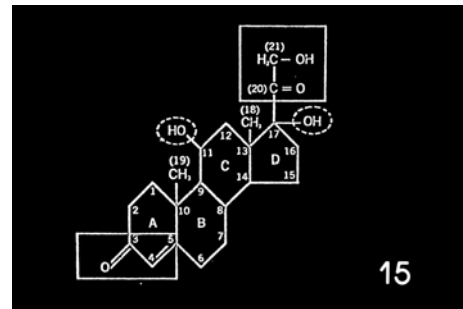


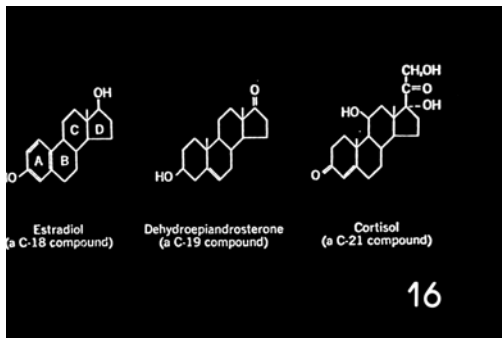
Adrenal Function

- chemistry of steroids/biosynthesis of cortisol, aldosterone & adrenal androgen
- pathophysiology of HPA axis disorders, secondary hypertension
- Laboratory Diagnosis of Cushing's, adrenal insufficiency, hirsutism/virilism, pheochromocytoma, primary aldosteronism

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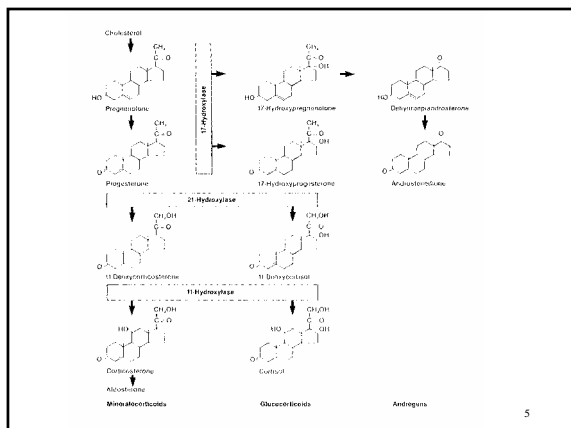


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Adrenal Steroids

- glucocorticoids & mineralocorticoids are 21-carbon steroids
- androgens are 19-carbon steroids
- adrenal androgens are 17-ketosteroids
- key adrenal androgen is dehydroepiandrosterone sulfate (DHEAS)
- testosterone is a 17-OH steroid - not a ketosteroid

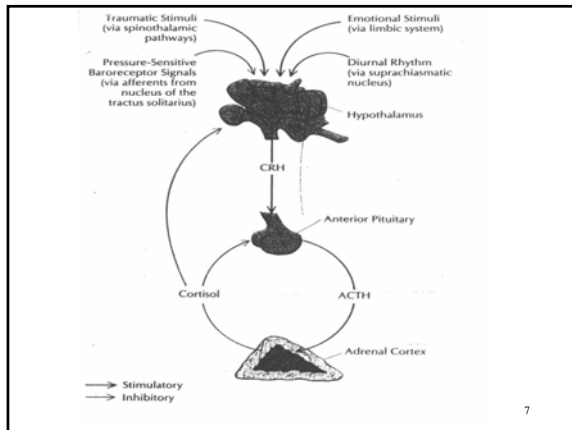
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Adrenal Biosynthesis

- cortisol is the result of 3 successive hydroxylations of progesterone at 17, 21 and 11
- aldosterone synthesis requires only 21 and 11 hydroxylation steps
- androgen requires only 17 hydroxylation

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Adrenal Pathophysiology

- free plasma cortisol inhibits biosynthesis and secretion of CRH and ACTH
- ACTH is synthesized as a large precursor, pro-opiomelanocortin (POMC)
- ACTH stimulates cortisol, adrenal androgen and under short-lived conditions - aldosterone

Adrenal Insufficiency

- autoimmune adrenalitis
- TB & systemic fungal infections
- AIDS & opportunistic infections
- acute hemorrhage or thrombosis (sepsis, anticoagulant therapy, antiphospholipid syndrome, clotting disorders)
- hypothalamic-pituitary disease
- glucocorticoid therapy

Lab Diagnosis: Adrenal Insufficiency

- Ruling out - low probability
 - 8:00 am serum cortisol
 - < 3 ug/dL confirms
 - > 20 ug/dL rules out
 - 8:00 serum cortisol 3 - 20 ug/dL
 - short corticotropin stimulation
- Primary vs Secondary
 - basal serum cortisol & ACTH

Short Corticotropin Stimulation

- 250 ug cosyntropin before 10:am
 - serum cortisol, before, 30 & 60 min post
- a low dose of 1 ug cosyntropin for Asthma patients on inhaled glucocorticoids
- any cortisol value > 19 ug/dL excludes
- insulin hypoglycemia test for inadequate responses

Cushing Syndrome

- | Corticotropin-dependent | Percent |
|---------------------------|---------|
| Cushing's disease | 68 |
| ectopic ACTH | 12 |
| ectopic CRH | < 1 |
| Corticotropin-independent | |
| adrenal adenoma | 10 |
| adrenal carcinoma | 8 |
| nodular hyperplasia | < 2 |
| pseudo-Cushing | < 2 |

Lab Diagnosis: Cushing's

- Screening
 - 24h urine free cortisol
- Confirmation
 - low dose dexamethasone
 - midnight serum cortisol
- Specific Diagnosis
 - ACTH
 - high dose dexamethasone
 - inferior petrosal sinus sampling

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Hirsutism/Virilism

- polycystic ovary syndrome
- idiopathic
- Drugs: minoxidil, cyclosporin, androgens, glucocorticoids, antiepileptics
- 21-hydroxylase deficiency
- Cushing syndrome
- adrenal tumors
- ovarian tumors

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Lab Diagnosis: Hirsutism/Virilism

- Basal & Dexamethasone Suppression of
 - serum total testosterone
 - serum DHEAS
 - 17-hydroxyprogesterone
 - serum cortisol
- ACTH stimulated 17-hydroxyprogesterone
- FSH & LH

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Lab Diagnosis Hirsutism/Virilism

- Rapidly developing Severe Virilism
 - marked inc in DHEAS indicate adrenal malignancy
 - total testosterone > 300 ng/dL and normal or slight inc in DHEAS indicate ovarian malignancy

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Lab Diagnosis Hirsutism/Virilism

- LH:FSH ratios > 2.0 favor polycystic ovary syndrome
- serum total testosterone < 150 ng/dL makes ovarian malignancy unlikely
- basal or ACTH stimulated 17-hydroxyprogesterone > 1500 ng/dL indicate 21-hydroxylase deficiency

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Pheochromocytoma:

- 24 hr urine Metanephrines
 - positive interferences
 - imipramine, monoamine oxidase inhibitors
 - negative interferences
 - radiographic contrast media
 - sensitivity: 98 - 99 percent
 - specificity: 98 percent

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Pheochromocytoma

- VMA
 - positive interferences
 - hydroxymandelic acid
 - negative interferences
 - monoamine oxidase inhibitors
 - sensitivity: 90 percent
 - specificity: 98 - 00 percent

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Pheochromocytoma

- Catecholamines- urine or plasma
 - positive interferences
 - stress, emotion, exercise, catecholamine containing nasal sprays & bronchodilators
 - highly sensitive; choice in MEA-II or in paroxysmal episodes
 - specificity may be a problem

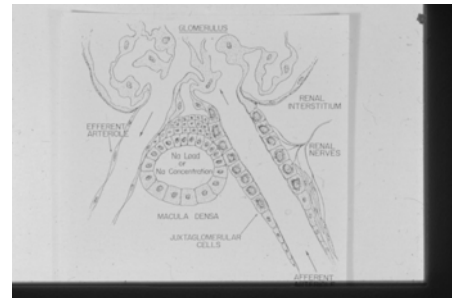
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Primary Aldosteronism

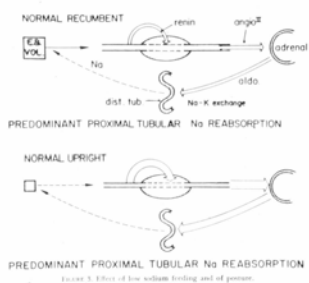
- Aldosterone producing Adenoma (APA)
- Idiopathic Hyperaldosteronism (IHA)

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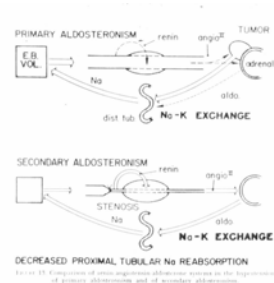
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Primary Aldosteronism: Laboratory Diagnosis

- Screening: spontaneous or easily provoked diuretic induced hypokalemia
- Detection: serum K, urine K,
plasma aldosterone (PAC)
plasma renin activity (PRA)
PAC:PRA ratio > 20 favors
primary aldosteronism

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Primary Aldosteronism

- Confirmation
 - off antihypertensives, spironolactone, diuretics, estrogen
 - high Na & K intake for 5 days
 - urine aldosterone > 14 ug/d favors disease
- APA vs IHA
 - > 33% rise in aldosterone &
18-OHB < 100 ng/dl favor IHA

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