REVIEW OF DISEASE
Hypertension is defined conventionally as a sustained increase in blood pressure $\geq$ 140/90 mm Hg, a criterion that characterizes a group of patients whose risk of hypertension related cardiovascular disease is high enough to merit medical attention\(^1\).

Blood pressure varies from minute to minute and is influenced by measurement technique, time of day, emotion pain, discomfort, hydration, temperature, exercise, posture and drugs. Actually the risk of both fatal and non fatal cardiovascular disease in adults is lowest with systolic blood pressure of less than 120 mm Hg and diastolic blood pressure less than 80 mm Hg, these risks increase progressively with higher systolic and diastolic blood pressure\(^2\).

**Table 3. Classification of blood pressure\(^{1,2}\)**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Blood Pressure mm Hg</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Normal</td>
<td>$&lt;120$ and</td>
<td>$&lt;80$</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120-139 or</td>
<td>80-90</td>
</tr>
<tr>
<td>Hypertension, stage 1</td>
<td>140-159 or</td>
<td>90-99</td>
</tr>
<tr>
<td>Hypertension, stage 2</td>
<td>$\geq160$ or</td>
<td>$\leq100$</td>
</tr>
<tr>
<td>Hypertension, stage 3</td>
<td>180 or</td>
<td>110</td>
</tr>
</tbody>
</table>

**Etiology\(^2\)**

**Essential Hypertension**

More than 90% of patients with sustained elevation of arterial blood pressure have essential hypertension with no identifiable cause. The term essential hypertension is evolved from the mistaken belief that high blood pressure was essential for adequate tissue perfusion.

**Remedial Hypertension**

A small percentage of patients may have potentially curable hypertension caused by renal disease, adrenal disease, coarctation of aorta, or another rare condition. Renovascular hypertension, which is considered the most prevalent remediable cause of hypertension, is estimated to cause hypertension in less than 0.5% of the hypertensive population.

**Drug-Induced Hypertension**

Hypertension may occur in upto 5% of patients who take oral contraceptives. Factors that may increase the likelihood of oral contraceptive hypertension include age greater than 35 years, smoking, obesity, and a family history. Other drugs may also significantly increase blood pressure. A double dose of the sympathomimetic diet drug Phenylpropanolamine (PPA) causes a significant increase in blood pressure to a peak of 173/103 mmHg. NSAIDs, cyclosporine, Recombinant Human Erythropoietin (rHuEPO), corticosteroids, MAOI and the products containing large amount of sodium may increase blood pressure.

**Pathophysiology\(^5\)**

Blood pressure is maintained within a fairly constant range, despite changes in posture and wide variations in the demand for blood supply. Early theories suggested that renal sodium retention expanded vascular volume, increasing cardiac output. The increased cardiac output was believed to have led to increased vascular resistance. Another theory suggests that inherited cellular defects caused intracellular sodium, leading to increase in ionic calcium and increased vascular tone and reactivity. A possible primary role of sympathetic nervous
system has also been suggested. It is likely that several interrelated mechanisms, rather than a single causative defect, control blood pressure in essential hypertension. A relationship called, "the deadly quarlet," or "syndrome X" has led to the theory that hyperinsulemia is a cause of hypertension. However, even with continued insights into the regulation of blood pressure, essential hypertension remains a process that must be controlled rather than a curable disorder.

Table 4. Effect of combined risk factor in total deaths per 1000 in the multiple risk factor intervention trial.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Men Age 35-45 yr Death/1000 Increase *</th>
<th>Men Age 46-57yr Deaths/1000 Increase *</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>5.4</td>
<td>19.3</td>
</tr>
<tr>
<td>DBP&gt;90</td>
<td>8.4</td>
<td>25.8</td>
</tr>
<tr>
<td>Cholesterol&gt;250 mg/ dL</td>
<td>10.0</td>
<td>25.4</td>
</tr>
<tr>
<td>Smoking</td>
<td>12.8</td>
<td>38.8</td>
</tr>
<tr>
<td>DBP+ Cholesterol</td>
<td>15.8</td>
<td>37.9</td>
</tr>
<tr>
<td>DBP+ Smoking</td>
<td>23.2</td>
<td>56.4</td>
</tr>
<tr>
<td>DBP/Cholesterol/Smoking</td>
<td>33.2</td>
<td>70.7</td>
</tr>
</tbody>
</table>

*Increase = deaths for men with risk factor / deaths for men with no risks.

Classification of Antihypertensive drugs by their Primary Site or Mechanism of Action⁵

A. Diuretics
1. Thiazides and related agents e.g. Chlorthalidone etc.
2. Loop diuretic e.g. Furosemide etc.
3. K⁺-sparing diuretics eg Spimolactone etc.

B. Sympathomimetic drugs
1. β Adrenergic antagonistics e.g. Atenolol etc.
2. α Adrenergic antagonistics e.g. Prazocin etc.
3. Mixed adrenergic antagonistics e.g. Carvedilol etc.
4. Centrally acting agents e.g. Clonidine etc.
5. Adrenergic neuron blocking agents e.g. Reserpine etc.

B. Calcium Channel blocker
e.g. Diltiazem etc.

C. Angiotensine Converting enzyme Inhibitors
e.g. Captopril etc.

D. Angiotensine-II receptor antagonists
e.g. Losartan etc.

E. Vasodilators
1. Arterial
e.g. Hydralazine etc.
2. Arterial and venous
e.g. Nitropruside etc.
HYPERLIPIDEMIA\textsuperscript{3, 4, 7, 8}

Cardiovascular disease is one of the leading causes of morbidity and mortality. Heart disease causes an estimated 5, 00,000 deaths every year. Risk factors associated with the development of cardiovascular disease include gender, age, cigarette smoking, diabetes, hypertension and hyperlipidemia. Hyperlipidemia, hypertension and cigarette smoking are considered treatable risk factors. Cholesterol and blood pressure reduction and smoking cessation have been proven to reduce the risk of cardiovascular disease. Hyperlipidemia and the medications used to lower cholesterol have received generous exposure. As a result, the public is aware that high cholesterol is a risk factor for cardiovascular disease.

Hyperlipidemia is defined as the presence in the blood of an abnormally high concentration of fats such as cholesterol, cholesterol esters, triglycerides and phospholipids. Studies have demonstrated that elevated low-density lipoprotein (LDL) level is an independent and proven risk factor for cardiovascular disease. Hypertriglyceridemia has been associated with certain lipoprotein disorders and with pancreatitis and uncontrollable diabetes mellitus, but has not been identified as an independent risk factor for cardiovascular disease\textsuperscript{1}. Hyperlipidemia is a major player in atherogenesis. Hypertension is also one of the primary risk factors for atherosclerosis. The significant reduction of fatal and nonfatal events observed in trials of primary and secondary prevention has confirmed that HMG-CoA reductase inhibitors reduce the risk of cardiovascular events well beyond the expected hypolipidemic effect. The large clinical trials like West of Scotland Coronary Prevention Study (WOSCOPS) have demonstrated significant reductions in the incidence of cardiovascular events in a 1 to 2 year time frame.

Treatment
1. Diet
2. Pharmacotherapy
3. Bile acid resins
4. Niacin
5. 3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase Inhibitors (HMG-CoA Reductase Inhibitors)
6. Fibric Acid Derivatives.

HMG-CoA Reductase Inhibitors
i. Atorvastatin
ii. Cerivastatin
iii. Fluvastatin
iv. Lovastatin
v. Pravastatin
vi. Simvastatin

These statins competitively inhibit the enzyme HMG-CoA reductase, which is responsible for the conversion of HMG CoA to mevalonic acid. Mevalonic acid is a precursor to cholesterol in its synthesis. When this process is inhibited, cholesterol production is reduced, which results in an upgradation of LDL receptors and further reduction of circulating free cholesterol. HMG CoA reductase inhibitors are the most potent LDL-lowering drugs available and generally are preferred in patients with elevated LDL because they are more effective and better tolerated than other cholesterol lowering agents. Statins reduce LDL by 20%-60%, decrease triglyceride by 10%-40% and increase HDL by 5%-15%. The statins generally are well tolerated but safety beyond 5 years has not been established. The most
common side effects are GI effects, including abdominal pain, flatulence, and constipation, which occur in approximately 3% of patients.

REFERENCES