PHEOCHROMOCYTOMA

Marina Nodelman, MD

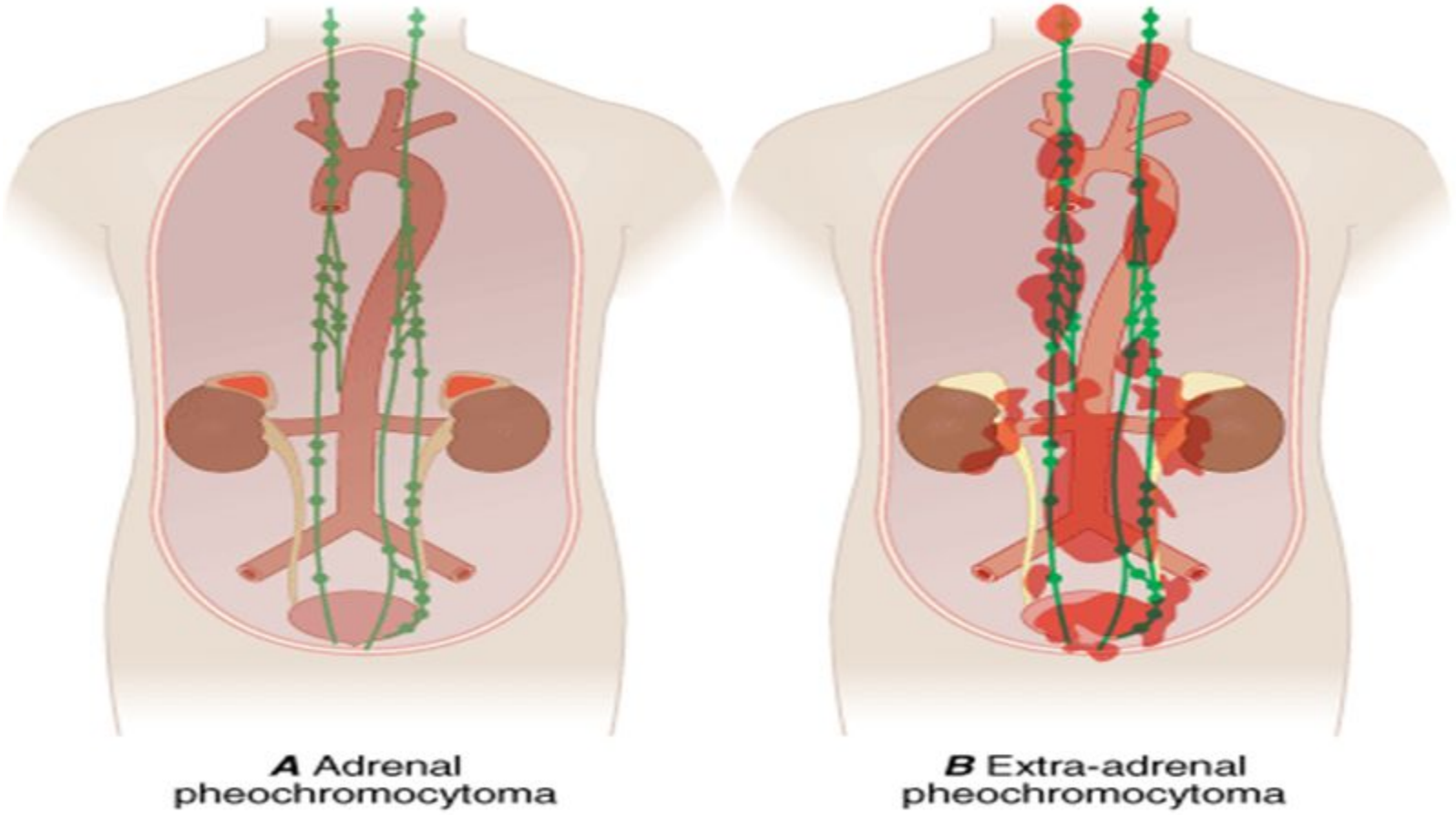
The Diabetes, Endocrinology and Metabolism Department

Pheochromocytomas

rare, catecholamine-secreting, vascular, neuroendocrine tumors arising from chromaffin cells of the adrenal medulla ~80%

extra-adrenal pheochromocytoma or paraganglioma (PGL) ~15–20%

Pheochromocytoma localization



A Adrenal pheochromocytoma

B Extra-adrenal pheochromocytoma

Epidemiology

- rare cause of secondary hypertension
- less than **0.2%** of patients with HTN
- incidence is approximately **0.8/100,000** p-y
- **0.05%** in the autopsy (report from China)
- occur at any age, most common in 40-50 y
- male and female equally

Tumor characteristics

- **~ 95%** of catecholamine-secreting tumors are in the abdomen
- **85-90%** of which are intraadrenal (PHEO)
- **10-15%** of catecholamine-secreting tumors are extra-adrenal (paraganglioma(
- **5-10%** multiple PHEO
- **~ 10%** malignant PHEO: local invasion into surrounding tissues and organs (kidney, liver) or distant metastases

Clinical presentation

- The “classic triad”: episodic headache, sweating, and tachycardia – rarely seen
- Blood pressure: paroxysmal hypertension (50%); persistent hypertension (30%) or normal BP(15%)
- Other symptoms: palpitations, tremor, pallor, dyspnea, weakness, syncope, panic attack, orthostatic hypotension, weight loss, polyuria, constipation, hyperglycemia, cardiomyopathy, pulmonary edema
- Paroxysmal elevations in BP, tachycardia, or arrhythmia during diagnostic procedures, surgery, induction of anesthesia, with certain foods or drugs

PHEO may bee asymptomatic

- incidental imaging discovery (incidentaloma)
- genetic survey
- autopsy

Familial pheochromocytoma

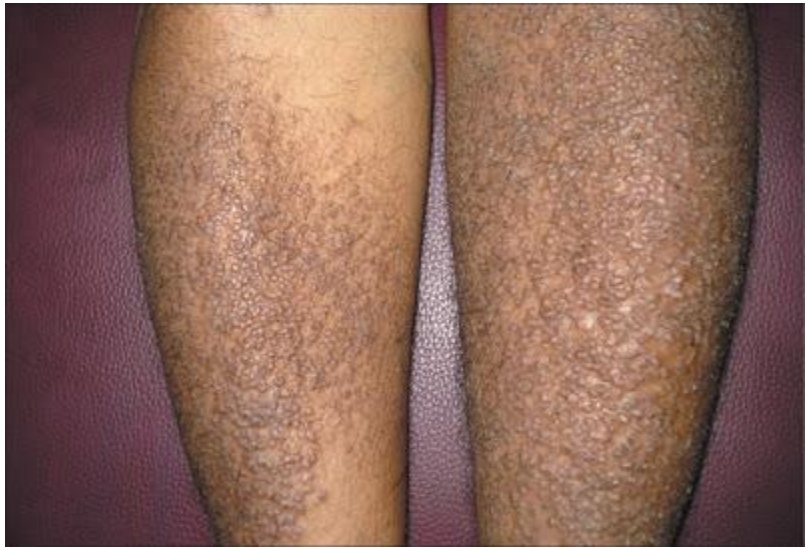
MEN 2 syndrome

- 95% autosomal dominant RET proto-oncogene mutation
- prevalence ~1/ 35,000 individuals
- ~ 50% of patients with MEN 2 syndrome develop PHEO in the adrenal glands
- rarely malignant
- younger age (30-40 years)

Familial pheochromocytoma

MEN 2A (Sipple's syndrome)

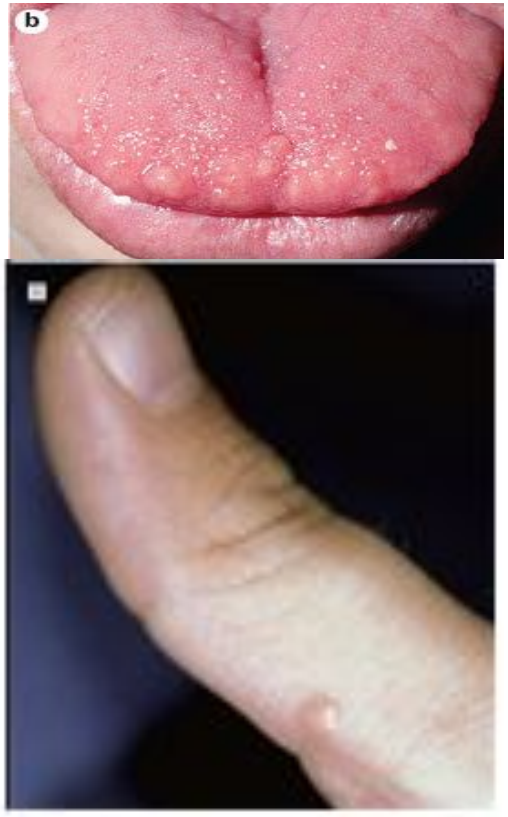
- medullary thyroid cancer (MTC) in all patients, PHEO in 50%, primary hyperparathyroidism in 20%, and cutaneous lichen amyloidosis in 5%



Familial pheochromocytoma

MEN 2B (mucosal neuroma syndrome)

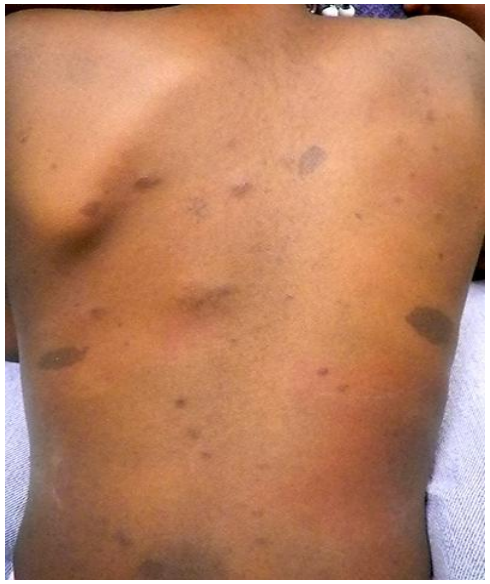
- MTC in all patients, PHEO in 50%, mucocutaneous neuromas, skeletal deformities, marfanoid habitus and intestinal ganglioneuromas (Hirschsprung's disease)



Familial pheochromocytoma

Neurofibromatosis type 1

- prevalence ~ 1/ 3,000 individuals
- neurofibromas, multiple café-au-lait spots, axillary and inguinal freckling, iris hamartomas (Lisch nodules), macrocephaly and cognitive deficits
- ~ 2% solitary, benign adrenal PHEO



Familial pheochromocytoma

von Hippel–Lindau disease (VHL)

- prevalence ~2–3/ 100,000 persons
- hemangioblastoma (cerebellum, spinal cord or brainstem), retinal angioma, clear cell renal carcinoma, pancreatic tumors, endolymphatic sac tumors of the middle ear
- bilateral or malignant PHEO, paraganglioma in the mediastinum, abdomen and pelvis

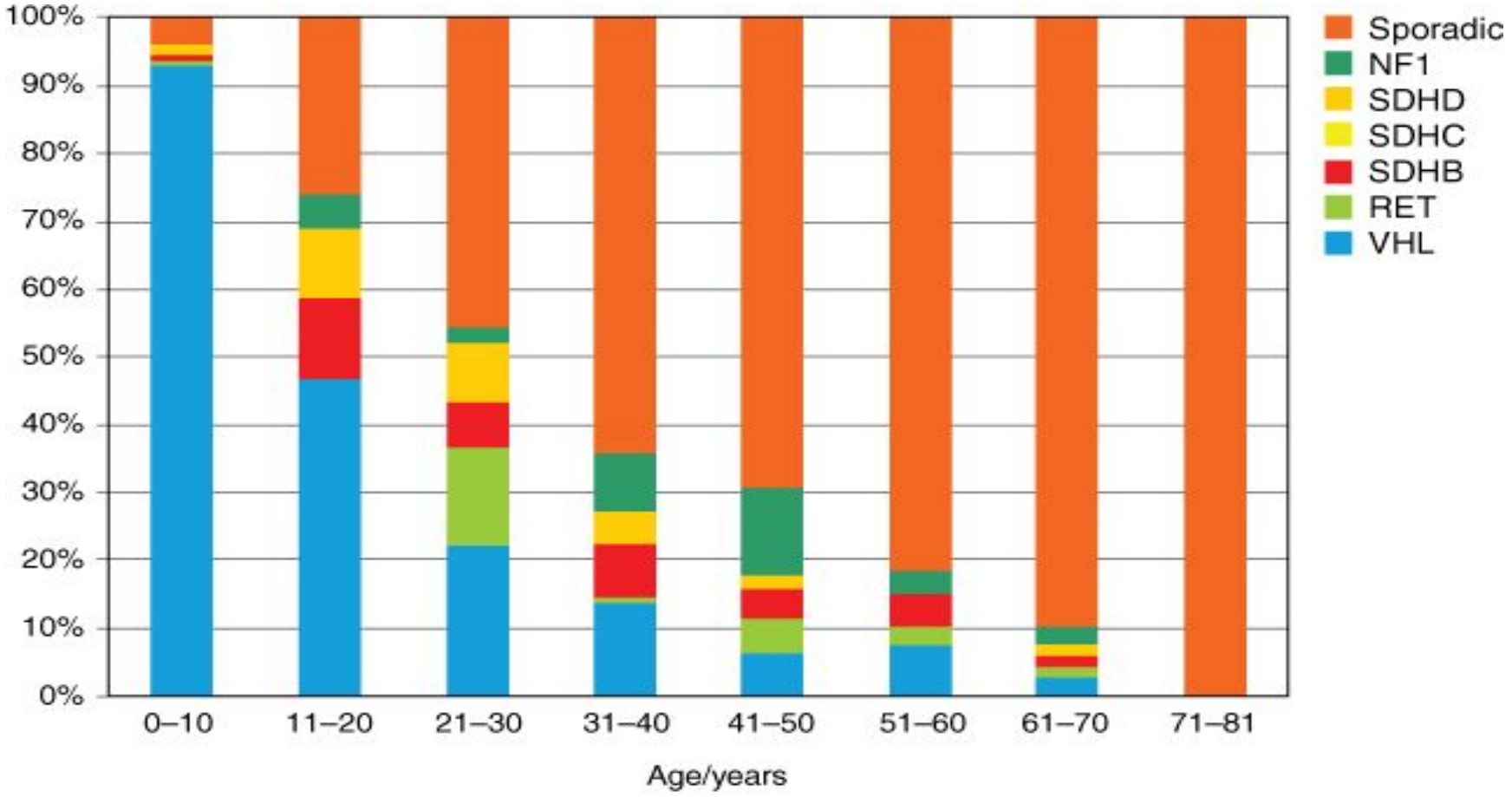
Familial pheochromocytoma

Familial paraganglioma syndromes

Paraganglioma syndrome type 1-4

- usually nonfunctional parasympathetic paragangliomas at skull base and neck
- sometimes adrenal pheochromocytoma
- type 4 may be malignant PHEO

Genetic vs. sporadic PHEO

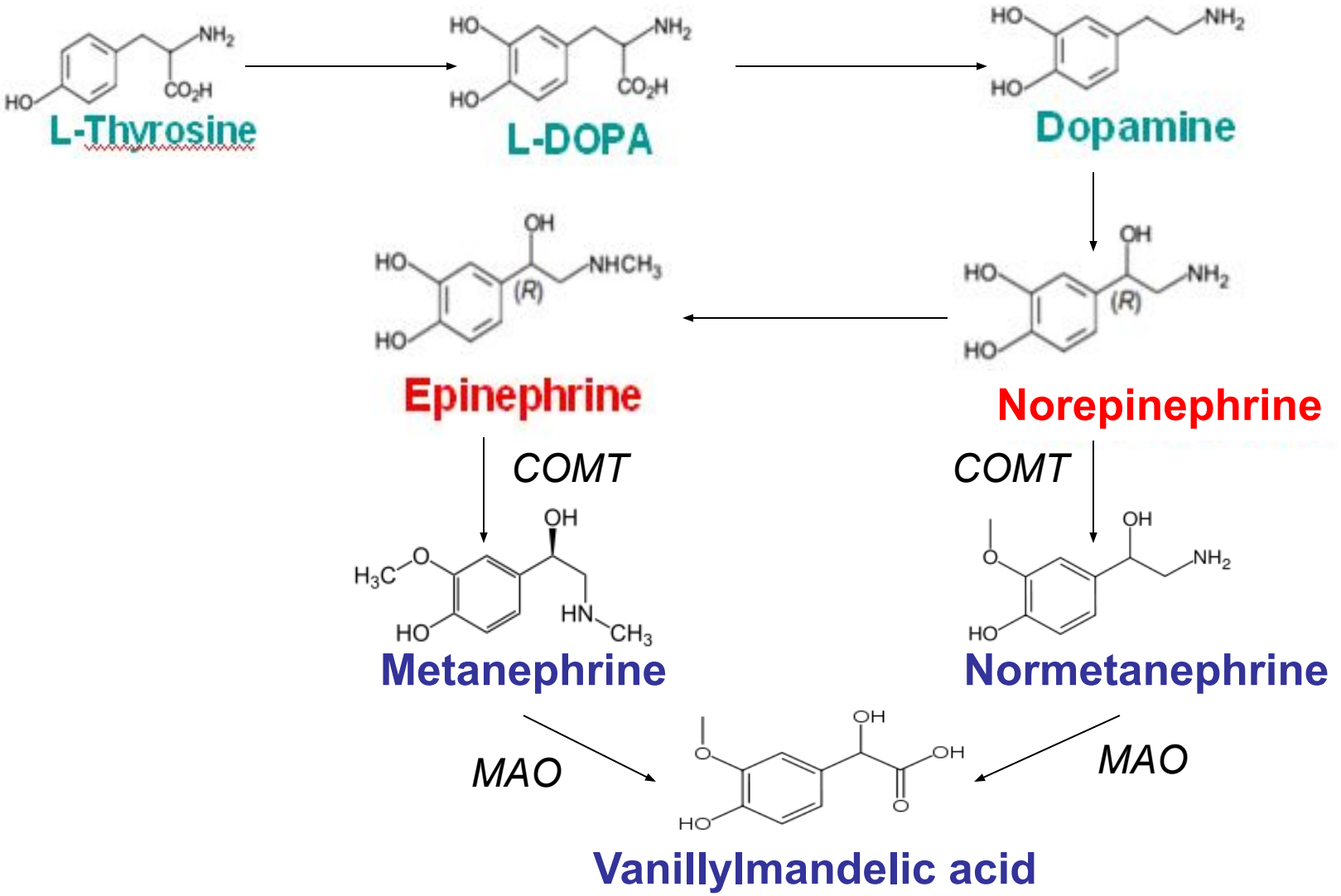


Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

?When to suspect PHEO

- Hyperadrenergic spells
- Resistant hypertension
- A familial syndrome that predisposes to PHEO (MEN2, NF1, VHL(
- A family history of pheochromocytoma
- An incidentally discovered adrenal mass
- Hypertension and new onset or atypical DM
- Pressor response to anesthesia, surgery, or angiography
- Onset of hypertension at a young age (<20 years)

Catecholemine metabolism



Pheochromocytoma diagnosis

- 24-hour urine collection for fractionated metanephrines and catecholamines
  - Norepinephrine >170 mcg/24 h
  - Epinephrine >35 mcg/24 h
  - Dopamine >700 mcg/24 h
  - Normetanephrine >900 mcg/24 h
  - Metanephrine >400 mcg/24 h

measurement of urinary creatinine to verify an adequate collection

may be false-positive

have to be used if clinical probability is low

Pheochromocytoma diagnosis

- Plasma fractionated metanephrines
  - metanephrine <0.3 nmol\l (fast), <0.5 nmo\l (non-fast)
  - normetanephrine <0.66 nmol\l (fast), <0.9 nmo\l (non-fast)

high predictive value of a negative test

high rate of false-positive tests

have to be used if clinical probability is high

Medications that may increase measured levels of catecholamines and metanephrines

Tricyclic antidepressants
Levodopa
Drugs containing adrenergic receptor agonists (eg, decongestants)
Amphetamines
Buspirone and most psychoactive agents
Prochlorperazine
Reserpine
Withdrawal from clonidine and other drugs
Ethanol

Pheochromocytoma diagnosis

- 24-hour urinary vanillylmandelic acid (VMA) excretion

  poor diagnostic sensitivity and specificity

- Chromogranine A in serum

  increased in 80% of patients with PHEO

  not specific for PHEO and may be seen with other neuroendocrine tumors (carcinoid), and in a variety of other conditions (atrophic gastritis, cirrhosis, CRF, PPI treatment …)

Pheochromocytoma imaging

CT or MRI of the abdomen and pelvis

Pheo Imaging characteristics

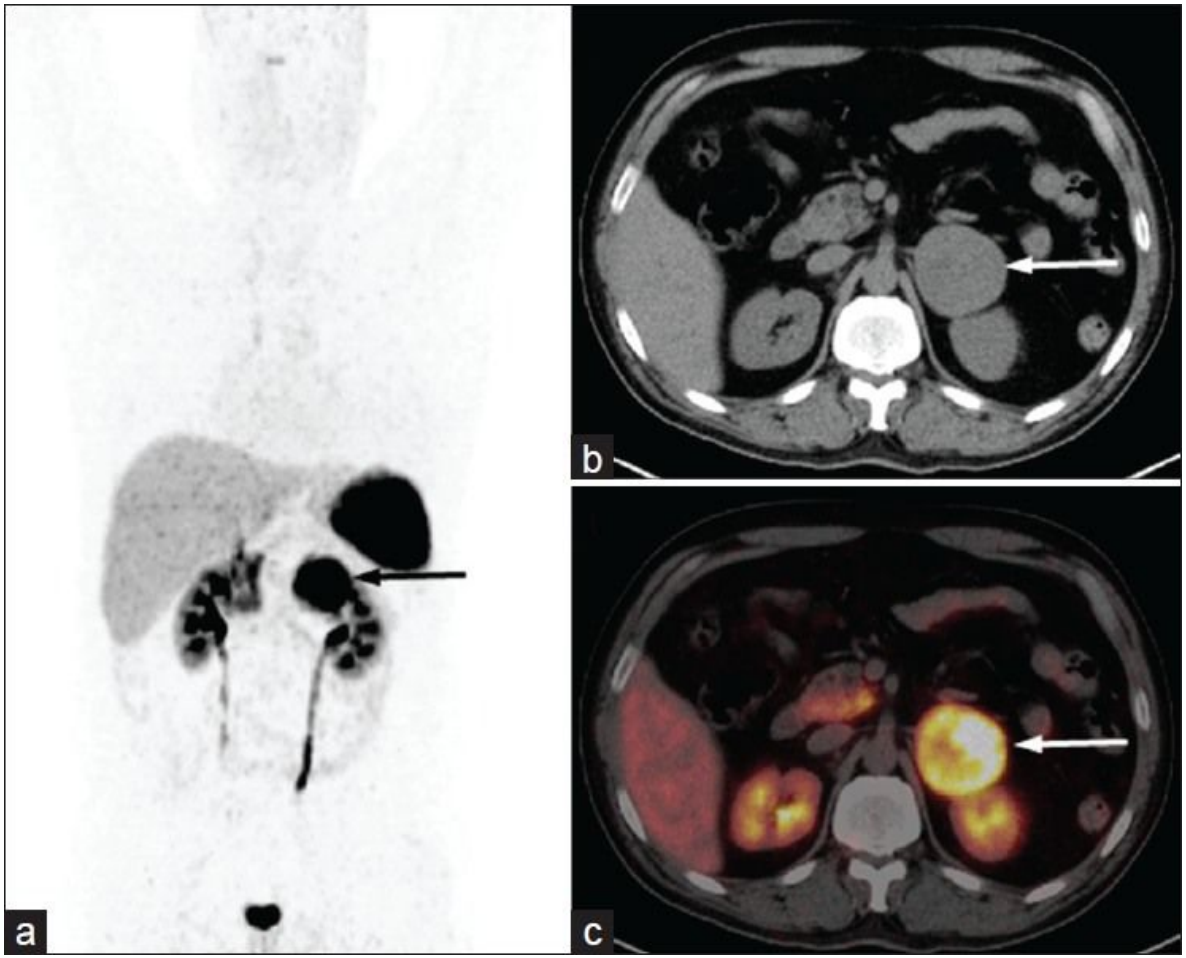
- Usually large size (>3 sm)
- May be bilateral
- Cystic and hemorrhagic changes
- Increased mass vascularity
- Increased attenuation on non-enhanced CT (>20HU)

Additional imaging: MIBG, FDG-PET, DOTATATE-Scan

Biopsy of suspected Pheo should be avoided!

Pheochromocytoma imaging

a- FDG-PET
b- abdominal CT
c- DOTATATE-Scan



Pheochromocytoma treatment

- all patients should undergo a resection of the Pheo (laparascopic or open adrenalectomy)

- preoperative medical therapy

✔ hypertension and tachycardia control:
target BP 120/80 mmHg
combined α-adrenergic blockade (Phenoxybenzamine, Prazocine, Doxazocine) and β-blockade (Deralin)

✔ volume expansion (high sodium diet, IV 0.9% NS)

- prevention of the hypertensive crisis during surgery (Nitroprusside, Phentolamine, Nicardipine)


THANK YOU FOR LISTENING