

Pituitary Disorders Evaluation and Management

National Nurse Practitioner Symposium
Keystone, Colorado
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3:30-5:00 PM

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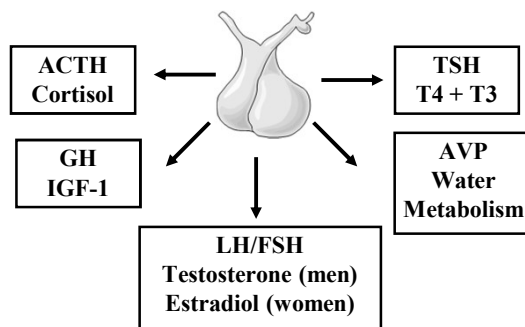
Disclosure

- Michael McDermott MD has no conflicts or disclosures in regard to this presentation.
- Any unlabeled/unapproved uses of drugs or products referenced will be disclosed.

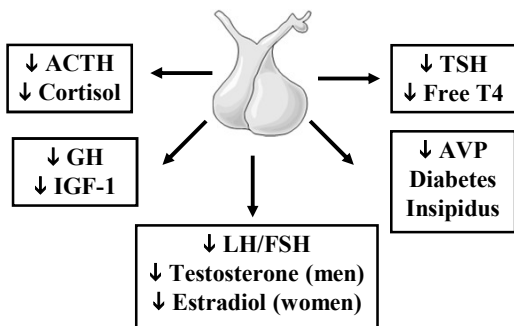
Learning Objectives

- Review the most common causes of pituitary disorders in the general population, and discuss situations where pituitary disorders may complicate other medical conditions
- Explain the recommended evaluation for patients with suspected pituitary conditions
- Discuss treatment strategies for the most common pituitary disorders

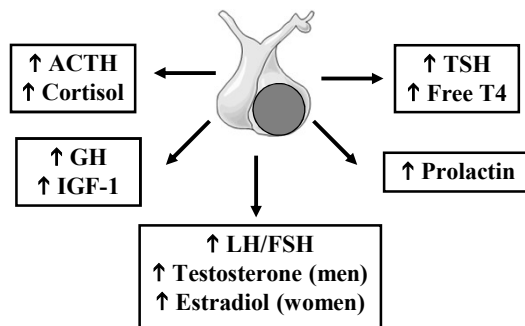
Pituitary Function

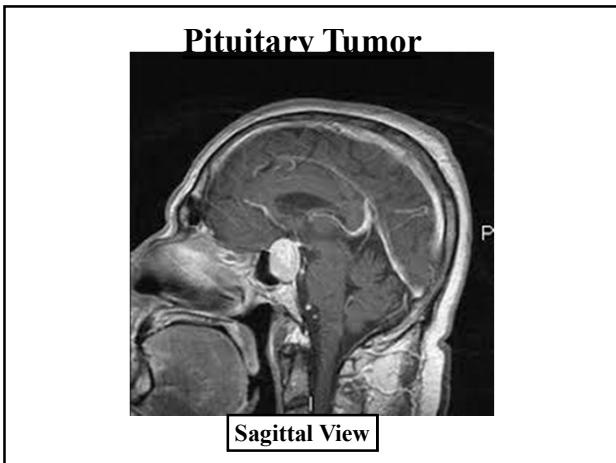
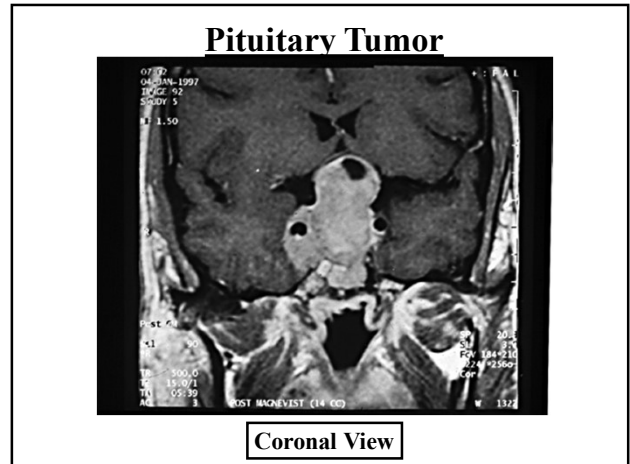
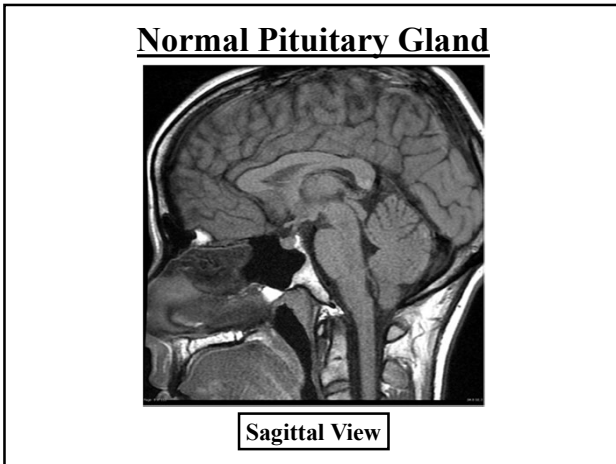
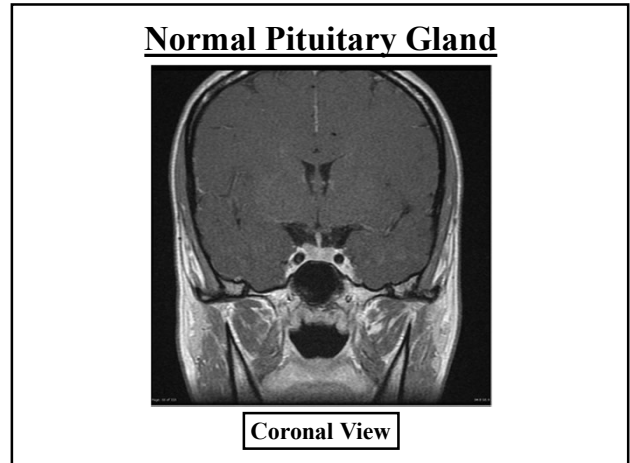
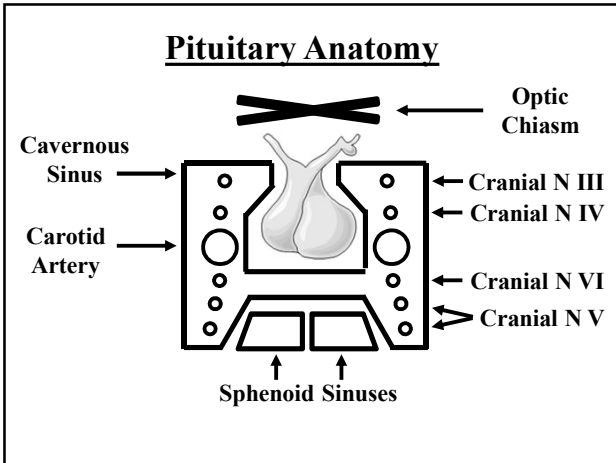


Hypopituitarism



Pituitary Tumors





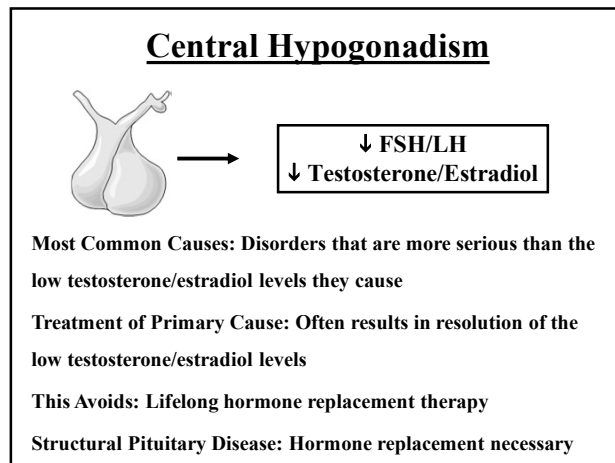
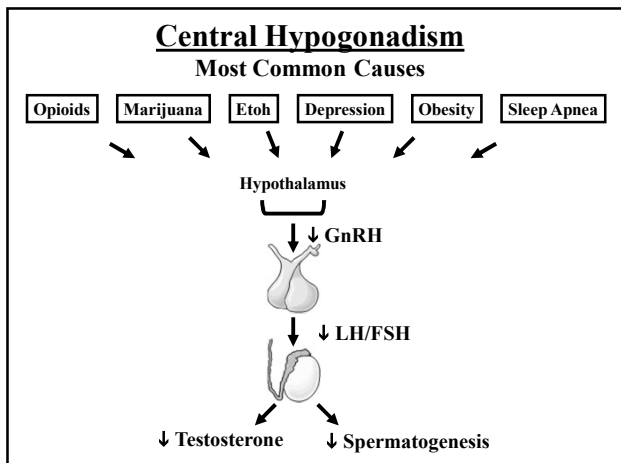
Case

51 yo man presents for treatment of low testosterone discovered in a Men's Health Clinic. He wants a second opinion.

PMH: Hypertension FH: HTN, CAD
 Medications: Metoprolol ROS: loud snoring
 Exam: BP 142/84 P 82 Ht 5'10 Wt 221 lb
 Normal general exam
 Labs: Testosterone 115 ng/dl, LH 2.1 uU/L, FSH 1.9 uU/L

What is the most likely cause of his low testosterone?

1. Pituitary macroadenoma
2. Anabolic steroid use
3. Sleep apnea
4. Klinefelter's syndrome



Case

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

Case

A 52 year old woman admitted with fever, dyspnea, cough, yellow blood-tinged sputum, and right pleuritic chest pain.

PMH: Rheumatoid Arthritis, Asthma FH: Asthma, COPD
Medications: Prednisone 7 mg QD, Intermittent Steroid Inhalers
Exam: BP 114/78 P 108 T 38.0 Ht 5'9 Wt 168 lb
Respiratory distress, Rales in RLL

Labs: WBC 14, 900, Na 136, K 4.3, Glucose 118, Creat 0.9
O2 Sat 82%

CXR: RLL infiltrate with probable right pleural effusion

What is the best management of her adrenal condition?

1. Continue Oral Prednisone 5 mg QD
2. Increase Prednisone to 50 mg QD
3. IV Hydrocortisone 200 mg QD
4. IV Hydrocortisone 200 mg + oral Fludrocortisone 0.2 mg QD

Central Adrenal Insufficiency
Glucocorticoid Induced

Supraphysiological Doses for ≥ 3 Weeks

Hydrocortisone: 15-25 mg/day

Prednisone: 5-7 mg/day

Prednisolone: 4-6 mg/day

Dexamethasone: 0.75 mg/day

Cooper M, N Engl J Med 2003; 348:727-34

Case

A 25 year old woman is admitted for nausea, vomiting and abdominal pain progressive over 3 days.

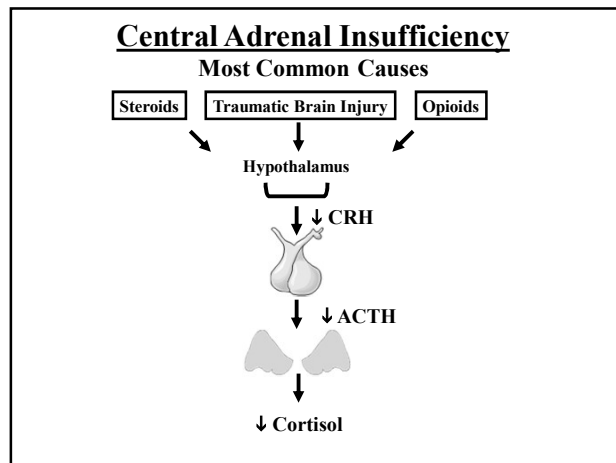
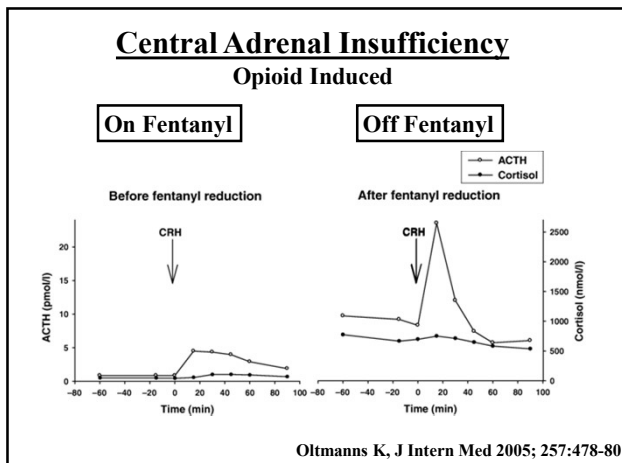
PMH: Sickle cell disease, Asthma FH: DM, HTN, CAD
Medications: Oxycodone, Methadone, Fluticasone PRN
Exam: BP 92/58, P 104

General: moderate distress Abdomen: diffusely tender

Labs: Glucose 88, Na 123, K 4.2, Creatinine 1.3
CBC: anemia, eosinophilia HCG: negative
Cortisol: 2 ug/dl ACTH 8 pg/ml

What is the most likely cause of her low serum cortisol?

1. Adrenal Infarction due to Sickle Cell Disease
2. Pituitary Infarction due to Sickle Cell Disease
3. Adrenal Axis Suppression from Inhaled Steroids
4. Adrenal Axis Suppression from Opioids



Central Adrenal Insufficiency Diagnosis

Serum Cortisol (8-9 AM Best)
 < 3 ug/dl Baseline OR
 < 18 ug/dl after Cosyntropin (250 ug)

Cortisol > 15 ug/dl
 Excludes AI

Plasma ACTH
 Normal or Low

Pituitary MRI May Show Pathology

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

Central Adrenal Insufficiency Treatment (When Structural Pituitary Disease Present)

Glucocorticoid Replacement

Hydrocortisone: 10-15 mg AM 5 mg PM
 OR
Prednisone: 4-5 mg/day

* Hydrocortisone Preferred

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

Central Adrenal Insufficiency 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
Home 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

Central Adrenal Insufficiency

Most Common Causes: Steroids, Opioids, TBI

Temporary Steroid Coverage for Stress Events: Often necessary

This Prevents: Adrenal Crisis

Structural Pituitary Disease: Glucocorticoid daily replacement and stress coverage needed

Case

A 58 year old woman was diagnosed with a non-secreting pituitary tumor 12 years ago. She had a transsphenoidal pituitary resection followed by radiation therapy for residual tumor. She was diagnosed with hypopituitarism 2 years ago. She was started on hydrocortisone and levothyroxine. She continues to experience fatigue, cold intolerance and constipation.

Meds: Hydrocortisone 15 mg AM, 5 mg PM, LT4 75 mcg QD.

Exam: BP 140/78 P 62 Ht 5'4" Wt 174 lb General: normal

Labs: TSH 0.2 mU/L (0.45-4.5), Free T4 1.0 ng/dl (0.8-1.8)

What treatment do you recommend first?

1. Reduce Levothyroxine dose
2. Increase Levothyroxine dose
3. Add Liothyronine (T3) therapy
4. Change to desiccated thyroid hormone

Central Hypothyroidism



Diagnosis: TSH ↓ and ↓ Free T4

- Pituitary Can't Make TSH

Treatment: Levothyroxine

Monitor: Free T4 (not TSH)

- Maintain Free T4 in upper half of reference range

Case

A 34 year old veteran sustained head trauma while deployed abroad. He now complains of fatigue, weight gain and low libido.

PMH: negative FH: negative Medications: Ibuprofen PRN

Exam: BP 110/68 P 82 Ht 6'3" Wt 215 lb

General: normal exam

Labs: Glucose 88, Na 132, K 4.0, Creat 1.1

TSH 0.5 mU/L, Free T4 0.6 ng/dl

Cortisol 1.8 ug/dl, ACTH 8 pg/ml

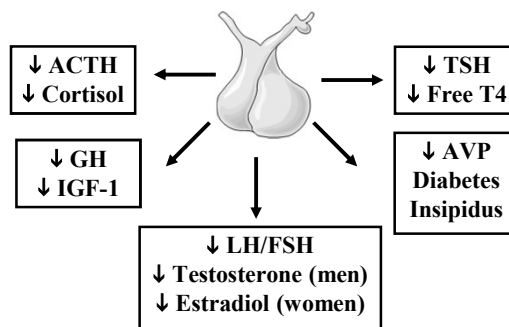
IGF-1 45 ng/ml (nl: 90-390)

Testosterone 120 ng/dl (nl: 300-1000), LH 1.7 mU/L

What treatment do you recommend first?

1. Levothyroxine replacement
2. Hydrocortisone replacement
3. Testosterone replacement
4. Growth Hormone replacement

Hypopituitarism



Hypopituitarism

Treatment

Central Adrenal Insufficiency

- Glucocorticoid Replacement (Hydrocortisone, Prednisone)
- Extra coverage for stress events

Central Hypothyroidism

- Levothyroxine: monitor Free T4 (not TSH)

Central Hypogonadism

- Treat Primary Causative Disorder
- Sex Hormone Replacement (Estrogen, Testosterone)

Growth Hormone Deficiency

- GH Replacement: monitor IGF-1

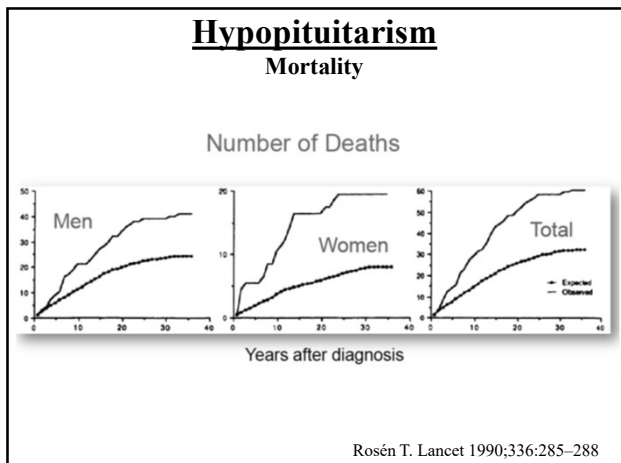
Diabetes Insipidus

- DDAVP (Nasal Spray, Oral)

Hypopituitarism

Treatment

Always Treat Adrenal Insufficiency First
(If Present)



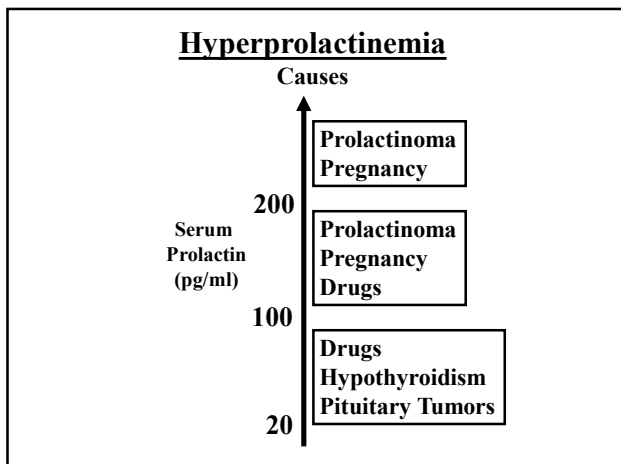
Case

A 32 year old woman notes the recent development of irregular menses and some breast tenderness.

PMH: Hypothyroidism, Bipolar Disease FH: HTN, Bipolar Dz
Meds: Levothyroxine, Levonorgestrel (Mirena), Olanzapine
Exam: BP 127/80, P 72, Ht 5'8" Wt 142 lb
Visual fields nl Thyroid nl Nipple ring, no breast discharge
Labs: Estradiol 88 pg/ml, LH 2.1, FSH 2.6,
TSH 6.2 mU/L (nl, 0.5-5.0), Prolactin 94 pg/ml

What is the likely cause of her elevated prolactin level?

1. Hypothyroidism
2. Nipple ring
3. Levonorgestrel
4. Olanzapine



- ### Hyperprolactinemia
- #### Causes - Medications
- Antipsychotics
 - Antidepressants
 - Anticonvulsants
 - Antihistamines
 - Antihypertensives
 - Anesthetics
 - Cholinergic Drugs
 - Dopamine Inhibitors
 - Estrogens
 - Opiates

Case

A 28 year old woman complains of progressive weight gain over the past 2 years. She has also had acne and thinning of her hair.

PMH: 2 normal pregnancies FH: Mother - Hypothyroidism
Medications: Oral Contraceptives
Exam: BP 132/86, P 78, Ht 5'6" Wt 188 lb
Thyroid - nl Skin -terminal hair on chin, pink striae on abdomen
Labs: Glucose 95 mg/dl, Na 142, K 4.2, Creatinine 0.9
Cortisol AM 34 ug/dl (nl: 5-25) After 1 mg Dex HS: 12 ug/dl
ACTH 35 pg/ml (nl: 10-85)
TSH 5.95 mU/L Testosterone 64 ng/dl (nl: 20-80)

What is the likely cause of her elevated cortisol level?

1. Cortisol Producing Adrenal Adenoma
2. ACTH Producing Pituitary Tumor
3. Mild Hypothyroidism
4. Oral Contraceptive

- ### Estrogen Effects on Cortisol
- Cortisol circulates bound to Cortisol Binding Globulin (CBG) and Albumin
 - High estrogen levels (OCPs and Pregnancy) increase CBG levels: ↑ serum total cortisol, nl free cortisol
 - High serum cortisol levels are seen in women using OCPs and in Pregnancy
 - Can cause a false diagnosis of Cushing's Syndrome

Case

A 25 year old woman developed a bilateral breast discharge about 6 months ago. Her menses have been irregular for the past year and absent for the past 4 months.

PMH: mild depression FH: Father – Crohn’s disease

Medications: Oral contraceptives, Escitalopram

Exam: BP 105/68 P 64 Ht 5’5” Wt 124 lb

Visual fields – normal Optic disk – normal

Thyroid normal Breasts – milky discharge

Labs: Estradiol 24 pg/ml, LH 3.0 mU/L, FSH 4.2 mU/L

Prolactin 332 pg/ml, HCG negative, TSH 1.2 mU/L

What is the most likely diagnosis?

1. Prolactinoma
2. Hyperprolactinemia due to Oral Contraceptives
3. Hyperprolactinemia due to Citalopram
4. Molar Pregnancy

Case

A 25 year old woman developed a bilateral breast discharge about 6 months ago. Her menses have been irregular for the past year and absent for the past 4 months.

PMH: mild depression FH: Father – Crohn’s disease

Medications: Oral contraceptives, Escitalopram

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Visual fields – normal Optic disk – normal

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Labs: Estradiol 24 pg/ml, LH 3.0 mU/L, FSH 4.2 mU/L

Prolactin 332 pg/ml, HCG negative, TSH 1.2 mU/L

What do you recommend now?

1. Pituitary MRI
2. Stop Oral Contraceptives and retest
3. Stop Citalopram and retest
4. Mammogram

Case

A 25 year old woman developed a bilateral breast discharge about 6 months ago. Her menses have been irregular for the past year and absent for the past 4 months.

PMH: mild depression FH: Father – Crohn’s disease

Medications: Oral contraceptives, Escitalopram

Exam: BP 105/68 P 64 Ht 5’5” Wt 124 lb

Visual fields – normal Optic disk – normal

Thyroid normal Breasts – milky discharge

Labs: Estradiol 24 pg/ml, LH 3.0 mU/L, FSH 4.2 mU/L

Prolactin 332 ng/ml, HCG negative, TSH 1.2 mU/L

MRI: 2 cm pituitary tumor abutting the optic chiasm

What treatment do you recommend?

1. Transsphenoidal Pituitary Surgery
2. Cabergoline
3. Stop Citalopram and retest
4. Stop Oral Contraceptives and retest

Prolactinoma

Women – Microadenoma or Macroadenoma

- Galactorrhea, Amenorrhea/Abnormal Menses
- Headaches, Visual Field Abnormalities (Macroadenomas)

Men – Macroadenoma

- Decreased Libido, Erectile Dysfunction
- Headaches, Visual Field Abnormalities

Prolactin Levels > 200 pg/ml (Tumor or Pregnancy)

- Prolactin 20-100 pg/ml (hypothyroidism or medications – especially anti-depressants)

Treatment

- Dopamine Agonist: Cabergoline, Bromocriptine
- Surgery for compressive tumors / aggressive growth

Case

A 42 year old woman complains of weight gain, fatigue, muscle weakness, and abnormal menses, progressive over the past year.

PMH: gestational diabetes FH: DM2, HTN

Medications: None

Exam: BP 145/93 P 76

Central obesity, facial plethora, facial rounding, supraclavicular fat pads, and purple axillary striae.

Labs: Fasting glucose 156 mg/dl, A1C 6.8%

Which of these is a good screening test for Cushing’s Syndrome?

1. AM Serum Cortisol
2. AM Plasma ACTH
3. 24 Hour Urine Cortisol
4. 8 mg Overnight Dexamethasone Suppression Test

Case

A 42 year old woman complains of weight gain, fatigue, muscle weakness, and abnormal menses, progressive over the past year.

PMH: gestational diabetes FH: DM2, HTN

Medications: None

Exam: BP 145/93 P 76

Central obesity, facial plethora, facial rounding, supraclavicular fat pads, and purple axillary striae.

Labs: Fasting glucose 156 mg/dl, A1C 6.7%
24 Hour Urine Cortisol 442 ug (nl < 55)

What would you order now?

1. Pituitary MRI
2. Plasma ACTH
3. Bedtime Salivary Cortisol
4. 1 mg Dexamethasone Suppression Test

Case

A 42 year old woman complains of weight gain, fatigue, muscle weakness, and abnormal menses, progressive over the past year.

PMH: gestational diabetes FH: DM2, HTN

Medications: None

Exam: BP 145/93 P 76

Central obesity, facial plethora, facial rounding, supraclavicular fat pads, and purple axillary striae.

Labs: 24 Hour Urine Cortisol 442 ug (nl < 55)

Plasma ACTH 45 pg/ml (nl: 10-85)

What is the most likely underlying disorder?

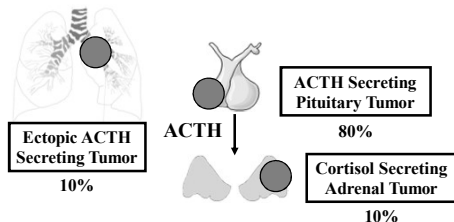
1. Ectopic ACTH Syndrome
2. Hypercortisolism due to Diabetes
3. Pituitary ACTH Secreting Tumor
4. Cortisol Producing Adrenal Adenoma

Cushing's Syndrome



Cushing's Syndrome

Endogenous



Cushing's Syndrome

Screening

Screening Tests

Positive Result

- 24 Hour Urine Cortisol Elevated ($\geq 2 \times$ nl)
- Bedtime Salivary Cortisol Elevated
- 1 mg DST* Cortisol > 1.8 ug/dl

*DST = Dexamethasone Suppression Test

Take: 1 mg Dex at 10-11 PM

Measure: serum cortisol next morning at 8:00 AM

Nieman L, J Clin Endocrinol Metab 2008; 93:1526-40
Endocrine Society Clinical Practice Guidelines

When you diagnose someone with Cushing's Disease, you have saved a life!

High Mortality Rate Untreated

Very Treatable

Case

A 44 year old man complains of has recently developed diabetes and presents for further evaluation. He has also noted pain in his hands and knees and occasional headaches.

PMH: DM2 (recent), Carpal Tunnel Syndrome FH: No Diabetes
Medications: Metformin

Exam: BP 138/92, P 72 Ht 5'11 Wt 173

Prominent supraorbital ridge Thyroid – mildly enlarged
Hands – increased soft tissue

Labs: Glucose 188 A1C 7.6% TSH 3.5 mU/L

What do you recommend to evaluate the cause of his diabetes?

1. 24 Hour Urine Cortisol
2. Serum Growth Hormone
3. Serum IGF-1
4. Thyroperoxidase (TPO) Antibodies

Acromegaly
Diagnostic Testing

- IGF-1: Elevated - Best Overall Test
- GH During OGTT: Failure to Suppress GH

Acromegaly. Clinical Practice Guidelines – Endocrine Society
Katznelson L. J Clin Endocrinol Metab 2014; 99: 3933-51

Acromegaly
Clinical Features



Acromegaly
Clinical Features



Acromegaly
Macroadenoma (70%)



Coronal View

Pituitary Conditions in Primary Care

- Central Adrenal Insufficiency most often results from exogenous glucocorticoid or opioid use
- Patients with Central Adrenal Insufficiency should receive stress steroid coverage for surgery and serious illness
- Hyperprolactinemia has multiple causes, the most common of which is medications that affect the Central Nervous System
- Drug induced hyperprolactinemia does not require treatment other than stopping the causative drug, if possible
- Cushing's Syndrome (CS) is not rare and is more common in patients with diabetes, hypertension and osteoporosis
- CS results from ACTH pituitary tumors (80%), ectopic ACTH tumors (10%) or cortisol producing adrenal adenomas (10%)
- Three good screens for CS: 24 hour urine cortisol, HS salivary cortisol, and overnight 1 mg dexamethasone suppression test
- The best screening test for Acromegaly is a serum IGF-1 level

Thank You

