Endocrine Emergencies

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Disclosure

Michael McDermott has no conflict of interest or relationships to disclose in relation to this educational activity.

Learning Objectives

- Discuss the diagnosis and treatment of **Thyroid Storm** and **Myxedema Coma**.
- Explain the evaluation and management for a **Rapidly Expanding Thyroid Mass**.
- Discuss the prevention, recognition and treatment of **Adrenal Crisis**, and the causes and effective therapies for **Hypercalcemic Crisis**.

Case 1

A 43 y.o. man presents with 5 month history of fatigue, excessive sweating, palpitations, muscle weakness, 55 lb weight loss and the recent onset of nausea and vomiting.

PE: BP 143/66 P 102

Thyroid: diffusely enlarged (35 gm)

Lab: TSH < 0.01 mU/L (nl: 0.5-5.0)

Free T4 3.9 ng/dl (nl: 0.8-1.8)

Total T3 423 ng/dl (nl: 90-180)

RAIU: 6 hr. = 57% **Scan: diffuse uptake**

He was given 15 mCi of I-131.

Case 1

He presents 15 days later with confusion, dyspnea, nausea, vomiting, and diarrhea.

PE: BP 162/60 P 125 T 101.8

MS: confusion CV: + rales, + S3, 1+ edema

Thyroid: diffusely enlarged (35 gm), tender

Lab: TSH < 0.01 mU/L (nl: 0.5-5.0)

Free T4 8.7 ng/dl (nl: 0.8-1.8)

Total T3 313 ng/dl (nl: 90-180)

Does he have thyroid storm (decompensated hyperthyroidism)?

1. **Not Likely**
2. **Possibly**
3. **Probably**
4. **Highly Suggestive**

Thyroid Storm

Decompensated Hyperthyroidism

Burch
Wartofsky

Thyroid Storm Score

80

Feature	Score	Feature	Score
Fever:		**Pulse:**	
99-99.9	5	99-109	5
100-100.9	10	110-119	10
101-101.9	**15**	120-129	**15**
102-102.9	20	130-139	20
103-103.9	25	>139	25
>103.9	30	Atrial fibrillation	10
CNS:		**CHF:**	
Absent	0	Absent	0
Mild (agitation)	10	Mild (edema)	5
Moderate (delirium)	**20**	Moderate (rales)	**10**
Severe (seizure, coma)	30	Severe (pulm edema)	15
GI:		**Precipitant History:**	
Absent	0	Absent	0
N, V, D, Pain	**10**	Present: **I-131 Therapy**	**10**
Jaundice	20		

Burch H, Wartofsky L. Endocrinol Metab Clin N Am, 1993; 22:263-78

Thyroid Storm: Precipitating Events

Rapid ↑ in Thyroid Hormone Levels:

- Thyroid Surgery
- Radioiodine Therapy
- Stopping Antithyroid Drugs
- Thyroid Palpation (vigorous)
- Contrast Dyes

Acute/Subacute Non-Thyroidal Illness:

- Non-Thyroidal Surgery
- Infection
- Trauma
- Pulmonary Embolus
- Myocardial Infarction
- Stroke
- DKA
- Parturition

Burch H, Wartofsky L. Endocrinol Metab Clin N Am, 1993; 22:263-78

Burch
Wartofsky

Thyroid Storm Score

Score Classification

- < 25 Unlikely
- 25-44 Suggestive
- ≥ 45 Highly Suggestive

Burch H, Wartofsky L. Endocrinol Metab Clin N Am, 1993; 22:263-78

Case 1

He presents 15 days later with confusion, dyspnea, nausea, vomiting, and diarrhea.

PE: BP 162/60 P 125 T 101.8

MS: confusion CV: + rales, + S3, 1+ edema

Thyroid: diffusely enlarged (35 gm), tender

Lab: TSH < 0.01 mU/L (nl: 0.5-5.0)

Free T4 8.7 ng/dl (nl: 0.8-1.8)

Total T3 313 ng/dl (nl: 90-180)

How would you treat this condition?

1. **Repeat Radioiodine Therapy**
2. **Urgent Thyroidectomy**
3. **High Dose Methimazole, Beta Blockers, Steroids and IV Fluids**
4. **Emergency Dialysis**

Thyroid Storm Treatment

Reduce Thyroid Hormone Synthesis

Propylthiouracil (PTU) traditionally preferred because of effects to ↓ T4 to T3 conversion.
But, no evidence that PTU is more efficacious than Methimazole (MMI) in Thyroid Storm.

Use Either ATD in High Dose
PTU: 600-1200 mg daily in Divided Doses
MMI: 60-120 mg daily in Divided Doses

Preparations
PTU: PO, NG Tube, or Rectally
MMI: PO, NG Tube, Rectally or IV

Cooper D, N Engl J Med 2005;352:905-17
Hodak S, Thyroid 2006;16:691-5

Thyroid Storm Treatment

Comparison of PTU vs MMI

Design: Comparative Effectiveness – Large Multicenter Database
Subjects: 1,383 Patients with Thyroid Storm
Outcome: In-Hospital Death or Discharge to Hospice

	PTU	MMI	
Number:	656 (47.4%)	727 (52.6%)	
Outcome:	8.5% (6.4-10.7%*)	6.3% (4.6-8.1%*)	P = 0.64

*95% CI

Conclusion: PTU vs MMI - no difference in mortality or adverse outcomes. Current guidelines merit reevaluation.

Lee SY. JAMA Open Network 2023; 6(4):e238655

Thyroid Storm Treatment

Reduce Thyroid Hormone Release

Cold Iodine

KI (PO): 5 drops QID [SSKI, Lugol]

NaI (IV): 1 g over 24 hours (if available)

SSKI: 50 mg I/drop

Lugol: 8 mg I/drop

Thyroid Storm Treatment

Reduce Heart Rate

Esmolol (IV): 500 ug / 1 min, the 50-300 ug/kg/min

Metoprolol (IV): 5-10 mg Q 2-4 hours

Propranolol (PO): 60-80 mg Q 4 hours

Diltiazem (IV): 0.25 mg/kd / 2 min, the 10 mg/min, or

(PO): 60-90 mg Q 6-8 hours

Thyroid Storm Treatment

Provide Glucocorticoid Support

Glucocorticoids IV - Stress Doses

Hydrocortisone (Solu-Cortef): 50 mg QID

Methylprednisolone (Solu-Medrol): 10 mg QID

Dexamethasone: 2 mg QID

Thyroid Storm Treatment

Support Circulation and Oxygenation

IV Fluids

Oxygen

Cooling (+/-)

Thyroid Storm Treatment

Treat Precipitating Cause

- Infection
- Stroke
- Pulmonary Embolism
- Myocardial Infarction
- Diabetic Ketoacidosis

Thyroid Storm Treatment

Reduce Thyroid Hormone Synthesis

- PTU (PO, NG, Rectal): 600-1200 mg daily
- Methimazole (PO, NG, Rectal, IV): 60-120 mg daily

Reduce Thyroid Hormone Release

- Sodium Iodide (IV): 1 gm over 24 hours
- Potassium Iodide (PO): 5 drops QID [SSKI]

Reduce Heart Rate

- Esmolol (IV): 500 ug over 1 min, then 50-300 ug/kg/min
- Metoprolol (IV): 5-10 mg Q 2-4 hours
- Propranolol (PO): 60-80 mg Q 4 hours
- Diltiazem (IV): 0.25 mg/kg over 2 min, then 10 mg/min
  (PO): 60-90 mg Q 6-8 hours

Glucocorticoids IV – Stress Doses

Support Circulation and Oxygenation

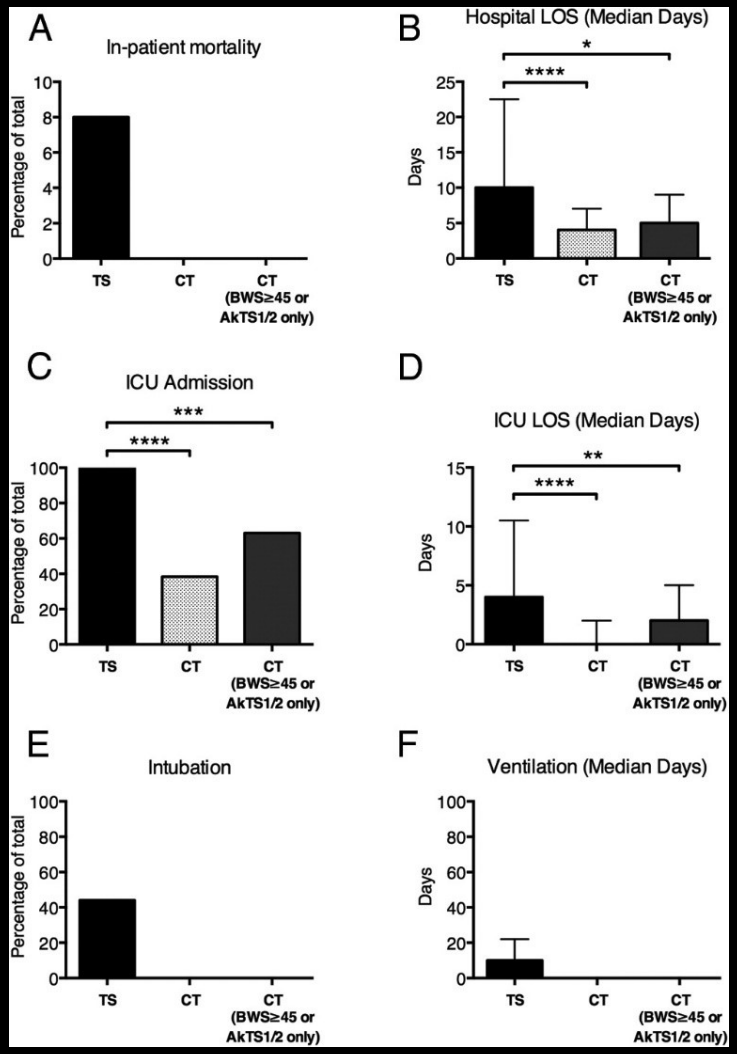
- IV Fluids, Oxygen, Cooling (+/-)

Treat Precipitating Cause

Thyroid Storm Treatment

Subjects: 25 Thyroid Storm c/w 125 Compensated Thyrotoxicosis

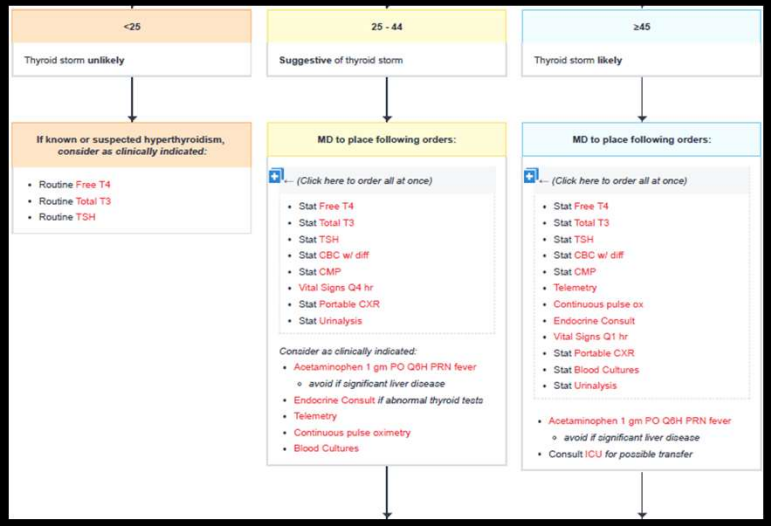
Thyroid Storm
Mortality: 8%

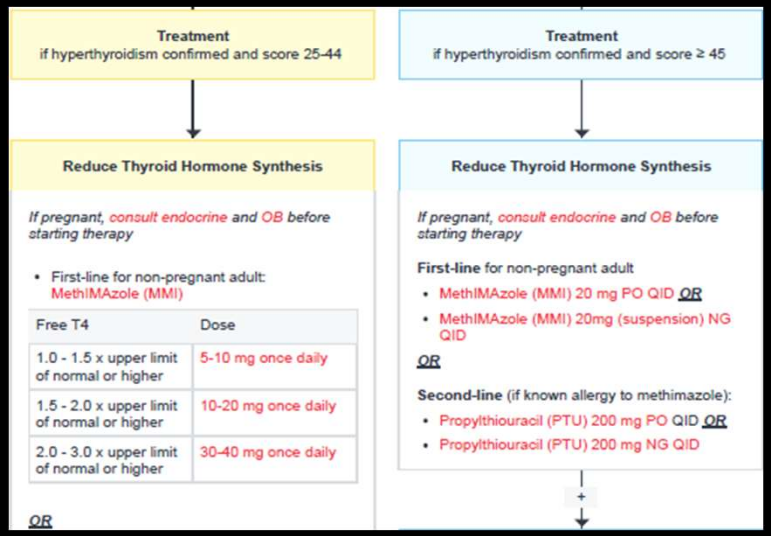


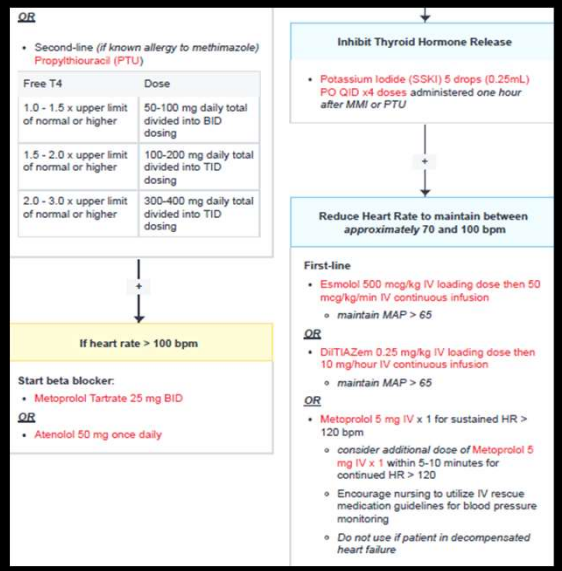
Angell T, .., Nguyen C, .., LoPresti J. J Clin Endocrinol Metab 2015; 100:451-9

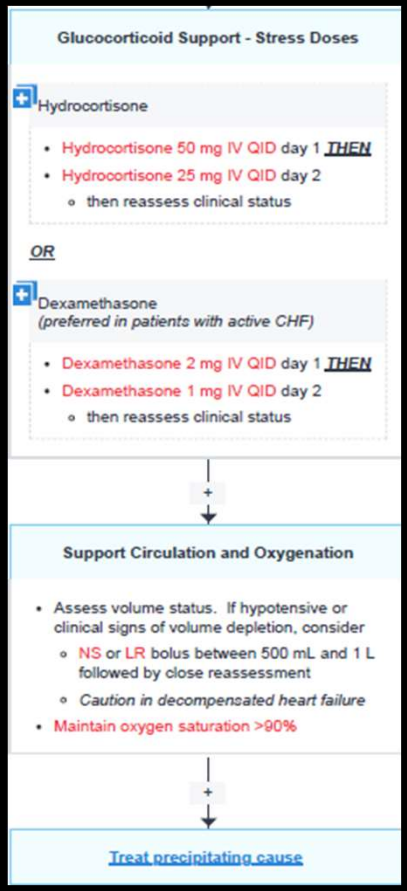
Thyroid Storm

Epic Pathway - UCH









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Mayson S, McDermott M

Case 2

A 68 y.o. woman presents to ED in a semi-comatose state. She is believed to be homeless. No other history.

PE: BP 95/60 P 48 R 12 T 32.2 C

MS: stuporous; responds to pain stimuli only

Neck: surgical scar; no thyroid palpable

Abd: bowel sounds absent

CV: distant heart sounds, no rales, no S3, 2+ edema

Lab: Na 127, K 4.4, CO2 28, Cr 1.8, Glucose 52, TSH 148 mU/L, PaO2 70 mmHg, PaCO2 50 mmHg CXR: Pneumonia

Does she have myxedema coma (decompensated hypothyroidism)?

1. **Not Likely**
2. **Possibly**
3. **Probably**
4. **Highly Suggestive**

Myxedema Coma

Decompensated Hypothyroidism

Popoveniuc
Wartofsky

Myxedema Coma Score

145

Feature	Score	Feature	Score
Temperature		**Cardiovascular**	
> 35 C	0	Bradycardia	
32-35 C	10	Absent	0
< 32 C	20	50-59	10
Central Nervous System		40-49	20
Absent	0	< 40	30
Somnolent /Lethargy	10	Other EKG Changes*	10
Obtunded	15	Pericardial/Pleural Effusion	10
Stupor	20	Pulmonary Edema	15
Coma/Seizures	30	Cardiomegaly	15
Gastrointestinal		Hypotension	20
Anorexia/Pain/Constipation	5	**Metabolic Disorders**	
Decreased Motility	15	Hyponatremia	10
Paralytic Ileus	20	Hypoglycemia	10
Precipitating Event		Hypoxemia	10
Absent	0	Hypercarbia	10
Present	10	Decreased GFR	10

*Other EKG Changes: QT Prolongation, Low Voltage, BBB, Non-Specific ST-T Wave Changes

Popoveniuc G, Wartofsky L. Endocrine Practice, 2014; 20:808-17

Popoveniuc
Wartofsky

Myxedema Coma Score

Score Classification

- < 25 Unlikely
- 25-59 Suggestive
- ≥ 60 Highly Suggestive

Popoveniuc G, Wartofsky L. Endocrine Practice, 2014; 20:808-17

Case 2

A 68 y.o. woman presents to ED in a semi-comatose state. She is believed to be homeless. No other history.

PE: BP 95/60 P 48 R 12 T 32.2 C

MS: stuporous; responds to pain stimuli only

Neck: surgical scar; no thyroid palpable

Abd: bowel sounds absent

CV: distant heart sounds, no rales, no S3, 2+ edema

Lab: Na 127, K 4.4, CO2 28, Cr 1.8, Glucose 52, TSH 148 mU/L, PaO2 70 mmHg, PaCO2 50 mmHg CXR: Pneumonia

How would you treat this condition?

1. **Oral Levothyroxine 25 mcg daily**
2. **IV Levothyroxine 300 mcg now, then 100 mcg QD, Steroids**
3. **High Dose Methimazole, Beta Blockers, Steroids and IV Fluids**
4. **Emergency Plasma Exchange**

Myxedema Coma Treatment

Replace Thyroid Hormone Deficit

Recommended

Levothyroxine: 200-500 mcg IV over 5 minutes, then

Levothyroxine: 50-100 mcg QD PO or IV

Can be Considered if Preferred and Available

Liothyronine: 50-100 mcg IV over 5 minutes, then
Levothyroxine: 50-100 mcg QD PO or IV

Levothyroxine 200-300 mcg IV + **Liothyronine** 20-50 mcg IV over 5 minutes, then **Levothyroxine** 50-100 mcg QD PO or IV + **Liothyronine** 20-30 mcg QD PO or IV

Myxedema Coma Treatment

Provide Glucocorticoid Support

Glucocorticoids IV - Stress Doses

Hydrocortisone (Solu-Cortef): 50 mg QID

Methylprednisolone (Solu-Medrol): 10 mg QID

Dexamethasone: 2 mg QID

Myxedema Coma Treatment

Support Circulation and Oxygenation

IV Fluids

Oxygen

Mechanical Ventilation (if needed)

Central Warming (if hypothermia severe)

Myxedema Coma Treatment

Treat Precipitating Cause

- Medication
- Infection
- Stroke
- Pulmonary Embolism
- Myocardial Infarction
- Diabetic Ketoacidosis

Myxedema Coma Treatment

Replace Thyroid Hormone Deficit

- **Levothyroxine 200-300 mcg IV over 5 minutes, then**

  Levothyroxine 50-100 mcg QD PO or IV

Provide Glucocorticoid Support

- **IV Glucocorticoids - Stress Doses**

Support Circulation, Ventilation and Oxygenation

- **IV Fluids, Oxygen, Mechanical Ventilation (if needed)**
- **Central Warming if Severely Hypothermic**

Treat Precipitating Cause

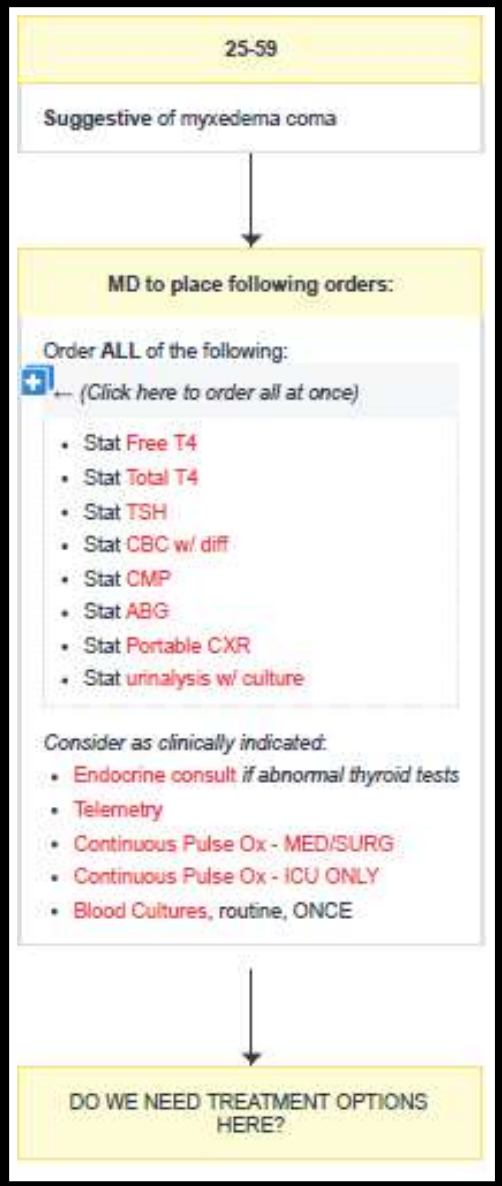
Myxedema Coma Treatment

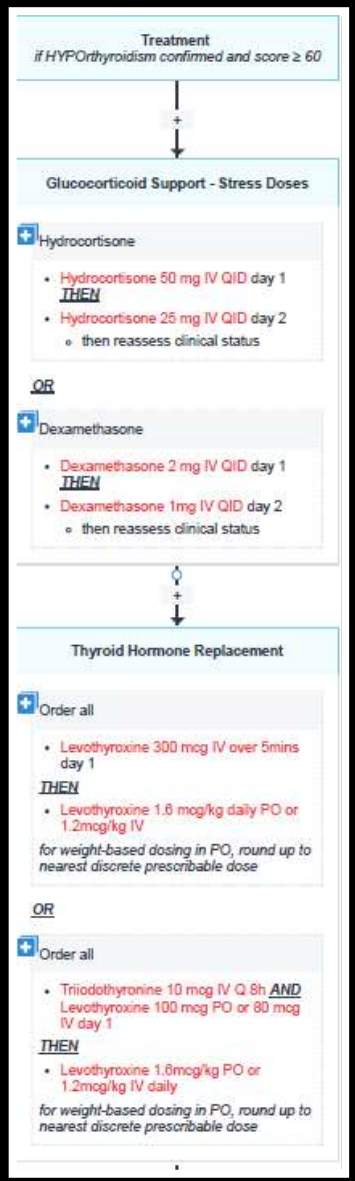
Case Series: **45 Myxedema Coma Patients Treated with 500 mcg IV Levothyroxine and Usual Support**

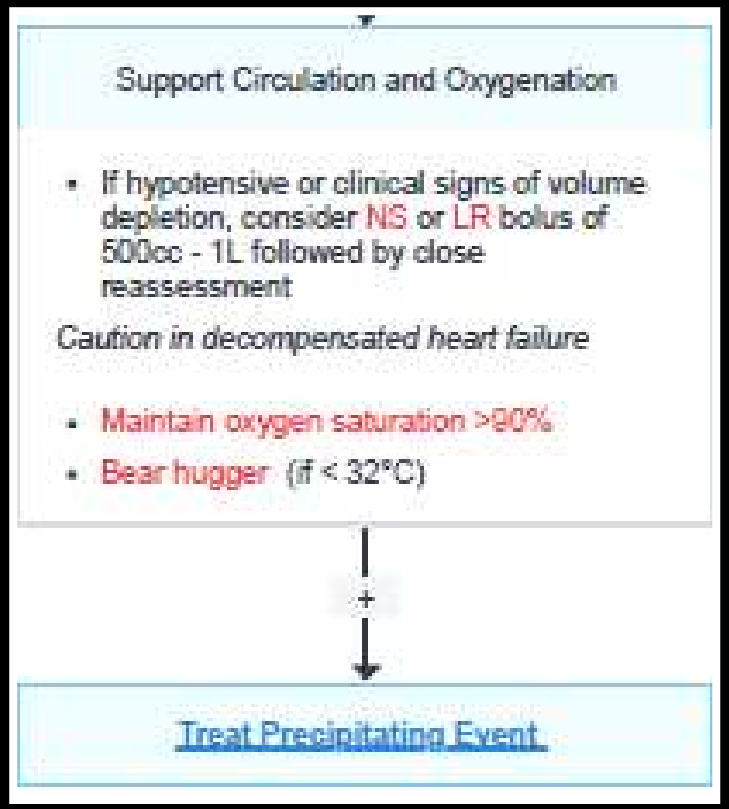
Myxedema Coma
Mortality: 8%

Nguyen C, Angell T, Wu K, LoPresti J. 84th Annual Meeting of American Thyroid Association, Coronado, CA, Oct 29-Nov 4, 2014

Myxedema Coma
Epic Pathway - UCH







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Mayson S, McDermott M

Case 3 + 4

A 42 yo woman found unconscious by husband with signs of dyspnea and vomiting and empty medicine bottles next to her. She had taken 15,000 mcg of levothyroxine + BP meds.

Lab: FT4 8.9 ng/ml (nl, 0.9-1.76), FT3 7.4 pg/ml (nl, 2.28-4.23)

Treatment: Beta Blocker, Cholestyramine, Plasmapheresis

A 20 yo man presents to ED with anxiety, agitation, palpitations and dyspnea. Meds: compounded LT3.

Lab: TT4 7.1 ug/dl (nl, 4.6-12)), TT3 14,982 ng/dl (nl, 80-200)

Capsule sent to Lab: LT3 = 10,794 ug of LT3 (1000 x > intended)

Li R. Ann Palliative Med 2021; 10:5839-45.
He ZH. Drugs in Context 2020; 9:2019

Massive Thyroid Hormone Overdose

Treatment

- Beta Blockers
- Cholestyramine
- Supportive Care (Fluids, O2, Stress Steroids)
- Consider Plasmapheresis
- Not Effective
  - Anti-Thyroid Drugs
  - Hemodialysis (T4 is protein bound)

Li R. Ann Palliative Med 2021; 10:5839-45.
He ZH. Drugs in Context 2020; 9:2019

Case 5

A 28 yo woman, competitive figure skater, presents to ED with high fever and sore throat. Started on Methimazole 20 mg BID two weeks earlier for Graves' disease

PE: BP 100/65 P 88 T 102.8

Neck: diffusely enlarged thyroid

Lab: TSH < 0.01, Free T4 6.4 ng/ml, Total T3 433 ng/ml

WBC 2,200, ANC 95

ATD Induced Agranulocytosis

- **Cause:** Idiosyncratic Reaction (likely autoimmune)
- **Diagnosis:** ANC < 500
- **Incidence:** 0.2-0.5% (1/200-1/500) ATD patients
- **Timing:** Usually in first 2-3 months of ATD RX
- **ATD Dose:** Usually ≥ 30 mg Methimazole or equivalent PTU
- **Pathogen:** Pseudomonas Aeruginosa most often
- **Treatment:**
  - Stop ATD
  - Antibiotics – broad spectrum
  - Granulocyte Colony Stimulating Factor (G-CSF) may shorten time to recovery – recommended by most authorities

Case 6

A 27 yo man presents with a rapidly enlarging neck mass causing difficulty breathing.

PE: Thyroid - occupied most of anterior neck, chin to sternum

Lab: TSH 12.4 FT4 0.72 TPO 15 LT4 100 mcg started

CT-PET: – diffusely enlarged thyroid, chin to superior mediastinum, high metabolic activity.

Transferred to UCH due to increasing respiratory distress.

CT-PET: – further thyroid enlargement over 3 months.

Thyroid Biopsy: Langerhans Cell Histiocytosis (BRAF +).

Further Evaluation: Diabetes Insipidus and Panhypopituitarism

Treatment: Steroids – minimal effect

Trametinib – resolution of goiter; DI/Panhypopituitarism persist

Rapidly Enlarging Thyroid Mass

- Anaplastic Thyroid Cancer
- Lymphoma of the Thyroid
- Medullary Thyroid Cancer
- Metastatic Carcinoma (esp. Lung)
- Riedel Struma (IgG4 Disease)
- Langerhans Cell Histiocytosis
- Primary Amyloid Goiter
- Suppurative Thyroiditis
- Thyroid Hemorrhage

Anaplastic Thyroid Carcinoma

Rapidly and Definitively Establish the Diagnosis

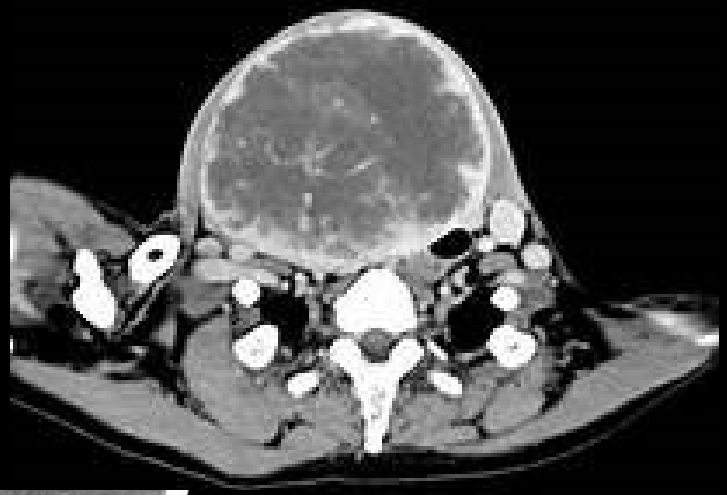
- **Differential Dx: Thyroid Lymphoma, SCC (H + N), Metastatic (Lung)**
- **Rapid Mutation Analysis**

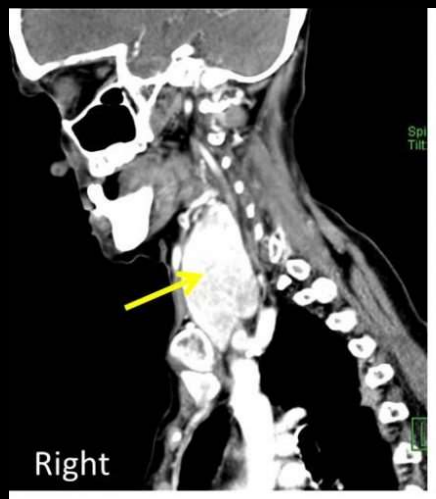
Rapid Response Team – Multidisciplinary

- **Surgeon, Radiation/Medical Oncology, Endocrinology, Palliative Care**

Bible KC. Thyroid 2021; 31:337-386

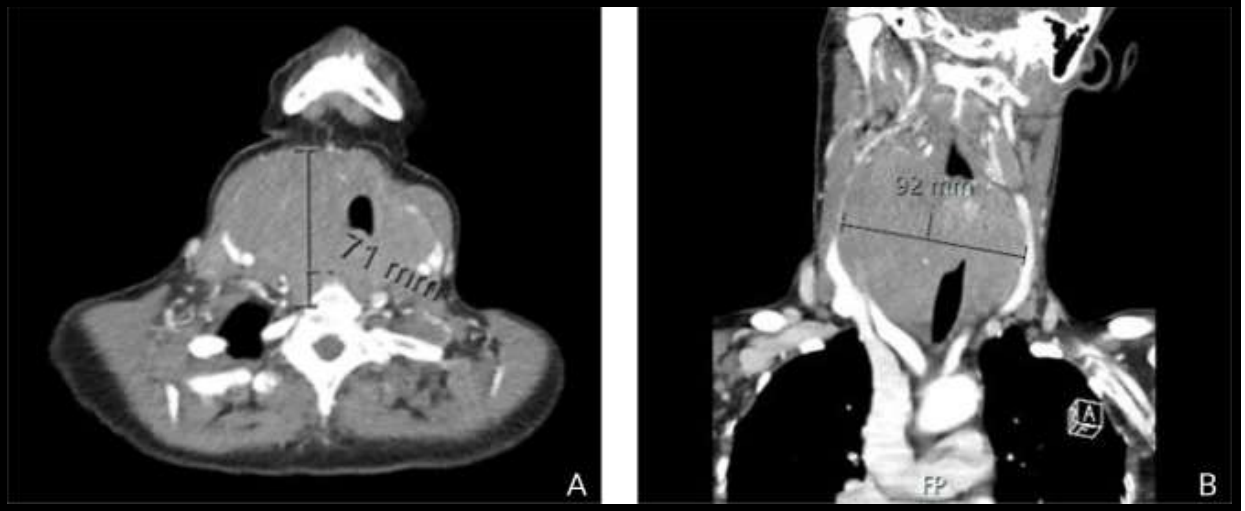
Anaplastic Thyroid Carcinoma





Bible KC. Thyroid 2021; 31:337-386

Thyroid Lymphoma



FNA Sensitivity: 45%-70%

Core Biopsy Sensitivity: 95%

- **Immunohistochemistry**
- **Flow Cytometry**

Elshout B. Eur J Case Rep Intern Med 2023; 10:003827

Case 7

29 year old man, recently immigrated from Japan, presents to the ED with myalgias and leg weakness for 3 days

Meds: No prescription or OTC meds

Exam: BP 148/82 P 94 T 98.7 R 20 O2 Sat 98% RA

Neuro: 3-4/5 muscle strength in proximal muscle groups
Sensory exam normal. Reflexes: reduced at most sites

Lab: CBC normal, Na 140, K 1.9, Glucose 135, Creat 0.77, AST 58 (nl, 10-30), ALT 71 (nl, 8-30), Alk Phos 166 (nl, 30-120)

What additional exam and lab tests are needed?

1. Serum CK and autoimmune anti-muscle antibody screen
2. Celiac Disease Panel and TPO screen
3. Serum Cortisol, Aldosterone, and ACTH
4. Thyroid palpation and serum TSH, Free T4, Total T3

Case 7

29 year old man, recently immigrated from Japan, presents to the ED with myalgias and leg weakness for 3 days. No Meds.
Exam: BP 148/82 P 94 T 98.7 R 20 O2 Sat 98% RA
Neuro: 3-4/5 muscle strength in proximal muscle groups
Sensory exam normal. Reflexes: reduced at most sites

Lab: TSH < 0.01 mU/L, Free T4 7.4 ng/dl (nl: 0.8-1.8), K 1.9, Cortisol 22 ug/dl, ACTH 35 pg/ml, Aldosterone 5.9 ng/ml/hr

What diagnosis does this strongly suggest?

1. **Adrenal Insufficiency associated with Graves' Disease**
2. **Acute Autoimmune Hypophysitis**
3. **Thyrotoxic Periodic Paralysis**
4. **Acute Primary Autoimmune Myopathy**

Thyrotoxic Periodic Paralysis

- Episodes of severe muscle weakness or paralysis associated with severe hypokalemia – potentially fatal.
- Mostly Asian Males with Thyrotoxicosis – not inherited.
- Sudden intracellular K shifts due to thyrotoxicosis induced increased sensitivity of Na-K-ATPase pump activity.
- Treatment
  - Potassium (Oral or IV) and Beta Blocker – Acute Event
  - Thyrotoxicosis Management – Prevent Future Events

Kung A. J Clin Endocrinol Metab 2006; 91:2490-5
Maciel R. Nat Rev Endocrinol 2011; 7:657-67

Case 8

A 30 year old Caucasian man with known Graves' disease presents with nausea, vomiting, weakness and dizziness.

Exam: **BP 90/60 with orthostatic drop**
P 105 with orthostatic increase
Skin: darky pigmented

Lab: **Na 121, K 6.8, Glucose 62, Creatinine 2.1, WBC 9,800**

What is the most likely cause of this presentation?

1. **Thyroid Storm**
2. **Primary Aldosteronism with Adrenal Crisis**
3. **Primary Adrenal Insufficiency with Adrenal Crisis**
4. **Secondary Adrenal Insufficiency with Adrenal Crisis**

Case 8

A 30 year old Caucasian man with known Graves' disease presents with nausea, vomiting, weakness and dizziness.

Exam: BP 90/60 with orthostatic drop
P 105 with orthostatic increase
Skin: darky pigmented

Lab: Na 121, K 6.8, Glucose 62, Creatinine 2.1, WBC 9,800

What is the best management for this condition?

1. IV Fluids, Prednisone 5 mg QD
2. IV Fluids, Hydrocortisone 300 mg day 1 and 100 mg day 2
3. IV Fluids, Fludrocortisone 0.2 mg QD
4. IV Fluids, Hydrocortisone 200 mg + Fludrocortisone 0.2 mg QD

Case 9

A 48 year old woman presents to your office with a 3 day history of fevers up to 102, non-productive cough, myalgias and arthralgias. She feels weak and has no appetite but is keeping down fluids.

PMH: Rheumatoid Arthritis **FH:** COPD, HTN

Medications: Prednisone 7 mg QD (years), Methotrexate

Exam: BP 136/83 P 88 T 38.7 Ht 5'9 Wt 168 lb
Mild diffuse ronchi

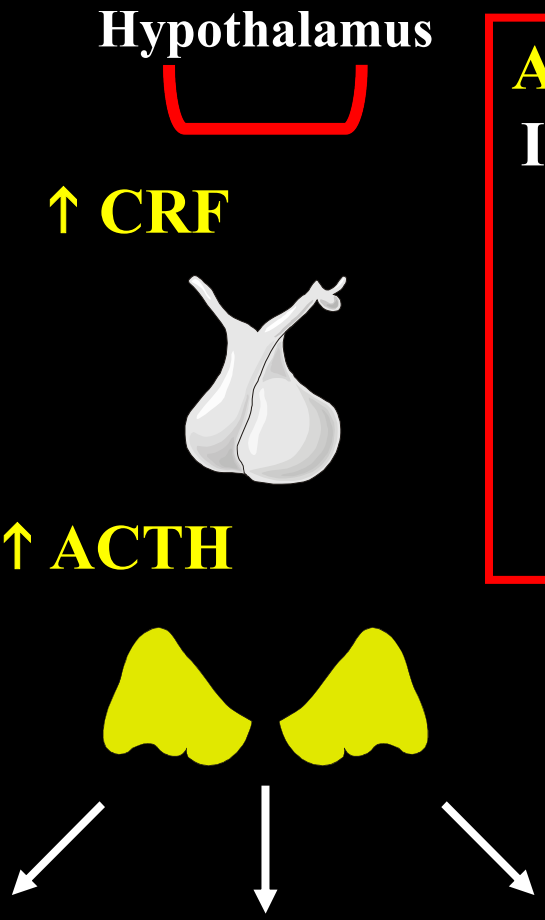
Labs: WBC 9, 800, Na 138, K 4.8, Glucose 104, Creat 0.9
O2 Sat 92%

Considering her long term steroid use, what is the best management of her steroid therapy?

1. Continue Oral Prednisone 7 mg QD
2. Double Prednisone dose for 2-3 days
3. Add Fludrocortisone 0.1 mg daily
4. IM Hydrocortisone 200 mg

Adrenal Crisis

Primary Adrenal Insufficiency



Autoimmune: Addison's Dz
Infectious: TB, Fungi, HIV
Infiltrative: Amyloid
Hemorrhage
Metastatic
Surgery
Metabolic*

***Adrenoleukodystropy**
***Adrenomyeloneuropathy**

Bornstein SR, J Clin Endocrinol Metab 2016; 101:364-89

Secondary Adrenal Insufficiency

↓ CRF

↓ ACTH

↓ Cortisol Nl Aldosterone ↓ Adrenal Androgens

Glucocorticoids
Opioids
Tumor
Surgery
Radiation
Infectious
Hemorrhage
Infiltrative
Metastatic

Fleseriu M. J Clin Endocrinol Metab 2016; 101: 3888-3921

Adrenal Insufficiency

Daily Treatment

Glucocorticoid Replacement (Primary + Secondary)

Hydrocortisone: 15-20 mg/day**

10-15 mg AM 5 mg PM

Prednisone: 4-5 mg/day

Dexamethasone: 0.75 mg/day

****Preferred**

Mineralocorticoid Replacement (Primary Only)

Fludrocortisone: .05-0.1 mg/day

Clinical Practice Guidelines – Endocrine Society
Bornstein SR, J Clin Endocrinol Metab 2016; 101:364-89

Adrenal Crisis

Prevention

Education about Stress Dose Changes

Glucocorticoid dose may need to be increased during intercurrent illness, fever and stress

Emergency Glucocorticoid Injection Kit

Glucocorticoid injection kit for emergency use.
Educate your patient on its' use.

Clinical Practice Guidelines – Endocrine Society
Bornstein SR, J Clin Endocrinol Metab 2016; 101:364-89

Adrenal Crisis

Prevention

Condition	Suggested Action
Home Illness with Fever	T > 38 C (100.4 F) 2 x dose for 2-3 days T > 39 C (102.2 F) 3 x dose for 2-3 days
Same but No Oral Intake	Hydrocortisone 100 mg SQ or IM
Surgery: Minor/Moderate	Hydrocortisone 25-75 mg/24 hr
Surgery: Major, Trauma, Medical Intensive Care	Hydrocortisone 100 mg IV, then 50 mg every 6 hours IV or IM

Clinical Practice Guidelines – Endocrine Society
Bornstein SR, J Clin Endocrinol Metab 2016; 101:364-89

Adrenal Crisis

Prevention

Injectable Glucocorticoids

Hydrocortisone (Solu-Cortef)

Methylprednisolone (Solu-Medrol)

Act O Vial – You Tube

Adrenal Crisis

Clinical Features

- Nausea, Vomiting, Abdominal Pain
- Hypotension, Tachycardia, Fever
- Hyponatremia, Hyperkalemia
- Hypoglycemia, Eosinophilia
- Cortisol < 3 ug/dl
- ↑ ACTH (primary), ↓ ACTH (secondary)

Adrenal Crisis

Treatment

Agent	Dose
Hydrocortisone (Solu-Cortef)	100 mg IV, then 200 mg/24 hr infusion x 24 hr, then 100 mg/24 hr infusion x 24 hr
Normal Saline (+/- D5)	1 Liter over 1 hour, then guided by individual needs

Treat the Precipitation Cause

Clinical Practice Guidelines – Endocrine Society
Bornstein SR, J Clin Endocrinol Metab 2016; 101:364-89

Case 10

A 19 year old man complains of a 2-3 week history of weakness, nausea and vomiting.

PE: BP 90/65 P 108 Dehydration

Lab: Ca 19.1 Phos 3.9 CBC normal

PTH < 1 pg/ml (nl: 10-65)

Is this considered a hypercalcemic crisis?

1. **Not Likely**
2. **Possibly**
3. **Probably**
4. **Definitely**

Hypercalcemic Crisis

Hypercalcemic Crisis

Definition

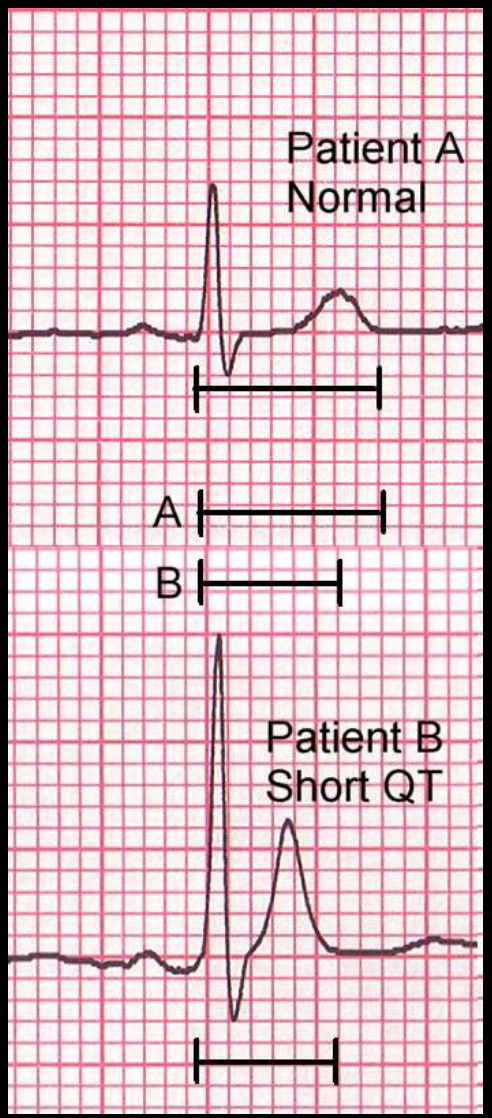
Serum Calcium ≥ 14 mg/dl

Clinical Features

Nausea, Vomiting
Dehydration
Mental Status Changes
Acute Kidney Injury
ECG Changes
Cardiac Dysrhythmias

Hypercalcemic Crisis

ECG Changes



Short QTC

Case 10

A 19 year old man complains of a 2-3 week history of weakness, nausea and vomiting.

PE: BP 90/65 P 108 Dehydration

Lab: Ca 19.1 Phos 3.9 CBC normal

PTH < 1 pg/ml (nl: 10-65)

What is the most likely cause of his hypercalcemia?

1. **Primary Hyperparathyroidism**
2. **Hypercalcemia of Malignancy**
3. **Milk Alkali Syndrome**
4. **Sarcoidosis**

Hypercalcemia

Classification

PTH Dependent

- Primary Hyperparathyroidism
- Lithium Induced Parathyroid Hyperplasia
- Familial Hypocalciuric Hypercalcemia (CaSR Mutation)

PTHrp / Cytokine Dependent

- Hypercalcemia of Malignancy

25 OH Vit D Dependent

- Vitamin D Toxicity

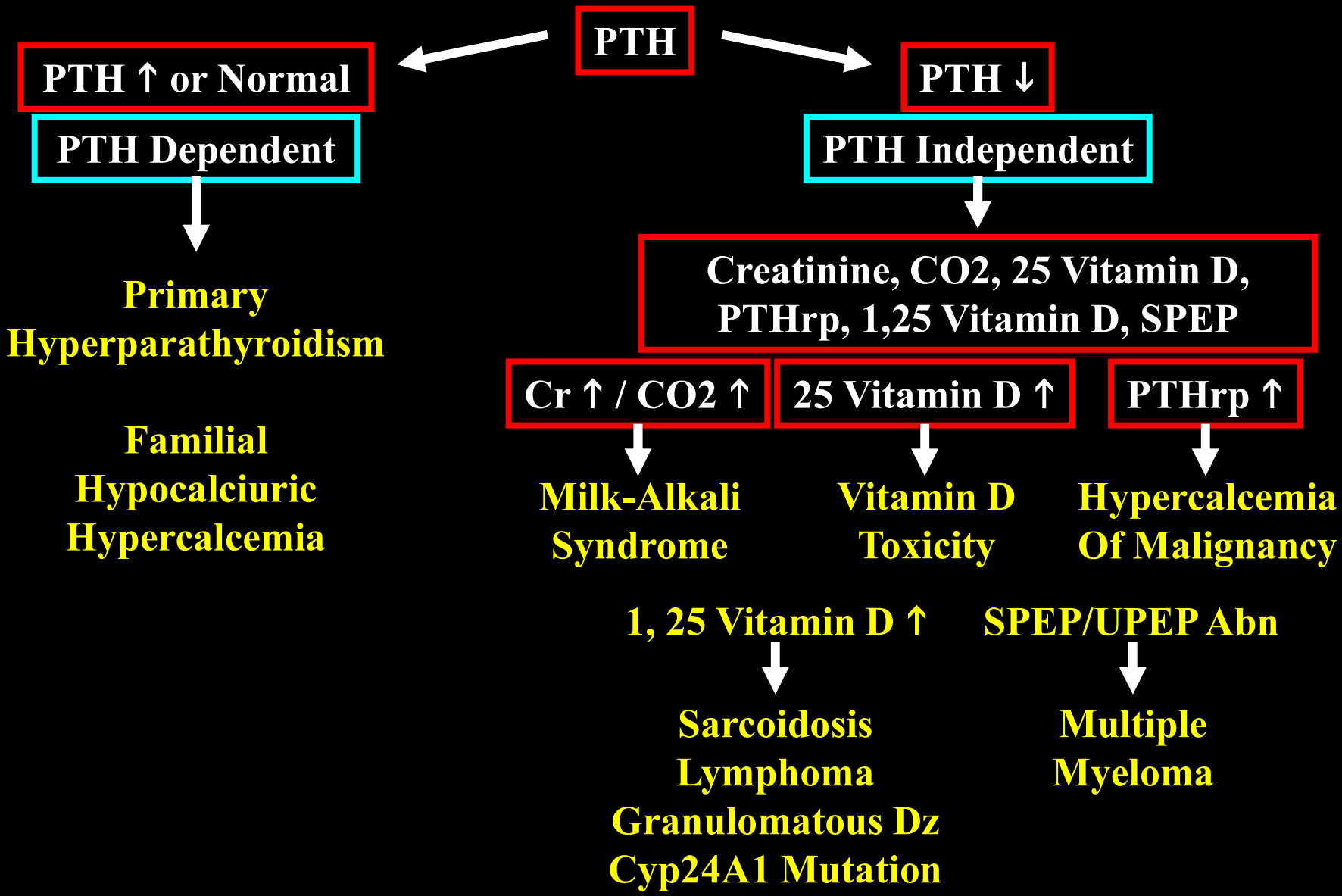
1, 25 (OH)2 Vit D Dependent

- Sarcoidosis
- Lymphomas
- Granulomatous Diseases
- Cyp24A1 Mutations

Other Mechanisms

- Milk Alkali Syndrome
- Hyperthyroidism
- Thiazide Diuretics
- Acute Renal Failure
- Adrenal Insufficiency
- Vitamin A Intoxication
- Immobilization

Hypercalcemia Evaluation



Hypercalcemic Crisis

Treatment Principles

Determine: the Cause

Understand: the Mechanism

Treat: the Cause and the Mechanism

Case 10

A 19 year old man complains of a 2-3 week history of weakness, nausea and vomiting.

PE: BP 90/65 P 108 Dehydration

Lab: Ca 19.1 Phos 3.9 CBC normal

PTH < 1 pg/ml (nl: 10-65)

How would you treat this condition?

1. **IV Fluids, SQ Calcitonin, then IV Bisphosphonate**
2. **IV Fluids, SQ Calcitonin, High Dose Steroids**
3. **IV Fluids, High Dose Steroids, Cinacalcet**
4. **Emergency Dialysis**

Hypercalcemic Crisis

Treatment Options

Medication	Mechanism	Onset	Duration
Normal Saline	↑ Renal Ca Loss	Hours	Short
Loop Diuretics	↑ Renal Ca Loss	Hours	Short
Calcitonin	↓ Bone Resorption	4-6 Hrs	48 Hrs
Bisphosphonates	↓ Bone Resorption	24-72 Hrs	2-4 Wks
Denosumab	↓ Bone Resorption	4-10 Days	4-15 Wks
Glucocorticoids	↓ Intest. Ca Absorption ↓ 1,25 Vit D Production by Mononuclear Cells	2-5 Days	Weeks
Calcimimetics	↓ PTH Production	-3 Days	Short
Dialysis (low Ca)	Removes Ca	Hours	Short

Shane E. Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism (6th Ed.) Am Soc Bone Min Research 2006; 179

Hypercalcemic Crisis

Treatment Recommendations

PTH / PTHrp Mediated

- Normal Saline Infusion
  - 200-300 ml/hr to keep urine output at 100-150 ml/hr
- Cinacalcet / Etelcalcetide
- Calcitonin SQ
  - 4 IU/kg; repeat 4-8 IU/kg every 6-12 hour for 48 hrs
- Zoledronic Acid IV, 4 mg
- Denosumab SQ, 120 mg
- Dialysis (Low Ca Bath)

Vitamin D Mediated

- Glucocorticoids
- Normal Saline Infusion
  - 200-300 ml/hr to keep urine output at 100-150 ml/hr
- Calcitonin SQ
  - 4 IU/kg; repeat 4-8 IU/kg every 6-12 hour for 48 hrs
- Zoledronic Acid IV, 4 mg
- Denosumab SQ, 120 mg
- Dialysis (Low Ca Bath)

Treat the Underlying Cause

Thank You