Federal Ministry of Health
Non-Communicable Diseases Directorate
&
Sudan Society of hypertension (SSH)
www.ssh-sd.org

Sudan Guidelines for the Management of Systemic Hypertension in Adults
First Edition 2011

Updated by Non-Communicable Diseases Directorate
&
The Sudan Society of Hypertension
April 2014

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1. the JNC7 the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure”

2. “WHO/ISH (international society of hypertension) Clinical Guidelines for the Management of Hypertension”

3. “British Hypertension Society Guidelines”

4. “ESC (European society of cardiology ) and ESH(European society of hypertension ) 2013 Guidelines for the Management of Arterial Hypertension”

5. International Society of hypertension in black guidelines for management of hypertension

6. 2014 Evidence-based Guideline for the Management of High blood Pressure in Adults

Report from the Panel Members Appointed to the Eighth joint national Committee (JNC 8)

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Sudan aspires to establish a sustainable systematic health development process for all citizens including prevention of non-communicable diseases and their complications to ensure a public well being. As a result, the Ministry of Health has adopted many health policies and programs one of which is establishing local guidelines for the Management of systemic Hypertension. This disease affects 20 percent of the population in Sudan, children and adults alike, and is a leading cause of cardiovascular, cerebrovascular and renal diseases.

The NCDs Directorate and the Sudan Society of Hypertension has an important role in translating guidelines and programs into practical plans of actions, unified in a protocol for early diagnosis and proper management of this health dilemma and its complications. These guidelines were prepared by the First Working Party of the Federal Ministry of Health Non-Communicable Diseases Directorate, the Sudan Hypertension Society and the Cardiology/ Medicine and Pediatrics Consultative Councils.

They have to develop, in collaboration with interested groups, research and evidence based knowledge database specific for issues related to our culture and heritage. These scientific resources should be made readily accessible online, and provide brochures and pamphlets for healthcare providers.

In this regard, we would like to express our deep appreciation to the members of the Sudan Society of Hypertension (SSH) and the NCDs for their efforts in developing these guidelines for the direct use by healthcare providers.

May all of us pray to Allah, the almighty for more success

Prof. Hassan Abuaisha
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<th>Description</th>
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<tr>
<td>AAFP</td>
<td>American Academy of Family Physicians</td>
</tr>
<tr>
<td>ACE</td>
<td>Angiotensin Converting Enzyme</td>
</tr>
<tr>
<td>ACEIs</td>
<td>Angiotensin Converting Enzyme Inhibitors</td>
</tr>
<tr>
<td>ARBs</td>
<td>Angiotensin II Receptor Blockers</td>
</tr>
<tr>
<td>BMI</td>
<td>Body Mass Index</td>
</tr>
<tr>
<td>BP</td>
<td>Blood Pressure</td>
</tr>
<tr>
<td>CABG</td>
<td>Coronary Artery Bypass Graft</td>
</tr>
<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
</tr>
<tr>
<td>CCBs</td>
<td>Calcium Channel Blockers</td>
</tr>
<tr>
<td>CHD</td>
<td>Coronary Heart Disease</td>
</tr>
<tr>
<td>CKD</td>
<td>Chronic Kidney Disease</td>
</tr>
<tr>
<td>CO</td>
<td>Cardiac Output</td>
</tr>
<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
</tr>
<tr>
<td>CRF</td>
<td>Chronic Renal Failure</td>
</tr>
<tr>
<td>CV</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>CVD</td>
<td>Cardiovascular Disease</td>
</tr>
<tr>
<td>CVP</td>
<td>Central Venous Pressure</td>
</tr>
<tr>
<td>CXR</td>
<td>Chest X-Ray</td>
</tr>
<tr>
<td>DASH</td>
<td>Dietary Approach to Stop Hypertension</td>
</tr>
<tr>
<td>DBP</td>
<td>Diastolic Blood Pressure</td>
</tr>
<tr>
<td>DM</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>EMAN</td>
<td>East Mediterranean Approach to Non-Communicable Diseases</td>
</tr>
<tr>
<td>ESC</td>
<td>European Society of Cardiology</td>
</tr>
<tr>
<td>ESH</td>
<td>European Society of Hypertension</td>
</tr>
<tr>
<td>FBS</td>
<td>Fasting Blood Sugar</td>
</tr>
<tr>
<td>FEC</td>
<td>Final Editing Committee</td>
</tr>
<tr>
<td>FMOH</td>
<td>Federal Ministry of Health</td>
</tr>
<tr>
<td>GDP</td>
<td>Gross Domestic Product</td>
</tr>
<tr>
<td>HDL</td>
<td>High Density Lipoprotein</td>
</tr>
<tr>
<td>HF</td>
<td>Heart Failure</td>
</tr>
<tr>
<td>HPT</td>
<td>Hypertension</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>IHD</td>
<td>Ischaemic Heart Disease</td>
</tr>
<tr>
<td>ISA</td>
<td>Intrinsic Sympathomymetic Activity</td>
</tr>
<tr>
<td>JNC</td>
<td>Joint National Committee</td>
</tr>
<tr>
<td>K</td>
<td>Korotkoff</td>
</tr>
<tr>
<td>LDL</td>
<td>Low Density Lipoprotein</td>
</tr>
<tr>
<td>LV</td>
<td>Left Ventricle</td>
</tr>
<tr>
<td>LVH</td>
<td>Left Ventricular Hypertrophy</td>
</tr>
<tr>
<td>NCDs</td>
<td>Non-Communicable Diseases</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non Steroidal Anti-Inflammatory Drugs</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean Arterial Blood Pressure</td>
</tr>
<tr>
<td>MI</td>
<td>Myocardial Infarction</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonant Imaging</td>
</tr>
<tr>
<td>OCP</td>
<td>Oral Contraceptive Pills</td>
</tr>
<tr>
<td>PHC</td>
<td>Primary Health Care</td>
</tr>
<tr>
<td>PP</td>
<td>Pulse Pressure</td>
</tr>
<tr>
<td>PPP</td>
<td>Power Parity per Head</td>
</tr>
<tr>
<td>RF</td>
<td>Risk Factor</td>
</tr>
<tr>
<td>RFT</td>
<td>Renal Function Test</td>
</tr>
<tr>
<td>RAA</td>
<td>Renin Angiotensin</td>
</tr>
<tr>
<td>SBP</td>
<td>Systolic Blood Pressure</td>
</tr>
<tr>
<td>SHTN</td>
<td>Sudan Society of Hypertension</td>
</tr>
<tr>
<td>SSH</td>
<td>Systolic Hypertension</td>
</tr>
<tr>
<td>SLE</td>
<td>Systemic Lupus Erythymatosus</td>
</tr>
<tr>
<td>SVR</td>
<td>Systemic Vascular Resistance</td>
</tr>
<tr>
<td>SR</td>
<td>slow release</td>
</tr>
<tr>
<td>TIA</td>
<td>Transient Ischemic Attack</td>
</tr>
<tr>
<td>TOD</td>
<td>Target Organ Damage</td>
</tr>
<tr>
<td>TPA</td>
<td>Tissue Plasminogen Activator</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>3D CT</td>
<td>3 Dimensions Computed Scan</td>
</tr>
</tbody>
</table>
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his document was the fruitful outcome of the dedicated efforts of a multitude of persons and institutions. It would not have been possible to produce these guidelines without the contributions, support and encouragement of a group of national consultants in the fields of internal medicine, cardiology, pediatric and public health. The Sudan Society of hypertension and the Consultative Councils in the Federal Ministry of Health were instrumental in leading the efforts which culminated in the production of this manual.

The Non-Communicable Diseases Directorate at the Federal Ministry of Health, (the policy making body) extends its deep gratitude and special thanks to the Sudan Hypertension Society and the Cardiology/ Medicine/ Pediatrics Consultative Councils for without their outstanding efforts and extensive deliberations over a long period of time, this outcome would not have been possible.

Dr. Zainab Swar Aldahab

Director/NCDs/FMoH
Introduction

Sudan health care system:

The official health care system of the Sudan is a three-tier system, which includes governmental health services provided by the Federal Ministry of Health, state ministry of health and armed forces. Health services are also provided through other bodies such as: universities, private sector (both for profit and non-profit), civil society and a newly established health insurance system.

Accessibility to services varies considerably between areas with the rural parts of the country suffering from inadequate coverage.

According to the 25 year strategy for the health sector (Sudan 2002-2027) rigidity of the organizational structure in the governmental health services at different levels and poor coordination between departments are some of the main problems facing the health care system of the country.

WHO estimates of national health accounts suggest that the percentage of the gross domestic product (GDP) for expenditure on health has been increasing over the 5 years (2000-2005) up to an estimated 4.7% in 2005, composed of both public and private expenditure, thus giving purchasing power parity per head (PPP) of about US$ 48.

Hypertension in Sudan:

It is estimated that there are one billion hypertensive individual globally. Hypertension is the third leading killer in the world, and four million people die annually as a direct result of hypertension. In the Eastern Mediterranean Region, the prevalence of hypertension averages 26% and it affects approximately 125 million individuals (1).

Hypertension has the highest prevalence among the major NCDs in Sudan (prevalence of 23.6% in Khartoum state, among adults (25 - 64 years) and (24.3%) in SHHS 2010 among adults. Hypertension accounts for 1.3% of the outpatient visits; it is represented as one of the 10 leading diseases treated in outpatient healthcare facilities, and also one of the 10 leading causes of death in Sudan (3).

The high prevalence of hypertension and its definite role in the development of cardiovascular disease puts hypertension control and prevention as one of the top priorities of the NCDs directorate in Sudan. The development of Sudan guideline for the management of hypertension is a cornerstone for the control and prevention of hypertension. These guidelines are intended to standardize the care and provide all health care providers with practical and up to date information regarding the management of hypertension.

Regarding the threshold of intervention the committee adopted a modified approach that is relatively lower than what is recommended by the above mentioned guidelines. Late patient presentation to healthcare facilities as well as irregularity of routine follow up prompted those lower threshold and shorter recommended intervals for follow up.
1-General issues

1.1 Target of the guidelines

To provide an accessible and comprehensive resource document for management of hypertension for health care professionals (Doctors, Nurses, pharmacists and all para medical personnel) at public and private sectors.

The guideline is aimed to be simple, practical and educational. Based on a concise protocol, it will be distributed to all health workers in primary, secondary and tertiary care levels

1.2 Objectives of the guidelines

1. To promote the primary prevention of hypertension and its cardiovascular complications by life style modification of high risk groups.
2. To increase the detection of under-diagnosed hypertension by routine screening and increase awareness of hypertension among the public.
3. To improve the treatment and control of hypertension to optimal levels. <
4. To reduce the risk of cardiovascular disease of treated hypertensive patients by pharmacological and non-pharmacological measures

1.3 Summary of the Recommendations

1- Measurement of blood pressure (BP) should be carried out regularly in all persons above 20 years of age even if they are asymptomatic.

2- Diagnosis of hypertension should be confirmed by the mean of two or more appropriate measured BP readings, on two or more visits using a validated machine except in emergency situations.

3- Assessment by focused history and examination should be performed to rule out secondary causes of hypertension and to assess for target organ damage (TOD).

4- Baseline investigations of a hypertensive patient include a complete blood count (CBC), renal function and electrolytes panel (RFT), urinalysis, fasting blood sugar (FBS) and fasting lipid profile

5- The risk of developing cardiovascular disease (CVD) can be estimated using either the categorical classification or the WHO risk prediction charts (if available).

6- The goal of BP level is <150/90 for patients 60 years and older and <140/90 for all patients between 18-59 years including those with co morbidities such as DM,CKD or CVD according to JNC 8

7- Life-style modifications should be recommended for all people with high BP and pre-hypertension. (120-139/80-89)

8. Initiate antihypertensive drug therapy if persistent systolic blood pressure (SBP) 140-159 and/or diastolic blood pressure (DBP) 90-99mmHg (stage 1) is obtained after one month follow up

9- Initiate antihypertensive drug therapy after two weeks of follow up if persistent SBP >160 and/or DBP>100mmHg mmHg. (stage 2) is obtained. 10- The use of calcium channel blockers (CCBs) or thiazide diuretics is recommended as first line therapy unless there are
compelling indications or contraindications for specific classes of antihypertensive drug

11-Combination therapy should be used when BP is >20/10 mmHg above the goals.

12- Unless contraindicated, low-dose aspirin (75-100 mg/day) is recommended for all people needing secondary prevention of ischemic CVD, and primary prevention in people with hypertension over the age of 50 years or who have a 10-year CVD risk ≥30% by using the WHO charts or moderate risk by using the categorical classification,

13-Statin therapy is recommended for all people with high BP complicated by CVD, irrespective of baseline total cholesterol or low-density lipoprotein (LDL) levels. Similarly, statin therapy is also recommended for primary prevention in people with high BP who have a 10-year CVD risk ≥20%, moderate risk or those more than 65 years of age

14-Advice is provided on the clinical management of hypertension in specific patient groups. These include the elderly, patients with diabetes mellitus, chronic kidney disease, in pregnancy and hypertension and surgery

15-A policy for follow-up care at primary and specialist care level is provided in these guidelines.
2- Definitions and classification of Hypertension

2.1 What is Blood pressure?
Blood pressure is the lateral force applied by the blood on the arterial walls. It is recorded in two numbers; the higher is the systolic pressure and the lower is the diastolic pressure. The measuring units are millimeters of mercury; both figures represent the force of blood against the arterial walls.

The higher systolic figure reflects the force of the left ventricle as it contracts in systole. The lower figure reflects the pressure of the blood during the brief time between “beats,” the ventricular diastole. While the pressure in the left ventricle at this time drops essentially to 0, the pressure in the aorta normally drops to about 80 mmHg in an adult. This pressure keeps the blood moving even between beats. (4, 5)

2.2 Definition of hypertension:

Hypertension is defined as that level of arterial blood pressure associated with doubling of long-term cardiovascular risk.

- Office BP of ≥140/90 mm Hg,
- Daytime ambulatory measurements of ≥135/85 mm Hg
- Or nocturnal measurements of ≥120/70 mm Hg

2.3 Classification

Provided that the readings are taken as the mean of two or more properly measured blood pressure readings, on two or more visits. (1)

- **Normal** blood pressure: is defined as level ≤ 120/80 mmHg, (1)
- **Pre hypertension:** is SBP of 120 – 139 and or DBP 80 – 89 mmHg. This group of patients is at increased risk for progression to hypertension and has significantly greater risk to develop future cardiovascular events than those with normal blood pressure. Therefore, they should be identified and managed separately. Clustering of cardiovascular risk factors (e.g., diabetes, dyslipidemia, obesity, and impaired glucose tolerance) is more prevalent in this group than in individuals with normal blood pressure. (1)

- **Isolated systolic Hypertension:** is defined as high systolic pressure more than 140) with normal diastolic pressure(<90). (1)

- **Hypertension can be classified into two stages according to the level of the blood pressure (Table 1). (6)**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic BP (mmHg)</th>
<th>Diastolic BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>And &lt;80</td>
</tr>
<tr>
<td>Pre hypertension</td>
<td>120---139</td>
<td>And /or 80---89</td>
</tr>
<tr>
<td>Stage 1</td>
<td>140---159</td>
<td>And /or 90---99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>&gt;160</td>
<td>And /or&gt;100</td>
</tr>
</tbody>
</table>

Simplified from JNC 7
2.4 Types of hypertension: (1, 6)

2.4.1 Primary hypertension: is defined as systemic hypertension of unknown cause that affects more than 95% of patients.

2.4.2 Secondary hypertension: affects less than 5% of the patients and is due to an underlying disorder.

2.4.2.1 Causes of secondary hypertension (table 2)

<table>
<thead>
<tr>
<th>Causes of systolic and diastolic hypertension</th>
<th>1-Renal</th>
<th>2-Endocrine</th>
<th>3-Exogenous hormones</th>
<th>4- Pregnancy-induced hypertension</th>
<th>5-Neurological disorders</th>
<th>6-Drugs</th>
<th>Causes of Systolic hypertension</th>
</tr>
</thead>
</table>

Rigidity of the aorta

Iatrogenic hypertension
3. Prevention of hypertension

3.1 Introduction

The WHO Expert Committee on Hypertension Control has stressed the importance of primary prevention of hypertension by preventing the rise of blood pressure, lowering blood pressure levels in the population and addressing modifiable risk factors in order to decrease cardiovascular morbidity and mortality. Applying these recommended measures is among the priorities of the Non-Communicable Diseases Directorate of Sudan Federal Ministry of Health (FMoH). These preventive policies are planned to take place at primary health care and community levels. *(1)*

3.2 Lifestyle modifications

To decrease the incidence of hypertension in the population, the following lifestyle modifications are needed:

- Weight control
- Increased physical activity
- Adopting the DASH eating plan

This can be achieved by improving communication between health providers and patients; this depends on the health provider's confidence and their ability to teach patients the necessary skills to follow the recommendations within the time available for preventive services. These goals can be achieved by training of the health providers and support of patients’ education and counseling.

3.3 Target groups for primary prevention:

- Pre-hypertensive patients.
- Individuals with family history of hypertension.
- Diabetic patients.
- Females with history of hypertension with pregnancy or toxemia of pregnancy.
- Individual with risk factors (e.g. smokers, overweight, sedentary lifestyle, unhealthy diet).

The approach should be directed also to: communities, schools, work sites, and food industries.

3.4 Primary prevention of hypertension at Primary Health Care (PHC) settings

The PHC facilities play a major role in early detection and treatment of hypertension.

PHC providers should:

BP should be measured regularly in all persons above 20 years of age; even if they are asymptomatic, at least once a year.

Advising patients with pre-hypertension and hypertension on lifestyle modifications, such as reduction of salt intake to 5g per day, which reduces risk of stroke (by 33%) and coronary heart disease (by 25%). Patients can also achieve significant reduction in blood pressure by making appropriate changes to their lifestyles.

3.5 Community approach to hypertension prevention

The community approach to hypertension prevention has high degree of generalization and cost-effectiveness. The objectives of Sudan’s Community Approach for hypertension prevention goes in line with the East Mediterranean Approach to Non-communicable diseases (EMAN) for primary hypertension prevention which aims at reducing the major risk factors for cardiovascular disease and their social and economic determinants. This could be achieved through launching community based programs that target both prevention and control of hypertension in addition to development of standards of care and cost effective case managements. This approach also emphasizes the importance of establishing effective collaboration between those implementing the community approach and the health authorities to sustain primary prevention.
4- Diagnosis and evaluation

4.1 Diagnosis of hypertension

Early diagnosis and management of hypertension is important so as to prevent its complications (1). Uncomplicated hypertension is usually asymptomatic or gives rise to minimal symptoms. Therefore, it usually goes unrecognized for several years and when obvious symptoms and signs develop this usually indicates the onset of target organ damage (TOD).

Anticipate hypertension in adults when the average of two or more SBP is ≥140 mmHg and/or DBP is ≥90 on at least two subsequent visits.

Inform patients clearly that a single elevated reading does not constitute a diagnosis of hypertension but is a sign that further observation is required. (1)

4.2 BP measurement technique and devices:

The person should be seated quietly for at least 5 minutes in a chair with the arm supported at the heart level. Caffeine, exercise, and smoking should be avoided for at least 30 minutes prior to measurement. No exogenous adrenergic stimulants e.g. nasal decongestants should be administered before measuring the blood pressure. (1)

- Use an appropriately sized cuff (cuff bladder encircling at least 80 percent of the arm) and the length should be one and half times the arm circumference to ensure accuracy. The examiner should have a larger and a smaller bladder available for fat and thin arms, respectively table(3)

<table>
<thead>
<tr>
<th>Arm circumference (cm)</th>
<th>Bladder size (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;33</td>
<td>13 X 24 (regular cuff)</td>
</tr>
<tr>
<td>33-42</td>
<td>17 X 32 (large cuff)</td>
</tr>
<tr>
<td>&gt;42</td>
<td>20 X 42 (thigh cuff)</td>
</tr>
</tbody>
</table>

- Inflate by 20 mmHg above the systolic BP (determined by the pulse) and deflate by 3 mmHg every second, Korotkoff sounds should be heard at least every 2 mmHg gradation of the mercury column.
- Take the mean of at least two measurements spaced by 1–2 minutes. Additional measurements might be needed if the first two are quite different (more than 5 mm Hg difference) and until the two readings are similar (8).
- Measure BP in both arms at first visit and take the higher value as the reference one.
- Take multiple measurements routinely in patients with irregular pulse (e.g. atrial fibrillation) and in older patients with systolic hypertension.
- Use phase I and V (disappearance) Korotkoff sounds 1 (8) to identify systolic and diastolic BP.

1 Korotkoff Phase I: begins with the sudden appearance of a faint, clear, tapping or thumping sound that gradually increases in intensity. Phase II: phase II begins when the sounds change to a loud “swishing” murmur. Phase III: the beginning of Phase III occurs
respectively. If the phase V goes to zero, phase IV (muffling) should be used to identify the diastolic blood pressure.

- Use a mercury sphygmomanometer or validated aneroid device. Make sure various parts e.g. rubber tubes, valves, amount of mercury, are kept in proper order. (1)
- Measure BP regularly in all persons above 20 years of age even if they are normotensive.
- Encourage the patients to monitor their BP at home and record the reading

4.3 Recommended response when hypertension is suspected during the first visit

<table>
<thead>
<tr>
<th>Initial BP measurement (mmHg)</th>
<th>Recommended response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or optimal</td>
<td>Recheck every year if the age above 40 years</td>
</tr>
<tr>
<td>Pre hypertension</td>
<td>Recheck every 6 months (treat if DM or CKD)</td>
</tr>
<tr>
<td>SBP 120-139 and/or DBP 80-89</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>Check every week for one month (treat if DM or CKD)</td>
</tr>
<tr>
<td>SBP 140-159 and/or DBP 90-99</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>Confirm with two readings every week for two weeks (treat if DM or CKD)</td>
</tr>
<tr>
<td>SBP &gt; 160 - and/or DBP &gt; 100</td>
<td></td>
</tr>
</tbody>
</table>

(7) Modified by the FEC

*If feasible, ambulatory or home BP monitoring should be considered in the following situations:

when the sounds assume a loud, distinct, knocking quality. These sounds are less intense than those of Phase I. Phase IV: begins when the sounds suddenly become muffled and have a faint murmur-like or “swishing” quality. Phase V: begins when silence develops.
4.4 Initial assessment of newly diagnosed hypertensive patient

Assess every new patient with hypertension through history taking, examination and investigations for:

1. Secondary causes.
2. Risk factors for cardiovascular diseases.
3. Contributory factors.
4. Target organs damage.
5. Associated clinical conditions.
6. Drug contraindications.

1- suspected white coat hypertension
2- suspected episodic hypertension
3- hypertension resistant to increased medication
4- symptomatic patients on antihypertensive medications
5- autonomic dysfunction
6- to evaluate whether antihypertensive therapy is moderating early morning B.P. surge
7- large variation in B.P. values
8- elevated office B.P. in pregnant women with suspected pre-eclampsia
9- to establish non dipper status or nocturnal hypertension
**Table (5) Initial assessment of newly diagnosed hypertensive patient**

| 1) Assessment of causes (Most common causes) (7) | Drugs: e.g. NSAID’s, oral contraceptive pills and steroids  
Renal parenchymal and Renal vascular disease (abdominal or loin bruit)  
Endocrine disease: pheochromocytoma, Conn’s syndrome, Cushing syndrome  
Coarctation of the aorta (radio-femoral delay or weak femoral pulses) |
|-----------------------------------------------|
| 2) Assessment of risk factors for cardiovascular diseases (10) | Systolic and diastolic BP levels  
Levels of pulse pressure (in the elderly)  
Age (> 55 years for males and >65 years for females)  
Smoking  
Dyslipidemia  
Total cholesterol 5.0 mmol/l (190 mg/dl)  
  1. LDL-C: 3.0 mmol/l (115 mg/dl)  
  2. HDL-C:  
      a. Male: 1.0 mmol/l (40 mg/dl)  
      b. Female: 1.2 mmol/l (46 mg/dl)  
  3. TG: 1.7 mmol/l (150 mg/dl)  
Diabetes Mellitus  
Impaired glucose tolerance (Fasting plasma glucose 5.6–6.9 mmol/L (102–125 mg/dl)  
Abdominal obesity (Waist circumference >102 cm (M), >88 cm (W))  
Family history of premature CVD: Male at age 55 years; Female at age 65 years) (2) |
| Assessment of contributory factors (1) | Overweight, Lack of exercise  
Excess alcohol intake (>3 units/day) - Excess salt intake  
Environmental stress |
| Target Organ Damage | Stroke, TIA, dementia, carotid bruits  
LVH and/or LV strain on ECG, heart failure  
Myocardial infarction, angina, CABG or angioplasty, Peripheral vascular disease  
Fundal hemorrhages or exudates, papilledema  
Proteinuria, Renal impairment (raised serum creatinine) |
| Associated clinical conditions | Diabetes- CVD–CHD- congestive heart failure-CKD  
Aortic disease-Peripheral arterial disease Hypercholesterolemia |
| Drug contraindications | The treatment of hypertension should be tailored to each patient according to the initial assessment. |

The treatment of hypertension should be tailored to each patient according to the initial assessment. (1)

4.5 Patient evaluation

4.5.1 Clinical history:

Ask about:

1. Duration of high blood pressure
2. Symptoms indicating presence of secondary hypertension.
3. Family history of cardiovascular disease, hypertension and/or hyperlipidemia.
5. Symptoms of target organ damage:
   - Eye: impaired vision
   - Brain: headache, vertigo, transient ischemic attacks, sensory or motor deficits.
- Heart: palpitation, chest pain, shortness of breath, swollen ankles
- Kidney: proteinuria, haematuria, generalized body swelling and encephalopathy due to uremia
- Peripheral arteries: cold extremities, intermittent claudication

7. Tobacco use
8. Diet
9. Exercise
10. Stress

4.5.2 Physical examination:
Check for:
1. Evidence of visceral obesity:
   - Body Weight, BMI, waist circumference (WCC), Hip circumference (HCC), WCC/HCC, mid arm circumference
2. Signs of secondary hypertension.
   - General features of Cushing syndrome.
   - Pulse for diminished and delayed femoral pulse and reduced femoral blood pressure (coarctation of the aorta)
   - Palpation of enlarged kidneys (e.g. polycystic kidney)
   - Auscultation of precordial or back murmurs (aortic disease) or abdominal murmurs ( renovascular hypertension)
3. Signs of target organ damage
   - Brain: Murmurs over neck arteries, motor or sensory defects
   - Eyes: Fundoscopic abnormalities
   - Heart: Cardiac enlargement, arrhythmias, gallops sound, pulmonary crackles, dependent edema.
   - Peripheral arteries: Absence, reduction, or asymmetry of pulses, cold extremities, ischemic skin lesions.

4.5.3 Investigations:
1. Urine strip test for Albumin and blood.
2. Serum creatinine and electrolytes.
3. Fasting blood glucose.
4. Fasting lipid profile.
5. Haemoglobin and haematocrit

4.6 Assessment of CVD risk

4.6.1 Methods:

The risk of developing CVD can be estimated using either the categorical classification or the WHO risk prediction charts annex (2).
The two methods of calculating the risk approximately estimate the risk of cardiovascular disease morbidity and mortality in the coming 10 years.

We highly recommend the use of WHO risk chart since it can give more precise assessment of the risk. However, the categorical method can be used when the risk assessment charts are not available.

4.6.2 Categorical classification: According to the level of the blood pressure and the presence or absence of the risk factors of cardiovascular disease hypertensive patients can be classified into three categories: low risk, medium risk, high risk. (see table below)

<table>
<thead>
<tr>
<th>Risk factor and disease history</th>
<th>Stage 1: SBP 140-159 and/or DBP 90-99</th>
<th>Stage 2: SBP &gt;160 and/or DBP &gt;100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors, no TOD</td>
<td>Low risk</td>
<td>Medium risk</td>
</tr>
<tr>
<td>1-2 risk factors or TOD</td>
<td>Medium risk</td>
<td>High risk</td>
</tr>
<tr>
<td>3 or more risk factors or TOD</td>
<td>High risk</td>
<td>High risk</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; TOD, target organ damage; *modified from the WHO and JNC 7

4.6.3 WHO Risk chart

The WHO/ISH risk prediction charts indicate 10-year risk of a fatal or nonfatal major cardiovascular event (myocardial infarction or stroke), according to age, sex, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus for WHO epidemiological sub-regions D annex (2).

There are two sets of charts one can be used in settings where blood cholesterol can be measured and the other set is for settings in which blood cholesterol cannot be measured.

Each chart can only be used in countries of the specific WHO epidemiological sub-region, in Sudan the recommended chart is the East Mediterranean region chart (EMRO)(1).

4.6.3.1 How to use the WHO risk prediction chart

Calculate a score based on several risk factors as a percentage chance, for example, if the score is 30% this means that there is a 30% chance of developing a cardiovascular disease within the next 10 years.

- **High risk** - if the score is 20% or more. (That is, a 2 in 10 chance or more of developing a cardiovascular disease within the next 10 years.)
- **Moderate risk** - if the score is 10-20% (between 1 in 10 and 2 in 10 chance).
- **Low risk** - if the score is less than 10% (less than a 1 in 10 chance)

(Risk assessment chart annex (2).
4.7 Mean arterial pressure (MAP)

4.7.1 Clinical significance

MAP is considered to be the perfusion pressure seen by organs in the body. It is believed that a MAP that is greater than 60 mmHg is enough to sustain the organs of the average person.

MAP is normally between 70 to 110 mmHg

If the MAP falls significantly below this number for an appreciable time, the end organ will not get enough blood flow, and will become ischemic.

Mean arterial pressure can be determined from:

\[
MAP = (CO \times SVR) + CVP
\]

Where:

- \( CO \) is cardiac output
- \( SVR \) is systemic vascular resistance
- \( CVP \) is central venous pressure and usually small enough to be neglected in this formula.

At normal resting heart rates MAP can be approximated using the more easily measured systolic and diastolic pressures, SP and DP:

\[
MAP \approx DP + \frac{1}{3}(SP - DP)
\]

or equivalently

\[
MAP \approx \frac{2}{3}(DP) + \frac{1}{3}(SP)
\]

or equivalently

\[
MAP \approx \frac{(2 \times DP) + SP}{3}
\]

or equivalently

\[
MAP \approx DP + \frac{1}{3}PP
\]

Where \( PP \) is the pulse pressure, \( SP - DP \)

At high heart rates MAP is more closely approximated by the arithmetic mean of systolic and diastolic pressures because of the change in shape of the arterial pressure pulse. (9, 10)
5.1 Goals of treatment:
The goal in the treatment of hypertension is to reduce the long term risk of cardiovascular morbidity and mortality. This requires:

- Treatment of modifiable risk factors such as; smoking, dyslipideamia, obesity, and diabetes mellitus.
- Proper management of associated clinical conditions, such as; congestive heart failure, coronary artery disease, transient ischemic attacks.
- The goal of BP level is $<150/90$ for patients 60 years and older and $<140/90$ for all patients between 18-59 years including those with co morbidities such as DM, CKD or CVD according to JNC 8.

5.2 Patient involvement:
Hypertension is a lifelong disease and its treatment requires commitment to lifestyle changes, taking regular therapy and regularly attending follow-up appointments.

Patient involvement in the treatment makes it more likely that the patient will adhere to the medication, thus achieving good control.

Effective involvement starts with adequate explanation of the nature of the disease, discussion of the risk factors that might lead to its development, and where appropriate the patient should be involved in the decision as to whether they should take lifestyle action or start drug therapy, and in particular decisions about which individual drugs they should take, possible side-effects and the likelihood that they may need to take at least two or more medications.

Adequate explanation of the all relevant information should be carried out in a simple layman terms. Special attention should be paid to uneducated people or those who have a low awareness of their disease, and the elderly since they may have difficulty in recalling the information. Moreover, a written plan should be provided to all patients in order to improve their adherence to treatment.

5.3 General guidance:
- Patients with isolated systolic hypertension have the same risk for developing cardiovascular events as those with high diastolic pressure. Therefore, they should be treated when the diagnosis is confirmed.
- Treating hypertension is associated with decrease in cardiovascular complications, including 35%-40% reduction in stroke incidence, 20%-25% reduction in myocardial infarction and $\geq 50\%$ reduction in heart failure.
- Establish a partnership with the patient and involve him/her adequately in formulating the management plan so as to encourage trust and adherence to treatment.
- Consider cultural beliefs and individual attitude in formulating a treatment plan.
- Involve the whole family to facilitate the adoption of healthy lifestyle and increase adherence to the therapy.

5.4 Plan of management after confirmation of pre hypertension and hypertension: table (3)
1. Non Pharmacological approach such as lifestyle modifications
2. Pharmacological therapy
Table 7: Plan of management after confirmation of pre-hypertension and hypertension

<table>
<thead>
<tr>
<th>Presence or absence of CVD risk factors and diseases</th>
<th>Pre Hypertension SBP 120-139 And/ Or DBP 80-89</th>
<th>Stage 1 HTN SBP 140-159 And/ Or DBP 90-99</th>
<th>Stage 2 HTN SBP &gt;160 And/ Or DBP &gt;100</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk factors (Low risk) or (score less than 10%)</td>
<td>Life style change Check BP every 6 months No BP intervention</td>
<td>Lifestyle change + Treatment if persistently high over one month Targeting BP &lt; 140/90</td>
<td>Lifestyle change + Drug treatment if persistently high over two weeks Targeting BP &lt; 140/90</td>
</tr>
<tr>
<td>1-2 risk factors (moderate risk) or (score 10-20%)</td>
<td>Lifestyle change + Check BP every 2 months No BP intervention</td>
<td>Lifestyle change + Treatment if persistently high over two weeks Targeting BP &lt; 140/90</td>
<td>Lifestyle change + Immediate Drug treatment (consider combination therapy) Targeting BP &lt; 140/90</td>
</tr>
<tr>
<td>≥3 risk factors or High risk (score is ≥ 20%) Or DM or established CKD or CVD</td>
<td>Life style change Check every month No BP intervention</td>
<td>Life style change + Immediate drug treatment Targeting BP &lt; 140/90</td>
<td>Life style change + Immediate Drug treatment Targeting BP &lt; 140/90</td>
</tr>
</tbody>
</table>

5.5 Lifestyle modifications:
Lifestyle modification prevents hypertension, decrease blood pressure, enhance antihypertensive drug efficacy and decrease cardiovascular risk. (1)

The lifestyle measures that should be considered in all patients are:

- Cessation of smoking: This the most important lifestyle measure for prevention of cardiovascular and non-cardiovascular diseases, including stroke and coronary heart disease.
- Weight reduction and physical exercise: Weight reduction reduces blood pressure in overweight patients by 1.6/1.1 mmHg for every kilogram of weight loss, and also has positive effects on associated risk factors such as diabetes, Hyperlipidemia and left ventricular failure. Weight reduction may be achieved by increase in physical exercise such as brisk walking for at least 30 minutes per day, most days of the week.

  NB: For poorly controlled hypertensive patients heavy physical exercise should be discouraged.
- Reduction of salt intake and other dietary changes: Reducing sodium intake to 2.4 g sodium or 6 g sodium chloride reduces SBP by 4-6 mmHg. Patients should be advised to avoid salted food, to eat more fish, potassium, fruit and vegetables and to reduce intake of saturated fat. This is achieved by adoption of Dietary Approach to Stop Hypertension (DASH) that is rich in fruits, vegetables and low-fat dairy foods (whole grains, poultry, fish and nuts) and increased amount of potassium, calcium, magnesium, dietary fiber and protein, and is reduced in fats, red meat, sweets and sugar. The combination of low sodium intake and DASH diet is more effective than either alone.
Table 4: Summary of the recommended lifestyle modifications

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate SBP reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight</td>
<td>5–20 mmHg/10kg</td>
</tr>
<tr>
<td>Adopt DASH</td>
<td>Consume a diet rich in vegetables, fruits, and a eating plan low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8–14 mm Hg</td>
</tr>
<tr>
<td>Dietary sodium</td>
<td>Reduce dietary sodium intake to no more than sodium chloride 2.4 g sodium or 6 g salt</td>
<td>2–8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity at least 30 minutes daily, most days of the week</td>
<td>4–9 mmHg</td>
</tr>
</tbody>
</table>

5.6 Pharmacological therapy:

5.6.1 General Guidelines (1)

- Once the selection of the most appropriate agent for initial therapy has been made; a relatively low dose of a single drug should be started, aiming for a reduction of 5 to 10 mm Hg in blood pressure at each step.
- Thus, there should be a gradual approach to antihypertensive therapy in order to avoid symptoms related to overly aggressive blood pressure reduction.
- Individualized therapy. Perhaps the most crucial factor in the selection process is the presence of one or more concomitant conditions, some that could be worsened by the drug chosen, others that could be improved.
- Drug combinations. Combinations of smaller doses of two drugs from different classes is better to take advantage of the differences in the dose-response curves for therapeutic and toxic (side) effects.
- It is better to choose long acting preparations providing effective, 24-hour control of hypertension in a manner that encourages adherence to the regimen.

5.6.2 Initiation of drug treatment

Is determined by presence or absence of compelling indications for the use of a specific drug:

- In patients without compelling indications, the drug therapy must be initiated by a thiazide diuretic or a long acting Calcium channel blocker.
- In patients with compelling indications, initial drug is based on outcome data- from clinical trials- for specific anti-hypertensive drugs in treatment of special groups according to benefits of drugs on the associated condition.

5.6.3 Compelling indication:

- Ischemic heart disease
  - In patients with stable angina, the drug of choice is a β-blocker, alternatively calcium channel blockers (CCBs) can be used.
- In patients with unstable angina or myocardial infarction initial drug therapy should be β-blockers and angiotensin converting enzyme inhibitors (ACEI).
- In post myocardial infarction angiotensin converting enzyme inhibitors (ACEI), β-blockers and aldosterone antagonists are recommended.

- **Heart failure**
  - For patients with asymptomatic ventricular failure, ACE inhibitors and β-blockers are recommended.
  - For patient with clinical heart failure, ACE inhibitors, β-blockers, angiotensin receptor blockers (ARBs), aldosterone blockers and loop diuretics are recommended.

- **Diabetes mellitus**
  - Combination of two or more drugs are needed to achieve blood pressure of <140/90 mmHg.
  - ACE inhibitors and ARB treatments decrease the progression of diabetic nephropathy and reduce albuminuria.
  - Thiazide diuretic, ACE inhibitors, β-blockers, angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs) are beneficial decreasing cardiovascular diseases and stroke incidence.

- **Chronic kidney disease (CKD)**
  - Patients with chronic renal disease should receive aggressive blood pressure management to delay further impairment of renal function and prevent cardiovascular complications. Three or more drugs are often needed.
  - In patients with Proteinuric CKD, usually defined as greater than or equal to 500 mg/day or higher, the blood pressure should be lowered to less than 130/80 mmHg.
  - In patients with nonproteinuric CKD, defined as less than 500 mg/day, the blood pressure should be lowered to less than 140/90 mmHg.
  - JNC 8 sets a target BP goal of <140/90 for all CKD patients whether proteinuric or not.
  - ACE inhibitors and ARBs have good effects on the prognosis of renal disease.
  - With advanced renal disease increased doses of loop diuretic combined with other drugs are needed.

- **Cerebrovascular disease**
  - For patients with ischemic stroke who are not treated with thrombolytic therapy, most consensus guidelines recommend that BP not be treated acutely unless the hypertension is extreme (SBP >220 mmHg or DBP >120 mmHg), or the patient has active ischemic coronary disease, heart failure, aortic dissection, hypertensive encephalopathy, acute renal failure, or pre-eclampsia/eclampsia. When treatment is indicated, cautious lowering of BP by approximately 15% during the first 24 hours after stroke onset is suggested.


To prevent intracerebral bleeding in patients with recent ischemic stroke whose blood pressures are very high, cautious reduction of blood pressure by about 10%-15% is needed and this can be achieved by carefully monitored infusion therapy.
### Table 5: Indications and contraindications of antihypertensive drugs

<table>
<thead>
<tr>
<th>Class of drug</th>
<th>Compelling indications</th>
<th>Possible indications</th>
<th>Caution</th>
<th>Compelling Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-blockers</td>
<td>Benign prostatic Hypertrophy</td>
<td>Postural Hypotension Heart failure</td>
<td>Urinary incontinence</td>
<td></td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Heart failure, LV dysfunction post MI Established CHD type I diabetic nephropathy secondary stroke prevention</td>
<td>Chronic renal disease type II diabetic nephropathy, proteinuric renal disease</td>
<td>Renal impairment PVD</td>
<td>Pregnancy Reno vascular Disease</td>
</tr>
<tr>
<td>ARBs</td>
<td>ACE inhibitor intolerance Type II diabetic Nephropathy Hypertension with LVH Heart failure in ACE-intolérant patients post MI</td>
<td>LV dysfunction post MI Intolerance of other antihypertensive drugs proteinuric renal disease, Heart failure</td>
<td>Renal impairment PVD</td>
<td>Pregnancy, Reno vascular Disease</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>MI Angina</td>
<td>Heart failure, PVD Diabetes (except with CHD)</td>
<td>Heart failure, PVD Heart block</td>
<td></td>
</tr>
<tr>
<td>CCBs (dihydropyridine)</td>
<td>Elderly Isolated systolic hypertension</td>
<td>Elderly, Angina</td>
<td>Asthma/COP D, heart block</td>
<td></td>
</tr>
<tr>
<td>CCBs (rate limiting)</td>
<td>Angina</td>
<td>MI</td>
<td>Combination with beta-blockade</td>
<td></td>
</tr>
<tr>
<td>Thiazide/thiazide-like diuretics</td>
<td>Elderly, Isolated systolic hypertension Heart failure, Stroke prevention</td>
<td></td>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Gout</td>
<td></td>
</tr>
</tbody>
</table>

#### 5.6.4 Other drugs used in the management of hypertensive patients

- **Aspirin**: Unless contraindicated, low-dose aspirin (75--100mg/ day) is recommended for all people needing secondary prevention of ischemic CVD, and primary prevention in people with hypertension over the age of 50 years or who have a 10-year CVD risk $\geq 30\%$.

- **Statin**: therapy is recommended for all people with high BP complicated by CVD, irrespective of baseline total cholesterol or low-density lipoprotein (LDL)-cholesterol levels. Similarly, Statin therapy is also recommended for primary prevention in people with high BP who are above 65 years or have a 10-year CVD risk $\geq 20\%$. The target is to achieve optimal cholesterol lowering (reduction of the total cholesterol by 25% or LDL-cholesterol by 30%) or achieves total cholesterol of 4.0 mmol/l or LDL-cholesterol of 2.0 mmol/l, whichever is the greatest reduction.
5.6.5 Selection of antihypertensive drugs

The selection of antihypertensive drug is based on the presence or absence of compelling indication as indicated on the table above.

- Use of a single drug

The use of a single antihypertensive drug increases the adherence to the medication. However, the response to the antihypertensive drugs is substantially different between patients and the use of single drug will reduce the BP by no more than 7-8%. Therefore, the use of single drug is indicated mainly for patients with mild hypertension (8).

When a single drug is chosen to treat hypertension, it is recommended to start with a low dose and gradually build it up until adequate blood pressure control is achieved. If the patient develops persistent side effects or the control is not achieved; try another drug from another class and if no response then two or three drugs should be combined (1).

- Use of combination therapy

Most of the patients will need to use more than one drug due to the heterogeneity in the pathogenesis of BP elevations and the multiplicity of pathophysiological mechanisms responsible for high levels of BP.

Combination therapy should be considered when blood pressure is >20/10 mmHg above the goal. It is generally recommended to use drugs with different modes of action when combination therapy is indicated. Fixed drug combinations are recommended to reduce the number of medications, which may enhance adherence to treatment (1).

The policy of combination therapy that we are recommending in our guidelines is modified from the British Hypertension Society Algorithm (ABCD). The algorithm is developed to improve the control of hypertension and it is based on the notion that the renin levels are different among different groups of people (Caucasian have high renin / Africans have low renin) (8).

In our guidelines we recommend starting treatment with diuretics or long acting calcium channel blockers (drugs with minimal effect on the renin-angiotensin system) and then to add a drug with strong effect on the rennin-angiotensin system e.g. Angiotensin converting enzyme inhibitors, or angiotensin receptor blocker.

NB: diuretics enhance the effects of beta blockers and ACE inhibitors in Africans.

5.6.6 Steps of combining the drugs are (6)

**FIRST STEP**: THIAZIDE DIURETIC OR CCBS + ACEI or ARB (low dose of 2nd drug)

**SECOND STEP**: THIAZIDE OR CCBS + ACEI or ARB (max. dose of 2nd drug)

**THIRD STEP**: THIAZIDE + CCBS + ACEI or ARB (low-. dose of 3rd drug)

**FOURTH STEP**: THIAZIDE + CCBS + ACEI or ARB or {B- BLOCKER OR α – Blockers OR SPIRONOLACTONE OR OTHER DIURETICS OR CENTRALY ACTING DRUGS}.(max. doses)

**Screen for secondary causes if still not controlled. Consider ambulatory BP monitoring**

(If there is any compelling indication that prevent following these steps, the patient should be treated accordingly)
6. Follow-up for patients with hypertension

6.1 Level of follow up

All the patients with essential hypertension can receive medical care at primary care level (non-specialist care).

Refer patient to specialist care if any of the following criteria is present:

- Secondary hypertension
- Age less than 40 years (younger patients may have secondary hypertension which need to be treated under specialist care)
- Blood pressure not controlled with the use of single drugs or two drugs
- Albuminuria.
- Hyperlipidaemia (cholesterol more than 8 mmol/l).

6.2 Frequency of the follow-up visits at PHC level

All patients with hypertension should be provided with regular follow-up, the follow-up intervals can vary from one week to one year according to patient’s condition.

Arrange follow-up visits as follows:

- Grade 1: Monthly until goal blood pressure is achieved, then every 3 to 6 months.
- Grade 2: every 2 weeks until goal blood pressure achieved then every 3 months.
- Grade 3: weekly until the goal blood pressure achieved then every 3 months.
- In the presence of co-morbidity as DM or heart disease might increase the follow-up frequency.

6.3 What to do during the follow-up visit

1. Check the blood pressure
2. Check adherence to medication
3. Advice and educate on lifestyle modification
4. Inquire about symptoms that indicate the presence of target organ damage (complication) e.g. breathlessness, chest pain
5. Examine for signs of target organ damage
6. Investigate as required;
   - One week after initiating ACEIs: Serum creatinine and electrolytes
   - Annual routine investigations: Lipid profile, renal function test and electrolytes
   - Other investigations are requested according to the symptoms of target organ damage and the presence of concomitant disease e.g. DM
7. Decide whether to continue the same management plan or to modify it.

6.4 Modifying the management plan: (13)

Increase the dose of antihypertensive drugs if adequate response is not achieved.
The increment of the antihypertensive dose depends on the maximum drug effect,
Plan the increment in the doses as follows:

- Diuretics: after one month
- ACEIs: 2 weeks to 1 month
- CCBs: 2 weeks to 1 month
- ARBs: 2 weeks to 1 month
Consider reduction or discontinuation of antihypertensive drugs if the targeted blood pressure achieved and maintained for a period of at least one year, features in favor of withdrawal are: (1)

- Low blood pressure before and after therapy.
- Control of the blood pressure with a low dose of medicine.
- Patient’s willingness to maintain healthy lifestyle.

In above cases decrease the doses of antihypertensive medications first and then stop it if a good response has been maintained. Keep the patient on regular follow even after discontinuing the medication to maintain the blood pressure under control.

7-MANAGEMENT OF HYPERTENSION CRISIS

7.1 Frequency:
Approximately 1% of hypertensive patients will develop acute elevations in blood pressure at some point in their life.

7.2 Types:
1. Hypertensive emergencies: These conditions are characterized by severe elevations in BP (>180/120 mmHg) complicated by target organ dysfunction (11)
2. Hypertensive urgencies: This term is used for patients with severely elevated blood pressure without acute end-organ damage.

7.3 Aims of Treatment
1. To reduce the BP safely to non-morbid levels.
2. To prevent end-organ damage.
3. To tackle co-morbidities.
4. To prevent precipitating ischemic attacks.

7.4 Hypertensive emergencies:
7.4.1 Clinical conditions that meet the diagnostic criteria for hypertensive emergencies are:
1. Hypertensive encephalopathy
2. Dissecting aortic aneurysm
3. Acute left ventricular failure with pulmonary edema
4. Acute myocardial ischemia
5. Eclampsia
6. Acute renal failure
7. Symptomatic microangiopathic hemolytic anemia

7.4.2 The Clinical manifestations of hypertensive emergencies
The clinical manifestations are those associated with end-organ dysfunction. Organ dysfunction is uncommon with diastolic blood pressures less than 130 mmHg except in children and in pregnant women [the absolute level of blood pressure may not be as important as the rate of increase]. In patients with longstanding hypertension a systolic blood pressure of 200 mmHg or elevations in diastolic pressure up to 150 mmHg may be well tolerated without the development of hypertensive encephalopathy, whereas children or pregnant women may develop encephalopathy with a diastolic blood pressure of only 100 mmHg.
• Hypertensive encephalopathy gives rise to headache, altered level of consciousness, and/or focal neurologic sign. On physical examination, these patients may have retinopathy with arteriolar changes, hemorrhages and exudates as well as papilledema.

• Cardiovascular manifestations may predominate, with angina, acute myocardial infarction, or acute left ventricular failure

• Renal manifestation: in some patients, severe injury to the kidneys may lead to acute renal failure with oliguria and/or haematuria.

• In pregnant ladies, the clinical features vary but may include visual field defects, severe headaches, seizures, altered mental status, acute cerebrovascular accidents, severe right upper quadrant abdominal pain, congestive heart failure, and oliguria. In the vast majority of cases, this process can only be terminated by delivery. The decision to continue the pregnancy or to deliver the baby should be made following consultation between medical and obstetric personnel.

• Aortic dissection should be considered a likely diagnostic possibility in patients presenting with acute chest pain and elevated blood pressure. Left untreated, about three-quarters of patients with type A dissection die within 2 weeks of an acute episode, but with successful initial therapy the 5-year survival rate increases up to 75%.

7.4.3 Evaluation and management of hypertensive emergencies

• Distinction between a hypertensive emergency (which involves TOD) and a hypertensive urgency on the basis of the clinical evaluation.

• Measurement of the blood pressure in both arms by a physician.

• Use appropriately sized cuffs in obese patients.

• Physical examination should include palpation of pulses in all extremities, auscultation for renal bruits, focused neurologic examination, and a fundoscopic examination.

• Investigations should include the following:
  1) Complete blood count
  2) Peripheral blood smear (to exclude a microangiopathic anemia),
  3) Electrolytes, blood urea, creatinine,
  4) Urinalysis
  5) Electrocardiogram.
  6) Chest radiograph should be obtained in patients with shortness of breath or chest pain,
  7) Head computed tomography (CT) scan should be obtained in patients with focal neurological deficits
  8) Chest CT scan or magnetic resonance imaging scan should be considered in patients with unequal pulses and/or evidence of widened mediastinum on the chest radiograph.

Remember that patients in whom an aortic dissection is considered should not undergo transesophageal echocardiography until the blood pressure has been adequately controlled.

7.4.4 Initial Therapeutic Approach (11)

• Treat patients with hypertensive emergencies in intensive care unit for continuous monitoring of BP and intravenous administration of an appropriate antihypertensive drug (table 1).

• Reduce mean arterial BP by no more than 25% (within minutes to 1 hour), then if stable, to 160/100–110 mmHg within the next 2–6 hours (this is the initial goal therapy).
- Avoid excessive falls in blood pressure that may precipitate renal, cerebral, or coronary ischemia. Therefore, short-acting Nifidipine is no longer considered acceptable in the initial treatment of hypertensive emergencies or urgencies.

- If this level of BP is well tolerated and the patient is clinically stable, implement further gradual reductions toward a normal BP in the next 24–48 hours.

- Exceptions to the above recommendations are:
  - Patients with an ischemic stroke in which there is no clear evidence from clinical trials to support the use of immediate antihypertensive treatment
  - Patients with aortic dissection who should have their SBP lowered to <100 mmHg if tolerated
  - Patients in whom BP is lowered to enable the use of thrombolytic agents.

7.4.5 Recommended antihypertensive agents for hypertensive crises table (8)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Preferred antihypertensive agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute pulmonary edema</td>
<td>nitroglycerin (up to 60 μg/min) and a loop diuretic if needed IV CCBs</td>
</tr>
<tr>
<td>Acute myocardial ischemia</td>
<td>Labetalol or Esmolol in combination with nitro-glycerin (up to 60 μg/min)</td>
</tr>
<tr>
<td>Hypertensive encephalopathy</td>
<td>Labetalol, Nicardipine, or Fenoldopam</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>Labetalol or combination of Nicardipine or Fenoldopam and Esmolol or combination of Nitroprusside with either Esmolol or intravenous Metoprolol</td>
</tr>
<tr>
<td>Eclampsia</td>
<td>Labetalol or CCBs, Hydralazine may be used in a non-ICU setting</td>
</tr>
<tr>
<td>Acute renal failure, microangiopathic anemia</td>
<td>Hydralazine or CCBs</td>
</tr>
<tr>
<td>Sympathetic crisis/cocaine overdose</td>
<td>Verapamil, Diltiazem, or Nicardipine in combination with a benzodiazepine</td>
</tr>
</tbody>
</table>

7.5 Hypertensive urgencies:
This term is used for patients with severely elevated blood pressure without acute end-organ damage

- Patients with hypertensive urgencies may benefit from treatment with an oral, short-acting agent such as captopril, (other drugs) followed by several hours of observation.
- Use alternative approach adjustment in their antihypertensive therapy, particularly the of combination drugs, or reinstitution of medications if noncompliance is a problem
- Check patient with hypertensive urgency in the refer clinic in a week time
- Reduce the blood pressure gradually. The term urgency led to overtreatment which is therefore not without risk.
Severe hypertension
BP >180/120

ACUTE TARGET ORGAN DAMAGE

NO

Urgency

Treatment:
- Oral, short-acting agent such as captopril,
  OR
  - Adjustment in their own antihypertensive therapy
  +
  - Several hours of observation.

Yes

Emergency

Treatment:
- Treated in intensive care unit, monitor BP continuously and use IV drugs
  - Select drug appropriate as indicated on table
  - In the 1st hour reduce BP by no more of 25% of the mean

Figure 1 Management of severe hypertension (11)
# Table (9) Hypertensive emergency drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Onset of action</th>
<th>Duration of action</th>
<th>Special indications</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitroprusside</td>
<td>0.25–10 μg/kg per min</td>
<td>Instantaneous</td>
<td>1–2 min</td>
<td>Most hypertensive emergencies, caution with high hand intracranial pressure cyanide intoxication or azotemia</td>
<td>Nausea, vomiting, twitching, thiocyanate toxicity (AVOID its use for more than 48 hrs to prevent the side effects)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydralazine</td>
<td>10–20 mg/IV</td>
<td>10–20 min</td>
<td>1–4 hrs</td>
<td>Eclampsia</td>
<td>Tachycardia, flushing, headache, or aggravation of angina</td>
</tr>
<tr>
<td></td>
<td>10–50 mg/IM</td>
<td>20–30 min</td>
<td>4–6 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labetalol</td>
<td>20–80 mg IV</td>
<td>5–10 min</td>
<td>min 3–6 hrs</td>
<td>Most hypertensive except acute heart failure</td>
<td>Vomiting, burning throat, postural hypotension scalp tingling</td>
</tr>
<tr>
<td></td>
<td>Bolus every 10 min, infusion 2 mg/min IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>250–500 μg/kg per min bolus then 50–100 μg/kg per min IV infusion may repeat bolus after 5 min or increase infusion to 300 μg/min</td>
<td>1–2 min</td>
<td>10–30 min</td>
<td>Aortic dissection preoperative</td>
<td>Hypotension, nausea, asthma, first degree heart block, heart failure</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>5–100 μg/min</td>
<td>2–5 min</td>
<td>5–10 min</td>
<td>Coronary ischemia</td>
<td></td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5–15 mg/h IV</td>
<td>5–10 min</td>
<td>15–30 min</td>
<td>Most hypertensive emergencies except acute heart failure; caution with coronary ischemia</td>
<td>Tachycardia, headache, flushing, local phlebitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>May exceed 4 hrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enalapril</td>
<td>1.25–5 mg every 6 hours</td>
<td>15–30 min</td>
<td>6–12 hrs</td>
<td>Acute left ventricular failure, avoid in acute myocardial infarction</td>
<td>Abrupt fall in BP in high renin states. Variable response</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>0.1–0.3 μg/kg per min</td>
<td>&lt;5 min</td>
<td>30 min</td>
<td>Most hypertensive emergency; caution with glaucoma</td>
<td>Tachycardia, headache, flushing Adrenergic inhibitors</td>
</tr>
<tr>
<td>Phentolamine</td>
<td>5–15 mg IV bolus</td>
<td>1–2 min</td>
<td>10–30 min</td>
<td>Catecholamine excess</td>
<td>Tachycardia, flushing, headache</td>
</tr>
</tbody>
</table>
7.6 Special consideration: Management of hypertension with acute stroke:
The management of BP during an acute stroke remains controversial. BP is often elevated in the immediate post-stroke period and is thought by some to be a compensatory physiologic response to improve cerebral perfusion to ischemic brain tissue. As a result, it has been common practice after acute cerebral infarction to reduce or withhold BP treatment until the clinical condition has stabilized. Nevertheless, it is recommended that: in patients with recent ischemic stroke whose SBP is >220 mmHg or DBP 120–140 mmHg, cautious reduction of BP by about 10–15 % is suggested, while carefully monitoring the patient for neurologic deterioration related to the lower pressure. If the DBP is >140 mmHg, a carefully monitored infusion of sodium Nitroprusside should be used to reduce the BP by 10–15 % (11).

The use of thrombolytic agents in ischemic stroke is affected by the BP level. SBP >185 mmHg or diastolic pressures >110 mmHg are contraindications to the use of tissue Plasminogen activator (TPA) within the first 3 hours of an ischemic stroke. Once a thrombolytic agent has been initiated, BP should be monitored closely, especially in the first 24 hrs (11).

7.7 Summary of treatment in hypertensive emergencies and urgencies

- The treatment should be established in an intensive care unit.
- In hypertensive urgency the recommended action is to reduce the BP within 24 to 48 hours by oral route.
- In patients with end organ damage rapid but controlled lowering of blood pressure is indicated to limit and prevent further organ damage. The type of antihypertensive should be selected according to the organ involved.
- Severe hypertension in the setting of an acute ischemic stroke, reduce the blood pressure should be reduced by no more than 10–15 % in the first 24 hours.
- In patients with intra cerebral hematomas lowering blood pressure is currently recommended only when the systolic blood pressure is greater than 200 mmHg or the diastolic pressure is greater than 110 mmHg.

Pregnant patients with systolic blood pressure greater than 180 mmHg or diastolic blood pressure greater than 110 mm Hg, should be treated by the intravenous route keeping the diastolic blood pressure over 90 to avoid fetal distress.
8. Special Groups

8.1 Hypertension in the elderly:

Older people show greater BP variability, so multiple measurements on several occasions are mandatory to confirm the diagnosis. It is also worth noting that seated and standing measurements be taken during initial assessment and after initiating therapy because of high prevalence of orthostatic hypotension (SBP falls ≥20 mmHg). Treatment may need to be titrated to the standing value. Lifestyle measures should be offered to all older people as they have been proven to be effective in reducing BP as they are in younger people.

Thiazide/thiazide-like diuretics are especially effective at lowering BP in older people as are dihydropyridine CCBs.

ARB-based therapy was shown to be more effective than beta blockers based therapy at reducing the risk of stroke and CVS mortality in people with ISH, so beta-blockers should be used when indicated, e.g. post MI, angina or HF. More than one drug can be used and logical combinations are outlined in the ABCD algorithm. (8)

8.2 Hypertension and pregnancy:

There is consensus for initiating treatment at BP level 150 – 160 mmHg SBP or 100-110 mmHg DBP or in the presence of target organ damage. There is concern that excessive lowering of BP leads to intrauterine growth restriction. Regarding the choice of anti-hypertensive therapy, methyldopa remains the drug of choice. CCBs (esp. long acting form of Nifidipine) and the vasodilator Hydralazine are commonly used as second line drugs. Labetalol can also be used as second line and esp. for resistant hypertension in third trimester. Beta-blockers frequently less used as it inhibits fetal growth.

ACE-inhibitors and ARBs are contraindicated during pregnancy. Thiazide/thiazide-like diuretics should be avoided as much as possible, as theoretically, they have the potential of reducing circulatory blood volume. (8)

8.3 Hypertension and diabetes:

The target blood pressure for diabetics with hypertension is <140/90 mmHg and combined therapy is usually needed to achieve this target. ACE-inhibitor or ARBs are the first line therapies. Other drugs that will be required to achieve targeted blood pressure are long acting CCBs, beta blockers and alpha blockers. In patients with renal impairment and/or edema, a loop diuretic may be required as an alternative to, or in addition to, thiazide and thiazide-like diuretics. A precaution to use of thiazides and thiazide-like diuretics is hyperglycemia. (10)

8.4 Diabetic nephropathy:

Type 1 diabetes and diabetic nephropathy:

The target B.P is <140/90 mmHg. Control of BP by using an ACEI slow the rate of decline of renal function in overt diabetic nephropathy and delay progression from the microalbuminuric phase to overt nephropathy. ACE-inhibitors have specific renoprotective properties in patients with incipient or overt type 1 diabetic nephropathy and are recommended as initial therapy. ARBs can be used as an alternative in patients with a persistent cough due to ACEI treatment. The ACE-inhibitors / ARBs should be titrated to the maximum dose. If the goal is not achieved by one medication then combined therapy is required. Drugs that can be used in combined therapy are low dose thiazide/thiazide-like, CCBs, beta blockers and alpha blockers (8)
Type II diabetes and diabetic nephropathy:

Anti-hypertensive therapy slows the progression of nephropathy in patients with type II DM.

ACE-inhibitors have similar action as in type I in preventing the progressing from microalbuminuria to overt nephropathy, but it is less clear whether they have specific renoprotective properties beyond BP reduction in overt nephropathy. There is now good evidence that ARB-based antihypertensive treatment can delay progression of micro-albuminuria to overt nephropathy and progression of overt nephropathy to end stage renal disease, so this benefit is complementary to the more substantial benefit achieved by improved BP control.(8)

8.5 Orthostatic hypotension:

Diagnosed by measuring standing and supine blood pressure; normally there is slight difference between the two measures but the presence of >20 mmHg difference in systolic or >10 mmHg diastolic blood pressure confirm the diagnosis of orthostatic hypotension.

The patient presents with dizziness or fainting on standing, eating or hot bathing. It is associated with the presence of impaired vasomotor reflexes (which are present in elderly), autonomic neuropathy (e.g. DM), antihypertensive medication and over diuresis. (1, 8)

Orthostatic hypotension is an obstacle to achieving good blood pressure control and its severity is strongly related to premature death, increased numbers of falls and fractures.

The presence of orthostatic hypotension necessitates slow-dose titration of antihypertensive drugs. Moreover, volume depletion should be avoided and a clear warning should be given to patients. (1, 8)

9. Resistant hypertension

9.1 Definition: (14)

Defined as blood pressure that remains above goal in spite of concurrent use of three antihypertensive agents of different classes and if tolerated, one of the three agents should be a diuretic. All agents should be prescribed at optimal doses (ie, 50% or more of the maximum recommended antihypertensive dose) Thus, patients whose blood pressure is controlled with four or more medications should be considered to have resistant hypertension

9.2 Causes of resistant hypertension (15)

1) Improper blood pressure measurements.

2) Volume overload:
   - Excess sodium intake.
   - Volume retention from kidney disease.
   - Inadequate diuretic therapy.

3) Drug induced or other causes:
   - Drugs: NSAIDs use, sympathomimetic (decongestants), oral contraceptive pills, corticosteroids, cyclosporine, erythropoietin
   - Cocaine/amphetamine + illicit drugs
   - Non-adherence to antihypertensive medication.
   - Inadequate antihypertensive doses.
   - Inappropriate drug combination.

4) Associated conditions:
   - Obesity.
   - Excess alcohol.
   - Obstructive sleep apnea (present in 50% of hypertensive patients)
9.3 Management approach (14):

1. Confirm resistant hypertension diagnosis and check for the following:
   - If adequate treatment is prescribed
   - If it is the appropriate treatment
   - If the patient is taking the pills or not
   - If BP is measured correctly

2. Exclude pseudo-resistance through the following:
   - Check adherence with prescribed medication
   - Obtain home, work or ambulatory BP readings to exclude white coat effect
   - Identify and reverse contributing lifestyle factors

3. Increase patients compliance with the medication: this can be achieved through:
   - Do proper education
   - Increase the frequency of the follow-up visits
   - Encourage self measurement of BP
   - Prescribe of drugs that least likely to cause adverse effect
   - Prescribe once a day regimen
   - Use of fixed dose combination
   - Use of less costly regimen
   - Acknowledge progress towards goals and the exclusion of other the drugs that can interfere with BP control.

4. Exclude secondary causes of hypertension

5. Adjust the pharmacological treatment:
   - Studies suggest that change in diuretics therapy (adding a diuretic, increasing the dose, or changing the diuretics class based on kidney function) will help 60% of these patients achieve BP goals.
   - The rationale behind the use of diuretics is that volume expansion seems to be the most frequent pathogenic finding in this group of patients. Fixed dose antihypertensive are very useful for patients with resistant hypertension, especially those with an adherence problem.
### Annex 1: Anti hypertensive Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose/mg/day</th>
<th>Doses/day</th>
<th>Mechanism of action</th>
<th>Special consideration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diuretics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiazides and related drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrochlorothiazid</td>
<td>12.5-25</td>
<td>1</td>
<td>They initially lower BP by reducing plasma extracellular fluid volume and cardiac output. Within 6–8 weeks, these parameters return toward normal and the lower BP is related to fall in peripheral resistance.</td>
<td>• Thiazides are more effective antihypertensive than loop diuretics, unless serum creatinine is 2.0 mg/ml or creatinine clearance 50 ml/min.</td>
</tr>
<tr>
<td>Chlorothalidone</td>
<td>12.5-25</td>
<td>1</td>
<td></td>
<td>• Without concomitant diuretics, antihypertensive drugs which do not block the RAA mechanism may cause sodium retention.</td>
</tr>
<tr>
<td>Indapamide</td>
<td>2.5</td>
<td>1</td>
<td></td>
<td>• Week diuretics may cause hypokalaemia particularly when combined with ACE inhibitors, K supplements or NSAIDS.</td>
</tr>
<tr>
<td><strong>Loop diuretics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide</td>
<td>20-320</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bumetanide</td>
<td>0.5-5</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethacrynic acid</td>
<td>24-100</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Torsemide</td>
<td>50-100</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>K sparing diuretics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>25-100</td>
<td>2-3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamterene</td>
<td>50-100</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Calcium antagonists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nondihydropyridine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verapamil</td>
<td>80-480</td>
<td>2-3</td>
<td>Block entry of calcium into smooth muscle cell Deltiazem and Verapamil blunt increases in exercise rate.</td>
<td>• May cause initial natriuresis, resulting in vasodilatation.</td>
</tr>
<tr>
<td>Verapamil SR</td>
<td>120-480</td>
<td>1-2</td>
<td></td>
<td>• Effect not blunted by NSAID.</td>
</tr>
<tr>
<td>Verapamil- covera HS</td>
<td>180-240</td>
<td>1</td>
<td>(bed time)</td>
<td>• Short acting agents may increase risk of ischaemic heart disease.</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>90-360</td>
<td>3-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diltiazem CD</td>
<td>180-360</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dihydropyridines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nifedipine</td>
<td>30-120</td>
<td>3</td>
<td></td>
<td>• Liquid Nifidipine reduces BP quickly but may precipitate cerebral and myocardial ischaemia.</td>
</tr>
<tr>
<td>Nifedipine GTS</td>
<td>30-120</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amlodipine</td>
<td>2.5-10</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felodipine</td>
<td>43952</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isradipine</td>
<td>2.51</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# ACE inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose</th>
<th>half-life</th>
<th>side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril</td>
<td>12.5-100</td>
<td>2-3</td>
<td>First dose may precipitate dramatic fall in BP but full effect may not appear for up to 7 to 10 days.</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5-4</td>
<td>1-2</td>
<td>Renal function test and K should be measured one week after starting the treatment to detect the presence of side effects</td>
</tr>
<tr>
<td>Fusinopril</td>
<td>10-40</td>
<td>1</td>
<td>Effect is potentiated by diuretics.</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>5-40</td>
<td>1</td>
<td>May cause hyperkalaemia in patients with renal failure, hypoaldosteronism and those receiving K-sparing diuretics or NSAID.</td>
</tr>
<tr>
<td>Perindopril</td>
<td>1-16</td>
<td>1-2</td>
<td>Particularly effective in patients with diabetic vasculopathy, heart failure or systolic dysfunction after myocardial infarction.</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25-20</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Trandolapril</td>
<td>1-4</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

# Angiotensin II receptor blockers

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose</th>
<th>half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan</td>
<td>25-100</td>
<td>1-2</td>
</tr>
<tr>
<td>Valsartan</td>
<td>80-320</td>
<td>1</td>
</tr>
<tr>
<td>Candesartan</td>
<td>8-32</td>
<td>1</td>
</tr>
<tr>
<td>Irbesartan</td>
<td>150-30</td>
<td>1</td>
</tr>
</tbody>
</table>

## A-Adrenergic receptors antagonists

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose</th>
<th>half-life</th>
<th>side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prazocin</td>
<td>2-20</td>
<td>1-2</td>
<td>Inhibition of NE release may lead to first-dose hypotension</td>
</tr>
<tr>
<td>Doxazocin</td>
<td>2-16</td>
<td>1</td>
<td>Useful for prostatic hypertrophy</td>
</tr>
<tr>
<td>Terazocin</td>
<td>1-20</td>
<td>1</td>
<td>In older patients, doxazocin may increase the risk of stroke and heart failure</td>
</tr>
</tbody>
</table>

## B- adrenergic receptor antagonists

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose</th>
<th>half-life</th>
<th>side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>25-100</td>
<td>1</td>
<td>The three most important differences in clinical use are cardio-selectivity, ISA and lipid solubility</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>50-200</td>
<td>1-2</td>
<td>Cardio-selectivity disappears when higher doses are given.</td>
</tr>
<tr>
<td>Non-cardioselective</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propranolol</td>
<td>40-240</td>
<td>1-2</td>
<td>Cardio-selectivity results in less metabolic side effects.</td>
</tr>
<tr>
<td>Nadolol</td>
<td>20-240</td>
<td>1</td>
<td>ISA causes less decrease in heart rate, renin release and cardiac output and less metabolic side effects.</td>
</tr>
</tbody>
</table>

# Cardioselective

<table>
<thead>
<tr>
<th>Drug</th>
<th>dose</th>
<th>half-life</th>
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</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>25-100</td>
<td>1</td>
</tr>
<tr>
<td><strong>With intrinsic sympathetic activity</strong></td>
<td></td>
<td></td>
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<td>----------------------------------------</td>
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</tr>
<tr>
<td>• Acebutolol</td>
<td>200-1200</td>
<td>2</td>
</tr>
<tr>
<td>• Pindolol</td>
<td>22190</td>
<td>2</td>
</tr>
</tbody>
</table>

**A- / B- blocker**

- Fall in blood pressure results mainly from decrease in peripheral resistance. α- / B- blocker is 10:1 for Labetalol and 4:1 for Carvedilol
- B-blockers are well suited for younger and middle-aged hypertensive particularly in patients with myocardial ischaemia and high level of stress. They may interfere with athletic performance.

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<tbody>
<tr>
<td>• Labetalol</td>
<td>200-800</td>
<td>2-3</td>
</tr>
<tr>
<td>• Carvedilol</td>
<td>3.75-25</td>
<td>2</td>
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</table>

**Acting within neurons**

- Frequently cause orthostatic hypotension and sexual dysfunction

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<tbody>
<tr>
<td>• Reserpine</td>
<td>0.05-.25</td>
<td>1</td>
</tr>
<tr>
<td>Depletes postganglionic adrenergic neurons of NE by inhibiting its reuptake in storage vesicles</td>
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<td></td>
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<tr>
<td>• Guenfancine</td>
<td>0.5-2.0</td>
<td>1</td>
</tr>
<tr>
<td>Inhibits release of NE from adrenergic neurons</td>
<td></td>
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</table>

**Central α-agonists**

- Central α-agonists have short half life, so when discontinued, the inhibition of NE release disappears and rebound hypertension occurs.

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<tbody>
<tr>
<td>• Methyle dopa</td>
<td>250-1500</td>
<td>2</td>
</tr>
<tr>
<td>A methyl NE, derived from methyldopa stimulates central α-adrenergic receptors reducing sympathetic outflow.</td>
<td></td>
<td></td>
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<tr>
<td>• Clonidine</td>
<td>0.1-0.6</td>
<td>2</td>
</tr>
<tr>
<td>Same action as Methyldopa but also inhibits NE release from pre-synaptic α- neurons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Clonidine TTS</td>
<td>0.1-0.3</td>
<td>once /week</td>
</tr>
<tr>
<td>Limited efficacy if given alone due to fluid retention and reflex sympathetic activation, so they should be given with a diuretics and B-blockers</td>
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**Direct vasodilatation**

- Hydralazine may cause lupus – like syndrome if dose >200 mg/day and in slow acetylators of the drug

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<tbody>
<tr>
<td>• Hydralazine combined</td>
<td>50-200</td>
<td>2-4</td>
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<tr>
<td>Direct relaxation of smooth muscle cells</td>
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<td></td>
</tr>
<tr>
<td>• Minoxidil</td>
<td>2.5-80</td>
<td>1</td>
</tr>
<tr>
<td>Limited efficacy if given alone due to fluid retention and reflex sympathetic activation, so they should be given with a diuretics and B-blockers</td>
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<td></td>
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</tbody>
</table>
Annex 2: East Mediterranean risk assessment chart

This chart can only be used for countries of the WHO Region of Eastern Mediterranean, sub-region D, in settings where blood cholesterol can be measured (see Table 1).
Figure 14. WHO/ISH risk prediction chart for EMR D. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus.

This chart can only be used for countries of the WHO Region of Eastern Mediterranean, sub-region D, in settings where blood cholesterol CANNOT be measured (see Table 1).
REFERENCES


3. (annual health statistical report 2008)

4. Hypertension Research Group*Clinical Epidemiology Unit, Department of Community Health Sciences.

5. Aga Khan University, Karachi Modified from JNC 7 and the Fourth Working Party of the British Hypertension Society guidelines (last updated in 2007):

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12. WHO Flow charts for prevention and management of major NCDs (for physicians and non-physician health workers), Year

