

# Memoranda/Mémorandums

## 1989 Guidelines for the management of mild hypertension: Memorandum from a WHO/ISH meeting\*

*The present guidelines were prepared by a subcommittee<sup>a</sup> of the WHO/ISH (International Society of Hypertension) Mild Hypertension Liaison Committee, and were finalized after discussion at the Fifth WHO/ISH Mild Hypertension Conference. They include the definition of mild hypertension, and describe blood pressure measurement, factors influencing the decision to begin treatment, methods of treatment, and follow-up. These guidelines are a revision of those published in 1986; they are based on the best available scientific evidence, and will be updated in the future to keep abreast of further developments in this field.*

Mildly raised blood pressure often presents a therapeutic problem calling for careful judgement in individual cases. Such patients are at increased risk of cardiovascular disease, whether or not symptoms are

present. Recent studies have shown that treatment of mild hypertension with antihypertensive drugs lowers cardiovascular morbidity and mortality. As many as 10–20% of the adult population are found to have mild elevation of blood pressure at one time or another, but the pressure is not persistently raised and not all of them should be treated with antihypertensive drugs.

The present guidelines give particular emphasis on non-drug measures as well as drug treatment and on the correction of other major risk factors for the prevention and treatment of cardiovascular disease.

### Definition of mild hypertension

#### *Blood pressure measurement*

Blood pressure is generally measured by the indirect method, using a mercury sphygmomanometer. Before measurement the patient should be seated for several minutes in a quiet room; the chair should provide comfortable back support. The arm muscles should be relaxed and the forearm supported with the cubital fossa at heart level (4th intercostal space). Blood pressure may also be measured supine and standing. In the supine position the arm should be supported at heart level. A cuff of suitable size is applied evenly and firmly to the exposed upper arm. Care should be taken to avoid tight sleeves. The standard cuff available in many countries is too small. A cuff for adults must have a bladder 13–15 cm wide and 30–35 cm long so as to encircle the arm. Larger cuffs are needed for fat arms and smaller ones for children. The cuff is rapidly inflated till the reading is about 30 mmHg above the level at which the pulse disappears, and then slowly

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deflated at approximately 2 mmHg per second. During this time the Korotkoff sounds are heard through a stethoscope placed over the brachial artery.

The pressure at which the sounds are first heard is the systolic pressure. The diastolic pressure (phase V) is the pressure at which the sound disappears. Most of the major studies have used the latter point, which may be significantly lower than the phase IV pressure (when muffling of sounds occurs). Because most of the data concerning treatment have been related to phase V diastolic pressure, this should be used when deciding on the need for treatment. The systolic and diastolic pressures should be measured at least twice over a period of at least 3 minutes; both should be recorded and the mean value should be used. It is also recommended that, on the first visit, the blood pressure be measured on both arms, and that in the elderly a measurement in the standing position be performed. Measurement by nurses or trained non-medical staff may reduce the problem of falsely high readings that may result from the presence of the physician ("white coat" effect).

Values obtained with semiautomatic devices and home blood pressure readings should not be equated with readings taken as described above but can be used as supplementary sources of information. Ambulatory blood pressure monitoring should be considered at present as a research tool but may be helpful in selected cases.

### **Mild hypertension**

There is a continuum of cardiovascular risk associated with blood pressure level: the higher the pressure the higher the risk. The dividing line between "normotension" and "hypertension" is not fixed. It reflects present judgement on the level at which intervention is justified. It is well established that lowering of even mildly or moderately elevated pressures reduces cardiovascular morbidity and mortality. However, a decision to intervene will depend not only on prospective benefits of intervention, but also on possible side-effects and costs.

Mild hypertension in adults is defined as a persistent resting level of diastolic blood pressure (DBP) (phase V) between 90 and 104 mmHg (12–14 kPa). "Borderline" hypertension (diastolic blood pressure 90–94 mmHg) accounts for about half of mild hypertensive patients. Community screening has shown that up to 20% of the population aged 50 years or above have diastolic pressures within the mild hypertension range at screening. With repeated measurement over periods of up to 3–6 months, the diastolic pressure of almost half of those within the mild range falls to levels below this range.

Persons whose resting values of diastolic blood

pressure remain persistently above 90 mmHg after repeated measurement are at increased risk of cardiovascular mortality and morbidity, and the risk clearly increases with the height of the diastolic blood pressure. Between 12% and 15% of such patients will develop moderate or severe hypertension (DBP > 105 mmHg) within 3–5 years, with a worse prognosis, while the remaining patients remain within the mild range. The risk of stroke is increased in patients with mild hypertension, and drug treatment has been clearly shown to reduce this risk. In populations with high plasma cholesterol levels, the major cause of cardiovascular mortality and morbidity in patients with mild hypertension is usually ischaemic heart disease. Lowering of blood pressure with drugs probably reduces the risk of non-fatal myocardial infarction and death from ischaemic heart disease, but the size of the benefit remains uncertain.

In practice, when the initial diastolic pressure averages 90–104 mmHg, measurements should be repeated on at least two further occasions during the next 4 weeks. With repeated measurements both systolic and diastolic pressures often fall substantially. It is therefore necessary to identify those patients with sustained high or increasing blood pressure.

All patients should be given advice to stop smoking, reduce obesity, limit alcohol as well as dietary saturated fat and salt, and take appropriate exercise. This advice to patients should be one part of the strategies to improve cardiovascular health. Management decisions should be made after discussion with the patient about the risks and benefits of various intervention strategies.

Practical guidelines are illustrated in the flow-chart (Fig. 1). The main points to note are:

#### *(1) Within 4 weeks from an initial measurement of DBP 90–104 mmHg*

- Patients whose DBP falls to below 90 mmHg should have further measurements at 3-month intervals for a year.
- If the DBP remains at 90–104 mmHg, institute appropriate non-drug treatment for all patients (see below); monitor the blood pressure on several occasions during the following 3 months.

#### *(2) After the first three-month period*

- If the DBP is 100 mmHg or above, non-drug measures should be reinforced and drug treatment should be instituted.
- If the DBP is 95–99 mmHg, reinforce non-drug measures and consider drug treatment, especially when other cardiovascular risk factors are present.
- If the DBP remains at 90–94 mmHg, reinforce

non-drug measures and continue long-term observation of the patient.

(3) *After a second three-month period*

- If the DBP is 95 mmHg or above, consider drug treatment even when other cardiovascular risk factors are absent.
- Patients whose diastolic pressures, after prolonged observation, remain between 90 and 94 mmHg also have an increased risk of cardiovascular disease. This is more marked when the systolic blood pressure is also elevated, as well as in smokers, diabetics, individuals with increased plasma cholesterol, and those with a family history of cardiovascular disease. Drug treatment should be considered for such patients at higher risk. Lower risk subjects, if not treated with drugs, should be further assessed at about 3-month intervals and appropriate non-drug measures should be maintained or reinforced.

## Drug treatment

### *Factors influencing initiation of treatment*

Factors other than diastolic blood pressure, which influence the decision to begin drug treatment, include the following:

(a) *Systolic blood pressure.* At any level of diastolic blood pressure an increased systolic blood pressure carries an additional risk. When the DBP is 90 mmHg or above, systolic blood pressure levels of 160 mmHg or greater favour an earlier start to drug treatment. Systolic blood pressures of 160 mmHg or greater associated with diastolic blood pressures below 90 mmHg (isolated systolic hypertension, which is particularly common in the elderly) carry a substantial additional risk. There is as yet no evidence of a reduced risk associated with reduction of an isolated systolic high blood pressure by any form of treatment. Until the results of controlled therapeutic trials (now under way) are available, the treatment of isolated systolic hypertension by non-pharmacological methods would appear reasonable.

(b) *Age.* The benefits of antihypertensive therapy are more conspicuous in older subjects. However, there is as yet no evidence that antihypertensive treatment is of benefit in persons aged 80 years and over. Although old age is no bar to drug treatment, caution is needed since side-effects may be severe. In elderly patients, blood pressure elevation can often be controlled by low-dose medication. Patients aged 70 and over who are in good general health should probably be treated in the same way as younger patients. Elderly hypertensive patients with cardiac failure benefit significantly from antihypertensive drug

treatment, even if given over a short period of time.

(c) *Sex.* Women have a lower risk of cardiovascular disease than men, and the evidence of benefit from treatment is less strong in women.

(d) *Cardiovascular signs.* Clinical, electrocardiographic, echocardiographic or radiological evidence of left ventricular hypertrophy or clinical, electrocardiographic or angiographic evidence of ischaemic heart disease is a clear indication to begin drug treatment. A history of cerebrovascular disease (e.g., transient cerebral ischaemia or stroke) is also a clear indicator to begin treatment.

(e) If there are signs of renal disease, e.g., raised plasma creatinine, haematuria or proteinuria, drug treatment should be started.

(f) A strong family history of stroke, heart disease or sudden death should influence the decision towards early drug treatment.

(g) Continued smoking, elevated fasting glucose, elevated serum cholesterol or creatinine all markedly increase the cardiovascular risk associated with high blood pressure and should influence the decision towards early drug treatment and the intensive use of appropriate non-drug measures.

(h) In developing countries costs may make it difficult to extend drug therapy to all individuals with mild hypertension as defined above. Detailed and sustained advice on modification of life-style should be of particular benefit in such circumstances, before resorting to drug therapy.

### *Evaluation of the patient*

A complete history and physical examination are essential. Factors of significance include (1) a family history of hypertension, hyperlipidaemia, ischaemic heart disease or stroke, (2) a personal history of symptoms suggestive of ischaemic heart disease, cardiac failure, or transient cerebral ischaemic episodes, as well as kidney disease or bronchospasm, (3) previous measurements of blood pressure, and (4) details of life-style, educational level, and sociological factors. There should be careful quantitation of smoking and alcohol consumption; weight gain since early adult life can provide a useful index of excess body fat. Patients should be questioned on the ingestion of pro-hypertensive substances or drugs, notably oral contraceptives, non-steroidal anti-inflammatory drugs, liquorice, carbenoxolone, etc. Physical examination should include measurement of weight and height, evaluation of heart size, examination of the optic fundi and evidence of arterial disease in the carotid, renal and peripheral arteries. Certain minimum investigations should be performed in all patients. These are analysis for blood, protein and glucose in the urine, microscopic examination of the urine, plasma potassium,

creatinine, cholesterol, uric acid and blood glucose estimations, and an electrocardiogram. Echocardiography is useful in assessing left ventricular hypertrophy. In selected cases, further investigations should be carried out to exclude curable causes of hypertension. The cost of investigations should be considered when a decision is made for a given patient.

## Methods of treatment

The goal is to lower the blood pressure to normotensive levels, or at least to lower the diastolic to below 90 mmHg. Recent trials have shown that an important predictor of risk is the level of blood pressure, particularly systolic blood pressure, achieved during treatment. Reduction in systolic blood pressure should also be an important goal of treatment.

### *Non-pharmacological interventions*

Several non-pharmacological interventions have been shown to lower the blood pressure in patients with mild hypertension. Weight reduction in overweight subjects, cessation of heavy alcohol consumption, regular exercise in sedentary patients and, in some patients, sodium restriction are effective in lowering the blood pressure. Efforts to reduce blood pressure using non-pharmacological methods should normally precede any decision about the necessity for drug treatment of mild hypertension. Note that some of these measures may take several months to become fully effective. If a decision is made to begin drug treatment, a structured programme of non-pharmacological intervention remains an essential component of the overall therapeutic programme.

**Added risks.** All the large-scale trials of treatment of mild hypertension have confirmed that treated hypertensive patients who smoke tobacco have a greater incidence of both stroke and coronary heart disease than equally treated hypertensive patients who do not smoke. Repeated advice as to how to discontinue smoking is therefore of major importance, and will need to be coupled with particular efforts to prevent consequent weight gain. Intensive advice programmes are more effective than haphazard admonitions.

Since high serum cholesterol levels and diabetes also unfavourably influence the long-term prognosis of hypertensive persons, nutritional counselling and, when appropriate, drug treatment are indicated to control these risk factors. If dietary measures are to be successful, a careful programme of motivation and dietary instruction and follow-up should be instituted. Since increased physical activity is also likely to reduce the risk of cardiovascular disease, it is appropriate in mildly hypertensive patients.

Alternative methods of contraception should

be recommended to women in place of oestrogen-containing oral contraceptives as these substances may raise the blood pressure as well as carry other cardiovascular risk.

### *Antihypertensive drugs*

Many drugs are available for the treatment of mild hypertension. These include diuretics, beta-adrenoceptor blocking drugs, alpha-blocking drugs, angiotensin-converting enzyme (ACE) inhibitors, calcium channel blocking drugs, serotonin antagonists, centrally acting drugs, and peripheral vasodilator drugs.

Most of these drugs are approximately equally effective in reducing blood pressure in patients with mild hypertension; the choice of drug used may be influenced by the individual patient's characteristics and responses. The cost of drug treatment is also an important consideration.

Treatment may be started with one of the following categories of drugs.

**Diuretic drugs.** Diuretics have been widely used as first-line antihypertensive therapy and have been shown to be clearly effective in the prevention of stroke. Particularly in large doses, they may cause a variety of unwanted metabolic effects, ventricular ectopics, and impotence, so that the dose should be kept as low as possible. Low-dose diuretics remain effective and cheap. They are also particularly valuable as ancillary treatment to enhance the effectiveness of other drugs. Combination of diuretics with potassium-sparing drugs, including ACE-inhibitors, may prevent potassium depletion.

**Beta-adrenoceptor blocking drugs.** Beta-blocking drugs are widely and effectively used to initiate treatment for mild hypertension. Numerous drugs of this type are available, some with cardio-selective properties, others with partial agonist activity, and others with alpha-blocking or vasodilator properties. Although beta-blockers have been shown to prevent secondary complications of a previous myocardial infarction, their role in primary prevention is not established.

Beta-blocking drugs should be avoided in patients with reactive airways obstruction, heart failure, peripheral vascular disease and, possibly, hyperlipidaemia. They are particularly useful in hypertensive patients with angina or rhythm disturbances.

**ACE-Inhibitors.** Angiotensin-converting enzyme inhibitors are effective in lowering blood pressure. They are generally well tolerated and have been shown not to exert untoward effects on serum lipids and glucose homoeostasis. Among possible adverse effects, persistent cough, angioedema and, in patients with reno-

vascular disease, deterioration in renal function have been reported. ACE-inhibitors may increase the risk of early fetal death and should be avoided in women considering child-bearing. Their safety profile is otherwise good. As with all recent classes of antihypertensive agents, the ability of ACE-inhibitors to reduce mortality in hypertension has not yet been tested in controlled clinical trials.

**Calcium antagonists.** There are three major classes of calcium antagonists with different characteristics (papaverine, dihydropyridine and benzodiazepine derivatives), but all are effective in lowering the blood pressure. Troublesome side-effects may include reflex tachycardia, ankle oedema, flushing and constipation. Like ACE-inhibitors, they do not have undesirable

metabolic effects and their safety profile appears good, but their ability to reduce mortality has not been tested in controlled clinical trials.

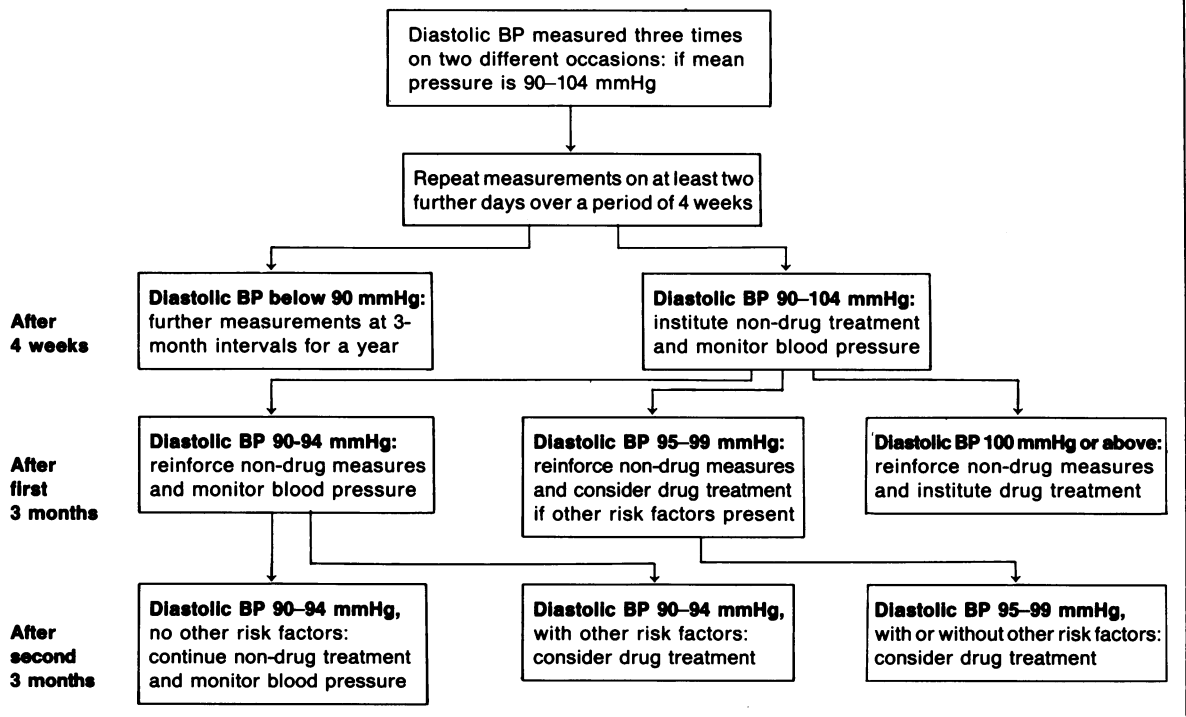
**Other classes.** Alpha-adrenergic blockers have been used for many years with successful reduction of blood pressure and limited side-effects. Centrally-acting drugs are also effective antihypertensive agents and have been used for many years, although the side-effect profile is less favourable than for the antihypertensive agents previously mentioned. Other interesting classes of compounds have recently been introduced, such as serotonin antagonists, but with all new classes and new antihypertensive compounds any recommendation for general use as a possible first choice has to await the result of extensive clinical experience.

Fig. 1. Definition, blood pressure (BP) measurement, and management of mild hypertension.

**DEFINITION:** 90–104 mmHg diastolic blood pressure (phase V)

**GOALS:** *diagnostic*—to provide a safe classification of patients

*therapeutic*—to decrease the diastolic blood pressure to below 90 mmHg; also to reduce systolic blood pressure if elevated.



**Combinations of drugs.** When a single drug is ineffective it is reasonable to substitute a different drug. If a single drug has been partly effective it may be preferable to add a small dose of a second drug rather than increase the dose of the first.

Effective combinations include: (1) thiazide diuretic with beta-blocker or angiotensin-converting enzyme inhibitor; (2) beta-blocker with dihydropyridine calcium antagonist; (3) angiotensin-converting enzyme inhibitor with calcium antagonist.

For reasons of convenience, cost and increased patient compliance, preparations that combine two drugs in a single tablet or capsule may be appropriate for many hypertensive patients, once the need and doses for the constituent drugs have been established. Non-drug measures should be continued in order to minimize the required number and doses of drugs and to control other risk factors.

**Follow-up**

During the stabilization period of treatment, patients need to be seen at regular intervals until the blood pressure levels are satisfactorily controlled. The main task of doctors during follow-up is to ensure that the target systolic and diastolic blood pressures are reached and maintained and that other risk factors are controlled. Gradual and careful lowering of blood pressure will minimize the side-effects and complications, and

will improve compliance. Sometimes telling a patient that he or she has hypertension ("labelling") may be followed by anxiety or mood changes; additional support, e.g., reassurance about prognosis, stress on the ability to lead normal active lives, and explanation of any new symptoms that may appear, is therefore particularly important. Self-measurement of blood pressure may be helpful to ensure compliance. After stabilization of blood pressure, follow-up visits at 3–6-month intervals may be adequate. During each visit the blood pressure should be measured, side-effects monitored, and non-pharmacological measures, particularly cessation of smoking and control of serum cholesterol and obesity, should be reinforced. The therapy should be adjusted accordingly. As a rule, antihypertensive therapy should be maintained indefinitely. Cessation of therapy in patients who had been correctly diagnosed as hypertensives (see above criteria and Fig. 1) is usually followed—sooner or later—by a return of blood pressure to pre-treatment levels. Nevertheless after prolonged blood pressure control it may be possible to attempt a careful progressive reduction in the dose or number of drugs used, especially in patients strictly observing non-drug treatment.

According to the drugs used, appropriate laboratory investigations should be performed at regular intervals.