Hypertension

(to access this via my wesbite

www.hypertensionclinic.co.nz

↓

Powerpoint Presentations And Teaching Materials

↓

FRACP Teaching 29.7.09)

JNC 7 Guidelines (2003)

Classification of Blood Pressure

Category	SBP		DBP
Normal	< 120	or	< 80
Prehypertension	120-139	or	80-89
Stage 1	140-159	or	90-99
Stage 2	> 160	or	> 100

Hypertension is the most important modifiable cardiovascular risk factor and the commonest cause of premature death in developed countries (and second only to maternal and childhood undernutrition in undeveloped countries)

•Continuum of increasing CV risk from SBP 115mmHg

• CV mortality doubles for every 10/5 increase in BP > 120/70mmHg

• High BP causes

- 35% of all cardiovascular deaths

- 50% of all stroke deaths

- 25% of all CAD deaths

- 50% of all congestive heart failure

- 25% of all premature deaths

- commonest cause of CKD overall and commonest cause of ESRD in older individuals

JNC-7 Blood Pressure Treatment

Treat to BP < 140/90 or < 130/80 in pts with diabetes or CKD

Start with lifestyle modifications

Without Compelling Indications

Stage 1	Stage 2
Thiazide for most	Thiazide + ACE-I ARB, BB, or CCB

With Compelling Indications

Drug(s) for compelling indications

↓

Not at goal BP

Optimise dosages or add additional drugs until goal BP achieved

Most people will require at least 2 drugs

More Recent Hypertension Guidelines

British Hypertension Society (2006)

European Society of Hypertension (2007)

Canadian Hypertension Education Programme (2009)

JNC-8 due out late 2009 or early 2010

Guidelines since JNC-7 have relegated beta blockers to 4th or 5th choice drug (except where complelling indications)

BHS guidelines say 1st drug for < 60 yrs ACE-inhibitor and > 60 years thiazide

Most hypertension is Essential Hypertension

Proportion of Essential/Secondary depends on definition of “secondary”

(eg if elevated BMI was a “secondary cause” 75% of patients would have it)

<u>Aetiology of Essential Hypertension is Complex</u>

-Multiple interacting mechanisms but important final common pathway is disordered renal sodium handling

- Primitive tribes with low daily Na intake (< 50mmol) do not get hypertension nor do they experience age-related increase in blood pressure

- 75-80% of individuals with essential hypertension have BMI > 25

Secondary Causes of Hypertension

Basic laboratory evaluation of *all* patients prior to conmencing antihypertensive therapy

12-lead ECG

FBC

Na, K, urea creatinine calcium

Fasting glucose + lipids

T4/TSH

Urine microscopy and albumin/creatinine ratio

When To Suspect a Secondary Cause of Hypertension

(1)Resistant Hypertension

(2)Clinical Clues

Resistant Hypertension Definition

A patient has Resistant Hypertension if BP > 140/90 (or > 130/80 with DM, CKD, or history of cardiovascular disease) despite

Optimal Doses

Of a Minimum of Three

Complementary Antihypertensive Medications

One of which is a Diuretic

Clinical Clues

History
• Polyuria/ nocturia/ muscle weakness
• Difficult hypertension in young women
• Snoring/apnoeas/somnolence
• Headaches/ palpitations/ diaphoresis esp in paroxysms
• Recent onset difficult hypertension in an older individual with peripheral vascular disease or smoker
• Headaches/ palpitations/ diaphoresis esp in paroxysms
• NSAID's/ Non-prescribed medications/ herbal remedies
• Dysthyroid symptoms

Exam
•Cushingoid features
• Bruits
•Radiofemoral delay

•*Lab*
• Low eGFR or abnormal urinary sediment
•Hypokalaemia / hypernatraemia/ alkalaemia/
•Hypercalcaemia
• Abnormal TFT

w1

Secondary (identifiable) Causes of Hypertension

- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Sleep apnoea
- Drug induced/ related
- Cushing's Syndrome or steroid therapy
- Phaeochromocytoma
- Coarctation of the aorta
- Thyroid/ parathyroid disease
- (Monogenic causes of hypertension – *rare but good for exams)*

Slide 12

w1 waltervdm, 11/07/2009

17 year old boy from Glen Eden with extended family in Northland presents to ED with a minor sporting injury. BP noted to be 180/110. He is admitted and BP does not settle below 160/90. Auntie says there is a family history of high blood pressure and strokes on his father's side.

Na 144 K 3.1 urea 5 creatinine 80 venous bicarb 31

Renin < 3mU/L (low) Aldosterone 900 ug/l (high)

Saline suppression test - aldo. non-suppressible

CT – no adrenal mass or hyperplasia

What is the next appropriate step?

(a) Bilateral adrenal venous sampling

(b) Genetic test for Glucocorticoid Remediable Hyperaldosteronism

(c)Start on spironolactone

(d) Start on low-dose dexamethasone

Primary Aldosteronism (Conn's Syndrome)

Autonomous overproduction of aldosterone by the adrenal glands
1-2% of mild hypertension
Up to 20% of resistant hypertension
Hypokalaemia is a late and variable manifestation;
More than 50% are normokalaemic

Aetiology

- bilateral adrenal hyperplasia (common)
- discrete aldosterone-producing adenoma
- unilateral adrenal hyperplasia (rare)

Diagnostic workup of suspected Primary Aldosteronism

Seated resting mid-morning plasma renin and aldosterone

↓

If suppressed renin (<10mU/l) **+** elevated aldosterone (> 400ug/l) **+** A/R ratio > 40

↓

Saline suppression test (2000 ml IV normal saline over 4 hours with per and post aldosterone)

↓

If post-aldosterone non-suppressible (> 200ug/l)

↓

Adrenal CT scan

↓ ↓

Unequivocal unilateral adenoma > 2.0cm

↓ ↓

Laparoscopic adrenalectomy

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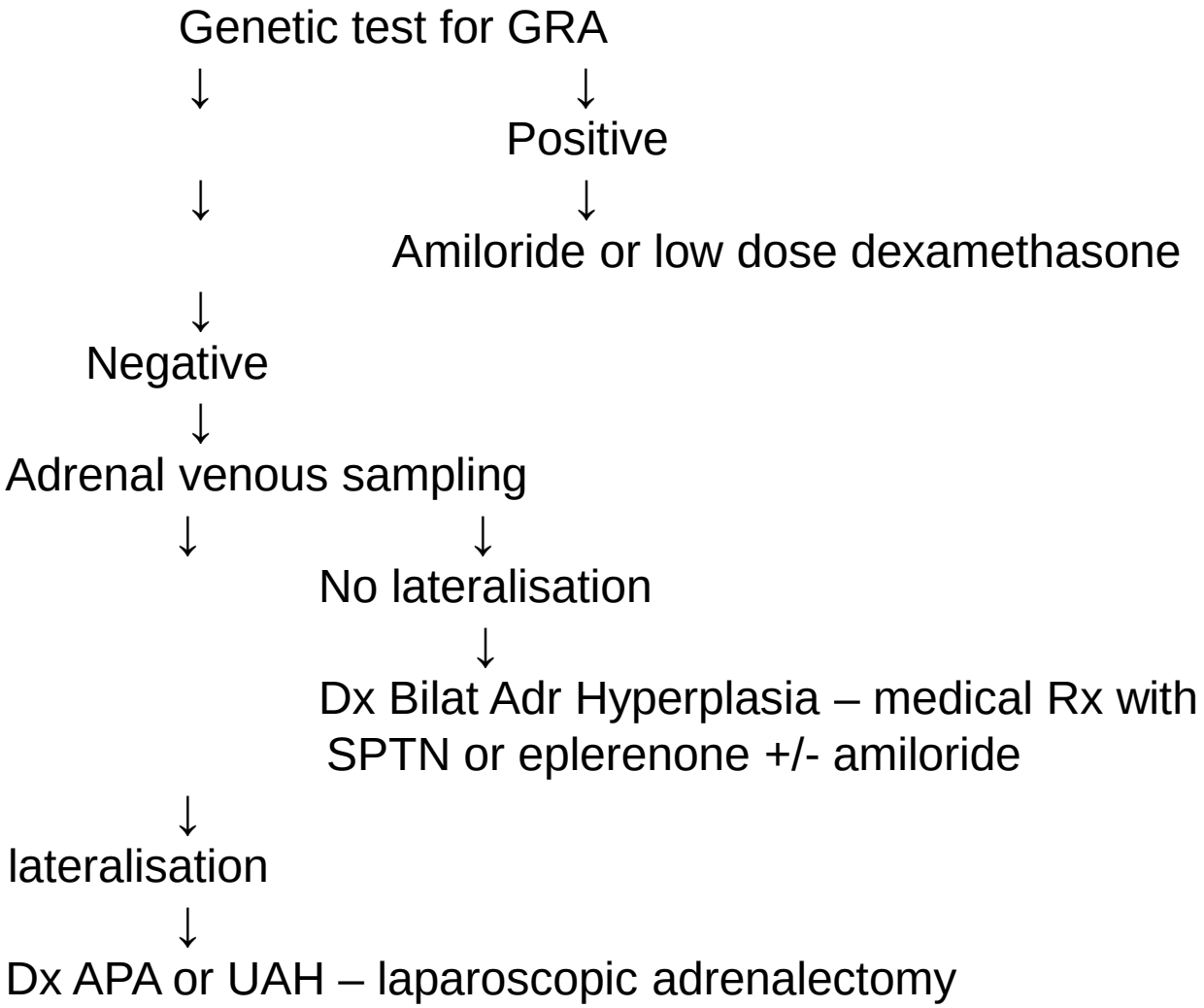
Normal **or** unilateral adenoma < 2cm **or** bilateral hyperplasia **or** unilateral hyperplasia

↓

Genetic test for GRA


Genetic test for GRA
Positive
Amiloride or low dose dexamethasone
Negative
Adrenal venous sampling
No lateralisation
Dx Bilat Adr Hyperplasia – medical Rx with SPTN or eplerenone +/- amiloride
lateralisation
Dx APA or UAH – laparoscopic adrenalectomy

Glucocorticoid Remediable Hyperaldosteronism

Suspect in patients with early onset familial hypertension

Biochemically indistinguishable from other causes of Primary Aldosteronism

-Adrenals normal or diffuse hyperplasia on CT

Diagnosis – PCR for the chimeric gene

Treatment

Low dose dexamethasone

Also responds to aldosterone antagonists and amiloride

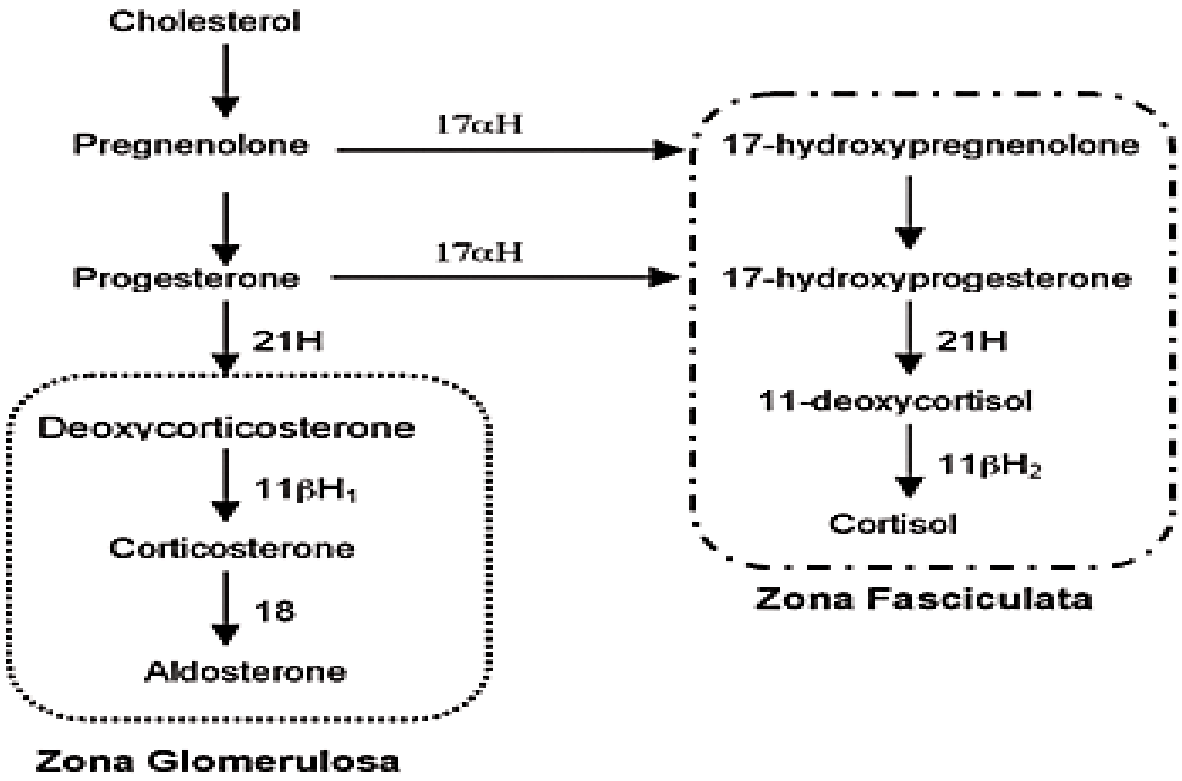


Figure 1. Normal biosynthetic pathways for cortisol and aldosterone. $11\beta H_1$ and aldosterone synthase are present only in the *zona glomerulosa*, and are regulated by angiotensin II. $11\beta H_2$ is present solely in the *zona fasciculata* and is regulated by ACTH. 21H= 21-hydroxylase. $11\beta H_{1\&2}$= 11β-hydroxylase isoenzymes 1 & 2; 18 = 18-hydroxylase/ aldosterone synthase. 17αH= 17α-hydroxylase.

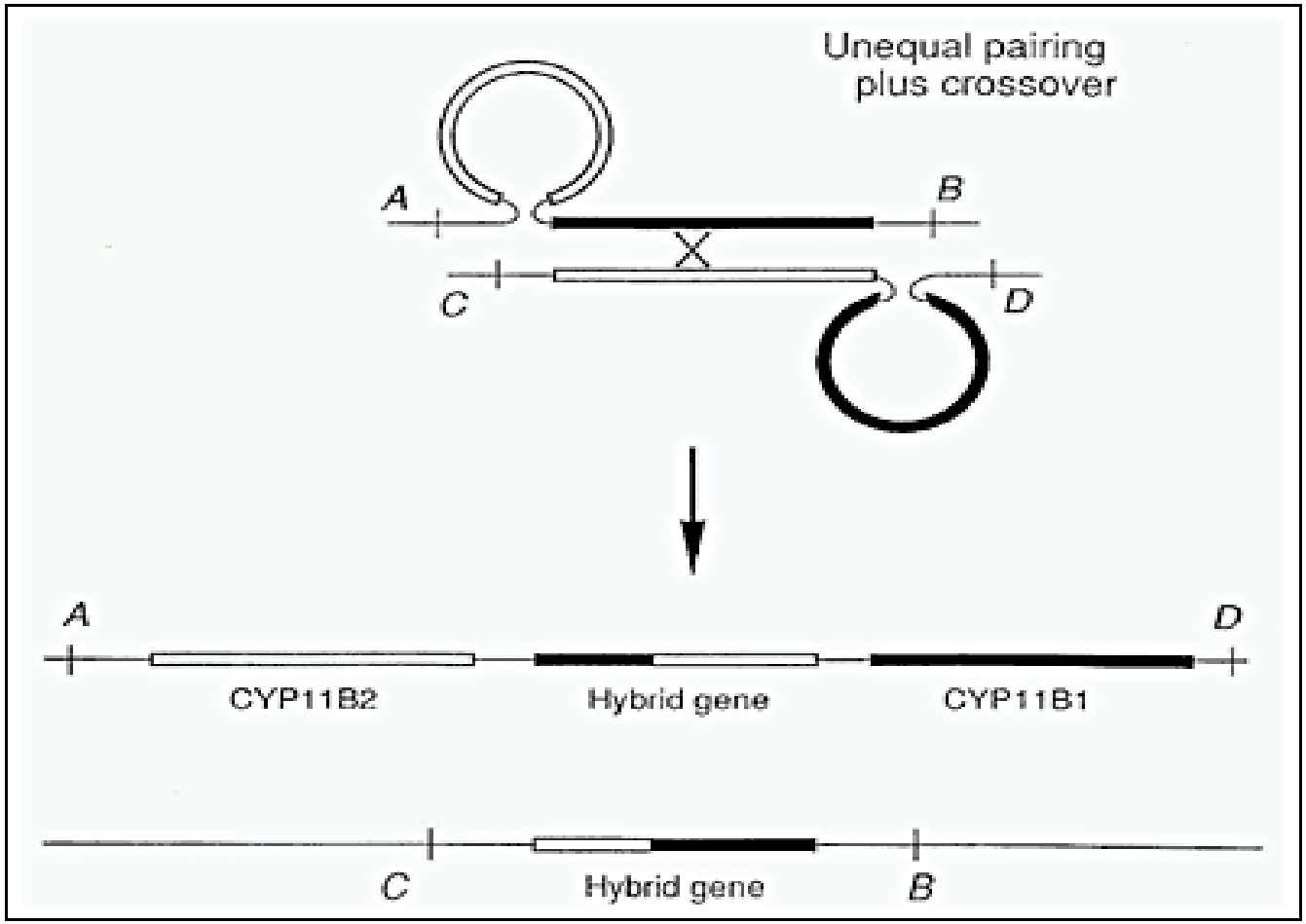

Unequal pairing
plus crossover
A
B
C
D
A
D
CYP11B2
Hybrid gene
CYP11B1
C
Hybrid gene
B

Table 1. Algorithm for GRA diagnosis and treatment.

Screening	
Recommended for hypertensive individuals who: - are diagnosed with primary hyperaldosteronism without demonstrable tumor - are young (especially children) and have suppressed plasma renin activity - have a family history of cerebral hemorrhage or hypertension before age 30 years - have refractory hypertension (hypertensive on 3 classes of agents including a diuretic) - are members of known GRA kindreds	
Diagnosis	
Dexamethasone suppression test	Easily performed. Dexamethasone 0.5mg every 6hrs x 2 days, normally aldosterone < 4ng/dl on day 3 at 8am
Genetic Test	Can be arranged through the international GRA registry (http://www.brighamandwomens.org/gra)
24 hour urinary 18-hydroxycortisol & 18-oxocortisol levels	Impractical since assays only available in specialized centers. Elevated > 2x upper limit of normal; a urinary level of 18-hydroxycortisol > 10nmol/l is diagnostic (5)
Treatment	
Glucocorticoids	Dexamethasone 0.125-0.25mg, or prednisolone 2.5-5mg daily, titrated to normotension.
Mineralocorticoid receptor antagonists	Eplerenone and spironolactone are effective treatment choices.
Sodium epithelial channel antagonists	Amiloride and triamterene have also been used successfully.
Non-directed anti-hypertensives	β-blockers and ACE-inhibitors are less likely to be efficacious in the setting of a suppressed renin-angiotensin system (9). Dihydropyridine calcium channel blockers can be useful adjunctive treatments to the above diuretic agents.

Prevalence of Diagnoses in Patients With an Incidentally Discovered Adrenal Mass (only ~ 13% are functional)

Condition Prevalence Per 10,000 Patients

Pheochromocytoma 650

Aldosterone-producing adenoma 700

Glucocorticoid-producing adenoma 3.5

Adrenal carcinoma 5.8

Monogenic Causes of Hypertension

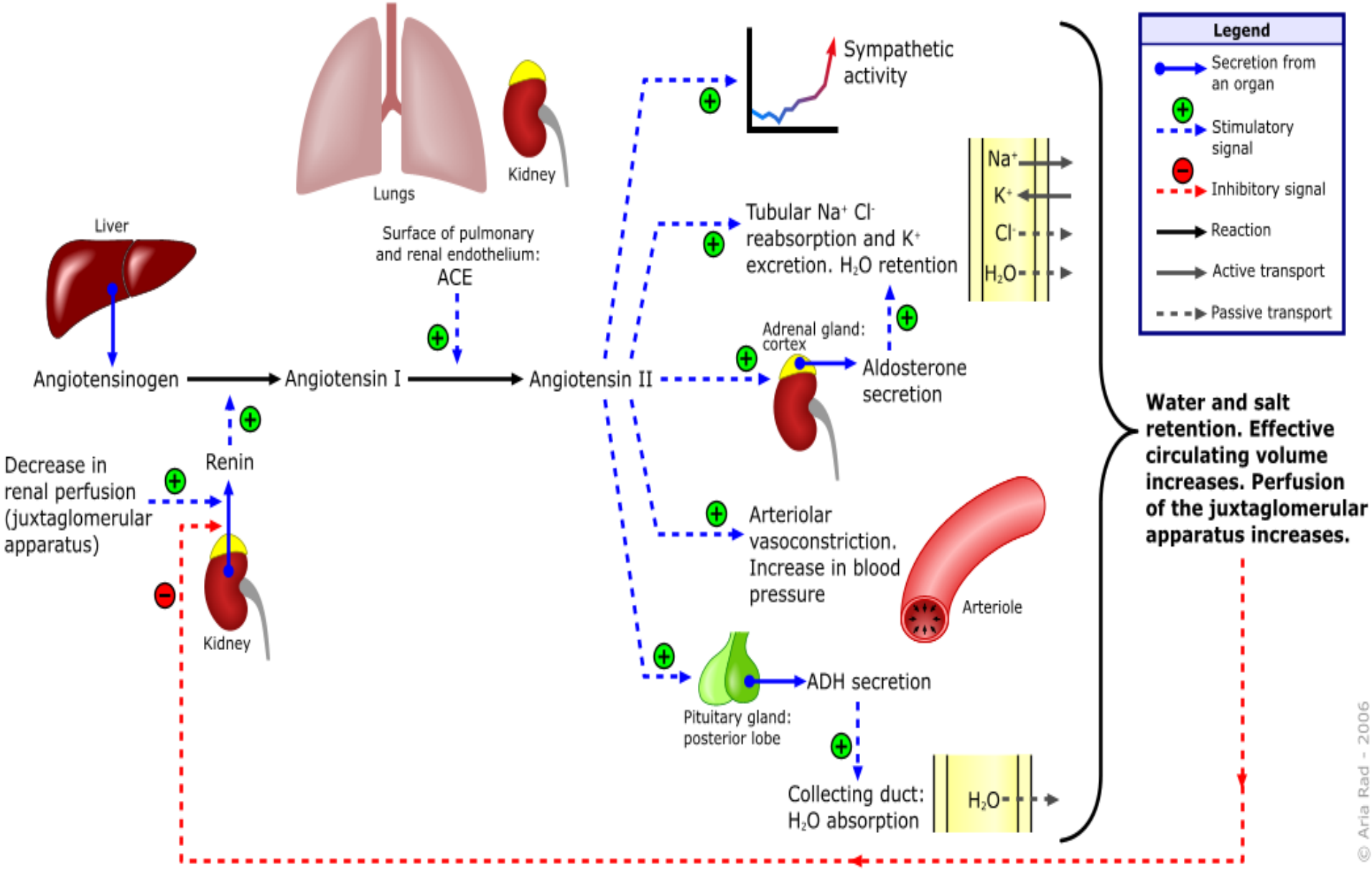
• monogenic (single gene) forms of hypertension involve gain-of-function mutations that result in overproduction of minerallocorticoids, or increased minerallocorticoid activity

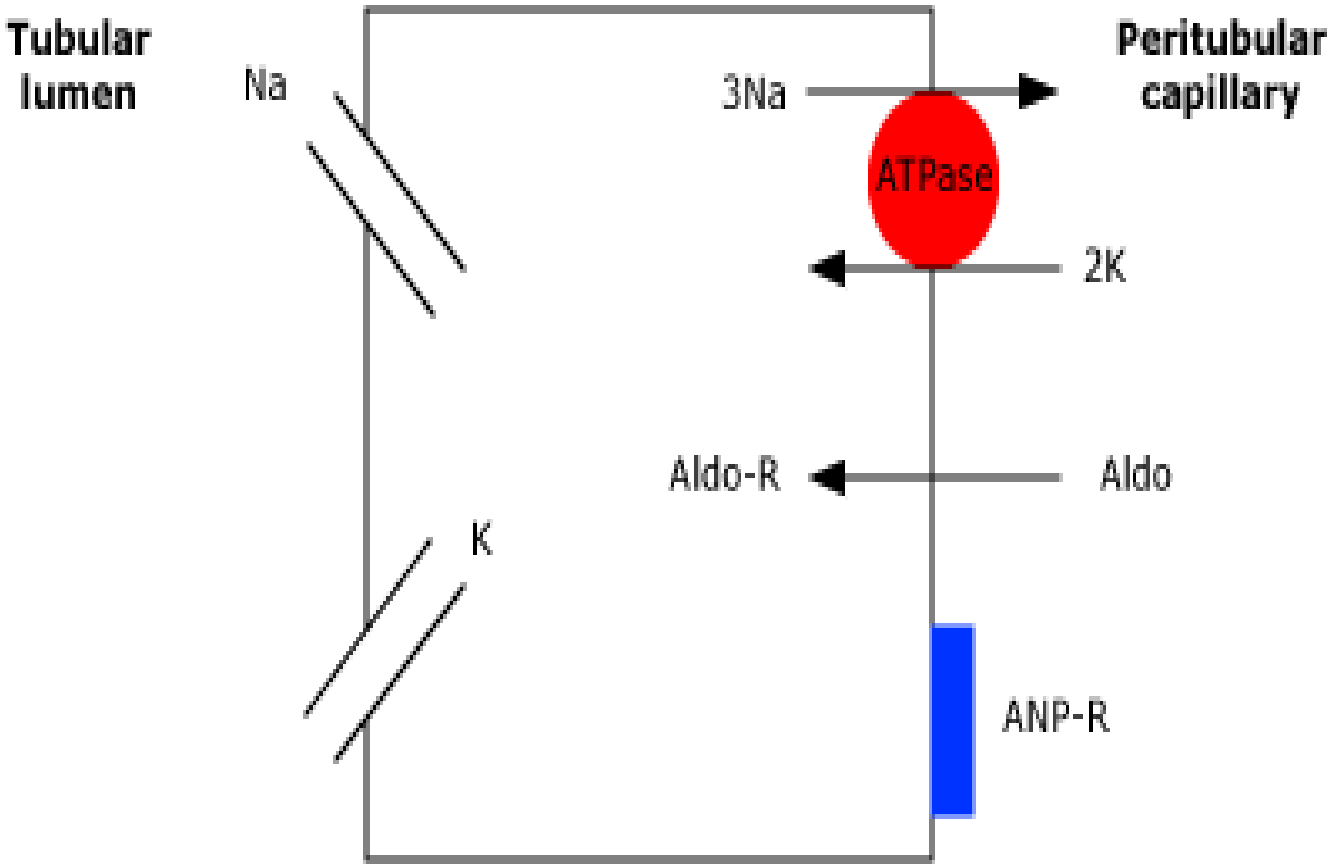
• clinical phenotypes include severe hypertension fromn birth, apparent volume expansion, suppression of plasma-renin activity and variable hypokalaemia

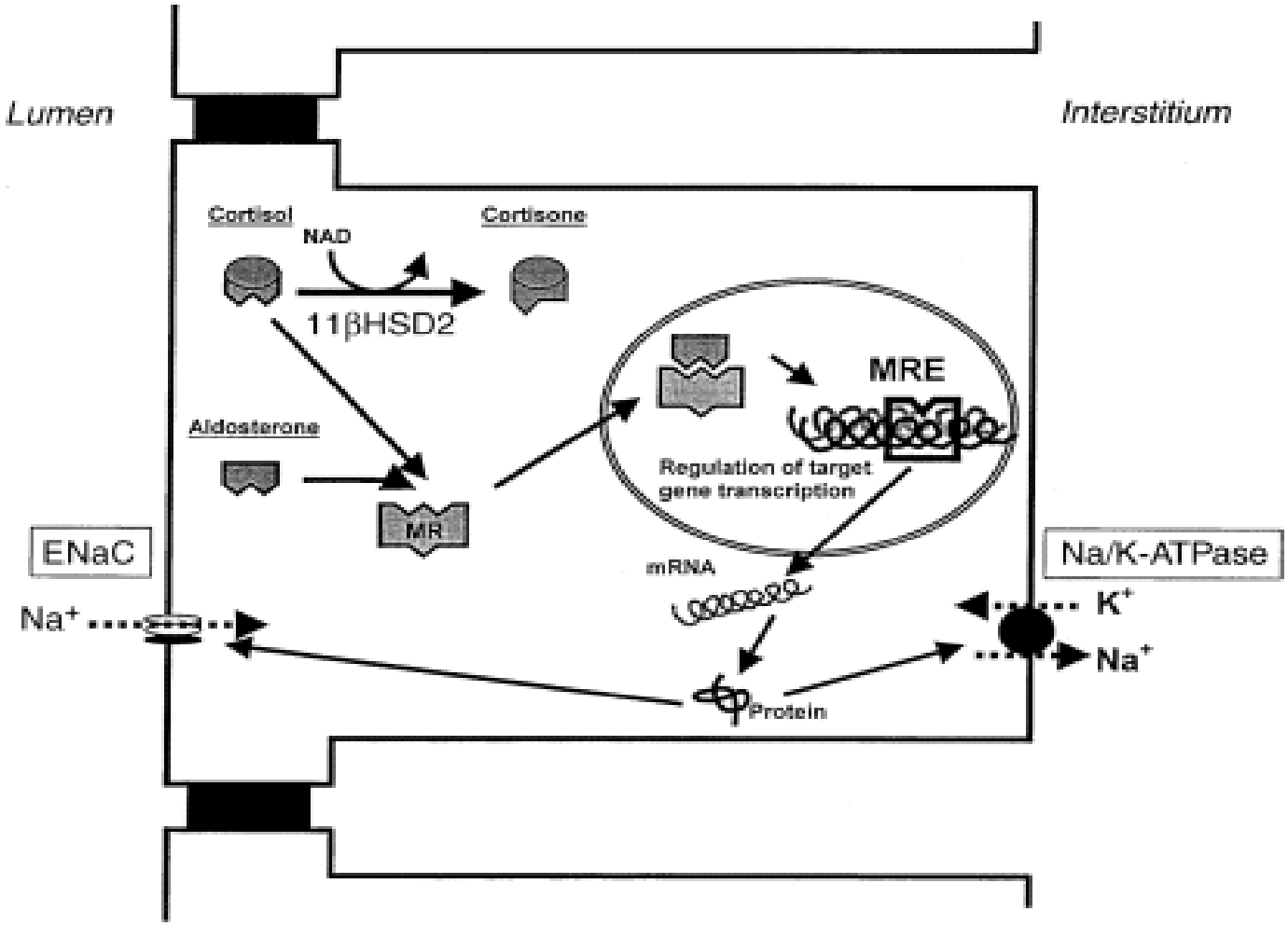
• Commonest is Glucocorticoid-Remediable Aldosteronism

- Congenital adrenal hyperplasia
- Glucocorticoid responsive hyperaldosteronism
- Apparent mineralocorticoid excess
  - Acquired
  - Hereditary
- Progesterone-induced hypertension (Activating MR Mutation)
- Liddle's Syndrome
- Gordon's Syndrome (PHA 2)
- Autosomal dominant hypertension with brachydactyly (chromosome 12)

Renin-angiotensin-aldosterone system




Tubular lumen
Na
3Na
Peritubular capillary
ATPase
2K
Aldo-R
Aldo
K
ANP-R


Lumen
Interstitium
Cortisol
NAD
Cortisone
11βHSD2
Aldosterone
MR
MRE
Regulation of target gene transcription
mRNA
ENaC
Na/K-ATPase
Na+
K+
Na+
Protein

17 year old girl with BP 170/110

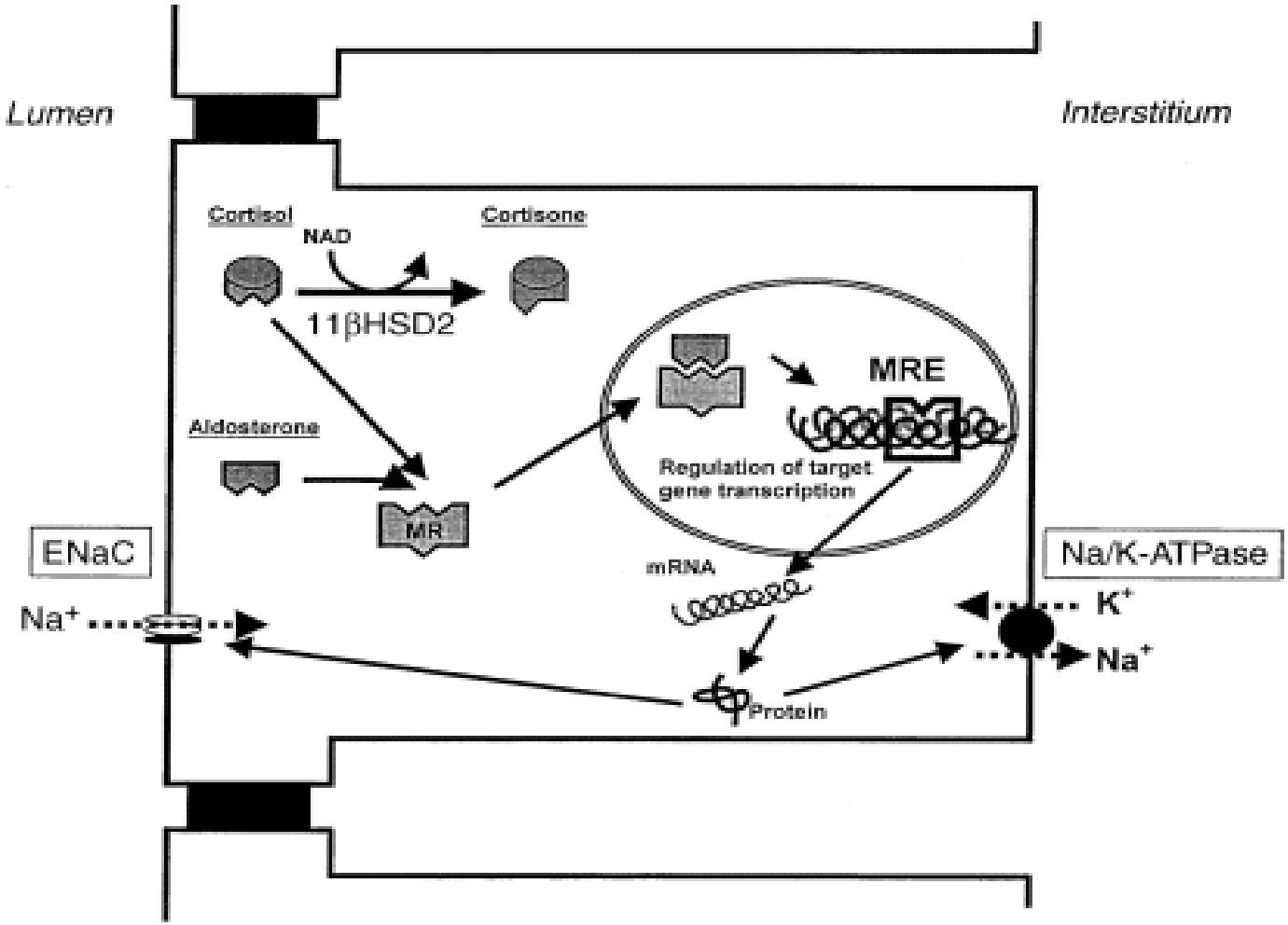
Family history of difficult hypertension

Na 140 K 3.1 creatinine 70 pH 7.43 HCO_3’ 34 Renin 2mU/l (low) Aldosterone 175ug/l (low)

Responsive to high dose spironolactone

<u>What is the diagnosis?</u>

Apparent Mineralocorticoid Excess


Lumen
Interstitium
Cortisol
NAD
Cortisone
11βHSD2
Aldosterone
MR
MRE
Regulation of target gene transcription
mRNA
ENaC
Na/K-ATPase
Na+
K+
Na+
Protein

Apparent Mineralocorticoid Excess – Hereditary

- Prevalence < 1%
- Mechanism: Autosomal dominant inheritance of inactivating mutation in 11beta hydroxysteroid dehydrogenase 2
- Presentation
  - Severe salt-dependent hypertension with hypokalaemia, low plasma renin and aldo, usually in childhood, can present in adulthood
- Diagnosis: Increase ratio of urinary tetrahydrocortisol (THF + 5 alpha THF) to tetrahydrocortisone (THE): ranga 6-50 (N = 1)
- Treatment High dose MR antagonists

62 year old woman with D2M for 12 years and hypertension for 10 years

Office BP 180/110

Today: Na 144 K 2.6 Bicarb 35 Cl 95

6 months ago: Na 138 K 4.5 Bicarb 26 Cl 101

Meds Valsartan, Frusemide, Verapamil, Vitamin E, Vitamin C, Ibuprofen, Herbal preparation

Apparent Mineralocorticoid Excess – acquired

Glycyrrhizic Acid (Licorice)

- Blocks 11BHSD 2
- Increases access of cortisol to minerallocorticoid receptor causing sodium retention + potassium loss

Glycyrrhizic Acid (50x sweeter than sugar) present in many herbal preparations to improve palatability, candies, medications, chewing tobaccos, teas, and present in 2/3 of Chinese herbal formulas

- 25 y/o male with new onset hypertension
- BP 200/115 HR 88, hypertensive retinopathy
- 1 + proteinuria
- Na 140 K 2.7 Cl 97 HCO_3 30 pH 7.44 pCO_2 45 Cr 90umol/l
- Spot urine K 40mmol/l
- Plasma renin 3mU/l (low) aldosterone 150ug/l (low)

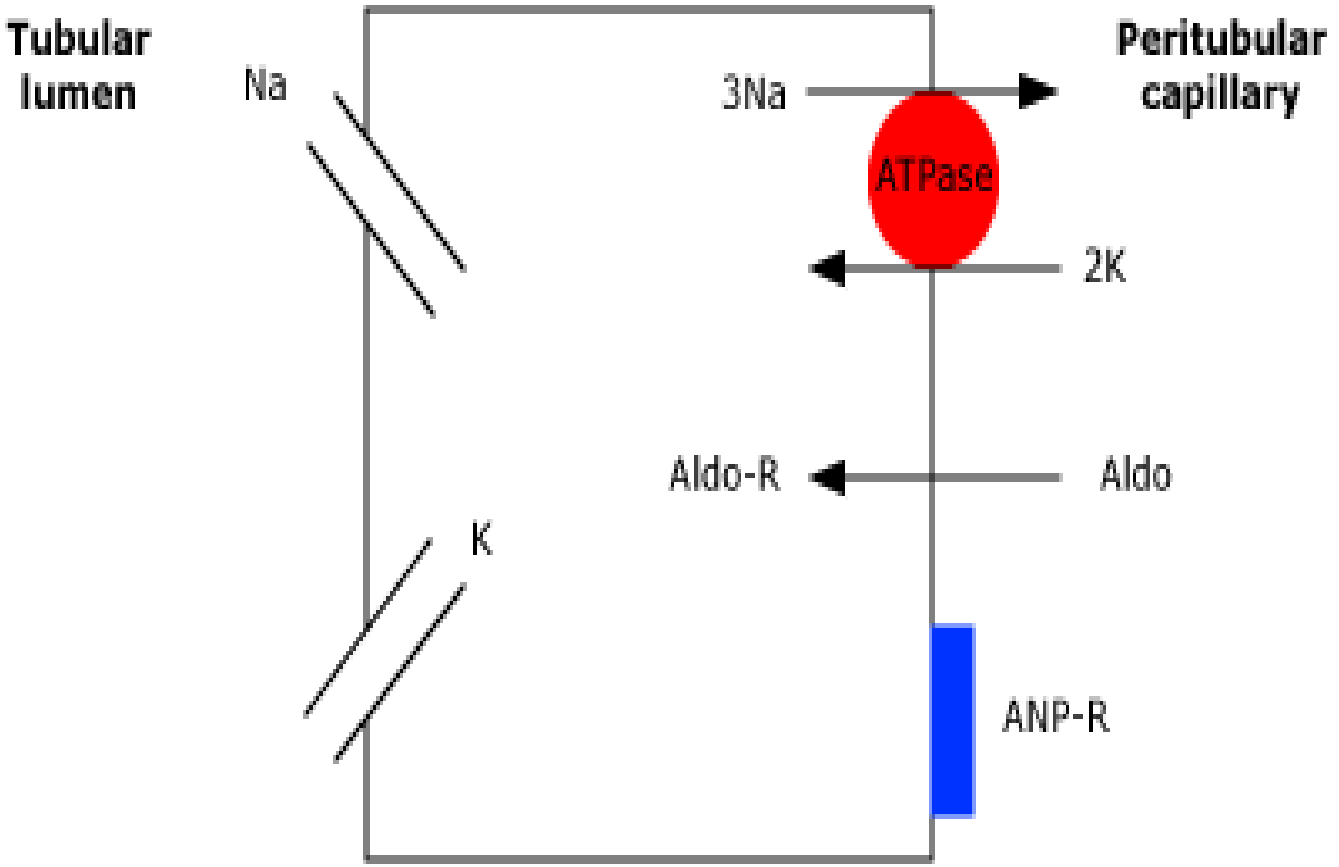
What is the diagnosis?

Clue:

unresponsive to spironolactone, but responsive to low Na diet and triamterene

Liddle’s Syndrome

(Pseudohypoaldosteronism type 1)


Tubular lumen
Na
3Na
Peritubular capillary
ATPase
2K
Aldo-R
Aldo
K
ANP-R

Liddle's Syndrome: Characteristic Features

- Prevalence < 1% hypertensives

- Mechanism

    Autosomal Dominant activating mutation(s) in ENaC of collecting duct

    Impaired regulatory mechanism leads to increased no. ENaC channels on luminal membrane

-Presentation: severe salt sensitive hypertension, hypokalaemia, low renin + aldosterone

- Presents in children and young adults

- Diagnosis – Genetic analysis of ENaC gene

- Treatment

    Responds to low protein diet and triamterene

    Cured by renal transplant

21 year old man with hypertension on 3 drugs and remains poorly controlled. Ongoing search for a secondary cause so far negative. Renin and Aldo levels are pending and in the meantime he is started on spironolactone 25mg daily which results in a severe exacerbation of his hypertension – necessitating urgent withdrawl of the drug

Later that year, his 24 year old previously normotensive sister develops severe hypertension and hypokalaemia late in the second trimester of pregnancy. Her renin and aldosterone levels are both low.

What is the diagnosis?

Mineralocorticoid Receptor Mutation *(Geller's Syndrome) (Pregnancy-Associated Hypertension)*

Rare genetic familial disorder where there is point mutation of the minerallocorticoid receptor resulting in a partially activated receptor.

Causes severe hypertension

Progesterone and spironolactone act as partial agonists

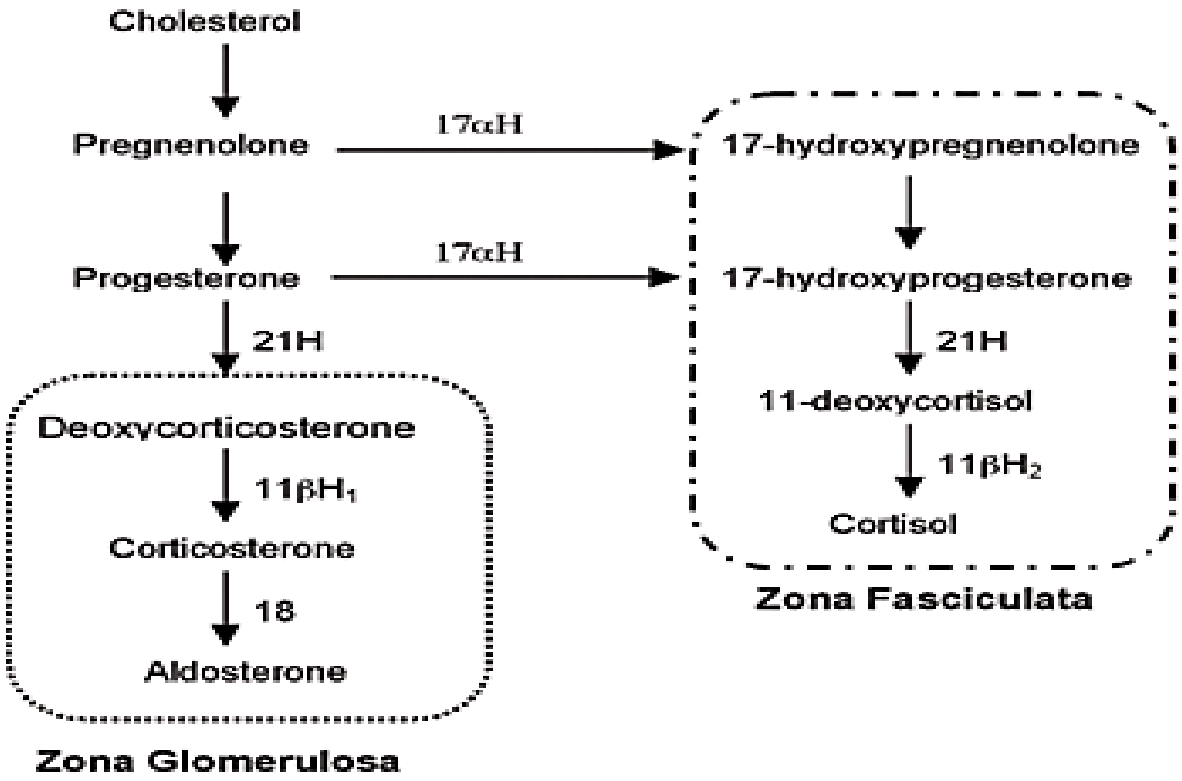
Suspect in women who present with severe hypertension and hyopkalaemia in 2nd or 3rd trimester of pregnancy.

The syndrome was discovered in a young male hypertensive whose 2 sisters experienced severe exacerbations of hypertension in pregnancy.

5 year old boy with precocious puberty hypertension and hypokalaemia

What is the likely diagnosis?

Congenital Adrenal Hyperplasia



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Hypertension and hypokalaemia

↓

Measure renin and aldosterone

↓

↑ renin + aldo	N or ↓ renin + ↑aldo	↓ renin + ↓aldo
↓	↓	↓
Malignant hypertension	Primary aldosteronism	Apparent mineralocortocoid excess – genetic (11BHSD2 mutation) – acquired (glycerrhetinic acid)
Renovascular	Idiopathic aldosteronism	
Diuretics	Glucorticoid remediable hyperaldosteronism	Cushing's Syndrome
Coarctation		DOC Excess
Renin-secreting tumour	Congenital adrenal hyperplasia	Liddle's Syndrome
Renal infarct		Activating MR Mutation
Vasculitis		

Gordon's Syndrome (Pseudohypoaldosteronsim type 2)

Familial hypertension/ Autosomal Dominant

Hyperkalaemia + metabolic acidosis (***one of the few causes of persistent hyperkalaemia with completely normal renal function***)

Normal (low) aldosterone levels

Responsive to NaCl restriction

Responsive to diuretics – especially thiazides

Possible mechanisms:

• Too much NaCl absorption by DCT

• Too much Cl^- absorption by collecting duct/ shunting voltage with less K secretion

• Impaired collecting duct apical K channel – less K secretion causes more NaCl absorption

(Mutant WNK proteins are though to be involved + could underlie any of these mechanisms)

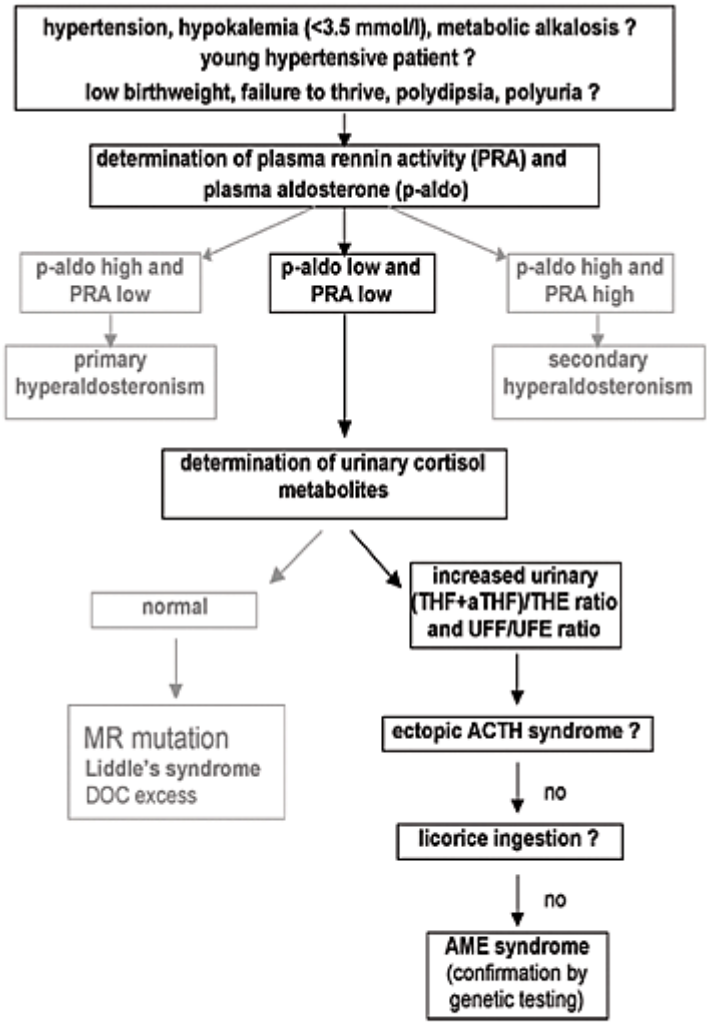


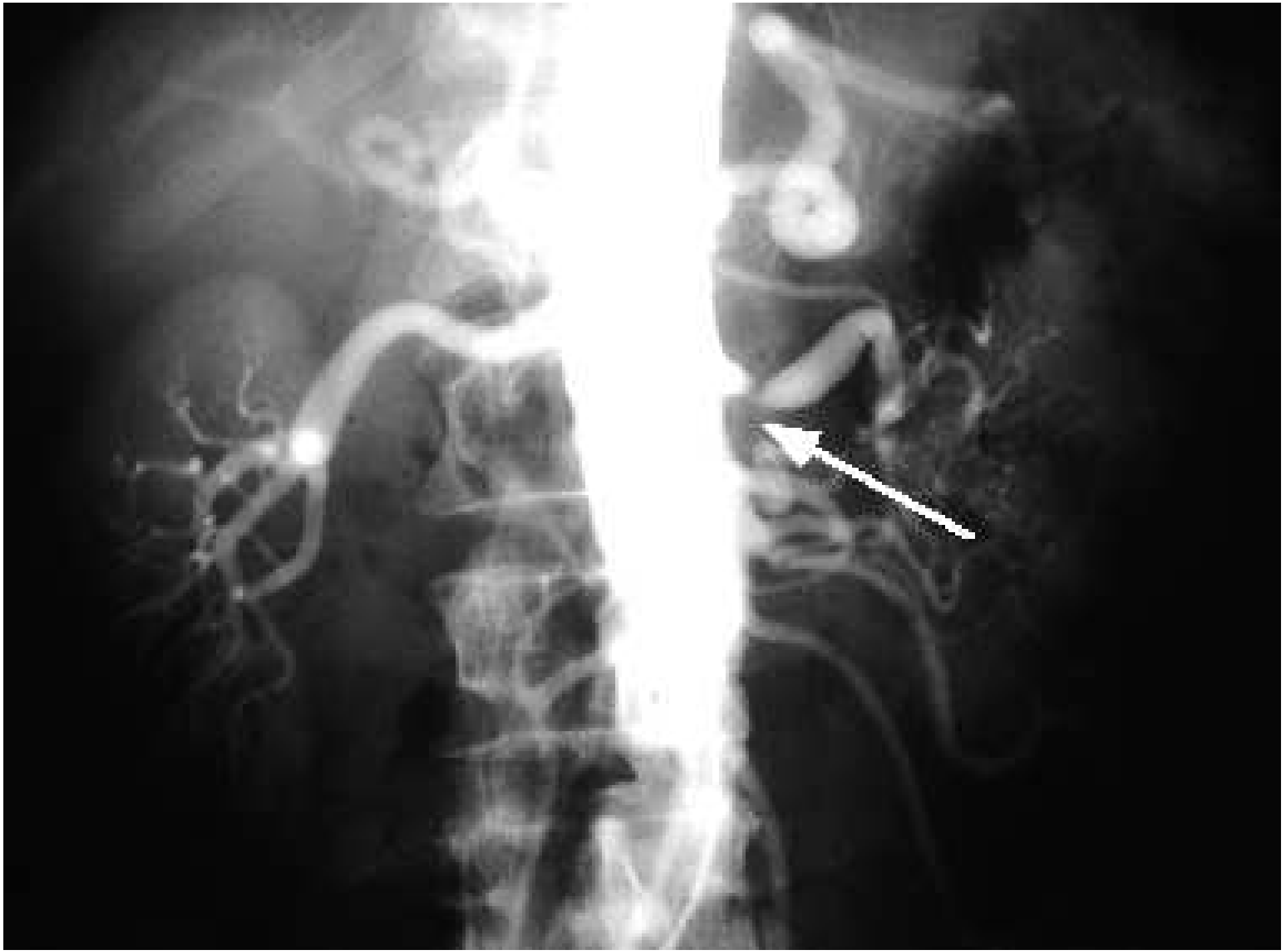
Figure 6. Flowsheet with guidelines for detecting Apparent Mineralocorticoid Excess (AME) syndrome. THF= tetrahydrocortisol; aTHF= allo-tetrahydrocortisol; THE= tetrahydrocortisone; UFF= urinary free cortisol; UFE= urinary free cortisone.

Renovascular Hypertension

Mr JH. European male aged 68

Chronic stable hypertension
Recent NSTEMI
Blood pressure normal on 2 agents (ACE-I and BB) creatinine 130 umol/l. Referred to an interventional cardiologist for coronary angiography – during the angiogram he makes incidental note (on single planar views) of what appears to be a severe left renal artery stenosis.

What should he do?



(1) PTA left renal artery

(2) PTA and stent left renal artery

(3) Nothing

Anatomical presence of renal artery stenosis is not on it's own a mandate for intervention!

Atherosclerotic renal artery stenosis – common (80%)

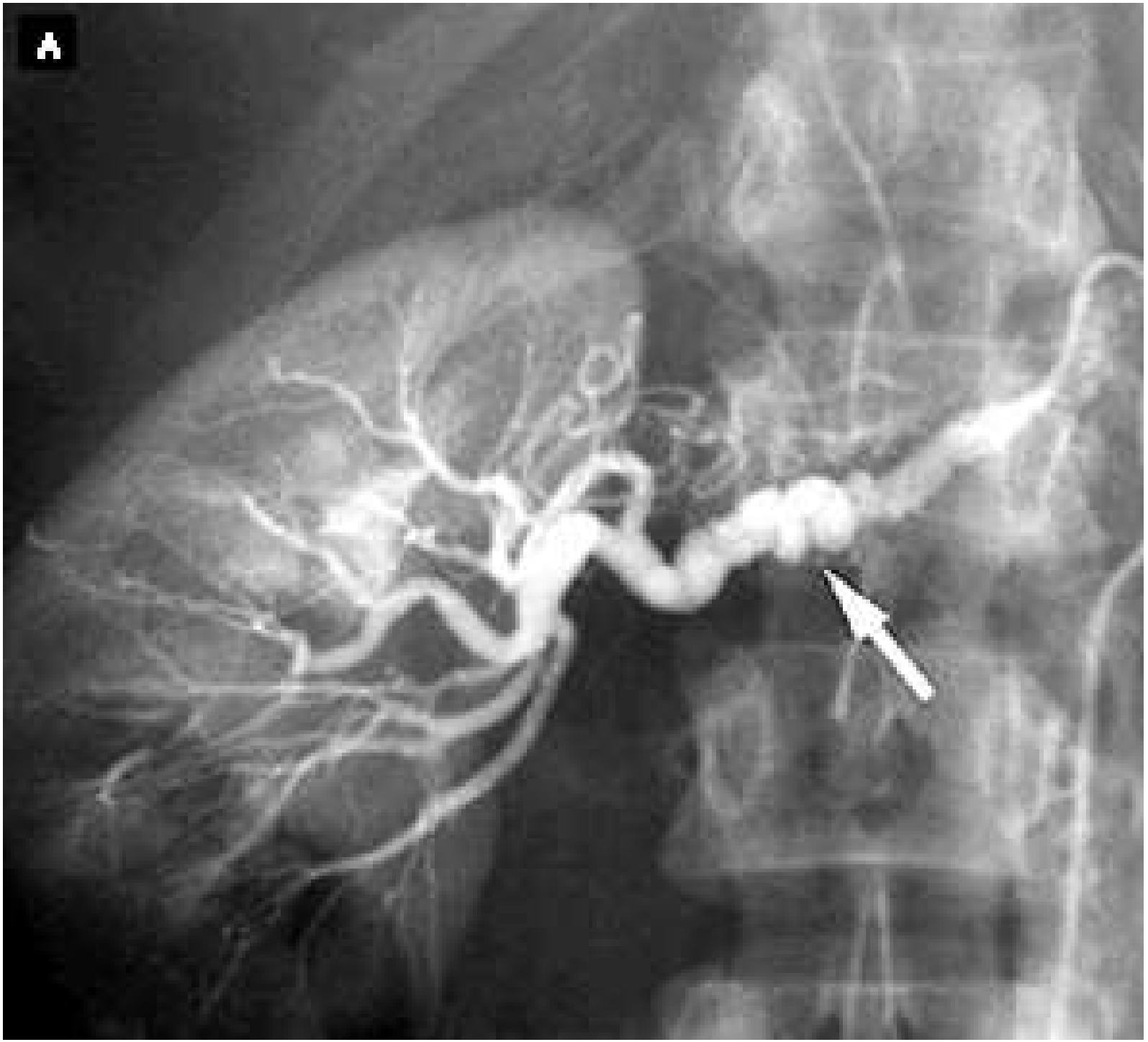
Fibrous renal artery disease less common (20%)

- Medial fibroplasia (FMH)
- Perimedial fibroplasia
- Intimal fibroplasia
- Medial hyperplasia

Fibrous renal artery disease

Suspect in young women with difficult hypertension. A woman under 40 (with no other clear secondary cause of hypertension) requiring > 2 antihypertensives for BP con trol should have an imaging test to exclude RAS.

MRA or DSA renal angiogram


A

Treatment of FMH is angioplasty

- low incidence of recurrence

Risk of renal arterial occlusion or CRF very low

Main benefit of intervention is BP control (reduce or remove need for antihypertensives)

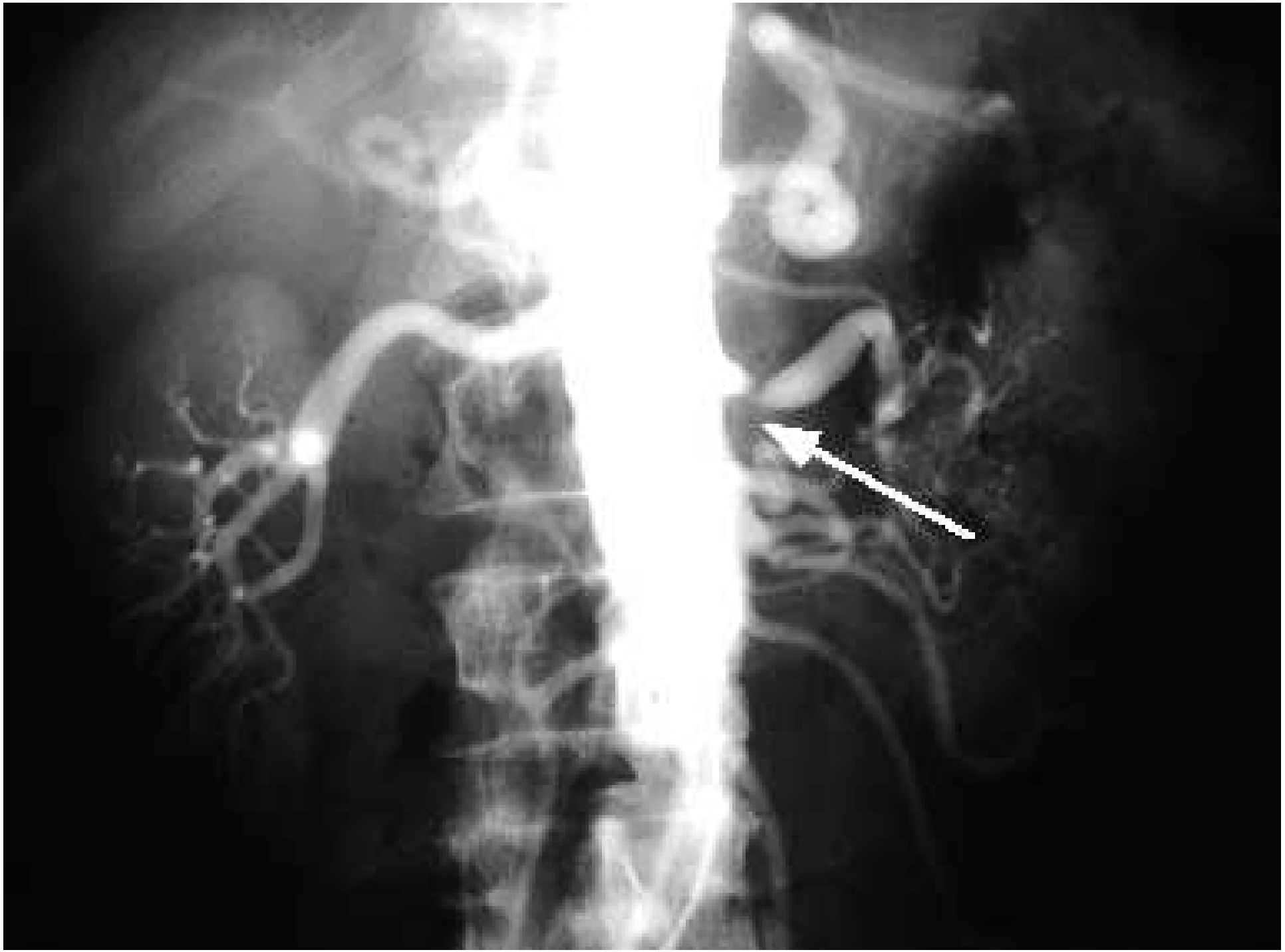
Atherosclerotic renal artery stenosis

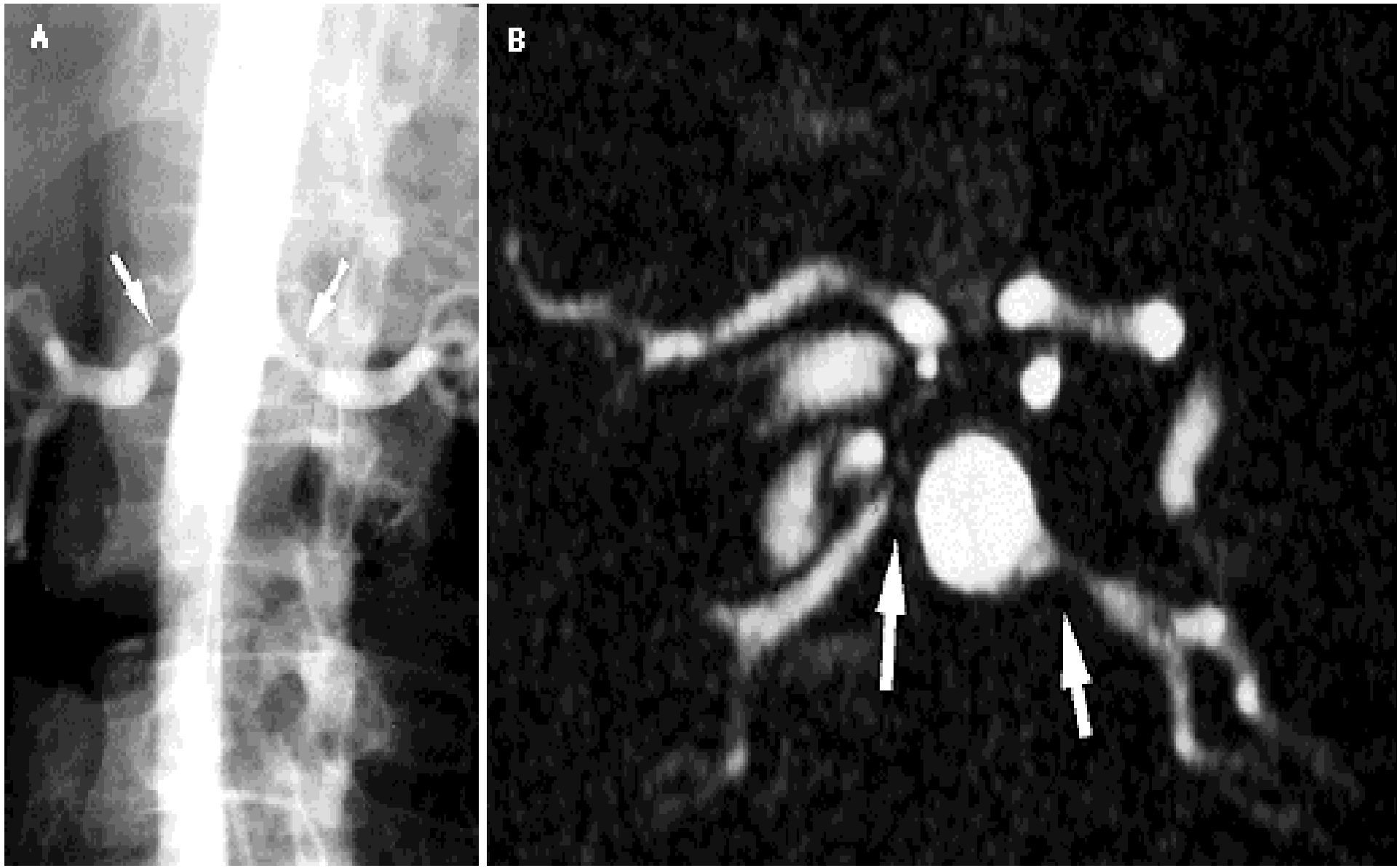
Clinical Syndromes

(1) Majority asymptomatic

(2) Renovascular hypertension

(3) Ischaemic nephropathy

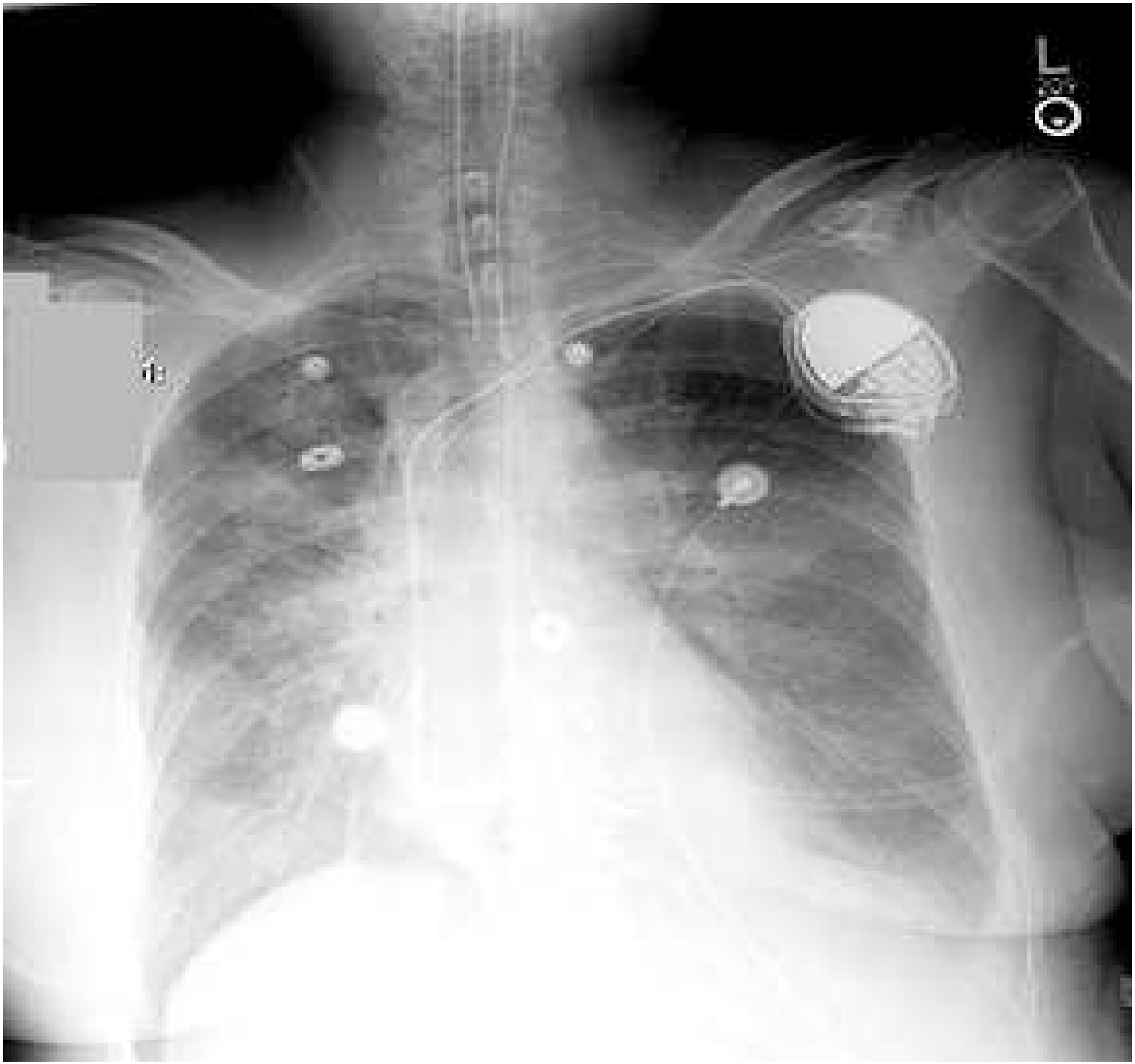



A
B

Most atherosclerotic RAS occurs in individuals over 50 with other evidence of vascular disease, particularly PVD and CAD

Clinical Clues

- Severe or refractory hypertension/ malignant hypertension
- Short duration of hypertension
- An acute elevation of creatinine – either spontaneous or following introduction of an ACE-inhibitor
- Assymetry of renal size (the artery supplying the smaller kidney is often occluded)
- “Flash” pulmonary oedema


L

How do we screen for renal artery stenosis?

Renal angiography is the gold standard but not usually performed first off.

Variety of less invasive procedures

(Plasma renin activity)

(Captopril renin test)

(Captopril renogram)

(Renal vein renin sampling)

(IVP)

MR angiography

Spiral CT with CT angiography

Duplex Doppler ultrasonography (good non-obese women under 50 – quite operator-dependent)

MR angiography is currently the most widely used screening test in NZ

- excellent sensitivity, but can tend to overcall the severity of a stenosis

What do we do when atherosclerotic renal artery stenosis has been detected on MRA or angiogram?

Factors to consider…

Low incidence of progresssion of stenotic lesions to occlusion

Most studies show equivalent outcome of angioplasty/ stenting for atherosclerotic RAS vs medical treatment

To date, no randomised clinical trial has clearly identified a group in whom intervention is superior to medical therapy

Angioplasty (particularly without stenting) can hasten the progression of stenotic lesions

No evidence that intervention in patients with controlled BP or stable renal function improves outcome

RAS is a marker for widespread vascular disease and bulk of excess mortality from CAD and stroke

(Possible) Predictors of beneficial outcome from intervention

Uncontrolled BP on several agents

Rapidly worsening renal function

Flash pulmonary oedema

Beneficial effect of ACEI on BP

ACEI-induced uraemia

Doppler resistance index < 80

What is a haemodynamically significant lesion??

More than 75% stenosis

or

More than 50% with

- post stenotic dilatation

or

- reduction in renal size

How can we functionally assess the haemodynamic significance of a stenosis?

Bilateral stenoses

Good BP response to ACE-inhibitor

Decrease GFR with ACE-inhibitor

Unilateral stenoses

Positive captopril renogram

Doppler resistance index (< 80 is most predictive determinant of response to revascularisation)

Assessment of a patient with known atherosclerotic RAS

Detection of atheromatous RAS > 50%

↓

Initiate lifelong therapy for atherosclerosis

↓

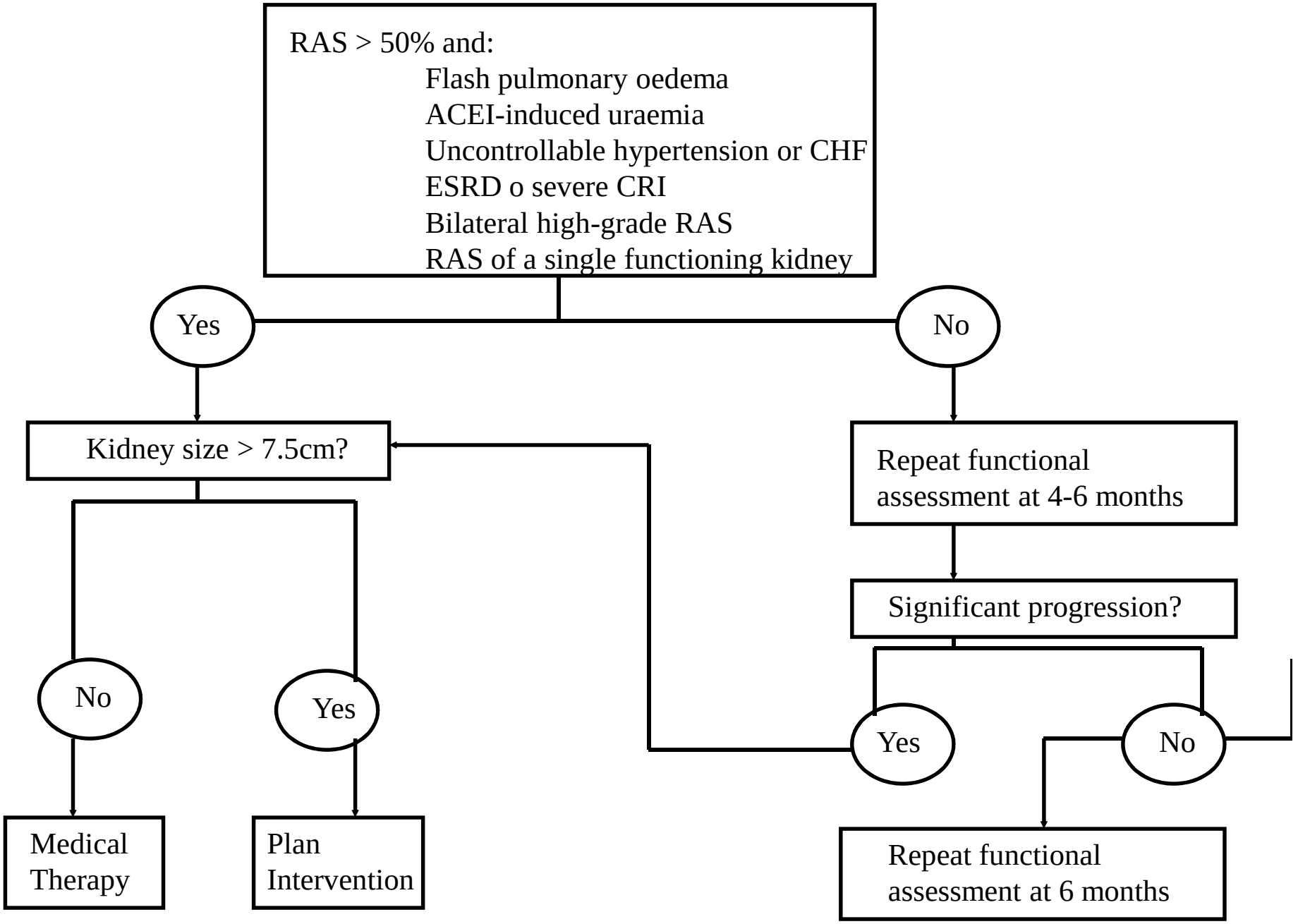
Optimise antihypertensive and medical therapy

↓

Undertake quantitative functional assessment

BP
Creatinine Clearance
Proteinuria
Single Kidney GFR
Renal Size
RAS Severity

Management


RAS > 50% and:
Flash pulmonary oedema
ACEI-induced uraemia
Uncontrollable hypertension or CHF
ESRD o severe CRI
Bilateral high-grade RAS
RAS of a single functioning kidney
Yes
No
Kidney size > 7.5cm?
Repeat functional assessment at 4-6 months
Significant progression?
No
Yes
Yes
No
Medical Therapy
Plan Intervention
Repeat functional assessment at 6 months

ACE-Inhibitors and RAS (creatinine rise > 25% on ACE-inhibitor)

ACEI-induced uraemia is a pointer to severe bilateral RAS and a predictor of re sponse to intervention

ACEI BP effect predicts BP response to intervention

ACEI most effective antihypertensives in RAS and should be used, provided renal function remains stable

ACEI-induced uraemia may be an indication for intervention even when BP and renal function OK (off ACEI) if another strong indication for ACEI therapy exists (eg cardiac indication)

What interventions are available?

PTA

Procedure of choice in FMH – low recurrence rate

In atherosclerotic RAS 40% restenosis in 1 year – reduced to 10% by PTA + Stenting

Surgical revascularisation

Up to 5% surgical mortality but low incidence of recurrent stenosis – some enthusiasts, but not widely used now except in patients requiring concomitant aortic surgery

Nephrectomy

High grade RAS, uncontrollable BP, small kidney with very low GFR on split renal function

Ongoing large randomised trials comparing medical therapy +/- angiopasty with stent placement

STAR

ASTRAL

CORAL

Mr JH should not have a “Drive-By” angioplasty because….

(1) Unilateral disease

(2) BP and renal function OK

(3) Tolerating an ACE-inhibitor

(4) Functional importance of the right RAS has not been assessed

(5) Severity of stenosis difficult to assess on single planar views

(6) No current clinical trial evidence that he is likely to benefit

(7) May actually end up being a harmful procedure

Take Home Messages

(1) Don’t look for RAS unless the patient has a probable indication for intervention eg uncontrolled BP or progressive renal failure

(2) Most people with RAS will die of CAD or stroke and cornerstone of management is treatment or cardiovascular risk factors

(3) The presence of significant RAS is on it’s own not an indication for intervention

(4) Intervention is indicated in a minority with narrowly defined parameters

Phaeochromocytoma

What are they?

Phaeochromocytomas are catecholamine-secreting tumours arising from chromaffin cells of SNS distingusihed by their embryonic derivation from primitive neural crest cells + their uptake of chromium salts. Most arise from the adrenal gland and 10% form extra-adrenal sites such as carotid body + abdominal sympathetic ganglia.

Incidence

< 0.1% of all hypertensives

Which catecholamines do they produce?

Noradrenaline predominantly, adrenaline produced more commonly by extra-adrenal and malignant phaeos

Clinical manifestations

Hypertension in 90% - paroxysmal in only 20-25%. Paroxysmal episodes ae assoc with other signs of catecholamine excess (tremor, tachycardia, hyperhydrosis, headache, + pupillary dilatation). Orthostatic hypotension may occur from decreased sympathetic reflexes reflecting down-regulation of adrenergic receptors. Weight loss may result from chronic hypermetabolism (5 H's – Hypertension, Headache, Hypermetabolism, Hyperhydrosis, Hyperglycaemia)// Pressor response to beta blocker is an important clinical clue, as is hypertensive criss during anaesthesia or surgery

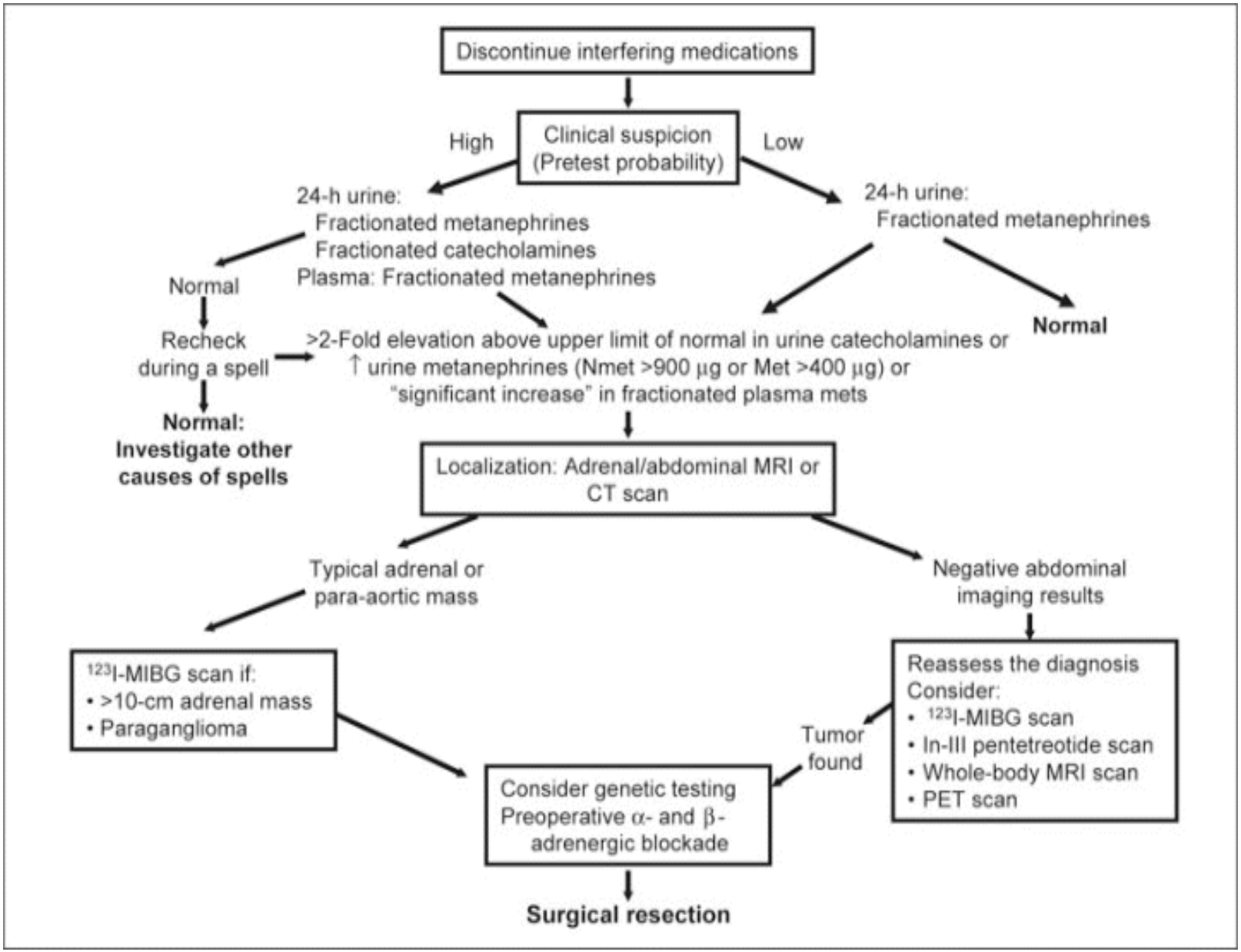
What is the rule of 10%

10% bilateral (both adrenals), extraadrenal, malignant, familial, paediatric

Associated conditions

Familial – neurofibromatosis, tuberous sclerosis, Sturge-Weber syndrome, von-Hippel-Landau disease, ataxia telangiectasia, MEN 2 (phaeo, PTH adenoma, medullary thyroid Ca), MEN 3 (phaeo, medullary thyroid Ca, mucosal neuromas, abdominal gangliomas, marfanoid body habitus)

Non-familial – cholelithiasis, Cushings syndrome, renal artery stenosis, Carney's triad (gastric leiomyosarcoma, pulmonary chondroma and paragangliomas)


Discontinue interfering medications
Clinical suspicion (Pretest probability)
High
Low
24-h urine: Fractionated metanephrines Fractionated catecholamines Plasma: Fractionated metanephrines
24-h urine: Fractionated metanephrines
Normal
Recheck during a spell
Normal: Investigate other causes of spells
>2-Fold elevation above upper limit of normal in urine catecholamines or ↑ urine metanephrines (Nmet >900 μg or Met >400 μg) or "significant increase" in fractionated plasma mets
Normal
Localization: Adrenal/abdominal MRI or CT scan
Typical adrenal or para-aortic mass
Negative abdominal imaging results
123I-MIBG scan if:
• >10-cm adrenal mass
• Paraganglioma
Reassess the diagnosis
Consider:
• 123I-MIBG scan
• In-III pentetreotide scan
• Whole-body MRI scan
• PET scan
Tumor found
Consider genetic testing
Preoperative α- and β-adrenergic blockade
Surgical resection

Which drugs increase measured levels of catecholamines + metabolites?

Tricyclic antidepressants, amphetamine, beta blockers (labetolol, sotalol), bendodiazepines, L-Dopa, methyldopa, ethanol, clonidine withdrawl

Imaging Studies?

CT, MRI. I-metaiodobenzyl-guanidine (MIBG) scintigraphy employs an isotope with afinity fo rcroomaffin tissue can be used to detect extra-adrenal tumours or to confirm that an adrenal mass is a phaeochromocytoma

Treatment

Surgical removal curative in 90%

Nonoperative treatment is combined alpha and beta blockade or inhibition of catecholamine synthesis with α-methyl-paratyrosine (can be used in pts with inoperable, recurrent, multicentric, or malignant phaeochromocytoma)

Perioperative management α-blockers are agents of choice, and phenoxybenzamine, a long-scting noncompetitive α-blocker is preferred. When tachycardia or arrhjythmias persist, beta-adrenergic blockade is indicated (but only after achieving α-blockade to avoid unopposed α-receptor stimulation

Chronic Kidney Disease

Commonest secondary cause of hypertension

NHANES Data

40% pf pts with CKD 2 (GFR 60-90) have BP > 140/90

75% of pts with GFR < 30 have BP > 140/90

Pathogenesis

Volume-dependent

Volume –independent

Hormonal

- Activation of RAAS
- Activation of sympathetic nervous system
- Endothelin -1

Miscellaneous

- NO deficiency,
- Disturbances in calcium metabolism + secondary hyperpartahyroidism
- Hyperuricaemia)

Sleep Disturbances

- Ubiquitous in severe CKD + ESRD
- Long-term sequelae may be caused by sympathetic activation (that outlasts the triggering stimulus)

Pharmacological treatment considerations in CKD hypertension

(1) Target BP is < 130/80

(2) Resistant hypertension is common

(3) Most pts require combinations of several drugs to achieve target

(4) Diuretics are (usually) indispensible/ lower GFR, more diuretic

- Most thiazides work down to GFR ~ 40ml/min
- Chlorthalidone effective down to ~ 30ml/mi
- < 30ml /min use frusemide in BD dose

(5) RAAS-blockers (ACE-inhibitors and ARB's) as part of a combination of antihypertensive drugs (usually including a diuretic), for the same level of BP lowering, slow progression of renal disease and have greater antiproteinuric effect than combinations which do not include RAAS blockers in patients with proteinuric renal diseases (diabetic and non-diabetic). There is no evidence that RAAS blockers confer this additional benefit in non-proteinuric renal diseases

(6) Calcium Channel Blockers are effective antihypertensives in CKD

- non-DHP CCB's have greater antiproteinuric effect (for same level of BP lowering) than DHP CCBs (but this effect is somewhat ameliorated when given in combination with RAAS-bockers

(7) Central alpha agonists

-Useful as add-on treatment in CKD where activation of SNS often contributes to hypertension

(8) Peripheral alpha blockers

-Pharmacokinetics not altered by CKD and dose-adjustments not required/ can cause salt and water retention but are useful add-on drugs in resistant hypertension (when diuretic therapy is being appropriately used)

(9) Beta blockers

- No special place in management of CKD hypertension/ non-renally clearedbeta blockers are easier to use/ carvedilol improved survival in a group of dialysis pts with LV dusfunction

Obstructive Sleep Apnoea

In all patients being evaluated for hypertension it is important to consider OSA as a contributory cause, and patients though to be at high risk evaluated with sleep studies

Most individuals with OSA also have the metabolic syndrome and “cure “ of hypertension with CPAP is uncommon

Meta-analysis of 12 placebo-controlled randomised trials of CPAP in OSA (*Haentjens et al Arch.Intern.Med.2007;167(8):757-764)* showed net reduction of 1.69mmHg in 24 hour MBP

Cushings Syndrome

Important cause of hypertension, but other clinical features usually more prominent.

Screening test is 24 hour urinary free cortisol

Drug-Induced/ Related

Multiple prescribed and proprietary medications can elevate blood pressure and are important to consider and ask about.

Important ones include:

NSAID's, glucocortocoids, minerallocorticoids, oestrogen and progesterone (as in the combined OCA), amphetamines, methylphenidate, sibutramineclozapine, antidepressants (MAOI's, selegiline, tricyclics, buspirone, fluoxetine), cyclosporin, tacrolimus, erythropoetion, alchohol, protease inhibitors

Thyroid and Parathyroid Disorders

Hypothyroidism – has been assoc with elevated diastolic BP

Hyperthyroidism – high cardiac output and reduced peripheral resistance – eleveted systolic pressuer and lowered diastolic pressure common

Primary hyperparathyroidism – common association with elevated blood pressure

Routine to check thyroid function and serum calcium as part of basic hypertension workup