

# Hypertension: Today

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## HISTORICAL PERSPECTIVE

**R**ev. Stephen Hales first measured blood pressure in 1733 and Huchard recognized in 1889 that high blood pressure could occur independently of nephritis. The development of simple clinical measurement of blood pressure by Basch, Riva Rocci, Recklinghausen and Korotokow generated rapid interest in this disease in the early part of this century. Frank in 1911 coined the term essential hypertension and four years later came the classic studies of Volhard and Fahr on the relationship between renal lesions and high blood pressure. The next couple of decades saw the accumulation of a great deal of knowledge regarding the physiological mechanisms of the control of blood pressure and the epidemiology, etiology, complications and management of hypertension. Large epidemiological studies were initiated which provided the data-base for the Chicago symposia in 1964. they were followed by a host of detection and intervention programmes in the U.S.A., Australia and many other countries. While tracing the history of hypertension it will be unfair not to mention the great stimulus provided to hypertension research by Sir George Pickering.

The amazing array of technological advances after the World War II has added new dimensions to our knowledge of various aspects of high blood pressure.

There is now a massive amount of information available on the subject some of it factual and rest hypothetical still. Hypertension strictly speaking may be an undesirable term because there is no definite point where normal blood pressure ends and pathologically raised levels begin. The division between the two is arbitrary. Blood pressure is a graded character with a unimodal distribution, and high blood pressure is the upper end of biologic continuum, and is thus a quantitative derangement from the norm.

### Definition

Population studies are necessary to determine the average mean blood pressure for a group of

people. The definition of hypertension may therefore vary in different population groups within a country. However keeping the limitations in view, the W.H.O. on the basis of global information has laid down arbitrary levels of systolic and diastolic pressure as criteria for defining hypertension. The U.S. joint National Committee on detection Evaluation and Treatment of hypertension defined it a little differently and Borhani likes to call the term mild hypertension a misnomer and would like to name diastolic BP 90 - 104 mm Hg. as stratum in measurement of blood pressure.

### Measurement of Blood Pressure

The initial recording of blood pressure should be the average of three readings taken at two different occasions. Moreover the basic rules concerning the patient, the instrument-its cuff size, the examiner and the environments under which blood pressure is being measured should be strictly observed, to obtain valid results. Basal blood pressure is ideal but casual pressures have been shown to be reproducible giving a good prognostic indication of the risk of complications and the effectiveness of treatment. They are therefore recommended for practical, clinical and epidemiological purposes. Falsely high readings resulting from the presence of the physician (white coat effect) can be reduced if the blood pressure is taken by nurses or non trained medical staff, or better still home blood pressure readings taken with semiautomatic devices. Self measurement may also ensure better compliance. the instruments used for self-monitored blood pressure blood pressure measurement should be regularly checked and calibrated against the physicians standard office manometer. The available methods for ambulatory blood pressure measurements are expensive and are currently not practical for widespread and general clinical application, but may be used for selected patients whose office blood pressure measurements do not correlate with the severity or lack of end organ damage.

The relative importance of systolic blood pressure has been debated. It depends on the force of

cardiac contraction. It increases as the aortic compliance falls. Diastolic blood pressure on the other hand increases with peripheral resistance and decreases with a fall in heart rate. Thus the factors increasing systolic blood pressure may not increase the diastolic blood pressure and vice versa. Also diastolic blood pressure is a much more important determinant of coronary artery blood flow whereas systolic blood pressure determines the peak pressure in the cerebral circulation. It has also been shown that down-ward fluctuations in diastolic blood pressure are more dangerous to the heart than the brain and this may be the reason why antihypertensive treatment is more beneficial in preventing strokes than heart attacks. Despite the divergence between systolic and diastolic blood pressure and the differences in the pathophysiological mechanisms affecting the two has not been established conclusively that either of them has a greater effect on morbidity or mortality. Systolic and diastolic blood pressure therefore, merit equal importance. Similarly isolated systolic hypertension may be as important as isolated diastolic hypertension

### **Epidemiology**

The prevalence of hypertension depends on the criteria used to define the condition as well as several other factors. The W.H.O. overall world figures vary between 8 - 18% while the prevalence in some highly industrialized countries is above 25%. In USA Hypertension Detection Follow-up Programme it was 23% with 60 million people having BP above 140/90 mm. In many developing countries there is a progressive increase in the prevalence of hypertension and according to a WHO report it is already at an epidemic stage in some of them. The prevalence of hypertension in some group in developing countries is now about the same magnitude as in Finland - a country with one of the highest viz 28% prevalence rate of hypertension among the middle age population.

There is no exact data available regarding the prevalence of hypertension in Pakistan, and according to a few available epidemiological surveys the rates vary widely between 7 - 17%. The preliminary results of a recent multicentre survey reveal the overall prevalence to be 9.33%, and females were affected more frequently 12.5% as compared to male counterparts 7.03%. The prevalence in all groups increased with age.

### **Etiology**

The precise etiology of any form of raised B.P is obscure. However, in up to 5% of hypertensives, there may be an identifiable cause. This figure may vary as a result of selection bias but a number of population based studies support the view that in 95% of all hypertensives there will be no recognizable cause. the extent of investigations which should be undertaken to exclude secondary causes may therefore be moderated by this knowledge. Extensive use of high technology diagnostic investigations may not only be unrewarding but definitely wasteful except in the subgroup of young hypertensives and in patients with clinical and laboratory evidence suggestive of a secondary cause.

Although our knowledge regarding the etiology of essential hypertension is grossly inadequate, a number of modifiable predisposing factors have already been identified and newer ones are being discovered. Essential Hypertension is said to be a heterogeneous disorder with complex interplay of multiple and interacting genetic and environmental factors. According to some workers it is a biochemical multiform. Genetic susceptibility provides the permissive background but it requires environmental factors to trigger the tendency. Thus the lifetime blood pressure trend of an individual is engendered by the impact of diverse environmental factors upon his genetic constitution. The degree of heritability of a biologic variable like blood pressure is an individual, has to be viewed in the context of his interface with the total environment. Hypertension may develop due to the cumulative action of many minor genes being above a certain threshold.

### **Pathogenesis**

The pathogenesis of primary hypertension and even of a number of cases of secondary hypertension is not possible to explain despite different approaches to hypertension research. The disease may be precipitated by various derangements in factors affecting the cardiac output and peripheral resistance, with the kidney providing the triggering mechanism. Twenty five years ago renin-angiotensin system was thought to contribute to blood pressure elevation only in patients with renovascular hypertension. The situation changed dramatically and the renin angiotensin system is now recognized as a major factor contributing to the regulation of

peripheral vascular resistance, and converting enzyme inhibitors are now being widely used to treat hypertension. The latest research has focussed its attention on angiotensin II, not only as a potent vasoconstrictor but more importantly as a trophic hormone or growth factor responsible for the structural changes in the arterial wall and heart. More recently it has been discovered that, in addition to the classic endocrine system in which ANG-II is generated in blood and reaches the great target organs via the circulation, the components of Renin Angiotensin System are also found in the tissues themselves especially in the vascular wall.

A new line of research has become increasingly absorbing in the past few years and this concerns the hypothesis that hypertension is part of a metabolic syndrome with cardiovascular consequences. The association of high blood pressure with obesity and diabetes both conditions with insulin resistance has been established for long. But hypertension is now associated with insulin resistance independently of overweight. A decreased insulin sensitivity and the compensatory insulin increase mark the start of metabolically blood pressure increase. It is postulated that essential hypertension is an insulin resistant state and this insulin resistant hypertension and insulin resistance is directly correlated with the severity of hypertension. Insulin resistant and hyperinsulinaemia are primary defects which induce hypertension per se by stimulation of tubular sodium absorption and expansion of extracellular fluid volume and by increasing sympathetic activity.

Multicultural dietary studies suggest that the level of habitual salt consumption in a society is linked to the prevalence of hypertension. It is estimated that industrialized societies absorb up to 100 times more salt than their prehistoric ancestors but some primitive societies still exist who consume little salt and in whom hypertension is virtually unknown. Although a very high intake of Sodium chloride (more than 14 g.d/day) will cause a detectable increase in blood pressure and a very low intake will reduce blood pressure, there are many unanswered questions regarding the relationship. It is possible that only genetically salt-sensitive person are prone to develop an increase in arterial pressure in response to a high salt intake, or else a high salt intake needs the presence of other markers or other environmental factors to produce high blood pressure.

Potassium is a major intracellular cation mainly involved in maintaining membrane potential. It has been postulated that it may have some correlation with the level of blood pressure or the pathogenesis of hypertension is as yet available. Trials of dietary potassium supplements in patients with essential hypertension have not yet produced convincing results.

Calcium, Magnesium and some trace elements have been implicated in the regulation of blood pressure. Arterial pressure is primarily regulated by contraction and relaxation of vascular smooth muscle. Calcium ion is directly involved in both neurogenic and hormonal interaction responsible for cellular and molecular processes producing smooth muscle contraction. Several epidemiological studies have suggested an inverse relationship between dietary intake of calcium and blood pressure. There is evidence that magnesium too may have a role in blood pressure regulation. But it is still highly premature to make any definite recommendations regarding changes in the dietary intake of Ca and mag. Again there are no firm data to suggest that any of the trace elements play a significant role in the pathogenesis of hypertension.

Excess of special nutrients like proteins may contribute to higher blood pressure while polyunsaturated fatty acids may have to opposite effect. Low energy food intake is believed to be associated with lower blood pressure levels. Caffeine and nicotine do cause an immediate rise in blood pressure but neither is associated with persistently elevated blood pressure.

A high intake of alcohol has been found to be associated with high blood pressure in a number of studies, but the mechanism of the association is not yet clear. There is no casual relationship between smoking and hypertension.

Psychological influences have been presumed to produce physiological effects including elevation of blood pressure. Acute psychological stress does not produce any sustained rise of blood pressure. However, major sociocultural changes involving long term exposure to adverse psycho-social circumstances due to rapid urbanization and mass migration may lead to hypertension. Such situations entail modification of many environmental factors simultaneously such as directly changes, noise, and the fears, apprehension and stress of the new environments. Cardiovascular diseases especially hypertension are associated with modern day

lifestyle of the industrialized world which are rapidly being imitated in the developing countries due to an explosion of mass media communication. For good reasons therefore these diseases are called diseases of lifestyles, the modern ills or the new communicable disease.

A higher prevalence of hypertension has been found in several studies in persons of lower social status, in lower income and less educated groups. Residence in urban or rural areas also has a bearing. High attitude has been claimed to have a beneficial effect on blood pressure. Highlanders generally manifest low average mean blood pressure. Regular physical exercise is generally believed to produce haemodynamic changes that minimize overall cardiovascular risk, but the evidence that it may directly reduce blood pressure is still weak. It may however, inculcate a healthier life-style including less intake of sodium, fat and alcohol more relaxation and less reaction to stress which may have a salutary effect on blood pressure.

### Management

The basic principles underlying management of hypertension include:-

1. Hospitalization In HTN crises, refractory and complicated HTN and HTN in pregnancy.
2. Appropriate diagnostic workup to find the cause of HTN and assess the target organ damage.
3. A known cause of HTN may not always be amendable to radical surgical treatment.
4. Once HIGH BP has persisted for sometime in a case of secondary HTN, it may no be abolished even after the cause is removed.
5. Education of the patient regarding the disease and its management allaying their fears and apprehensions.
6. Withdrawal of prohypertension drugs like contraceptives, NSAID.
7. Using the simplest possible regime of drugs.
8. Combination of drugs with different modes of action in smaller doses thus minimizing the dose dependent side effects.
9. Avoidance of precipitous reduction of blood pressure except in crisis.
10. Recognizing that HTN is not always a life long disease
  - a. Stepwise reduction of drugs and their eventual Withdrawal is possible in some cases.

- b. Spontaneous remissions may occur in some cases.

The goal of treatment of hypertension is to achieve and maintain the both systolic and diastolic at normotensive levels and to prevent morbidity and mortality due to hypertensive vascular disease.

### Non-pharmacologic Approach

Non-pharmacologic approaches should be used as definitive intervention initially in cases of mild hypertension and as an adjunct to drug therapy in all cases of hypertension. In mild hypertension without any complications there is no hurry to institute drug therapy and a trial of nonpharmacologic therapy should be continued for 3-6 months. This includes wt. reduction, restriction of sodium, relaxation and biofeedback therapies, regular aerobic exercise programmes, modification of dietary fats - and giving up smoking. All this virtually amounts to a change of life-style and will require proper counselling which is time consuming. Nonpharmacologic therapy is, therefore difficult to institute and it is certainly easier to prescribe a pill. Moreover NPT has no commercial advocates to convince the medical practitioners.

### Drug Therapy

Drug treatment is indicated in cases where nonpharmacologic therapy alone has failed and initially in all cases of moderate to severe hypertension. Other factors influencing the decision to initiate drug therapy and the choice of drugs are, target organ involvement, presence of other concomitant diseases, race, age, etc. and the limitations imposed by their side effects and cost effectiveness. The latter factor is especially pertinent in the developing countries, because antihypertensive drug therapy is invariably required for life and involves the largest use of long term drug therapy. It is also the most important determinant of compliance.

Drug therapy of hypertension was in the docks for quite some time because of the severe disabling side effects produced by the older drugs. They were regarded as a greater nuisance than the discomforts of the disease itself. But with the advent of newer less toxic drugs, this conflict has vanished and drugs are no longer prosecuted for harming the patients. It may be said that the hypotensive drugs introduced over the last decade have almost revolutionized the

treatment of hypertension. They have not only transformed the prognosis but also the pattern of death in both benign and malignant phase. Drug treatment increases the expectation of life 6 - 8 times in malignant hypertension.

A wide variety of drugs is available today and since the advent of hexamethonium in 1940 a huge number of drugs have been introduced for the control of hypertension. They have multiple sites of action and here is a diversity of their proven and postulated mechanisms of action. There is as yet no ideal or universal drug. Each individual patient and various subgroups of patients may require and respond differently to drugs. The drug groups which have stood the test of time and are still in use are the sympatholytics-centrally acting, ganglion blockers, adrenergic receptor blockers-diuretics, vasodilators, calcium channel blockers, ACEI and a miscellaneous group.

Various regimens of those drugs have been advocated over the past two decades the referred care therapy, sequential or stepped care and individualized stepped care approaches, and monotherapeutic substitution deletion approach. Further modifications of these regimens and newer regimens will be proposed in future. New drugs and new analogs of the existing drugs will be launched with massive promotional campaigns. But prudence demands that the physician should temper his selection of drugs based on cost effectiveness, side effects and compliance. There should be no hurry to prescribe the latest and most expensive ACEI in the market. The 1988 report of the US Joint National Committee and the 1989 WHO/ISH guidelines for the management of mild hypertension recommend the simplest regimes in the minimal possible dosage. The diuretics and beta blockers despite their metabolic and other side effects may still be the cheapest and most effective drugs in the majority of patients of mild hypertension if used judiciously.

Since HTN is a life long disease and its treatment with or without drugs has to be continued indefinitely, the impact of the disease itself and the treatment on the quality of life should be an important factor in selecting the regimen of treatment. The management therefore should be individualized to ensure the desired quality of life according to the needs of each patient.

### Prevention

Essential Hypertension today is a major public

health problem in the developed as well as the developing countries because of the high rates of prevalence and its importance as a risk factor for cardiovascular disease. Although further research is needed and will continue to be carried out in various population groups around the globe, some definitive recommendations can certainly be made on the basis of the available data for the present. Primary prevention of hypertension is a highly desirable goal and is certainly possible to achieve by applying the two complementary approaches viz. the high risk strategy and the mass strategy. The nonpharmacologic modalities now established as standard intervention in the management of hypertension should be instituted for primary prevention in the group at high risk as well as in populations at large.

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