Take Home Messages in Endocrinology

Carolyn Becker, MD

Overview

- Diabetes
- Thyroid
- Pituitary
- Adrenal
- Hypoglycemia

Diagnostic Criteria for T2DM

- Diabetes should be diagnosed when A1C is $\geq 6.5\%$.
  - Diagnosis should be confirmed with a repeat A1C test except in symptomatic subjects with plasma glucose levels $>200$ mg/dl.
- Prevention efforts should target patients with A1C of between 5.7 and 6.5%.
  - The risk for diabetes based on levels of glycemia is a continuum; therefore, there is no lower glycemic threshold at which risk clearly begins.
  - The categorical clinical states pre-diabetes, IFG, and IGT fail to capture the continuum of risk and will be phased out of use.

Treatment Goals

<table>
<thead>
<tr>
<th>Treatment Goals</th>
<th>Approximate A1C Lowering ~ A1C Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>1.0-2.0</td>
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<tr>
<td>Sulfonlureas</td>
<td>1.0-2.0</td>
</tr>
<tr>
<td>Repaglinide</td>
<td>1.0-2.0</td>
</tr>
<tr>
<td>Glitazone</td>
<td>0.5-1.4</td>
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<tr>
<td>Exenatide</td>
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<tr>
<td>Sitagliptin</td>
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<tr>
<td>Nateglinide</td>
<td>0.5-1.0</td>
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<td>Acarbose, Miglitol</td>
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<tr>
<td>Pramlintide</td>
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</table>
Patient with A1C 10% on maximum metformin & glipizide

a) Pioglitazone  
b) Exenatide  
c) Sitagliptin  
(d) Bedtime basal insulin (e.g. NPH, glargine, detemir)

ADVANCE, ACCORD, VADT

What have we learned?

• High-risk patients with diabetes can be safely targeted to an A1c of 7.0-7.5%  
• No evidence that a specific glucose-lowering regimen is better or worse  
• CV benefit of lower glucose levels, if any, accrues over years  
• Pts earlier in their disease derive benefit  
• Significant hypoglycemia may be associated with CV risk

AACE/ADA Recommended Target Glucose Levels in ICU Patients

• ICU setting:
  – Starting threshold of no higher than 180 mg/dL  
  – Once IV insulin is started, the glucose level should be maintained between 140 and 180 mg/dL  
  – Lower glucose targets (110-140 mg/dL) may be appropriate in selected patients  
  – Targets <110 mg/dL or >180 mg/dL are not recommended

<table>
<thead>
<tr>
<th>Not recommended</th>
<th>Acceptable 110-140</th>
<th>Recommended 100-150</th>
<th>Not recommended</th>
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Summary of Major Diabetes-Hypertension Studies: ALLHAT, ACCOMPLISH, UKPDS, HOT and HOPE

• Lower BP prolongs life  
• Goal < 130/80 mmHg  
• First Line: ARB or ACEI  
• Second Line: CCB, or Thiazides  
• Third Line: B-blockers  
• Most patients require combination therapy

Patient with Symptoms of Hyperthyroidism

• Weight loss, palpitations, nervousness, heat intolerance, sweating for 3 weeks  
• TSH <0.01 (0.5-5.0)  
• Free T4 3.4 (0.8-1.8)

What would you do now?

a) Check thyroid antibody levels  
b) Refer for thyroid ultrasound  
(c) Refer for thyroid (scan and) uptake  
d) Start methimazole
Common Causes of Thyrotoxicosis

Overproduction of Thyroid Hormone
- Grave's disease
- Toxic nodule
- Toxic multinodular goiter

Leakage of Thyroid Hormone
- Thyroiditis
  - Painless, e.g. postpartum
  - Painful

High $^{131}$I Uptake

Low $^{131}$I Uptake

Treatment of Hyperthyroidism

High Uptake
(Grave's, toxic nodules)
1. Radioactive Iodine
2. Methimazole or PTU
3. Surgery

Low Uptake
(thyroiditis)
- Resolves on its own
  - NSAIDs if pain

Thyroid Nodule on Exam or Incidentally on Imaging

Initial Diagnostic Evaluation of Nodular Thyroid Disease

FIRST STEP
TSH

NOT INDICATED
Radionucleotide scans
Antithyroid antibodies
$T_4$, FT$_4$, T$_3$
CT or MRI

Evaluation of Thyroid Nodules

Check TSH

Low
Radionucleotide Scan

Normal or High
Fine Needle Aspiration
(nodules > 1 cm)

Evaluation of Pituitary Lesions

- Mass effects
- Pituitary hyperfunction
- Pituitary hypofunction
Screening for Pituitary Hormone Excess

- PRL
- GH
- ACTH
- TSH
- LH/FSH

Screening for Pituitary Hormone Excess

- PRL *
- GH - IGF-1
- ACTH - 24 hr UFC or 1 mg O/N DST
- TSH - TSH, T4/T3
- [LH/FSH - LH, FSH, free a-subunit, E2/T]

Evaluation for Hypopituitarism I

- Corticotroph (ACTH)
  - fasting a.m. cortisol
  - Cortrosyn stimulation test
  - insulin tolerance test
- Thyrotroph (TSH)
  - T4 (and TSH)
- Gonadotroph (FSH, LH)
  - premenopausal woman - menstrual history
  - postmenopausal woman - FSH
  - men - testosterone + LH, sperm count

Evaluation for Hypopituitarism II

- Somatotroph (GH)
  - Provocative tests:
    - Insulin tolerance test, arginine/GHRH, L-dopa, glucagon, vasopressin, exercise
  - Other:
    - IGF-1
    - IGFBP-3

Primary Treatments

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<th>Mass &lt; 1 cm, No hormone excess</th>
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<td></td>
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Primary Treatments

Observation
- Mass < 1 cm, No hormone excess

Surgery
- Hormone excess (except PRL)
- Mass effects
- Apoplexy
- Diagnosis
- Progression
- Intolerance
- Prior TX

Medical
- High Prolactin
Therapy
- Excess growth hormone

Medical
- High Prolactin
Therapy
- High growth hormone

Radiation
- Refractory GH excess

Hormone Replacement Therapy

<table>
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<tr>
<th>Deficiency</th>
<th>Replacement</th>
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<tbody>
<tr>
<td>ACTH</td>
<td>Hydrocortisone/prednisone</td>
</tr>
<tr>
<td>TSH</td>
<td>Levothyroxine</td>
</tr>
<tr>
<td>FSH, LH</td>
<td>Men-testosterone</td>
</tr>
<tr>
<td></td>
<td>Women-estrogen &amp; progesterone</td>
</tr>
<tr>
<td>GH</td>
<td>hGH</td>
</tr>
<tr>
<td>Vasopressin</td>
<td>ddAVP</td>
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Causes of Hyperprolactinemia

I. Physiologic
- Menstrual cycle
- Pregnancy
- Nursing
- Nipple stimulation
- Stress

II. Pharmacologic
- Dopamine antagonists
- Phenothiazines
- Haloperidol
- Risperidone
- Metoclopramide
- Domperidone
- Amipryline
- Antihypertensives
- Methyldopa
- Reserpine
- Verapamil
- Clonidine

III. Pathophysiologic
- Primary hypothyroidism
- Primary hyperplasia
- Cystic renal failure
- Chromosomal defects
- Polycystic ovarian syndrome
- Idiopathic
- Macroprolactinemia
- Hypothalamic/pituitary lesions
- Macroadenomas
- Other medications?
- Birth control pills?
- Check TSH
- Stalk compression?

Pheochromocytoma:
Consider in the Evaluation of...
- HYPERTENSION
- Severe pressor response to anesthesia
- Family history of pheo or MEN
- Adrenal “incidentalomas”

Pheochromocytoma
Frequency of Symptoms

- Headache 43-80%
- Sweating 37-71%
- Palpitations 44-71%

- Pallor 42-44%
- Nausea 10-42%
- Tremors 30-38%
Endocrine Evaluation for Secondary Hypertension

1. Pheochromocytoma
   - Plasma metanephrines
   - 24 h urine for metanephrines, free catechols

2. Hyperaldosteronism
   - Fasting AM PAC & PRA → PAC/PRA > 20 suggests primary hyperaldosteronism

3. Cushing’s
   - 24 h urine free cortisol or 1 mg O/N dexamethasone suppression test

Adrenal Insufficiency

- Non-specific symptoms
  - Weakness
  - Fatigue
  - Anorexia/weight loss
  - GI symptoms
  - Hypoglycemia

- Other symptoms (if mineralocorticoid insufficiency)
  - Hypotension
  - Postural dizziness

ACTH Stimulation Test

- A serum cortisol of >18 µg/dL → normal adrenal reserve
- A subnormal response → adrenal insufficiency
  - Primary: normal or high ACTH
  - Secondary: Low ACTH

Treatment

- Glucocorticoid replacement
  - For 1° and 2° adrenal insufficiency
- Mineralocorticoid replacement
  - Only for 1° adrenal insufficiency
  - In 2° (pituitary disease) aldosterone secretion is maintained by the renin-angiotensin system and serum K+

Non-Diabetic Patient with Low Glucose & Symptoms

Must get labs to evaluate when the glucose is LOW
- Glucose
- Insulin
- C-peptide
- Sulfonylurea (SFU) screen
- Others

C-peptide Secreted with Insulin

- Proinsulin
  - B Chain
  - C-peptide
  - A Chain

- Insulin
  - A Chain
  - C-peptide

- C-peptide
  - C-peptide
  - B Chain
When Glucose is Low (<50)

- **INSULIN HIGH**
  - C-peptide high
  - SFU negative → insulinoma
  - SFU positive → sulfonylurea effect
  - C-peptide low → surreptitious insulin use

- **INSULIN LOW**
  - Liver, heart, or kidney failure; sepsis, ETOH, Cortisol or GH deficiency, nonpancreatic tumors, inborn errors of metabolism, inanition