Endocrine Emergencies

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Agenda

1- thyroid storm

2- myxedema coma

3- hypocalcemia

4- hypercalcemia

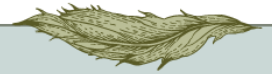
5- adrenal insufficiency

6- phechromocytoma

7- pituitary apoplexy

Thyroid storm

Thyrotoxic crisis ('thyroid storm')

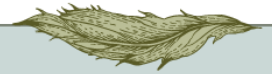


- This is a rare but life-threatening complication of thyrotoxicosis.
- It is a medical emergency and has a mortality of 10% despite early recognition and treatment.
- Mortality is most frequently associated with serious underlying medical conditions.
- Urgent specialist endocrine input should be sought in cases of suspected 'thyroid storm', both to confirm the diagnosis and provide advice on appropriate treatment.

Thyroid storm precipitating factors

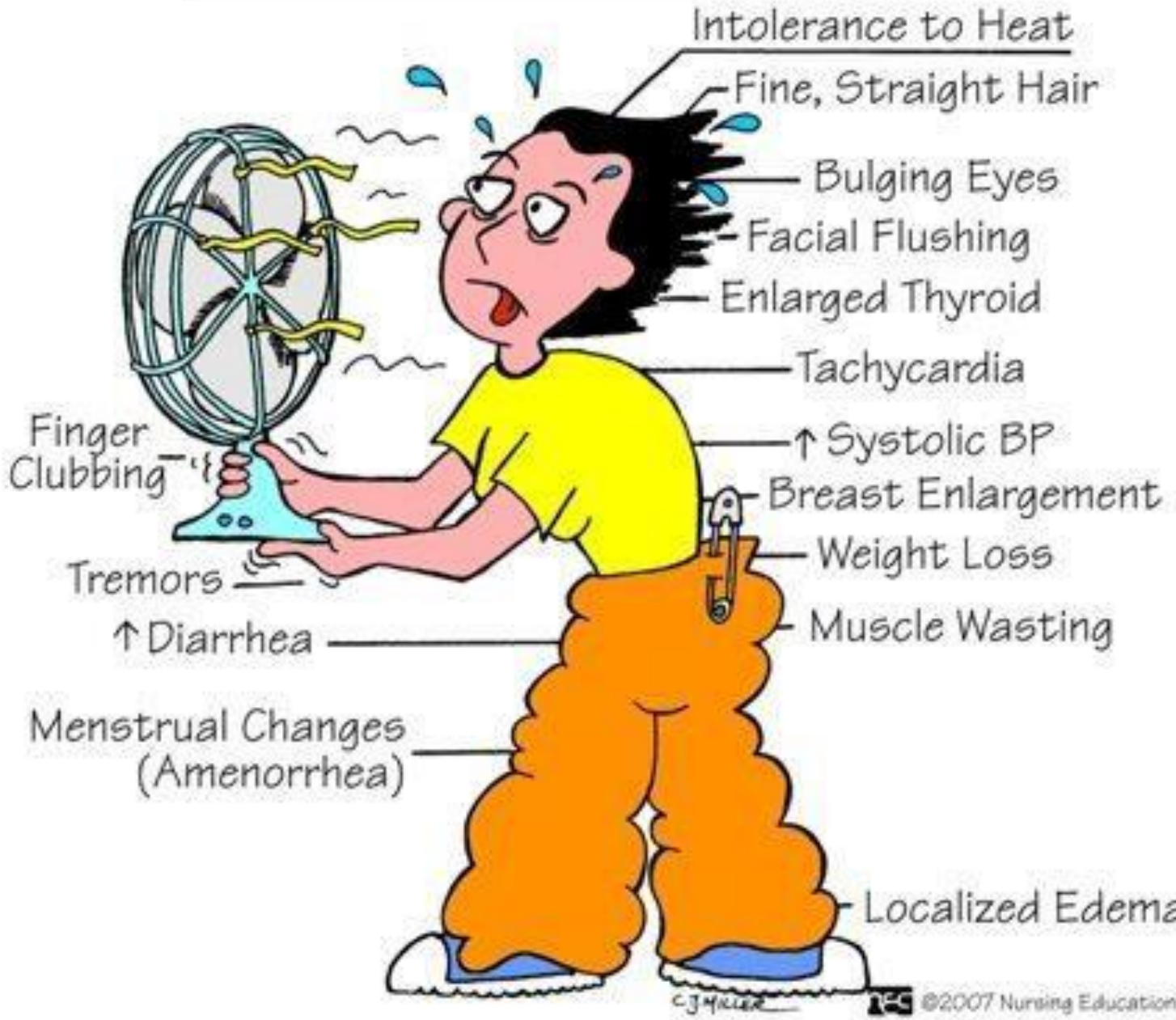
- acute illness (e.g., stroke/CVA, infection, trauma, diabetic ketoacidosis)
- surgery (especially on the thyroid)
- Radio-iodine treatment
- Abruptly stopping treatment of hyperthyroidism
- Exposure to iodinated contrast
- Acute ingestion of high dose of thyroid hormone
- Medications

Symptoms



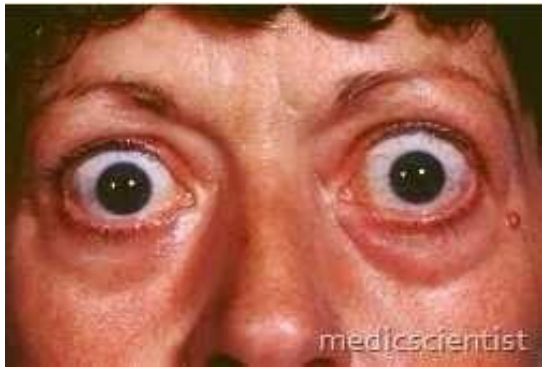
- General symptoms
  - Fever
  - Profuse sweating
  - Weight loss
  - Respiratory distress
  - Fatigue
- GI symptoms
  - Nausea and vomiting
  - Diarrhea
  - Abdominal pain
  - Jaundice
- Neurological symptoms
  - Anxiety / agitation
  - Altered behavior
  - Seizures, coma
- Cardiac symptoms
  - Palpitation
  - Hypotension
- Symptoms of hyperthyroidism

HYPERTHYROIDISM



Physical examination

- Hyperpyrexia >41
- Exessive sweating
- Cardiovascular signs
  - Hypertension with wide pulse pressure
  - Tachycardia
  - Signs of HF
  - Cardiac arrhythmias (SVT eg, atrial flutter & fibrillation are more common than ventricular tachycardia)
- Neurological signs
  - Agitation and confusion
  - Hyperreflexia and transient pyramidal signs
  - Tremors , seizures
  - Coma
- Signs of thyrotoxicosis
  - Orbital signs
  - Goiter



Laboratory studies

- Free T4 and free T3 are elevated
- TSH is suppressed
- There is no much difference in thyroid hormone levels between hyperthyroidism and thyroid storm
  - The difference is how the hormone levels affect the body systems
- The diagnosis of thyroid storm is based upon the presence of severe and life-threatening symptoms (hyperpyrexia, cardiovascular dysfunction, altered mentation) in a patient with biochemical evidence of hyperthyroidism (elevation of free T4 and/or T3 and suppression of TSH).
- There are no universally accepted criteria or validated clinical tools for diagnosing thyroid storm

Diagnostic criteria for thyroid storm

Thermoregulatory dysfunction	
Temperature (°F | °C)	
99 to 99.9 | 37.2 to 37.7	5
100 to 100.9 | 37.8 to 38.2	10
101 to 101.9 | 38.3 to 38.8	15
102 to 102.9 | 38.9 to 39.4	20
103 to 103.9 | 39.4 to 39.9	25
≥104.0 | >40.0	30
Central nervous system effects	
Mild	10
Agitation	
Moderate	20
Delirium	
Psychosis	
Extreme lethargy	
Severe	30
Seizure	
Coma	

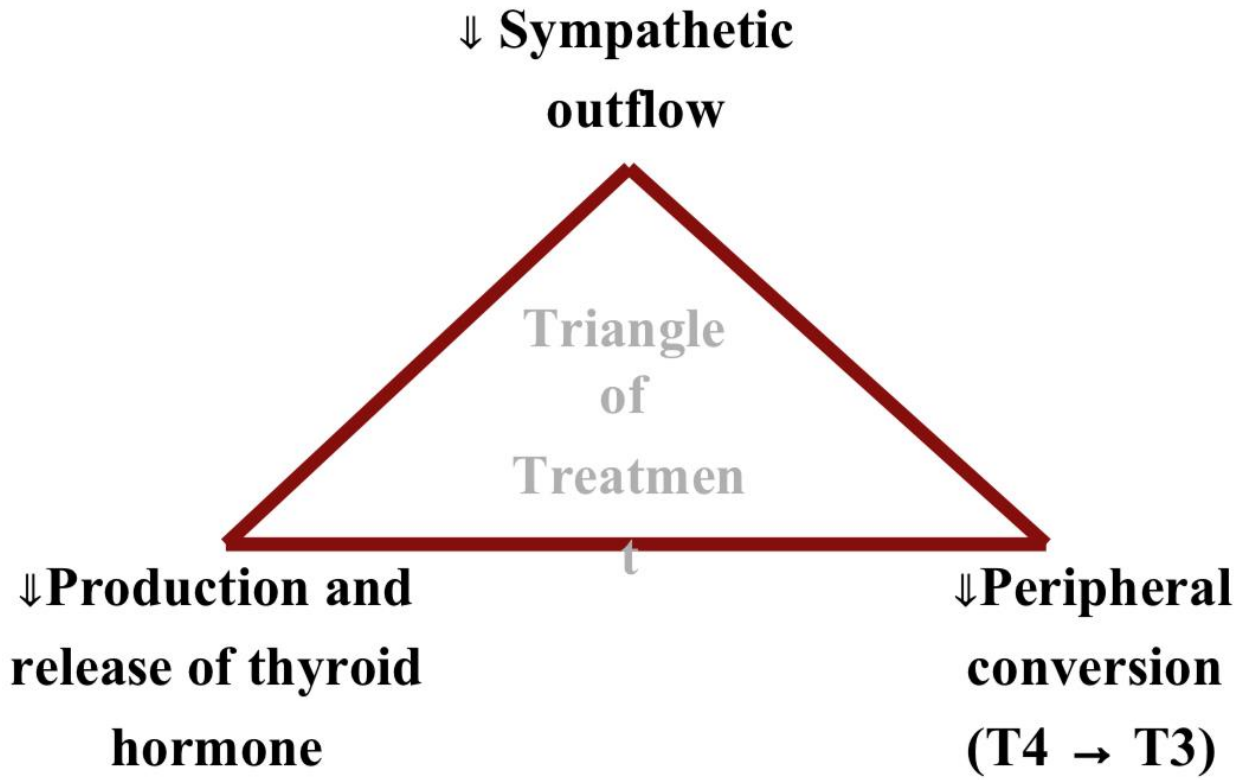
Cardiovascular dysfunction	
Tachycardia	
99 to 109	5
110 to 119	10
120 to 129	15
130 to 139	20
≥140	25
Atrial fibrillation	10
Heart failure	
Mild	5
Pedal edema	
Moderate	10
Bibasilar rales	
Severe	15
Pulmonary edema	
Precipitant history	
Negative	0
Positive	10

Gastrointestinal-hepatic dysfunction	
Moderate	10
Diarrhea	
Nausea/vomiting	
Abdominal pain	
Severe	20
Unexplained jaundice	

- A score of 45 or more is highly suggestive of thyroid storm,
- whereas a score below 25 makes thyroid storm unlikely.
- A score of 25 to 44 is suggestive of impending storm
- While this scoring system is likely sensitive, it is not very specific

Management

- Management requires
  - intensive monitoring and supportive care,
  - identification and treatment of the precipitating cause
  - measures that reduce thyroid hormone synthesis



Treatment of Thyrotoxic crisis :

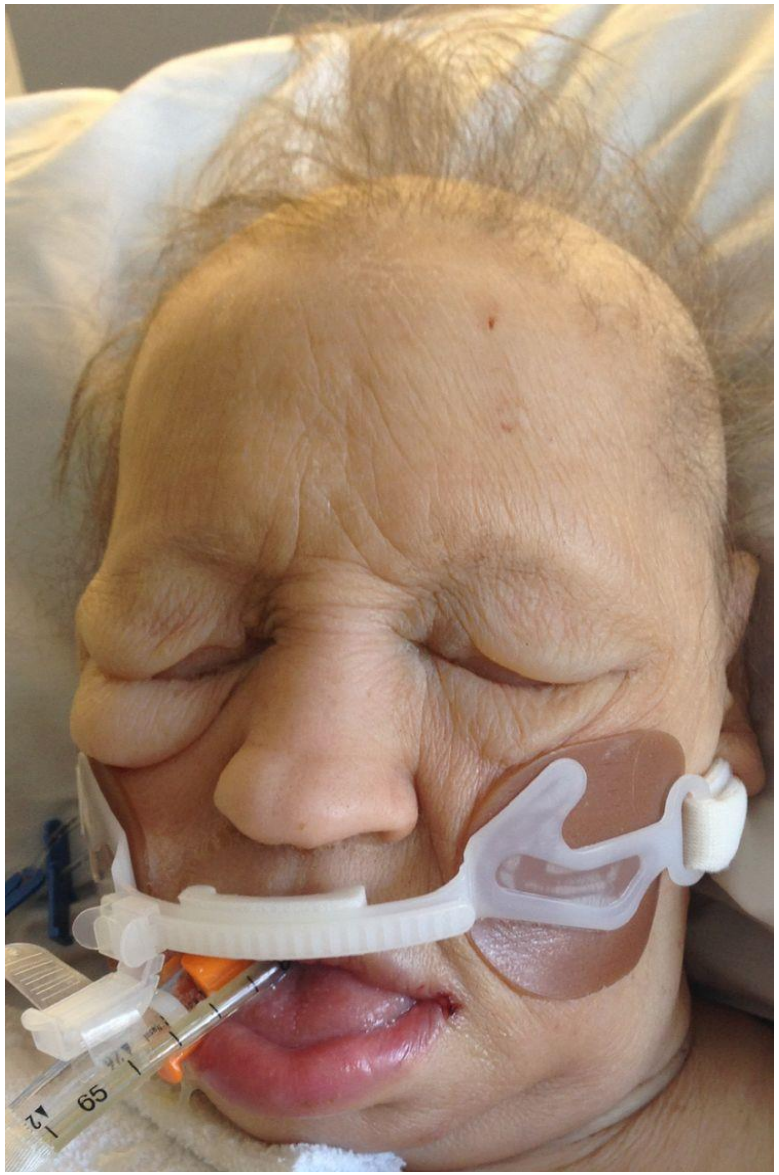
- **Propranolol** in full dose is started immediately for tachyarrhythmia
  - **Dose**: either orally (80 mg 4 times daily) or intravenously (1–5 mg 4 times daily).
  - **Mechanism:**
    - It blocks the peripheral effects of thyroid hormone.
    - decrease T4 → T3 conversion
    - reduce tachycardia and other adrenergic manifestations
- **Propylthiouracil** :
  - **Dose** : 600 loading dose then, 200 mg/6h. (orally, rectally ornasogastric tube) .
  - **MOA**: It inhibits the synthesis of new thyroid hormone & prevents the peripheral conversion of T 4 to T3.
  - Clinical effects may appear within 1 hour.
- Both **glucocorticoids** (hydrocortisone 100 mg IV every 8 hours) and **iodine** are important in reducing the conversion of T4 to active T3
- **Sodium ipodate**, a radiographic contrast medium (500 mg per day orally),
  - will restore serum T3 levels to normal in 48–72 hours.
  - Where sodium ipodate is not available, potassium iodide or Lugol's solution are reasonable alternatives.
- After 10–14 days the patient can usually be maintained on **carbimazole** alone.
- Plasmapheresis

Management

- Supportive care
  - Fluids , glucose
  - Oxygen
  - Cooling
  - Acetaminophen
    - Avoid aspirin: since it displaces T4 from TBG, resulting in increase in free T4.
  - Phenobarbital
  - Digoxin if indicated

Drug	Typical adult dose	Action
Antithyroid agents		
propylthiouracil (also called PTU)	1,200 – 1,500 mg/day, given in 200 – 250 mg increments PO or via gastric tube	Prevents production of more T_4 and T_3 in the thyroid, and blocks the conversion of T_4 to T_3 outside the thyroid.
methimazole (Tapazole)	120 mg given in 20 mg increments PO or via gastric tube	Prevents production of more thyroid hormone.
Iodides		
Lugol's solution	10 drops twice a day PO or via gastric tube	Blocks release of stored thyroid hormone from thyroid gland.
saturated solution of potassium iodide (Pima, SSKI)	8 drops every 6 hours PO or via gastric tube	
Glucocorticoids		
dexamethasone (Decadron)	2 mg every 6 hours, PO or IV	Blocks conversion of T_4 to T_3.
hydrocortisone	100 mg IV every 8 hours	
Beta-blockers		
propranolol (Inderal)	1 mg/min IV as required, then 60 – 80 mg every 4 hours PO or via gastric tube	Reduces symptoms (tachycardia, tremor, restlessness) caused by a heightened response to catecholamines; blocks conversion of T_4 to T_3.
esmolol (Brevibloc Injection)	500 mcg/kg/min for 1 minute, then 50 – 100 mcg/kg/min for 4 minutes	

Myxedema Coma



Myxedema Coma

- **A rare life-threatening complication of severe hypothyroidism**
- **The condition usually occurs in patients with untreated or insufficiently treated long-standing hypothyroidism .**
- **Precipitated by :**
  - Infection
  - Exposure to cold temperatures
  - **Trauma**
  - **Burns**
  - Cerebrovascular accidents (CVA)
  - **MI , CHF**
  - **Medications- sedatives, narcotic or potent diuretics**

Clinical picture

- Most patients have a history of Hypothyroidism.
- Some patients may have developed hypothyroidism after thyroidectomy or radioactive iodine therapy for hyperthyroidism. However, some patients will have undiagnosed hypothyroidism and myxedema coma will be the initial presentation .
- Altered level of consciousness, delirium or COMA
- Profound hypothermia (24-32.2 C)
- Respiratory depression with CO2 retention
- **symptoms of Hypothyroidism**

HYPOTHYROIDISM

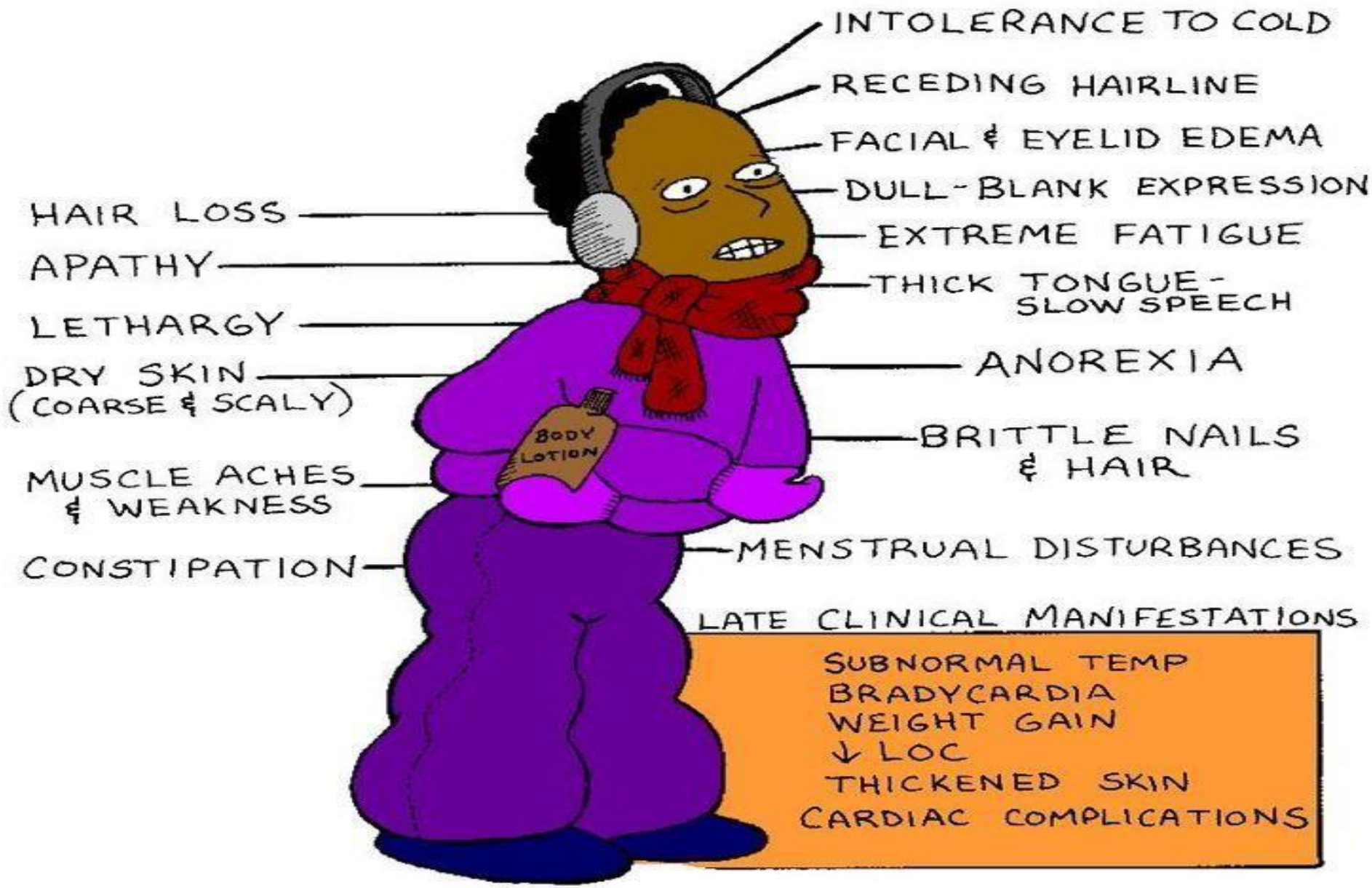
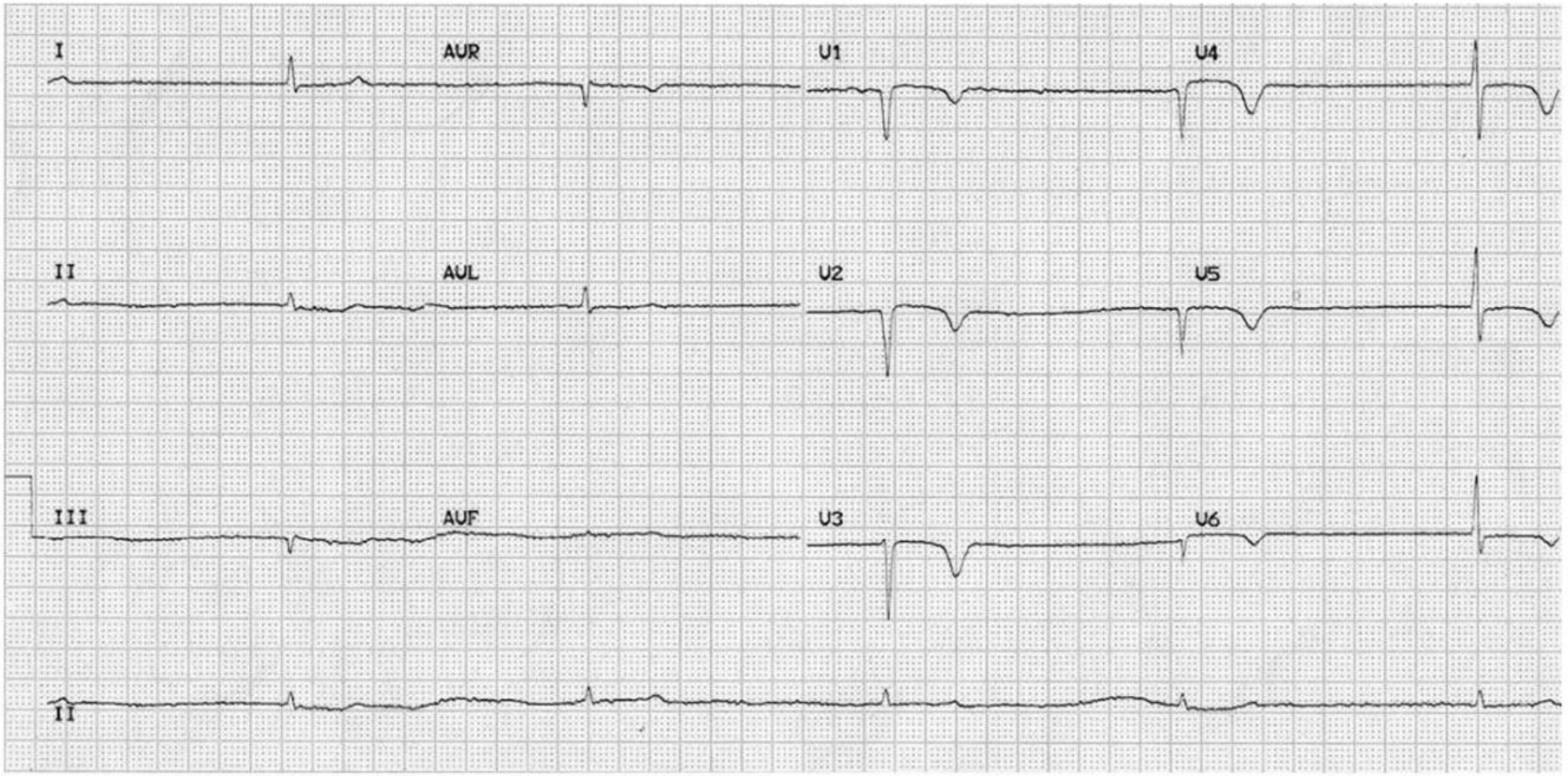


Table 2. Clinical features of myxedema coma

History	Physical Exam
• Thyroid hormone non-adherence • History of precipitating event • Increasing confusion, behavioural changes, and/or decreasing level of consciousness on collateral history • Symptoms of chronic hypothyroidism. For example (not exhaustive): o Fatigue o Cold intolerance o Weight gain o Constipation	• Vitals o **Hypothermia** o Bradycardia o Refractory hypotension o Bradypnea o Hypoxia • Altered mental status: o Confusion o Agitation o Psychosis o Seizures o Lethargy o Coma • Signs of chronic hypothyroidism. For example (not exhaustive): o Elevated BMI o Dry skin o Coarse hair o Large tongue o Broad nose o Anasarca o Thyroidectomy scar

Investigations

- Laboratory studies:
  - TFTs- High TSH and T3/T4 low (if low/normal TSH with low T3/T4 consider pituitary or hypothalamic hypothyroidism)
  - Other tests : Electrolytes (HYPOnatremia) ,KFTs-serum creatinine (high;decreased renal perfusion), CBC (Anemia,R/O infection) , blood glucose(HYPOglycemia), HYPERlipidemia , cortisol, cosyntropin stimulation test.
- Chest radiography:
  - may show signs of cardiomegaly, pericardial effusion, congestive heart failure, or pleural effusion
- ECG:
  - sinus bradycardia, low-amplitude QRS complexes, a prolonged QT interval, flattened or inverted T waves, or arrhythmias.
- If the diagnosis is suspected, immediate management is necessary before confirming the diagnosis.



This is the admission ECG of a 79-year old man who was referred to ICU with coma, hypothermia, severe bradycardia and hypotension refractory to inotropes.

TSH was markedly elevated with an undetectable T4.

The ECG shows marked bradycardia (30 bpm) with low QRS voltages (esp. in the limb leads) and widespread T-wave inversions, typical of severe myxedema.

Management

- **ICU** setting with **continuous cardiac monitoring**
- Airway maintenance- intubation may be needed
- Thyroid hormone replacement - Parenteral thyroxine (levothyroxine) Loading dose of 300 – 600 µg then 50-100 µg daily.
  - Because the rate of conversion of T4 to the active hormone T3(liothyronine) can be reduced in these patients, the addition of T3 along with T4 has been recommended.T3 has a quicker onset of action than T4, as increases in body temperature and oxygen consumption has been reported to be faster with T3 therapy compared to T4. T3 therapy is given as bolus of 5-20 µg IV and to be continued at a dosage of 2.5-10 µg every 8 hours.
  - Measurement of thyroid hormones every 1-2 days is suggested. Failure of TSH to decrease or of thyroid hormone levels to increase suggests the need to increase doses of T4 and/or add T3.
  - The treatment is changed to the oral form once the patient is able to take medications by mouth.

Management

- Glucocorticoids Therapy:
  - Patients with 1ry hypothyroidism may have concomitant 1ry adrenal insufficiency while patients with 2ry hypothyroidism may have associated hypopituitarism and 2ry adrenal insufficiency. The other rationale for the treatment with corticosteroids is the potential risk of precipitating acute adrenal insufficiency caused by the accelerated metabolism of cortisol that follows T4 therapy.
  - Hydrocortisone at a dose of 50 – 100 mg every 8 hours is administered .
  - An alternative is dexamethasone at a dose of 2-4 mg every 12 hours. Dexamethasone has the advantage of not affecting the serum cortisol concentration and can be used immediately without affecting the results of the ACTH stimulation test, which can be performed at any time. If the test is normal, corticosteroids can be stopped without tapering

Management

- Supportive measures –
  - Treat hypothermia with passive rewarming; using ordinary blankets and a warm room
  - treat associated infection
  - correct severe hyponatremia with saline and free water restriction
  - correct hypoglycemia with intravenous dextrose
  - hypotension is usually corrected with thyroid hormone therapy . If BP continues to be low, cautious use of IV fluids with normal saline is advised. Refractory hypotension can be cautiously treated with vasopressors
- Avoid fluid overload
- Avoid sedation

Prognosis

- **Myxedema coma has a high mortality rate ~50% , And survival depends on early recognition and treatment.**

Acute hypocalcemia

definition of acute hypocalcemia

Sudden and severe decrease in level of ionized calcium (below 2.0 mEq/dL) or total serum level of calcium (below 8.5 mg/dL).

Causes of acute hypocalcemia

- Increased phosphate levels
  - Chronic kidney disease
  - Phosphate therapy
  - Tumor lysis syndrome
- Hypoparathyroidism
  - Surgical: after neck exploration (thyroidectomy, parathyroidectomy)
  - Congenital deficiency (DiGeorge's syndrome)
  - Idiopathic hypoparathyroidism
  - Severe hypomagnesaemia

- Resistance to PTH
  - Pseudohypoparathyroidism
- drugs
  - Calcitonin, bisphosphonate, cimetidine, phenytoin, phenobarbital, gentamicin, heparin, theophylline, loop diuretics and glucocorticoids.
- Others
  - Sepsis
  - Acute pancreatitis
  - Citrated blood in massive transfusion
  - Metabolic alkalosis

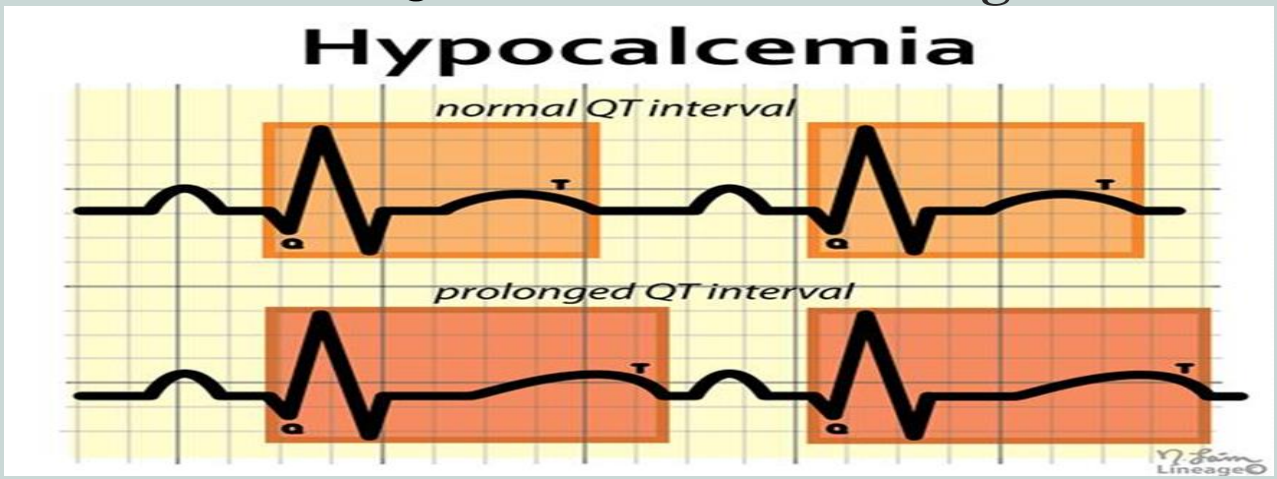
Clinical Picture

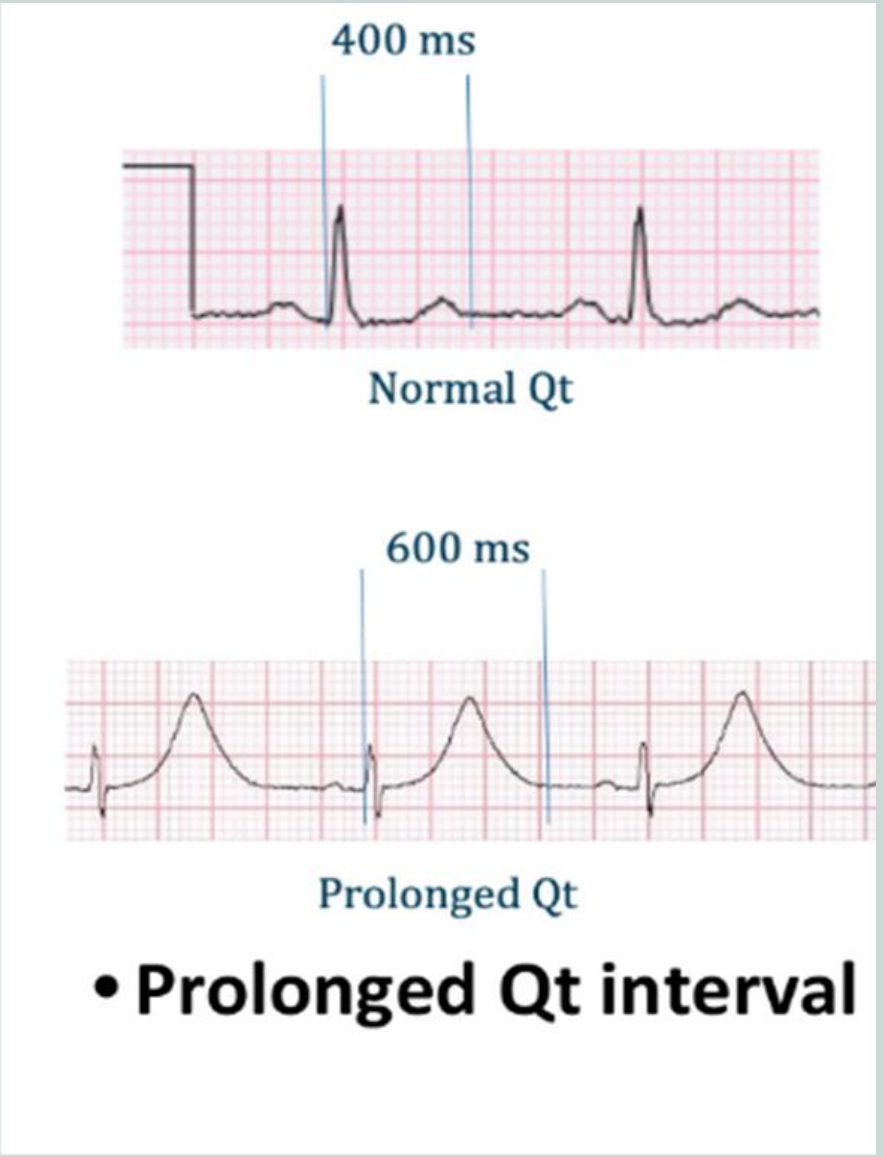
- Symptoms:
- circumoral and distal extremity paresthesias, irritability, fatigue, muscle cramps, anxiety, and tetany (including carpopedal spasm).
- Followed by convulsions, laryngeal stridor, dystonia, and psychosis.

- Signs:
- Hyperreflexia
- Trousseau’s sign (inflation of the sphygmomanometer cuff above systolic pressure for 3 minutes induces tetanic spasm of the fingers and wrist)
- Chvostek’s sign (gentle tapping over the facial nerve causes twitching of the ipsilateral facial muscles)
- Severe hypocalcemia may cause papilledema and frequently a prolonged QT interval on the ECG.

Chvostek's sign

Trousseau's sign





Investigations

Laboratory studies

- Serum calcium.
- Ionized Ca++
- Serum phosphate, magnesium, BUN and creatinine levels.
- PTH levels
- CBC
- Amylase and lipase

Electrocardiography

- ECG findings may include a prolonged QT interval, sinus bradycardia, complete heart block, ventricular arrhythmia, and ventricular fibrillation.

Radiology

- X-ray for metacarpals, showing forth metacarpals which occur in pseudohypoparathyroidism

Treatment of hypocalcemia

- Patients with acutely symptomatic hypocalcemia should be treated with 10 mL of 10% calcium gluconate infused intravenously over 10–15 minutes, followed by a maintenance infusion of 1–2 mg/kg/hour over 6–12 hours.
  - Calcium must be given cautiously to patients receiving digitalis because calcium can worsen digoxin toxicity or cause sudden death.
- b. For asymptomatic patients, oral therapy with elemental calcium (with or without vitamin D) may be all that is required. The rapid intravenous administration of calcium to asymptomatic patients with mild to moderate hypocalcemia is contraindicated because doing so can cause severe cardiovascular, neuromuscular, or renal complications.

Acute hypercalcemia

Definition of acute hypercalcemia

Is a medical condition characterized by a sudden and severe increase in the total calcium level (exceeding 10.5 mg/dL) or an ionized calcium level (exceeding 2.7 mEq/L).

Causes of acute hypercalcemia

- Endocrine
  - Primary and tertiary hyperparathyroidism
  - Pheochromocytoma
- Malignancy
  - SCC of lung, breast cancer, and myeloma.
  - Production of osteolytic factors by tumors.
  - PTH-related protein secretion.

- Granulomatous disorders
  - Sarcoidosis
  - Tuberculosis
- Medications
  - Excessive vitamin D or A intake
  - Thiazide
  - Lithium
  - Hormonal therapy for breast cancer
- Miscellaneous causes
  - Dehydration
  - Excess calcium ingestion
  - milk-alkali syndrome.

Clinical Picture

- Symptoms:
- Mild hypercalcemia is frequently asymptomatic, but more severe hypercalcemia can produce a number of symptoms:
- Weakness, depression, confusion, lethargy, personality changes, nausea, vomiting, anorexia, constipation, headache, abdominal pain.

- Signs:
- Signs of dehydration.
- Decreased mental status.
- Decreased motor strength, hyporeflexia.
- Hypertension.

Investigations:

Laboratory studies

- Serum calcium, phosphate
- Ionized calcium
- Serum PTH
- 24-hour urinary calcium
- Renal function – usually normal but should be measured as a baseline.

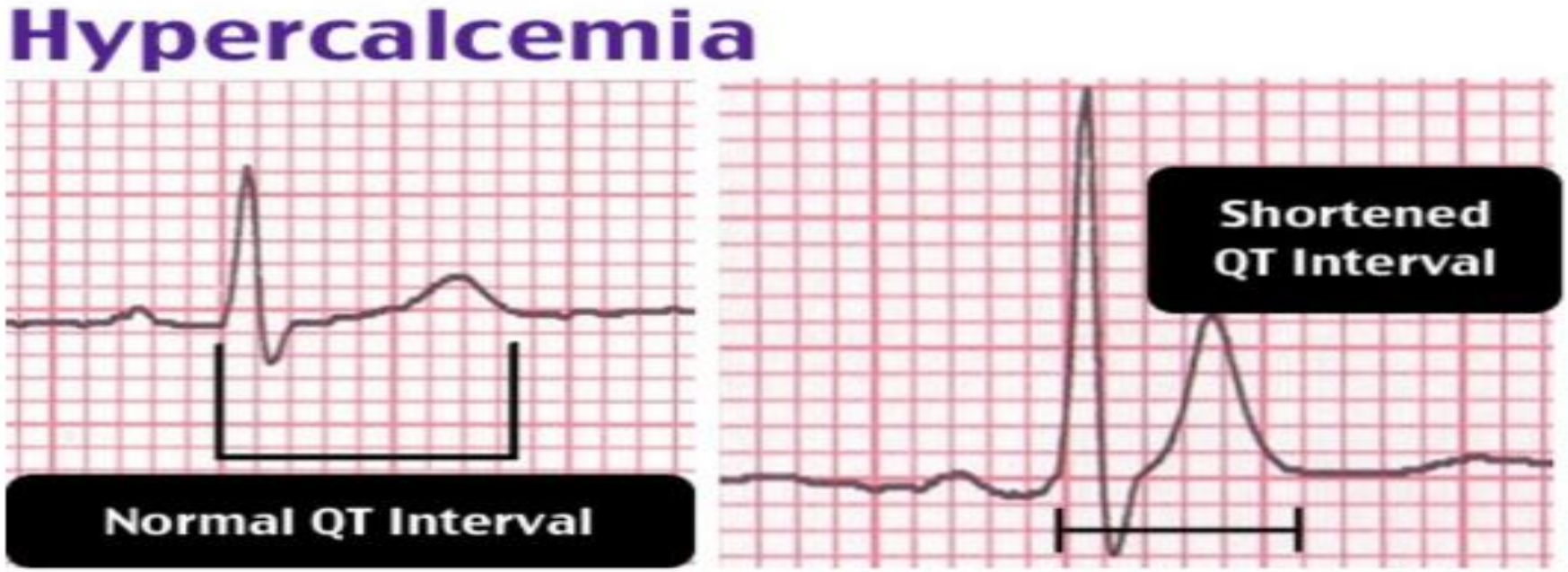
Electrocariography

- ECG abnormalities include shortening of QT interval, widening of T waves, bradyarrhythmias, bundle branch block, and second-degree and complete heart block.

Radiology

- Chest x-ray: check any abnormality in the lung, such as granulomatous diseases like sarcoidosis or TB.

ECG Hypercalcemia shortened QT interval



Treatment

Emergency Box 19.2

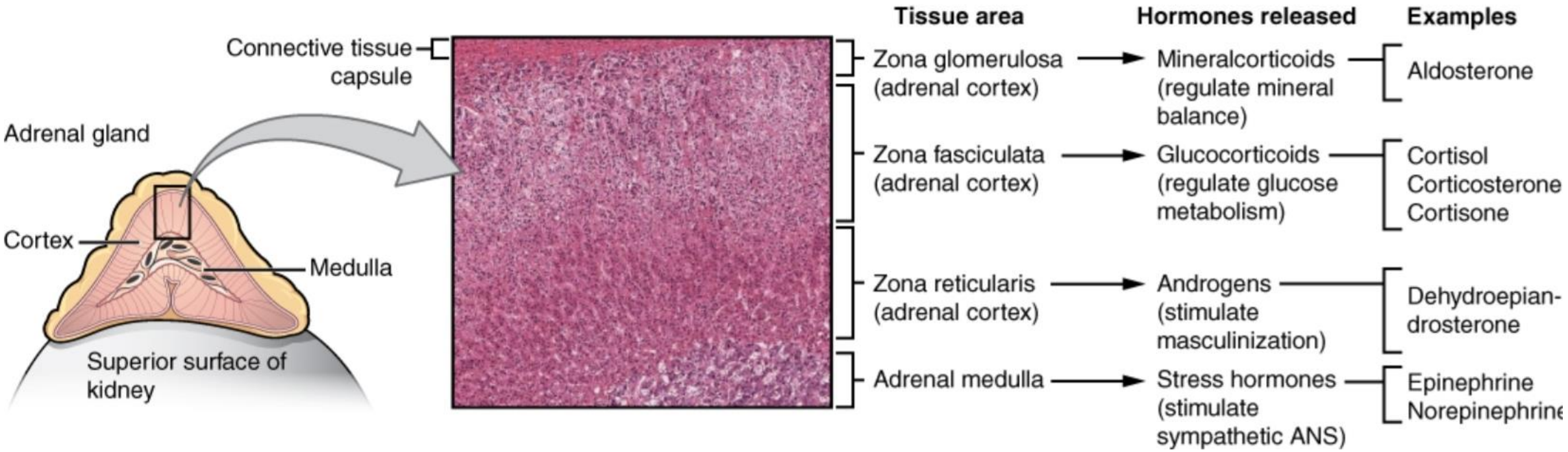
Treatment of acute severe hypercalcaemia

Acute hypercalcaemia often presents with dehydration, nausea and vomiting, nocturia and polyuria, drowsiness and altered consciousness. The serum Ca^{2+} is over 3 mmol/L and sometimes as high as 5 mmol/L. While investigation of the cause is under way, immediate treatment is mandatory if the patient is seriously ill or if the Ca^{2+} is above 3.5 mmol/L.

- **Rehydrate** at least 4–6 L of 0.9% saline on day 1, and 3–4 L for several days thereafter. Central venous pressure (CVP) may need to be monitored to control the hydration rate.
- **Intravenous bisphosphonates** are the treatment of choice for hypercalcaemia of malignancy or of undiagnosed cause. Pamidronate is preferred (60–90 mg as an intravenous infusion in 0.9% saline or glucose over 2–4 hours or, if less urgent, over 2–4 days). Levels fall after 24–72 hours, lasting for approximately two weeks. Zoledronate is an alternative.
- **Prednisolone** (30–60 mg daily) is effective in some instances (e.g. in myeloma, sarcoidosis and vitamin D excess) but in most cases is ineffective.
- **Calcitonin** (200 units i.v. 6-hourly) has a short-lived action and is little used.
- ***Oral* phosphate** (sodium cellulose phosphate 5 g three times daily) produces diarrhoea.

Adrenal crisis

Adrenal gland



1. Lack of cortisol
    a. GI symptoms—anorexia, nausea and vomiting, vague abdominal pain, weight loss
    b. Mental symptoms—lethargy, confusion, psychosis.
    c. Hypoglycemia—Cortisol is a gluconeogenic hormone.
    d. Hyperpigmentation
    e. Intolerance to physiologic stress
2. Low aldosterone
    a. Sodium loss, causing hyponatremia and hypovolemia, which may lead to:
        - Hypotension, decreased cardiac output, and decreased renal perfusion.
        - Weakness, shock, and syncope.
    b. Hyperkalemia (due to retention of potassium).

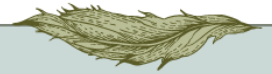
Adrenal insufficiency

1. Primary adrenal insufficiency (Addison disease)
    a) Idiopathic (thought to be autoimmune disease) is the most common type in the industrialized world.
    b) Infectious diseases—these include tuberculosis (most common cause worldwide) and fungal infections. Causes also include cytomegalovirus, cryptococcus, toxoplasmosis, and pneumocystis.
    c) Iatrogenic—for example, a bilateral adrenalectomy.
    d) Metastatic disease—from lung or breast cancer.

Adrenal insufficiency

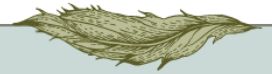
2. Secondary adrenal insufficiency
    a) Patients on long-term steroid therapy—This is the most common. When these patients develop a serious illness or undergo trauma, they cannot release an appropriate amount of cortisol because of chronic suppression of CRH and ACTH by the exogenous steroids.
    b) Hypopituitarism (rare)—due to a variety of insults.
3. Tertiary adrenal insufficiency—hypothalamic disease.

Adrenal crisis



- An acute and severely symptomatic stage of adrenal insufficiency
- Adrenal crisis may result from:
- an acute exacerbation of chronic insufficiency, usually caused by sepsis or surgical stress.
- adrenal hemorrhage (eg, usually septicemia-induced Waterhouse-Friderichsen syndrome [fulminant meningococcemia]) and anticoagulation complications.
- Steroid withdrawal is the most common and almost exclusively causes a glucocorticoid deficiency.

Clinical features



- Weight loss
- Weakness
- Pigmentation
- Anorexia
- Nausea
- Postural hypotension
- Abdominal pain (can mimic acute abdomen)
- Hypoglycemia
- Fever and decreased level of consciousness

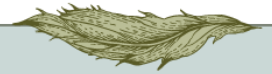
Work up

- Labs
  - Complete blood count
  - Electrolyte levels
  - BUN level
  - Creatinine level
  - Cortisol level/ACTH
  - Serum calcium levels
- Imaging
  - A CT scan of the abdomen may show hemorrhage in the adrenals, calcification of the adrenals (seen with tuberculosis), or metastasis.
  - In cases of secondary adrenal insufficiency, a head CT scan may show destruction of the pituitary (ie, empty sella syndrome) or a pituitary mass lesion.

Work up

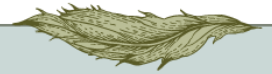
- Adrenocorticotropic hormone (ACTH) stimulation test
- Normal response is indicated when the cortisol peak exceeds 18 ug/dL in response to ACTH stimulation.
- Note: In emergent situations, do not delay treatment of presumed adrenal insufficiency during diagnostic testing. Treatment with dexamethasone allows ACTH stimulation testing without affecting or interfering with the measurement of serum cortisol levels.

Management



- Emergency department care includes the following:
- Maintain airway, breathing, and circulation in patients with adrenal crisis.
- Use coma protocol (ie, glucose, thiamine, naloxone).Use aggressive volume replacement therapy (dextrose 5% in normal saline solution [D5NS]).
- Correct electrolyte abnormalities (hypoglycemia, hyponatremia ,hyperkalemia ,hypercalcemia)

Management



- Administer hydrocortisone 100 mg intravenously (IV) every 6 hours
- Administer fludrocortisone acetate (mineralocorticoid) 0.1 mg every day as needed.
- Note: Mineralocorticoid administration is usually not necessary for treatment of secondary adrenocortical insufficiency.
- Once the patient stabilizes, usually by the second day, the corticosteroid dose may be reduced and then tapered. Oral maintenance can usually be achieved by the fourth or fifth day.
- Always treat the underlying problem that precipitated the crisis.

Pheochromocytoma

Introduction

Catecholamine-producing tumors that arise from sympathetic paraganglia cells that are collection of adrenaline-secreating chromaffin cells of the adrenal medulla or from sympathetic ganglia if extra-adrenal.

Curable if diagnosed and treated, but may be fetal if undiagnosed.

Etiology:

- Idiopathic (most cases)
- Genetic (associated with MEN2, von Hippel-Lindau)

Clinical presentation

HTN— Bp is persistently high, with episodes of severe HTN (paroxysmal).

Sever pounding headache.

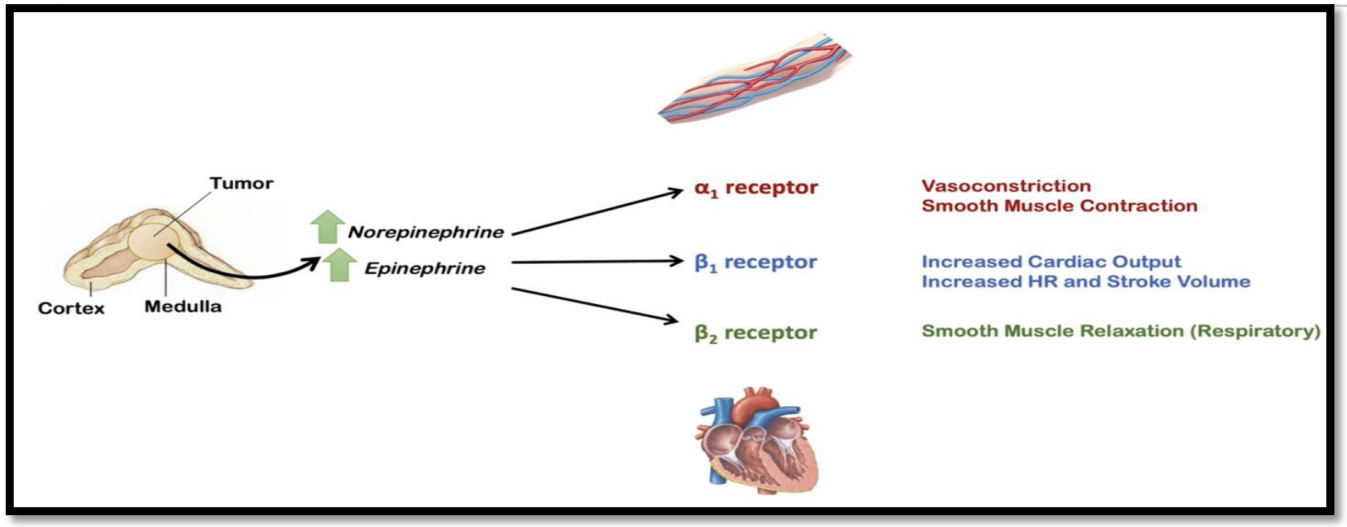
Inappropriate severe sweating.

Tachycardia.

Palpitations, with sudden severe HTN.

Anxiety.

Feeling of impending doom.



Rule of 10s for pheochromocytoma

- 10% are familial
- 10% are bilateral (suspect MEN type ll)
- 10% are malignant
- 10% are multiple
- 10% occur in children
- 10% are extra-adrenal

Risk factor

- Combined HTN + DM
- Refractoty HTN
- HTN in young person without a family history
- Dilated cardiomyopathy of unknown cause.
- Hx HTN during procedures, with ingestion of tyramine-containing foods, or use of MAO inhibitors.
- Family Hx of pheochromcytoma .
- Family Hx of MEN2, neurofibromatosis, or von hippel-Lindau disease.

Diagnosis

Urine screen test

- First line diagnostic test.
- 24-hour urinary Metanephrine and catecholamines.
- Preferred for screening of low-risk individuals.

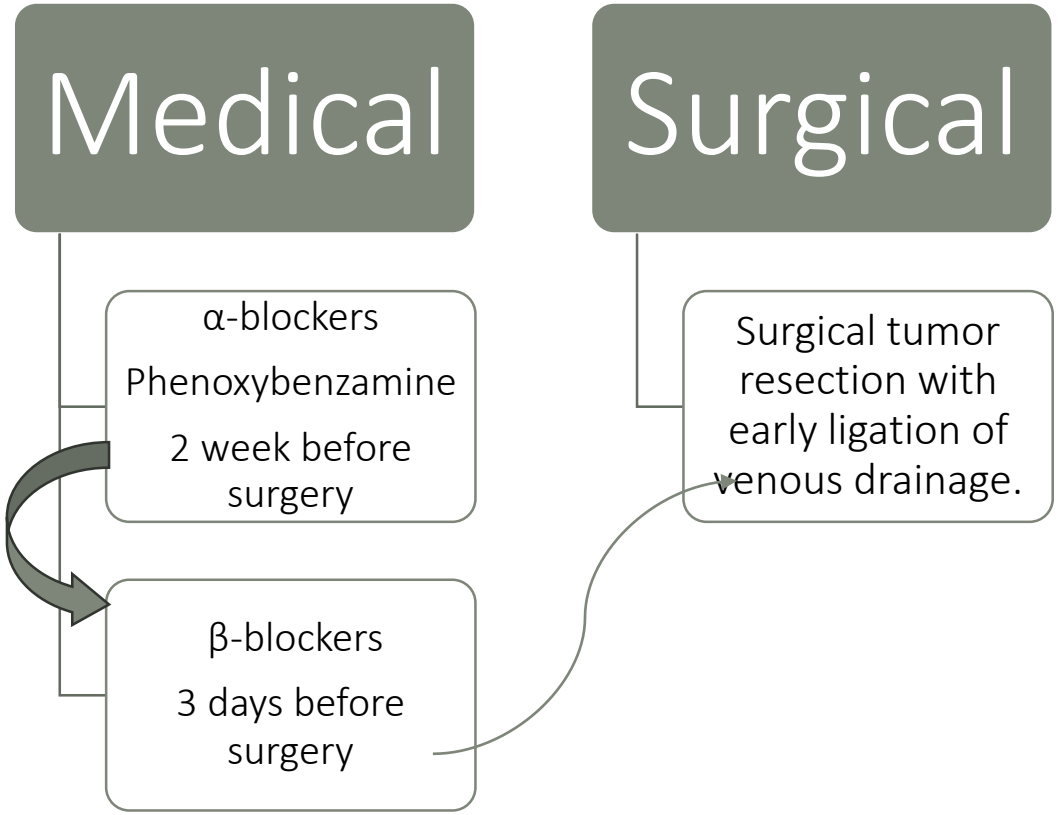
Plasma metanephrines level

- In patients who carry a high pretest probability of disease .

Tumor localization tests

- CT
  MRI
  MIBG

Management


Medical
Surgical
α-blockers
Phenoxybenzamine
2 week before surgery
β-blockers
3 days before surgery
Surgical tumor resection with early ligation of venous drainage.

Pituitary apoplexy

Introduction

a neurosurgical emergency caused by hemorrhage or infarction of the pituitary gland, which typically occurs within a pituitary adenoma..

It may occur in a normal gland during and after child birth (sheehan syndrome), or with head trauma or in patient on anticoagulation therapy.

Clinical presentation

severe headache.

N/V

meningismus

vertigo.

visual defects.

fluctuating consciousness.

Risk factors

1. Diabetes with microvasculature changes.
2. radiotherapy.
3. concurrent warfarin use.

Diagnosis

Ct / MRI of head and pituitary

Hormonal studies :

- Deficiency of at least one of the anterior pituitary hormones (GH and ACTH are most common deficiencies).

Management

Hormonal

- Dexamethasone (glucocorticoid support and relief of cerebral edema)

Surgical

- Transsphenoidal pituitary decompression

REFERENCES

- Kumar & Clark's clinical medicine 8th edition
- UpToDate
- Davidson's 24th edition
- Step up to medicine 5th edition
- Medscape
- Medstudy 16th edition

Thank you