, Used to determine the Glomerular Filtration Rate (GFR), If one kidney fails or is removed, the other kidney – if normal – can increase its filtration so there is no decrease in creatinine clearance. Requires a 24 hour urine collection and serum creatinine level. Creatinine Clearance = UV/P. U=mg/dl of creatinine excreted in 24 hours, V=ml/minute of urine volume, P=Serum creatinine in mg/dl. **Interfering factors:** Exercise, High-meat diet, Incomplete urine collection lowers value. **Increased:** Exercise, Pregnancy, High cardiac output syndromes. **Decreased:** Impaired kidney function, CHF, Dehydration…

Ferritin: Reference Ranges: Male 12-300 ng/ml, Female 10-150 ng/ml, The most sensitive blood test for iron deficiency anemia, **Increased:** Inflammatory disease, Hemochromatosis, hemolytic anemia, alcoholism, **Decreased:** Iron-deficiency anemia, Severe protein deficiency, Dialysis

Fibrinogen: Reference Range: 200-400 mg/dl, **Critical Value:** <100 is associated with spontaneous bleeding, Used primarily to diagnose bleeding disorders. Diets with a large amount of polyunsaturated oils decrease fibrinogen levels, **Increased:** Acute inflammatory reactions, Trauma, Acute infection, Cigarette smoking… **Decreased:** Liver disease, Advanced carcinoma, Malnutrition

Folic Acid (Folate): Reference Range: 5-25 ng/ml, Used to asses nutritional status, **Increased:** Pernicious anemia, Vegan or vegetarianism, **Decreased:** Malnutrition, Malabsorption, Pregnancy, Megaloblastic anemia, Hemolytic anemia…

HLA-B27 Antigen (HLA=Human Leukocyte Antigen): Normal Finding – Negative, **Positive:** AS, RA, Celiac disease, Reiter's, Psoriasis, …

Homocysteine (HCY): Reference Range: 4-14 micromol/L Used to evaluate risk of vascular disease (and several other conditions), Deficiency of B6, B12, and Folic acid is the most common non-genetic cause of high homocysteine, Homocysteine is an intermediate metabolite of methionine, **Increased:** Risk of vascular disease, Malnutrition, Renal failure.

Magnesium: Reference Range 1.3-2.1 mEq/L, Most organ functions depend on magnesium – it is critical in almost all metabolic processes, Most magnesium is bound to ATP and is involved in it's phosphorylation, Deficiencies often lead to cardiac irritability and arrhythmias. **Increased:** Renal insufficiency, Addison's disease, Hypothyroidism… **Decreased:** Malnutrition, malabsorption, Hypoparathyroidism, Alcoholism, Diabetic acidosis

Thyroid Stimulating Hormone (TSH): Reference Range 2-10 microU/ml, Used to diagnose primary hypothyroidism and differentiate it from secondary (pituitary) and tertiary (hypothalamus) hypothyroidism. TSH is stimulated by thyroid-releasing hormone (TRH) from the hypothalamus. Both TRH and TSH are stimulated by low levels of T_3 and T_4 so both TRH and TSH are elevated when the thyroid hormones are low. **Increased:** Primary hypothyroidism, **Decreased:** Secondary or tertiary hypothyroidism, hyperthyroidism, Suppressive thyroid medication

Triiodothyronine (T_3): Reference Ranges 20-50 years old 70-205 ng/dl, >50 years old 40-180 ng/dl, Used primarily to diagnose people with hyperthyroidism and to monitor replacement and suppressive therapy, Less useful than T_4 for diagnosing hypothyroidism because many other conditions can decrease T_3 levels. **Increased:** Primary hyperthyroid states i.e. Grave's, Acute thyroiditis e.g. Hashimoto's (levels decrease in later stages), **Decreased:** Hypothyroidism (myxedema, cretinism, surgical ablation), Pituitary insufficiency, Hypothalamic failure, Iodine deficiency..

Total Thyroxin (T_4) aka Thyroid Hormone or Tetraiodothyronine: Reference Range 4-12 mcg/dl, **Critical Values:** <2 mcg/dl may result in myxedema coma, >20=Thyroid Storm, Includes both free and bound thyroxin (almost all of it is bound), Used to diagnose thyroid disorders and to monitor therapy, **Increased & Decreased:** Same as T_3

Urinalysis

Overview

Urine is derived from the filtration of blood. All end-products of metabolism are excreted in the urine along with waste products. Some products can be found in urine that are not detectable in blood such as Bence-Jones proteins.

Types of Urine Specimens:

First Morning Specimen: Represents all the urine produced over the previous 6-8 hours and provides more information than a random specimen. It is more concentrated due to the overnight fast and is therefore more likely to detect abnormalities.

Random Urine Specimen: Used for screening for illegal drugs. Convenient if timing is not important.

Timed Urine Collection: Urine collected at a pre-determined time such as testing glucose and/or insulin 2 hours after a meal. Also used for collecting at specific times due to natural cycles such as early-morning cortisol levels.

Double-Voided Specimen: The patient empties the bladder then provides the specimen shortly afterward. This most accurately reflects blood concentrations at that time.

Collection Methods

Routine Specimen: Requires no preparation. A non-sterile container can be used.

Mid-stream Clean-catch Specimen: The urinary meatus must be carefully cleaned. The cleaning agent must be removed. The stream is started, then stopped, then started and collected in a sterile container.

Twenty-four Hour Collection: This method reduces false negatives. <u>All</u> urine produced during the 24 hours must be collected or the interpretation will not be accurate.

Other methods include: **Urethral catheterization, Suprapubic aspiration,** and **Pediatric Collection**

Urinalysis – Normal Findings:

Appearance; Clear
Color: Amber yellow
Odor: Aromatic
Protein: None or a trace
Specific Gravity: 1.005-1.030
Leukocyte esterase: Negative
Nitrites: None

Ketones: None
Bilirubin: None
Urobilinogen: 0.01-1.0 Ehrlich units/ml
Crystals; None
Casts: None
WBCs: 0-4 per low power field (lpf)
WBC casts: None
RBCs: No more than 2
RBC casts: None

Urinalysis – Abnormal Findings

Appearance and Color:

Cloudy may indicate pus or fat or other abnormal solute

Straw color indicates dilute urine. **Dark amber** indicates concentrated urine, **Dark red** may indicate bleeding from the kidney, **Bright red** indicates bleeding from the lower urinary tract (or beet ingestion), **Dark Yellow** may be from bilirubin (thick yellow foam on the specimen is another indication of bilirubin) **Green** may indicate pseudomonas, **Brown** may be from eating rhubarb.

Odor: Sweet or Acetone = ketoacidosis, **Foul odor** = urinary tract infection, **Fecal odor** = possible fistula

pH: Alkaline urine can be caused by bacteria or a diet high in vegetables and fruit. **Acid urine** can be caused by acidosis, starvation, dehydration, or a diet high in meat, meat products, or cranberries.

Protein: An indicator of kidney problems. The combination of proteinuria and edema is called **nephrotic syndrome**.

Specific Gravity: a measure of hydration and kidney function. High SG = concentrated. Low SG = dilute

Leukocyte Esterase and Nitrites: Both are indications of bacteria in the urine

Glucose: Diabetes, increased intracranial pressure, endocrine disease

Ketones: a sign of uncontrolled diabetes, Fasting – starvation, High-protein diet, Alcoholism, or Febrile illness esp. in infants and children

Bilirubin: Conjugated bilirubin is water soluble and can spill into the urine, An indication of biliary obstruction such as gallstones, It can also indicate liver injury or drug toxicity

Urobilinogen: Made from bilirubin in the intestine by bacteria. High bilirubin and High urobilinogen indicates **hemolysis**. High bilirubin plus Low urobilinogen indicates an **obstruction** or defects in bilirubin metabolism.

Crystals: Indication of kidney stone formation. The type of crystal is determined by the urine pH

Casts: Usually associated with proteinuria

Hyalin Casts: Normally present, esp,. after strenuous exercise

Granular Casts: exercise or renal disease

Fatty Casts: nephrotic syndrome, fatty emboli from bone fractures

Waxy Casts: chronic renal disease or renal failure

Anemia

Anemia Defined: A decrease in hemoglobin (or hematocrit)

Classification of Anemia by Pathology:

Factor Deficiency Anemia: Iron, B_{12}, Folic acid, or some combination of the three

Production Defect Anemia: Failure of blood-forming organs to produce or deliver mature RBCs to the peripheral blood due to conditions such as marrow fibrosis or neoplasm, chemical toxins, severe infection, widespread malignancy…

Depletion Anemia: From peripheral blood loss, hemorrhage, hemolysis…

Classification of Anemia by RBC Morphology: Microcytic, Normocytic, Macrocytic

Factor Deficiency Anemia:

Iron Information: 70% is in the hemoglobin, 30% is stored in the bone marrow, liver, spleen, and reticulum cells. Absorption is increased by **vitamin C** and by taking iron supplements 45-60 minutes before eating. Absorption is decreased by coffee, tea, dairy products, and foods with high fiber content. Iron needs are increased in pregnant and lactating women.

Transferrin transports iron. Most iron is stored and **ferritin**.

Other General Information: With blood loss from acute bleeding, the anemia is initially normocytic and normochromic. If bleeding continues, the RBCs become microcytic and hypochromic. Bleeding is the most common cause of anemia. Common causes of bleeding include hemorrhoids, GI bleeding (peptic ulcer, carcinoma), reproductive tract in women.

Laboratory Tests for Iron Deficiency:

Peripheral Blood Smear:

May appear normal in the early stages. RBCs become microcytic and hypochromic in later stages, MCV may decrease, RDW increases, Reticulocytes are normal in uncomplicated iron deficiency, but will increase with acute blood loss.

Serum Iron: A sensitive indicator of possible iron deficiency. **Decreased:** Iron deficiency, Anemia of severe chronic disease, severe physical stress, **Increased:** Hemolysis, Iron overload, Estrogen therapy, Acute hepatitis…

Serum Ferritin: The major iron storage compound. The most sensitive test for iron deficiency other than bone marrow iron stain, <10 ng/ml is almost always diagnostic of iron deficiency.

Free Erythrocyte Protoporphyrin aka Zinc protoporphyrin: If iron is not available, zinc binds with the protoporphyrin. **Increased:** iron deficiency, lead poisoning, inflammation, malignancies…

Total Iron Binding Capacity: An estimate of serum transferrin. Is increased in uncomplicated iron deficiency and decreased with decreased transferrin.
Decreased Serum Iron + Decreased TIBC suggests chronic disease
Decreased Serum Iron + Increased TIBC suggests iron deficiency
Decreased Serum Iron + Decreased Transferrin Saturation suggests thalassemia minor

Bone Marrow Iron Stain: The gold standard for iron deficiency. It requires bone marrow aspiration.

Vitamin B_{12} Deficiency:

Caused By: Lack of Intrinsic Factor, Lack of or low gastric acid, Dysbiosis, Pancreatic disease, Fish tapeworm, Drugs, Malabsorption syndromes

Can appear low due to: Actual deficiency, Large dose of vitamin C, Pregnancy, Folic acid deficiency, Chronic iron deficiency

Megaloblastic Anemia: Caused by a lack of B_{12} and/or Folic acid. **Methylmalonic acid (MMA)** assay is a functional test for B_{12} deficiency. MMA will be increased in the blood and the urine. Elevated MMA indicates deficiency even when serum B_{12} is normal. MCV and LDH will be increased.

Pernicious Anemia (PA): B_{12} deficiency due to the lack **of intrinsic factor (IF)**. It is most often seen in northern Europeans age 40 or older although incidence is increasing among Hispanics and African Americans. It can be idiopathic or due to gastrectomy. The definitive test for PA is the **Shilling** test, however false positives are common – up to around 30%.

Folic Acid Deficiency: Megaloblastic anemia that would be indistinguishable from PA without the Shilling test. The two must be differentiated because treating PA with folic acid will relieve symptoms, but the neurological damage of B_{12} deficiency will continue. Can be **caused by:** Dietary deficiency, Chronic alcoholism, Malabsorption, Pregnancy, Oral contraceptives…

Depletion Anemia: There are two types of depletion anemia
Loss of RBCs due to bleeding
Destruction of RBCs i.e. hemolysis

Production Defect Anemia: Due to one or more of the following:
Failure of the marrow to incorporate adequate supplies of raw material
Failure of the marrow to release mature RBCs
Destruction of RBC precursors in the marrow
Etiological factors may include:

Myelofibrosis, Neoplasm, Aplastic anemia, Anemia associated with systemic disease. Associated conditions can include radiation, chemicals, cytotoxic drugs, rubella, herpes zoster, hepatitis C and others. About 50% of production-defect anemia cases are idiopathic.