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Question of the etiology of essential hypertension

Richard R. Flebbe
University of Nebraska Medical Center

THE QUESTION OF THE ETIOLOGY OF ESSENTIAL HYPERTENSION

BY

RICHARD A. FLEBBE

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OUTLINE

PART I

INTRODUCTION

In choosing as a subject for a thesis, one so controversial as that of the question of the etiology of essential hypertension, I do so advisedly, well knowing that in a short time there may be no such subject. It is hard to understand how such a common symptom as high blood pressure could be so thoroughly investigated by medically minded men over a period of half a century and still remain so largely unexplained. That this has happened is not a reflection upon those who have labored upon the problem, but is rather, an indication of the complexities encountered.

The purpose of the medical profession is to keep people well and to aid in overcoming illness when it has occurred. The ancients used amulets, incantations, vile mixtures and the laying on of hands in their treatment of the sick. The methods of modern medicine in the treatment of hypertension is no far cry from these methods of the ancients. Nowhere is there less reason and more empiricism. The mechanic must know the reason for its failure before he can repair the motor. The physician, to get the best results in treatment, should know the cause of the disease. Unlike the mechanic, he

cannot dismantle the living machine and find its defective mechanism. Here he is at a disadvantage. How much of a disadvantage is shown by our lack of understanding of the problem of essential hypertension. The primary causes and effective methods of treatment of the vast majority of cases of hypertension are still unrecognized.

Recent experimental work has been so spectacular in nature that many of the profession are prone to lose sight of the older but equally well substantiated observations of workers prior to Goldblatt. It would be impossible to review and evaluate the mass of literature which has accumulated, relative to the etiology of essential hypertension. However, after reading some of the better known papers on the subject, I have formed a few more or less personal opinions regarding the etiological complex of the symptom of essential hypertension. Undoubtedly, these ideas will change in the future. Nevertheless, the process by which they were reached has been an instructive one and when new studies concerning hypertension are presented, I will have a basis upon which to evaluate them.

Before essential hypertension can be intelligently treated, we must have a more perfect understanding of its etiology. Undoubtedly, most of the groundwork has

been done toward this end. This paper is intended to present known and suspected facts regarding the etiology and, perhaps, to hazard a guess as to what the nature of the final concept will be. In effect it is a protest against the growing tendency to consider the height of the blood pressure as an index of the degree of ischemia of a kidney. The question of the etiology of essential hypertension has not been fully answered. When it is answered in all its phases, there will no longer exist the concept of primary hypertension as we know it today.

It is not fitting that one so inexperienced as I should attempt a criticism of wise and well-informed writers. In reading their papers, however, I may form opinions. It is this view that I will attempt to present, knowing that in doing so, the writer benefits much more than does the reader.

Historical Notes*:

The measurement of blood pressure, which today is accepted as a routine procedure both by the physician and the layman, is rather a modern innovation even though a clergyman, the Reverend Stephen Hales, first demonstrated the phenomenon of blood pressure as long ago as 1733 (1). Hales measured the pressure in the femoral artery of a horse by means of a long glass tube, the

trachea of a goose, and a brass cannula. The disadvantages and inaccuracy of such an instrument applied to the estimation of blood pressure in humans was probably evident even at that time and clinical use of blood pressure estimations did not become common until 250 years later.

Since 1828, when Poiseuille introduced the mercury manometer (1), blood pressures have been expressed in millimeters of mercury. The Poiseuille type of manometer is still used in experimental laboratories. Almost all important contributions in connection with the question of hypertension have been made since 1896 when Riva-Rocci introduced his pneumatic cuff and manometer, essentially the same instrument as the sphygmomanometer used today (2).

After Bright's (3) reports on his one hundred cases of chronic renal disease, it became gradually evident to medical men that there was some relation between kidney disease and hypertrophy of the heart. In 1856, Traube proposed the theory that high blood pressure was the connecting link between these two conditions. For many years kidney disease was considered to be the universal cause of hypertension.

Late in the nineteenth century the concept of essential hypertension began to develop. In 1874, Mahomed

(4), spoke of the "pre-albuminuric stage of Bright's disease", and cited cases of hypertension in which there was no demonstrable evidence of kidney lesions. Mahomed emphasized his belief that in all of these cases, a Bright's disease would eventually develop. Von Basch, in 1893 (2), wrote of cases of hypertension in which symptoms of arteriosclerosis were not present and termed the condition "latent arteriosclerosis". Allbutt (5), in England, became the leading proponent of the theory that a high blood pressure could exist without the presence of clinically significant renal disease. He called this condition "hyperpiesia".

In the United States, Janeway in 1913, (6) wrote that the disease underlying high arterial pressure is predominantly a disease of the circulatory system and is best designated as hypertensive cardiovascular disease, either primary or secondary when preceded by an inflammatory nephritis. Moschowitz (1919) (7), believed that it is a mistake to classify hypertension as nephritic, arteriosclerotic or essential, and stated that all of these were phases of the same disease. He spoke of a persistent hypertension as "representing a decompensation of the circulation". His views coincided almost exactly with those of Mahomed.

Frank, in 1911, introduced the expression "essentielle hypertonie" (2), which term, has become, in this country, essential hypertension, a term which includes those cases of chronic hypertension which cannot be demonstrated to have developed as a result of inflammatory kidney disease or urinary obstruction. This concept of essential hypertension is rather indefinite and is defined entirely in negative terms. It is a confession of ignorance on the part of the modern medical profession as to the true nature of the symptom complex classified as primary hypertensions.

Definition: Explanation of Subject Matter:

It can be easily seen that essential hypertension is not a disease entity, but a complex of conditions which have two things in common: an abnormally high arterial blood pressure, and the absence of a primary inflammatory or obstructive renal lesion. The terms, essential and primary hypertension, will be used interchangeably although, strictly speaking, they are not synonymous. We wish to write of that large group of cases of clinically evident arterial hypertension in which the primary cause cannot be definitely proven and it is in this sense that the terms essential hypertension or primary hypertension will be used.

The Meaning of "Hypertension":

Before a patient can be labeled as hypertensive, his blood pressure must be compared with a standard which is taken as normal for the patient's age group. There is by no means universal agreement upon what this standard should be. The blood pressure varies somewhat with age but how much of this variation is normal is difficult to determine.

Alvarez (8) has noted that blood pressure levels rise rapidly during adolescence, then drop in the years from seventeen to twenty-five, normally remain here until about fifty years and then gradually rise. He considers 130 mm. systolic as normal. Bell and Clawson (9) consider 120 mm. systolic as normal at twenty years and anything over 150 mm. as abnormal after forty years of age. These authors note Hunter's observations of blood pressure, the normal at twenty years being 120 mm. systolic and 80 mm. diastolic, increasing 2 mm. systolic and 1 mm. diastolic every five years up to sixty years, at which age the average is 135 mm. systolic and 89 mm. diastolic. True hypertension has been defined by Boas and Shapiro (10) as a condition in which the diastolic pressure is consistently above 90 mm. of mercury regardless of age.

A very interesting survey was made in 1939 by Robinson and Brucer (11) who studied the blood pressures of over 10,000 persons during a period of ten years. From the observations made in this series, the authors defined the normal range of systolic blood pressure in men and women as being between 90 and 120 mm. systolic and 60 and 80 mm. diastolic. They observed that the higher levels of blood pressure show greater and more erratic yearly variations and conclude that blood pressures normally change very little with age after adolescence. The tendency among clinicians seems to be to set a lower standard for normal blood pressures but to take repeated readings before calling a patient hypertensive.

It is obviously difficult to set a standard and adhere strictly to it. The difference of 1 or of 5 mm. of mercury in the reading should not decide a patient's status. In general, it seems advisable to consider 130 mm. systolic and 85 mm. diastolic as the upper limits of normal in patients up to forty years of age and anything above 150 mm. systolic and 90 mm. diastolic as hypertension at any age; provided, of course, that the patient has the benefit of repeated readings and demonstrates a consistent elevation of the blood pressure above these limits.

PART II

GENERAL CONSIDERATIONS

Incidence:

In 1924, according to Fahr's (12) estimates, 70,000 persons died in the United States of cardiac failure in hypertension. Twice this number died either directly or indirectly from the effects of hypertension. According to this writer's estimates, 50% of all organic heart disease in persons over forty-five years of age is hypertensive in nature. These estimates are probably conservative ones.

The large majority of these cases are truly essential hypertension. Brown (13) states that despite recent advances in the study of hypertension, 98% of cases must still be classified as "essential". Other estimates are only a little lower. (2)

If Janeway's (16) figure of five years as the average duration of life following onset of hypertensive symptoms, is taken as correct, and the number of deaths per year from essential hypertension is taken as 130,000, then there are at least a half million cases of symptomatic essential hypertension in the United States today. Factors which may have some bearing on the etiology of this common condition are discussed in the following pages.

Race:

Conclusive evidence that certain races are more liable to, or are more immune to, hypertensive disease has not yet been presented. The accepted views that blood pressures in the more energetic, ambitious and high strung peoples of North America and North and Central Europe have more of a tendency to become elevated, cannot be proven. It seems to be true, however, that the incidence of hypertension in China is very low. Foster (14) states that hypertension in Chinese is rare and that the average blood pressure is lower in this race. Interestingly, according to this author, the blood pressure of occidentals living in China are lower than at home and the average for these foreigners is about the same as for the local Chinese. The observations of Tung (15) corroborate these views. Harris (16) supports the belief that Chinese blood pressures are distinctly lower than those of Caucasions, but maintains that blood pressures of foreigners in China do not fall and that hypertension among these people is as common as it is in Western countries.

Negroes are not usually considered to be of the high strung, hypertensive type but Allen (17) found, in a study of 1000 negro factory worker, that 56% suffered

from cardio vascular abnormalities the predominant symptom being hypertension which was present in 45% of the cases. This incidence was conclusively higher than in a similar control group of whites. The higher rate of hypertension might be attributed at least partially to the high incidence of syphilis in the colored race.

Sex:

Bell and Clawson (9) state that hypertension occurs in males more often than females in a ratio of 14:10. Janeway (6), on the other hand, found the condition to be more common in women. Fishberg believes that, considering the common occurrance of essential hypertension in pregnant women, the incidence is significantly higher in females. Alvarez (8) observed that "the blood pressures of the women are more uniform than those of the men and they average 11 mm. lower". It is generally agreed that after middle age the incidence of hypertension is about the same in both sexes.

Any dispute as to the incidence of hypertension in the two sexes seems to be out of order. High arterial pressure occurs in both sexes and whatever the cause, physiological factors peculiar to one sex or the other appear to be unimportant in the consideration of etiology of essential hypertension as a whole.

Age:

The problem of age in hypertension is considered to some extent elsewhere. Age probably has some bearing on the etiology of the condition as indicated by the high incidence in those past middle age. Whether this relationship is any closer than the ordinary senescence which occurs as the body grows older, is yet to be determined. The age at time of death in a series studied by Bell and Clawson (9) indicated the maximum incidence as being between 50 and 70 years. The youngest patient was thirteen years of age and 91% were over forty years of age. These writers claim that 15% of persons over fifty years of age have essential hypertension. The renal type of hypertension shows the highest incidence under the age of forty years. Janeway (6) and Fahr (12) report essentially similar age distribution.

Alvarez (8) reported, in 1923, what he termed a 'surprising' incidence of hypertension in young people. He states, "In the first place it was found that hypertension is not a disease of old age alone; it is found commonly among young people, healthy enough to go to college. Furthermore, the pressure does not increase with age as we have always thought". He found that 45% of the college men in the series had pressures above

130 mm. and 22% above 140 mm. Diehl and Sutherland (18) claim that most of these apparent hypertension were due to nervousness and in a similar study report the presence of high blood pressure in 6% of students studied. It appears that the true incidence is somewhere between these two extremes. Nevertheless, hypertension is relatively common at any age.

What, then, does age have to do with hypertension? Is the higher incidence in elderly people due to anything more significant than the more lengthy exposure to the trauma of living? These questions are unanswered at the present time.

Occupation:

The role of occupation in hypertension is indefinite. It is a common belief that the people who live under constant mental strain are more prone to develop high blood pressure. Although this is not proven, it is evidently quite well founded in fact. This does not mean that the well-to-do business executive or professional man is any more liable to hypertension than the poor relief worker. Hypertension is decidedly not a class disease. Fishberg (2) points out that there is a high incidence of essential hypertension in dispensary patients. Allen's (17) series shows a high incidence

among factory workers. Hypertension, especially of a moderate degree is supposed to be very common among railroad employees. (19)

In my opinion, occupational factors play a very minor part in any attempt to explain the etiology of hypertension, and further study along this line, while perhaps interesting, will never explain the cause of elevated blood pressures.

Bodily Habitus:

Larimore (20) states that the sthenic habitus is accompanied by a higher blood pressure than is the asthenic habitus. Terry (21) believes that most obese women who seek medical attention suffer from hypertension. Allen (17) notes that at all ages there was a tendency to hypertension in overweight negroes and that above forty years of age 78% of persons, twenty pounds or more overweight, suffered from hypertension.

Wood and Cash (22) found that in normal and hypertensive dogs the systolic blood pressure rises with weight gain and falls with weight loss. The diastolic pressure varies only a little.

The majority of observers note an increase of the incidence of hypertension in the obese. It seems physiologically sound to believe that the increase in vascu-

lar area occurring in an overweight individual would lead to a compensatory rise in blood pressure. One of the most successful means of treating essential hypertension in overweight individuals is by means of reducing diets. Nevertheless, as Bell and Clawson (9) point out, many obese persons do not have hypertension, and the disease is frequent in underweight individuals. This factor will be discussed further with the metabolic phases of the etiology of hypertension.

Heredity and Constitutional Factors:

When considering etiological factors in hypertension, heredity must not be overlooked. Numerous authors have noted a familial tendency to the hypertensive state. (2, 5, 23, 24, 25) According to Brown (13), Morgagni in 1769, recorded cases of apoplexy which he believed were influenced by hereditary factors.

Hines (23) has presented a study of the family histories of about 900 patients with and without hypertension. He found that a positive history of hypertensive cardio-vascular disease was five times as frequent in persons who had hypertension or were hyper-reactors to stimulus test, as in normal persons. No hyper-reactor was found who did not have one hypertensive parent. In the study of ten pairs of twins in the family groups it

was found that the types of blood pressure reaction followed an inherited pattern. From these findings, he concluded that the trait is a dominant characteristic and postulated that the inherited quality might be a vasomotor system which reacts excessively to certain external or internal stimuli and eventually results in the development of essential hypertension in many cases.

Quinan (26) makes the interesting observation that high arterial tension occurs more frequently in left handed than in right handed people. Considering that sinistrality is accepted as hereditary, he concludes that hereditary predisposition is a definite factor in the etiology of hypertension and hypertension is another indication of the supposed constitutional inferiority of left handed people.

Brown (13), Weiss (24) and Fishberg (2) are impressed by the importance of hereditary factors in the etiology of hypertension. Bell and Clawson (9) sum up the status of the question of heredity thus: "If inheritance is accepted as a fact, there still remains the question as to what is inherited. Is a subnormal arterial system or an unstable vasomotor system inherited?" When this question is answered a large part of the mystery of essential hypertension will be solved.

PART III

THEORIES OF ETIOLOGY

Physiology:

Before proceeding further it would seem wise to discuss the manner in which an elevation of blood pressure can be produced by alterations in the physiology of the circulatory system.

The maintenance of a normal blood pressure depends upon the following factors (1):

1. The pumping action of the heart.
2. The peripheral resistance.
3. The volume of blood in the arterial system.
4. The viscosity of the blood.
5. The elasticity of the arterial walls.

Conceivably, the blood pressure might be raised to an abnormal level by a variation in one or more of these factors. Broadly speaking, the first four of the above factors are concerned with the systolic pressure while the diastolic pressure is maintained largely through the elasticity of the walls of the great arteries. A high systolic pressure might then result from an increased cardiac output, an increase in blood volume, a heightened blood viscosity, an increased peripheral

resistance, or a combination of these factors.

According to Weiss and Ellis (28), the cardiac output, the circulating blood volume and the mean velocity of the blood are unchanged while the peripheral resistance is almost doubled in most cases. Burwell and Smith (29) concluded from a study of both normal and hypertensive individuals that the minute volume of the blood did not show significant changes in the hypertensives. Freeman and Page (30) and others (31, 46) have presented evidence to indicate that the blood volume is not measurable increased in essential hypertension. Austrian (32) in 1911, showed that the viscosity of the blood in hypertensives is not increased and may be even decreased. According to Prinzmetal and his associates (33), the blood viscosity is normal.

The one remaining variable factor responsible for the rise in blood pressure, as indicated by the above observations and supported by work of numerous other investigators (34, 35, 36), is an increased peripheral resistance. The mechanism through which this change is initiated remains unexplained. It may be due to a nervous or a humeral mechanism or to intrinsic changes in the walls of the vessels themselves leading to a spasm of the smaller blood vessels throughout the body. (34)

Freeman and Page (30) suggest that known factors which normally control the arterial pressure are not significant in the production of hypertension.

Endocrine Factors:

In the study of the causation of essential hypertension some of the most promising investigation has been done. Cases of hypertension which in years past would have been classified as essential, now should properly be classed as secondary hypertension because of definite demonstrable glandular pathology which accounts for the elevation of pressure. These instances are a small portion of the total, however, and at least 95% of cases of non-renal hypertension remain in the primary group.

The glandular components in the etiology of hypertension, according to Hutton (37), are pituitary, adrenal and thyroid. Hutton has obtained symptomatic relief and reduction of hypertension in several cases through the use of low dosage irradiation to the pituitary and adrenal regions. In addition to these three glands, the gonads, the liver and the pancreas will be considered.

Adrenals: One of the oldest theories of the cause of high blood pressure is that of a hyper-secretion of

the suprarenal glands. The strong pressor effect of the secretion of these glands is well known and the temptation to explain hypertension on this basis is great. The fact that in Addison's disease the blood pressure is low lends support to the hyperepinephrinemia theory of hypertension.

Collins and Wood (38) found that adrenelectomy lead to a fall in the blood pressure of hypertensive dogs, but the pressure never reached the normal level. These men feel that it is unlikely that the adrenal cortex is involved specifically in the etiology of experimental hypertension. Page (39) offers the reasonable explanation that in dogs made hypertensive by constriction of the renal arteries, the endocrine glands are chiefly concerned with maintenance of the body in a state that can physiologically respond to this by the development of a compensatory hypertension.

It is impossible to demonstrate an increase of epinephrine in the blood of hypertensive individuals, and this fact, together with experiments such as those of Jeffers, Lindauer and Leukens (40) in which hypertension is shown to persist following bilateral adrenelectomy, has led to an almost complete abandonment of the epinephrine theory of hypertension. An interesting note

in this line is that of Goldzeiher and Sherman (41) who found a hypertrophy of the muscle tissue of the suprarenal veins in cases of hypertension and also an abnormal distribution of dye injected into the vessels of the suprarenal glands, which they are unable to explain.

It is an accepted fact that suprarenal tumors can cause hypertension. Although the type of lesion is not constant and the precise mechanism is unknown, a small group of cases demonstrate adrenal tumors as the basis of hypertension. This type of hypertension is particularly found in younger individuals. (42) Hutton (37) noted the frequent simultaneous occurrence of hypertension and diabetes mellitus, and observed that the most significant finding in the hypertensive cases was grossly enlarged or frankly tumorous suprarenal glands.

In the final analysis of the etiology of hypertension, abnormalities of the adrenal secretions may not have the role of the primary factor. It is my impression, however, that they will be found to play an important part in the mechanism which leads to the production of hypertension in a goodly percentage of the cases.

Thyroid: There is considerable difference of opinion as to the part that the thyroid gland plays in

hypertension. Fishberg (2) believes that the elevation of blood pressure in hyperthyroidism is not a true hypertension. This seems to be paradoxical, although Boas and Shapiro (10) speak of a special syndrome of diastolic hypertension with tachycardia, increased B.M.R., loss of weight, nervousness and other indications of hyperthyroidism.

Experimentally, nothing can be proven regarding the relationship of the thyroid gland to hypertension. Glenn and Lasher (43) found that total thyroidectomy in dogs does not effect either the production or the maintenance of experimental hypertension.

Riseman (44) found clinical improvement of hypertension following thyroidectomy. In his series, after excision of the gland, there was often a rise of the systolic blood pressure after exercise as high or higher than that before operation, but this rise was asymptomatic.

A very reasonable view is that of Bisgard (45) who believes that there are two types of hypertension occurring with hypertension. Those in which the hypertension coexists with the hyperthyroidism as a separate entity and a second type in which the hyperthyroidism causes the hypertension or precipitates or exaggerates a latent

vascular disorder.

In hypothyroidism the blood pressure is usually low. This is not universally true and both Hutton (37) and Fishberg (2) note cases in which the opposite condition exists. As in cases of hypertension with other types of endocrine disfunction, the symptom cannot be attributed directly to the malfunctioning thyroid gland but must be explained on the basis of a more complicated imbalance of the entire endocrine system as well as the closely associated vegetative nervous system.

Gonads: Alvarez (8) observes that, generally speaking, women have an average blood pressure lower than that of men of similar ages until the time of the menopause, and then it becomes actually higher. He also observes that in hypertensive young women there are often symptoms of hypofunctioning ovaries. He attributes to the actively functioning ovary, the ability to prevent a hypertension in women with the hereditary tendancy to high blood pressure. According to his theory, at the time of the menopause this power is lost and the symptoms of hypertension develop.

It is a common observation that hypertension may occur in young women in whom an artificial menopause has been caused by radio therapy. The results of

treatment of these cases with ovarian extracts are not conclusive. Polak and his associates (47) have noted an elevation of blood pressure in women over forty and at the climacteric, who have had hysterectomies because of fibroids of the uterus. If the ovaries are not removed in these women the elevation is not so marked and if there is no intercurrent disease the blood pressure eventually recedes.

According to Schaeffer (48), in cases of hypertension occurring at the menopause there is a substantial reduction of the hypertension after the administration of theelin. There is evidently an incretory imbalance at this time with an actual lack of follicular hormone.

Page (39) observes that neither the ovaries or testes are essential for the maintenance of high blood pressure in dogs with induced hypertension.

It is probable that some cases of essential hypertension may be explained on the basis of hypo-functioning gonads. Nevertheless, the great majority of cases cannot be explained on this basis.

Pituitary: Because of the well known pressor qualities of extract of the posterior lobe of the pituitary, this gland was early incriminated as a cause of hypertension, despite the fact that in classic cases of

definite pituitary hyperfunction there are no significant changes in the blood pressure of the patients.

Cushing (49, 50) and his syndrome of basophil adenoma are well known. However, the exact pathology occurring in this syndrome is not known. It is true that hypertension occurs with basophil adenomas of the pituitary. It is also true that basophil adenomas occur without hypertension. Also many cases of Cushing's syndrome occur with adrenal cortex hyperplasia or tumors without the basophil adenoma of the pituitary. (2)

Cushing's theory that essential hypertension is due to excessive pituitary pressor substance in the blood stream is apparently not well grounded. Investigators (51, 52) have been unable to demonstrate such an increase. Another theory of Cushing (50), who believes that the extent of the basophil invasion of the neurohypophysis is an index of the activity of the pituitary, seems also groundless. Spark (53) found no greater basophil invasion of the neurohypophysis of hypertensives than of a group of normal controls.

Page and Sweet (54) found that preliminary hypophysectomy in dogs did not prevent the rise in blood pressure established by renal ischemia, although the rise did tend to be transient in nature. On the other

hand, these investigators found that once the hypertension was established in these experimental animals, it could be reduced somewhat by hypophysectomy. A similar reaction was observed in normal animals.

It appears that pituitary function may be necessary for the establishment of a hypertension. The idea that pathology in the gland itself is responsible for hypertension is apparently untenable except in that small group of cases where neoplastic change can actually be demonstrated. Even here it is questionable in view of the association of the basophil adenomas with bodily changes involving different types of tissue. (24)

Rather, it seems that the pituitary, as the chief gland of the body, reacts to pathology elsewhere in such a manner that a compensatory rise in blood pressure might result. What the condition is, which initiates the reaction, and what the mechanism of the reaction is, must yet be determined.

Pancreas: Fisher (55) demonstrated that there must be additional substances to insulin secreted by the pancreas, necessary for life, when he noted that depancreatized dogs, supported by insulin, died of fatty infiltration of the liver.

In the past few years there has been some little

interest in a substance, thought to be of pancreatic origin, which has a vasodilating effect. (56) Wolffe (57) used this substance to treat arteriosclerotic gangrene with surprising results. Later he used this vasodilating substance of the pancreas in the treatment of essential hypertension. In some of his cases there was an appreciable lowering of the blood pressure under this treatment. Herbison and Roberts (58), doing similar work, observed that the blood pressure changes varied directly with the amount of pancreatic substance used.

Other workers have supported these observations, (59), and Kraut, Frey and Bauer (56) found that this so-called pancreatic hormone was very active in opposing the action of adrenalin, a strong pressor substance.

In view of these observations, a very attractive theory can be postulated: Hypertension may be the result of a deficiency of a vasodilating substance produced by the pancreas in much the same way that diabetes mellitus is the result of a deficiency in insulin.

At the present time, this theory can be neither proved or disproved. Additional work will undoubtedly be done along these lines in the near future and it is

possible, if not probable, that in many cases at least, the question of the etiology of hypertension will then be answered.

Liver: While this organ probably has no etiological relation to primary hypertension, for the sake of completeness, it should be mentioned here. MacDonald (60), Major (61), Levin (62), and James, Laughton and MacCallum (63) have reported cases of hypertension successfully treated by the use of liver extract. The chemical nature of the "antipressor" substance, which is thought to cause the lowering of the systolic and diastolic blood pressures in some hypertensive patients, is unknown. Burnett (64) notes the similarity of the reaction of the liver extract and histamine and offers biochemical evidence to indicate that the liver extract consists of histamine in combination with some other substance.

While attempts to connect the liver with the etiology of hypertension would seem ill advised, there is the possibility of utilizing liver extract in the symptomatic treatment of certain early cases of essential hypertension.

Metabolic:

Although in the past few years, the stress which

has been placed on this phase of the problem of hypertension has decreased, metabolic factors were long considered as the chief causes concerned in hypertension. Even though no very clear-cut ideas were presented, treatment was based almost entirely upon attempts at regulation of various metabolic factors. Thus in Allbutt's (5) discourse on management of hypertension, we see diet, massage, exercise and climate as the chief considerations with drug therapy in a minor place and no mention of surgery. Many of the principles here put forth still apply, however, and some consideration must be given to the various phases of metabolism possible concerned in the etiology of essential hypertension.

Cholesterol: One of the most characteristic findings in essential hypertension is arteriosclerotic change in the vascular tree. One of the theories of the production of arteriosclerosis depends upon the assumption that lipids and, more specifically, cholesteral derivitives, are deposited in the walls of the vessels in increased amounts leading eventually to an arteriosclerosis. Because of these considerations, early attempts to explain essential hypertension postulated an increase in the cholesterol of the blood stream.

Present indications are that there are no significant changes in the lipid content of the blood. Although some authors (65, 66) maintain that there is a definite hypercholesteremia in essential hypertension, others (67, 68, 69) consider it questionable. Page, Kirk and Van Slyke (70) flatly state: "Theories of the genesis of arterial changes in essential hypertension based on prepresumed hypercholesteremia or on an elevation of the cholesterol:phosphatid ratio are without basis." Weiss (24) believes that hypercholesteremia may be a result rather than a cause of hypertension.

Probably there is a change of the blood cholesterol level in some cases of hypertensive arterial disease. This change may be primary or secondary or entirely unrelated. Many cases of hypertension must occur with normal blood cholesterol levels and it is doubtful if the lipids of the blood stream have a significant part in the causation of primary hypertension. Yet they may have, and so abnormalities of the blood lipids should be kept in mind when searching for the cause of any given case of hypertension.

Guanadine: Major (71) has been the leading proponent of the theory that excess guanadine base, circulating in the blood is responsible for essential hypertension.

He was able to produce a rise of blood pressure in animals by giving certain guanadine compounds. He later admits that his test may have not demonstrated guanadine but some other substance, and his work is not at all conclusive. Pfiffner and Myers (72) found what they thought was an elevated guanadine level in some cases. DeWesselow and Griffiths (73) found an elevated blood guanadine in nine of twenty-three cases of hypertension but noted gross fluctuation of the guanadine level in individual cases without corresponding alterations in the blood pressure. Weiss (24) does not hold with the guanadine theory and believes Major's claims to be invalid.

Major (74) in his last article on the subject, concludes: "The blood of certain patients suffering from arterial hypertension contains something which is present in greater amounts than in normal blood." To which statement most authorities will agree. The "substance" is probably not guanadine.

Calcium and Potassium: That calcium ion is vagotonic is well known. Out of this fact grows the theory advanced by Reid (75) that in hypertension the calcium content of the blood serum is lowered, thus lowering the vagal influence and the vasoconstrictor action of

the sympathetics is relatively unopposed. Then the pressor actions of various substances become manifest by an arterial hypertension.

In order to validate this theory, the calcium content of the blood would have to be demonstrably lowered. Kylin (76) claimed to have shown this to be true. Addison (77) has reported success in treatment of essential hypertension by the administration of large doses of calcium chloride. Engelbach (78) believes that there is a definite relationship between hypocalcemia, parathyroid deficiency and hypertension.

More recent work has caused doubt as to the validity of the hypocalcemia theory. In pregnancy, a hypocalcemic condition should be most conspicuous. Steiglitz (79) investigated forty-seven cases of pregnancy complicated by hypertension and was unable to find a constant variation between the calcium content of the blood and the hypertension. In this series the average calcium levels of the patients were the same as in a series of controls and Steiglitz concluded that hypocalcemia was not a major factor in arterial hypertension of pregnancy.

Other investigators (80) have been unable to demonstrate a relationship between the potassium:calcium ratio and uncomplicated cases of hypertension. In

patients with cardiac complications the potassium level is somewhat high. This is considered to be a result rather than a cause of hypertension.

At this time the possibility of hypocalcemia being an etiological factor in some cases of essential hypertension should not underestimated. It seems settled, however, that Reid's (75) hypothesis: "A diet deficient in calcium is the primary cause of arterial hypertension", is definitely an over-statement of fact.

Protein: One of the oldest and most commonly believed theories regarding essential hypertension places protein in the role of the primary etiological factor. The hypertension being an end result either of kidney damage due to end products of protein metabolism or of intrinsic changes in the vascular system resulting from a high protein intake. Several observers claim to have caused hypertension by high protein diets. Newburgh (81) and others (82) caused Bright's disease by feeding this type of diet. Nuzman and his associates (83) induced an experimental hypertension in this way and suggested that the elevation of blood pressure was due to renal injury brought about by the high acid or alkaline ash residue of the high protein diet.

Opposed to these findings are those of Anderson (84)

Drummond and Crowden (85), as well as others (24), who have been unable to demonstrate evidence of kidney damage or hypertension resulting from an excessive protein intake. Clinical observations seem also generally opposed to the protein theory of hypertension. Observers (86, 87) are unable to note any variation in the blood pressure of hypertensive patients in relation to the intake of protein food. They could neither lower the blood pressure of these patients by reducing the protein food or elevate it by increasing the protein intake. One of the most interesting observations in this line is that of Lieb (88) on Stefannsson, the arctic explorer, who after nine years subsistance on an exclusively protein diet had a blood pressure of 115/55.

Jackson, Sherwood and Moore (89) found no convincing evidence that peptide nitrogen of the blood in hypertension rises sufficiently to be of etiological importance.

It is possible that protein is an etiological factor in the production of hypertension in susceptible individuals. However, as Fishberg (2) points out, there is not very good evidence that excess of protein in the diet results in essential hypertension. We must certainly look much farther than this in explaining the

great majority of cases of unexplained hypertension.

Carbohydrate: Joslin (90) and Kramer (91) have noted the high incidence of diabetes in association with hypertension, especially in patients over forty. Kramer believes that it is unlikely that the diabetes, through hyperglycemia can produce hypertension. When hypertension occurs in these patients it can be explained on other grounds. Herrick(92) demonstrated that often a high glucose concentration in the blood is associated with hypertension and advocated treatment of high blood pressure by means which would reduce the blood sugar. Mohler (93) also noted the hyperglycemia, but observed that the relation of blood pressure to blood sugar level is not at all constant and believed that the blood pressure findings depend upon other factors than the lesions of diabetes.

As Weiss (24) observes, there seems to be no adequate proof that carbohydrate metabolism, per se, is concerned in the etiology of essential hypertension. Nevertheless, there seems to be some relationship between the pancreas and some cases of hypertension as is pointed out elsewhere. The relationship of this organ to carbohydrate metabolism is well known and it is conceivable that in the future essential hypertension and

disturbances of sugar metabolism may be found to be much more closely linked than is now supposed. The observation of Herrick (92) that hypertension, hyperglycemia and obesity often occur in the same patient is valid and the fact that these peculiarities have a familial tendency, as noted elsewhere, seem to point to a constitutional factor responsible for the entire group.

Purines: Another phase of metabolism which has been much discussed in relation to hypertension is that of the purines, because of the supposed frequency of the occurrence of hypertension in gouty individuals. (94) Rosenbloom (95) observed that hypertension was only present during the acute attacks of gout. Allbutt (5) speaks of hypertension in cases of "irregular gout". The facts probably are that when gout and hypertension occur together they are independent of each other (24). It is doubtful if further investigation along this line would shed any light on the question of the etiology of essential hypertension.

Sodium Chloride: Another common belief is that salt retention causes high blood pressure. The layman is especially prone to incriminate the excessive use of table salt as the basis of his high blood pressure.

This belief does not appear founded in fact. Numerous observers (87, 96, 97, 98, 99, 100) have failed to find any relationship between either the sodium chloride intake or the sodium chloride level in the blood and the level of the blood pressure. Sodium chloride seems definitely eliminated as a cause of primary hypertension.

Toxic:

Tobacco and Alcohol: Among the many evils attributed to the use of tobacco is essential hypertension (2, 5). It has been shown that nicotine can induce elevation of the blood pressure in experimental animals (101, 102). Clark (103) states that in the novice, tobacco causes a fall in blood pressure while in the habitual smoker it may cause a slight elevation.

Riseman and Weiss (104) note that in their survey there is a higher incidence of essential hypertension in females than in males. Although at one time this observation might have been used as indirect evidence that tobacco is not significant as an etiological factor in essential hypertension, the rising number of female smokers makes the observation valueless in these modern times. Weiss (24) believes that tobacco should not be considered as the cause of hypertension.

It is certainly true that the largest percentage

of smokers do not develop high blood pressure and there is no evidence available to indicate that hypertension is more common in smokers than in non-smokers. Thus we are forced to minimize the part that tobacco has in the etiology of hypertension.

Alcohol has also often been accused of causing high blood pressure (3, 5). Without reviewing the literature it may be stated that at this time alcohol is fairly definitely ruled out as an etiological factor (2, 5, 24). It may be said to have a casual relationship to hypertension in that alcoholism may lead to obesity and together with the obesity may serve to initiate hypertension in a predisposed individual.

Lead: Weiss (24) states that inasmuch as it is well known that lead compounds cause a constriction of smooth muscle, it is possible that lead is responsible for a few cases of arterial hypertension. The survey of Harris (105) revealed that 39% of a series of painters with symptoms of lead poisoning were definitely hypertensive. Fishberg (2) believes that lead is the only toxic inorganic element which has been shown to cause high blood pressure. Aub (106) states that the late manifestations of lead poisoning are largely degenerative as shown by the appearance of arteriosclerosis,

contracted kidneys and a resulting high blood pressure.

It seems clear that lead is a specific etiological factor in occasional cases of hypertension. Whether this hypertension is primary or secondary has not been shown. From the pathological findings it appears to be secondary. At any rate, the possibility of plumbism should be kept in mind in the study of cases which are apparently "essential" hypertension.

Intestinal Auto-intoxication: Until about 1925, it was believed that products of bacterial putrefaction in the intestine might give rise to toxic products which when absorbed, would cause essential hypertension (5, 107). Such products can be isolated in the intestinal contents (2). If these products were responsible for high blood pressure, constipation should be a definite factor in the etiology of hypertension. This does not seem to be the case. Alvarez and his associates (108) could find no correlation between constipation and hypertension. The present concept does not include the possibility of intestinal auto-intoxication as an important etiological factor.

Infection and Allergy:

Infection: As in most syndromes, there have been many attempts to explain essential hypertension on an

infectious basis; not as a specific infectious disease but rather as an aftermath of various specific and non-specific infections.

Probably the infection which most persistently is labeled as pre-hypertensive is syphilis. Stoll (109) notes that many cases of arterial hypertension are associated with prenatal syphilitic infection. He lists lues as the most significant factor in causation of pathologic arterial changes and hypertension as one of the most common late manifestations of congenital syphilis. In a series of fifty cases of hypertension of unknown etiology 90% were syphilitic. In a few of these cases specific treatment gave satisfactory results in controlling the hypertension. Moschowitz (110) observed several patients with hypertension directly traceable to syphilis.

On the other hand, Walker and O'Hare (111) noted a higher incidence of syphilis in a series of control cases than in their series of hypertensive patients. Baruch (112) lists typhoid, tonsillitis, scarlet fever, diphtheria and rheumatism in that order, ahead of syphilis as precursors of hypertension. This writer speaks of infection as one of the triad of factors responsible for hypertension but suggests that the course and

sequelae of the disease is determined by the inherited "organ inferiority" of the individual. Weiss (24) believes that while infection has an indirect etiological role in many cases of hypertension, this hypertension is of the secondary type as in pyelonephritis. Allbutt (5) and Fishberg (2) attach very little importance to the infectious theory of essential hypertension except in the case of syphilitic aortitis, which often leads to a compensatory elevation of blood pressure.

It is apparent that there are no infections regularly associated with hypertension except those concerned in the etiology of the secondary type. While an occasional case of essential hypertension may seem to be directly associated with a specific infection, these considerations shed only a little light on the question of etiology in the majority of cases.

Allergy: Another interesting explanation of the cause of hypertension has to do with vascular allergy.

O'Hare, Walker and Vickers (113) demonstrated a family history of hypertension in 68% of their cases. Considering this evidence of hereditary predisposition to the disease, they point out that heredity is the foremost clinical criterion of allergy. They were able to demonstrate that migraine, which is supposedly of

allergic origin, preceded 50% of their cases of hypertension.

Mosenthal (114) described a case of hypertension which was caused by specific articles of food. This case was controlled by removing these articles of food from the diet. Such a phenomenon could easily be explained on an allergic basis. Woldbott (115) believes that some cases of previously unexplained hypertension may be caused by allergy because of their association with other typically allergic manifestations. Some of these cases react favorably to an allergin-free diet.

Cohen, Fineberg and Rudolph (116), on the other hand, observe that hypertension and allergy are found only infrequently in the same patient. They conclude that there is no relationship between blood pressure level and allergins.

Investigation in this field is somewhat limited and as Weiss (24) points out, further study might be very fruitful. There has been rather an over-emphasis of allergy in the last decade but this should not lead us to lose sight of the fact that allergy might be and probably is, a potent factor in the causation of some cases of hypertension. We must admit that essential hypertension is a symptom of multiple etiology and

allergy is conceivably one of these.

The Nervous System:

That the nervous system has a large part in the maintenance of blood pressure cannot be denied. That this normal control might become unbalanced and cause abnormal blood pressure is entirely reasonable. The factors concerning the nervous mechanism governing blood pressure can be classified as: central nervous system, vegetative nervous system, and psychic. Disorders of any of these might cause an elevation of blood pressure.

Organic lesions of the central nervous system can cause severe and protracted hypertension as is noted in cases of bulbar poliomyelitis. To presuppose such lesions in all cases of hypertension is out of the question. Laycock (117) in 1873, proposed that morbid states of the cerebellum, medulla and spinal cord might cause Bright's disease. Cushing (118), in 1901, postulated that an increase of intracranial tension occasions a rise in blood pressure which tends to find a level slightly above that of the pressure exerted by the medulla. We often see evidence of this phenomenon in the elevated blood pressure which follows intracranial lesions such as tumors and hemorrhage.

Bordley and Baker (119) feel that it is likely that vascular changes in the brain stem might explain the occurrence of hypertension. Anrep and Starling (120) state that cerebral anemia can cause an elevation of blood pressure. Davidson and Brill (121) regard changes in the central nervous system as secondary to the hypertension. Part of the generalized arteriolar changes which result from the hypertension, if localized primarily in the brain, might cause "hypertensive encephalopathy". Cutler (122) was unable to demonstrate any significant anatomical changes in the blood supply to the vasomotor center and states that if high blood pressure is due to lack of blood supply to the vasomotor center, this condition is not caused by visible change in the arteries of the region.

It is an accepted fact that the vegetative nervous system regulates, at least to some extent, the normal blood pressure; the sympathetic system with its constrictor effect, being inhibited by the parasympathetic system, especially through the carotid sinus and aortic depressor reflexes. Among the first observers to incriminate the vegetative nervous system in cardiovascular disease were DaCosta and Longstreth (123) who claimed to have demonstrated a constant

lesion of the renal plexus and advanced the theory that this lesion caused Bright's disease, postulating that similar lesions of the cardiac plexus might explain cardiac hypertrophy. This work has never been substantiated.

Another attractive theory is that various lesions, Such as atheromatous changes in the carotid sinus, might lead to loss of the parasympathetic depressor control and result in an elevation of blood pressure. Weiss and Baker (124) review the work which indicates that, following the removal of the intercarotid and aortic nerves in animals, chronic hypertension develops. These men feel that, as patients with normal carotid sinuses often have hypertension, local pathology in the sinus is probably not important in the causation of high blood pressure. In many of their patients stimulation of the carotid sinus caused a drop in blood pressure, indicating that the carotid sinus reflex was active and functioning. Keele (125) was unable to establish any relationship between the degree of atheromatous change in the sinus or aorta and the presence of a hypertension. He noted that these atheroma are very common, are mainly related to the age of the patient, and are usually associated with involvement elsewhere.

Opposed to the theory discussed above is its antithesis, that increased pressor stimulation through the sympathetic system might overpower the parasympathetic effects and cause a hypertension through constriction of the peripheral vessels. It is commonly accepted that there is a constriction of the arteriolar system in hypertension (2, 28, 126). The possibility of stimulation of the vasomotor center through ischemia, causing an increase in sympathetic tone has been already mentioned.

The work of Prinzmetal and Wilson (36), and of Pilkering (127) indicates that the vascular hypertonus is not vasomotor in origin but seems to consist of an intrinsic spasm of the vessels themselves. In view of the failure to get satisfactory results in the surgical treatment of hypertension by sympathectomy, the theory of sympathetic pressor etiology of essential hypertension seems untenable except in occasional cases.

It is universal knowledge that blood pressure may be affected by fear, anger, excitement and other psychic manifestations. Frequently, blood pressure readings must be repeated during physical examinations in order to get a true indication of the blood pressure level. The type of patient most frequently suffering from hypertension has been discussed to some extent

elsewhere but will be considered more in detail here.

Numerous statements indicating that patients with hypertension are of the high-strung, nervous type, with driving personalities and that hypertension is a product of our modern high speed life appear in the literature, (7, 128). The truth is that people were dying of apoplexy in the time of Hippocrates.

Moschowitz (7) observes that hypertension occurs most frequently in that type which is the direct antithesis of a child. Patek and Weiss (129) note that the following symptoms and signs occur more frequently in hypertensive patients than in controls: overexcitability, impulsiveness, tendency to worry, negative hippus, absence of sinus arrhythmia, negative oculo-cardiac reflex, "white" dermatographic reaction to pressure, and a tendency to telangiectasis. In the hypertensive patients the influence of the sympathetic system seems to be more pronounced. Ayman and Pratt (130) as well as Davis (131) note that the early symptoms associated with hypertension are probably psychic in origin and closely resemble the symptomatology of patients with neurosis. Riseman and Weiss (104) feel that psychic conditions may play a more important part in hypertension than is realized. Menninger (132) notes that some

hypertensive patients show gross abnormalities of emotional status but, as Stieglitz (128) points out, there is no proof as to whether the hypertension is the cause or the result of these changes. Excellent results have been reported in the treatment of essential hypertension by various procedures essentially psychological in nature (132, 133). In this light, Menninger makes the interesting observation that any treatment, regardless of nature, benefits the hypertensive patient, at least for a time.

It seems to me that the part of the nervous system in the etiology of hypertension has been in the past somewhat underestimated. Of course, everyone is willing to grant that brain tumors and the like can cause hypertension and that psychological factors may play at least a precipitating or aggravating part in many cases. However, investigators too often lose sight of the fact that no matter what the primary causative agent is, it must exert its effect through a mechanism essentially nervous in character. Be the causative agent hormonal, metabolic, toxic, nervous or renal in origin, reflex nervous activity must play an important part. An abnormal nervous mechanism, then, could distort the bodily reaction to a stimulus which might not be abnormal

in such a way that the reaction became abnormal. No attempt is made to place pathology of the nervous system in the primary etiologic role but it seems evident that the nervous system is as much a part of the chain of factors which produce the final picture of hypertension as is the vascular system itself.

Local Vascular Resistance in the Kidney:

Experimental hypertension has been produced repeatedly by various methods which produce local disturbance in the renal circulation. These procedures may be classified as follows:

1. Excision of varying amounts of renal tissue. (134, 135, 136, 137)
2. Damaging the kidneys with roentgen rays causing fibrosis. (138)
3. Local renal venous stasis. (139)
4. Partial ligation of renal arteries. (140)
5. Compression of the renal arteries by adjustable clamps. (141, 142)

Of these methods, that of Goldblatt (141) is the most easily controlled and has been carried out numberless times with one result - the elevation of the blood pressure. The mechanism of this means of production of hypertension has not been satisfactorily explained.

There are the possibilities of a nervous reflex mechanism, a humeral mechanism or a combination of these. It has been shown that this type of experimental hypertension is not prevented by denervation of the kidney, (30, 143), resection of the splanchnic nerves (144), or complete sympathectomy (145). Page (39) demonstrated that the adrenal glands were not concerned in the production of this type of hypertension.

Therefore, by elimination, the process must be primarily on a humeral basis. It is assumed that some chemical substance is released by the ischemic kidney which, when circulated in the blood stream, causes a vasospasm which results in hypertension (34). There is an abundance of experimental evidence that indicates that this may be true. The pressor substance which is found in saline extracts of normal kidney is found to be present in larger amounts in the extract of a contralateral kidney in which ischemia has been produced by Goldblatt's method (33). Goldblatt (142) showed that excision of the ischemic kidney after hypertension had been established, caused the blood pressure to return to normal. In cases of secondary hypertension, dramatic cures have been reported following the removal of the effected kidney (146, 147, 148)

On the other hand, the blood of a Goldblatt dog when transferred into another dog is no more pressor than the blood of a normal dog (149). Friedman and Prinzmetal (149) were unable to cause a significant change in blood pressure by cross transfusions of large volumes of whole blood between patients with malignant hypertension and persons with normal blood pressure.

We must admit that the exact mechanism of the hypertension caused by local disturbances in the renal circulation is not known. The work along this line has been largely experimental rather than clinical, and the correlation between the experimental hypertension and clinical essential hypertension has not been shown. There is a vast difference between the relatively acute process of the experimental elevation of blood pressure and that which takes place clinically over a long period of years.

Blackman (150) observes that 86% of a series of fifty cases of essential hypertension showed marked atheromatous occlusion of the renal arteries and implies that the hypertension is explained on this basis. This is a little difficult to believe in view of the well known fact that arterial changes always come as a result of hypertension and whether they are the cause

of it is not known. As Menninger (132) points out, one of the mistakes to which investigators are most prone is in assuming that any of the phases of hypertension are due to another phase of it.

As has already been explained, the most characteristic feature of essential hypertension is a condition of increased vascular resistance, due to a narrowing of the arteriolar system. Not only are the arterioles of the kidney more resistant to blood flow, but throughout the body there appears to be a norrowing of these vessels (36, 151). Weiss and Ellis (28) have observed that the average peripheral resistance in hypertensive patients is twice as great as in normal patients. It might be assumed then, that the hypertension results from the decreased blood flow through the kidney. In order to accept this theory we should be forced to admit that the renal arteriolarsclerosis is both the cause and the effect of the hypertension. This may be so; however, it does not appear that any conclusive evidence has yet been presented to settle the question.

Until recently the conception generally had been that primary or essential hypertension is not of renal origin. Since the publishing of Goldblatt's work, the tendency has been growing to explain every case of

essential hypertension upon a renal ischemia basis. When the pendulum again swings back it will probably be found to be a fact that some cases of hypertension are explained on this basis but by no means all of them. Nevertheless, if renal ischemia can be shown to cause 5% or 10% of the cases of hypertension, this is a forward step and narrows the field of the so-called essential hypertensions by just that much.

PART IV

DISCUSSION

It is difficult to evaluate the work which has been done regarding the etiology of hypertension. In doing so one must consider the great number of fallacies encountered. Many of the methods used have been inaccurate. There has been too great a tendency to explain one phase of the symptom complex concerned in hypertension in terms of another coexisting phase. Clinical data is often woefully incomplete. Most important of all, experimental work has lead to broad generalizations which cannot be supported practically. In too many cases the worker is so concerned with details that the problem as a whole is forgotten.

Thus we see an almost universal attempt to find one explanation for all cases of essential hypertension. It is my belief that this single explanation will never be forthcoming. Furthermore I believe that most cases of hypertension, which appear to be idiopathic, can be explained in terms already covered in the literature. By this I do not mean that the explanation will always be the same. Far from it. It must be remembered that high blood pressure is a symptom, not a disease. We do not attempt to explain all abdominal pain on the basis of

stomach pathology, all hematuria on the basis of kidney pathology or every headache on the basis of brain tumor. Then why should we attempt to explain every elevation of blood pressure on the basis of one or two all-inclusive theories?

It seems to me that the most progress in this field will be made when the practitioner begins to sharpen his diagnostic tools to the point that he can differentiate between cases which now he throws into the common wastebasket of essential hypertension. Not only will this call for an increased clinical acuity in this field but it will require establishment of new laboratory methods and refinements of old ones.

One fact seems well established - that the elevation of blood pressure in essential hypertension is brought about by a narrowing of the arterioles throughout the body, thus increasing peripheral resistance. How this narrowing is brought about is still unknown and it is with this problem that investigators seem most concerned. While they are thus occupying themselves patients continue to suffer from hypertension. If physicians would utilize what is already known about the etiology of hypertension, much suffering could be prevented. Instead, they blindly search for a universal panacea.

It is true that treatment based on this concept of the etiology of hypertension would be difficult. It would partake of the fields of preventative medicine, endocrinology, psychiatry, neurology, urology and internal medicine. In fact, it might become a specialty in its own right.

It matters little to the diabetic how insulin alleviates his symptoms. What he wants and what he pays for is the alleviation. In the same way a hypertensive patient is not concerned with the yet unknown mechanism which causes a narrowing of his arterioles. If the pathology or abnormality which causes this mechanism to act is found and corrected the peripheral resistance should be reduced and the hypertension corrected.

Conclusion:

With careful study etiology could be definitely established in many cases of what are now known as essential hypertension. Once this etiology is established treatment should follow as indicated. One method of treatment should not be empirically used for all cases of primary hypertension in the hope of affecting a miraculous cure. It seems definitely established that hereditary predisposition plays an important part and that various types of pathology cause a reaction in

predisposed individuals which leads to elevation of the blood pressure. Tumors or malfunction of the various endocrine glands, metabolic abnormalities, plumbism, infection and allergy, psychic and nervous disorders and disturbances of the renal circulation can all furnish the added stimulus which leads to the establishment of the hypertension. Essential hypertension should not be considered as a disease entity. It should rather be considered as a symptom of a myriad of abnormal conditions. Diagnostic ability should be utilized to the utmost in determining the nature of this condition. Once the nature of the pathology is determined, it, not the hypertension, should be treated. When this occurs the concept of essential hypertension will disappear.

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