ENDOCRINE EMERGENCIES – CRITICAL CARE

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- You are on call in MICU, ED just admitted a 40 yo woman with CHF. The patient complains of palpitations, anxiety, weight loss, and mild ankle edema for few months. ROS diarrhea, increased appetite and insomnia.
- PE fine smooth skin, chemosis, mildly enlarged thyroid, mild hand tremor, tachycardia of 135 bpm, SM I/VI apex, no radiation

Q

- Which of the following tests will be diagnostic?

a. Echocardiogram w/ LVEF and wall motion

b. Ultrasensitive TSH

c. Serial cardiac enzymes

d. HIV test

e. Urine drug screen

- Which is the best treatment option?

a. Furosemide IV

b. Methimazole or Propylthiouracil

c. Heparin IV drip, ASA and beta blockers

d. HAART

e. Counseling for drug addiction

Thyroid Disease

- Thyrotoxicosis (Thyroid storm)
- Myxedema coma

Thyroid Gland

- Thyroid gland secretes thyroxine (T_4) and triiodothyronine (T_3)
  - modulate energy utilization and heat production, also facilitate growth.
- Biosynthesis of T_4 and T_3 occurs by iodination of tyrosine molecules in thyroglobulin.
- Dietary iodine is essential for synthesis of thyroid hormones.
- Secretion of free T_4 and T_3 into the circulation occurs after proteolytic digestion of thyroglobulin, which is stimulated by thyroid-stimulating hormone (TSH).

- T_4 and T_3 are tightly bound to serum carrier proteins: thyroxine binding globulin (TBG), thyroxine binding pre-albumin, and albumin.
- The unbound or free fractions are the biologically active (0.04% of the total T_4 and 0.4% of the total T_3).
- Normally, the thyroid gland secretes T_4, T_3 and reverse T_3 (biologically inactive form of T_3).
- Most of circulating T_3 is derived from T_4 in the peripheral tissues.

- Hypothalamic thyrotropin-releasing hormone (TRH) is transported through the hypothalamic-hypophyseal portal system to the anterior pituitary gland, stimulating synthesis and release of TSH.
- TSH -> increases thyroidal iodide uptake and iodination of thyroglobulin , release of T_3 and T_4 from the thyroid gland.
- Hypersecretion of TSH causes thyroidmegaly (goiter).
- Circulating T_3 exerts negative feedback inhibition of TRH and TSH release.

Thyroid evaluation

- Determining serum thyroid hormone levels
- Imaging thyroid gland: size and architecture
- Measuring thyroid autoantibodies
- Performing a thyroid gland biopsy by FNA

Thyrotoxicosis
(Thyroid storm)

- Thyroid hormones increase basal metabolic rate by increasing oxygen consumption and heat production.
- Hypermetabolic state → elevated circulating thyroid hormones.
- Manifestations are due to the direct physiologic effects of the thyroid hormones as well as to the increased sensitivity to catechol amines.
- Life-threatening complication of hyperthyroidism.

Q

- Your decided to check TSH in an ICU patient that was just admitted and find out that her TSH level is low. Which of the following tests results suggest subclinical hyperthyroidism?

a. Increased free T_4 and suppressed TSH (low)

b. Normal free T_4 and suppressed TSH (low)

- Which of the following is not a cause of thyrotoxicosis (thyroid storm):

a) Graves Disease

b) Toxic multinodular goiter

c) Iodine deficiency

d) Hashimoto thyroiditis

e) Postpartum

Precipitants of Thyrotoxicosis

- Thyroid surgery
- Withdrawal of antithyroid drugs
- Radioactive iodine therapy or iodinated contrast materials
- Thyroid palpation
- Massive thyroid hormone overdose
- Trauma, labor and delivery

Causes of Thyrotoxicosis

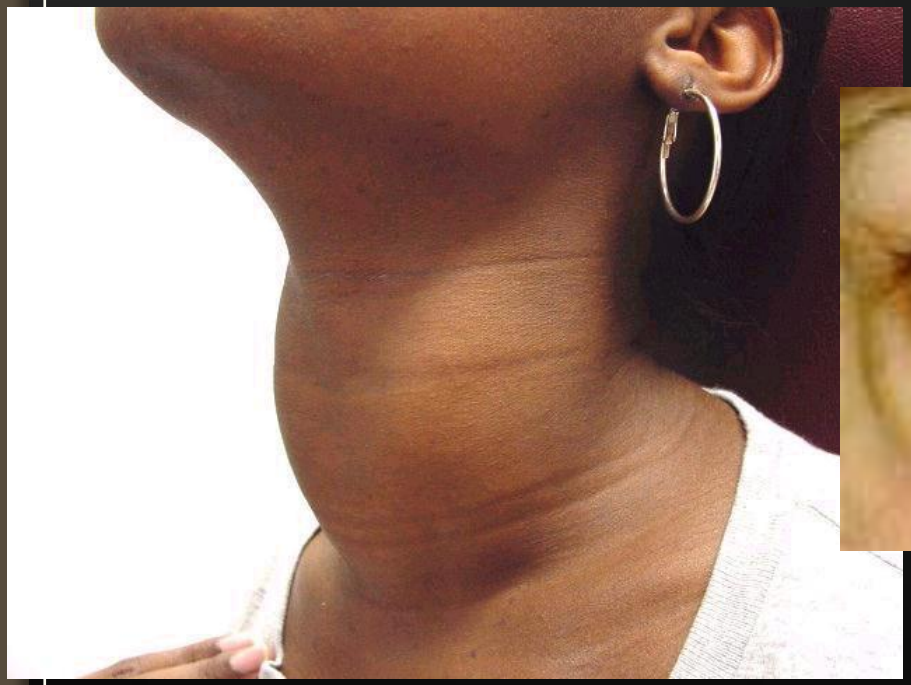
- Graves disease
- Toxic adenoma (solitary)
- Toxic multinodular goiter

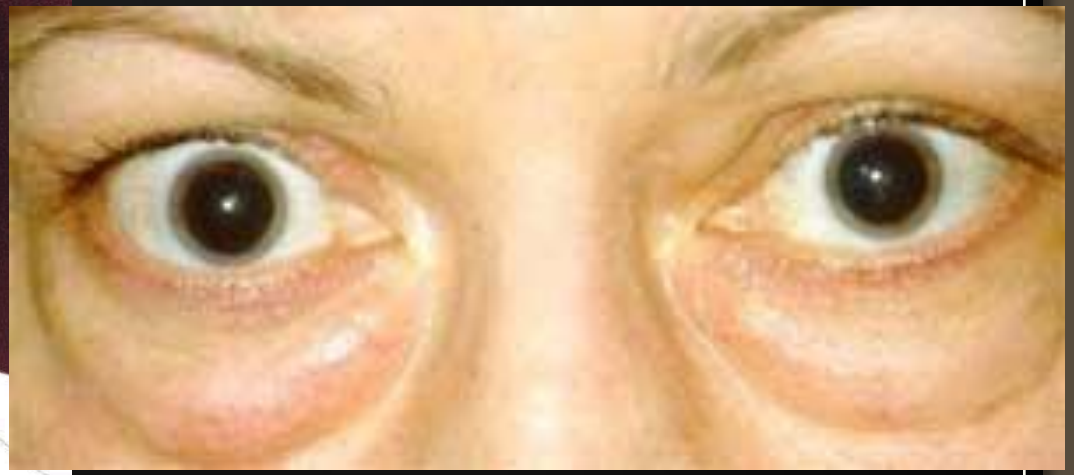
Less common:

- Subacute thyroiditis
- Hashimoto's thryroiditis
- Thyroiditis factitia
- Postpartum

- Graves disease is the most common cause of thyrotoxicosis, more common in women, peak incidence of 20 to 40 yrs of age, may be autoimmune, with one or more features:
  - Goiter
  - Thyroitoxicosis
  - Eye disease (from proptosis, extraocular muscle paralysis to loss of sight)
  - Thyroid dermopathy

Clinical manifestations





A patient is admitted to MICU for atrial fibrillation. Which of the following signs and symptoms will not suggest thyrotoxicosis?

a) Fine tremor

b) Delayed relaxation of DTRs

c) Warm Skin

d) Thyromegaly

e) Exophthalmos

Clinical manifestations

Symptoms	Signs
Nervousness	Tachycardia
Heat intolerance	Atrial fibrillation
Fatigue and weakness	Wide pulse pressure
Palpitations	Brisk reflexes
Increased appetite	Fine tremor
Weight loss	Proximal limb-girdle myopathy
Oligomenorrhea	Chemosis

A 27 yo woman is admitted to MICU with low grade temperature, jaundice, tachycardia, anxiety, mild leg edema. Which of the following will confirm your suspicion of thyroitoxicosis?

a) Normal TSH but elevated T_3 and T_4

b) TFT normal but increased thyroxine binding globulin

c) Low cortisol

d) Undetectable TSH with elevated T_3 and T_4

e) None of the above

Diagnosis

Thyroid function tests:

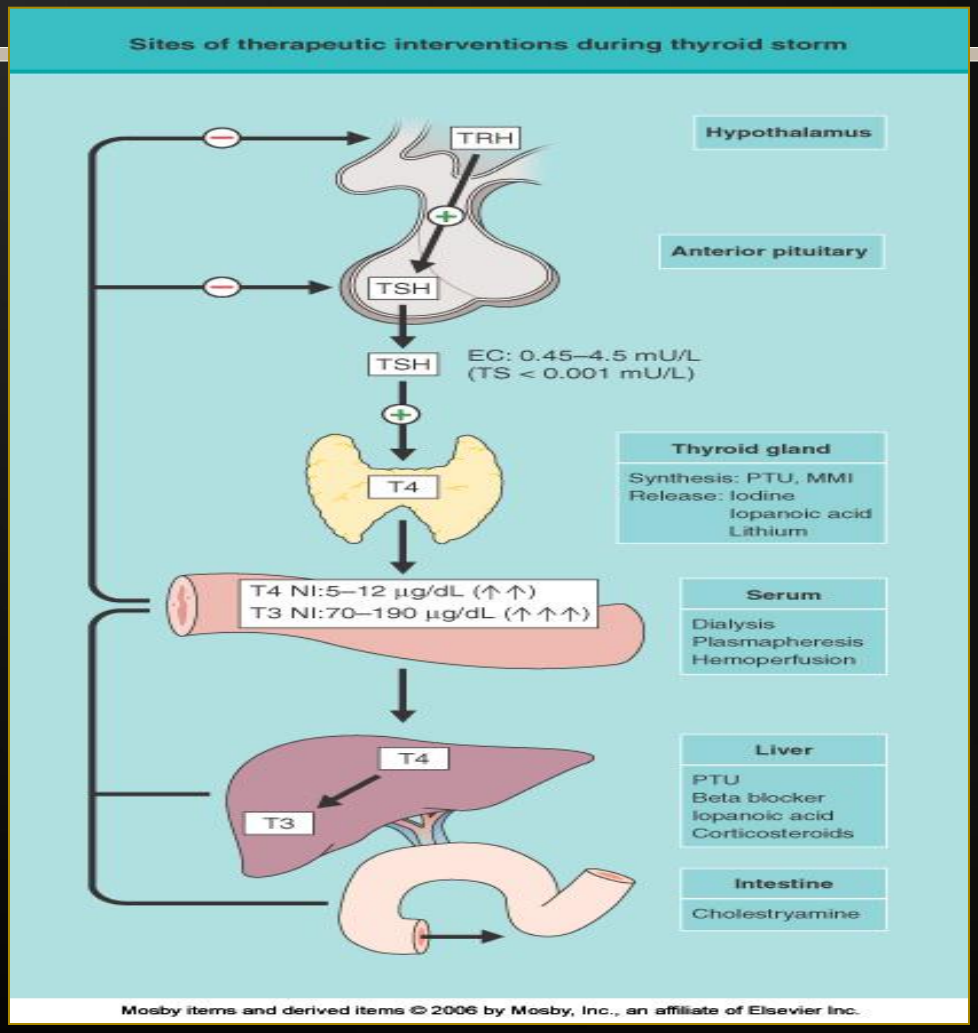
- An elevated T_4 and/or T_3 and a suppressed TSH confirm the diagnosis.

- T_3 is typically more elevated than T_4 due to concomitant conversion of T_4 to T_3

Treatment

- 3 treatment modalities:
  - Antithyroid drugs
  - Radioactive iodine
  - Surgery

Treatment


Sites of therapeutic interventions during thyroid storm
TRH
Hypothalamus
Anterior pituitary
TSH
TSH
EC: 0.45–4.5 mU/L
(TS < 0.001 mU/L)
Thyroid gland
Synthesis: PTU, MMI
Release: Iodine
Iopanoic acid
Lithium
T4
T4 NI:5–12 µg/dL (↑↑)
T3 NI:70–190 µg/dL (↑↑↑)
Serum
Dialysis
Plasmapheresis
Hemoperfusion
T4
T3
Liver
PTU
Beta blocker
Iopanoic acid
Corticosteroids
Intestine
Cholestryamine
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Q

- The 40 yo woman that you diagnosed and treated for thyrotoxicosis is complaining of sore throat, fever, fatigue, WBC is 1500/mm^3, which is your next step?

a. Observe the patient, repeat WBC in 2 months

b. You do not need to be concerned since patient with thyrotoxicosis usually have very low white blood cell count

c. Perform blood cultures, urine culture and start broad spectrum antibiotics, the patient has septic shock

d. Discontinue methimazole

e. Perform a bone marrow biopsy

Treatment

- Thiocarbamide drugs: propylthiouracil (PTU), methimazole and carbimazole block thyroid hormone synthesis by inhibiting thyroid peroxidase.
- PTU also partially inhibits peripheral conversion of T_4 to T_3.
- Available oral only. Treatment should continue for 1 to 2 yrs until spontaneous remission. 40 to 50% of pts remain in remission, relapse patients undergo surgery or radioactive iodine treatment.
- Side effects: pruritus and rash (5%), cholestasis, acute arthritis, and rarely, agranulocytosis (0.5%) = discontinue medication and consult ASAP if fever or sore throat.

Treatment

- Acute phase thyrotoxicosis → Beta blockers for tachycardia, HTN and atrial fibrillation.
- Radioactive iodine benefits are superior to surgery and antithyroid drugs, however, most pts become hypothyroid (80%). Effective in 6 weeks to 3 months. Treatment of choice in adults with Graves disease. Contraindicated in pregnancy.
- Patients should be euthyroid before treatment.
- Surgery is indicated in pts with large goiter and obstructive symptoms or multinodular gland or pts deciding pregnancy within the next year.

Treatment

- Premed with antithyroid drugs 6 weeks prior to surgery is recommended.
- Blocking the release of thyroid hormone from the stores in the colloid is achieved by iodine and lithium carbonate.
- 2 weeks prior to surgery, oral saturated solution of potassium iodide is administered daily to decrease the vascularity of the gland.
- Cx: persistent hypoparathyroidism and recurrent laryngeal nerve palsy occurs in < 2% post-op

Treatment

- Glucocorticoids reduce T_4 to T_3 conversion (? direct effect on the underlying autoimmune process)
- Hyperthermia is better treated with antipyretics and peripheral cooling (no salicylates, can displace thyroid hormone from the serum binding sites)

A 65 yo woman is admitted to MICU obtunded, bradycardic, hypotensive, w/ elevated $PaCO_2$, neg cardiac enzymes, and mild pericardial effusion by echo. Which of the following medications will have the highest benefit?

a) Thyroid hormone replacement

b) TPA

c) Heparin IV

d) B-blockers

HYPOTHYRODISM

- Clinical syndrome cause by deficiency of thyroid hormones.
- Slowing of metabolic processes and is reversible with treatment.
- Usually primary (thyroid failure)

HYPOTHYRODISM

- The most common cause is autoimmune thyroiditis (Hashimoto thyroiditis).
- Isolated or polyglandular failure syndrome type II (Schmidt syndrome, IDDM, adrenal insufficiency, pernicious anemia, vitiligo, gonadal failure, hypophysitis, celiac disease, myasthenia gravis, and primary biliary cirrhosis).
- Iatrogenic causes: ^{131}I therapy, thyroidectomy, and lithium or amiodarone.
- Iodine deficiency or excess.

Clinical manifestations

Adults
Fatigue
Cold intolerance
Weight gain
Constipation
Menstrual irregularities
Dry, coarse, cold skin
Delayed relaxation of reflexes
Bradycardia

MANIFESTATIONS OF MYXEDEMA COMA

MYXEDEMA COMA
Hypothermia
Extreme weakness
Stupor or coma
Hypoventilation
Hypoglycemia
Hyponatremia

Cardiovascular Manifestations of Myxedema Coma

CV Myxedema Coma
Bradycardia
Decreased cardiac contractility
Increased peripheral vascular resistance
Decreased systolic blood pressure
Increased diastolic blood pressure
Pericardial effusion

Diagnosis

- Precipitating factors are:
  - Cold exposure
  - Infections
  - Psychoactive drugs
- Diagnosis:
  - Elevated TSH and low total and free T_4
- Hypercholesterolemia is frequent, elevated CK and anemia normochromic

EUTHYROID SICK SYNDROME

- It is seen in acute illness.
- Low total T_4 and occasionally low free T_4 with normal or mildly elevated TSH.
- It does not require any treatment.

Treatment

- Synthetic levothyroxine (half life is 8 days), usual dose is 75 to 150 mcg per day (1.6 mcg/kg/day, starting dose).
- Pts with cardiac disease or elderly, may start with 25 mcg daily and increased gradually every few weeks.
- Monitor TSH 6 weeks after a dose adjustment.
- In myxedema coma: 300 to 400 mcg of levothyroxine IV loading dose followed by 50 mcg daily, hydrocortisone and IV fluids.
- Most pts improve in 1 to 3 days.

A 20 yo male developed N/V/D, abdominal pain for 3 days. In ED, his BP is normal, AG is 25, pH 7.15, glucose 325 mg/dl, creatinine 2.4 mg/dl, moderate serum ketones. Which is the etiology of the metabolic acidosis?

a) Lactic acidosis
b) Ketoacidosis
c) Renal failure
d) Hypotension
e) The pt does not have metabolic acidosis

DKA

- DKA is more common in IDDM, pts with absolute or relative insulin deficiency.
- Hyperglycemia = glucose > 250 mg/dL.
- Ketosis = moderate to severe ketonemia
- Acidosis = pH ≤ 7.30 or HCO_3^- < 15 mEq/L.

DKA

- Poorly controlled / compliance.
- DKA is the most common cause of death in IDDM in pts < 40 years of age.
- DKA and NKH can occur in both type I or type II diabetes.

DKA associated metabolic and plasma abnormalities

- Dehydration
- Increased serum osmolality (≥ 320 mOsm/kg)
- Increased AG (> 12 mEq/L)
- Increased serum amylase
- Leukocytosis
- Hypertriglyceridemia

DKA: precipitating factors

- Infection (30%)
- New onset diabetes (25%)
- Problems with insulin administration (20%)
- Stress
- Illicit drug use

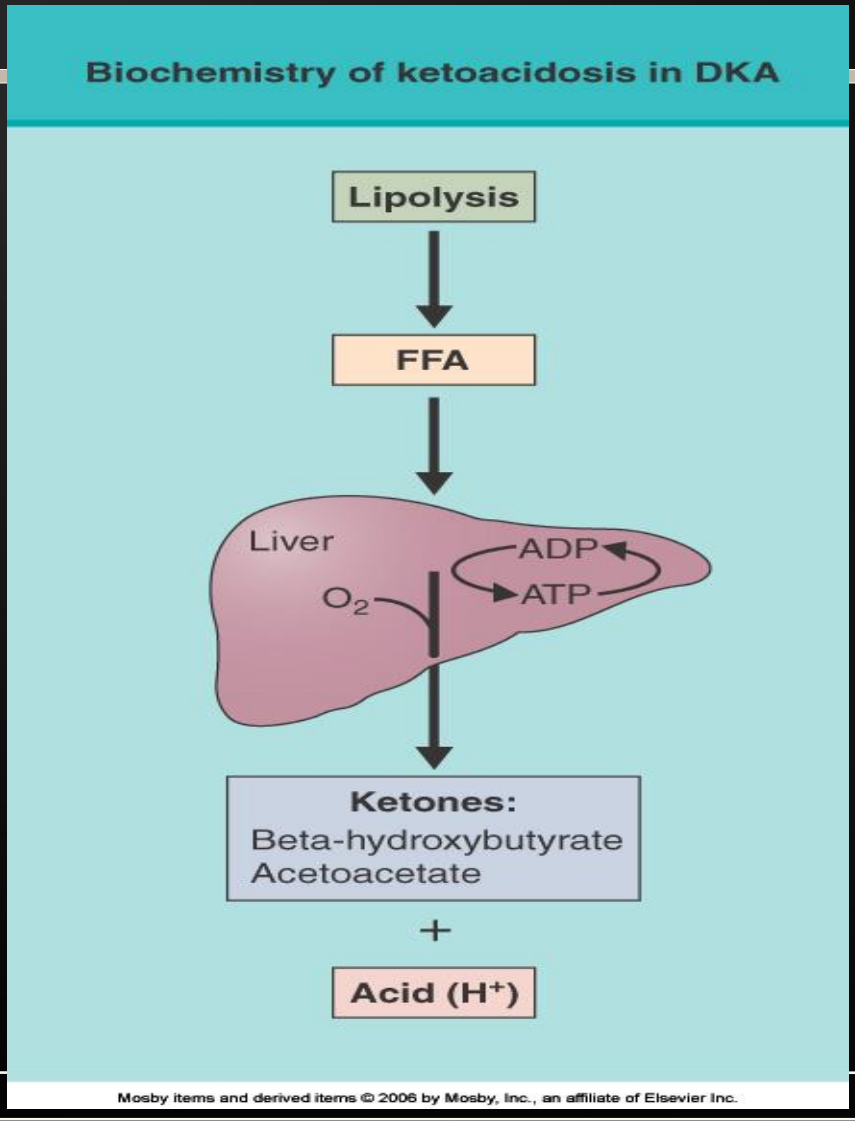
DKA

- Insulin deficiency and raised insulin counter-regulatory hormones (glucagon, growth hormone, cortisol, catecholamines) result in increased hepatic glucose production and decreased peripheral glucose utilization.
- Leading to hyperglycemia and hyperosmolality with consequent osmotic diuresis, electrolyte loss (Na^+, K^+, PO_4^+, $Mg^{+,}$ Ca^+ and Cl^-) and dehydration.

DKA

- Insulin deficiency causes lipolysis - release of FFAs from adipose tissues, which are oxidized in the liver to produce ketones.
- Diminished peripheral utilization of ketones during insulin deficiency results in ketosis and metabolic acidosis.

Pathogenesis



DKA Clinical Manifestations	
Nausea	Tachycardia
Vomiting	Orthostatic hypotension
Polydipsia	Poor skin turgor
Thirst	Warm or dry skin
Abdominal pain	Dry mucous membranes
Weakness	Hyperventilation or Kussmaul breathing
Fatigue	Ketones on the breath (fruity odor)
Anorexia	Weight loss
Polyuria	AMS or coma

DKA - HNK

Feature	DKA	HNK
Age	< 40 yr	> 60 yr
Duration of symptoms	< 2 days	> 5 days
Plasma glucose	< 600 mg/dL	> 600 mg/dL
Serum sodium	Nl or low (130-140 mEq/L)	Nl or high (145-155 mEq/L)
Serum potassium	Nl or high (5-6 mEq/L)	Nl (4-5 mEq/L)
Serum bicarbonate	< 15 mEq/L	> 15 mEq/L
Ketone bodies	Positive	Negative
pH	< 7.35	> 7.3
Serum osmolality	Usually < 320 mOsm/Kg	Usually > 320 mOsm/Kg
Fluid deficit	Approx 6 to 10 L	Approx 6 to 15 L
Cerebral edema	Rare clinical	Very rare
Prognosis	3 – 10 % mortality	10 – 20 % mortality
Course	Insulin required usually	Insulin not required usually

Diagnosis

- Search for precipitating cause is crucial.
- Correct sodium (add 1.6 mEq of sodium for each 100 mg/dL of glucose above normal)
- Differential diagnosis: other causes of metabolic acidosis such as lactic acidosis, acute renal failure, and alcoholic ketoacidosis

Q

Which is the most important initial treatment in patients with DKA or HNK?

a) Insulin IV

b) IV volume replacement with NS (at least 2 L in the first hour)

c) DVT prophylaxis

d) Electrolyte replacement

e) ACE-I

Treatment DKA

- The most important therapy of DKA is the restoration of circulating volume with maintenance of cardiac output and renal function.
- Fluid deficit is 4 to 10 L and approx 2 L should be infused in the first hour.
- Rapid normalization of plasma glucose is not necessary and maybe harmful.
- IV fluid improves hyperglycemia and acidosis by improving circulatory volume and renal blood flow, and reducing counter-regulatory hormones, particularly catecholamines

Treatment DKA

- Initially, insulin bolus of 0.15 units/kg followed by an infusion at a rate of 0.1 U/kg.
- Insulin suppresses lipolysis, ketogenesis, and hepatic glucose production, and augments glucose disposal in the skeletal muscle.
- The goal is to reduce glucose by 50 to 100 mg/dL per hour.
- Once the glucose is around 200 or 250 mg/dL, decrease of glucose level should slow --> fluids should include dextrose
- IV insulin should continue until ketones are cleared and anion gap has closed
- Then transition to subQ insulin

Treatment DKA

- Cardiac dysfunction may occur if pH <7.0 (<6.9).
- Potassium may be elevated initially because of the systemic acidosis but as glucose falls and pH normalizes, the K^+ decreases rapidly and should be corrected.
- $PO4^-$ and Mg^+ need to be followed and corrected as needed.

HYPERGLYCEMIC HYPEROSMOLAR STATE (HNKS)

- Almost always occurs in type 2 DM, elderly and physically impaired with limited access to free water.
- Pathogenesis is similar to DKA but with more severe hyperglycemia, relative absence of acidosis and ketonemia, and greater degree of dehydration.
- Increased lactic acid secondary to poor tissue perfusion.
- Insulin resistance is usually present with normal or elevated levels of serum insulin.

HNKS

- Up to 40% of pts > 65 yo may have undiagnosed DM.
- Precipitating factors include infection, intestinal obstruction, mesenteric thrombosis, PE, peritoneal dialysis, heat stroke, hypothermia, subdural hematoma, severe burns, and drugs.

Treatment HNK

- Fluid losses for glycosuria are higher than DKA. Water deficit between 6 to 15 L.
- Serum sodium levels are > 150 mEq/L in half of the patients (greater water loss than Na)
- DKA and HNK patients are at high risk for thrombotic events, DVT prophylaxis is necessary
- Insulin to slowly decrease glucose concentration over 24 to 48 hrs
- Glucose should be measured every hour
- All the patients should be referred for diabetic education

A 38 yo woman with N/V/D, weakness presents to ED. BP is low but improves after receiving IV fluids. Which of the following test results in ED will help you to suspect adrenal insufficiency?

a) Leukocytosis with bandemia

b) Hyponatremia, hyperkalemia and eosinophilia

c) Elevated creatinine

d) History of drug abuse

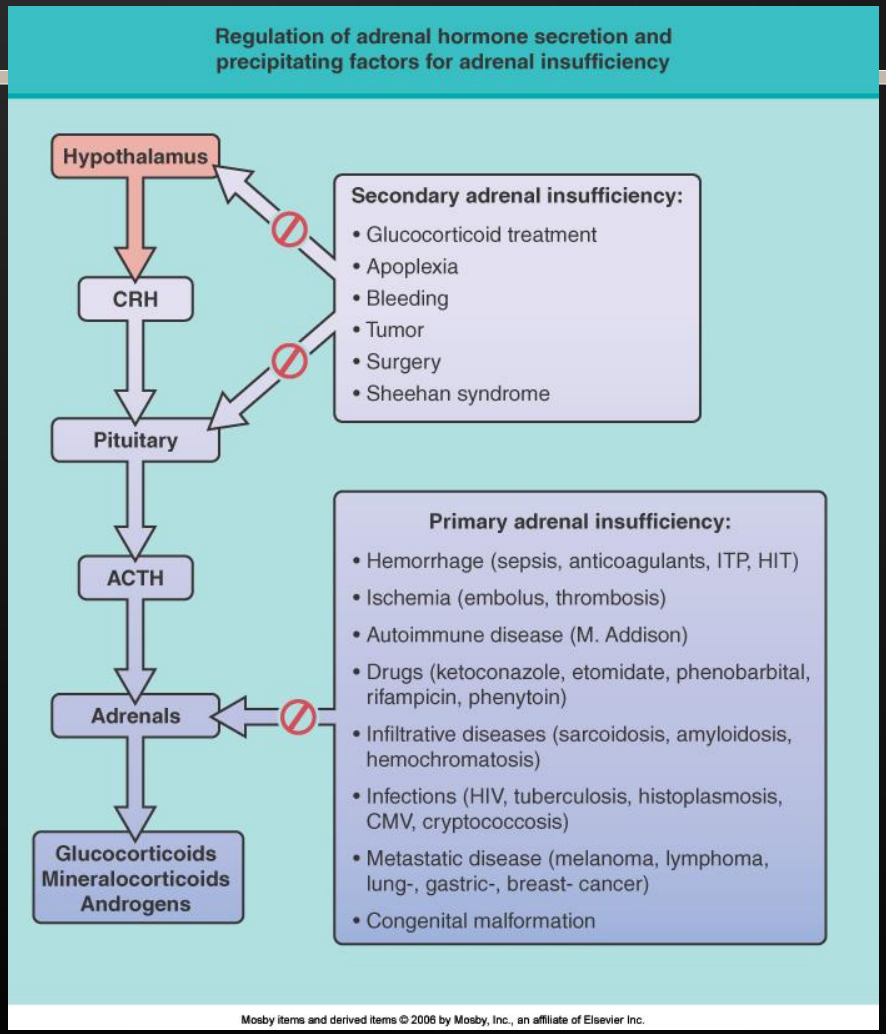
Adrenal insufficiency

- Primary: destruction or dysfunction in the adrenal cortex
- Secondary: resulting from ACTH hyposecretion
- The most common cause is autoimmune destruction of the adrenal gland (Addison's disease).
- Addison's disease may be part of 2 distinct autoimmune polyglandular syndromes:
  - Type I (hypoparathyroidism, adrenal insufficiency, mucocutaneous candidiasis); usually affects children
  - Type II (Addison disease, autoimmune thyroid disease (Graves or Hashimoto) and IDDM; also known as Schimdt Syndrome, adults).

Adrenal insufficiency

- Deficiency of glucocorticoids, mineralocorticoids, and androgens (first two are important in an acute crisis).
- Glucocorticoids are essential for homeostasis within the immune and CV systems.
- Mineralocorticoids are essential for water and electrolyte balance through regulation of renal fluid and sodium reabsorption and potassium excretion.

Adrenal insufficiency



In stress, the adrenal hormone production may become insufficient to meet the current elevated needs.

Clinical manifestations of adrenal insufficiency
Anorexia
Weight loss
Increasing fatigue
Vomiting
Diarrhea
Salt craving
Muscle and joint pain
Abdominal pain
Postural dizziness (orthostatic hypotension)
Increased pigmentation (extensor surfaces, palmar creases, and buccal mucosa)

Laboratory
Hyponatremia
Hyperkalemia
Mild metabolic acidosis
Azotemia
Hypercalcemia
Anemia
Lymphocytosis
Eosinophilia
Hypoglycemia (children)

Diagnosis

- High index of suspicion is key.
- Acute adrenal insufficiency is a medical emergency and treatment should not be delayed.
- Plasma cortisol concentration > 34 mcg/dL rules out the diagnoses of adrenal insufficiency.
- Plasma cortisol concentration < 20 mcg/dL in shock is consistent with adrenal insufficiency.

Diagnosis

- Critically ill pts with severe sepsis or septic shock may have “relative adrenal insufficiency”.

Treatment

- Life-threatening disease, treatment may be started before the results are available.
- First line is saline solution to correct fluid and sodium deficit.
- Second line is hydrocortisone 100 to 200 mg IV bolus followed by 50 mg every 6 hrs.
- Pts using chronic corticosteroids or known to have adrenal insufficiency require additional glucocorticoids when they undergo stressful procedures or suffer significant medical illness.

THANK YOU ☺

A 35 yo male with thyrotoxicosis is admitted to MICU. Which of the following medications are not indicated?

a) Digoxin

b) Methimazole or propylthioracil

c) Oral contrast or lithium prior thionamids

d) Beta blockers

e) Glucocorticoids