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1999 WHO/ISH HYPERTENSION GUIDELINES - HIGHLIGHTS & ESH UPDATE

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Introduction

- The 1999 WHO/ISH Hypertension Guidelines (1) provide recommendations that are based on the collective expert interpretation by a Guidelines Subcommittee of the available evidence from epidemiological studies and from clinical trials.
- The primary aim is to offer balanced information to guide clinicians, rather than rigid rules that would constrain their judgment about the management of individual patients, who will differ in their personal, medical, social, economic, ethnic, and cultural characteristics.
- The WHO/ISH Guidelines are written for a global audience from communities that vary widely in the nature of their health system and in the availability of resources. The goal, however, remains universally the same, that is to lower blood pressure and other risk factors in order to reduce the risk of cardiovascular disease.
- ESH has endorsed the 1999 WHO/ISH Hypertension Guidelines. This ESH Update integrates recent knowledge from the clinical trials CAPPP, STOP-2, ALLHAT, NORDIL, INSIGHT, HOPE, HOT, UKPDS and SYST-EUR.

Table 1.
1999 WHO/ISH definitions and classification of BP levels

Category	Systolic BP (mm Hg)	Diastolic BP (mm Hg)
Optimal BP	<120	<80
Normal BP	<130	<85
High-Normal BP	130-139	85-89
Grade 1 Hypertension (mild)	140-159	90-99
Subgroup: Borderline	140-149	90-94
Grade 2 Hypertension (moderate)	160-179	100-109
Grade 3 Hypertension (severe)	≥180	≥110
Isolated Systolic Hypertension	≥140	<90
Subgroup: Borderline	140-149	<90

When SBP and DBP fall into different categories, the higher should apply.

Clinical evaluation - what should be done?

The clinical and laboratory evaluation of the hypertensive patient has four aims:

- to confirm a chronic elevation of BP and determine the level, e.g. measure BP several times under standardized procedures.
- to exclude or identify secondary causes of hypertension
- to determine the presence of target organ damage and quantify its extent
- to search for other cardiovascular risk factors and clinical conditions that may influence the prognosis and treatment.

Minimum routine investigations:

- Clinical and family history
- Full physical examination as described in medical textbooks
- Laboratory investigations, including:
  Urinalyses for blood, protein, and glucose
  Microscopic examination of urine
  Blood chemistry of potassium, creatinine, fasting glucose, and total cholesterol
- Electrocardiography (ECG)

Situations in which ambulatory BP monitoring or home BP should be considered:

- Unusual variability of BP over the same or different visits
- Office ("white coat") hypertension in subjects with low cardiovascular risk
- Symptoms suggesting hypotensive or transient hypertensive episodes
- Hypertension resistant to drug treatment

Average 24 hour or home BP values of around 125/80 mm Hg correspond to office BP of 140/90 mm Hg. Reliable information about the long-term prognostic value of ambulatory and home BP is awaited.

Table 2.
Stratifying risk and managing drug treatment

	Blood pressure and 10 year risk levels (mm Hg)		
Additional risk factors[1] and disease history	Grade 1 MILD 140-159/90-99	Grade 2 MODERATE 160-179/100-109	Grade 3 SEVERE ≥180/110
No other risk factors	LOW RISK (<15%) DRUGS??[a]	MEDIUM (15-20%) DRUGS?[b]	HIGH RISK (20-30%) DRUGS
1-2 additional risk factors	MEDIUM DRUGS?[b]	MEDIUM DRUGS	VERY HIGH RISK DRUGS
3 or more additional factors or target organ disease[2] or diabetes	HIGH RISK DRUGS	HIGH RISK DRUGS	VERY HIGH RISK DRUGS
Associated clinical condition[3]	VERY HIGH RISK - DRUGS COMPULSORY		

All patients should be educated on smoking cessation, weight reduction, moderate alcohol consumption, reduction of salt intake and increased physical activity.

[1] Age (men>55, women >65 years), smoking, total cholesterol >6.5 mmol/L, family history of premature cardiovascular disease.

[2]Table 2B. **Identifying target organ damage**

Organ	Condition	Investigation
Heart	Left ventricular hypertrophy Diastolic dysfunction	ECG, echocardiography, X-ray Echocardiography
Kidney	Slightly reduced renal function Albuminuria	Serum creatinine 106-177 µmol/L Dip stix
Large arteries	Atherosclerotic plaque (aorta, carotid, iliac, femoral)	Ultrasound, X-ray
Eye fundi	Narrowing of retinal arteries	Fundoscopi

[3] Cerebrovascular disease, coronary heart disease or heart failure, renal disease including diabetic nephropathy and renal failure (serum creatinine >177 µmol/L), dissecting aneurysm, symptomatic arterial disease and advanced hypertensive retinopathy.

[a] Monitor BP and other risk factors for 6-12 months; begin drug treatment if SBP ≥150 or DBP ≥95 mmHg, otherwise continue to monitor.

[b]Monitor BP and other risk factors for 3-6 months; begin drug treatment if SBP ≥140 or DBP ≥90 mmHg, otherwise continue to monitor.

Table 3.
Which drug treatment should be used? Results for primary cardiovascular endpoints of recent trials comparing "newer" drugs vs. diuretics/beta-blockers in hypertension

Acronym	Pts. no.	Age range	Drug	RR and 95% CIs
CAPPP (2)	10,985	25-66	captopril	1.05 (0.90-1.22)
STOP-2 (3)	6,614	70-84	CCBs/ACEIs	0.99 (0.84-1.16)
ALLHAT (4)	24,335	≥55	doxazosin	1.03 (0.90-1.17)
NORDIL (5)	10,948	50-74	diltiazem	1.00 (0.87-1.15)
INSIGHT (6)	6,321	55-80	nifedipin GITS	1.11 (0.90-1.36)

There were no differences in primary outcomes in any trials, so in uncomplicated hypertension all regular first-line drugs could be used.

Principles of drug treatment

- Beneficial effects on morbidity and mortality have been proven from blood pressure lowering per se (2-7). Thus, all main classes of antihypertensive drugs are suitable for the initiation and maintenance of BP lowering therapy.
- In many cases, begin with the lowest available dose in an effort to reduce adverse effects. If needed, consider increasing the dose of the initial drug or use appropriate drug combinations to maximise BP lowering efficacy while minimising side effects. Change to other drug or combination if little response or poor tolerability. Combinations of beta-blocker and verapamil/diltiazem may cause heart blocks and combinations of ACEIs/ARBs and K^+-sparing diuretics may cause hyperkalaemia.
- The use of long-acting drugs provides 24-hour efficacy on a once daily basis and improves adherence to therapy. This may provide greater protection against the risk of major cardiovascular events and the delelopment of target organ damage.
- The goal of antihypertensive treatment (8,9) should be to achieve "optimal" or "normal" BP in young, middle-aged, or diabetic subjects (below 130/85 mm Hg), and at least "high-normal" BP in elderly patients (below 140/90 mm Hg).
- Treatment with cholesterol-lowering statin is usually recommended if total cholesterol ≥6.5 mmol/l or ≥5.2 mmol/l if two additional risk factors or diabetes.
- Acetylsalicylic acid 75 mg once daily prevents myocardial infarction provided good blood pressure control, especially in men (10).

Table 4.
Main compelling indications and contraindications

Class of drug	Compelling indications	Compelling contraindications
Diuretics		
Thiazide-type	Isolated systolic hypertension Heart failure, diabetes	Low K^+
Furosemide	Heart failure, renal failure	Low K^+
K^+-sparing	Heart failure, low K^+	High K^+, renal failure
Beta-blockers	Coronary heart disease Heart failure, tachyarrythmia Migraine headache	Heart block Decompensated heart failure
ACE Inhibitors	Heart failure Coronary heart disease (11) Diabetic nephropathy	High K^+ Bilateral renal artery stenosis Pregnancy
Calcium Antagonists		
Dihydropyridines	Isolated systolic hypertension Angina pectoris (AP)	
Diltiazem	AP, tachyarrythmia	Heart block
Verapamil	AP, tachyarrythmia	Heart block
Alpha-blockers	Prostatic hyperplasia	Orthostatic hypotension
Angiotensin II Antagonists	Heart failure Diabetic nephropathy	High K^+ Bilateral renal artery stenosis Pregnancy

Target BP is <130/85 mm Hg if compelling cardiovascular indication (8,9).

Treatment of hypertension in type-2 diabetes mellitus

Hypertension in type-2 diabetes mellitus (blood pressure ≥140 mm Hg systolic and/or ≥90 mm Hg diastolic) should be treated with one or more drugs to achieve a target <130/85 mm Hg (8,9). Benefits in preventing major cardiovascular events have been shown with diuretics, beta-blockers, ACE-inhibitors and calcium-antagonists, i.e. all classes of drugs tested (11-14). Usually, combinations are needed. Benefits in preventing renal deterioration have been shown with ACE-inhibitor (14), with calcium anatagonist (6), with their combination (15) and with the angiotensin II antagonists losartan (RENAAL) and irbesartan (IRMA, IDNT).

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