



# Current guidelines in the treatment of hypertension

**Dr. Yui-ming Lam** MBBS, MRCP(UK), FHKCP, FHKAM(Medicine)

Department of Medicine, Queen Mary Hospital, The University of Hong Kong



Dr. Yui-ming Lam

*This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 July 2006.*

## Introduction

Hypertension (HT) is one of the most common diseases encountered in daily clinical practice. It is a major risk factor for coronary heart disease (CHD), heart failure, cerebral vascular disease and renal disease. A meta-analysis of observational studies involving more than one million individuals without prior histories of stroke or heart disease demonstrated that death from CHD and stroke increases continuously and linearly from blood pressure (BP) as low as 115 mmHg systolic and 75 mmHg diastolic.<sup>1</sup> An increment of 20 mmHg in systolic blood pressure (SBP) or 10 mmHg in diastolic blood pressure (DBP) in middle-aged and elderly persons is associated with a 2-fold increase in cardiovascular disease (CVD) mortality throughout the entire range of BP. This article will review the recently published important clinical trials and guidelines for the treatment of HT.

## New Classification of Blood Pressure

Because of new data on lifetime risk of HT and the rise of the risk of cardiovascular complications associated with levels of BP previously considered to be normal, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7),<sup>2</sup> published in 2003, has introduced a new classification of BP (Table 1). Individuals in the category of prehypertension (preHT), especially those with BP in the range of 130-139/80-89 mmHg, are at elevated risk for progression to HT and should be advised to practise lifestyle modification.

**Table 1. Classification of blood pressure (BP) for adults ages 18 and older**

Category	Systolic BP mmHg	and	Diastolic BP mmHg
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Hypertension, Stage 1	140-159	or	90-99
Hypertension, Stage 2	≥160	or	≥100

This classification is based on the average of two or more properly measured, seated BP readings on each of two or more office visits.

## Patient evaluation

The initial assessment of patients with HT begins with the medical history and physical examination. Routine laboratory tests include electrocardiogram, chest X-ray,

urine analysis, complete blood count, liver and renal function test, fasting blood glucose level and lipid profile. The objectives are to reveal identifiable causes of HT (table 2), assess other cardiovascular risk factors (table 3) and look for the presence of target organ damage (table 4). Further work up and other diagnostic test will depend on the results of initial assessment.

**Table 2. Identifiable causes of hypertension**

- Renovascular disease
  - renal artery stenosis
- Chronic renal disease
  - glomerulonephritis
  - polycystic disease
- Endocrine disease
  - Cushing's disease/syndrome
  - phaeochromocytoma
  - primary hyperaldosteronism
  - hyperthyroidism
  - hyperparathyroidism
  - acromegaly
- Aortic disease
  - coarctation of aorta
- Drugs
  - oral contraceptive
  - NSAIDs; cyclooxygenase 2 inhibitors
  - steroids
  - sympathomimetics (anorectics, decongestants)
- Sleep apnoea
- Excessive alcohol intake

**Table 3. Other major cardiovascular risk factors**

- Age (male older than 55 and female older than 65)
- Family history of premature cardiovascular disease (male under age 55 and female under age 65)
- Diabetes mellitus
- Hyperlipidaemia
- Cigarette smoking
- Obesity (body mass index ≥ 30 kg/m<sup>2</sup>)
- Estimated glomerular filtration rate <60 ml/min or microalbuminuria
- Physical inactivity

**Table 4. Target organ damage**

- Heart
  - left ventricular hypertrophy
  - heart failure
  - angina pectoris or prior myocardial infarction
  - prior percutaneous coronary intervention or bypass surgery
- Brain
  - transient ischaemic attack or stroke
- Peripheral arterial disease
- Chronic renal disease
- Retinopathy



## Treatment of hypertension

### Goals of therapy

The goal of antihypertensive therapy is to reduce the cardiovascular and renal morbidities and mortalities. Most patients, especially those at or above 50 years old, will reach the DBP goal once SBP is at goal. Therefore, the main focus should be on achieving the SBP goal. Treating SBP and DBP to levels that are <140/90 mmHg is associated with a reduction in cardiovascular complications. In patients with diabetes mellitus (DM) and renal disease, the BP goal should be <130/80 mmHg.<sup>3,4</sup>

### Non-pharmacological management of hypertension - lifestyle modifications

A healthy lifestyle is an important step for the prevention of HT and all person with preHT and HT should try to adopt a healthy lifestyle. Component of lifestyle modifications include weight reduction in patients who are overweight or obese, limit alcohol consumption for drinkers, regular exercise and diet adjustment. Weight loss is the most effective non-pharmacological measure for the treatment of HT.<sup>5</sup> Body mass index (BMI) should be maintained between 18.5 and 24.9 kg/m<sup>2</sup>. Alcohol consumption elevates BP both acutely and chronically. Clinical studies show that SBP falls by 2 to 4 mm with reduction in alcohol intake.<sup>6</sup> For unrelated health reasons, alcohol consumption is not recommended for nondrinkers; for drinkers, intake should be limited to 1 oz of alcohol per day (2 oz of 100-proof whiskey, 8 oz of wine, or 24 oz of beer) in most men and half that amount in women and small men.<sup>1</sup> At least 30 minutes of moderately intense physical activity, such as brisk walking, swimming, or bicycling, carried out at least 3 times per week (preferably once per day) can lower BP in hypertensive individuals. Studies suggest that such moderate activity may lower SBP by 4 to 9 mm Hg.<sup>7,8</sup> A diet low in sodium and high in fruits, vegetables, and calcium is also helpful in treating hypertension.<sup>9</sup>

### Pharmacological Treatment

#### Which class should be the first line medication?

There are abundant clinical data proved that lowering BP with different antihypertensive medications, including thiazide-type diuretics, beta-blockers (BBs), calcium channel blockers (CCBs), angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), will reduce the complication of hypertension.<sup>10</sup> In the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial<sup>11</sup> (ALLHAT, n = 42418), there was no difference in the rate of fatal CHD or non-fatal MI in patients assigned to chlorthalidone (thiazide-type diuretic), amlodipine (CCB) or lisinopril (ACEI). There was also no difference in the all cause mortality. The doxazosin (alpha blocker) arm was stopped prematurely because of a reported excess of cardiovascular events (principally congestive heart failure). Thiazide-type diuretics is generally well tolerated and it enhances the antihypertensive efficacy of most other drug classes. Together with their low cost, thiazide-type diuretics should be used as initial therapy for most patients with HT.

#### Is monotherapy adequate for the control of BP?

Most patients with HT will require 2 or more antihypertensive medications to achieve their BP goals.

In ALLHAT11, less than 30% of participants achieved goal BP (<140/90 mmHg) on monotherapy. A second drug from a different class should be added if a single drug in adequate dose fails to control the BP. For patients with BP >20/10 mmHg above goal, initial treatment with 2 drugs is recommended by JNC 7. The initiation of more than one drug offers the potential advantage of achieving goal BP faster and avoiding dose-related adverse effects of individual drugs by producing greater BP reduction at lower doses of the component agents. However, particular caution is advised in those persons at risk of postural hypotension such as some older patients and patients DM or autonomic dysfunction.

#### Are newer antihypertensive drugs better than older ones?

In the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm<sup>12</sup> (ASCOT-BPLA, n = 19257), patients were assigned either amlodipine +/- perindopril (ACEI) as required or atenolol +/- bendroflumethiazide as required. The amlodipine-based regimen significantly reduced fatal and non-fatal stroke, total cardiovascular events and procedures, and all-cause mortality compared with the atenolol-based (BB) regimen. Patients in the amlodipine group also had less non-fatal MI and fatal CHD but were statistically not significant. The difference in the outcomes may partly be related to better BP control in the amlodipine-based regimen (2.7/1.9 mmHg lower). Beta blockers are known to be ineffective for BP lowering in elderly patients and the results of the ASCOT-BPLA may just be reporting the inferiority of atenolol.<sup>13-15</sup>

#### Special considerations for patients with other comorbidities

Hypertensive patients with certain comorbidities may benefit from specific drug classes (Table 5).<sup>2</sup> The drug selections for these compelling indications are based on favourable outcome data from large clinical trial. Therapeutic decisions in such patients should be directed at both the compelling indication and BP lowering.

Table 5. Guidelines for treatment of HT based on compelling indications

Compelling indication	Recommended drug classes
- High coronary disease risk	Thiazide, BB, ACEI, CCB
- Post MI	BB, ACEI, aldosterone antagonist
- Heart Failure	Thiazide, BB, ACEI, ARB, aldosterone antagonist
- DM	Thiazide, BB, ACEI, ARB, CCB
- Chronic kidney disease	ACEI, ARB
- Recurrent stroke prevention	Thiazide, ACEI

## New definition and classification of HT proposed by American Society of Hypertension (ASH)

In order to identify and treat individuals who are at risk for CVD at an earlier point in the disease process, the writing group of the ASH has proposed a new definition and classification of HT in 2005.<sup>16</sup> Hypertension is defined as a progressive cardiovascular syndrome arising from complex and interrelated etiologies. Early markers of the syndrome are often present before blood pressure elevation is observed; therefore hypertension cannot be classified solely by discrete blood pressure



thresholds. Progression is strongly associated with functional and structural cardiac and vascular abnormalities that damage the heart, kidneys, brain, vasculature, and other organs, and lead to premature morbidity and death. The writing group omits the preHT category in JNC 7 and classifies individuals into normal, stages 1, 2, and 3 HT (Table 6). This classification emphasises that therapeutic decisions should base on global cardiovascular risk instead of a single risk factor (high blood pressure).

**Table 6. Classification of BP proposed by ASH**

Normal	People with 0 cardiovascular risk factors, no identifiable early CVD markers and no target organ damage. BP usually < 120/80 mmHg.
Stage 1	People classified as preHT according to JNC 7 who have cardiovascular risk factors or early disease markers, but no target organ damage. BP usually between 120/80 mmHg and 139/89 mmHg.
Stage 2 (JNC 7 stage 1)	People have BP $\geq$ 140/90 mmHg and/or $\geq$ 2 disease markers or evidence of early target organ damage.
Stage 3 (JNC 7 stage 2)	People have blood pressure $\geq$ 140/90 mm Hg and/or clinical evidence of overt target organ damage or CVD or have had cardiovascular events.

### Summary

Tight BP control is fundamental for prevention of CVD in patients with HT. A healthy lifestyle should be recommended to all individuals with preHT and HT. For hypertensive patients, the goal of treatment is to reduce the BP <140/90 mmHg and <130/80 mmHg for those with DM or chronic kidney disease. Thiazide-type diuretics should be used as initial therapy for most patients but majority of them will need 2 or more medications to achieve treatment goal. Specific drug classes may provide additional benefits for hypertensive patients with certain comorbidities besides BP lowering. Future development may focus on early initiation of pharmacological treatment to prevent progression of hypertension and reduce cardiovascular complications.

### References

- Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903-13.
- Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 Report. *JAMA*. 2003;289(19):2560-71.
- American Diabetes Association. Treatment of hypertension in adults with diabetes. *Diabetes Care*. 2003;26(suppl 1):S80-S82.
- National Kidney Foundation Guideline. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Kidney Disease Outcome Quality Initiative. Am J Kidney Dis*. 2002;39(suppl 2):S1-S246.
- National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. *Obes Res*. 1998; 6: 51S-209S.
- Xin X, He J, Frontini MG, et al. Effects of alcohol reduction on blood pressure. *Hypertension*. 2001; 38: 1112-7.
- Kelly GA, Kelly KS. Progressive resistance exercise and resting blood pressure. *Hypertension*. 2000; 35: 838-43.
- Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure. *Ann Intern Med*. 2002; 136: 493-503.
- Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med*. 2001;344:3-10.
- Turnbull F, Neal B, Algert C, et al. Effects of different blood-pressure-lowering regimens on major cardiovascular events: results of prospectively designed overviews of randomized trials. Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2003;362:1527-35.
- The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the antihypertensive and lipid lowering treatment to prevent heart attack trial (ALLHAT). *JAMA* 2002;288:2981-97.
- Dahlof B, Sever PS, Poulter NR, et al, for the ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet*2005;366:895-906.
- Duerden M.ASCOT-BPLA. *Lancet* 2006;367:206.
- Fuchs FD, Gus M, Ribeiro JP.ASCOT-BPLA. *Lancet* 2006;367:205.
- Donzelli A, Malliani A.ASCOT-BPLA. *Lancet* 2006;367:205-6.
- Giles TD, Berk BC, Black HR, et al; the Hypertension Writing Group. Expanding the definition and classification of hypertension. *J Clin Hypertens*. 2005;7:505-12.

### MCHK CME Programme Self-assessment Questions

Please read the article entitled "Current guidelines in the treatment of hypertension" by Dr. Yui-ming Lam and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 July 2006. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

- Hypertension is a major risk factor for coronary heart disease, heart failure, cerebral vascular disease and renal disease.
- Apart from hypertension, other major cardiovascular risk factors include old age, family history of premature cardiovascular disease, diabetes mellitus, hyperlipidaemia, cigarette smoking, obesity, impaired renal function and physical inactivity.
- According to JNC 7, a person with blood pressure of 130/85 mmHg is suffering from stage 1 hypertension.
- Weight loss is the most effective non-pharmacological measure for the treatment of hypertension.
- In hypertensive patients with diabetes mellitus or renal disease, the BP goal should be <130/90 mmHg.
- A diet low in sodium and high in fruits, vegetables, and calcium may help to reduce blood pressure
- According to JNC 7, beta-blockers should be the first line antihypertensive medication for most patients.
- In ALLHAT, there is no significant difference in the rate of fatal coronary heart disease, non-fatal MI and all cause mortality between patients treated with amlodipine, lisinopril or chlorthalidone.



9. In more than 2/3 of hypertensive patients, blood pressure can be adequately controlled by a single medication.
10. In ASCOT-BPLA, the amlodipine-based regimen significantly reduced fatal and non-fatal stroke, total cardiovascular events and procedures, and all cause mortality when compared with the atenolol-based regimen.

### ANSWER SHEET FOR JULY 2006

Please return the completed answer sheet to the Federation Secretariat on or before 31 July 2006 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

#### Current guidelines in the treatment of hypertension

**Dr. Yui-ming Lam** MBBS, MRCP(UK), FHKCP, FHKAM(Medicine)

*Department of Medicine, Queen Mary Hospital, The University of Hong Kong*

1  2  3  4  5  6  7  8  9  10

Name: \_\_\_\_\_ HKID No. \_\_\_\_\_ - \_\_\_\_\_ X X (x)

Signature: \_\_\_\_\_ Contact TelNo.: \_\_\_\_\_

#### Answers to June 2006 issue

#### Paediatric CT Radiation Risks: What you should know

1. F    2. T    3. T    4. F    5. T    6. F    7. F    8. F    9. T    10. T