

TYPES OF ESSENTIAL HYPERTENSION AND THEIR RELATIONSHIP TO THERAPY*

ALYS LIPSCOMB, M.D.
Fellow in Medicine

STATISTICS¹ show that more than 500,000 persons in this country die each year as a result of hypertensive vascular disease. It has been estimated that hypertension affects 20 to 40 per cent of the population.^{2,3} This implies that there is no consistently effective therapy for high blood pressure in spite of the numerous reports of medications, dietary schedules and surgical procedures, each of which is reported to give good results in 50 to 85 per cent of patients. In 1929 Ayman⁴ listed 200 separate remedies which had been recommended during the preceding decade. The table lists 8 widely diverse treatments offered in the past twenty-five years. The favorable results reported are comparable. A rational explanation of why psychotherapy, oral ingestion of thiocyanates, restriction of dietary sodium and operations upon the sympathetic nervous system should exact similar physiological responses is obscure. The only obvious possibility is that some hypertensive persons respond to attention and care in the same way regardless of "specific" treatment. If this is the correct interpretation all statistics will be difficult to construe unless this factor can be eliminated.

TABLE

Therapy	Author	Date Published	Per Cent Patients In Whom Blood Pressure Was Lowered
Low Sodium	Allen, F. M. et al.	1922	61
	Selman	1923	60
	Allen, F. M.	1925	60
	Vogel	1928	74
	Grollman et al.	1945	66
	Bryant et al.	1947	76
	Kempner	1944-1945	64
(Rice Diet)			
Psychotherapy	Buck	1937	66
Liver Extract	MacDonald	1927	60
Watermelon Seed Extract	Wilkinson	1927	82
	Althausen et al.	1929	73

*Lower Fellowship Prize Thesis, 1948, condensed.
Robert D. Taylor, M.D., advisor

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Thiocyanate	Nichols	1925	66
	Bolotin	1932	68
	Barker	1936	50
	Kurtz et al.	1941	78
Phenobarbital	Gruber	1925	85
Sympathetic Nervous System Surgery	Craig et al.	1939	52
	Smithwick	1947	66
	Peet et al.	1946	81

Differentiation of known causes of hypertension is important. From the great pool of patients formerly classified as essential hypertensives, one is now able to delineate properly, prognosticate accurately and treat better such widely diverse pathologic states as pheochromocytoma, Cushing's syndrome, adreno-genital syndrome, coarctation of the aorta, polycystic kidney disease, chronic glomerulonephritis, unilateral kidney disease, and polycythemia vera. Before separation of each of these into proper niches, one factor was shared commonly; namely, hypertension. It is to be hoped that other specific causes of elevated arterial pressure may be defined more accurately so that definitive therapy may be instituted. A step in that direction, meager though it be, is the grouping together of patients exhibiting similar characteristics. The present report outlines the manner in which hypertension is classified on the Research service of the Cleveland Clinic.

Method of Study

History and Physical Examination

In arriving at a diagnosis of the type of hypertension existing, analysis of the time of onset and duration of high blood pressure is important. A patient who is first found to have hypertension at the age of 50 probably has a quite different disease from one who is hypertensive at 20. The true age of onset can usually be determined by careful interrogation of all previous examiners for life insurance, school, athletic endurance, draft boards, etc.

Family history should be carefully explored. In those cases where heredity is a factor, it is not unusual that the type and course of the disease is similar throughout a family.

Since the cerebral blood vessels are not easily examined, one must depend upon symptoms and signs of cerebral vascular insufficiency. These have been recently reviewed by Taylor and Page,⁵ and consist of occipital and nuchal pains, vertigo, paresthesia, paresis and paralysis (transient or permanent), and nosebleeds.

The most valuable index of cardiac status in the highly emotional, hypertensive patient is not dyspnea, palpitation, or substernal distress, but rather an estimate of the ease with which he can carry on daily activities.

Manifestations of hyperactivity of the autonomic nervous system must be noted. The most common are a diffuse blotchy red blush over the neck and upper thorax, excessive perspiration, lacrimation and peristalsis. There are episodes of tachycardia and wide fluctuations of blood pressure.

As for the physical examination, the most important single feature is inspection of the ocular fundi. A careful estimate of degree of arteriolar constriction and sclerosis of hemorrhages, exudate and papilledema, should be recorded (Mann and Taylor).⁶ Appraisal of the degree of medial sclerosis of the peripheral arteries and the presence or absence of pulsations in the vessels of the legs, are diagnostic aids which are often overlooked.

Laboratory Studies

The electrocardiogram utilizing the standard limb and precordial leads, and the teleoroentgenogram as suggested by Ungerleider and Clark⁷ for the measurement of cardiac size, are adequate for establishing the degree of cardiac disease.

The renal vascular bed not only comprises 20 per cent of the body's arterioles, but lends itself admirably to examination. In lieu of elaborate clearance tests which record renal blood flow, and filtration rate, the Addis examination is the best measure of renal vascular integrity. The latter measures tubular function by establishing ability to concentrate urine. It allows quantitative measurement of proteinuria, cylindruria, hematuria, and pyuria. Intravenous urography is a rough measure of diodrast clearance, and often excludes or demonstrates anatomical disease of the urinary tract. Occasionally cystoscopy and retrograde pyelography are necessary to account for unexplained pyuria or hematuria.

Nomenclature

These methods have made it possible to separate patients commonly referred to as having essential hypertension into four usually distinct and characteristic groups. (1) Essential hypertension; (2) malignant phase of essential hypertension; (3) hypertensive diencephalic syndrome; and (4) generalized arteriosclerosis with hypertension.

Essential Hypertension

True essential hypertension may be defined as a disease of unknown causes characterized by persistently increased peripheral resistance due to arteriolar constriction with cardiac augmentation which leads to progressive arteriolar sclerosis. It usually begins in the late teens or early twenties. Initially there are transient elevations of pressure without demonstrable vascular disease. After five or ten years, the blood pressure, both systolic and diastolic, is consistently elevated. The retinal arterioles by this time may show narrowing but little, if any, sclerosis. The results of other examinations are often within normal limits. Within the succeeding decade arterial pressure becomes more sharply

and constantly elevated. Retinal arteriolar constriction is supplemented by sclerosis. The left ventricle of the heart and renal vascular beds fall short of normal functional capacity. In the next ten years, that is by the fifth or sixth decades, symptoms of vascular incompetence appear and insufficiency of cerebral, cardiac, and renal vascular beds can be demonstrated easily.

This disease generally lasts twenty to thirty years. It usually becomes a problem to the physician and patient only in the last ten to fifteen years of its course. There are deviations from the typical course; an occasional patient dies at 25 years of age or earlier of congestive heart failure or cerebral hemorrhage. Some may have hypertension for fifty years and experience a normal life expectancy. However, it is fairly safe to say that a patient with true essential hypertension does not survive past the age of 60.

Malignant Phase of Essential Hypertension

The malignant phase of essential hypertension is a clinical diagnosis. It is based upon the presence of hypertensive vascular disease with papilledema and hemorrhagic retinopathy. It may appear at any age from 7 to 50, unheralded and lightning-like in a person without known vascular disease. Usually, however, it is engrafted upon a pre-existing essential hypertension and rarely upon hypertensive diencephalic syndrome. It occasionally complicates arteriosclerosis, but this is the result of advanced nephrosclerosis and is often comparatively benign.

In addition to the retinal lesions, there is evidence of extensive cardiac and renal change as the result of fulminant necrotizing arteriolitis. Death in malignant hypertension is usually due to renal failure, although some are attributable to congestive heart failure, cerebral hemorrhage, and rarely coronary thrombosis with myocardial infarction.

The course of this phase of the disease varies from one to five years, more often the shorter period.

Hypertensive Diencephalic Syndrome

Hypertensive diencephalic syndrome was described by Page (1938).⁸ It usually appears in women who have great emotional sensitivity. The blood pressure is highly labile. The most characteristic sign is the appearance of a diffuse, blotchy red blush over the neck and upper thorax with any emotion. There is excessive lacrimation and perspiration, particularly palmar. Hyperperistalsis is always present with emotion and is often audible. Tachycardia is frequent and with the elevated basal metabolic rate which is found among hypertensive patients, leads to a diagnosis of thyrotoxicosis. Thyroidectomy, which is often performed, has no value.

In spite of blood pressures that are intermittently extremely variable (250/150 to 130/80 mm.Hg) the course of this disease is prolonged. Vascular disease may be minimal at 55 or 60 years of age. The patients usually die eventually of cerebral hemorrhage and only rarely, of subsequent malignant hypertension and renal failure.

To this group may be added certain highly emotional persons frequently of Jewish or Southern European extraction who show all of the signs and symptoms mentioned except the characteristic blush. Such patients have a more striking component of hyperactivity of the intestinal tract. They complain of gaseous dyspepsia, epigastric pain, functional constipation and diarrhea. The course is even more kindly as far as vascular disease is concerned, and more unpredictable as to variations in blood pressure. Tension may be extreme (240/150 mm.Hg) for a few weeks or months; later with the advent of some degree of serenity, it can be normal.

Generalized Arteriosclerosis with Hypertension

Generalized arteriosclerosis with high blood pressure makes its appearance at approximately 50 years of age. Documentary evidence of the onset is particularly important in this group. Hypertension may be discovered during routine examination; or the patient may present himself for examination because of headache, giddiness, or fatigue. Elevation of blood pressure is primarily systolic; however, at times, the diastolic pressure may be as high as 120 or 130 mm.Hg. The pulse pressure nevertheless is invariably great and usually exceeds 100. The pressure is further characterized by its lability. The retinal arterioles show predominate sclerosis with minimal or absent constriction. The peripheral arteries are usually thickened and tortuous. A chest film will indicate tortuosity, elongation and often calcification of the aorta. Depending upon the degree and duration of hypertension, the heart shadow shows evidence of left ventricular hypertrophy.

Kidney function is, as a rule, moderately impaired so that the Addis test shows a maximum ability to concentrate urine to a specific gravity of about 1.020; the urea clearance is approximately 50 per cent of normal and there is a trace of albuminuria.

This condition usually responds well to any therapy which decreases cardiac output, be it bed rest, sedation, reduction of body weight, or relief of headache, giddiness, or fatigue. The blood pressure can generally be maintained at or near normal levels by diligent application of any of the above remedies. Should the patient die of the disease, it is from cerebral hemorrhage or coronary thrombosis and at 65 to 90 years of age. Many succumb to carcinoma or infectious diseases.

Observations

The lability of pressure and the ease with which it can be reduced in several of these conditions may account in part for the frequency with which favorable effects are reported from treatment in "essential hypertension." To test this possibility, 600 consecutive patients with hypertension were classified carefully and the results of treatment analyzed in each group.

Of the 600 hypertensive persons, 320 (53.3 per cent) had essential hypertension. The average age of 237 (39.6 per cent) was 44.3 years, all of whom

had well established hypertensive disease. The remaining 76 (12.7 per cent of the total) averaged 34.8 years of age and had early essential hypertension or were in the stage in which blood pressures were labile and above normal inconstantly. The sex distribution was 57 per cent men and 43 per cent women. There were 39 or 6.5 per cent who had the malignant phase of essential hypertension. Of these 29 were men. This group had an average age of 46.5 years.

Those with the diencephalic syndrome and its allied type of labile hypertension, numbered 47 or 7.8 per cent of the total. All but 5 of these were women. The average age of this group was 41.4 years.

Among those whose hypertension was believed to be secondary to arteriosclerosis, there were 183 patients which comprised 30.5 per cent of the total. The average age of this class was 57.8 years and the sex distribution was about equal with 47 per cent women.

There were 18 patients who fit into none of these classifications. Ten had chronic glomerulonephritis, 1 polycystic kidney disease, 1 chronic pyelonephritis, 5 simple vasomotor lability and 1, Kimmelstiel-Wilson's disease.

Thus, of these 600 patients 51 per cent had blood pressure which varied spontaneously or could be reduced with ease by many simple measures. This large group is therefore unsuitable for any study which depends upon changes of arterial blood pressure as the only method of measuring the results of treatment.

Comment

The analysis presented in no way detracts from the brilliant results which follow certain kinds of therapy offered to patients with severe essential hypertension or the malignant phase of the disease. Various types of sympathectomies have aided and prolonged the lives of hundreds of patients. Thiocyanate alone and in conjunction with sedatives has relieved distressing symptoms such as headache so that otherwise disabled people can lead useful lives. Dietary programs that sharply restrict the intake of sodium have been gratifyingly effective in many cases of severe vascular disease. If these measures were always effective, however, the incidence of early death from hypertension should have receded rather than increased.

The appearance, undoubted though inconsistent, of good results from such varied methods of treatment poses a problem. The problem is to establish means for selecting those patients who will respond to a particular type of treatment in a predictable manner. When this can be done, much time, effort and expense will be saved, and what is more important, such knowledge could well lead to further clarification of the mechanisms responsible for high blood pressure and its attendant blood vessel disease. Progress may be retarded if approximately 50 per cent of the patients with essential hypertension, whose blood pressures are inconstantly elevated are included in therapeutic studies whose results depend upon measured reduction of blood pressure.

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