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Understanding Adrenal Diagnosis and Management

ACOi 2023 October 11-14 Tampa • Hybrid

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Private Solo Practice in Carson City, NV
Kirksville College of Osteopathic Medicine 1989
Post grad Osteopathic Hospitals Suburban Detroit
Endocrinologist Carson Tahoe Health
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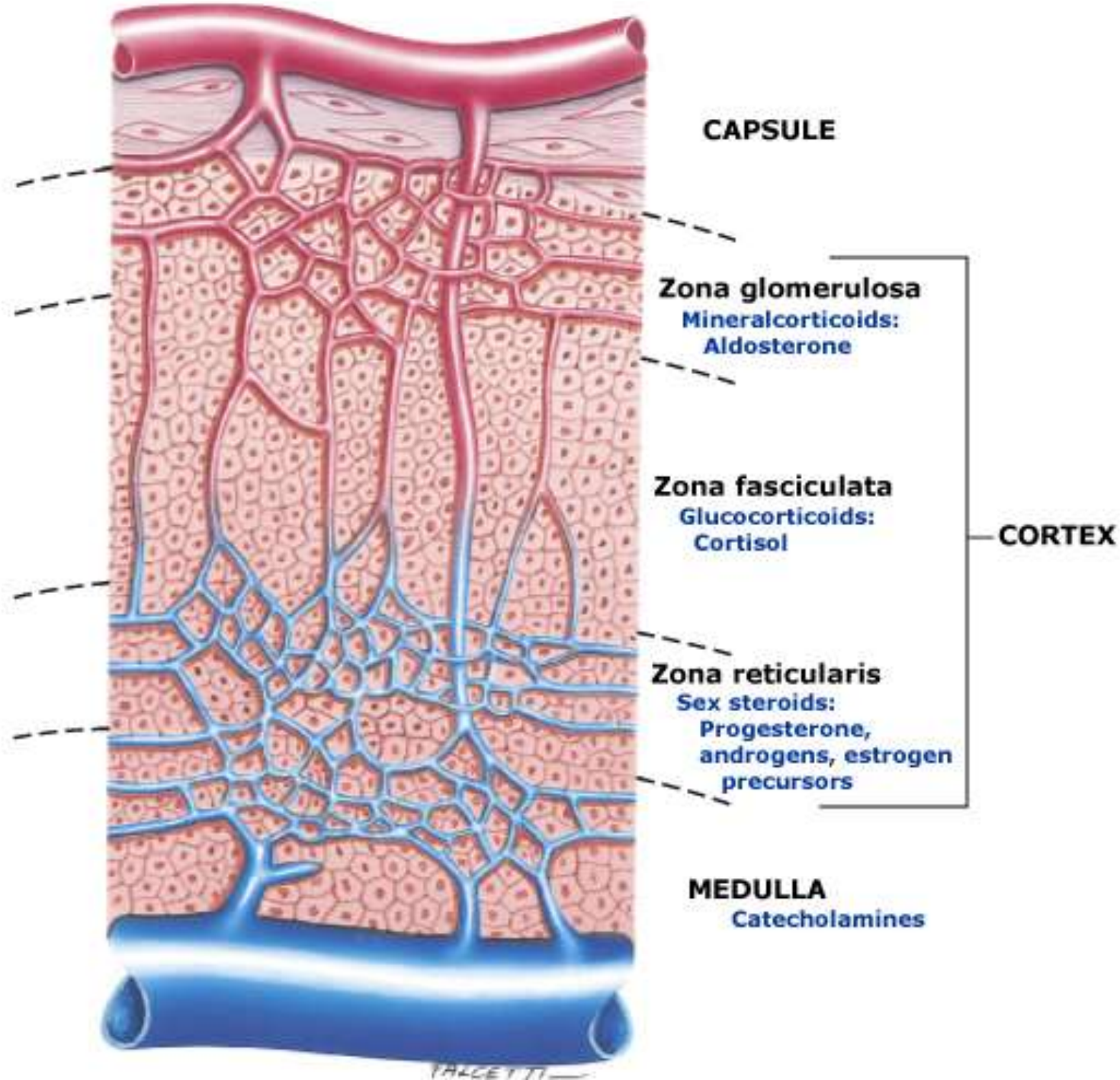
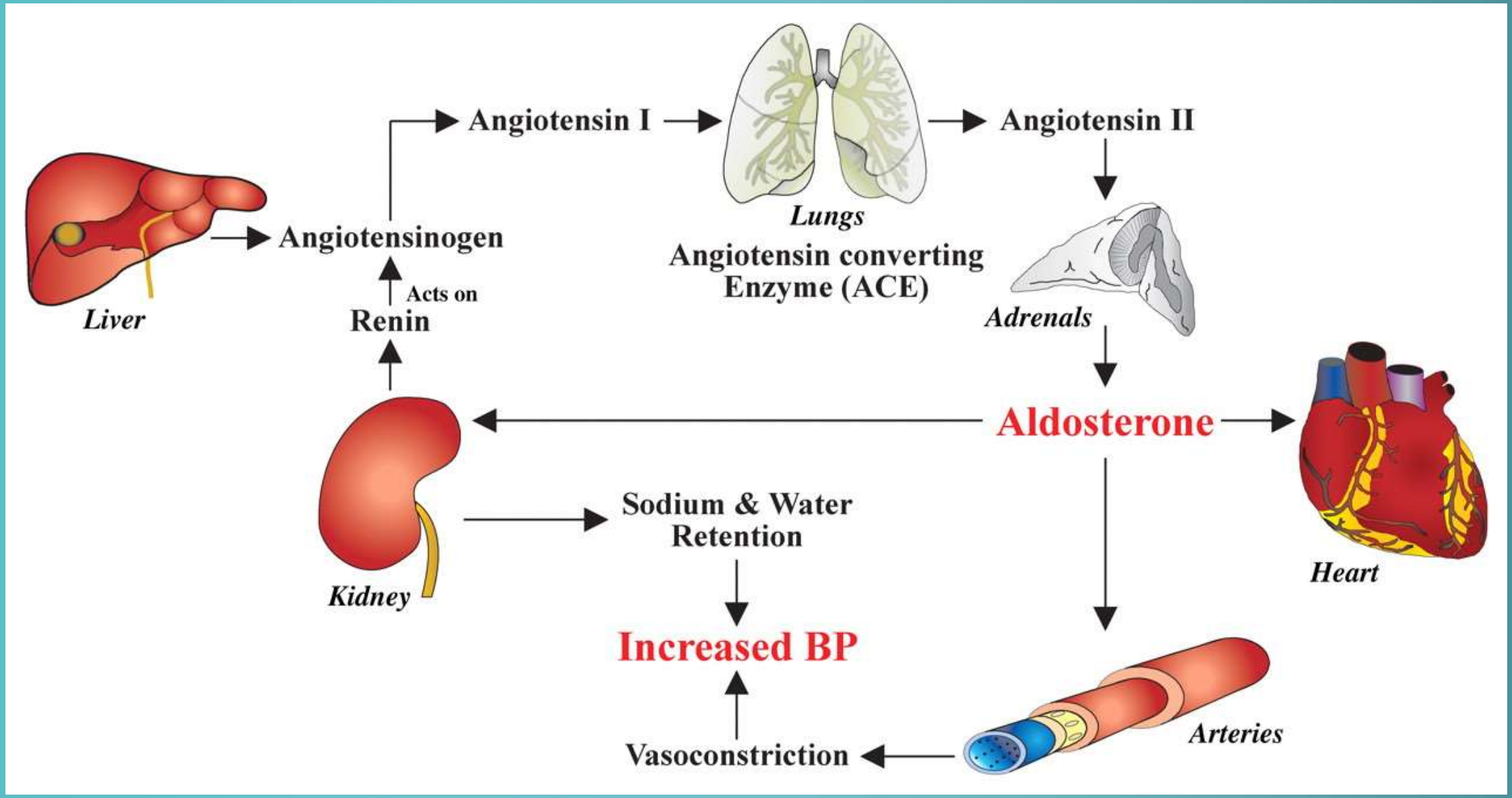
Principle Centered Medicine

- Framework for patient care centered in the whole patient
- Consider body, mind, spirit in the pathway to health
- Seeking the full health potential of the patient
- Focus on getting to the bottom of the problem for endocrine etiology
- Seeking a diagnosis to apply Rational Therapy based in scientific endocrine principles


CAPSULE
Zona glomerulosa
Mineralcorticoids:
Aldosterone
Zona fasciculata
Glucocorticoids:
Cortisol
Zona reticularis
Sex steroids:
Progesterone,
androgens, estrogen
precursors
CORTEX
MEDULLA
Catecholamines

Zona Glomerulosa

- Mineralocorticoids: aldosterone
- Angiotensin II/renin regulation by sympathetic tone; High potassium will stimulate and ACTH
- Increase in aldosterone leads to salt and water retention
- Increase in Angiotensin II leads to vasoconstriction

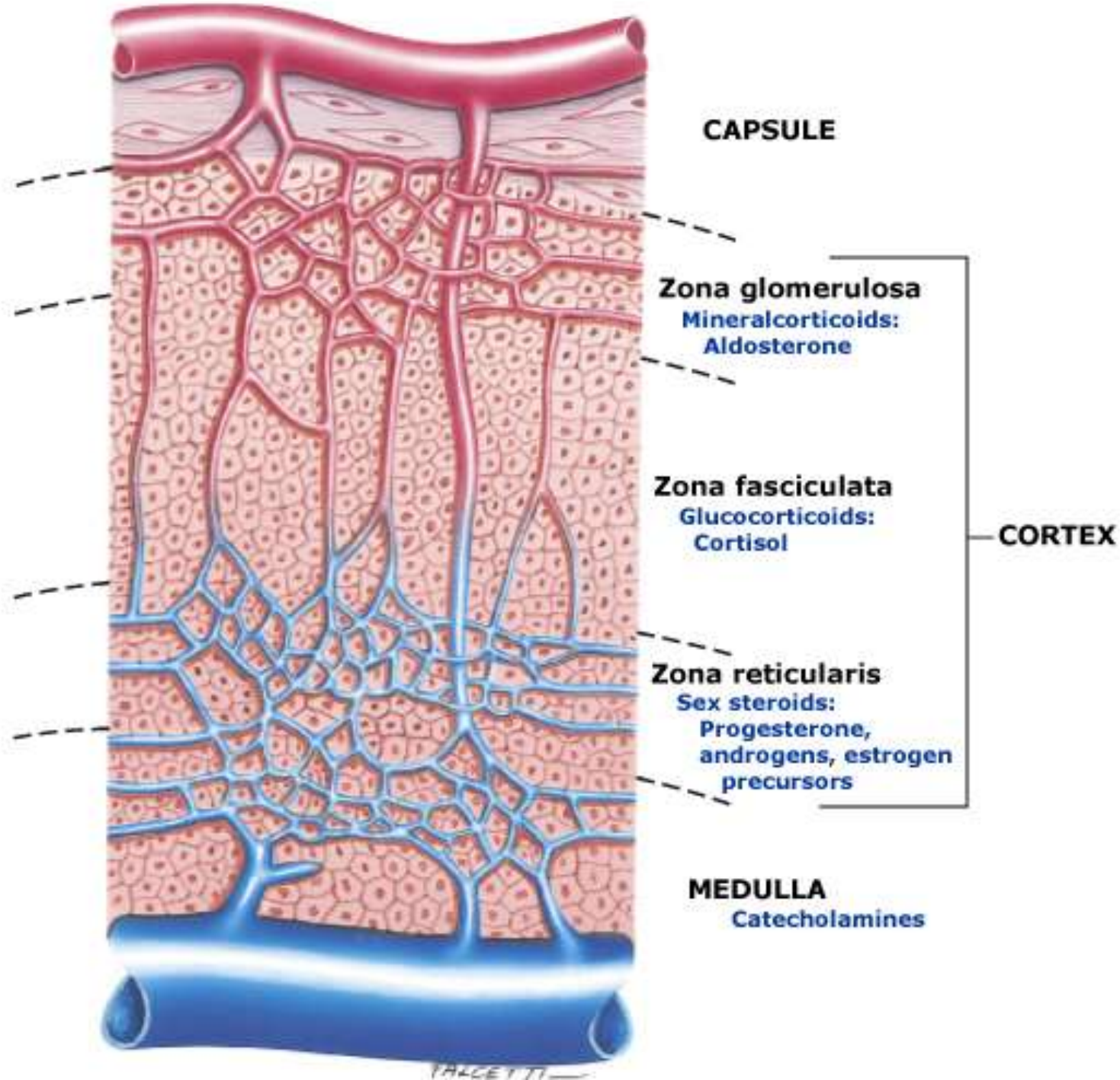


Zona Fasiculata and Reticularis

- Glucocorticoids: Cortisol
- Androgen: DHEAS
- Estrogens, Progesterone
- Regulated by ACTH

Adrenal Medulla

- Catecholamines
- Regulated by autonomic nervous system
- Patient with a neoplasm in this area may have symptoms of poorly controlled BP, diaphoresis, headache = Pheochromocytoma
- Think of pheochromocytoma when it seems unusual for the patient to have hypertension (HTN). No family history, lean, young patients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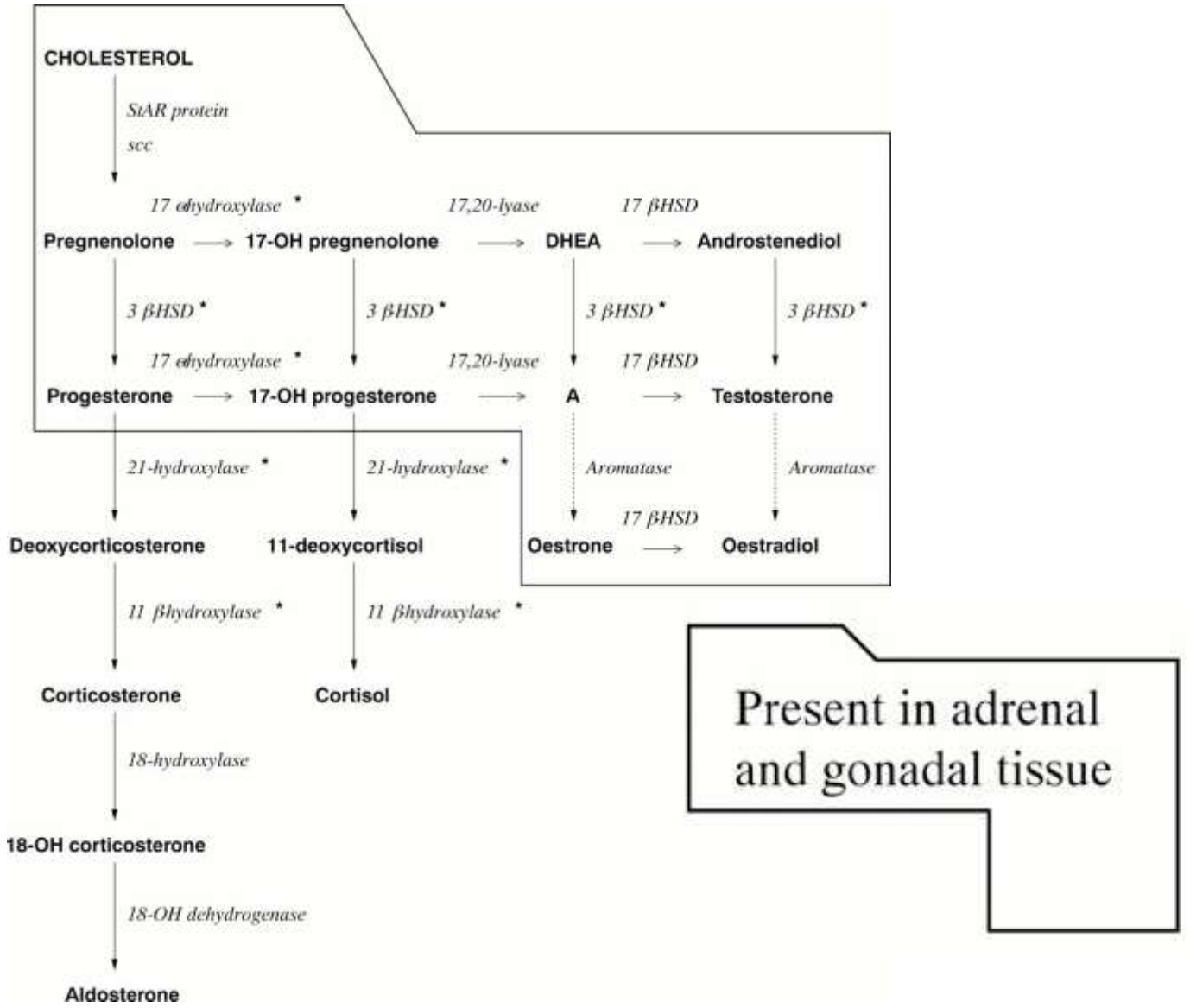
Steroid Production Pathway (steroidogenesis)

- Baseline substrate = cholesterol
- Precursors: DHEAS , DHEA,17-OH progesterone
- End products: estradiol, cortisol, aldosterone



20 year old female

- Weight loss, easy tanning, nausea, vomiting, abdominal pain, weakness, lightheaded
- BP=70/30, tan, confusion

Laboratory

- Hyponatremia
- Hyperkalemia
- Low glucose
- Elevated BUN/Cr
- Vitiligo

- Deficiency of all steroids

Diagnosis

- **Primary**
- **Adrenal Insufficiency**

Laboratory

- AM cortisol, ACTH
- Cortrosyn (ACTH) stimulation IV or IM Baseline, 30 min and 60 minute values for cortisol
- If Aldosterone drawn with Cortrosyn stimulation, response blunted
- **Cortisol ≥ 18mcg/dL with Cortrosyn stimulation, assuming a normal baseline cortisol; With IM high dose ACTH cutoff ≥ 16 mcg/dL using standard immunoassays

Laboratory

- Cortrosyn is ACTH. If you draw ACTH level, make sure it is done before the ACTH is given for the test
- Cortisol binding globulin (CBG) is bound to cortisol and is higher patient estrogen, lower in low protein state as in nephrotic syndrome or in malnourished patient
- Older immunoassays vs new immunoassays vs LC-MS/MS with cut off 14 to 15 mcg/dL for modern cortisol assays
- Baseline cortisol < 2 mcg/dL predicts poor response to ACTH stimulation

Etiology

- 80 % Autoimmune/Idiopathic
- 20 % Tuberculosis
- Other: Vascular, infectious, AIDS, trauma, mets, meds, congenital adrenal hyperplasia

Autoimmune Etiology

- Addison Disease
- May be associated with other autoimmune conditions, as in Hashimoto or vitiligo

50 year old female

- Similar symptoms to index patient: low to low normal BP, fatigue weakness
- No change in skin color
- COPD

Laboratory

- Low sodium
- Normal potassium– {Suggests normal aldosterone production}
- Low ACTH or inappropriately normal when the end organ value is low

Additional History

- History of long term steroid use IV and oral treatment
- Recent change in pharmacy
- Prednisone not renewed
- Presents with fever and lung infiltrate

Diagnosis

- **Secondary Adrenal Insufficiency**

Etiology

- Steroid dependent
- Tumor, infection, radiation, surgery, trauma involving hypothalamic region or pituitary

Physical findings in AI

- Fever
- Generalized abdominal tenderness
- Postural hypotension
- Look for precipitating infection
- Careful with consideration for surgical abdomen
- Surgery could precipitate adrenal crisis if adequate steroids are not on board

Adrenal Insufficiency

- Electrolyte imbalance: Hyponatremia, Hyperkalemia in primary adrenal insufficiency
- Hypotension and medical crisis
- Hyponatremia without hyperkalemia in secondary adrenal insufficiency, less likely to result in adrenal/medical crisis

Electrolyte imbalance in AI

- 85 to 90 % of patients have hyponatremia
- Mineralocorticoid deficiency results in sodium loss and volume depletion and increased Vasopressin secretion due to loss of cortisol
- Hyperkalemia in 60 to 65 % of patients
- Rare hypercalcemia

Imaging

- Consider CT of the adrenals for primary adrenal insufficiency
- MRI of the brain for secondary adrenal insufficiency unless the cause is evident
- CT Adrenals: primary----small adrenal glands

Treatment at diagnosis in Crisis

- IV hydrocortisone 100 mg q 6-8 hrs wean as tolerated to daily oral dose of 25 mg daily/divided
- Saline and glucose
- Supportive and correcting precipitating factors
- Primary adrenal insufficiency: Florinef as aldosterone replacement
- If steroids < 30 days in general medical treatment, do not necessarily need to wean slowly

Crisis Intervention

- Surgery
- Acute illness
- Additional steroids IV and/or PO
- Home illness: short course of double dose steroids
- Observe sodium, potassium and BP; Pt can follow BP at home for crisis intervention

25 Year Old Female

- Weight gain, hirsutism, diabetes, osteoporosis
- Abdominal obesity, striae, acne, hypertension, capillary fragility, amenorrhea

Diagnosis

- **Cushing Syndrome**

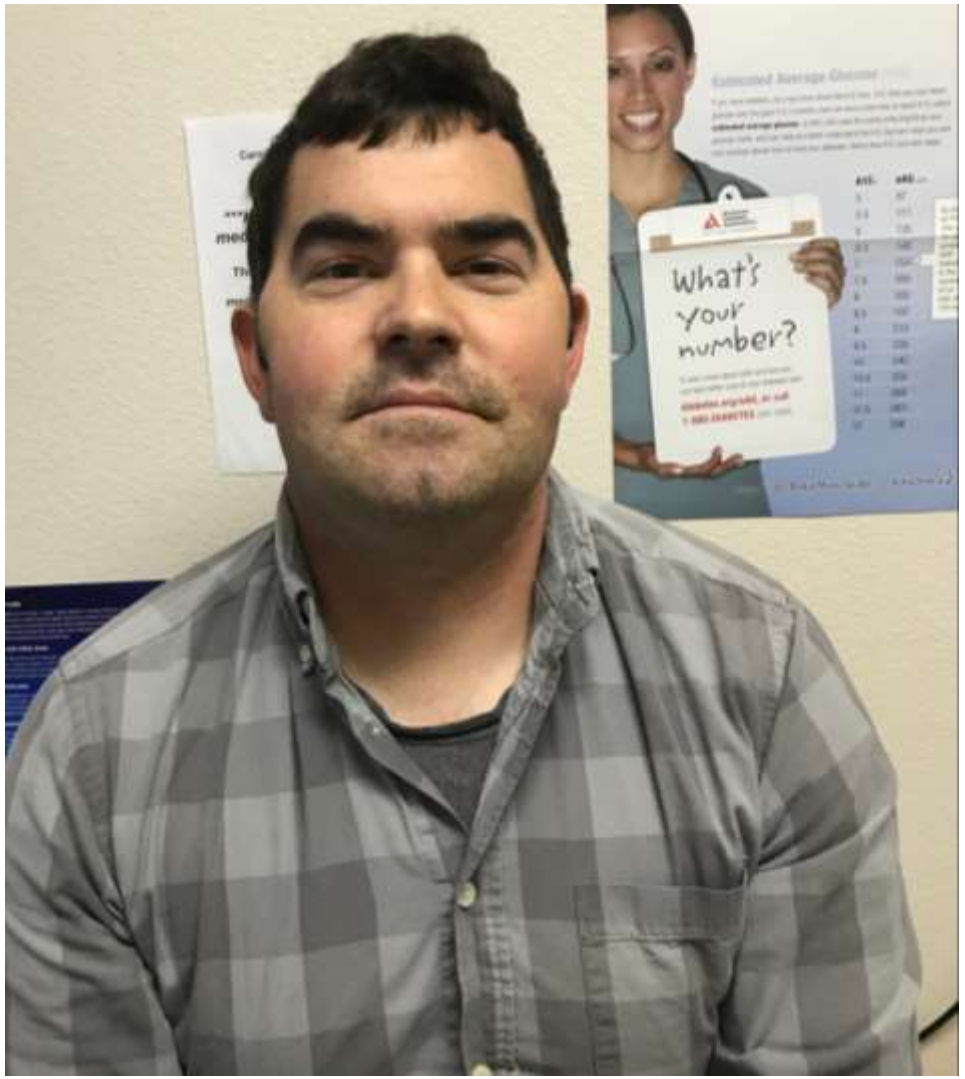
Laboratory

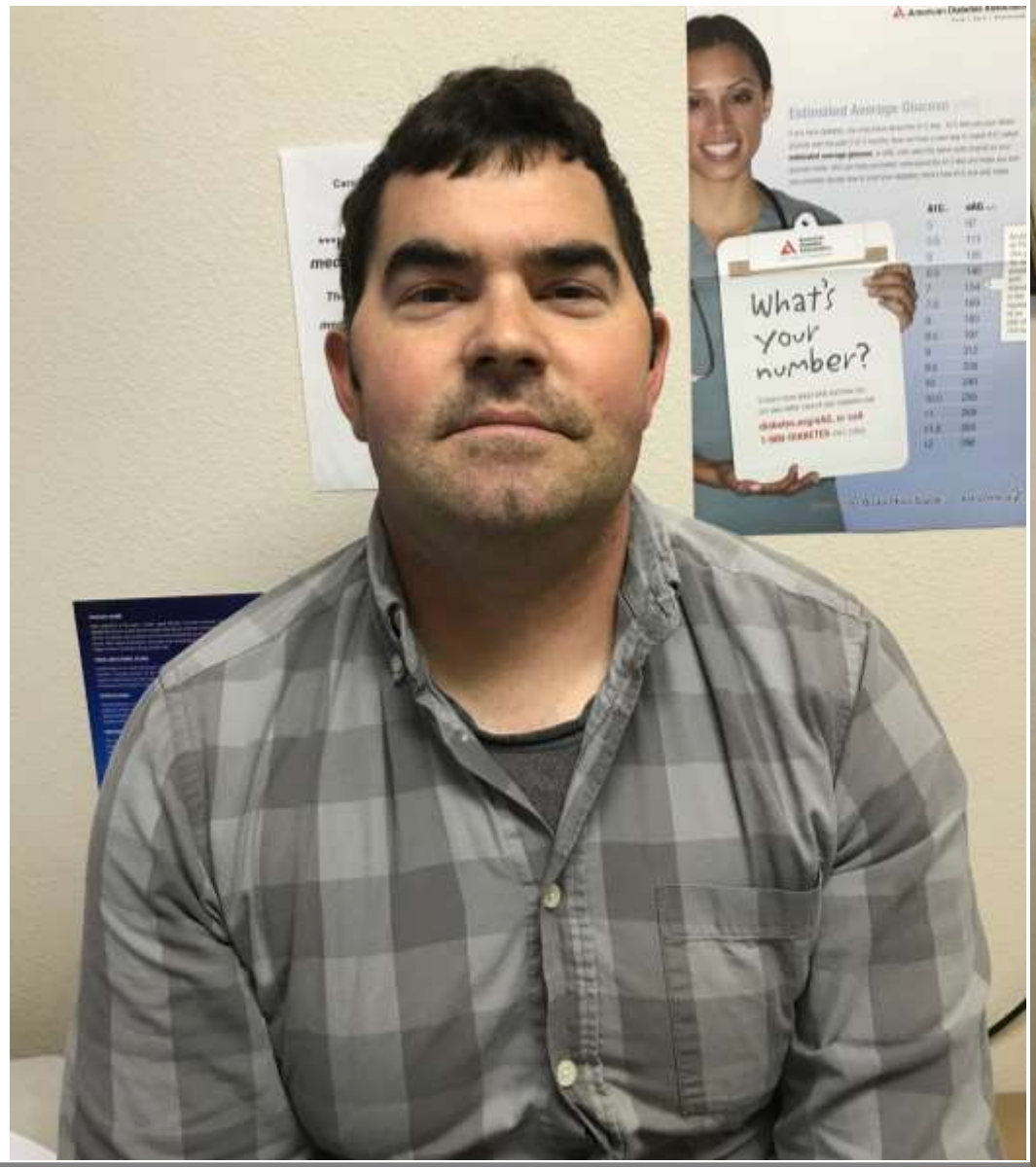
- 1 mg overnight dexamethasone suppression testing; 1 mg Dex 11 pm with 8 am cortisol next day; suppression < 1.8 excludes excess cortisol
- 24 hour urine free cortisol at least a few times normal result
- Hypokalemia, hyperglycemia
- Some false positives


Pregnancy Striae

Differential Diagnosis

- Cushing disease: Cushing syndrome due to pituitary adenoma/high ACTH---dependent
- ACTH Independent vs ACTH Dependent
- Exogenous steroids
- Adrenal adenoma or hyperplasia
- Ectopic: lung tumor


What's your number?



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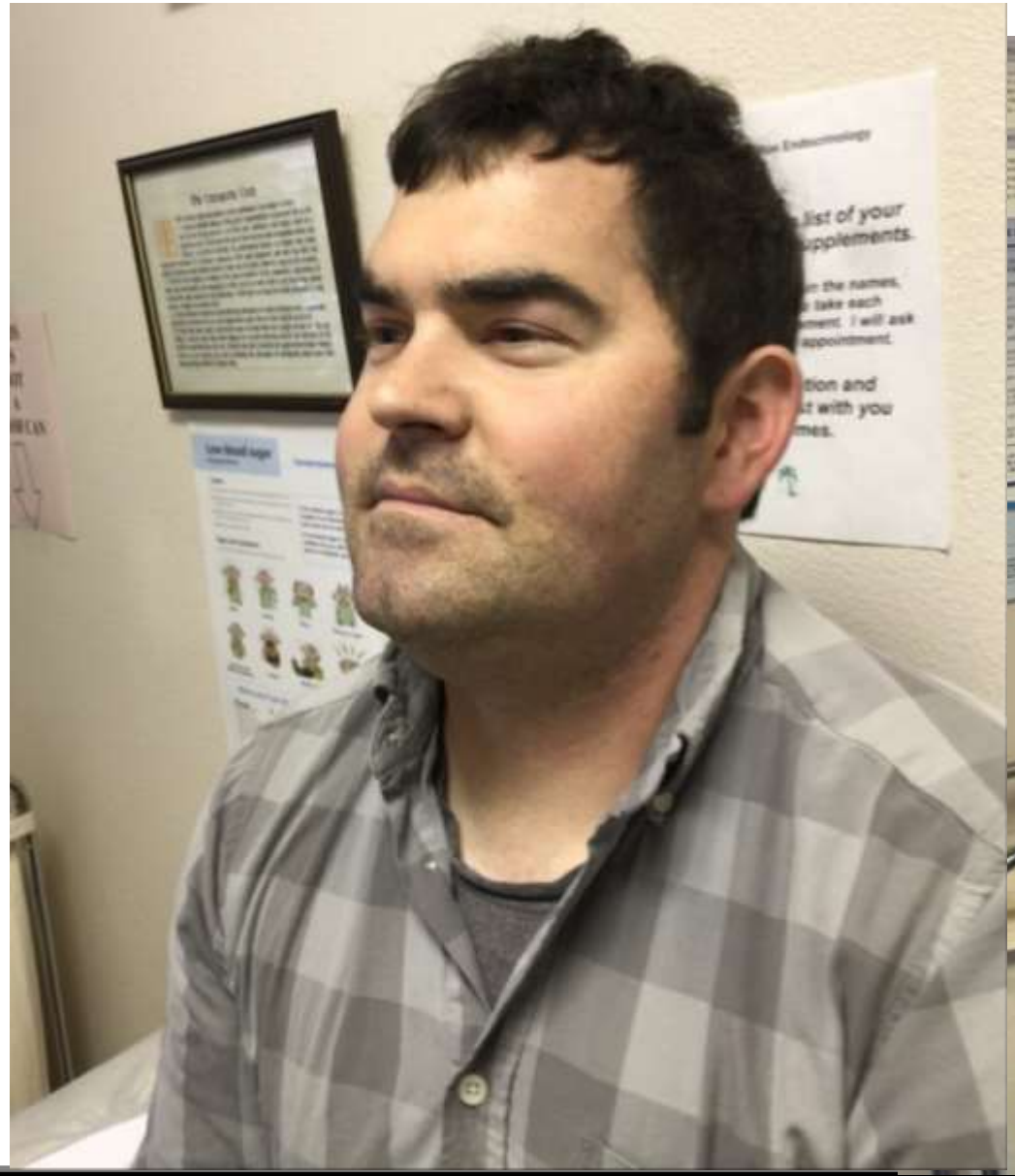

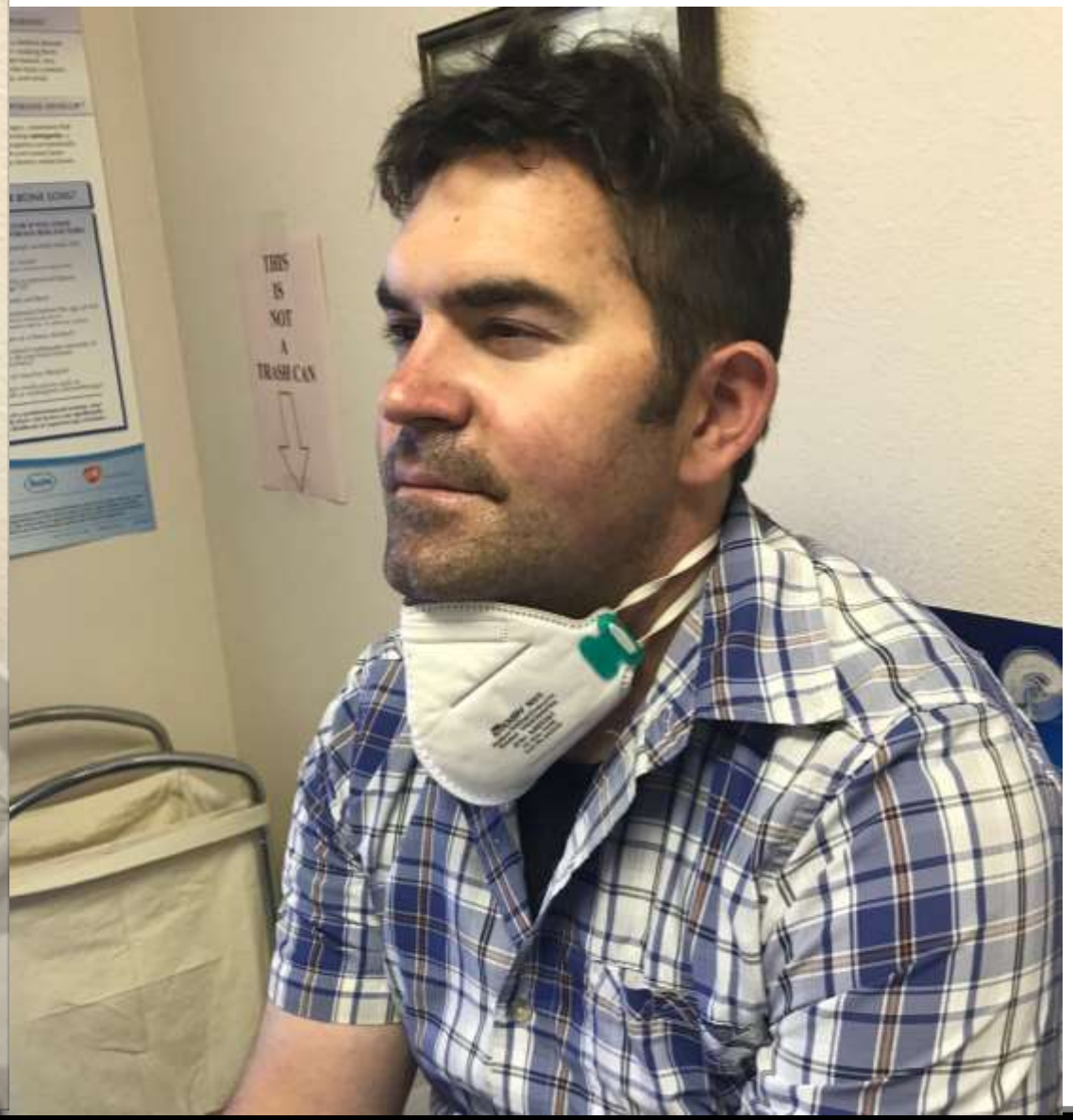

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Differential Diagnosis

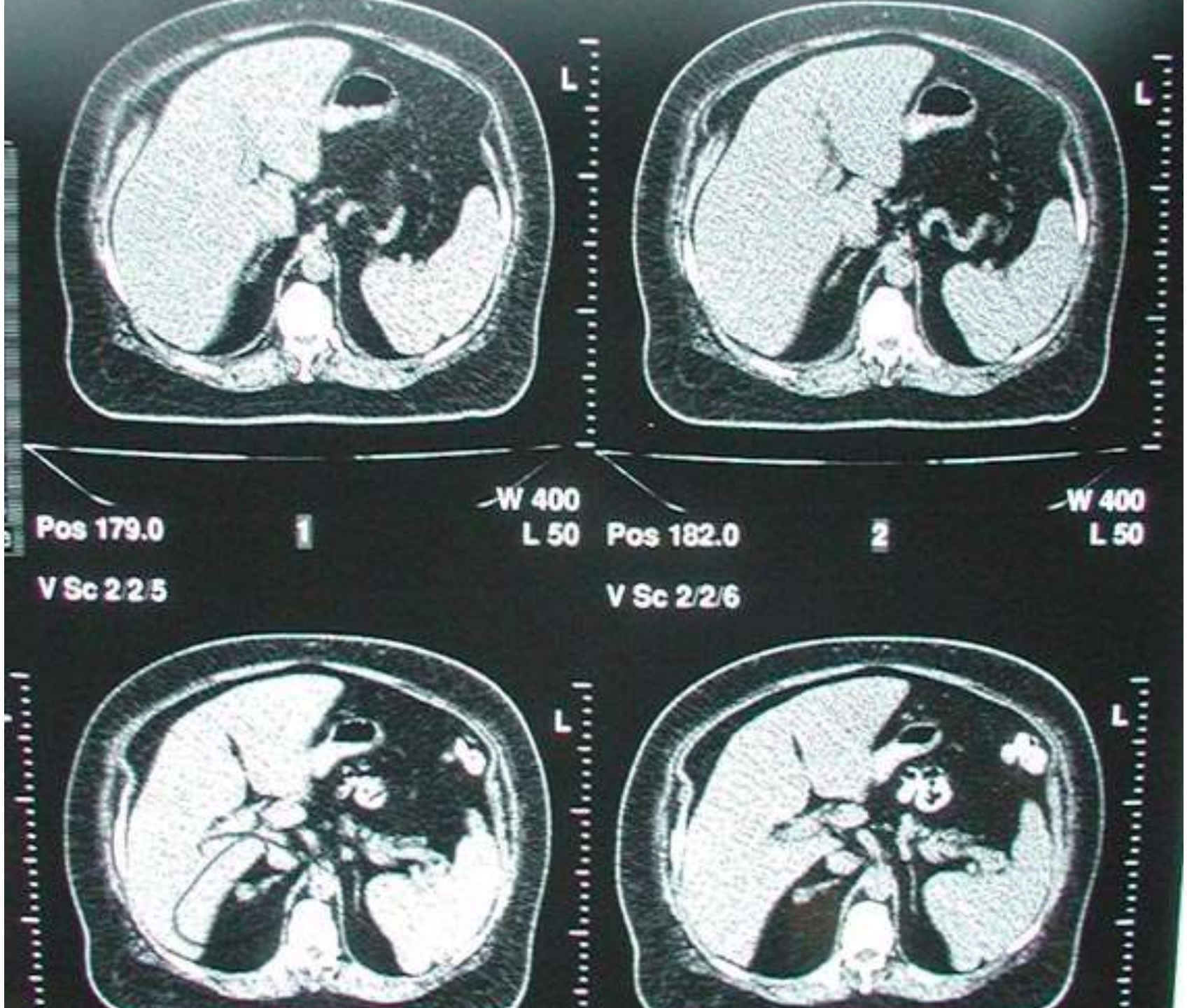
- Cushing disease and ectopic have higher ACTH>>>>ACTH Dependent
- Adrenal disease is ACTH independent
- Clarification required with additional dexamethasone testing including urinary testing

Imaging

- Cushing disease: MRI of the pituitary
- Cushing syndrome: CT or MRI of (adenoma vs hyperplasia) adrenals
- Ectopic: localize source

Treatment

- Pituitary: surgery, radiation, anti-adrenal drugs
- Ectopic: surgery, drugs
- Adrenal: surgery, drugs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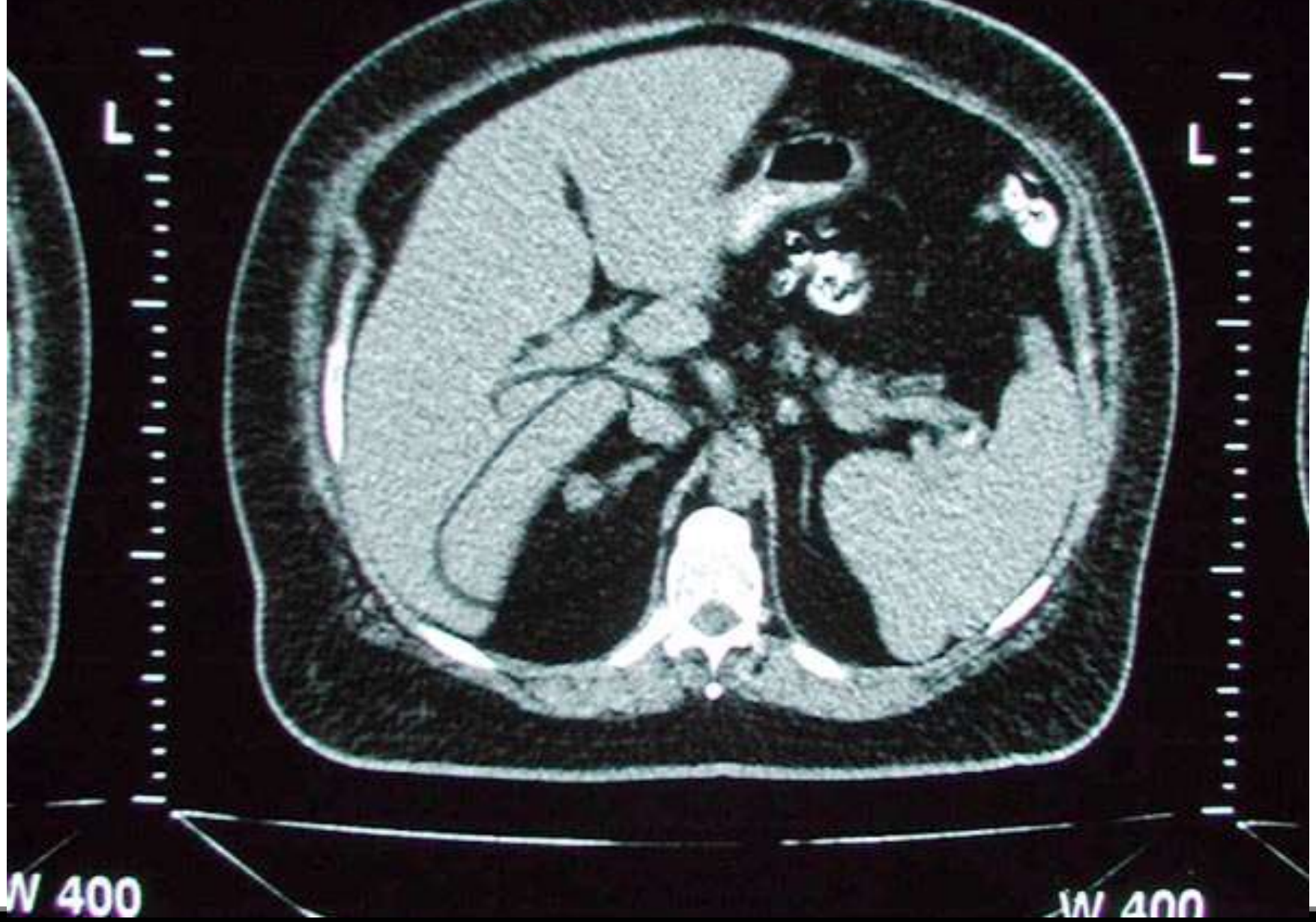
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Incidental Adrenal Adenoma

- Benign adenomas common
- Avoid imaging until biochemical diagnosis
- Evaluation important with coexisting HTN, hypokalemia, hirsutism

Adrenal Incidentaloma

- Lesions discovered “inadvertently in the course of diagnostic testing or treatment for other clinical conditions that are not related to the suspicion of adrenal disease”

Prevalence

- In autopsy series 2.1 %
- More identified with better imaging
- Prevalence of 4.3 % in patients with a previous diagnosis of cancer
- Higher with aging at 7 % in 70 +
- More lesions in women—related to who is being tested

Causes

- Pathology: Cancer patients ¾ mets, No history of cancer 2/3 benign
- 70 % non-functioning in patients without endocrine symptoms
- 5-10 %-----Cushing Syndrome, subclinical

Natural History of lesion size

- 25 % of lesions larger than 6 cm represent adrenal cancer
- Up to 25 % of adrenal lesions may grow 1 cm, but the significance of size change is not known
- Adrenal Cancer rapid growth “doubling time”

Adrenal Carcinoma

- Metastatic at diagnosis
- Presents with weight loss
- Rapid onset
- Typical excessive activity of steroidogenesis pathway, not typical insufficiency

Natural History of function

- Up to 20 % may develop a functional component
- Development of function more common in larger neoplasms (3 cm)---this evidence can depend on study follow-up length and methods
- Less than 3 cm neoplasms rarely change in function

Adrenal Incidentaloma Diagnosis

- Function
- Surgical resection vs non-surgical treatment
- Malignant vs benign

35 Year Old female

- Hypertension, poorly controlled multiple meds
- Hypokalemia
- Thin
- Metabolic alkalosis

Diagnosis

- **Hyperaldosteronism**

Hyperaldosteronism

- Biochemical work-up first
- Low renin/high aldosterone is primary
- High renin/high aldosterone is secondary
- Elevated 24 hour urine aldosterone on high sodium diet and off diuretics
- Saline Suppression Testing

Hyperaldosteronism

- Adrenal adenoma (Conn Syndrome) “APA” Aldosterone Producing Adenoma
- Idiopathic Hyperaldosteronism “IHA” with bilateral disease

Secondary Hyperaldosteronism

- Sodium restriction
- Renal disease
- High Potassium intake
- Pregnancy
- Diuretics

Localization testing

- Cat Scan
- Nuclear imaging with Iodocholesterol
- **Adrenal venous sampling—Gold Standard**

Adrenal Venous Sampling Summary

RE: Male DOB: 1942

	Aldosterone (ng/dL)	Cortisol (ug/dL)
Basal:		
Right adrenal vein	1	4.3
Left adrenal vein	221	10.2
Peripheral Arm	12	12.3
POST ACTH:		
Right adrenal vein	4	108.1
Left adrenal vein	16430	>150
Peripheral Vena Cava	71	14.4
Peripheral Femoral Vein	46	18.9

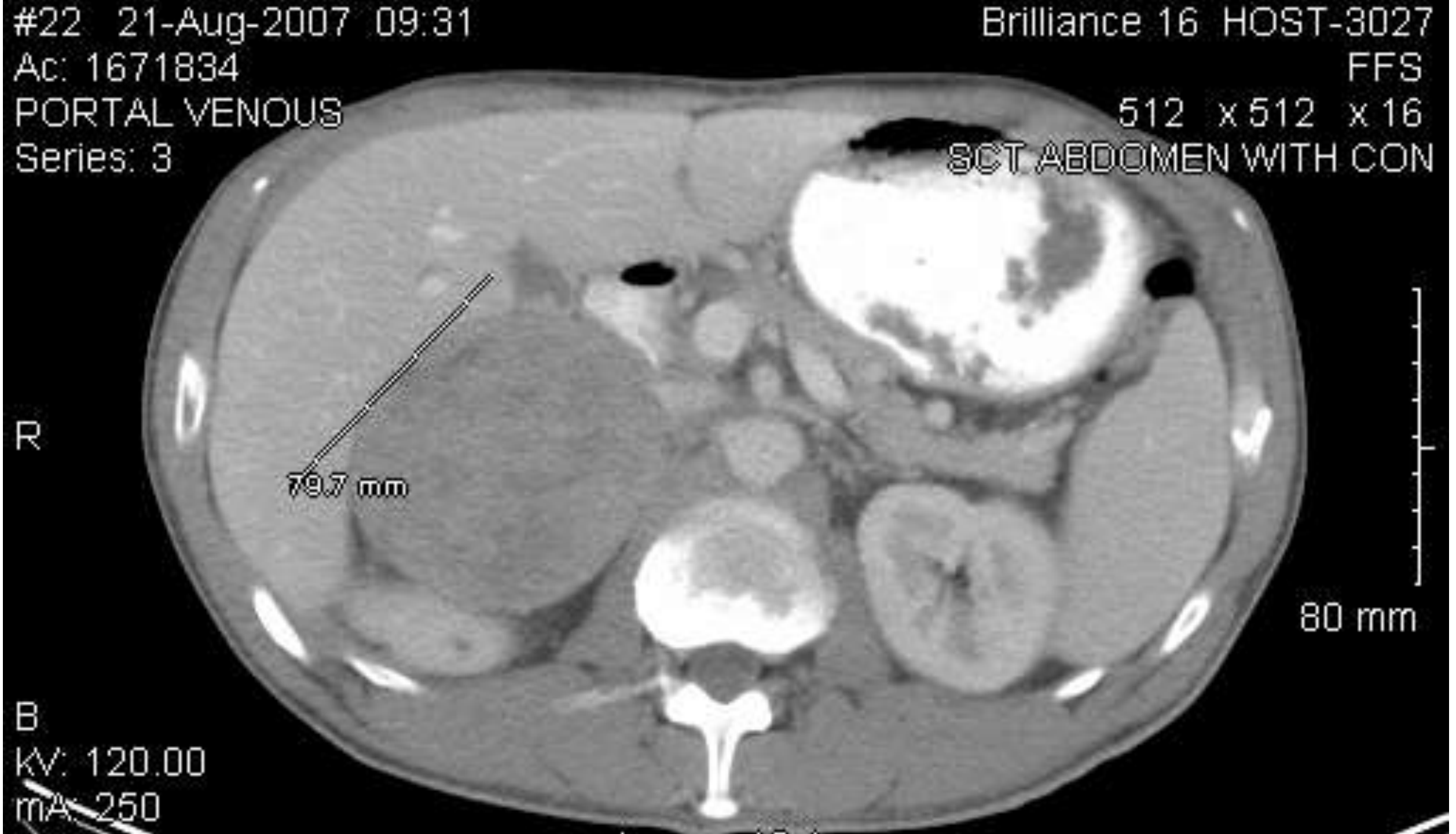
Treatment

- Aldosterone producing adenoma: surgery; takes 6 months for final htn results, may have underlying essential HTN but hypokalemia should resolve; Spironolactone in patients with poor surgical risk

- Bilateral adrenal disease: restrict sodium, spironolactone use, no surgery

40 Year Old Male

- Hypertension unresponsive to meds
- Normal electrolytes
- Thin
- Headache, palpitations
- Abdominal pain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Diagnosis

- **Pheochromocytoma**

Laboratory

- Check 24 hour urine fractionated metanephrines
- Serum fractionated metanephrines
- 24 hour urine testing off BP meds if possible

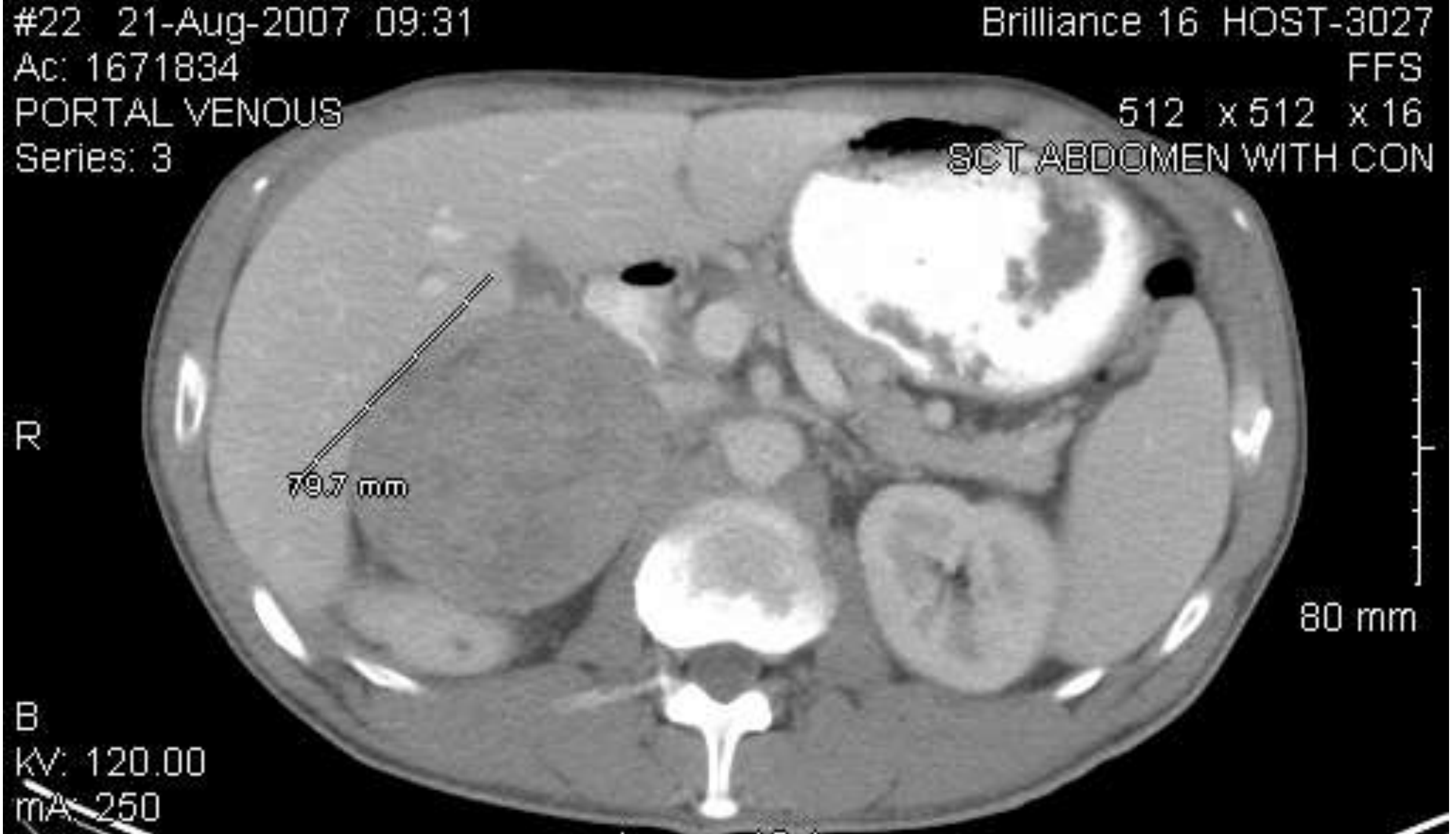
Imaging

- MRI or CT: MRI may help with difference in signal intensity T1/T2---bright signal in pheo

- MIBG (Metalogobenzylguanidine) nuclear imaging tracer concentrates in catecholamine producing cells

Treatment

- Alpha blockers preferred
- Avoid Beta Blockers, which can precipitate a pheo crisis without alpha blockade on board
- Avoid adrenal biopsy of a lesion that is not yet evaluated for pheochromocytoma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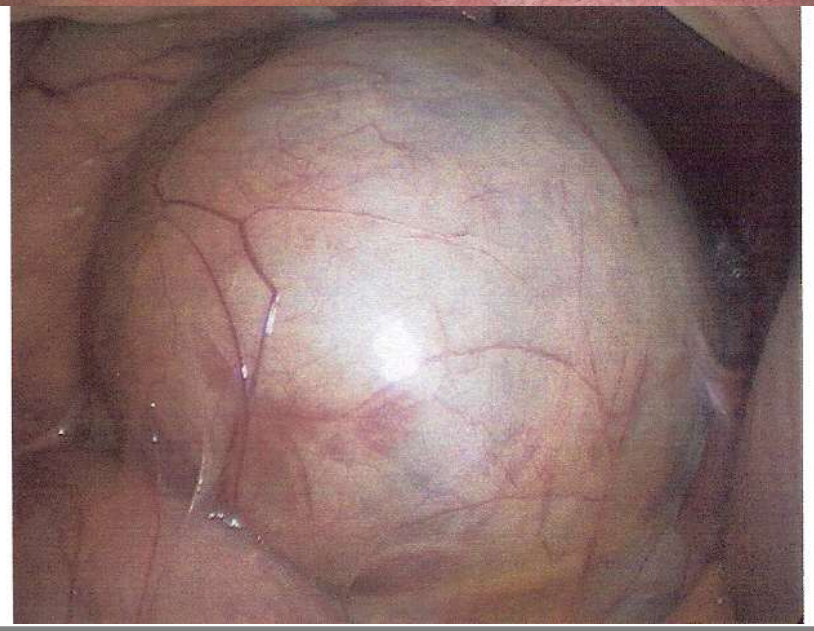

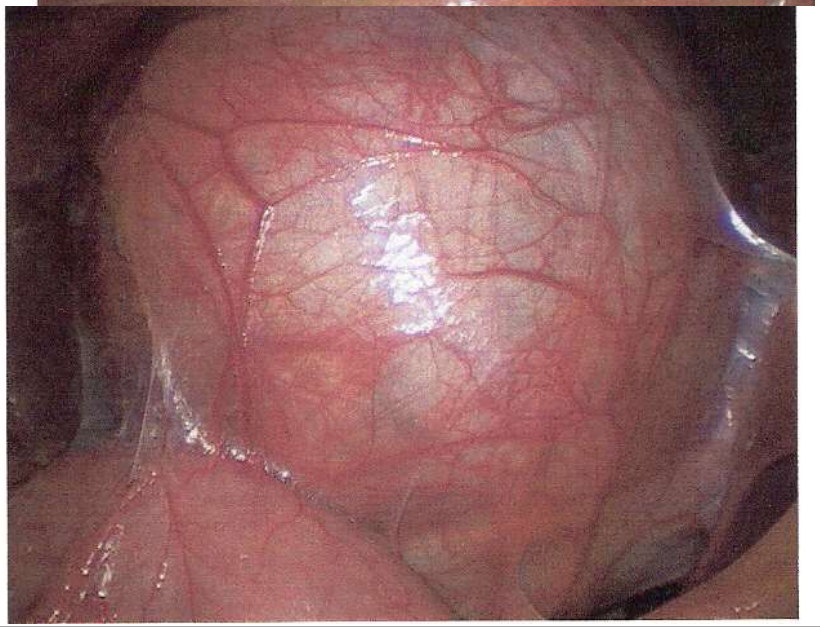


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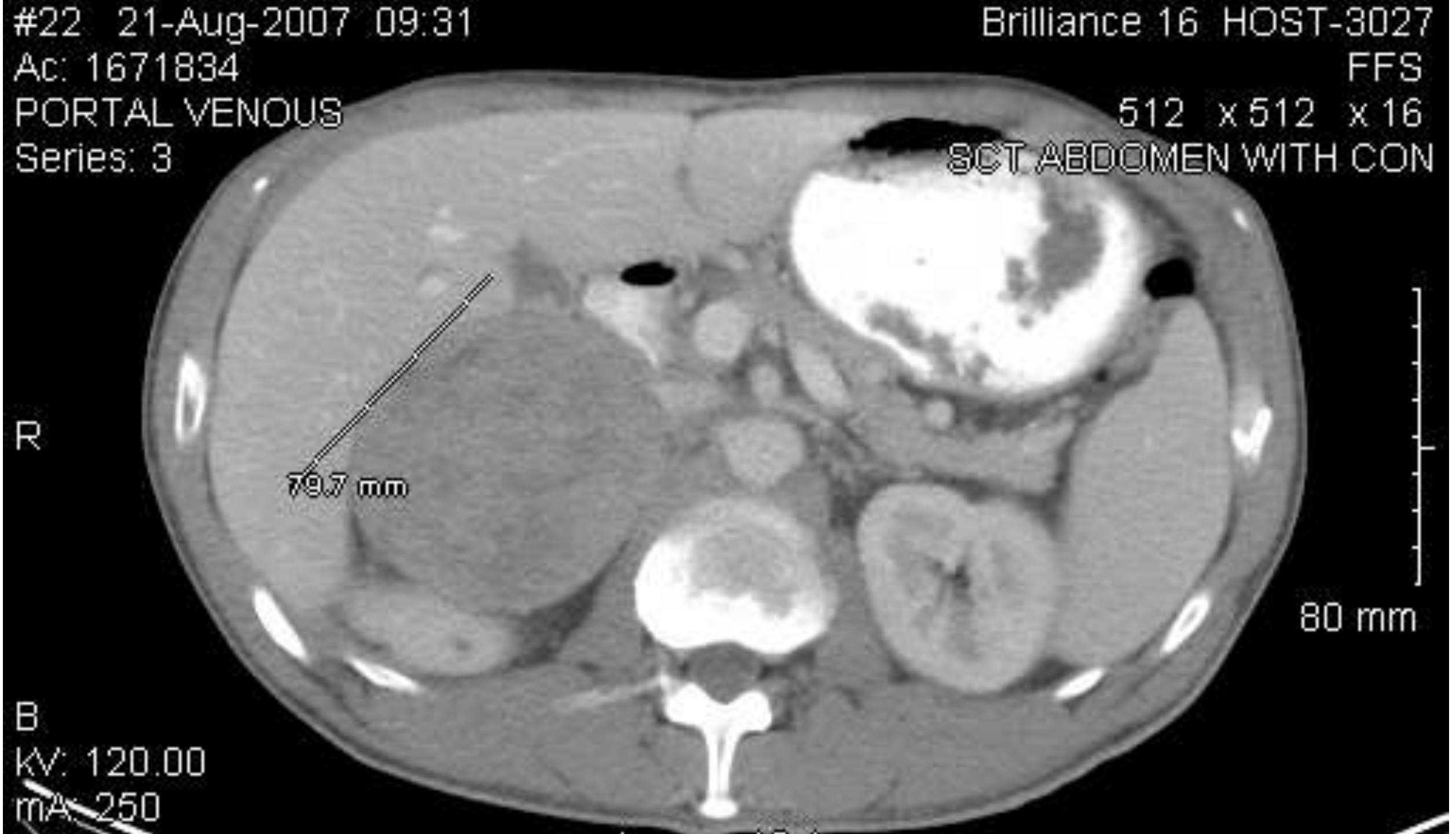
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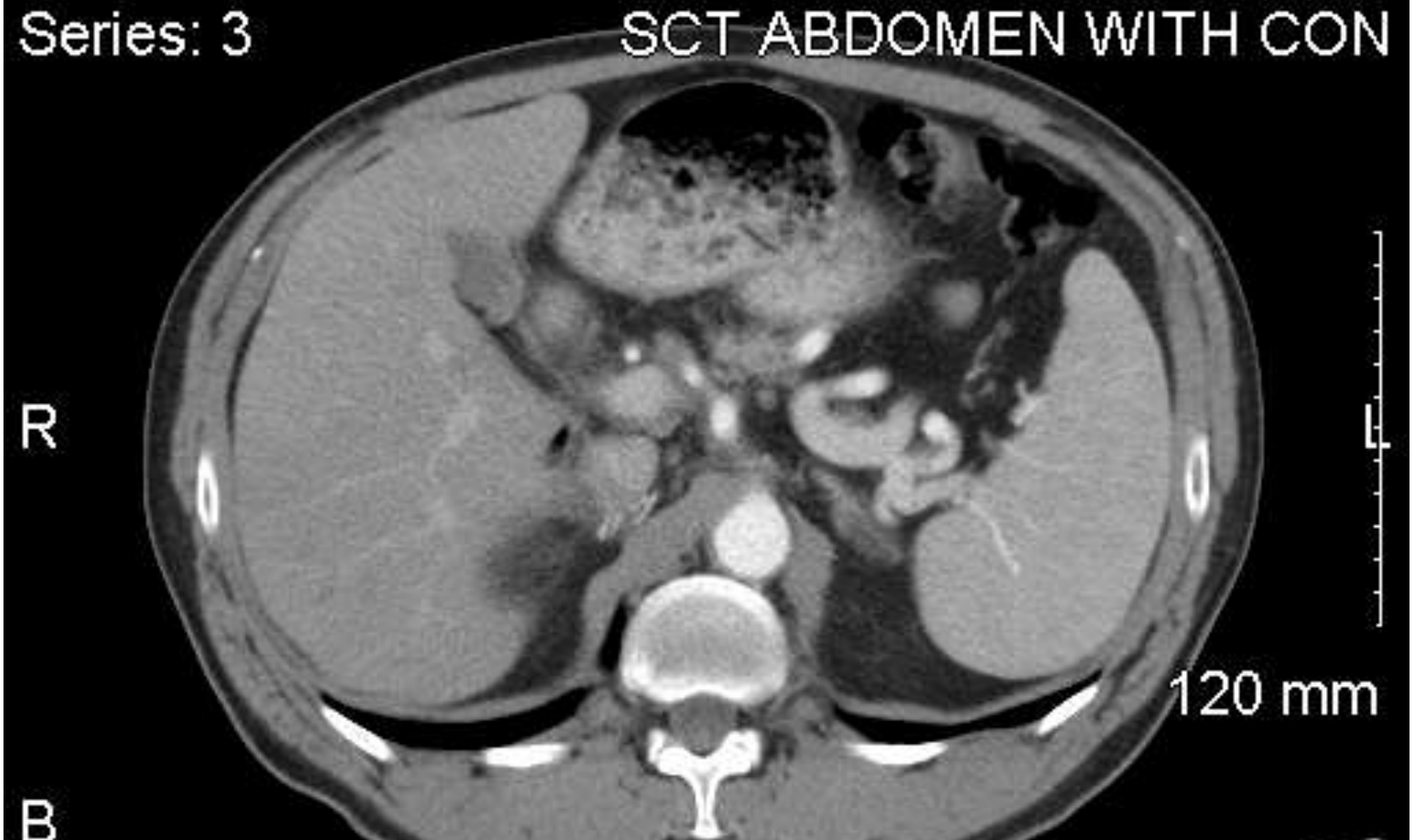
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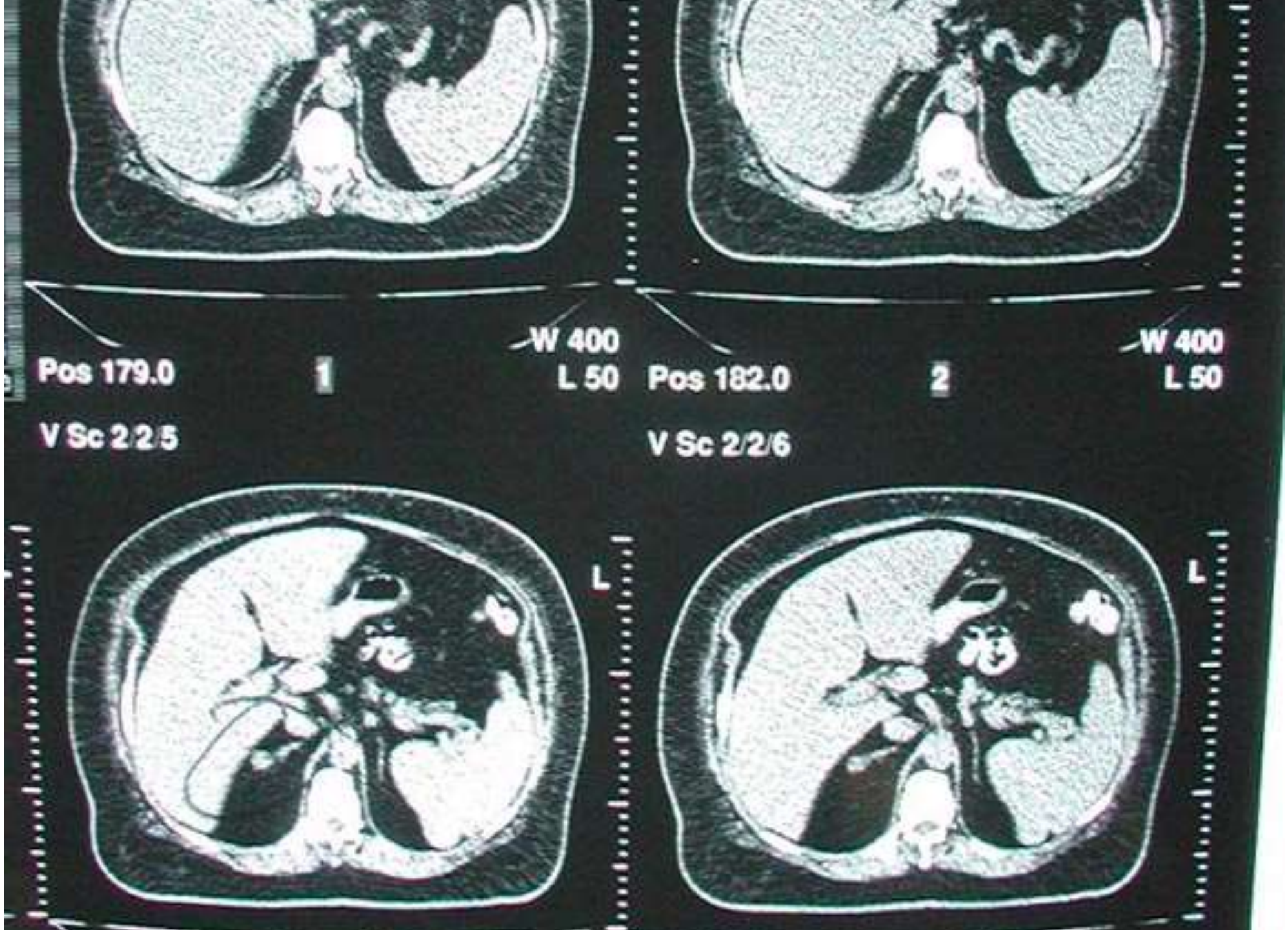
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