HIGH BLOOD PRESSURE *

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ARTERIAL hypertension is a common clinical finding in most forms of medical practice. It may be an integral part of a variety of renal, vascular, endocrine and neurological disorders. In each such instance the visceral disease is regarded as the cause of the hypertension, and indeed in many instances the cure or relief of the visceral disease, if achieved, is accompanied by a return of the blood pressure to normal levels. When no such organic disease is discernible as the cause arterial hypertension graduates by default into the ranks of diseases with the title of essential hypertension, and we must still, for practical purposes, look upon it as a disease entity rather than as a feature of some other underlying condition. This in no way denies the accepted academic belief that a basic lesion will eventually be disclosed. When this happens essential hypertension will join all its cousins as only an outstanding clinical feature of some other pathological process. Essential hypertension may indeed turn out to be not one disease but a variety of diseases.

Essential hypertension, however, constitutes by far the most important of all forms of hypertension, accounting for 80 to 85 per cent. of all cases of hypertension. It has been estimated that one-fifth of the population is hypertensive, and there is little doubt that, as Cabot wrote in 1926, " Hypertension is more common than all other forms of heart disease put together." Essential hypertension, or rather its effects on heart, brain or kidneys, probably constitutes the most important single non-traumatic cause of morbidity and death after the age of forty.

We remain in ignorance of the cause of this common disorder. Although the circle of the light of knowledge on this subject has widened rapidly in the past decade, it has not yet illuminated the most important corner of the room. As the result of the brilliant research during the past ten years or more of Goldblatt in the United States and Houssay in South America, and many others, much information is now available regarding the mechanism of production of renal hypertension. Renal ischæmia, induced experimentally by partial constriction of the renal artery, is followed by sustained hypertension which is not prevented or cured by denervation of the kidney, section of the splanchnic nerves, or section of the anterior spinal nerve roots. This hypertension is due to a direct humoral action upon the

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arterioles. The blood pressure of a non-hypertensive nephrectomised animal is elevated when an ischæmic kidney from a hypertensive animal is transplanted into it. Transplantation of a normal kidney does not affect the blood pressure. Plasma from the vein of an ischæmic kidney has a marked vasoconstrictor effect.

Purified preparations of the pressor substance (commonly known as renin) are inactive, but are reactivated when added to plasma. Renin with renin-activator has been called angiotonin, and this has been isolated in crystalline form. Various experiments have shown that normal kidney tissue forms a substance which antagonises or inhibits angiotonin, and such a " renin inhibitor " has been prepared, has been shown to be effective by oral administration in lowering the blood pressure in hypertension and has given encouraging results in a few human cases.

In chronic nephritis in human beings, renal ischæmia results from the readily observed and well-authenticated vascular narrowing. In unilateral renal disease such as chronic pyelonephritis associated with hypertension, removal of the diseased kidney is followed by a fall in the blood pressure to normal.

The burning question is whether and how far this experimental work on renal hypertension is applicable to human essential hypertension. That the hypertension is due to peripheral vasoconstriction is accepted, but the cause of this vasoconstriction is unknown. It has been observed histologically that the kidneys of hypertensive patients show arteriolar lesions of endothelial hyperplasia, medial hypertrophy and hyaline degeneration of the intima which non-hypertensive kidneys do not show, and yet the arterioles in other sites do not show this difference between hypertensive and non-hypertensive cases. It may therefore be that renal arteriolar constriction is the primary factor with renal ischæmia and hypertension following, even though impairment of renal function does not occur until late in the disease. However, even if this is the mechanism behind essential hypertension the original cause of the renal arteriolar constriction remains to be elucidated. The striking lability of the blood pressure in the earlier phases, the excessive rises which result from emotional or other stimuli, and the great reduction which may follow rest and sedation are strong arguments against a fundamental renal cause. Heredity, constitutional factors such as obesity, endocrine disturbances such as the menopause, nervous factors such as emotional strain may one or all be involved.

Essential hypertension does not arise suddenly except in the rare form of " malignant " hypertension. The much more common benign form develops slowly over many years and its progress may be divided into stages. These stages of course merge imperceptibly into one another and the rapidity of progress through them is very variable.

The initial phase is characterised by an unduly labile blood pressure, systolic and diastolic components showing a tendency to rise temporarily

into zones of frank abnormality, such as 150-160/95-100 mm., while at other times subsiding to levels which are commonly regarded as normal, such as 130/80-85. The elevations may take place during periods of emotional tension, but are also evident under the stimulus of cold, for the hypertensive or " prehypertensive " subject frequently exhibits an excessive reaction to the pressor effects of cold applied to the extremities, the systolic pressure rising by more than 20 mm. and the diastolic by more than 15 mm. The specificity of the cold pressor test for early hypertension has been questioned. The lower levels are attained during quiet rest, or sleep, and for considerable periods of each day the heart and arteries are not faced with any increased loading. There is considerable possibility that normal blood pressures may be recorded on at least some of a series of routine examinations. It would appear that the vasoconstriction responsible for the rises in blood pressure is due to increased nervous tone, since rest with or without sedation can be shown to result in a fall to normal levels. The sodium amytal test serves to demonstrate this lability of the blood pressure The patient is given 3 grains of sodium amytal by mouth hourly for three hours and the blood pressure is recorded before, during, and after this period. The patient may go to sleep and not waken even when the blood pressure is measured or he may lie in a quiet drowsy state. The lowest figures are usually obtained soon after the third dose has been given, and in this early stage of the disease the minimum pressures recorded are well within the normal range.

In this initial stage of essential hypertension there may be no symptoms whatever, and the hypertension may be an accidental observation in the course of examination for some other purpose. Other patients complain of headaches, fatigue, lack of concentration and dizziness. These symptoms are strikingly similar to those of psychoneurosis, and are observable with equal frequency in patients with normal blood pressure. This fact and the common absence of any symptoms at all make it possible that the symptoms are not directly due to the hypertension. An exception may have to be made in the case of headache, for there is experimental evidence that the headache may be due in these cases to stretching of the cranial or cerebral arteries. It need hardly be emphasised that there is no evidence of renal disease or impairment at this stage and no sign of cardiac enlargement.

As the years go by the daily periods of hypertension become longer and the levels higher, though normal pressures are still attained during sleep and under the influence of sedatives. A higher proportion of observations of the blood pressure now show hypertension and the likelihood of observing normal pressures at routine examinations becomes less. However, the peripheral vessels have not yet become organically narrowed but are still spastically constricted. Removal of nervous vasoconstrictor tone by sedation is still capable of inducing normal or nearly normal pressures.

In this second stage again there are commonly no symptoms whatever, though the same apparently neurotic symptoms may persist, and if headache is a feature of the case it may become more severe and more frequent. As a rule, too, signs of the effects of prolonged hypertension are lacking, but early left ventricular enlargement may now be found especially radiologically, and the mitral first and aortic second sounds may be accentuated. Spastic narrowing of the retinal arteries may be seen.

In the third stage the general level of blood pressure is set still higher, *e.g.* 200-250 or more/110-150. The pressure remains elevated during repose and the amytal test induces a modest reduction, or no reduction at all. Permanent narrowing of the peripheral arterioles has now occurred as the result of medial hyperplasia and fibrosis and intimal thickening. There is evidence of the effects of prolonged arterial hypertension. The most easily detectable and the most important of these is enlargement of the left ventricle. In the absence of cardiac valvular lesions left ventricular enlargement in the middle-aged or elderly adult is almost always an expression of prolonged hypertension. Other features are arterial hardening, hypertensive retinitis and slight or moderate impairment of renal function as indicated by an impaired urea clearance test or a lowering of the maximum attainable specific gravity of the urine.

It is common now for patients to notice some diminution in exercise tolerance, but this may be gradual in development and may not attract the patient's attention sufficiently to take him to his doctor or even to interfere with his normal pursuits. The patient who has headaches in conjunction with hypertension continues to suffer from them and the same neurotic symptoms may persist. Cerebral vaso-spastic attacks are quite common. However, in spite of the advanced stage of the disease, there still may be no symptoms whatever.

In the fourth stage breakdown occurs. Here is the irreversible end result of years, maybe decades, of arterial hypertension. A cerebral or coronary vascular accident may suddenly kill a patient who has not previously complained of any symptoms, and it is only at autopsy that evidence is obtained of preceding prolonged hypertension. However, nearly one-half of hypertensive patients eventually exhibit congestive cardiac failure with or without auricular fibrillation or other cardiac arrhythmia, and succumb after a variable period of relapses and partial remissions. Angina pectoris, coronary thrombosis or cerebral vascular accident, not immediately fatal, may bring the patient to a greatly reduced state of activity or a trying state of bed-ridden paralysis. Impairment of renal function is common but renal failure and uræmia account for less than 10 per cent. of deaths from essential hypertension. Intermittent claudication and gangrene are among the other terminal manifestations of the process.

With the onset of congestive failure or after the occurrence of a coronary thrombosis the blood pressure, especially the systolic

component, falls, and this is to be regarded as an ominous rather than an advantageous feature. Headaches, formerly severe, may now disappear and the last months or years of the patient's life, distressing enough, may be freed from this added distress.

There is little need in this terminal phase for any test of lability. The increased load has been in existence for many years and the secondary degenerative results are now firmly established.

In endeavouring to assess the prognosis in any given case of essential hypertension a number of factors fall to be considered. So-called malignant hypertension, though fortunately uncommon, occurs mainly in younger persons, particularly in the fourth and fifth decades. As its name implies it pursues a rapid course, usually ending fatally within two years. In people of this age it is therefore unwise to offer a prognosis without observing the patient's progress over at least a few weeks. A rapid increase in the hypertension, the development of papillœdema and retinal hæmorrhages, and the finding of evidence of gross and advancing impairment of renal function will indicate a rapid termination. The majority of patients follow a relatively slow and benign course through the stages I have outlined and it may be five, ten, or twenty years from the discovery of hypertension in the first or second phases before the final breakdown. Essential hypertension developing in women at the menopause is often well tolerated for ten to twenty years, while if it is detected first in the age period 60-70, with no gross signs of cardiovascular damage, it may not shorten life. In women the prognosis is about twice as good as in men.

However, in general, the expectation of life of anyone suffering from essential hypertension is materially less than in comparable non-hypertensive subjects. Mortality is lowest when the systolic blood pressure is in the range 90-110 mm. (tuberculosis excluded), somewhat higher in the range 110-130 mm., and it then rises steeply with further elevations.

Patients whose blood pressures are very labile, in whom rest and sedation or the amytal test show a marked fall to normal or nearly normal levels, have a much better outlook than persons with elevated pressures which are incapable of much reduction by these measures even though the latters' figures during active ambulant existence may actually be lower. For instance, a patient whose blood pressure under ambulant conditions is 230/120 mm. but falls to 145/90 when tested, may live five to ten years longer than another with an ambulant pressure of 200/110 mm. which falls only to 180/105.