# The Pathogenesis of Hypertension with Special Emphasis on Endocrine Causes

THESIS

Submitted in Partial Fulfilment for the Degree of Master in Medicine


BY

Ahmed Gamal Mostafa Ahmed

MB.B.CH

Supervised

BY

Professor Dr: Ahmed Ghareeb

Prefessor of Medicine and Chairman of Endocrinology Unit.Ain Shams University

Dr : Mohamed A.Fikry

Assist professor of Medicine

Ain Shams University

Dr: Aboul Ela El-Desoky

Consultant Physician in Medical Service of the Army Forces

Dr : Hussien El. Damasy

Lecturer of Medicine

Ain Shams University

Dr : Badawi Labib

Lecturer of Medicine

Ain Shams University




1979

ACKNOWLEDGMENT

I would like to express my deepest gratitude and thanks to my professor Dr. Ahmed Ghareeb for his unfailing advice, generous help and revision of this work.

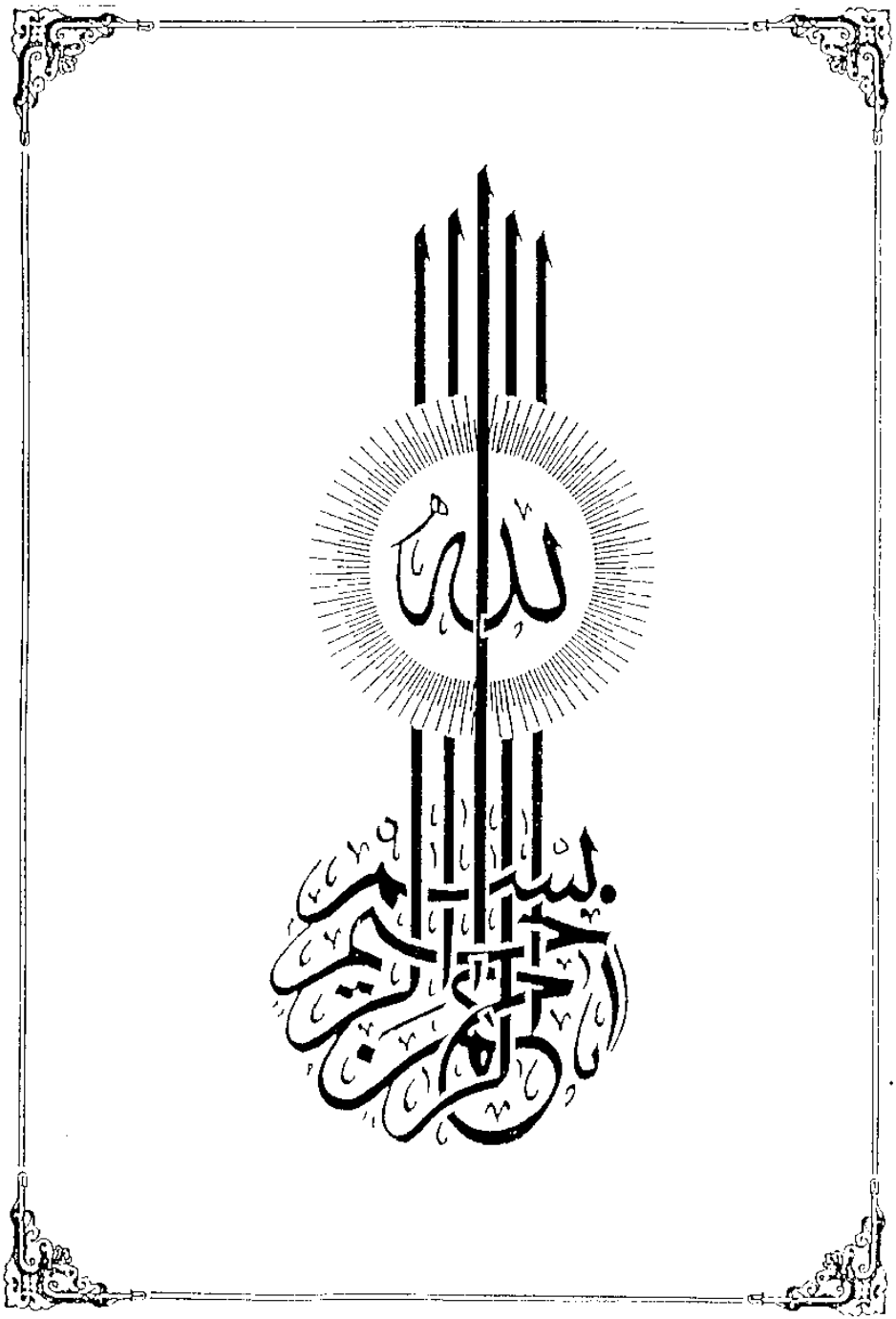
I wish also to express my sincere gratitude to assist professor Dr. Mohamed A. Fikry for his suggesting the topic of this thesis, continuous encouragement and revision of this work.

Thanks are to Dr. Aboul Ela El-Desoky who cordially offered much of his knowledge and experience in this work and in my life.

My deepest gratitude and thanks is also to Dr. Hussien El Damasy for his kind advice and enlightening discussions of the whole work.

I would like to thank Dr. Badawi Labib for his kind closed supervision.

Last but not least thanks to every one who gave me help and advice.



CONTENTS

## Aim of the work

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The pathogenesis of hypertension seems to be multifactorial. Still the pathogenesis of essential hypertension is not precisely obvious.

The aim of this work is to try to explore some aspects of the pathogenesis of essential hypertension as compared with those of endocrine etiology and in patients with hypertension due to Cushing's disease dealt with at the Endocrine unit Ain Shams University.

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# Introduction

Although the cause of elevated blood pressure remains elusive in the majority of instances, it is now well accepted that sustained elevation of blood pressure for an extended period of time in itself may result in significant vascular damage throughout the body. The vascular deterioration is usually evident in the brain, the heart and the kidneys.

In 1949, Dublin et al stated that the mortality rises steadily and markedly with increasing elevation of both systolic and diastolic pressure. Bechgaard, Kopp and Nielsen (1956) after having observed about 1000 hypertensive patients over varying periods of time, up to 22 years, showed that increasing levels of blood pressure are associated with a significant decrease in survival rates, especially in men. At the end of an average follow up period of 19 years, only one fifth of the men and about half of the women with hypertension survived.

The vast of data gathered in 1959 for the society of Actuaries on 4,000,000 lives and 102,000 deaths (of insurable individuals) established that life expectancy at virtually all ages varies inversely with elevated arterial pressure.

Thus, the final effect of uncontrolled hypertension appears to be a shortening of life in many cases. The final common pathway is through vascular disease of the brain heart kidneys, and other organs.

In malignant hypertension the brunt of vascular damage lies on the Eyes and Kidneys. Before 1935, no truly effective

treatment for hypertension was available and most physicians shared the view that none was needed.

Blood pressure was supposed to be elevated to perfuse tissues through thickened blood vessels of high resistance. According to this view, lowering the blood pressure could only result in inadequate perfusion of organs, with consequent worsening of the clinical picture. This was, in a sense, a most reassuring concept for the simple reason that no satisfactory means of lowering arterial pressure was available.

The introduction of sympathectomy for the treatment of hypertension, described by Peet (1935) and Smithwick (1940) represents the first effective technique for obtaining sustained blood pressure reduction in hypertensive patients. The results achieved between 1938 and 1947 with extensive sympathectomy demonstrated for the first time that lowering of the blood pressure was effective in reducing mortality in patients with malignant or severe hypertension (Smithwick et al., 1959).

Since about 1950, many potent pharmacologic agents have become available for effectively lowering blood pressure in most cases.

In 1958 Moyer and coworkers completed a study of the effect of therapy in 133 hypertensive patients. They provided evidence that effective pharmacologic control of the hypertension significantly decreased morbidity and mortality among patients with malignant hypertension.

In 1967, the veterans Administration Hospitals started a prospective study on the effect of therapy on morbidity and mortality in patients with hypertension with diastolic pressures between 115 and 129 mm Hg.

Early evidence during the follow-up period indicated an important decrease in morbidity and mortality in the hypertensive patients who were effectively treated.

The more recent extensive survey by the Veterans Administration Hospitals (1970) provides another demonstration that antihypertensive therapy is capable of lowering the incidence of death and of adverse events such as heart failure, strokes, retinal changes and nephrosclerosis even in patients with moderate diastolic hypertension between 105 and 114 mm Hg. This study also suggested that diastolic blood pressure between 90 and 104 mm Hg may require treatment. Final demonstration for this group has not been provided. The clinician today would usually treat a diastolic pressure above 105 mm Hg and probably above 90 mm Hg, at least in certain patients. With the increasing number of pharmacologic agents for the treatment of hypertension and with the acceptance of appropriate drug combinations for effective therapy. He may select the most appropriate drug (or combination) for the individual clinical situation.

The prognosis for the hypertensive patient is influenced by the cerebral, cardiac and renal complications. The purpose of therapy, therefore, is to reduce high blood pressure and therapy help to curt the cerebral, cardiac and renal effects of hypertension.

At birth blood pressure is about 80/40 mm Hg. and rises gradually until at the age of 20 it is about 120/70 mm Hg. At the age of 50 - 60 the pressure is approximately 150/90 mm Hg. With increasing age the systolic pressure often continues to rise as the aorta become increasingly rigid. However, in many individuals and throughout some societies e.g in some pacific islands, there is no rise with age. In the younger age groups males, on average, have higher pressures than females, but this tendency is reversed after the age of 45 (Julian 1977).

No mention has been made of the posture of the patient when the blood pressure is measured. The diastolic pressure is different when lying or standing as there is normally increase of 5-10 mm Hg. In diastolic pressure when a patient s stands. Moreover, the diastolic pressure may be first elevated on lying rather than when standing, this observation is unexplainable.

During exercise the systolic pressure rises and hence for comparability of measurments, blood pressure should be measured after a few minutes rest. An important factor which will elevate an otherwise normal blood pressure is obesity. Clinically it is often possible to induce a measurable fall in blood pressure by weight reduction. The mechanism for increased systolic and diastolic pressure in obesity is unknown. Psychological stress may lead to a sustained increase in the blood pressure. It can be reduced to normal by gaining the ability to control our own autonomic system. Behavioral methods for

the treatment of hypertension are begining to be explored but because they are time consuming they are difficult to apply.

Long term prognosis is worse in the younger patient, as he has potentially more years in which to suffer morbidity. Men tolerate uncontrolled hypertension less than do women for reasons which are not understood. In the States Negroes develop hypertension earlier in life and often more severly with resulting higher mortality than age-matched white hypertensives taking a similar diet, the explanation is unknown.

There is thus a number of general factors which have to be considered when assessing a hypertensive patient. Also there is some fallacies that must be constantly borne in mind when measuring blood pressure e.g the blood pressure in obese subject may appear to be higher than it realy is, owing to the unreliability of the cuff method of measurment when applied to a fat limb. Lower pressures may be recorded by direct arterial puncture. Under certain conditions e.g during a rigor when there is intense vasoconstriction or when the main artery to the limb is partly occluded, the blood pressure reading may be much lower when measured by the cuff method than when measured by direct arterial puncture.

## Definition and Clas_ification of Hypertension

Definition:

The World Health Organization (WHO) defined hypertension as a single sitting or recumbent blood pressure exceeding $\frac{160}{95}$. values below $\frac{140}{90}$ were considered to be normotensive. Individuals whose blood pressure fell between these two limits were not classified.

A later report of the world Health Organisation stated that reading between $\frac{140}{90}$ and $\frac{160}{95}$ in persons below 30 years of age should be regarded with suspecion. In practice, the term "borderline hypertension" is used to describe such individuals. atients with borderline hypertension have unique features. heir blood pressure rise with age and the rise is steeper than n normotensive subjects. Their mortality and cardiovascular orbidity rates are exces ive and they exhibit numerous pathoysiologic abnormalities. Exceptions are described but in the ajority of populations the blood pressure increases with age.

Consequently, the WHO practice of disregarding the age in lood pressure clas ification is not acceptable. For adults he following classification appears reasonable:-

- Normotension:

(a) age between 17 and 40 : blood pressure less than $\frac{140}{90}$

(b) age 41 - 60 blood pressure less than $\frac{150}{90}$

(c) age over 60 blood pres ure less than $\frac{160}{90}$

2- Hypertension:

(a) blood pressure above $\frac{160}{100}$ at age 17 to 60

(b) blood pressure above $\frac{170}{100}$ over age 60

3- Borderline Hypertension:

Blood pressure reading between the hypertensive and normotensive range.

Classification of Hypertension:

(1) Etiological Classification:

Despite considerable research and advances and improvement in diagnostic methods, in a large majority of patients, the etiology of hypertension remains unresolved. Consequently, in high specialized centres where elaborate diagnostic procedures are regularly and systematically applied, close to 95% of adult patients are found to have essential hypertension. The etiological classification shown in table (1). In practice it is well known that "essential" hypertension runs in families and a genetic factor plays a major role.

2) Clinical classification:

This classification is used for patients who can be adequately examined in order to assess the severity of hypertension for purposes of patient referral, decisions regarding the urgency and choice of treatment, and clinical research.

Complications of arterial hypertension are directly related to the level and duration of the elevated blood pressure, but the rate of progression in individual patients is very variable.

In addition to dependable blood pressure readings, clinical assessment of hypertension requires an examination for pressure-related organ changes. Basic tools for clinical classification are the physical examination, fundus copic examination, urine analysis, assessment of renal function and electrocardiogram. These are used in conjunction with the average of multiple blood pressure readings. As shown in table (2).

Therapeutic Classification:

The objective here is to determine whether a subject requires treatment. A classification based on sitting casual blood pressures has recently been proposed by the National High Blood pressure Education program in the united states. According to this classification, subjects with a blood pressure below $\frac{160}{95}$ do not require treatment. If subjects had an initial reading above $\frac{160}{95}$ but on another day their diastolic blood pressure is below 95, they also do not require treatment.

A subject whose initial blood pressure was above $\frac{160}{95}$ and on the second examination the diastolic reading was between 95 and 105 requires observation but the decision regarding treatment may be individualized. Finally all patients whose initial diastolic reading was above 120 or whose second diastolic readin

was between 105 and 120 require treatment. In this group three further subgroups of increasing degree of severity of blood pressure are recognized:-

(1) Diastolic blood pressure 105 - 120 .

(2) Diastolic blood pressure 120 - 140 .

(3) Diastolic blood pressure 140 mm Hg. the most severe group requires "individualized hospitalized therapy".

Fundus Examination in Hypertension:

The fundi are primarily examined for signs of hypertensive damage. The duration of hypertension can roughly be assessed by the amount of arteriolar damage present. It is customary to grade the fundi when viewed through an ophthalmoscope into four categories:-

Grade I : Mild narrowing of the retinal vessels is present and the blood pressure may be only slightly raised.

Grade II: Arteriolar-venous nipping correlates with a relatively mild pressure.

Grade III: Arteriolar-venous nipping with Haemorrhages and exudates. This suggests a moderately severe hypertension which must rapidly be reduced.

Grade IV: Papilloedema and usually also haemorrhages and exudates. Pointing to "malignant hypertension".

Table -1- Classification of Hypertension By Etiology

A. Essential hypertension.

B. Renal.

1- Parenchymal

- acute glomerulonephritis
- chronic nephritis; glomerulonephritis; pyelonephritis; heredity; irradiation; lupus erythematosis.
- polycystic kidney disease
- Hydronephrosis
- Renin-producing tumor
- Diabetic nephropathy

2- Renovascular

- Fibromuscular arterial stenosis.
- Atherosclerotic arterial stenosis.
- Renal infarctions.
- Polyarteritis.

3- Trauma

- Perirenal hematoma.
- Renal arterial thrombosis
- Renal arterial dissection

C. Endocrine (Curable)

1- Thyroid

- hyperthyroidism, hypothyroidism

D. Neurogenic (transient and reversible).

- Respiratory acidosis.
- Brain tumor.
- Encephalitis.
- Bulbar poliomyelitis.
- Familial dysautonomia.
- Acute porphyria.
- Quadriplegia.
- Extra adrenal chromaffin tumors.
- Paragangliomas.

E. Mechanical interference with flow -A-V fistulas (paget's disease, patent ductus arteriosus).

- Aortic insufficiency.
- Coarctation of the aorta.
- Atherosclerotic systolic hypertension.

F. Exogenous.

1- Poisoning: lead and thallium

2- Medication: sympathetic amines.

- MAO inhibitor combined with ephedrine or tyramine