

A case of hypertension

Jürgen Abela

You are consulted by MB, a 58 year old lady. She is single and works as a manager with a leading advertising agency, keeping up with a lot of deadlines. During the visit, which was mainly related to some minor elbow complaint, you discover a raised blood pressure of 170/95 mmHg. Subsequent visits confirm the raised blood pressure. She is known to suffer from dyslipidaemia, with a LDL-cholesterol of 4.5mmol/L and a total cholesterol of 6.3mmol/L. MB does not smoke. How would you manage this case?

Introduction

Hypertension is a common condition, and continues to be one of the most important causes of death and illness.¹ At a public health level, it is expected to increase in frequency and affect 1.5 billion people by 2025.² Hypertension is not only a disease in itself but also a strong risk factor for the development of cardiovascular disease (Figure 1 and 2). In fact it is estimated to be implicated in 35% of all atherosclerotic events.³

There is great benefit in treating hypertension which benefit should stimulate doctor and patient alike to strive for consistent control (Figure 3). Translated into NNT's (Numbers Needed to Treat), this means that:

- In the presence of hypertension and additional risk factors, a 12 mmHg reduction in Systolic BP (SBP) over ten years will prevent one death for every 11 patients treated
- In the presence of cardiovascular disease or target organ damage, only nine patients would require such BP reduction to prevent death.⁴

For some reason, it seems that this benefit is not being exploited to the full and it is estimated that less than 10% of patients with hypertension have their blood pressure adequately controlled.⁵

Definition

Blood pressure has a continuous (bell-shaped) distribution, with a continuous range of blood pressures from the lowest to the highest, with the majority in the middle. Thus defining what is "raised blood pressure" is a matter of contention, compounded by the fact that there is a proportionate increase in risk of cardiovascular disease with increasing levels of blood pressure. Such risks both increase with age.

Most guidelines regard **140/90 mmHg** as the threshold above which one can use the term hypertension. In special circumstances which are deemed to be at high risk of cardiovascular events, namely diabetes, chronic kidney disease or in the context of secondary prevention of cardiovascular disease, this threshold is lowered to **130/80 mmHg**. The USA guidelines of 2003 (JNC 7) have complicated the debate further by using the term "pre-hypertension".⁶ However this adds no benefit to the management; on the other hand it may cause undue anxiety in patients who are not hypertensive.

Jürgen Abela MD, MRCP
 Floriana Health Centre, Department of Primary Care, Malta
 Email: jurgena@maltanet.net

Once hypertension is confirmed, as is the case with our patient MB, one can proceed to:

1. Exclude any identifiable causes of the raised blood pressure (secondary hypertension).
2. Look out for concomitant cardiovascular disease and in the absence of a past history of cardiovascular events (as is the case with MB) carry out cardiovascular disease risk assessment.
3. Explain to the patient what is happening and arrive to an agreed management plan.
4. Offer treatment in a holistic way by using non-pharmacological as well as pharmacologic treatment. The treatment should be aimed at lowering the blood pressure as well as lowering the cardiovascular risk of the patient as much as possible.
5. Offer a follow-up service which is acceptable to the patient.

Essential vs Secondary Hypertension

Of all patients diagnosed with hypertension, 95% fall in the category of essential (or idiopathic) hypertension, while 5% will fall in the category of secondary hypertension. In the latter category there is usually a well-defined disease process or contributory factor which would raise the blood pressure (Table 1). Over the last few years, there has been increasing awareness about the importance of the Renin-Angiotensin System (RAS) as the mechanism for essential hypertension. This hormonal axis even contributes to the differences seen between races in the expression of hypertension, response to treatment regimens and potential complications.⁷

The problem is how to identify the patients who will fall in each category. Many guidelines quote age as an important determinant; the younger the patient, the higher the probability of secondary hypertension. While this is certainly true, problems arise in defining the cut-off age limit, and what to do with patients who are close to this age limit.

A more pragmatic approach involves using age as an important guiding tool but aiding oneself with a good systemic

enquiry and general examination, especially in the first visit. Besides reassuring the patient, this will help guide the clinician to focus on the necessary investigations. As a routine, the European Society of Hypertension (ESH)⁸ suggests the following baseline investigations in all hypertensive patients:

- ECG
- Complete blood count
- Serum electrolytes, creatinine, liver function tests
- Fasting lipid profile and fasting plasma glucose
- Urine analysis

The ESH guidelines go even further and suggest that each hypertensive patient should have an echocardiogram and carotid ultrasound. However, this may not be practical, and is often reserved as second line investigations in cases with specific signs and symptoms.

Cardiovascular risk assessment

Following the initial diagnostic work-up, the cardiovascular risk of the patient may be calculated. As is well known, the more risk factors present, the higher is the risk of developing cardiovascular disease, their effect being synergistic.

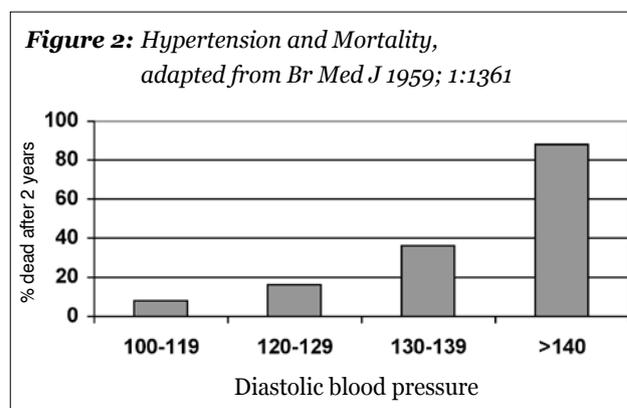
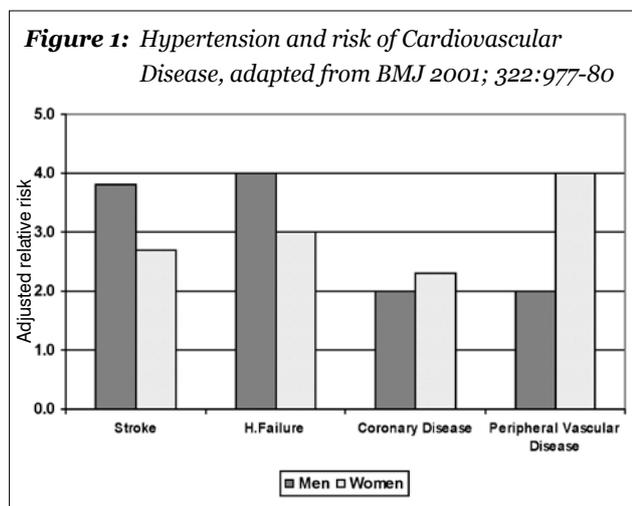
The aim of carrying this risk assessment is twofold, as it:

- Allows proper evaluation and tailoring of treatment to the individual.
- Can be used as an educational tool, motivating the patient to improve his position with regard to risk.

There are various charts available, the two most commonly used being the SCORE charts and charts derived from the Framingham cohort. Both use systolic blood pressure as an index, as this has been shown to be an important determinant of cardiovascular risk.⁹

Certain situations are deemed high risk by definition. These are listed below:

- Diabetes (coined as *coronary disease equivalent* for the first time by the National Cholesterol Education Programme of the USA)¹⁰
- Chronic kidney disease



- Familial hypercholesterolaemia and related inherited disorders
- Past history of cardiovascular disease (e.g. transient ischaemic attack, cerebrovascular accident)
- Associated clinical condition (e.g. peripheral vascular disease).

Admittedly, these risk estimation charts are not complete, and although they contain a relation of the major risk factors related to BP (age, systolic blood pressure level, smoking, gender and cholesterol level), they have certain well-noted limitations – they tend to underestimate the risk in younger patients and do not take into consideration other risk factors such as sedentary lifestyle, family history and obesity. Besides, they do not address the variation in risk between different ethnic groups.

Some guidelines stratify patients according to blood pressure levels and number of risk factors present (JNC 7 and ESH). However, they are often rather cumbersome to use and not quite patient-friendly.

Explanation to patient and choosing an agreed management plan

Due to the poor control of hypertension, this step is very important, since it will definitely motivate the patient. Admittedly, with a busy clinic, clinicians can easily fall in the trap of “dishing out” the fanciest drug of the moment, omitting to explain why the patient needs to be treated and why the particular drug was chosen.

It is estimated that up to 50% of patients do not abide by their treatment schedule. Benson and Britten have highlighted the fact that there are a variety of reasons for not taking treatment.¹¹ Contrary to what many doctors think, side effects are not the only reason for not taking prescribed medication. In one study, only one out of 38 patients interviewed declared that he/she was taking treatment for the benefits related to lowering blood pressure.

It is important to consider also the practical side of treatment namely that all guidelines are based on data obtained in trial settings. Targets set are difficult to achieve even in trial settings; in the recent ASCOT (Anglo-Scandinavian Clinical Outcomes Trial) study, only 32% of patients with diabetes and 60% of patients without diabetes achieved the recommended targets.¹²

Extrapolating standards and treatment protocols from trials to everyday life seems a rational step; however this is often not so and here is where many guidelines may be regarding as failing.¹³ Financial aspects to treatment, motivation, lack of follow-up and inadequate communication between patient and clinician are possible causes why this extrapolation is not so easy to make.

Table 1: Causes and Contributory factors in Hypertension, adapted from JNC 7 and the European Hypertension Society Guidelines for Primary Care Physicians)

Causes

- Drugs e.g. NSAIDs, OCP's, steroids, liquorice, sympathomimetics
- Renal Disease – past present or family history
- Renovascular disease
- Pheochromocytoma
- Conn's Syndrome
- Coarctation of the aorta
- Cushing's syndrome

Contributory Factors

- Overweight
- Excess alcohol
- Excess salt intake
- Lack of exercise
- Environmental Stress

NSAIDs – non-steroidal anti-inflammatory drugs
OCP – oral contraceptive pill

Figure 3: Event reduction with controlled hypertension, adapted from the J Hypertens 2003; 21:10

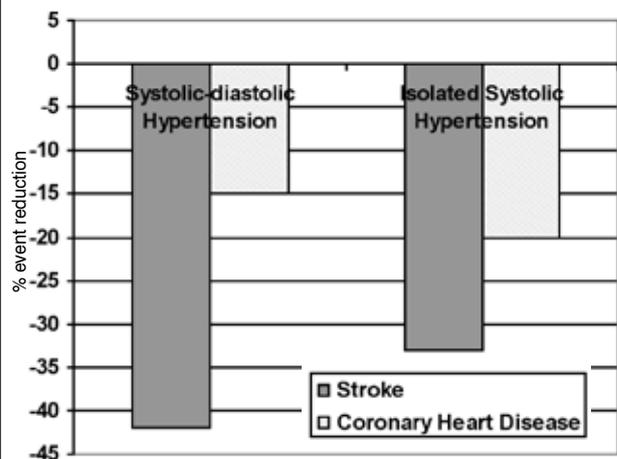
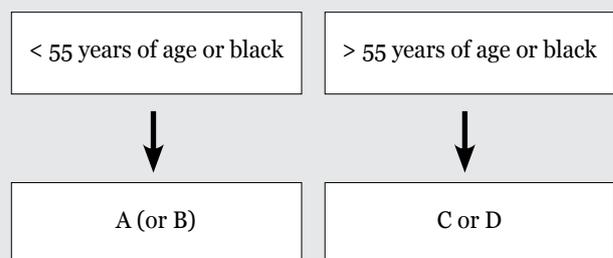


Figure 4: A(B)CD for initial drug prescribing, adapted from J Hum Hypertens 2004; 18:139-185



NB – A = ACEI or ARB; B = beta blocker; C = Calcium channel blocker; D = Thiazide diuretic. Recent evidence suggests that beta blockers are no longer regarded as first line therapy except in special circumstances (NICE 2006)

Treatment

The aim of treatment in the context of hypertension is to lower the overall cardiovascular risk, besides lowering the blood pressure. There are two fundamental components to treatment:

- Lifestyle modifications
(Therapeutic Lifestyle Changes – TLCs)
- Pharmacological treatment.

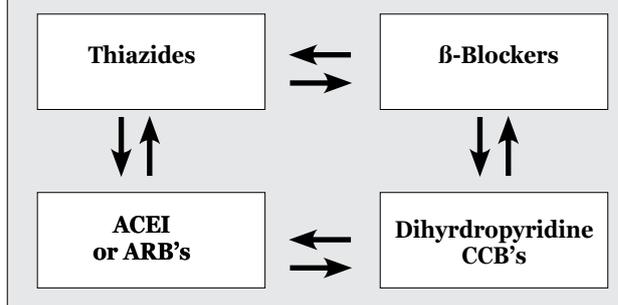
Therapeutic Lifestyle Changes (TLCs)

The adoption of TLCs in the management plan will further increase the efficacy of any medications administered, lower further the cardiovascular risk of the patient, and most importantly empower the patient in the management of his disease. Admittedly, because of many social pressures, such TLCs are sometimes difficult to achieve.

TLCs include:

1. *Weight reduction in overweight or obese patients, aiming at a body mass index (BMI) of 20 – 25.*
2. *DASH (Dietary Approaches to Stop Hypertension) eating plan.* This type of eating plan is poor in fats and cholesterol and rich in potassium, calcium, magnesium,

Figure 5: The Birmingham Hypertension Square,
adapted from *J Hum Hypertens* 1998; 12: 761-3



protein and fibre, through consumption of fruit, vegetables and low-fat dairy products.

3. *Restricting dietary sodium* is well known to reduce blood pressure effectively.
4. *Physical activity.* Regular physical activity has been shown to lower significantly both systolic and diastolic blood pressure levels.¹⁴
5. *Moderation in the consumption of alcohol*
Smoking cessation does not *per se* lower blood pressure, but it lowers the overall cardiovascular risk.

Table 2: Compelling indications and contraindications of the major drug classes

Drug Class	Indications	Contraindications
Thiazide diuretics	ISH, heart failure, elderly	Gout; also associated with increased incidence of diabetes especially when combined with a beta blocker
β-Blockers	Angina, post-MI, possibly in heart failure at reduced dosage, tachyarrhythmias, women of child bearing age	Asthma, COPD, PVD; also associated with increased incidence of diabetes especially when combined with a thiazide diuretic
Calcium channel blockers (dihydropyridine group)	ISH, elderly, Angina, PVD, pregnancy, hyperlipidaemia	
Calcium channel blockers (non-dihydropyridine group)	Angina, tachyarrhythmias	Heart block, heart failure, never to be combined with beta blockers
ACEI	Heart failure, post-MI, type I diabetic nephropathy, LVD, hyperlipidaemia	Pregnancy, bilateral renal artery stenosis, PVD
ARBs	Heart Failure, Diabetic nephropathy, ACEI induced cough, LV dysfunction, hyperlipidaemia	Pregnancy, PVD, renovascular disease
α-Blockers	Prostatic Hyperplasia; hyperlipidaemia; third line add-on agent	Heart failure, orthostatic hypotension

COPD – Chronic Obstructive Pulmonary Disease; PVD – Peripheral Vascular Disease; LVD – Left Ventricular Dysfunction; ACEI – Angiotensin Converting Enzyme Inhibitor; ARB – Angiotensin Receptor Blocker; ISH – Isolated Systolic Hypertension; post-MI – post Myocardial Infarction

Pharmacological Treatment

This can be divided into two major classes:

- Drug therapy to lower cardiovascular risk
- Drug therapy to lower blood pressure.

Drugs lowering cardiovascular risk

Aspirin and **statins** are the two drug classes commonly used in this setting. Aspirin has been well documented to prevent cardiovascular events in the context of secondary prevention.¹⁵ In the primary prevention settings, there is some debate as to when to prescribe aspirin, but a sensible approach would be to give aspirin to patients who are deemed high risk (e.g. diabetes) or who have a cardiovascular risk of more than 5% (for SCORE charts) or 20% (for Framingham charts) in the next ten years.

As regards statins, numerous trials have shown that they have a beneficial effect on the cardiovascular system which goes beyond the lipid lowering effect. In the context of secondary prevention it has been adequately shown that statins are beneficial even when cholesterol levels are within acceptable ranges.¹⁶

As regards primary prevention, again, prescribing should be guided by the cardiovascular risk since there is no consensus as to the lipid levels adequate for prescribing; the trend is that with each set of guidelines issued, the prescribing threshold is lowered further. However it sounds reasonable that patients with cardiovascular risk of less than 5% (SCORE) or 20% (Framingham) over the next ten years should be prescribed a statin, if their total cholesterol is >5.0 mmol/L or LDL-cholesterol >3.0 mmol/L in the absence of a compensatory high HDL cholesterol level.

Blood pressure-lowering treatment

All major drug classes have been shown to be more or less equally effective in lowering blood pressure.¹⁷ The major benefit with the exception of particular situations is mostly derived from the actual blood pressure lowering, rather than the drug class used. In recent head-to-head comparisons β -blockers have done worse than all other drug classes and they are being side-lined as first line therapy except in certain situations such as angina or in the aftermath of myocardial infarction.¹⁸

The last few years have seen an array of trials being carried out with the intent of studying various drug classes and their beneficial effect. There are still many heated debates about the preferred first line drug and whether to use drug combinations or not.

The issue of preferred first line treatment is slowly being clarified. This issue is a non-issue in itself, since many patients will need more than one medication to effectively lower their BP. After the ALLHAT study, it was concluded that thiazides should be used as first line;¹⁹ but recently there has been an increased awareness of the racial differences in hypertension, and such blanket statements are not very accurate. In fact the most recent NICE guidelines have adopted the BHS 2004 model of A(B)CD

(Figure 4), contrary to the JNC 7 and the ESH guidelines, both of which were issued in 2003. The A(B)CD model reflects the difference in response between individuals, due to different mechanisms causing hypertension; black people and elderly individuals tend to have low renin levels, and thus respond better to calcium channel blockers or thiazide diuretics; while younger people and white population tend to have high renin levels and respond better to RAS blockers such as angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARBs).

Further additions of drugs should be done according to recognized beneficial drug combinations (Figure 5).

As regards fixed drug combinations, they should ideally be used once the patient is stabilized and any side effects of the individual components monitored adequately. These fixed drug combinations certainly encourage compliance.

Table 2 summarizes the major indications and contraindications in line with recent evidence from trials. Moxonidine and Rilmenidine, are centrally acting agents which are useful especially in resistant hypertension. Further longitudinal studies of mortality and morbidity are needed for both drugs.

Follow-up

During follow up visits, it is important to cover a number of issues including:

- a. Blood pressure response to treatment
- b. Discuss side effects from medications
- c. Encourage the patient to continue with a successful treatment plan
- d. Look out for complications
- e. Discuss any difficulties which may crop up.

As regards follow-up, this needs to be agreed with the patient. Generally, people are now very conscious about hypertension, and in some cases, the concern verges on the obsessional. There are no fixed time frames recommended for follow-up frequency and this depends on the individual case, with co-morbidities and need of laboratory tests usually influencing the frequency of visits.

However, in routine cases it would be ideal to monitor at monthly intervals until the blood pressure settles to an acceptable level. High BP levels would warrant a more frequent **initial** review. Following attainment of the target blood pressure, it is recommended that follow-up visits should be carried out on a **three-to-six month interval basis**. There is no difference in control obtained between three month follow-up or six month follow-up²⁰ and ultimately, individual clinical judgement should prevail.

In this particular case

Since MB has been confirmed to have hypertension through serial readings, it would be advisable to carry out some baseline biochemical assessment and ECG as outlined above. Once

the results are known, then treatment can be initiated. It is important to emphasise the need of regular exercise and to adopt a healthy way of eating (small portions spread throughout the day and a diet low in salt and saturated fats). Her CVD risk is less than 5% for the next five years (SCORE charts). Hence there is no need to start aspirin. It would seem sensible to start MB on a calcium channel blocker (given the high systolic value) and proceed to combining it with an ACEI given that both of these drugs are lipid neutral. If she fails to lower her cholesterol through TLCs, one could give a low dose statin (e.g. simvastatin 10mg) to lower her cholesterol and in so doing lower also her cardiovascular risk.

References

- Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ; Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet*. 2002 Nov 2;360(9343):1347-60
- Kearney PM, Whelthorn M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005; 365:217-23
- Kannel WB. Blood Pressure as a cardiovascular risk factor: prevention and treatment. *JAMA* 1996; 275: 1571-6
- Ogden LG, He J, Lydick E, Whelton PK. Long-term absolute benefit of lowering blood pressure in hypertensive patients according to the JNC VI risk stratification. *Hypertension* 2000; 35: 539-43
- Primates P, Brookes M, Poulter NR. Improved hypertension management and control: results from the health survey for England 1998. *Hypertension* 2001;38(4):827-32
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL 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;289:2560-72
- Morris B. Hypertension and ethnic group. *BMJ* 2006;332:833-36
- Practice Guidelines Writing Committee. Practice Guidelines for Primary Care Physicians: 2003 ESH/ESC Hypertension Guidelines. *J Hypertens* 2003;21:10
- Prospective Studies Collaboration. Age-specific relevance of usual BP to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet* 2002;360:1903-1913
- Third report of the National Cholesterol Education Programme (NCEP). Expert panel on detection, evaluation and treatment of high blood cholesterol in adults (ATP III) final report. *Circulation* 2002;106:3143-421
- Benson J, Britten N. Patients' decisions about whether or not to take antihypertensive drugs: qualitative study. *BMJ* 2002;325:873-8
- Dahlof B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, et al. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendrofluzide as required in the Anglo Scandinavian Clinical Outcomes Trial – Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomized controlled trial. *Lancet* 2005;366:895-906
- Mant J, McManus RJ, Hare R. Applicability to primary care of national guidelines on blood pressure lowering for people with stroke: cross sectional study. *BMJ* 2006;332:635-7
- Little P, Margetts B. The importance of diet and physical activity in the treatment of conditions managed in general practice. *BJGP* 1996;46:187-92
- Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomized trials of anti-platelet therapy for prevention of death, myocardial infarction and stroke in high risk patients. *BMJ* 2002;324:71
- MRC/BHF Heart Protection Study Collaborative group. MRC/BHF Heart Protection Study of cholesterol lowering with Simvastatin in 20536 high risk individuals: a randomized placebo controlled trial. *Lancet* 2002;360:7-21
- Blood Pressure Lowering treatment Trialists' Collaboration. Effects of blood pressure lowering regimens on major cardiovascular events: results of prospectively designed overviews of randomized trials. *Lancet* 2003;362:1527-45
- The National Collaborating Centre for Chronic Conditions. Hypertension – Management of hypertension in adults in primary care: partial update to NICE 2004. Available from <http://www.nice.org.uk>
- 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;356:1955-64
- Birtwhistle RV, Godwin MS, Delva MD, Casson RI, Lam M, MacDonald SE, et al. Randomized equivalence trial comparing three month and six month follow-up of patients with hypertension by family practitioners. *BMJ* 2004; 328: 204-10