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rattibha.com ♥

1/ 📢Hello #MedTwitter

This month's @ASPNeph Renal Imaging Webinar was all about #Pheochromocytoma!

Here are a few "pheo facts" I learned! #tweetorial #nephtwitter

Let's start with a poll.

Which of the following is true about pheochromocytoma (PCC)?

2/Answer: D All of the above

(PMID: 24893135 & 30603807)

💥 PCC & Paraganglioma (PGL) are catecholamine secreting tumors arising from chromaffin cells

PCC 👉Adrenal medulla = 80-85%
PGL 👉Extra-adrenal =10-15% ➡️symp chain (abdo/chest/pelvis) or parasymp chain (head&neck)

3/ 💡Many will recall the “Rule of 10s” 💡

10% Malignant

10% ➕Family history

10% Bilateral

10% Extra-adrenal

But..

💣This rule does not hold true for children💣

⚡In particular, inherited PCC/PGL more likely in children⚡

📌 Up to 80% in some studies! (PMID:24169644)

4/ Which Syndromes are associated with PGLs/PCCs?

5/Ans: D

📌Von Hippel Lindau: PCC (often B/L) or PGL in ~10-20%. Noradrenergic phenotype.
Gene: VHL TSG

📌MEN2: PCC in ~ 50%. Adrenergic phenotype.
Gene: RET

📌NF1: ⬇️ common ~2-3%. Usually solitary PCC.
Gene: NF1

⚡All =AD inheritance⚡
Source:

http://UptoDate.com

6/⚡Many other susceptibility genes identified ⚡

Genetic mutations can be divided into 2 groups:
📌Genes encoding proteins
🔼Hypoxia inducible factors: VHL, SDH, EGLN1 & HIF2A
⏩Kinase Signalling pathway: RET, NF1, TMEM127

⚡Genetic Testing is recommended in all children

7/ Approximately how common is the classic triad of episodic headache, sweating and palpitations in children?

8/ The classic triad 🔺 has been reported in up to 54% of children (PMID: 24825268)

🌟Average age ~ 11-13 years
🌟M>F 2:1

Other symptoms:
🌟anxiety 🌟⬇️weight🌟visual change🌟 polydipsia/uria 🌟⬆️glucose🌟tremor 🌟flushing 🌟abdo pain 🌟 diarrhoea 🌟 pallor 🌟syncope

9/🧨Hypertension is common (60-90%)
🔥Sustained > paroxysmal in children
🔥BP can be normal
🔥Look for abnormal ABPM eg. “non-dipping”

🧨 Orthostatic Hypotension can be a presenting feature (epinephrine secreting tumours)

(PMID: 30603807)

10/ Let's Review catecholamine production & metabolism!

Catecholamines are produced by metabolism of Tyrosine👉 DOPA👉Dopamine 👉Norepinephrine 👉 Epinephrine

⚡Metanephrines are the o-methylated products of catecholamine metabolism⚡

(PMID: 30603807)

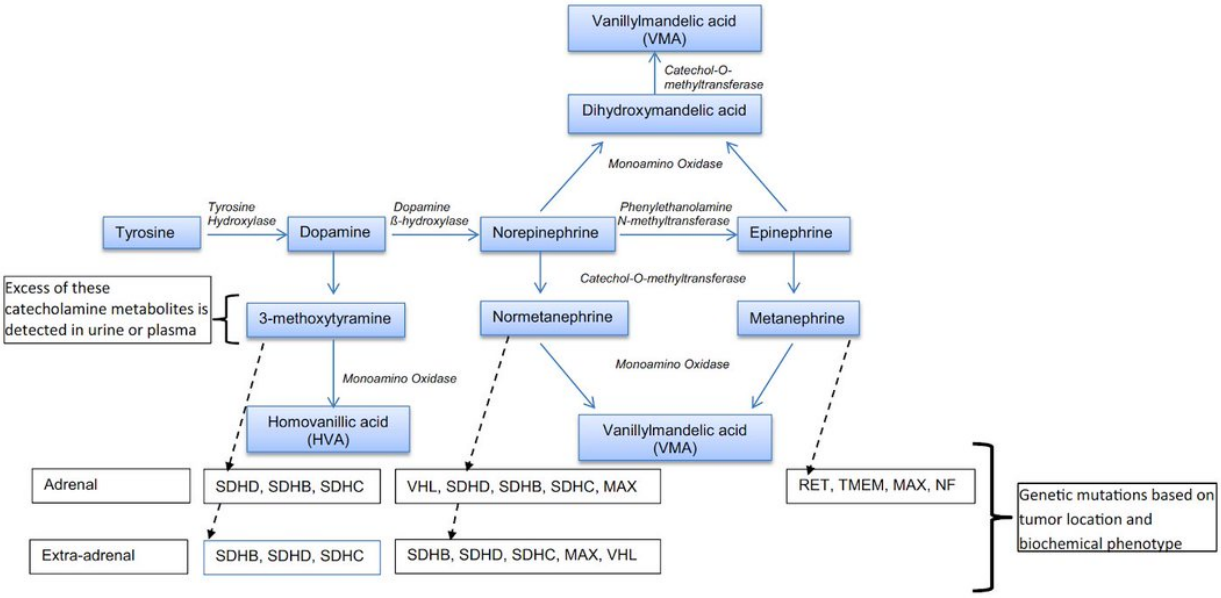

Fig. 1 Catecholamine metabolism and genetic mutations associated with hormonally active tumors. Combining information from figures in Lenders et al. [2] and Fishbein et al. [15]

11/ 1st line of invx is biochemical testing

⚡Catecholamines or metanephrines can be tested
⚡Plasma metanephrines more sens/specific than urine
⚡Suspect false ➕ if level <3-4 x normal

⏰ Patient should be supine x 30mins for plasma sample
👶 Use age appropriate cut-offs

12/ Which of the following medications can cause elevation of catecholamines?

13/ All the above

⚡Sympathomimetics, SSRIs, MAO inhibitors, α/β blockers➡️false ⬆️catecholamines
⚡Acetaminophen interferes w/ liquid chromatography
⚡Stop medications ~2 wks prior to testing
⚡If not,➡️ Clonidine suppression test
(PMID: 21615192, 28752085, 21651412)

TABLE 4 | Factors associated with false positive and false negative testing of metanephrines.

False positives
Medications (3)
Calcium channel blockers
Beta blockers
Mood stabilizers: tricyclic antidepressant, buspirone
Sympathomimetics: amphetamine, ephedrine
Stimulants: caffeine, nicotine
Dopaminergic agents: levodopa, alpha-methyldopa
Acetaminophen
Age
Increase in plasma metanephrines with age (51)
Posture
Increase in plasma metanephrines in seated versus supine position (52, 53)
Exercise (52)
High catecholamine diet (54)
Hypertension (3)
Obstructive sleep apnea (53, 55)
Stroke (3)
Renal impairment (56)
False negatives
Small tumors, usually <2 cm in size in normotensive patients being screened initially or for recurrence
Dopamine-secreting tumors

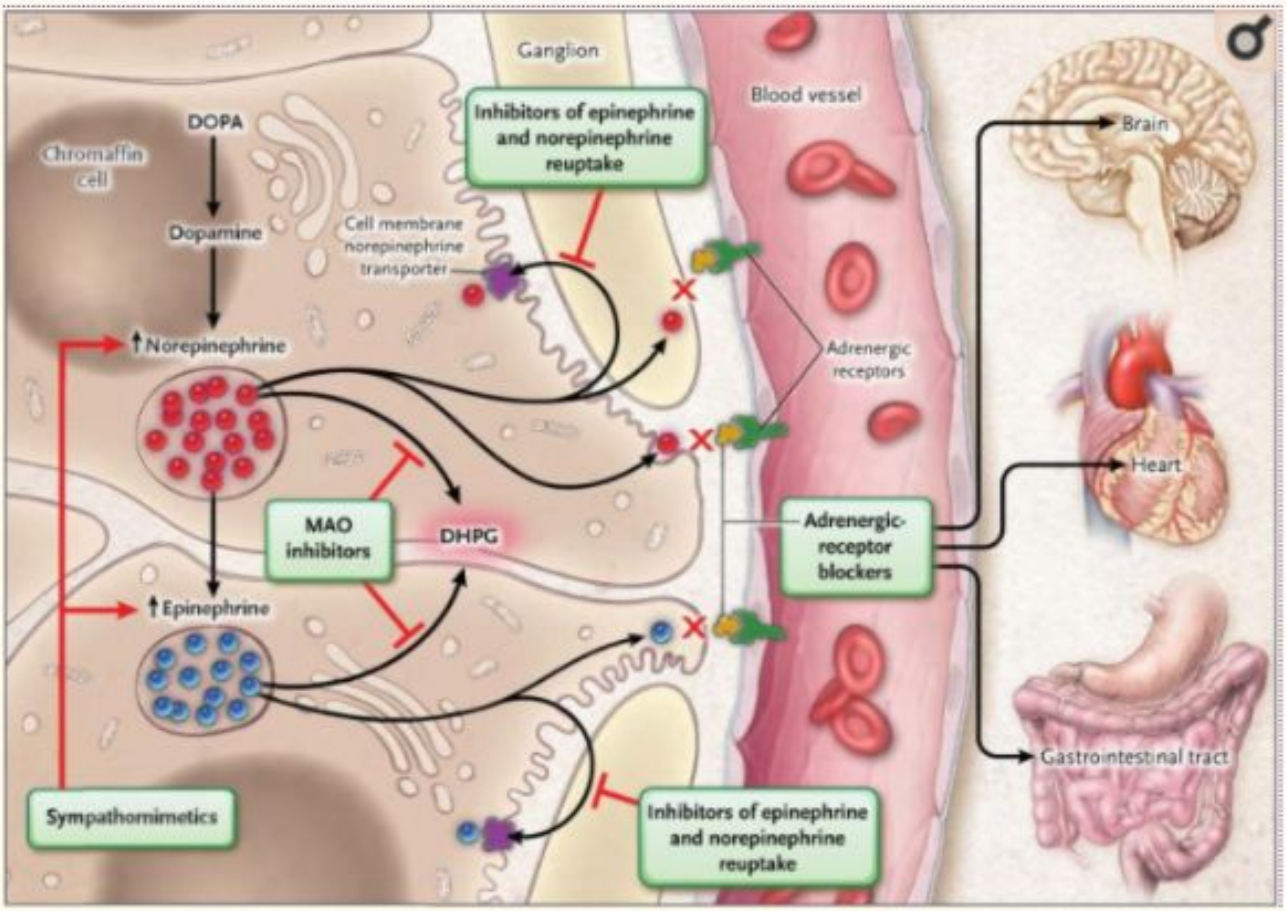

Figure 1

Mechanisms of Pharmacologic Interference with Catecholamines and Metanephrines

Sympathomimetic agents such as ephedrine, amphetamine, caffeine, and nicotine increase the release of norepinephrine and epinephrine. Monoamine oxidase (MAO) inhibitors block the conversion of norepinephrine and epinephrine to dihydroxyphenylglycol (DHPG), leading to increased concentrations and availability of these two catecholamines. Drugs that inhibit norepinephrine and epinephrine reuptake, such as serotonin–norepinephrine reuptake inhibitors (e.g., venlafaxine), "selective" serotonin-reuptake inhibitors, and tricyclic antidepressants, lead to increased concentrations of norepinephrine and epinephrine in the synaptic clefts. The α-adrenergic-receptor blockers and β-adrenergic-receptor blockers reduce the effects of catecholamines on end organs such as the brain, heart, gastrointestinal tract, and others. DOPA denotes dihydroxyphenylalanine.

PMID: 21651412

14/ Biochemical results can help classify the tumour:

📌Adrenergic:⬆️ E&NE, M & NM, VMA

📌Noradrenergic:⬆️ NE, NM, VMA

📌Dopaminergic:⬆️ Dopamine, HVA

15/ Imaging ▶️localise tumour & identify mets

CT & MRI both ➡️ good sens & specificity

📌Features can include:

⬆️attenuation on non-con CT (most >20 HU)

⬆️vascularity, cystic or hemorrhagic change

🕐Delayed contrast washout

⬆️ T2 signal on MRI

Source:

http://uptodate.com

16/ Functional imaging can be used to:
📌Localise tumour when CT/MRI negative
📌Identify metastatic/multifocal disease
📌Follow-up screening

Functional imaging may include integrated PET CT/MRI or scintigraphy

Let's review some options🔎

17/ MIBG Scintigraphy:
📌Iobenguane I-123 is a compound similar to NE
📌Uptake at adrenergic tissue
📌Uptake in normal adrenals can by asymmetrical
📌Correlate with CT/MRI

PMID: 21803186

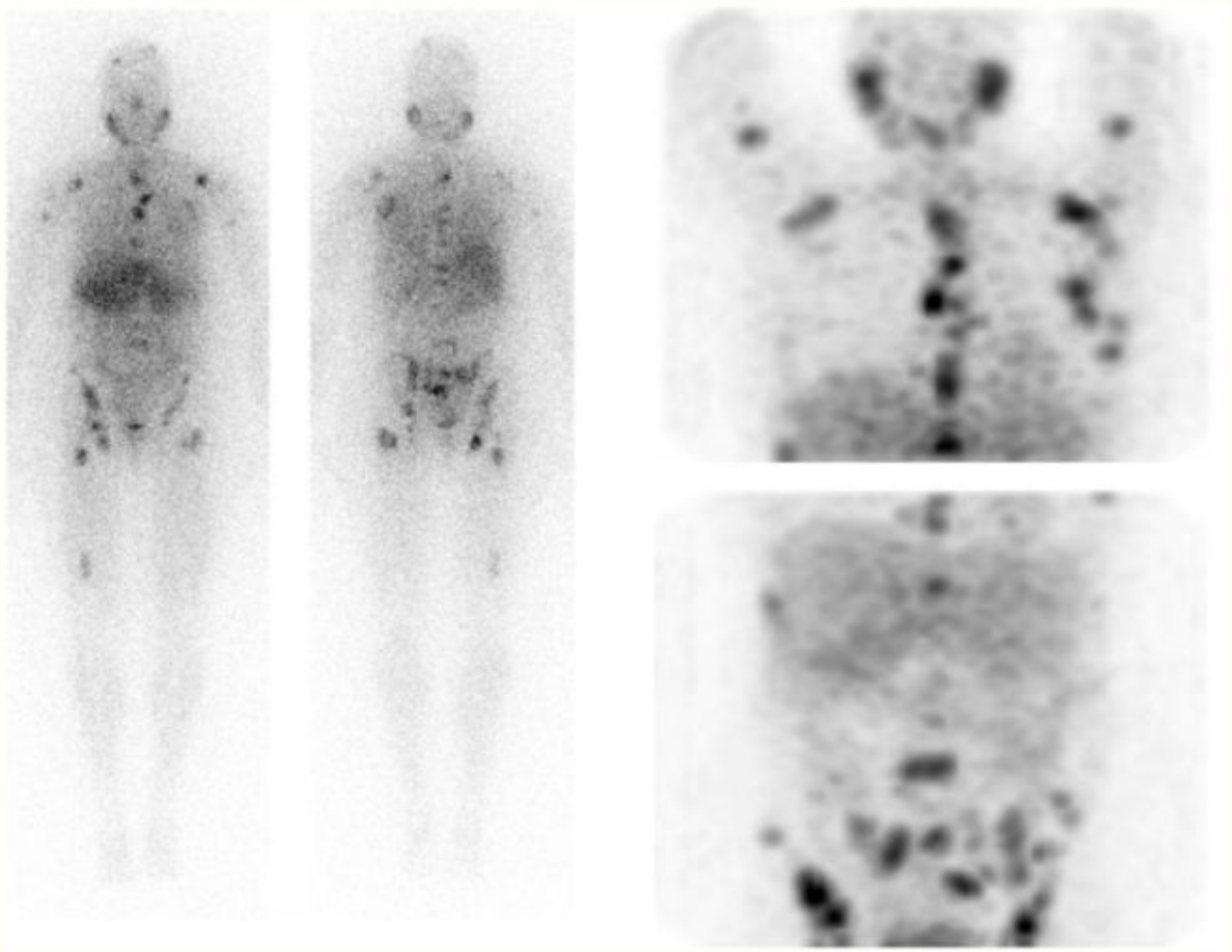

Figure 1

Whole body (left) and anterior reprojected images (right) with [^{123}I]-MIBG of a patient with PHEO; multiple metastatic lesions are seen

PMID: 21803186

18/ FDG PET:

📌FDG is a glucose analogue

📌Useful in tumours with ⬆️ glycolytic activity

Ga68 DOTATATE PET:

📌Somatostatin analogue

📌Good uptake in well-differentiated tumours

📌⬆️ Sensitivity & ⬆️Resolution

📌⬇️ Radiation

PMID: 19372492

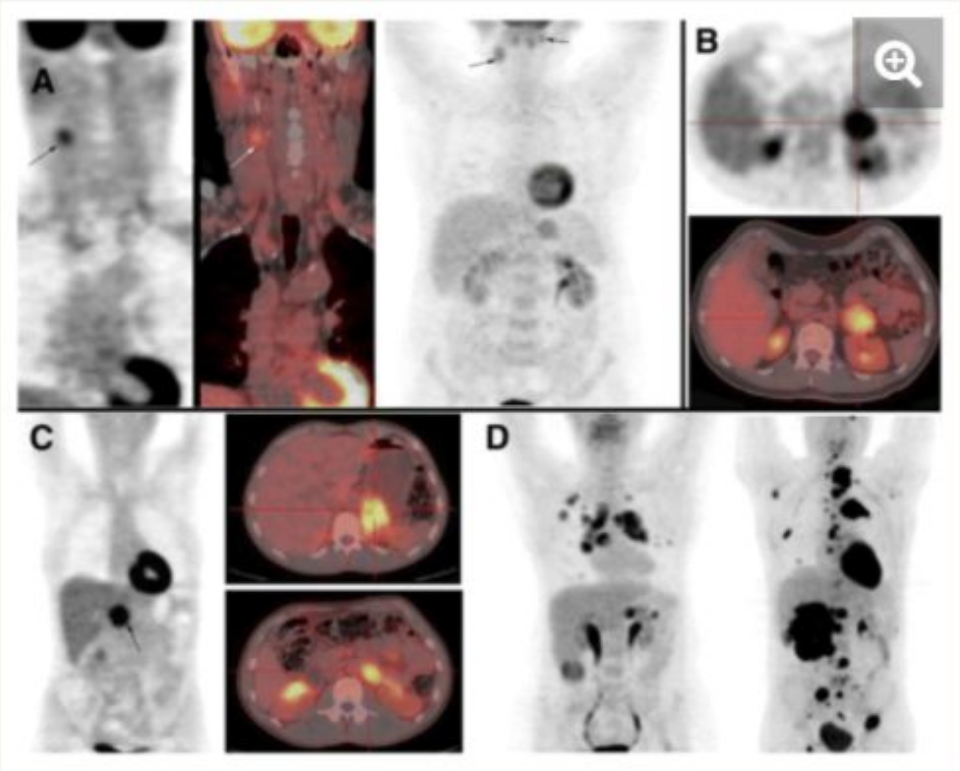

FIGURE 1.

Download figure | Open in new tab | Download powerpoint

(A) Cervical paraganglioma (patients 13 and 12). Patient 13 is SDHB patient with right glomic paraganglioma (arrow), as seen on coronal ^{18}F-FDG PET (left) and fusion imaging (middle). Patient 12 has bilateral cervical paraganglioma, as seen on coronal ^{18}F-FDG PET (right). (B) Left pheochromocytoma (patient 3), as seen on axial ^{18}F-FDG PET (top) and fusion imaging (bottom). (C) Abdominal nonmetastatic tumors (patients 7 and 10). Patient 7 has abdominal right paraganglioma, as seen on coronal ^{18}F-FDG PET (left). Patient 10 is VHL patient with left pheochromocytoma (top right) and paraganglioma at left renal hilum (bottom right), as seen on axial fusion imaging. (D) Metastatic pheochromocytoma (patients 19 and 28). Patient 19 has recurrent pheochromocytoma, as seen on maximum-intensity-projection image (left). Patient 28 is SDHB patient with metastatic pheochromocytoma, as seen on maximum-intensity-projection image (right).

PMID: 19372492

19/ This helpful diagram from a comprehensive review or PCC/PGL (PMID:30603807) summarises an approach to diagnostic evaluation:

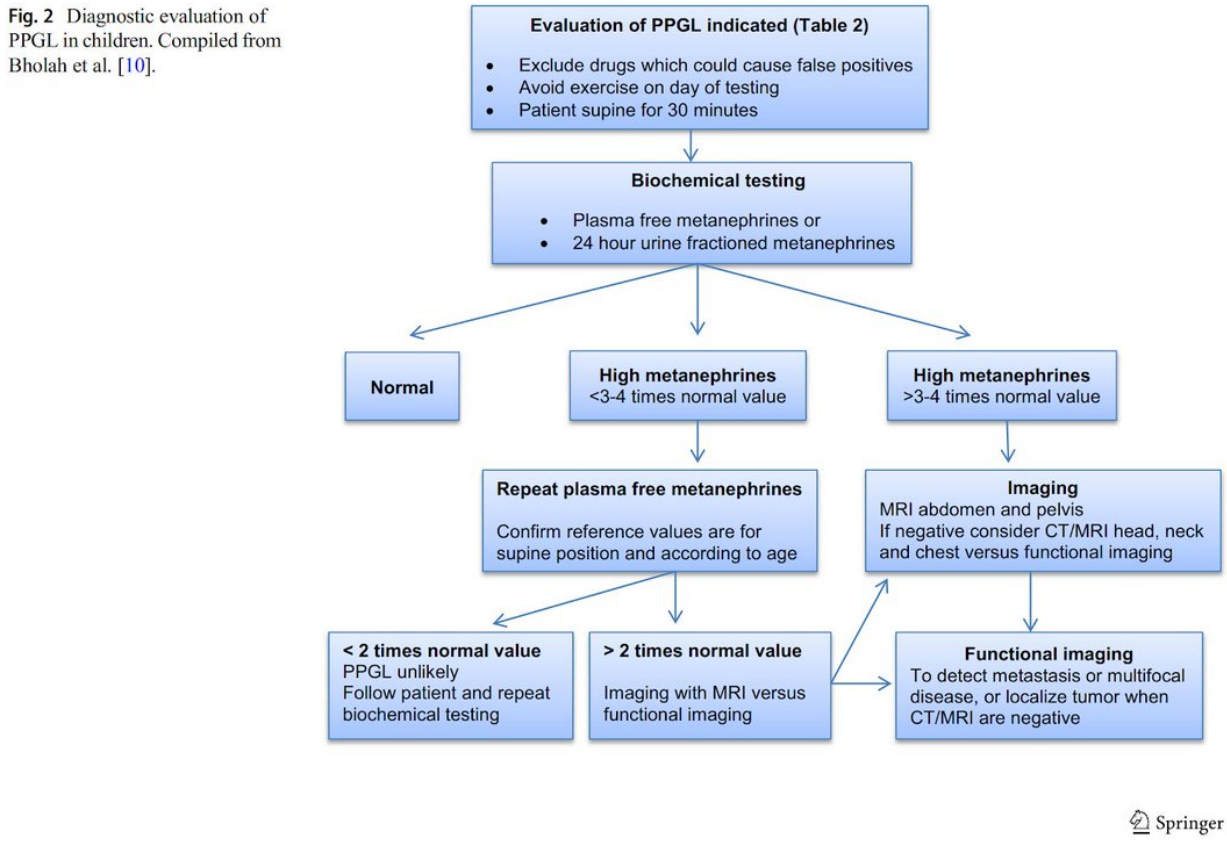

Fig. 2 Diagnostic evaluation of PPGL in children. Compiled from Bholah et al. [10].

20/ 💡 Surgical removal of a PCC/PGL can trigger a life threatening catecholamine storm💨⚡

This can cause:

👉Hypertensive Crisis

👉Arrhythmias

👉Myocardial infarction

👉Stroke

⚡Also post-operatively a drop in catecholamines can lead to 🔽 BP

21/ Aim of medical management is to prevent fluctuations in BP & post op 🔽BP

Always THINK 🅰️ before 🅱️
Start with alpha blockers before beta blockers!

⚡Initial use of beta blockers ➡️unopposed alpha action ➡️catecholamine storm 💨⚡

22/ There are no internationally approved protocols for management of PCC/PGLs

The table below summarises a suggested approach (PMID:30603807)

⚡Metyrosine = tyrosine hydroxylase inhibitor ⛔ catecholamine synthesis +/- alpha blockers can 🔽 BP lability peri-op

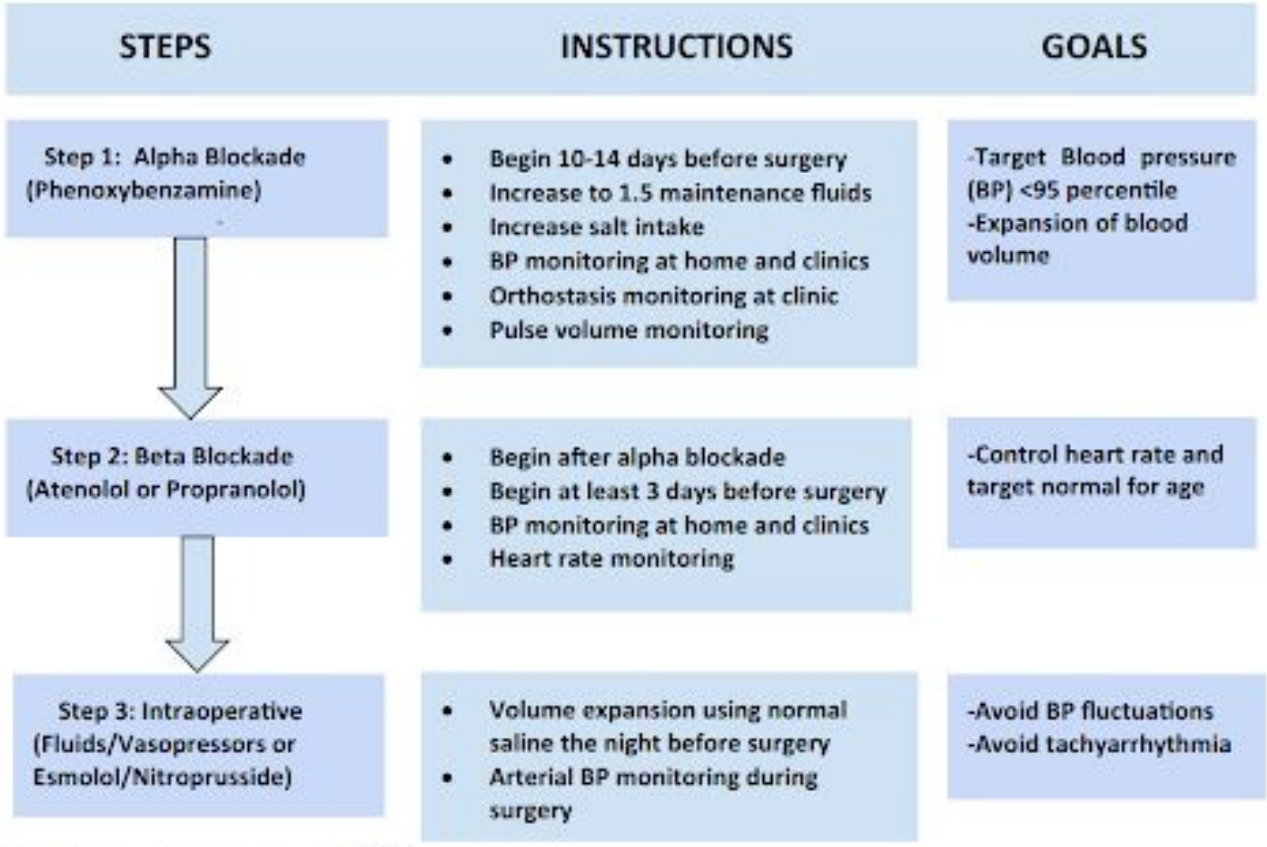

Fig. 4 Systematic approach to management of PPGL

23/ Take home points:

⚡PCC/PGL are rare

⚡Only ~50% have classic symptom triad

⚡Genetics testing for all children

⚡Biochemistry ➡️CT/MRI➡️Functional imaging

⚡Remember 🅰️before 🅱️to avoid a catecholamine storm!!

Thanks #ASPNeph #FellowFOAMgroup @drM_sudha @RoshanPGeorgeMD

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