THE TREATMENT OF HYPERTENSION IN HOSPITAL OUTPATIENTS AND COMMUNITY POPULATIONS IN DAR ES SALAAM



A STUDY OF COMPLIANCE AND EFFECTIVENESS OF CONTROL

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PATRICK J.M. LYIMO

DECLARATION

I declare that the whole of this work has not been submitted for a degree in any other University.

.....
Signature of Candidate

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SUMMMARY

Hypertension is a rapidly increasing problem in Tanzania (1). It presents earlier in life and with much more severe complications than in White patients (2). Its impact is seen in the increasing work-load in our hospital outpatient clinics and in the increasing number of malignant hypertension, heart failure, stroke and chronic renal failure among hospital admissions.

A study was carried out to identify all hypertensive patients within a randomly selected community in a Dar es Salaam urban population and to follow them up prospectively for 12 months using pharmacological and non-pharmacological treatment. Their monthly mean blood pressures and one year morbidity were calculated and compared between hypertensive patients who were treated with the ussual step-care pharmacological treatment and those who were followed up on non-pharmacological treatment only. Similarly, monthly mean blood pressures for the hypertensive patients who completed 12 months of regular follow-up in the community were compared with mean blood pressures for the patients who did not complete 12 months of follow up. Factors which were associated with good or poor patient compliance to treatment in the hypertensive populations were elucidated.

A similar study was done using the Records Department in Muhimbili Medical Centre to assess the prevalence of hypertension among our hospital outpatient clinic population in 1983 and 1984. Blood Pressure records of identified hypertensive patients were documented for a period of 5 years up to 1988 and the degree of blood pressure control as well as compliance compared with the results obtained in the community study.

A total of 797 community subjects were screened for hypertension during the initial survey which was done at the beginning of the community study. 138 subjects out of this community population qualified for follow up in the community study. Of the 138 community subjets 70 patients were hypertensive using World Health Organization definition, the remaining 68 patients had borderline hypertension. Prevalence of hypertension in the community studied therefore, was found to be 8.8%.

Out of the 138 community patients 20 patients with borderline hypertension and 8 patients with blood pressure above 160/95 mmHg were lost for follow up. The remaining 110 patients were followed up monthly for one year in the community study. Of these 48 (43.6%) patients had borderline hypertension, 50(45.5% patients had mild hypertension, 11(10%) patients had moderate hypertension and 1 (0.9%) patient had severe hypertension.

The median age for the 62 hypertensive community patients (blood pressure > 160/95 mmHg) was 45 years (range 25-80 years). Their mean blood pressure at the beginning of study was 180/106 mmHg (range 160/94-236/132 mmHg). Only patients who had initial systolic blood pressure of 160 mmHg and above and/or initial diastolic blood pressure of 95 mmHg were considered for treatment in the community study.

The borderline hypertensive patients in the community population were included in the study in order to determine the behaviour of borderline hypertension when followed up regularly without treatment for one year. The median age for the borderline group was 40 years (range 17-77 years) and their mean blood pressure was 151/93 mmHg.

The hospital study consisted of 420(18.4%) hypertensive patients out of the 2287 new patients refered to Muhimbili Medical outpatient clinics from January 1983 to December 1984. Of the 420 hypertensive patients 349 (83.1%) patients had never been on anti-hypertensive treatment before. Their mean blood pressure was 170/108 mmHg with range 140/90 - 200/134 mmHg).

22(6.3%) of the 349 patients who had not been on treatment were started on anti-hypertensive treatment in the medical outpatient clinic with blood pressure below 160/95 mmHg. 156(44.7%) and 157(45.0%) patients who had

not been on treatment had mild and moderate hypertension respectively. Only 14 (4.0% of this group had severe hypertension. Isolated systolic hypertension was not found in the hospital and community population in this study.

Non-compliance was a problem both in the hospital and in the community study population presenting with 379 (90%) and 77(70%) hospital and community patients respectively discontinuing follow up before the end of study period.

Better compliance in treatment in the community patients was associated with having Islamic religious education (P=0.04) and aged 40 years and above (P=0.08). There was no significant difference in compliance between males and females and between those who were illiterate and those who had formal education.

There were 2 heart failure and 1 stroke cases observed among the 42 community hypertensive patients who did not complete 12 months of follow up. Only 1 of the 33 compliant community hypertensive patients developed heart failure during the whole study period. The overall one year morbidity in the community study population was 2.4 times higher in the group which did not complete 12 months of follow up than in group which complied with treatment. The mean initial blood pressures for the compliant and non-compliant groups as shown in table below were not statistically different.

The community hypertensive population responded favourably to both the non-pharmacological and pharmacological treatment. Weight reduction was objectively found to be the most important factor in reducing blood pressure in the non-pharmacological treatment group. Their mean body mass index dropped from 24.0. at the beginning of study to 22.6 after 12 months of follow up. This was associated with a mean fall of 15/10 mmHg from their initial blood pressure.

The hospital hypertensive study population showed two unique features in their mean blood pressure during the 5 years of follow up. Patients who started the clinic with a blood pressure below 160/95 mmHg showed a gradual rise in mean blood pressure over the first 2 years of follow up thereafter remaining higher than their initial level up to the end of study. Those who started with higher blood pressures showed a significant drop in blood pressure but none achieved a diastolic blood pressure below 100 mmHg.

INTRODUCTION

Hypertension, once a rare finding in the African population has nowadays reached an alarming rate which compares with rates in some of the developed countries. It occurs at a much younger age group than in the white population and presents with more severe complications, death frequently occuring from cerebro-vascular accidents, congestive heart failure or uraemia (2).

Hypertension is increasingly becoming a common problem in many African hospitals both in the outpatient clinic and among medical admissions. In Dar es Salaam, Tanzania, and Lusaka, Zambia, hypertension was found to be the third most common heart disease among hospital admissions. Valvular and cardiomyopathic heart diseases were the leading causes in both countries (1,3).

Hypertension and its associated complications have been found to be very common in the coastal regions of Tanzania (1) This was thought to be associated with the high amounts of salt consumed by the coastal people along with their traditional meal of kingfish popularly known as "nguru". The fish needs enormous amounts of salt for its preparation and when eaten results in a greater intake of salt.

Unexplained heart failure is a significant problem in East Africa. Over 50% of these heart failure cases are associated with previously underlying hypertension. Most

of these hypertensive patients who develop unexplained heart failure have been going around with undetected hypertension and their blood pressure remains in the normotensive, or even hypertensive state, for months before it starts to rise again. Evidence from developed countries indicates that with better living conditions, adoption of Western life styles, and an increase in life expectancy, a greater increase in the incidence of hypertension, as well as the other non-communicable diseases may result. The incidence rates of many of these non-communicable diseases are now higher in some developing countries still beset with other economic, social and health problems than in some developed nations. Tanzania, in particular is one of these countries. Its per-capita expenditure on health is only about US $ 1.00 per year but the prevalence of hypertension in some of the urban populations studied is higher than in some of the developed countries.

More and more people are having their blood pressure measured. As more asymptomatic people are being found to have an elevated blood pressure, the need to identify those with sufficiently elevated levels to justify therapy has been an increasing problem in clinical practice. The problem is compounded by the wide variation in blood pressure throughout the day and night both in persons whose levels remain normal and in those with high levels (4). In some cases these variations accompany

physical activity and emotional stress, but in others it is without obvious cause. In a few patients, markedly high readings clearly indicate serious disease requiring immediate treatment. But in most, initial readings are not as high as to indicate immediate danger, and the diagnosis should be substantiated by repeated readings. The reason for such action is obvious; the diagnosis of hypertension imposes a heavy psychological, and socio-economic burden, and implies a commitment to lifelong therapy.

A great deal of effort has been devoted to the search for a dividing line between "normotension" and "hypertension". It has been known for over a century that the actual blood pressure varies enormously during the day and that the relationship between actual blood pressure and mortality is quantitative; the higher the pressure the worse the prognosis.
So is the incidence of coronary heart disease, severity of changes in the renal arteries, size of the heart, frequency of cerebrovascular haemorrhage, and every other variable capable of measurement (5,6). The dividing line between "normotension" and "hypertension" therefore becomes an artefactual one. For practical purposes hypertension has been defined by the World Health Organisation as a systolic blood pressure of 160 mmHg or above and/or a diastolic blood pressure of 95 mmHg or above, while normotension is 140/90 mmHg or below (7).

Borderline hypertension is any value between 160/95 and 140/90 mmHg.

Even though hypertesion is a preventable and treatable disease, most cases remain either undetected, untreated or uncontrolled (8,9). There is a strong evidence that treatment of hypertension decreases morbidity and mortality (10-12). Hypertension is the single most important risk factor in strokes, both atherothrombogenic and haemorrhagic (13). In a recent report from Ethiopia, of 48 patients with cerebrovascular accidents, 62.5% had hypertension (14). Similar high rate of hypertension in stroke patients has been reported in Tanzania (15).

Hypertension screening programmes carried out in developed as well as in underdeveloped countries have shown that 10-30% of the general population suffer from hypertension (9,16,17). Indeed, hypertension is a serious public health problem that should be tackled by the community, using resources and health services already in existence. Emphasis should be stressed on primary rather than secondary prevention particularly in underdeveloped countries where resources and health budget may not be enough to meet the expensive costs of treating hypertensive patients.

Non-compliance is a problem of extreme importance in the treatment of hypertension. The rate of non-compliance is

particularly high in this part of the world where awareness of the disease in the population is generally low. As many as half of the newly diagnosed hypertensives may drop out of care within one year of initiation of treatment. Studies from developed countries commonly report that only one third of hypertensive patients take medication as prescribed, one third take it erratically and one third never take it at all.

Long term morbidity and mortality associated with high blood pressure is a subject which has not been studied in our hypertensive population. The inadequate availability of community screening facilities and lack of the supporting funds has led to failure to define the magnitude of the problem in our developing countries . Lack of a properly coordinated health care system contributes in the failure to trace treatment defaulters and assess their long-term morbidity and mortality. This does not apply only to hypertension but also to many of the other chronic medical conditions including diabetes and infectious diseases like pulmonary tuberculosis.

SECTION I: OBJECTIVES OF THE STUDY, STUDY POPULATION AND METHODOLOGY

BROAD OBJECTIVE:

To determine the magnitude of hypertension in medical out- patient clinics in Muhimbili Medical Centre and in an urban community in Dar es Salaam, to assess the adequacy of blood pressure control and to evaluate factors affecting compliance in the hypertensive patients both in hospital and in an urban primary health care centre.

SPECIFIC OBJECTIVES:

1. To establish the proportion of all medical outpatients diagnosed to have hypertension and assess their level of blood pressure control during a 5 year period of treatment.

2. To establish the prevalence of hypertension in a randomly selected urban community and find out whether treating hypertensive patients within their locality improves the degree of compliance and blood pressure control.

3. To study factors affecting treatment compliance in the management of the African hypertensive patient in Tanzania.

4. To study the applicability of non-pharmacological treatment in Tanzanian hypertensive patients.

5. To compare morbidity and mortality between the treated hypertensive patients and the patients who do not comply with anti-hypertensive therapy.

SUBJECTS AND METHODS:

Two different groups of hypertensive patients were studied; those treated at Muhimbili Medical Centre outpatient clinic from January 1983 to December 1988, and a hypertensive population randomly selected from an urban community in Dar es Salaam. The clinic study group included all patients who were registered for the first time in the medical outpatient department of Muhimbili Medical Centre with the diagnosis of hypertension from January 1983 through December 1984. Most patients were referred from peripheral clinics around the City and from the other non-medical clinics in the Centre. A few were registered without evidence of any referral note.

A thorough review of each case note was carried out from the first day to the last day of attendance at the clinic. All parameters for each patient's identification were extracted. Blood pressure was recorded at each clinic visit of all attendancies up to the last date of

attendance and means for each year upto 5 years were calculated. It was not possible to trace patients who appeared to have stopped attending the clinic prematurely.

The second part of the study was a community-based prospective study done at Tandale, one of the Dar es Salaam Urban sub-divisions. This study was a continuation of a larger study which the author and other members of the Department of Medicine at Muhimbili Medical Centre carried out to determine the prevalence of diabetes mellitus and impaired glucose tolerance, hypertension, epilepsy, and hypercholesterolaemia among people above 14 years of age.

During this initial survey procedures were explained to the community, consent obtained and the subjects were asked to meet at their community administrative building. Every individual had blood pressure measured twice within an interval of 2 hours on their first day of survey. All measurements were made with subjects seated using a mercury sphygmomanometer. Use was made of two medical assistants who were given rehearsal sessions of blood pressure measurement technique before embarking on the survey. These two assistants and the author would measure a subject each and the author would randomly counter-check their readings without their prior information. A variation table was kept for the two readings. All subjects who were found with blood pressure readings

above 140/90 mmHg were also counter-checked by the author.

All readings were made to the nearest 2 mmHg using Korotkov phase V for the diastolic level. All study subjects were asked to come back on the following day for the results of their tests. Subjects who had a blood pressure above 140/90 mmHg had a third measurement taken on the day of results and the mean of the 3 readings considered as the individual's actual blood pressure. About 53.1% of the estimated study population was screened over a period of two weeks.

At the end of this initial study the author then sent letters to all subjects whose blood pressures had remained in the hypertensive range according to the definition given below. The letters clearly explained what the main study had discovered as the subjects medical problems and that the author was going to establish a special clinic within the same locality which would provide free medication and follow up for all the hypertensive patients who had been found in the survey.

These hypertensive subjects formed the study population for the hypertension community study. They were all instructed to report back to the treatment centre which had been established in the health centre located very close to their community administration building.

All letters were distributed by their community and political leaders. Subjects who did not respond to the recall letters were followed to their homes by the author or a paid assistant through the help of these political leaders. No force or threats were used to patients who refused to turn up for treatment or follow up.

Each patient after the initial visit was given monthly appointments for the subsequent 12 months of follow up. The clinic opened on every Saturday morning and was run by one medical assistant, who had taken part in the initial survey, and a nurse. The author attended the clinic regularly for the first 6 months of the study to initiate, supervise or change treatment accordingly. The initial response of the patients was rather slow, the last patient on the register reponded to the recall letter and home visiting 6 months after starting the clinic.

The first patient from the hypertensive register was selected using random number tables. This and the subsequent alternate patients were started on the step-care regimen of anti-hypertensive agents.

The remaining half was left without any anti-hypertensive drug but instead instructed on non-pharmacological therapy. Each individual in this group was repeatedly educated on the importance of using the non-pharmacological techniques of reducing their blood

pressure. Particular emphasis centred on stopping smoking, reducing salt intake to almost tasteless food, reducing body weight, reducing alcohol consumption and increasing daily physical activity.

Baseline information was obtained for all these parameters at the beginning of study. Repeat weight measurement was done at 12th month of follow up.Body mass index at the beginning and at the end of study was calculated and compared between the pharmacological and non-pharamacological treatment group. A thirty day supply of folic acid was given to the non-pharmacological group to ensure regular follow-up of patients and to maintain motivation. All the non-pharmacological patients whose diastolic blood pressures were 115 mmHg and above or those whose subsequent blood pressure rose to this level were given the ussual step-care anti-hypertensive therapy. All the pharmacological treatment group, except 4 who were found to have diabetes mellitus and those whose blood pressure was less than 160/95 mmHg, were initially given 5 milligrams of bendrofluazide daily for a month before considering adding a second drug. The pharmacological group patients who had blood pressure below 160/95 mmHg were given folic acid like the non-pharmacological group. The other drugs which were available were reserpine and methyldopa.

All the patients in the two groups were told that the medicine they were receiving was for lowering blood

pressure and that it worked better when taken regularly. The drug register was not shown to the medical assistant who measured the blood pressure up to the end of the study. This register was kept by the nurse who entered the blood pressure and issued medicine. The author's duty was to examine the blood pressure trends and make appropriate treatment alterations, whereever it was required, for the whole study population.

Finally, home visits were made after 18 months (when every regularly attending patient had completed 12 months of follow up) to all subjects who had disappeared from follow up and enquiry made on the following questions; reason(s) for failure to attend,presence of shortness of breath impairing ability to perform ussual duties or work, shortness of breath on lying flat on bed at night, painless swelling of both ankles occuring during the last 18 months, and evidence of stroke occuring within the period of study. Blood pressures of all those found at home were measured at the end of interrogation when everyone was relaxed. This was followed by a quick physical examination to look for evidence of stroke or heart failure.

Data analysis was done at this juncture but the project is continuing with yearly reviews of all the hypertensive study population who are now under the care of the medical assistant with no more placebo. Morbidity and mortality differences will be compared between patients

who continue taking their medicine regularly and those who do not.

DEFINITION OF HYPERTENSION:

NORMOTENSION - - - Systolic blood pressure equal to or below 140 mmHg and/or diastolic blood pressure equal to or below 90 mmHg.

BORDERLINE HYPERTENSION - - - Blood pressure between 140/90 and 160/95 mmHg

MILD HYPERTENSION Systolic blood pressure equal to or above 160 mmHg and or diastolic blood pressure equal to or above 95 mmHg. but not exceeding 200/109 mmHg.

MODERATE HYPERTENSION - - - Diastolic blood pressure of and including 110 to 130 mmHg

SEVERE HYPERTENSION - - - Diastolic blood pressure above 130 mmHg

ISOLATED SYSTOLIC HYPERTENSION - - - Systolic blood pressure above 200mmHg with diastolic blood pressure below 95 mmHg

SECTION II: REVIEW OF LITERATURE

PREVALENCE OF HYPERTENSION

Hypertension, once a rare finding in the African population has nowadays reached an alarming rate when compared with rates in some of the developed countries (9,16,17). It occurs at a much younger age group than in White counterparts and presents with more severe complications, death frequently occuring from cerebral haemorrhage, uraemia or congestive heart failure.

Observations 40 to 50 years ago in Africa are typified by the remarks of C.P. Donnison in 1929 during the 2 years he stayed in a native hospital in Kenya (18). He saw an approximate total number of 1800 admitted patients and none was found with an elevated blood pressure. His observations were further strengthened by autopsy findings of Vint less than 10 years later (19). In a study of 1000 autopsies of Africans in Kenya, Vint did not find a single case of essential hypertension, nor did the medical records of the colony show evidence of its occurrence.

Since these early observations there have been several subsequent studies which have shown increasing rates of hypertension in the African continent (20-22). Most African authors have recorded a prevalence of 10 to 20 percent of hypertension in the community (23, 24). A

higher prevalence of hypertension (41%) has been recorded among the South African urban Zulu females aged 40 to 55 years (25).

Changes in environmental and host factors like acculturision, stress, obesity, dietary salt intake and town migration have been suggested as contributing to the rising rates of hypertension in Africa (20,21).

The lowest prevalence rates of hypertension found among rural Zulu men aged 31 - 40 years in 1976 (1%) and among rural Tanzanians in the late 1970's (2 - 3%) do not nowadays apply to most of the urban populations studies in Africa (26). Makene et al in Tanzania showed that hypertension was a very common medical problem in the coastal regions of Tanzania (1). This was thought to be associated with the high amounts of salt consumed by the coastal people along with their traditional meal of kingfish, popularly know as "Nguru". The fish needs enormous amounts of salt for its preparation and preservation. Eating the delicacy results in an increased intake of salt.

Hypertension is a common cause of cardiovascular admissions in many African hospitals. In Dar es Salaam, Tanzania, and Lusaka, Zambia hypertension was found to be third most common heart disease among hospital admissions (1,3). Valvular and cardiomyopathic heart diseases were the leading causes in both studies. In Mulago Hospital,

Uganda, hypertension accounted for 30% of all cardiovascular admissions while in Lusaka, Zambia it accounted for 37% (27.28).

Unexplained heart failure is a significant problem in East Africa. In one study, it accounted for 11% of 712 patients with heart failure (29). Foster, in his study of 28 patients with unexplained heart failure discovered the existence of previously underlying hypertension in over 50 percent of them (30). Most of these patients remained in the normotensive or even hypotensive state for many months before their blood pressure started rising again. This evidence suggests a higher prevalence of undetected hypertension among our hypertensive population.

The clinical significance of the use of the traditionally prepared salts has been known for over two centuries. Fries, in some of his reviews discussed the use of salt substitutes in various parts of the world including Africa, and the association of these low salt diets with low incidences of hypertension (31,32).

The association of the traditional salt with a low incidence of hypertension in Kenya has been suggested by anecdotal reports and observation. Shaper made an extensive study of blood pressure among various groups of Africans including the Samburu nomadic warriors of Kenya. He showed that in almost all the low pressure groups, salt intake in the form of sodium chloride was very low

and in those in whom a rise in blood pressure had been associated with such social change as joining the Kenyan army or the environmental change of rural to urban migration, the salt intake had almost always increased considerably (33).

Current available evidence suggests that the sodium: potassium ratio is just as important as the low sodium diet in protection against high blood pressure with potassium providing a kind of prophylaxis against sodium toxicity (34, 35).

Such evidence is not only compatible with the probable prophylactic value of the traditional salts in maintaining a low blood pressure but would also explain why hypertension was apparently unknown in the Kavirondo Gulf in Kenya in the 1920s when only the traditional salt was being used (36). The nomadic peoples of Somalia, Kenya and Tanzania normally live on a diet consisting mainly of milk, meat and blood. They are a lean, active people in whom the blood pressure does not rise with age and in whom there is apparently no clinical or electrocardiographic evidence of hypertension. Their body physique, the continued activity associated with pastoral life, diet and lack of urban stresses are some of the factors which may account for the relative absence of hypertension in these unique populations (37).

Hypertension as a risk factor for cardiovascular diseases has been recognized in industrialized countries since the 1950s. Numerous studies have examined blood pressure levels among different populations. Awareness of hypertension and the effects of drug treatment are well documented in most of these countries where anti-hypertensive drug therapy has been established. Many surveys have also been carried out to examine blood pressure levels and the magnitude of hypertension and associated complications in developing countries. What is obvious, however, is the fact that there have been very few studies from developing countries which have reported on the indicators of hypertension control in the African community, such as, the proportion of persons aware of their hypertension and the proportion of anti-hypertensive treated persons with adequate blood pressure values (26).

Furthermore, there may be very few developing countries which can afford drug treatment for all their hypertensive populations.

As suggested in the most recent World Health Organisation review paper by Nissinen et al, non-pharmacological therapy of avoiding obesity, excess salt intake and excess alcohol is probably the best solution for controlling hypertension in developing countries (26)

PHYSIOLOGY OF BLOOD PRESSURE

The function of the circulation is to preserve the constancy of the millieu interieur of Claude Bernard, that is, the composition of the extracellular fluids on which cellular function depends. This means the delivery of the appropriate amount of blood at an appropriate pressure to each organ according to its needs. The exchange of oxygen, carbon dioxide, glucose, sodium, potassium and all other substances takes place partly by filtration, but chiefly by diffusion through the endothelium of the capillaries.

SYSTOLIC, DIASTOLIC AND PULSE PRESSURE

The stroke output of the left ventricle is received into the aorta and its large branches which expand to accommodate it. The pressure that expands the aorta is the difference between systolic and diastolic pressures, that is, the pulse pressure. Because of the shape of the pulse wave, mean pressure is always closer to diastolic than sytolic. Hence diastolic pressure is both theoretically and empirically, a better guide to severity of the rise of mean pressure than systolic.

MECHANISM OF ESSENTIAL HYPERTENSION

Arterial pressure is the product of cardiac output and peripheral resistance. Cardiac output in turn is dependent on four inter-related factors:-

1. Myocardial contractile state (contractility, inotropic state or the position of the heart's force-velocity curve),

2. Preload i.e. the length of cardiac muscle at the onset of contraction.

3. After load - the tension which the muscle is called upon to develop during contraction.

4. Heart size.

Peripheral resistance is determined by the intrinsic physical characteristics of the resistance vessels, i.e. the ratio of lumen to wall thickness as well as the neurohumoral influences that act on vascular smooth muscle; the latter include the neurotransmitters noradrenaline, a vasocontrictor, and in some vessels, acetylcholine, a vasodilator. Humoral and locally acting substances include angiotension II (a vasocontrictor) and prostaglandins and kinins (vasodilators). Hypoxia and products of metabolism, such as hydrogen ions, lactic

acid, and perhaps most important, adenosine, also exert potent local vasodilating influences.

For arterial pressure to rise, there must be an increase either in cardiac output or peripheral resistance, or both. Theories of pathogenesis of essential hypertension have suggested increases in either cardiac output or peripheral resistance as the initiating events.

In 1963, Borst and Borst Geus proposed that "hypertension is part of a homeostatic reaction to deficient renal sodium output". The proposed abnormality in renal function i.e reduced sodium excretion at normal arterial pressure, might be secondary to (1) a primary tubular defect, (2) excessive increase in mineralocorticoid activity, (3) decreased renal kallikrein-kinin and postaglandin activity, or (4) local increases in vasoconstrictor activity (angiotension II or the sympathetic nervous system) reducing renal blood flow and secondary sodium excretion. Regardless of the mechanism of salt retention, according to this concept, blood volume rises because of the increased sodium retention, raising central venous pressure and preload, and thereby cardiac output, i.e. systemic blood flow. However, tissues have the intrinsic capacity to regulate this overperfusion down to appropriate levels by increasing the local vascular bed and causing arteriolar constriction. The rise in arterial pressure which results from the vasoconstriction serves as negative feedback by

increasing cardiac after-load, thereby depressing stroke volume and cardiac output.

As has been shown by Guyton (38, 39), and others (40,41), the elevated arterial (renal perfusion) pressure also increases the urinary excretion of sodium thereby serving as a source of negative feedback and reducing blood volume, central venous pressure, preload, and ultimately cardiac output. Thus the end result of this process would be increased peripheral resistance and arterial pressure, with all other parameters including blood volume and renal sodium excretion, remaining normal. Indeed, this sequence has been documented in experimental human and animal hypertension.

It is interesting to note that when a group of untreated young hypertensive patients was initially studied, cardiac output was normal or slightly increased and peripheral resistance was normal (42). Over the next 10 years cardiac output fell and peripheral resistance rose. A similar conversion from initially high cardiac output to increased peripheral resistance has been described by other authors (43).

Although this traditional pattern is suggested by the majority of authors it may not be universally applied to all patients with essential hypertension. On the one hand, in a few patients a high output state may be

present even after 20 years (44). On the other hand, peripheral resistance is often abnormally high even in those patients with initially high output states. The expected response to an increased cardiac output is vasodilatation with a fall of peripheral resistance. Thus, "normal" resistance in the presence of a high cardiac output is actually abnormally elevated, constituting the primary mechanism of the hypertension (45). Those patients with persistently expanded blood volume who would be expected to have a relatively low peripheral resistance have an even higher resistance than those with greately reduced volume (46). The pattern described above where a state of high cardiac output changes to high peripheral resistance is thought to be the underlying basic physiological change in systemic hypertension. One possible mechanism for the change is the process of autoregulation, a property intrinsic to resistance vessels, in which an increase in blood flow beyond the needs of the tissues leads to vasoconstriction. As this descreases blood flow and brings supply and demand into balance, an increased arteriolar tone occurs which when sustained leads to development of hypertension.

The fact that a normal cardiac output is found in most patient with essential hypertension suggests that either the studies have not been performed early enough in the course of the disease or that this theory is incorrect in

that a change in peripheral resistance is actually a primary rather than secondary event.

Such primary elevation in peripheral resistance can occur either because of an increase in factors tending to produce vasocontriction, a reduction in factors producing vasodilatation, or a change in arterial smooth muscle i.e. an increase in muscle mass or an increase in its responsiveness and/or sensitivity to vasocontrictor stimuli. Each theory has its advocates. Thus, the hypertension associated with emotional stress, some neurologic disorders, and perhaps early essential hypertension is accompanied by increased plasma or urine levels of noradrenaline. Presumably, this reflects augumented neural releases of the vasocontrictive adrenergic neurotransmitter which is responsible for the increased arterial pressure. Secondly, there is an increased vascular response to vasoconstrictor agents such as angiotensin II and noradrenaline, in many patients with essential hypertension. Finally, since the 1930's hypertensive patients have been known to exhibit a decrease in the urinary excretion of kinins, and thus it is possible that reduced vasodilator activity could also result in increased peripheral resistance and arterial pressure.

The "primary increase in peripheral resistance" hypothesis and the "deficient renal sodium output theory" are not necessarily mutually exclusive. For example, an

increased retention of sodium enhances vascular reactivity, at least to angiotension II, in normotensive subjects. Thus, a primary defect in sodium excretion could simultaneously increase both cardiac output and peripheral resistance. It appears that all the factors mentioned above play some role in the development of essential hypertension. Hypertension may be best regarded as a multifactorial disease related to abnormalities of the regulatory mechanisms normally concerned with the control of systemic vascular resistance, sodium excretion, blood volume, cardiac output, and ultimately arterial pressure. The specific parameter which is improperly regulated may differ from patient to patient.

SYMPATHETIC NERVOUS ACTIVATION:

Increased sympathetic nervous activity could raise blood pressure in a number of ways alone or in concert with catecholamine stimulation of renin release, by causing arteriolar and venous constriction, by increasing cardiac output or by altering the normal renal pressure volume relationship (47).

Renin release is directly stimulated by sympathetic discharge. Although plasma renin is usually normal in patients early in the course of hypertension, such "normal" levels may be inapropriately high, since both the higher level of blood pressure and the relatively

overfilled vascular bed should serve to shut off the release of renin. The combination of high catecholamines and renin-angiotension levels may then result in a disturbed pressure natriuresis. It has been suggested that constant repetition of such alerting stimuli might lead to labile and then sustained hypertension (48). Folkolov has shown that this functional change is followed quickly by structural alterations that thicken the vessel wall (49).

GENETIC PREDISPOSITION:

Familial correlations relative to blood pressure levels have been found in infants as young as 6 months of age, supporting a genetic mechanism (50).

In studies of twins and family members in which the degree of familial aggregation of blood pressure is compared to closeness of genetic sharing, the genetic contribution has been estimated to be as low as 30 percent to as high as 60 percent (51). The blood pressure of parents was much more closely related to that of their natural children than to that of their adopted children sharing the same environment (52). These data support a predominant role for heredity in the family resemblance regarding blood pressure.

THE INHERITED DEFECT:

Children of hypertensive patients have shown a greater blood pressure response to psychological stress, which was further accentuated after they ingested two additional grams of sodium chloride for 2 weeks (53). Although exposure to high levels of stress may induce hypertension regardless of the genetic substrate, it is obvious that not all who are exposed to stress develop it. A genetically determined heightened response to stress and sodium would be in keeping with the findings of Falkner et al (53). This is thought to be determined by the Pickering Polygenic inheritence theory as opposed to the Platt's theory of inheritance of a single dominant gene.

NEUROGENIC HYPERTENSION:

It is over 100 years since the depressor nerves were first descovered and about 50 years since Hering described the carotid sinus mechanisms. At first is seemed likely that this might be very important in the pathogenesis of hypertension but several animal studies have cast doubt. Neurogenic hypertension caused by cutting the so called "buffer" nerves (carotid sinus and aortic baroreceptors) differ from essential hypertension in several respects. First, the pressure is extremely variable; second, there is a disproportionate tachycardia; third, the pressure may return to normal at

night; and fourth, the degree of arteriolar and cardiac hypertrophy is less marked.

AGEING AND BARORECEPTOR SENSITIVITY IN HYPERTENSION:

There is a marked diminition in baroreceptor sensitivity with increasing age and with increasing levels of resting mean arterial pressure. Gribbin et al in 1971 showed that in any age group the subjects resting arterial pressure is closely related to the baroreceptor sensitivity (54). It is not yet clear whether the loss of reflex control is the cause of hypertension or if the bororeceptors are damaged secondarily by hypertension. The carotid sinuses are one of the most common sites in the body for the development of atheroma and whatever the cause of hypertension in any given individual ineffective baroreceptors contribute strongly to impaired homeostasis of arterial pressure.

THE ROLE OF THE CENTRAL NERVOUS SYSTEM AND PSYCHOLOGICAL FACTORS:

Studies on spontaneous hypertensive (SHR) rats have shown an abnormal nervous reaction to environmental stimuli. They show sharper and more sustained rises in arterial pressure when their cages are disturbed compared with normal controls. These studies implicated the central

nervous system in the genesis of high blood pressure. The problem in man is that although there is a clear relation between mental or emotional stress and a temporary rise in blood pressure, there is no evidence that this leads to a sustained rise. This should not, however, be held as evidence against a relation between mind and hypertension, since adequately controlled studies would be impossible to carry out. What constitutes a stress to one subject would not necessarily do so for another. The mechanism by which mind affects arterial pressure could be either by central influence on sympathetic efferent neurones or by central resetting of the baroreceptor sensitivity to render reflexes less effective.

THE ROLE OF THE KIDNEY IN ESSENTIAL HYPERTENSION;

PRESSURE NATRIURESIS:

When a normal kidney is exposed to higher arterial pressure it quickly excretes extra sodium and water, the process of pressure natriuresis, which would shrink fluid volume and restore normal pressure (55). This resetting of the pressure natriuresis curve has been explained by increased resitance within the renal efferent arterioles, which could arise from exposure to increased amounts of,or increased sensitivity to angiotensin II or catecholamines (56 - 57).

PLASMA VOLUME:

The reset pressure-natriuresis curve would result in a relatively greater volume within the circulation for the level of blood pressure. A relatively expanded plasma volume has been measured in at least 80 percent of hypertensive patients compared with the expected and observed progressive decrease in volume with increasing blood pressure among normotensive subjects (58).

This relatively increased plasma volume, inappropirately high for blood pressure, would overfill the vascular bed. Although there may be an absolute increase in plasma or extracellular fluid volume, the vascular bed is also likely to be somewhat smaller in response to the vasoconstrictive action of the increased levels of catecholamines and angiotensin.

NATRIURETIC HORMONE:

When plasma volume is expanded, renal excretion of sodium is increased, in part by the action of a circulating natriuretic hormone, whose function is widely recognised (59). Natriuretic substances have been shown to be present in the blood and urine of both normal and hypertensive subjects whose blood volume is expanded (60, 61). In animals, the hormone appears to come from the

hypothalamus (62). Increased circulating levels of an endogeneous inhibitor of Na/K ATP-ase, which shares immunological determinants with the cardiac glycoside, digoxin, and which has been called "endoxin" has been measured in both volume expanded dogs (63) and hypertensive monkeys (64). This may well be putative natriuretic hormone. Another natriuretic factor has been extracted from cardiac atrial tissue (65).

The hormone increases natriuresis by inhibiting Na/K ATP-ase activity in the kidney thereby reducing active sodium reabsorption beyond its renal site of action. There is evidence that the natriuretic hormone acts upon Na/K ATP-ase activity in leucocytes and vascular smooth muscles (66 - 67). The inhibition of extra renal Na/K ATP-ase would diminish the active extrusion of sodium from cells by the Na/K pump mechanism.

INTRACELLULAR SODIUM AND CALCIUM:

Blausten showed that an increase in intracellular sodium enhances a sodium-calcium exchange mechanism and thereby increases intracellular calcium (68). He calculated that a rise of 0.5 mmol/l of intracellular sodium could give rise to an increase in intracellular calcium of 4 to 40 uml/l which is enough to increase the resting tone of vascular smooth muscle by 50 percent. The increase in intracellular calcium is translated into an increase in

vascular resistance by its binding to myofilament regulatory protein and stimulation of myosin phosphorylation (69). Calcium channel blockers owe their activity to this basic change.

SALT INTAKE AND HYPERTENSION

The influence of sodium intake on hypertension remains a major debatable issue. Those who believe in the salt hypothesis think that there is a strong association between salt intake and the incidence of hypertension and its cardiovascular complications such as stroke. Japan, which has a high salt intake also has an above average incidence of hypertension. On the other hand primitive populations of Amazonian and some parts of Africa who have a sodium intake of less that 10 mmol/per day have no or a very low incidence of hypertension. Their blood pressure does not show a rising trend with age.

Opponents of the salt theory point out that within a population there is no evidence that an individual's arterial pressure is associated with salt intake. Studies of spouses with similar salt intake have not shown marked variation of blood pressure with salt intake. A negative correlation between blood pressure and salt intake has been demonstrated in several other studies as well.

De Wardener has postulated a defect in the renal excretion of sodium in hypertension, as mentioned above,

which in turn leads to an increase in circulating natriuretic hormone. The same defect can be detected in normotensive relatives of hypertensive subjects.

ROLE OF RENIN IN ESSENTIAL HYPERTENSION:

The role of renin in hypertension is reported to be limited by many authors (70,71). Most patients with essential hypertension have normal levels of circulating renin. Since high blood pressure in the renal afferent arteriole should suppress the release of renin from juxtatglomerular cells through the baroreceptor mechanism, the presence of normal renin level may be considered inapropriate. Thus, the normal negative feed-back between blood pressure and renin release may be imperfect in hypertension, resulting in inappropriately high renin levels which may contribute to the hypertension. This is supported by the fact that blood pressure falls when hypertension is treated with angiotensin converting enzyme inhibitors. The same enzyme, however, is responsible for the inactivation of the vasodepressor bradykinin so that the fall of blood pressure could as well reflect bradykinin accumulation and not necessarily indicate a role of renin.

On the other hand, those hypertensive subjects with low renin levels, which seem more appropriate to essential hypertension, may owe their levels to increased

sensitivity of adrenal receptors to angiotensin. Less renin-angiotensin would be required to maintain the required body fluid volume. This is evidenced by the fact that when low renin patients are given exogeneous angiotensin there is a super normal rise in plasma aldosterone (72). The possible mechanism for low renin hypertension is thought to be due to expanded body fluid volume which in turn increase renal perfusion and therefore tending to switch off renin output.

PROSTAGLANDINS:

Recently, prostaglandins that act at their site of synthesis have been shown to produce physiologically important effects on the blood pressure. Prostacyclin, synthesized within the vessel wall, is vasodilatory, thromboxane A, released from platelets, is vasoconstrictive (73).

The major site of prostaglandin action relative to hypertension may be in the kidney. Prostaglandin E^2, is synthesized mainly in the renal medulla by medullary interstitial cells. When prostaglandin E_2, or the precursor, arachidonic acid, is infused into the renal artery, renal vasodilatation, increased renal blood flow, and natriuresis follow. Thus, prostaglandin E2, may protect against ischaemia. When renal blood flow is compromised, both renin and prostaglandins are released.

By this mechanism the kidney can raise systemic blood pressure via renin angiotensin without deminishing renal blood flow, since intrarenal prostaglandins would counteract the effects of intrarenal angiotensin (74).

A deficiency of prostaglandin E2 might then lead to hypertension by impairing renal function and permitting fluid retention as well as by accentuating the ill-effects of renin-angiotensin. Decreased levels of prostaglandin E2 have been measured in hypertensive patients and have been related to decreased renal blood flow and sodium excretion (75)

There are other reno-medullary lipids which have been identified to have a definite anti-hypertensive effects in animals. This is yet to be proved in human.

OBESITY:

Despite the possible over-estimation of blood pressure in the obese because of the use of relatively small sphygmomanometer cuffs, true hypertension is more common among these individuals (75) and adds to their risk of developing ischaemic heart diseases (76,77). The association of obesity with hypertension has been particularly obvious in children and young adults (78). It is hoped that prevention of obesity will reduce the incidence of hypertension. Until recently, several

factors have been incriminated in obese persons with high blood pressure: 1. the potential falsely elevated blood pressure by using an inappropriate size of blood pressure cuff, 2. the role of excessive dietary sodium intake in person with excessive food intake and 3. the increased body mass itself being responsible for the abnormally elevated pressures (79).

The expanded intravascular volume that is associated with an increased cardiopulmonary volume increases venous return to the heart and cardiac output, and hence, an elevated blood pressure (80 81).

Although sodium may play an important role in the development of obesity hypertension, many authors have refuted the notion after observing that blood pressure will fall in the setting of a liberal sodium intake as long as calories are reduced.

INSULIN, OBESITY AND HYPERTENSION:

Hyperinsulinaemia is a well known feature of obesity. More recently, the detailed physiology of the insulin resistance associated with essential hypertension has been characterised (82). It is as yet unclear whether these two abnormalities are inherited or acquired by some environmental developments during the evolution of hypertension. Since essential hypertension has

substantial genetic component (83), it is quite possible that at least some of the abnormalities in glucose metabolism may be inherited and could even be linked to such abnormalities as increased sodium-lithium counter-transport (84). The insulin resistance of hypertension appears to be strongly linked to body fat distribution (85,86). Thus, upper body fat (central or abdominal) obesity is more frequently associated with hypertension, hyperlipidaemia, and diabetes than is lower body fat obesity. Central fat distribution is commoner in males.Indeed, upper body fat distribution appears to be a stronger predictor of high blood pressure than total body mass (87). The relative genetic and environmental determinants of fat distribution are as yet not understood. But the role of androgens is being explored and there is evidence they may regulate fat distribution and hepatic sensitivity to insulin (88).

INSULIN AND THE CIRCULATION:

Insulin affects the circulation in a number of ways. Under certain circumstances it can promote sodium retention by the kidney, stimulate sympathetic nervous system, and alter vascular tone directly.

Insulin's natriuretic effect on the kidney is well established (89). This is most dramatically evidenced in the clinical setting of uncontrolled diabetes where sodium retention can be substantial (90.91). Insulin does

not appear to affect renal haemodynamics but rather appears to have a direct action on the renal tubule. Thus, it appears that insulin plays a role in the natriuresis of fasting and natriuresis of refeeding (92). Insulin, however, does not appear to be the exclusive determinant of sodium metabolism in this setting since both inorganic acid and glucagon also play a role (93,94). Insulin's effect appears to be most dramatic in the setting of sodium depleted states such as fasting and uncontrolled diabetes.

INSULIN, THE SYMPATHETIC NERVOUS SYSTEM AND VASCULAR TONE:

The mechanism by which insulin stimulates the sympathetic nervous system is unknown but it is possible that it may occur through a central action perhaps in insulin sensitive areas in the hypothalamus leading to vasodilation. Insulin also has a direct vasodilatory action on the vascular bed (95). However, in hypertension insulin works through elevation of the circulating nonadrenaline as well, thus over-riding the weak vasodilatory action (96,97,98).

ETHNOL INTAKE

In the Framingham cohort, the prevalence of hypertension in those who drank more than two ounce of ethanol or

three mixed drinks a day was higher than in those who drank less (99).

This association is independent of age, adiposity, and smoking (100). On the other hand those who drink one or two ounces of ethanol a day have less coronary heart disease than either teetotallers or heavy drinkers (101).

SMOKING AND HYPERTENSION

Cigarette smoking raises the blood pressure, probably through the nicotine induced release of noradrenaline from adrenergic nerves (102). Yet when smokers quit, a trivial rise in blood pressure may occur, probably reflecting a gain in weight (103).

HYPERTENSION AND DIABETES MELLITUS:

Between 30 and 50 percent of patients with non-insulin dependent diabetes (NIDDM) have hypertension (104, 105). In Nigeria hypertension was found to occur more commonly among diabetic subjects than in the general population after the age of 50 years (106). The prevalence of hypertension was noted to increase with duration of the diabetes. Although it is unclear whether the diabetic state per se has a role, hypertension is usually present at the time of diagnosis of NIDDM suggesting that

diabetes is not the cause of the hypertension in many cases (107,108). Insulin resistance is common in NIDDM (109). It is believed by some that during the pre-clinical evolution of NIDDM, particularly in those who are obese and insulin resistant, a period of prolonged hyperinsulinaemia occurs (110,111).Ultimately, it would appear that the beta cell becomes exhausted, resulting in a transition from Insulin compensated glucose intolerance to frank insulopenic diabetes. Thus, hypertension may have been initiated in these patients during the prolonged "silent" period of hyperinsulinaemia. With established diabetes, hypertension may become self-sustaining once renal damage has ensued.

Hypertension is present in about two - thirds of long-standing diabetic patients with the intracapillary glomerulosclerosis described by Kimmelstiel and Wilson (105). Hypertension in the early diabetic subject may be related to an exaggerated pressure responsiveness to noradrenaline observed in patients without renal insufficiency (112)

Hypertensive diabetic patients experience a lot of problems during the course of their illness. With progressive renal insufficiency and autonomic neuropathy, they may have few functioning juxtaglomerular cells and a reduced ability to stimulate the release of renin. As a result, very low renin levels are frequently observed, with a tendency towards the syndrome of hyporeninaemic

hypoaldosteronism. If hypoglycaemia develops because of too much insulin or other drugs, severe hypertension may occur as a result of stimulated sympathetic activity.

Nearly all anti-hypertensive drugs have some significant disadvantage when used in diabetic subjects (113 114). The choice of any drug will clearly depend on the type of diabetes, adverse effects of the drugs concerned, presence of complications and the presumed pathophysiology of hypertension.

Diuretics, for example, may exacerbate their carbohydrate intolerance, probably by inducing potassium deficiency. Those who are brittle and prone to hypoglycaemia may have problems if they are given beta blockers, since their protective catecholamine response would be blunted and severe hypoglycaemia might develop without warning.

Despite all these limitations, thiazide diuretics and beta blockers remain the initial drugs in the treatment of diabetic hypertensive subjects used in combination where one is inadequate (115).

POLYCYTHAEMIA:

Polycythaemia vera is frequently associated with hypertension in about one- third of subjects. This is

because of the markedly increased circulatory volume and cardiac output associated with the blood hyperviscosity.

GOUT:

Twenty five to 50 percent of individuals with untreated essential hypertension have hyperuricaemia (116). In 71 male hypertensive subjects asymptomatic hyperuricaemia was associated with decreased renal blood flow, presumably a reflection of nephrosclerosis (117). When diuretics are used, the uric acid level rises further. However, even after prolonged exposure patients with diuretic-induced hyperuricaemia do not develop urate deposition, so that treatment for the elevated uric acid level is unnecessary (118). Nonetheless, gout may be precipitated in those who are genetically susceptible.

SECONDARY HYPERTENSION

Essential hypertension accounts for 90 - 95 percent of all hypertensive cases. The remainder consists of secondary hypertension. Most of them are extremely rare and pricise figures hard to obtain. Despite their rarity there are number of conditions in which appropriate treatment may cure hypertension. Nearly all forms of secondary hypertension are related to an alteration in hormonal function and/or renal function.

The commonest cause of secondary hypertension, according to Berghind et al are chronic renal disease (2.4 - 5%), renovascular diseases including pre-enclampsia and enclampsia (0,2 - 1%), coarctation of aorta (0,1 -0,2%) and endocrine hypertension (0,2 - 0,8%) (119 - 121).

RENAL HYPERTENSION

Hypertension produced by renal disease is the result of either (1) a derangement in the renal handling of sodium and fluids leading to volume expansion or (2) an alteration in renal excretion of vasoative materials resulting in a systemic or local change in arteriolar tone. The main sub-divisions are renovascular hypertension, including pre-enclampsia and enclampsia, and renal parenchymal hypertension. A simple explanation for renal arterial hypertension is that decreased

perfusion of renal tissue due to stenosis of a main or branch of renal artery elevates the renin-angiotensin axis. The angiotensin elevates arterial pressure by direct vasoconstriction, by stimulation of aldosterone secretion with resultant sodium retention and/or by stimulating the adrenergic nervous system. In practice only about one half of patients with renovascular hypertension have elevated absolute levels of renin activity in peripheral plasma, although when renin measurements are referenced against an index of sodium balance, a much higher fraction have inappropriately high values.

Activation of the renin-angiotensin system also has been offered as an explanation for the hypertension in both acute and chronic renal parenchymal disease. The difference between renovascular and renal parenchymal hypertension is that the decreased perfusion of renal tissue in the later case results from inflammatory and fibrotic changes involving multiple small intra renal vessels. Alternately, renal parenchymal hypertension may be a result of the damaged kidneys (1) producing an unidentified vasopressor substance other then renin, (2) failing to produce a necessary humoral vasodilator substance which may be a prostaglandin or bradykinin, (3) failing to inactivate circulating vasopressor substance and/or failing to dispose sodium whose retention together with water leads to hypertension. The hypothesis involving sodium

retention being particularly attractive is supported by the observation that those patients with chronic pyelonephritis or polycystic renal disease who are salt wasters do not develop hypertension, and by the observation that removal of salt and water by dialysis or diuretics is effective in controlling arterial pressure in majority of patients with uraemia.

A relatively recently described form of renal hypertension results from the excess secretion of renin by juxtaglomerular cell tumors or nephroblastomas. The initial presentation is similar to that of hyperaldosteronism with hypertension, hypokalaemia and over-production of aldosterone although the peripheral renin activity is elevated instead of being subnormal. Patients also present with normal vein renin concentration without a renal artery lesion.

COARCTATION OF AORTA:

Coarctation of the aorta is usually diagnosed in childhood but it may be missed and present with hypertension later in life. It is often refractory to treatment. The male to female ratio is estimated to be 2:1 and may be associated with other congenital abnormalities such as Turner's Syndrome, patent ductus arteriosus, septal defects, mitral valve lesions, septal hypertrophy and bicuspid aortic valves. The mechanisms of

hypertension in coarctation is thought to be more than just the mechanical effects alone because some patients may remain hypertensive even after reconstructive surgery. Changes in activity of the renin-angiotensin system as well as re-setting of the baroreceptors have been postulated as being contributory.

ENDOCRINE HYPERTENSION:

(i) ORAL CONTRACEPTIVES

The most common cause of endocrine hypertension is that resulting from the use of oestrogen containing oral contraceptives. In countries where contraceptive are wildly used this has been found to be the most common form of secondary hypertension. The mechanism producing the hypertension is likely to be secondary to activation of the renin-angiotensin-aldosterone system. Thus, both volume (aldosterone) and vasoconstrictor (angiotensin II) factors are important. The oestrogen component of oral contraceptive agents stimulates the hepatic synthesis of renin substrate, which in turn favors the increased production of angiotensin II and secondary aldosteronism. Women taking oral contraceptives have increased plasma concentrations of angiotensin II and aldosterone with some increase in arterial pressure. However, only about 5 percent actually have an increased arterial pressure above 140/90 mmHg. In about half, the hypertension will remit within 6 months of stopping the drug.

Why some women taking oral contraceptive develop hypertension and others do not is unclear but may be related to (1) increased vascular sensitivity to angiotensin II, (2) the presence of mild renal disease, (3) familial factors, (4) age above 35 years, and/or (5) obesity. Some authors have suggested that the oral contraceptives are simply unmasking patients with essential hypertension.

(ii) ADRENAL HYPERTENSION

Adrenal hypertension is a feature of a variety of adrenal cortical abnormalities. In primary aldosteronism there is a clear relationship between the aldosterone induced sodium retention and the hypertension. Normal individuals given aldosterone develop hypertension only if they ingest sodium. Since aldosterone causes sodium retention by stimulating renal tubular exchange of sodium for potassium, hypokalaemia is a prominent feature in most patients with primary aldosteronism, and the measurement of serum potassium provides a simple screening test. Primary aldosteronism may be secondary either to a tumour or bilateral adrenal hyperplasia. It is important to distinguish these two conditions pre-operatively, as usually the hypertension in the latter is not modified by operation.

The sodium retaining effect of large amount of glucocorticoids also offers an explanation for the hypertension in severe case of cushing's syndrome. Moreover, increased production in mineralocorticoids also has been documented in some patients with cushing's syndrome. Hypertension in many cases of cushing's syndrome does not seem to be volume dependent, and investigators have speculated that it may be secondary to glucocorticoid induced production of renin substrate (angiotensin mediated hypertension) or a steroid induced change in vascular reactivity.

In patients with phaechromocytoma increased secretion of adrenaline and noradrenaline by a tumor most often located in the adrenal medulla causes excessive stimulation of adrenergic receptors, which results in peripheral vasoconstriction and cardiac stimulation. This diagnosis is confirmed by demonstrating increased urinary excretion of adrenaline and noradrenaline or their metabolities such as vanillmandelic acid.

(iii) PREGNANCY INDUCED HYPERTENSION

With diastolic blood pressure exceeding 84 mmHg at any time during gestation foetal abnormality increases, especially when accompanied by proteinuria (122). Normal blood pressure falls during the course of normal pregnancy to levels lower than those found in non-pregnant women (123). This is why different criteria are

needed for diagnosis of hypertension in pregnancy. In most cases, this involves a rise in blood pressure of 30/15 mmHg or more, or an absolute level greater than 140/90 mmHg on two or more occations taken at least 6 hours apart.

The underlying lesion in this case is an imbalance between placental mass and blood flow (124). Some women predisposed to pre-enclampsia have impaired placental blood flow as in those with diabetes mellitus or pre-existing chronic hypertension. Others have increased placental mass as in those with multiple gestation and molar pregnancy (125). Primigravidas have the greatest predisposition to enclampsia because they have both increased placental mass and inadequately developed blood supply to the placenta.

Normal pregnant women are relatively insensitive to the pressure effects of angiotensin because of production of high levels of prostaglandins, especially prostacyclins, by the placenta (126). A relative reduction in placental perfusion would lead to decreased prostaglandin production and increased sensitivity to angiotensin thus elevating the pressure.

Other theories

1. Primary alteration in placental function may occur in pregnancy and lead to slow intravascular coagulation and later blood pressure elevation (127).

2. The presence of a kind of immunological mechanism which would better explain the higher incidence of pre-enclampsia in first pregnancies, its familial tendency and its association with an enlarged placenta (128).

(iv) **ACROMEGALY**

Excessive growth hormone in adulthood is commonly associated with hypertension. The disease is also complicated by coronary atherosclerosis, cardiac hypertrophy and heart failure

(v) **HYPERCALCAEMIA**

Hypertension occurs in one third of patients with hyperparathyroidism. It is thought to result from renal parenchymal damage by nephrolithiasis and nephrocalcinosis which occurs in this disease. However, increased calcium levels alone can have a direct vasoconstrictive effect. In some cases the hypertension disappears when the hypercalcaemia is corrected.

SECTION III: WHAT IS KNOWN ABOUT TREATMENT OF HYPERTENSION

NON-PHARMACOLOGICAL TREATMENT:

Interest in the use of various non-pharmacological therapies from the treatment of hypertension has risen markedly in the past 10 years (129 - 132). This started after many physicians became concerned with the polypharmacy in the stepped care approach as well as the various toxic effects of anti-hypertensive agents, the diminished quality of life caused by the adverse effects of drugs, poor patient compliance and cost. The non-pharmacological therapies most commonly recommended include weight reduction (133 - 135), sodium restriction (136 - 138), reduced alcohol consumption (139 - 140), exercise (141 - 144) and behavioural modification (145 - 147).

Evidence indicates that non-pharmacological therapy is successful especially in the mild-hypertensive group. Techniques improving adherence are being popularized and patients seem increasingly willing to accept changes in lifestyle.

The underuse of non-pharmacological therapies has been attributed to excitement over newly available drugs and the massive advertising campaigns to promote their use.

Moreover, when physicians decide to treat a condition, they expect immediate results with virtual certainty. Certainly these expectations were justified when a majority of patients had fairly severe hypertension. However, as the large number of patients with mild hypertension enter the picture, a more relaxed, gradual approach to their management seems likely to be adopted. A committee representing the World Health Organisation and the International Society of Hypertension, after analysing data from several trials of treatment of mild hypertension, offered this conclusion in 1982: "The first line treatment for people with mild hypertension should be observation, perhaps combined with general health measures such as weight reduction and restriction of salt intake". (148,149).

DIETARY SODIUM RESTRICTION:

Previously in this review evidence was presented incriminating the typically high sodium content of the diet of people living in acculturised, industrialized societies as a cause of hypertension. Once hypertension is present, salt restriction will help lower the blood pressure. This has been demonstrated by several experimental studies in man (150, 151). It is important to emphasize moderate reductions only, i.e. to levels of 2g. (88 mmol) of sodium per day. More rigid restriction is impractical and the excess potassium loss which follows will stimulate mechanisms which will counter the

anti-hypertensive effect through the sympathetic nervous system and activation of the renin-angiotensin-aldosterone system (152 , 153). A significant reduction in blood pressure was seen in 60 to 70% of hypertensive patients subjected to diets containing 3-5g (90-150 mmol) of salt per day (154,155). In the 1940s Kempner reported a reduction of blood pressure in more than 65% of 500 patients subjected to a rice-fruit water diet containing 100 mmol of sodium per day (156). Similar observations have been reported in patients with accelerated hypertension (157). Houston and Kaplan in separate studies have demonstrated that with essential hypertension, the higher the blood pressure the greater the effect of sodium restriction (158, 159). The Intersalt Study on normotensive population also demonstrated the association between very low salt intake and low blood pressure as well as the absence of a rise of blood pressure with age (160). The situation is more encouraging for the combination of drug therapy and sodium restriction. Ram et al showed that sodium restriction could be combined with a lesser dose of a diuretic agent to obtain a blood pressure reduction equivalent to that obtained with a full dose of the thiazide diuretic agent and unmodified by sodium intake (150). Moreover the degree of hypokalaemia was less on the former regimen. Langford and colleagues showed that a low sodium diet in patients who had been treated for hypertension for 5 years and who were then withdrawn from

medication substantially slowed the relapse of hypertension (161).

It is difficult to follow a diet that is markedly depleted in sodium. Reduction of sodium to 100 mmol per day is the best that most American studies have obtained in free living individuals. Compliance is difficult and rarely ascertained in clinical practice.

WEIGHT REDUCTION:

After a critical review of 21 published studies on the effects of weight loss on hypertension, it was concluded that weight loss is effective in reducing blood pressure (162). The most quoted study is the Israel Study where 81 hypertensive patients were placed on a diet restricted to 800 to 1200 calories a day for 2 months with all loosing at least 3 kilograms. During the study, all but two experienced a significant reduction in blood pressure related to the degree of weight loss. The mean fall was 26/20 mmHg among sub-groups receiving no anti-hypertensive drugs, and 37/23 mmHg in those receiving anti-hypertensive drugs. This decrease occurred despite increased sodium intake which they were given to compensate for the reduced dietary volume.

ALCOHOL AND COFFEE:

Moderate consumption of alcohol, less than 2 ounces of ethanol a day, appears to protect early development of atherosclerosis in the hypertensive population (163, 164). It does so probably by increasing the level of high-density lipoproteins (165). Heavier drinking significantly increases the likelihood of hypertension (166). Excessive consumption of coffee, 3 cups or more, is associated with elevated blood pressure probably by activating the sympathetic nervous system (167).

EXERCISE:

Isometric exercised such as weight lifting, pushing, and pulling may be harmful to the hypertensive subject. During isometric exercises blood pressure rises often to very high levels by a reflex mechanism (168). The few documented studies on isotonic exercises show a slight reduction in blood pressure, although the effect may be related to the coincidental weight loss usually achieved (169).

A group of Chilean women undertook a 30 minute exercise three times weekly. Their blood pressures fell significantly but returned to their basal levels after stopping the exercise 3 months later (170)

INFLUENCE OF BIOFEEDBACK OR TRANSCENDENTAL MEDITATION

Because of the association of hypertension with Western society and its absence in certain less developed cultures attempts have been made to lower arterial pressure by meditation or mental relaxation. The subject is given information about the level of arterial pressure and asked to try to raise or lower his pressure. Patel et al and several other authors have reported successful use of this method (171-173). The only set-back is that the arterial pressure changes obtained with this technique are therapeutically insignificant and a great deal of dedication and time is required for its success.

It is important to note that most of these non-pharmacological trials have been applied and well studied in the developed countries where the population activity, diet and the prevalence and degree of obesity differ much from the Tanzanian population. The amount of weight reduction which may be required in our hypertensive subjects may be far less than in their Western hypertensive counterparts where obesity is a major health problem. Our hypertensive patients may be already doing a lot in terms of physical activity compared to their counterparts who may spend most of their time in a car or office . The importance of studying these factors in our population does not need to be emphasized. This study was designed to determine the magnitude of hypertension in

our medical clinics, and in an urban community and to evaluate treatment and problems associated with blood pressure control in these two African Population.

PHARMACOLOGICAL TREATMENT OF HYPERTENSION:

(i) THE BENEFIT OF DRUG THERAPY.

Protection from the complications of hypertension by drug therapy was shown first for malignant hypertension and heart failure as early as the 1950's (174). Thereafter in 1967 drug therapy was shown to be of value in patients with diastolic levels between 115 and 129 mmHg, and diastolic levels between 104 and 115 mmHg in 1970(175 - 176). The benefit of treatment is directly proportional to the level of the blood pressure elevation. In the hypertensive group with diastolic blood pressure of 115 - 129 mmHg, the Veterans Administration Cooperative (VAC) study group in 1967 demonstrated that treatment versus placebo reduced fatal and non-fatal events by 93% per year (175). Treatment benefited 28 out of every 100 persons receiving therapy per year. Under these circumstances it would appear that lowering moderately to severely elevated blood pressure by any means is desirable and that the side effects of the regimen are of less concern.

In the second part of the VAC study (1970), patients with diastolic blood pressures of 90 - 104 mmHg and 105 - 115 mmHg were also studied, comparing treatment and placebo (176). Statistically significant benefit was demonstrated only for the later class of hypertension. There was a

favourable but non-significant trend in the hypertension class with diastolic blood pressure of 90 - 104 mmHg.

In the hypertension Detection and Follow up Program (HDFD) of 1979, mild hypertension treated by stepped care reduced the 5 years mortality by 20.3% when compare with a similar group of controls (177). A more careful analysis of the data shows only 1.5 person per 100 treated for 5 years received benefit. In other words treatment must be maintained for a significantly long time to benefit a mildly hypertensive patient. This realization underscores the need to look closely at how blood pressure is lowered and whether it is really beneficial to use pharmacological therapy to treat mild hypertension.

(ii) COST EFFECTIVENESS AND ANTI-HYPERTENSIVES:

Cost effectiveness analysis provides a yardstick by which the cost of medical treatment can be examined in relation to health benefits conferred. Alternative uses of the health resources and different health care prognoses can thereby be compared. Studies have shown that it is not cost-effective to treat mild hypertension as a primary way of preventing stroke or heart attack. While this may not be applicable to the other severities of hypertension it becomes an important fact when considering treatment of hypertensive patients with

diastolic blood pressure of 90 to 104 mmHg.Mild hypertension in many studies constitutes over 70% of the general hypertensive population.

(iii) THE DEGREE OF RISK:

The overall increase in long term cardiovascular risk from even a mild degree of hypertension has been amply documented (178). But it is well known that the majority of patients with mild hypertension do not suffer apparent harm over a few years. The majority of those patients who entered the Australian trial with diastolic pressures between 95 and 109 mmHg experienced a lowering of blood pressure over the next 4 years without treatment and those whose diastolic pressure stayed below 100 mmHg had no excess morbidity or mortality (179). On the other hand in 12.2% of the placebo treated group, blood pressure progressed to 110 mmHg or higher, indicating the need for continued surveillance of all patients identified as mild hypertensive.

(iv) COMPLIANCE WITH HYPERTENSION TREATMENT:

Compliance is the degree to which a patient's behaviour corresponds to the advice and instrtuctions given. In hypertension treatment, compliance would include not only taking medications as prescribed but also such things as keeping follow up appointments and making recommended lifestyle changes such as dietary modifications.

In blood pressure control non-compliance is a problem of extreme importance. As many as half of newly diagnosed hypertensives may drop out of care within one year of initiation of treatment. Of those remaining under medical care, only about two thirds take medications, regularly or irregularly and not all of them achieve significant lowering of blood pressure (180). Poor compliance has been found as a primary reason why many community surveys have reported only 20 to 30 percent of known hypertensives as being under adequate blood pressure control (181). It is a common finding from several sources that one third of hypertensive patients take medication as prescribed, one third take it erratically, and one third never take it (182).

Several factors have been postulated as having the potential to affect compliance.

(a) **SOCIOECONOMIC STATUS:**

Age, sex, race and income have not been found to have any significant association with compliance. Individuals of all social and demographic strata may be non-compliers.

(b) **PERSONALITY:**

Studies have also been made of psychological and personality traits. It has not been possible to demonstrate any specific personality association with non-compliance (182). However, it is possible that the more anxious personality may make more frequent visits to the clinic.

EDUCATION:

The effect of health education on compliance has also been studied. Knowledge about hypertension is not sufficient to ensure compliance. Health education has only been found to increase knowledge but does not improve blood pressure control (183). There is evidence however, that patient understanding of the therapy given may improve compliance.

SIDE EFFECTS:

The commonly held belief that fear of side effects from anti-hypertensive medication is a major cause of non-compliance has not been documented (184).

SECTION IV: **RESULTS**

THE MUHIMBILI CLINIC STUDY POPULATION

There were a total of 2287 newly registered patients in all the medical outpatient clinic (excluding the neurology,diabetes and gastroenterology clinics). Of these 420 (18.5%) were diagnosed to have hypertension and followed up in the clinics. These consisted of 233 (55.5%) females and 187 (44.5% males). Their median age was 43 years (range 15 - 80 years). 349 (83.1%) out of the 420 hypertensive population in the hospital study had never been on anti-hypertensive treatment before. These had mean blood pressure of 170/180 mmHg and a range of 146/90 to 240/160 mmHg. 71 (16.9%) patients were already receiving anti-hypertensives when they were refered to our medical outpatient clinics. Their mean blood pressure before starting treatment could not be established but it was 141/86 mmHg with a range of 100/60 to 200/134 mmHg in their first day of clinic attendance at Muhimbili.

Distribution of the 349 hospital study population which had not been on anti-hypertensive treatment when first refered to the follow up clinic is shown by age, sex and severity of hypertension in table 3 and 4 below. 114 (38.6%) of these were below 40 years of age and 181 (61.4%) had 40 years and above. The remaining 54 patients did not have ages recorded in their notes.

The preponderance in the upper age group remained the same in all the four different levels of hypertension.

22 (6.3%) of 349 hypertensive hospital population were started on anti-hypertensive treatment with blood pressure which was on the borderline range. Neither the borderline group nor the remaining group with blood pressure above 160/95 mmHg had blood measured more than once before they were started on anti-hypertensive therapy. Of the remaining hypertensive patients 156 (44.7%), 157 (45.0%) and 14 (4.0%) had mild, moderate and severe hypertension respectively. There were no patients noted with isolated systolic hypertension.

Of the 71 hospital study patients who were already on treatment 59 (83.1%) patients had blood pressure below 160/95 mmHg, 1 (1.4%) patient had mild, 2 (2.8%) had moderate and 9 (12.7%) had severe hypertension when first seen in the medical outpatients clinics.

Compliance to treatment among the hospital populations is shown in table 7 and figure 1 below. There were 163 (38.8%), 86(20.5%) and 56(13.3%) patients remaining in the follow up clinic by the end of 1,2 and 3 years of follow up respectively. Only 40 (9.5%) out of the 420 patients were still attending by the end of 4 years and these attended the clinic regularly up to the end of 5 years. The proportion of female patients who complied

with treatment was higher than that of the male patients (26 (11.1%0) versus
14 (7.5%)), and patients who were aged 40 years and above had a better treatment compliance than those below 40 (29 (11.5%) versus 11 (6.5%)). The difference noted above was statistically significant at 1% level in both cases.

Figure 2 below shows the mean systolic and mean diastolic blood pressure in 4 groups of the hospital study population who discontinued treatment after 1, 2, 3 and 4 years of follow up, and in a fifth group which continued to attend up to 5 years. The change in both systolic and diastolic blood pressure from time first seen to time last seen is also shown for each group on the same figure.The group which dropped out within the first year of follow up had significantly less fall of their mean blood pressure than the rest of the group ($P<0.05$).

Figure 3 shows a significant fall in blood pressure from mean initial levels in all the hospital hypertensive study population (except the borderline group) during the first 2 years follow up. Thereafter, mean diastolic blood pressures did not fall below 100 mmHg and mean systolic pressures did not drop significantly below 160 mmHg. Patients who started the clinic with blood pressure below 160/95mmHg showed a gradual rise in mean systolic and mean diastolic blood pressure in the first 2 years of follow up and remained high to the end of study. Mean diastolic pressure changed from 86 mmHg at the

beginning of clinic to 95 mmHg at the end of two years of follow up.

THE COMMUNITY STUDY POPULATION

A sample population of 1500 people from an urban community was identified. 797 (53.1%) of these came for hypertension screening during the initial survey. A total of 138 patients had blood pressure above 140/90 mmHg measured in 3 different occations at the beginning of study. Of these 70 patients had blood pressure meeting the World Health Organization definition of hypertension, the remaining 68 patients had borderline. The prevalence of hypertension in the community study, therefore, was 8.8%. None of these hypertensive patients had evidence of end-organ damage from history, physical examination and the results of urine tested during the survey.

A total of 28 out of the 138 community subjects were omitted from the study. 27 out of these were omitted after failing to trace their households and the subjects had not turned up for follow up in the community study. One patient died of pulmonary tuberculosis having stopped both anti-tuberculous and anti-hypertensive treatment.

The remaining 110 hypertensive patients qualified for follow up and analysis in the community study. Of these 48 (43.6%) patients had borderline hypertension, 50

(45.5%) patients had mild hypertension and 11 (10.0%) patients had moderate hypertension. Only 1 (0.9%) patient had severe hypertension at the beginning of the community study.

The median age for the 62 hypertensive community patients (blood pressure > 160/95 mmHg) was 45 years (range 25 - 80 years). Their mean blood pressure at the beginning was 180/106 mmHg (range 160/94-236/132 mmHg). The median age for the 48 borderline community hypertensive population was 40 years (range 17-77 years). Their mean initial blood pressure was 151/93 mmHg.

As in the hospital population, the community study population showed a female and older age group excess at all different levels of blood pressure with the exception of the borderline group where males predominated.

There were 64 (58.2%), 33 (30.0%) and 32 (29.1%) patients still attending the clinic at the end of 3,6,9, and 12 months of follow up respectively. The largest number of patients lost to follow up in the community study occurred within the first 6 months. There were no significant losses after the ninth month of follow-up when 76 (70%) patients had stopped coming to the follow-up clinic. 26 (33.8%) out of the 76 patients who were aged 40 years and above showed good compliance to treatment attending for the whole of the 12 months of follow up. This percentage was higher (P=0.08), than the percentage of the under 40

year patients who completed 12 months of follow up. (34% versus 21%).There was no significant difference between men and women in the number of patients who completed 12 months of follow up.

Three broad categories of educational status were identified from the community study. Those who had obtained formal education of any grade 48 (43.6%), those who had religious education, mainly muslims 14 (12.7%) and the ones who had none 48(43.6%). The religious education group had significantly better compliance than the rest of the group with 7(50%) patients attending regularly to the end of study (P=0.04). There was no significant difference in the compliance rate between the group with formal education and the illiterate group.

There was a significant drop in both mean systolic and mean diastolic blood pressure in the group which was treated with pharmacological agents starting immediately after the initial visit. The non-pharmacological treatment group took a longer time to show a significant drop in their mean blood pressure. The borderline group which had been left without any pharmacological or non pharmacological advice had their mean systolic pressure falling back to normal after 3 months of follow-up. The blood pressur rise seen after the sixth months in the borderline and non-pharmacological patients was not statistically different from their initial levels.

The mean body mass index (BMI) for the community study population was 24.6. A significant fall of the BMI occured only in the non-pharmacological treatment group. Their BMI changed from 24 at the beginning of study to 22.6 at the end of study. This change was significantly different from the change noted in the pharmacological treatment group whose BMI actually went up (P=0.02).

There were no drug side effects reported by the pharmacological treatment group population. One patient from the compliant group presented with congestive heart failure. None in this group had a stroke during the whole period of study.

There were two patients found with congestive heart failure and one patient with stroke during the home visits carried out at the end of the study to the patients who had absconded follow up. This stroke had occurred within the period of study and was non-fatal.

SECTION V:

DISCUSSION

PREVALENCE OF HYPERTENSION IN THE OUTPATIENT POPULATION:

High blood pressure was found to be a common problem in our hospital medical outpatient clinics. It accounted for more than 18% of all the newly referred patients during the two years of enrollment. Similar high rates have been reported elsewhere by other African authors. Azinge in Nigeria, demonstrated a steady increase in the number of new hypertensive patients diagnosed annually in their clinic. The number rose from 7.2% in 1965 to 23.2% in 1975 (185). The figure obtained in our clinic was probably an underestimation of the true value if the rate of increase noted in Azinge's study was applied on our hypertensive clinic population.

Hypertension is a chronic problem which needs life-long patient follow up and treatment. The prevalence of hypertension (excluding borderline) in the community study was 8.8%. This was not different from what had been reported earlier by another author in the same city (186). The prevalence in the clinic population is likely to increase with increasing social development. This work-load on hypertension alone may later exceed the manpower and resources available at the clinics. Drug availability may require diversion of most of the

available meagre health budget to anti-hypertensive drugs. On the other hand the hypertensive population in this study showed a remarkably high default rate which slowed the rate at which the hypertensive patients accumulated in the clinics.

CLASSIFICATION OF HYPERTENSION BY LEVEL OF BLOOD PRESSURE

Studies indicate that morbidity and mortality related to high blood pressure increases directly proportional to the level of systolic and diastolic blood pressure beginning at levels well below 140/95 mmHg (187). However, in practice a blood pressure in excess of 160/95 mmHg is considered the point at which a patient can be diagnosed as hypertensive, particularly if the elevation is reproduced on at least two occations.

The classification used in this study agrees with the classification proposed by the World Health Organization whereby the borderline hypertensive patients with blood pressure between 160/95 and 140/90 mmHg need regular follow up only without administration of pharmacological treatment. It is not unusual to have a large proportion of these patients becoming normotensive after a period of observation. Twenty four (50%) of the 48 borderline patients in this study became normotensive after only one month of follow up.

The long term prognosis of patients with mild hypertension, diastolic blood pressure of 95 to 109 mmHg, has not been shown statistically to be economically improved by pharmacological treatment (188 - 190). Bursten et al showed that as many as 28% of their study subjects with mild hypertension became normotensive without any medication during the clinic follow up (191). Similar findings have been reported by several other investigators (192 - 194).

71 (16.9%) of the 420 hospital study patients had been on anti-hypertensive therapy at the time of referal to the hospital outpatient clinics. No drug free washout period was given to these patients and it was difficult to tell whether the apparently normal blood pressures seen in some of the patients in this group was a result of the treatment or if the patients had not been hypertensive from the beginning of their treatment. Another problem was seen among the hospital study population with initial blood pressure above 160/95 mmHg. Anti-hypertensive treatment was started to all patients without obtaining at least a second blood pressure reading.

CHARACTERISTICS OF THE HOSPITAL AND THE COMMUNITY STUDY POPULATION

The clinic study was a retrospective one in which 2 years of enrollment were required to obtain a sample size of

420 patients. Since the retrospective registers were available only upto 1983 it was not possible to increase the number further without affecting the duration of follow up. With the community hypertension prevalence of 8.8% and an estimated Dar es Salaam population of half a million people aged above 14 years the city was estimated to have a total hypertensive population of 39,000 patients (195).

This means that only a negligible fraction of these hypertensive patients (420 out of the 39,000) attended the hospital for treatment. It is unlikely that a significant number of those unregistered hypertensive patients would have been getting treatment from the smaller clinics in the city considering the overall drug shortages and the high cost of anti hypertensive medicines which have existed in the city hospitals.

40% of the hospital study population started the clinic with moderate and severe hypertension while only 20% of the community study population had initial blood pressure lying in this high range. This difference was attributed to the effect of selection of patients with higher blood pressure being referred to the hospital clinics leaving the ones with lower blood pressure in the smaller hospitals where expert advice was not required.

There was an overall female and older age group excess in the hypertensive population in both the clinic and the community study.

Most of the females in the study population were found to be housewives who did not have the opportuniy to get their health services from clinics other than those in the public hospitals. Similarly the older age group patients were more likely to have been unemployed and their income inadequate to pay for treatment from the private clinics in the city. This may have explained why the two groups of populations predominated in the study.

PATIENTS COMPLIANCE

Lack of compliance was a major observation in this study. The problem was greater in the clinic than in the community study population with 90 and 70 percent of patients respectively having disappeared from follow up by the end of the study period.

In a study done by Kitai et al in Harare, Zimbabwe, noncompliance was found to be highest in the first few months of follow up (196). Similar results were obtained by the author both in the clinic and the community studies. Patients' atitudes, beliefs and lack of education,as well as social environment and poor communication between patients, doctors and pharmacists were implicated to be responsible for the low compliance by Nyimweza in a similar study in Zimbabwe (197).

The poorer compliance observed among the hospital study population could be explained by many factors most which were eliminated during the community study. Patients in the community study who had no distance to travel had significantly better compliance than the clinic population. There were no queues during the community study and patients were given an adequate supply of medicine throughout the period of study.

The higher non-compliance rate which occured within the first few months of treatment was probably a results of the asymptomatic nature of hypertension. Patients who continued attending were probably the group of patients who had other underlying symptoms particularly because of the higher number of the older age group in this population. On the other hand, patients appeared to be more motivated in the first few months of treatment. However, because of the asymptomatic nature of hypertension again patients soon lost motivation after not having felt significantly different from the pre-treatment state.

It is shown from figure 2 below that patients who dropped out from the study earlier had a higher mean blood pressure in their last clinic visit than those who did not ($P<0.05$). This indicated that the disappearance of patients did not imply improvement of their hypertension. Over 85% of the Harare patients studied by Nyimweza

mentioned above were given less anti-hypertensive drugs by their pharmacists than what had been prescribed. The situation in our clinic was probably worse than that of Harare where patients had a better degree of blood pressure control

In a study by Wuraga in one rural Zambian community there was no single social or demographic factor which was associated with non-compliance to anti-hypertensive treatment (198). This was similar to what was observed in this study where the sex and age differences did not alter compliance. There was no difference in compliance between patients who had formal education and the illiterate ones. It was interesting to not a significantly better compliance among patients who had Islamic religious education compared to the rest of the community group (P=0.04).

BLOOD PRESSURE CONTROL

The hospital study population showed a general trend of falling blood pressure with treatment up to the second year of follow up. The rise of blood pressure which was observed in the second half was most likely a result of inadequate treatment in the clinics either because of underdosage or inadequate drug supply to cover the long waiting periods to the next clinic appointment which were noted to be an average of 3 months. This fact was more

clearly demonstrated by the borderline hypertensive group shown in figure 3 below. All the patients who were referred to the clinic while on anti-hypertensive therapy were having relatively normal or borderline blood pressures with a mean blood pressure of 141/86 mmHg at the time of initial registration. As soon as they started attending the clinic their mean blood pressures rose to significantly high levels and remained so throughout the 5 years of follow up.

The community study population which was put on pharmacological treatment showed a rapid response to treatment with their mean blood pressures falling to borderline levels in the third month of follow up. Theirü mean blood pressure normalized after the first 6 months and remained low to the end of study.

The non-pharmacological treatment group took longer to achieve control of their blood pressure. This could be explained by the long period of time which was required to achieve the significant weight loss that was observed in this group only.

All the borderline community study population had their mean blood pressure falling to normotensive levels from the third month of follow up despite their not being on pharmacological or non-pharmacological treatment.

EFFECTS OF TREATMENT ON MORBIDITY

Lack of drug side effects in the community study probably indicates the need for establishing a better study design in future studies. On the other hand almost all (99% of the 110 community study patients) had borderline, mild and moderate hypertension, and very few of them required high doses of the anti-hypertensives. This was probably the reason why there were no side effects reported in this study group. Lack of side effects would tend to suggest that the low compliance observed was not due to drug adverse reactions. This observation concurs with findings reported by Haynes study from the Western World (182).

The overall one year morbidity in the community study population appears to be 2.4 times higher in the group which did not complete 12 months of follow up than in the compliant group. This difference in morbidity between the two groups, however, was not statistically different probably because of the small sample sizes. The non-compliant group had two heart failure cases and one stroke case occurring during the period of study. There were no deaths which could be associated with hypertension during the whole period of study. The only death which occurred was due to pulmonary tuberculosis in a patient who had defaulted from both our clinic follow-up and the anti-tuberculous agents.

There was no stroke observed in any of the 33 patients who had completed their 12 months of follow up. The only heart failure case reported in the compliant group occurred in a patient who was on the non-pharmacological therapy. The symptoms resolved immediately after starting the patient on anti-hypertensive therapy.

Almost all of the 797 subjects who came for the initial screening did not know what hypertension was. None knew the association between high blood pressure and heart failure or stroke. It was a popular belief among the population studied that stroke resulted from possession of a bad ghost and that its treatment required a magician who would drive the ghost away. This type of thinking could have contribed to the low compliance rate both in the clinic and the community population.

SECTION VI:

CONCLUSIONS:

Hypertension is a major problem both in our medical outpatient clinics and in our urban community accounting for more than 18% and 8.8% of the clinic and community population respectively. Very few of our community population knew the meaning of high blood pressure or the association of hypertension, heart failure and stroke.

Less than 1% of the hypertensive population in Dar es Salaam get their treatment from Muhimbili Medical Centre, the only centre where free and more regular drug supply can be guaranteed. Over 90% of all the hypertensive patients referred to our medical outpatient clinics and 70% of those treated at our community dispensaries default from treatment after a short period of follow up. Of the patients who attend the medical outpatient clinic at Muhimbili for treatment of moderate to severe hypertension none will achieve a diastolic blood pressure of less than 100 mmHg even after 5 years of treatment.

Treatment of hypertensive patients in the community using their own people and simple anti-hypertensive drugs improves blood pressure control very effectively provided patients show a regular attendance.

Non-compliance in the treatment of hypertension remains significantly high whether patients are treated in a

consultant hospital or when treatment is given within their own village where travel distance and long waiting times in queues have been eliminated.

Non-compliance to treatment is a risk factor in the development of heart failure and stroke among our hypertensive population. Regular treatment by pharmacological or non-pharmacological therepy may reduce the overall morbidity.

Use of non-pharmacological treatment in the treatment of hypertension in African community may be as effective as using pharmacological treatment in reducing high blood pressure although it takes longer to achieve the same level of blood pressure.

RECOMMENDATIONS

1. Mass campaigns through radio and newspapers should be encouraged to improve knowledge of the meaning of high blood pressure and the association of heart failure and stroke with hypertension. Regardless of their educational status people should be educated on the importance of non-pharmacological methods of treating hypertension like weight and salt reduction.

2. Treatment policies should be established to ensure better patient compliance and more effective control

of blood pressure. This will avoid administering drugs to patients who do not need them or whose morbidity cannot be altered because of irregular drug availability and poor patients compliance.

3. Mild and borderline hypertensive patients form the majority in the clinic and community hypertensive population. This is the group which responded most to non-pharmacological therapy in the community study. A large proportion of the anti-hypertensive drugs consumed by the hypertensive patients could be reduced by putting more emphasis on this modality of treatment particularly in males and under 40 years old patients whose compliance to pharmacological treatment has been shown to be poor.

4. To reduce the work-load of hypertension at Muhimbili Medical Centre outpatient clinics a similar system like the one used for tuberculosis and leprosy patients should be established at health centre level. Enough thiazide diuretics and reserpine should be supplied to the health centres where proper registers of the hypertensive patients should be kept. Proper training should be given to the Medical Assistants to handle the hypertensive population within the Health Centres' catchment area. The same referral system like that of tuberculosis and leprosy should be reinforced in the treatment of hypertension.

Table 1: **HOSPITAL STUDY POPULATION BY SEX AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY : THE OVERALL POPULATION**

SEX	BORDERLINE + BELOW	MILD	MODERATE	SEVERE	TOTAL	%
MALE	37	70	73	7	187	44.5
FEMALE	56	86	84	7	233	55.5
TOTAL	93	156	157	14	420	100.0
%	22.1	37.1	37.1	3.3	100	

Table 2: **HOSPITAL CLINIC STUDY POPULATION BY AGE AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY: THE OVERALL POPULATION**

AGE GROUP (years)	BORDERLINE + BELOW	MILD	MODERATE	REVERE	TOTAL	%
<40	33	52	47	6	138	40
40+	46	80	82	8	216	60
TOTAL	79	132	129	14	354*	100
%	22.3	37.3	36.4	4	100	

* 66 unknown ages

TABLE 3: HOSPITAL STUDY POPULATION BY SEX AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY: THE GROUP WHICH HAD NEVER BEEN ON ANTI-HYPERTENSIVE TREATMENT WHEN FIRST SEEN IN THE CLINIC

SEX	BORDERLINE	MILD	MODERATE	SEVERE	TOTAL	%
MALE	8	70	73	7	158	45.3
FEMALE	14	86	84	7	191	54.7
TOTAL	22	156	157	14	349	100.0
%	6.3	44.7	45.0	4.0	100.0	

TABLE 4: HOSPITAL STUDY POPULATION BY AGE AND SVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY: THE GROUP WHICH HAD NEVER BEEN ON ANTI-HYPERTENSIVE TREATMENT WHEN FIRST SEEN IN THE CLINIC

AGE(YEARS)	BORDERLINE	MILD	MODERATE	SEVERE	TOTAL	%
< 40	9	52	47	6	114	38.6
40 +	11	80	82	8	181	61.4
TOTAL	20	132	129	14	295*	100.0
%	6.8	44.7	43.7	4.7	100.0	

* 54 unknown ages

TABLE 5: HOSPITAL STUDY POPULATION BY SEX AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY: THE GROUP WHICH HAD STARTED ON ANTI-HYPERTENSIVE TREATMENT BEFORE THEY WERE SEEN IN THE CLINIC

SEX	BORDERLINE + BELOW	MILD	MODERATE	SEVERE	TOTAL	%
MALE	19	-	-	4	23	32.4
FEMALE	40	1	2	5	48	67.6
TOTAL	59	1	2	9	71	100.0
%	83.1	1.4	2.8	12.7	100.0	

TABLE 6 HOSPITAL STUDY POPULATION BY AGE AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY: THE GROUP WHICH HAD STARTED ON ANTI-HYPERTENSIVE TREATMENT BEFORE THEY WERE SEEN IN THE CLINIC

AGE (YRS)	BORDERLINE + BELOW	MILD	MODERATE	SEVERE	TOTAL	%
<40	37	1	1	-	39	54.9
40+	22	-	1	9	32	45.1
TOTAL	59	1	2	9	71	100.0
%	83.1	1.4	2.8	12.7	100.0	

Table 7: **COMPLIANCE IN THE HOSPITAL STUDY POPULATION SHOWN BY AGE GROUP AND SEX**

Sex/Age	Number of patients completed 5 years of follow up	Number of patients not completed 5 years of follow up	Total
SEX MALE	14 (7.5%)	173	187
FEMALE	26 (11.1%)	207	233
AGE <40 YRS	11 (6.5%)	157	168
>40	29 (11.5%)	223	252
*EDUCATION	-	-	-

* Not showed in majority of the case notes.

Table 8: **COMMUNITY STUDY POPULATION BY SEX AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY**

SEX	BORDERLINE	MILD	MODERATE	SEVERE	TOTAL	%
MALE	26	17	4	-	47	42.7
FEMALE	22	33	7	1	63	57.3
TOTAL	48(43.6%)	50(45.5%)	11(10%)	1(0.9%)	110	100

Table 9: COMMUNITY STUDY POPULATION BY AGE AND SEVERITY OF HYPERTENSION AT THE BEGINNING OF STUDY

AGE(yr)	BORDERLINE	MILD	MODERATE	SEVERE	TOTAL	%
<40	22	8	3	-	33	30.0
>40+	26	42	8	1	77	70.0
TOTAL	48(43.6%)	50(45.5%)	11(10%)	1(0.9%)	110	100

Table 10: **COMPLIANCE IN THE COMMUNITY STUDY POPULATION SHOWN BY AGE, SEX AND TYPE OF EDUCATION**

		Number of patients completed follow up	Number of patients not completed follow up	Total	P-value
Age(Yrs)	<40	7 (21.2%)	26	33	
	>40	26(33.8%)	51	77	0.08
Sex	Male	13(27.7%)	34	47	
	Female	20(31.7%)	43	63	0.3
Educ.	Formal	15(31.3%)	33	48	0.2
	Religious	7 (50%)	7	14	0.04
	None	11(22.9%)	37	48	
TOTAL		33 (30%)	77	110	

Table 11: MEAN BODY MASS INDEX AT THE BEGINNING AND AT THE END OF STUDY IN COMMUNITY PATIENTS WHO COMPLETED 12 MONTHS OF FOLLOW UP

Mean BMI	Initial	At 12 months
Pharmacological group	25.2	26.4
Nonpharmacological group	24.0	22.6*
Whole population	24.6	24.5

* P = 0.02

Table 12: **MORBIDITY IN THE COMPLIANT (33 PATIENTS) AND IN THE NON-COMPLIANT (42 PATIENTS) POPULATION IN THE COMMUNITY STUDY**

Morbidity	Patients who completed follow up (33 pts).	Patients who did not complete follow up (42 pts)
Drug side effects	-	-
Congestive heart failure	1 (3%)	2 (4.8%)
Stroke (non fatal)	-	1 (2.4%)
Total	1 (3%)*	3 (7.1%)

*P=0.2

FIG. 1 : PROPORTION OF PATIENTS CONTINUING TO ATTEND THE OUTPATIENT CLINIC THE END OF EACH YEAR OF FOLLOW UP.

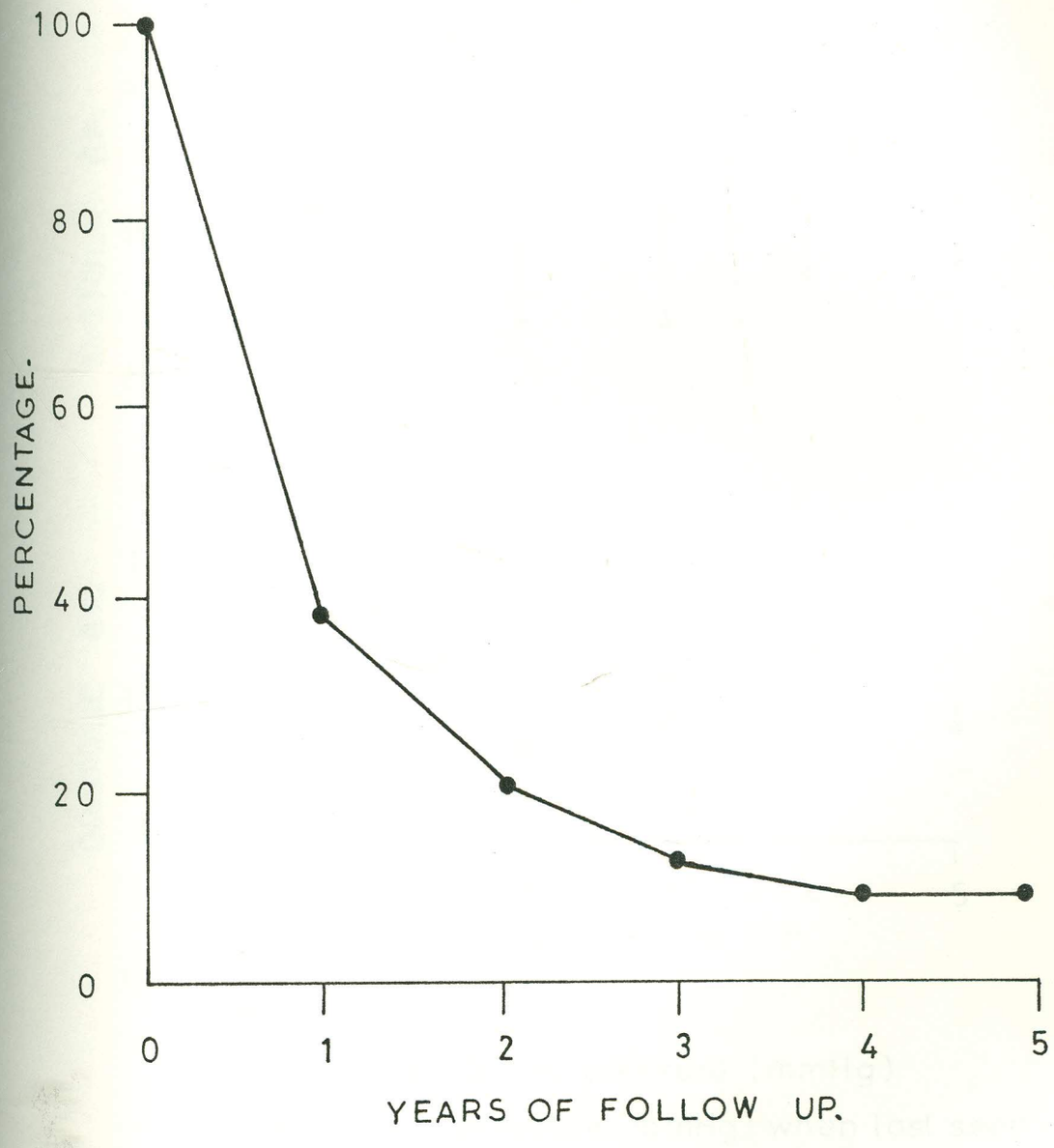
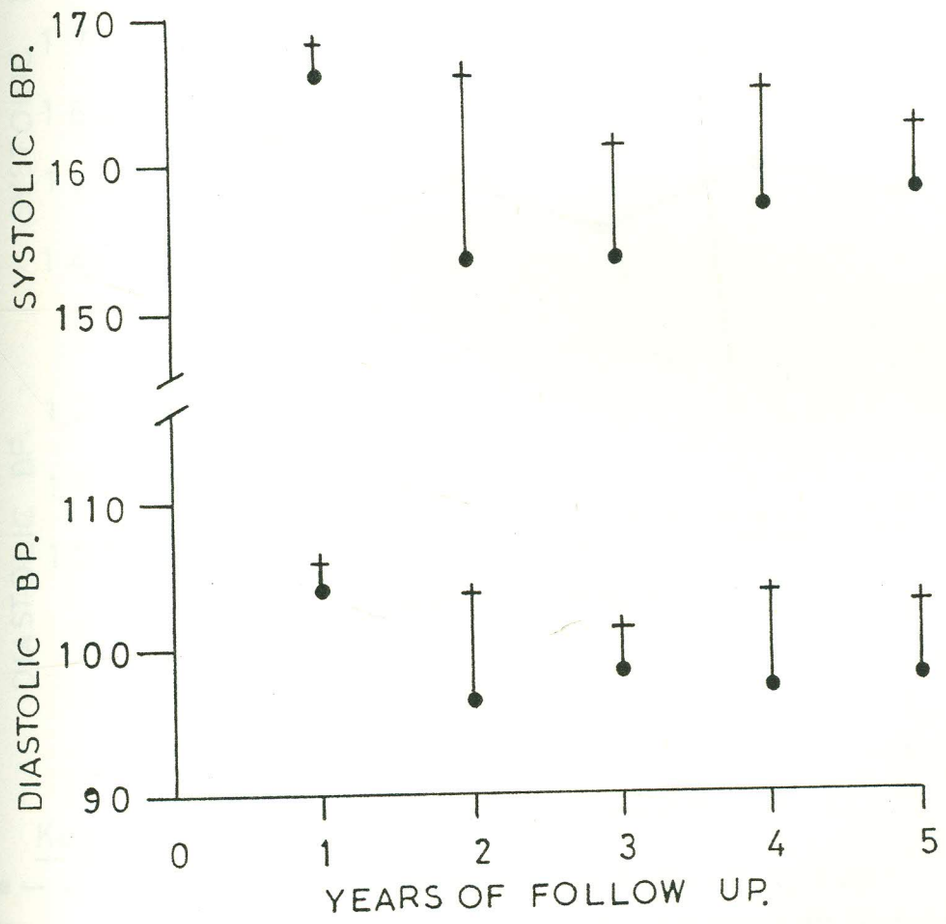


FIG 2 : FIVE GROUPS OF HOSPITAL STUDY POPULATION WITH THEIR MEAN SYSTOLIC AND MEAN DIASTOLIC BLOOD PRESSURE AT THE BEGINNING OF STUDY AND AT THE END OF THE YEAR WHEN EACH GROUP WAS LAST SEEN IN THE CLINIC.

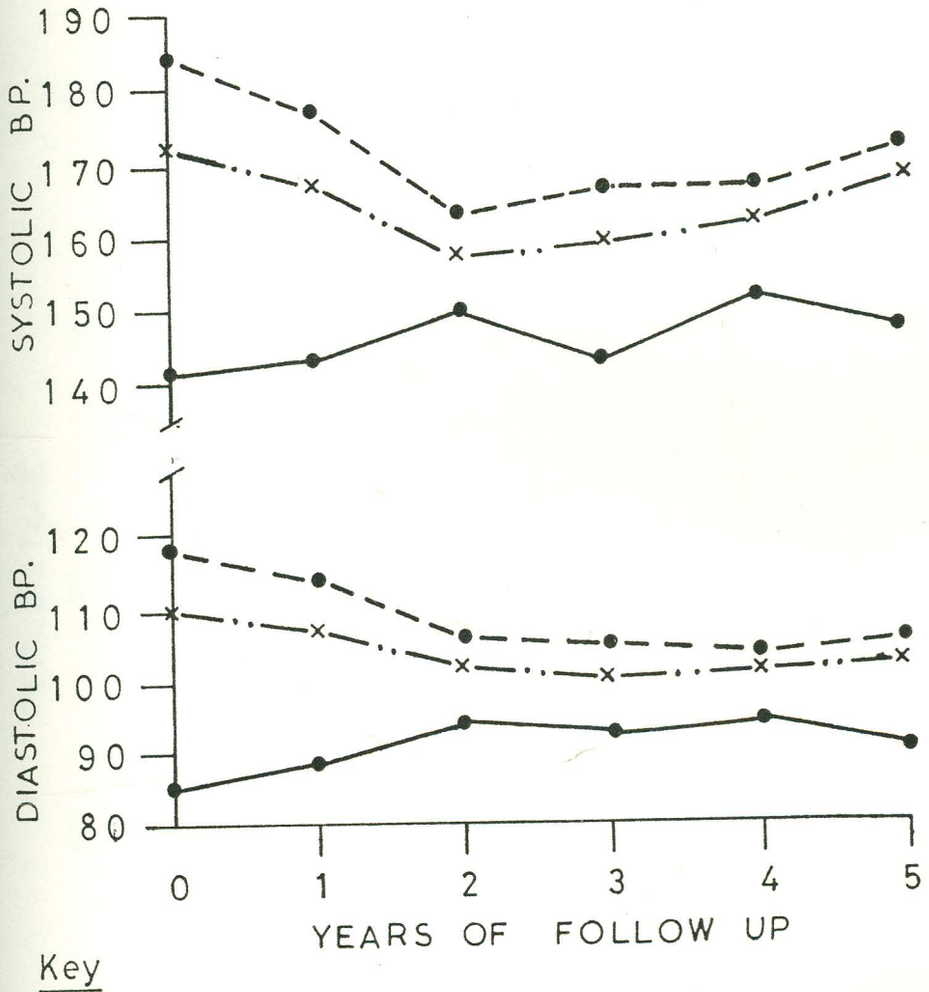


Key:

+ = Initial blood pressure (mmHg).

• = Blood pressure (mmHg) when last seen.

FIG. 3: MEAN SYSTOLIC AND MEAN DIASTOLIC BLOOD PRESSURE IN 3 GROUPS OF HOSPITAL STUDY PATIENTS FOR EACH OF THE 5 YEARS OF FOLLOW UP



Key

●— — —● Moderate to severe hypertensive group.

×—··—× All hypertensives excluding those with initial blood pressure below 160/95 mmHg.

●——● Patients with initial blood pressure below 160/95 mmHg.

FIG. 4 PROPORTION OF COMMUNITY PATIENTS CONTINUING TO ATTEND AT THE END OR EACH THREE MONTH PERIOD OF FOLLOW UP.

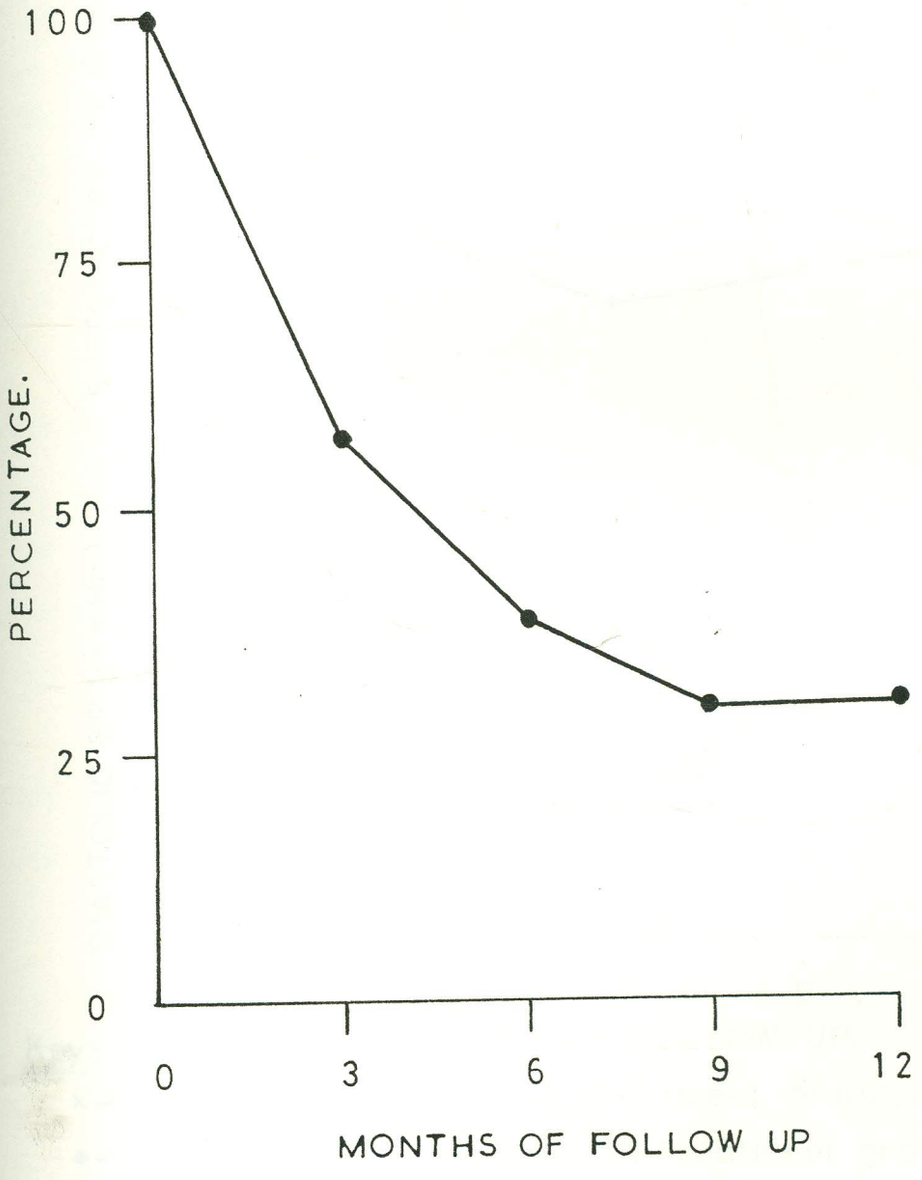
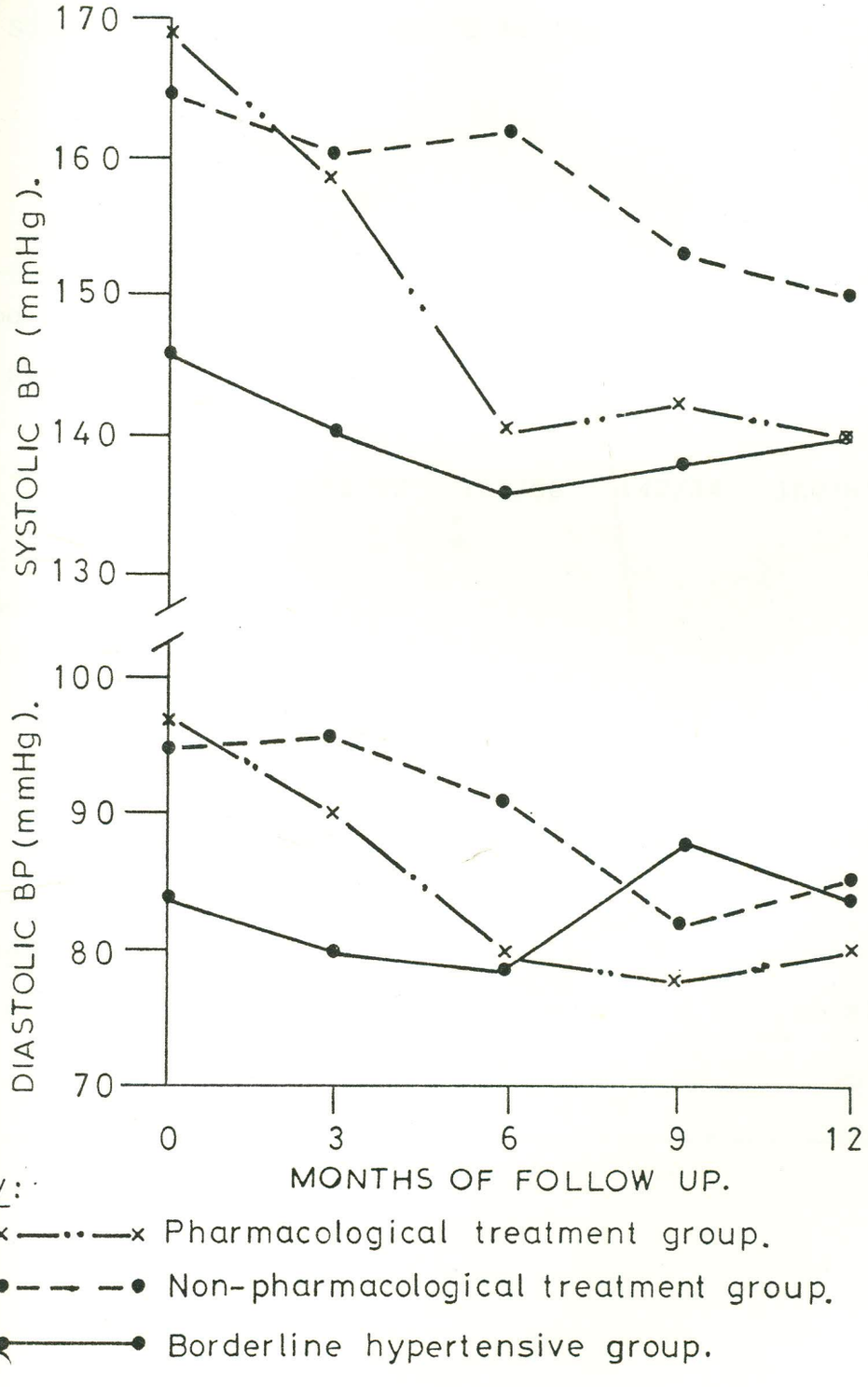


FIG. 5 MAEN BLOOD PRESSURE (mmHg) AT THE BEGINNING OF STUDY AND AT THE END OF 3, 6, 9 AND 12 MONTHS OF FOLLOW UP IN THE PHARMACOLOGICAL, NON-PHARMACOLOGICAL AND BORDERLINE COMMUNITY PATIENTS.



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