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Essential hypertension

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ESSENTIAL HYPERTENSION

DEFINITION

Essential hypertension is a disease of unknown etiology, characterized by a persistent and progressive rise in both the systolic and diastolic blood pressure. All pathologic anatomic changes characteristic of the malady are secondary, being the effect of the hypertension upon the individual.

It has been recognized as a disease entity largely through the efforts of Sir Charles Allbut who calls it hyperiesia. His original definition reads as follows: "Hyperiesia is a malady in which at or towards middle life, blood pressure rises excessively: a malady having a course of its own, and deserving the name of a disease." He goes on to say: "Of hyperiesia I have never offered an explanation or nothing more than conjecture. I have been content to distinguish it as a clinical series from recognized forms of Bright's Disease" (16).

It has been variously known as the prealbuminuric stage of Bright's disease (Mahomed), latent arteriosclerosis (Von Basch), presclerosis (Huchard) and hypertensive cardiovascular disease

(Janeway).

All these names indicate that certain pathologic involvements accompany or are entailed by the increased blood pressure. This is true in most instances but not necessarily so. For this reason and because such changes, when present, are always a secondary phenomena, the terms essential hypertension and hyperiesis describe the malady more accurately. By some authors the disease has been called benign essential hypertension because of its slow course and the very marked recuperative power the failing heart possesses in this condition. The disease in some instances, however, is characterized by a rapid progress and is far from benign. The term "malignant hypertension" has been widely used during the past few years. It describes those cases of essential hypertension with distinct kidney involvement and a tendency to renal insufficiency and uremia. It is doubtful whether this serves any useful purpose; it might clarify the character of the disease a good deal if these diagnoses were made as essential hypertension with complicating arteriosclerosis of the kidney and uremia (1).

ANATOMY AND PHYSIOLOGY OF BLOOD PRESSURE

Behind the clinical findings of increased arterial tension lies a very definite foundation of altered anatomic structure and changed physiologic activity. An understanding of this foundation of concrete change and perverted function of the vascular walls is fundamental to any clear conception of the processes of disturbed vascular tension, and particularly essential in forming the basis for logical, curative therapy. Hypertension is a progressive, gradual process, slow but persistent in development. The anatomic foundation, therefore, also develops slowly and gradually with the result that at various stages in the disease the pathologic picture is different (2).

Any understanding of the abnormal is dependent upon a clear conception of the normal, either in structure or function. Although a complete description of the normal vascular anatomy and physiology is unnecessary, a brief review is desirable, (2).

The blood vascular system is composed of four types of structures: the heart, the arteries, the capillaries and the veins. Each of the four units of the blood vascular system has different

and individual functions in addition to the common function of being tubes for the conduction and direction of the blood. These individual functional characteristics are responsible for individual structural differences. The heart, besides being a part of the vascular system, supplies the energy for the propulsion of the blood. In addition to being a blood vessel it is, therefore, also a pump, a regularly contracting muscular organ, supplied with four semi-independent chambers, separated by special valve structures to prevent any reversal of flow. The large arteries, such as the aorta, femorals or brachials on the other hand have essentially no role to play in the propulsion of the blood other than a maintenance of the intra-vascular pressure. They are, therefore, but poorly equiped with muscular tissue and their walls are structurally chiefly composed of elastic connective tissue. Muscle cells are not adapted for or able to maintain sustained force or resistance (2).

The smaller arteries, however, in addition to the function of carrying the moving blood stream have the very important function of controlling the distribution of the blood. For example, during digestion the smaller arteries and the arteriales of

the digestive tract relax their walls, the lumina become larger and the volume of blood flow through the digestive structures is greatly increased. Simultaneously, the peripheral vessels of the skeletal system contract, forcing more blood into the splanchnic portion of the vascular bed. Because of this added function of distribution the smaller arteries must have the power of independent contractility and dilation and, therefore, their walls are well equipped with smooth muscle fibers.

The capillaries, or minutest blood vessels, have the important additional function of diffusion or transportation through their walls of the oxygen and food brought by the fresh arterial blood, and the reversed diffusion into the blood of carbon dioxide and other chemical waste, permitting of adequate tissue respiration. Of necessity, the capillary walls are very thin (2).

The veins, in contrast to the arteries, heart or capillaries, are essentially passive tubes or ducts and their walls are not characterized either by extreme strength or elasticity like the larger arteries, or by independent contractility like the smaller arteries, or by free permeability like the capillaries (2).

The nerves of the arterial walls enter via the tunica externa and are composed of both medullated and non-medullated fibers. These nerve fibers belong to the sympathetic autonomic system and consist, therefore, of a preganglionic fiber arising in the central nervous system and a post-ganglionic fiber arising from the cell of some sympathetic ganglion. A very important fact regarding the vasoconstrictor fibers is that they are constantly in action to a greater or less extent. This fact is demonstrated by the simple experiment of cutting them. If the sympathetic nerve in the neck is cut in the rabbit, the blood vessels of the ear become dilated. If the splanchnic nerves on the two sides are cut the intestinal region becomes congested, and the effect in this case is so great that the general arterial pressure falls to a very low point. From these and numerous similar experiments we may conclude that normally the arteries - that is, the arterioles - are kept in a condition of tone by impulses received through the vasomotor fibers (3).

As stated in the above paragraphs, the vasoconstrictor fibers emerge from the cord over a definite region, and they exhibit constant tonic

activity. It has been shown, moreover, that if the cord be cut anywhere in the cervical region all of the constrictor fibers lose their tone; a great vascular dilatation results (3) in both the splanchnic and skin areas. We may infer from this fact that the vasomotor paths originate from nerve cells in the brain and that their tonic activity is to be traced to these cells. Such a group of cells exists in the medulla oblongata, and forms the vasoconstrictor center (3).

THE MECHANISM OF MAINTENANCE OF BLOOD PRESSURE

Harvey, over three hundred years ago, was the first to prove, step by step, the mechanism of the circulation, clarifying the vast confusion of theory that had existed previously (2). Arterial pressure is dependent upon several separate, distinct and individually variable factors (5). These several factors are found to vary continually under normal conditions while in pathologic states they may and do undergo great and permanent changes, which are reflected as either transient or permanent variations in blood pressure (6). Arterial blood pressure at any given time is the sum of these factors plus their reciprocal relations. Not

only may one vary independently of the other, but they are capable also of most complicated interaction (6).

1. HEART ENERGY

The heart is a force pump of intermittent action and is the most important factor in the circulation as it is the fountain head of all energy (6). All of the five inherent properties of the cardiac muscle share in this, rhythmicity, excitability, contractility, conductivity and tonicity (4). The factors that affect the heart's efficiency to this end are the factors that influence the output of blood per minute from the heart. They are as follows: (1) the diastolic filling of the ventricles; this is dependent upon (a) the venous pressure, (b) the length of diastole, and (c) the cardiac tone; (2) the completeness of systolic emptying; (3) the number of beats per minute or cardiac rate; (4) the efficiency of the valves of the heart. The cardiac cycle may be divided into two parts: (a) systole, or the period of contraction and (b) diastole, or the period of cardiac relaxation and rest. During systole the ventricular pressure in the left ventricle rises, the semi-

lunar valves open, with the propulsion of the blood onward into the aorta; the pressure rises in both ventricle and aorta to the systolic pressure. This pressure is then maintained in the ventricle almost to the end of systole, driving the blood out into the aorta and the smaller vessels. With the relaxation at the close of systole the pressure in the ventricles falls and the semilunar valves close. Diastole now commences. The venous pressure causes the tricuspid and mitral valves to open and the blood fills the ventricles at a rate dependent upon the venous pressure. The amount of distension produced in the ventricle by a given venous pressure is determined by the cardiac tone - the greater the tone the less the distension. When this inflow is completed the diastole proper ends and the remainder of the cycle is occupied by a period of rest or diastasis (5).

Any increase in the rapidity in the discharge of blood from the heart (increase in volume output per minute) will, the other factors remaining constant, cause a rise in systolic blood pressure. Conversely any diminution in the pulse rate or volume output will cause a reduction in systolic blood pressure. On the other hand a compensatory

relation between the heart rate and the volume output may permit either or both (if inversely) to be altered without any appreciable change in blood pressure (4, 6).

2. ARTERIAL ELASTICITY

The elasticity and tonicity of the arteries serve to convert the intermittent flow of blood from the heart into a constant current. The arteries are distended during cardiac systole, thereby accomodating themselves to the increased blood volume; during diastole they contract, thereby maintaining a certain degree of blood pressure (6). Recently it has been suggested that the muscular elements in the arterial wall are active in this regard, as well as the elastic tissue (1). If the elasticity of the arteries is impaired, as may occur in arteriosclerosis, and the vessels become more or less rigid instead of being distensible and contractile, the systolic pressure is much increased and the diastolic pressure has a tendency to approach zero (1).

3. PERIPHERAL RESISTENCE

Peripheral resistance is that factor, ever present in the circulatory system, which tends

to retard and prevent the forward movement of the circulating blood (6). It is apparent that without resistance there can be no pressure, and it is equally apparent that the following law is applicable: the greater the resistance, the higher the pressure, other things being equal (4). In the human body this is a complicated factor, being dependent in part upon (a) the diminishing diameter of the conducting tubes, particularly in the arterioles and capillaries; (b) internal friction; (c) the length of the vessels and (d) the innumerable branching of the arterial tree (6). The chief factor that we have to consider in maintaining peripheral resistance is constriction of the vascular bed, the resistance of the arterial walls to stretching and relaxation. This resistance depends primarily upon the degree of constriction (7) and the total length of vessel area under constriction and varies inversely as the square of the radius of the vessels. When changes in resistance occur from changes in viscosity of the blood, a correction takes place in altered vasomotor tone, either by constriction or relaxation, in an attempt to compensate for the change (6).

4. ARTERIAL TONUS

If the factors previously mentioned, the cardiac output, the minute volume of the blood, the elasticity of the arteries and the peripheral resistance, remain comparatively constant, the explanation for a sustained rise of blood pressure can only be found in the increased tonicity of the arteries (1).

The factors influencing the degree of vascular constriction are manifold. Not only may there be constriction as a result of the circular or spiral smooth muscle fibers of the tunica media, but there may be shortening of the vascular bed by contraction of the longitudinal fibers. A constriction equivalent to 12 per cent contraction of the circular muscle fibers reduces the cross-section of a vessel to 70 per cent of its previous size, or reduces the area by almost one-third. This statement of fact serves to emphasize the tremendous effect upon peripheral resistance, or in other words the mean diastolic pressure, of generalized changes in peripheral vasomotor tone (2).

5. VISCOSITY OF THE BLOOD

Increase in the viscosity of the blood increases the resistance to its passage through the vessels and in consequence tends to the elevation of blood pressure and vice versa. Clinically, thus far, no definite relationship has been established between the degree of hemic viscosity and the height of blood pressure (5).

NORMAL VALUES FOR HUMAN BLOOD PRESSURE

Few functions of the body have been so extensively studied as human blood pressure. The data gathered from examinations of large groups of population under conditions that obtain in ordinary everyday life rather than under basal conditions, have been statistically studied and inferences drawn as to normal values with relation to age, race, sex and many other factors. Such data obtained from "wholesale" examination of school children, college students, athletes, candidates for life insurance, army and navy recruits, etc., indicate that in adults between twenty and sixty five years the average systolic blood pressure determined by the auscultatory method increases gradually from 110 mm. ($\pm$ 10) to 140 ($\pm$ 10). This

has led to formulation of the general rule that systolic pressure is approximately equal to 100 plus the age of the individual with the reservation that pressures above 150 are probably excessive at ages beyond fifty years (25).

Alvarez found that the arithmetical mean for women between the ages of sixteen to forty years to be 115 mm., the extreme variations ranging from 85 to 155 mm. Similarly, the average pressures for men were found to be 126.5 mm., with variations ranging from 90 to 175 mm. Alvarez concluded that systolic pressures over 140 for young men and 130 for young women should be considered abnormal.

Statistical studies of diastolic pressures are less numerous and the conclusions are often at variance. This is probably due to the varying criteria used. According to Symonds and Mackenzie the average diastolic pressure rises gradually between twenty and sixty years, the average figures at different age limits being roughly between 80 and 93 mm. Statistics gathered by Wiggers for over twenty-five years indicate that diastolic pressures in young men and women range between 70 and 85 mm. with readings of 95 or 100

a very exceptional occurrence (25). We may therefore conclude that 70 to 90 mm. Hg represents a reasonably liberal range within which diastolic pressures may be expected to fall between the ages of twenty to sixty years. Pressure relations of 120/80 at twenty years; 140/90 up to forty years, and 150/90 up to sixty-five years probably express the highest expected values. This gives pulse-pressures of 40, 50 and 60 mm. respectively: in other words pulse-pressure gradually increases with age (25).

Under basal conditions, i.e., with the subject resting in bed and three to five hours after a meal, blood pressures tend to be lower than under average conditions of activity. The decrease varies but may amount to 15 or 30 mm. for the systolic pressure and a 5 to 10 mm. drop in diastolic pressure. A similar decline of pressure occurs during sleep unless disturbing dreams occur, in which case an actual elevation of pressures may be obtained (20). Changes in posture appear to act differently on various subjects; change from a recumbent to a standing position may cause either an elevation or drop in systolic pressure. During physical exercise pressures rise rapidly at first,

then fall somewhat and are maintained at a sustained hypertonic level (20, 25).

Daily and monthly variations in blood pressure as studied by Brown, Mueller and Aymin show many interesting facts. There is a rise in blood pressure as the day progresses, with three definite rises during the day after each meal. In the early afternoon the pressure begins to rise, and by early evening it has reached its highest peak. During the first two hours of sleep there is a marked fall in blood pressure and by 4 A. M. it has reached its minimum in normal persons. The blood pressure is lower in summer than in winter, and the minimum is during the months of August and September (23).

Olienis (32) considers the normal systolic pressure (at rest) in childhood to be 90 to 105, in middle age 130 to 140 and after the sixtieth year 140 - 150. In women it is five to ten mm. lower than in men. The diastolic pressure is two-thirds of the systolic and the pulse-pressure is one-third of the systolic pressure. That the systolic blood pressure depends essentially on the force of the heart, while the diastolic blood pressure is essentially the gauge of the peripheral re-

sistance, which means the amount of tonus particularly in the arterioles is stated by Olienis. He also states that the systolic blood pressure is less reliable as an index of the patient's condition than the diastolic pressure because the systolic pressure is much more subject to variation by psychic and other evanescent conditions than the diastolic pressure (32).

ETIOLOGY

Various theories have been advanced to explain the etiology of essential hypertension but none has been satisfactory (7, 8, 1). At the outset one may say that up to the present no satisfactory solution has yet been arrived at (8). It is probable that an increased tonicity of the arteries is responsible for the disease, though what brings about the increased tonicity is an open question (1).

INCIDENCE: The incidence of hypertension is given by Frost as 1.74 per cent in examining 146,992 cases for life insurance; Knight finds similar figures, 1.6 per cent with a blood pressure above 140 mm. in 500,000 candidates for life insurance (1). Stieglitz states that 7.2 per

cent of the adult white American males have hyperpiesis and that the insurance statistics are low probably because many persons knowing of their hypertension are never examined for insurance (2). Diehl and Sutherland determined that in 5,122 male college students in the University of Minnesota after eliminating the cases of "secondary", transient and intermittent hypertension, there was a group comprising 1.6 per cent in which the augmented blood pressure (above 140 mm.) was persistent. All of these figures, except Stieglitz, show the incidence of essential hypertension to be about 1.6 per cent in the "normal population".

HEREDITY: There is a very distinct hereditary factor associated with essential hypertension (9, 1, 2, 7, 8). This has been stressed, apparently with good judgment, as being one of the most important etiological factors. Ayman, after extensive work in this field, is of the opinion that valuable evidence can be obtained by studying the blood pressure in a large number of hypertensive and non-hypertensive families, with an effort to obtain the blood pressure readings of all of the available relatives in two or more genera-

tions. The results were that there is an unusually high incidence of elevated blood pressure readings in the children, brothers, sisters and parents of subjects with essential hypertension as compared with similar relatives of subjects with normal blood pressure (9). Barach states that it is generally concluded that hereditary tendency plays a prominent role in the life history of patients with hypertension (13). Weitz has taken up this subject in as thorough and exhaustive a manner as any one; he proves statistically that hypertension is a familial disease affecting women as well as men. Alvarez, Wulzen and Mahoney conclude that hypertension seems to be an inherited pecularity, the appearance of which can be suppressed in women so long as the ovaries function well (10). O'Hare (11) found that in 68 per cent there was a definite family history of vascular disease. Exactly what functional disturbance is inherited is not clear; however, it may be regarded as an established fact that hypertension is prone to be transmitted from one generation to the next (1).

AGE INCIDENCE: Although essential hypertension is usually found in people after the age of

forty, it is by no means confined to that group. It is occasionally seen in children and not uncommon in young adults (7). It begins most frequently, however, between the ages of forty and fifty. Janeway's statistics show that 80 to 90 per cent of his cases occurred between the fortieth and sixty-ninth years. It appears, therefore, that it is a disease frequently beginning at the age of forty and continuing from that time on, the blood pressure rising slightly year after year (1).

SEX INCIDENCE: It is extremely difficult to decide whether essential hypertension is more prevalent in the male or in the female sex. Much stress has been placed of late on the fact that it is likely to occur in women at the time of the menopause (1, 2). In dispensary practice the disease is more common in women than in men. In private practice the opposite seems to hold true, although in neither instance is the preponderance of one sex over the other very noticeable. A great deal of confusion has occurred because cases of essential hypertension have not been sharply differentiated from nephritis (1).

MODE OF LIFE: There has been a tendency

to ascribe inordinate importance to nervous strain in the production of hypertension and to consider the high strung, hard driven city dweller as particularly subject to this condition. This conception is being gradually modified with the development of the idea that the inherited characteristics of an individual have more bearing than his mode of life.

CHEMICAL AND ENDOCRINE STUDIES: An enormous number of observations have been made on the chemistry of the blood, urine and even the tissues in connection with hypertension. There is no proof that chemical changes have any bearing on the etiology of hypertension, though they may be of great importance in connection with the mechanism of the disorder (17).

The question of the guanidine content of the blood of hypertensive patients has been exhaustively studied by Major (18). He suggests that the excess of guanidine found in the blood of essential hypertensives may be the result of a failure to excrete this substance, even though the normal non-protein nitrogen content of the blood suggests an adequate renal function (18). When

the excretory power of the kidney was tested by giving methyl guanidine sulphate by mouth, it was found to be definitely impaired as far as this substance was concerned, when compared with normal controls. He also finds that in the hypertensive the excretion of the allied body creatinine, when injected intravenously, may be definitely defective even though the creatinine content of the blood is at a normal level. He concludes that it is possible that in hypertension retention of guanidine may occur as the result of a specific excretory failure on the part of the kidney. In dogs a prolonged rise of pressure was found to occur when the blood guanidine was raised by injection of methyl guanidine sulphate to a figure corresponding to that found in the blood of human hypertensives (18).

Major's work is of interest since in guanidine we have a product of normal metabolism which is capable of producing a prolonged rise of blood pressure, but at best the case for guanidine as a factor in the production of the hypertensive state is far from strong. Felix has pointed out, although many guanidine derivatives are pressor in action, others are actually depressor, while others

again, such as arginine, produce no effect upon the blood pressure. It is generally believed that creatinine is the most efficiently eliminated of all the nitrogenous waste products and that in renal inadequacy it is the last of these bodies to show appreciable accumulation in the blood; even when renal inadequacy has reached a stage at which considerable nitrogenous retention is present, the quantity of guanidine in the blood is not necessarily increased (19).

The substances known to exert pressor effects being derived from the metabolism of meat, it has been suggested that hypertension may be produced in certain individuals through hepatic disorders. It is thought that the liver under certain circumstances may fail to detoxify the products of decomposition absorbed from the intestinal tract; such products, having pressor qualities, may cause spasm of the vascular system which in turn leads to permanent hypertension (17).

Abnormal sugar metabolism has been investigated by a number of observers as a possible cause of hypertension. Glucose, uric acid and cholesterol are not "pressor" substances and cause no elevation of pressure when injected into animals,

but they must be considered briefly. Statistical studies by Rosenbloom failed to show that diabetes per se predisposes to hypertension. Joslin found that diabetics under thirty-five years of age tend to have pressures slightly below normal figures: after this age the average diabetic shows a pressure that exceeds normal by a small margin. However, diabetes is a rather frequent late complication of hypertension, and it has been suggested that such a condition is due to sclerosis of the arterioles of the pancreas. A decline in glucose tolerance is noted in certain cases of hypertension (O'Hare). Herrick found hyperglycemia in some (10 to 30 per cent) of his patients with hypertension and suggested that a meatless diet containing an excess of carbohydrates might have been responsible (15). However, Voegelin found no evidence of either hyperglycemia or deficient glucose tolerance in hypertension. Mosenthal doubts that hyperglycemia can produce hypertension. Kramer finds diabetes and hypertension not uncommonly associated after middle life and suggests a common etiology (17).

Cholesterol metabolism has been under study in recent years in connection with the etiol-

ogy of arteriosclerosis in general and hypertension. The fact that obesity is associated so often with hypertension has aroused the question whether an abnormal lipoid metabolism might lead to both obesity and hypertension. Westphal found hypercholesterinemia in 71 per cent of cases of hypertension. Glaser points out that cholesterol is elevated in such conditions as diabetes, obesity, arcus senilis, albuminuric retinitis, essential hypertension and various other conditions that are frequently associated clinically. It has been suggested that cholesterol may infiltrate the walls of the arteries, that the vessels then become impregnated with calcium and that arteriosclerosis supervenes. At present there seems to be more reason to incriminate lipoid metabolism in the etiology of large vessel sclerosis than in genuine hypertension (17).

Several observers have found relatively low calcium contents in the blood of patients with hypertension. It has been thought that a high K/Ca ratio predisposes to smooth muscle spasm and to hypertension. However, observations by Stieglitz on the calcium metabolism during nephritis of pregnancy with hypertension throw some doubt on this hypothesis. At best, the relation of calcium

to the etiology of essential hypertension may be said to be unproved (2).

Weiss and Weinstein state that neither changes in potassium-calcium ratio nor changes in hypercholesteremia can be considered as playing a fundamental role in the development of essential hypertension. Elevation of the potassium and cholesterol levels observed in one group of patients with hypertension is the result rather than the cause of changes in the cardiovascular system in essential hypertension (22).

The above observations showing that certain cases of arterial hypertension show increased amounts of blood sugar, blood uric acid and blood cholesterol are of considerable interest since they suggest possible metabolic disturbances in this disease. The difficulty in assigning a specific effect to them lies in the fact that neither glucose, uric acid nor cholesterol are pressor substances. It should be further recalled that diabetes, a disease in which the blood sugar is regularly increased, shows no elevation of blood pressure as a constant rule; that gout and leukemia, in which the blood uric acid is elevated, usually show normal blood pressure values and that

diseases in which the blood cholesterol is usually increased, such as cholelithiasis, lipoid nephrosis, atherosclerosis and diabetic acidosis do not show an increase in blood pressure as a constant or essential feature (18).

The ovary is apparently in a most intimate manner concerned with the causation of high blood pressure. In women in the climacteric one finds in the manner of its origin, its symptoms and its course the classical form of essential hypertension. The mechanism of the causation of the hypertension is still unexplained. The earlier the menopause the more often is it associated with hypertension. Artificially sterilized women, whether by operation or by exposure to X-ray show a high incidence of high blood pressure (44).

Warfield states, "The symptoms which accompany such increased tension are thought by some to be due to the lack of inhibitory action of ovarian secretion upon the thyroid, pituitary and adrenal glands" (7). Alvarez, Wulzen and Mahoney conclude that hypertension is an inherited peculariity, the appearance of which can be suppressed in women so long as the ovaries are functioning (10). The ovary is apparently intimately associated with

the causation, but the nature of the mechanism is not understood (44).

It was a natural result of the discovery of a pressor body in the adrenal gland that disturbances in the level of the arterial blood pressure should be attributed to excessive or defective secretion of adrenalin. This theory of hypertension has never won any general recognition, although many suggestive facts may be adduced in its favor, and although it has been vigorously advocated by the French school.

Among the arguments put forward for an adrenal factor in the production of permanent hypertension are the changes reported in the adrenal glands of hypertensive subjects, the alleged increase in adrenalin content of hypertensive blood, the vascular lesions produced by adrenalin injections, and the frequent association of glycosuria, possibly of adrenal origin, with hypertension. More definitely significant, however, is the occurrence of permanent hypertension, accompanied by cardiovascular and renal lesions resembling those of essential hypertension, in patients in whom are found tumors arising from the chromaffin cells of the adrenal medulla, the so-called paraganglio-

mata (29).

It would seem that there is no adequate evidence that adrenalin is the factor concerned in the production of the raised blood pressure in essential hypertension. Admittedly, persistent hypertension is occasionally associated with the presence of adrenal paragangliomata, and in such cases the raised blood pressure is almost certainly the result of over-secretion of the hormone by the tumor. Such cases, although unimportant numerically, are theoretically significant since they show that over-secretion of adrenalin may ultimately produce permanent hypertension and that vascular and renal lesions resembling those found in essential hypertension may result (31).

The pituitary is known to yield an active principle which is capable of affecting the blood pressure. From its posterior lobe a substance, vasopressin, can be extracted which on intravenous injection into anaesthetised animals produces a rise of pressure far more prolonged and sustained than that which follows the injection of adrenalin. Despite the remarkable vasomotor activity of vasopressin we know little of its physiological role in the maintenance of the circulation or of its

manner of secretion; it is even uncertain whether it reaches the blood stream directly or indirectly by way of the cerebrospinal fluid (17).

In normal individuals it was found by Moffat that the intramuscular injection of pituitrin produced a very brief rise in blood pressure, which is succeeded by a fall in the systolic pressure, the diastolic pressure remaining practically unchanged, and the pulse pressure diminishing - an effect which may well result from coronary constriction. In hypertensive patients the fall was more marked than in healthy (28).

From what has been said it would appear that neither the two natural hormones, pituitrin and adrenalin, nor guanidine and its derivatives are likely to be the bodies concerned in the production of the raised blood pressure in the great majority of hypertensive patients.

SINUS HYPERTENSION: Although it is probable that experimental damage to the renal tissue in animals leads to hypertension, there is only one experimental method by which a permanent elevation of the blood pressure can be produced - the destruction of the aortic and sinus nerves.

These so-called buffer nerves exercise a tonic inhibitory action on the circulatory centers of the medulla; their removal is followed by definite and persistent hypertension. The assumption that atheromatous changes in the vaso-sensitive zone leads to such loss of sensitivity as to put out of action the inhibitory tonus of the buffer nerves is not borne out by post mortem findings. The nerve-endings in atheroma of the sinus are found to be normal on histological examination (19, 25).

KIDNEY DISEASE: It is well known since the publication of Bright's famous essay that a constant high blood pressure and renal disease are associated. This has led many to believe that every instance of enduring increased arterial tension is thus brought about. As one pathologist after another and many clinicians have gathered experience there has been an ever increasing number of autopsies recorded in which a persistent hypertension was present during life and a perfectly normal kidney was found at the post mortem examination. This does not mean that Bright's disease (Janeway 1913) is not productive of hypertension, but it does signify that essential hypertension is

a malady occurring independently of any lesion in the kidneys.

It is held by many that sclerosis of the smaller arteries is more pronounced in the kidney than it is in other organs in essential hypertension, this frequently being so without any other obvious change, either functional or pathological, in the kidney itself. That the kidney produces any specific substance which has a direct effect on the vascular system is doubtful, nor is there evidence to indicate that tissue extracts of the kidney have any specific action either in raising or lowering the vascular tension. Petrovsky reports some interesting experiments in which he found by perfusing a kidney with Ringer-Locke solution that the perfusate contained a substance which exerted a pressor action on the systemic vessels and augmented the cardiac action. He could not claim that this was specific for the kidney as he found a somewhat similar effect produced by perfusates of other organs. Some have claimed that hypertension is due to the initiation of a vascular spasm in the vessels of the kidney, from which it spreads to other organs. Theories like this, based upon a modicum of suggestive evi-

dence, have not so far been amenable to experimental proof (20).

OBESITY: There is general argument that a condition of obesity predisposes to hypertension. This tendency has been shown by Fisk to be as follows:

Overweight	Normal B.P. Group	High B.P. Group
10-15%	9.3%	11.0%
15-20%	7.5%	9.5%
over 20%	12.6%	25.5%

This table shows that, while there is only a slightly greater tendency to hypertension among individuals with slight or moderate obesity, the tendency to hypertension is twice as high in the group markedly obese as in those of normal weight.

In Dunham's studies weight was related to blood pressure as follows:

Underweight

40 or more lbs.	B.P. 123/77
30-39 lbs.	121/76
20-29 lbs.	123/77
10-19 lbs.	122/77
1-9 lbs.	124/78

Overweight

1-9 lbs.	B.P. 125/79
10-19 lbs.	127/81
20-29 lbs.	128/82
30-39 lbs.	129/82
40 or more lbs.	134/85

Thus it is clear that undernutrition has no effect on pressure in otherwise healthy men, while obesity creates a distinct liability to hypertension. This is one of the few features of hypertension about which there is general agreement, reports having been made to the same effect by many other observers (17).

TOXIC PRODUCTS: "Auto-intoxication" and "intestinal toxemia" are terms that have found their way into the literature as causes for hypertension. The basis for this assumption is not clear. Alvarez, McCalla and Zimmerman in their work along this line conclude that their findings do away with the idea that "intestinal auto-intoxication" bears a causal relation to hypertension (26).

Concerning the possibility of toxic bodies whether produced within the body or affecting it from the outside the evidence is largely negative (1).

It has been part of the tradition relating to hypertension to accuse tobacco, coffee, alcohol and press of activity of being more or less responsible for the condition. However, it is impossible to prove a definite case against any one

of them so far as the actual etiology of hypertension is concerned. In the first place, if there is any difference between sexes in their liability to hypertension, women take first place. This is true even in populations in which the use of alcohol and tobacco among women may be negligible. Few women, moreover, are definitely subject to physical and mental stress in the manner to which men are accustomed. Weitz found blood pressure readings no higher among alcoholics than among other persons. As a result of statistical studies on 5,520 persons Fisk concludes "it is not possible to say that tobacco is an outstanding factor in the causation of high blood pressure, although it undoubtedly is a factor in individual cases." King (17) states "tobacco has no relation to the actual cause of hypertension except in rare instances. No case has been made directly against alcohol, but obesity of alcoholic origin is a real liability. Tea and coffee may play a small role in etiology if used to excess. There is no evidence that the 'pace of modern life' is concerned in the actual etiology, though it undoubtedly may hasten the sequelae."

ARTERIOSCLEROSIS: Arteriosclerosis has

in the past been considered as the cause of hypertension. Narrowing of the arterioles through "arteriocapillary fibrosis" (Gull and Sutton) was supposed to result in permanently high blood pressure by an increased resistance in the peripheral circulation. Gradually the true situation has evolved and it is realized that the changes in the smaller arteries are secondary to a persistent high blood pressure and that the original conception of the pathological process had reversed the relation of cause and effect. The vascular lesions in hypertension are practically never general, but are confined to certain organs which vary in each instance; usually the changes predominate in the spleen, pancreas, liver, brain and heart. Symptoms referable to these and other organs manifest themselves in direct proportion to the extent of the arteriosclerotic lesions.

TYPE OF PERSONALITY

It has long been believed that patients with arteriolar essential hypertension have special physical and emotional reactions to life: in other words that such patients have a special type of personality. If this is true, then the knowledge

and application of this fact may not only aid this diagnosis and therapy of this disease, but may afford insight into its etiology. Unfortunately, the evidence for this idea of a specific hypertensive type consists almost wholly of clinical impressions.

In accord with many writers on this aspect of the subject Mosenthal (1) states that arteriolar (essential) hypertension "occurs rather more frequently in the highstrung, nervous, or irritable individual." Likewise O'Hare says that "almost all have been of a nervous temperament throughout life." Herrick (15) believes that hypertensive patients have an "ill-balanced personality" whose chief tendencies are "pressure of activity and over-earnestness." He says further that they are "serious, earnest, conscientious, enthusiastic at work, at their infrequent play, and too often at table." Barach (13) finds that early in life hypertensive patients have "a certain instability, restlessness, a lack of confidence and shirking of responsibility. During middle life they frequently are restless or ineffectual, or they may be abnormally active and intensive in their special field of endeavor." Moschcowitz (14) has presented one of the most detailed and inter-

esting descriptions of the hypertensive type. He has observed among other things that "the greatest proportion of patients with hypertension are terribly tense and pursue their vocation with tremendous seriousness, and worry over trivialities. In consequence, they are irritable. They are the antithesis of the child. They do not play. They have no time for play. They have narrow intellectual horizons." In general, the above writers believe that hypertensive patients tend to be highstrung, serious and overactive.

The study made by Ayman seems to confirm the often mentioned clinical impression that persons with arteriolar (essential) hypertension tend to have certain emotional and physical reactions much more frequently and intensely than comparatively healthy people of the same age group and with normal blood pressure. The impressions are that hypertensive patients tend to be highstrung individuals who either display quick temper or are easily excited within themselves. They tend to be unusually sensitive, being hurt by little things. In youth and often persisting to later life they tend to blush easily, to be easily embarrassed, and to be unusually shy. In dealing with the events of

life, however minute, they tend to be unusually serious and worry over trivialities. Physically, whether symptomless or not, the hypertensive individual seems to be an unusually rapid walker, even when in no special hurry. They often tend to eat or talk rapidly. In general, they tend to be unusually active physically, in their domestic, occupational and social activities. This does not infer that every person with a hypertensive type of personality has or will develop arteriolar (essential) hypertension. Neither is it meant that every hypertensive patient has the type of personality above presented. However, in most of the hypertensive patients the above described personality type is present (33).

Elliott, however, states that undoubtedly this individual as described may be identified in the vascular clinic but he is merely one of a crowd and that all types appear to contribute to the group, short and tall, thin and obese, active and slothful, gay and morose. If attributes common to all exists, they appear to be impersonal and biologic rather than personal and temperamental (21).

Not only does the middle-aged hypertensive

patient tend to be of a certain personality type, but the intensive studies done by Ayman indicate that he has always been of that type. It seems likely, therefore, that the hypertensive personality is present and recognizable in early life. This likelihood is further confirmed by the study of Ayman's younger hypertensive group, which already at an average age of 26 show exactly the same type of personality reactions to life as the older group. It is also significant that about 80 per cent of this group are the children of known hypertensive patients.

The recognition of the hypertensive personality may be of definite aid in the diagnosis of early arteriolar (essential) hypertension especially in the presence of a positive family history of vascular disease (33).

MORTALITY

A study of mortality statistics readily demonstrate that hypertension is one of the most common causes of death, probably being equal in importance to cancer or tuberculosis. Fahr comes to the conclusion from a conservative statistical study that 23 per cent of all deaths in persons

over fifty years of age are the result of that form of cardiac disease which is secondary to hypertension (1).

The two most frequent causes of disability or death are cerebral hemorrhage and heart failure. These two particularly cover the direct mortality from hypertension. Deaths from uremia are comparatively infrequent. In Christian's statistics 25 per cent died of cerebral lesions, 32 per cent of cardiac failure and 4.5 per cent of uremia. This is probably a fair representation of the average (21).

PATHOGENESIS

The following is the theory put forth by Dr. E. J. Stieglitz, who has done a great amount of research work in connection with hypertension, in an effort to explain the pathogenesis of essential hypertension (35).

1. Irritation of Arterioles

2. Spasticity (Smooth Muscle)

3. Hypertrophy of Arterial Muscle

4. Spasticity (Increased by Hypertrophy)

5. Fatigue (Of Muscle)

6. Hyperirritability (Of Muscle)

7. Exhaustion (Degeneration of Muscle)

8. Fibrosis to replace degenerated muscle fibers

9. Arteriolarsclerosis

The diagram represents a crude attempt at visualizing the "pathogenesis of the arteriolar changes in hypertension" (35).

The vicious cycle of fatigue or the perpetuating factor is represented by steps 4-5-6-4 (24).

Step 1. There occurs irritation of the arterioles by almost anything (toxins, protein excess, bacterial poisons, condiments, vasomotor hypertonia, etc.), which results, of course in

Step 2. Increased tonus or spasticity of the smooth muscle of mesial layer of the arterioles.

Step 3. If such increased tonus continues any length of time hypertrophy of the muscle

is inevitable, as hypertrophy follows increased work anywhere.

Step 4. Because of such hypertrophy, with a continuation of the original irritation, the spasticity becomes even more marked.

Step 5. But muscles are not adapted to continuous strain, as is well known, and such continuous hypertonia or spasticity leads to fatigue.

Step 6. Fatigue (to be sharply differentiated from exhaustion) makes muscle cells more irritable and hyperirritability results.

Such hyperirritability is also seen in the nervous mechanism. We all become cranky, fussy, irritable, when very tired. With such a lowered threshold mild irritation or stimulation leads to an exaggerated response of more spasticity.

Thus a vicious circle is set up: steps 4-5-6-4. This is called "the perpetuating factor in hypertension" (2) as it continues to operate, although the original sources of irritation in Step 1 have ceased to exist. It may also be termed "the vicious circle of fatigue" (24).

Step 7. If fatigue continues to exhaustion, the muscle cells degenerate, die and fail. Thus simultaneously with the activity of

the vicious cycle, some cells are slowly exhausted.

Step 8. As these fall by the wayside, replacement with connective tissue takes place; fibrosis occurs.

This is not an invasive process or an aggressive cirrhosis; the connective tissue proliferates to support the crumbling framework of the vascular wall as a scaffolding to protect it. Eventually the greater portion of the arteriolar medial muscle is replaced and the final stage is

Step 9. Arteriolarsclerosis.

Up to Step 7 the processes are reversible biologically; fatigue may be relieved by rest, hypertrophy may subside. Beyond Step 7, with fibrotic replacement of exhausted muscle, the processes are irreversible and not amenable to therapy. Characteristic, of course, of the spastic earlier phases is the variability of the diastolic tension; inversely, after fibrosis occurs, diastolic tension is fixed and rigid. Therefore, we may use the variability of the diastolic tension as an index to the degree of permanent change; the more variable the diastolic tension is, the less the actual sclerosis.

Of course all of these processes are slow

and gradual; taking years to develop. Probably in various structures various phases of this procession occur simultaneously and there is no sharp transition between the steps.

CLINICAL PATHOLOGY

Essential hypertension is a distinctively functional disease. At present there is no known anatomical basis for the malady. The anatomical changes which occur are entirely dependent upon the blood pressure; that is, they are the result of mechanical stress put upon the tissues that maintain the circulation. The changes become manifest in the heart and in the blood vessels (1).

After a time the cardio-vascular system responds to the stress of the continued high blood pressures of essential hypertension by structural changes which are permanent. The heart hypertrophies and enlarges to the left, the "coeur de sabot" of French radiologists (48). This hypertrophy occurs early in the disease. With sclerosis of the coronary arteries there is degeneration of the heart muscle, with areas of replacement fibrosis. Involvement of the aorta occurs late in the disease (30). It is remarkable to what degree the heart may hypertrophy under these conditions.

Such hearts are among the largest encountered. The weight of the heart in a given case of hypertension depends upon the degree and duration of the peripheral resistance and the nutrition of the myocardium (38).

Ziskin studied the size of the heart by means of Roentgen-ray measurements, taken from six foot plates of the heart. The cardiothoracic ratio was used as the index of enlargement. A gradual increase in the cardiothoracic ratio was noted with the increase of blood pressure. In the groups with a blood pressure of 190 or over, definite cardiac enlargement was found. The beginning of hypertrophy, however, could not be determined, for it is known that early hypertrophy can not be detected by X-ray (42). Bell and Clawson, in their study of 420 cases of hypertension at autopsy, found the weight of the heart increased in 70 per cent of 220 cases with known hypertension (38).

Changes in the electrocardiogram offers definite evidences of involvement of the myocardium in hypertension. Changes in conduction, evidence of ventricular preponderance and changes in the QRS and T waves were the predominant signs found in these cases. Ziskin did not find ab-

normal electrocardiographic signs frequently until he reached the group with a systolic pressure of 170. Here he found 24 per cent showing abnormal signs. Evidence of arborization block is the most frequent sign noted in this group. With the increase of blood pressure, negative T waves, depression and elevation of the S-T phase occur also with increasing frequency. These findings indicate that the heart is involved quite early in this group of patients (42).

Bell and Clawson, in their study of necropsy material of hypertension, found only 10 per cent of the cases without notable signs of coronary disease. Fifty-five per cent showed coronary disease of a moderate degree, and 35 per cent of a severe degree (38). A comparison, therefore, of the electrocardiographic signs with the pathology found at autopsy would indicate that coronary disease begins early in hypertensive patients.

As a result of the hypertension, the arteries become the seat of arteriosclerosis. Arteriosclerosis occurs because of the consistent stress and strain brought about by the increased pressure. In some individuals the change comes on very slowly, in others rapidly. The visceral

arteries are more frequently the site of lesions than those of the extremities. This is in contrast particularly with the senile or decrescent type of arteriosclerosis, in which the arteries of the limb are prone to suffer most (1). This arteriosclerosis occurs most extensively in the smaller arteries, to which the term "arterioles" is commonly used to designate small precapillary vessels composed of muscle and endothelium with little or no other tissue (38). In essential hypertension the kidney arterioles are involved much more frequently and far more intensively than those of any other portion of the body. Arteriosclerosis is a common finding in the spleen, pancreas, liver and brain. Involvement of the splenic arterioles occurred in about two-thirds of Fishberg's cases (45), the pancreatic in about half, the hepatic in less than a third and the cerebral in about one fifth of the cases. But the lesion usually was not very marked, rarely being even nearly as intense or diffuse as in the kidney. There is no constancy about the involvement of these organs; any one or more of them may be involved in a given case. The most marked arteriolar changes in these organs are found only in association with a very

advanced process in the renal arterioles. Another organ in which arterisclerosis is quite often found is the suprarenal gland (45).

Wagener believes that a majority of the patients with essential hypertension show some sclerosis of the retinal arterioles (42). Sclerosis of the retinal arteries (which are, of course, arterioles) of the hypertension type is characterized by generalized constriction of the calibre of the arteries with exaggerated arterial reflex stripe, irregularities in the lumen of the arteries and arteriovenous compression (47). The retinitis of severe benign hypertension is characterized by scattered cotton wool patches and hemorrhages, and mild, more or less generalized, edema of the retina in which, in the later stages powdery, punctate, white exudate may appear. In the more malignant type of hypertension, to this picture is added edema of the disc, which may vary in degree from mere hyperemia and marginal blurring to an elevation of several diopters.

PROGNOSIS

When discussion is undertaken of the prognosis or treatment of any pathologic state, the

etiology of which is unknown, difficulties are at once met. To this rule essential hypertension is no exception (15). Essential hypertension although serious does not justify the routine bad prognosis often given it. With good renal function and no cardiac symptoms many of these patients can live a long and fairly active life. Some of the world's best workers have had hypertension for long periods before it hampered their effective activity (27).

Brochbank states that high blood pressure is far from being incompatible with old age (11).

It is important to evaluate both renal and cardiac involvements at intervals before forming a prognosis because this alone can give us any idea of rate of progression. It is worth while in first studying one of these patients to take the pressure early in the examination and later to get the patient relaxed, diverted and in bed to see what happens to the blood pressure. A marked fall under these circumstances followed by a rise on slightly exciting the patient is valuable evidence toward some of the factors producing the condition, which may be removed subsequently in the therapeutic management of the patient. When this is true, prog-

nosis is better. In general an increased systolic pressure with proportionately less increase in diastolic pressure is of better prognostic import than a proportionately equal increase in each. A relatively high diastolic pressure indicates a more serious condition than the converse; this type is less influenced by treatment than the latter (27).

Ophthalmoscopic examination is of great value in telling us the condition of a group of small vessels and one in intimate association with the important cerebral arteries. With evident changes in the retinal vessels cerebral hemorrhage is more probable. Prognosis depends on the condition of cerebral vessels, myocardium and coronary arteries and on renal function rather than on height of blood pressure (27).

The salient points in the prognosis of high blood pressure may be summarized. Unfavorable features are a family history of cardiovascular disorders, a relatively high diastolic pressure and, chiefly, evidence of degeneration in certain selected parts of the cardio-vascular system. These evidences are of marked arteriosclerotic changes in the cerebral, retinal, coronary, renal or pancreatic arteries or in the aortic arch.

Signs of myocardial weakness make for a bad prognosis. Among the functional tests, that revealing a lack of normal response to effort on the part of the pulse rate and blood pressure, when existing with advanced structural changes in the circulatory system, is a not unimportant item in an unfavorable prognosis. This is especially true where both systolic and diastolic pressures are fixed at high levels and do not vary after effort (15).

Of the favorable features the following may be mentioned. Hypertension in the absence of demonstrated organic cardiovascular changes may not shorten life. High blood pressure with predominant changes in the larger peripheral vessels and with little changes in aorta or retinal vessels may be viewed with much less concern than those with marked changes in smaller arteries. This is particularly true of cases with normal diastolic pressures and of those without albuminuria and glycosuria. Cases retaining their capacity to respond by a normal or exaggerated rise in blood pressure after effort carry a better prognosis than do those in which this capacity is lost (15).

SYMPTOMATOLOGY AND CLINICAL DEVELOPMENT

It is generally agreed that there may not

be any symptoms, especially in the early stages of essential hypertension (11). Elliott (21), in his discussion of the symptomatology states that during the early stage, there are few or no subjective symptoms and the existence of hypertension is usually accidentally revealed. Goodridge, in his discussion in Cecil says that in many instances essential hypertension may exist for years before it produces symptoms which interfer with the daily routine and comfort of the patient (30).

Riseman and Weiss in their extensive study of the symptomatology based on an analysis of the records of 1090 uncomplicated cases selected from 1628 cases of hypertension discovered among the patients visiting the medical outpatient department of the Boston City Hospital during a forty-two months period, compiled the following charts (39):

SYMPTOMS OF HYPERTENSION

Based on the Records of 1090 Patients with Elevated Blood Pressure and No Related Disease

Symptoms	No. of Cases	Per cent
Headache	473	43.3
Dizziness	440	40.3
Aches and pains	422	38.7
Dyspnea	302	27.7
Nycturia	283	25.9
Nervousness	144	13.2
Palpitation	143	13.1
Tinnitus	129	11.8
Weakness	126	11.6
Insomnia	61	5.6
Epistaxis	61	5.6
Precardial pain	58	5.3
Numbness and tingling	48	4.4
Edema	46	4.2
Spots before the eyes	44	4.0
Hot flashes	24	2.2
Cramps	17	1.6
Nausea or vomiting	13	1.2
Blurred vision	11	1.0
"Angiospasm"	9	0.8
Throbbing	7	0.6
Hemoptysis	6	0.6
Fainting spells	6	0.6
No symptoms	129	11.8

Headaches occurred in 43.3 per cent of their cases. The location varied but the headache was constant for each individual. The discomfort occurred at any time of the day but was most frequently noted in the early morning or evening. The character varied from sharp to dull pain, but it was usually steady; less frequently did a patient complain of a throbbing headache.

Dizziness, a symptom which was almost as frequent (40.3 per cent), occurred in varying degrees of severity. It usually consists of a sense of giddiness or light headedness but occasionally it is true vertigo. It is most frequent immediately after rising in the morning and after retiring at night. Dizziness and headache commonly occur together or alternately in the same individual.

Somatic aches and pains are of various sorts: sharp, dull, or aching, but usually vague and indescribable. The location and distribution is usually bizarre and visceral pain very infrequent. These vague yet very real complaints appear to have no common basis. Douthwaite suggested that the pains might be due to a stretching of the blood-vessels as could occur with the patient's increased activity, but Riseman and Weiss could find no constant relationship to exist between pains and motion.

Dyspnea on exertion was recorded in 27.7 per cent of the 1090 cases and in no instances did there appear to be enough evidence to justify a diagnosis of myocardial insufficiency.

Nycturia occurred in 25.9 per cent of the cases. This symptom may be caused by various conditions and it is often difficult to determine the

etiology in any single instance.

"Nervousness" was a term used to denote a variety of closely related symptoms. It included a tendency to worry, to become easily upset, or to become excited over matter of little importance, etc., and this was present in 13.2 per cent of Riseman's series.

Palpitation of the heart was found in 13.1 per cent of the cases and it was quite often associated in patients who had dynpnea.

Riseman and Weiss conclude from their studies that headache, dizziness, aches and pain, dyspnea and nycturia alone or in combination were by far the most frequent complaints of the patient with essential hypertension (39).

Copeland in his series of cases reports the following chart (34):

Headache	24.8 per cent
Vertigo	21.6
Precardialgia	11.2
Dyspnea	9.6
Nervousness	6.4
Symptomless	5.6
Weakness	4.8
Palpitation	4.0
Pedal edema	3.2
Hot flashes	3.2
Epistaxis	1.6
Eye symptoms	1.6
Insomnia	0.8
Dyspepsia	0.8
Joint pains	0.8

In this series forty-six per cent of all inaugural symptoms fall into one of two groups, namely, headache or vertigo. The one symptom which occurred most frequently was headache, thirty-one patients out of 100 possessing it.

CHIEF COMPLAINT IN RELATION TO BLOOD PRESSURE

Blood Pressure	150	160	170	180	190	210	220	230	240	Tot.
Number of cases	9	29	21	14	6	4	5	2	6	96
Headache %	22	14	24	7	17	25	20	50	17	20
Palpitation %	11	18	5	14	17	0	0	0	0	10
Dyspnea %	11	15	19	29	0	25	20	0	50	17
Dizziness %	0	7	9	29	0	0	--	0	33	8
Pain %	0	15	0	0	0	25	20	0	0	5
None %	56	31	43	14	66	0	40	0	0	32

In this table Ziskin shows the percentage of the chief symptoms complained of according to the height of the blood pressure (42). Headache was the most frequent symptom complained of, being present in 20 per cent of the entire group. The frequency of the complaint does not seem to vary greatly with the increase of blood pressure. Dyspnea is the next most common complaint and was present in 17 per cent of the cases. Palpitation was the chief complaint in 10 per cent of the cases and was noted only in the cases with systolic pressures of 190 or less, and not in the cases with systolic pressure of 200 or more. Dizziness was a variable

symptom, being complained of by only 8 per cent in his entire group.

Hypertension in its earlier and milder stages may last for years without producing any considerable discomforts and limitations of the individuals activity (37).

Early in essential hypertension systolic pressure is not high and varies greatly from day to day and the diastolic is but slightly elevated. There follows a period more or less prolonged when compensation is perfect and the patient in the main remains in satisfactory bodily comfort. During this interval lasting often months or years, the elevated pressure remains merely an object of more or less apprehensive interest to both patient and physician, the degree of elevation meanwhile undergoing steady but slow increase on both systolic and diastolic sides.

Hypertension is a malady that in its development affects the blood flow generally and consequently the function of all the internal organs more or less. Because of their extreme dependence on adequate blood supply, the heart, the brain and the kidneys display the greatest disturbance of function. Clinical manifestations involving one

or more of these organs develop in every case of hypertension as it advances, although many times it is difficult to decide which organ is more severely affected. We should not wait for gross manifestations such as edema, angina or cerebral disturbance to develop. We should watch very carefully for the earliest evidence of progressive organ involvement. Intensive study is indicated. In periodic examinations we should be on the watch for significant developments (21).

There exists no single criterion that will enable one to predict much in advance of the event when cerebral hemorrhage, heart failure or uremia is impending. The heighth of the blood pressure cannot be trusted to foretell it, unless perhaps it be the diastolic level. A pressure of 130 mm. or over on the diastolic side is a wearing strain that neither heart nor artery is apt to tolerate for long periods of time. On the other hand, extravagant heights of systolic pressure are often borne tolerantly. The determining factor in prognosis is not then necessarily the blood pressure record but the patient's organ resistance - the ability of his heart and cerebral arteries to stand the strain. This all-important factor in unfortun-

ately not determinable as is the blood pressure in mathematical terms. Clinical manifestations of functional decline announce to the observer what may be expected.

Every patient with persistent hypertension is a potential cardiopath. If he escapes apoplexy and death from intercurrent illness, he will eventually succumb to some form of heart failure. Aside from myocardial fibrosis resulting from associated coronary disease the failing heart of hypertension shows less structural change than would be expected. It is more "heart defeat" than "heart failure", cardiac decompensation being more the result of increased functional load than myocardial degeneration. This is shown by Fishberg's recent anatomical studies in which the arterioles of the myocardium were found involved very infrequently. Since the hypertensive heart fails from fatigue, then should there be some way of preventing or at least postponing this devlopment. If we are to accomplish anything in this direction, we must be keenly on the alert for the earliest evidence of progressive muscle deficiency. These are nearly always subjective in character and not necessarily such as to direct attention especially to

the heart. The patient may remark that he has observed a certain decline in the efficiency of his perceptive faculties so that he is less keen than he was. He lacks the normal healthy feeling of refreshment after a good night's rest. He confesses to uncharacteristic emotional instability, is less able to tolerate tobacco or is inordinately depressed after coitus. More definite and suggestive are increasing dyspnea and fatigue after moderate effort, rapid pulse, palpitation, postprandial oppression, vertigo on sudden alterations of the body posture, pain and constriction in the chest, and so forth. He may assert that his discomforts, when referred to the chest, are relieved by belching and consequently ascribes them to indigestion or error in diet. Recurrent premature contractions are highly suggestive, especially if they are increased by effort. Most significant of all is a permanent increase in heart rate. Other things being equal, a change from the deliberate slow and measured heart beat ordinarily present in high blood pressure to one persistently more rapid signifies the advent of myocardial insufficiency. It is a fair presumption that this rapid rhythm represents an effort on the part of the ventricle to compensate by increase of

stroke for reduced volume output. Progressive elevation of diastolic pressure is to be watched with the greatest concern and when observed, the urine, blood nitrogen derivatives and ocular fundi should be carefully studied. Decline of systolic pressure, if not attributable to therapeutic measures and if associated with increasing subjective discomfort, possesses unfavorable significance, pointing to myocardial exhaustion. Edema, alternating pulse, gallup rhythm, nocturnal asthma, need no emphasis as to their implications (21).

Cerebral developments are less easy to foretell. Failure of mental alertness, persistent occipital headaches, vertigo, transient disturbance of speech, memory or vision, retinal hemorrhages are among significant warnings.

The urine should be analyzed at regular intervals and a kidney function test or blood nitrogen estimation made when indicated and at least twice a year as a routine, in order that uremia may not creep in unawares.

COMPLICATIONS

In a review of the complications occurring in 500 patients seen in consultation and private practice Paullin finds that the organ which

bears the greatest burden of the advancing attack of hypertension is the heart, which undergoes a cycle of changes; dilatation and hypertrophy, development of murmurs, cardiosclerosis, angina pectoris, disturbances of rhythm, congestive heart failure and coronary occlusion. Cardiac complications caused 137 (27.4%) of the patients to seek medical advice. Second in importance are the complications referable to the central nervous system: tinnitus, sever vertigo, cerebral arises and apoplettic seizures; these complications caused 121 (20.2%) to seek medical relief. Next in importance are the changes in the vascular system as evidenced by the development of arteriosclerosis, dilatation of the aorta and aneurysm. The above are but links in a chain upon which the development of other complications greatly depends. Renal impairment, although not of a severe degree, eventually occurs as a late complication in only a small number of individuals. Severe renal disease occurred in a small percentage (41).

Christian in a discussion on Paullin's article says that what is described as complications are what other writers describe as symptoms and the physical findings of hypertension. They may vary

at the time of observation, but after all the symptoms and physical findings of hypertension are the result of various changes or complications that are going on in the vascular system (36).

TREATMENT

Since hypertension is considered to be a compensatory process there is no more reason to treat it per se than to treat a case of compensated valvular lesion. A certain amount of hypertension is absolutely necessary to the individual's well-being. Were it possible to reduce the high pressure to normal, there would not be sufficient driving force to send the blood to the vital organs in the brain and cerebral anemia would result. The high blood pressure is, however, a combination of the necessary hypertension and the hypertension due to some added factor. It is this latter element in hypertension which we should endeavor to eliminate (7).

Given a patient with high blood pressure, the first question that arises is whether or not to treat the hypertension at all. In some mild cases it is far better not to mention the increase in blood pressure, lest the patient be made intro-

spective about his difficulties and thereby produce a condition of increased nervous tension which would lead to greater and greater blood pressure. A tactful suggestion to the patient to slow down may be enough. The physician, however, should keep his eye on such a patient from time to time to note the rate of development of the vascular disease and to treat him when necessary. In most cases the hypertension must be treated because the pressure is usually greater than is necessary for mere compensation and because the greater the pressure the more rapid the increase in the arteriosclerosis, and the secondary changes in the various organs (43).

The treatment of essential hypertension starts then with a careful history to determine what systems are involved and to what extent, what is the mode of living of the patient, how many hours of sleep, how much exercise, how much relaxation, the type of work and how many hours are spent at it, the degree of responsibility, etc. Of course the amount of treatment and the ability of the patient to carry it out will vary with each individual (43).

REST: Of all the remedies tried, physical and mental rest have appeared to produce the most

certain results. The reason why rest in bed may not only lead to a diminution of the hypertension but to a cessation of unpleasant symptoms must be that there is less demand made upon the circulation (40). Nervous tension, worry and excitement increase vascular spasm; consequently these individuals should invariably be cautioned against such things with an insistence that will leave no doubt in their minds. Meals elevate blood pressure and augment heart load. In Mosenthal and Short's studies it was noted that the greatest drop in pressure usually manifested itself well within half an hour after lying down and that the subsequent blood pressure when sitting or upright position was resumed, often did not return to the initial level for a considerable period. This shows that a half-hour rest or nap after meals systematically practiced may have far-reaching consequences. Postprandial rest and relaxation, both physical and mental, should be insisted upon from the earliest stages of high blood pressure. As the case advances, greater and greater emphasis should be places upon this invaluable therapeutic aid (21). The patients must be cultivated to take a placid attitude of no hurry and no worry. They should be taught to perform their work

in a routine and systematic manner and they should sleep at least eight to ten hours nightly (32). Regular and long hours of sleep, avoidance of sudden strain and of activities leading to excessive fatigue should be insisted upon. Periodic vacations, preferably with change of scene and interest, should be recommended. With the advent of dyspnea following meals or usual activity, greater restrictions should be enforced. Every other week-end in bed is an excellent practice for patients engaged in active business and one of the very best therapeutic measures we have is a week or two in bed with business excluded four times a year as a routine. The fact that pressures rise again to former levels after the patient gets about does not disqualify the procedure. For a time at least the strain has been relieved and circulatory reserve is improved thereby (21).

DIETING: Diet therapy in essential hypertension, so far as it has been specialized, is predicated on the old and no longer tenable interpretation of hypertension as an associate condition or consequence of chronic nephritis. This applies particularly to the principles of protein restric-

tion and of salt privation. In the great majority of cases of this form of high blood pressure there is no demonstrable decline in the excretory efficiency of the kidneys. With normally functioning kidneys, it is consequently difficult to regard these diet practices as rational procedures.

Strouse and Mosenthal, the the case of strict protein restriction, and O'Hare and Walker, Mosenthal and others in the matter of salt privation, appear to justify the above statements (21). Underfeeding may reduce blood pressure. It does this presumably by lowering the vital qualities of various tissues, the cardiac muscle, the musculature and elastic tissue of the arteries, the nervous system and the blood, which interest us most in their relation to hypertension; but the whole body is concerned. By the method of subcaloric, especially sub-maintenance protein feeding, blood pressure may be lowered; this, however, may be undesirable from two points of view, which must be constantly kept in mind. First the efficiency of the individual becomes impaired: fatigue, drowsiness, weakness, "neurasthenia" develop. Second, the very organ we wish to have in the best possible physical state to combat the ravaging effects of

hypertension, the heart, deteriorates. However, a large percentage of hypertension patients are more or less obese. Vaquez refers to a "hypertension de luxe" occurring in heavy feeders. These types of patients well benefit by underfeeding whether enforced by either qualitative or quantitative methods. Faber's tables show that, as a rule, with the treatment for obesity there occurred a fall in blood pressure - a loss of 8 to 16 pounds being associated on an average with a drop of from 15 to 30 mm. in systolic pressure. The closest attention should be given to enforcing the principles of diet moderation and the avoidance of all excess in eating, but except under special circumstances or to meet some definite indication, such as obesity, the practice of dietary depletion should not be enforced without a careful checking of its effect from time to time (21). Alcohol, tea and coffee in moderation exercise no harmful effect upon the disease (40).

TOBACCO: The use of tobacco is not generally contraindicated in arterial hypertension unless, as is sometimes observed, patients show a hypersensitivity to it by an accentuation of symptoms and an elevation of blood pressure. In such

hypertensive patients even very small amounts of nicotine may be responsible for serious symptoms and complications. The use of tobacco in such patients is to be permanently prohibited (49).

BOWELS: The bowels should be kept free and daily action without straining assurred. Rupture of minute cerebral vessels leading to severe hemorrhages occurs occasionally during straining. There is a rather marked tendency to constipation in patients with severe hypertension, although in mild cases constipation is not always present. Magnesia magma and phenolphthalein are useful laxatives in keeping the bowels functioning normally. Not infrequently the establishment of a regular regimen is followed by definite improvements in the general symptoms and a lowering of the arterial pressure (49).

PHYSICAL THERAPY: The practitioners of physical therapy have not been inactive in this field. Marx found a lasting decrease in seven of twenty-one patients treated with light baths and subjective improvement was noted in nineteen. Gutman favors the use of all types of physical therapy including light baths, vibrations, auto-

condensation and colonic lavage, but especially the latter. Carbon dioxide baths are also recommended. Diathermy has been used and as is so often the case, with subjective improvement but without any appreciable change in the blood pressure. Animal experiments indicate that it does not affect the blood pressure favorably. Tarbett found that 50 per cent of his cases were helped by warm tub baths after two or three weeks course (46). Shaw says the sole reason for using hot baths is that they relieve some patients from some of their symptoms, notably headaches, although they provoke them in others (40). Oliensis (32) advises moderately warm baths, electric cabinet baths, massage, hydrotherapy in general and diathermy as they are beneficial because of their relaxing effect on the vasomotor system causing dilitation of the arterioles, capillaries and venules. They lower temporarily both the systolic and diastolic blood pressures and the patients experience subjective improvement.

VENESECTION: Venesection is frequently indicated for relief of symptoms, particularly headache (50). The blood pressure is reduced only transiently by this procedure yet subjective relief

may last over weeks or months.

DRUGS: 1. Vasodilatation - Vasodilators were formerly resorted to a great deal in the treatment of hypertension. Their effect appears to be limited to emergencies, to dilate the arteries in such conditions as angina pectoris; they have not proved themselves of any great value, however, in the treatment of essential hypertension. The vasodilators in use today are shown in the following chart:

Drug	Dosage	Mode of Administraa tion
Amyl nitrite	3 min.	Inhalation
Nitroglycerin	1/100 to 1/10 gr.	Tablet
Nitroglyeerin	1 min.	Spiritus glycerylis nitratis
Sodium nitrite	½ to 2 gr.	Solution in water
Erythroltetranitrate	¼ to 2 gr.	Tablet
Benzyl benzoate	5 to 20 min.	20% alcoholic solution.
Potassium sulphocyanate	1 to 2 gr.	Dissolved in water, t.i.d. after meals
Bismuth subnitrate	5 to 10 gr.	Powder or capsule, t.i.d.

Amyl nitrate is the best drug for emergency use. The duration of the lowering effect of these drugs upon blood pressure is least for the nitroglycerin, more prolonged for the sodium nitrite and greatest for the erythroltetranitrate.

O'Hare (43) states that the drugs aimed directly at the reduction of pressures are of little value. These include calcium chloride, alone or in conjunction with atropine, the so-called antispasmodics such as benzyl benzoate, akineton, the various nitrites, etc. The nitrites have their place in the treatment of hypertension only in such places as the symptomatic relief of angina pectoris, nocturnal smothering and cramps in the extremities.

Stieglitz highly extols bismuth subnitrate in 5 gr. doses three to four times daily. This is given for weeks or months, gradually reducing the dose until none is given. He claims that he has good results and that they last some months. He has proved that the subnitrate is decomposed in the intestine to the nitrite and thus the vasodilator action of the nitrite is continuous. Warfield, however, has not been able to duplicate the good results claimed by Stieglitz (24, 7).

Bruen states that the bismuth subnitrate, even in largest therapeutically practicable dosage, does not develop sufficient nitrite action to exert any demonstrable effect on the blood pressure or symptoms of essential hypertension under the conditions of rigorously controlled experiment (52).

Ayman could find no discernible effects on the blood pressure of essential hypertensive patients with the use of crystalline ovarian follicular hormone (Theelin and Theelol). He used daily doses as high as 350 rat units over 3 month periods (51).

Elliott and Nuzum report that there is no constant or frequent deviation from the reported normal cardiovascular response to the subcutaneous injection of epinephrin and pituitrin in patients with essential hypertension (53).

Ayman in his work on potassium thiocyanate in essential hypertension finds that potassium thiocyanate has a hypotensive effect but it also has a toxic effect and which practically always occurs simultaneously. These are produced by large doses given for long periods. He states that "after a careful analysis of the symptoms of the patients before toxic symptoms set in, no definite evidence of specific relief was obtained. Just as many patients were relieved to the same degree by the control treatment as by the thiocyanates (54).

Considerable work has been done with liver extracts and O'Hare quotes letters he has

received from Dr. Major of Kansas City and Dr. MacDonald of Toronto. Dr. Major stated that "we are seeing a fall in blood pressure in from 80 per cent to 90 per cent." Dr. MacDonald wrote, "In selected cases of hypertension we are obtaining falls in pressure in 60 or more per cent and are obtaining relief from associated symptoms in approximately 90 per cent. In many cases the relief from symptoms is marked where no fall in pressure occurs and, as a general rule, the relief from symptoms is out of all proportion to the fall in pressure" (43).

Fisher and Blashill find that the administration of liver extract with sedatives and nitroglycerin has proven to be the most effective treatment in their series of essential hypertensive patients (55).

Cucurbocitrin or watermelon seed extract, in capsules, 300-450 mg. daily is of questionable value in the treatment of essential hypertension (32).

Pacyl, a crystalline choline derivative, has been used with apparently beneficial results abroad, not only on increased blood pressure but on the failing blood sugar regulation and the de-

creased intestinal glandular secretions of elderly people. Palmer, however, did not note any subjective improvement in the patients in which he used pacyl (46).

Certain sedatives such as the various members of the barbituric acid derivatives and perhaps the chloral group which have a relative affinity to the vasomotor and other vegetative centers, are of great benefit. Phenobarbital in a half grain dose twice daily lowers the blood pressure desirably in many patients; in others it prevents undesirable fluctuations (49).

Numerous other drugs have been advocated for the treatment of essential hypertension but none have been generally accepted.

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