The Endocrine System

- Disease of the Pituitary Gland
- Diseases of the Thyroid
- Disease of the Adrenal Glands
- Diabetes Mellitus
- Lipid Disorders

Endocrine System

Maria Alonso, CDE, PA-C
Pituitary Anatomy

- Small pea-sized gland at the base of brain
- Located in the “Sella Turcica”
- Functions as “The Master Gland”
- Attached below hypothalamus by stalk
- Large anterior lobe (adenohypophysis)
- Smaller posterior lobe (neurohypophysis)
- The optic chiasm lies directly above
- Supplied by internal carotid artery

Pituitary Gland

**PITUITARY ANATOMY**

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- Located in the “Sella Turcica”
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- Attached below hypothalamus by stalk
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Quick Review: Hypothalamic Pituitary Axis

- Neurosecretory cells send messages from brain to hypothalamus
- Hypothalamus sends chemical hormones to the pituitary gland
- Pituitary gland secretes hormones to the thyroid gland, adrenal glands, and gonads
- Negative feedback mechanism finishes the loop

Quick Review

**Hypothalamus**

GnRH, GH, SS, TRH, DA, CRH

**Anterior Pituitary**

ACTH, Prolactin, TSH, GH, FSH/LH

**Hypothalamus**

GnRH, GHRH, SS, TRH, DA, CRH

**Posterior Pituitary**

Oxytocin, ADH

Quick Review: Hypothalamic Pituitary Axis

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# Pituitary Disorders

- **Hypopituitarism – Congenital causes**
  - Hypothalamic gene defects
  - Pituitary gene defects
  - Hormone receptor gene defects
  - Anencephaly, neural tube defect
  - Pituitary aplasia, usually fatal at birth
  - Kallmann syndrome: X-recessive GnRH defect with hypogonadism, delayed puberty, osteoporosis, anosmia

- **Hypopituitarism- Acquired causes**
  - Tumors are the most common cause in adults
  - Irradiation for other cranial tumors
  - Vascular: bleed, infarct, Sheehan’s
  - Inflammatory: sarcoidosis, TB
  - Metabolic: Fe deposits/hemochromatosis, amyloidosis, illness, malnutrition

**Empty Sella Syndrome:**
- Unable to see gland on imaging due to any of above. May have shrunk or flattened.

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# Hyperpituitarism

## Acquired Causes

- Tumors are the most common cause in adults
- Irradiation for other cranial tumors
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**Empty Sella Syndrome:**
- Unable to see gland on imaging due to any of above. May have shrunk or flattened.
Pituitary Tumors

- Microadenomas (<10 mm)
- Macroadenomas (>10mm)
- Rarely malignant
- Locally invasive
  destroy hormone producing cells
  compresses gland or hypothalamus

Types of Adenomas

- Prolactinoma prolactin/hypogonadism and galactorrhea
  (25-40%) (Lactotroph)
- Null cell no active hormone (10-25%)
- Somatotroph GH/acromegaly and gigantism (10-15%)
- Corticotroph ACTH/ Cushing’s (10-15%)
- Gonadotroph FSH/LH (15-20%)
- Thyrotroph TSH/ hyperthyroidism (1%)

Clinical Manifestations

- Mass effect
  headaches
  bitemporal hemianopsia
  Diplopia
- Symptoms based on hormone involved
Treatments
- Medical therapy: decreases hormone and tumor
dopamine agonist - Bromocriptine replace hormones (thyroid/adrenal)
- Surgical excision
  Transsphenoidal
  Gamma Knife/ Stereotactic Non-invasive Radio Surgery

Prolactinoma 25-40%
- Occurs M/C 20-50 yo
- Hyperprolactinemia
- Hypogonadism
  negative effect on GnRH reduction in LH and FSH
- Females - galactorrhea, oligomenorrhea, amenorrhea
- Males - headache, visual disturbance, impotence

Prolactin
- Dopamine inhibits prolactin secretion
- Estrogen, TRH, and GHRH positively effect prolactin secretion
- Excess can be caused by lactation, tumors, drugs, hypothyroidism, hypothalamic dysfunction
### Prolactinoma
- **Work up:**
  - BHCG, prolactin level, TSH
  - CT/MRI of the Brain
- **DX:**
  - excessive exercise
  - Hx chest wall surgery
  - chest trauma
  - renal failure
  - cirrhosis
- **TX:**
  - dopamine agonist - Bromocriptine
  - Surgical excision

### Excessive Growth Hormone Secretion
- **Acromegaly** – adults
  - After epiphyseal closure
- **Gigantism** – children
  - Before epiphyseal closure (excessive height)

### Excessive Growth Hormone
- **98% cases adenomas is the cause**
- **Usually mixed cell tumors**
- **Increase risk** - DM, HTN, CAD
Physical Manifestations

- Enlargement of extremities
  - hands doughy / large hands
- Coarse facial features
  - prominent mandible, brow, nose, lips, tongue
- Coarse, oily, thick skin
- Organomegaly

Prominent jaw/ Brow

Public domain available at:
http://commons.wikimedia.org/wiki/File:Acromegaly_facial_features.JPEG

Hands doughy / Large hands

Public domain available at:
http://commons.wikimedia.org/wiki/File:Acromegaly_hands.jpg
### Related Conditions
- **Musculoskeletal**
  - Hypertrophy of joint cartilage and synovial tissue
  - Carpal tunnel syndrome
- **Cardiac**
  - Left ventricular hypertrophy
  - Diastolic dysfunction
- **Metabolic**
  - Insulin resistance, glucose intolerance, DM

### Related Conditions
- **Musculoskeletal**
- **Cardiac**
- **Metabolic**
Labs/ Diagnostic Tests
- Labs
  - GH and IGF-1: 5x normal in acromegaly
  - Prolactin, glucose
  - Liver enzymes, Blood urea nitrogen (BUN)
  - Calcium
  - Serum FT4 and TSH
  - Glucose Suppression test = Diagnose
  - Glucose should suppress GH, in acromegaly it does not
- Imaging: MRI

Treatment
- Surgical (50% success w/macroadenomas)
- Radiotherapy
- Medical Therapy
  - Dopamine Agonist - (brocriptine)
  - GH Receptor Antagonist - (Pegvisomant)

Dwarfism
Less than 4'10" is height
- Disproportionate - skeletal dysplasia
  - Achondroplasia
  - Short-trunk dwarf
- Proportionate - medical or genetic conditions
  - Growth hormone deficiency

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Achondroplasia

- Mutations in the FGFR3 gene
- Autosomal dominant
- Short stature < 4'10"
- Overweight
- Short limbs
- Prominent brow
- Midfacial hypoplasia

Growth Hormone Deficiency

- Insufficient GHRH from hypothalamus
- Insufficient production of GH by pituitary
- Genetic Mutation- GHRHR, GH1
- Acquired- tumors/irradiation
- Idiopathic- M/C
- Genetic disorders- Turner, Noonan, PWS
- SGA

Stimulation Test

- Gold Standard Insulin Tolerance Test (ITT), then another agent clonidine, L-Dopa, glucagon, arginine or GHRH should cause an increase in GH levels
- Stimulation test measures the level of growth hormone (GH) in the blood after stimulation
- The test measures the ability of the pituitary gland to release GH under stimulation
**GROWTH HORMONE REPLACEMENT**

- Somatotropin given as daily SQ injection until bone fusion (Bone Age)
- May not need further treatment as adults, consider repeating stimulation test
- Side effects include headaches, carpal tunnel, SKFE, arthralgias, and edema
- Monitor for scoliosis

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**Diabetes Insipidus**

- Vasopressin (ADH): Anti-Diuretic Hormone
- Synthesized in hypothalamus: stored and released from posterior pituitary
- Two Main forms:
  - Central (neurogenic): deficiency of ADH, low secretion, most commonly seen
  - Nephrogenic: resistance to ADH

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**Central Diabetes Insipidus = LOW ADH**

Disruption of the normal production, storage and release of ADH

- **Primary**: No organic lesion, autoimmune
- **Secondary**: damage to hypothalamus or pituitary stalk
  - Trauma, tumor or illness
Nephrogenic DI = High ADH

- Caused by a defect in the kidney tubules interferes with water reabsorption, therefore do not respond to ADH
- Causes: genetic disorder (seen shortly after birth), CKD, or drugs (lithium)

Other Rare Causes

- Congenital Nephrogenic DI: defective expression of renal vasopressin receptors
  - Familial X-linked trait
- DI of Pregnancy: Last trimester
  - Oligohydramnios
  - Pre-eclampsia
  - Hepatic dysfunction

Clinical Features

- Polydipsia
- Polyuria (5-15L daily)
- Colorless urine (dilute)
- Dehydration and electrolyte imbalance
Diagnosis

- Fluid deprivation test
- Excessive intake of fluid (primary polydipsia)
- Defect in ADH production
- Defect in the kidneys' response to ADH
- Desmopressin stimulation test
- U/A
- Consider MRI
- Diff Dx: psychogenic polydipsia

Treatment of DI

- Central DI: Desmopressin (DDAVP), Carbamazepine
- Nephrogenic: Thiazide diuretics, indomethacin, amiloride (combo)

HYPOTHALAMIC-PITUITARY - THYROID AXIS

Public domain available at: http://commons.wikimedia.org/wiki/File:Thyroid_hormone_feedback.png
Thyroid Gland

- Hypothyroidism
- Hyperthyroidism

THYROID ANATOMY

- Largest endocrine gland in body
- Two lobes connected by "isthmus"
- Protected by thyroid cartilage

FUNCTION

- T4 is the main hormone secreted
- Only 20% of T3 is secreted from thyroid
- Iodine + tyrosine makes the T3 and T4
- T3 is 3-4 times as active as T4
- T3 and T4 exist as free and protein bound
**THYROID IMAGING**
- Ultrasound (U/S) is useful to identify nodules
- U/S guided Fine Needle Aspiration for Dx
- Nuclear scans with radioactive iodine-123 or technetium-99m
- Radioactive iodine uptake test (RAIU) evaluates function and helps determine amt. RAI for tx

**Diseases of the Thyroid Gland**
- Hyperthyroidism
  - Graves’ Disease
  - Thyroid storm
- Hypothyroidism
  - Hashimoto’s thyroiditis
- Thyroiditis
- Neoplastic Disease

**Hyperthyroidism**
- Thyrotoxicosis is the clinical syndrome
- More common in women, 2% of society
- Most common cause is Graves’ Disease
- Older patients do not show classic signs
Hyperthyroidism:
- Other causes:
  - Toxic nodules
  - Thyroiditis
  - Iodine induced
  - Exogenous hormone

Hyperthyroidism in Pregnancy
- Graves'- most frequent cause
- BHCG-a stimulator of thyroid gland
- Decrease TSH & elevated FT4
- Neonatal mortality 6%

Graves’ Disease
- Women > Men (8:1)
- Onset 20-40 yrs.
- Autoimmune disorder
- Thyroid stimulating immunoglobulin antibody
- Association with other autoimmune disorders
  - SLE, pernicious anemia, RA, DM type 1, MG
Graves’ Disease

- Affects TSH receptors
- TSH secretion
- Stimulate glandular growth
- Diffuse, symmetric enlargement/goiter
- Nontender
- Thyroid cancer can coincide w/ Graves’

Signs Specific to Graves’

- Ophthalmopathy: Exophthalmos
- Pretibial myxedema
- Thyroid bruit

EXOPHTHALMOS

- Mucopolysaccharides/lymphocytes
- Causes protrusion of globe
- Look of astonishment
- "Stellwag's sign" - infrequent blinking
- Upper lid lag on downward gaze
- Each eye can be affected differently
- May see weak upward gaze, diplopia
- Excess tearing, photophobia, gritty feel
<table>
<thead>
<tr>
<th>Thyrotoxicosis Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Nervousness, insomnia, irritability</td>
</tr>
<tr>
<td>- Hand tremor, hyperactivity, tremulousness</td>
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<tr>
<td>- Excessive sweating, heat intolerance</td>
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<tr>
<td>- Wt. Loss (despite appetite)</td>
</tr>
<tr>
<td>- Diarrhea, freq. defecation</td>
</tr>
<tr>
<td>- Palpitations (tachyarrhythmias)</td>
</tr>
<tr>
<td>- Muscle weakness</td>
</tr>
<tr>
<td>- Menstrual irregularities</td>
</tr>
</tbody>
</table>
Diagnosis of Graves’

- T3 and free T4 levels elevated
- TSH level extremely low or undetectable
- Anti-thyroglobulin antibodies (TGA)
- Anti-thyroid peroxidase antibodies (TPO)
- 24 hr RAIU given orally is increased (T4 can be normal = T3 toxicosis)

Don’t forget false positives!

- Drugs
- Auto immunity
- Acute illness
- High estrogen states
- Psychiatric illness
- AIDS
- Acute use steroids

Treatment Types

- Antithyroid drugs
- Ablation
- Beta blockers — Used to treat symptoms
Antithyroid Drugs
block conversion of T4 to T3

- **Propylthiouracil (PTU)**
  - taken three x daily
  - used in severe cases, pregnancy and breastfeeding
- **Methimazole (Tapazole)**
  - taken daily, slower to decrease T3
- **Levels checked 4 weeks after TX started**
- **Side effects:**
  - Agranulocytosis, thrombocytopenia, anemia, hepatitis, dermatitis, vasculitis, pneumonitis, hypoglycemia, urticaria,

Radioiodine 131 (RAI)

- Used in older patients
- Prior PTU/MMI reaction or failure, or poor compliance.
- Not to be used in pregnancy/nursing
- Stop antithyroid meds 3-5 days prior
- RAIU used to determine dosing
- Improvement seen after 4-6 weeks
- Almost 80% are cured with one dose
- At least 50% will become hypothyroid in a year

Surgical- Thyroidectomy

- Indicated for large obstructing glands, malignant nodules, or pregnancy
- Must be euthyroid before surgery
- Potassium iodide may be given prior
- **Complications:**
  - recurrent laryngeal nerve damage
  - bleeding
  - hypoparathyroidism
### Keys to Choosing Tx

- Non-pregnant Graves’ patients
- Methimazole + Beta blocker
- RAI
- Preg + Graves’ = PTU (“P’s”)
- RAI: Elderly with Graves’, solitary toxic nodule

### Thyroid Storm

- Rare complication of thyrotoxicosis
- Precipitating factor:
  - Stressful illness
  - DKA
  - Severe trauma
  - Thyroid surgery
  - Infection
  - Childbirth
- High mortality rate:
  - 20% pts. (coma or die)

### Clinical Manifestations & Tx

- Marked delirium
- Severe tachycardia
- Vomiting
- Diarrhea
- Dehydration
- High fever
- Supportive therapy:
  - IVF, cooling blankets, glucose
  - PTU q 6 H
  - Methimazole q 1H
  - Beta blockers
  - Iodine
  - Hydrocortisone
### Hypothyroidism
- 0.8-1.0% population
- 3 x more common women
- Onset adulthood and insidious
- Primary (90-95%)
- Autoimmune associated with other non-endocrine abnormalities
  - pernicious anemia, RA, SLE, Sjogren’s, and Myasthenia Gravis.

### Primary Hypothyroidism
**Auto immune**
- Hashimoto’s thyroiditis
- End-stage Graves’ Disease

### Primary Hypothyroidism
**Iatrogenic**
- Radio Iodine therapy
  - Gland shrinks
- Thyroidectomy
- Medications
  - Lithium
  - Amiodorone
  - Interferon
**Other Causes**

- **Infiltrative Process**
  - Amyloidosis
  - Lymphoma
  - Scleroderma

- **Congenital Hypothyroidism**
  defects in enzymes

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**Secondary Hypothyroidism**

Failure of the pituitary gland or hypothalamus

- Neoplasm
- Surgery
- Sheehan’s syndrome

Cause deficiency in TSH or TRH → low TSH, low FT4

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**Hashimoto’s Thyroiditis**

- Chronic Lymphocyte Thyroiditis
- Most prevalent form of thyroid autoimmune disease
- Genetic propensity → HLA-B8
- Hypothyroidism initial manifestation
- Hyperthyroidism < 5% patients – self limiting or long standing
- Hashitoxicosis, transient hyperthyroidism (severe)
- Graves’ → TSI (thyroid stimulating immunoglobulins)
- Hashimotos → TSH receptor blocking antibodies
### Myxedma Coma
- Life-threatening hypothyroidism
- Obturation, CO2 retention, coma
- Altered mental status is hallmark
- Can be precipitated by sepsis
- High mortality, treat in ICU
- Thyroxine bolus 300mcg, then 100mcg daily
- Hydrocortisone 100mg IV bolus

### Hypo: Signs
- Dry skin
- Coarse hair
- Thickened puffy features
- Non-pitting edema
- Carpal tunnel syndrome
- Slow relaxation of DTR
- Loss lateral portions of eyebrows
- Bradycardia
- Goiter (Hashimoto: rubbery, non-tender, possibly nodular)

### Hypo: Symptoms
- Fatigue, lethargy, weakness
- Heavy menstrual periods (menorrhagia)
- Slight weight gain
- Cold intolerance
- Constipation
- Slow mentation, inability to concentrate
- Depression
- Diminished hearing
### Hypothyroidism Lab Values
- **Primary:** High TSH, Low FT4
- **Secondary:** Low TSH or normal, Low FT4
- **Antibody titers:** present
- **Anti-thyroglobulin antibodies (TGA)**
- **Anti-thyroid peroxidase antibodies (TPO)**
- **T3 not a good test**
- **Subclinical Hypothyroidism:** mild elevated or high normal TSH, serum FT4 normal

### Hypothyroidism Treatment
- Levothyroxine (T4) Synthroid
- Dose ranges 25mcg to 200 mcg daily
- The T4 is converted into T3
- Start lower in elderly
- Adjust dose every 4-6 weeks
- Once stable, check levels twice yearly

### Symptoms Key Words
<table>
<thead>
<tr>
<th>Hyper</th>
<th>Hypo</th>
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<tbody>
<tr>
<td>Increase appetite</td>
<td>Fatigue/Lethargy</td>
</tr>
<tr>
<td>Nervous</td>
<td>Depressed</td>
</tr>
<tr>
<td>Loose stools</td>
<td>Constipation</td>
</tr>
<tr>
<td>Irritability</td>
<td>Weakness</td>
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Thyroiditis
- Acute suppurative (rare)
- Subacute painful (Dequervain's)
- Drug-induced (Amiodarone)
- Chronic lymphocytic (Hashimoto's)
- Fibrous thyroiditis (Riedel's)

Nontoxic Goiter
- Thyroid levels are usually normal
- Slowly enlarging thyroid gland over years
- 5% of US population
- Women > men
- Usually asymptomatic unless impinging
- Endemic in iodine deficient areas

Solitary Thyroid Nodules
- Common in population, women > men
- Nodule must be over 1cm to be palpated
- Thyroid adenoma most common benign nodule
- Nodule of adenoma is encapsulated
  - Follicular adenoma is most common
  - Hürthle (oxyphil)
  - Papillary adenoma are very rare
- Bleeding into nodule causes pain, enlargement
- Most nodules are benign (95%)
Solitary Nodule Work Up
- History: Head or neck irradiation
- Physical exam: thyroid, lymph, systemic
- Tests: labs, US, RAIU, FNA
- Capsular invasion & vessel infiltration are hallmarks of malignancy
- Nodules that concentrate iodine are “hot”, those that do not are “cold”
- Solitary nodules rarely cause extension or pressure symptoms

Thyroid Cancer
- Rapid growing
- Painless
- Single hard lesion
- More common in women 3:1
- Worse in men
- 9% of thyroid cancers are fatal

Thyroid Cancer Types
- Papillary most common, least aggressive
- Follicular type often metastasizes
- Anaplastic type (bad!) mainly >60 yo, least common
- Medullary type- C cells, elevated calcitonin, found with MEN syndrome
- Thyroid lymphoma seen in Hashimoto’s
Treatment of Thyroid Cancer

- Total vs near total thyroidectomy
- Lymph node dissection if needed
- Radiation therapy
- Radioactive iodine therapy
- Chemotherapy as an adjunct
- T4 replacement will be needed

Parathyroid gland

- Hypoparathyroidism
- Hyperparathyroidism

Review PTH

- Increase osteoclastic activity in bone → Ca⁺⁺ into circulation
- Increase renal tubular reabsorption of Ca⁺⁺
- Inhibits absorption of phosphate and bicarb by renal tubule
- Synthesis 1,25 dihydroxycholecalciferol by kidney (active form of Vit.D)

Parathyroid gland

1. Hypoparathyroidism
2. Hyperparathyroidism
Hypoparathyroidism
- Most commonly seen following thyroidectomy, surgical removal parathyroid adenoma.
- Di George's syndrome.
- Congenital cardiac anomalies.
- Damage heavy metals such as copper, Wilson's disease, or iron (hemochromatosis, transfusion hemosiderosis).
- Granulomas.
- Riedel's thyroiditis.
- Magnesium deficiency (malabsorption chronic ETOH).
- Pseudohypoparathyroidism.

Clinical Features S&S
- Cardiac arrhythmias, prolong QT interval.
- Rickets, osteomalacia.
- Neuromuscular irritability.
  - Circumoral/fingers, toes numbness, tingling.
  - Tetany: hyperactive DTR, Chovostek's Sign, Trousselau's sign.
- Cataracts.
- Nails – thin, brittle.
- Skin – dry, scaly.
- Loss hair (eyebrows).
- Defective teeth (childhood).

Think Hypocalcemia!
- Chovostek's sign:
  - Tapping facial nerve elicits contraction of facial muscles.
- Trousselau's sign:
  - Inflating BP cuff to pressure higher systolic BP x 3 minutes to elicit carpal spasms.
Labs and Treatment

Labs
- Low Calcium
- Low PTH
- High phosphate
- Alkaline phosphatase normal

Treatment
- IV calcium gluconate severe
- Calcium & Vit D maintenance

Hyperparathyroidism

- PRIMARY
- SECONDARY

Primary Hyperparathyroidism

- High PTH, High Ca⁺
- Excessive secretion of PTH by one or more glands
- Women 3x more common
- Pt's > 50 yo
- Single parathyroid adenoma (80%)
- Hyperplasia (20%)
- Carcinoma (<1%)
### Secondary Hyperparathyroidism

- **High** PTH, **Low** or **Normal** Ca²⁺
  - Chronic Renal Failure
  - Vitamin D deficiency

### Signs and Symptoms

- **Bones**
- **Stones**
- **Groans**
- **Psychiatric overtones**
- **Other signs**

### Bones

- Bone aches
- Arthralgia
- Pathologic fx’s –
- Osteitis fibrosa cystica
  - “brown tumors” or cysts of the jaw
<table>
<thead>
<tr>
<th>Stones (urinary tract manifestations)</th>
<th>Groans</th>
<th>Psychiatric Overtones</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Renal stones</td>
<td>■ Muscle pain</td>
<td>■ Depression</td>
</tr>
<tr>
<td>■ Nephrocalcinosis</td>
<td>■ Weakness</td>
<td>■ Fatigue</td>
</tr>
<tr>
<td>■ Polydipsia</td>
<td>■ Pancreatitis</td>
<td>■ Anorexia</td>
</tr>
<tr>
<td>■ Polyuria</td>
<td>■ PUD</td>
<td>■ Sleep disturbance</td>
</tr>
<tr>
<td>■ Hypercalcemia induced nephrogenic DI</td>
<td>■ Gout</td>
<td>■ Anxiety</td>
</tr>
<tr>
<td></td>
<td>■ Constipation</td>
<td>■ Lethargy</td>
</tr>
</tbody>
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Other signs

- Shortened QT interval (EKG)
- Decreased DTR

Laboratory

- Elevated PTH, Ca++ (confirms diagnosis)
- Ca++ > 10.5 mg/dL, phosphate < 2.5 mg/dL
- Hypercalciuria, elevated Alkaline Phosphatase (bone disease)
- The best immunoradiometric assay

Treatment

- Surgery
- Medical
  - IV hydration
  - Bisphosphonates
  - Furosemide
AVOID:
- Large doses of……
  Vit A, Vit D and Calcium
  (Antacids/ supplements/additives)
- Thiazide diuretics

Adrenal Glands
- Cushing’s syndrome
- Corticoadrenal insufficiency
- Neoplastic Disease

Adrenal Hormones
- Glucocorticoids = Cortisol
- Mineralcorticoids = Aldosterone
- Androgens: precursors of sex steroids
- Catecholamines: epinephrine and norepinephrine
**Glucocorticoids = Cortisol**
- Help body respond to stress
- Maintain BP
- CV function
- Slow immune system inflammatory response
- Maintain levels of glucose
- Regulate protein/fat/carbohydrate metabolism

**Mineralcorticoids = Aldosterone**
- Maintains blood pressure
- Maintains water and salt balance
- Help kidneys retain Na⁺, excrete K⁺

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**ACTH**
- Hypothalamus
- Pituitary Gland
- Adrenal Cortex
- Glucocorticoids

Public domain available at:
http://commons.wikimedia.org/wiki/File:ACTH_Negative_Feedback.svg

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(becoming Rutgers July 1, 2013)
**ACTH**
- Adrenocorticotropic hormone
- Hypothalamus →CRH→ pituitary
- Pituitary → ACTH
- ACTH stimulates adrenal cortex → cortisol
- Excess ACTH → adrenal hyperplasia
- Deficiency ACTH → adrenal atrophy
- Cortisol inhibits CRH & ACTH secretion

**Cushing’s Disease**

**Excess ACTH**
- Cushing’s disease (ACTH excess) is caused by ACTH secreting pituitary microadenoma
- Cushing’s syndrome (cortisol excess) is the effects of excess cortisol on the body
- Women affected 8 times more often
- Cushing’s disease accounts for 70% of Cushing’s syndrome

**Causes**
- Iatrogenic Cushing’s Syndrome (most common cause)
- ACTH secreting adenoma of pituitary = Cushing’s Disease (43%) (second most common cause)
- Adrenal Adenoma and Carcinoma (10-15%)
- Ectopic ACTH (10-15%)
### Cushing’s Disease

- Central obesity
- Hirsutism
- Moon face
- “buffalo hump”
- Purple striae
- Lanugo hair
- Acne
- Easy bruising
- Supraclavicular fat pads
- Protuberant abdomen
- Thin extremities
- HTN
- Increase infections

### How to Diagnose Cushings Disease?

1. **Initial screening**
   - Low dose Dexamethasone suppression test
   - 24 hour free urinary cortisol level

### What is my source of ACTH?

- High dose Dexamethasone Suppression test
  - > 50% suppression cortisol → pituitary
    - MRI of pituitary
  - < 50% suppression cortisol → ectopic ACTH tumor
    - CT of appropriate region
Ectopic ACTH producers
- Small cell carcinoma (lung) "Oat cell"
- Thyroid, thymomas
- Pancreatic islet cell

Treatment of Cushing’s
- Iatrogenic Cushing’s: Taper steroids
- Pituitary Cushing’s: transphenoidal removal of pituitary adenoma
- Adrenal adenoma or carcinoma: adrenalectomy

Corticoadrenal Insufficiency
"Addison’s disease"

[Image of adrenal gland]
### Causes of Destruction or Dysfunction of Adrenal Cortices

<table>
<thead>
<tr>
<th>Primary (ACTH independent)</th>
<th>Secondary (ACTH dependent)</th>
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<tr>
<td>Autoimmune</td>
<td>Steroids</td>
</tr>
<tr>
<td>Adrenalectomy</td>
<td>Hypopituitarism</td>
</tr>
<tr>
<td>Infection (TB/fungal)</td>
<td>Trauma</td>
</tr>
<tr>
<td>Bleed</td>
<td>ACTH deficiency</td>
</tr>
<tr>
<td>Metastatic</td>
<td></td>
</tr>
<tr>
<td>Congenital</td>
<td></td>
</tr>
</tbody>
</table>

### Corticoadrenal Insufficiency “Addison’s disease”

- Autoimmune destruction: most common cause Addison’s disease in 80% spontaneous cases
- Infectious diseases – tuberculosis: most common cause worldwide
- Iatrogenic: B/L adrenalectomy
- Metastatic
- Secondary adrenal insufficiency: abrupt cessation of exogenous steroids
  - Pituitary failure

### Clinical Features

- GI symptoms: anorexia, N/V, vague abdominal pain, wt. loss
- Mental: lethargy, confusion, psychosis
- Hypoglycemia
- Hypotension (orthostatic)
- Hyperpigmentation – knuckles, elbows, knees, post. neck, palmar creases, nail beds (primary insufficiency)
- Other: irregular or absent menses
Diagnostic Labs

- **Serum Na⁺ low** (90%)
- **Serum K⁺ high** (65% primary disease)
- Fasting glucose low
- Low levels of AM cortisol (<3 mcg/dL), high ACTH (> 200 mg/dL) = diagnostic
- Low ACTH = secondary
- Eosinophilia, neutropenia, lymphocytosis

Cosyntropin test (stimulation)

- Give ACTH (cosyntropin - parenterally)
- Measure serum cortisol 30-60 min
- Normal rise to at least 20 mcg/dL
- Less than rise of 20 mcg/dL – suspicious for adrenal insufficiency

Treatment

- **Hydrocortisone** - glucocorticoid
  - Prednisone 20-40mg po QD
  - Hydrocortisone 50-100mg q6hr IV (*stress situations*)
- **Fludrocortisone** - mineralocorticoid
  - Florinef 0.1-0.2mg po QD
  - Ensure adequate salt intake

Hydrocortisone – glucocorticoid
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- Florinef 0.1-0.2mg po QD
- Ensure adequate salt intake
**Pheochromocytoma**
- Rare cause of HTN, age 40-60 onset
- Most are due to unilateral medullary tumor
- Bilateral type tends to run in families
- Rule of 10%: 10% bilateral, 10% extra-adrenal, 10% malignant, 10% familial, 10% pediatric, 10% show no HTN
- Palpitations, diaphoresis, and headache
- Picture of refractory or labile HTN

**Presentation and Laboratory Values**
- Family Hx of pheochromocytoma or MEN
- First do 24hr urine catecholamines (avoid caffeine, vanilla, fruits)
- False (+): shock, hypoglycemia, stress, clonidine withdrawal, TCAs, and MAOIs
- Clonidine suppression test if above equivocal

**Treatment**
- Adrenergic blockade for 3-4 weeks
  - Phenoxybenzamine PO
  - Phentolamine IV
- Surgical laparoscopic adrenalectomy
- Follow up catecholamine testing needed
- Adjunctive radiation and chemotherapy
An 8 yr. old boy presents with his mother who states that he has become overweight during the past year and has little energy, sleeps more, and is cold all the time. His growth curve has fallen from the 50th% to the 5th% for height, but his weight has increased from the 50th% to 90th%. On PE he is obese, has thin hair, immature facies, and slowed reflexes. What is the cause of his symptoms?

1. Acromegaly
2. Cushing’s syndrome
3. Dwarfism
4. Hypothyroidism

A 28 yr. old presents to the ED with confusion and agitation. He appears intoxicated and is unable to provide a history. On exam he has mild proptosis, is tachycardic with regular rhythm, neck fullness, a fine tremor, and brisk reflexes. While in the ED he vomits x 3. All labs are normal. What is the most likely diagnosis?

1. Addison’s disease
2. Diabetic ketoacidosis
3. Thyroid storm
4. Toxic adenoma
A 28 yr. old presents to the ED with confusion and agitation. He appears intoxicated and is unable to provide a history. On exam he has mild proptosis, is tachycardic with regular rhythm, neck fullness, a fine tremor, and brisk reflexes. While in the ED he vomits x 3. All labs are normal.

What is the most likely diagnosis?

1. Addison’s disease
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Where is thyroid-stimulating hormone (TSH) produced?

1. Anterior pituitary
2. Posterior pituitary
3. Zona fasciculata
4. Zona glomerulosa

Where is thyroid-stimulating hormone (TSH) produced?

1. Anterior pituitary
2. Posterior pituitary
3. Zona fasciculata
4. Zona glomerulosa
Over the past year a 21 yr. old female has developed amenorrhea and milky nipple discharge. She is not taking any medications and is sexually active but doesn’t wish to become pregnant. Her serum HCG is negative; prolactin 300 mg/dL; MRI reveals a 3 mm mass in the pituitary.  What is the most appropriate therapy at this time?

1. Bromocriptine (Parlodel)
2. Monthly IM medroxyprogesterone
3. Sequential OC’s
4. Transphenoidal tumor resection

A 25 yr old presents with extreme weakness and dizziness. On PE he appears depressed; BP 90/70. He has dark skin and hyperpigmented creases on his palms. Labs: low sodium; high potassium, calcium and urea. What is the most likely diagnosis?

1. Addison’s disease
2. Cushing’s syndrome
3. Pheochromocytoma
4. Primary hyperaldosteronism
A 25 yr old presents with extreme weakness and dizziness. On PE he appears depressed; BP 90/70. He has dark skin and hyperpigmented creases on his palms. Labs: low sodium; high potassium, calcium and urea. What is the most likely diagnosis?

1. Addison’s disease
2. Cushing’s syndrome
3. Pheochromocytoma
4. Primary hyperaldosteronism

A 46 yr old male complains that he has developed coarse facial features and a large prominent jaw. He states that his shoe size has increased over the last year despite no weight gain. What additional finding will most likely be found on PE?

1. Atrophy of the digits
2. Deepening voice
3. Dry skin
4. Enlarged testes
A 19 yr. old male presents to the ED with acute fatigue, vomiting, diarrhea, and anorexia. On PE he has postural dizziness and pigmented buccal mucosa. Labs indicate hyponatremia, hyperkalemia and glucose of 50 mg/dL. What is the most likely diagnosis?

1. Adrenal insufficiency
2. DM, type 1
3. Myxedema
4. Pheochromocytoma

Diabetes Mellitus
What is Diabetes Mellitus?
- A disorder of carbohydrate metabolism
- Lack of insulin
- Insulin resistance
- Both insulin deficiency and resistance

Classification
- Type 1 - little or no endogenous insulin production
- Type 2 – insulin resistance and/or deficiency
- Gestational
- LADA (type 1.5)- latent autoimmune diabetes in adults (+) GAD
- MODY- maturity onset diabetes of the young

Epidemiology
- Nearly 26 million people in the US have diabetes, 7 million of whom may be undiagnosed and unaware of their condition
- Research examining A1C levels found that 35% of U.S. adults aged 20 years or older had pre-diabetes (50% of those aged 65 years or older are considered pre-diabetic); an estimated 79 million Americans aged 20 years or older have pre-diabetes
Pathogenesis of DM type 1
- Hereditary predisposition (HLA-DR gene)
- Autoimmune (90% islet cell AB)
  - Islet Cell Cytoplasmic Autoantibodies (ICA)
  - Glutamic Acid Decarboxylase Autoantibodies (GADA)
  - Insulinoma-Associated-2 Autoantibodies (IA-2A)
  - Insulin Autoantibodies (IAA)
- Autoimmune destruction of beta cells
- Infiltration of pancreas with T-lymphocytes

Pathogenesis of DM type 2
- Genetically linked
- Inadequate insulin secretion
- Peripheral insulin resistance
- Accelerated hepatic glucose production

Type I vs. Type II
- Onset: Sudden
- Age: Typically young
- Body: Usually thin
- Ketosis: Common
- Autoantibodies: Present
- Endogenous insulin: low or absent

- Onset: Gradual
- Age: Mostly adults
- Body: Usually obese
- Ketosis: Rare
- Autoantibodies: Absent
- Endogenous insulin: normal, increased, decreased
Risk Factors

- Age (> 45 years old)
- Obesity
- Sedentary Lifestyle
- Ethnicity (African-American, Hispanic, Asian)
- Family history
- HTN, hypercholesterolemia, high triglycerides
- Gestational diabetes, having a child >9lbs
- PCOS

Diagnostic Criteria

<table>
<thead>
<tr>
<th></th>
<th>FBS</th>
<th>GTT</th>
<th>A1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Blood Sugar</td>
<td>&lt;100 mg/dL</td>
<td>&lt;140 mg/dL</td>
<td>&lt;5.7%</td>
</tr>
<tr>
<td>Prediabetes</td>
<td>100-125 mg/dL</td>
<td>140-199 mg/dL</td>
<td>5.7-6.4%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>≥126 mg/dL</td>
<td>≥200 mg/dL</td>
<td>&gt;6.5%</td>
</tr>
</tbody>
</table>


Screening Guidelines

- Asymptomatic individuals with risk factors should be screened for diabetes if they are overweight (BMI > 25 kg/m2) and have additional risk factors
- Beginning at age 45 for those without other risk factors
- Those with normal results and low risk should be re-tested at three-year intervals

### Testing Recommendations: Child

- **Overweight**: Age 10 yrs or onset of puberty
  - BMI > 85th percentile for age and sex
  - Weight for height > 85th percentile
  - Weight > 120% ideal for height
- **Plus 2 risk factors**
  - Family history
  - Race
  - Acanthosis nigricans, HTN, dyslipidemia, PCOS, SGA
  - Maternal history of DM or GDM
- **Frequency every 3 years**

### Signs & Symptoms

- Polyuria, polydipsia, polyphagia
- Infections
- Weakness
- Lethargy
- Numbness and tingling
- Blurry vision
- Weight loss

### Diabetes Complications

- **Microvascular Complications**:
  - Retinopathy
  - Neuropathy
  - Nephropathy
- **Macrovascular Complications**:
  - CVD- atherosclerosis – 1st cause of death
  - Poor immune function
  - Complicated infections
Morbidity and Mortality
- Leading cause of kidney failure, nontraumatic lower-limb amputations, and new cases of blindness among adults in the US
- Major cause of heart disease and stroke
- 1 in 3 suffer from severe periodontal disease
- Seventh leading cause of death in the US

**Diabetic Retinopathy**
- Cataracts
- Glaucoma
- Proliferative retinopathy neovascularization, scarring
- Non-Proliferative retinopathy hemorrhages, exudates, microaneurysms, venous dilatation

**Diabetic Neuropathy**
- **Peripheral neuropathy** (LE > UE)
  - distally symmetric,"stocking glove pattern" loss sensation
- **Autonomic**
  - Gastroparesis, urinary retention, postural hypotension, impotence, fecal incontinence
  - Silent MI

**DM leading cause of Blindness**
Diabetic Nephropathy
- High glucose levels cause polyuria-renal hyperfiltration
- Chronic hyperfiltration leads to kidney damage
- Proteinuria – early indicator of renal disease
- Rapid progression to dialysis once creatinine reaches 3-4 mg/dl

ESRD-DM most common reason for HD

Systemic Vascular Changes
- Atherosclerosis
- Hypertension
- CAD
- PVD
- Stroke

Poor immune function
- Vaginitis
- Periodonitis
- UTI
- Sinusitis
- Otitis externa/ media
- Cellulitis
Complicated Infections
- Gram negative pneumonias
- Infected ulcers
- Gram negative sepsis

Diabetic immunosuppression
- Fungal infections
- Thrush
- Aspergillus
- Cholecystitis/ cholangitis
- Pyelonephritis

Hypoglycemia
- Signs and Symptoms
  - FS < 70 mg/dL
  - Tachycardia, sweating, tremors, nausea, hunger, anxiety
  - Confusion, coma, seizure, death

**Tx:** 15 grams of glucose
4 oz OJ or soda, 3-4 glucose tabs, 5-6 hard candies, glucagon IM
DKA - Diabetic Ketoacidosis

- Usually occurs in type 1 (insulin insufficiency)
- Diagnostic criteria:
  - PG >250
  - Ph <7.35
  - Bicarb <15
  - High anion gap
  - Serum/urine ketones
- Signs/Symptoms:
  - Polyuria, polydipsia
  - Weakness, stupor (Kussmaul breathing)
  - Tachycardia, tachypnea (to compensate pH)
  - Nausea/vomiting
  - Fruity breath

Treatment of DKA

- Regular insulin IV 0.1 units/kg bolus - then 0.1 units/kg/hr
- Fluid replacement w/ normal saline 3-4 L/8 hrs
- Sodium bicarb if pH <7.0
- Potassium replacement (20-30 meq/ 2-3 hrs after therapy started)
- Glucose < 250mg/dL add 5% dextrose to fluids

Hyperosmolar Hyperglycemic State (HHS)

- Usually occurs in type 2 (osmotic diuresis due to hyperglycemia -> dehydration, insulin secretion suppresses ketolysis)
- K+, Mg+, are lost along w/ water & Na+
- Severe dehydration:
  - Cardiac profusion compromise: tachycardia, low CO, low Mg+ & K+
- Diagnostics Criteria:
  - PG >600 mg/dL
  - Serum osm >310
  - No acidosis
  - No ketones
  - Bicarb >15
- Triggers: infection, AMI, pancreatitis, poor compliance

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**Treatment**

**Hyperosmolar Hyperglycemic State**

- Saline replacement - (6-10 L)
- Regular Insulin IV (15 units/IV, 15 units SQ)
- Potassium (10 meq to initial fluids)
- Magnesium (2 gm to initial fluids)
- Once glucose <250md/dL – 5% dextrose to fluids

---

**Dawn Phenomenon**

- End result of a combination of natural body changes that occur during sleep
- Between 3 AM & 8 AM, your body starts to increase the amounts of counter-regulatory hormones (GH, cortisol, & catecholamines).
- These combined events cause your body's blood sugar levels to rise in the morning
- M/C in type 1

---

**Somogyi Effect**

- "rebound hyperglycemia"
- The cause is more "man-made" - a result of poor diabetes management
- Refers to pattern of high morning sugars preceded by an episode of hypoglycemia
- Check blood sugars between 2-3 AM

---

**Dawn Phenomenon**

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- Between 3 AM & 8 AM, your body starts to increase the amounts of counter-regulatory hormones (GH, cortisol, & catecholamines).
- These combined events cause your body's blood sugar levels to rise in the morning
- M/C in type 1
Treatment & Management of DM

- Self monitoring
- Insulin/ oral medications
- Diet and exercise
- Patient education

Self Monitoring

- Used to adjust medication
- Improves glycemic control
- Patient's involvement in their care

Balanced Diet

- Moderate caloric restriction
- Moderate weight loss 5-9 kg goals
- Spacing meals (especially carbs)
- Approach depends on lifestyle
- Very low calorie diet usually NOT effective for long term goals!

Public domain available at: http://commons.wikimedia.org/wiki/File:Glucose_test.JPG
Exercise

- Improves glucose tolerance
- Promotes good circulation
- Maintains good muscle tone
- Helps maintain normal body weight
- Reduces insulin requirements
- Recommendation 150min/week

Oral Anti-diabetic Agents (OAD)

- Sensitizers- Inhibit the release of glucose from the liver; improve sensitivity to insulin
  - Biguanides- Metformin (Glucophage, Fortamet, Glumetza, etc)
  - Thiazolidinediones (TZD) PPARy (gamma)
- Rosiglitazone (Avandia), Pioglitazone (Actos)
- *Bladder Cancer, CHF

Oral Anti-diabetic Agents (OAD)

- Secretagogues- Stimulate the release of insulin from the pancreas
  - Sulfonylureas (SU)
  - Glipizide (Glucotrol), Glimepiride (Amaryl), Glyburide (DiaBeta, Glynase)
  - Meglitinides
  - Repaglinide (Prandin), Nateglinide (Starlix)
Oral Anti-diabetic Agents (OAD)

- Dipeptidyl peptidase-4 inhibitors (DPP-4) - inhibitors inhibit the degradation of incretins (GLP-1 and GIP)
  - Saxagliptin (Onglyza), Sitagliptin (Januvia), Linagliptin (Tradjenta)
- Alpha-glucosidase inhibitors (AGI) - Slow the breakdown of starches and some sugars
  - Acarbose (Precose), Miglitol (Glyset)

Non-insulin Injectables

- Amylin mimetics - It slows the rate at which glucose is absorbed from the intestine, reduces the production of glucose by the liver by inhibiting the action of glucagon
  - Pramlintide (Symlin)
- Incretin mimetics - GLP-1 agonist - Enhances insulin secretion by the pancreatic beta-cell, suppresses inappropriately elevated glucagon secretion, slows gastric emptying which produces satiety
  - Liraglutide (Victoza), Exenatide (Byetta), Exenatide extended-release (Bydureon)

Human Insulin Profiles
(Rapid and Intermediate Acting, Premix)

<table>
<thead>
<tr>
<th>INSULIN</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novolin® (R), Humulin® (R) Regular</td>
<td>30-60 min</td>
<td>2-4 hrs</td>
<td>5-8 hr</td>
</tr>
<tr>
<td>Novolin® (N), Humulin® (N) NPH</td>
<td>1-3 hrs</td>
<td>4-10 hrs</td>
<td>18-24 hrs</td>
</tr>
<tr>
<td>Humulin® 70/30, Novolin® 70/30</td>
<td>30-60 min</td>
<td>Varies</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Humulin® 50/50</td>
<td>30-60 min</td>
<td>Varies</td>
<td>Up to 24 hrs</td>
</tr>
</tbody>
</table>
**Insulin Analogs**

Basal (Long-acting) Bolus (Fast-acting)

<table>
<thead>
<tr>
<th>INSULIN</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levemir®</td>
<td>1 hr</td>
<td>Steady over time</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Lantus®</td>
<td>1 hr</td>
<td>Steady over time</td>
<td>Up to 24 hrs</td>
</tr>
<tr>
<td>Novolog®</td>
<td>5-15 min</td>
<td>30-90 min</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Apidra®</td>
<td>5-15 min</td>
<td>30-90 min</td>
<td>3-5 hr</td>
</tr>
<tr>
<td>Humalog®</td>
<td>5-15 min</td>
<td>30-90 min</td>
<td>3-5 hr</td>
</tr>
</tbody>
</table>

**Treatment in DM**

- Type I: Insulin (basal / bolus)
- Type II:
  1. Diet and Exercise (First Step)
  2. Oral medication
  3. Insulin (if no glycemic control, severe hyperglycemia fasting BG > 240)

***Start with one Lifestyle changes- then add Metformin (drug of choice) if fails, use second agents different class***

**Preventive Care**

- Hgb A1C every 6 mo (if controlled)
- FBS, AC & HS+ bedtime
- Microalbuminuria yearly
- BUN/Cr yearly

- Dilated eye exam yearly
- Foot exam each visit (yearly DPM)
- Cholesterol yearly
- BP each visit
- Stop smoking
Hypoglycemia

- Self induced: medications
- Immunopathologic (rare) – anti-insulin antibodies to insulin receptors
- ETOH related hypoglycemia
- Tumors – pancreatic B-cell, extra-pancreatic
- Symptoms at or below 60 mg/dL, impairment of brain function 50 mg/dL
- Whipple’s Triad: hx of hypoglycemic symptoms, fasting blood glucose of 40 mg/dL or less, immediate recovery upon admin. glucose

Metabolic Syndrome

Need 3 of 5 to diagnose

- HDL < 40 male, < 50 female
- Elevated BP ≥ 135/85
- Elevated Triglycerides ≥ 150 mg/dL
- Fasting BG 100-125 mg/dL
- Waist Circumference > 35"F, >40"M

Lipid Disorders

- Hyperlipidemia
- Hypertriglyceridemia
**Hyperlipidemia**
- Most important and modifiable risk factor for CAD → accelerates atherosclerosis
- Primary Disorder: Familial Dyslipidemia Syndrome
- Secondary Disorder
  - Endocrine: hypothyroidism, DM, Cushing’s
  - Nephrotic syndrome, Chronic liver disease
  - Medications: steroids, estrogen, thiazide diuretics
  - Pregnancy

**First Step:**
**Screening and Risk Assessment**
- All adults ≥ 20 yrs. fasting lipoprotein profile → Every five years
- LDL Levels alone
- Cigarette smoking
- HTN (BP ≥ 140/90 or on HTN med)
- Low HDL < 40 mg/dL
- Family History of premature CAD (CAD in male first degree relative < 55, female first degree relative < 65)
- Age Men > 35, women > 45

**Values and Risk Assessment**
- LDL
  - < 100 = desirable
  - 100-129 = above optimal
  - 130-159 = borderline high
  - ≥ 160 = very high
- HDL Cholesterol
  - < 40 = low
  - ≥ 60 = high
- Total Cholesterol
  - < 200 = desirable
  - 200-239 = borderline high
  - ≥ 240 = high
- Triglycerides < 125
- TC:HDL ratio < 4.5

**Total < 200**
- LDL < 100 (no CAD)
- LDL < 70 (+CAD)
- Triglycerides < 125
- TC:HDL ratio < 4.5
### Screening and Clinical Features

- No risk factors (if previously not screened)
- 35 Men
- 45 women
- Family Hx
- HTN
- Smoking
- DM
- Low HDL
- Age

- Asymptomatic
- Severe hyperlipidemia
  - Xanthelasma: yellow plaques on eyelids
  - Xanthoma – hard yellow masses on tendons

### Treatments

- Dietary Changes
  - Lowering fat intake (saturated fats, cholesterol)
  - Food rich in Omega 3-fatty acids (fish)
  - Fiber

- Exercise: Increase HDL

- Drug Therapy

### Drug Treatment of Hyperlipidemia

- **HMG CoA reductase inhibitors (statins)**
  - Most potent
  - Lower LDL
  - Monitor CPK, LFT

- **Niacin**
  - Decrease TG levels, Decrease LDL, Increase HDL
  - Use in Diabetes
  - Most potent: HDL, TG levels
  - Flushes/flushing effect

- **Bile acid-binding resins (cholestyramine, colestipol)**
  - Increases TG levels
  - Good for use in combination with statins or niacin in high risk pts.
  - Third line agent for LDL
  - GI side effects

- **Fibrates (gemfibrozil)**
  - Lower VLDL, Increase HDL
  - Use if above fail
  - GI side effects, gynecomastia, gallstones, wt. gain

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Treatment of Hypertriglyceridemia

- Reduce weight
- Reduce amount saturated fat, trans fat, cholesterol in diet
- Reduce ETOH use
- Exercise
- Lower carbohydrate intake
- Increase meats high in Omega-3 fatty acids
- LOVAZA® (omega-3-acid ethyl esters)
  - SE: burping, infection, flu-like symptoms, upset stomach, and change in sense of taste

A 42 yr. old obese woman with a hx of Type 2 DM x 4 mos. presents for follow-up after initial attempts at diet and exercise for control. She has gained 10 lbs and her BMI is now 30.5. On this visit her HgbA1c is 8; serum creatinine is normal.

What is the best management?

1. Bedtime insulin (NPH)
2. Metformin (glucophage)
3. Glipizide (Glucotrol)
4. Continue diet & exercise efforts

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What is the best management?

1. Bedtime insulin (NPH)
2. Metformin (glucophage)
3. Glipizide (Glucotrol)
4. Continue diet & exercise efforts
A 66 yr old male was found wandering the streets by the police. There are no signs of trauma. Vitals: BP 90/54, P 115, R 12. PE reveals mild dehydration and mental confusion w/o focal neurological findings. Labs are: glucose 759, Na 124, K 3.0, Cl 102, CO2 37, BUN 63, CR 1.0. What is the most appropriate first step in treatment?

1. Glucagon
2. Insulin
3. Phosphate
4. Saline

Which of the following glucose-lowering agents acts by decreasing insulin resistance and increasing glucose utilization?

1. Acorbase (Precose)
2. Glipizide (Glucotrol)
3. Metformin (Glucophage)
4. Pioglitazone (Actos)
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1. Acorbase (Precose)
2. Glipizide (Glucotrol)
3. Metformin (Glucophage)
4. Pioglitazone (Actos)

A 15 yr. old male presents with extreme fatigue and frequent urination day and night which he attributes to increased water intake to “quench his thirst.” Exam indicates a slender male with postural hypotension. What is the best initial step to establish a diagnosis?

1. ACTH
2. HgbA1C
3. Plasma glucose
4. Serum AM cortisol

A 15 yr. old male presents with extreme fatigue and frequent urination day and night which he attributes to increased water intake to “quench his thirst.” Exam indicates a slender male with postural hypotension. What is the best initial step to establish a diagnosis?

1. ACTH
2. HgbA1C
3. Plasma glucose
4. Serum AM cortisol
A 50 yr. old male presents for a routine visit. He states that he could “stand to lose a few pounds” but is otherwise in good health. PMH and family hx reveal no risk factors. Exam reveals abdominal obesity (waist circumference 45 in.) and BP 142/90. What additional finding would confirm a dx of metabolic syndrome?

1. Fasting glucose 98 mg/L
2. HDL 45 mg/dL
3. LDL 120 mg/dL
4. Triglycerides 200 mg/dL

A 49 yr. old with a hx of Type 2 DM presents after receiving a non-fasting cholesterol of 235 at a community health fair. Which of the following is the best management?

1. Diet & exercise advice
2. Fasting lipid profile
3. HMG Co-A reductase inhibitor
4. Reassurance that results are OK
A 49 yr. old with a hx of Type 2 DM presents after receiving a non-fasting cholesterol of 235 at a community health fair. Which of the following is the best management?

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2. Fasting lipid profile
3. HMG Co_A reductase inhibitor
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2. Fasting lipid profile
3. HMG Co_A reductase inhibitor
4. Reassurance that results are OK

A 52 yr old postmenopausal woman presents with chest pain suggestive of angina. Exercise stress test is positive. Fasting labs: glucose 92, T. Chol. 271, LDL 127, HDL 31, Trigl. 375. What is the best therapy for this patient?

1. Atorvastatin (Lipitor)
2. Cholestyramine (Questran)
3. Estradiol
4. Niacin

A 52 yr old postmenopausal woman presents with chest pain suggestive of angina. Exercise stress test is positive. Fasting labs: glucose 92, T. Chol. 271, LDL 127, HDL 31, Trigl. 375. What is the best therapy for this patient?

1. Atorvastatin (Lipitor)
2. Cholestyramine (Questran)
3. Estradiol
4. Niacin
Thank you and good luck!

References

- Cecil Textbook of Medicine, 22nd Edition. Lee Goldman, MD, Dennis Ausiello, MD.
- http://commons.wikimedia.org/wiki/Main_Page