

# Endocrinology

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# Lecture Modules

- Thyroid
- Parathyroid
- Pituitary
  - Prolactinoma
  - Growth hormone adenoma
- Adrenal
  - Cushing's syndrome
  - Addison's disease

A 32 yo female presents with symptoms of weight loss of 5 kg and palpitations. PMHx is negative. The exam is unremarkable except for pulse 96 and regular. Skin is mildly sweaty. Which labs match your suspected diagnosis?

- A. TSH = 17 (high), free T4 = 0.3 (low)
- B. TSH = 3.2 (normal), free T4 = 1.2 (normal)
- C. TSH = 0.1 (low), free T4 = 0.1 (low)
- D. TSH = 0.1 (low), free T4 = 2.1 (high)

# Correct answer is D

- This is a typical presentation of hyperthyroidism
- The most common cause of hyperthyroidism is Grave's disease
- Consider checking thyroid-stimulation immunoglobulins (TSI)
- Can also check free T4 and free T3 levels
- T3 toxicosis: TSH suppressed, normal free T4, elevated free T3
- T4 converted to T3 at the cellular level

# Hyperthyroidism

- Confirm with radioactive Iodine scan
- Graves – diffuse uptake of the tracer
- Hashimoto's – cold scan
- Hot nodule – most likely benign adenoma, confirm with bx

# Hyperthyroidism treatment

- Radioactive ablation with I-131
  - TSH/free T4 followed, and lifelong levothyroxine replacement started
- Methimazole or propylthiouracil (PTU)
  - Some patients spontaneously recover after treatment for 2-3 years
  - Be aware of agranulocytosis on PTU or methimazole
  - Check CBC anytime such a patient has a fever
- Surgical removal of the thyroid
  - Subtotal thyroidectomy

# Subacute Thyroiditis

- Inflammation in the thyroid from a viral/inflammatory event
- Thyroid releasing hormone due to inflammation
- TSH suppressed, free T4/free T3 elevated
- Cold scan as the thyroid is not taking up Iodine to make more hormone
- The thyroid is tender/painful in this instance
- Treat with NSAIDS, sometimes oral steroids
- Beta blockers inhibit the peripheral conversion of T4 → T3 and can decrease sx in addition to controlling the pulse

A 43 yo female presents with sx of fatigue and constipation over the past 3-4 months. Which labs are most consistent with a diagnosis of subacute hypothyroidism?

- A. TSH = 6.3 (0.4 – 4.0) and free T4 = 1.2 (0.8 – 1.8)
- B. TSH = 0.2 and free T4 = 2.2
- C. TSH = 12.2 and free T4 = 0.5
- D. TSH = 0.3 and free T4 = 1.6



# Correct answer = A

- With both subacute hyper- and hypothyroidism, the TSH is low or high (respectively) while the free T4 and free T3 are normal.
- The usual treatment is to repeat labs in three months.
- Many patients revert to normal
- Some patients become overly hyper- or hypothyroid.

# Cautions with hyperthyroidism or overtreating with levothyroxine

- Palpitations
- Atrial fibrillation and other tachyarrhythmias
- Osteoporosis

# Hypothyroidism

- Autoimmune inflammation and damage of thyroid leading to a loss of thyroid function
- Hashimoto's thyroiditis
- Postpartum thyroiditis
- Can check thyroid antibodies – not necessary
- TPO – thyroid peroxidase antibodies
- Replace with levothyroxine, lower starting doses in older patients

# Unusual endocrinopathies

## General comments

1. These conditions are all unusual – they are not common.
2. When you see a patient for the same complaint the third time, back up and expand your differential dx.
3. Serendipity is a friend.  
“I’d rather be lucky than good” – Vance White, my Father-in-law
4. Watch out what you order – you may find something

# My experience

1. All 10-15 cases of hyperparathyroidism were lab pick ups  
Elevated  $Ca^{++}$  → elevated PTH
2. Prolactinomas are common in infertility workups
3. Cushing's syndrome: one patient
4. Addison's disease: 3-5 pts all with pre-existing diagnosis
5. Sheehan's syndrome: 2 pts with pre-existing diagnosis  
asking for refills of replacement hormones

# WADAO

- Weak And Dizzy All Over.
- Usual work up?
- CBC, CMP, TSH, UA
- All normal except  $\text{Ca}^{++} = 10.7$  (nl 8.5-10.4)
- Repeat  $\text{Ca}^{++} = 11.1$
- DDx?

Which of the following should be not included in the DDx of  $\text{Ca}^{++}$  of 10.7 and 11.1?

- A. Sarcoidosis
- B. DiGeorge's Syndrome
- C. Breast cancer
- D. Hyperparathyroidism



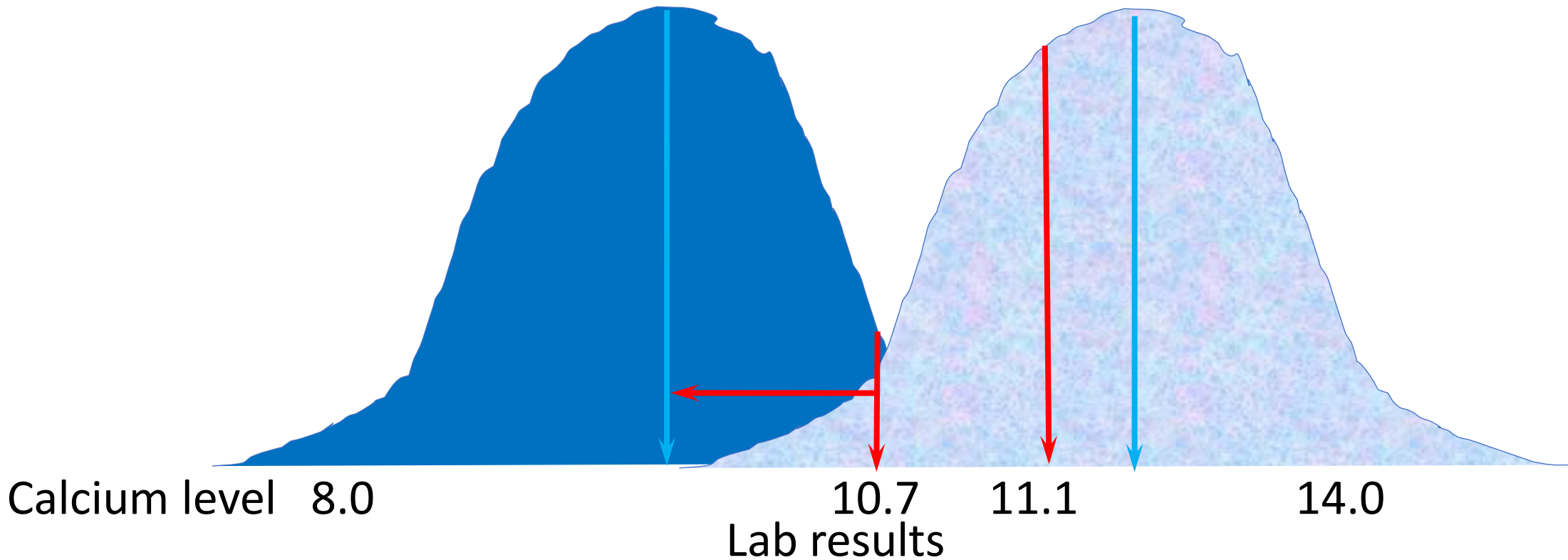
Correct answer = B

1. All of the listed conditions can cause hypercalcemia except DiGeorge's syndrome.
2. DiGeorge's syndrome is a congenital absence or lack of parathyroid substrate leading to *hypo*-calcemia.

# Regression to the Mean

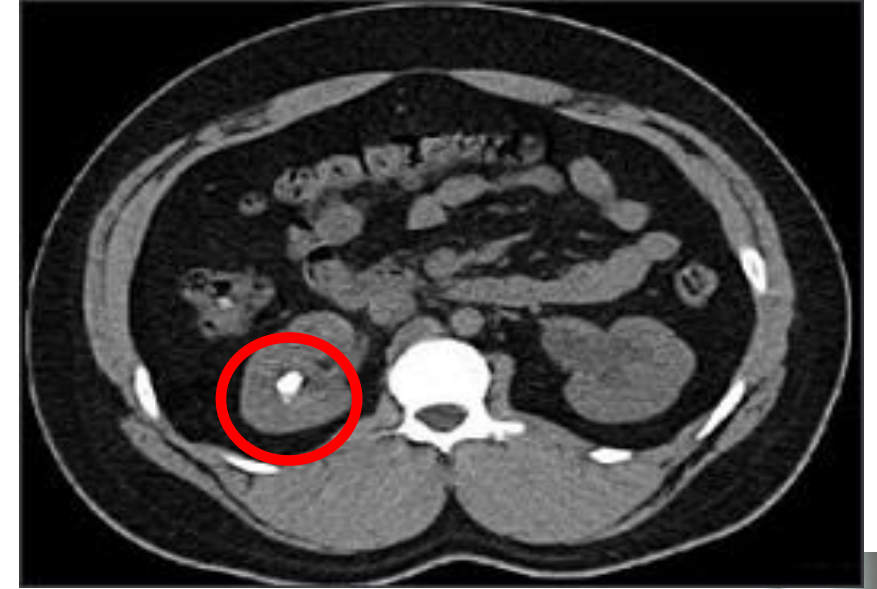
Normal population

Abnormal population



# Hyperparathyroidism

- Brittle bones
- Renal stones
- Gastric groans
- Psychic moans



The most common presenting symptom of hyperparathyroidism is:

- A. Nephrolithiasis
- B. Bone pain from osteitis fibrosa cystica
- C. Confusion
- D. Asymptomatic

# Correct answer is D

## Hyperparathyroidism

1. **80%** or more of patients are **identified by routine testing**
2. In most asymptomatic patients, the  $\text{Ca}^{++}$  is 1.0 mg/dL or less above the upper limit of normal (10.5 – 11.5 mg/dL)
3. Nephrolithiasis occurs in 15-20% pts
4. Of those with nephrolithiasis, <5% have HPTH.
  - Or, 95% of patients with kidney stones do NOT have hyperparathyroidism

Silverberg SJ, Bilezikian JP. Evaluation and management of primary hyperparathyroidism. J Clin Endocrinol Metab. 1996;81(6):2036.

Parks J, Coe F, Favus M. Hyperparathyroidism in nephrolithiasis. Arch Intern Med. 1980; 140(11):1479.

# Hyperparathyroidism

1. Symptomatic patients are considered surgical candidates
2. History of nephrolithiasis → surgery
3. The majority of asymptomatic patients remain asx over time, with the PTH and Ca<sup>++</sup> remaining stable.
4. Cure rates of bilateral neck exploration and minimally invasive parathyroidectomy are in the 95-98% range.
5. Follow bone mineral density (BMD) and renal function in patients not receiving surgery.

27 yo female with primary infertility and irregular menses. She runs regularly, 2-3 miles 3x/week. Height and weight stable at 5'6", 135 lbs, normal blood pressures. Married 3 years, 2 years unprotected intercourse

Which of the following is the most likely cause of her infertility?

- A. Cushing's syndrome
- B. Prolactinoma
- C. Sarcoidosis
- D. Sperm antibodies

# Correct answer is B

## Prolactinoma

1. Common symptoms at presentation in women include:
  - A. Infertility (48%)
  - B. Headache (39%)
  - C. Oligo- or amenorrhea (29%)
  - D. Galactorrhea (24%)
2. Prolactin inhibits the secretion of GnRH and thus FSH and LH.



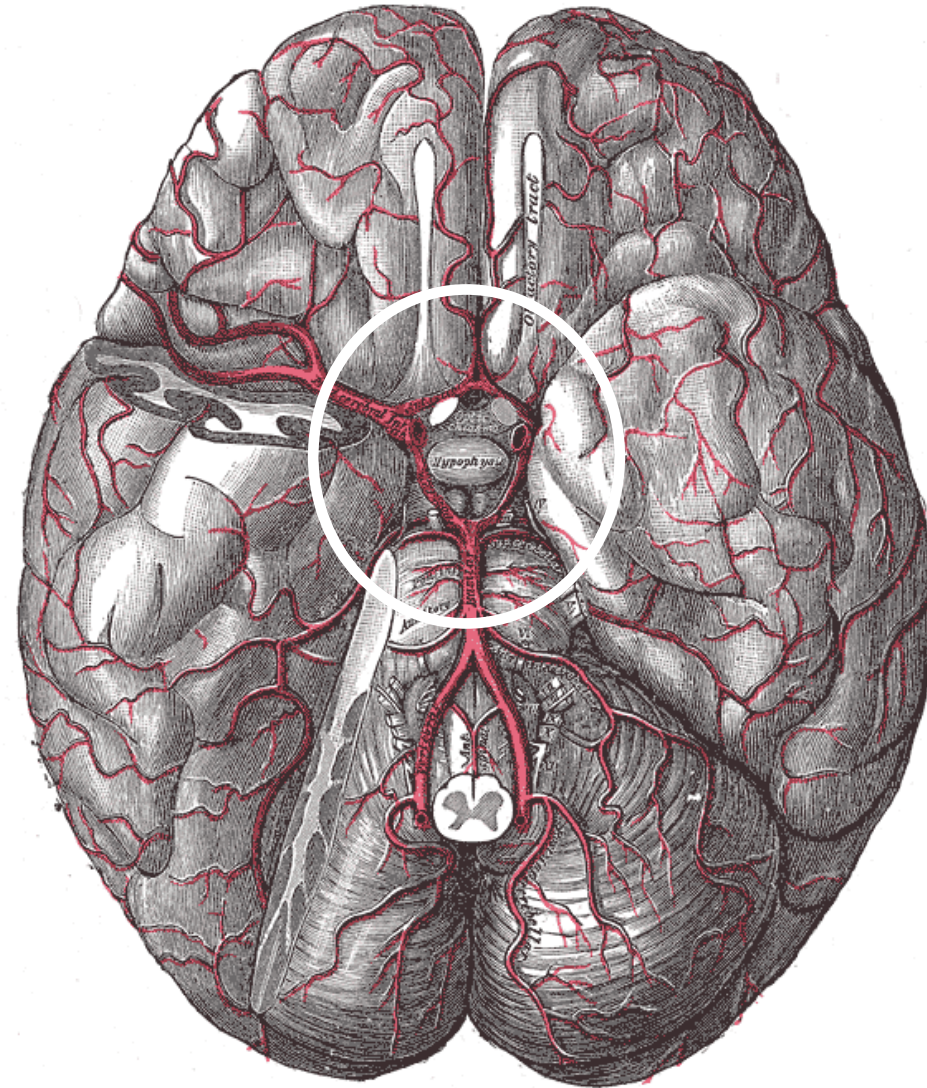
# Prolactinoma

1. Diagnosis made with elevated prolactin level
  - A. Normal range 5-20
2. Prolactin levels  $> 100$  often associated with sx
3. Levels 50-100 may cause amenorrhea or oligomenorrhea
4. Levels 20-50 often asymptomatic
5. The workup of infertility should generally include a prolactin level

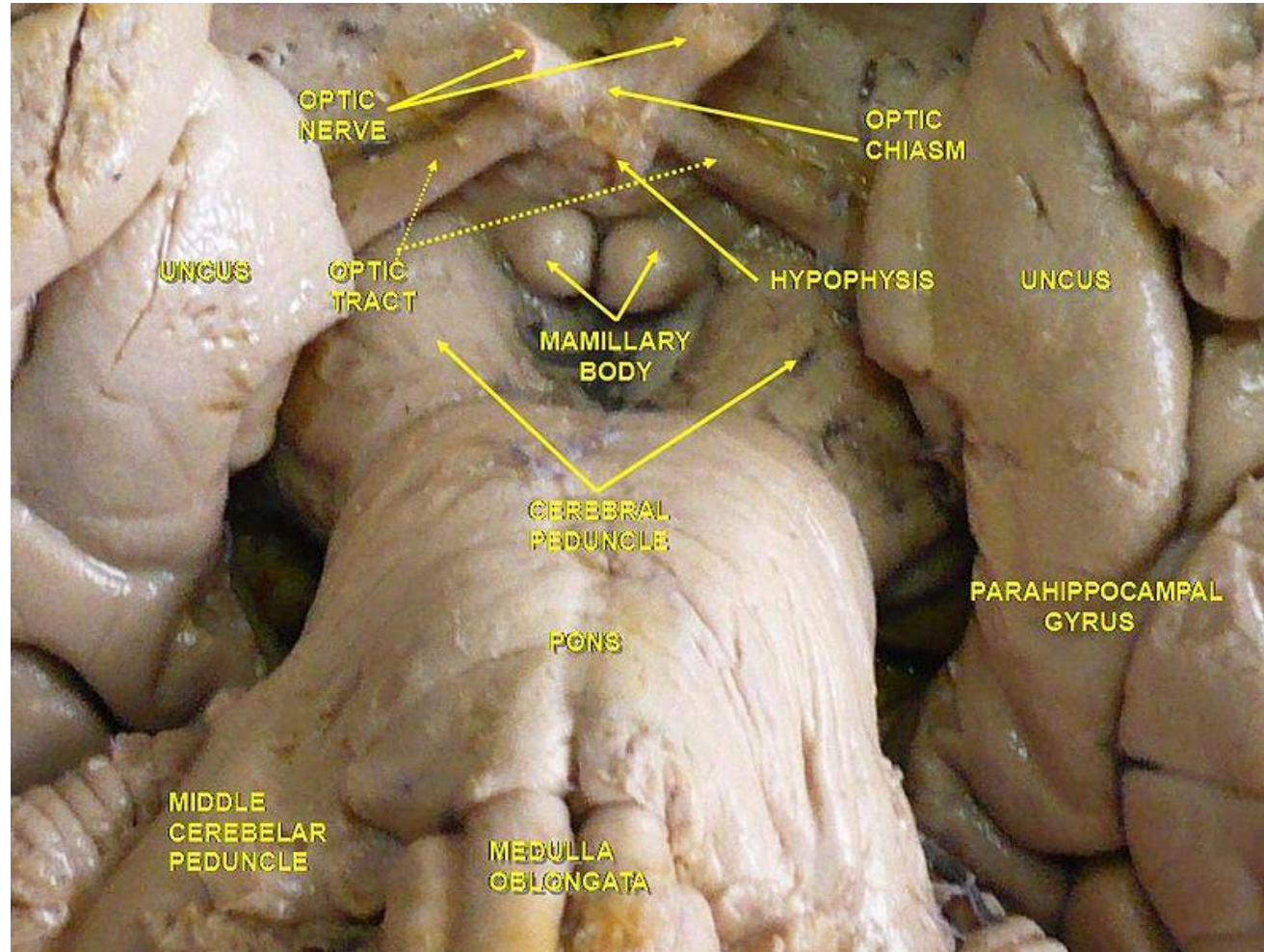
There are donuts ...and there are donuts



All patients with an elevated prolactin level should receive an MRI



# Location, location, location



# Medications that increase prolactin

1. First generation antipsychotics: chlorpromazine and **haloperidol**
2. Second generation antipsychotics: **risperidone** and others
3. Antidepressants: TCAs, SSRIs, others
  - A. Citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
4. Antiemetics and GI drugs: **metoclopramide**
5. Verapamil and methyldopa (Aldomet)
6. Opioids: methadone, morphine, others

# Prolactinoma - Treatment

1. Indications for treatment:
  - A. Existing or impending neurologic symptoms
  - B. Symptoms of hyperprolactinemia
2. Macroadenoma – size > 1 cm
  - A. Higher likelihood of progressing
3. Microadenoma – size < 1 cm
  - A. 95% do NOT progress

1. Sisam DA, Sheehan JP, Sheeler LR. The natural history of untreated microprolactinomas. *Fertil Steril.* 1987;48(1):67
2. Schlechte J, Dolan K, Sherman B, Chapler F, Luciano A. The natural history of untreated hyperprolactinemia: a prospective analysis. *J Clin Endocrinol Metab.* 1989;68(2):412

# Prolactinoma - Treatment

1. Dopamine agonists for all patients with hyperprolactinemia:
  - A. Cabergoline (\$15 USD/month, March 2023, GoodRx)
    - i. Less side effects than bromocriptine, esp. nausea
    - ii. Once or twice weekly dosing, 0.25-0.5 mg 2x/wk
  - B. Bromocriptine 1.25 mg bid
  - C. Pergolide withdrawn from US market in 2007 due to increased risk of valvular heart disease



# Prolactinoma - Treatment

1. Start dopamine agonist and follow patient symptoms, prolactin level, and size by MRI.
2. Consider transphenoidal surgery for:
  - A. Insufficient response to dopamine agonist
  - B. Large macroadenoma

Patient presents with mild headaches on and off for 2-3 months. What do you observe?



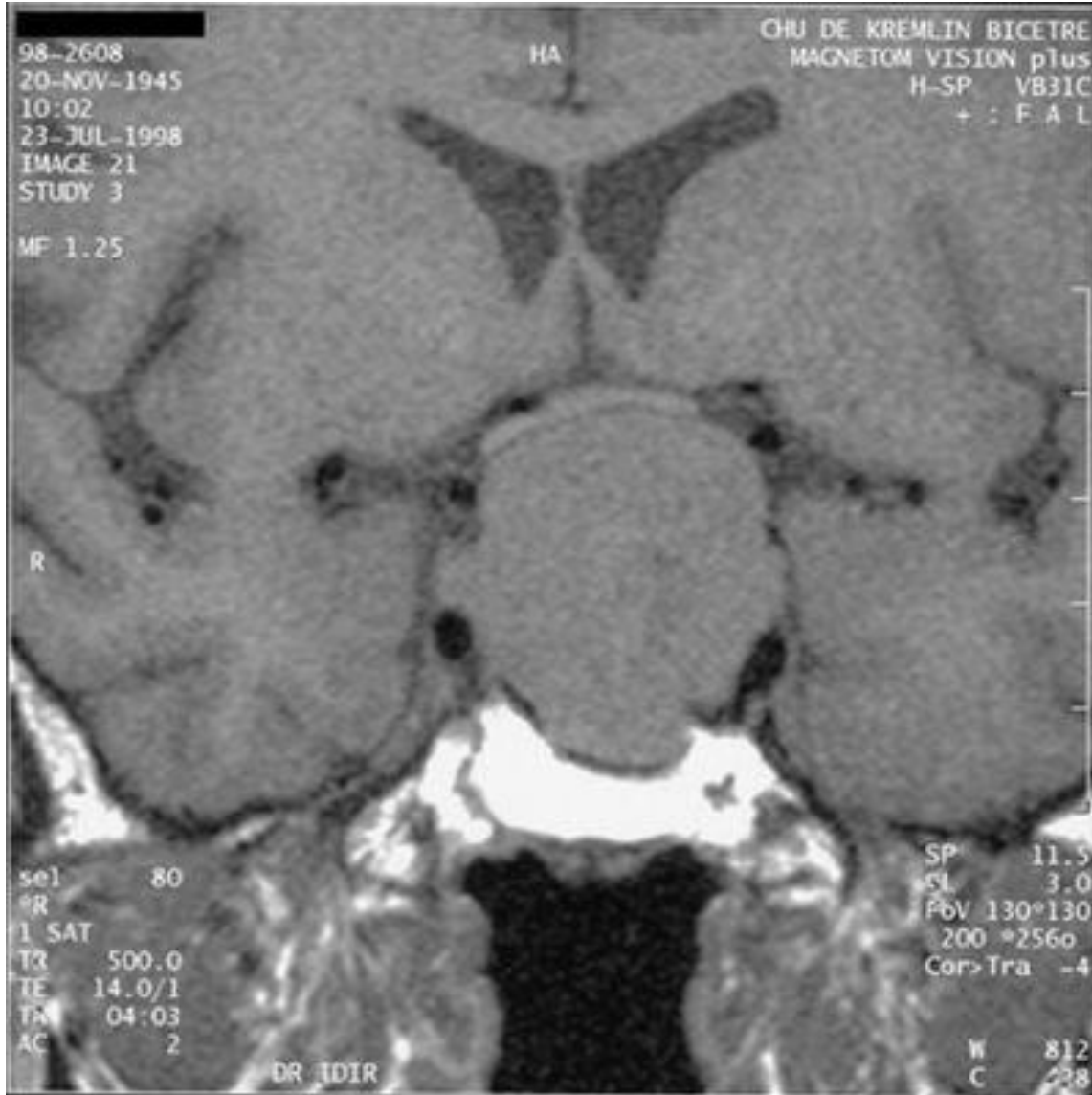
Diagnosis?

**Acromegaly**

# Observations

1. Prominent Supra-orbital ridge (Frontal bossing)
2. Jutting lower jaw...macrognathism
3. Patient may note need to resize rings, need for larger gloves and shoes
4. Patient may have signs/symptoms  
mass:  
Headache, visual changes





# Acromegaly

1. Diagnosis confirmed with Insulin-like growth hormone – 1 level (IGF-1).
2. Growth hormone release is periodic and noncontinuous.
3. IGF-1 levels are stable.
4. Use MRI to localize and characterize tumor.

# Acromegaly - Treatment

1. Transphenoidal surgery for:
  - A. Microadenoma
  - B. Macroadenoma that can be completely excised
  - C. Macroadenoma with neurologic compromise
2. Somatostatin analogues to inhibit release of GH and subsequent IGF-1
  - A. Octreotide and lanreotide
  - B. Cabergoline – second line





Pt with HTN:  
Thick cheeks  
Stretch marks  
...and “X” marks  
the spot

# Cushing's syndrome

# Symptoms of Excess ACTH

- Weight gain
- Central obesity
- Hypertension
- Proximal muscle weakness
- Diabetes
- Depression or psychosis
- Osteoporosis
- Easy bruising
- Menstrual disorders
- Violaceous striae
- Acne
- Hirsutism

# Symptoms of Excess ACTH

1. Excess ACTH is called Cushing's syndrome
2. If the excess ACTH is coming from the pituitary, then it is called Cushing's disease
3. Think of a steroid overdose and you'll have the symptoms of excess ACTH

## Signs of Excess ACTH

- Central obesity
- Moon facies
- Buffalo hump
- Muscle wasting of the extremities
- Cataracts
- Glaucoma
- Hypertension
- Diabetes

# Cushing's Syndrome – Diagnosis and Treatment

1. Two of three first line tests should be abnormal
  - A. 24 hour urinary cortisol
  - B. Dexamethasone suppression test
  - C. Late evening salivary cortisol
2. The result is usually 2-3X abnormal in a patient with Cushing's syndrome
3. MRI of brain to localize and characterize lesion
4. Transphenoidal surgery is curative in 70-80% cases

# Cushing's syndrome

## Key points

1. The symptoms and signs of Cushing's syndrome result from steroid excess.
2. Steroid excess can be a paraneoplastic syndrome (oat cell cancer in the lung)
3. Use the 24 hour urine and dexamethasone suppression test to aid in diagnosis as cortisol has a pulsatile secretion.

# Case of WADAO

1. Mrs. Smith is a 37 yo female who presents to your office complaining of feeling weak and dizzy all over (WADAO) for the previous two months
2. PMHx – she has stable vitiligo for 10 years
3. Social – married 15 years, two young children, stable family, homemaker



# Physical Exam

- VS: BP 85/40, P 86, RR 14, T 98.4, PO<sub>2</sub> 98%
- Skin: tanned
- Oral mucosa: brownish discoloration on buccal mucosa
- The remainder of the exam is otherwise normal

# Labs

- BMP/Chem7

- Na+ 132
- K+ 5.2
- Cl- 101
- HCO<sub>2</sub><sup>-</sup> 23
- BUN/Cr 17/0.9
- Glucose 87

- CBC, TSH, UA normal

37 yo female with fatigue, BP 85/40, dermal hyperpigmentation, Na<sup>+</sup> 132, K<sup>+</sup> 5.2. The most likely Dx is:

- A. Dysthymia
- B. Conn's syndrome with aldosterone excess
- C. Addison's disease with adrenal insufficiency
- D. Waterhouse-Friedrichsen syndrome

## Correct answer is C – Addison's DZ

1. Classic patient presentation of Addison's disease.
2. Patients with dysthymia feel generally down but do not have lab or vital sign abnormalities.
3. Aldosterone excess → elevated sodium and low potassium.
4. WF is a result of meningococcal sepsis and life-threatening adrenal crisis. This patient is not septic.

# Adrenal Insufficiency

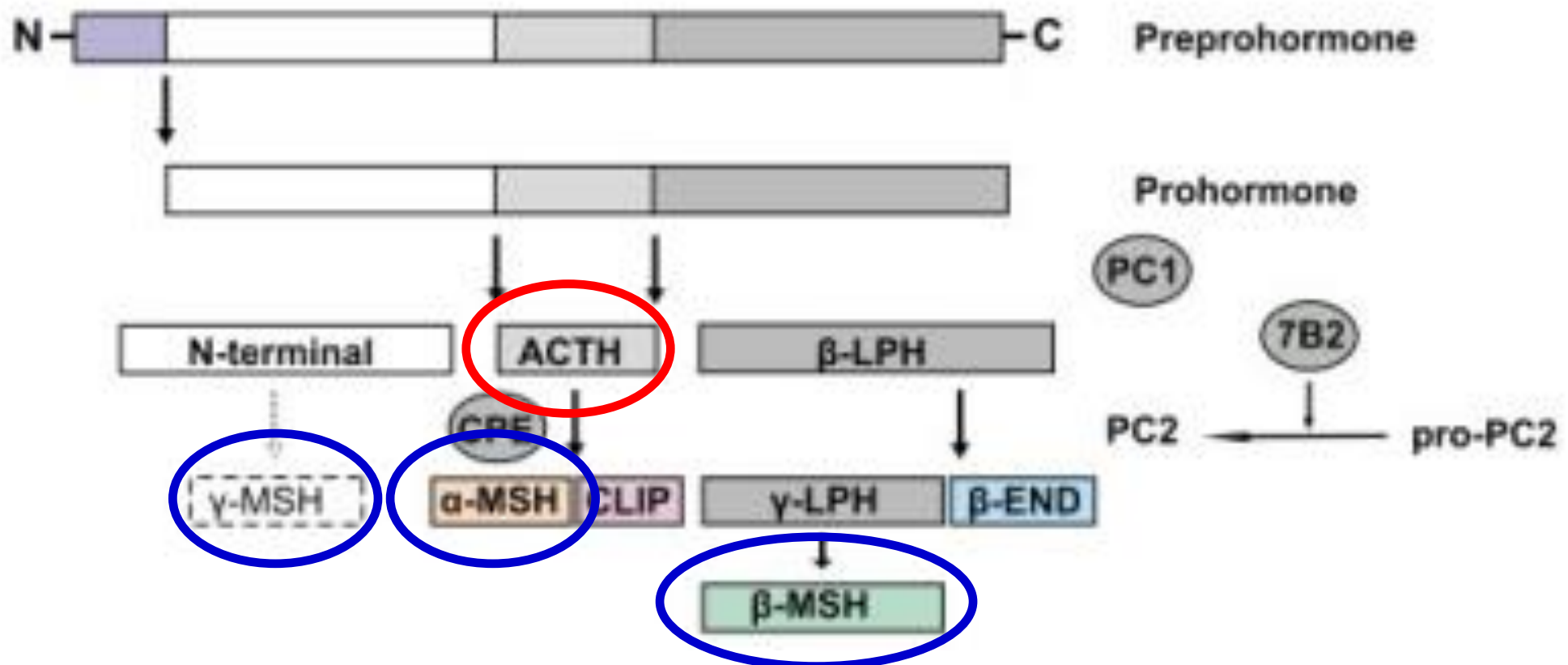
- This is a life-threatening disorder that results from a deficiency of glucocorticoids
  - Primary causes from adrenal failure
  - Secondary causes from disruption of the hypothalamic-pituitary axis (HPA)





# Why the Tan?

## Pro-Opiomelanocortin (POMC)



MSH = melanocyte stimulating hormone



JFK



# Addison's disease

## Key points

1. Review the vital signs and electrolytes when considering this diagnosis
2. Hyperpigmentation can be a late finding
3. Treat with hydrocortisone urgently with a patient in crisis

## Best Practice Recommendations

1. Use the astute history and physical exam to guide the evaluation in patients for endocrinopathies
2. Order tests to best support the working diagnosis
3. Work closely with endocrinology colleagues to provide optimum care for patients.

# Thank you

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