

Endocrine Emergencies

- Neuroendocrine response to Critical illness
- Thyroid storm/Myxedema Coma
- Adrenal Crisis/Sepsis
- Hyper/Hypocalcemia
- Hypoglycemia
- Hyper and Hyponatremia
- Pheochromocytoma crises

CASE

76 year old man presents with urosepsis and is Admitted to MICU. He has chronic renal insufficiency. During his hospital course, he is intubated and treated With dopamine. Thyroid studies are performed for Inability to wean from ventilator.

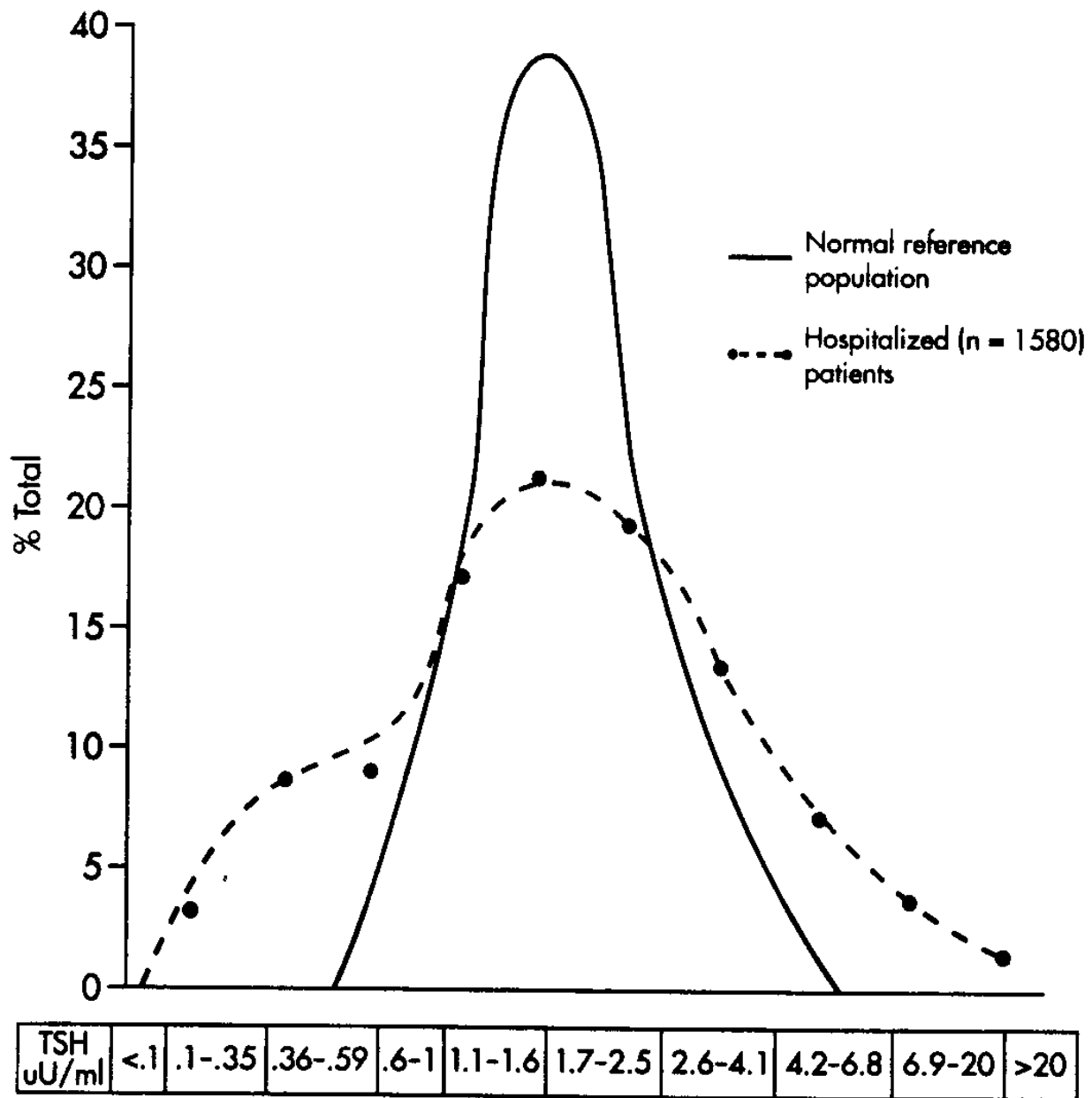
What labs do you want?

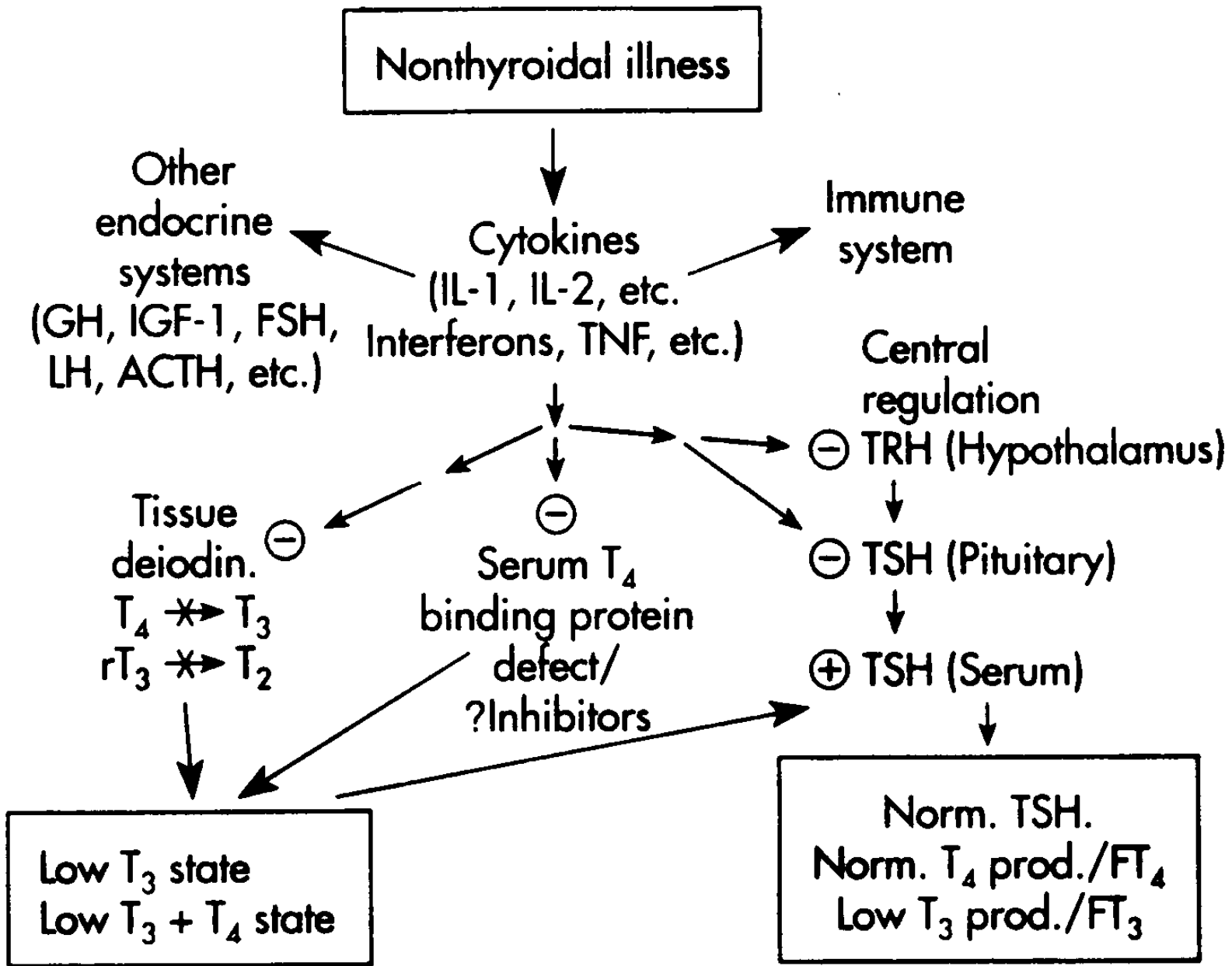
Assessment of Thyroid Function

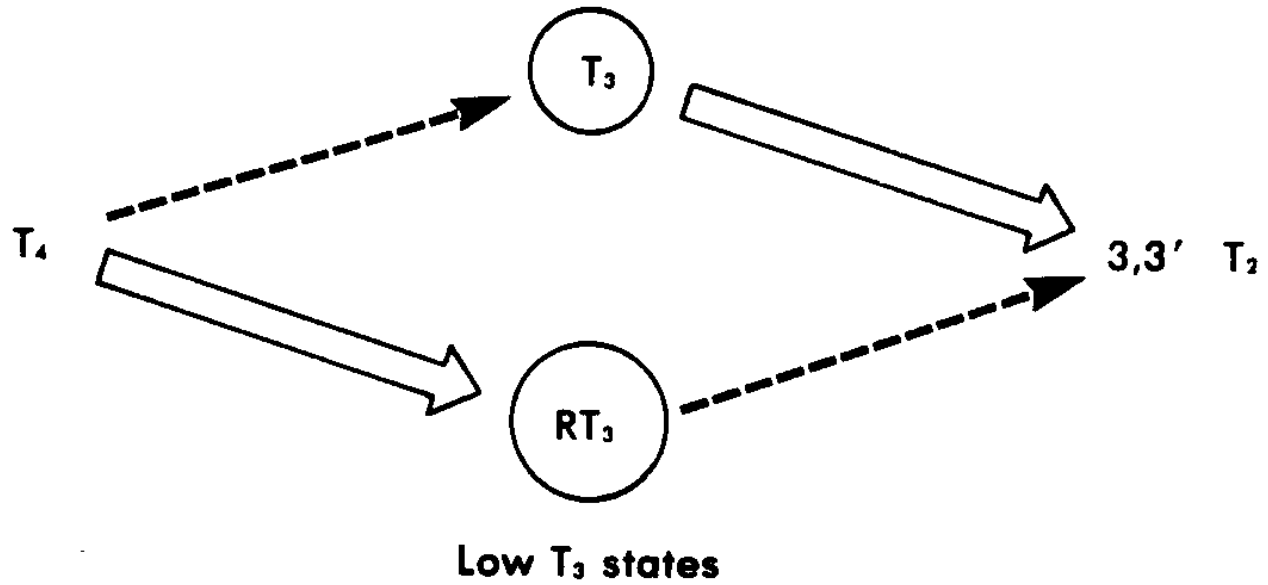
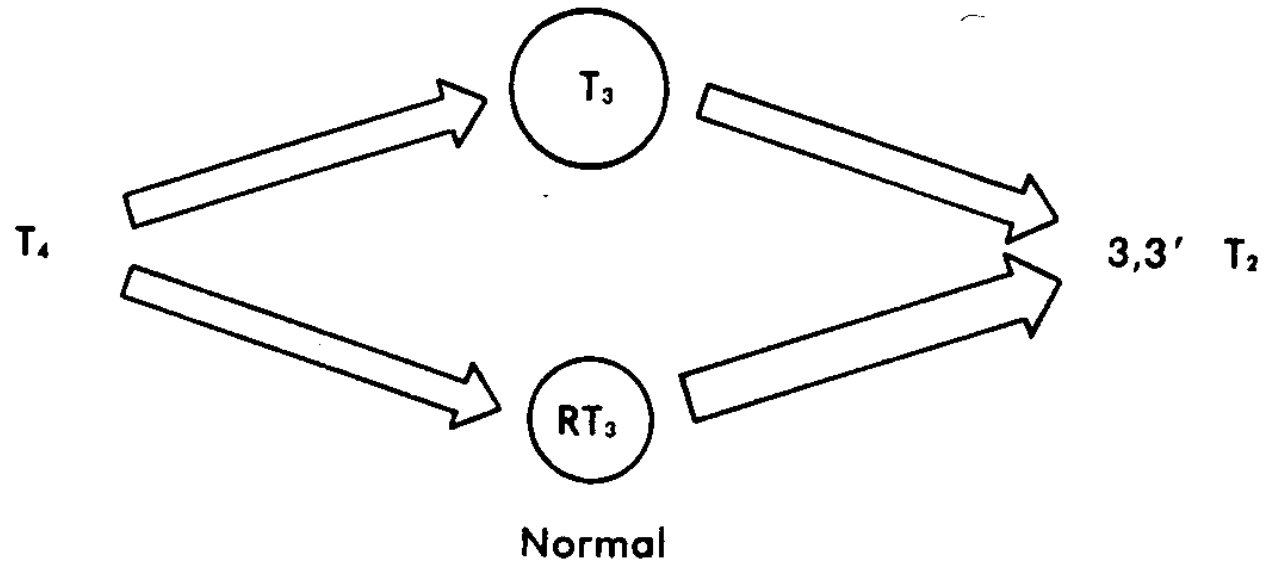
- Hormone Levels: Total T4, Total T3
- Binding proteins: TBG, (T3*) Resin uptake
- Free Hormone Levels: TSH, F T4, F T3, Free Thyroid Index, F T4 by Eq Dialysis
- Radioactive Iodine uptake (RAIU); primarily for DDx of hyperthyroidism
- Thyroid antibodies; TPO, Anti-Thyroglobulin, Thyroid stimulating immunoglobulins, Th receptor antibodies

Labs:

T4	2.4 ug/dl	(5-12)
T3U	40%	(25-35)
FTI	1.0	(1.2-4.2)
FT4	0.6	(0.8-1.8)
TSH	0.2 uU/ml	(.4-5.0)







Non-thyroidal illness

- Hypothesis: NTI vs 2° Hypothyroidism
 - RT3 ↑ in NTI and ↓ in Hypothyroidism
- Hypothesis: NTI vs Hyperthyroidism
 - TT3 ↓ in NTI and in ↑ Hyperthyroidism

- 75 year old woman with history of hypothyroidism is found unresponsive in her home during a cold spell in houston. No heat in the home.
- Exam: T° 95, BP 100/60, P 50, RR 8
- Periorbital edema, neck scar, no rub or gallop, distant heart sounds, crackles at bases, peripheral edema
- ECG: Decreased voltage, runs of Torsade de pointes
- Labs? Imaging?



- CXR: cardiomegaly
- Glucose 50
- Na⁺ 120, K⁺ 4, Cl 80, HCO₃⁻ 30
- BUN 30 Creat 1.4
- ABG: pH 7.25, PCO₂ 75, PO₂ 80
- CK 600
- Thyroid studies pending
- Management:

Manifestations of Myxedema Coma

- Precipitated by infection, iatrogenic (surgery, sedation, diuretics)
- Low thyroid studies
- Hypothermia
- Altered mental status
- Hyponatremia
- $\uparrow pCO_2$
- $\uparrow CK$
- \uparrow Catecholamines with \uparrow vascular resistance
- Cardiac: low voltage, Pericardial effusion, impaired relaxation with \downarrow C.O.

What are the signs of hypothyroidism?

- Bradycardia
- Coarse hair
- Delayed relaxation of deep tendon reflexes
- Dry, cool, pale skin
- Goiter or Surgical Scar
- Hoarseness
- Nonpitting edema (myxedema)
- Puffy eyes and face (orbitopathy)
- Slow movements
- Slow speech
- Thinning lateral third of eyebrows



Myxedema coma: Precipitating or exacerbating factors

- Hypothermia
- CVA
- CHF
- Infection
- GI bleeding
- Trauma
- Discontinuation of meds
- Drugs
 - Anesthesia
 - Sedatives
 - Tranquilizers
 - Narcotics
 - Amiodarone
 - Lithium carbonate
 - Raw Bok Choy

Multifaceted treatment

- Treat precipitating event!
- R/O upper airway obstruction
- Mechanical ventilation until full recovery of consciousness
- IV volume repletion
 - 0.45 NS + D5 or D10
 - NS + D5 or D10 if hyponatremic
 - LT4 should correct Na⁺
- Passive warming;
 - Avoid rapid rewarming → vasodilatation

Management of Myxedema

- Levothyroxine intravenously (100 ug – 200 ug loading dose + 100 ug/day)
 - IV dose is 50% of oral dose
- IV hydrocortisone 100 mg Q 8
- IV antibiotics
- Maintain intravascular volume (cautious use of diuretics)
- ?T3 use: Call endocrine first

Management of Primary Hypothyroidism

- Levothyroxine 1.6 ug/Kg is average maintenance dose (Adults .075-.15 mg/d)
- Absorption impaired by Iron, Calcium, antacids, carafate; best taken fasting

- 30 year old presents with atrial fibrillation w/ RVR 180/min, BP 100/70, Temp 104, delirious. Family notes nausea/vomiting and diarrhea for > 1 week. 50 lb weight loss of past year.
- Exam: warm moist skin, tremulous, mild proptosis. Visible goiter with bruit. Generalized shotty lymphadenopathy. +S3 gallop with hyperdynamic precordium and bilateral crackles. Spleen tip palpable.
- CTA: Enlarged thyroid and anterior mediastinal mass appears to be thymus, cardiomegaly with increased interstitial markings.
- Labs?

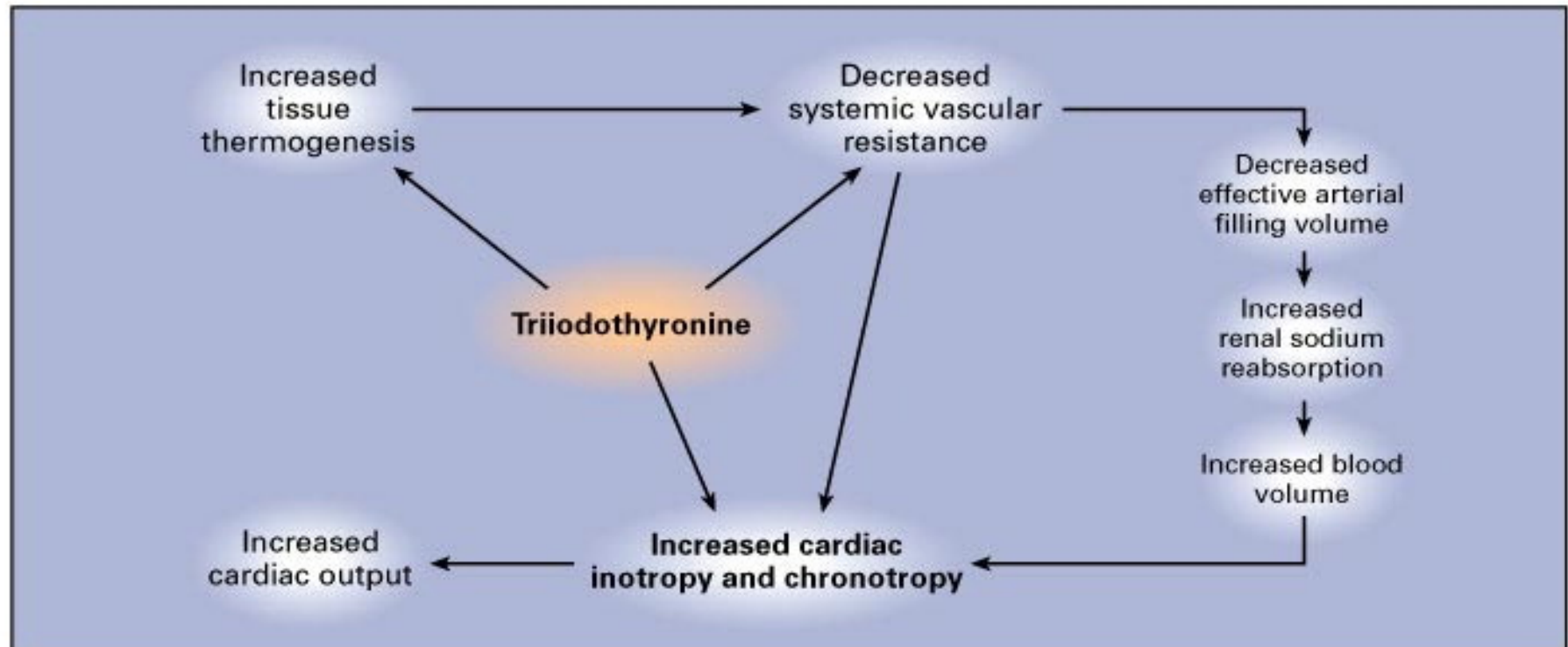
Labs

- Lytes normal
- Hg 10, WBC 4K, 60% lymphs, no bands, PLT 80K
- Calcium 11, AST/ALT 60/60, Alk P 200
- Thyroid studies pending

Decompensated thyrotoxicosis: “Thyroid storm”

- Multisystem decompensation of pre-existing thyrotoxicosis
 - Thermoregulatory
 - Neuropsychiatric
 - Gastrointestinal
 - Cardiovascular
- Etiology?

Effects of Thyroid Hormone on Cardiovascular Hemodynamics.



Klein I, Ojamaa K. N Engl J Med 2001;344:501-509.



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Thyroid Storm

- Precipitated by infection or iatrogenic
- Tachyarrhythmia
- Fever $> 104^{\circ}$
- Altered mental status
- Other manifestations of thyrotoxicosis

Burch-Wartofsky Index

<u>Thermoregulatory Dysfunction</u>	
99 - 99.9	5
100 – 100.9	10
101 – 101.9	15
102 – 102.9	20
103 – 103.9	25
104 or higher	30
<u>Central nervous system</u>	
Absent	0
Mild (agitation)	10
Moderate (delirium, psychosis, lethargy)	20
Severe (seizures, coma)	30
<u>Gastrointestinal – hepatic</u>	
Absent	0
Moderate (diarrhea, N/V, pain)	10
Severe (unexplained jaundice)	20

<u>Tachycardia</u>	
90 – 109 bpm	5
110 – 119 bpm	10
120 – 129 bpm	15
130 – 139 bpm	20
140 or higher	25
<u>Atrial fibrillation</u>	10
<u>Congestive heart failure</u>	
Mild (pedal edema)	5
Moderate (bibasilar rales)	10
Severe (pulmonary edema)	15

Sum of ≥ 45 : highly suggestive
 Sum of 25–44: suggestive
 Sum below 25: unlikely

Multifaceted treatment

- Treat precipitating event!
- Stop thyroid hormone synthesis
- Stop release of preformed hormone
- Stop T4 → T3 conversion
- Control adrenergic effects
- Supportive therapy
- **Assess cardiac function!**

Management of Thyroid Storm

- Methimazole 20 Q 6-8 hours or PTU ~400 mg + 200 mg Q 4 hrs per NG or rectal
- β blockers (propranolol, metoprolol, esmolol) – Contraindicated if systolic failure
- Iodine (SSKI, Lugol's, contrast, amiodarone)
- Glucocorticoids (hydrocortisone 100 mg Q 8 hrs)

Alternative regimens

- Lithium carbonate 300 mg q8 hr
- Potassium perchlorate 1 g daily
- Cholestyramine 4 g q6 hr
- Charcoal hemoperfusion
- Plasmapheresis

- Hyperthyroidism ~ Atrial arrhythmias
- Hypothyroidism ~ ventricular arrhythmias, prolonged QT, acquired Torsade de pointes

- 65 year old man with chronic atrial fibrillation on coumadin presents after MVA.
- Unresponsive, intubated, hypotensive, tachycardic, afebrile with generalized ecchymoses over abdomen and arms.
- IV resuscitation with saline without change in BP. Started on norepi but still hypotensive.
- Labs?

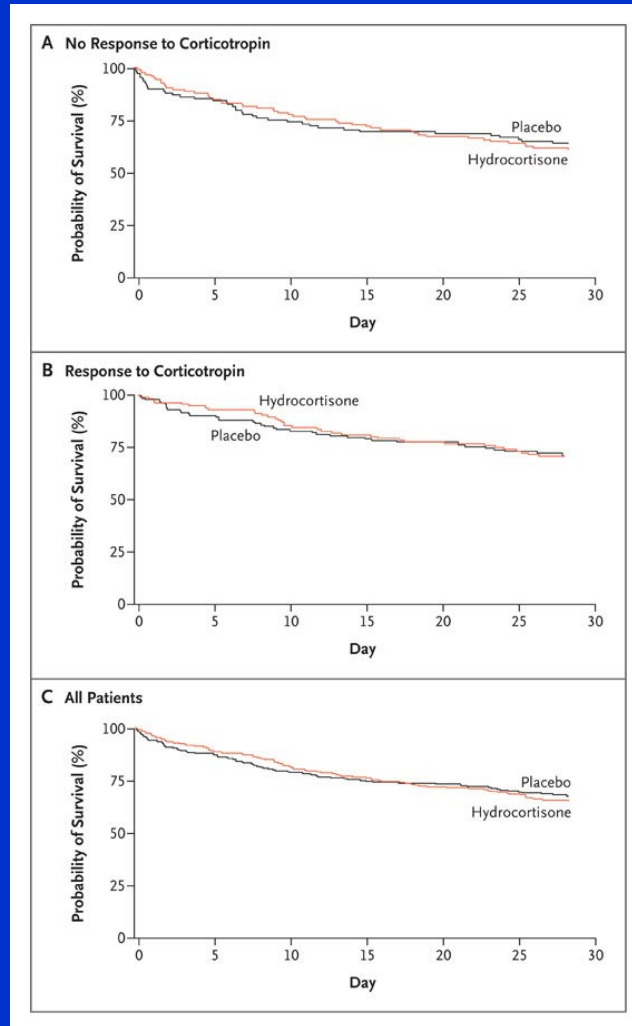
- HCT; 40, Na⁺ 144, K⁺ 3.8, Cl 95, HCO₃ 10
- WBC 20K with left shift
- ALT 900

- Management:

Acute vs Chronic Adrenal Insufficiency

- Anorexia, abdominal pain, wt loss
- Orthostasis
- Salt craving, hyperpigmentation, vitiligo
- Other autoimmune endocrinopathies: hypothyroidism, DM-1, PA, SLE, etc
- HyperKalemia, hyponatremia, acidosis, hypoglycemia
- **Acute adrenal insufficiency → hypotension unresponsive to pressors**

Kaplan-Meier Curves for Survival at 28 Days

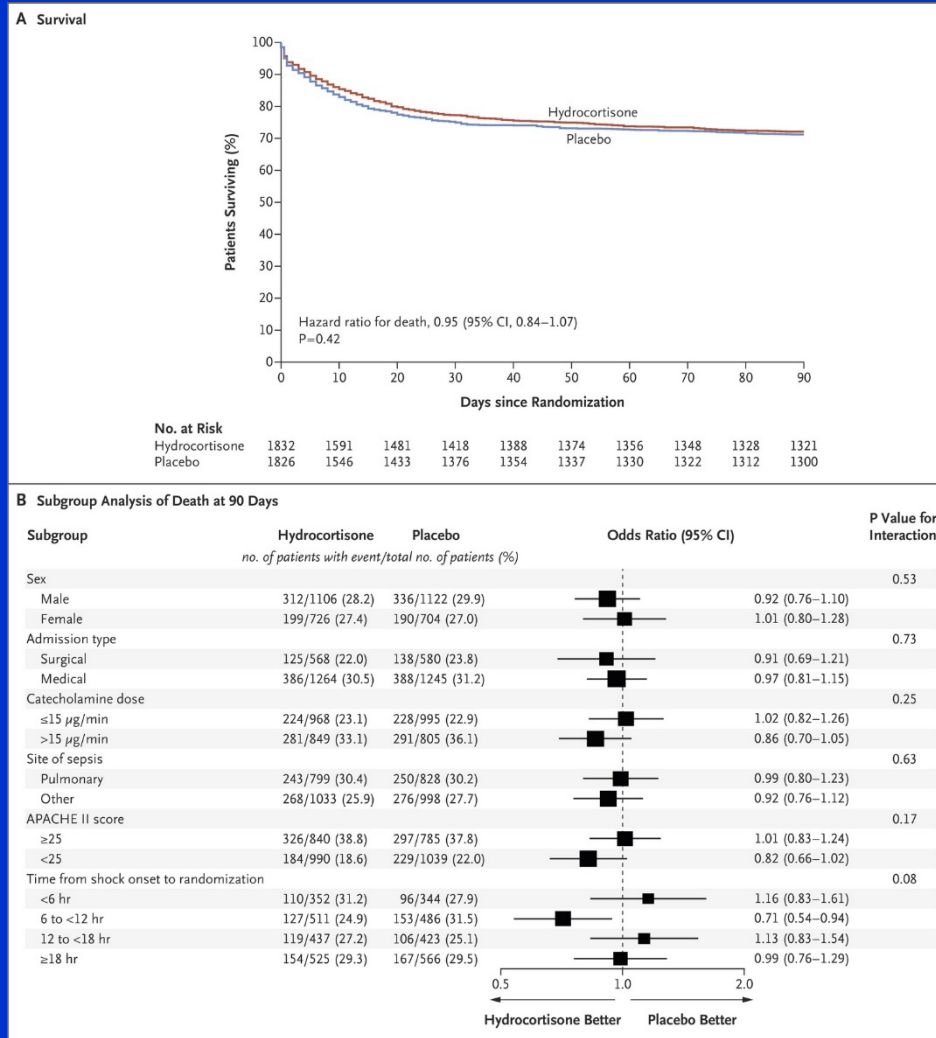


Sprung C et al. N Engl J Med 2008;358:111-124



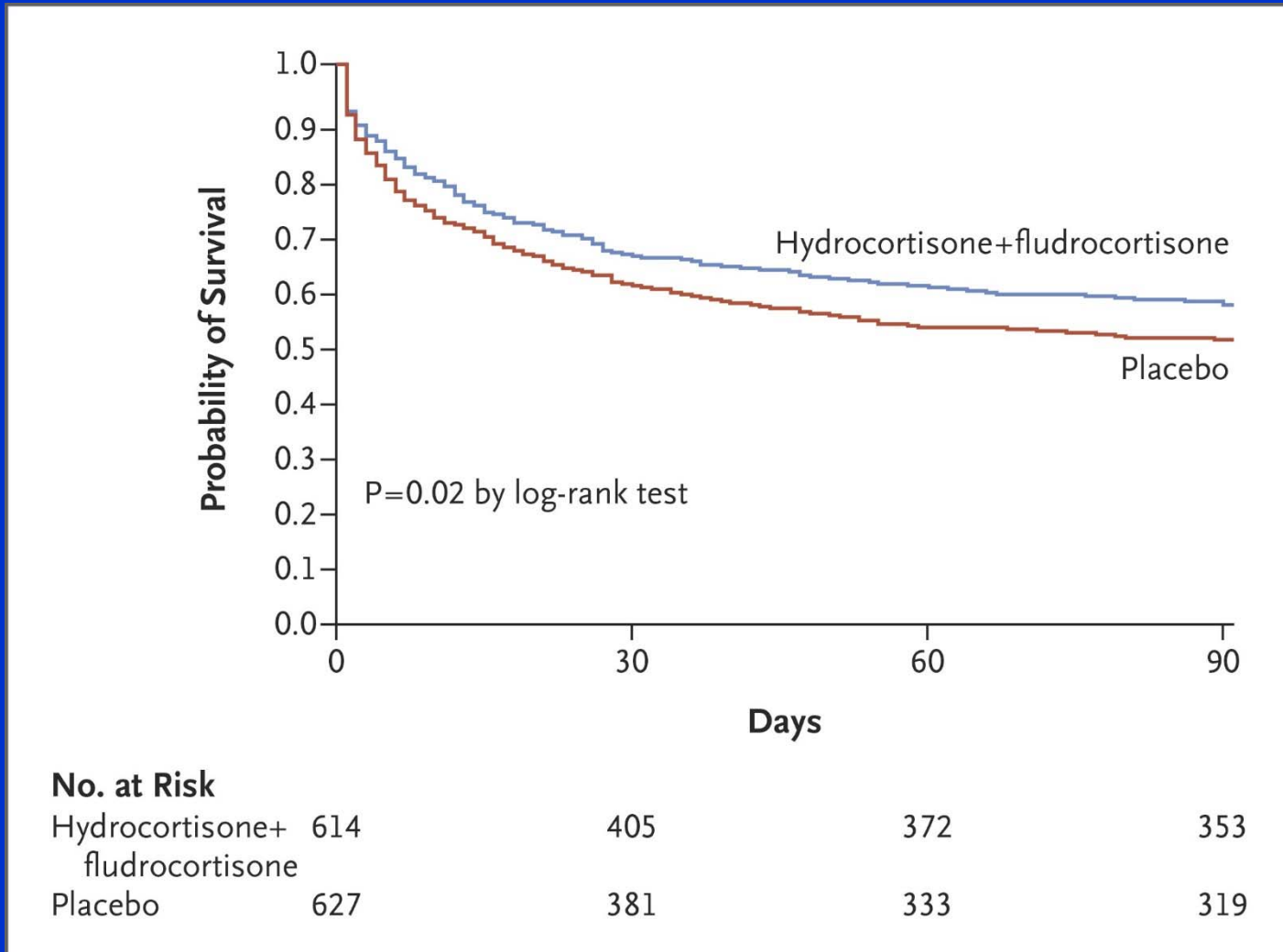
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Rate of Survival and the Risk of Death at 90 Days, According to Subgroup.



Venkaresh B et al. N Engl J Med 2018;378:797-808

90-Day Survival Distributions.



Annane D et al. N Engl J Med 2018;378:809-818



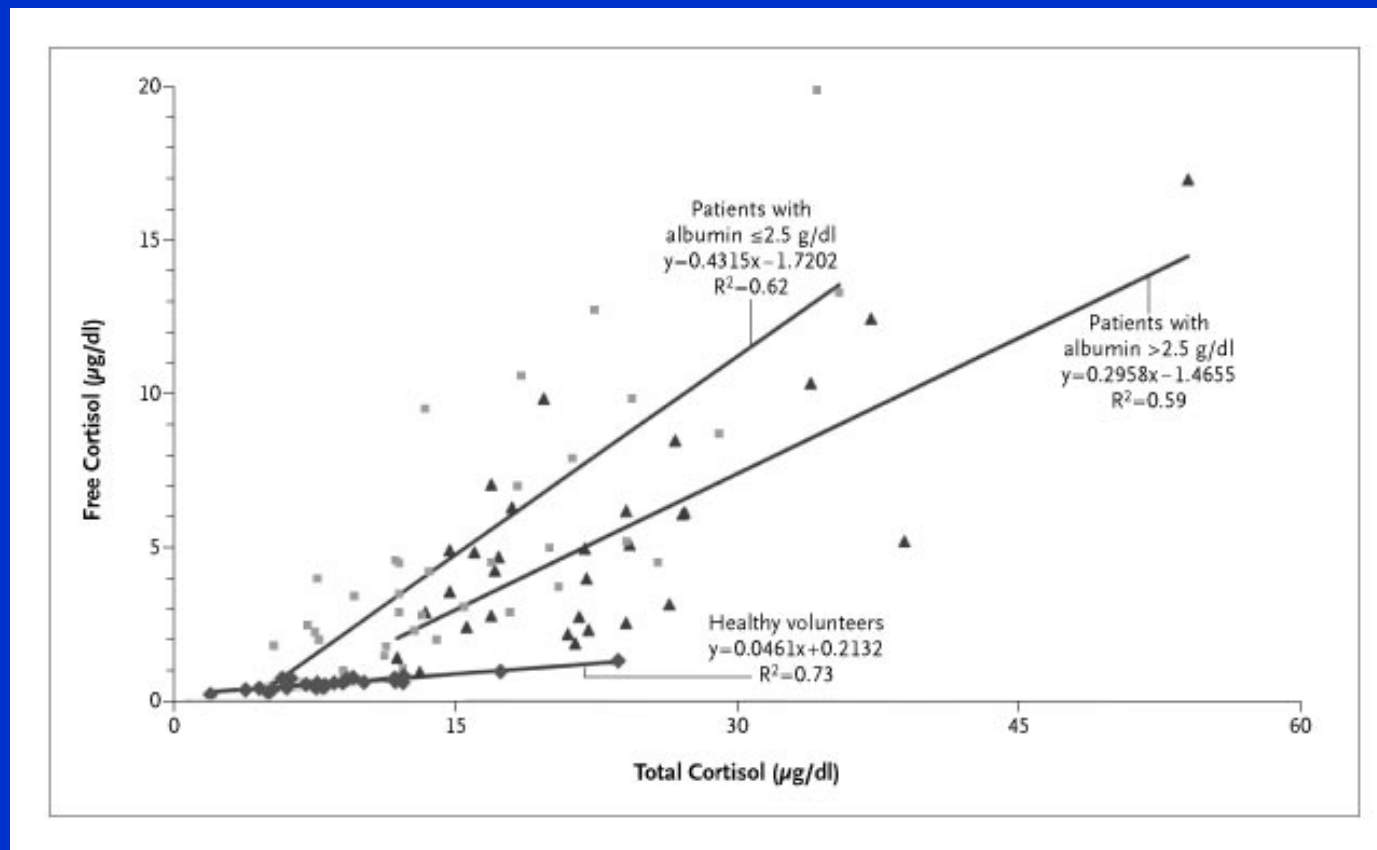
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Conclusions

- In this trial involving patients with septic shock, 90-day all-cause mortality was lower among those who received hydrocortisone plus fludrocortisone than among those who received placebo.
- Hydrocortisone 50-mg IV Q6 hours + fludrocortisone 50- μ g tablet through a nasogastric tube once daily in the morning. Trial agents were administered for 7 days without tapering.



Scatter Plots and Regression Lines of Base-Line Serum Total Cortisol and Free Cortisol Concentrations in 66 Critically Ill Patients with Serum Albumin Concentrations [\leq]2.5 g per Deciliter (Squares) or $>$ 2.5 g per Deciliter (Triangles) and in 33 Healthy Volunteers (Diamonds)



Hamrahian, A. H. et al. N Engl J Med 2004;350:1629-1638



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Management of Adrenal Crisis

- IV saline
- Equivalent doses of glucocorticoids:
 - Hydrocortisone 100 mg Q 8 hrs
 - Methylprednisolone 20 mg Q 8 hrs
 - Dexamethasone 4 mg Q 8 hrs
- ?mineralocorticoids



Diagnosis?

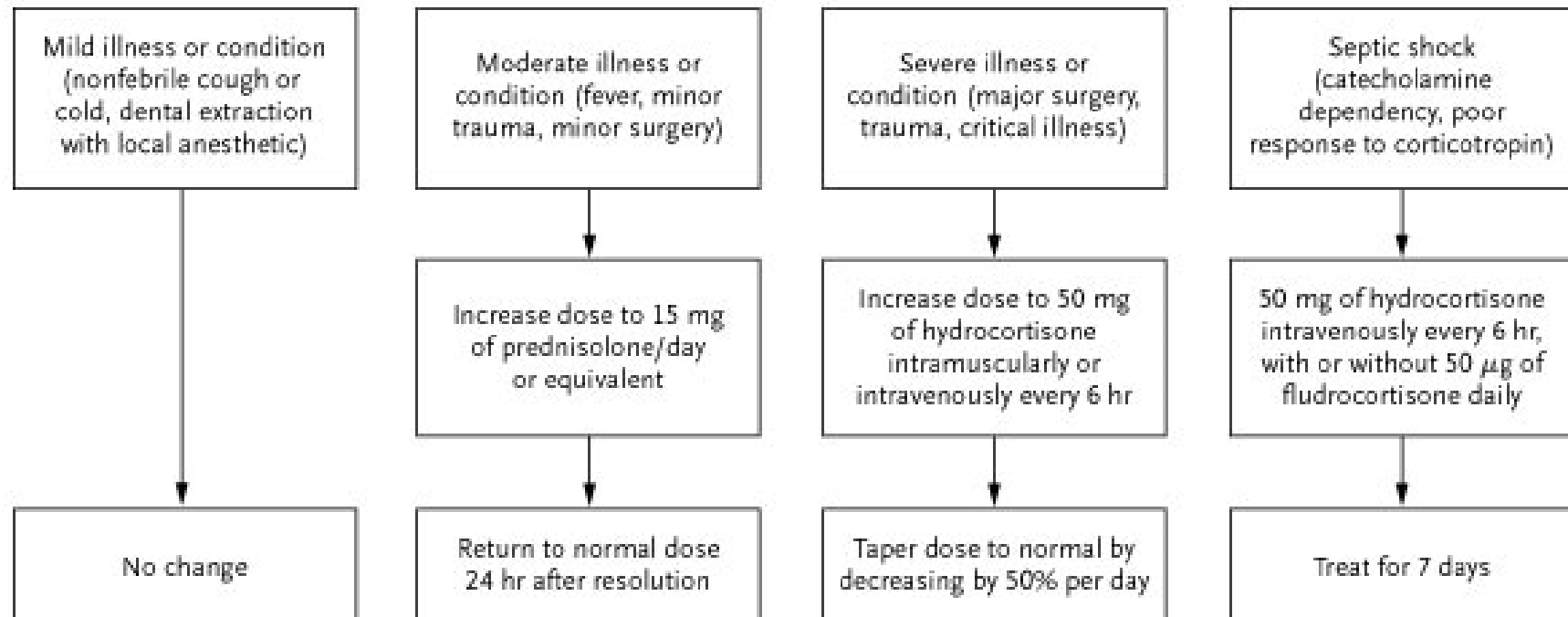
Etiology?

Associated diseases?

Cosyntropin Stimulation Test

- Measure basal serum cortisol
- Administer IV/IM cosyntropin
 - 1 ug
 - 250 ug
- Measure 30 ± 60 minute serum cortisol
- Any value over 18-20 ug/dl demonstrates adequate adrenal reserve

Suggested Corticosteroid-Replacement Doses during Intercurrent and Acute Illness in Patients with Proven or Suspected Adrenal Insufficiency, Including Those Receiving Corticosteroid Therapy



Cooper, M. S. et al. N Engl J Med 2003;348:727-734



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- 50 year old man presents to ER unresponsive with dry mucous membranes. MR shows only hiatal hernia with GERD.
- Calcium 14, Phosp 6, Creatinine 4, BUN 80
- Labs?

Hypercalcemia

- Hyperparathyroidism
- Hypercalcemia of Malignancy
 - PTH-rp, IL-1, IL-6, TNF- α
- Vitamin D related:
 - Granulomatous diseases (Sarcoid)
 - Lymphomas, leukemias
- Medications
- Other: Immobilization, hyperthyroid, Addison's

Evaluation of Hypercalcemia

- Ionized Calcium
- Intact PTH
- PTHrP
- 1,25 Vitamin D
- Urinary Calcium/creatinine

Medications associated with hypercalcemia

- Thiazides; may unmask hyperparathyroid
- Lithium; may unmask hyperparathyroidism
- Vitamin D; increased 25 vitamin D levels
- Vitamin A
- Milk-Alkali syndrome: increased phosph, renal disease
- TPN or aluminum toxicity

Treatment of Hypercalcemic Crisis

- Hydration with IV saline (Add furosemide **ONLY** after volume repleted)
- Zoledronic acid 4 mg over 15 min or Pamidronate IV 30-90 mg over 6 hours
- Denosumab SQ 120 SQ
- Calcitonin 4 units/Kg SQ every 6-8 hours
 - Mild efficacy and early tachyphylaxis
- Glucocorticoids only for responsive illnesses (sarcoid, myeloma, Vitamin D, etc)
- Other: Dialysis

A 67-year-old man is admitted to the hospital after being found unresponsive and intoxicated at home. Family members report that he has a history of hypertension treated with atenolol and a history of alcoholism. He lives alone and has been resistant to assistance with meals and chores. He takes no other medication.

On physical examination, the patient is lethargic but arousable and smells strongly of alcohol. Vital signs are normal except for a pulse rate of 105/min. Mucous membranes are dry. No pain is elicited on abdominal examination. Chvostek sign and Trousseau phenomenon are noted.

After an electrocardiogram shows tachycardia (heart rate to 105/min) and a prolonged corrected QT interval (0.49 s), the patient is given intravenous fluids with added thiamine and folate.

Labs?

Laboratory studies (before administration of thiamine, folate, and calcium):

Amylase 110 units/L

Blood urea nitrogen 33 mg/L (11.8 mmol/L)

Creatinine 1.4 mg/dL (124 μ mol/L)

Ethanol 249 mg/dL (0.25 g/dL) (normal, <1.0 mg/dL)

Ionized calcium 0.7 mmol/L [1.0-1.3 mmol/L]

Phosphorus 2.1 mg/dL

Additional labs?

Hypocalcemia

- Tetany
- Laryngospasm
- Convulsions

Evaluation of Hypocalcemia

- Ionized calcium
- Phosphorus
- Alkaline Phosphatase
- Magnesium
- iPTH
- 25 hydroxy Vitamin D
- 1,25 dihydroxy Vitamin D

Hypocalcemia

- Low Phosphorus = high PTH state
 - Vitamin D deficiency
 - Hungry bones syndrome
- High Phosphorus
 - Hypoparathyroid
 - Renal Disease
 - Parathyroid resistance (pseudohypoparathy)

Treatment of Hypocalcemia

- IV Calcium Gluconate 10% (**National shortage**) – alternative Ca Cl – need central line
10-20 ml in D5W over 10 minutes until symptoms resolve (.5-1.5 mg/kg/hr with ECG monitoring or 10-15 mg/kg over 6-8 hr)
- Oral Calcium 2-10 gm/day
- Calcitriol (IV or PO)
- Replace electrolytes: K⁺ and Mg⁺⁺

- 80 year old woman with history of dementia presents after a fall and found to have R hip fracture, admitted to Geriatrics.
- Ortho consulted and found to be non surgical candidate.
- On day 4, am glucose by lab was 45
- Labs?

Common Causes of Hypoglycemia

- Drugs, Drugs, Drugs, Drugs, Drugs
 - Sulfonylureas
 - Alcohol
 - Sulfa
 - Pentamidine
- Associated disorders
 - **Sepsis**
 - End Stage Renal Disease
 - Liver disease
 - Endocrine (glucocorticoid deficiency, hypothyroidism)
 - Neoplasia (IGF-II)
 - Autoimmune disease (anti-IR ab's)
- Endogenous insulin production

Diagnosis of Hypoglycemia

- Venopuncture ONLY. DO NOT TRUST FINGERSTICK GLUCOSE VALUES!!
- Whipples Triad: Documented hypoglycemia, Symptoms, and Resolution of symptoms with treatment
- Critical Sample Concept: Must measure GLUCOSE, INSULIN, C-PEPTIDE, CORTISOL, etc. ON SAME SAMPLE AT TIME OF HYPOGLYCEMIA < 50 MG/DL

Protocol for 72 hour fast

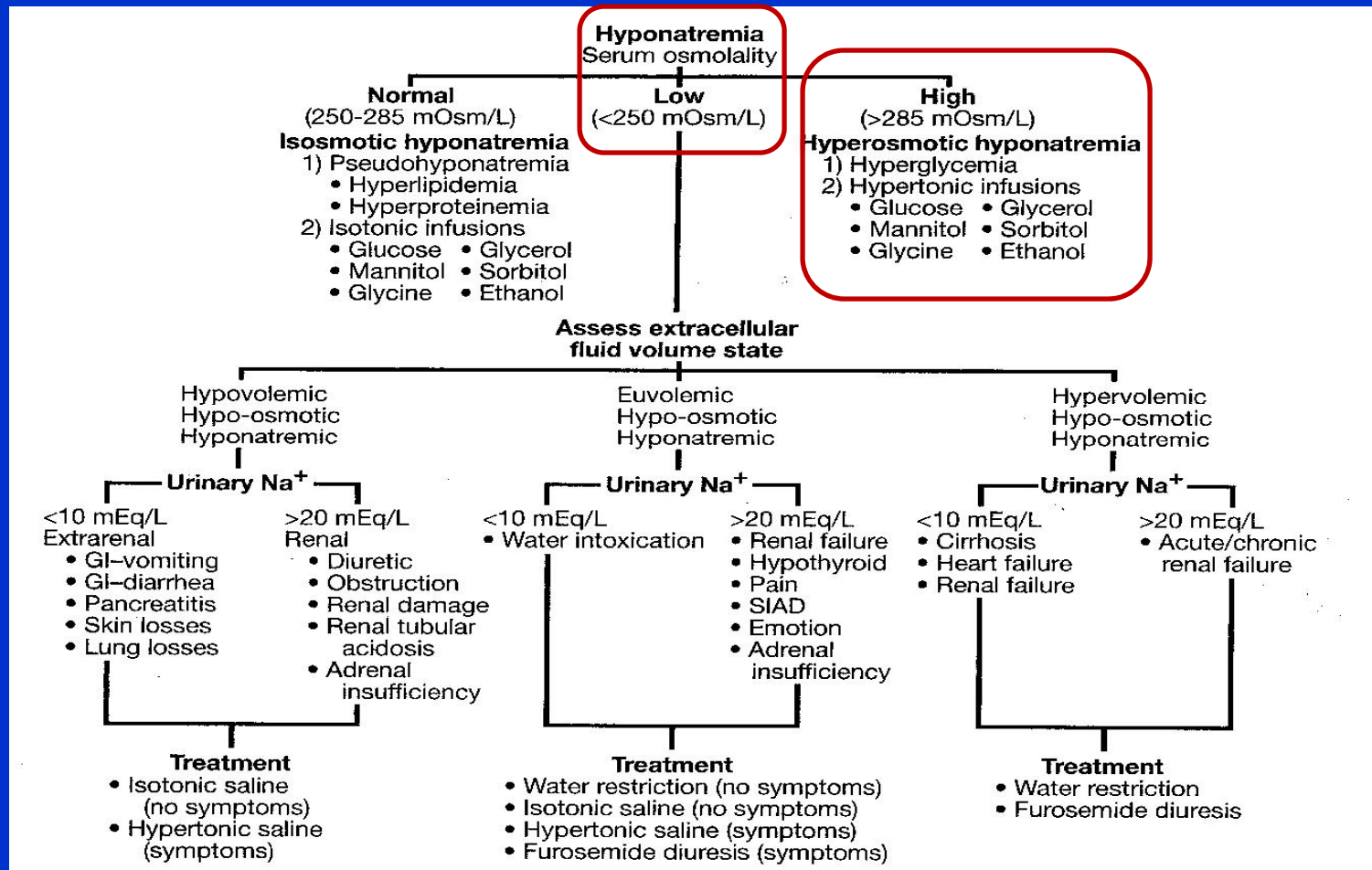
- Essential meds only, calorie and caffeine free beverages, pt should be active
- Measure glucose, insulin, C-peptide, proinsulin in **SAME** specimen Q 6 hours
- End fast when glucose < 45 mg/dl AND patient has symptoms and signs of hypoglycemia (include sulfonylurea level in same specimen)

Management of Hypoglycemia

- IV glucose
- Parenteral or enteral feedings (nocturnal)
- Glucagon
- Glucocorticoids
- Growth Hormone

- 80 year old woman presents unresponsive after seizure at home. Na⁺ 103 on admission.

Diagnostic Approach



Hyponatremia

Hypovolemic Hyponatremia

- Diuretics
- GI losses
- Adrenal insufficiency

Hypervolemic Hyponatremia

- CHF
- Cirrhosis

Euvolemia Hyponatremia

- SIADH
- Psychogenic polydipsia
- Diuretics with sufficient free water replacement

Serum osmolality	273 mosm/kg (278-305)
Urine osmolarity	518 mosm/kg (50-1200)
Urine sodium	52 meq/L
Uric Acid	3 mg/dL (4.0-8.5)

Evaluation of a patient with Hyponatremia

Urine osmolality

- Used to distinguish between inappropriate ADH secretion and primary polydipsia
- Patients with primary polydipsia have appropriately dilute urine
(urine osm < 100 , low specific gravity)
- Most patients have SIADH, higher urine osm >300 mosm/kg

Evaluation of a patient with Hyponatremia

Urine sodium

- Helps to distinguish hypovolemic hyponatremia and euvolemic hyponatremia

SIADH urine Na >40 meq/L

Hypovolemia urine Na <25 meq/L

Chronic hyponatremia

- Goal- initial correction rate upto 1 mEq/L/h in the first 3-4 hours in patients with distressing symptoms.
- Limit serum Na correction to less than 10 mEq/L in the first 24 hours [4-6 mEq/L if risk is high].
- Rapid correction can occasionally lead to osmotic demyelination especially in patients with volume depletion, cortisol deficiency and thiazide induced hyponatremia.
- Hypotonic fluids/Desmopressin can be used to slow (or reverse) rate of rise

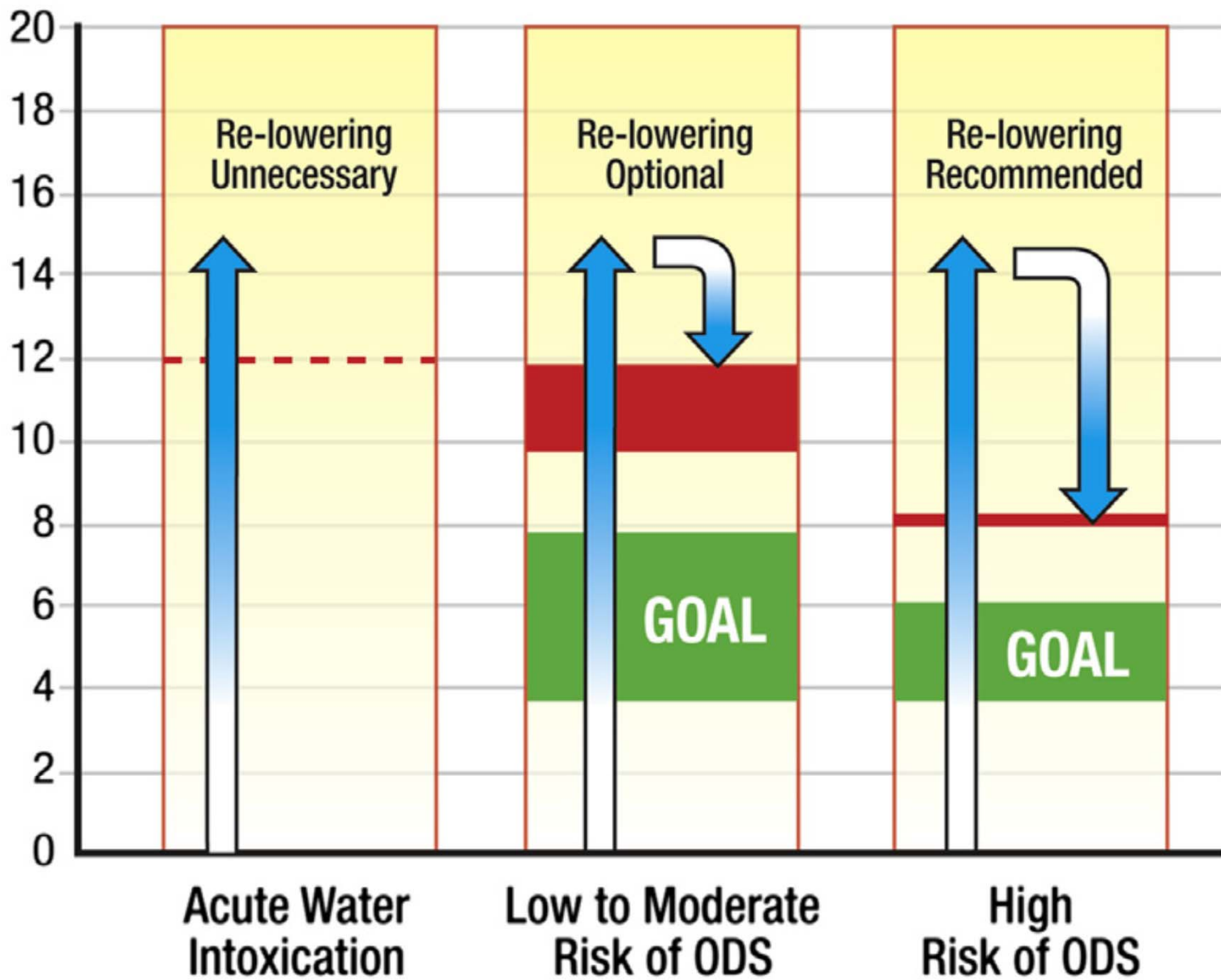
SIADH

- Fluid restriction is the mainstay of therapy in chronic SIADH and mild to moderate hyponatremia.
- Principles:
 1. All fluids including water should be restricted
 2. Degree of restriction depends on urine output plus insensible loss
 3. Several days of restriction are usually needed for a significant rise in plasma osmolality
 4. Only fluid and not sodium should be restricted due to ongoing natriuresis

Treatment of Severe Symptomatic Hyponatremia

- Hypertonic (3%) saline at a correction rate of 1.5 to 2 meq/L/h for the first 3-4 hours. Goal is to raise plasma Na concentration to not more than 10 meq/L in the first 24 hours and not more than 18 meq/L in the first 48 hours.
- Stop aggressive treatment once symptoms resolve or a safe serum Na (over 120meq/L) is achieved or the above goal is reached.
- Measure the serum Na every 2-3 hours initially.

Change in Serum Sodium Concentration
in First 24 Hours, mmol/L



Pharmacologic therapy for SIADH

- Vasopressin receptor antagonists: tolvaptan (oral)
- Demeclocycline- induces nephrogenic DI.
Dose: 600-1200 mg/day in divided doses, takes 3-4 days for the maximal effect
Disadvantage: nephrotoxic
- Salt tablets (+ Lasix)
- Treat the underlying cause of SIADH if possible.

- 60 year old man presents with severe headache and lapses into coma. CT shows large intraventricular bleed. Urine output increases to 1 liter/hour.
- Labs several hours later show Na^+ 160
- Additional labs:
- Management:

Diabetes Insipidus

- Hypernatremia with dilute urine/polyuria >3 L/d;
 - Urine osm < serum osm
- DDAVP 1 ug → urine osm > 400 with ↓ urine output
- Follow: urine output > 300/hr for 2 consecutive hours or >1 L/8 hrs, U Sp Gravity, Uosm, Serum Na⁺
- Do not write scheduled DDAVP until there is a clear pattern of requirement
- Rx DDAVP 1 ug Q 12 hrs IV

A 38-year-old man presents with a hypertensive urgency with headaches and palpitations. The patient also reports experiencing a pressure sensation when swallowing solid foods for the past year and daily diarrhea for the past 2 months. His personal medical history is unremarkable. His younger brother has nephrolithiasis, and his father died of a hypertensive crisis and cardiac arrest at age 62 years while undergoing anesthesia induction to repair a hip fracture.

On physical examination, BP 220/140, P 110/min regular. He appears pale and apprehensive. A mass is palpated in the right lobe of the thyroid gland. No cervical lymphadenopathy is palpable.

Results of laboratory studies show a serum calcium level of 10.6 mg/dL (2.7 mmol/L) and a thyroid-stimulating hormone level of 1.9 μ U/mL (1.9 mU/L).

A chest radiograph is normal. A thyroid ultrasound confirms a 1.4-cm mass in the right lobe of the thyroid gland.

Evaluation of Pheochromocytoma

- Episodes of Headaches, Palpitations, Sweating
- Sustained or episodic hypertension
- Tachyarrhythmias
- **Serum metanephrines***
- 24 hr urine for VMA, fractionated metanephrines and catecholamines
- CT or MRI of adrenals

Management of Pheochromocytoma

- α blockers (phenoxybenzamine, phentolamine, doxazosin, prazosin)
- Alternate meds: CCB, ACE-I
- β blockers (propranolol, metoprolol): Only after adequate α blockade, Use in small doses
- Saline hydration

Endocrine Consult