**Vesalius SCALpel™ : Adrenal**

**Embryology**

neural crest cell migration
- cortex mesoderm, medulla ectoderm and neural crest
- ectopic: organ of Zuckerkandl aortic bifurcation, along aorta, broad ligament, uterus

adrenal mass: 9% of autopsies, incidentaloma on CT most benign cortical adenoma
- size is best indicator of malignancy: 92% > 6cm malignant; inhomogeneous, irregular
- functional adrenal mass most commonly adrenocortical neoplasm, produce cortisol
  - 30% clinically apparent: 20% androgens, 10% estrogens, 2% aldosterone, 35% mixed
- 2/3 of adrenocortical carcinoma hormonally active
  - rapid onset Cushings syndrome with virilization
  - complete resection only chance of cure

**Cortex**

- glomerulosa: aldosterone, faciculata: cotrisol, reticularis: androgens, estrogens
- cortisol: stress -> hypothalamus production CRF -> ant pituitary -> ACTH -> adrenal
  - diurnal variation, high AM, low PM
- glucocorticoids
  - stimulate hepatic gluconeogenesis
  - inhibit protein synthesis (inhibit wound healing)
  - inhibit fibroblast activity (inhibit wound healing)
  - lipolysis
  - increase response to gluconeogenic hormones
  - increase glycogen synthesis
  - increase uptake glucose
  - inhibit bone formation (osteoporosis)
    - negative calcium balance
  - anti-inflammatory
    - inhibit leukocyte mobilization
    - decrease migration of inflammatory cells
    - decrease production inflammatory mediators (interleukins, leukotrienes, bradykinins)
- Cushing's
  - iatrogenic steroid (glucocorticoid) administration most common
  - syndrome: adrenal adenoma, hyperplasia or, carcinoma, ectopic, iatrogenic
    - ectopic most commonly (15%) small cell lung Ca, 15% primary adrenal tumor, bronchial carcinoid, bilateral adrenal hyperplasia
      hyperpigmentation most commonly from ectopic
      17 hydroxyprogesterone high
  - disease: pituitary adenoma -> ACTH (70% source of ACTH)
  - differential diagnosis
    - 24h urine free cortisol most sensitive Dx
    - lo dose (1 mg) dex to confirm

AM plasma cortisol suppressed < 3 normal; elevated = syndrome
corticotropin releasing hormone (CRH) elevated in disease, normal in ectopic
hi does dex suppression: suppresses pituitary adenoma, not ectopic or adrenal
plasma ACTH differentiates pituitary/ectopic source from adrenal
if other tests inconclusive, inferior petrosal sinus sampling differentiates source ACTH

aldosterone

decrease in blood pressure stimulates release renin from renal tubules -> liver where angiotensinogen is converted to angiotensin 1, lung enzyme converts to angiotensin 2, potent vasoconstrictor, stimulates adrenal release of aldosterone which causes tubular reabsorption Na in exchange for K and H, water reabsorption, increased vascular volume

aldosteronoma 1% of hypertensive patients

imaging may miss bilateral micronodular disease, idiopathic hyperaldosteronism

if miss on CT 60% bilateral hypersecretion

unilateral adrenalectomy not effective

venous sampling can differentiate

increased BP, hypokalemia, alkalosis, feedback decreases renin

Dx: decreased K (necessary for diagnosis), increased plasma/urine aldosterone, suppressed plasma rennin (aldosterone/renin ratio), increased Na,

aldosteronoma 65%, idiopathic 35%, rare adrenal carcinoma

adenoma: younger, women, more severe hypertension, hypokelemia

salt loading and postural test no change in aldosterone

CT small,< 2cm, solitary (70%), solitary cortical adenoma, 30% hyperplasia, rare Ca

primary see decreased plasma rennin

idiopathic: male, older

salt loading drops aldosterone

postural test aldosterone increases

medical Rx: K-sparing diuretics (spironolactone most effective)

secondary hyperaldosteronism from hypovolemia

Na load, captopril decrease aldosterone

spironolactone, ACE inhibitors, diuretics affect aldost measure: withhold

adrenalectomy cures 80% of hypertension, 90% normalization of K

bilateral hyperplasia treated with spironolactone

androgens

<5% of male testosterone

increased in Cushings

congenital adrenal hyperplasia

autosomal recessive defect in cortisol synthesis (21 alphahydroxylase deffic.)

causes increase ACTH production -> adrenal hyperplasia -> incr androgen

associated defect aldosterone production, severe electrolyte and fluid loss

adrenal insufficiency

etiologies: cortisol administration, autoimmune, bilateral adrenal hemorrhage, (Waterhouse-Friedrichson), heparin induced, adrenalectomy, adrenal mets, infection

symptoms: vascular collapse (no aldosterone, fluid loss), abdominal pain, nausea, weakness, fever, decreased mentation
adrenal crisis, hypotension, responds to cortisol
lab: hyponatremia, hyperkalemia, hypoglycemia (no cortisol), increase BUN/Cr (vol loss), decreased glucocorticoid level
stress dose for surgery in chronic hypothalamus/pit/adrenal axis
major : 100-150mg/d hydrocortisone X 2-3d
(older recommendation 300-400 excessive, unnecessary)
minor surgery: (hernia) 25mg/d, moderate 50-75mg X 1-2d
hydrocortisone short half life: 3 doses/d
no taper necessary
3/4 of septic patients who respond poorly to fluid resuscitation have relative adrenal insufficiency
df: failure to increase cortisol level by at least 9mcg/dl in response to ACTH
supplement with 200mg/d plus mineralocorticoids, benefits sepsis Rx

**Medulla**

pheochromocytoma
24h urinr VMA, metanephrine (serum catechols elevated in essential HTN)
90% adrenal medullary tumor, 3X as bright as liver on T2 MRI image
MIBG (methyoiodobenzylguanidine: norepi analogue) scan for primary sporadic, extra-adrenal, low sensitivity, rarely identifies other sites or changes plan: no advantage over MRI
rule of 10s: 10% extraadrenal, bilateral, child, familial, malignant
most sporadic unilateral
many congenital (MENIIA, B, VonRecklinhausen) bilateral
laparoscopic adrenalectomy for pheo: risk of seeding malignant?
alpha blockade (penoxybenzamine = major alpha blockade; now prefer selective alpha 1 antagonist [prazosin] or calcium channel blocker) pre-op functional tumor, subsequent beta blockade if still tachycardic after alpha (no early beta: chronically volume contracted due to alpha stimulation, beta could cause hypotension), proportional to initial symptoms
pheo during pregnancy: untreated 50% maternal mortality, higher fetal mortality
hypertension, sweating, tachycardia may be mistaken for pre-eclampsia
urine protein elevated in pre-eclampsia, not pheo
treat with alpha block and adrenalectomy first and second trimester
third trimester immediate alpha block (decreased fetal mortality), then controlled C-section
vaginal delivery absolutely contraindicated (BP instability, abruptio)
MS and phenothiazine can precipitate pheo crisis

**Incidentaloma**

41% benign adenoma, 19% metastasis, 10% adrenocortical malignancy, 9% myelolipoma, 8% pheo
check aldosterone/renin, corticoids, catechols

adrenal met

FNA only of other malignancy present, suspect met and would change plan: 75% positive
lymphoma, lung, breast common; also melanoma, renal, leukemia, ovarian
resection of solitary adrenal met can increase survival

**References:**

Pasieka J. What's new in general surgery: endocrine surgery. JACS 199(3), Sept. '04: 437-445.