Introduction
Hypertension is a highly prevalent condition in Singapore, affecting 27% of our adult population. It is an established risk factor for stroke, myocardial infarction, renal failure, congestive heart failure, progressive atherosclerosis and dementia. Treatment of hypertension has been shown to be able to reduce these complications and overall cardiovascular mortality and morbidity. In reality, it may surprise some to know that the 1998 data for Singapore shows that only 66% of patients with hypertension are on treatment, among whom, only 30% are treated optimally.

How to Diagnose?
A clinical and family history followed by physical examination is essential. Standard laboratory investigations should include urinalysis (for blood, protein, glucose and microscopy) and blood chemistry (for electrolytes, creatinine, urea, fasting glucose and full lipid profile) and finally, a 12-lead electrocardiogram (ECG). These are to guide the physician in assessing the patient's global cardiovascular risk and screen for evidence of Target Organ Damage (TOD) and possible secondary hypertension.

Technique
It is imperative that the technique of recording blood pressure (BP) be correct before making a diagnosis of hypertension. Patients should be seated for 5 minutes prior to any measurements, with feet on the ground and arms rested at the level of the heart. Patients are to be reminded that they should not smoke or consume caffeinated drinks at least 30 minutes before the consultation. The BP cuff used should be of sufficient size to encircle 80% of the arm of the patient. A small cuff will overestimate a person's blood pressure reading. Using palpation of the radial artery to ascertain the systolic blood pressure, the cuff should be quickly inflated to about 30 mmHg above the palpated systolic blood pressure. Systolic blood pressure (SBP) is the reading at which the Phase I of the Korotkoff sound is heard and diastolic blood pressure (DBP) is at Phase V, when the sound disappears completely but not Phase IV when the sound is muffled.

Systolic versus diastolic blood pressure
Historically, diastolic pressure has been used to guide management of hypertension only because isolated systolic hypertension (SBP > 140, DBP < 90) was an exclusion criterion in major clinical trials in the 1970's and 80's. But we now know from large meta-analyses, that both SBP and DBP correlate closely with increasing risks of cardiovascular complications. The increased risks actually start at 115/75 mm Hg and for every rise in 20 mm Hg in SBP, there is a doubling of cardiovascular events. Regardless, all guidelines suggest monitoring both readings closely. The severity of hypertension is graded according to the component (SBP or DBP), which falls into the higher grade. This issue is actually not that crucial because the diastolic component will almost always track the systolic component with adequate treatment.

Further Investigations
While clinic measurements over several visits are usually adequate to diagnose hypertension, occasionally it is necessary to exclude white-coat hypertension or secondary hypertension. Hypertension may be diagnosed confidently in those with evidence of TOD and ambulatory monitoring is not indicated under these circumstances except perhaps to assess response to therapy.

The diagnosis of hypertension may need to be confirmed with 24-hour ambulatory BP test under the following circumstances:
1. Young patients
2. Variable home or office BP
3. Possible hypotensive episodes with treatment

The cause of hypertension is multifactorial and the vast majority will fall into the category of primary or essential hypertension. In minority of cases, a patient may suffer from hypertension secondary to an underlying pathology i.e. “secondary hypertension”. Clinical suspicion for a secondary cause may be aroused if clinical examination and history are abnormal (e.g. Cushingoid features, stigmata of pheochromocytoma, radiofemoral pulse deficit, murmur in coarctation of aorta, polycystic kidneys and labile blood pressure). The presence of abnormal biochemistry investigations such as hypokalaemia and left ventricular hypertrophy on resting electrocardiogram should also alert one to possible secondary causes and to ascertain the severity of the hypertension.

When to Treat?
The decision to treat and the target BP to lower to will depend on 2 sets of information about the patient that a physician will need to obtain in his clinical assessment. These include (1) The absolute SBP and DBP and (2) his global cardiovascular risk.

It is imperative to note that all patients with diagnosed hypertension...
hypertension (defined as BP >140/90 mmHg) will require treatment (either lifestyle modifications and/or pharmacological intervention) regardless of his risk factors. The lowering of this treatment threshold has been a constant theme in practice guidelines published by various national and regional bodies, including our Ministry of Health (MOH) Clinical Practice Guidelines released in 2000.

Common ground
All the guidelines agree on several important points which are:
1) Awareness and treatment of hypertension is still wholly inadequate
2) Non-pharmacological measures are essential
3) Individual risk from hypertension is a continuum and there are different targets depending on individual risk factors
4) Most patients will require 2 or more types of medications.

Treatment Goals
The treatment target goals should be 140/90 mmHg for all uncomplicated hypertensives. In specific subgroups, it may be necessary to lower the BP to even lower levels such as 130/80 mmHg for patients with diabetes mellitus. In patients with nephropathy and proteinuria, the target level should be 120/75 mmHg.

How To Treat
Non-Pharmacological
Lifestyle modification is generally recommended as first line therapy. Studies have shown that a diet comprising plenty of fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, and nuts, with limited fats, red meat and sweets can reduce blood pressure significantly. Combining a low salt diet also had an additive effect on BP lowering. Patients with the lowest salt intake also had the largest decrease in BP, and this applied to normotensive subjects as well. Regular exercise has also been shown to reduce SBP and DBP by 7.4 and 5.8 mmHg respectively. Regular exercise of low to moderate intensity (4-10 METs) 3 times a week for 20 minutes each is usually adequate to achieve optimum health benefits. There appears to be a flat dose response curve and excessive exercise does not appear to confer added cardiovascular benefit. Smoking cessation must be encouraged although there is no evidence of a direct causal relationship.

Those that are suitable for a 3-6 month trial of non-pharmacological treatment alone are those with only 1-2 risk factors or less (see Table 1 for risk factors) and/or BP less than 180/110 mmHg. Non-pharmacological treatment alone is not suitable for those with Associated Clinical Conditions (ACC)/TOD (Table 2) or severe hypertension (more than 180/110) mmHg.

First Line Drugs
All classes of antihypertensive drugs may be used in the initial treatment of patients with uncomplicated hypertension. However, specific agents may be used in those with co-morbidities. For example, hypertensive patients with coronary artery disease will benefit from the use of beta-blockers, while those with concurrent heart failure should receive angiotensin converting enzyme inhibitors or diuretics. Other issues that may be considered include cost, patient preference and tolerance.

The most recent attempt to demonstrate which drug

<table>
<thead>
<tr>
<th>Class of Drug</th>
<th>Compelling Indications</th>
<th>Possible Indications</th>
<th>Compelling Contraindications</th>
<th>Possible Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Heart failure, Elderly patients, Systolic hypertension</td>
<td>Diabetes</td>
<td>Gout</td>
<td>Dyslipidaemia, Sexually active</td>
</tr>
<tr>
<td>Beta-Blockers</td>
<td>Angina, After myocardial infarct, Tachyarrhythmias</td>
<td>Heart failure, Pregnancy, Diabetes</td>
<td>Asthma and chronic obstructive pulmonary disease, Heart block</td>
<td>Dyslipidaemia, Athletes and physically active patients, Vascular disease</td>
</tr>
<tr>
<td>ACEi</td>
<td>Heart failure, Left ventricular dysfunction, After myocardial infarction, Diabetic, Nephropathy</td>
<td>Heart failure, Pregnancy, Diabetes</td>
<td>Heart block</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Calcium Channel Blocker</td>
<td>Elderly patients, Systolic Hypertension</td>
<td>Angina, Peripheral vascular disease</td>
<td>Heart block</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Alpha-Blockers</td>
<td>Prostatic Hypertrophy</td>
<td>Glucose intolerance, Dyslipidaemia</td>
<td>Heart failure</td>
<td>Orthostatic hypotension</td>
</tr>
<tr>
<td>ARB</td>
<td>Side effects with other drug classes e.g. cough with ACEi</td>
<td>Heart failure, Pregnancy, Bilateral renal artery stenosis, Hyperkalaemia</td>
<td>Heart failure</td>
<td>Orthostatic hypotension</td>
</tr>
</tbody>
</table>
provides the best first line choice was the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) study\textsuperscript{12}. In this large study (n = 33357), a diuretic (Chlorthalidone) was compared to 1) ACE-I (Lisinopril) 2) Calcium Antagonist (Amlodipine) and 3) Alpha-blocker (Doxazosin). The Doxazosin arm was terminated early by the safety committee in February 2000 due to a higher incidence of stroke and cardiovascular events\textsuperscript{13}. The results suggest a lower incidence of heart failure among those treated with a diuretic when compared to an ACE-I or calcium antagonist. Sub-group analyses however suggest that this was mainly due to the large (32%) numbers of African-Americans (who tend to respond poorly to ACE-I) randomized into the trial\textsuperscript{14}.

However, the apparent superiority of diuretics over and ACE-I was not shown in the Second Australian National Blood Pressure Study (ANBP2) consisting of an older (age 65 to 84 years old) and predominantly white population\textsuperscript{15}. This study in fact suggested that in that cohort, ACE-Is have a slight advantage in preventing myocardial infarction. The results of ALLHAT and ANBP2 are not as contradictory as they first appear as the patients recruited into these 2 trials were quite dissimilar in terms of their age and racial demographics. The importance of individualization of drug therapy in light of these new findings was reiterated in a recent editorial\textsuperscript{16}.

### Combination Therapy

Combination therapy has been demonstrated in various trials to be needed to reach the desired target BP goal. Some favoured combinations which are known to have synergistic effects include beta-blockers and calcium antagonists, ACE-inhibitors and diuretics, ACE-inhibitors and calcium antagonists. This can be summarized in Figure 1. Using the right combination has been shown to increase efficacy of treatment\textsuperscript{17} but is largely academic if 3 or more medications are needed to reach target BP.

![Figure 1: ABCD Rule](image)

**Key:**
- A = Angiotensin Converting Enzyme Inhibitors
- B = Beta-blockers
- C = Calcium Antagonists
- D = Diuretics

Solid lines represent combinations which are potentially synergistic. Dashed lines represent combinations which lack synergy as they act on similar pathways, but may be unavoidable if dual therapy is unsuccessful.

### What else to treat

**Aspirin**

The addition of aspirin in patients with hypertension who are at a low risk is generally not necessary, as the benefit of reduction in ischaemic events must be balanced against the risk of a significant bleed either in the brain or in the gastrointestinal system. Recent meta-analyses suggest the use of a global risk score to assess the risk versus benefit of aspirin in those without established ischaemic heart disease\textsuperscript{18}. The American Heart Association has proposed that aspirin may be considered in a patient with a 10 year risk of developing cardiovascular disease of more than 10\%\textsuperscript{19}, the British Hypertension Society was slightly more conservative and advised aspirin in those with a 10 year risk of 15\%\textsuperscript{20}. As diabetics have a cardiovascular risk equal to someone with a prior myocardial infarction\textsuperscript{21}, both guidelines consider this group of patients as having the risk of another event similar to one who already has established cardiovascular disease, hence both advise aspirin as primary prevention in diabetics. MOH guidelines advise aspirin use in those with satisfactory blood pressure and “high” as well as “very high” cardiovascular risks (e.g. 3 – 4 risk factors). Diabetics for reasons mentioned above would automatically qualify\textsuperscript{7}.

### Cholesterol Lowering in Hypertension

The additive benefits of lipid lowering in hypertension was shown recently in the (Anglo-Scandinavian Cardiac Outcomes Trial – Lipid Lowering Arm) ASCOT-LLA\textsuperscript{22} study. The ASCOT
study was essentially a hypertension study comparing a new (calcium channel blocker / ACEi) against an older (beta-blocker / diuretic) combination21. While results from the main study are still pending, results from ASCOT-LLA were published recently. In ASCOT-LLA, patients were randomized to either atorvastatin or placebo if their total cholesterol was less than 6.5 mmol/l and most patients had at least 3 to 4 other risk factors in addition to hypertension, hence this was a reasonably high risk cohort. Follow up was for 3.3 years and although the relative risk reduction in cardiac event was an impressive 36%, the addition of atorvastatin was shown to reduce the absolute risk by only 3.0 to 1.9 % for MI / fatal Coronary Heart Disease and by 2.4 to 1.7 % for fatal / non-fatal stroke.

The data from the ALLHAT AT-LLA study did not show a significant benefit in terms of mortality in lipid lowering in well controlled hypertensive patients with a mean LDL of 3.8 mmol/l. There was a small and non-significant decrease in cardiovascular event24. Some have commented that this could be due to the prevalent use of non-study statin in the placebo arm as the difference in LDL was only 0.6 mmol/L after 4.8 years of follow-up25. The data from ASCOT-LLA and ALLHAT AT-LLA are again consistent with current guidelines that emphasize attainment of target BP and global risk stratification when considering therapy for primary prevention.

Conclusions

While many of our patients have heard of hypertension, many are not diagnosed and even among those who are diagnosed, many are not treated optimally. With its increasing prevalence due to an ageing population and obesity, it is important that the treatment of hypertension be taken seriously to bring about maximal cost-benefit outcomes.

Table (MOH 2000 Hypertension Guidelines)

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt; 130</td>
<td>&lt; 85</td>
</tr>
<tr>
<td>High-Normal</td>
<td>130 - 139</td>
<td>85 - 89</td>
</tr>
<tr>
<td>Grade 1 (mild)</td>
<td>140 - 159</td>
<td>90 - 99</td>
</tr>
<tr>
<td>Grade 2 (moderate)</td>
<td>160 - 179</td>
<td>100 - 109</td>
</tr>
<tr>
<td>Grade 3 (severe)</td>
<td>&gt; 180</td>
<td>&gt; 110</td>
</tr>
<tr>
<td>Isolated Systolic Hypertension*</td>
<td>&gt; 140</td>
<td>&lt; 90</td>
</tr>
</tbody>
</table>

* Isolated systolic hypertension is graded according to the same level of systolic BP

Cardiovascular Risk Factors

1. Levels of systolic and diastolic BP (Grades 1-3)
2. Age (Men > 55 years; Women > 65 years)
3. Smoking
4. Family history of premature cardiovascular disease (Men = 55 years; Women 65 years)
5. Total cholesterol > 6.5mmol/L (250 mg/dL)
6. Reduced HDL cholesterol < 0.9mmol/L (35 mg/dL)
7. Raised LDL cholesterol > 3.4mmol/L (130 mg/dL)
8. Diabetes Mellitus

APPENDIX I - USEFUL LINKS
2. Framingham risk calculator from the National Heart, Lung and Blood Institute (downloadable 60kb Microsoft Excel file) http://hin.nhlbi.nih.gov/atpiii/riskcalc.htm

REFERENCES


