HE latest joint guidelines on the management of arterial hypertension from the European Society of Hypertension and the European Society of Cardiology follow on from the recently published guidelines of the UK National Institute for Health and Clinical Excellence (NICE), the Joint British Societies and the American JNC 7 guidelines, and the just-published American Heart Association Scientific Statement for the Treatment of Hypertension in the Prevention and Management of Ischaemic Heart Disease.

Hypertension is being misdiagnosed in as many as a third of all patients attending for routine blood pressure measurement.

In empathy with our colleagues in general practice who have to wrestle with this bevy of recommendations (as well as many other guidelines), Jan Staessen and I have to wrestle with this bevy of recommendations (as well as many other guidelines), while undoubtedly based on evidence, also reflects the complex relationship between the influence of respective authorities in the process and the bias of their individual interests, which ultimately influences the final interpretation of data. This failure to update all multi-authored guidelines, and the European guidelines are no better, or worse, than others in this regard. The fact is that doctors who follow guidelines "should realize that recommendations can never replace sound clinical judgment or take precedence upon the personal interaction between patient and doctor." In the following brief review of the European guide line, I have of necessity confined to areas where I believe guidance that was lacking previously is now provided, but I will also highlight aspects of hypertension management that in my opinion, have not been addressed adequately.

**Definition of hypertension**

Systolic and diastolic blood pressures are independently and similarly predictive of stroke and coronary mortality, and both must be taken into account in defining hypertension. The contribution of pulse pressure to outcome is small, particularly in individuals aged less than 55 years, whereas, in middle aged and elderly hypertensive patients with cardiovascular risk factors or associated clinical conditions, pulse pressure shows a strong predictive value for cardiovascular events. Blood pressure has a unimodal distribution in the population and the relationship with cardiovascular risk is continuous down to systolic and diastolic levels of 115-110mmHg and 75-70mmHg, respectively. For various well-founded reasons, the European guidelines do not adopt the American JNC 7 guideline approach to unifying the normal and high normal blood pressure categories into a single entity termed 'prehypertension'. The European classification is shown in Table 1.

**Blood pressure measurement**

According to the WHO, about 1 in 3 adults worldwide has high blood pressure, and an additional 1 in 3 with high-normal blood pressure is confirmed when measured a second time. The guidelines advise against the use of a single measurement to confirm hypertension because there is a 10% chance that it will be missed (false negative) by the clinician, particularly if there is no other information available. Blood pressure measurement must be repeated at least two times, preferably in the morning and evening. Missed visits and equipment failure may also occur, and the automatic measurement on a single visit can be grossly inaccurate but which still forms the basis of definitions and classifications as listed in Table 1. Is there any other test in use in medicine with such a provenance? There might be some excuse for persisting to use an inaccurate technique if we had no other methodology. But the European guideline states that cross-sectional and longitudinal studies have shown that office blood pressure has a limited relationship with 24-h ambulatory blood pressure measurement (ABPM) which: (i) correlates with hypertension-related organ damage and its changes by treatment more closely than does office blood pressure; (ii) has a relationship with cardiovascular events that is dependent on a measure of daytime and nighttime pressure, and (iii) measures more accurately than clinic blood pressure the extent of blood pressure reduction induced by treatment, because of a higher reproducibility over time and an absent or negligible white-coat effect.

One would have thought that these advantages should lead to the logical recommendation of the automated technique as the preferred method of measurement. But no — the guideline ignoring the above, goes on to recommend "multiple blood pressure measurements, taken on separate occasions over a period of time" to overcome the "large spontaneous variations both during the day and between days, months and seasons".

The guideline further acknowledges that white-coat hypertension (individuals with elevated office blood pressures and normal daytime ABPM) is a masked hypertension (individuals with normal office blood pressures and elevated daytime ABPM), each of which has no distinguishing clinical characteristics, may each occur in some 15 percent of the population. This leads to the salutary conclusion that hypertension is being misdiagnosed in as many as a third of all patients attending for routine blood pressure measurement. If we are going to base guidelines on recommendations on evidence, surely the time has come when the recommendations from experts must be that doctors who are prepared to diagnose and treat hypertension with or without the benefit of ABPM are in breach of best clinical practice.

**Hypertension within the total risk profile**

Though hypertension is listed by the WHO as the first cause of death worldwide, elevated blood pressure should never be managed in isolation from other relevant risk factors, such as dyslipidaemia, smoking, diabetes, etc. Evidence is now available that in high-risk individuals thresholds and goals for antihypertensive treatment, as well as other treatment strategies, should be different from those recommended in lower risk individuals. The European categorization of total risk as low, moderate, high and very high added risk has the merit of simplicity; the term added risk refers to the risk additional to the above average one (see Figure 1).

**Target organ damage**

A key concession of the European guideline is devoted to searching for subclinical organ damage where evidence for the additional risk of each subclinical alteration is absent and the proposed cut-off values are justified. These include estimates of creatinine clearance by the Cockcroft-Gault formula, or of glomerular filtration rate by the MDRD formula, microalbuminuria, and an elevated daytime ABPM by the large spontaneous variance of the distribution, which begs the question whether any specified measurement can be considered to be normal. The Joint British Societies, for example, plead for the harmonization of office and ABPM values, but the evidence is not there.

**Table 1: Definitions and classification of blood pressure (BP) levels (mmHg)**

<table>
<thead>
<tr>
<th>Category</th>
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<th>Diastolic</th>
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<td>&lt; 120</td>
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<td>≥ 180</td>
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Isolated systolic hypertension should be graded (1,2,3) according to systolic blood pressure values in the ranges indicated, provided that diastolic values are <90mmHg. Grades 1, 2 and 3 correspond to classification in mild, moderate and severe hypertension, respectively. These terms have been now omitted to avoid confusion with quantification of total cardiovascular risk.

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bunionaratus; concurrent left ventricular hypertrophy on echocardiography or sign of non-fulfilment of target blood pressure and renal disease.

When to treat

The decision to start antihypertensive treatment should be based on two criteria, i.e.: 1. The level of systolic and diastolic blood pressure as classified in Table 2. The level of total cardiovascular risk as illustrated in Figure 2. Choice of drug

Comparative randomized trials show that for similar blood pressure reductions, differences in the incidence of cardiovascular morbidity and mortality between different drug classes are small, thus strengthening the conclusion that their benefit largely depends on blood pressure lowering per se. However, the European guideline does clarify certain issues in relation to treatment.

Beta-blockers: Beta-blockers (in combination with thiazide diuretics) fared badly compared to amlodipine in combination with perindopril in the ASCOT-PRoOF study. The British recommendations are that beta-blockers should not be used as first-line treatment. However, in the European guideline, the proven benefit of beta-blockers in patients with angina pectoris, heart failure and a recent myocardial infarction and the potential advantages of the newer beta-blockers, restore the beta-blockers as an option in this high-risk group. Subsequent antihypertensive treatment strategies Interestingly, some of the newer drugs also stage a comeback in the American Heart Association/American College of Cardiology practice guidelines. In particular, the guideline recommends beta-blockers as the first-line therapy in hypertensive patients with ischaemic heart disease. However, because beta-blockers tend to favor an increased heart rate, they have adverse effects on lipid metabolism and increase (compared with other drugs) the incidence of new onset diabetes, these should not be the drugs of choice in hypertensives with multiple metabolic risk factors including the metabolic syndrome. This applies also to thiazide diuretics, which have diuretic and diabetogenic effects when used at high doses. These disadvantages may not apply, however, to vasodilator blockers, such as carvedilol and nebivolol, which have less or no dysmetabolic action, as well as a reduced incidence of new onset diabetes compared with classical beta-blockers.

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ARBs vs ACEs: The European guideline considers the recent claim that angiotensin receptor antagonists might provide less protection against myocardial infarction than other antihypertensive agents, such as ACE inhibitors. However, this has not been confirmed by a comprehensive meta-analyses published recently, which shows the incidence of myocardial infarction to be similar to that occurring with other drugs. Direct comparisons between the overall and cause-specific cardiovascular endpoints recommend angiotensin receptor antagonists and ACE inhibitors are, therefore, awaited with interest.

Lifestyle modification

There is an interesting admission of failure in the European guideline, which acknowledges the edges of the failure of lifestyle modification in preventing cardiovascular events in hypertensive patients, and the notoriously poor long-term compliance to their recommendation. This viewpoint is also stated in the recently published American guidelines, which go a little further by stating: “Although hypertension, hypercholesterolemia, cigarette smoking, obesity, and sedentary lifestyles are potentially modifiable risk factors for IHD (ischemic heart disease), it has never been proven that lifestyle modifications can reduce clinical events in individual patients.” We need to be clear as to how these views should be interpreted. Neither guideline is advocating that lifestyle modification should be abandoned. In fact, the European guideline states: “The lifestyle measures that are widely agreed to lower blood pressure or cardiovascular risk, and that should be considered in all patients, are: smoking cessation, weight reduction in the context of an adequate diet and reduction of alcohol consumption; physical activity; 5) reduction of salt intake, and avoidance of fruit and vegetable intake and decrease in saturated and total fat intake.”

However, both the European and American guidelines are placing the imperative for drug treatment in context by emphasizing the importance of implementing behaviour modification (as a part of the medical management) as soon as possible; gone should be the day when prescribing antihypertensive medication had to await the response to lifestyle modification — to do so, especially in high-risk patients, is only facilitating the onset of stroke and heart attack. The message is clear: in patients with elevated blood pressure, lifestyle measures to lower blood pressure levels are achieved the greater the reduction in systolic and stroke heart attack. Therapeutic approach in special conditions

The European guideline provides useful information on the intricacies of drug treatment in the elderly (who are prone to the effects of excessive treatment); patients with diabetes mellitus (who require opportunistic blood pressure control to prevent premature cardiovascular disease in particular); patients with cerebrovascular disease (in whom the PROGRESS trial using the ACE inhibitor perindopril in association with the diuretic indapamide showed a 30 per cent reduction in recurrent stroke (both haemorrhagic and ischemic) in treated patients); patients with coronary artery disease (in whom the rationale for administering angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists, in patients with a recent acute coronary event is particularly well-founded; all likelihood of complicated by systolic dysfunction); patients with diabetes mellitus and hypertension (in which hypertension is the most important risk factor and which increases the risk of cardiovascular morbidity and mortality by approximately two to five-fold with a marked increased risk in the risk of embolic stroke); patients with non-diabetic kidney disease in whom blood pressure should be lowered to at least 120/80 mmHg; women receiving hormone replacement therapy; patients with the metabolic syndrome (in whom careful selection of medication is required to avoid worsening the metabolic abnormalities); and patients with resistant hypertension (usually defined as hypertension unresponsive to treatment with at least three drugs and in whom spironolactone may be an effective additional drug). Treatment of associated risk factors — especially those of stroke

The European guideline recommends concomitant use of a statin in patients up to the age of at least 80 years who have established cardiovascular disease, peripheral artery disease, previous stroke or coronary heart disease, or diabetes. This recommendation is based largely on the evidence of the ASCOT study, where administration of 10mg/day of atorvastatin in more than 10,000 hypertensive patients reduced total cardiovascular events by 36 per cent and stroke by 27 per cent.

Poor blood pressure control

Poor blood pressure control is one of the singular frustrations of 20th Century medicine, which shows little sign of abating as we move into this century. The European guideline reminds us that in most clinical trials (concerning blood pressure lowering as opposed to clinical practice) the achieved average systolic blood pressure remained above 140mmHg, and even in trials achieving average blood pressure values 140/90mmHg the control rate included at most 60 to 70 per cent of the patients. The situation in practice is of course; worse. and the ‘rule of halve’ operates across Europe half of the population over the age of 50 years has elevated blood pressure. Half of these people are unaware that their blood pressure is high; half of those who know that they have hypertension are untreated; of those receiving drug treatment only two of five have normal blood pressure and all of this despite the fact that we know that normotension was achieved in Ireland we would prevent at least 5,000 of the 10,000 strokes occurring every year, as well as significantly reducing heart attack.

Whose responsibility is blood pressure control?

It is always easy to blame the doctor for failing to achieve blood pressure control, but as the European guideline points out, the responsibility for control rests with the patient. Patients with elevated blood pressure have to become involved in comprehensive care management and advice; they must also be prepared to question advice (if blood pressure control is not optimal) why this is so and they must also ask why they are often often denied ABPM that will provide information on their blood pressure pattern. This cannot be provided by any other methodology. But it is reasonable for general practitioners to provide a facility that the Government will not reimburse?

As the guideline states: “Health providers sometimes wrongly consider the management of hypertension as the purview of few-minute visits, and reimburse doctors accordingly. They often see guideline recommendations as an attempt to reduce cost and limit reimbursement to high-risk conditions defined by arbitrary cut-offs. Therefore, policy makers and all those responsible for the reimbursement of drug should be involved in the development of a comprehensive preventive program. Which is where Minister for Health Ms Mary Harney and the HSE (Health Service Executive) Department should take the stage, and might I suggest that they could begin by excluding the treatment of uncontrolled hypertension and thereby dramatically reduce the occurrence of stroke (and other cardiovascular sequelae of hypertension) by firstly providing all general practitioners with the facilities to perform and interpret ABPM on all hypertensive patients.”

References