Endocrine Pathology Assignment

Robbins: Chapter 24

Wheater, Endocrine

Clinical Lab Source:

- Adrenal cortex panel,
- ACTH and ACTH stimulation test,
- Calcium, ionized and free,
- Calcitonin,
- Diabetic ketoacidosis panel,
- Pheochromocytoma,
- Endocrine emergencies,
- GTT,
- PTH,
- Pituitary panel,
- Thyroid antibodies,
- Thyroid panel,
- TSH following TRF,
- T4,
- FTI,

Slides: All slides listed on the master list and in the manual for endocrine. There aren’t that many.

Paper cases at the end of this unit.

Online case: Mr. Harvey’s seizure, this should be case 10 on the website.
Endocrine Pathology

The endocrine system undoubtedly represents the original method of cellular communication and must have come along about as soon as multicellular organisms began to evolve. By a simple system of peptide and steroid chemical signals, a multicellular organism can keep all members informed and to a great extent coordinate metabolism and growth. It’s basically a system of “runners” carrying messages to various parts of the body using the existing transport system of the blood vessels. Pretty slick really.

The hormones interact with specific receptors and trigger changes in cell metabolism. We now recognize three basic receptor categories:

- Surface membrane receptors

  - polypeptide (pituitary) and amine (catecholamines)

  - transducer G and second messenger concept

  - cAMP and tyrosine kinase system

  - calcium and calmodulin in some cases

- Cytoplasmic receptors

  - Steroid hormones fit this category.

  - Penetrate lipid membrane and bind with receptor, bring about nuclear changes.

  - Gene activation -> transcription -> translation

- Intranuclear receptors
Example is thyroid hormone. Receptor is principally in nucleus
- Gene activation -> transcription -> translation

Pathology of the endocrine system revolves around three basic problems:

- **Too much hormonal activity**

- **Too little hormonal activity**

- **Space occupying lesions and/or malignant growth**

Specifics from the history and physical, and especially laboratory, are essentially to making the correct diagnosis. You will need to be very familiar with hormone measurements and the assessment of their metabolites or unique alteration in physiology.

I. Pituitary pathology

Anterior and posterior

Too much, too little and especially “space occupying” lesions causing gland destruction!
A. Space occupying lesion as in adenoma. (What does the term “benign” mean?)

- enlarged Sella Turcica

- visual field defects (temporal field loss bilateral)

- pituitary gland failure due to compression atrophy

- many adenomas are non-functional, but some do produce a specific stimulating hormone which may lead to other hyperactive gland states.

- prolactin secreting adenomas most frequent

- GH

- ACTH

<table>
<thead>
<tr>
<th>Table 26-1. Pituitary Adenomas</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
</tr>
<tr>
<td>Prolactin cell adenoma</td>
</tr>
<tr>
<td>Growth hormone cell adenomas</td>
</tr>
<tr>
<td>Mixed growth hormone–prolactin adenomas</td>
</tr>
<tr>
<td>ACTH cell adenomas</td>
</tr>
<tr>
<td>Gonadotropin cell adenomas</td>
</tr>
<tr>
<td>Null cell adenomas</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone cell adenomas</td>
</tr>
<tr>
<td>Other pleurithymonal adenomas</td>
</tr>
</tbody>
</table>

ACTH, adrenocorticotropic hormone.

Ref: Robbins, Pathologic Basis of Dis.

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B. Hypopituitarism

- space occupying lesion results in destruction of gland.

- pituitary adenoma

- craniopharyngioma (Rathke’s Pouch Remnant tumor)

- failure of hypothalamus

- suprasellar tumors

- Sheehan’s Syndrome (aseptic necrosis)

- postpartum necrosis

- failure of lactation may be first clue

- DIC

- failure of all systems “downstream”

- gonad function, adrenal, thyroid ...

- known as Panhypopituitarism
- Empty Sella syndrome? Pressure atrophy of pituitary
  - increased CSF pressure in conjunction with too large aperture for hypophyseal stalk.

- Hypothalamic and suprasellar tumors

C. Posterior pituitary (remember posterior pit is actually extension of hypothalamus)

- ADH deficiency
  - neoplastic or inflammatory destruction (abscess) of hypothalamus
  - surgical or irradiation ablation
  - severe head injuries
  - unknown

- ectopic ADH production
  - tumors other than pituitary. Lung cancer
II. Thyroid, as before, too much, too little and tumors (remember, this term just means enlargement or swelling).

A. Physiology, TRF, TSH, T-3 and T-4

B. Laboratory measurement of thyroid function

1. This is really important and unfortunately can be confusing.

2. Levels of TRF and TSH are helpful and their diagnostic values should be self evident

3. Here are the ones that are commonly used and what they apply to:
   - Sensitive TSH
   - T4 = measurement amount of all T4, protein bound and free
     - bound fraction = about 99%
   - TBG
   - albumin
   - pre-albumin
   - knowing what effects the levels of these is important as they can influence the amount of total T4, and thereby the test results.
- Free T4

- T3 by RIA = actual measurement of the amount T3 in a patient’s serum.

- FTI (free thyroxin index) = a computed value, with no label, that is a pretty good indicator of what the “Free T4” is. In other words, that that is available for metabolism.

### Drugs and their effects on Thyroid Function Tests

<table>
<thead>
<tr>
<th>Increased TBG</th>
<th>Estrogen, Oral Contraceptives, Heroin, Clofibrate, Fluorouracil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased TBG</td>
<td>Androgens, Glucocorticoids, L-Asparaginase</td>
</tr>
<tr>
<td>Increased T4</td>
<td>Drugs that Elevate the TBG, Extrathyroidal Thyroid Hormone</td>
</tr>
<tr>
<td>Decreased T4</td>
<td>Drugs that Decrease the TBG, Phenytoin, Carbamazepine, Rifampin, High Doses of Glucocorticoids, Dopamine</td>
</tr>
<tr>
<td>Decreased T3</td>
<td>Glucocorticoids, Propranolol, Iodine Containing Drugs and Contrast Agents, Dopamine</td>
</tr>
<tr>
<td>Increased TSH</td>
<td>Dopamine Antagonists, Chlorpromazine, Haloperidol, Iodine Containing Drugs</td>
</tr>
<tr>
<td>Decreased TSH</td>
<td>Extrathyroidal Thyroid Hormone, Glucocorticoids, Dopamine, Levodopa, Dopamine Agonists, Apomorphine, Pyridoxine</td>
</tr>
</tbody>
</table>
C. Hyperthyroidism (thyrotoxicosis) Too much in a big way!

1. the biggies: (1) Graves’s, (2) toxic multinodular goiter, (3) toxic adenoma

2. Clinical

- heat intolerance

- warm, moist and flushed skin

- Eye changes in some cases

- **Cardiac** - resting tachycardia - palpitations - arrhythmias - may be fatal

- thyrotoxic cardiomyopathy

3. Many causes.

<table>
<thead>
<tr>
<th>Table 29-2. DISORDERS ASSOCIATED WITH HYPERTHYROIDISM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Common</strong></td>
</tr>
<tr>
<td>Diffuse toxic hyperplasia (Graves disease)</td>
</tr>
<tr>
<td>Toxic multinodular goiter</td>
</tr>
<tr>
<td>Toxic adenoma</td>
</tr>
<tr>
<td><strong>Uncommon</strong></td>
</tr>
<tr>
<td>Acute or subacute thyroiditis</td>
</tr>
<tr>
<td>Hyperfunctioning thyroid carcinoma</td>
</tr>
<tr>
<td>Chorionicarcoma or hydatidiform mole</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone–secreting pituitary adenoma</td>
</tr>
<tr>
<td>Neonatal thyrotoxicosis associated with maternal Graves disease</td>
</tr>
<tr>
<td>Struma ovarii (ovarian teratomatous thyroid)</td>
</tr>
<tr>
<td>Iodide-induced hyperthyroidism</td>
</tr>
<tr>
<td>Iatrogenic (exogenous) hyperthyroidism</td>
</tr>
</tbody>
</table>
a. Graves’ Disease - antibody stimulation of TSH receptor

(Diffuse toxic hyperplasia)

- most common cause of hyperthyroidism

- young women - exophthalmos
  - variable changes in skin

- antibodies in two classes
  - stimulating
  - binding

- cause? Bad CD4 and helper cells?

- appearance of thyroid
  - diffusely enlarged
- microscopic shows hyperplasia of follicular epithelium
  and scalloping at edges of colloid.

- variable lymphocytic infiltrate

b. Toxic multinodular goiter (goiter just means enlargement, and does not
  say anything specific about thyroid activity)

c. Toxic adenoma.

  - an isolated, encapsulated benign tumor of follicular cells
    arranged in follicles secreting hormone in an unregulated manner.

d. Excess peripheral conversion of T4 to T3 (T3 thyrotoxicosis)
D. Hypothyroidism, again many causes, but the name says it all.

1. Genetic - Cretinism (sporadic)

2. Iodine deficiency may lead to “endemic Cretinism”

3. Destruction of gland
   - surgical removal
   - inflammatory destruction
   - radiation injury

4. Hypothalamic and/or pituitary failure

5. Clinical
   - Myxedema is the term used for older children or adults
   - cold intolerance
- peculiar peripheral “edema”

- photophobia

- changes in hair, skin and voice (funky sense of humor)

- large tongue

- cardiac
E. Tumors (remember this just means swelling or enlargement)

1. Non-neoplastic

   - Goiter

     - definition

     - Simple vs multinodular

     - toxic vs non-toxic

     - gross

     - microscopic
2. Neoplastic - but benign

- adenomas - different cell types and degrees of maturation of follicles

- basic observations

- encapsulated
- compression of normal tissue at margins
- cells and follicles look different than surrounding tissue

- follicular, micro follicular, Hurthle cell
3. Malignant “thyroid tissue” origin

- cell of origin

- follicular

- interstitial cells (calcitonin producing)

- Microscopic appearance defines type: Papillary, follicular, mixed and anaplastic.

- Papillary carcinoma - papillary growths with malignant cells on the surface of the papillae.

- nuclear grooves

- Orphan Annie eyes

- Psammoma bodies
- Follicular carcinoma:
  - fairly well defined follicular arrangements, but no capsule

- Mixed follicular and papillary pattern.
- Anaplastic
  - very aggressive
  - malignant cells have the superficial appearance of lymphocytes, but are not.

- Medullary = C cells
  - amyloid like material

General stuff
  - contributing factors

  - rarely hyperactive

  - mets
4. Malignant “other”
   - malignant lymphomas on rare occasions may arise primarily in thyroid
   - met from somewhere else is exceedingly rare: breast and melanoma

F. Inflammatory conditions:

1. This is a major source of pathology, especially hypothyroidism after the
   inflammatory conditions has run its course and left the thyroid
   “burned out.”

2. Lots of possibilities, bacterial, viral, but immune mediated is big ticket item.

3. Immune compromised patient

   - bacteria, staph, strep, TB

4. Immune mediated

   a. Hashimoto’s - also known as struma lymphatosa (the word “struma”
      gets substituted a lot for “thyroid,” so be on the look out.

      - women over men 5:1

      - measurable antibodies in serum
- micro shows marked lymphoid infiltrate with **germinal centers** within the thyroid tissue itself.

- leads to hypothyroidism

- other autoimmune conditions; SLE, Sjogren’s, PA, rheumatoid arthritis, even Grave’s disease.

b. Reidel’s struma (?autoimmune)

- Marked atrophy and sometimes profound fibrosis involving even surrounding structures. Leads to hypothyroidism.

5. De Quervain’s (subacute granulomatous thyroiditis, giant cell thyroiditis)

   a. Probably virally mediated

   b. Female to male 3:1
c. These folks are sick with fever, painful and enlarged thyroid.
   - Complain of sore throat or earache.

d. Characteristic microscopic findings.

III. Parathyroid: Come from pharyngeal pouches just like thymus. Most have four, but not everyone.
   - chief cells: PTH
   - water clear cells: glycogen
   - Oxyphil cell: fine granular cytoplasm, glycogen containing
   - PTH - 84 amino acids in circulating active form
     - mobilizes Ca from bone
     - lowers phosphate by promoting renal excretion
     - increase renal reabsorption of Ca
     - promotes renal production of vitamin D

A. Primary hyperparathyroidism = hypercalcemia

1. Sx: “stones, bones, abdominal groans and psychic moans”
   - urinary stones
   - ulcers of stomach, nausea and vomiting
   - muscle weakness
   - lethargy and depression
   - osteitis fibrosa cystica and generalized bone wasting
2. Causes of primary hyperparathyroidism
   - adenoma (75-80%)

   - diffuse or nodular hyperplasia (10-15%)

   - parathyroid carcinoma (<5%)

B. Secondary hyperparathyroidism = hypercalcemia

1. Renal failure leading to phosphate retention and secondary parathyroid hyperplasia
2. Hyperplasia or adenomas
3. Renal osteodystrophy
C. Non-endocrine causes

- paraneoplastic syndromes

  - squamous cell cancer of lung

  - breast cancer

  - bladder cancer

  - renal cancer

  - ovary cancer

  - vitamin D intoxication

D. Hypoparathyroidism

1. SX

  - increased neuromuscular excitability

  - contractures of muscles of eyes, mouth and nose (Chvostek’s sign)

  - tetany

  - irritability and rarely psychosis
- cataracts
- prolonged QT on EKG, possible heart block
- basal ganglia calcifications with Parkinson-like movements

2. Causes:

- surgical removal with the thyroid
- congenital absence
- autoimmune destruction

3. Pseudohypoparathyroidism

- end-organ insensitivity
- characteristic physical appearance
- Labs

High PTH, low calcium, high phosphate

Low urinary cAMP

Pseudopseudo........ All the outside manifestations, but normal PTH
E. Interpretation of serum calcium levels

1. Very tightly controlled ion in the serum

2. Must know protein as approximately ½ is protein associated (bound)

3. Total 8.5-10.5 mg% (varies a little for children)

   - The “ionized (free) fraction is the “working” calcium, this is what you want to know! You see. If you have a high serum protein, say as in multiple myeloma, you will have a correspondingly high total calcium, but the “free calcium” will still be in the right range.

   At pH of 7.4, free calcium = 4.4-5.4 mg%

4. Isolated parathyroid hormone levels are not very useful. You must know the calcium, and put the value in context with the clinical situation. Here are some examples:

<table>
<thead>
<tr>
<th>Ca in mg%</th>
<th>PTH in pg/ml</th>
<th>What the heck does it mean?</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.8-10.8</td>
<td>100-600</td>
<td>Normal, expected value</td>
</tr>
<tr>
<td>11-16.2</td>
<td>&gt;300</td>
<td>Primary hyperparathyroidism</td>
</tr>
<tr>
<td>&lt;9.4</td>
<td>&gt;800</td>
<td>Secondary hyperparathyroidism</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Renal failure</td>
</tr>
<tr>
<td>&lt;7.5</td>
<td>&lt;300</td>
<td>Hypoparathyroidism</td>
</tr>
<tr>
<td>&lt;7.0</td>
<td>350-700</td>
<td>Pseudohypoparathyroidism</td>
</tr>
</tbody>
</table>
IV. Endocrine Pancreas

A. Diabetes

Carbohydrate

Fats

Proteins

Hyperyglycemia

SMALL VESSEL DISEASE !!

Interplay of genetics and environment

Type I

Genetic susceptibility

Trigger

Autoimmune

<table>
<thead>
<tr>
<th>Table 20-2. TYPES OF DIABETES MELLITUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Diabetes</strong></td>
</tr>
<tr>
<td>Type 1 (previously insulin-dependent diabetes mellitus, IDDM)</td>
</tr>
<tr>
<td>Type 2 (previously non-insulin-dependent diabetes mellitus, NIDDM)</td>
</tr>
<tr>
<td>Genetic defects of β-cell function (including maturity-onset diabetes of the young [MODY])</td>
</tr>
<tr>
<td>Chromosome 2, HNF 4α (MODY1)</td>
</tr>
<tr>
<td>Chromosome 7, glucokinase (MODY2)</td>
</tr>
<tr>
<td>Chromosome 12, HNF 1α (MODY3)</td>
</tr>
<tr>
<td>Mitochondrial DNA</td>
</tr>
<tr>
<td>Other genetic defects</td>
</tr>
</tbody>
</table>

**Secondary Diabetes**

Infectious

Congenital rubella

Cytomegalovirus

Endocrinopathies (e.g., adrenal, pituitary tumors)

Drugs (corticosteroids, pentamidine, Vaco)

Other genetic disorders (e.g., Down syndrome)

Gestational diabetes mellitus

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<table>
<thead>
<tr>
<th>Table 20-3. TYPE 1 VS. TYPE 2 DIABETES MELLITUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type 1 (IDDM)</strong></td>
</tr>
<tr>
<td><strong>Type 2 (NIDDM)</strong></td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>Onset &lt;30 yr</td>
</tr>
<tr>
<td>Normal weight</td>
</tr>
<tr>
<td>Decreased blood insulin</td>
</tr>
<tr>
<td>Anti-insulin cell antibodies</td>
</tr>
<tr>
<td>Ketoadidosis common</td>
</tr>
<tr>
<td><strong>Genetics</strong></td>
</tr>
<tr>
<td>50% concordance in twins</td>
</tr>
<tr>
<td>HLA-A linked</td>
</tr>
<tr>
<td><strong>Pathogenesis</strong></td>
</tr>
<tr>
<td>Autoimmunity, immunopathologic mechanisms</td>
</tr>
<tr>
<td>Severe insulin deficiency</td>
</tr>
<tr>
<td><strong>Islet cells</strong></td>
</tr>
<tr>
<td>Insulin early</td>
</tr>
<tr>
<td>Marked atrophy and fibrosis</td>
</tr>
<tr>
<td>β-cell depletion</td>
</tr>
<tr>
<td><strong>Onset &gt;30 yr</strong></td>
</tr>
<tr>
<td>Normal or increased blood insulin</td>
</tr>
<tr>
<td>No anti-insulin cell antibodies</td>
</tr>
<tr>
<td>Ketoadidosis rare</td>
</tr>
<tr>
<td>90% to 100% concordance in twins</td>
</tr>
<tr>
<td>No HLA association</td>
</tr>
<tr>
<td>Insulin resistance</td>
</tr>
<tr>
<td>Relative insulin deficiency</td>
</tr>
<tr>
<td>No insulin</td>
</tr>
<tr>
<td>Focal atrophy and amyloid deposits</td>
</tr>
</tbody>
</table>

HNF, hepatocyte nuclear factor.

Type II

genetic predisposition

obesity

release defect

dergorgan resistance
Long term 

microangiopathy 

nonenzymatic glycosylation 

irreversible advanced glycosylation end products (AGE) 

Intracellular hyperglycemia (sorbitol) 

Diabetic renal disease 

glomerulus 

interstitial 

Tubules
Papillary necrosis

Infections everywhere
Pancreatic islet cell tumors and hyperplasia

A. May be hormonally active or not.

1. Activity depends on cell of origin

B. Beta-cell tumors; insulin secreting (insulinoma)

1. Attacks of hypoglycemia (<50 mg%)

2. Attacks are characterized by CNS symptoms

3. Promptly relieved by administering glucose

4. Similar syndrome is seen with diffuse beta cell hyperplasia

   - infants born to diabetic mothers

C. Zollinger-Ellison Syndrome (gastinoma)

1. Numerous and recurring ulcers

2. Measurable hyperacidity

3. About 20% of gastinomas occur out of the pancreas
D. Alpha-cell tumors (glucagonoma)

E. VIPoma

1. Raging squirts

V. Adrenal: two separate functional units; cortex and medulla

A. Cortex: three layers (salt, sugar, sex)

1. Cortisol principal steroid
   - steroid hormones are protein bound in the circulating blood
   - unbound is active, binds to specific cell transport protein
   - DNA binding sites and regulates transcription
   - inhibits glucose uptake, protein catabolism, increases bone reabsorption.

2. Aldosterone
   - sodium retention

3. Testosterone
   - masculinizing effects

B. Pathology: same as for all, too much, too little and tumors.
C. Cushings syndrome

1. Sx
   - central obesity
   - moon face
   - hirsutism
   - Buffalo hump
   - hypertension
   - osteoporosis
   - abdominal stria
   - weakness

2. Iatrogenic
3. Cushings disease

4. Ectopic ACTH
   - small cell cancer of lung
   - carcinoids (rarely)
   - thymomas (rarely)

5. Autonomously functioning adrenal cortical adenoma
- most of these are actually not hormonally active (or at least respond the same as the rest of the gland), but about 20% of cases of Cushing’s Syndrome are attributed to functional cortical adenomas.

6. Carcinomas of the adrenal cortex

 - rare

 - generally show hirsutism because of intermediates of metabolism

D. Hyperaldosteronism - hypertension and sodium retention

1. Adenoma - Conn’s syndrome

2. Hyperplasia of glomerulosa (often bilateral) (65%)

3. Rarely adrenal cortical carcinoma
E. Congenital enzyme deficiency leading to *Adrenogenital syndromes*

1. Intermediates of metabolism cause virilizing effects
   - ambiguous genitalia in newborn

2. Adrenal cortical hyperplasia (ACTH stimulation to make adrenal work)
3. 21-hydroxylase deficiency, a mixture of symptoms, but involves
- salt wasting (inability to make adequate mineralocorticoids)
- androgenizing effects (intermediates of metabolism that leak from the adrenal cortical cells)

F. Hypoadrenalism

1. General considerations

- pituitary vs gland
- acute or chronic

- “crisis” must be able to increase adrenal cortical output with stress, here people cannot.

Table 26-5. ADRENOCORTICAL INSUFFICIENCY

<table>
<thead>
<tr>
<th>Primary Insufficiency</th>
<th>Secondary Insufficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of cortex</td>
<td>Hypothalamic pituitary disease</td>
</tr>
<tr>
<td>Idiopathic (autoimmune)</td>
<td>Neoplasms, inflammation (sarcoidosis, tuberculosis, pyogenic, fungal)</td>
</tr>
<tr>
<td>Infection (mycobacteria, fungi)</td>
<td>Hypothalamic pituitary suppression</td>
</tr>
<tr>
<td>AIDS, opportunistic microbes</td>
<td>Long-term steroid administration</td>
</tr>
<tr>
<td>Acute hemorrhagic necrosis (Wasserhous-Friderichsen syndrome)</td>
<td>Steroid-producing neoplasms</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td></td>
</tr>
<tr>
<td>Sarcoidosis, hemochromatosis</td>
<td></td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td></td>
</tr>
<tr>
<td>Metabolic failure in hormone production</td>
<td></td>
</tr>
<tr>
<td>Congenital adrenal hypoplasia</td>
<td></td>
</tr>
<tr>
<td>Drug- and steroid-induced inhibition of adrenocorticotropic hormone or cortical cell function</td>
<td></td>
</tr>
</tbody>
</table>
2. Primary (gland itself) acute adrenocortical insufficiency ADRENAL CRISIS

   - Waterhouse-Friderichsen syndrome

   - DIC

3. Addison’s Disease (Primary chronic adrenocortical insufficiency)

   - chronic destructive process of adrenal gland (destroyed about 90%)

   - Autoimmune

   - TB

   - metastatic cancer

   - SX

   - weakness and fatigue
- nausea
- hypotension and postural dizziness
- weight loss
- hyperpigmentation

4. Secondary adrenocortical insufficiency (pituitary or hypothalamus failure)

- with no ACTH trying to drive the gland, there is no hyperpigmentation

G. Medulla

1. Not much with respect to loss of function

2. Catacholamines, epi, norepi and dopamine

3. Pheochromocytoma (Tumor secreting epi and norepi)

- 85% arise in adrenal medulla
  - this means that 15% are extra glandular
  Zuckerandl (Zuckerwho?)
- Isolated or associated with other conditions (ie familial)
- MEN syndromes
- SX
  - hypertension (sustained or paroxysmal)
  - CHF
  - headache
  - psychological changes (fear, anxiety)
  - syncopal episodes

- Appearance

  - often large

  - areas of necrosis and hemorrhage

  - maybe hard to find viable tumor (this the case with one in your set)

- can see secretory granules with EM

  - malignant one is not always easy to distinguish from benign

  - mets most reliable, can’t count on local extension
- Neuroblastoma
  - Childhood tumor of autonomic ganglia cell origin

  - 15% of childhood tumors

  - Adrenal origin most common

  - Extra-adrenal, thoracic

  - Measure urinary HVA
VI. MEN

A. Neural crest cells

1. APUD cells

2. Where do they come from and where do they go?

B. MEN I, Wermer’s syndrome - Parathyroid, pancreas and pituitary

1. Parathyroid adenomas or hyperplasia
   - renal stones

2. Pancreatic islet cell tumors
   - gastrin (ZE syndrome with multiple GI ulcers)
   - insulin
   - PIP

3. Pituitary
   - non-functioning adenomas (but these are space occupying lesions)

   - rarely one adenoma will make ACTH, so may have secondary Cushing’s

4. Mutation on chromosome 11 (tumor suppressor gene?)
C. MEN II (IIa) *Sipple’s syndrome* - medullary thyroid carcinoma and pheochromocytoma syndrome.

1. Parathyroid tumors are rare
2. C-cell hyperplasia of thyroid leading to medullary carcinoma of thyroid making calcitonin (may make prolactin, ACTH or serotonin)
3. Pheochromocytoma (often extra-adrenal), benign
4. Linked to mutation on chromosome 10 (*RET* proto-oncogene)

D. MEN IIb - *mucosal neuroma syndrome*

1. Much the same as MEN IIa, but with

   - neuromas, neurofibromas and/or ganglioneuromas of
     - lips
     - face
     - oral cavity
     - eyes
     - GI tract

2. The presence of the neuromas may lead to early diagnosis
Endocrine Pathology Case Studies

Case 1.

HISTORY: This 12-year-old girl was referred for evaluation of short stature. Both parents were above the 50th percentile for height.

PHYSICAL FINDINGS: Normally proportioned young girl, height 94cm (third percentile 138cm), weight 35kg (25th percentile). Visual field exam showed bitemporal hemianopsia.

LABORATORY FINDINGS:
urinalysis: specific gravity: 1.018; pH: 5.0; RBC: 0/hpf; WBC: 1/hpf; casts: 0/lf; epithelial cells: 1/lf; hemoglobin: neg; bilirubin: neg; urobilinogen: neg; ketones: neg; glucose: neg; protein: neg
sodium: 140 mEq/l
alkaline phosphatase: 50 U/L (normal: 30-115)
growth hormone: 3 ng/ml (normal: greater than 10 ng/ml)
growth hormone, lysine challenge: 3 ng/ml
growth hormone, hypoglycemic challenge: 3.1 ng/ml
skull x-rays: enlarged sella turcica, fluffy suprasellar calcifications

Based on the history, what do you suspect is the best diagnosis? The most likely cause for this child's short stature is? This patient's visual field defect is most likely due to what?

Case 2.

HISTORY: This 41-year-old housewife was seen as an outpatient complaining of severe weakness, headaches and nosebleeds of about 2-months duration. She is taking no drugs other than aspirin and reports nothing of further significance in her medical history.

PHYSICAL FINDINGS: The patient is not acutely ill. BP: 168/112 mm Hg.

LABORATORY RESULTS:
sodium: 140 mEq/l
alkaline phosphatase: 50 U/L (normal: 30-115)
growth hormone: 3 ng/ml (normal: greater than 10 ng/ml)
growth hormone, lysine challenge: 3 ng/ml
growth hormone, hypoglycemic challenge: 3.1 ng/ml
serum electrolytes- K: 2.8 mEq/L (N=4.0-4.8) Na: 154 mEq/L (N=142-147)
24-hour urine sample-elevated calcium, elevated potassium, low specific gravity

CLINICAL COURSE: The patient was treated surgically and is now free of diseases.

Based on the history and physical findings, what do you think is ultimately responsible for this patient's distress? Complications of the far advanced untreated form of this disease might include?

Case 3.

HISTORY: This 19-year-old female college student was seen as an outpatient complaining of fatigue, nervousness and palpitations
of several months duration. Following the recommendation of a friend she had been subsisting on a diet of brown rice and brown sugar for the past 8 months.

PHYSICAL FINDINGS: The patient was thin and apprehensive appearing. Her pulse was rapid but strong; her skin warm and her hair thin and of very fine texture. Lymph nodes were palpable bilaterally in the cervical, axillary and inguinal areas. The thyroid gland was slightly enlarged and slightly tender.

LABORATORY RESULTS:
- serum T-4-elevated
- serum T-3-elevated

CLINICAL COURSE: The patient was admitted to the hospital and preparations were made for surgical treatment. On the day before the operation her temperature rose suddenly to 40C and she experienced severe diarrhea and vomiting; palliative treatment was instituted and the surgery performed on schedule. She is now in relatively good health although not cured of the basic disease.

What is the most likely diagnosis for this woman’s

What histological findings would you expect?

Other laboratory tests that might be helpful?

Why is she not actually “cured” of this disease and what other conditions might you be on the look out for?

Case 4.

HISTORY: This 61-year-old diabetic woman was referred because of enlargement of the thyroid gland. The gland had increased in size over the past two years but she was asymptomatic.

PHYSICAL FINDINGS: Firm, nonmovable thyroid gland 3 times normal size. Remainder of exam unremarkable.

LABORATORY RESULTS:
- T-3 (tri-iodothyronine) assay: 100 ng/dl (normal 50-170)
- T-4 (thyroxine) 7.5 mcg/dL (normal 4.5-11.0 mcg/dL)
- TSH 14.5 U/L (normal 0.3-6.0 U/L)

CLINICAL COURSE: At operation the thyroid gland was uniformly gray and rubbery and was about 3 times normal size.

The most likely diagnosis in this case is?

What can you diagnose from the laboratory tests?
Why is the thyroid gland 3 times the expected size?
What other laboratory test would be helpful in confirming your diagnosis?
Two new endocrine patients have just shown up

Mrs. JG is a 38-year-old woman presents with a history of 60 lb weight gain over the past six months. Physical examination reveals truncal obesity, hypertension, a round face, and abdominal cutaneous striae.

- Hx and physical?
- Differential dx?
- Basic evaluation?
- Diagnostic tests?

Mr. JK is a 43-year-old man is admitted to the hospital for progressive weakness and loss of 50 pounds during the previous 6 months. The patient reports that he has "no desire to eat anything". Physical examination reveals hypotension as well as hyperpigmentation of the skin of the extremities and the face and neck.

- Hx and physical?
- Differential dx?
- Basic evaluation?
- Diagnostic tests?