

ESH-ESC Guidelines for the Management of Hypertension

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Abstract

The following is a brief statement of the 2003 European Society of Hypertension (ESH)-European Society of Cardiology (ESC) guidelines for the management of arterial hypertension.

The continuous relationship between the level of blood pressure and cardiovascular risk makes the definition of hypertension arbitrary. Since risk factors cluster in hypertensive individuals, risk stratification should be made and decision about the management should not be based on blood pressure alone, but also according to the presence or absence of other risk factors, target organ damage, diabetes, and cardiovascular or renal damage, as well as on other aspects of the patient's personal, medical and social situation. Blood pressure values measured in the doctor's office or the clinic should commonly be used as reference. Ambulatory blood pressure monitoring may have clinical value, when considerable variability of office blood pressure is found over the same or different visits, high office blood pressure is measured in subjects otherwise at low global cardiovascular risk, there is marked discrepancy between blood pressure values measured in the office and at home, resistance to drug treatment is suspected, or research is involved. Secondary hypertension should always be investigated.

The primary goal of treatment of patient with high blood pressure is to achieve the maximum reduction in long-term total risk of cardiovascular morbidity and mortality. This requires treatment of all the revers-

ible factors identified, including smoking, dislipidemia, or diabetes, and the appropriate management of associated clinical conditions, as well as treatment of the raised blood pressure per se. On the basis of current evidence from trials, it can be recommended that blood pressure, both systolic and diastolic, be intensively lowered at least below 140/90 mmHg and to definitely lower values, if tolerated, in all hypertensive patients, and below 130/80 mmHg in diabetics.

Lifestyle measures should be instituted whenever appropriate in all patients, including subjects with high normal blood pressure and patients who require drug treatment. The purpose is to lower blood pressure and to control other risk factors and clinical conditions present.

In most, if not all, hypertensive patients, therapy should be started gradually, and target blood pressure achieved progressively through several weeks. To reach target blood pressure, it is likely that a large proportion of patients will require combination therapy with more than one agent. The main benefits of antihypertensive therapy are due to lowering of blood pressure per se. There is also evidence that specific drug classes may differ in some effect or in special groups of patients. The choice of drugs will be influenced by many factors, including previous experience of the patient with antihypertensive agents, cost of drugs, risk profile, presence or absence of target organ damage, clinical cardiovascular or renal disease or diabetes, patient's preference.

Key Words:

Guidelines · Hypertension · Blood pressure

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ESH-ESC-Leitlinien zur Behandlung der Hypertonie

Zusammenfassung

Im Folgenden wird eine kurze Übersicht über die Leitlinien 2003 der Europäischen Gesellschaft für Hypertonie (ESH) und der Europäischen Gesellschaft für Kardiologie (ESC) zur Behandlung der arteriellen Hypertonie gegeben.

Der enge Zusammenhang zwischen dem Blutdruck und dem kardiovaskulären Risiko macht die Definition der Hypertonie schwierig. Da sich Risikofaktoren bei Hypertoniepatienten häufen, sollte eine Risikoanalyse durchgeführt werden, und die Entscheidung über die Behandlung sollte nicht nur vom Blutdruck allein abhängig gemacht werden, sondern auch

von anderen Risikofaktoren, Zielorganschäden, Diabetes und kardiovaskulärem bzw. renalem Schaden sowie weiteren Aspekten des Patienten. Allgemein als Normwerte gelten Blutdruckwerte, welche in der Arztpraxis oder in der Klinik gemessen werden. Die ambulante Blutdrucküberwachung kann klinische Relevanz haben, wenn anlässlich einer oder verschiedener Konsultationen in der Arztpraxis gemessene Blutdruckwerte beträchtlich divergieren oder wenn hohe Blutdruckwerte bei Patienten mit ansonsten geringem globalem kardiovaskulärem Risiko gemessen werden. Stellt man eine eindeutige Diskrepanz zwischen den Blutdruckwerten fest, welche zu Hause

Schlüsselwörter:

Leitlinien · Hypertonie · Blutdruck

oder in der Arztpraxis gemessen werden, kann eine Medikamentenresistenz vermutet werden. Sekundäre Hypertonieformen sollten immer genauer abgeklärt werden.

Das primäre Ziel bei der Behandlung von Hypertoniepatienten ist die maximale Reduktion des Langzeitrisikos einer kardiovaskulären Gefäßerkrankung und der Gesamtsterblichkeit. Dies bedarf einer Behandlung aller identifizierbaren reversiblen Faktoren inklusive Rauchen, Dislipidämie und Diabetes sowie einer angemessenen Behandlung assoziierter klinischer Befunde und der Behandlung des erhöhten Blutdrucks per se. Auf der Basis der gegenwärtigen Evidenz sollten sowohl der systolische als auch diastolische Bluthochdruck drastisch gesenkt werden, und zwar bei Hypertonikern unter 140/90 mmHg, ggfs. sogar tiefer, wenn dies toleriert wird, und bei Diabetikern unter 130/80 mmHg.

Der Lebensstil sollte nach Möglichkeit bei allen Patienten verbessert werden, einschließlich Patienten mit hochnormalem Blutdruck und Patienten, die

eine medikamentöse Therapie benötigen. Ziel ist es, den Blutdruck zu senken sowie andere Risikofaktoren und sonstige klinische Befunde unter Kontrolle zu halten.

Bei den meisten, wenn auch nicht allen Patienten mit Bluthochdruck sollte man die Therapie langsam beginnen und die Zielwerte kontinuierlich über mehrere Wochen anstreben. Um den Zielwert zu erreichen, benötigt ein großer Teil der Patienten eine Kombinationstherapie mit mehr als einem Wirkstoff. Die hauptsächlichlichen Vorteile der Antihypertensiva basieren auf der Blutdrucksenkung an sich. Es gibt klinische Indizien dafür, dass spezifische Medikamentengruppen in ihrer Wirkung oder bei speziellen Patientengruppen etwas variieren. Die Medikamentenwahl wird von vielen Faktoren beeinflusst, wie dem bisherigen Ansprechen des Patienten auf Antihypertensiva, Medikamentenkosten, Risikoprofil, möglichen Zielorganschäden, kardiovaskulären Erkrankungen, Nierenerkrankung, Diabetes oder speziellen Präferenzen des Patienten.

Introduction

The following is a brief statement of the 2003 European Society of Hypertension (ESH)-European Society of Cardiology (ESC) guidelines for the management of arterial hypertension. The reader should refer to the original guideline document for detailed management recommendations and a critical assessment of the evidence for the recommendations [1].

Because of the continuous relationship between the level of blood pressure and cardiovascular risk, the definition of hypertension is arbitrary (Table 1).

When a patient's systolic (SBP) and diastolic blood pressure (DBP) fall into different categories, the higher category should apply. Isolated systolic hypertension can also be graded (grades 1, 2, 3) according to SBP values in the ranges indicated, provided diastolic values are < 90 mmHg.

Since risk factors cluster in hypertensive individuals, risk stratification should be made and decision about the management should not be based on blood pressure alone but also according to the presence or absence of other risk factors, target organ damage, diabetes, and cardiovascular or renal disease, as well as on other aspects of the patient's personal, medical and social situation (Tables 2 and 3).

Blood Pressure Measurement

BP values measured in the doctor's office or the clinic should commonly be used as reference [2–5]. 24-h ambulatory blood pressure monitoring may be considered

of additional clinical value, when considerable variability of office blood pressure is found over the same or different visits, high office blood pressure [6–8] is measured in subjects otherwise at low global cardiovascular risk, there is marked discrepancy between blood pressure values measured in the office and at home, resistance to drug treatment is suspected, or research is involved [2–4, 9–11]. Self-measurement of blood pressure at home should be encouraged in order to provide more information for the doctor's decision, and improve patient's adherence to treatment regimens. Self-measurement of blood pressure at home should be discouraged whenever it causes patients anxiety or induces self-modification of the treatment regimen [12]. It should not be forgotten that normal values are different for office, ambulatory, and home blood pressure.

Table 1. Definitions and classification of hypertension.

Tabelle 1. Definitionen und Klassifikation der Hypertonie.

Category	Systolic (mmHg)	Diastolic (mmHg)
Optimal	< 120	< 80
Normal	120–129	80–84
High normal	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	< 90

Table 2. Stratification of risk to quantify prognosis. ACC: associated clinical conditions; DBP: diastolic blood pressure; SBP: systolic blood pressure; TOD: target organ damage.

Table 2. Risikostreuung für die Prognoseberechnung. ACC: assoziierte klinische Befunde; DBP: diastolischer Blutdruck; SBP: systolischer Blutdruck; TOD: Zielorganschaden.

Other risk factors and disease history	Blood pressure (mmHg)				
	Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 SBP 140–159 or DBP 90–99	Grade 2 SBP 160–179 or DBP 100–109	Grade 3 SBP ≥ 180 or DBP ≥ 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1–2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more risk factors or TOD or diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
ACC	High added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

Physical Examination for Secondary Hypertension and Organ Damage

Signs suggesting secondary hypertension and organ damage include features of Cushing’s syndrome [13–15], skin stigmata of neurofibromatosis (pheochromocytoma), palpation of enlarged kidneys (polycystic kidney), presence of abdominal murmurs (renovascular hypertension), precordial or chest murmurs (aortic coarctation or aortic disease), diminished and delayed femoral and reduced femoral blood pressure (aortic coarctation, aortic disease). Murmurs over neck arteries, motor or sensory defects may show brain damage. Fundoscopic abnormalities [16] may suggest retinal damage. Location and characteristics of apical impulse, abnormal cardiac rhythms, ventricular gallop, pulmonary rales, dependent edema may be present when heart is affected [17].

Laboratory Investigations

Routine tests must include plasma glucose (preferably fasting), serum total cholesterol, serum high-density lipoprotein (HDL) cholesterol, fasting serum triglycerides, serum uric acid [18] and creatinine, potassium, hemoglobin and hematocrit levels. Urinalysis (dipstick test complemented by urinary sediment examination) must be made and an electrocardiogram must be taken [19, 20]. Recommended tests include echocardiogram [21–23], carotid (and femoral) ultrasound, C-reactive protein [24], quantitative proteinuria (if dipstick test positive), and funduscopy (in severe hypertension). Extended evaluation (domain of the specialist) must be carried out when complicated hypertension exists which deteriorates cerebral, cardiac and renal function. Secondary hypertension must be searched for, and plasma renin, aldosterone, corticosteroids, and catecholamines have to be measured. Renal and adrenal arteriography can be made by ultrasonography, and comput-

Table 3. Factors influencing prognosis. DBP: diastolic blood pressure; HDL: high-density lipoprotein; IMT: intima-media thickness; LDL: low-density lipoprotein; LVMI: left ventricular mass index; M: men; SBP: systolic blood pressure; W: women.

Table 3. Faktoren, welche die Prognose beeinflussen. DBP: diastolischer Blutdruck; HDL: High-Density-Lipoprotein; IMT: Intima-media-Dicke; LDL: Low-Density-Lipoprotein; LVMI: linksventrikulärer Masseindex; M: Männer; SBP: systolischer Blutdruck; W: Frauen.

Risk factors for cardiovascular disease used for stratification

- Levels of SBP and DBP
- Men > 55 years
- Women > 65 years
- Smoking
- Dislipidemia (total cholesterol > 6.5 mmol/l, > 250 mg/dl, or LDL cholesterol > 4.0 mmol/l, > 155 mg/dl, or HDL cholesterol M < 1.0, W < 1.2 mmol/l, M < 40, W < 48 mg/dl)
- Family history of premature cardiovascular disease (at age < 55 years M, < 65 years W)
- Abdominal obesity (abdominal circumference M ≥ 102 cm, W ≥ 88 cm)
- C-reactive protein ≥ 1 mg/dl

Target organ damage (TOD)

- Left ventricular hypertrophy (electrocardiogram: Sokolow-Lyon > 38 mm; Cornell > 2 440 mm * ms; echocardiogram: LVMI M ≥ 125, W ≥ 110 g/m²)
- Ultrasound evidence of arterial wall thickening (carotid IMT ≥ 0.9 mm) or atherosclerotic plaque
- Slight increase in serum creatinine (M 115–133, W 107–124 μmol/l; M 1.3–1.5, W 1.2–1.4 mg/dl)
- Microalbuminuria (30–300 mg/24 h; albumin-creatinine ratio M ≥ 22, W ≥ 31 mg/g; M ≥ 2.5, W ≥ 3.5 mg/mmol)

Diabetes mellitus

- Fasting plasma glucose ≥ 7.0 mmol/l (≥ 126 mg/dl)
- Postprandial plasma glucose 11.0 mmol/l (> 198 mg/dl)

Associated clinical conditions (ACC)

- Cerebrovascular disease: ischemic stroke; cerebral hemorrhage; transient ischemic attack
- Heart disease: myocardial infarction; angina; coronary revascularization; congestive heart failure
- Renal disease: diabetic nephropathy; renal impairment (serum creatinine M > 133, W > 124 μmol/l; M > 1.5, W > 1.4 mg/dl), proteinuria (> 300 mg/24 h)
- Peripheral vascular disease
- Advanced retinopathy: hemorrhages or exudates, papilledema

er-assisted tomography (CAT). For brain assessment brain magnetic resonance imaging may be used [25].

Goals of Treatment

The primary goal of treatment of the patient with high blood pressure is to achieve the maximum reduction in the long-term total risk of cardiovascular morbidity and mortality. This requires treatment of all the reversible risk factors identified, including smoking, dyslipidemia, or diabetes, and the appropriate management of associated clinical conditions, as well as treatment of the raised blood pressure per se. On the basis of current evidence from trials, it can be recommended that blood pressure, both systolic and diastolic, be intensively lowered at least below 140/90 mmHg and to definitely lower values, if tolerated, in all hypertensive patients, and below 130/80 mmHg in

diabetics, keeping in mind, however, that systolic values below 140 mmHg may be difficult to achieve, particularly in the elderly.

Lifestyle Changes

Lifestyle measures should be instituted whenever appropriate in all patients, including subjects with high normal blood pressure and patients who require drug treatment. The purpose is to lower blood pressure and to control other risk factors and clinical conditions present. The lifestyle measures that are widely agreed to lower blood pressure or cardiovascular risk and that should be considered, are: smoking cessation, weight reduction, reduction of excessive alcohol intake, physical exercise, reduction of salt intake, increase in fruit and vegetable intake, and decrease in saturated and total fat intake.

Indications and Contraindications for the Major Classes of Antihypertensive Drugs

Class	Conditions favoring the use	Compelling	Possible
Diuretics (thiazides)	Congestive heart failure Elderly hypertensives Isolated systolic hypertension Hypertensives of African origin	Gout	Pregnancy
Diuretics (loop)	Renal insufficiency Congestive heart failure	Renal failure Hyperkalemia	
Diuretics (anti-aldosterone)	Congestive heart failure Post-myocardial infarction		
β -blockers	Angina pectoris Post-myocardial infarction Congestive heart failure (uptitration) Pregnancy Tachyarrhythmias	Asthma Chronic obstructive pulmonary disease A-V block (grade 2 or 3)	Peripheral vascular disease Glucose intolerance Athletes and physically active patients
Calcium antagonists (dihydropyridines)	Elderly Isolated systolic hypertension Angina pectoris Peripheral vascular disease Carotid atherosclerosis Pregnancy		Tachyarrhythmias Congestive heart failure
Calcium antagonists (verapamil, diltiazem)	Angina pectoris Carotid atherosclerosis Supraventricular tachycardia	A-V block (grade 2 or 3) Congestive heart failure	
ACE inhibitors	Congestive heart failure LV dysfunction Post-myocardial infarction Nondiabetic nephropathy Type 1 diabetic nephropathy Proteinuria	Pregnancy Hyperkalemia Bilateral renal artery stenosis	
AT ₁ blockers	Type 2 diabetic nephropathy Diabetic microalbuminuria Proteinuria LV hypertrophy ACE inhibitor cough		
α -blockers	Prostatic hyperplasia (BPH) Hyperlipidemia		

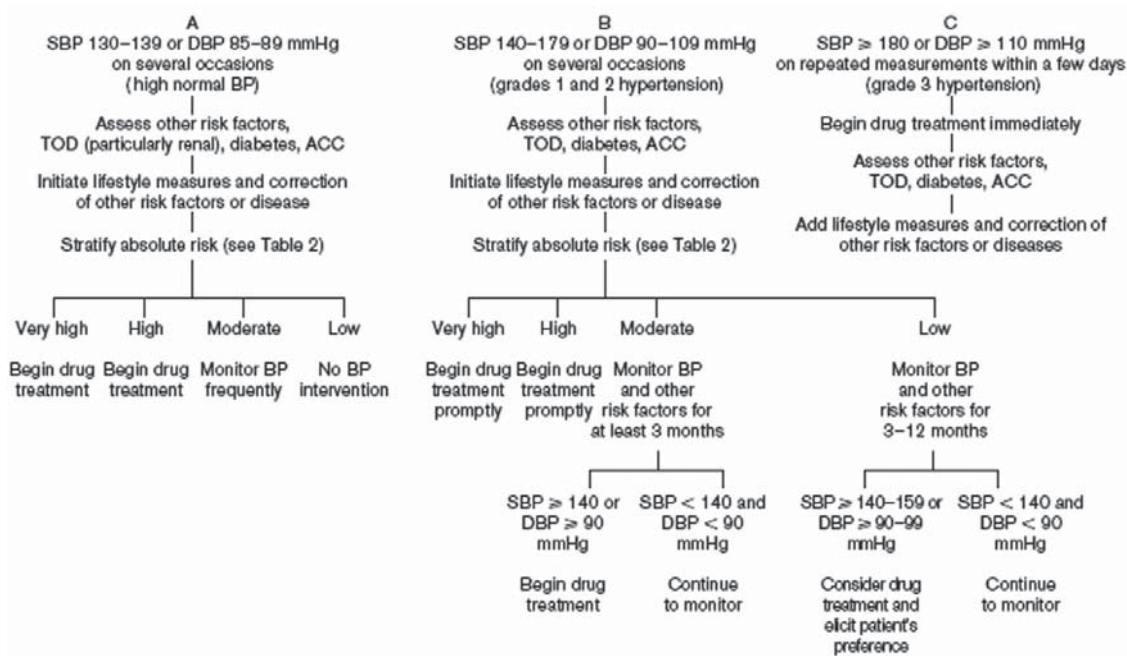


Figure 1. Initiation of hypertensive treatment. Decision based on initial blood pressure levels (A, B, C) and total risk level. ACC: associated clinical conditions; BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure; TOD: target organ damage.

Abbildung 1. Beginn der Hypertoniebehandlung. Entscheidung basierend auf den ersten Blutdruckmessungen (A, B, C) und Gesamtrisiko; ACC: assoziierte klinische Befunde; BP: Blutdruck; DBP: diastolischer Blutdruck; SBP: systolischer Blutdruck; TOD: Zielorganschaden.

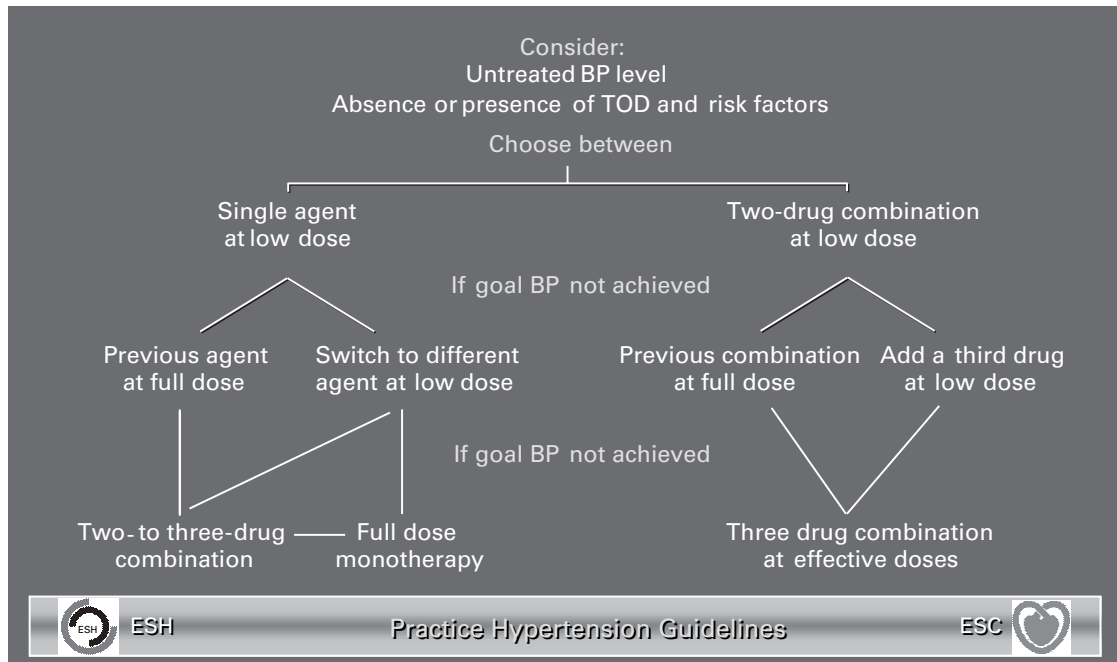


Figure 2. Choice between monotherapy and combination therapy. BP: blood pressure; TOD: target organ damage.

Abbildung 2. Wahl zwischen Mono- und Kombinationstherapie. BP: Blutdruck; TOD: Zielorganschaden.

Monotherapy Versus Combination Therapy

In most, if not all, hypertensive patients, therapy should be started gradually and target blood pressure values achieved progressively through several weeks (Figure 1).

To reach target blood pressure, it is likely that a large proportion of patients will require combination therapy with more than one agent [26]. According to the baseline blood pressure and the presence or absence of complications, it appears reasonable to initiate therapy either with a low dose of a single agent or with a low-dose combination of two agents (Figure 2). There are advantages and disadvantages with either approach [27].

Choice of Antihypertensive Drugs

The main benefits of antihypertensive therapy are due to lowering of blood pressure per se [28]. There is also evidence that specific drug classes may differ in some effect or in special groups of patients [28]. Drugs are not equal in terms of adverse effects, particularly in individual patients. The major classes of antihypertensive agents – diuretics, β -blockers, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor antagonists – are suitable for the initiation and maintenance of therapy. Emphasis on identifying the first class of drugs to be used is probably outdated by the need to use two or more drugs in combination in order to achieve goal blood pressure. Within the array of available evidence, the choice of drugs will be influenced by many factors, including: previous experience of the patient with antihypertensive agents, cost of drugs, risk profile, presence or absence of target organ damage, clinical cardiovascular or renal disease or diabetes, patient's preference.

Antihypertensive Therapy in the Elderly

There is little doubt from randomized controlled trials that older patients with systolic-diastolic or with isolated systolic hypertension [29] benefit from antihypertensive treatment in terms of reduced cardiovascular morbidity and mortality [30]. Initiation of antihypertensive treatment in elderly patients should follow the general guidelines but should be particularly gradual, especially in frail individuals. Blood pressure measurement should also be performed in the erect posture, to exclude patients with marked postural hypotension from treatment and to evaluate postural effects of treatment. Many elderly patients will have other risk factors, target organ damage, and associated cardiovascular conditions, to which the choice of the first drug should be tailored [31]. Many elderly patients need two or more drugs to control blood pressure, particularly since it is often difficult to

lower systolic blood pressure to below 140 mmHg [30]. In subjects aged 80 years and over, a recent meta-analysis concluded that fatal and nonfatal cardiovascular events, but not mortality, are reduced by antihypertensive therapy [29].

Antihypertensive Therapy in Diabetics

Nonpharmacological measures (particularly weight loss and reduction in salt intake) should be encouraged in all patients with type 2 diabetes, independently of the existing blood pressure. These measures may suffice to normalize blood pressure in patients with high normal or grade 1 hypertension and can be expected to facilitate blood pressure control by antihypertensive agents. The goal blood pressure to aim at during behavioral or pharmacological therapy is below 130/80 mmHg [32]. To reach this goal, most often combination therapy will be required. It is recommended that all effective and well-tolerated antihypertensive agents are used, generally in combination. Available evidence indicates that renoprotection benefits from the regular inclusion in these combinations of an ACE inhibitor in type 1 diabetes and of an angiotensin receptor antagonist in type 2 diabetes. In type 2 diabetic patients with high normal blood pressure, who may sometimes achieve blood pressure goal by monotherapy, the first drug to be tested should be a blocker of the renin-angiotensin system. The finding of microalbuminuria [33, 34] in type 1 or 2 diabetics is an indication for antihypertensive treatment, especially by a blocker of the renin-angiotensin system, irrespective of the blood pressure values [35–37].

Antihypertensive Therapy in Patients with Deranged Renal Function

Before antihypertensive treatment became available, renal involvement was frequent in patients with essential hypertension. Renal protection in diabetes has two main requirements: strict blood pressure control (< 130/80 mmHg and even lower) [38], if proteinuria is > 1 g/day, lowering proteinuria [35, 36, 39] to values as near to normal as possible. To reduce proteinuria, either an angiotensin receptor blocker or an ACE inhibitor is required [40]. To achieve the blood pressure goal, combination therapy is usually required, with addition of a diuretic and a calcium antagonist. To prevent or retard nephrosclerosis in hypertensive nondiabetic patients, blockade of the renin-angiotensin system appears more important than attaining very low blood pressure, but evidence is so far restricted to African-American hypertensives, and suitable studies in other ethnic groups are required. It appears prudent, however, to lower blood pressure intensively in all hy-

pertensive patients with deranged renal function [41]. An integrated therapeutic intervention (antihypertensives, statins, antiplatelet therapy, etc.) frequently has to be considered in patients with renal damage.

Resistant Hypertension

Resistant hypertension is defined as blood pressure over 140/90 mmHg despite the use of three antihypertensive agents one of which is a diuretic [42]. Causes of resistant hypertension include unsuspected secondary cause [43], poor adherence to therapeutic plan, continued intake of drugs that raise blood pressure, failure to modify lifestyle including weight gain and heavy alcohol intake (i.e., binge drinking), volume overload due to inadequate diuretic therapy, progressive renal insufficiency, high sodium intake. *Causes of spurious resistant hypertension include isolated office (white-coat) hypertension, and failure to use large cuff on large arm.*

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