Pheochromocytoma

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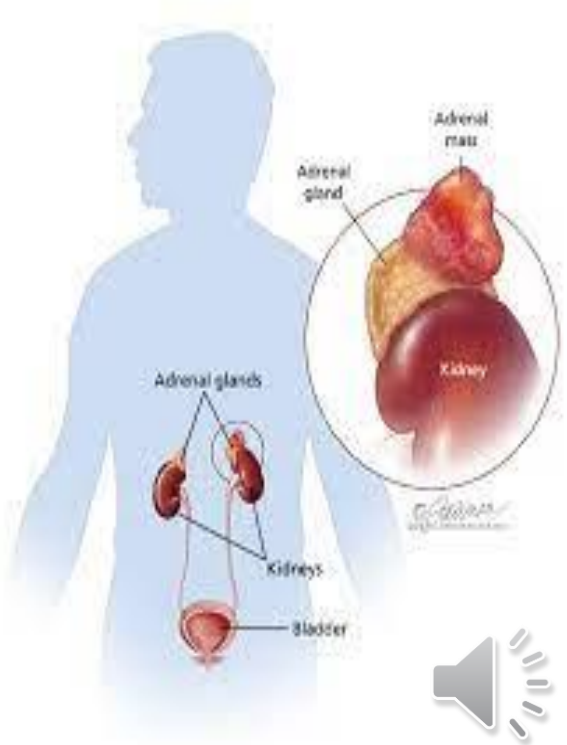
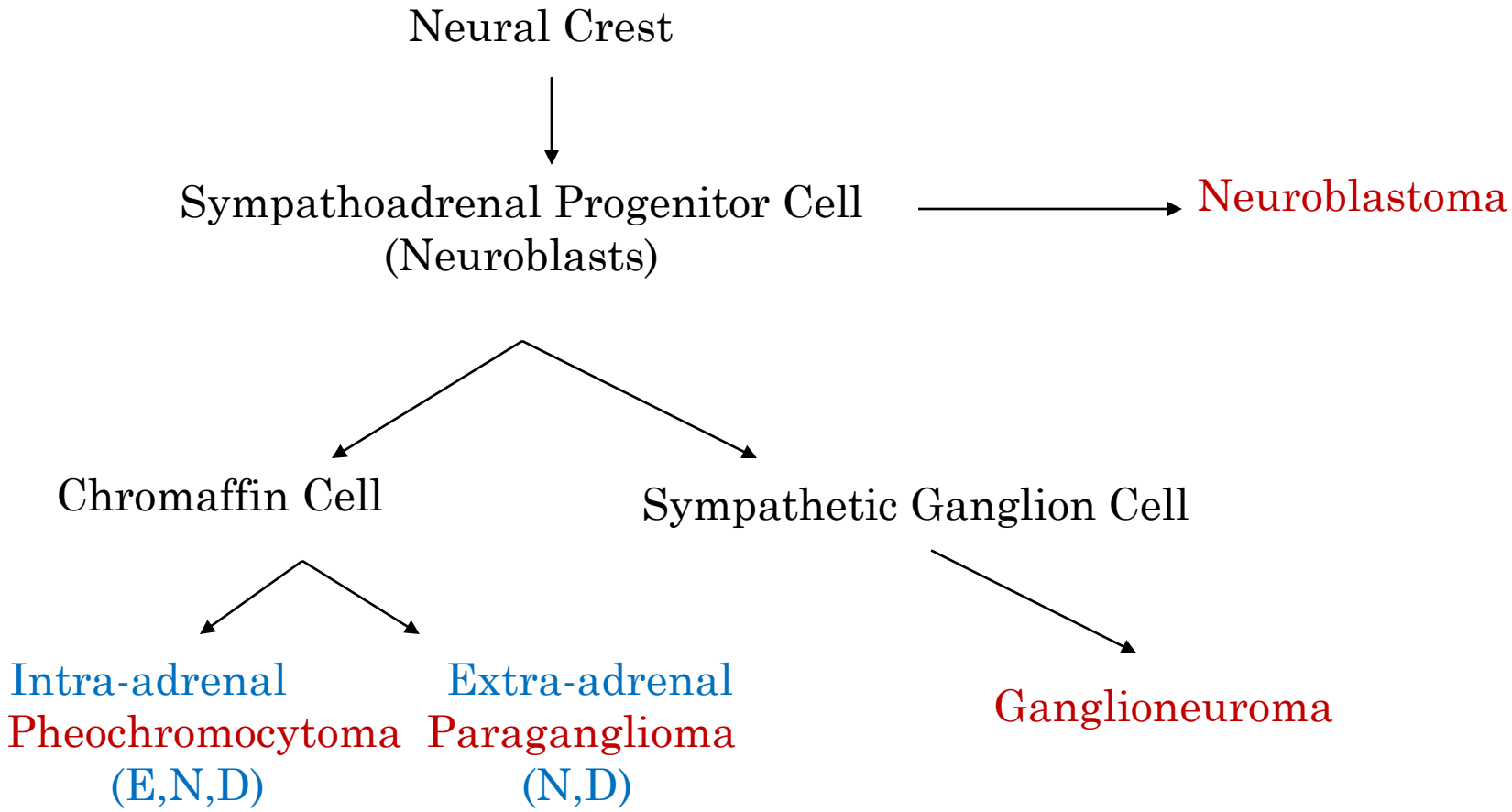
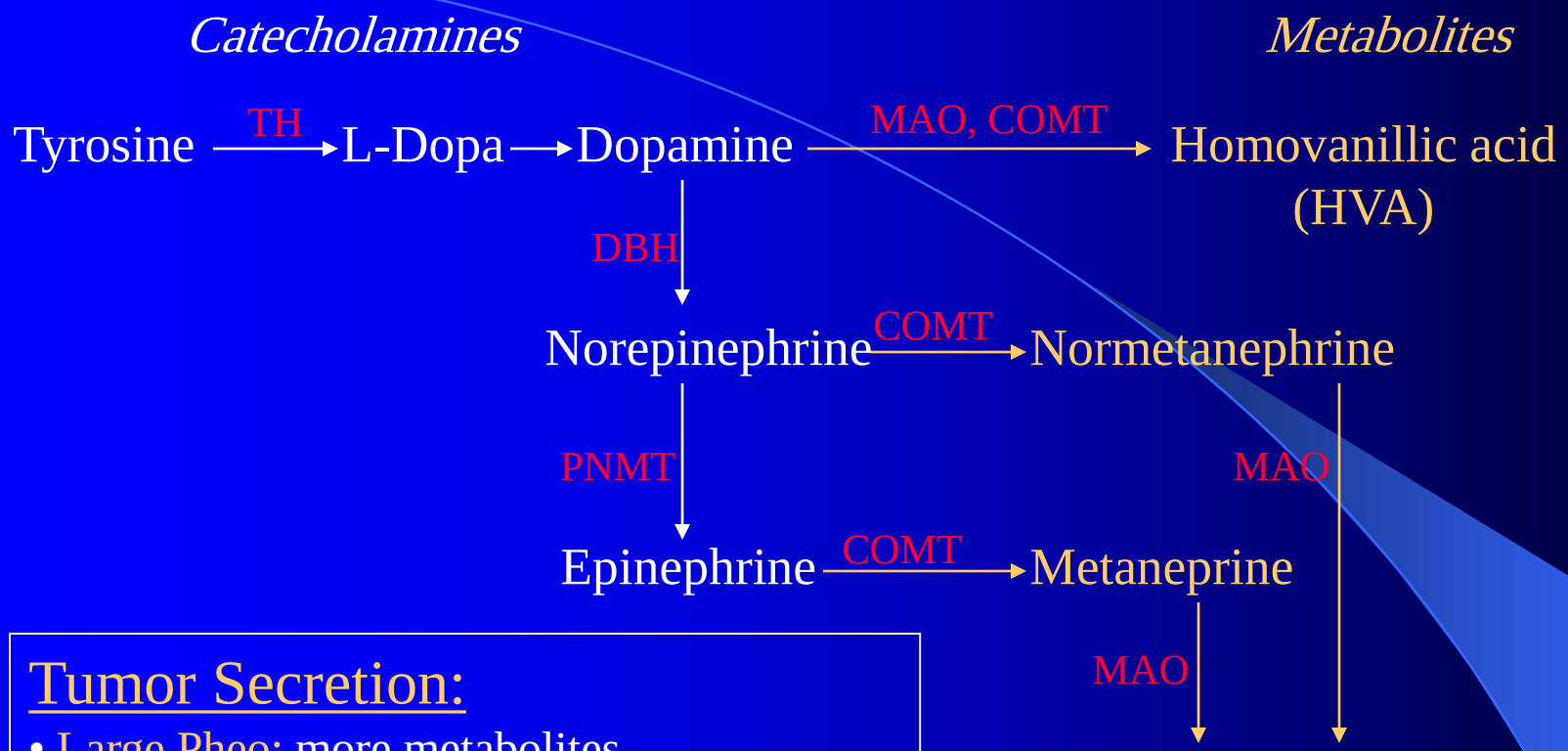


OUTLINE

1. **Catecholamine Physiology/Pathophysiology**
2. **Clinical Presentation**
    1. Epidemiology
    2. Signs & Symptoms
3. **Diagnosis**
    1. Biochemical
    2. Localization
4. **Management**
    1. Medical
    2. Surgery
    3. Peroperative
    4. Pregnancy

Catecholamine Producing Tumors





Tumor Secretion:

- Large Pheo: more metabolites
- Small Pheo: more catecholamines
- Sporadic Pheo: Norepi > Epi
- Familial Pheo: Epi > Norepi
- Paraganglioma: Norepi
- Paraganglioma(neck&skull base): Dopamine
- Gangioneuroma: Norepi
- Malignant Pheo: Dopamine, HVA

Adrenergic Receptors

catecholamines → catecholamine-O-methyl transferase → metanephrines

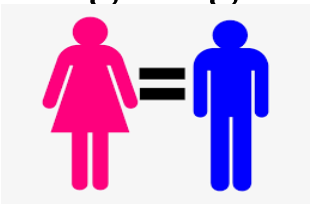
- **α adrenergic effects (α1, α2)**
  - intense vasospasm
  - hypertension

- **β-adrenergic effects (β1,β2,β3)**
  - vasodilatation
  - diaphoresis
  - tachycardia

Epidemiology:

- less than 0.2 percent of patients with hypertension
- Annual incidence of **pheo** is approximately 0.6-0.8 per 100,000 person-years

- most common in the 4th to 5th decade
- average age: 47 years / average tumor size was 4.9 cm

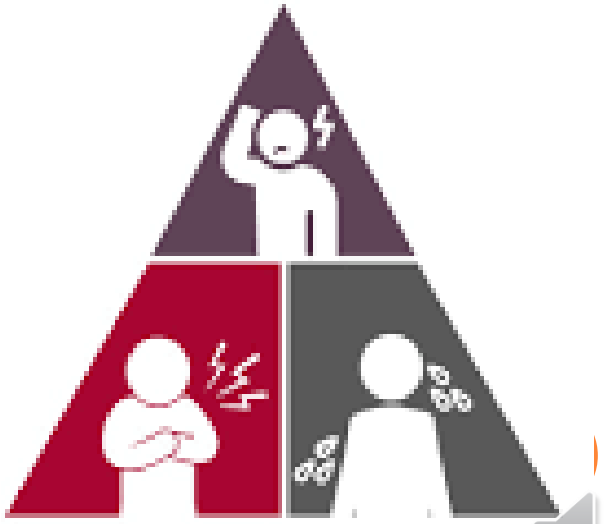


- most tumors are sporadic
- 40 % of patients have a familial disorder

Clinical Presentation:

- present in 50 percent of patients
- typically paroxysmal
- headache, palpitation, sweat (24 %) + HTN = specific
- HTN: sustained (50%) or paroxysmal (8%) or combined hypertension (36%)
- normal blood pressure(5-15%)

- The five P's:
  - Pressure (HTN) 90%
  - Pain (Headache) 80%
  - Perspiration 71%
  - Palpitation 64%
  - Pallor 42%
    - Paroxysms (the sixth P!)



Clinical Presentation:

Paroxysms, 'Spells':

- 10-60 min duration (80%)
- Frequency: daily to monthly
- Spontaneous
  - Diagnostic procedures, I.A. Contrast (I.V. is OK)
  - Drugs (opiods, unopposed β-blockade, anesthesia induction, histamine, ACTH, glucagon, metoclopramide)
  - Strenuous exercise, movement that increases intra-abdo pressure (lifting, straining)
  - Micturition (bladder paraganlgioma)

- panic attack-type symptoms (particularly in pheochromocytomas that produce epinephrine)

Clinical Presentation…

- Pheochromocytoma crisis

  rare occasions

  hypertension or hypotension

  hyperthermia (T >40°C),

  mental status changes,

  other organ dysfunction

  emergent surgery?

Less Common Symptoms:

- insulin resistance, hyperglycemia
- visual blurring, papilledema
- weight loss, polyuria, polydipsia, constipation, increased ESR, leukocytosis, psychiatric disorders, fear of death, secondary erythrocytosis, sudden death
- heat intolerance
- Cardiomyopathy
- Lactic Acidosis (case report)
- Paraneoplastic (Cushing's)

Less Common Symptoms:

Two **rare** presentations of pheochromocytoma:

- Orthostatic hypotension:
  - ECFv contraction
  - Loss of postural reflexes
  - Tumor release of epinephrine
- Rapid cyclic fluctuations (every 7 to 15 minutes) of hypertension and hypotension can occur via an uncertain mechanism

Indications for biochemical testing

- Classic triad
- Hyperadrenergic spells (self-limited episodes of nonexertional palpitations, diaphoresis, headache, tremor, or pallor).
- Onset of hypertension (age, <20 years), resistant hypertension, or hypertension with new-onset or atypical diabetes mellitus
- A familial syndrome MEN2 , VHL ,NF 1
- A family history of pheochromocytoma
- Adrenal incidentaloma
- Pressor response during anesthesia, surgery, or angiography
- Idiopathic dilated cardiomyopathy
- A history of gastric stromal tumor (GIST) or pulmonary chondromas
- Orthostatic hypotension in a hypertensive patient (?)

Biochemical Tests:

- 24h urine collection:
  - catecholamines, metanephrines, vanillymandelic acid (VMA), (+/-dopamine, 3-methoxytyramine)
  - liquid chromatography with tandem mass spectrometry versus HPLC with electrochemical detection

- measurement of fractionated catecholamines (epinephrine, nor epinephrine, and dopamine) is less sensitive, but clearly elevated values (>2 ULN) are also diagnostic.
- VMA in urine : a lower sensitivity of 68 %

- Plasma:
  - Free metanephrines, normetanephrine, +/- 3-methoxytyramine
  - increase in metanephrines has a mean sensitivity of 97% and a specificity of 93% .

Biochemical Tests: When? Which?

- low index of suspicion: 24-hour urinary fractionated catecholamines and metanephrines

  (Resistant hypertension, Hyperadrenergic spells)

- high index of suspicion: plasma free metanephrines

  (FH, genetic syndrome, resected pheo, adrenal mass)

  predictive value of a negative test is extremely high

- sensitivity will be lower and specificity will be higher for hereditary compared with sporadic pheochromocytoma

Positive Test:

1) reference values should be established from subjects who are sampled after supine rest.
2) ideal reference population consists of patients who were suspected for a Pheo but in whom a Pheo was ruled out.
3) reference values for plasma normetanephrine should be adjusted for age while this is not necessary for others

Table 2. Age-Related Upper Cut-off Values for Plasma Metanephrines and 3-Methoxytyramine

Age, yr	Normetanephrine, nmol/L	Metanephrine, nmol/L	3-Methoxytyramine, nmol/L
5–17	0.47	0.45	0.10
18–29	0.58	0.45	0.10
30–39	0.70	0.45	0.10
40–49	0.79	0.45	0.10
50–59	0.87	0.45	0.10
>60	1.05	0.45	0.10

Jacques etal, Endocrinol Metab 2017;32:152-161

Positive Test:

- 24-hour urine fractionated metanephrines and catecholamines:
  - Normet >900 mcg/24 hours or met >400 mcg/24 hours (total meta >1000)
  - Norepinephrine >170 mcg/24 hours
  - Epinephrine >35 mcg/24 hours
  - Dopamine >700 mcg/24 hours
- Plasma free metanephrines:
  - supine, resting,fasting, indwelling cannola:
    exclude pheochromocytoma if met <0.3 nmol/L and/or normet <0.66 nmol/L
  - seated, ambulant, nonfasting:
    exclude pheochromocytoma if met <0.5 nmol/L and/or normet <0.9 nmol/L

Discontinue Interfering Drugs:

- Ideal: no drug
- TCA
- at least 2 weeks
- 4 times plasma half-life
- physical stress or illness
- hospitalization
- No physical activity (12 h)
- No smoking (12 h)
- clonidine suppression test

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

Renal Failure:

- Urinary catecholamines and metabolites may be invalid if advanced CKD
- Plasma measurements may also be compromised by increased sympathetic outflow
- In hemodialysis without pheo, plasma catecholamines and metabolites concentrations may be increased 2-3 times above ULN.
- Plasma free metanephrines : more suitable

Adrenal Incidentaloma:

- 3 to 10 % of adrenal incidentalomas prove to be pheo
- Asymptomatic adrenal mass was the initial presentation in 25-60 % of the cases*
- noncontrast CT attenuation is < 10 HU, biochemical testing for pheo is not needed
- biochemical tests in incidentaloma > 2 cm in diameter are negative, a functioning adrenal pheo is excluded
- Small pheo (<2 cm) may not be biochemically detectable

(followed with both imaging and repeat biochemical testing)

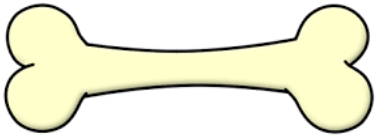
* Yu etal. Am J Med. 2009;122:85–95

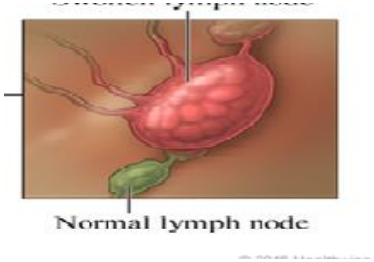
Malignant Potential:

- 10 % of all tumors are malignant
- are histologically and biochemically = benign
- local invasion into surrounding tissues and organs
- distant metastases occur as long as 53 years after resection
- long-term follow-up is indicated in all patients
- Tumor size > 5 cm / PGL /advanced age /high dopamine / (SDH) subunit B mutations are more likely to develop metastatic disease
- WHO = all pheo & para have some metastatic potential

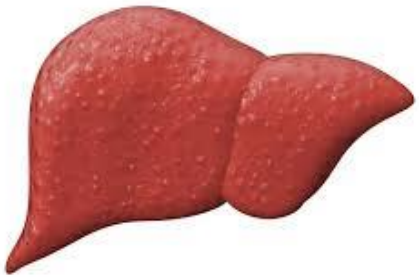
Metastatic Pheochromocytoma:

- Only metastases are the proof for a malignant pheo
- updated WHO classification of endocrine tumors has replaced the term “malignant pheochromocytoma” with “metastatic pheochromocytoma
- Pheochromocytoma:





- Paraganglioma:



Metastatic Pheochromocytoma:

- Most metastatic pheochromocytoma or paraganglioma are sporadic tumors
- Patients with heritable Pheo in whom metastatic disease develops, SDHB mutations account for up to 43% of cases, followed by VHL, SDHD, and NF1 mutations
- **Treatment:**

surgical resection

use of targeted radiolabeled carriers

(e.g., 131I-MIBG or 90Y-DOTATATE and 177Lu-DOTATATE),

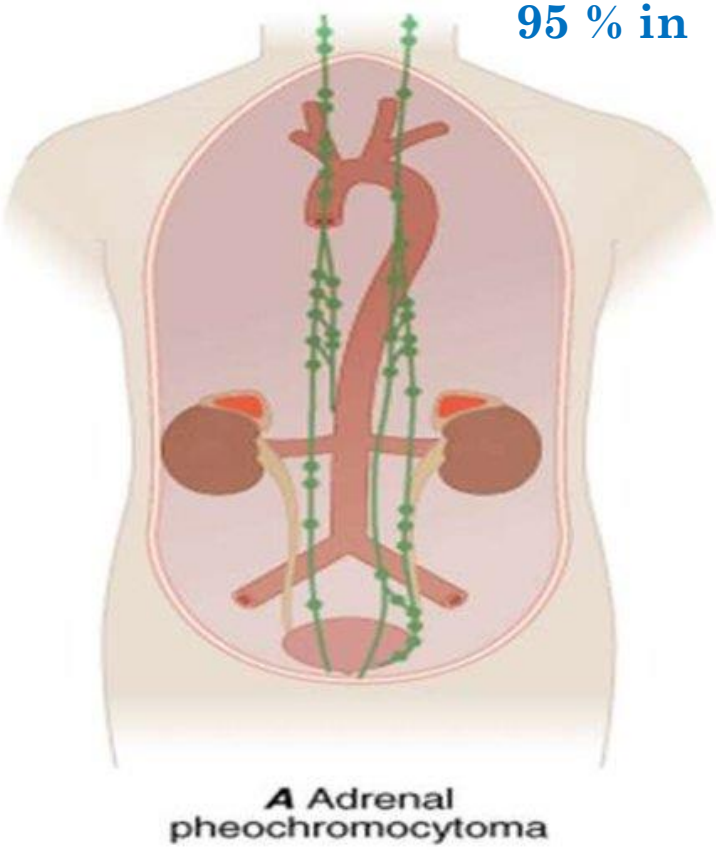
thermal ablation

chemotherapy (cyclophosphamide, vincristine ,darcarbazine)

external irradiation

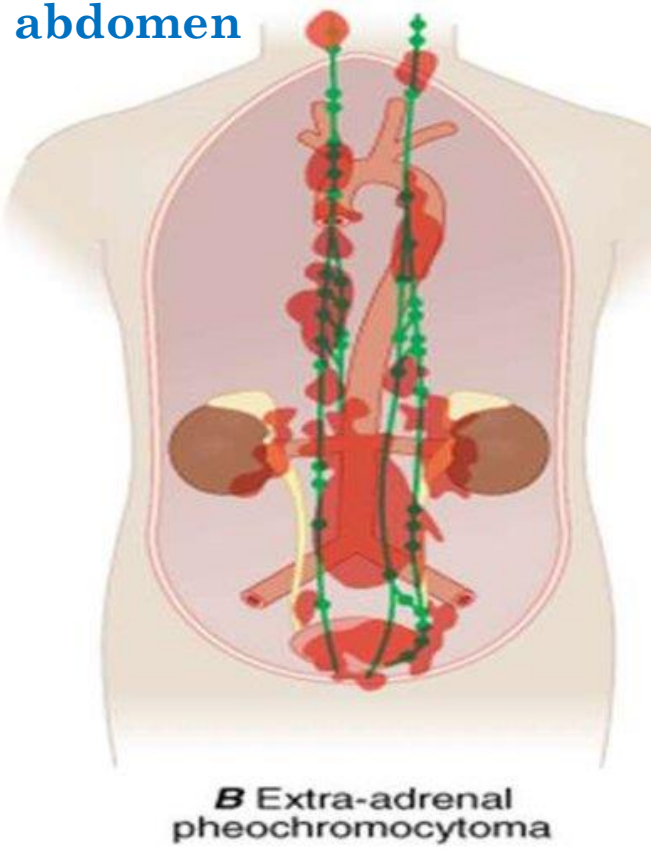
Pheochromocytoma localization

95 % in abdomen



A Adrenal pheochromocytoma

85 to 90 %

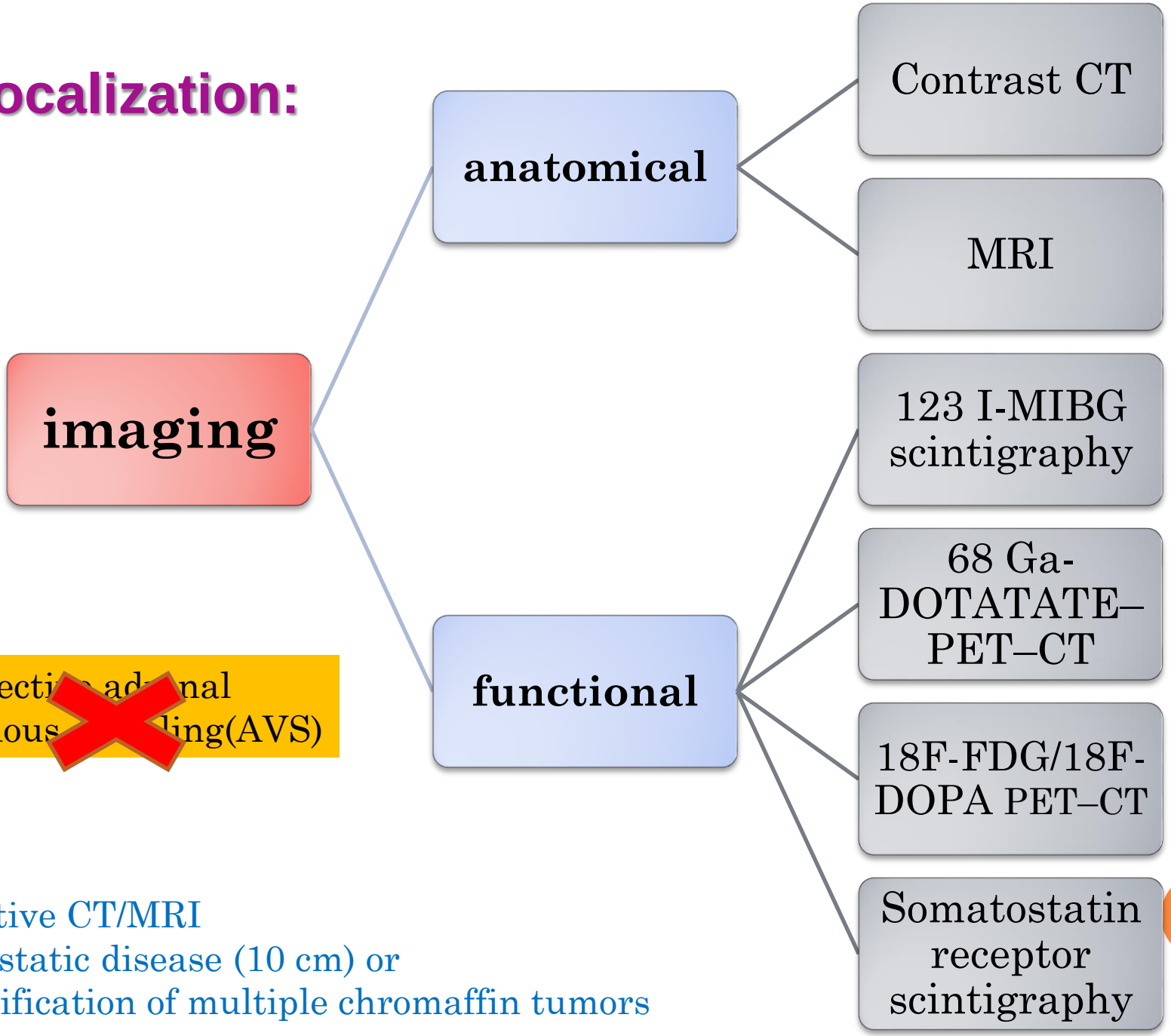


B Extra-adrenal pheochromocytoma

10 to 15 %

5%:
sup and inf abd
bladder
thorax
skull base
neck
pelvis

Localization:

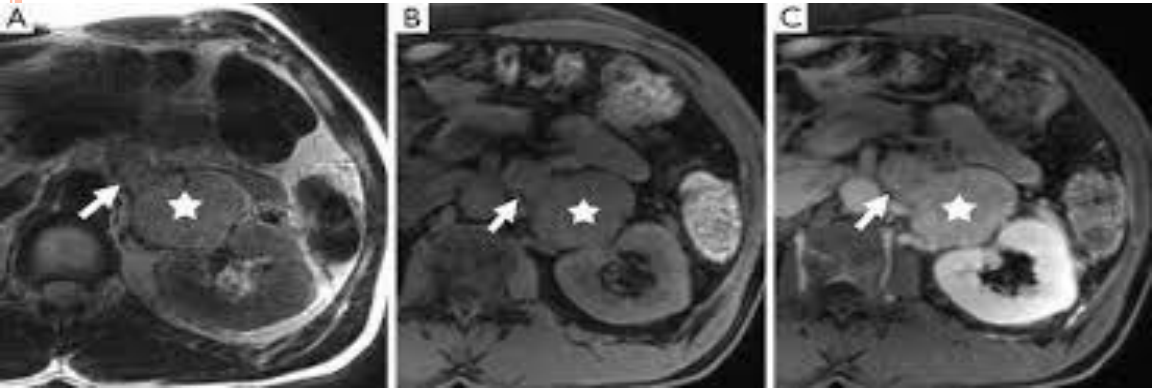


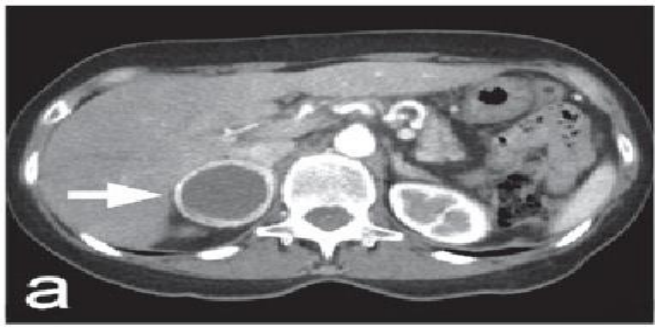
Selecti[illegible] ad[illegible]nal venous [illegible]ling(AVS)

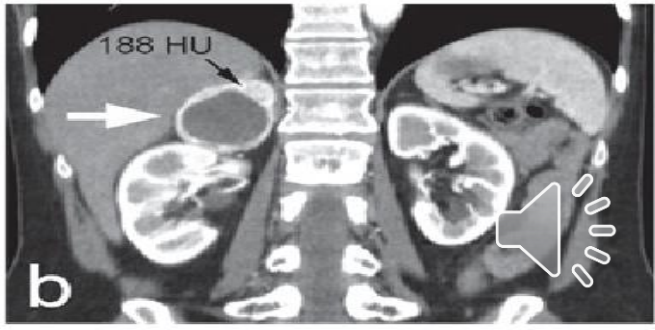
negative CT/MRI
metastatic disease (10 cm) or
identification of multiple chromaffin tumors

Contrast CT / T2 weighted MRI

- increased vascularity
- delay in contrast washout
- cystic and hemorrhagic changes
- high signal intensity on T2-weighted MRI

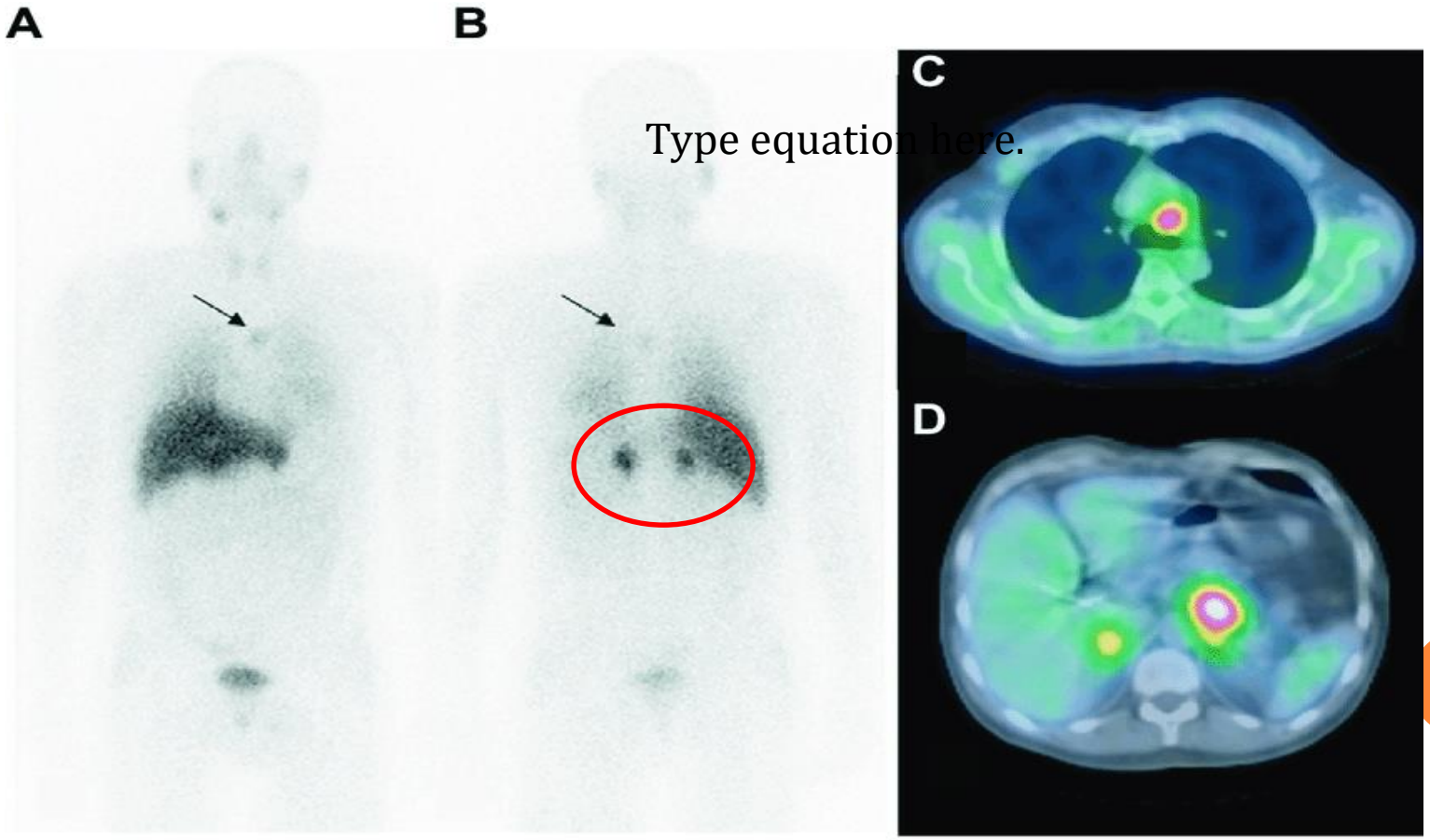






123 I-MIBG SCINTIGRAPHY

- Ligand: 123-metaiodobenzylguanidine
- sensitivity for adrenal pheo is excellent (nearly 100%)
- Identify metastatic patients responsive I-131 MIBG



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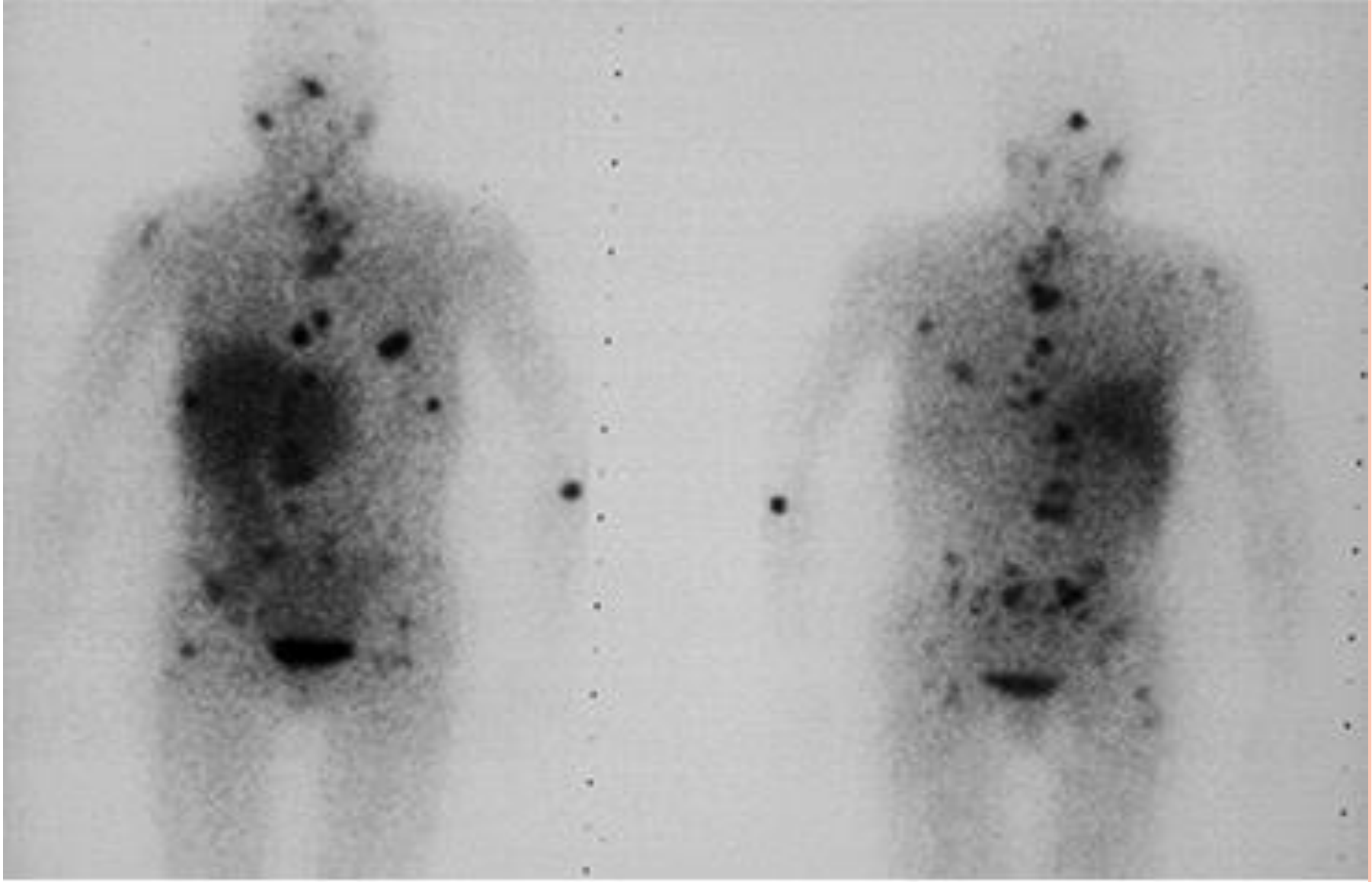


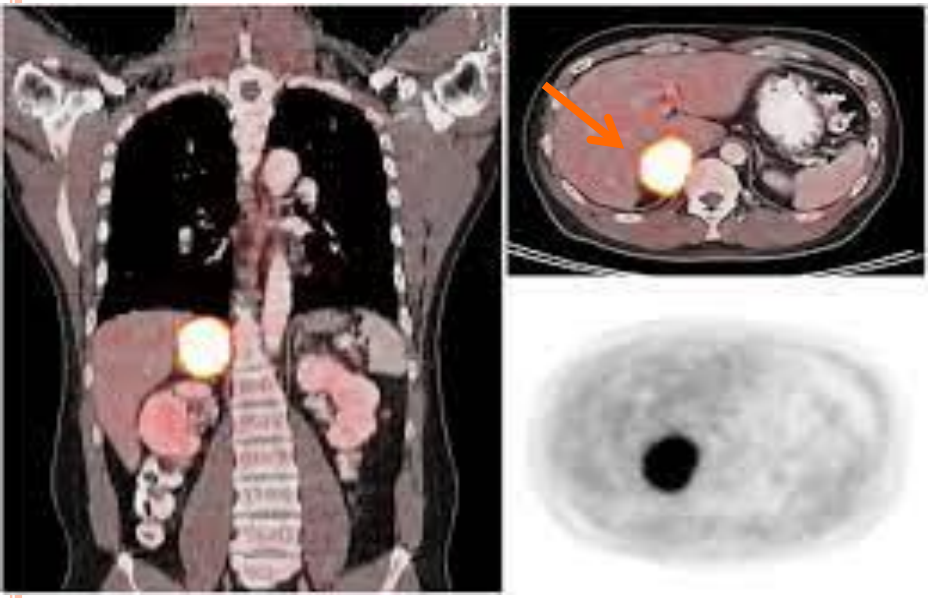
Diffuse metastatic pheochromocytoma 123-I-meta-iodobenzylguanidine scan from a 41-year-old woman shows diffuse metastatic pheochromocytoma. Courtesy of William F Young, Jr, MD.

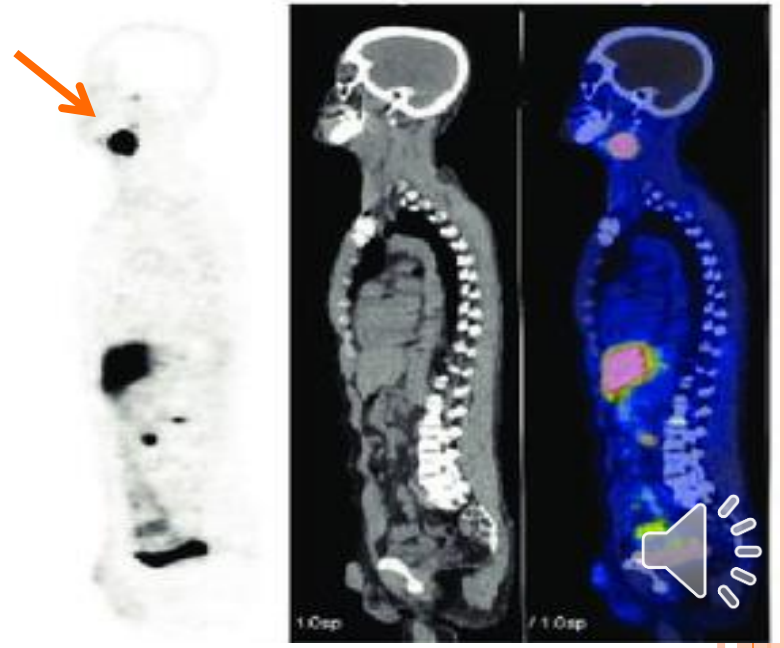
- **18F-FDG–PET–CT**

  Ligand:18F-fluorodeoxyglucose

- **68 Ga-DOTATATE–PET–CT**

  Ligand:68Ga-labeled DOTA(0)-Tyr(3)-octreotide





EXPERIMENTAL AND THERAPEUTIC MEDICINE 15: 3151-3160, 2018

Current diagnostic imaging of pheochromocytomas and implications for therapeutic strategy (Review)

FILIP ČTVRTLÍK[1], PAVEL KORANDA[2], JAN SCHOVÁNEK[3], JOZEF ŠKARDA[4], IGOR HARTMANN[5] and ZBYNĚK TÜDÖS[1]

Tumor	Functional imaging
Sporadic pheochromocytomas	123I-MIBG &PET imaging
Head and neck paragangliomas	18F-DOPA & 18FDG PET/CT
Retroperitoneal paragangliomas	18F-DOPA PET/CT
Metastatic pheo & para	18F-DOPA & 18FDG PET/CT

EXPERIMENTAL AND THERAPEUTIC MEDICINE 15: 3151-3160, 2018

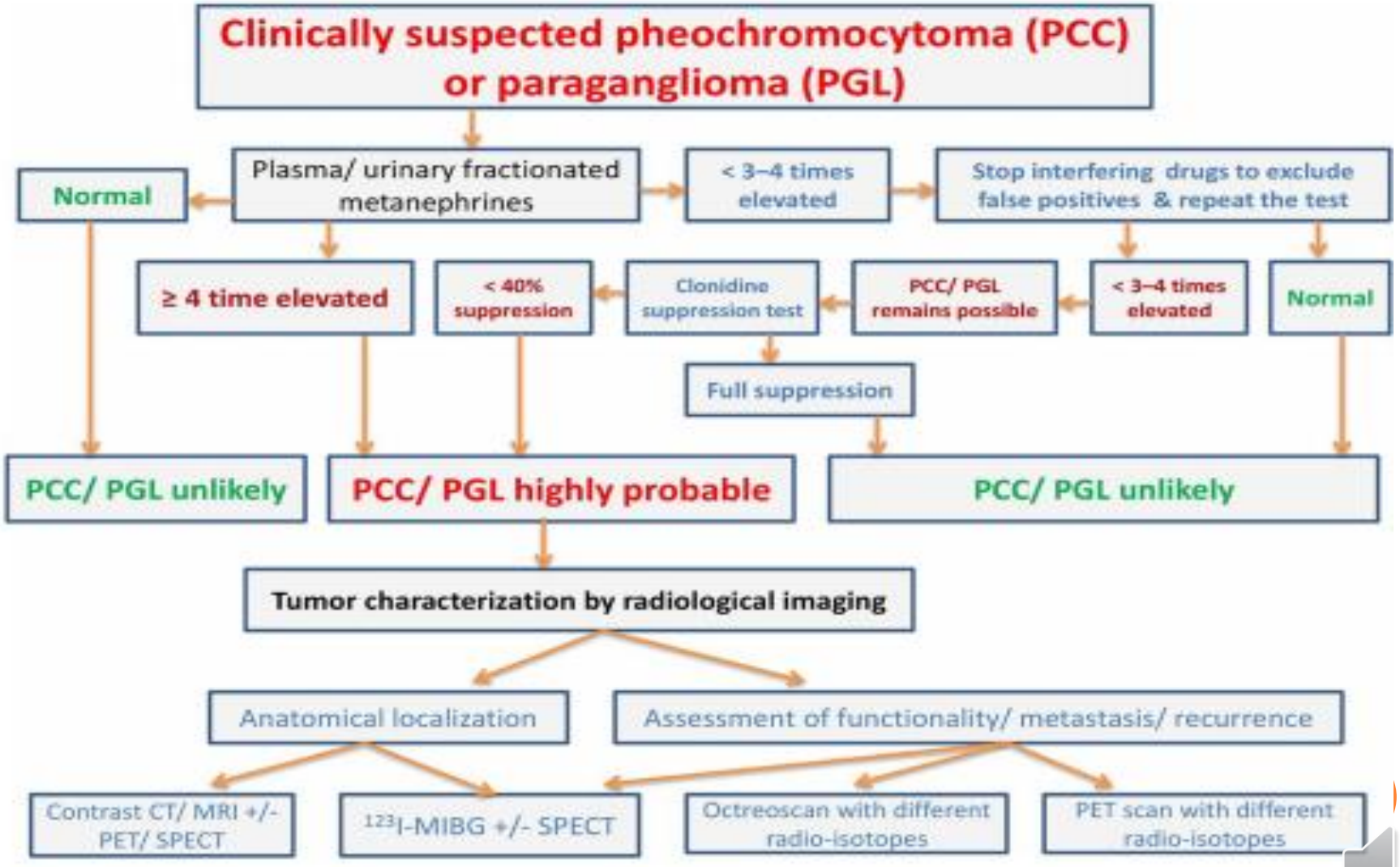
Approach to Pheochromocytoma and Associated Syndromes According to the Clinical Scenario.*

Table 1. Approach to Pheochromocytoma and Associated Syndromes According to the Clinical Scenario.*

Clinical Scenario	Initial Biochemical Testing and Imaging	Follow-up Biochemical Testing and Imaging
Signs and symptoms on presentation (e.g., resistant hypertension or paroxysms of hypertension, palpitations, perspiration, headaches, and markedly elevated metanephrines or catecholamines)	Perform abdominal contrast-enhanced CT or MRI; if abdominal imaging is negative, consider MRI of skull base, neck, chest, and pelvis	Measure metanephrines postoperatively and then annually; if bilateral pheochromocytomas were removed with cortical-sparing surgery, document normal glucocorticoid secretory function with cosyntropin-stimulation test
Incidentally discovered adrenal or retroperitoneal mass with attenuation >10 Hounsfield units on unenhanced CT	If levels of metanephrines are clearly elevated, perform contrast-enhanced CT or MRI; if mass is >10 cm in diameter or is extraadrenal, search for additional paragangliomas or metastatic disease with ^{123}I-MIBG scintigraphy, ^{68}Ga-DOTATATE–PET–CT, or ^{18}F-FDG–PET–CT	If a pheochromocytoma or paraganglioma was resected, measure metanephrines postoperatively and then annually
Patient identified as carrier of disease-causing mutation		
RET mutation	Measure metanephrines and perform abdominal MRI; measure serum calcitonin and calcium; seek endocrine surgery consultation if thyroid gland not previously resected	Measure serum calcitonin, metanephrines, and serum calcium annually
VHL mutation	Measure metanephrines; perform MRI of the brain, spinal cord, and abdomen; perform ophthalmoscopy	Measure metanephrines yearly; perform MRI of the brain, spinal cord, and abdomen; perform ophthalmoscopy; if no tumor found, monitor every 2 or 3 years
SDHA, *SDHB*, or *SDHD* mutation	Perform MRI of skull base and neck, thorax, retroperitoneum, and pelvis; alternatively, perform ^{68}Ga-DOTATATE–PET–CT; also measure metanephrines	Measure metanephrines yearly; if a pheochromocytoma or paraganglioma was removed, perform MRI of the surgical region annually for yr 1–3; for body areas that had no tumors, perform MRI every 3 yr
SDHC or *SDHAF2* mutation	Measure metanephrines; perform MRI of skull base and neck or ^{68}Ga-DOTATATE–PET–CT	If a paraganglioma or pheochromocytoma was removed, perform MRI of the surgical region annually for yr 1–3; for body areas that had no tumors, perform MRI every 3 to 5 yr
MAX or *TMEM127* mutation	Measure metanephrines; perform MRI of the abdomen or ^{68}Ga-DOTATATE–PET–CT	Measure metanephrines yearly; if a pheochromocytoma or paraganglioma was removed, perform MRI of the surgical region annually for yr 1–3; perform MRI of the abdomen every 3 yr
Neurofibromatosis type 1	Measure metanephrines	If hypertension or clinical symptoms develop, measure metanephrines

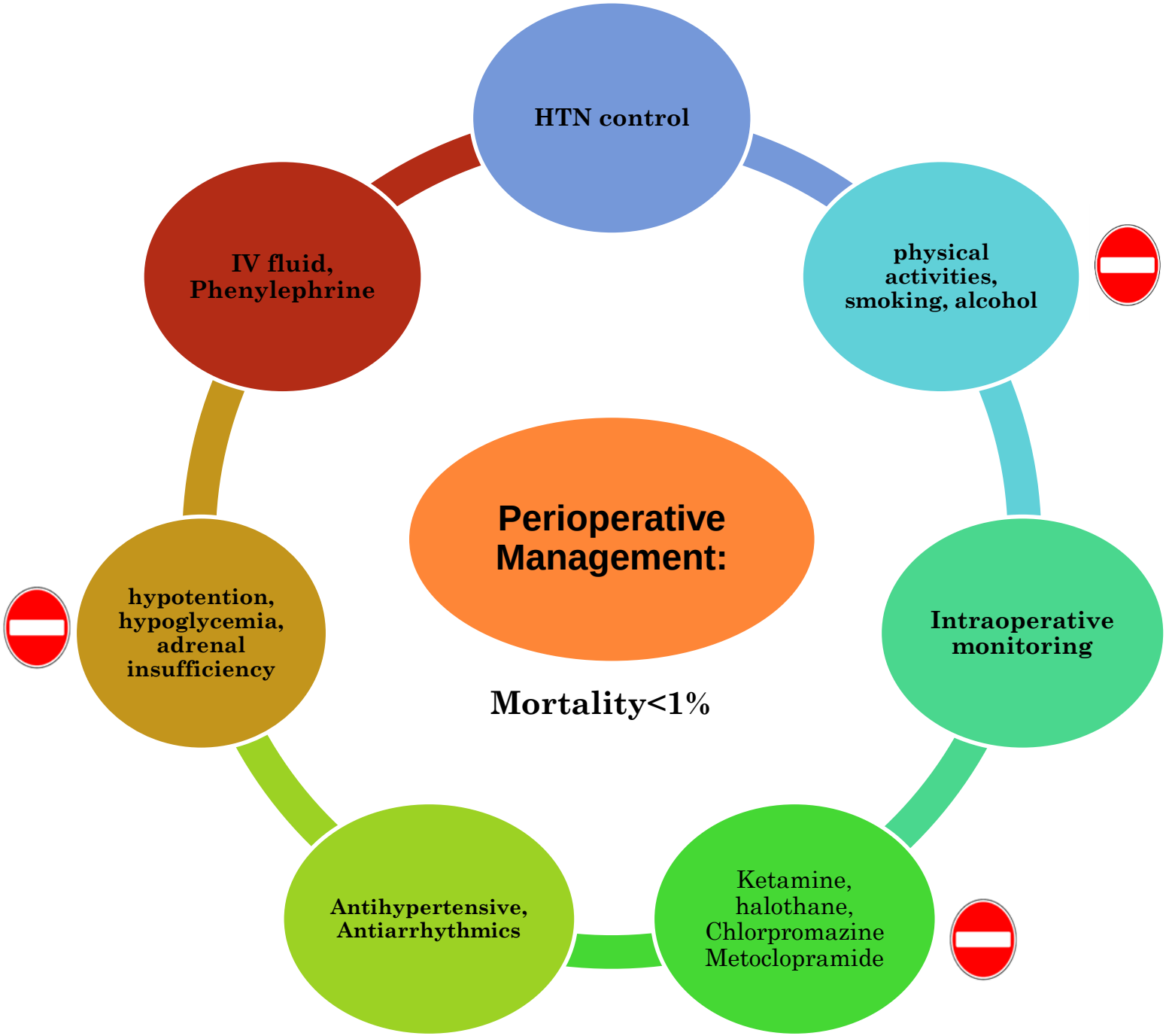
* The term metanephrines refers to metanephrine and normetanephrine. CT denotes computed tomography, ^{18}F-FDG ^{18}F-fluorodeoxyglucose, ^{68}Ga-DOTATATE ^{68}Ga-labeled 1,4,7,10-tetraazacyclododecane–1,4,7,10-tetraacetic acid–octreotate, ^{123}I-MIBG ^{123}I-labeled metaiodobenzylguanidine, MRI magnetic resonance imaging, and PET positron-emission tomography.

Algorithm for the usual diagnostic evaluation of PCCs & PGLs



Treatment:

- Surgical resection
- Laparoscopic adrenalectomy retroperitoneal approach
- When?
- started at least 7-14 days before surgery.
- Combined α- and ß-adrenergic blockade is standard Tx
- target BP <120/80 mm of Hg with a standing systolic BP >90 mm of Hg
- Liberal intake of salt(5 g) and fluids 3 d after α- blocker
- Intra-operative hemodynamic monitoring


HTN control
physical activities, smoking, alcohol
Intraoperative monitoring
Ketamine, halothane, Chlorpromazine Metoclopramide
Antihypertensive, Antiarrhythmics
hypotention, hypoglycemia, adrenal insufficiency
IV fluid, Phenylephrine
Perioperative Management:
Mortality<1%

Treatment:

- α-adrenergic blockade:

  nonselective = phenoxybenzamine

  10 mg BD increased 30 mg TDS

  selective α1 blockade = doxazosin P & T

  1 mg daily increased 10 mg BD

  a high-Na diet (5000 /d) & generous fluid intake (2.5 l /d)

- ß-adrenergic antagonist:

  extended-release metoprolol 25 mg daily up to 100 mg BD HR of 80 b/ min

  propranolol 10 mg/QID

Treatment:

- Calcium Channel Blockers (CCBs)

  add on therapy

  first-line agents

- Metyrosine

  inhibitor of tyrosine hydroxylase, rate-limiting enzyme in the biosynthesis of catecholamine

  due to severe adverse effects its use is reserved for the management of large tumors and prior to radiofrequency ablation of metastatic disease

- IV drug (intraoperatively)

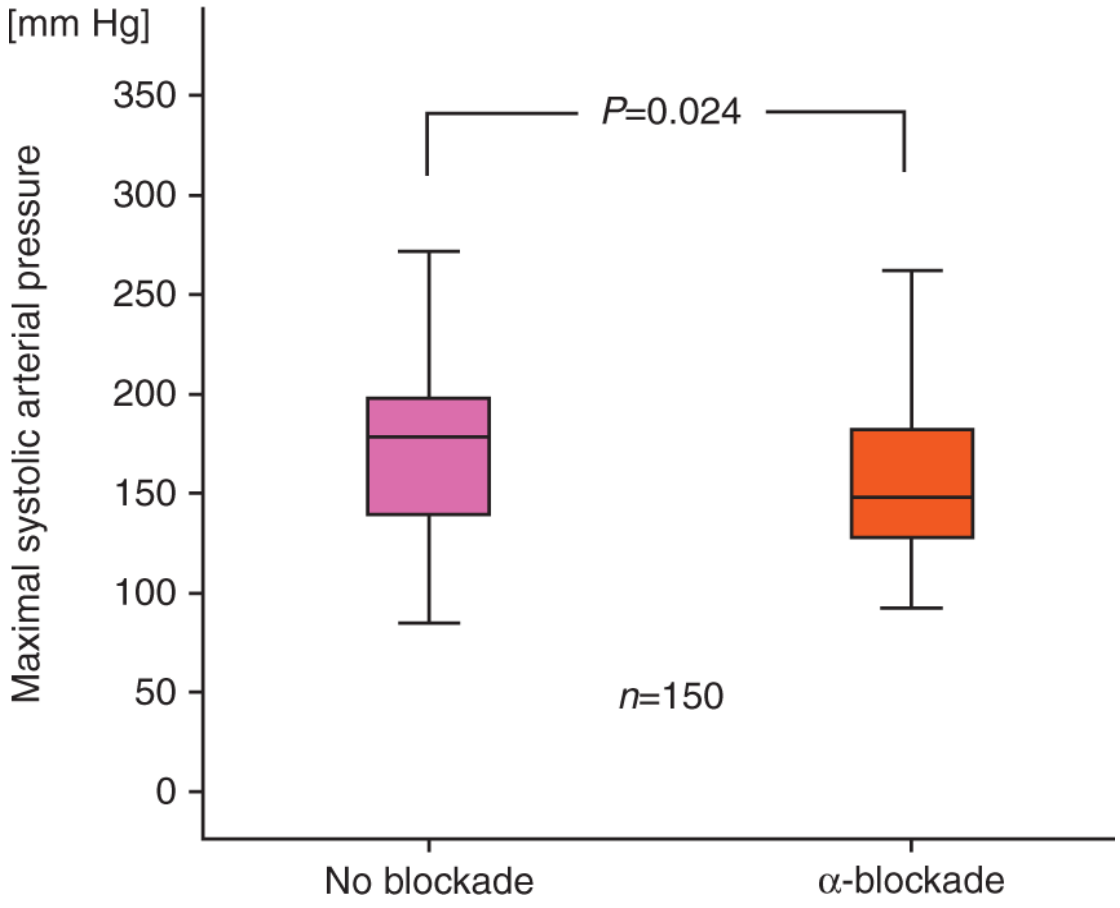
  phentolamine, sodium nitropruside, nitroglycerine, nicardipine and hydralazine.

Treatment:

Drug	Usual dosage range
Phenoxybenzamine (non-selective α-blocker)	Oral: 20–100 mg/ day in divided doses. Intravenous: 1 mg/ kg/ day (maximum)
Phentolamine (non-selective α-blocker)	Bolus doses of 2.5–5 mg intravenously as required
Doxazosin (α_1-adrenergic blocker)	1–16 mg/ day in divided doses 1–3 times/ day
Prazosin (α_1-adrenergic blocker)	2–15 mg/ day in 2-3 divided doses
Terazosin (α_1-adrenergic blocker)	1–5 mg/ day (maximum dose 20 mg/ day)
Propranolol (non-selective β-blocker)	40–240 mg/ day in 2–3 divided doses
Metoprolol (cardio-selective β-blocker)	50–400 mg/ day in 2 divided doses
Bisoprolol (cardio-selective β-blocker)	2.5–20 mg/ day
Labetalol (α_1 and non-selective β-blocker)	Oral: 200–400 mg/ day in 2 divided doses Intravenous: 300 mg/ day (maximum)
Nicardipine (calcium channel blocker)	Oral: 30–60 mg twice daily Intravenous: 15 mg/ hour (maximum)
Amlodipine (calcium channel blocker)	2.5–10 mg daily
Nifedipine (calcium channel blocker)	30–120 mg once daily (sustained-release orally)
Verapamil (calcium channel blocker)	120–240 mg once daily (sustained-release orally)
Metyrosine (tyrosine hydroxylase inhibitor)	1000–4000 mg orally in 3–4 divided doses
Nitroglycerine infusion	5 – 100 μ grams/ minute (for hypertensive crisis)
Sodium nitropruside infusion	10–200 μ grams/ minute (for hypertensive crisis)

Perioperative α-receptor blockade in phaeochromocytoma surgery: an observational case series†

H. Groeben[1,*], B. J. Nottebaum[1], P. F. Alesina[2], A. Traut[3], H. P. Neumann[4] and M. K. Walz[2]



no difference in the incidence of excessive hypertensive episodes between groups
and
no major complications occurred.

Br J Anaesth, Volume 118, Issue 2, February 2017, Pages 182–189, https://doi.org/10.1093/bja/aew392

Familial Pheochromocytomas:

- 40 % of patients have a familial disorder
- more likely to be bilateral adrenal pheochromocytomas, extra adrenal, multiple
- hereditary tumors typically present at a younger age than sporadic neoplasms

- autosomal dominant inheritance

- multiple endocrine neoplasia type 2 (MEN2) (50)
- Von Hippel-Lindau (VHL) syndrome (10 to 20)
- neurofibromatosis type 1 (NF1) (0.1 to 5.7)

Curr. Treat. Options in Oncol. (2020) 21: 85

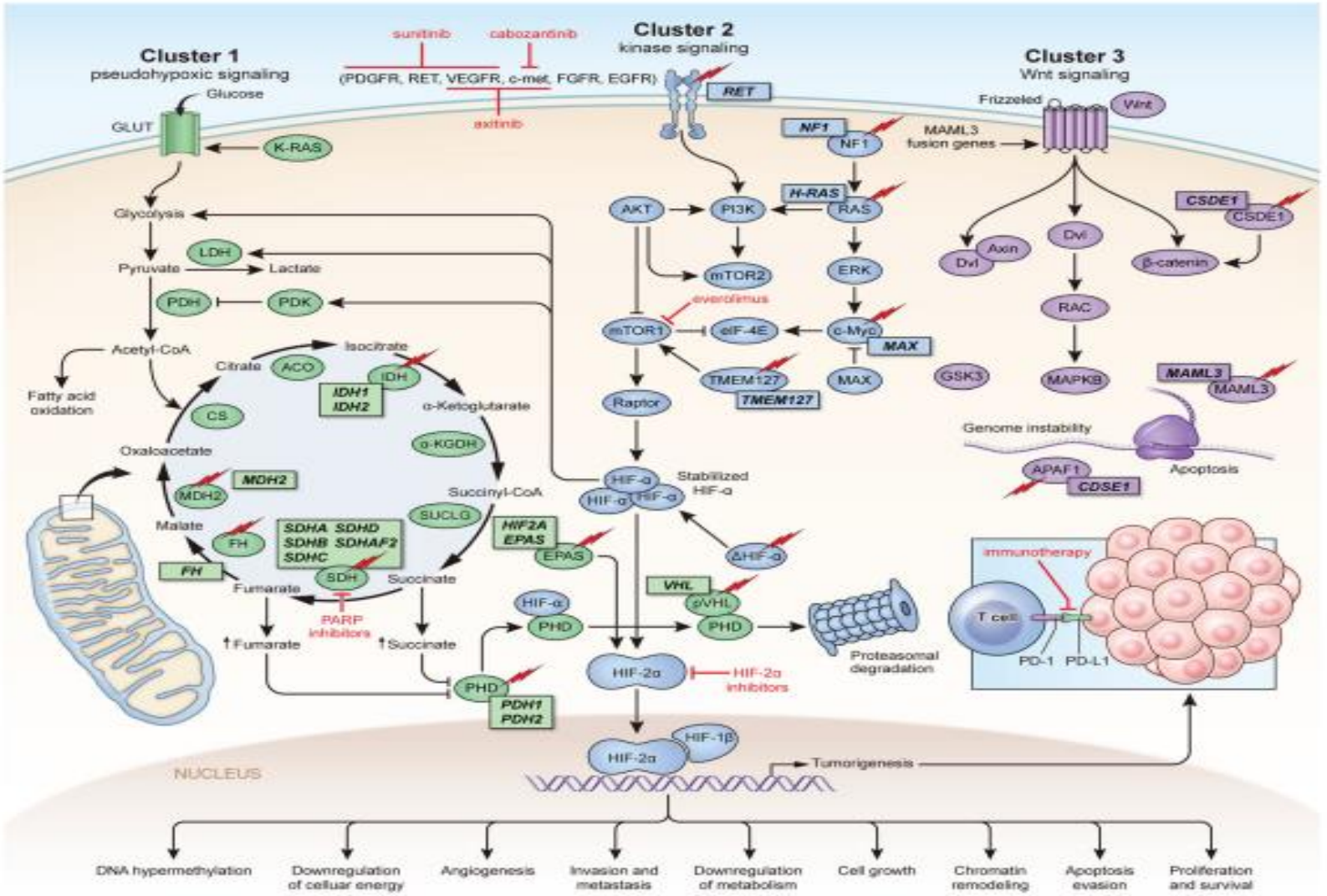


Fig. 1. Genetics and molecular pathways for pheochromocytoma and paragangliomas. Clusters I, II, and III with molecular-targeted options. Cluster I PHEOs/PGLs, also known as the pseudohypoxia group, are characterized by mutations in *SDHA*, *SDHB*, *SDHC*, *SDHD*, *SDHAF2*, *FH*, *VHL*, and EPAS1 [20]. Cluster II PHEOs/PGLs, also known as the kinase signaling group, are characterized by mutations in *RET*, *NF1*, *TMEM127*, *MAX*, and *HRAS* [16]. The Wnt signaling group (cluster III) includes mutations in the genes *CSDE1* and *MAML3* [73, 74].

Genetic Testing:

- 32–79 % of cases were associated with mutations => **all**
- 11%-24% of PHEO/PGL with apparently **sporadic** have genetic mutations

When?

- Paraganglioma
- Bilateral adrenal pheo
- Unilateral adrenal pheo and a FH of pheo/parag
- Unilateral adrenal pheo onset at a young age (<45 years)
- Other clinical findings suggestive of one of the syndromic disorders

Characteristics of Pheochromocytoma-Associated Syndromes.*

Table 2. Characteristics of Pheochromocytoma-Associated Syndromes.*

Gene	Syndrome	Nonchromaffin Tumors	Transmission	Adrenal Tumors	Head and Neck Tumors	Extraadrenal Tumors†	Multiple Tumors	Metastatic Tumors‡	Family History§
				frequency (percent)					
VHL	VHL	Retinal and CNS hemangioblastomas, RCC, pancreatic neuroendocrine tumor, ELST	Autosomal dominant	>50	<1	10–24	>50	1–9	25–50
NF1	NF1	Cutaneous neurofibromas, malignant peripheral-nerve-sheath tumor, breast cancer	Autosomal dominant	>50	<1	1–9	25–50	1–9	10–24
RET	MEN-2	Medullary thyroid carcinoma, hyperparathyroidism	Autosomal dominant	>50	<1	<1	>50	<1	25–50
SDHA	PGL5	Rarely also pituitary adenoma, GIST, RCC	Autosomal dominant	25–50	25–50	25–50	1–9	1–9	1–9
SDHB	PGL4	Rarely also pituitary adenoma, GIST, RCC	Autosomal dominant	25–50	25–50	25–50	10–24	25–50	10–24
SDHC	PGL3	Rarely also pituitary adenoma, GIST	Autosomal dominant	1–9	>50	<1	10–24	Not reported	10–24
SDHD	PGL1	Rarely also pituitary adenoma, GIST, RCC	Autosomal dominant, maternal imprinting	10–24	>50	10–24	>50	1–9	25–50
SDHAF2	PGL2		Autosomal dominant, maternal imprinting	1–9	>50	Not reported	>50	Not reported	>50
MAX	No name	Rarely also RCC	Autosomal dominant	>50	<1	1–9	>50	1–9	25–50
TMEM127	No name		Autosomal dominant	>50	1–9	<1	25–50	10–24	1–9

* For multiple endocrine neoplasia type 2 (MEN-2), von Hippel–Lindau disease (VHL), and neurofibromatosis type 1 (NF1), the frequencies of the characteristics shown are for patients with chromaffin tumors, since such tumors do not develop in all patients with these syndromes. CNS denotes central nervous system, ELST endolymphatic-sac tumor of inner ear, GIST gastrointestinal stromal tumor, HPT hyperparathyroidism, PGL paraganglioma syndrome (PGL1 through PGL5 denote paraganglioma syndromes 1 through 5), and RCC renal-cell carcinoma.
† These tumors consist of retroperitoneal, pelvic, and thoracic tumors.
‡ These tumors consist of metastatic pheochromocytoma and paraganglioma.
§ Shown is the frequency of a family history of components of the given syndrome.

HP Neumann et al. N Engl J Med 2019;381:552-565.

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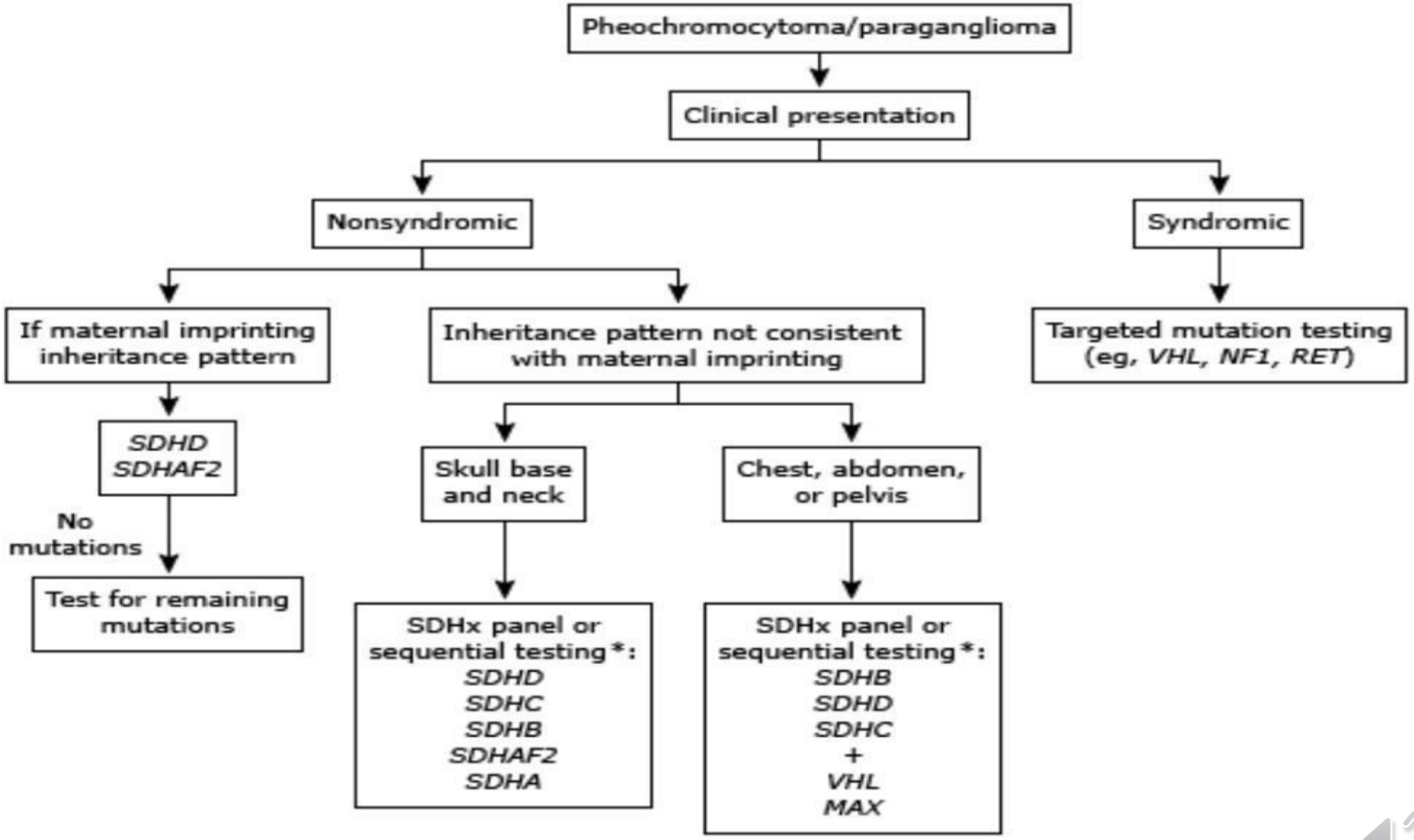
Proposed Genetic Testing Algorithm:



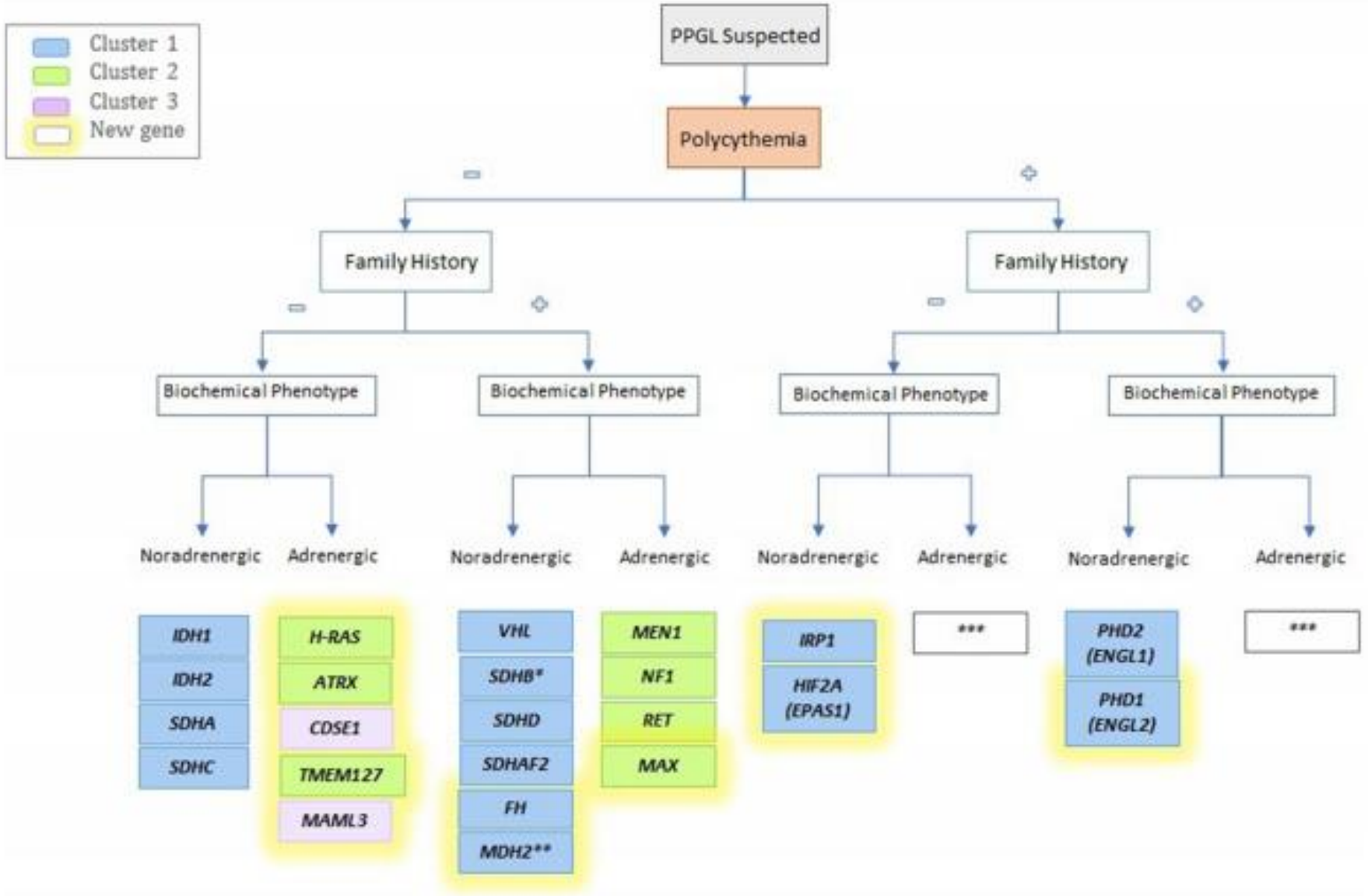


FIGURE 3 | Schematic algorithm for identifying a possible driver mutation of the newly identified genes mutation. *Often family history is absent; **Unknown; ***Not described yet.

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Neuroendocrine Cancers (JR Strosberg, Section Editor)

Check for updates

Emerging Treatments for Advanced/Metastatic Pheochromocytoma and Paraganglioma

Maran Ilanchezhian, BS[1]
Abhishek Jha, MD[2]
Karel Pacak, MD, PhD, DSc[2]
Jaydira Del Rivero, MD[3,4,*]

(cluster I) Pseudohypoxia group

- Antiangiogenic therapy
- Hypoxia-inducible factor (HIF) inhibitors
- Immunotherapy
- Poly (ADP-ribose) polymerase (PARP) inhibition

(cluster II) Kinase signaling group

- (mTOR) inhibition

(cluster III) Wnt signaling

- no

Pheochromocytoma in Pregnancy:

- rare cause of hypertension during pregnancy
- (0.007%) versus HTN during pregnancy (5–10%)
- tumors can become symptomatic in any period of gestation
- supine position may allow the gravid uterus to compress the tumor, causing paradoxical supine hypertension
- Diagnosis as in nonpregnant women
- unexplained peripartum cardiomyopathy
- MRI & Sono
- Maternal and fetal mortality rates are high

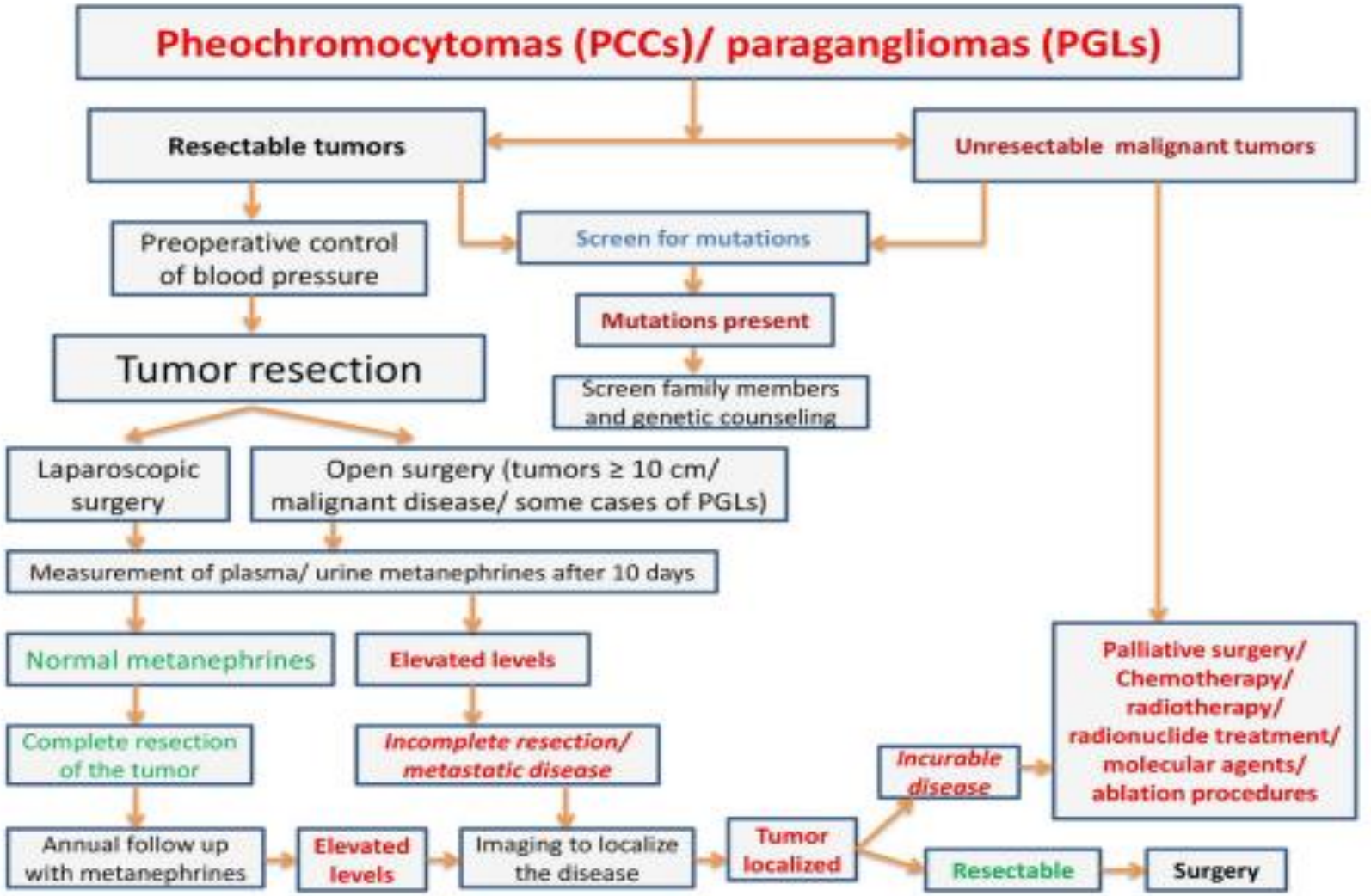
Pheochromocytoma in Pregnancy:

- alpha-adrenergic blockade , beta-adrenergic blockade
- CCB can be added
- Labetalol no longer recommended
- Methyldopa no longer recommended
- drugs should be avoided: GCS, anti-emetics, thiopental, ketamine
- surgery if the fetus is previable (less than 24 weeks of gestation) second trimester
- medical management when the pregnancy is further along
- Cesarean section is the preferred mode ?
- monitor the neonate closely during the first days

Surveillance:

- plasma or urinary metanephrine should be checked only after ten days of the surgical resection
- Hypertension can persist in up to 25-50 % of cases
- Postoperatively, asymptomatic patients should undergo annual biochemical testing and crosssectional digital imaging of the operated area annually for at least 3 years , every 2 to 3 years (high risk patients: lifelong)
- Recurrence (16%) : familial, malignant, extraadrenal & right adrenal tumor
- first-degree relatives of a mutation carrier should be testing
- asymptomatic mutation carriers should be offered clinical surveillance and management specific to the gene
- patients and clinicians understand the concept of disease penetrance

Algorithm for management and follow up of patients with PCCs and PGLs



Pheo : Revised "Rule of Ten"

- 10% extra-adrenal (closer to 15%)
- 10% occur in children
- 10% familial (closer to 40%)
- 10% bilateral or multiple (more if familial)
- 10% recur (more if extra-adrenal)(16%)
- 10% malignant
- 10% discovered incidentally(up to 60%)

Thank you