SECONDARY HYPERTENSION - EVALUATION

CASE PRESENTATION

A 17 YEARS OLD MALE COLLEGE STUDENT- CAME TO THE HOSPITAL WITH CHIEF COMPLAINTS OF :

- HEADACHE,
- BLURRING OF VISION AND
- VOMITINGS SINCE 2 DAYS

PRESENT HISTORY

HE WAS APPARENTLY ASYMPTOMATIC 2 DAYS BACK TO START WITH HE HAD BLURRING OF VISION IN BOTH EYES ,

HEADACHE OVER OCCIPETAL REGION WHICH IS ASSOCIATED WITH 2 EPISODES OF NON PROJECTILE, NON BILIOUS VOMITINGS CONTAINING INGESTED FOOD PARTICLES SINCE 2 DAYS.

HEADACHE IS MORE SEVERE IN EARLY MORNING HOURS

BOWEL AND BLADDER HABITS ARE REGULAR

NO H/O LOSS OF CONSCIOUSNESS,HEAD INJURY,LOOSE MOTIONS,FEVER,PALPITATIONS,PERIORBITAL EDEMA,HEMATURIA,WEIGHT LOSS/GAIN,COLD/HEAT INTOLERANCE,SNORING,DAY TIME SOMNALENCE,BURNING MICTURITION.

PAST HISTORY

H/o similar complaints 3 months back and diagnosed as hypertension and advised antihypertensives but he is not taking medicines regularly.

No h/o diabetes mellitus ,renal disease and other chronic illness

Not a known smoker/alcoholic

Near vision (myopia) since 7years wearing spectacles of power -2.0 in both eyes

Family history

Born out of consanguineous marriage

One brother- both had hypertrophic pyloric stenosis –operated (ramstead pyloroplasty) at 3 months of age.

His Father is an essential hypertensive on treatment.

TREATMENT HISTORY: He is not taking any drug regularly.

RELEVANT POSITIVE HISTORY

- Young male with occipital headache,blurring of vision in both eyes and non projectile vomitings since 2 days
- Headache over occipital region and more in early morning hours.
- H/o similar complaints 3months back and diagnosed as hypertension on irregular treatment.
- Myopic(power,-2.0) on spectacles since 7 years
- Born out of consanguineous marriage.
- One brother- both had hypertrophic pyloric stenosis at the age of 3 months and operated (ram stead pyloroplasty).
- His father is an essential hypertensive on treatment.

ON EXAMINATION

Patient moderately built and moderately nourished

On general examination- No pallor, cyanosis, icterus, clubbing, lymphadenopathy, pedal edema,No raised JVP

VITALS:PR-92/min, normal rhythm,volume, character, no radioradial delay and no radio femoral delay, all peripheral pulses felt

Temp- Afebrile, RR-20/min

BP-210/120 mmHg on left and right arm in supine position

Systemic examination:

Heart-s1 s2 heard, No murmurs

Lungs-BAE+,clear

P/A- Visible linear scar mark noted in epigastric region
Soft, nontender, No organomegaly
No palpable mass felt in the abdomen
Bowel sounds heard and No bruit heard in the abdomen on auscultation

CNS-Concious, coherent,well oriented to time,place and person
No focal neurological deficit.

Fundoscopy showed Grade I Hypertensive retinopathy

Investigations

Blood group-O +ve
Hb- 15.3 gm/dl
TLC- 13,300 cells/cu.mm
- Neutrophils-83% (40-75)
- Lymphocytes-15%(20-45)
- Eosinophils-2%(1-6)

PLT- 2.56 lakhs/cu.mm
B.UREA- 75 mg/dl
S.CREATININE- 1.7 mg/dl
Na+- 136 meq/l
K+- 3.9 meq/l
CL^- - 102 meq/L

CUE
Albumin- +++
Sugars- nil
Pus cells-8-10/hpf
RBC-nil
no casts

RBS- 91mg/dl
VMA quantitative assay-
4.3 mg/24hrs (1-11)
2D ECHO-Concentric LVH,
No RWMA
HIV & HbsAg-Non reactive

USG ABDOMEN showed B/L grade 3 renal parenchymal changes with normal sized kidneys

USG ABDOMEN DOPPLER was negative for Renal artery stenosis

CT brain was S/O possible PRES (Posterior reversible encephalopathy syndrome)

ABNORMAL-TLC-13,100 cells/cu.mm

CUE-Albumin-3+,pus cells:8-10/hpf

Blood urea-75mg/dl,Sr.creatine-1.7mg/dl

2D ECHO-Concentric LVH

USG Abdomen-B/L grade 3 renal parenchymal disease

DIAGNOSIS ?

RELEVANT POSITIVE summary

- Young male with occipital headache more in early morning hours, blurring of vision in both eyes and non projectile vomitings since 2 days
- H/o similar complaints 3months back and diagnosed as hypertension on irregular treatment.
- Myopic (power,-2.0) on spectacles since 7 years
- Born out of consanguineous marriage.
- One brother- both had hypertrophic pyloric stenosis at the age of 3 months and operated (ram stead pyloroplasty).
- His father is an essential hypertensive on treatment.
- BP:210/120mm of Hg,
- Investigations:TLC-13,100 cells/cu.mm
  CUE-Albumin-3+,pus cells:8-10/hpf
  Blood urea-75mg/dl,Sr.creatine-1.7mg/dl
  2D ECHO-Concentric LVH
- **Fundoscopy** showed Grade I Hypertensive retinopathy
- USG ABDOMEN showed B/l grade 3 renal parenchymal changes with normal sized kidneys
- USG ABDOMEN DOPPLER was negative for Renal artery stenosis
- CT brain was S/O possible PRES (Posterior reversible encephalopathy syndrome)

HYPERTENSION

- Current clinical criteria for defining hypertension generally are based on the average of **two or more seated blood pressure readings** during each of two or more outpatient visits.

- A recent classification recommends blood pressure criteria for defining - normal blood pressure, prehypertension, hypertension (stages I and II), and **isolated systolic hypertension**, which is a common occurrence among the **elderly** .

Table 14.50 Classification of blood pressure levels of the British Hypertension Society

Category	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Blood pressure		
Optimal	<120 and	<80
Normal	120–129 and/or	<80–84
High normal[a]	130–139 and/or	85–89
Hypertension		
Grade 1 (mild)	140–159 and/or	90–99
Grade 2 (moderate)	160–179 and/or	100–109
Grade 3 (severe)	≥180	≥110
Isolated systolic hypertension		
Grade 1	140–149	<90
Grade 2	>160	<90

The European Societies of Hypertension and Cardiology Guidelines 2007 are based on clinical blood pressure and not values for ambulatory blood pressure measurement. Threshold blood pressure levels for the diagnosis of hypertension using self/home monitoring are >135/85 mmHg. For ambulatory monitoring, 24-hour values are >125/80 mmHg. If systolic blood pressure and diastolic blood pressure fall into different categories, the higher value should be taken for classification.

[a]Equivalent to prehypertension.

- Blood pressure tends to be higher in the early morning hours, soon after waking, than at other times of day. Myocardial infarction and stroke are more common in the early morning hours.
- Night time blood pressures are generally 10–20% lower than daytime blood pressures, and an attenuated night time blood pressure "dip" is associated with increased cardiovascular disease risk
- **White coat hypertension-** High blood pressure readings are found when measured by the physician, but not when the patient measures at home. Evidence of anxiety-induced sympathetic phenomena such as tachycardia, perspiration, cold hands, tremor, and/or pupil dilation will usually be present

HOW DO WE MEASURE BLOOD PRESSURE

- Before the blood pressure measurement is taken, the individual should be seated quietly in a chair (not the exam table) with feet on the floor for 5 min in a private, quiet setting with a comfortable room temperature.

- At least two measurements should be made. The center of the cuff should be at heart level, and the width of the bladder cuff should equal at least 40% of the arm circumference; the length of the cuff bladder should be enough to encircle at least 80% of the arm circumference.

- It is important to pay attention to cuff placement, stethoscope placement, and the rate of deflation of the cuff (2 mmHg/s).

- Systolic blood pressure is the first of at least two regular "tapping" Korotkoff sounds, and diastolic blood pressure is the point at which the last regular Korotkoff sound is heard.

Primary Essential Hypertension

- Essential hypertension is the term applied to the **95%** of hypertensive patients in which elevated blood pressure results from complex interactions between multiple genetic and environmental factors

Secondary Hypertension

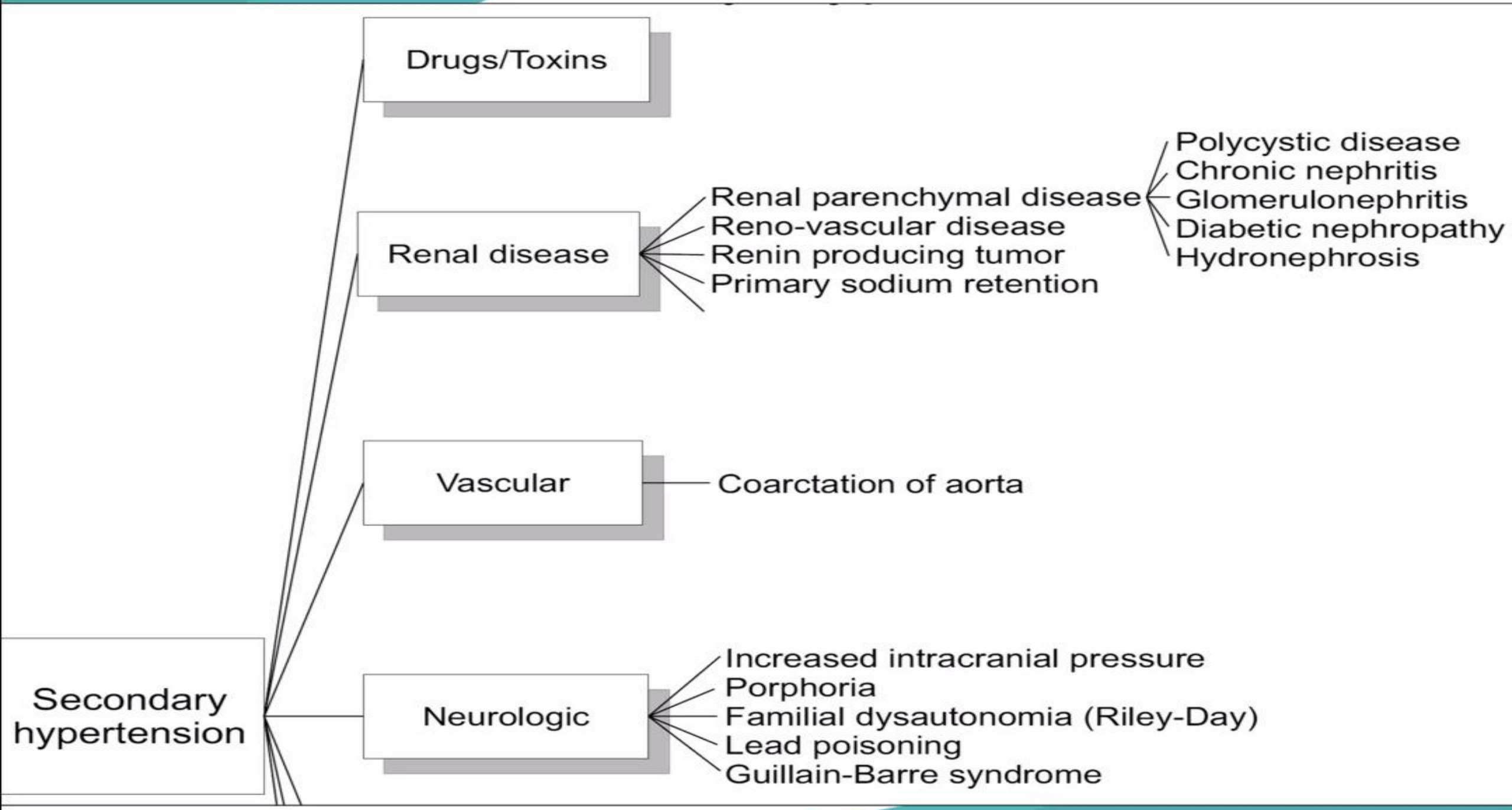
- It accounts for only **5-7%** of hypertensive patients

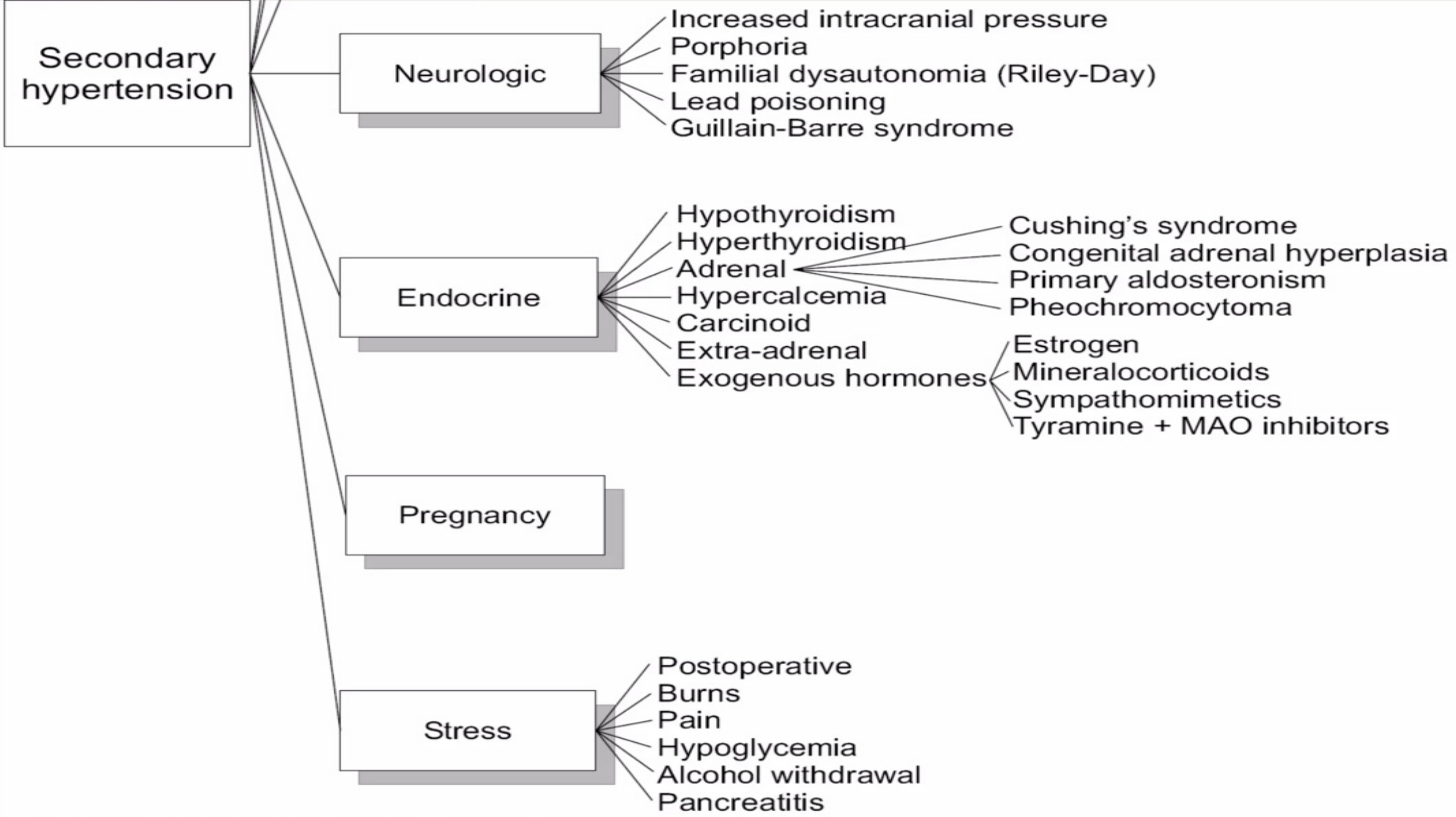
Secondary hypertension should be suspected in patients in whom hypertension develops at an early age, those who first exhibit hypertension when over age 50 years, or those previously well controlled who become refractory to treatment

When to suspect secondary hypertension clinically?

- Absence of family history of hypertension
- Severe hypertension > 180/110 mm Hg with onset at age < 20 years or > 50 years
- Difficult-to-treat or resistant hypertension with significant end-organ damage features
- Presents with combination of pain (headache), palpitation, pallor and perspiration – 4 P's of phaeochromocytoma
- Persons with Short and thick neck – Obstructive Sleep Apnoea
- Polyuria, nocturia, proteinuria or hematuria – indicative of renal diseases

- Absence of peripheral pulses, brachiofemoral delay and abdominal or peripheral vessel bruits
- History of polycystic renal disease or palpable enlarged kidneys
- Cushingoid features, multiple neurofibromatosis
- Significant elevation of plasma creatinine with use of ACE inhibitors
- Hypertension in children
- History of snoring, daytime somnolence, obesity


Secondary hypertension
Drugs/Toxins
Renal disease
Renal parenchymal disease
Polycystic disease
Chronic nephritis
Glomerulonephritis
Diabetic nephropathy
Hydronephrosis
Reno-vascular disease
Renin producing tumor
Primary sodium retention
Vascular
Coarctation of aorta
Neurologic
Increased intracranial pressure
Porphoria
Familial dysautonomia (Riley-Day)
Lead poisoning
Guillain-Barre syndrome


Secondary hypertension
Neurologic
Increased intracranial pressure
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Endocrine
Hypothyroidism
Hyperthyroidism
Adrenal
Cushing's syndrome
Congenital adrenal hyperplasia
Primary aldosteronism
Pheochromocytoma
Hypercalcemia
Carcinoid
Extra-adrenal
Exogenous hormones
Estrogen
Mineralocorticoids
Sympathomimetics
Tyramine + MAO inhibitors
Pregnancy
Stress
Postoperative
Burns
Pain
Hypoglycemia
Alcohol withdrawal
Pancreatitis

Hypertension in Chronic Kidney Diseases

- There are two forms of kidney diseases causing hypertension

a) Renal parenchymal and b) Renovascular causes

- **Renal parenchymal diseases** :
  - Chronic glomerulonephritis
  - Chronic interstitial nephritis
  - Pyelonephritis
  - Nephrocalcinosis
  - Neoplasms
  - Glomerulosclerosis
  - Analgesic nephropathy
  - Polycystic kidney disease
  - Gout with renal failure
  - Obstructive nephropathy

Polycystic Kidneys

Renovascular Hypertension

Etiology: **Atherosclerosis**

Takayasu's arteritis

Fibromuscular dysplasia

Other causes

- **Aortic/renal dissection**
- **Thrombotic/cholesterol emboli**
- **Post transplantation stenosis**
- **Post radiation**

➢ The most common cause of renovascular hypertension in **India** is **Takayasu's syndrome (progressive aortoarteritis**) though atherosclerotic renovascular disease is also being recognised more often now in early patients.

➢ The most common cause of renovascular disease in Western population are atherosclerotic disease in 60% of elderly population and fibromuscular dysplasia in 35% of young.

- A **Para umbilical bruit** is heard in 50-60% of patients with renovascular hypertension and 10% cases of essential hypertension. A **diastolic renal bruit** is more specific than systolic bruit.

- Clinically, macroalbuminuria (a random urine albumin/creatinine ratio >300 mg/g) or microalbuminuria (a random urine albumin/creatinine ratio 30–300 mg/g) are early markers of renal injury.

- Proteinuria is a reliable marker of the severity of chronic kidney disease and is a predictor of its progression. Patients with high urine protein excretion (>3 g/24 h) have a more rapid rate of progression than do those with lower protein excretion rates.

Investigations :

- In patients with **moderate degree of suspicion** of renovascular hypertension, **non-invasive** tests are recommended initially which are--

1)Colour Doppler Ultrasound (CDUS)-to know the renal artery stenosis

2)CT angiography and

3)MRI angiography.

4)99Tc – DTPA and 123 I – Hippuran scan.

These tests give functional status of CKD.

MRI angiography has higher sensitivity (90%) and specificity (92%).

- In patients with **high degree of suspicion**, direct selective **renal arteriography** is recommended.
- **Conventional angiography**, though invasive, is the **gold standard test.**

Other tests:

Captopril Screening Test-Test sensitivity is excellent but specificity is poor

Method: Patient maintains normal salt intake and receives no diuretics and withdraw all antihypertensives 3 weeks before the test, if possible

· Patient should be seated for at least 30 minutes; draw venous blood sample and measure baseline plasma renin activity

· Dilute 50 mg of captopril in 10 mL of water; patient immediately drinks the solution and after 60 minutes, draw venous blood samples and measure stimulated plasma renin activity

Interpretation

Test is positive in the presence of:

· Stimulated plasma renin activity of **12 ng/mL/hr or more** and

· Absolute increase in plasma renin activity of **10 ng.mL.hr or more**

➢Intra-arterial injection with **digital subtraction angiography (DSA**) may be used.

➢Once the diagnosis is confirmed, **renal angioplasty with stenting is the treatment of choice**.

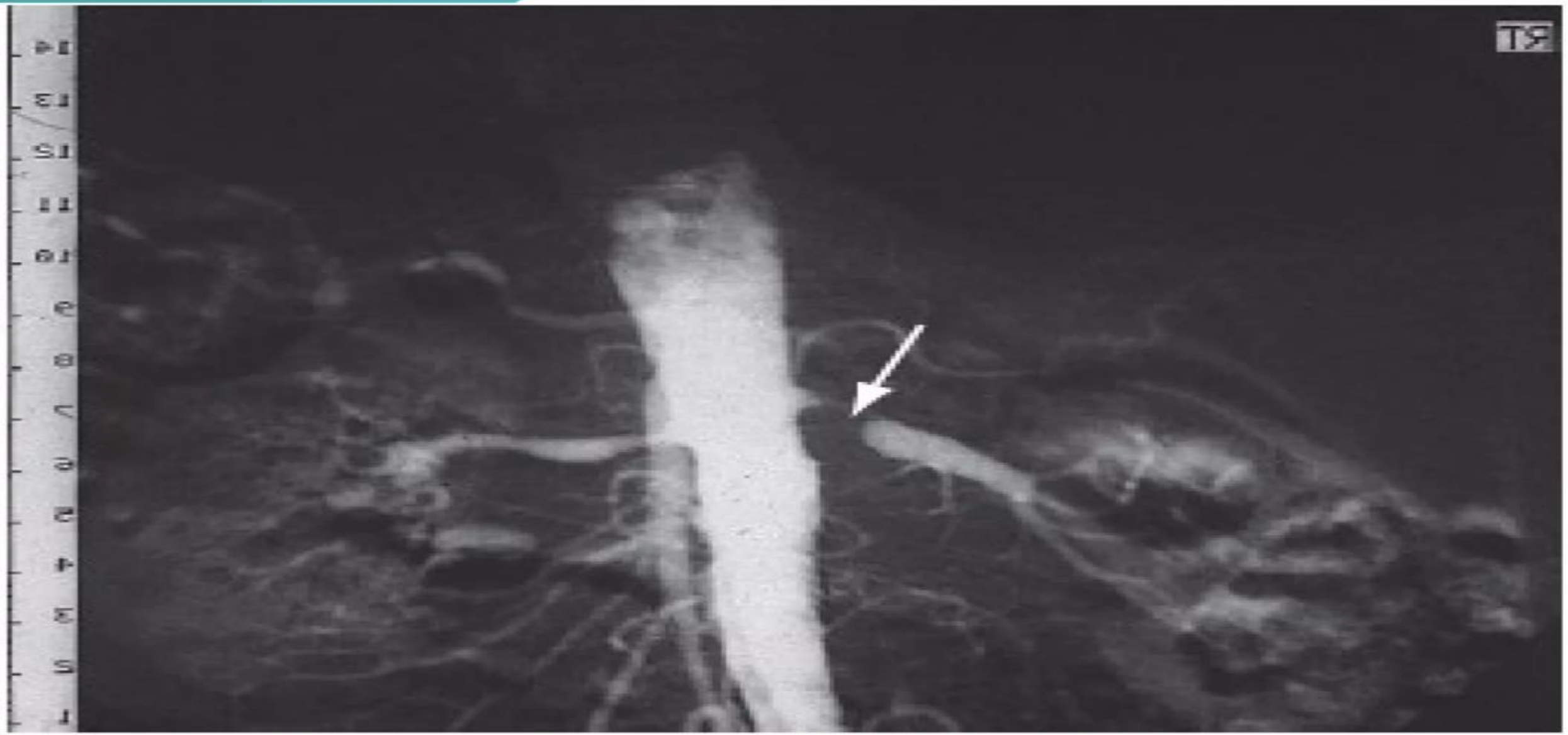
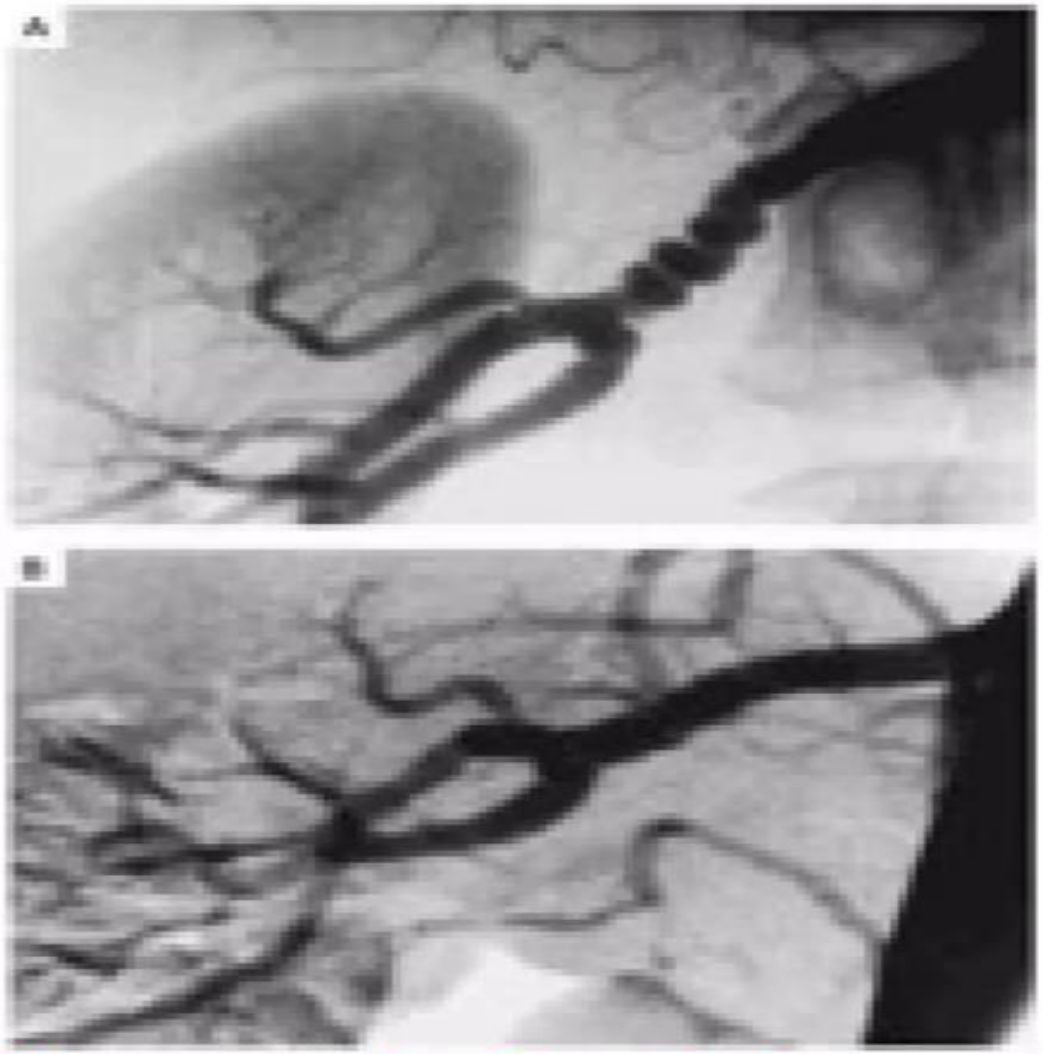
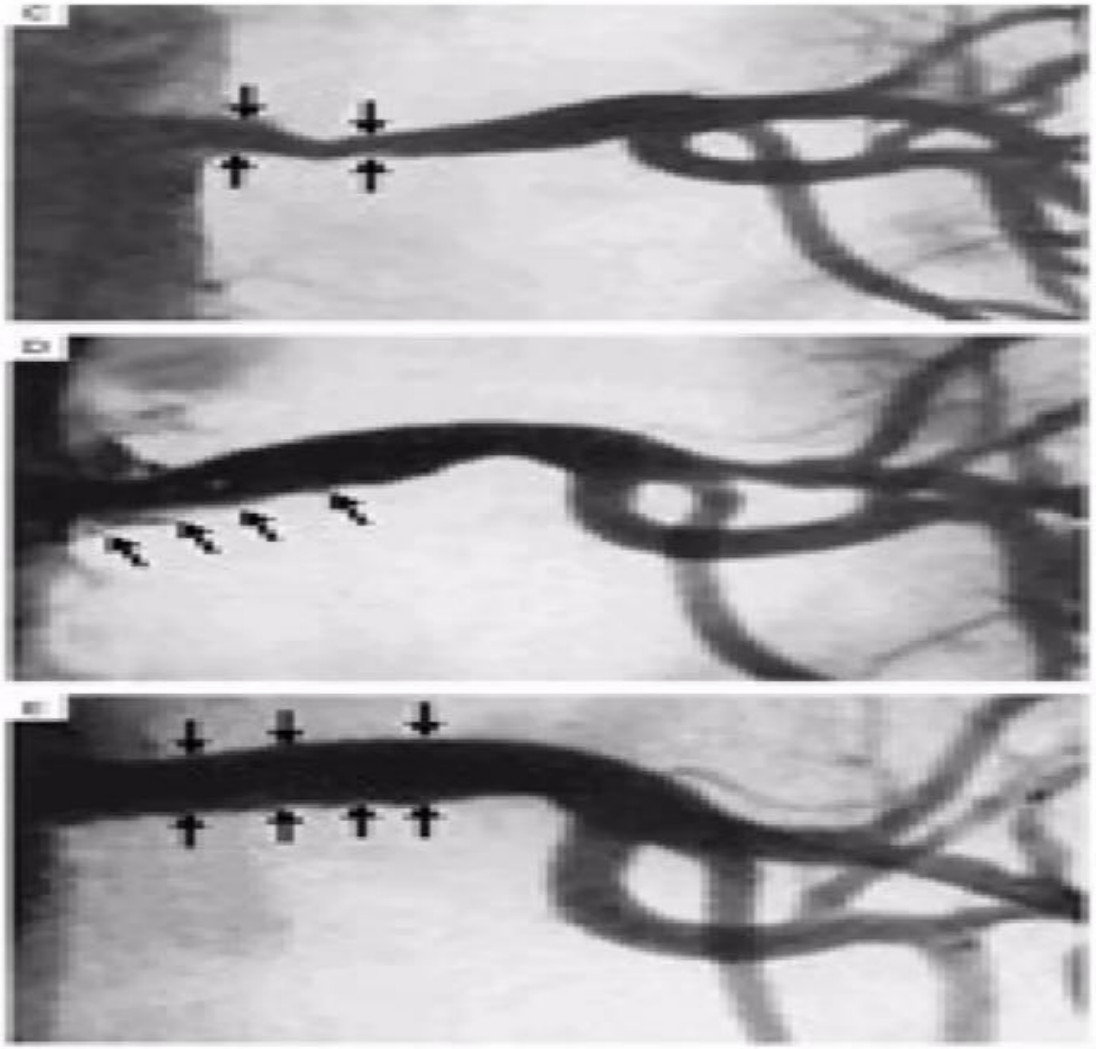


Figure 14.118 Digital subtraction angiography, showing typical unilateral atheromatous renal artery stenosis with post-stenotic dilatation (arrow).



Fibromuscular Dysplasia, before and after PTRA



Atherosclerotic RAS before and after stent

Endocrine causes

1.Pheochromocytoma

- It is a chromaffin cell tumor which are mostly adrenal and unilateral. These may be extra-adrenal in 10% of the cases and bilateral in 10% of the cases. 10% of all cases are familial and 10% are malignant
- Episodic hypertension, postural fall, pallor, throbbing headache, palpitations and perspiration are suggestive clinical features
- Features may be provoked by triggers such as tyramine-containing foods (beer,cheese,wine), pain, trauma, drugs (clonidine, TCA, opiates)

Investigations

- **Screening tests:** Plasma and urinary biochemical assay for
  a) free catecholamines,
  b) metanephrines and
  c) vanillyl-mandelic acid (VMA).

These tests have high specificity (99%) and sensitivity (85-90%)

- Following drugs should be withdrawn for 48 hours before doing these tests: α methyldopa, β blockers, clonidine, penicillins.
- Patients can be continued on CCBs and ACE inhibitors during evaluation.

Medications That Can Cause False-Positive Elevations of Plasma and Urinary Catecholamines or Metanephrines

Medications	Catecholamines NE	Catecholamines E	Metanephrines NMN	Metanephrines MN
Tricyclic antidepressants	+++	—	+++	—
Phenoxybenzamine	+++	—	+++	—
Labetalol*	+++	—	+++	—
Monoamine oxidase inhibitors	—	—	+++	+++
Sympathomimetics	++	++	++	++
Caffeine	++	++	?	
Levodopa, Carbidopa	++	—	?	
Cocaine	++	++	?	
Acetaminophen*			++	
Buspirone*				+++

Tumor localisation is done by- CT scan and MRI of the abdomen

- **MIBG labelled with I-131** is the **most specific** way of diagnosing adrenal and extra adrenal pheochromocytomas and PET scan using18 F-fluorodeoxy glucose is also useful
- Once localised, **surgery** should be offered to all the patients. Mortality from surgery is now less than 5%.
- For pre-operative preparation, control of blood pressure is important and can be achieved with **oral phenoxybenzamine 10 mg once daily**, to be increased slowly. Oral prazosin and terazosin preferentially block post-synaptic α1-receptors on vessel wall and leave pre-synaptic α 2- receptors. As a result, tachycardia is less of a problem
- B-blockers may be given to these patients to control tachycardia and arrhythmias, only after α-blockers have been started

2. Primary Aldosteronism

- Primary aldosteronism is due to excess aldosterone secretion by the adrenal adenomas and occasionally due to bilateral adrenocortical hyperplasia
- Clinical presentation
  - May be asymptomatic; headache, muscle cramps, polyuria
  - Hypokalemia (K normal in 40%), metabolic alkalosis
  - Retinopathy
- This is suspected in a case of hypertension showing **persistent hyokalaemic metabolic alkalosis** in the absence of diuretic therapy

Investigations

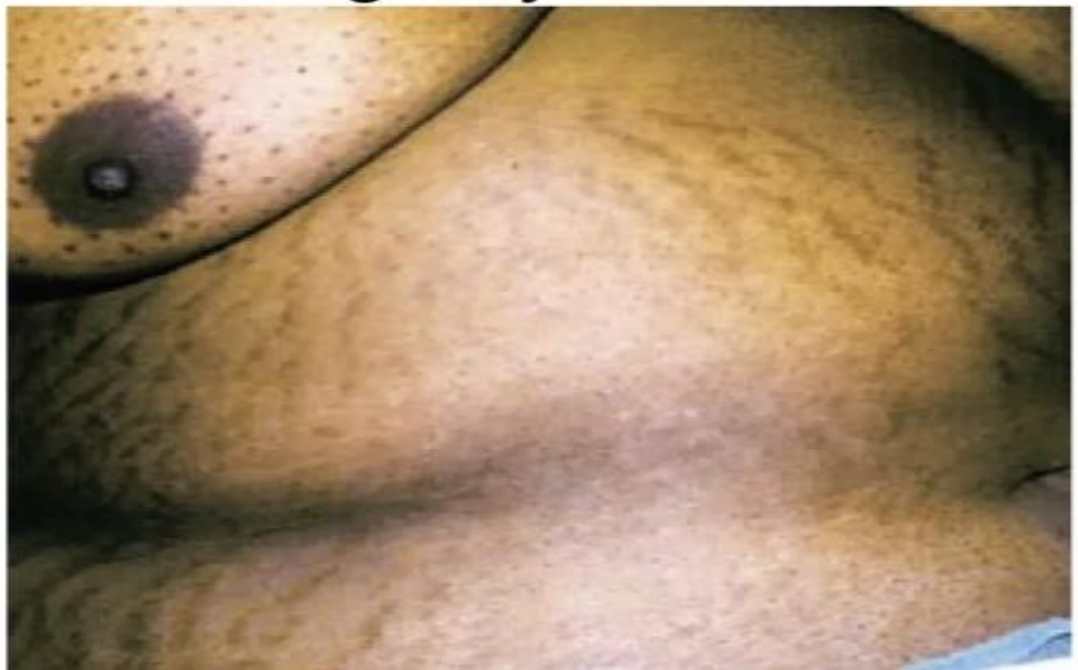
- Plasma Aldosterone to Plasma Renin Activity (PRA) ratio **more than 20 to 25** (normal < 10) is 95% sensitive and 75% specific for Primary Hyper Aldosteronism
- **Confirmatory test**: by demonstrating failure to suppress plasma aldosterone to <277 pmol/L (<10 ng/dL) after IV infusion of 2 L of isotonic saline over 4 h;. **Alternative confirmatory tests** include failure to suppress aldosterone in response to an oral NaCl load, fludrocortisone, or captopril.
- It is usually diagnosed by imaging techniques- CT Scan, adrenal scintigraphy with 6 beta-[I131]iodomethyl-19-nor cholesterol after dexamethasone suppression (0.5 mg every 6 h for 7 days)

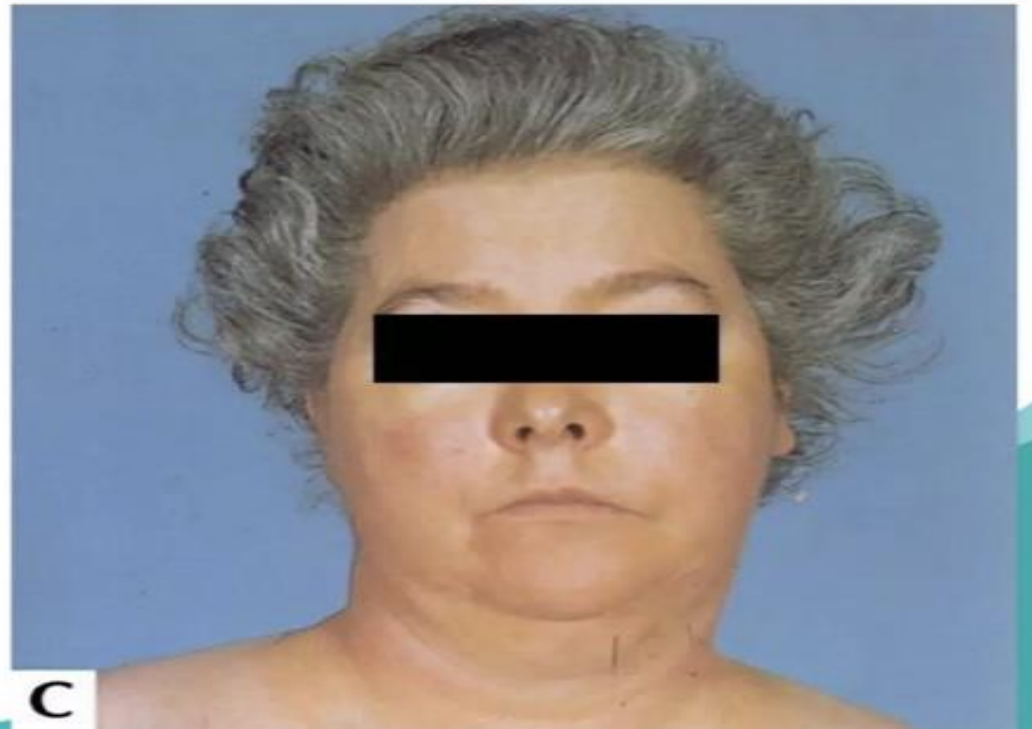
TREATMENT

- Surgical removal of adrenal tumor, can be done laparoscopically
- Pretreatment for 3-4 wks with spironolactone minimizes postoperative hypoaldosteronism and restores K to normal levels

3. Cushing's Syndrome

- **Etiology**: Pituitary microadenoma, Iatrogenic (steroid use), Ectopic ACTH and adrenal adenoma
- **Clinical presentation-**Sudden weight gain,truncal obesity, moon facies, abdominal striae, DM/glucose intolerance, HTN,proximal muscle weakness, skin atrophy, hirsutism/acne
- Hypertension is present in approximately 80% of patients with Cushing's syndrome.





Screening test:

- **24 Hr Urine free cortisol: >90ug/day is 100% sensitivity and 98% specificity**
- **false +ve result in Polycystic Ovarian Syndrome and depression**
- **Recent evidence suggests that late night salivary cortisol is also a sensitive and convenient screening test**

Confirmatory test:

- **Low dose dexamethasone suppression test----Give 1mg dexamethasone** at 11 p.m. and draw a sample of blood at 8 a.m. for cortisol measurement **(>100nmol is +ve)**

- **CT/MRI Scan of head (pituitary) and chest (ectopic ACTH tumor)**

TREATMENT

a) Cushings disease/ pituitary adenoma

- Transphenoidal resection
- Pituitary irradiation
- Bromocriptine, octreotide

b) Adrenal tumors - adrenalectomy

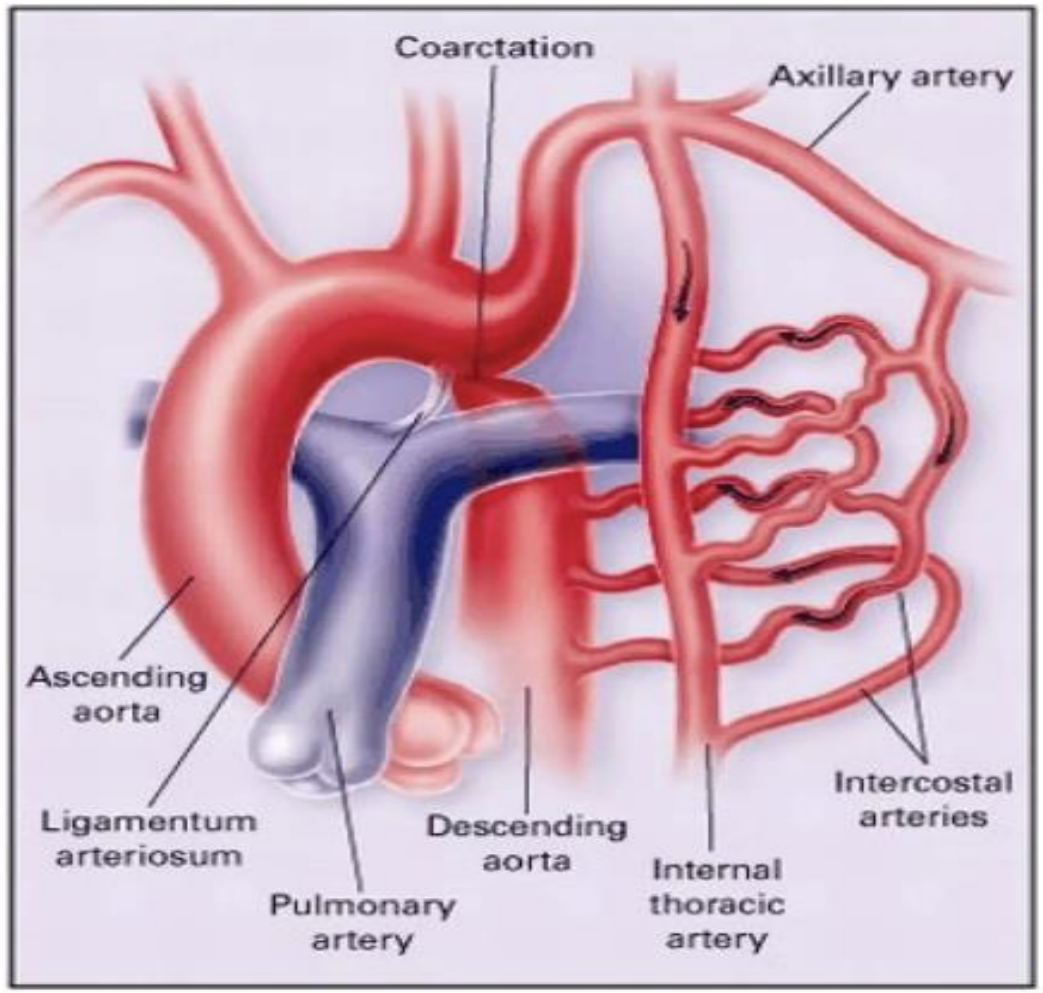
Removal of ACTH tumor

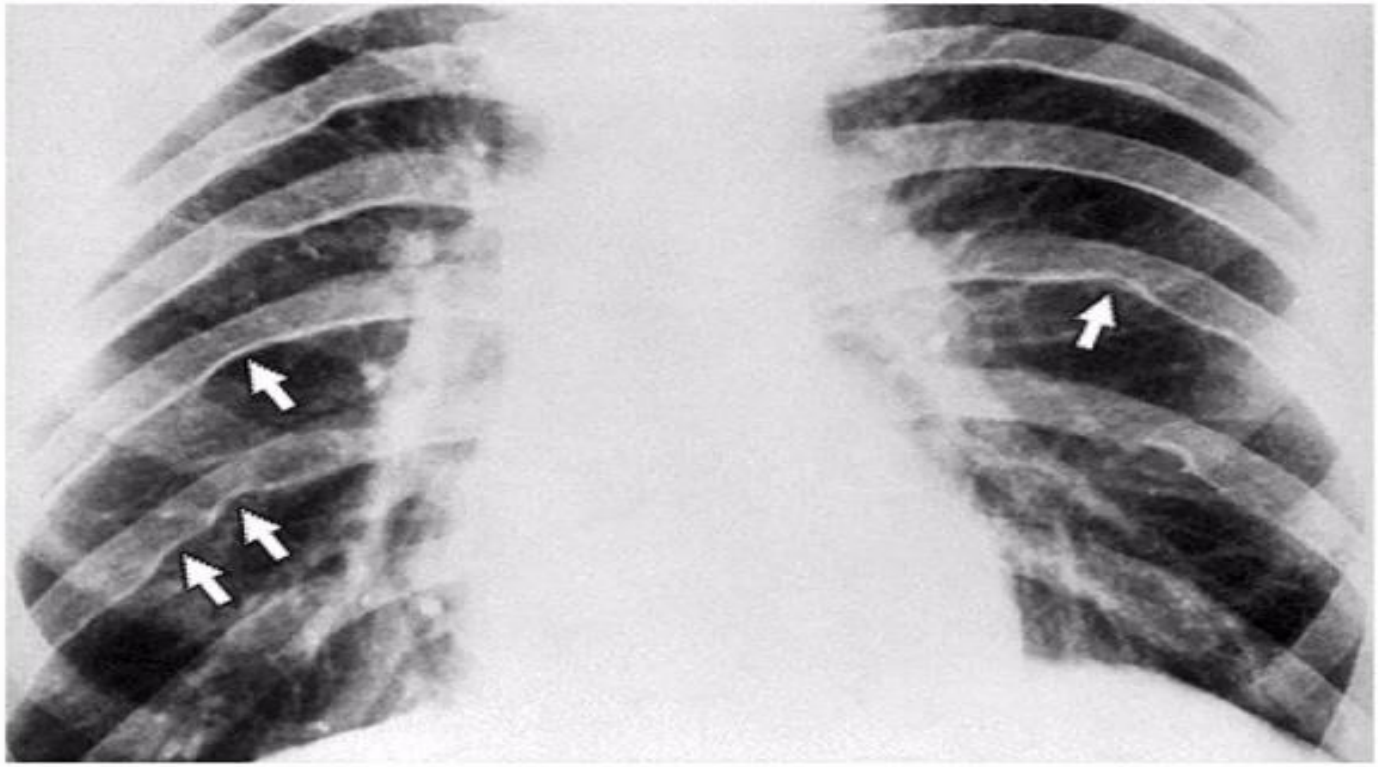
4. Coarctation of the aorta

Coarctation of the aorta consists of localized narrowing of the aortic arch just distal to the origin of the left subclavian artery.

- Collateral circulation develops around the coarctation through the intercostal arteries and the branches of the subclavian arteries and can result in a lower transcoarctation gradient by enabling blood flow to bypass the obstruction.
- **Congenital defect, male>female**
- **Clinical presentation:**
  - **Differential systolic BP in arms and legs (=DBP)**
  - **May have differential BP in arms if defect is proximal to Left subclavian artery**
  - **Diminished/absent femoral artery pulse**
  - **Often asymptomatic**
  - **Associated with Turners syndrome, bicuspid Aortiv valve**
- **If uncorrected, 67% will develop LV failure by age 40 and 75% will die by age 50**

Coarctation of Aorta





Inferior rib notching

- Surgical Rx, long term survival better if corrected early

5. Hypertension associated with pregnancy

- During pregnancy, a blood pressure of 140/90 mmHg is considered to be abnormally elevated and is associated with an increase in perinatal morbidity and mortality.

- In all pregnant women, the measurement of blood pressure should be performed in the sitting position, because the lateral recumbent position may result in a blood pressure lower than that recorded in the sitting position.

- The diagnosis of hypertension requires the measurement of two elevated blood pressures, at least 6 h apart.

- Hypertension during pregnancy is usually caused by pre eclampsia, chronic hypertension, gestational hypertension, or renal disease.

- **Pre eclampsia**: new onset of hypertension (blood pressure >140/90 mmHg) and proteinuria (>300 mg/24 h) after 20 weeks of gestation

- ***Severe preeclampsia*** :Marked elevation of blood pressure (>160/110 mmHg), severe proteinuria (>5 g/24 h), or evidence of central nervous system (CNS) dysfunction (headaches, blurred vision, seizures, coma), renal dysfunction (oliguria or creatinine > 1.5 mg/dL), pulmonary edema, hepatocellular injury (ALT > 2-fold the upper limits of normal), hematologic dysfunction (platelet count < 100,000/L or disseminated intravascular coagulation), or placental dysfunction (oligohydramnios or severe intrauterine growth restriction).

- **HELLP syndrome**: Hemolysis, *e*levated *l*iver enzymes, *l*ow *p*latelets

6. Estrogen use / oral contraceptives

- A small increase in blood pressure occurs in most women taking oral contraceptives.

- This is caused by volume expansion due to increased hepatic synthesis of angiotensinogen and consequent activation of the renin–angiotensin–aldosterone system.

- Postmenopausal estrogen does not generally cause hypertension, but rather maintains endothelium-mediated vasodilation.

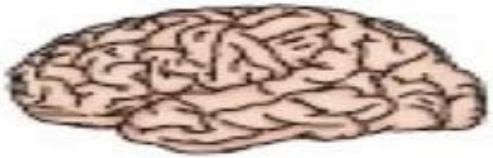
Other important secondary causes :

- **Thyroid disorders:** hypothyroidism and hyperthyroidism
- **Sleep apnea syndrome** is one of the common causes of reversible hypertension. **Polysomnography** is diagnostic. No specific drugs have proven superior in sleep apnea but **use of C-PAP improves the hypertension**
- **Acute stressful situations** cause intense sympathetic discharge and may temporarily induce hypertension.
- Common conditions include acute mental stress, hypoglycaemia, acute intermittent porphyria, exposure to cold, burns, perioperative period and post head injury.

Drugs that Raises Blood Pressure

- Immunosuppressive agents-Cyclosporine, tacrolimus, corticosteroids
- NSAID's--Ibuprofen, naproxen, piroxicam
- COX-2 inhibitors--Celecoxib, rofecoxib, valdecoxib
- Estrogens
- Weight-loss agents--Sibutramine, phentermine,ephedrine
- Minerocorticosteroids—Fludrocortisone
- Antiparkinsonian—Bromocriptine
- Monoamine oxidase inhibitors—Phenelazine
- Anabolic steroids—Testosterone
- Sympathomimetics—Pseudoephedrine
- Stimulants--Nicotine, amphetamines

complications

Organ	Problem	
	Atherosclerosis Aneurysms Aortic dissections	
	Haematuria Uraemia Proteinemia	Chronic kidney disease
	Pulmonary oedema Myocardial infarction Left ventricular hypertrophy	Cardiac failure
	Haemorrhage / infarction Seizures Vascular dementia	Stroke / TIA
	Haemorrhages Exudates A-V nipping Papilloedema	Blindness

Fundoscopy is an essential part of the examination of any hypertensive patient . The abnormalities are graded according to the Keith-Wagener classification:

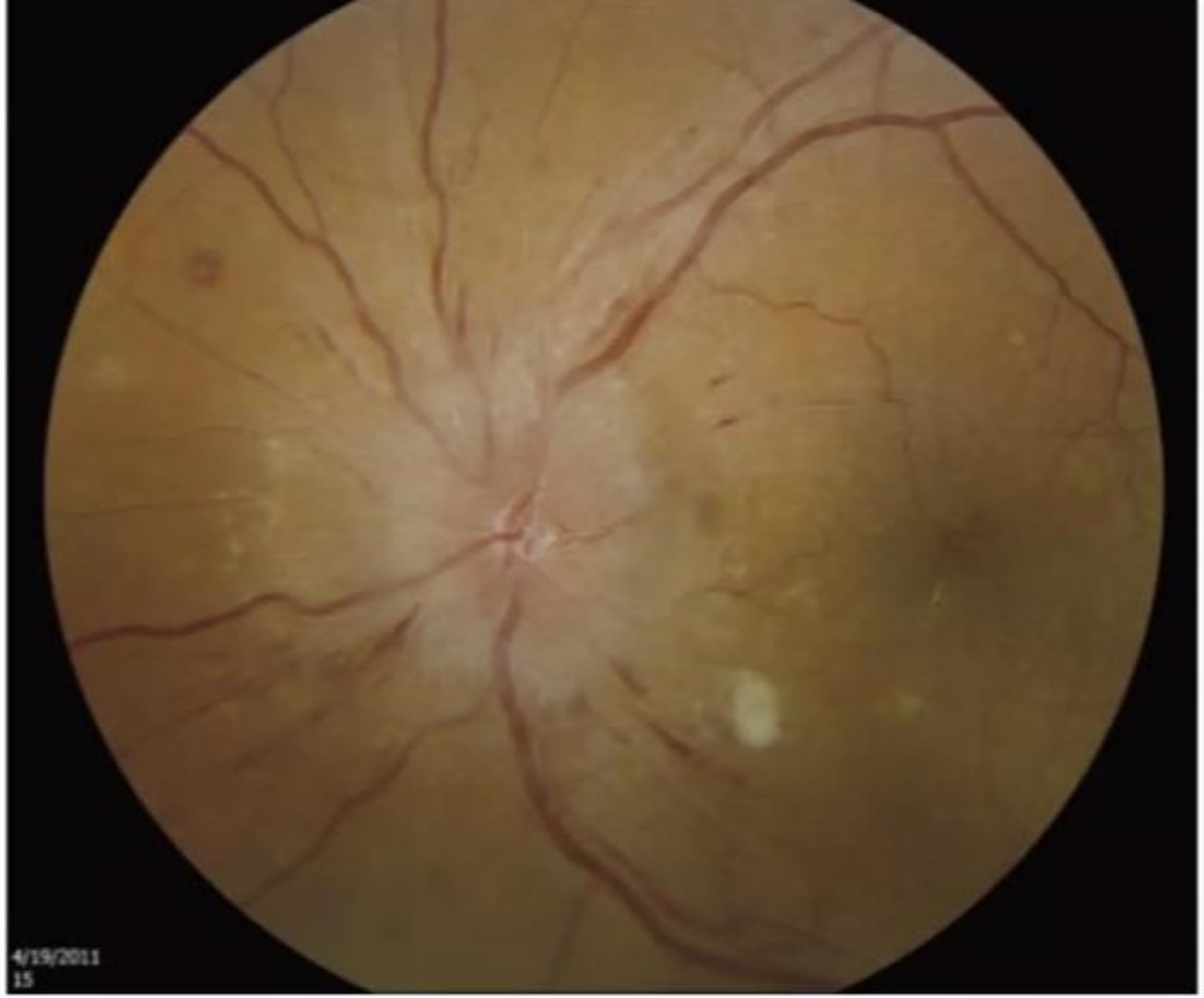
Grade 1 – Tortuosity of the retinal arteries with increased reflectiveness (silver wiring)

Grade 2 – grade 1 plus the appearance of arteriovenous nipping produced when thickened retinal arteries pass over the retinal veins

Grade 3 – grade 2 plus flame-shaped haemorrhages and soft ('cotton wool') exudates actually due to small infarcts

Grade 4 – grade 3 plus papilloedema (blurring of the margins of the optic disc)

Grades 3 and 4 are diagnostic of **malignant hypertension**.



▲ **Figure 11–2.** This image shows severe acute hypertensive retinopathy with papilledema, intraretinal hemorrhages, nerve fiber layer infarcts (cotton-wool spots) and arteriovenous nicking. Retinal arteries show irregular thinning. (Used, with permission, from Dr. Richard S.

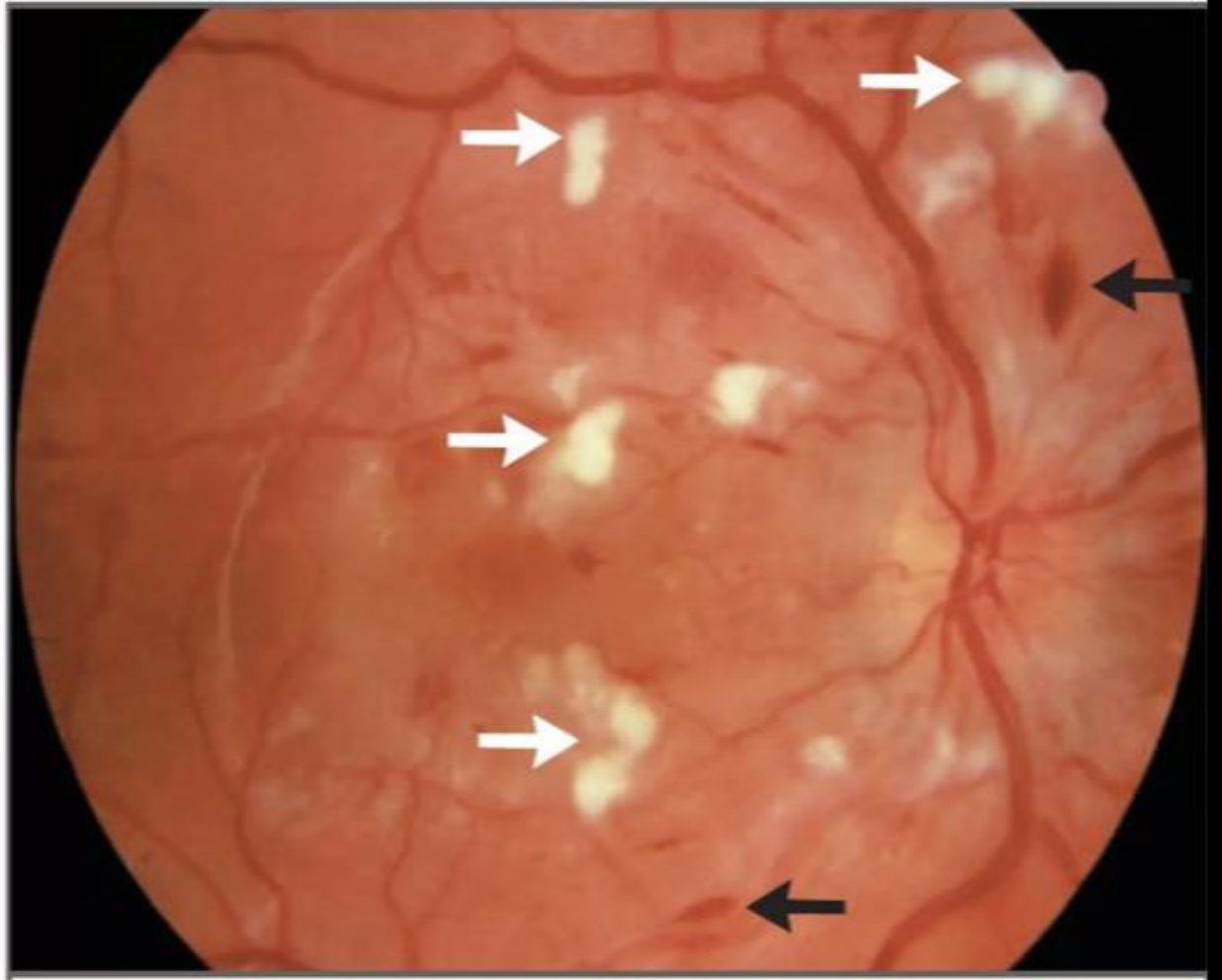


Figure 3. Example of Malignant Hypertensive Retinopathy.

Multiple cotton-wool spots (white arrows), retinal hemorrhages (black arrows), and swelling of the optic disk are visible.

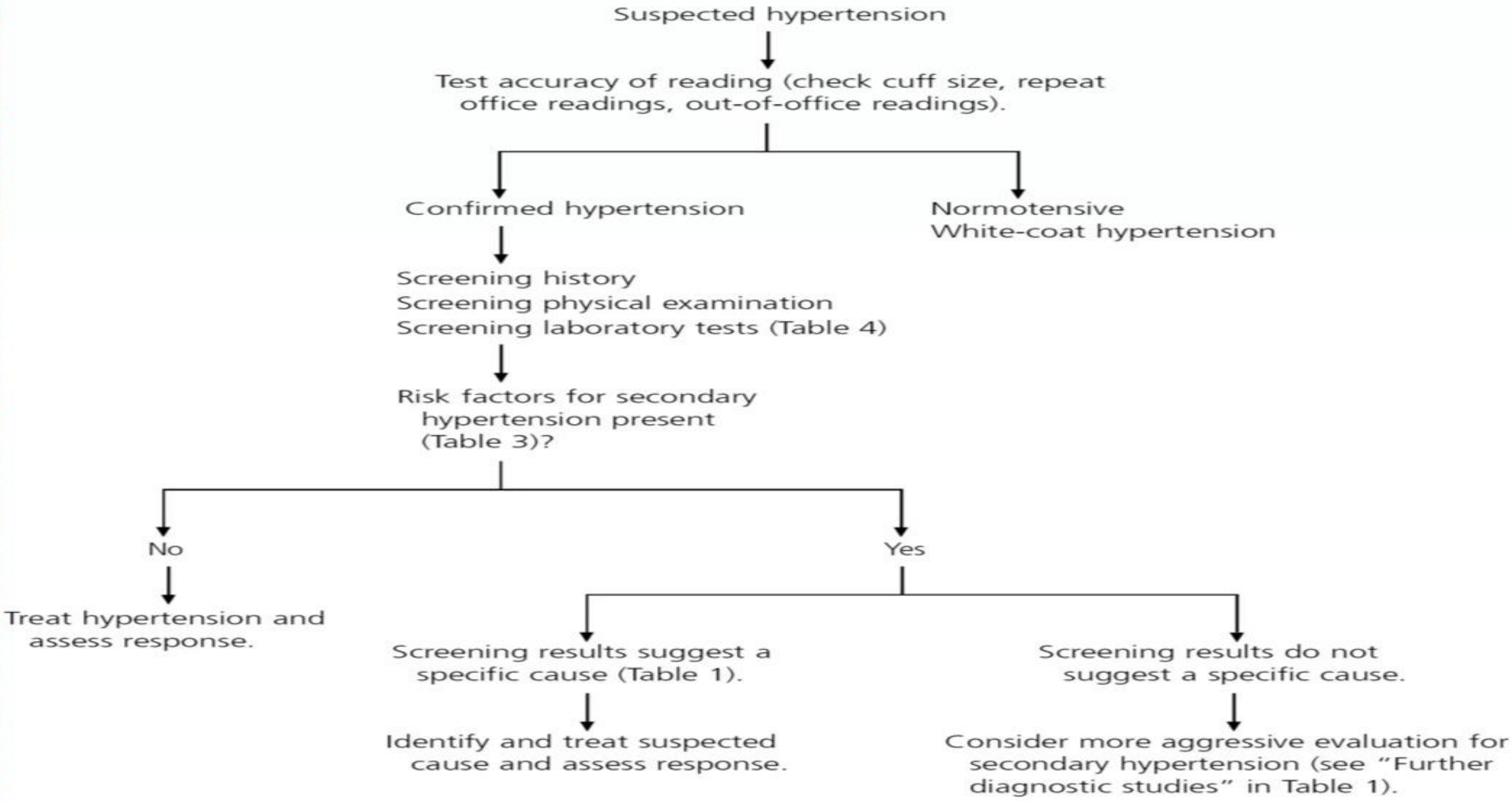
Summary

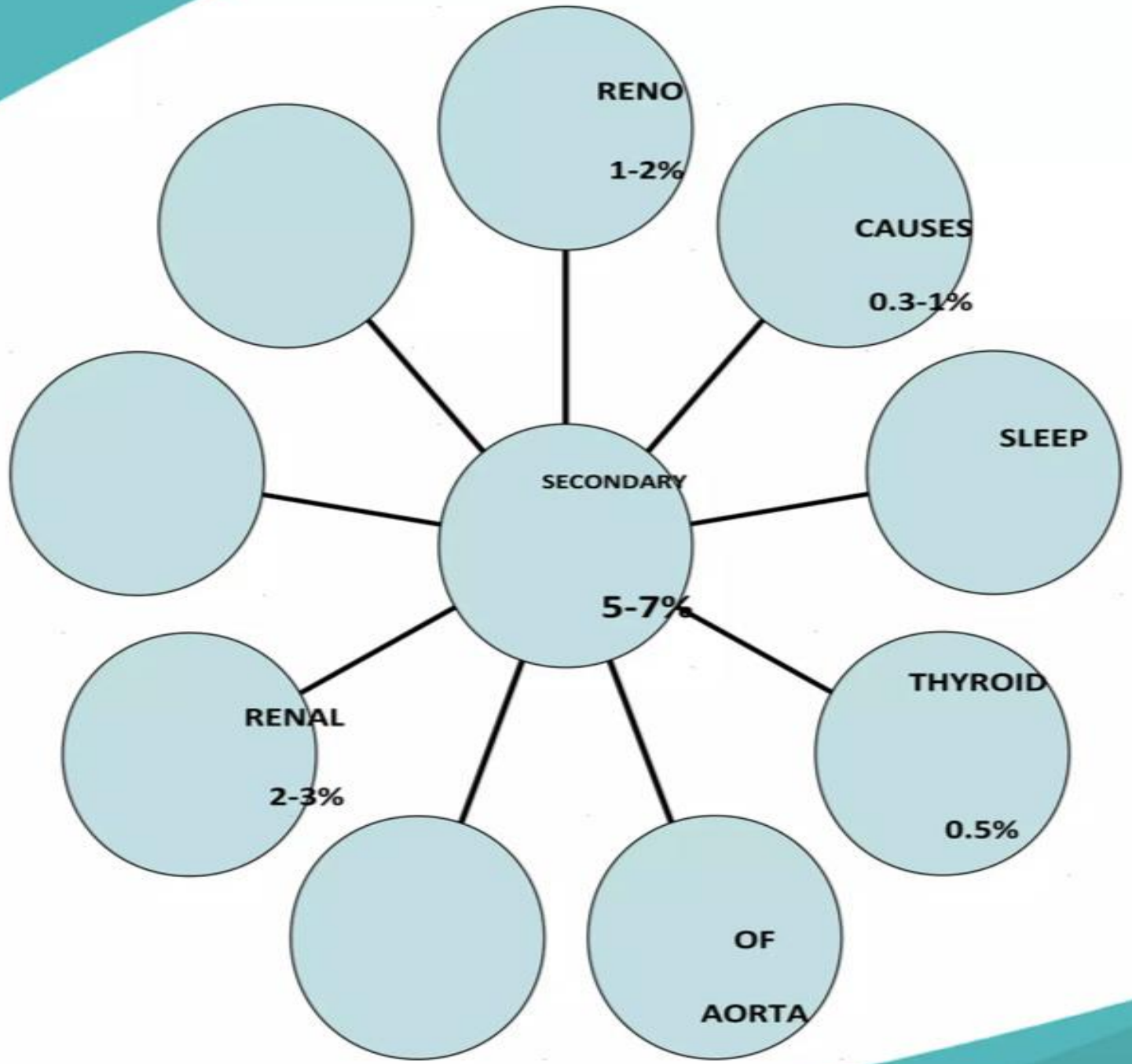
- The initial assessment of a hypertensive patient should include a complete history and physical examination to confirm a diagnosis of hypertension

- Clues to secondary hypertension include onset at a young age (<20), abrupt onset of hypertension, blood pressure difficult to control requiring high dosages of two or more drugs, and very high or labile blood pressure.

- Headaches with severe hypertension are occipital and worse in the morning.

Evaluation for Secondary Causes of Hypertension





PARENCHYMAL

Findings That Suggest Secondary Hypertension

Findings	Disorder suspected	Further diagnostic studies
Paroxysmal hypertension, headaches, diaphoresis, palpitations, tachycardia	Pheochromocytoma	Urinary catecholamine metabolites (vanillylmandelic acid, metanephrines, normetanephrines Plasma free metanephrines
Fatigue, weight loss, hair loss, diastolic hypertension, muscle weakness	Hypothyroidism	TSH levels
Heat intolerance, weight loss, palpitations, systolic hypertension, exophthalmos tremor, tachycardia	Hyperthyroidism	TSH levels
Kidney stones, osteoporosis, depression, lethargy, muscle weakness	Hyperparathyroidism	Serum calcium, parathyroid hormone levels
Headaches, fatigue, visual problems, enlargement of hands, feet, tongue	Acromegaly	Growth hormone level

Findings That Suggest Secondary Hypertension

Findings	*Disorder suspected*	*Further diagnostic studies*
Use of sympathomimetics, perioperative setting, acute stress, tachycardia	Excess catecholamines	Confirm patient is normotensive in absence of high catecholamines.
Decreased or delayed femoral pulses, abnormal chest radiograph	Coarctation of aorta	Doppler or CT imaging of aorta
Weight gain, fatigue, weakness, hirsutism, amenorrhea, moon facies, dorsal hump, purple striae, truncal obesity, hypokalemia	Cushing's syndrome	Dexamethasone-suppression test
Use of drug in Table 2	Drug side effect	Trial off drug, if possible
High salt intake, excessive alcohol intake, obesity	Diet side effects	Trial of dietary modification
Erythropoietin use in renal disease, polycythemia in COPD	Erythropoietin side effect	Trial off drug, if possible

Findings That Suggest Secondary Hypertension

Findings	*Disorder suspected*	*Further diagnostic studies*
Snoring, daytime somnolence, obesity	Obstructive sleep apnea	Sleep study
Hypernatremia, hypokalemia	Aldosteronism	Ratio of plasma aldosterone to plasma renin activity, CT scan of adrenal glands
Renal insufficiency, atherosclerotic cardiovascular disease, edema, elevated blood urea nitrogen and creatinine levels, proteinuria	Renal parenchymal disease	Creatinine clearance, renal ultrasonography
Systolic/diastolic abdominal bruit	Renovascular disease	Magnetic resonance angiography, captopril (Capoten)-augmented radioisotopic renography, renal arteriography