Endocrine Disease: Practical, Evidence-Based, Clinical Pointers

B. Wayne Blount, MD, MPH
JenCare & Emory
Learning Objectives

1. Identify the diagnosis and management of the common types of hypothyroidism, hyperthyroidism, & thyroid nodules.

2. Discuss the work-up of pituitary masses.

Additional slides for your study:

– Adrenal Problems
– Parathyroid Problems
– Male Hypogonadism
Disclosure Statement

Dr. Blount has nothing to disclose.

The AAFP has selected all faculty appearing in this program. It is the policy of the AAFP that all CME planning committees, faculty, authors, editors, and staff disclose relationships with commercial entities upon nomination or invitation of participation. Disclosure documents are reviewed for potential conflicts of interest and, if identified, they are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.
Question 1

A 17 yo WF c/o “swelling” in her neck x 2-3 wks. 5-lb wgt gain and somewhat tired. ROS neg

PE: 5’10”, 155 lb, BP 132/80, P 80, AF, thyroid diffusely enlarged, smooth & NT; remainder WNL
1. What single test would you order for this patient?

   A. T4
   B. RT3U
   C. TSH
   D. Ultrasound
1. What single test would you order for this patient?

A. T4
B. RT3U
C. TSH
D. Ultrasound

C. TSH (85%)

A (3%)
B (2%)
D (10%)
Hypothyroidism

- Female-male = 6:1
- Prevalence: 1 in 300 people
  - In US
- Causes:
  - Hashimoto’s*
  - Ablation
  - 2ndary: Lithium, interferon, amiodarone
  - Transient causes
  - Central causes
Presentation

Fatigue**
Dry skin
Hair loss
Hoarseness*
Slow DTRs*
Depression
Myalgia*
Macroglossia
Lateral eyebrow thinning*

Weight gain
Cold intolerance**
Coarse hair
Goiter
Constipation
Concentration loss*
Hyperlipidemia*
Bradycardia
Diagnosis

• Hx & PE:
  – Look for presentations

• Lab:
  – TSH
  – Thyroid antibodies?
  – Others C/W Dx: High CPK, LDL, TGs, proteinuria, normocytic anemia
2. Which of the following is true?

A. All brands of levothyroxine are bioequivalent
B. The usual starting dose in the non-elderly is 1.6 mcg/kg/day
C. The usual starting dose in the non-elderly is 1.2 mcg/kg/day
D. You should recheck a TSH 3 weeks after a dosage change
2. Which of the following is true?

A. All brands of levothyroxine are bioequivalent

B. The usual starting dose in the non-elderly is 1.6 mcg/kg/day

C. The usual starting dose in the non-elderly is 1.2 mcg/kg/day

D. You should recheck a TSH 3 weeks after a dosage change

- A: 22%
- B: 31% (Correct)
- C: 34%
- D: 13%
Treatment

• Start @ 1.6 mcg/kg/day

• Start lower in the elderly (1.0-1.25) (Even 25 – 50 mcg/day)

• Re-evaluate 5-6 wks after dosage change

• Different products = different bioavailability
Treatment Principles

• Avoid desiccated thyroid (doesn’t work in many)
• Avoid triiodothyronine (doesn’t work in many)
• Too much causes osteoporosis & A Fib
• Take on fasting stomach & wait 30 mins before eating. (Can do a weekly dosing)
• Watch other interactions:
  – Iron, sucralfate, cholestyramine, antacids, anticonvulsants, grapefruit, amiodarone, lithium, SSRIs, retinoids
Treatment Principles

- If TSH WNL but patient not feeling well, consider:
  - Getting TSH to < 2.5. If still not to par,
  - Problems with conversion of T4 to T3
- Nutrient deficiency:
  - Heavy metals: selenium, chromium, zinc, iron, copper, mercury, lead
  - Iodine
  - Vitamins: A, B2, B6, B12, D, E
Conversion Problems

Meds:

- Steroids
- OCPs
- Chemotherapy
- Lithium
- SSRIs
- Phenytoin
- Iodinated contrast agents

- Theophylline
- Beta blockers
- Fluoride
- Opiates
- Estrogen
Conversion Problems

- Stress
- Aging
- ETOH
- Fasting
- Radiation
- Cruciferous vegetables (in excess)
- Receptor antibodies
- Low ferritin
- Pesticides
- Soy (excess)
- Hemochromatosis
- Smoking
- Kidney dz
Question 3.

A 42-yo WM c/o fatigue, weight loss, voracious appetite, hand tremor, HAs, decreased exercise tolerance; all x 4 weeks.

PE: 6’0”, 150 lb, thyroid diffusely large and NT, + fine hand tremor.
3. Which of the following lab tests are indicated?

A. TSH
B. T4
C. T3
D. Thyroid antibodies
E. All of the above
3. Which of the following lab tests are indicated?

A. TSH
B. T4
C. T3
D. Thyroid antibodies
E. All of the above

- E. All of the above (88%)
- A. TSH (11%)
- D. Thyroid antibodies (1%)
Hyperthyroidism

- Female-Male = 8:1
- Prevalence: 0.2 %
- Causes:
  - Graves
  - Multinodular goiter
  - Adenoma
  - Thyroiditis
  - Ingestion
Presentation

- Nervousness
- Palpitations
- Heat intolerance
- Tremor
- Fatigue*
- Insomnia
- HA*

- Irritability*
- Weight loss
- Increased appetite
- Hyperdefecation
- Mental changes*
- DOE*
Diagnosis

• Hx: Ask about presenting Sx

• PE:  Weight  BP
      Pulse  Thyroid
      CV    Neuromuscular
      Eye   Skin
Workup of Hyperthyroidism

- TSH (Duh!)
- Free T4 & T3: A Rec
- CBC: B Rec
- Radioactive uptake scan: A Rec
- “Maybes”: ESR, ultrasound, thyroid antibodies: C Rec
- All of above are after a good Hx & PE
Question 4.

Patient lab results:

- Low TSH
- High T3 & T4
- Scan: Diffuse increased uptake
4. The most likely diagnosis is:

A. Hashimoto’s
B. Graves
C. Multinodular goiter
D. Ingestion
E. Amiodarone administration
4. The most likely diagnosis is:

- A. Hashimoto’s (7%)
- B. Graves (89%)
- C. Multinodular goiter (4%)
- D. Ingestion (0%)
- E. Amiodarone administration (0%)
Graves Disease

• Most common cause of hyperthyroidism
• Caused by TSH receptor-stimulating antibodies.

• Other Causes of Hyperthyroidism:
  – Hashimoto’s
  – Amiodarone
  – Postpartum thyroiditis
  – Metastatic thyroid cancer
  – Iodine
  – Hyperemesis gravidarum
Differential Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Graves</th>
<th>Adenoma</th>
<th>Multinodular</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TSH</strong></td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Scan</strong></td>
<td>Diffuse uptake</td>
<td>Nodule</td>
<td>Multiple nodules</td>
</tr>
<tr>
<td><strong>T4</strong></td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>
5. The preferred definitive treatment for Graves disease is:

A. Surgery
B. Radioactive iodine ablation
C. Antithyroid drugs
D. Close monitoring
5. The preferred definitive treatment for Graves disease is:

- A. Surgery (7%)
- B. Radioactive iodine ablation (78%)
- C. Antithyroid drugs (13%)
- D. Close monitoring (3%)
Graves Disease

• Radioactive iodine is the TOC: A Rec
  – Except perhaps in cases with ophthalmopathy: B Rec

• Surgery is uncommon today

• Drugs: PTU or methimazole; & beta blockers
• Insufficient evidence for Chinese herbal meds: I Rec, Cochrane 2007
Graves Disease Treatment

- Methimazole much safer than PTU
- With PTU risk of serious liver injury is:
  - Adults: 1:10,000
  - Peds: 1:2,000
- PTU now considered a 2nd-line agent
  - EXCEPT during pregnancy & lactation
- A Rec FDA: June, 2009
  - Monitor aminotransferases & CBC in both: C Rec
Question 6.

A 46-yo WF c/o neck mass x 6 wks

Review of systems: negative

PE: All WNL except palpable 2-cm firm mass in right lobe of thyroid
6. What is the initial diagnostic test for this patient?

A. TSH
B. Fine-needle aspiration
C. Nuclear thyroid scan
D. Surgery
6. What is the initial diagnostic test for this patient?

A. TSH
B. Fine-needle aspiration
C. Nuclear thyroid scan
D. Surgery

45% ✓ A. TSH
35% B. Fine-needle aspiration
20% C. Nuclear thyroid scan
0% D. Surgery
Thyroid Nodules

• Work up all nodules
  – 1 in 20 is malignant

• Start with TSH* SOR A

• TSH results determine further workup
Nodule Workup

If LOW TSH

- Ultrasound
- I-123 SCAN
  - COLD
    - FNA
  - HOT
    - ENDOCRINE OR SURGERY

NML OR HIGH TSH

- Ultrasound
- FNA
How Do We, FM, Encounter Pituitary Problems?

• Symptom presentation
  – Neuro Sx
  – Hormonal abnormalities

• The “Incidentaloma”
  – (Nonfunctioning pituitary tumors)
Clinical Presentation

- Most common are endocrine abnormalities – hyper- or hypo-secretion of pituitary hormones: Sx depend on hormone secreted
- HA
- Vision changes – bitemporal hemianopsia and superior temporal defects
Endocrine-Active Pituitary Adenomas

- Prolactin – Amenorrhea, galactorrhea, impotence
- Growth hormone – Gigantism and acromegaly
- Corticotropin – Cushing’s disease
- TSH - Hyperthyroidism
Differential Diagnosis of a Sellar Mass

• Benign Tumors
  – Pituitary adenoma (most common sellar mass)
  – Craniopharyngioma
  – Meningiomas

• Malignant Tumors
  – Primary
    • Germ cell tumor
    • Sarcoma
    • Chordoma
    • Pituitary carcinoma
  – Metastatic
    • Lung
    • Breast
So, How Do We Evaluate These Pituitary Masses?

- Radiologically
  - MRI with and without gadolinium

- Hormonally
  - Oversecretion
  - Undersecretion
Summary

- 3 Major Thyroid Problems
  - Use TSH to start diagnosis in all 3
- Pituitary Masses: The Work-up

Extras:
Subclinical Disease
The Thyroid in Pregnancy
Male Hypogonadism
The Parathyroid Disorders
Adrenal Disorders
Bibliography

1. Am Thyroid Assoc Management Guidelines For Thyroid Nodules. 2009
5. Wiersinga WM. Thyroid disease manager. [http://www.thyroidmanager.org/chapter/adult-hypothyroidism/](http://www.thyroidmanager.org/chapter/adult-hypothyroidism/)
Answers

1. C
2. B
3. E
4. B
5. B
6. A
Supplementary Slides
Good Reasons for Endocrine Consult

- Heart Disease
- Age < 18
- Myxedema Coma
- Pregnancy
- Unresponsive to therapy
- Presence of nodule
- MEN syndrome
Common ECG Findings in Hypothyroidism

- Bradycardia
- Flattened T Waves
- Low voltage
Myxedema Coma (HypOthyroidism)

- Rare: 0.22 per million
- Labs: Hyponatremia, hypercapnia, hypoxia, anemia; High: CPK, prolactin, & lipids
Other Causes of Hyperthyroidism

• Hashimoto’s will have tender neck, fever, dysphagia, high ESR or CRP

• Postpartum thyroiditis:
  – Prevalence = 7.5%
  – Usually within 1 yr of parturition
Graves Disease Treatment

- In pregnancy, PTU is TOC in 1st Trimester
- Switch to methimazole in 2nd & 3rd trimesters
- If breastfeeding, PTU is preferred as less is transferred thru milk
Graves Pharmacotherapy

• Joint decision-making

• Medical treatment is for 18 months and then attempt to wean: B Rec, Cochrane, 2009
  – Success rate of 30%-50%, but
  – Recurrence in those is 50%
Risk for Cancer in a Nodule

- Children
- Age < 30 or > 60
- Radiation
- Rapid growth
- Obstructive Sx
- Cvcl lymph-adenopathy

- Males
- Fam Hx
- Hardness
- > 4 cm
- Voice Diff
# Sonographic Evidence of Cancer in a Nodule

<table>
<thead>
<tr>
<th>Feature</th>
<th>PPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taller than wide</td>
<td>59.8</td>
</tr>
<tr>
<td>Solid appearance</td>
<td>49.4</td>
</tr>
<tr>
<td>Microcalcifications</td>
<td>38.6</td>
</tr>
<tr>
<td>Irregular margins</td>
<td>28.2</td>
</tr>
<tr>
<td>Purely cystic nodule is highly unlikely (&lt; 2%)</td>
<td></td>
</tr>
</tbody>
</table>
# What to Do with FNA Results

<table>
<thead>
<tr>
<th>Result</th>
<th>Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>Observe</td>
</tr>
<tr>
<td>Malignant</td>
<td>Excision</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Excision</td>
</tr>
<tr>
<td>Nondiagnostic</td>
<td>Repeat FNA</td>
</tr>
</tbody>
</table>
Positive FNA?

- 5% of samples

- Types of cancer
  - Papillary: Most common
  - Medullary
  - Anaplastic: Usually older pts
Thyroid Cancer Rx?

- Refer
- Surgery
- Metastasis determines prognosis
Workup of Multinodular Thyroid for Cancer

- Dynamic Contrast Medium-Enhanced MRI (DCE-MRI) is more accurate than FNA in detecting cancer in a multinodular gland: B Rec, Tezelman. Archives of Surgery, 2007
- Negative Predictive Value = 100%
  - For FNA, it’s 58%
  - PPV: DCE-MRI = 78.5%; FNA = 100%
  - Diagnostic accuracy: DCE = 90%; FNA = 71%
If You Cannot Do a DCE-MRI for Multinodular Goiter

- Start with a TSH
- Get an ultrasound
- FNA anything suspicious found on U/S
- If unsure, refer
6. Which of the following organizations recommends screening for ASx thyroid dz?

A. USPSTF
B. AAFP
C. ACP
D. AACE
Only the ACP & Am Thyroid Assoc

- ACP: Only in women > 60 YO
  - Not in men
- ATA: All adults > 35 YO q 5 years
- USPSTF & AHRQ give it an I recommendation
Subclinical Hypothyroidism

- Prevalence: 5%-17%
- Risk for progression to overt dz: 8%-18%
- Look for Sx
- Treat if TSH > 10, attempting conception, or + thyroid peroxidase Ab
- Be observant for overtreatment: Osteoporosis, A Fib
- Treatment does NOT result in improved survival or morbidity, nor QOL nor Sx: A Rec, Cochrane, 2007
Subclinical Hyperthyroidism

- Subclinical hyperthyroidism: Any antithyroid drug is effective. A Rec, Nygaard; AFP’s Clinical Evidence Concise. 2007;76:1014-7.
- Prevalence: 0.1%-6%
- Risk higher in women, age > 60, + antibodies
- Higher osteoporosis, death from CV causes, A Fib
- Joint decision-making for treatment or not
The Thyroid in Pregnancy

• Pregnancy has profound impact on the thyroid.
• Pregnancy can be called a stress test for the thyroid.
• Esp. hypothyroidism during pregnancy is harmful to maternal & fetal health & to child’s future intellectual development
The Thyroid in Pregnancy
(Nice to Know, not on Test)

• Thyroid can increase 10% in size.
• A 50% increase in thyroid hormones and in iodine need.
• 10% of gravid women in 1st trimester will be + for thyroid peroxidase or thyroglobulin Abs.
  – 16% of them have hypothyroidism
  – 33-50% develop pp thyroiditis
The Thyroid in Pregnancy

- Levothyroxine is indicated with overt hypothyroidism
- Levothyroxine is indicated for subclinical hypothyroid (SbHypo) with + TPO Abs
- Gravid women with SbHypo not treated should have TSH & T4 checked q 4 weeks til 16-20 wks & then ≥ once from 26-32 wks
The Thyroid in Pregnancy

- Treatment not needed for isolated low T4
- Women already on levothyroxine should increase dose by 25-50% @ pregnancy. Go to 9 doses/week
- Antithyroid meds are NOT indicated for women with gestational hyperthyroidism
- For Graves, use PTU in 1st trimester, then methimazole
The Thyroid in Pregnancy

- During PP thyroiditis toxic phase, don’t need antithyroid meds.
- Check TSH q 2 months after toxic phase
- Can try to wean off replacement @ 6-12 months after starting Rx
- No radioactive iodine scanning during pregnancy
Pituitary Masses

- What is the differential diagnosis of a lesion within the pituitary?
- What is the prevalence of previously unrecognized pituitary tumors?
- What is the appropriate evaluation of this abnormality?
Pituitary Masses

- 10-15% of all primary brain tumors
- 20-25% of pituitary glands at autopsy found to have adenomas
- 70% of adenomas are endocrinologically secreting (? study bias?)
- 25% of those with MEN-I develop pituitary adenomas
- Etiology is unknown
- Not associated with environmental factors
Radiological Evaluation of a Sellar Mass

- MRI with and without gadolinium
  - Gadolinium contrast
    - Normal pituitary takes up gadolinium more than does CNS tissue
    - Microadenomas often take up gadolinium less than normal pituitary
- CT
  - Calcification in a craniopharyngioma or a meningioma is seen better by a CT than by MRI
- PET Scan
  - Uptake by adenoma was 2-3 X greater than by craniopharyngiomas or meningiomas
Hormonal Evaluation of a Sellar Mass

- Evaluation for potential pituitary hormone oversecretion
  - Prolactin
  - IGF-1 or growth hormone, 2 hours post 100 gm glucose load
  - 24 hour urine free cortisol or 1 mg overnight dexamethasone suppression test
  - Free T4, TSH
Hormonal Evaluation of a Sellar Mass

• Testing for Pituitary Undersection
  – Free T4 and TSH
  – Serum cortisol and ACTH A(8:00 and 9:00 AM)
    • Cortisol less than 3 meg/dL on two occasions, suggests adrenal insufficiency
    • Cortisol > 10 meg/dL is rarely associated with adrenal insufficiency
    • Cortisol of 3-10 meg/dL needs further testing
      – Insulin tolerance test
      – Metyrapone test
Hormonal Evaluation of a Sellar Mass

- Testing for Pituitary Hormone Undersecretion
  - Free testosterone, LH – (male)
  - Estradiol, FSH – (female)
  - Growth hormone deficiency
    - If ACTH, TSH and gonadotropin deficiency exists and baseline GH is low, no further testing needed
    - Otherwise stimulation with two agents
      - Insulin, clonidine
Male Hypogonadism

Decrease in one or both of the two major functions of the testes.

<table>
<thead>
<tr>
<th>Hypogonadism</th>
<th>Pathology</th>
<th>Gonadotropins</th>
<th>Testosterone</th>
<th>Sperm count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td>Testicular failure</td>
<td>Elevated</td>
<td>Low/low nl</td>
<td>Low/low nl</td>
</tr>
<tr>
<td>Secondary</td>
<td>Gonadotrope failure</td>
<td>Low or low nl</td>
<td>Low/low nl</td>
<td>Low/low nl</td>
</tr>
</tbody>
</table>
Male Hypogonadism

Symptoms

- Decreased libido
- Decreased energy
- Decreased sexual hair
- Infertility
- Erectile dysfunction
- Loss of muscle mass
- Decreased bone density
Male Hypogonadism

Primary
- Chromosomal abnormalities
  - Klinefelter syndrome XXY
- Infections
- Trauma
- Cryptorchidism
- Drugs
- Chemotherapy
Male Hypogonadism

• Secondary
  – Pituitary tumors
  – Infiltrative disease
  – Idiopathic hypogonadotropin-hypogonadism
  – Kallmann Syndrome

• Androgen resistance
  – 5 alpha reductase deficiency
  – Androgen receptor abnormalities
Male Hypogonadism

Total testosterone (AM draw)
  Abnormal
    ↓
    Repeat testosterone (consider Free T), FSH, LH
      ↓
      Low T, Low FSH, LH
        ↓
        Secondary hypogonadism
          ↓
          Low T, High FSH, LH

Primary hypogonadism

FSH, LH

Prolactin, MRI,

T4, TSH

Primary hypogonadism
Male Hypogonadism

Therapeutic options

• Androgen replacement
  – Testosterone enanthate or cypionate
    • Transdermal delivery
      – Androgen 5 mg patch daily
      – AndroGel 1% 5 mg daily

• Stimulating spermatogenesis
  – hCG, and hMG
  – GnRH
History

- Symptom onset
- Testicular size
- Breast enlargement
- Behavioral abnormalities
- Chemotherapy or radiation therapy
- Alcoholism
- Visual field defects
- Medications
Examination

- Testicular size
- Pubic hair
- Gynecomastia
- Muscle mass
- Body proportions
- Fundoscopy & visual fields screening
# Laboratory Testing

<table>
<thead>
<tr>
<th>Testosterone</th>
<th>Semen analysis</th>
<th>Gonadotropins (LH/FSH)</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low/low nl</td>
<td>Low sperm ct</td>
<td>Elevated</td>
<td>Primary hypogonadism</td>
</tr>
<tr>
<td>Low/low nl</td>
<td>Low sperm ct</td>
<td>Low/low nl</td>
<td>Secondary hypogonadism</td>
</tr>
</tbody>
</table>
Evaluation of Men with Androgen Deficiency

Confirmed low testosterone

Check LH+FSH (SA if infertility)

High gonadotropins – 1o

Low/low nl gonadotropins – 2o

Karyotype

Prolactin, other pituitary hormones, iron studies, sella MRI
Testosterone Replacement

- Primary goal is to restore testosterone levels to the laboratory reference range
- Prescribe only for patients with confirmed hypogonadism
- Role in “treating” decline in testosterone levels with aging uncertain
- Multiple preparations
  - Oral
  - Intramuscular
  - Transdermal
  - Buccal
Oral Testosterone Preparations

- Alkylated testosterone more slowly metabolized by liver than native testosterone
- May not induce virilization in adolescents
- Untoward effects
  - Cholestatic jaundice
  - Peliosis hepatis
  - Hepatocellular carcinoma
Intramuscular Testosterone

- Enanthate and cypionrate esters of testosterone
- Lipophilic, leading to sustained release from muscle depots
- Side effects related to dosing or administration
- Regimens of 100 mg q wk to 300 mg q 3 wks acceptable
- Goal is a mid-cycle level near the middle of the laboratory reference range
Transdermal Testosterone

• **Patch (Androderm)**
  – Apply to skin of upper arms and torso
  – Delivers 5 mg testosterone/24 hr in continuous manner
  – Approximately 1/3 of patients develop significant contact dermatitis

• **Gels (AndroGel, Testim)**
  – Apply to skin of upper arms and torso
  – Usually dosed as 5.0 g or 10.0 g of gel to deliver 50 mg or 100 mg testosterone, respectively in a continuous manner
  – Reports of contact dermatitis and gel odor uncommon
Desirable Effects of Testosterone Therapy

- Virilization (incompletely virilized men)
- Increased libido and energy
- Improved erectile function?
- Increased muscle mass and strength (8-10 wks)
- Increased bone mass (full effect ~ 24 mo)
Untoward Effects of Testosterone Therapy

- Pain at injection site (IM preparations)
- Contact dermatitis (patch >> gel)
- Acne or oily skin
- Gynecomastia
- Aggressive behavior (adolescents)
- Short stature (adolescents)
- Increased prostate volume/PSA
- Urinary retention (BPH exacerbation)
- Sleep apnea
- Erythrocytosis
Contraindications to Testosterone Therapy

• Very high risk of adverse outcomes
  – Prostate cancer
  – Breast cancer

• High risk of adverse outcomes
  – Undiagnosed prostate nodule
  – Unexplained PSA elevation
  – BPH with severe urinary retention
  – Erythrocytosis
  – NYHA Class III or IV heart failure
Pre-treatment Screening

- Digital rectal exam
- History of urinary retention (urodynamic studies, bladder US PRN)
- History of sleep apnea symptoms (polysomnography PRN)
- PSA (urology referral if > 4 ng/mL)
- CBC
Treatment Monitoring

• Serum testosterone
  – IM testosterone: midpoint between injections, level near middle of reference range
  – Patch: 3-12 hrs after applying new patch
  – Gel: timing not critical
  – Buccal pellet: immediately before or after new pellet

• Prostate
  – DRE @ 3 months, then annually
  – PSA @ 3 months, then annually
  – Prostate biopsy if PSA > 4 ng/mL, PSA increases by > 1.4 ng/mL in 12 months, or PSA velocity > 0.4 ng/mL/yr

• Red cell mass
  – CBC at 3 months, then annually
  – If Hct > 54%, stop therapy, monitor for return to reference range, then resume therapy at a lower dose
Pituitary Masses
Disorders of the Pituitary with Oversection

- Prolactinoma
- Cushing’s syndrome
- Acromegaly
- Gonadotroph Adenomas
Symptoms of Hyperprolactinemia

Women
More gonads and breast
Hypogonadal
Infertility
Oligomenorrhea
Amenorrhea
Galactorrhea
Mass effect
Headache
Visual defects
Hypopituitarism rare

Men
More mass effect
Hypogonadal
Impotence
Infertility
Mass effects
Headache
Visual defects
Hypopituitarism (rare, but more common than in women)
Hyperprolactinemia – Differential Diagnosis

Physiologic Causes

- Pregnancy
- Nipple stimulation
- Emotional or physical stress
Hyperprolactinemia – Differential Diagnosis

Associated disease states

- HYPOTHYROIDISM
- HYPOTHYROIDISM
- HYPOTHYROIDISM
- Chronic Renal Failure
- Cirrhosis
- Adrenal insufficiency
- Chest wall lesions/Spinal cord lesions
Hyperprolactinemia – Differential Diagnosis

Medications (Prolactin levels usually < 100)

<table>
<thead>
<tr>
<th>Neuroleptics</th>
<th>Monomine-oxidase inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricyclic antidepressants</td>
<td>Opioids</td>
</tr>
<tr>
<td>Cocaine</td>
<td>SSRIs</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>High estrogen</td>
</tr>
<tr>
<td>Verapamil</td>
<td>Methyldopa</td>
</tr>
<tr>
<td>Cimetidine</td>
<td></td>
</tr>
</tbody>
</table>
Hyperprolactinemia – Differential Diagnosis

Primary pituitary disease
- Prolactinoma
- Acromegaly
- Cushing’s syndrome
- Empty sella syndrome
- Lymphocytic hypophysisitis
Prolactinoma

- 40-50% pituitary adenomas
- Rarely increase in size
- Clinical features
  - 18% spontaneous miscarriages, corrected with treatment
  - ↓ BMD 20-25%
  - Gynecomastia
- Laboratory features
  - Serial prolactin levels
  - Macroprolactin
Prolactinoma - Diagnosis

- Prolactin correlates with tumor size
- Rule of 200’s
  - Prolactin level > 200 is almost always a prolactinoma
    - Normal is < 25
- Thorough history and physical exam to consider
- Differential Dx
- Pregnancy test
- Thyroid function studies (TSH and Free T4)
- MRI with contrast or CT scan with coronal cuts
- Formal visual field examination if > 10 mm in size
- Evaluation of remainder of pituitary function, if indicated
Treatment

• Aims: fertility, potency, bones, tumor size
• Prolonged drugs may result in reversal (10-15%)
• Dopamine agonists:
  – Bromocriptine, quinagolide, cabergoline (long-acting, but not for women who desire pregnancy)
  – Side effects differ between drugs
  – Rapid reduction of prolactin levels
  – Tumor shrinkage in 70-90%
Prolactinoma - Treatment

Indication

• Tumor size - Macroadenoma (>10 mm in size)
• 94% of microadenoma remain unchanged at 6 years of follow up

Symptoms

• Asymptomatic microadenoma may be followed by MRI at baseline, 1 year and 2 years
• Serial PRL values
Prolactinoma - Treatment

- Symptomatic patients, Macroadenoma or enlarging microadenoma
  - Medical therapy – Treatment of choice
    - Dopaminergic agonist
      - Bromocriptine
      - Carbergoline
  - Surgical removal (70% cure): Rsvd for med failures
    - Transphenoidal hypophesectomy
    - Complete ablation difficult with large tumor
  - Pituitary irradiation
Cushing’s Syndrome

- 10-15 per million in general population
- Higher prevalence in patients with:
  - Diabetes
  - Obesity
  - Hypertension
  - Osteoporosis

- Peak Incidence in 25 – 40 yo
  - No evidence-based guidelines
Cushing’s Syndrome

- Full-blown syndrome fatal 50% at 5 yr untreated
- May have few typical features
- Usually microadenoma
- Good discriminants:
  - Central obesity
  - Ecchymoses *
  - Plethora *
  - Proximal weakness *
  - Osteopenia/osteoporosis
  - Hypertension
  - WBC > 11.0
  - Purple striae > 1cm wide *
- Other features: myopathy, hirsutism, opportunistic infections, loss of libido (male)
- * = Most specific signs
## Cushing’s Syndrome

### Clinical Characteristics of Cushing Syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity (centripetal)</td>
<td>94%</td>
</tr>
<tr>
<td>Facial plethora</td>
<td>84%</td>
</tr>
<tr>
<td>Hirsutism</td>
<td>82%</td>
</tr>
<tr>
<td>Menstrual disorder</td>
<td>76%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>72%</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>58%</td>
</tr>
<tr>
<td>Back Pain</td>
<td>58%</td>
</tr>
<tr>
<td>Striae</td>
<td>52%</td>
</tr>
<tr>
<td>Acne</td>
<td>40%</td>
</tr>
</tbody>
</table>
Cushing’s Syndrome
Clinical Characteristics of Cushing’s Syndrome

Psychological symptoms 40%
Bruising 36%
Congestive heart failure 22%
Edema 18%
Renal Calculi 16%
Headache 14%
Polyuria/Polydipsia 10%
Hyperpigmentation 6%

Diagnosis is usually delayed because Sx are nonspecific
Laboratory Diagnosis

- 1st step is to determine hypercortisolemia
- Cortisol levels (circadian cycling)
  - AM cortisol may be normal
  - Raised midnight cortisol
- 24-hr urinary free cortisol
  - Not affected by obesity, drugs, medical conditions
  - Need to measure creatinine (ratio unreliable)
  - 4x normal unequivocal, lower uncertain
- Midnight salivary cortisol
  - Raised in medical/psychiatric illness
Laboratory Diagnosis

- Dexamethasone suppression testing
  - Corticotrophs retain some sensitivity to glucocorticoid feedback
    - 0.5mg q 6h for 2 days (low dose)
    - 2mg q 6h for 2 days (high dose) – suppresses in pituitary CS
  - Sensitivity & specificity vary widely

- 2nd step is to determine the source of the hypercortisolemia
Diagnosis

- Inferior petrosal sinus sampling
  - Best test for localising ACTH-dependent Cushing’s syndrome
  - Cushing’s syndrome: petrosal > peripheral ACTH
  - Ectopic ACTH: petrosal = peripheral
  - Diagnostic accuracy better when CRF given (↑ACTH in Cushing’s syndrome)
- MRI of head; if negative then adrenal
- ACTH level
Diagnosis

- 3rd step is to exclude exogenous exposure
- 4th step: exclude physiologic causes

- Do one of the above tests TWICE
- Variability of levels and suboptimal sensitivity & specificity
- Last step: refer
Addison’s Disease

• Primary: Atrophy or destruction of adrenal glands.
• 2ndary: Inadequate secretion of ACTH from pituitary
• Diagnostic tests:
  – Serum electrolytes
  – Blood glucose
  – CBC
  – CT scan of adrenals
  – MRI of adrenals
Addison’s Disease

• Clinical presentation
  – Malaise, fatigue
  – Hyperpigmentation
  – Low Blood Pressure
  – Weight loss
  – N&V
  – Muscle cramps
  – Irregular menses
  – Salt craving

• Treatment
  – Replace:
    • Cortisol
    • Aldosterone
Parathyroid

- **Hyperparathyroid**
  - Overproduction of PTH from glands
    - Most often a tumor
    - Can be due to severe CKD

- **Hypoparathyroid**
  - Only 900 cases per year in U.S.
  - I would not expect any questions on such an uncommon disease
  - Treatment is to restore calcium & mineral balance thru Ca+++ & Vit D supplements
Hyperparathyroid

• Presentation:
  – Bone pain
  – Depression
  – Frequent urination
  – Kidney Stones
  – Nausea
  – Loss of appetite

• Treatment:
  – Locate & remove tumor surgically