# HOW WOULD I MANAGE A 40-YEAR-OLD BANK EXECUTIVE WITH A BLOOD PRESSURE OF 145/85?

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## INTRODUCTION

Hypertension can be defined pragmatically as that level of blood pressure above which the use of antihypertensive treatment does more good than harm. For many years, the institution of antihypertensive therapy was recommended only for blood pressures in excess of 160/90 mmHg. Indeed, until recently the recommendations of the British Hypertension Society still used this arbitrary cut-off value.[1] Blood pressure levels, however, are continuously related to the risk of cardiovascular disease, and even within the normotensive range, patients with the lowest levels of blood pressure have the lowest rates of cardiovascular disease.[2] Even the concerns about a 'J-curve', where mortality increases with lower blood pressure levels, have been considerably allayed by the recent publication of the Hypertension Optimal Treatment (HOT) study, which does suggest that we should be aiming for treated blood pressures lower than previously recommended.[3] This has led to modifications in previously published guidelines, with an introduction of the concept of 'absolute risk' for cardiovascular disease, and careful assessment of associated co-morbidity (such as diabetes) and hypertensive 'target organ damage'.[4,5] If either diabetes or target organ damage are present, more aggressive management of hypertension is now recommended.

Many national and international surveys reveal that hypertension is underdiagnosed, that those diagnosed are often not on therapy, and that many of those treated are inadequately controlled.[6-8] In particular, the Health Survey for England reported that the detection and management of hypertension in the United Kingdom remains far from optimal.[8] The symptomless nature of the disease means that many patients with hypertension remain undiagnosed, and once diagnosed often wonder why they need to take antihypertensive therapy for the rest of their lives. With the increasing age of the general population, the prevalence of hypertension (and its complications) is likely to rise rather than decrease, with increasing implications for health-care provision.

## INITIAL CONSULTATION

The aims of the initial consultation are to establish a firm diagnosis of hypertension, to exclude or identify secondary causes of hypertension, to determine the presence of target organ damage and define its extent, and to look for other cardiovascular risk factors and conditions which may influence prognosis.

As hypertension is essentially an asymptomatic disease, it is of vital importance to establish good rapport with the patient from the outset, explain the rationale for investigation, treatment and follow-up, so as to diminish the problems of non-compliance and patients being lost to follow-up.

Measurement of blood pressure should be meticulously performed on several occasions with the patient in the sitting position, using either a mercury sphygmomanometer or a validated non-invasive electronic blood pressure measurement device (for example, the OMRON HEM 705CP), which has passed tests of accuracy suggested by the British Hypertension Society. The patient should always be allowed to sit for several minutes prior to measuring the blood pressure. An 'alternative adult' cuff with a rubber bladder of 13 cm x 35 cm (or greater, 15 x 30 cm, if to be used on obese arms with arm circumference >33 cm) should be applied and placed at the level of the heart. Furthermore, Korotkoff Phase 5 (disappearance) sounds should always be used to measure the diastolic pressure.

As a minimum set the following initial investigations would be performed: (1) urinalysis for blood, protein and glucose; (2) measurement of serum potassium, creatinine, glucose and cholesterol levels; and (3) a 12 lead ECG. Not all centres would routinely perform 24-hour urinalysis in all patients, but as urinary sodium excretion reflects sodium consumption, this can give useful information regarding compliance with a low salt diet. Guidance for further investigations should come from the clinical history, a full physical examination and routine investigations. Indeed, more detailed investigation should be considered for those in whom a clinical suspicion of an underlying cause of hypertension exists, those with moderate to severe hypertension (especially if they fail to respond to treatment), young hypertensives (<35 years old), those with raised serum creatinine, abnormal urinalysis (with blood, protein or cells), or hypokalaemia or those who have a large postural drop in blood pressure.

## RISK STRATIFICATION

Treatment of hypertension is aimed at reducing future cardiovascular events, and therefore assessment of other risk factors is important for decisions regarding management.

Several different methods for assessing cardiovascular risk have been proposed. It is clear that intuitive estimates of risk are very inaccurate.[9] The British Hypertension Society recommends the use of a computer program or a coronary heart disease risk chart, both of which are based on the Framingham risk function.[10] These programs may not be widely available in clinics, and for this specific use, the more simplified table recommended in the WHO/ISH hypertension guidelines may be more applicable.[4] For the purposes of further discussion, 'low-risk' refers to a ten-year risk of stroke, or myocardial infarction below 15%, 'medium-risk' - 15-20%, 'high-risk' - 20-30% and 'very high-risk' at 30% or greater.

To stratify risk, the smoking history, the presence of

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hypercholesterolaemia (total cholesterol >6.5mmol/l) and family history of premature cardiovascular disease can help segregate this 40-year-old bank executive (assuming his blood pressure remains at 145/85mmHg) into low-risk (no risk factors), medium-risk (one to two risk factors) or high-risk (all three risk factors). The presence of diabetes or target organ damage - such as left ventricular hypertrophy, proteinuria, mild renal dysfunction, evidence of atherosclerotic plaques and hypertensive retinopathy - would also place this man in a 'high-risk' group. If there was evidence of cerebrovascular disease, ischaemic heart disease, symptomatic peripheral vascular disease or renal dysfunction then he would fall into the 'very high-risk' group.

## MANAGEMENT

In all patients, regardless of level of risk, institution of lifestyle measures is appropriate. These include: smoking cessation, weight reduction, moderation of salt intake and of alcohol consumption, and increase in physical activity or regular exercise.

In patients at 'high-risk' of cardiovascular events, pharmacological therapy should be instituted, to achieve a target blood pressure of <140/85mmHg (130/80mmHg in diabetics).[10] In those at 'medium-risk' further reassessment over three to six months is recommended, with institution of pharmacological therapy if the blood pressure remains greater than 140/85 mmHg. In the 'low-risk' group it is probably adequate to reassess in six to 12 months, with institution of therapy if the blood pressure still remains high.

Nevertheless, the ideal antihypertensive pharmacological strategy has yet to be determined. Reduction in cardiovascular events associated with blood pressure reduction is not related to the properties of a particular drug rather than to the reduction in blood pressure *per se*. More evidence of mortality and morbidity benefit is in print about the older classes of antihypertensive drugs, such as the thiazides and beta-blockers, than there is with the more modern drugs, such as the calcium antagonists or the ACE inhibitors, but evidence for use of the latter classes is accumulating.

### *Antihypertensive agents*

The choice of particular drug type depends upon the presence of co-existing disease, the patient's age, race and sex and economic implications.

Regardless of the initial choice of antihypertensive agent, certain general principles apply. To reduce side-effects, drugs should be started at a low dose. The use of long-acting, once-daily preparations is generally recommended, in order to improve compliance, and prevent large fluctuations in blood pressure which can be dependent upon wide variation in circulating concentrations of the antihypertensive agent.

In general, as the prevalence of hypertension in the Western world exceeds 25% of the population, prescription of the least expensive drugs will result in significant savings in health care expenditure. The thiazides and beta-blockers are the least expensive agents, and as both have extensive trial data supporting their usage, they should probably form first-line therapy unless they are contraindicated in the particular individual. Thiazides should be avoided in gout, and in sexually active males, whilst the beta-blockers should be avoided in asthma. The calcium antagonists are more expensive, but were shown in more recent studies of isolated systolic hypertension to have mortality and morbidity benefits. They have relatively few contraindications, but can often lead to troublesome oedema. The calcium channel blockers also tend to be more effective than beta-blockers and ACE inhibitors as monotherapy in black hypertensive patients.

At present, the long-term outcome data for antihypertensive drugs such as the ACE inhibitors and angiotensin receptor antagonists, which act primarily on the renin-angiotensin system are less extensive, but good theoretical reasons exist for prescribing these drugs in diabetic patients. These compounds, especially the ACE inhibitors, are the drugs of choice in patients with reduced left ventricular function, for example, as a result of previous myocardial infarction. Angiotensin II antagonists are useful antihypertensive agents, with a good side-effect profile - in particular, they rarely have the troublesome dry cough commonly seen with the ACE Inhibitors. Black/Afro-Caribbean hypertensive individuals respond less well to drugs acting on the renin-angiotensin system, and these patients often require between two and four times the dose of ACE inhibitor to achieve a response similar to that observed in non-black patients. This apparent resistance to therapy is due to the tendency towards a low-renin, salt-sensitive state and a lower cardiac output, with increased peripheral resistance. These differences disappear when higher doses of the ACE inhibitors, angiotensin receptor antagonists and beta-blockers are used, or if a diuretic is used in combination with these agents. Younger black patients also tend to be more responsive than the elderly, as a result of their tendency to show normal renin levels. The potentially life-threatening complication of ACE inhibitor induced angioedema is four- to five-fold more common in black patients.

The final major drug class, alpha-adrenoceptor blockers, again have little outcome data published on them, and their first-line use should probably be restricted to males with prostatic symptoms. Unfortunately it is the effect on the urinary tract (stress incontinence) which prevents more extensive use in females.

### *Aspirin*

The use of low-dose aspirin in hypertension is more contentious. The recent HOT study suggested that aspirin (75 mg) should be used in patients whose blood pressure is well controlled on therapy, who are at high risk of cardiovascular events and who are at low risk of bleeding.[3] Whilst there appeared to be a significant reduction in the incidence of myocardial infarctions, aspirin did not reduce the incidence of stroke, and also resulted in an excess of gastrointestinal bleeding.

### *Lipid-lowering therapy*

The HMG-CoA reductase inhibitors (statins) have been shown in primary and secondary prevention studies to reduce major cardiovascular events, with subgroup analysis demonstrating similar benefits in hypertensive patients. The current guidelines are fairly conservative, but recommend prescription of statins to those with a total cholesterol >5.0 mmol/l and either previous vascular disease, familial hypercholesterolaemia, or perceived to be at very high risk of cardiovascular events (>30% at ten years).[10] Ongoing studies, such as the ALLHAT and ASCOT trials will establish the value of lipid-lowering therapy in hypertensive patients.

FOLLOW-UP

By the time of subsequent visits, the initial investigations should be available, and these may suggest the need for further investigations. For example, a low serum potassium should prompt renin and aldosterone measurements to exclude the possibility of an underlying Conn's syndrome. The response to therapy should also be reassessed, and the patient asked specifically about side-effects. This is important as many patients will not openly volunteer sexual dysfunction or incontinence caused by their drug therapy.

If the drug is well tolerated, and there is a reasonable reduction in blood pressure, but the blood pressure still falls short of treatment goals, then an increase in the dose is sensible. If there is little response, or if the patient is intolerant of the first agent, it should be substituted with an alternative antihypertensive agent. Many antihypertensive drug combinations are synergistic, and therefore it is often preferable to add in a second agent rather than increasing the dose of the first agent. This has the added advantage of using drugs at low dose, thereby decreasing the chance of the adverse effects with high dose monotherapy. The problem of poor compliance on multi-drug regimens has been aided by the increasing availability of fixed low-dose combinations, such as Zestoretic (lisinopril plus thiazide), Cozaar Comp. (losartan plus thiazide) or Tarka (trandolapril plus verapamil).

There are logical add-on therapies and less logical combinations, and appropriate synergistic combinations are demonstrated in the 'Birmingham Hypertension Square' for add-in drugs in the management of hypertension (Figure 1). For example beta-blockers work well with the dihydropyridine calcium antagonists, and by offsetting tachycardia and sympathetic stimulation, they may actually reduce side-effects. Good evidence exists of synergy between the thiazide diuretics and the beta-blockers, the ACE inhibitors and the angiotensin II receptor antagonists. Similarly, the calcium antagonists work well in combination with the classes of drugs which block the generation or effects of angiotensin II.

By contrast there are some drug combinations which are not particularly effective and some may be unsafe. Little synergy exists between thiazide diuretics and the dihydropyridine calcium antagonists. The addition of an ACE inhibitor to a beta-blocker also tends to be less effective because the beta-blockers will already have blocked renin release. Using the Birmingham Hypertension Square, the clinician should opt to approach the Square from any corner, with first-line drugs chosen logically. The optimal second-line agents are immediately adjacent and indicated by the arrows.

We would consider 24-hour ambulatory blood pressure monitoring (ABPM) at the second or subsequent visits if there were features to suggest 'white coat' hypertension, if there was unusual variability of blood pressure readings, when symptoms suggest the possibility of hypotension, or if the blood pressure was still greater than 150/90 mmHg on a regimen of three or more antihypertensive agents. 'Routine' ABPM is not indicated in patients with evidence of hypertensive target organ damage, or in patients at high cardiovascular risk, as such patients will require treatment. Similarly, in patients with borderline or mild hypertension, no target organ damage and low cardiovascular risk, ABPM is probably unnecessary as these patients will not require urgent initiation of pharmacotherapy. It should be noted that all outcome trials in hypertension have been based on clinic blood pressure measurement, and guidelines on usage of ABPM to guide treatment are still lacking.

## BIRMINGHAM HYPERTENSION SQUARE

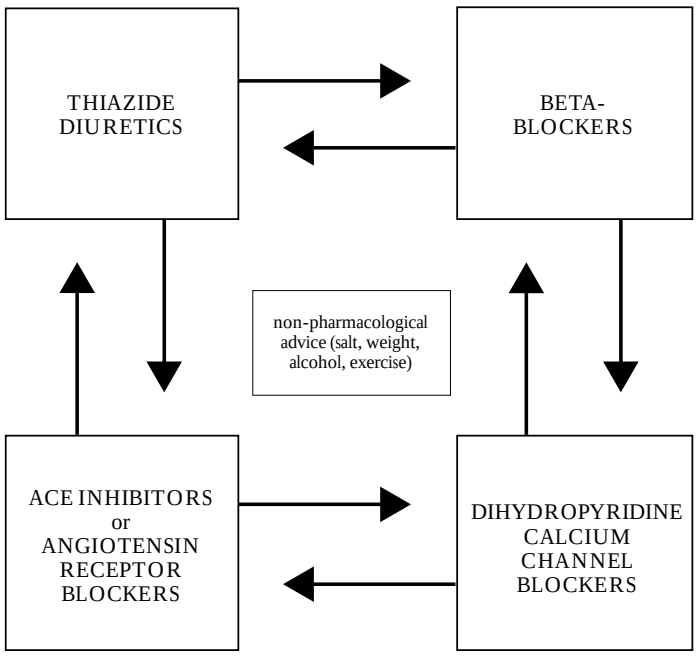


FIGURE 1
The 'Birmingham Hypertension Square' for the optimal choice of add-in drugs for the management of resistant hypertension. Regardless of which drug is initially used as monotherapy, logical add-on drugs are dictated by the directional arrows.

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