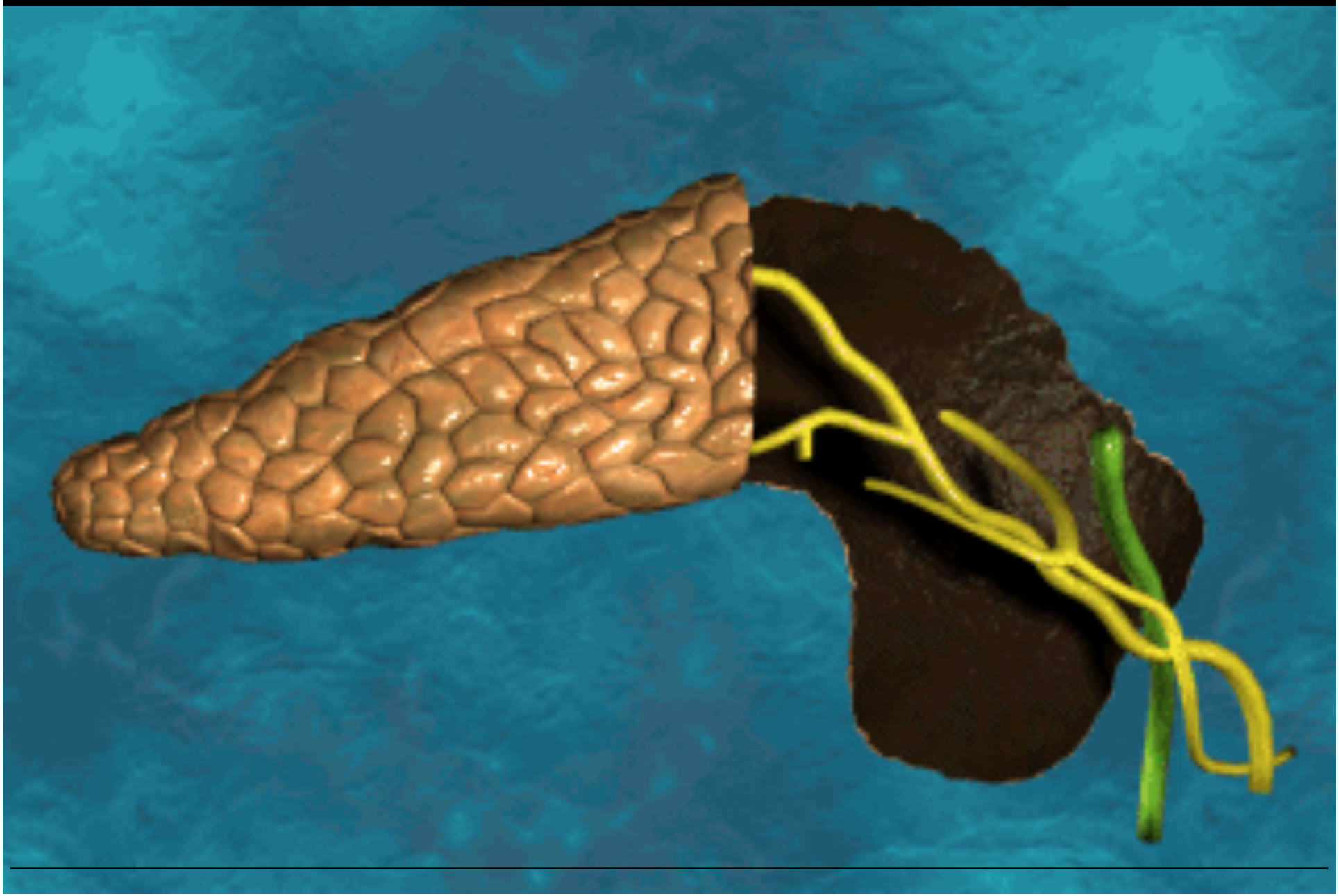
Endocrine / Electrolyte / Acid Base



Hypoglycemia (1)

- Glucose is the sole energy source for the brain
- Symptoms of hypoglycemia depend on the glucose level and the rate of glucose drop
- Hypoglycemia can mimic stroke,TIA, epilepsy, MS, psychosis, Stokes-Adams
- Counterregulatory hormones (glucagon and epinephrine) cause the release of glycogen from the liver

Hypoglycemia (2)

- Sympathomimetic symptoms: sweating, tremor, pallor (vasoconstriction), anxiety, nausea
- Sympathomimetic symptoms can be masked by beta blockers
- Neuroglycopenia symptoms: dizziness, psychosis, confusion, coma

Always consider hypoglycemia in an unresponsive patient – check a rapid blood glucose level

Hypoglycemia (3)

- Differential diagnosis
  - Insulinoma
  - Medications / drugs / alcohol
  - Extrapancreatic neoplasm
  - Hepatic disease (depletion of glycogen stores)
  - Deficiency of counterregulatory hormones
  - Critically ill, stressed infants, hypothermia
  - Dumping syndrome
- Artifactual
  - Continued glycolysis by WBCs in lab tube
  - Leukemia, polycythemia

Hypoglycemia (4)

- Distinguishing excess endogenous insulin from excess exogenous insulin
  - Pancreas cleaves proinsulin to insulin plus immunoreactive C-peptide
  - Excess endogenous insulin has measurable C-peptide (not so with excess exogenous insulin)

Hypoglycemia (5)

- Standard treatment options
  - D_{50}
  - D_{25} (peds)
  - D_{10} (neonates)
  - Glucagon 1 mg IM/IV (converts liver glycogen to glucose)
  - D_{10} drip if recurrent or overdose
  - Hydrocortisone (adrenal insufficiency)
  - **Octreotide** – **inhibits insulin secretion** and helps prevent rebound hypoglycemia in the setting of glucose infusion treatment of refractory **sulfonylurea-induced hypoglycemia**

Oral Agents In Diabetes Treatment (1)

- Two classes: hypoglycemics & antihyperglycemics
- Hypoglycemic agents:

  Sulfonylurea agents
  - Chlorpropamide, tolbutamide, acetohexamide tolazamide, glipizide, glyburide, glimepiride
  - Stimulate pancreatic insulin secretion
  - Cause profound hypoglycemia in overdose
  - Long duration of action
  - Chlorpropamide also can cause SIADH

  Repaglinide (Prandin)
  - Can also cause hypoglycemia

Oral Agents In Diabetes Treatment (2)

- Antihyperglycemic agents
- Less likely to cause hypoglycemia in overdose

Metformin

- Rarely causes lactic acidosis

Alpha-glucosidase inhibitors

- Inhibit intestinal hydrolysis of polysacharides
- Oral sucrose will not be absorbed

Thiazolodenediones (Avandia/Actos)

- Limited overdose experience
- Can worsen CHF
- Other side effects

Hypoglycemia Pearls

- **Always admit if sulfonylurea overdose**
  - Most symptomatic in 4 hours (can be delayed)
  - **Octreotide** inhibits insulin secretion
- Give thiamine with glucose in hypoglycemic malnourished patients
- Glucagon may not be effective in chronic alcoholics, those with liver disease or infants with low, liver glycogen stores

Diabetic Ketoacidosis Pathophysiology

- Relative lack of insulin + stressors causes hyperglycemia
- Hyperglycemia-induced osmotic diuresis causes polyuria, dehydration, hypovolemia, electrolyte loss (K, Mg, Phos)
- Switch over to fat breakdown for energy source causes ketonemia (acidosis)
- Metabolic acidosis causes compensatory hyperventilation (Kussmaul respirations)

Precipitants of DKA

- The "I's" have it!
  - Infection (UTI, pneumonia, pancreatitis)
  - Infarction (e.g. AMI)
  - Infraction (noncompliance)
  - IUP (pregnancy)
  - Ischemia (CVA)
  - Illegal (substance abuse)
  - Iatrogenic (drug interactions)
  - Idiopathic (new onset DM)

Fluids / Bicarbonate in DKA

- Initial fluid resuscitation for hypovolemia
- Replace electrolytes (phosphate, potassium)
- Insulin drip (**after checking potassium**)
- Sodium bicarbonate is rarely indicated
  - The hazards of bicarbonate use include
    - Paradoxical CSF acidosis
    - Decreased oxygen-hemoglobin dissociation (shifts curve to left)
    - Overload of sodium
    - Hypokalemia, hypophosphatemia
    - Cerebral edema in children

Sodium / Phosphate in DKA

- Pseudohyponatremia

  (*Hyperosmolar as opposed to hypoosmolar state)

  - Sodium is artifactually ↓1.6 mEq/L for every 100 mg/dL ↑ glucose over 100

Hypophosphatemia is possible:
Respiratory depression, muscle weakness
CHF, decreased mental status
(failure to generate adequate ATP)

Potassium in DKA

- Serum K^+ level may be elevated, normal or low
- Initial hypokalemia indicates massive total body depletion (usual deficit is 3-7 mEq/L)
- Replacement recommendations
  - K < 3.3: Hold insulin, give 40 mEq per hour until ≥ 3.3
  - K ≥ 3.3 but < 5.0: give 20-30 mEq in each liter IVF to keep K 4-5 mEq/L
  - K ≥ 5.0: No replacement but check Q2 hr
- **Serum potassium will decline with insulin and correction of acidosis** (drives K^+ into cells)
- Cardiac arrest in DKA is often 2° to precipitous hypokalemia (insulin therapy, acidosis correction or fluid therapy with increased urinary losses)

Complications of DKA Treatment

- Hypoglycemia due to excess insulin
  - Add glucose administration when glucose = 250 mg/dl
- Hypokalemia is associated with insulin administration, bicarbonate, hydration
- Bicarbonate therapy causes CSF acidosis
- Cerebral edema
  - Patients at risk: Young, new onset DM
  - Controversial: Possibly 2^0 to over-hydration, rapid osmotic changes, hypoxemia, sodium bicarbonate

Alcoholic Ketoacidosis (1)

- Binge drinking with heavy alcohol consumption and decreased food intake for several days (starvation ketosis)
- Imbalance of insulin levels and counter-regulatory hormones
- Ethanol metabolism inhibits gluconeogenesis
- Abdominal pain, nausea, vomiting, dehydration, disorientation

Alcoholic Ketoacidosis (2)

- Alcohol levels are usually low or negative and glucose is often mildly elevated with low bicarbonate and high anion gap
- Urinary ketones may be weakly positive
- Treatment: Glucose + saline (D5NS), thiamine and potassium repletion

The major and earliest ketone produced from fat breakdown is beta-hydroxybutyrate, but the lab-measured ketone is acetoacetate. Therefore, lab tests for ketones may be falsely negative.

Hyperosmolar Hyperglycemic Non-ketotic State HHNS (1)

- Similar to DKA but has important distinctions
  - No ketoacidosis
  - Glucose is usually higher, often >1000
  - Serum osmolality is often greater than 350
  - Most often occurs with NIDDM
  - Higher mortality than DKA
  - DKA has shorter onset
- Precipitating factors include
  - Infection, especially pneumonia
  - Myocardial infarction
  - CVA
  - GI bleed
  - Pyelonephritis
  - Pancreatitis
  - Uremia
  - Subdural hematoma
  - Peripheral vascular occlusion

Hyperosmolar Hyperglycemic Non-ketotic State HHNS (2)

- Common comorbid conditions
  - Renal insufficiency
  - Vascular disease
  - Poor access to water

HHNS is often the initial presentation of NIDDM

- Common associated medications
  - Diuretics
  - Propranolol
  - Corticosteroids
  - Calcium channel blockers
  - Phenytoin
  - Cimetidine

Hyperosmolar Hyperglycemic Non-ketotic State HHNS (3)

Physical findings

- Dehydration
- Altered sensorium
- Focal neurologic findings (often mistaken for a stroke)
- Coma is rare

Treatment

- Normal saline
- Average fluid deficit 8-12 liters
- ½ of deficit in first 12 hours, rest over next 24 hours
- Initial 1-2 liter bolus as clinically indicated
- Insulin infusion (usually lower doses than in DKA)

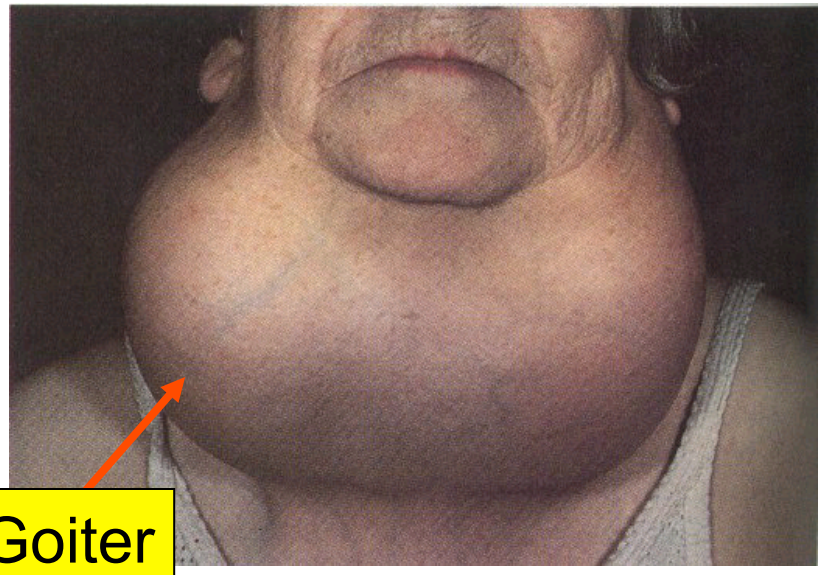
Cerebral edema possibly 2° to rapid fluid replacement or the severity of the condition

Thyroid Hormones

- TRH from hypothalamus stimulates TSH release from anterior pituitary
- TSH stimulates thyroid gland
  - Thyroid hormones ($T_{3,\,[20\%]}T_{4\,[80\%]}$) are synthesized and released
  - Thyroid hormone production depends on iodine intake. Excess iodine blocks hormone release
- T_3 is biologically 4x more active than T_4
- T_3 and T_4 provide feedback inhibition of TSH release
- T_3 and T_4 act on cells
  - Increase rate of cell metabolism
  - Increase rate of protein synthesis

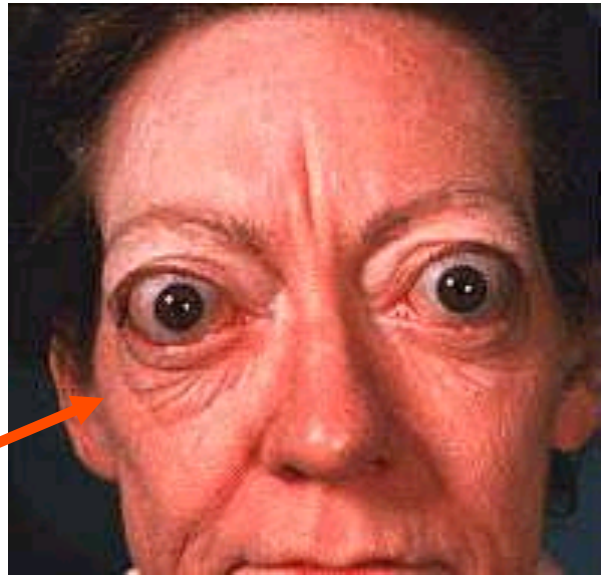
Hyperthyroidism (1)

- Causes
  - Graves' disease (most common):
    - An autoimmune disorder (thyroid-stimulating immunoglobulins mimic the action of TSH)
  - Toxic thyroid adenoma, toxic multi-nodular goiter
  - Thyroiditis
  - Pituitary adenoma
  - Excess iodine in diet



Hyperthyroidism (2)

- Signs and symptoms
  - Nervousness, tremor, insomnia
  - Heat intolerance, sweating
  - Weakness, weight loss, hair loss
  - Tachycardia, palpitations
  - Hyperdefecation
  - Irregular menses
  - Goiter / thyroid bruit
  - Exopthalmos (Grave's only), lid lag (the lids move more slowly than the eyes)



Hyperthyroidism (3)

Pre-tibial Myxedema

- Rare manifestation of Graves' disease
- Bilateral, elevated, firm dermal nodules and plaques
- Skin yellow or waxy
- Accumulation of mucopolysaccharides

Hyperthyroidism (4)

- Risk factors: female, family history, other autoimmune disease
- Lab: Increased T_3 and T_4, decreased TSH
- Treatment
  - Beta blockers
  - PTU
  - Radioactive iodine
  - Surgery

Thyroid Storm (1)

- A life-threatening complication of hyperthyroidism. May not be directly related to magnitude of excess thyroid hormone
- Precipitating events include
  - Withdrawal of antithyroid medications
  - Administration of IV contrast
  - Thyroid hormone overdose
  - Pneumonia
  - CVA
  - Pulmonary embolus
  - Toxemia of pregnancy
  - Diabetes

Thyroid Storm (2)

Thyroid storm is a clinical diagnosis
The hallmark is **CNS dysfunction**

- Other diagnostic criteria include
  - Temperature > 38 ˚C
  - Tachycardia out of proportion to the fever
  - Exaggerated peripheral manifestations of thyrotoxicosis, including tremor and weakness
- No laboratory tests distinguish thyroid storm from simple hyperthyroidism – it is a clinical diagnosis

Thyroid Storm (3)

- Thyrotoxicosis / thyroid storm is associated with
  - Elevated free T_4 level
  - Decreased TSH level
  - Hyperglycemia
  - Hypercalcemia
  - Elevated LFTs
  - Low cholesterol

Thyroid Storm Treatment

- **Five step ORDERED** approach
  1. General supportive care: IV fluids, correct electrolyte imbalance, **corticosteroids** (decrease peripheral conversion of T_4 to T_3), no ASA (displaces thyroid hormone from thyroglobulin)
  2. Blockade of peripheral thyroid hormone effects: **Propranolol** 1 mg to 10 mg titrated to symptoms
  3. Blockade of thyroid hormone synthesis: **PTU** (also inhibits peripheral conversion of T_4 to T_3)
  4. Blockade of thyroid hormone release: **iodine** given one hour after PTU
  5. Identification and treatment of precipitating events

Apathetic Thyrotoxicosis

- Rare disorder seen in elderly patients
- Lethargy, slowed mentation, apathetic facies
- Goiter is usually present
- **Droopy eyelids** are common
- **No exophthalmos**, stare or lid lag
- Symptoms of apathetic hyperthyroidism may be masked because of underlying organ dysfunction
- Resting unexplained tachycardia
- Resistant atrial fibrillation and CHF are common

Hypothyroidism (1)

- Causes
  - Treatment of Graves' disease
  - Iodine deficiency in diet
  - Autoimmune destruction of thyroid gland (e.g. Hashimoto's)
  - Lithium therapy for bipolar disorder
  - Amiodarone
  - Pituitary and hypothalamic disorders (rare)

Hypothyroidism (2)

- Signs and symptoms
  - Weakness, lethargy
  - Cold intolerance
  - Hypothermia
  - Weight gain
  - Constipation
  - Dry, thick skin
  - Generalized nonpitting edema (myxedema)
  - Prolonged, heavy periods

Hypothyroidism (3)

- Clinical signs of severe hypothyroidism include
  - Dermatologic: coarse, waxy skin, loss of lateral third of eyebrows, scant pubic hair, puffy face and extremities (myxedema)
  - CNS: slowed mentation, altered mental status, psychosis ("myxedema madness"), coma
  - Cardiac: CHF, bradycardia, hypotension, cardiomegaly, pericardial effusion, low voltage

Hypothyroidism (4)

- Lab
  - Low T_4, elevated TSH (unless problem with hypothalamus or pituitary)
  - Elevated lipids
  - Hyponatremia (dilutional)
  - Anemia
- Myxedema coma
  - Hypoxemia
  - Hypothermia

Myxedema Coma (1)

- The end of the spectrum of hypothyroidism
- Life-threatening, rare, elderly females, winter
- Precipitating factors include
  - Stressors: MI, infections, trauma, cold exposure
  - Drugs are metabolized slower and therefore have increased effects (narcotics, tranquilizers, beta blockers, amiodarone)
  - Non-compliance with thyroid replacement

Myxedema Coma (2)

- Signs
  - "Hung up" reflexes (prolonged relaxation phase of DTRs)
  - Hypothermia
  - Non-pitting periorbital edema (puffy eyelids)
  - Generalized non-pitting edema

Myxedema Coma (3)

- Treatment
  - Supportive care: Rewarming, fluid support, search for underlying cause
  - Specific treatment
    - IV thyroxine (T_4). May require large doses
    - IV T_3 is not recommended (can cause V-tach)
  - **Corticosteroids** (because of possible unrecognized adrenal or pituitary insufficiency)

Adrenal Gland

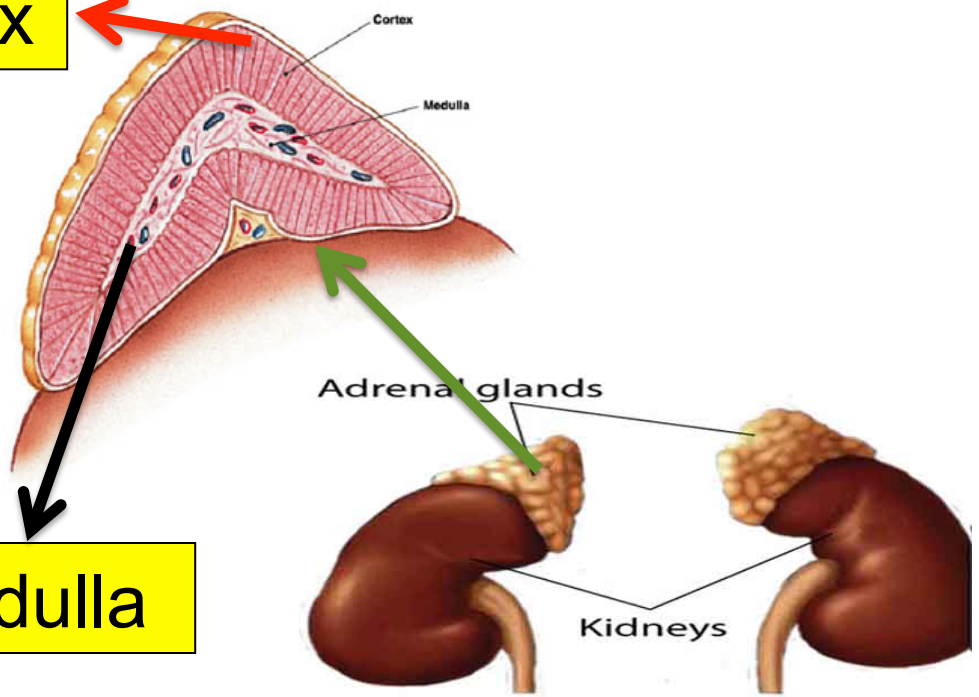
- Clinical manifestations primarily due to
  - Cortisol (affects metabolism of most tissues, glucose regulation, increases blood glucose)
  - Aldosterone (renal Na^+ reabsorption & K^+ excretion)

Cortisol
Aldosterone
Sex hormones

Cortex

Epinephrine
Norepinephrine

Medulla



Adrenal Insufficiency (1)

Primary Adrenal Failure

- Idiopathic (autoimmune): Addison's Disease
- Infiltrative, infectious
  - Sarcoid, amyloid
  - TB, fungal, septicemia
- Hemorrhage, infarction
- Neoplastic
- Drugs (etomidate)
- Bilateral adrenal failure is associated with meningococcemia (Waterhouse-Friderichsen)
  - Presents with abdominal pain, vomiting, fever, hypotension
- Diagnosis by serum cortisol level or corticotropin stimulation test

Hyperpigmentation is seen in Addison's disease

Adrenal Insufficiency (2)

- Secondary adrenal failure
  - Due to hypopituitarism
- Tertiary adrenal failure
  - Usually iatrogenic from prolonged steroid use **(most common cause overall)**
  - Causes adrenal atrophy
  - Usually due to oral steroids; rarely may be due to inhaled or topical steroids
- Laboratory abnormalities include
  - Hyponatremia (most common abnormality) +/- hyperkalemia, eosinophilia (all most common in chronic insufficiency), hypoglycemia
- Acute presentation
  - Fever and refractory hypotension
  - Consider in malignancy

Adrenal Crisis (Insufficiency)

- Treatment
  - D5NS +/ - D50%
  - Hydrocortisone
  - Pressors
- Mortality from adrenal crisis due to
  - Shock
  - Dysrhythmias (hyperkalemia)
  - Underlying disease

Hyperadrenalism (Cushing's Syndrome)

- Excess cortisol
  - Prolonged steroid use (most common)
  - Adrenal neoplasm, pituitary microadenoma
  - ACTH-secreting carcinoma (small cell, pancreatic, bronchial carcinoid)

- Signs and Symptoms
  - Truncal obesity, hypertension, hirsutism, edema, glucosuria, $\uparrow Na^+$
  - Moon facies, buffalo hump, purple striae
  - Treatment: Stop steroids, treat cause

Syndrome of Inappropriate Secretion of Antidiuretic Hormone

- Normally, ADH is secreted in states of dehydration
  - ADH increases renal H_20 reabsorption
  - ADH is inhibited in over-hydration (dilutes urine)
- SIADH: Inappropriate ADH secretion (inhibits urine production resulting in fluid retention and dilutional hyponatremia)
- **Inappropriately concentrated urine in the setting of low serum osmolality (low sodium) and normovolemia = SIADH**
- Causes include **CNS** (tumor, infection, CVA, injury), **Lung** (infection including TB, fungal), **Drugs** (chlorpropamide, vasopressin, diuretics, vincristine, thioridazine, cyclophosphamide)

Diabetes Insipidus

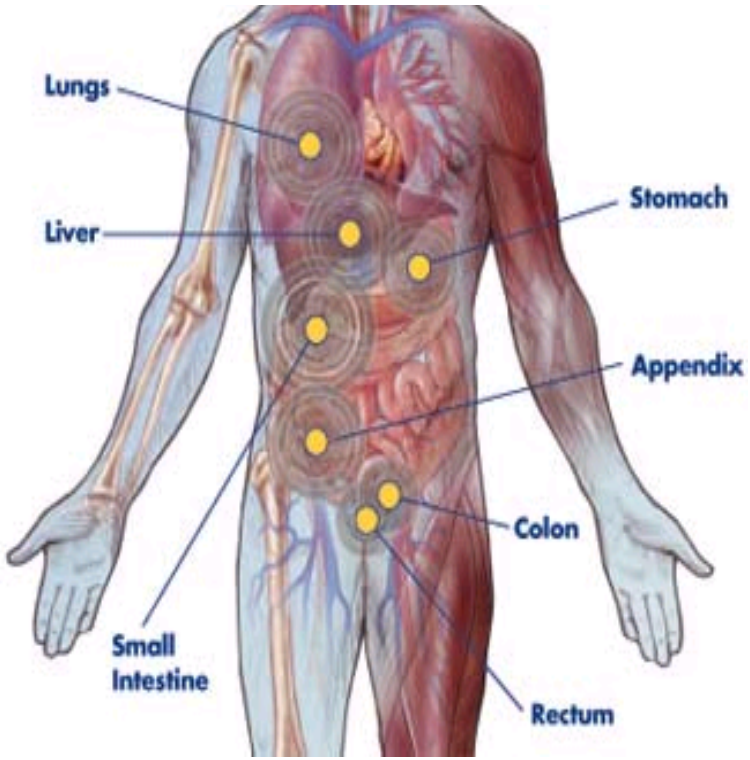
- Symptoms similar to DM – excess urination and increased thirst and fluid intake
- Lack of ADH activity
  - Central: Failure to secrete ADH (head trauma, neoplasm, pituitary surgery)
  - Nephrogenic: Kidney not responding to ADH (lithium toxicity, hypokalemia, hypercalcemia, nephrotoxic drugs)
- Presents with polydipsia, polyuria
- **Lab: Dilute urine in the face of concentrated serum (hypernatremic and hyperosmolar)**
- Central DI will concentrate urine with ADH; nephrogenic DI will not respond
- Treatment
  - Central = Desmopressin (synthetic vasopressin = DDAVP)
  - Nephrogenic = Hydrochlorothiazide

Pheochromocytoma

- Rare cause of treatable hypertension
- Often diagnosed at autopsy
- Can be malignant
- Tumor of adrenal medulla cells (secretes norepinephrine)
- Diagnosis: catecholamines and metabolites (VMA) in 24 hour urine
- **5 Ps** (paroxysmal spells) in a 20-45 y/o patient
  - **Pressure** (sudden increased hypertension)
  - **Pain** (headache, chest pain, abdominal pain)
  - **Perspiration**
  - **Palpitations**
  - **Pallor**

Carcinoid Syndrome

- Carcinoid tumor: Circumscribed tumors occurring in small intestine, appendix, stomach, colon
- Tumor secretes serotonin, prostaglandins and other bioactive substances
- Attacks of **skin flushing, watery stools**, hypotension, vasodilation, edema, ascites and bronchoconstriction



- Attacks can last from minutes to days
- Occurs in 10% of carcinoid tumor patients

Electrolyte / Acid Base Disturbances

Hyponatremia

- Usually due to too much water relative to sodium
- Symptoms depend on level and rate of drop
  - Early: Nausea, headache
  - Late: Lethargy, seizures
  - Symptoms often start around 120 mEq/L

Classification of Hyponatremia

- Hypovolemic hyponatremia (clinically dehydrated)
  - Na^+ loss > free water loss
  - GI losses (vomiting, diarrhea)
  - Renal losses (diuretics)
  - Excess skin losses (sweating, burns)
- Hypervolemic hyponatremia (edematous states)
  - CHF (decreased effective circulating volume leads to ADH release)
  - Liver cirrhosis (same as CHF)
  - Renal disease (nephrotic syndrome, renal failure)
  - Decreased free water excretion
- Euvolemic hyponatremia
  - SIADH (syndrome of inappropriate ADH secretion)
  - Psychogenic polydipsia
  - Hypothyroidism

Pseudohyponatremia

- Hyperglycemia
  - Free water osmotically drawn out of cells and into serum, leading to lower serum Na^+ (Remember **Na^+ drops 1.6 mEq/L for every 100 mg/dL increase in glucose over 100**)
- Hyperlipidemia, hyperproteinemia
  - Displaces sodium from the lab specimen

Hyponatremia Treatment (1)

- **Depends upon etiology, chronicity and severity**
- Hyponatremia that develops slowly should be corrected slowly
- Hypovolemic hyponatremia
  - Replace fluid deficits with NS
  - 100-150 mL/hr
- Euvolemic hyponatremia
  - Correct underlying cause
  - Water restriction (+/- furosemide if $Na^+ < 120$)

Hyponatremia Treatment (2)

- Hypervolemic hyponatremia
  - Goal is to increase Na^+ and H_2O loss
  - Salt and water restriction
  - Diuretics to increase Na^+ loss
    - Caveat: May worsen hyponatremia because water leaves in excess of Na^+
  - Faster correction: IV NS & loop diuretics (furosemide)

Hyponatremia Treatment (3)

Life-threatening symptoms

- Severe hyponatremia (Na^+ < 120 **PLUS** CNS abnormalities)
  - Goal is to raise level to **>120 mEq/L**
  - **Rise in Na^+ should be no greater than 0.5-1.0 mEq/L per hour (1-2 mEq/L per hour if seizures)**
  - Hypertonic saline (3%) 25-100 mL/hr
  - Furosemide (Lasix) 20-40 mg IV
  - Too-rapid correction
    - CHF
    - Central pontine myelinolysis (CPM)

Central Pontine Myelinolysis

Results from too rapid correction of hyponatremia

- Occurs 24-48 hours after rapid correction
- Symptoms include confusion progressing to cranial nerve deficits to quadriparesis to locked-in syndrome; dysphagia, dysarthria, paresis
- Concomitant use of furosemide (Lasix) has been shown to decrease incidence of CPM

Hypernatremia

- Too little water relative to Na^+
- Most commonly due to free water loss or decreased intake
- Common in infants and debilitated elderly (limited access to water or impaired thirst)
- Also seen with elevated aldosterone levels or diabetes insipidus
- Irritability, doughy skin turgor, coma

Treatment of Hypernatremia

RESTORE PLASMA VOLUME FIRST!

- May calculate total body water by formula
  - TBW = Wt (kg) x 0.6

Water deficit in liters =
TBW x ([current Na/ 140] -1)

- Replace calculated water deficit over 48 hours
  - Start with NS not D5W
  - May use diuretic to increase Na^+ excretion
  - **Target 0.5 mEq/hr correction**
- Severe volume depletion: NS bolus

Too-rapid correction may result in cerebral edema

Hypokalemia (1)

- Most common electrolyte abnormality in patients with weakness
- EKG changes: Decreased T waves, increased U waves, ventricular dysrhythmias
- Causes
  - Decreased intake (e.g. NPO)
  - Increased output
    - Renal losses
      - Diuretics, osmotic diuresis
      - Increased aldosterone
      - Magnesium deficiency
      - Renal tubular acidosis
    - GI losses: Vomiting, diarrhea, NG suction

Hypokalemia (2)

- Shift of K^+ into cells
  - Alkalosis (protons move out of cells to restore pH; K^+ moves in to maintain electrical neutrality)
  - Insulin-mediated transport
  - Catecholamine-mediated transport
- Potassium is primarily an intracellular ion (30:1)
  - Mild hypokalemia may represent severe total body deficits (especially in the setting of acidosis)
  - Serum levels determine adverse effects

Hypokalemia Treatment

- Treat after urine output established
- Oral replacement safest
- Correct acid-base abnormality
- IV replacement: No more than 40 mEq/L and no faster than 40 mEq/hour
- Hypokalemia often is associated with hypomagnesemia

Magnesium required for Na/K pump

- In severe hypomagnesemia, potassium supplements will continue to be excreted in the urine
- **Resistant hypokalemia: Replace Mg^{++} & K^{+}**

Hyperkalemia Causes

- Lab error: Hemolysis (most common), thrombocytosis, leukocytosis, ischemic blood
- Increased intake (rare)
- Decreased output (renal failure or low aldosterone)
  - Aldosterone causes sodium and water retention resulting in elevated BP and loss of K in the urine
  - Aldosterone is blocked by spironolactone (a K-sparing diuretic)
- Redistribution (lack of insulin, acidosis, digoxin toxicity, tissue damage, succinylcholine)

Hyperkalemia Signs and Symptoms

- Usually asymptomatic
- May have muscle weakness
- Cardiac
  - EKG changes: Peaked T waves, increased PR, flattened P waves, increased QRS width
  - Dysrhythmias: Conduction blocks (BBB), bradycardia, sine wave pattern, asystole

Hyperkalemia Treatment

- Correct acidosis
- Calcium gluconate 10% (10-20 mL) antagonizes the effects of high K^+, especially cardiac
  - Quick onset, shortest acting
- D50 + insulin, bicarbonate, beta agonists
  - Shift K^+ extracellular to intracellular
- Exchange resins polystyrene (Kayexalate) orally or by enema to remove and lower total K^+
- Dialysis if above fails

Don't use calcium in hyperkalemia with digitalis toxicity → cardiac arrest

Calcium Metabolism

- Parathyroid hormone: Increases total serum Ca^{++}
  - Osteoclast stimulation (bone resorption)
  - Renal resorption
  - GI absorption
- Vitamin D
  - Synthesized by kidney
  - Activated by skin exposure to sun
  - Essential for GI absorption
- Kidneys (dual role)
  - Synthesize vitamin D
  - Reabsorb filtered Ca^{++}

Hypercalcemia

- Causes
  - **P**arathyroid: hyperparathyroidism (most common)
  - **A**ddison's disease
  - **M**ultiple myeloma
  - **P**aget's disease (during immobilization)
  - **S**arcoidosis
  - **C**ancer
  - **H**yperthyroidism
  - **M**ilk-alkali syndrome
  - **I**mmobilization
  - **D** vitamin
  - **T**hiazide diuretic

PAM P SCHMIDT

Hypercalcemia Features

Stones, bones, moans (psych) and groans (abdominal)

- Neuro: AMS, hyporeflexia, weakness
  - Increased nerve and muscle resting membrane potentials
- EKG: Shortened QT, BBB, heart block
  - Hyp**ER**calcemia = Short**ER** QT
- Renal: Polyuria, polydipsia, nephrogenic DI, calculi
- GI: Abdominal pain, nausea, constipation
- PUD, pancreatitis
- Skeletal: Bone pain / fractures
- Metastatic calcifications

Hypercalcemia Treatment

- IV saline – 2-4 L
  - Dilutes calcium and increases GFR thereby increasing the calcium load excreted by the kidney
- Bisphosphonates (zoledronic acid / pamidronate)
  - Inhibit osteoclast function and decrease bone resorption – response seen within 2-4 days, nadir at 7 days). Used once hydration has been completed
- Loop diuretics (furosemide)
  - Facilitates calcium excretion but are advised only after hydration achieved
- Less often used options
  - Calcitonin (inhibits bone resorption)
  - Steroids (increase renal losses of calcium)
  - Dialysis

Hypocalcemia Causes

- Hypoparathyroidism (surgical)
- Renal failure
- Vitamin D deficiency
- Pancreatitis
- Hypomagnesemia (Mg^{++} necessary for PTH activity)
- Drugs: Phenytoin, cimetidine, phosphates (extensive list)
- DiGeorge Syndrome

Hypocalcemia Signs & Treatment

- Decreases nerve and muscle resting membrane potential
- Signs & Symptoms
  - Paresthesias, hyperreflexia, seizures
  - Chvostek's sign: Twitch of corner of mouth on tapping facial nerve in front of ear
  - Trousseau's sign: Carpal spasm when BP cuff is inflated above systolic BP
  - EKG: Prolonged QT / inverted T waves
    - Hyp**O**calcemia = L**O**nger QT
- Treatment
  - Goal is to raise Ca^{++} to low normal levels
  - Calcium gluconate
  - Magnesium

Hypermagnesemia

- Causes: Renal failure, iatrogenic
- Symptoms: Weakness, hyporeflexia, respiratory depression, heart blocks
- Treatment: IV calcium (the same as with high potassium), dialysis

Hypomagnesemia

- Causes: Malnutrition, alcoholism, diuretics
- Symptoms: Similar to hypocalcemia and hypokalemia; serum levels can be normal in spite of significant deficit
- Treatment: IV magnesium

Phosphorus Metabolism

- GI tract absorption
- Excreted and reabsorbed in kidneys
- PTH lowers serum phosphorous by blocking renal resorption
- **Usually inverse relationship with calcium**
  - ↑Ca^{++} = ↓phosphate
  - ↓Ca^{++} = ↑phosphate

Hyperphosphatemia

- Causes: ↓PTH, renal failure, increased vitamin D, many problems associated with ↑Ca^{++}
- K^{+}, Mg^{++} and phosphate (major intracellular components) travel together, ↓ of one = ↓ of the others
- Symptoms are usually from associated hypocalcemia and hypomagnesemia
- Treatment
  - Oral phosphate binding gels
  - Treat hypocalcemia if necessary

Hypophosphatemia

- Phosphate is involved in the function of all hematologic cell lines (i.e. red cells / WBC / platelets)
- Causes
  - ↑ PTH, malignancies with ↑ CA^{+2}
  - Hyperventilation (respiratory alkalosis)
  - Hyperalimentation (common)
  - Decreased oral intake (alcoholics)
  - DKA (12-24hrs s/p tx)
- Symptoms and signs
  - Muscle weakness, respiratory depression, altered mental status, CHF, hemolytic anemia, rhabdomyolysis
- Treatment
  - Oral phosphate for minor cases
  - IV phosphate if symptomatic

Anion Gap (1)

- Anions = negatively charged ions
- Calculates unmeasured anions
- Electroneutrality: Plasma has no net charge
- Measured cation: Na^+
- Measured anions: Cl^- and HCO_3^-
- Unmeasured cations: Ca^{++}, Mg^{++}
- Unmeasured anions: Organic acids, proteins, phosphates and sulfates

Calculation: $Na^+ – (Cl^- + HCO_3^-) \leq 12$

Anion Gap (2)

- Decreased anion gap
  - Measured: Occurs if there are less positive charges or more negative charges
  - Unmeasured: Occurs if there are more positive or less negative charges
  - Hypoalbuminemia (less unmeasured anions)
  - Multiple myeloma (excess positively charged IgG paraproteins), hypercalcemia, hypermagnesemia, lithium toxicity
  - Bromide intoxication (mistaken for chloride)

Anion Gap (3)

- Increased anion gap metabolic acidosis:

"MUDPILES"

Methanol
Uremia
DKA, AKA, starvation ketosis
Phenformin or paraldehyde
Iron or INH
Lactic acidosis
Ethylene glycol
Salicylates

Lactic Acidosis

- The most common cause of metabolic acidosis
- Lactate is produced by anaerobic glycolysis
- Causes: Hypoperfusion or hypoxia
  - Medical conditions: Seizures, renal insufficiency, hepatic failure, infection, neoplasm (especially, leukemia, lymphoma and myeloma)
  - Drugs and toxins: Ethanol, toxic alcohols (also produce organic acidosis), metformin (rare, associated with renal failure), antiretrovirals

Non-gap Acidosis

- Normal anion gap metabolic acidosis
- Loss of bicarbonate with a corresponding loss of Na^+
  - Therefore the equation is balanced on both sides with no increase in the anion gap
- Non-gap metabolic acidosis: **"HARD UP"**

Hypoaldosteronism
Acetazolamide
Renal tubular acidosis
Diarrhea
Ureterosigmoidostomy
Pancreatic fistula

Metabolic Alkalosis (1)

- H^+ loss or HCO^-_3 excess
- Differential diagnosis
  - Loss of gastric acid (vomiting, NG suction)
  - Excess diuresis
  - Mineralocorticoids
  - Increased citrate or lactate due to transfusions of Ringer's lactate
  - Antacids (e.g. milk-alkali syndrome, results from high calcium intake + absorbable alkali-like antacids = hypercalcemia and metabolic alkalosis)
  - Dehydration

Metabolic Alkalosis (2)

- Increase of renal Na^+ resorption with K^+ and H^+ secretion causes bicarbonate generation
- Chloride-sensitive
  - Chloride loss: Vomiting, diuretics
  - Volume depletion
- Chloride-insensitive
  - Euvolemia or hypervolemia
  - Excess mineralocorticoids
  - Examples: renal artery stenosis, renin-secreting tumor

Osmolality

- Determined by the concentration of low molecular weight solutes
- Primarily determinants: Sodium, chloride, glucose and BUN
- A difference between the measured and calculated osmolality of >10 is an osmolal gap
- An osmolal gap indicates the presence of other, unmeasured, low molecular weight solutes (ethanol, ethylene glycol, methanol, isopropyl alcohol, mannitol or glycerol)

Formula to calculate serum osmolality:
2Na +Glu/18 + BUN/2.8 = 280-295 (normal)

ENDOCRINE QUESTIONS

The treatment of diabetic ketoacidosis may result in which of the following complications?

A. Cerebral edema
B. Hypokalemia
C. Worsening CSF acidosis
D. Hypoglycemia
E. All of the above

A patient has a 600 mg/dl serum glucose. What is the expected serum sodium level (normal = 140)?

A. 150mEq/L
B. 146mEq/L
C. 132mEq/L
D. 123mEq/L
E. 120mEq/L

The most common etiology for metabolic acidosis is:

A. Lactic acidosis
B. Diabetic ketoacidosis
C. Alcoholic ketoacidosis
D. Non-ketotic hyperosmolar acidosis
E. Toxic ingestion

A 26 y/o female patient presents with an acute onset of confusion, fever, tremor, weakness and tachycardia. She is given propranolol 1 mg IVP. What is the most appropriate next medication to administer?

A. PTU
B. Digibind
C. Thyroxine
D. Iodine
E. Magnesium sulfate

A patient arrives after new onset tonic/clonic seizures. The patient's medical history includes psychogenic polydipsia. Which is most consistent with this diagnosis?

A. Na^+ = 165; urine maximally concentrated
B. Na^+ = 142; urine maximally concentrated
C. Na^+ = 115; urine maximally dilute
D. Na^+ = 150; urine maximally dilute
E. Na^+ = 110; urine maximally concentrated

Which of the following is associated with a non-gap metabolic acidosis?

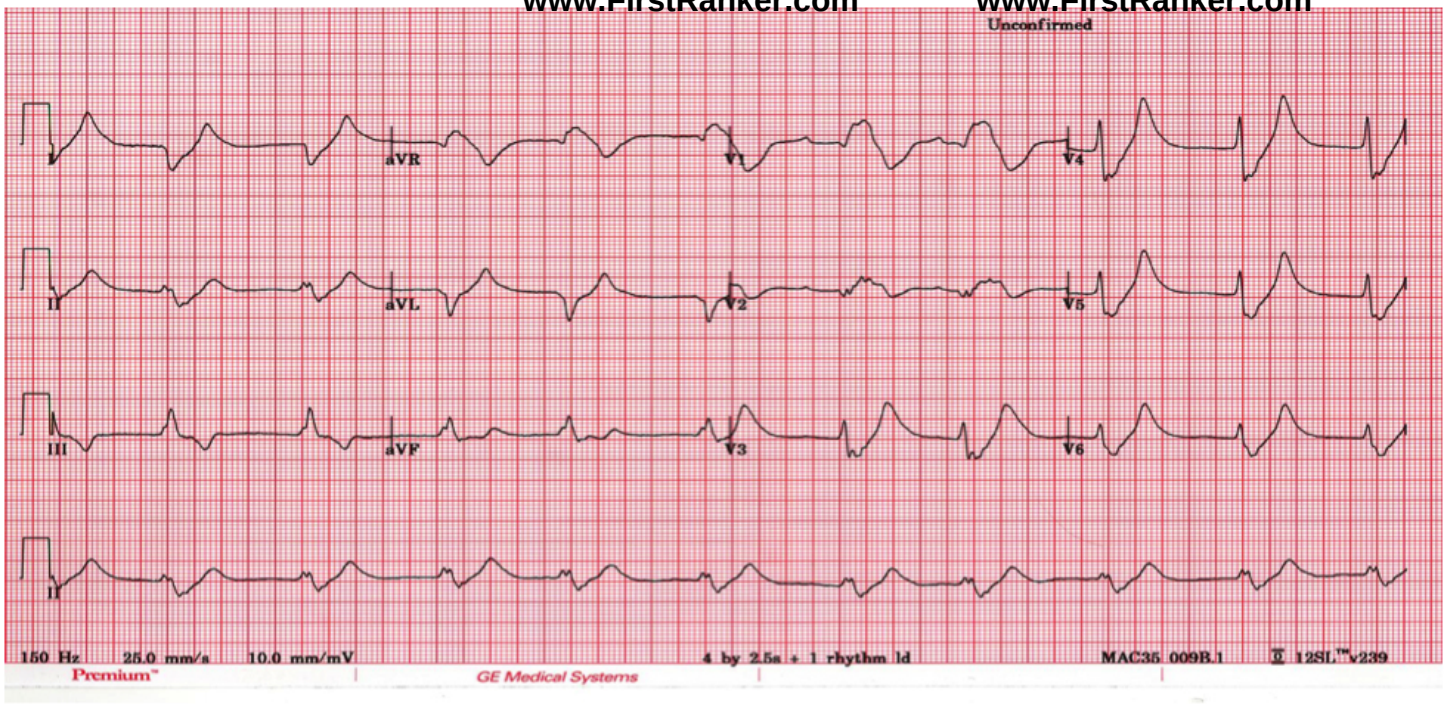
A. Diarrhea
B. Pancreatic fistula
C. Renal tubular acidosis (RTA)
D. Acetazolamide
E. All of the above

Which of the following entities causes an elevated anion gap acidosis?

A. Isoniazid toxicity
B. Bromide toxicity
C. Multiple myeloma
D. Hypoalbuminemia
E. Hypoaldosteronism

The treatment of hypercalcemia includes which of the following:

A. Hypertonic saline diuresis
B. Hemodialysis
C. Vitamin D
D. Hydrochlorothiazide
E. Pamidronate



Which of the following is the most appropriate treatment?

A. Thrombolytic administration
B. FAB
C. D50
D. Calcium chloride
E. Passive external re-warming

Which of the following is typical of hypokalemia?

A. J waves on EKG
B. Magnesium toxicity
C. Peaked T waves
D. Inhibits atrial and ventricular dysrhythmias
E. Flaccid paralysis

What is the most common electrolyte abnormality associated with adrenal insufficiency?

A. Hyponatremia
B. Hyperkalemia
C. Hyperglycemia
D. Decreased eosinophil count
E. Hypercalcemia

The common findings in myxedema coma include which of the following?

A. Hyperthermia
B. Hypoglycemia
C. Hypernatremia
D. Low cholesterol
E. Elevated T4

A 78 y/o patient had a gradual onset of confusion. The patient's GCS = 10 and GLC = 946. Serum ketones = neg. Which statement is true?

A. This patient is in DKA

B. Over-aggressive glucose reduction and hydration may result in cerebral edema

C. More common in IDDM

D. Precipitated by dietary indiscretions

E. Mortality rate lower than DKA

Which of the following statements is correct regarding alcoholic ketoacidosis?

A. Always associated with hyperglycemia
B. Is associated with alcohol levels > 300
C. Beta-hydroxybutyrate is the predominant ketone found in AKA
D. ETOH metabolism promotes gluconeogenesis
E. Should be treated with an insulin infusion

A 23 y/o type 1 diabetic patient quit taking his insulin. His blood gas = 7.18/30/99/100% RA. What should be done first for this patient?

A. Replete his potassium
B. Administer 2 amps of $NaHCO^3$ IVP
C. Give 2 liters of normal saline IV
D. Administer phosphate
E. Regular insulin bolus and infusion

Octreotide is effective in which of the following situations?

A. Metformin overdose
B. Sulfonylurea overdose
C. Hypoglycemia from insulinoma
D. Hypoglycemia associated with chronic liver disease
E. Ace inhibitor overdose

Treatment with hypertonic saline may result in which of the following?

A. Reflex hyponatremia
B. Diabetes insipidus
C. Hypotension
D. Hypokalemia
E. Central pontine myelinolysis

Which is true regarding diabetes insipidus?

A. The least common drug-related cause is lithium

B. In nephrogenic DI, the kidney responds to exogenous infusion of ADH

C. The urine is typically very concentrated

D. Head trauma is a rare cause

E. Results from decreased secretion or response to ADH

A patient is documented to have true fasting hypoglycemia with sugars measured as low as 30. Your differential diagnosis should include which of the following?

A. Small cell lung CA
B. Diabetes insipidus
C. Cushing syndrome
D. Liver disease
E. Hyperthyroidism

Regarding adrenal insufficiency, which of the following is true?

A. Histamine release associated with etomidate results in relative adrenal suppression
B. It is associated with meningococcemia
C. It rarely results in refractory hypoglycemia
D. It is never associated with hypothyroidism
E. It is a self-limited disease

Endocrine Answer Key

1. E
2. C
3. A
4. A
5. C
6. E
7. A
8. E
9. D
10. E
11. A
12. B
13. B
14. C
15. C
16. B
17. E
18. E
19. D
20. B