SECONDARY HYPERTENSION

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Abstract:
Approximately 5-10% of patients with hypertension have an identifiable cause, which is defined as secondary hypertension. The etiology of secondary hypertension varies with age of presentation. Screening for secondary causes of hypertension should be considered in the young (less than 30 years), hypertension resistant to treatment with three antihypertensives, sudden increase in BP in previously stable hypertensive patients and in patients presenting with severe hypertension. Primary aldosteronism, phaeochromocytoma, Cushing’s syndrome, hypothyroidism, hyperthyroidism, obstructive sleep apnoea, renal parenchymal disease, renal artery stenosis and coarctation of the aorta are some of the causes of secondary hypertension. Laboratory investigations must be sent depending on the clinical features suggestive of a secondary cause. Management of secondary hypertension is tailored to the underlying cause and includes medical and surgical interventions.

INTRODUCTION
Uncontrolled hypertension is associated with increased risk of acute myocardial infarction, left ventricular failure, stroke, renal failure and death. In the majority of cases, when the exact etiology of hypertension is unknown it is referred to as ‘essential hypertension’. Approximately 5-10% of patients with hypertension have an identifiable cause, which is defined as secondary hypertension. The etiology of secondary hypertension varies with different age groups. It is not essential to screen each patient for secondary hypertension as it is expensive, laborious and time consuming. Screening should be based on patient characteristics or when there is a greater likelihood of an identifiable cause. This review highlights the etiology, diagnosis and management of secondary hypertension in younger adults (19-39 years) and in middle aged populations (40-64 years).

Etiology of secondary hypertension:
The etiology of secondary hypertension varies with age of presentation (Table 1). The etiologies are almost similar in children (0-12 years) and adolescents (12-18 years). Overweight and obesity have recently been recognized as important causes of hypertension in adolescent age group. More recently, obstructive sleep apnea has been recognized as one of the important causes of secondary hypertension in middle aged adults. Drug related hypertension is another important cause of hypertension in the middle aged group (19-64 years). The most common type of drugs that may be associated with an increased risk of hypertension are NSAIDS, glucocorticoids, oral contraceptive pills, weight reducing pills like phenylpropanolamine and sibutramine, stimulants like amphetamines and cocaine. (See Table-3)

Who should be screened for secondary hypertension?
Early detection of a secondary cause and management can prevent end organ damage. The general characteristics of patients which may favor a diagnosis of secondary hypertension include:
REVIEW ARTICLE – Secondary hypertension

a) **Age:** onset of hypertension below 30 years of age without any other risk factors (family history, obesity, etc);

b) **Increased blood pressure in prepubertal children;**

c) **Resistant hypertension** - when blood pressure > 140/90 mmHg despite being on three antihypertensive at maximum doses (including one diuretic);

d) **Patients presenting with severe hypertension** >180/90mmHg or presenting with a hypertensive emergency;

e) **A sudden increased in BP** in previously stable hypertensive patients;

f) **Non-dipping of blood pressure at night** on ambulatory blood pressure monitoring or reverse dipping;

g) **Presence of end organ damage at the time of presentation** - left ventricular hypertrophy, hypertensive retinopathy

h) **Presence of typical symptoms suggestive of any definite cause** - (Eg. hypokalemia and hypertension in primary aldosteronism; hypertension, flushing and palpitation in pheochromocytoma)

i) **Atherosclerotic disorders** like coronary artery disease (CAD), peripheral vascular disease (PVD) and flash pulmonary edema suggestive of renal artery stenosis.

Always look for a clue which may point towards one important cause of secondary hypertension. An overview of clinical presentations of secondary causes of hypertension is shown in **Table-2.**

**Approach to secondary hypertension in a young adult (18-40 years):**

Prior to investigating a patient for secondary hypertension physician should confirm that patient blood pressure has been accurately measured using correct positioning with an appropriately sized cuff. Ambulatory blood pressure monitoring play a central role in evaluating secondary causes of hypertension, it can helps in excluding white coat hypertension, assess treatment-adherence , confirm the presence of resistant hypertension, and assess the dipping status. Modifiable risk factors like diet, alcohol intake, smoking, drugs that can increase the blood pressure showed be reviewed. Trial for stopping the offending drugs should be considered if there is no definite contraindication. Details of clinical history should be taken prior to evaluation (overview of clinical presentation shown in Table-2). The algorithm for evaluation of secondary hypertension is shown in **Figure-1.**

**Table-1: Etiology of Secondary Hypertension**

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Most common etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children (birth to 12 years)</td>
<td>Renal parenchymal disease</td>
</tr>
<tr>
<td></td>
<td>Coarctation of the aorta</td>
</tr>
<tr>
<td></td>
<td>Cushing’s syndrome</td>
</tr>
<tr>
<td>Adolescents (12 to 18 years)</td>
<td>Same as in children</td>
</tr>
<tr>
<td></td>
<td>Obesity and overweight</td>
</tr>
<tr>
<td>Young adults (19 to 39 years)</td>
<td>Thyroid dysfunction</td>
</tr>
<tr>
<td></td>
<td>Fibromuscular dysplasia</td>
</tr>
<tr>
<td></td>
<td>Renal parenchymal disease</td>
</tr>
<tr>
<td></td>
<td>Aldosteronism</td>
</tr>
<tr>
<td></td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td></td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td>Middle-aged adults (40 to 64 years)</td>
<td>Aldosteronism</td>
</tr>
<tr>
<td></td>
<td>Thyroid dysfunction</td>
</tr>
<tr>
<td></td>
<td>Obstructive sleep apnea</td>
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<tr>
<td></td>
<td>Cushing syndrome</td>
</tr>
<tr>
<td></td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Older adults (65 years and older)</td>
<td>Atherosclerotic renal artery stenosis</td>
</tr>
<tr>
<td></td>
<td>Renal failure</td>
</tr>
<tr>
<td></td>
<td>Hypothyroidism</td>
</tr>
</tbody>
</table>
## Table-2: Overview of clinical features and investigations for Secondary hypertension

<table>
<thead>
<tr>
<th>Clinical condition</th>
<th>Signs and Symptoms</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary aldosteronism</td>
<td>Hypertension, Hypokalemia, Hypokalemia related weakness, fatigue, cramps and muscle weakness</td>
<td>Aldo / PRA ratio (ARR) : ≥20</td>
</tr>
<tr>
<td>Phaeochromocytoma</td>
<td>Paroxysmal Hypertension, headache, palpitation, perspiration</td>
<td>24 hrs urinary metanephrines and nor-metanephrines Plasmap metaenephrines</td>
</tr>
<tr>
<td>Cushing's Syndrome</td>
<td>Weight gain, moon facies, striae mark abdomen, proximal muscle weakness and hyperpigmentation</td>
<td>Mid night cortisol, 8 AM cortisol, mid night/ 8 AM ACTH, 24 hours urinary cortisol -over-night dexamethasone suppression -high dose dexamethasone suppression test MRI pituitary / CT abdomen</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Weight gain, pedal edema, constipation, cold intolerance</td>
<td>TSH, T4 and FT4 (free thyroid hormone)</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>Weight loss, palpitation, sweating, heat intolerance and goiter</td>
<td>TSH, T4 and FT4 (free thyroid hormones) and thyroid uptake study</td>
</tr>
<tr>
<td>Obstructive sleep apnoea</td>
<td>Day time somnolence, snoring, Obesity, acanthosis nigricans and large neck</td>
<td>Sleep study (polysomnography)</td>
</tr>
<tr>
<td>Renal parenchymal disease</td>
<td>Nocturia, pedal edema, poor height</td>
<td>Urea, creatinine, urine routine, urine sediment and ultrasound abdomen</td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>Uncontrolled hypertension, flash pulmonary edema, increased creatinine with ACE-inhibitors, renal bruit and other atherosclerotic disease</td>
<td>Renal Doppler, renal angiography</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>Headache, epistaxis, delayed pulse in LL, BP difference (&gt;20/10 mmHg) between upper limb &gt; limber limbs. Interscapular ejection murmur</td>
<td>Color Doppler and echocardiography</td>
</tr>
</tbody>
</table>

## Table-3: Medications associated with Hypertension

<table>
<thead>
<tr>
<th>Medications associated with Hypertension</th>
<th>NSAIDs</th>
<th>Glucocorticoids</th>
<th>Estrogen</th>
<th>Diet pills</th>
<th>Stimulants</th>
<th>Decongestants</th>
<th>Tyrosine kinase inhibitors</th>
<th>Psychiatric medicines</th>
<th>Immunosuppressive agents</th>
<th>VEGF-1 inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>Cyclooxygenase-2 inhibitors, Ibuprofen, Naproxen</td>
<td></td>
<td></td>
<td></td>
<td>Amphetamines, Cocaine</td>
<td>Phenylephrine hydrochloride, Naphazoline hydrochloride</td>
<td>Sunitinib, Sorafenib</td>
<td>Buspirone, Carbamazepine, Clozapine, Fluoxetine, Lithium, Tricyclic antidepressants, Velnafexinie and Monoamine oxidase inhibitors</td>
<td>Cyclosporine A, Tacrolimus</td>
<td>Avastin</td>
</tr>
</tbody>
</table>
Algorithm for evaluation of secondary hypertension

History and examination
- Age, BMI (obesity), family history of resistant hypertension
- Drug induced?
- Target organ damage (fundoscopy)

Further evaluation
- 24 hours ambulatory blood pressure measurement (ABM)
- Exclude white coat hypertension
- Pseudo resistance hypertension
- Dipping status and heart rate

Investigations:
Urea, creatinine, CBC, urine routine, urine sediment, X-ray, TSH, lipid profile, urine protein / creatinine ratio, Ultrasound Abdomen, ECHO heart

Look for a clue to secondary causes as shown in Table-3

Primary hyperaldosteronism (Hypokalemia + Hypertension)
- Aldosterone / PRA ratio (ARR)
- CT Abdomen if ARR > 20

Phaeochromocytoma
- 24 hours urine metanephrine / normetanephrine
- If elevated > 3 times
- CT abdomen and MIBG

Cushing’s syndrome
- 8 AM & midnight – Serum cortisol
- 8 AM & midnight – ACTH
- 24 hours urinary free cortisol
- 1 mg (ONDST)
- 8 mg Dexamethasone suppressant test
- MRI pituitary for Cushing’s disease
- CT abdomen for adrenal Cushing’s syndrome
- PET scan for ectopic Cushing’s syndrome

Obstructive Sleep Apnea syndrome
Polysomnography

Fig.1 - Algorithm for evaluation of secondary hypertension
Common causes of secondary hypertension

Obstructive sleep apnea:
Obstructive sleep apnea (OSA) has recently been identified as one of the important causes of secondary hypertension in the middle aged group (20-60 years) of age. According to the American sleep association, obstructive sleep apnea (OSA) is a sleep-related breathing disorder that involves a decrease or complete halt in airflow despite an ongoing effort to breathe. It occurs when the muscles relax during sleep, causing soft tissue in the back of the throat to collapse and block the upper airway. This leads to partial reductions (hypopneas) and complete pauses (apneas) in breathing that last at least 10 seconds during sleep.

Clinical profile: Most patients present with snoring loudly during sleep, daytime sleepiness, headache, lack of concentration and irritability. Typical patients are overweight or obese having a large neck, double chin and marcoGLOSSIA.

Hypertension in OSA: OSA may produce surges in systolic and diastolic pressure that keep the mean blood pressure levels elevated at night. In many patients the blood pressure may remain elevated during the daytime, when breathing is normal. The mechanisms of hypertension in OSA includes sympathetic nervous system over activity and alterations in vascular function and structure that are caused by oxidant stress and inflammation.

Diagnosis and treatment: The diagnosis of OSA requires overnight sleep testing (polysomnography) in the sleep laboratory. An echocardiogram is essential to determine ventricular function, pulmonary arterial hypertension and right ventricular dysfunction. Continuous positive airway pressure (CPAP) at night can abolish apneas, thereby preventing intermittent arterial pressure surges and restoring the nocturnal "dipping" pattern. However CPAP treatment has only a modest beneficial effect on daytime blood pressure.

Primary hyperaldosteronism
Primary hyperaldosteronism (PA) constitutes of approximately 10% of all cases of hypertension and should be considered in a patient presenting with hyperkalemia and hypertension. The risks of cardiovascular, cerebrovascular and renal related morbidity are disproportionately higher in PA when compared to the degree of hypertension. In PA, adrenal adenoma may constitute about 1/3rd of the cases. Bilateral adrenal hyperplasia contributes to the remaining 2/3rd.

Clinical profile: The diagnosis of PA is usually made in 2 to 6th decade particularly in patients with resistant hypertension. Hypokalemia is commonly seen (in 9-37% of cases of PA) and may be spontaneous or induced by medications like diuretics. The symptoms of hypokalemia include periodic muscle weakness, muscle cramps and tetany.

Hypertension in PA: Hypertension in PA is typically moderate to severe and may be resistant to commonly used antihypertensive agents. The mechanism of hypertension is attributed to excessive aldosterone mediated absorption of sodium and water from the distal tubules of the kidneys.

Diagnosis and management:
The aldosterone / renin ratio (ARR) is the preferred screening test. The ARR is commonly expressed as a ratio between plasma aldosterone concentration (PAC) in ng/dL or pmol/L and plasma renin activity (PRA) in ng/ml/ hour. A combination of an ARR of 20 or higher and a PAC level of at least 15 ng/dL is found in more than 90% of patients with a surgically confirmed aldosterone producing adenoma (APA). Drugs interfering with the PAC/PRA ratio which mainly include the thiazide diuretics and mineralocorticoid receptor antagonists (aldactone and eplerenone) should be stopped at least 6 weeks prior to test being undertaken. An increased ARR should be confirmed by a confirmatory test to differentiate between adenoma and bilateral adrenal hyperplasia. Some of the confirmatory tests are the a) oral sodium loading test b) saline infusion test c) fludrocortisone suppression test and d) captopril challenge test.

A CT adrenal should be performed in all suspected patients with an elevated ARR. A typical adrenal adenoma is characterized by a hypodense nodule of size around 2 cm diameter. If the size of
the adrenal lesion is more than 4 cm, an aldosterone producing carcinoma should be suspected.\textsuperscript{32}

\textbf{Figure-2.} CT scan features of aldosterone producing adenoma (white circle).

Surgical resection is the definite treatment of PA\textsuperscript{33} A unilateral form of the disease should be further established by bilateral adrenal venous sampling in patients older than 40 years (when one side is an adenoma and other side a mildly bulky adrenal).\textsuperscript{34} In bilateral adrenal hyperplasia, treatment is always medical, with aldosterone receptor antagonist (spironolactone, eplerenone) being preferred.\textsuperscript{35} Gynecomastia is one important long term adverse effect seen with spironolactone therapy. Familial hyperaldosteronism like glucocorticoid remediable hypertension should be excluded if there is a family history of young onset hypertension. This clinical condition is rare and the blood pressure usually responds to a physiological dose of glucocorticoids.\textsuperscript{36}

\textbf{Cushing’s syndrome}

An iatrogenic cause of Cushing’s syndrome is more common than the endogenous causes of Cushing’s syndrome. Endogenous Cushing’s syndrome is further classified into ACTH dependent and ACTH independent Cushing’s syndrome. (See Box 1)

\textbf{Box 1. Cushing’s syndrome – Etiology}

\begin{itemize}
    \item \textbf{Iatrogenic}
    \item \textbf{Endogenous causes}
    \begin{itemize}
        \item \textbf{ACTH dependent} - Pituitary adenoma, ectopic ACTH secreting tumour (lungs, thymic carcinoid, pancreatic cancer)
        \item \textbf{ACTH independent} - Adrenal adenoma/carcinoma
    \end{itemize}
\end{itemize}

\textbf{Hypertension in Cushing’s syndrome:}

Hypertension is a one of the major and frequent manifestations (80\%) of Cushing’s syndrome.\textsuperscript{37} The association between glucocorticoid excess and hypertension is complex and still poorly understood though several mechanisms have been hypothesized. In patients with Cushing’s syndrome the severity of hypertension is more common in ectopic Cushing’s. In pituitary and adrenal Cushing’s the severity of hypertension may be correlated with the duration of hypercortisolim.

\textbf{Management:} The definitive treatment of Cushing’s syndrome is surgical resection of the tumour. This includes trans–sphenoidal excision of the pituitary adenoma in pituitary Cushing’s disease, excision of ectopic ACTH secreting tumour, and excision of benign cortisol producing adrenal adenomas / localized non invasive adrenal carcinomas. The cure rate is much lower in malignant tumours. In persistent disease, which includes either an ectopic / pituitary disease, bilateral adrenalectomy is an option. Bilateral adrenalectomy is associated with increased risk for development of Nelson syndrome. In adrenal carcinoma with secondary metastasis, medical treatment with mitotane is the main option.
Control of blood pressure is essential prior to any surgical procedure. Multiple anti hypertensive medications may be required along with mineral corticoid receptor blockade (aldactone) to control the blood pressure. Angiotesin receptor blockade and angiotensin converting enzyme inhibitors is preferred since there is up regulation of the RAAS (Renin angiotensin aldosterone system).

Medical treatment is an option for patients waiting for surgery and patients not fit for a surgical procedure and in cases with persistent disease. Ketocanaezloe is preferred to other medications due to its low cost and lower adverse effects compared to mitotane. Cabergolone alone or in combination with ketoconazole has been found to be effective in controlling hypercortisolemia in ACTH dependent pituitary Cushing’s syndrome.40

Phaeochromocytomas
The phaeochromocytomas and paragangliomas constitute about 0.2- 0.6% of cases of secondary hypertension.42 Phaeochromocytomas (PCC) are tumors arising from the chromaffin cells of the adrenal medulla and paragangliomas are benign tumours that arise from the neuroendocrine tissue of the sympathetic and parasympathetic chains.41 The phaeochromocytomas and sympathetic paragangliomas usually synthesize and secrete catecholamines while 1/3 of cases of parasympathetic derived paragangliomas secrete only dopamine.

Clinical profile: The most common presentation of PCC is hypertension that is found in approximately 90% of cases.43 Additional symptoms seen in phaeochromocytomas are palpitations, anxiety, sweating and headache. Phaeochromocytomas can be familial in nature. The familial syndromes associated with pheochromocytomas include a) multiple endocrine neoplasia (MEN-2A and 2 B), Von Hippel Lindau syndrome (VHL) and neurofibromatosis type -1(NF-1).45 Paragangliomas are also hereditary in nature, the mutation of the gene encoding different subunits of the SDH enzyme complex is associated with a familial paraganglioma syndrome (PGL).46 Clinical examination gives a clue to the diagnosis in many cases (Eg. marfanoid habitus in MEN-2b). The presence of corneal thickness on ophthalmological evaluation favors the diagnosis of MEN-2b.47

Hypertension in phaeochromocytoma: is either sustained or paroxysmal in nature. Some patients develop a paroxysmal rise in blood pressure in the setting of sustained hypertension. However 5-10% of cases are normotensive. The dopamine secreting tumours may present with hypotension rather than hypertension.

Diagnosis and treatment: The diagnosis of phaeochromocytomas and paragangliomas is primarily based on
a) Measurement of urinary and plasma fractionated metanephrines and catecholamines levels - elevation of urinary nor–metanephrines and metanephrines 3 times above the normal range is diagnostic.
b) Imaging with CT abdomen - a heterogeneous lesion with areas of cystic, necrosis (haemorrhage) and a HU value > 20 are suggestive of phaeochromocytomas.50

c) Functional imaging with an MIBG scan. - The increased uptake on MIBG confirm the diagnosis of phaeochromocytoma. It has 100% specificity but a low sensitivity.48,49

Figure-4: CT abdomen with large pheochromocytoma (white arrow) with features of necrosis.

Newer diagnostic modalities include Somatostatin receptor scintigraphy performed with octreotide, an analogue of somatostatin (DOTATATE PET scan).51
nephriti, interstitial renal diseases, congenital renal disease (polycystic kidney disease) and reflux nephropathy are among the most common causes of resistant secondary hypertension. The mechanisms of hypertension in renal parenchymal disease include a) activation of the renin angiotensin system b) activation of the peripheral sympathetic nervous system c) decreased synthesis of vasodilatory substances and d) sodium and water retention.

The initial laboratory investigations in such cases may include urea, creatinine, and urine for sediment, urine culture, urinary protein and renal ultrasound. Patients with renal parenchymal disease should be promptly referred to a nephrologist for further evaluation of causes and also for long term management. The goal of treatment in cases of renal parenchymal disease is control of blood pressure, reduction of proteinuria and prevention of further worsening of renal function.

**Renal artery stenosis (RAS)**

Renal artery stenosis is one of the most important causes of secondary hypertension and constitutes about 1-5% of cases.

**Clinical profile:** Females are found to be more affected than men. Fibromuscular dysplasia is more common amongst young adults between the ages of 15-50 years. Atherosclerosis related renal artery stenosis is more common above 50 years of age.

The pathogenesis of hypertension in RAS is related to a reduced perfusion to the kidney that activates release of renin, which subsequently stimulates the angiotensin system and retention of salt and water.

**Diagnosis and treatment:** The presence of an audible bruit is suggestive of RAS and patients should be investigated to determine the diagnosis. A renal Doppler should be performed as a screening test prior to any invasive investigation. Angiography is considered as the diagnostic test of choice for RAS. CT/ MRI angiography are equally accurate in diagnosis of RAS.

Treatment of RAS includes definitive treatment (endovascular / surgical), control of hypertension and treatment of modifiable risk factors. Prior to any revascularization procedure, all patients should receive life style modification (salt...

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**Figure-5:** MIBG uptake on right side suggestive of pheochromocytoma.

The definitive treatment of phaeochromocytomas is complete resection of the adrenal tumor. Preoperative preparation is essential to avoid crises during induction of anaesthesia and during tumor manipulation. Preoperative preparation strategies include initiating alpha blockade (Prazosin XL, Phenoxybenzamine) 7-10 days prior to surgery for control of blood pressure along with liberal water and salt intake (8-12gm) to expand the plasma volume.

Once adequate alpha blockade is achieved, beta blockers should be started 48-72 hours prior to surgery to control the heart rate to ≤ 80/min. Calcium blockers and other anti-hypertensives may be added if it becomes difficult to achieve good blood pressure control (<140 of SBP) prior to surgery. About 10% of patients fail to achieve a normal blood pressure following surgery which is attributable to vascular remodeling due to a prolonged duration of exposure to catecholamines or related to underlying essential hypertension.

**Renal parenchymal disease**

Renal parenchymal disease constitutes approximately about 2.5-5%, of cases of secondary hypertension. Renal diseases such as glomerulo...

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**CMI 13:3**

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July 2015
Thyroid disorders:
The signs and symptoms of thyroid disorders are predominately related to the effects of thyroid hormone on the cardiovascular system. These include an increase in heart rate, cardiac contractility and blood volume and a decrease in peripheral vascular resistance. The decrease in mean arterial pressure (secondary to decreased peripheral vascular resistance) stimulates the RAAS system which results in increase sodium re-absorption from tubules and water retention. In patients with thyrotoxicosis an excess of thyroid hormone can increase the cardiac output, systolic blood pressure and widen the pulse pressure. Hyperthyroidism has been described as one of the important causes of isolated systolic hypertension. Treatment with anti thyroid drugs (carbimazole and PTU) and beta blockers reverse thyroid hormone excess related cardiovascular manifestations.

On the other hand hypothyroidism is associated with diastolic hypertension in about 30-40% of cases. The diastolic hypertension in hypothyroidism occurs due to an alteration of endothelial function, impaired vascular smooth muscle (VSM) relaxation and an increase in systemic vascular resistance. Thyroid hormone replacement can restore the endothelial function and lead to a normalization in blood pressure.

Primary Hyperparathyroidism:
Primary hyperparathyroidism (PHPT) is characterized by persistent elevation of serum calcium levels due to autonomous over-production of parathyroid hormone (PTH). Nearly 80-85% of cases of PHPT are caused by parathyroid adenoma and the rest by parathyroid gland hyperplasia or by parathyroid cancer.

Clinical profile: The common symptoms of PHPT include a) classical bone symptoms (bone pain, joint pain, trivial trauma related fracture, osteitis fibrosa cystica and reduced bone mineral density) and b) renal symptoms (polyuria, kidney stones, hypercalciuria, and rarely nephrocalcinosis) . Atypical manifestations involving cardiovascular, neurocognitive and gastrointestinal systems are occasionally seen.

Hypertension in PHPT: Recent studies showed that 40-60% of patients with of PHPT have arterial hypertension. The prevalence is definitely higher when compared to the general population. The proposed mechanisms of hypertension in PHPT include a) activation of renin and angiotensin system b) activation of peripheral sympathetic nervous systems c) altered vasodilatory response or structural changes of resistance vessels d) enhanced vascular constriction to pressor hormones like catecholamine. Other cardiovascular manifestations of PHPT include left ventricular hypertrophy, conduction abnormalities and arrhythmias.

Management: Surgical resection of parathyroid adenoma cures > 95% of cases of PHPT. NIH -2013 guidelines must be followed when surgery is recommended in patients with PHPT. It is essential to localize the site of tumor prior to surgery, when solitary adenoma is suspected. Combinations of imaging technology are performed to localize the parathyroid adenomas, which include an ultrasound of the neck, Technetium-99m-methoxyisobutylisonitrile (99mTc-sestamibi or MIBI) along with single photon emission computed tomography.
(SPECT). The cardiovascular manifestations of PHPT are shown to be reversed following successful parathyroidectomy.73

Coarctation of the aorta
Coarctation of the aorta is a constriction of the aorta located near the ligamentum arteriosum and the origins of the left subclavian artery. This clinical condition presents alone or associated with other congenital cardiac lesions. Symptoms may not present before adulthood if it is an isolated lesion. Diminished and delayed pulses in the right femoral artery compared with the right radial or brachial artery are an important clue to the diagnosis of a coarctation of the aorta. Presence of a systolic murmur over the anterior chest, bruits over the interscapular region, and visible notching of the posterior ribs on a chest x-ray are diagnostic. The main cause of death is related to cardiovascular complications which include heart failure, aortic dissection or rupture, endocarditis, endarteritis, cerebral hemorrhage, ischemic heart disease, or concomitant aortic valve disease.74 The mechanism of hypertension is an activation of the renin-angiotensin system secondary to the reduction of renal blood flow.75 Color Doppler Echo cardiology is the screening method of choice. CT scan and MRI can also be used for diagnosis.76 Early surgical intervention, even percutaneous balloon angioplasty appears to be equally effective. Patients with coarctation of the aorta require lifelong follow up, for control of hypertension and monitoring of other cardiovascular complications.77,78

Conclusions
• Secondary hypertension constitutes about 5-10% of all hypertensive patients. It requires a high index of suspicion to recognize this subgroup of hypertensives.
• Clinical symptoms and a detailed bed side examination always provide clues to the diagnosis. Appropriate step-wise investigations should be performed while evaluating such patients.

• Screening for secondary hypertension should not be considered in all patients as it is time consuming, labor intensive and costly.
• In patients with a potentially reversible cause of hypertension, early detection and treatment are important to minimize / prevent irreversible damage to target organs and to reduce long-term morbidity and mortality.

References:
REVIEW ARTICLE – Secondary hypertension


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Serendipity in the history of medicine – Louis Pasteur

Serendipity is defined as ‘luck that takes the form of finding valuable or pleasant things that are not looked for’ (Merriam-Webster dictionary). The most well known serendipitous discovery in medicine was the discovery of penicillin by Alexander Fleming who found that an accidentally open petri dish with staphylococcal culture grew a fungus that produced a substance that killed the bacteria. Not so well known is Louis Pasteur’s discovery of anthrax and rabies vaccines. Pasteur’s assistant, Charles Chamberland had been instructed to inoculate some chickens with a cholera culture after Pasteur went on holiday. Chamberland failed to do this, but instead went on holiday himself. On his return, the month-old cultures (after they were inoculated) made the chickens unwell, but instead of the infections being fatal, the chickens recovered completely. Chamberland assumed an error had been made, and wanted to discard the apparently faulty culture when Pasteur stopped him. Pasteur guessed the recovered animals now might be immune to the disease and went on to develop vaccines against anthrax and rabies using this knowledge. The notion of a weak form of a disease causing immunity to the virulent version was not new; this had been known for a long time for smallpox. The difference between smallpox vaccination and anthrax vaccination was that the weakened form of the latter disease organism had been “generated artificially”, so there was no need to find a naturally weak form of the disease. This discovery revolutionized work in infectious diseases, and Pasteur gave these artificially weakened diseases the generic name of “vaccines”, in honour of Jenner’s discovery. Pasteur produced the first vaccine for rabies by growing the virus in rabbits, and then weakening it by drying the affected nerve tissue. (Source: en.wikipedia.org)