High blood pressure—ancient, modern and natural

R. G. SINCLAIR, M.B., Ch.B., D.Obst.R.C.O.G.
Falkirk

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HISTORICAL BACKGROUND

ALTHOUGH increasing understanding and successful treatment of hypertension are recent developments, study of the heart and circulation goes back much further, and disorders of the heart and blood vessels are frequently mentioned in ancient writings. The Ebers Papyrus, dated about 500 B.C. mentions the heart which is regarded as the principal vital organ and the Egyptians knew that the pulse could be felt in many parts of the body and that it was in time with the heart beat. The Aztecs of Mexico mentioned angina pectoris in their writings and a feature of Chinese medicine from ancient times has been diagnosis by palpation of the pulse which became elaborated into a complex pulse lore.

Blood pressure was first estimated by Stephen Hales (1677–1761) who was one of the outstanding English physiologists of the eighteenth century and the signs of left ventricular hypertrophy were described in 1819 by Laennec. Richard Bright mentioned thickening of the large renal arteries in the illness which bears his name, and by 1836 had studied 100 cases of renal disease, and arterial hypertension was shown to be the link connecting renal disease with cardiac hypertrophy by Traube in 1856.

A great deal of work was done during the latter half of the nineteenth century on the relationship between cardiac hypertrophy and hardening of the arteries and the theory was advanced that high blood pressure might be due to intra-arterial tension, although increased heart action was considered the primary cause at the time. Allbutt’s (1859) recognition of ‘hyperpiesia’ as a condition independent of chronic nephritis and arteriosclerosis, and belief that elevated intra-arterial tension might cause both arterial and arteriolar disease have since been proved experimentally. Most clinicians associated hypertension with chronic Bright’s disease until Mahomed (1881) first recognized the condition later named ‘essential hypertension’ by Janeway (1913) and Mahomed also suggested that hypertension causes the renal vascular affections found at necropsy. Huchard (1889) advanced the idea of a generalized angiosclerosis involving heart, arteries, veins and capillaries. The pressor properties of extracts of suprarenal medulla were discovered by Oliver and Schaefer in 1895 and nine years later Vaquez produced the theory that hypertension results from increased secretion of adrenaline. So within a century, more progress has been made than in the previous thousand years, and although the journey was far from over, instruments were available for accurate study of the condition and the way was paved for the search for treatments. The end of the nineteenth century saw the beginning of a trend towards specialization in medicine and the field of cardiology. Walter Holbrook Gaskell (1874–1914) studied the innervation of the heart and Sir Lauder Brunton noticed the effect of nitrates in the relief of pain in angina pectoris.

Estimation of blood pressure was first used as a routine procedure by Potain in Paris and in this country by Albutt, and in 1903 William Einthoven produced the first electro-
cardiograph and Janeway (1913) first used the term hypertensive cardiovascular disease. In 1914, Volhard and Fahr produced a classical clinical and pathological work on the classification of hypertension and they put forward the important contribution of the recognition of the benign and malignant phase of essential hypertension, and thus there came to be recognized a disease, primary or essential hypertension, characterized by raised arterial pressure, cardiac hypertrophy and wide-spread vascular disease. In 1922 a case of phaeochromocytoma associated with hypertension was investigated and reported by Liebbe and five years later the first operation on this condition was successfully performed by Mayo. Although suggested by various earlier authorities, sympathectomy as a treatment for hypertension was first initiated by Rowntree and Adson in 1925, and subsequently more extensive operations were devised by Adson, Peet, Smithwick and others.

There has thus evolved the concept of a level of arterial blood pressure which is considered to be too high, which to-day we divide into the two groups of essential and secondary hypertension. Essential hypertension means hypertension without evident cause and is characterized by elevated arterial pressure and its cardiovascular consequences. It is sometimes called primary hypertension to indicate that the hypertension comes first and the cardiovascular changes follow. It is defined by exclusion and what is excluded is called secondary hypertension to indicate that a specific lesion precedes the hypertension. The following conditions have been considered as precursors of hypertension; pyelonephritis, vascular lesions of the kidneys, including for example unilateral renal artery stenosis and polyarteritis nodosa, coarctation of the aorta, phaeochromocytoma and Cushing's syndrome and other diseases causing secondary hypertension have become better known, for example post-toxaemic hypertension.

Aetiology of hypertension

Previously, it was considered that essential hypertension was a specific disease entity. There was disagreement as to whether it was the arterial pressure or the vascular disease or some other factor that was the basic abnormality and the difference between hypertensive patients and normotensive patients was considered to be one of kind not of degree. The assumption that essential hypertension represented a specific disease entity meant that there has been an intense search for a unique cause, but this has never been found. Nervous and hormonal influences have been invoked, such as overaction of the vasomotor nerves, inaction of the carotid sinus and depressor reflexes, disorder of the vasomotor centre, overproduction of adrenaline or noradrenaline, of adrenal cortical steroids, of posterior pituitary substance, of anterior pituitary substance, of renin and of numerous other less-well-authenticated substances. Essential hypertension has also been regarded as due to an inherited fault caused by a gene behaving as a Mendelian dominant, as a disorder of adaptation, as a psychosomatic disorder expressing a defect of personality, as a disease of 'stress' and as a dietary disease due to the excessive ingestion of protein, salt or some other dietary constituent.

Hamilton, Pickering, Roberts and Sowry (1954), however, put forward the concept that this assumption was without any substantial justification and they suggested that differences between normal subjects and those with essential hypertension were quantitative. They described essential hypertension as the name given to a condition of high blood pressure in which no specific lesion had been found to account for the high blood pressure. Essential hypertension represented the right-hand end of frequency distribution curves that show continuous variations. They felt that there was no clear dividing line between hypertension and normality and the difference was quantitative, not qualitative. The justification for retaining the concept of essential hypertension was that, at any age, the higher the arterial pressure, the less the expectation of life. The view is advanced by Pickering (1955) that the syndrome of malignant hypertension represents the effects of
hypertension provided it is sufficiently severe and that it can occur in the course of any kind of hypertension. He is of the opinion that it is correct to speak of hypertension ‘in the malignant phase’ and has shown that the serious damage caused by the highly-elevated blood pressure can be minimized or even reversed by reducing the blood pressure. Blood pressure, he suggests, like other quantitative characteristics such as height and weight, is distributed in the population as a continuous series. Most people are near the average for their age, some have higher pressures and some lower, and those at the highest end of the curve are liable to certain hazards and so are classified as suffering from hypertension. The individual's position in this continuous distribution depends on the interaction of heredity and environment. Some support for the work of Pickering and his colleagues comes from the work of Miall and Oldham (1958 and 1963) who have investigated factors influencing blood pressure in the general population of a mining valley and an agricultural area of South Wales. They also found that arterial pressure is a graded characteristic inherited multi-factorially in much the same manner as height or somatotype and furthermore, those engaged in light occupations had higher pressures than those doing heavy manual labour. These authors consider that much of the familial resemblance in blood pressure may result from environmental factors. They suggest that blood pressure is a physical characteristic analogous to obesity and that both are continuously variable with no natural boundary separating normal from abnormal. When either weight or blood pressure is increased there are increased risks, and both are probably influenced in the same kind of way by environmental and genetic factors. This concept has been emphasized repeatedly by Pickering as in the St Cyres lecture (1965). He again stated his belief that arterial pressure is a quantity. It is not a quality with two alternatives, good and bad, normal and raised.

Platt (1959) however, has examined the work of Pickering and his colleagues and gives reasons for doubting their hypothesis concerning the nature of hypertension. Platt points out that if essential hypertension is an inherited tendency to develop high blood pressure in middle life, then there must be two populations, in one of which blood pressure rises significantly in middle age and this should be shown by a bi-modal frequency distribution curve of blood pressure in middle age. He found such bi-modality when, in order to obtain homogenous age samples, he obtained pressure distribution curves from siblings aged 45–60 years, of patients aged 45–60 with high blood pressure, using the data of Pickering and his associates (1955) and Soby (1948). In fact, the siblings separated into two groups, those who did and those who did not inherit the disorder from their parents.

Pickering's concept of hypertension is attractive in its simplicity and is difficult to disprove. The theory would certainly be more convincing if the distribution curve of blood pressure in the middle-aged population was Gaussian, but it never is. This shows well in the famous study of blood pressure in the population of Bergen by Bøe and his co-workers (1956). He showed that the distribution curve of the systolic pressure for males up to about the age of 40 years is nearly Gaussian. Over 40 years the Gaussian shape is lost and the probable interpretation is that there is a composite curve due to the overlapping of two populations. In one of these the average systolic blood pressure remains at no more than 140mms Hg in middle age, though the range of pressure is from the unusually low of about 110 mms Hg to the unusually high of about 180mms Hg. Superimposed is another population (essential hypertension) with a mean systolic pressure of about 200–210mms Hg and a range which might be from 170 to 240 mms Hg and the shape of the curve certainly suggests that this is the case.

Further controversy on the aetiology of essential hypertension was started by the publication of a paper by Morrison and Morris (1959) which purported to show that essential hypertension was inherited as a simple dominant, but this evidence has been challenged by several workers, among whom were Oldham, Pickering, Roberts and
Sowry (1960). Therefore it would appear that the aetiology of essential hypertension is multifactorial and it is the resultant of a number of factors that operate in greater or lesser degree in the population at large. The first factor is age, as arterial pressure tends to rise with age, the second is inheritance, but the mechanisms involved are complex and controversial; the third group includes environmental, metabolic and endocrine influences.

High blood pressures are more commonly found in older subjects and a rough guide to the expected systolic level (in mms Hg) is postulated as 100 plus age in years. This was well shown by a study of 74,000 men and women in the United States of America by Master, Dublin and Marks (1950). Platt (1963) made a study of 179 cases of severe hypertension and their 350 available sibs. He was concerned not with people whose blood pressure was a little higher than the average for their age, but with people whose hypertension was severe enough to require treatment because it was a threat to their continued survival. He chose a diastolic pressure of 125 mms Hg or over as the dividing line, and the mean diastolic pressure was in fact between 140 and 150 mms Hg. An interesting difference in age incidence was noted in cases diagnosed as secondary hypertension. Cases of secondary hypertension were fairly evenly distributed between all age groups from 15 to 60 years. Two thirds of the essential hypertension group who were sufficiently severe to require hospital investigation and treatment were in the age range 45 years to 60 years. This is information of great practical value to the clinician, suggesting that the younger the person the more likely is the hypertension to be due to some underlying cause. The smaller number over the age of 60 years could well be because hypertensive patients of this age are less frequently referred to hospital. Platt had previously noted this in 1948.

It has been suspected for a long time that inherited factors were concerned in the genesis of hypertensive cardiovascular disease. The evidence concerning the mode of inheritance is of three kinds and consists of studies of family histories, measurements of blood pressure in twins, and measurement of blood pressure in the relatives of patients with essential hypertension. Weitz (1923) found a history suggestive in one or both parents in 76.8 per cent of 82 patients with essential hypertension and a similar history in the parents of 30.3 per cent of 267 control patients over 44 years, attending his clinic for complaints other than cardiovascular. O’Hare, Walker and Vickers (1924) found positive family histories in 68 per cent of 300 cases of essential hypertension and in 37.7 per cent of 436 control patients, and Platt (1947) by personal enquiry, obtained similar findings.

Family histories, however, are not a particularly accurate guide to high blood pressure in so far as they may omit a considerable proportion of the family. Measurement of blood pressure on monozygotic and dizygotic twins is of great importance as evidence of the extent to which arterial pressure defects are inherited factors. Stocks (1930) investigated arterial pressure in twins ages 3–15 in London schools and showed a greater co-relation between monozygotic than dizygotic pairs. Weitz (1923) recognized the possible fallacies in family history studies and he therefore measured the blood pressure in 93 brothers and sisters of 42 patients with essential hypertension and noted that the incidence of hypertension was greater in them than in 359 control subjects of similar age (over 45 years). In 1934 Ayman measured the blood pressure in 1,525 members of 277 families, by collecting as many relations as possible when they came to visit patients in the wards. He considered that his figures provided evidence for a hereditary factor in hypertension but not for the mode of inheritance. The most extensive measurements were those of Sobyche (1948) who measured the pressures in relatives of 186 patients with hypertension related to nephrosclerosis. From these observations, and scrutiny of identical families, Sobyche considered that both nephrosclerosis and essential hypertension were inherited through a gene behaving as a Mendelian dominant...
and having a frequency in the population of 30–40 per cent. In 1947 Sowry, Hamilton and Pickering started their own observations, their intention being to investigate further Sobye’s hypothesis. They suggested that the concept of Mendelian dominant inheritance was unsupported and they thought that the inheritance was probably multifactorial.

The idea that essential hypertension is a psychosomatic disease and therefore arises chiefly through the agency of the mind, has many adherents and it is well known that the arterial pressure can be dependent upon the emotional state of the subject at the time of measurement. People who are agitated and anxious tend to have elevated pressures and emotional stimuli usually cause a higher rise in the blood pressure of people with hypertension than those whose blood pressure is normal. Pickering (1955) however, in a review of the relevant literature, concluded that the extent to which environmental factors, operating through the medium of the mind, are important in producing high blood pressure remains an entirely open question. There is nothing inherently improbable in the idea, but at the same time there is nothing conclusive about the evidence. No one doubts that the environment influences the level of blood pressure in the casual readings. However, there is no proof that environmental influences of the kind known as the stress of modern life have any effect on the establishment of continued hypertension. Attempts to establish environmental (including psychological) causes for essential hypertension have largely been a failure. Ostfield (1964) amongst others, has tried to make personality studies of hypertensive and normotensive persons. He compared groups with essential hypertension with renal hypertension and with normal blood pressures which were similar in age, sex, race, education, employment and marital status. There were no important differences in the groups.

Rapidly accumulating data from animal experiments and human studies indicate that in the presence of a sustained elevation of the systemic blood pressure, disturbance of water and electrolyte metabolism is almost invariable. In addition, the now accepted association between the renin-angiotensin system and aldosterone emphasizes how extremely complex some of the metabolic aspects of hypertension have become.

Indications that sodium and chloride were of possible pathogenic significance in hypertension date from the beginning of this century when therapeutic restriction of salt was first tried. In subsequent years, the use of such a regime was advised in the belief that its beneficial effects were caused more by poor chloride intake than restriction of sodium (Allan and Sherrill 1922, Martini 1938) and indeed Kempner (1948) attributed the undoubted effectiveness of his rice diet in hypertension to its low protein and possible ‘enzyme effects’ rather than its low sodium intake. Grollman and Harrison (1945) while investigating the effect of various diets on the blood pressure and survival of hypertensive rats, showed that drastic restriction of sodium both lowered the pressure and prolonged survival. Furthermore, they demonstrated that this effect could be achieved by other salt-free foods and was not limited to unpalatable rice diets, nor was the effect confined to hypertensive animals, but applied equally well to man. Recent carefully-controlled clinical studies have endorsed the hypotensive efficacy of the rice diet and other low-salt dietary regimens in the management of essential hypertension (Watkin et al. 1950, Corcoran et al. 1951 and 1966, Dustan 1960). Subjective improvement and sustained fall in diastolic and systolic pressures have been achieved in a substantial number of patients and in addition, decrease in heart size, resolution of retinal vascular damage and significant improvement in the electrocardiogram were often noted.

Interesting indirect circumstantial evidence of a close co-relation between sodium intake and the incidence of hypertension is also found in the results of epidemiological studies (Dahl and Love 1957, Dahl 1960), which show that hypertension is virtually absent in certain primitive races and in a selective Japanese farming community, the members of which appear to live on diets with very meagre salt content. In contrast,
a relatively high incidence of hypertension is found in similar communities in other areas of Japan where there is a normal or high daily sodium consumption. Similarly, it has also been shown that rats, after continued ingestion of excessive quantities of salt, develop diastolic hypertension (Menelly et al. 1961). It is interesting in passing to note that the Eskimos and Sikhs who have a large protein intake and the Chinese and the Hindus who are largely vegetarians, rarely suffer from hypertension.

General appreciation of the fact that elevation of the systemic blood pressure was a common finding in Cushing's syndrome and in patients on prolonged corticosteroid therapy, whereas hypotension was usual in Addison's disease or following bilateral adrenalectomy, led to intensive investigation of adrenal function in essential hypertension. The results of these studies, however, are inconclusive, although an increase in aldosterone production has been reported in patients with malignant hypertension (Genest et al. 1958; Laragh et al. 1960). There is an increase in both the intracellular sodium and water content of many tissues (liver, brain, heart, muscle, skin and blood) and expansion of the extracellular fluid spaces has been demonstrated in experimental hypertension and in human isotope studies (Laramore and Grollman 1950, Green and Sapirstein 1952, Grollman and Shapiro 1953). Recently, Brown et al. (1966) showed the close reciprocal relationship between plasma renin concentration and plasma sodium.

In contrast to essential hypertension, in secondary hypertension there is the aetiological factor provided by the specific lesion and this specific diagnosable disease process precedes or is associated with the hypertension. Renal disease, either bilateral or unilateral is thought to be a frequent cause of secondary hypertension and chronic pyelonephritis is now recognized to be a much commoner cause than chronic nephritis. During the past ten years much interest has been aroused in the ischaemic kidney with an abnormal, thrombosed or narrowed renal artery. Goldblatt (1964) showed that moderate constriction induced benign hypertension without impairment of renal secretion, and severe constriction induced malignant hypertension with characteristic terminal sclerotic lesions.

The syndrome of pre-eclampsia usually appears in the last trimester and is common in primigravida, affecting about eight per cent in Great Britain. It has been felt for some years that hypertension appearing before the 24th week of pregnancy and unaccompanied by albuminuria is a different disease process and indicates pre-existing hypertensive disease or an inherited tendency towards hypertension. A further rise in blood pressure and the appearance of albuminuria later in pregnancy in such patients indicates a superimposed pre-eclampsia. Confirmation of this clinical classification has been provided by renal biopsy studies (Altcher 1961, Hopper et al. 1961). The cause of pre-eclampsia is still uncertain but there is increasing evidence that placental ischaemia plays an important part. The hypertension can be reproduced by transfusion of blood from pre-eclamptic women (Tatum and Mule 1962) and a pressor substance (hysterotonin) has been detected in the placenta, amniotic fluid and uterine venous blood of patients with pre-eclampsia (Hunter and Howard 1961). This may be the cause of the hypertension and the arterial spasm which can be seen in retinal and conjunctival vessels. The pathogenesis of the oedema remains obscure; it has some similarities to nephrotic oedema but develops at a higher level of plasma protein.

REFERENCES

HISTORICAL BACKGROUND


AETIOLOGY OF HYPERTENSION


(To be concluded)