5-1-1934

Systemic hypertension : with special reference to etiology of essential hypertension

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Systemic Hypertension; With Especial Reference to Etiology of Essential Hypertension

Senior Thesis
1934
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Omaha, Nebraska April 10, 1934
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>II.</td>
<td>The Blood Pressure Mechanism</td>
<td>3</td>
</tr>
<tr>
<td>III.</td>
<td>The Development of the Hypertensive Picture</td>
<td>5</td>
</tr>
<tr>
<td>IV.</td>
<td>Incidence of Hypertension</td>
<td>15</td>
</tr>
<tr>
<td>V.</td>
<td>Classifications of Hypertension</td>
<td>17</td>
</tr>
<tr>
<td>VI.</td>
<td>Race and Age in Hypertension</td>
<td>25</td>
</tr>
<tr>
<td>VII.</td>
<td>The Clinical Picture of Hypertension</td>
<td>27</td>
</tr>
<tr>
<td>VIII.</td>
<td>Morbidity and Pathology</td>
<td>41</td>
</tr>
<tr>
<td>IX.</td>
<td>The Kidneys in Hypertension</td>
<td>46</td>
</tr>
<tr>
<td>X.</td>
<td>The Peripheral Vascular Bed in Hypertension</td>
<td>52</td>
</tr>
<tr>
<td>XI.</td>
<td>The Etiology of Essential Hypertension</td>
<td>60</td>
</tr>
<tr>
<td>XII.</td>
<td>Conclusion</td>
<td>88</td>
</tr>
<tr>
<td>XIII.</td>
<td>Case Report</td>
<td>89</td>
</tr>
<tr>
<td>XIV.</td>
<td>Bibliography</td>
<td>90</td>
</tr>
</tbody>
</table>
The problem of hypertension has always been a stumbling block to the practicing physician and to those interested in research, and although much work and speculation has been brought forth, it is still a perplexing problem.

Practical therapy can be of benefit only on the grounds of proven etiology, and the knowledge of adequate and correct therapy is one of, if not the most important of, a doctor's chief prerequisites. It would seem, therefore, that the etiology of a problem is of prime importance.

Authors have propounded various terms for this condition - known as hypertension, namely, primary or secondary, genuine, and transient hypertension; others include systolic or diastolic hypertension, hyperpiesia, and malignant hypertension, etc. To avoid confusion if possible in this paper, the word hypertension, unqualified, shall designate all types of systemic vascular disease with high blood pressure with some causative background evident and "essential hypertension" shall be a type of the above of unknown origin. The former is understood to have a systolic rise of more than a transitory period and the diastolic is not necessarily elevated. In the latter both systolic and diastolic are considered to be raised above normal.

"There are no diseases so little understood, and so difficult of comprehending, and so far beyond the control
of art, as chronic affections of the heart. Their characters are so ill defined, so difficult is it to distinguish the idiopathic affections of this organ from those cases in which its functions are sympathetically disturbed, so impossible to anticipate with certainty by the symptoms the presence of the disease there; in short, so intimately are the functional disorders of the heart connected with those of the brain, that an attempt to arrange systematically the disease, or lay down definite rule of treatment may be considered as impossible" (62).

Although many small streams of research have formed since the time of the above quotation, which was typical of about 1833, and many of these streams have joined to form larger rivers, still the open sea of complete knowledge has not been reached. One hundred years later finds many a modern physician still at a loss concerning the heart and its "idiopathic" or "sympathetically disturbed affections". It would seem that modern medicine has not progressed as rapidly along this line as is evidenced by discoveries in other branches of endeavor.

This paper is merely a collection of facts concerning hypertension and especially the etiology of essential hypertension; it is futile to draw conclusions, and furthermore, the author is in no position to do so at the present time.
The Riva Rocci sphygmomanometer was the first adequate means of accurately estimating systolic blood pressure. Harvey Cushing introduced this instrument into the United States in the first years of this century (31). This determination of blood pressure depended upon the palpation of the radial artery and the first pulse felt after obliterating the blood flow, was taken as the systolic pressure.

The auscultatory method of determining blood pressure, described by Korotkoff in 1905, made the estimation of the diastolic pressure practical. As will be noted by Stone (59), the diastolic pressure is of prime importance. In this latter method, when the cuff is first rapidly inflated to a point beyond the extinction of the pulse, and then gradually deflated, a series of sounds are heard by means of a stethoscope over the brachial artery; these sounds are divided by Wiggers into five periods;

(1) As the pressure falls there is a sudden appearance of a clear sound, as the first flow of blood occurs through the compressed artery. This corresponds to the systolic pressure.

(2) The sound becomes more continuous like a murmur.

(3) The sound becomes progressively louder.

(4) The sounds suddenly become muffled.

(5) The sounds disappear.

According to most observers the phase (4) corresponds to the diastolic pressure (82).
Arterial pressure is a resultant of the two effects:

(a) The rate at which blood enters the arterial system from the heart

(b) The rate at which blood leaves the arterial system through the peripheral resistance.

It is evident that the pressure will be altered by varying either of the two factors - peripheral resistance or output of the heart. The cardiac output will depend on the stroke volume of the heart and on the pulse rate (82). The maintenance of arterial pressure may be explained by the following cycle - 60 cc. of blood is forced through the aortic semilunar valves into the aorta by the contraction of the left ventricle of the heart; the aorta distends and its elasticity drives on that portion of blood, which is the whole principle but is found more so in the arteries and especially the arterioles. This gradually decreasing wave of distension is what we feel on the radial artery or any exposed artery as the pulse.

The arterial pressure can best be interpreted by looking upon it simply as the result of four main mechanical factors acting on the blood stream - namely, the propulsive force of the heart beat, the volume of blood, the resistance of the peripheral arterial bed (which should include the aortic valve) and the viscosity of the blood, the latter and the cardiac output being but rarely affected by any deviation from normal. If the pressure is abnormally high or low it becomes a symptom; it is never a disease (3).

The normal arterial tension in healthy adults ranges
from 110 mm. to 140 mm. of Hg. systolic and from 70 mm. to 85 mm. of Hg. diastolic pressures, gradually rising to the higher figures with increasing age (58). Mosenthal gives 120 over 80 as standard pressure readings (85). As will be shown, blood pressure is a fluctuating state of normality; it is dynamic and not static. To state definite values for normal blood pressure is of value only to insurance companies.

Very recently, C. P. Clark (85) has formulated a method of establishing theoretical blood pressure values. Having devised a constant and inserting it in the following equation, he is able to reach theoretical readings:

\[
K = \frac{\text{Body Weight}}{\sqrt[3]{\text{Weight} \times \text{Height} \times \text{Blood Pressure}}}
\]

\[
K \approx 0.01208
\]

This is a comparatively new idea and has not been proven by any means, although on several individuals it was accurate to 2 mm. of Hg.

The first step toward the understanding of the significance of blood pressure was taken by William Harvey (1628) when he gave a correct concept of the qualitative aspects of the circulation. Giovanni Alphonso Borelli (1680), probably during his twelve years of friendship with Malpighi in Pisa, made observations on the blood flow in the arteries; but Rev. Stephen Hales, a minister of Teddington, was the first investigator to
give an account of direct measurement of the blood pressure in animals. Hales, with his background of Newtonian physics, gave clear evidence that he considered arterial blood pressure one of the fundamental aspects of haemodynamics. In his "Statical Essays, Vol. 2, Containing Haemostatics," published in 1740, he describes his first experiment.

"In December I caused a mare to be tied down alive on her back. Having laid open the left crural Artery about three inches from her belly, I inserted into it a brass Pipe, whose bore was one sixth of an inch in diameter; and to that, by means of another brass Pipe which was fitly adapted to it, I fixed a glass Tube, of nearly the same diameter, which was nine feet in length: Then untying the ligature on the Artery, the blood rose in the tube eight feet three inches perpendicular above the level of the left Ventricle of the heart: But it did not attain to its full height at once; it rushed up about half way in an instant, and afterwards gradually at each Pulse twelve, eight, six, four, two, and sometimes one inch: When it was at its full height, it would rise and fall at and after each Pulse two, three, or four inches; and sometimes it would fall twelve or fourteen inches, and have there for a time the same Vibrations up and down at and after each pulse, as it had when it was at its full height; to which it would rise again, after forty or fifty Pulses."

He was also interested in the blood pressure of man. "If we suppose, what is probable", he says, "that the blood would rise seven and one half feet high in a tube fixed to the carotid artery of a man......." This is the first suggestion
of a definite quantitative estimate of blood pressure in man. (31)

Hales's observations were not appreciated or extended until almost a century after his death when Poiseuille (1828), a French observer, introduced the U-shaped mercurial manometer, thus bringing observations within reasonable space (14).

Poiseuille and later C. Ludwig (1858) and Vierordt (1855) undertook a systematic study of the significance of blood pressure in the mammalian circulation and established its importance permanently.

The impetus toward recognition of the clinical importance of the blood pressure in man, however, was not given by these learned and outstanding experimenters but by the clinical and post-mortem observations of physicians of the 19th Century.

Bertin in 1824 and Hope in 1832 claimed an association between hypertrophy of the left ventricle and cerebral hemorrhage. In 1836, Richard Bright of London published his well-known thesis, "Cases and Observations Illustrative of Renal Disease Accompanied with the Secretion of Albuminous Urine," in the first volume of Guys Hospital Reports. He believed the kidney to be the chief promoter of derangement of other organs and that is a wise and fair conclusion if one considers the evidence then available. In attempting to explain the frequent finding of hypertrophy of the left ventricle, Bright says, "This naturally leaves us to look for some less local cause, for the unusual efforts to which the heart has been impelled: and the two most ready solutions appear to be, either, that the altered quality of the blood affords irregular and animated stimulus to
the organ immediately; or, that it so affects the minute and capillary circulation as to render greater action necessary to force the blood through the distant subdivision of the vascular system." This hypothesis of Bright's, based on finding an association between contracted kidneys and cardiac hypertrophy, stimulated the curiosity of investigators interested in diseases of the kidneys and cardiovascular system more than any other clinical observation in this field. It was this stimulus that eventually led to the recognition of primary (essential) hypertension as different from the nephritis of Bright.

That Bright was not generally accepted by his contemporaries is shown by the fact that thirteen years later Walsche definitely claimed that Bright's disease was not essentially a renal disease, but primarily a blood disease. Quoting Walsche's statement, "The true explanation seems to be, that the state of the blood prevents the kidney from acting properly on the elements it is accustomed to excrete, not that its own functional aptitude is at the outset seriously impaired; in other words, it is probable that in the commencement the renal cells are still quite able to separate urea, if healthy constituted blood were offered to them by the vessels." Walsche's concept is a distinct step in the establishment of a clinical picture of primary or essential hypertension.

Johnson (1856) in his significant work "On the Diseases of the Kidney, Their Pathology, Diagnosis and Treatment, with an Introductory Chapter on the Anatomy and Physiology of the Kidney", states that as a result of changes in the blood, the small vessels
contract and the muscle hypertrophies. Johnson's concept still implicates the kidney as the primary cause of the disturbance but clearly introduces a functional factor, namely, the contraction of the small vessels, into the mechanism of the disease. According to Johnson the "toxic blood" is not able to nourish the tissues and the minute arteries resist its passage. Johnson, is is evident, was the originator of the present theory of pressor substances in the blood of hypertensive individuals (63). As a result of this resistance, both cardiac and arterial muscular tissue hypertrophy. A somewhat similar view was held by Traube (1856) who claimed that the small vessels of the kidneys contracted, water is-retained, and as a result increased work is put on the heart.

But all advances still adhered to Bright's original belief that in all cases of bilateral kidney involvement the cardiac and vascular changes are secondary to primary disturbance of kidney function.

The concept of a diffuse primary disease of the arteriolar system was introduced into pathology and clinical medicine through the observations of Gull and Sutton (1872). These two authors presented evidence that a condition exists in which a diffuse "hyalin-fibrosis" of the arteriolar system is present throughout the body, that "vascular changes" are, or may be, independent of renal disease; and that renal change in chronic Bright's disease with contracted kidney, when present, is but a part of a general morbid condition. They were the first to point out clearly that kidney tissue may be "healthy" with
marked cardiac hypertrophy and widespread arterio-capillary fibrosis. Thus was established by Gull and Sutton the morphological concept of a primary disease of the arteriolar system (31).

Virchow in 1872 was the first, apparently, to note the association of early arteriosclerosis and nephritis with narrow aorta. Lancereaux (1891) believed that the majority of nephritides, are the result of congenital aplasia of the vascular system; even in the 80's, he believed that increased intravascular tension was the cause of the condition (53).

The progress of clinical medicine was hampered by lack of accurate instruments for the study of cardiovascular diseases. Vierodt, C. Ludwig and Marey were three outstanding physiologists of the late 19th Century to make contributions along that line. But the results obtained with these instruments were inexact as Pascal's Law (that fluids exert pressures in all directions) was not taken into consideration. Results varied, therefore, with the anatomic location and the size of the artery.

Riva Rocci of Pavia (1896) was the first to eliminate the fundamental error in methods previously used. He applied a wide rubber tubing around the arm which, when inflated, exerted approximately the same pressure in every direction. This was a much simpler instrument than those formerly tried, less expensive and gave more accurate readings. It has contributed more than any other device to knowledge concerning the state of the cardiovascular system (31).

Nearly 200 years ago, scions of old continental clinics were pondering over "spastic constrictions" of the peripheral
blood vessels and "vehement agitation" of the blood leading to idiopathic hemorrhages without preceding diseases; and prescribed sedatives and nitro-bodies "in order to allay the spasm, and to bring the disorderly circulation of the blood back again to order." In course of time this "vehement agitation" was termed high blood pressure (22).

The separation of primary essential hypertension from primary bilateral kidney disease was first achieved by a group of London clinicians. In 1874 Frederique Mohamed described the "prealbuminuric stage" of kidney disease. He proves that elevation of the blood pressure may be present without clinical evidence of kidney involvement. He observed that elevation of blood pressure often precedes the appearance of albumin in the urine, and observation only recently confirmed by Kylin (1926). He suggested, therefore, that the vascular condition caused the albuminuria rather than that the albuminuria caused the vascular condition. On account of this deviation his work had little influence on the conception of the nature of hypertension entertained at the time.

The value of the general significance of elevated blood pressure is adequately expressed by Mohamed when he says: "The occasional appearance of sugar in the urine does not prove the existence of diabetes, nor does the presence of albumin on one occasion indicate nephritis. But as the constant occurrence of sugar and albumin in the urine may safely be assumed as proof of the presence of disease, so also the persistence of high pressure in the arterial system may be regarded as a fair indication of
what we may expect to follow.......

All of which is a very modern statement considering that we can say but little more today about hypertension than Mohamed did in the above statement (31).

Soon after Mohamed, Samuel v. Basch of Vienna, in 1887, brought out more significant observations. v. Basch claimed there was no relationship between arterial and venous pressure in circulatory failure, in opposition to Traube. He also observed that severe circulatory failure may be present both with normal and with elevated blood pressure. v. Basch also suspected that failure of the circulation occurred in a group of conditions with different mechanisms, but similar symptomatically; this concept is still unappreciated by many investigators today. He definitely stated that in arteriosclerosis the arterial blood pressure is very high. He urged routine blood pressure readings on all patients.

With the introduction of the sphygmomanometer into clinical medicine by von Basch, recognition of the type of case now termed essential hypertension was inevitable. Indeed, von Basch himself, who made over 100,00 blood pressure estimations, was very well acquainted with our present essential hypertension, which he termed "latent arteriosclerosis". In 1893, he wrote observations which he had been making for many years. "There are numerous cases in which examination reveals a high tension of the pulse, but the other characteristics of out-spoken arteriosclerosis are either absent or but minimal." von Basch viewed the stage of isolated hypertension as a precursor of arterio-
sclerosis; hence his term latent arteriosclerosis. (57).

With the morphological contributions of Gull and Sutton and the clinical observations of Mohamed and v. Basch, the foundations of the understanding of primary arterial hypertension were laid. Sir Clifford Allbutt (1895) in England, Huchard (1899) in France, and Pal (1905) in Vienna did much to urge the profession to a realization of the enormous frequency of preternaturally high blood pressure in the absence of clinically significant morphological changes in the kidneys and arteries.

Allbutt arrived at a recognition of the occurrence of isolated hypertension through following patients with increased arterial tension over periods of many years. He mentions in particular one lady with high blood pressure whom he watched for 18 years, but "years passed on and the dreaded Brights disease never appeared" until she finally died of cerebral hemorrhage. Allbutt named such cases hyperpiesia, after the predominant symptom and brought order into the previously confused hypertension - kidney disease - arteriosclerotic group by differentiating:

1. Hyperpiesia, in which high blood pressure dominates the clinical picture with little renal involvement.
2. Brights Disease, the true renal disease, with or without high blood pressure.
3. Decrescent arteriosclerosis, the senile atheroma of the large arteries, not necessarily associated with high blood pressure.

Almost simultaneously with Allbutt, Huchard recognized the frequency of non-nephritic hypertension. He wrote: "arterial
hypertension is the cause of arteriosclerosis; it precedes by a longer or shorter time the evolution of the various diseases (arterial cardiopathies and nephritides) which are themselves dependant on the vascular sclerosis." To emphasize the fact that the hypertension antedates the sclerotic changes in the vessels and kidney, he termed the condition "presclerosis".

Gradually, the relationship between the degenerative diseases of the larger and smaller arteries of various organs and certain clinical manifestations became recognized. Thus a closer relationship was found between high blood pressure, cerebral accident, angina pectoris, coronary occlusion and secondary kidney involvement. Sawada (1904) found normal blood pressure readings in arteriosclerotic cases. This, together with previous observations, once more focused attention on the problems of the relationship between arteriosclerosis of the large and small vessels and hypertension. The etiologic relationship between the vascular and kidney pathology was extensively re-investigated with not always uniform results, (31).

In this country the disease was first extensively studied by Janeway, and since by Moschowitz, Christian, O'Hare, Keith, Wagener and Kernohan, Bell and Clawson and many others. Recently the studies of Volhard and Fahr (1914) have partially clarified the situation (31).

At present this disease, the pre-albuminuric stage of chronic Brights disease of Mohamed, the latent arteriosclerosis of von Basch, the hyperpiesia of Allbutt, the pre-sclerosis of Huchard, the hypertensive cardiovascular disease of Janeway, the
benign and malignant sclerosis of Volhard and Fahr - is most widely known in this country as essential hypertension, a term introduced by Frank (essentielle Hypertonie, really essential hypertonia). All that the term essential hypertension means is non-nephritic hypertension - absence of primary renal disease (57).

Few diseases strike more terror to lay people than does heart disease. And rightly it should. The menace of heart disease with hypertension and its subsequent threat of cardiac failure is increasing. Of all diseases, those in the group entitled cardiovascular-renal are the greatest cause of death today, it being estimated that approximately 140,000 deaths annually are attributable to such vascular disease in the United States alone. A study of the literature indicates roughly that the incidence of hypertension in the general population is about 40 per cent (71). The incidence of hyperpiesis has been calculated to be about 7.2 per cent in adult white American males, according to Stieglitz (58). Department of Hygiene, Harvard University, found 10 per cent of 3,598 cases with systolic blood pressure of 140 mm. (74). Fifteen per cent of deaths in persons over 50 years of age are due to primary hypertension (44). 23 per cent of deaths in persons past 50 are due to hypertension believes Johnson (63). Ten per cent of total deaths in United States are due to consequences of high blood pressure (49). Eighty-five per cent of
oases of apoplexy are associated with hypertension, say Bell and Clawson (44). The Nebraska Department of Health records in its vital statistics that the incidence of apoplexy in 1928 was 86.2 per 100,000 population and that the 1932 figure has reached 93.3 — an increase of 7.1 in four years. As a cause of death heart disease has assumed greater and greater proportions in this part of the world until now it leads all other causes, having far outstripped tuberculosis, pneumonia, and malignant disease, the other three most common fatal diseases (56).

The high incidence of the condition in the United States and its apparent relation to our high-powered type of life has prompted some writers to term this the "American disease". Competition and abnormal strivings will accelerate the mechanism of hypertension in any race (37). Waller states, "Hypertension is not only a disease of the individual — it is a disease of American life; it is reflected in the tension under which every individual in America lives. Unlike the European, who, when he has enough for a comfortable living, retires to a life of leisure, the American, when he becomes rich, wants to become richer, and in doing so, in many instances, shortens his expectation of life" (18). That the modern pace merely hastens hypertension, if at all, is King's conclusion (3).

Hypertension selects its quota from the intellectual group of the community — professional men, business executives, and others whose loss is keenly felt, suffering most. The stricken individual is often taken suddenly from his life activity at the most productive and valuable period of his career (63).
Apparently the incidence of arterial hypertension is increasing, according to Stieglitz, in recent years, perhaps because of the increased tension and pace of modern life and partly because of the prolongation of the average span of life through prophylaxis and more adequate therapy in earlier years (58). This span of life is said to have been greatly lengthened - nearly 15 years since 1880, and is due and only due, says Waller, to a decrease in infant mortality and a saving of child life and not with the saving of adult life. It is highly probable that it has been shortened and that is the price of success among Americans (18).

Relatively speaking, for as many names for hypertension in the literature, there are as many different classifications of hypertension; for every new aspect presented to the profession, there are two classifications to represent it. And it appears that not until the key to this subject is found will there be uniformity of agreement on classification. Perhaps the fault lies not so much in disagreement as it does in lack of unified understanding of terms applied to this condition. But until the question of etiology is settled there seems no solution, for today every classification and every concept is as good as another, although deduction causes us to favor one or another.

"To classify cases of disease according to their pathologic agent or process, and not by solely naming the region affected or the function disturbed, is the ideal of scientific
progress in medicine", says Cabot (56). The following are a few of many classifications - some fulfilling in a way Cabot's ideal and others less so.

Marshall, Belfast, Ireland, divides hypertension into eight classes. The first is the hypertension of arteriovenous aneurysm; the second that associated with congenital stenosis of the aorta. Third, is the hypertension that occurs in hyperthyroidism, which disappears often with removal of a portion of the over-active thyroid gland. Fourth, is the very interesting condition, paroxysmal hypertension that has come to the notice both of pathologists and of clinicians within the last few years. This type is limited to those cases in which tumors were found in the region of the suprarenal gland. Fifth, is the hypertension that is associated with eclampsia or the acute glomerulonephritis of pregnancy. Then comes the subdivided group which Allbutt particularly stressed, essential hypertension. The subsidiary types are called benign, severe benign or early malignant and malignant (20).

Halls-Dally of London contends that "High blood pressure naturally falls into four main clinical groups:

1. The simple high arterial pressure without symptoms.
2. High arterial pressure due to arterial spasm (modern pace etiology and may develop into arteriosclerosis).
3. High arterial pressure in association with thickening of arteries and enlargement of the heart.
4. High arterial pressure in association with kidney disease (from retention with chronic Bright's disease)." (14). Stieglitz of Chicago classifies hypertension into (1) those
in which the arterial disease is yet young, angiospasm being the causative agent of increased peripheral resistance and the blood pressure is found to be variable and reducible and (2) those of long standing with arteriolar sclerosis and a rigid blood pressure. Hypertension with nephritis, to Stieglitz, is a separate clinical picture; it is a hypertension with complications (this is not by any means universally accepted). (58).

According to Riesman of Philadelphia, the most important clinical types of hypertension are: (1) Accidental hypertension - This accompanies aortic insufficiency, heart block, some cases of hyperthyroidism and is more or less normal in these conditions. (2) Nephritic hypertension - In this the hypertension is intimately connected with disease of the kidney and is apparently secondary to it; a rather compensatory mechanism. (3) Arteriosclerotic hypertension - This seems to start as a spastic arteriolar process which eventually passes into the stage of sclerosis and in many respects is like nephritic hypertension but does not have early renal involvement. (4) Essential hypertension - This is the "unknown quantity" which is the cause of the renal involvement. Riesman disagrees with Fishberg's view (57) that essential hypertension is a primary disease of the kidney with arteriolitis and that therefore, essential hypertension is a form of nephritic hypertension (25).

Backer of Yale declares "hypertension is elevation of blood pressure above the normal level. There are three types: (a) Transitory or acute, resulting from emotional disturbances with an excessive response. There is said to be a vasomotor instability which may lead to a permanent hypertension.
(b) Intermittent or fluctuating, which is most frequently observed in women at the menopause. Recovery is usual, although, some authors believe it may become permanent. (c) Permanent or chronic, in which a repeated finding of high blood pressure readings is necessary before the diagnosis can be made on this observation alone. "(22).

Stieglitz of Chicago presents an "emotional hypertension" which in his previous grouping (58) would be classed as an early, angiospastic type. "It has long been known that emotional stimuli cause variations in the arterial tension. These variations are encountered both with conscious and subconscious emotional changes. When sleep is restless and disturbed by dreams, extraordinary elevations in arterial tension have been recorded (Mac William 1923)." (30).

Janeway states "The most prominent symptoms associated with high blood pressure are circulatory rather than renal. The disease underlying high arterial pressure is best designated hypertensive cardiovascular disease, either primary or secondary when preceded by an inflammatory nephritis." (8).

Fineberg of New York has grouped hypertension into the following categories etiologically: (1) hypertension associated with glomerulonephritis, (2) essential hypertension, a makeshift inclusive class into which all baffling cases are thrown and (3) hypertension associated with various disease conditions such as Graves disease, myxedema, adrenal tumors, valvular heart disease and arteriovenous aneurysm.

Clinically, however, one may group patients with high blood pressure into those with systolic and those with diastolic
hypertension. Under the latter, with the systolic up too, may be classed the nephritic, essential, myxedema and adrenal tumor types. Under the systolic group with low diastolic blood pressure, are types associated with aortic insufficiency, Graves disease, arteriovenous aneurysm (the increase being due to increased systolic ejection) and complete heart block (increase being due to long diastole whereby the vascular bed empties and the ventricles adequately refill); there is also a large unexplained group included of elderly patients with benign cases and running a prolonged course - sclerosis of the aorta and the large vessels at autopsy is a probable factor in the etiology (29).

Hines of the Mayo Clinic, a recent observer, presents the following classification of hypertension:

Primary or Essential Hypertension

1. Preorganic, functional
2. Organic, benign, intermediate forms, malignant

Secondary forms of Hypertension

1. Glomerular nephritis and toxemia of pregnancy
2. Arteriosclerosis
3. Aortic heart disease and arteriovenous fistula
4. Coarctation of the aorta
5. Tumors of chromaffin tissue; paroxysmal forms
6. Hyperthyroidism
7. Intracranial lesions (37).

Blackford and Wilkinson of Seattle have formulated a very concise, all inclusive classification which includes the following: (1) physiologic, (2) circulatory defects, (3) par-
oxysmal hypertension, (4) toxic, (5) renal, (6) neurogenous vasospasm. According to Cabot (56), this classification nears the ideal but it would seem that (3) and (6) are apt to be considered as duplicates (64).

The designating of "essential hypertension" as a "makeshift waste-paper" group by Fineberg of New York (29), would indicate it to be an easy means for a physician to shirk searching diligently for the etiologic cause of a case of hypertension. This group should include only those cases which have no apparent etiology and then and only then is the group of value.

Merely the nomenclature of this condition "essential hypertension" indicates its depths. The bulk of the literature on hypertension is on the etiology of essential hypertension, inspite of which the question is still unsettled.

For a clinical classification of essential hypertension, McCloound of Minneapolis holds the following as practical:

1. benign (mild) shows diastolic under 115 mm.; no impairment of heart or kidneys.

2. severe benign - the diastolic is over 115 mm. with evidences of impairment of vital organs and often with changes in the retina.

3. malignant hypertension - the diastolic is 130 to 150 mm. or higher, perhaps with marked impairment of vital organs with special changes in the retina and retinal vessels.

Insurance companies would class all three as decidedly malignant (13).
DuBois of Portland states that "hypertension is divided into "essential" and malignant - they are probably one and the same process, the so-called malignant form being a rapid form of the same pathologic picture which occurs in essential hypertension. It is a late phase of essential hypertension ending in uremia; it is essential hypertension with renal failure." (48).

Keith of Rochester in 1927, antedating McCloud some three years, classes this condition as mild or benign, severe or malignant, and adds a term "severe benign" as a division of this malignant type of hypertension; McCloud has made only minor changes in this. (45).

Fishberg of New York declares the malignant phase of essential hypertension designates cases characterized anatomically by presence of necrosis and endarteritis of renal arterioles and clinically by acutely progressive renal insufficiency (57).

The term hereditary hypertension is suggested by Glomset for the disease which now generally is known as essential hypertension. He found a very high percentage of hereditary factors in the etiology of this condition (24).

All cases of essential hypertension are potentially malignant, according to Yater, in that death will occur from the effects of hypertension if the patient does not succumb to some other pathological condition earlier. The terms benign and malignant as applied to essential hypertension should, therefore, be abandoned. Cases of essential hypertension may better be designated as cardiac form, cerebral form, renal form,
combined form or generalized form, according to the manner of failure. This is a most simple manner of handling cases of essential hypertension (17).

It is suggested by Rice that the simple words "temporary" and "persistant", when properly qualified will cover the entire field of this disease and that the word "malignant" is misleading to many. The word has frequently been given to a terminal condition with widespread pathology which, itself, may cause the hypertension and the blood pressure may be nothing more than a small measurable part of the whole (1).

Smith divides essential hypertension into five groups:

1. The initial stage which is a type of constitutional hypertonic reaction. The blood pressure is not much above normal.

2. The primary stage is the beginning of labile hypertension, with the blood pressure varying between 150 to 200 mm. Hg. Frequently the blood pressure will return to normal (which is consistent with Ayman (41)). Subjective symptoms are in evidence.

3. Secondary stage - blood pressure ranges between 180 to 200 mm. Hg. - normalcy is never attained; patient is seriously ill.

4. Tertiary stage - the blood pressure is found constantly between 200 to 220 mm. Hg. - there is practically no fluctuation; cardio-vascular-renal pathology becomes apparent.

5. Final stage - A. arteriosclerosis markedly affecting
cerebral and coronary arteries with apoplexy and angina attacks.

B. arteriosclerosis involving the kidneys with insufficiency and uremia.

C. myocardial degeneration with decompensation. (75).

Repeating, since very few have the same conception of essential hypertension and its definite pathology, one might infer that disagreement lies in many names rather than the disease.

Concerning the incidence of this condition, Donnison (1929) found practically no hypertension among the aboriginal African negroes but the succeeding generations of American negroes have hypertension in more severe form than members of the white race. There is a low incidence of hypertension among the Chinese. The higher classes of Orientals have hypertension in degrees comparable to Occidentals (37). In contradistinction, Cadbury (1922) comments upon the rareness of hypertension among the Chinese, although chronic nephritis is very common. Also, DuBois states that "the Oriental living under our conditions in the United States can develop hypertension as well as his white neighbor - contradicting Harris and still others (48).

The age limits of this disease do not appear to be
definite; extremes of the life span have been included, but the majority of evidence would generally indicate middle life. 90.6 per cent of cases are over 40 years, 74.3 per cent are over 50 years of age at time of death (44). It affects especially individuals of 40 to 50 and 50 to 60 years; exceptionally it is found between the ages of 20 and 25, says Kylin (79). In 81 cases of malignant hypertension, it is evident to Marshall that the condition is not a disease of old age; it is a disease of youth and middle age. Patients as young as eight years of age are known but the majority are between 30 and 50 years (20). Stieglitz contends hypertension is a disorder occurring far more frequently in middle and later life (58). Briscoe believes essential hypertension occurs about the time of middle age or older, in persons who have lived not wisely, perhaps, but too well (28). The maximum incidence appears between 50 and 70 years states Bell (44). The average age of manifest cases was 49 years according to Cabot (60). Of 327 cases studied over a period from 5 to 10 years, the average age of this group is now 61 years and only 30 have died - 9.2 per cent, seven of which had no relation to blood pressure (30).

Blackford found hypertension two times as frequently in women and one half of them are without symptoms; hypertension in men is usually accompanied with symptoms (64). Bell found hypertension in males 3.2 per cent more than women (44). "Males in active cases are 12 to 5 over women, in latent cases it is 14 to 5" (60). The preponderance of men with high blood pressure over women is 15.8 per cent says Janeway (8).
Nephritic hypertension is more common in the male and begins in rather early life, about the age of 30, according to Raab (23). Before the age of 20, the percentage of occurrence is higher in men than women; it is equal in the fourth decade; after 40 there is a decided rise in frequency in women, presumably associated with menopause. Hypertension follows more slowly in men but at 60, the distribution is again about equal between the sexes (Gager) (3).

Recognizing the fact that there are cases of this condition in the young adult, why is it? He has not had time to work hard, to lead a life of strain. And why the few signs? Although there seems no adequate answer, it is a fact that the young adult is going through a period of adjustment, a period not without strain and worry.

Hypertension is no more than a symptom and occurs, for more than a transitory period, in the following conditions:

1. Essential hypertension. This is the most common disease characterized by hypertension.
2. Diffuse glomerulo-nephritis in all its stages.
3. Urinary obstruction, prostatic enlargement, bilateral calculus disease, etc.
4. Toxemia of pregnancy.
5. Lead poisoning.
6. Increased intracranial tension in brain tumors.
7. Polycystic kidneys.
8. Rarely in amyloid contracted kidneys; as a rule these have no hypertension.
9. In some cases of protracted anuria or severe oliguria due
to mercurial or other necrotizing nephroses.

10. In rare instances of tumors of either the cortex or medulla of the suprarenal gland.

11. In certain other endocrine disturbances, notably ovarian hypofunction and diseases of the thyroid gland. The nature of these cases is much disputed.

12. Periarteritis nodosa involving the renal vessels.

13. Very rarely as a result of widespread destruction of the renal parenchyma by suppurative disease.

14. In the so-called Gaisboeck type of polycythemia, though it seems these are coincidental cases of essential hypertension, and polycythemia vera, or secondary erythrocytosis due to emphysema or cardiac insufficiency.

15. In some instances of depressive psychoses.

16. In coarctation of the aorta there may be hypertension in the upper extremities with normal pressure in the lower extremities.

The beginning of all hypertension must be due to arterial spasm, whether it is produced by environmental stimulation, acute toxins, physiological disorders, or psychic disturbances, and a considerable number of people in every community will respond to these various stimuli more readily and more profoundly than the others. During the first four or five years of these reactions, the hypertension may be "temporary" and small injuries to the vascular system may, or do, disappear, but finally the majority follow their destinies and the repeated stresses, infections, the menopause, years of national depression, and wider
and wider oscillations of the hourly and daily changes in arterial tension finally produce widespread vascular changes that make certain a "persistent" hypertension. Any temporary hypertension may become permanent or persistent if any one of a 100 emotional, economic or physical stresses cannot be removed or relieved during the years. An easy analysis of the individual with a single word or two that states the background which produces the hypertension, would effectively remove the criticism that our "ignorance in the fields of blood pressure is profound". Temporary hypertension is a symptom of a tense and intense nervous system, and does not produce dizziness, flushing, neck-ache, palpitation, insomnia or indigestion, but is a minor symptom of a complex, and unless the physician can spare a few minutes to exercise his judgement, the sphygmomanometer should be set aside and the blood pressure disregarded (1).

An increase of blood pressure above the normal upper limits is common and is called hypertension. Before we can consider, however, such hypertension as pathological, if it is slight in degree, we must rule out physiological effects. Exertion and excitement, either alone or more effectively in combination, can cause an appreciable increase of systolic pressure above the normal, in large part through sympathetic nerve action on the circulation. At the heighth of vigorous exertion, the systolic blood pressure may be as high as 180 to 200 mm. of Hg., and even so great a rise as 120 mm., from 140 to 260 mm., has been recorded. Excitement alone has much less marked effect than exertion, but it always has to be taken into consideration; for
example, in physical examinations for insurance, for admissions into services like the army, or for important appointments, excitement may result in a temporary elevation of from 20 to 50 mm., as from 130 to 160 mm. or even more. Local anesthesia for surgical operations often raises the blood pressure, probably through this factor of nervous excitement. Pain may also send the pressure up, attacks of gout, lead colic, or other severe paroxysmal attacks of pain, have been noted to cause temporary increase in systolic blood pressure of as much as 50 to 100 mm. The Valsalva experiment (attempt at forceful expiration with the glottis closed) also raises the blood pressure (systolic) even to 180 mm. of Hg. for a few beats, but with a sharp fall immediately afterwards. The diastolic pressure is influenced either physiologically or pathologically, as a rule, far less than is the systolic pressure. There is, as a matter of fact, a tendency in exercise for the diastolic pressure to fall, thus increasing quite markedly the pulse pressure along with the total circulation to meet the needs of the increased metabolism. With marked rise of systolic pressure and little change in diastolic pressure, as a result of exercise, the pulse pressure may approach 100 mm. and has been known to exceed 150 mm. of Hg.

The systolic blood pressure in essential hypertension varies from 150 mm. of Hg. to 300 mm. or slightly more, and the diastolic pressure, lagging along behind, but also elevated, varies from 95 to 180 mm., although usually much nearer the first figure. Common readings in essential hypertension are 220 systolic and 120 diastolic. The increase in pressure that may occur with exertion, excitement, and other such factors, is generally much
more marked in cases of essential hypertension than in normal people. Also, spontaneous temporary variations of 50 mm. or more may occur in such cases, making it necessary sometimes to test the blood pressure repeatedly at several different times in order to establish the usual hypertensive levels for these patients. (56).

Cabot says "Emotion of every kind has long been recognized as having an important influence on the heart's action and functions, and is a factor we dare not neglect in investigating the etiology of heart disease, and especially of sudden cardiac failure.... There are few of us who have not had occasion to note the development of serious cardiac symptoms from the trouble arising out of untoward domestic affairs, the worry of an unsuccessful business, or even the wear and tear of a too successful business which has outgrown the physical powers of its manager" (60).

Briscoe contends that an extreme instability of arterial tone with responses in fluctuations of 50 mm. or more can no longer be considered physiologic; it becomes a potential hypertensive phenomenon (28).

Transient hypertension (emotional tachycardia) was known to Balfour who describes a case of his, a clergyman, who was in perfect health with no apparent disease, marked arteriosclerosis, or effects of disease; he was temperate and negative familiarily. This was not a "paroxysmal tachycardia", as recognized in those days; it lasted for years. Quoting Balfour, "This case is instructive as showing, in the first place, how efficient a cause of cardiac enlargement the mere natural loss of arterial elasticity
is, even in those who are perfectly healthy and temperate" (60).

The clinical picture of hypertension is relatively clear cut. Irrespective of etiology, this "cardio-vascular-renal" syndrome, in any one of its forms, offers no special difficulties, generally, in diagnosis; the results of the disease are usually quite apparent, it is the causative agent underlying the disease that prevents a complete understanding. To warrant this term hypertension, the increase in pressure must be permanent, and 160 mm. of Hg. may be taken as an arbitrary figure for the minimum of hypertension, believes Osler (83). Many authorities use 140 mm. as the minimum level.

Hypertension may persist from a few to twenty years with few symptoms, but finally, if neither cerebral nor kidney complications develope, the heart symptoms appear. The onset is insidious. Breathlessness and slight tachycardia are early signs of a cardiac embarrassment. Nocturnal dyspnea occurs later - awaking the patient with severe sudden dyspnea; this is typical of the hypertensive heart. Anginal attacks are common and may cause death insidiously. Frank pulmonary bleeding is seen and often it is nasal or from the gastro-intestinal tract; this is a serious form of hypertension by many writers. Later the right heart fails and typical cardiac decompensation ensues with congestion and some lowering of blood pressure (34).

According to Briscoe, nervousness, irritability and easy fatiguability and headaches are among the earliest signs of this
syndrome (cardio-renal). Precordial distress and dyspnea on exercise may be preeminent. The systolic blood pressure is commonly 250 mm. of Hg. The higher the diastolic pressure the greater the work thrown on the heart due to loss of normal elasticity and efficiency of the arteries and the worse the prognosis. The heart becomes hypertrophied and in any case, sooner or later, evidences of cardiac defeat appear if the patient survives the other complications of a disturbed circulation. Edema and ascites may be looked for. Dilatation of the aorta is almost invariable. In only 10 per cent of cases is true chronic nephritis present with hypertension and arteriosclerosis which must be differentiated from the hypertensive type of sclerosis - so-called essential hypertension. This may appear to be a distinction without a difference and indeed, it is claimed by some that all nephritis is vascular in origin, but it must be admitted that the clinical course of the two is quite different (28).

Symptoms are merely the manifestation of local circulatory failure, points out Stieglitz; the symptomatology is divisible into 3 groups: those symptoms resulting from cardio-circulatory failure, from malcirculation of the central nervous system and those dependent upon renal inadequacy (58). Ziskin believes that headache is the first sign (pressure 160 to 180 mm.), then palpitation and dyspnea (51). Cabot (60) maintains that hypertensive heart disease in its earlier and milder stages may last for years without producing any considerable discomforts or limitations of the individual's activities.

Osler states that what may be termed "hypertension hypochondriasis" is common; the patients suffer more from knowing

- 33 -
that hypertension is present than from the hypertension itself. They study their blood pressure figures as some do those of the stock market (83).

The physical signs of hypertension were described first and in a classical manner by Traube (1870) and are as follows:

1. A hard pulse which offers great resistance to compression and was compared by older clinicians to a taut iron wire. It is important that hardening of the vessel wall due to arteriosclerosis should not be confused with increased intra-arterial tension; the two phenomena have no obligate connection with one another. Despite high arterial tension the pulse may be very small as a result of hypertonicity of the arterial wall. The pulse tracing has a gradual ascent, a rounded or flattened apex, and a downstroke in which the dicrotic notch is either absent or situated very high; quite often the pulse is anacrotic.

2. Evidence of left ventricular hypertrophy in the absence of valvular disease. Before notable dilatation has taken place, recognition of this condition is difficult and often impossible. Nevertheless, one is rarely in error in assuming the presence of such hypertrophy if hypertension has been present for some time.

3. Accentuation of the second sound over the aortic area. The sound is loud, often ringing in quality and may be reduplicated. It is by no means constant in all cases; lack of accentuation may be due to emphysema or obesity.
or may not be so obvious (57).

Granger (33) states, "essential hypertension is a condition characterized by a persistant systolic blood pressure of 145 mm. of Hg. or over, and a left ventricular hypertrophy without demonstrable cause, though, the hypertension may exist in the early stages without cardiac enlargement." DuBois (48) says essential hypertension is a symptom and includes all chronic hypertension, which neither clinically nor anatomically can be demonstrated to have arisen from previous inflammatory disease of the kidney, or urinary obstruction. "Malignant hypertension" is a rapid general deterioration with early death, a form differing only in degree of severity from the usual syndrome of hypertension, according to Balfour (61). Johnson, the intestinal toxemia theorist, presents a toxemic syndrome which includes headache, malaise, nervousness, nausea, and bad taste in mouth; the signs are coated tongue, foul breath, muddy pallor to skin, slight icteric tint to sclera and sticky perspiration (63).

Ayman of Boston believes there is a personality type of patient with essential hypertension. These patients react more frequently and intensely to emotional and physical stimuli than do comparatively healthy people. They are high strung, quick tempered and unusually sensitive. They lead active lives in any thing they undertake to do. "The middle aged hypertensive patient says he has been that type as long as he can remember." The psychoneurotic individual's picture is of short duration, although similar, lasting as long as the existance of the emotional upset, while hypertensive picture is of life long
duration. The neurasthenic is not physically hyperactive, only emotionally. The presence of such a picture should indicate prophylactic measures of treatment according to Ayman (10). Moschcowitz describes a "type patient" - the antithesis of the "child" in makeup and temperament, a combination of psychic and physical characters in whom hypertension is apt to occur. Our present civilization does much to precipitate the picture. (53).

Briscoe differentiates essential hypertension and chronic nephritis with hypertension as follows: "The onset of essential hypertension is insidious, frontal headaches, and slight dyspnea. The patient looks well, color is good, is usually over weight, blood pressure is raised, especially the diastolic. The heart is hypertrophied. Urine may be normal. The course runs 15 or more years and death occurs by cerebral hemorrhage, cardiac failure or rarely uremia."

The chronic nephritic with hypertension is usually 10 or more years younger and looks ill, anemic and cachetic. The urine is of low specific gravity and may or not contain albumin. There is a morbid disturbance of kidney function shown by a lowered phthalein output and often retention of nitrogen. The duration is shorter, death occurs in uremia 3 to 5 years after onset. "It is common to see a man well past seventy with hard, beaded, tortuous arteries who shows little evidence of mental or physical decay. If such changes occur before middle age, the life expectancy is much reduced." (28)

The average length of life after the first symptom according to Millet is 3.2 years (49).
The presence of a raised diastolic pressure is not only indicative generally of an essential hypertension, but is indicative of bad prognosis and amount of sclerosis in arterioles. Says Bain (19), "hyperpiesia is a malady in which there is a raising of both systolic and diastolic blood pressures. The pressures must be sustained and in the diagnosis, the diastolic is the more important." A sustained systolic of 150 and 90 diastolic should be regarded as potential hyperpiesia. Should true hyperpiesia develope both pressures will tend to rise progressively (19). Stone believes diastolic is less influenced by factors which disturb the systolic pressure such as exercise, emotion, fear or digestion and if above 100, signifies essential hypertension irrespective of the systolic (59). Granger believes the diastolic of great importance in diagnosis (33). Stieglitz is of the same opinion, as is McCloud (13).

However, Sawada (1904) found normal blood pressure readings in arteriosclerotic cases. Ayman makes the paradoxical statement that the disease may exist with normal blood pressure, and he found it so in 56 percent of a series of unselected cases. A five to twenty minute rest period before taking pressure readings eliminates such factors as excitement, emotion, and exercise, which lead to false readings at the beginning of an examination (41). Janeway puts no belief in the fact that conclusions can be drawn from the height of the blood pressure. He saw cases with extraordinary high pressures live for 6 years, and others with moderate elevation die in a much shorter time (18).
Marshall found as much variation in diastolic as systolic pressure readings; he took diastolic readings at the change of sounds (20).

Retinal artery changes are one of the best means we have of obtaining information concerning degree of sclerosis of arterioles; it is prognostic as well as diagnostic in many cases.

Cowin (15) says retinal arteriosclerosis is of two types clinically - hypertensive and senile types. The characteristics of the former are general constriction of the calibre of the artery with exaggeration of the arterial reflex stripe, irregularities in the lumen of the arteries and arteriovenous congestion. The retinitis of severe benign hypertension is known by scattered cotton-wool patches and hemorrhages, mild generalized edema of the retina in which, late, may appear punctate white exudates. In the retinitis of malignant hypertension, there is added to this picture an edema of the disc (15).

Retinal changes were normal in 50 per cent with no cases of hemorrhage or exudate says Marshall, contradicting Keith who believes papilloedema to be the striking feature of all cases (20). Keith (45) avers retinal changes indicate a bad prognosis in spite of the patients relatively active life and apparent well-being. Ziskin (51) says eye-ground studies give earliest and most direct information regarding the hypertensive process - he had 37 per cent positive findings.
Essential hypertension is marked by a decreased carbohydrate metabolism, and subnormal lime values, increased cholesterol values and increase of the uric acid values in the blood. The leukocyte picture shows slight changes as observed in inner secretory disturbances. The mononuclear cells are increased. There is often a slight eosinophilia. The adrenaline blood pressure reaction in essential hypertension shows a vagotonic type after intravenous as well as subcutaneous application of the adrenaline according to Kylin (79). The electrocardiograms were largely normal with no great left ventricular predominance as expected (20).

Diagnosis depends on history or presence of hypertension, cardiac enlargement to the left, the characteristic "sock" shaped x-ray shadows, systolic apical murmurs, gallop rhythm, E.K.G. with inverted T wave in leads one and two, or left ventricular preponderance, retinal arteriosclerosis, evidence of kidney damage with fixed specific gravity of urine or retention of non-proteid Nitrogen in blood (34).

In toxemia of pregnancy which commonly causes aggravation of symptoms of primary hypertension, one must consider by way of differential diagnosis that toxemia of pregnancy does not cause cardiac hypertrophy, that sclerosis of retinal arteries indicates primary hypertension, that in a simple toxemia of pregnancy, the blood pressure returns to normal within one month after the uterus is emptied and that an uncomplicated toxemia of pregnancy seldom causes renal insufficiency. (44).
The prognosis in temporary hypertension is favorable, and in persistent hypertension it is better than in most of the other incurable diseases says Rice (1).

Says Clifford Allbutt, "High blood pressure is an attempt of the organism to maintain the equilibrium of its circulation". The conclusion to be drawn from such a statement is that it is worse than useless to lower the blood pressure in these cases unless one can at the same time remove the cause (27).

It might be well at this point to mention the work of Brown, Hines, Briggs and others on the reactability of persons to cold stimulus (38) (54) (67), as a means of classifying and even foretelling hypertension.

There was found to be a definite response in systolic and diastolic blood pressures to local application of stimuli - systolic 8.9 mm. of Hg. rise, diastolic 7.5 mm. in normal individuals. Those with hypertensive family histories showed 30.1 mm. systolic and 21.1 mm. diastolic; early essential hypertension showed 32.0 mm. systolic and 21.4 diastolic; essential hypertension with organic changes showed 38.4 mm. and 22.5 mm. Arteriosclerosis without hypertension showed 13.1 and 10.8, while with hypertension advanced to 29.1 and 16.0.

"It remains to be proved whether those without hypertension but who have exaggerated responses will develop hypertension ultimately." (38). This should be of benefit to insurance companies. 75 per cent of these hyperreactors have
a positive family history for hypertension or apoplectic death and at least 98 per cent of subjects with essential hypertension have hyperreactive responses (54).

The morbidity and immediate causes of death in this condition are rather constant. The term "hypertensive heart disease" expresses the belief that almost all of the enlarged hearts not due to valvular disease or pericardial adhesions, develops as an organic response to vascular hypertension, however produced, whether nephritis, arteriosclerosis, or what not. These cases are three times as frequent as rheumatic valve lesions whether manifest or latent. When manifest the ratio is reduced to 2 to 1 (60). Complication most met with - myocardial insufficiency (49). Steiglitz is of the same opinion. The knowledge of hypertension of any considerable duration is a priori evidence of myocardial injury (61). Stone claims any sustained high diastolic pressure ends usually in cerebral hemorrhage or myocardial defeat (59). A sudden drop of as much as 60 mm. in systolic pressure should indicate an unsuspected coronary catastrophe, says Marshall (20). Apoplexy constitutes the most dramatic and startling complication of vascular disease (58). Through continuation of the wear and tear upon a struggling heart, if there is no reduction in the diastolic pressure or peripheral resistance, complete
exhaustion supervenes and the classical clinical picture of acute cardiac decompensation ensues (58). Balfour makes a similar statement. Quoting from McMullen (34), "The left ventricle bears the load with the prolonged hypertension and of necessity increases in size of chamber and the muscular wall increases in thickness. The weight, 400 to 750 grams, is contrasted with 250 grams, the normal weight.

The valves appear normal and the muscle may show no changes, perhaps an occasional case with a scar or some fibrosis. Probably functional changes occur in the muscle of a metabolic and chemical nature which result in cessation of function without organic changes that we are able to recognize. It is a death due to overwork and muscle fatigue (34).

Rheumatic heart with mitral stenosis is thought by some to form a triad along with hypertension and granular kidneys (3).

Janeway (8) lists the causes of death: (1) gradual cardiac insufficiency, (2) uremic symptoms, (3) apoplexy, (4) acute infection - complicating, (5) angina pectoris, (6) unrelated causes, (7) edema of lungs - acute. In Granger's series (33), death was due to cardiac failure in 52 per cent, cerebral vascular accidents in 31 per cent, uremia in 5 per cent and intercurrent diseases in 11 per cent.

After a time the cardio-vascular system responds to the stress of these continued high pressures by structural changes, which are permanent. The heart hypertrophies and enlarges to the left, the "Coeur de Sabot" of French radiologists.
Obliterative changes take place in the arterioles; the intima hypertrophies and the lumen may become quite obstructed. This arteriolar hyperplasia affects chiefly the kidney, pancreas, spleen and suprarenals. The muscular tissue hypertrophies, the elastic tissue degenerates and fibrous tissue takes its place; this phenomenon is best seen in the retinal fields. With second stage of hyperpiesia an increased blood pressure is necessary to maintain circulation. In the third stage of the disease, the cardio-vascular system wears out, and death occurs, either by the bursting of a cerebral artery, or from failure of the circulation consequent on the exhaustion of the heart. Occasionally, without the necessary head of blood, elimination through the kidneys fails and death from coma occurs (19).

It is true that at necropsy of an individual who suffered from essential hypertension, one almost invariably encounters a triad of lesions - cardiac hypertrophy, arteriosclerosis, and certain renal changes. Investigations have indicated very strongly that each of these morphological abnormalities is a result and not a cause of hypertension. The changes in the kidney are secondary to disease of the small arteries - the so-called arteriolosclerosis which must be sharply differentiated from the arteriosclerotic kidney in which the larger vessels are damaged and is a part of a general arteriosclerosis of old individuals. This latter type - the
arteriosclerotic - very seldom causes hypertension and is of little clinical significance. Bell and Clawson found no arteriolosclerosis in 10 per cent of essential hypertension cases, Wallgren had eight cases of essential hypertension in which the renal arterioles showed no changes other than those corresponding to the age of the individuals. Kauffmann presented one case with normal kidneys and no arteriolosclerosis who was known to have had hypertension for 12 years. In the case of suprarenal tumor with great hypertension (heart wt. 880 grams) reported by Oppenheimer and Fishberg, the renal changes were minimal, and the same has been true in other similar cases in the literature.

Cases of essential hypertension without renal lesions at necropsy are decidedly exceptional. More commonly examination reveals well-marked arteriolosclerosis and foci of atrophy of the parenchyma despite the fact that macroscopically there may be no evidence of disease. Characteristically the picture is as follows: Usually the capsule is adherent, often so firmly that there is considerable laceration of the kidney substance as the capsule is stripped. In other instances, the capsule comes off readily despite the presence of contraction and granulation. If the kidney is contracted, there is an increase in the fatty capsule and the adipose tissue in the hilus. The size of the kidneys vary greatly. As a rule, however, the amount of contraction is less than in the secondary contracted kidney. The surface is granular, and slightly uneven. The general color of the surface is usually a brownish or grayish
red (red granular kidney). The kidney substance is tough and hard. The cortex is greatly thinned, and the borders between cortex and medulla are often not clearly defined. In the early stages, little atrophic areas near the surface may be the only abnormality noted. The arteries are rigid, have thickened walls, and gape. The glomerular changes are found in various stages of destruction and are a result of the arteriolosclerosis. There is a narrowing of the interlobular or afferent arteriole with hyalinization and a resulting atrophy of the tubule from that glomerulus - atrophy of disuse. The intact units hypertrophy and show signs of regeneration if the damage has not been very great.

The stage of renal insufficiency due to necrosis and endarteritis of the renal arterioles is thus merely one phase - always the terminal one, so far as we know - of those cases of essential hypertension in which it occurs. It is probably a severe variety of essential hypertension and is to be viewed as an exaggeration of the same process that is documented in the usual case of essential hypertension by arteriolosclerosis. Volhard's theory accords that the malignant phase is ushered in by occurrence of angiospasm whereby arteriosclerosis accelerates to endarteritis depending on the severity and permanence of the vascular constriction.

This phase is not of general occurrence and arteriolosclerosis is the only usual finding but if angiospasm were to be proven as the initiating factor toward the malignant phase we would still be more ignorant as we have no inkling of the
cause of angiospasm. Constitutional weakness of the arterioles as an explanation is purely a hypothesis. Not many authors agree with Fishberg findings. (57).

Much difference of opinion exists as regards, first, whether the increased resistance results from a generalized involvement of the vascular bed or not and, second, what the relation of hypertension to the kidneys may be.

It must be remembered that the kidneys contain a very peculiar and extensive vascular bed. There is an ideal system set up for the filtration of the watery contents of the blood into the urine including only two delicate layers of epithelium, one of the capillary and the other of the capsule at the head of the tubule. In the course of production of three liters of urine it has been estimated that 1000 to 1500 liters of blood pass through the kidneys a day. Such a system, through which so much blood flows with its benign and noxious contents, is unusually exposed to damage from irritating substances in the blood.

The theory behind the terminology of essential hypertension has been that this form of hypertension exists without apparent association with any known pathological state. According to the usual functional tests the renal activities seem normal in the earlier stages of hypertension, and the blood chemistry is generally normal. For these reasons it has been customary to state that the kidneys are normal until
the latter stages of hypertensive disease. Inspite of this, some clinicians have felt that it is impossible to separate accurately the cases of hypertension from those of chronic nephritis. Allen has described changes in the water and salt economy of patients with hypertension; he believes hypertension due to abnormal vascular resistance with retention of salt and water. There is a delay in water filtration as shown by the frequent occurrence of nocturia in hypertension. Whether the secretion of guanidine bases is found eventually to have a causal relation to hypertension or not, Major has shown that it is no longer safe to assume that patients with hypertension who show normal renal function by the usual tests actually have normal functioning kidneys.

Jaffe believes the mischief to begin at the glomeruli, which are probably, he thinks, thrown into repeated spasm thru the influence of irritant substances circulating in the blood. Hence the original lesion should be sought in the glomerular tufts. Lee found hypertension often associated with an atrophic kidney - increased connective tissue and disappearance of glomeruli; patients with moderate hypertension showed no lesion, while pressures exceeding 200 mm. of Hg. presented the kidney lesion. Hasenfield pointed out that small vessel sclerosis is common in the splanchnic area, whereas arteriosclerosis of the large vessels tends to involve the brain, aorta and extremities. G. Evans described "diffuse hyperplastic sclerosis" as more commonly found in the kidney than any other organ, and was found in the spleen and kidney if found in any organ. The kidney, pancreas and spleen are reported involved with marked
regularity while the other changes are quite variable. Certainly much of these changes in other structures is secondary to the hypertension itself, such as retinal arteriolar degeneration based on renal disease. Most of the evidence points to the glomeruli and the arterioles of the kidney as the initial site of the pathogenesis of hypertension: the changes in other structures, with the possible exception of the splanchnic area, are probably secondary to the hypertension.(3).

To account for the relationship between renal disease and hypertension, two theories have become prominent: (1) Retention of a toxic substance in the blood, but it must be assumed that it is held back by certain kinds of diseased kidneys and not by others; for not all kidney disease, retentions, etc. cause hypertension, (2) Reflex irritation of the vasomotor center or the sympathetic ganglions resulting in generalized increased tonus of arterioles. Theoretically, this idea is consistent with our present knowledge of the phenomenon. Obstruction in the kidney alone cannot cause hypertension, since the vascular area involved is too small. One must assume that the renal lesion in some way causes generalized increase of arteriolar tone. The simplest interpretation of this is a reflex, although it has not been proved. But the basis of the reflex must still be explained. There is always a narrowing and closure of either glomerular capillaries or arterioles or of both. There will be decreased amount of blood per unit of time to a kidney area if the blood pressure remains constant. Therefore to compensate the loss of secretory function, the
blood pressure increases to get more blood through a smaller working area in the same unit of time. The reflex nature of the process has not been proven. (44).

The still dominant tradition of the continental school avers that an abnormal function must necessarily be the result of a morphological change, so the idea that hypertension is the result of arterial and renal disease holds sway. It is becoming increasingly apparent, however, that an association of a lesion with a functional change does not always necessarily imply that this change is the result of the lesion. The lesion may represent an end-result of influences in which the functional change is the main or important factor.

Correlation of pathologic evidence and clinical data reveal striking discrepancies: 1. Hypertension was present although at post-mortem there was little evidence of arterial or vascular disease. These cases are not rare by any means, 2. Renal and vascular disease, sometimes even marked, may be present, although the patient at no time had hypertension. 3. There is no relation whatever between the grade of the hypertension and the extent and gravity of the arterial or renal lesion. These are serious obstacles to a rational explanation of hypertension on a renal or vascular basis and the problem of the cause of hypertension is once again an open issue.

Evidence is accumulating that the renal and vascular lesions are a result of the hypertension. In this conception, hypertension is not a "symptom" but the disease itself. In other words, function may not be interpreted in terms of anatomy, but reversely. (51).
Peripheral resistance is of importance in the causation of hypertension and its consequence arteriosclerosis and nephritis. In the lesser circulation, this is proved by the fact that, in cases of mitral stenosis, even in young individuals, marked arteriosclerosis of the pulmonary vessels, and arterio-capillary fibrosis of the lung are present; while the systemic arteries in cases of general vascular hypertension show arteriosclerosis, the pulmonary vessels are free. There is evidence that a congenital stenosis of the isthmus of the aorta or a congenital narrow aorta (aorta augusta) may be the cause of hypertension, arteriosclerosis and nephritis. (51).

Is renal arteriolosclerosis always present in cases of hypertension as found by Fishberg (57) in all his 72 cases? He included all arterioles and some are relatively quite large. Bell found 10.6 per cent of 368 cases did not show renal arteriolosclerosis. Sufficient studies are available to show that general arteriolosclerosis does not occur in cases of hypertension. The part of the arteriolar system that is organically narrowed is relatively small, even in the extreme cases, so that a case of hypertension cannot be explained on the purely anatomical basis of organic arteriolar disease. One must believe that increased tonicity of the arterioles is chiefly responsible for the increased peripheral resistance (44).

Sclerotic changes in the afferent arterioles of the renal glomeruli are almost pathognomonic and are the most common pathological finding contends Granger (33). Definite sclerosis of the afferent glomerular arterioles is rarely, if
ever, seen except in association with hypertension (44). It is seen that the association between hypertension and kidney disease is very definite, there being very few of the kidney conditions unattended by increase in the blood pressure. It can hardly be said, however, that kidney disease is usually the cause of hypertension. It is better to assume that the toxic agent responsible for the pathological condition in the kidney is also responsible for the arterial hypertension, is Mark's belief. (16).

The term essential hypertension as identifying a hypertensive state of the body without impairment of the kidney function cannot be rigidly applied. This is illustrated by the fact that practically all of the cases of arterial hypertension showing kidney impairment, detected by the methods used, would have been classified as "essential hypertension" in the past. There was a trend for the degree of impairment of renal reserve to parallel the height of the arterial blood pressure in Ellis's series, particularly the diastolic. There was no correlation to be made between the degree of renal damage and the age of the patients, the symptoms, or the known duration of the disease (7). On the whole the evidence seems to favor the hypothesis that hypertension causes renal arteriolosclerosis (44). Most cases of arteriosclerosis and nephritis with hypertension at some time were cases of "essential hypertension". (53).

Why such a localized reduction of the arteriolar-capillary bed should be responsible for elevation of blood pressure is a mystery and the proof of it is still forthcoming. Krehl suggests on good grounds that the hypertension and the renal vascular
changes may both result from a common unknown cause, says Foshay (77).

The conception that hypertension results from increased peripheral resistance in the vascular tree due to arteriolar narrowing is now accepted by all students of the subject. Arteriosclerosis and arteriolar thickening in hyperpiesia, although varying in degree and distribution, is as constant a finding as is cardiac hypertrophy, and in many cases dominates the pathological picture. Nevertheless, the increased peripheral resistance cannot be regarded as resulting from organic thickening of the walls of the arterioles. The absence of a true generalized arteriosclerosis, the fact that clinically hypertension precedes the arteriolar changes, the variability of the blood pressure in hypertension, and the acuteness of the onset of the condition in cases of acute nephritis and urinary obstruction constitute sufficient proof that hypertension must result from a functional vasoconstriction of the arterioles and that the arteriolar lesions are the results of the elevation of blood pressure.

Various investigators of the subject differ considerably as to the nature and distribution of the arteriolar lesions in cases of hypertension. Fishberg (57) states that arteriosclerosis has a very characteristic distribution in the various organs and divides them into three groups: (1) the kidney, which is
invariably involved to a greater extent than elsewhere; (2) the spleen, pancreas, liver and brain involved in a considerable proportion of cases; (3) the skin, skeletal muscles, myocardium, lungs, gastro-intestinal tract and thyroid, which are only rarely involved and then to an insignificant extent. On the contrary, Kernohan, Anderson, and Keith have found the arterioles in skeletal muscle uniformly involved. Several plausible reasons to explain these discrepancies occur to us. Undoubtedly, the duration and severity of the hypertension are important factors. Even more important, perhaps is the fact that all studies, with one exception, were qualitative in character, actual measurements of the vessels not being made. "We have been during this study, repeatedly struck with the inaccuracy of attempting to estimate the ratio of the thickness of the wall to the size of the lumen of the vessel without making measurements." Post-mortem material was used and post-mortem contraction cannot account for the endothelial proliferation and the increase in muscle nuclei that were found. Shrinkage affects the whole tissue and since the measurements are expressed as ratios, the end-results, theoretically, should not be disturbed. In the 15 cases, a decrease in the wall to lumen ratio was found, in each instance involving every tissue with the exception of the myocardium - the kidney, pancreas, liver, heart and spleen being used. This change, hypertrophy of the media, proliferation of the intima, and marked reduction in the ratio of wall to lumen with no actual signs of degeneration or changes similar to those of senile retrogression, accounted
for the thickening nearly entirely in the liver, to a lesser extent in the pancreas, whereas in the kidney and spleen, the degenerative changes were the prominent ones. It is plausible to assume that these findings in the arterioles of the internal organs, namely muscular hypertrophy, results either from increased intravascular tension or more likely from constantly increased tonicity of their walls. This adds support to the functional theory of the causation of hypertension (2).

Keith and Kernohan found that changes in the ratio of the lumen diameter to thickness of the arteriolar wall were apparent. In normal patients, with a biopsy of the pectoralis muscle, the ratio averaged 1 to 2. In benign cases it averages 1 to 1.4. In the malignant and severe benign or early malignant, the ratio often approached 1 to 1 (21).

It seems to be acceptable, says Rice, that the constant and usually first lesion of arterial hypertension is a sclerosis of the arterioles and that the difference is only one of degree whether the disease by early, malignant or hypertensive without hypertension. The kidneys may show the principle involvement, but the essential lesion is widespread and very soon the larger vessels will show some sclerosis. It also seems to have been proved that stiffening of the large vessels only, primarily affects the systolic pressure and that sclerosis of the small vessels permanently increases the diastolic pressure. The heart must enlarge although the hypertrophy, during the first years, is principally physiological and finally the aorta widens and becomes sclerosed (1).
Stieglitz (58) presents his conception of the changes which probably occur in the circulatory system where hypertension exists.

The vicious circle of fatigue or the perpetuating factor is represented by steps 4 - 5 - 6 - 4 - 5 etc.

The diastolic tension represents the peripheral resistance to the circulation and therefore, indirectly, is an expression of the tonus of the arterioles. Hypertension is an arteriolar disease. The systolic tension represents the diastolic resistance plus the force of the left ventricle to overcome this resistance. Therefore, in the absence of thyrotoxicosis or aortic valvular disease, a liberal pulse pressure is desirable. The diagram represents a crude attempt at visualizing the "pathogenesis of the arteriolar changes in hypertension."
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 a continuous hypertonia or spasticity leads to fatigue.

Step 6

Fatigue (to be sharply differentiated from exhaustion) makes muscle cells more irritable, and a hyper-irritability results. Such hyper-irritability 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 vicious cycle is set up: steps 4 - 5 - 6 - 4.
This is called "The perpetuation factor in hypertension," 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."

Step 7

If fatigue continues to exhaustion, the muscle cells
degenerate, die and fail. Thus simultaneously with the act-
ivity of the vicious circle, 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 frame-work 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

Arteriolar sclerosis
Up to step 7 the processes are reversible biologically;
fatigue may be relieved by rest, hypertrophy may subside. Be-
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 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 (58).

An increase in peripheral resistance in maintaining an increased blood pressure is of prime importance, but as yet obscure, says Moschcowitz (53). The view that hypertension is due to statically increased resistance offered by organic lesions of the arterioles is untenable is held by Fishberg. A true generalized arteriosclerosis does not exist in association with essential hypertension, and therefore, cannot be the cause of the latter. Arteriosclerosis is a pathologic exaggeration of physiologic changes, resulting from the increased wear and tear incidental to the hypertension (65).

During the ascending period of life, there is excessive intermittent tonicity of the smaller arteries associated with abnormal intermittent intravascular stress and strain. Pathologic wearing of the vascular tissue could be postulated. The first response to this excessive work is hypertrophy - a
physiologic response. With mesial hypertrophy, true organic narrowing takes place in the lumen whereupon rising levels of systolic and diastolic blood pressure would be expected. This is recognized as clinical hypertension, probably an irreversible condition as indicated by lack of response to therapeutic endeavors according to Brown (54).

The peripheral vessels play little or no part in hypertension. There is a relationship between small vessel sclerosis as in retinal arteries and high blood pressure. Hypertension is not associated only with sclerosis of retinal arteries but must assume sclerosis of small vessels to be more or less general; the changes may be microscopic and are often overlooked, but are present, says O'Hare (52). Primary hypertension does not appear to be caused by vascular disease, but it puts an additional strain on the arterial system which accelerates and intensifies arterial degeneration. It is, however, probable that when a severe arteriolosclerosis of the kidney has developed, the circulatory obstruction tends to raise the blood pressure to higher levels is Bell's contention (44).

Balfour believes more than just aging arterioles causes increased blood pressure - he looks to the tissues themselves as aging and losing elasticity which cannot be renewed either as in arterioles (61). Development of malignant hypertension with albuminuria and early renal insufficiency come as a result of vasospasm and arteriolar injury, and not as a result of primary glomerulonephritis, says Koenigsberger (42).

The histologic differences between arteriolosclerosis and some of the forms of arteriosclerosis may be due to differ-
ences in the structure of the walls or in the function of the arterioles and larger arteries rather than to dissimilarity of etiology. The common statement that "arteriosclerosis has no connection with hypertension" is incorrect is Bell's belief (44).

The etiology of hypertension is of especial interest, particularly essential hypertension. It has baffled medical men since the significance of high blood pressure became apparent. The various theories follow, largely frank quotations.

The mere fact that the disease has been termed essential hypertension is evidence that the cause is unknown. The etiology is not one source of injury, but a combination of various insults and irritations, often occurring simultaneously, says Stieglitz. "Hypertension is a 'disease' only on nosologic grounds. A morphological background is still lacking and hypertension must be interpreted in terms of pathologic physiology rather than in those of anatomy." (53).

The following is a summary, by Waller (18), of the various factors which have been held to be implicated in the etiology.

1. Hereditary influence
2. Infection (past or present)
   a. general systemic infection
   b. focal infection with dissemination of organisms
   c. focal infection with dissemination of toxins

- 60 -
3. Intoxications (non-infectious)
   a. Exogenous: (1) lead, arsenic
      (2) alcohol
      (3) diet - excess of meat, general
           excess, condiments, constipation
   b. Endogenous

4. Metabolic
   a. pregnancy
   b. fatigue
   c. endocrine disturbance

Janeway (8) concludes the range of etiologic factors
is so great as to demand an extensive critical study to yield
anything more than the usual text-book catalogue of all the
diseases and vices of the human race as the causes of any
disease, the origin of which is obscure.

Osler has said that the quality of the tubing with
which one is born may influence the occurrence and severity of
the disease, and this is born out by numerous investigators.

50 to 75 per cent of subjects with essential hyper-
tension will give definite positive family history of cardio-
vascular-renal disease, according to Hines (37). Glomset (24)
found a very high percentage of hereditary factors in the
etiology of this condition. Kylin says "hypertension appears
in certain families". (79). A series of 485 patients with
hypertension, 480 of whom gave direct parental history of hyper-
tension, apoplexy, congestive heart failure or sudden death, was found by Allan (71). Heredity was apparent in 33 per cent of Marshall's group (20). Allan found evidence that suggests this condition may prove to be a dominant unit trait. 37.6 per cent familial vascular disease was found in 436 general hospital admissions; 76 per cent of 300 unselected permanent hypertension cases showed definite familial tendency to some form of hypertension and its sequelae and complications (66). Taking blood pressure readings of 2,400 High School children, it was found that 39 per cent with high blood pressure knew of such in their families, while only 10 per cent without high blood pressure knew of high blood pressure in their families. Thus the term "hereditary hypertension" is coined by Glomset (24). Weitz found that parents of hypertensive patients rarely reached old age; after the age of 55, half the brothers and sisters of hypertensive individuals either showed hypertension or were already dead (3). Draper and his co-workers think that the disorder itself is not inherited but is rather a system or tissue defect which may find expression in a variety of fundamentally related clinical entities (3). Ayman found a tendency to arteriolar (essential) hypertension in three successive generations. In the third generation the hypertension had already appeared in the second decade of life. Fishberg (57) believes this "constitutional hypertension" group makes up a large, numerically important, section of essential hypertension cases.
In older works, syphilis is almost invariably accorded a prominent place among the causes of "chronic interstitial nephritis," and in recent years it has been placed as a factor in the etiology of essential hypertension. The combination of syphilitic aortitis and true (diastolic) hypertension is not uncommon but this does not prove its etiologic potency, avers Fishberg (57). Anti-syphilitic treatment is not notable in lowering hypertension in syphilitic subjects. "Syphilis has little, if any, importance in causing hypertension to enter the malignant phase" - from Fishberg.

Palmer (74) finds no definite correlation between hypertension and any of the infectious diseases, which is contrary to Barach, who found typhoid and diphtheria prominent. Marshall claims typhoid and syphilis were rare causes of hypertension, but that the acute Exanthemata were present in histories of 50 cases (20). Foci of infection are most common cause - Millet (49). The history of onset suggests acute tonsillitis probably of streptococcic origin as the chief etiologic factor (42). Sprunt blames typhoid and nasopharyngeal infections as the two outstanding offenders. Bowers found dental sepsis and tonsillar infection. Ophuls feels that sepsis in a broad sense is responsible (3). Palmer found no correlation between infectious diseases and hypertension (74).
That lead poisoning is a cause of chronic hypertension, is a well known fact. Whether, in the cases of long standing hypertension in lead poisoning, hypertension of renal origin is added to the original, non-nephritic hypertension as the kidney lesions develop, is a question not yet decided. It seems plausible that during the period when lead is present in the body, hypertension is due to direct vasoconstriction action of the metal on the arteries and, perhaps, the capillaries. But such an explanation does not hold for the cases in which chronic hypertension remains for years after the intake of lead has stopped, and it can no longer be demonstrated in the urine, unless one assumes that lead is fixed in the tissues - resulting in an arteriosclerotic kidney, which is the case. But the arteriosclerotic kidney only develops over a protracted period and cannot account for the hypertension that is often seen in the early stages of the intoxication. Thus the confusion remains, states Fishberg (57).

Alcohol has, of course, been reckoned among the causes of essential hypertension, as it has been considered to be at the root of so many affections. Marshall could obtain but eight alcoholic histories from 100 cases of essential hypertension (20). Blood pressure of alcoholics is no higher than in other persons, King believes (3). That the use of alcohol stimulates excessive ingestion of fluid and food, usually resulting in obesity, all of which are factors to bring out a latent hypertensive tendency, is subscribed to by King (3) and Fishberg (57).
The withdrawing of tobacco, in a case reported, was responsible for a drop of 55 mm. systolic and 45 mm. diastolic pressure readings and, with discontinuation of treatment, promptly rose again to previous heights, according to Sanguinetti (27). Nicotine in the hands of a novice does cause a rise in the systolic pressure, Fishberg says, but men who have smoked for years have normal or even low blood pressures, showing that smoking per se does not cause this condition, which has been one of the chief bogies flaunted by the anti-smoking propagandists. "There may be damage done to the circulatory apparatus by smoking, but it is not effected through the medium of hypertension" is Fishberg's opinion (57).

There is no convincing evidence as yet presented that an excess of protein in the diet results in essential hypertension or any other variety of Brights disease (Fishberg believing all hypertensions a form of a kidney disease). Faber (1924) observed an individual who had been a vegetarian for 12 years, but nevertheless had a systolic blood pressure of 220 mm. Thomas (1927) found the Eskimo, whose diet is practically carnivorous, to have no increased incidence of hypertension. High protein diet with rabbits did produce hypertension according to Nuzum. Cited (57)

Gluttony has long been held a leading cause of hypertension. This may be true indirectly, and, in some cases, restriction of diet does cause a moderate drop in blood pressure. On the other hand, there are many persons who have partaken of a seeming-
ly excessive dietary throughout a long life, and who have normal blood pressures. And there are many individuals with hypertension who have always eaten sparingly. It appears more probable that hypertension results from an excess of food over a long period of time only in those persons who have a constitutional predisposition to hypertension - the superalimentation is an "inciting cause" (57).

Examinations by the Life Extension Institute showed that there is a definite relation between obesity and hypertension. The following table is indicative of this relation.

<table>
<thead>
<tr>
<th>Over weight</th>
<th>Normal blood pressure group</th>
<th>High blood pressure group</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 15%</td>
<td>9.3%</td>
<td>11.0%</td>
</tr>
<tr>
<td>15 to 20%</td>
<td>7.5%</td>
<td>9.5%</td>
</tr>
<tr>
<td>over 20%</td>
<td>12.6%</td>
<td>25.5%</td>
</tr>
</tbody>
</table>

Fisk (1923) has shown the tendency of obesity to predisposition to hypertension. It has been shown by Dunham's study that under-nutrition has no effect on pressure in otherwise healthy men, while obesity creates a distinct liability to hypertension (3). Rose believes diet is a large factor, and overweight is frequently associated with high blood pressure. Weight reduction by a suitable diet reduces blood pressure in a high percentage of these cases (73). A group of thirty obese hypertensive women exhibited a marked lowering of sugar tolerance. A second group of fat individuals without hypertension showed no hyperglycemia. Reduction of weights often lowers blood pressure.
and shows normal sugar tolerance curves. It seems reasonable to assume that there is no one factor definitely responsible for the combination of obesity, hypertension and hyperglycemia (12). Probably hypertension and obesity together are an expression of some underlying disturbance of metabolism and both may be inherited characteristics (51).

Obesity, like hypertension, is often an inherited characteristic, and it seems probable that the same constitutional type is predisposed to both obesity and hypertension. The fact that reduction in weight in obese individuals may be accompanied by a reduction in blood pressure - though, this is far from always the case - is not an indication that obesity causes hypertension, for dietary restriction may have a similar effect on the blood pressure of thin persons concludes Fishberg (57).

Essential hypertension, obesity and diabetes mellitus are a common triad and rather points strongly to a constitutional peculiarity being responsible for both diabetes and the hypertension. It is possible that arteriosclerosis of the pancreas due to hypertension may be responsible in some cases for the disturbance in carbohydrate metabolism (57).

Hyperpiesia will probably be found to be a deficiency disease. As noted by Ismail, it has something in common with diabetes. In both diseases the usual time of onset is in the early middle age; both run a prolonged course, have a certain familial tendency, and are frequently found together. As in diabetes, hyperpiesia is much more severe when it occurs in
young people, and its course is more rapid: the so-called malignant hypertension of Keith and Wagener (19).

Ziskin (51) finds no relation of hypertension and constipation. Palmer agrees with him. Rose, on the contrary, believes that the group of hypertension cases, due to gastrointestinal conditions, outnumbers those from all other causes combined. (73). Johnson proposes intestinal toxemia as one of the "inciting causes" of hypertension; treatment lowers blood pressure which returns if treatment is stopped. (63). Rose believes streptococci and staphylococci in the bowel, which he found with stool cultures to run as high as 10 to 50 per cent, have an influence. "The effects of the elimination of such abnormal intestinal flora are remarkable."

The allergists enthusiasm in his field did not escape including hypertension.

Three Cleveland men find hypertension and allergy infrequently associated in the same patient. These patients feel better with allergic symptoms controlled, but the hypertension persists. They found no relation between blood pressure levels and the allergens (4).

Vaughan states that "angiospasm is the characteristic phenomenon of anaphylaxis, although definite proof of this is still lacking." Coca and his school have demonstrated that in anaphylaxis, the blood contains substances which contract un-
striped muscle tissue. Kaufmann asserts sensitiveness to heat to be a feature of essential hypertension histories and Duke has proved this sensitiveness to be an allergic manifestation. Heredity and allergy have been associated, and the heredity and hypertension combination is accepted in some cases.

Kylin describes three cases of simultaneous bronchial asthma and essential hypertension. Mosenthal found an individual with controllable essential hypertension when certain starchy foods were eliminated from the diet; apparently a typical allergic phenomenon. Kylin and others report cases of inverted epinephrin reactions in some essential hypertension cases; they observed a fall of blood pressure. Such an inverted reaction can be obtained in some allergic diseases.

"The conclusion is drawn that a certain number of cases of 'essential hypertension' are allergic in origin and showed improvement on allergen-free management. (5)."

Endocrine disorders have had much support as a factor in this subject of etiology.

Goldzieher says: "The relation between the climacterium in women and hypertension is striking and many theories of functional disturbance of ovary and hypertension incidence have been built up. The frequency of hypertension in artificially sterilized women is particularly noteworthy and so is the coincidence of myoma and hypertension."

Fluhmann's finding of an excess of the anterior pituitary sex hormone in women past the menopause, helps to
explain Goldzieher's observation. Maranon opined that the adrenals took on added activity at the menopause and that the body became more sensitive to adrenalin. Some cases of hypertension are relieved by injections of corpus luteum; it is known that corpus luteum depresses pituitary function. Cited (70).

Inasmuch as menopausal hypertension appears in only a relatively small fraction of women, Alvarez and Zimmermann (1926) believe that such hypertension comes on only in women who have a hereditary tendency to hypertension, which becomes manifest only with the loss of the ovarian secretion, the mechanism of which is still unknown. This is also Fishberg's viewpoint. (57). Goiter and the menopause constitute definite predisposing factors, though the mechanism is not clear (3).

Gutman believes women of the essential hypertension type are in reality pituitropic individuals. In 1919, Neubauer noted the association of hypertension and hyperglycemia and offered the theory that excessive activity of the suprarenals was the underlying factor. Hutton concludes, "The changes found in the pituitary in cases of hypertension, chronic nephritis and secondary contracted kidneys, the occurrence of adrenal pathology in cases of hypertension and arteriosclerosis, the occurrence of identical sugar curves in diabetes and essential hypertension, the relief of hypertension by x-raying the adrenals, point to hyper-function of the pituitary and adrenals as the most likely cause of the condition." (70).

Johnson believes not many cases can be explained by endocrine imbalance (63). Suprarenal tumors may be accepted as a definite form of secondary hypertension but not as a cause
of primary hypertension (44). Pheochromocytomas sometimes produce constant hypertension (6). Eclampsia, hypertension and basophilic adenomas of neurohypophysis will be seen to be interrelated, says Cushing (69).

Thyrotoxicosis produced elevation of blood pressure in about 33 per cent of a series. With thyroidectomy, 80 per cent showed improvement, and 47 per cent were reduced to normal. The longer the duration of the thyrotoxicosis (especially as in toxic adenoma), the greater the tendency to hypertension (35).

Concerning the role of the endocrine glands in essential hypertension, there is no definite knowledge as to how the disturbance in internal secretion produces the increased tonus of the arterioles which is the immediate cause of the hypertension, whether this is accomplished through the intermediary of the nervous system or through a humoral mechanism. Cited (57).

The possible presence of a pressor substance in the blood of patients afflicted with essential hypertension, has aroused much speculation and many hypotheses.

By analogy with other systems of the body, it is probable that a chemical agent is responsible. It may be that this substance is normally in excess and the fine adjustment is made by a hormone, which converts it into something which can be excreted by the kidney. Bain and Major found pressor substances in normal urine which was absent in urine of hypertensive individuals. If the hormone is inadequate, the arterioles will
be over stimulated and the blood pressure will have to rise to compensate for the arteriolar obstruction to circulation. According to the degree of hormonal deficiency, various grades of hyperpiesia will result. Over work and worry are important secondary factors which will aggravate an already aggravated state still further (19).

Wakerlin and Bruner (11) studied the action of blood serum of essential hypertension patients and of a normal blood pressure group on the tone of arterial segments from the mesenteric arteries of beees. They found evidence of a pressor substance, but there was no significant difference in action of normal and hypertensive sera. They did find evidence of a spontaneous rhythmic motor activity in arterial musculature deprived of its extrinsic innervation.

Danzer, Brody and Miles (1926) had found pressor effects on animals when injected in suitable amounts with blood of hypertensive patients. Curtis and Moncrieff found no such results in their work; washed corpuscles of the same patients caused no results with injections (32).

Attention has been directed to certain amines, which may be produced by bacterial decomposition of proteins. One of these, tyramine, causes a marked elevation of the blood pressure and is rapidly absorbed from the intestinal tract, according to Higgins (76). Hare has demonstrated a ferment in the liver capable of destroying tyramine, which opens up a most enticing field for further investigation (76).

Another product of protein disintegration has been suspected - namely indican, which is destroyed by the liver.
An excess was found, by Waller, in 72 per cent of cases; it is evident that this must be due either to an excess production or to a loss of hepatic oxidative power. There was no constipation or intestinal disturbance to account for the excess indican, through a gastro-intestinal toxemia. Amino-acid nitrogen was increased in 68 per cent. Renal disease has no marked increased amino-acid retention, so Waller concludes, it is due to liver degeneration most likely, to over-production, or retention from a renal disease (18).

Elliot (72) says the pressor hypothesis should not be lightly abandoned, but should be subjected to further experimental work for confirmation or refutation.

A most recent work by Gillespie, brings out the presence of an unstable chemical compound, adenosine triphosphoric acid, found in carefully attended muscle preparations, which, the failure to find heretofore, was laid to improper handling of experiments and consequent metabolic changes - namely, the loss of the pentose from the purine base which compound now becomes inactive. This unstable adenosine triphosphoric acid is said to lower blood pressure. Is this a natural means the tissues possess of increasing blood supply to a part and its surroundings to compensate for increased muscle activity? Speculating on its significance in essential hypertension, it might be said that the lack of this dilating substance could cause angiospasm, which is held by many authorities to be an "inciting cause" of hypertension on a hereditary basis. The cause of angiospasm is not known. Perhaps this discovery will mark the beginning of the understanding of essential hypertension.
Major has been a most enthusiastic follower of this pressor hypothesis, with especial reference to the possibilities of methyl guanidine. He states, "We wish to emphasize that we do not yet know that the substance which gives this increase in color reaction (Major's test for presence of guanidine) in the blood of hypersensitives is methyl guanidine or some guanidine compound. Observations suggest, however, that the blood of these people contains something which is present in greater amounts than in normal blood."

Normal control results did not exceed 0.2 mgm. per 100 cc. of blood of methyl guanidine. In the hypertensive patients, most of them showed an increase of blood "methyl guanidine"; some failed to show an increase in this pressor substance (36).

No theory, says Foshay, dependent upon circulating pressor compounds, is exempt from the criticism that, whereas, the toxin must bathe vessels in both the lesser and greater circulations, the pulmonary or lesser circulation almost never participates in the hypertension (77). Higgins believes it is reasonable to assume that the chemical changes in the body may be the result and not the cause of this phenomenon (76).

Neusser described two cases of hypertensive disease in young adults, terminating in cerebral hemorrhage, in which cancer of the suprarenal gland was found, but no disease of the kidneys. Vaguez (1904) observed frequent coincidence of suprarenal hyperplasia and hypertension. Huelse (1922) was unable to find epinephrin in venous or arterial blood of either nephritic or essential hypertension patients. Epinephrin was found in
the renal vein and as far in the circulation as the right heart, though, no further. This would seem fatal to this once promising theory - "the beautiful dream of adrenalinemia", as Janeway called it. Cited (57).

There is little support for the hypothesis that hypercholesterinemia is concerned in the production of essential hypertension, although, Westphal (1925) finds such true in 71 per cent of his cases; Buerger (1930) found no relation between blood pressure and cholesterol content of the blood, and Fishberg also denies this - in fact hypercholesterinemia in essential hypertension was found to be rarely striking (57).

Mac Donald (1925) and Major (1925) observed that liver extracts produce a particularly striking depression of blood pressure in many cases of essential hypertension, but Major found little effect on normal blood pressure. The nature of the depressor substance in the liver is not known, although it is thought to be histamine, choline or peptone by such men as James, Laughton and Burnett. This action of liver extract is no more convincing than to suppose that relief from an asthmatic paroxysm by epinephrin shows that the suprarenal medulla is diseased in asthma. "As yet there is no substantial evidence that any abnormality of liver function exists in essential hypertension" states Fishberg (57).

The suggestion has been made that a change of increased viscosity of the blood may be a cause of essential hypertension. No such increase has been noted, even in cases of polycythemia
rubra (which has a greatly increased viscosity) was there any marked rise in blood pressure (25).

That the carotid sinus is the center of an etiological picture, is a view held by many authorities.

In denervating the carotid sinuses and sectioning pressor nerves of rabbits, a rise of blood pressure was noted. No evidence of epinephrin was found in the peripheral blood; blood sugar was always normal - DeGoat's findings. (68).

Hering in 1923 showed that the slowing of the pulse after pressure on the side of the neck is due, not to a reflex engendered by pressure of the vagus as had long been believed, but to a reflex engendered by pressure on the bifurcation of the common carotid artery. Where the common carotid divides into its internal and external branches, there is an ampulla-like dilatation, which Hering has termed the carotid sinus. In its walls are sensory nerve endings, the mechanical stimulation of which initiates a reflex that lowers the blood pressure and slows the heart. Hering found that the sensory nerves leading from the proximal aorta - long known, especially in the rabbit, as the depressor nerve, but which he terms the aortic nerves - and the carotid sinus nerves together form a unified system that serves to prevent excessive rises in blood pressure - the "blood pressure restrainers". The normal stimulus of the "restrainers" is the pressure within the aorta and the carotid sinus. Hering has shown that if these restrainers are cut in animals, striking
arterial hypertension results.

"This", says Fishberg, "does not prove it to be analogous to hypertension in man, for pressure on the carotid sinus produces the same results in essential hypertension cases as it does in normal cases in the human." Cited (57). Some clinicians, however, have had results of some sort in the irradiation of the carotid sinus.

Bordley and Baker in 1926 formulated the theory that hypertension was due to arteriosclerosis of the blood vessels of the medulla oblongata; Anrep and Starling (1925) had found that a decreased blood supply to the vasomotor center caused a general rise in systemic blood pressure. Bordley and Baker found arteriosclerosis in long standing hypertensions and the reverse in normal controls. Cutler (1928) found no such results (48). Tuthill with 24 hypertension cases found 12 with changes in medulla and of the 35 normal blood pressure controls used, six had arteriosclerosis in medulla. Tuthill, therefore, concludes against the theory (26). Granger (33) states, "Vascular lesions of the medulla, affecting the vasomotor center, probably may produce a rise in systemic pressure, but there is no proof that a hypertension does not precede such lesions."

Ruehl (1927) found no evidence that the medulla suffers from deficient circulation in essential hypertension cases; others claiming arteriosclerosis at the base of the brain to be responsible. Arteriosclerosis, moreover, is frequently absent.
From this location in such cases (57).

From experiments by Raab (23), the conclusion was reached that the symptoms of essential (not nephritic) hypertension can be considered due to a local need of oxygen and the accumulation of lactic acid in the vasomotor centers of the brainstem as a consequence of local circulatory disturbances (spasms, sclerosis). The actual level of the blood pressure in hypertension would accordingly be composed of the sum of the stimulus through lactic acid plus the pathologically increased responses to the stimulus of the normal carbon dioxide tension of the blood and of different kinds of sensitive and emotional stimuli.

The experimental results correspond to the following characteristic features of essential hypertension: (1) high blood pressure, (2) hypersensitivity of inhalation of carbon dioxide (increase pressure) and to hyperventilation (decrease pressure), (3) hypersensitivity to peripheral sensitive stimuli and (4) weakened or inverted effect of epinephrin.

"This evidence is adequate", says Fishberg, "as far as it goes, but not sufficient to be conclusive". (57).

The vicious fatigue-cycle of Stieglitz (58) needs but a continued irritating substance acting on arteriolar musculature, or what, to set up a Gull and Sutton (31) type of arteriosclerosis. Zimmer contends the use of purified table salt which is lacking
in Nature's components of calcium, potassium and magnesium can initiate such a cycle. The normal ratio of these cations in the vertebrate vascular system is for Na: K: Ca: Mg - 100: 6: 3: 1, the sodium being antagonistic to the others.

Na-excess leads to alteration of stimulus reception and conduction and increased irritability on cell membranes. If such holds for arteriolar musculature, it would appear to be an adequate "inciting cause" of this subject. A dietary salt which is balanced in the proportions of sodium to sodium antagonists is a theoretical preventative. (43).

O'Hare and Walker (77) have demonstrated that salt plays little or no part in either the origin or treatment of hypertension.

Muzum (1926) presented evidence that disturbance of the acid-base balance through an excessive dietary ratio of acid-ash foods produces hypertension and renal injury. It was due to excessive acidity and not excess protein ingestion. Acid-base balance effects renal secretion and this disturbance may affect changes elsewhere in the body such as water balance or vascular tone (58).

In view of the close interrelationship between the vegetative nervous system, the glands of internal secretion and the inorganic ions, brought out especially by the researches of Kraus and Zondek, it seems very possible that study of the inorganic ions in the blood might appreciably further understanding of the nature of essential hypertension is Fishberg's prediction (57).
Up to this point, various theories of the cause of essential hypertension have been elicited, such as infectious disease, obesity, endocrine imbalance, ionic constellation upset, pressor substances, etc., all of which have their faults and good points according to critics. The subject of vasomotor control and its part in the etiology of essential hypertension bears much weight with a good many investigators as well as clinicians.

The height of the blood pressure is largely regulated by the tonic activity of the chief vasomotor center, situated in the medulla in the region of the fovea inferior of the fourth ventricle. The activity of the vasomotor center is not entirely automatic, but is influenced both reflexly and by changes in the chemical composition of the blood (e.g., of the hydrogen-ion concentration). In addition to this chief vasomotor center in the medulla, it is stated that there also are subsidiary vasomotor centers in the lateral horns of the thoracic cord which function when the medullary center is eliminated. As to whether they are true centers entertains some doubt.

Hypertension, as a result of alterations in the activity of the vasomotor center, is encountered clinically, and can be produced experimentally. Such is found in increased intracranial tension clinically, and Cushing (1902) and others have shown that compression of the medulla leads to an immediate rise in general blood pressure. "Blood pressure changes in the vasomotor center cause reverse changes in blood pressure in the rest of the body" - as shown by Anrep and Starling.
The same mechanism, anemia of the vasomotor center, is apparently responsible for the hypertension that results from asphyxia; this may possibly be due to the accumulation of waste products, for perfusion there with acid fluid, produces hypertension. Fear and emotion, of cortical origin, surely, in the last analysis, causes a rise in blood pressure.

The neurogenic-constitutional predisposition, while not thoroughly understood, seems to consist in the inheritance of a peculiar type of vasomotor tone, in the presence of which, certain factors, which can be called "inciting causes", act as stimuli to elevate blood pressure. This elevation goes through a temporary phase and thence rises more permanently and finally progresses through the well known pathologic cycle as Fishberg has demonstrated.

Backer concludes from all the physiologic data to date that (1) the autonomous innervation of the arterial system responds to a multiplicity of stimuli, (2) that the autonomous structures, that is, the nerve tracts affecting peripheral arterial resistance, are manifold, and (3) the combination of these circumstances allows a wide variety of physiologic and pathologic possibilities of changes in the peripheral arterial resistance, and these pathologic possibilities depend, as a whole, upon a primary cardinal condition inherent in and inseparable from the structural and functional character of the individual autonomous nervous system. The incidence of hypertensive disease depends upon the fundamental fabric of the particular autonomous nervous system as such, whether it will res-
pond to any stimuli whatsoever, with an abnormal pressor effect upon the peripheral blood vessels. Essential hypertension is solely a manifestation of a certain abnormal type of constitution; whether this is associated with other abnormalities, as endocrine imbalance, etc, is not known. Backer asks the question, "Does the person of the opposite constitutional type have low blood pressure?" It remains to be seen (22).

Blackford (64) maintains there is involved a constitutional hypertonicity of the autonomic neuro-vascular control in a large majority of instances.

Rountree believes there is an unknown factor in the etiology which is not understood as yet. He inclines to the view that "in the beginning at least, the arteries are not so much at fault as they are sinned against, chiefly through the vasomotor centers and sympathetic system". Vasoconstriction (the physiologic vascular spasm) is replacing in part the older idea of anatomic narrowing and fibrosis; both are important but the former has not received the consideration it merits (13).

Brown at Mayos is inclined toward a hyperreactive sympathetic vasomotor mechanism based on constitutional abnormality or imbalance and a subsidiary factor of "wear and tear" from any emotional agent which will modify or activate the constitutional factor. This hyperreactive mechanism possibly can be acquired. His classification:

I Constitutional or "x" factor, expressed as
   a. Hypersensitive vasomotor center
   b. Abnormal reactor mechanism
arteriolar tissue
sympathetic nerve endings
endocrine factors

II Subsidiary or accelerating factors of "wear and tear"
   a. environmental agents
   b. toxic or infectious agents (39) (54)

Hines at Mayos states, "If the hypothesis is valid, that there is a constitutional basis for these exaggerated responses, it would be anticipated that they could be demonstrated years before the development of clinical degrees of the disease (37).

Palmer (74) found a larger proportion of the nervous or neurotic types among patients with systolic pressures above 140 than those showing systolics below this level.

Quoting Higgins, "A rational conclusion from observations on the various aspects of hypertension, is that we are dealing with a clinical entity which has its initiating stimulus in a preceding generation and because of the inability to make adequate environmental adjustment, an imbalance of vascular tonus follows with its attendant results (76).

Many recent investigators have arrived at the conclusion that psychic factors play an important role in the causation of essential hypertension. It has long been known that various emotions and other mental processes may produce transitory or even long-continued elevations of blood pressure. Many persons with essential hypertension are irritable, unable to relax and
under constant strain; if poor, they worry about family and finances. But not all hypertensive cases show such a picture, in fact, many are quite the reverse. Some cases demonstrate the fact that the hypertension caused the anxiety and irritability and are manifestations of the disease and not the cause.

"In all probability, emotional and mental strains play purely an accessory role in the genesis of essential hypertension, serving to precipitate or aggravate the increased inherited constitutional predisposition to essential hypertension", concludes Fishberg (57).

The etiology of hypertension is anything which irritates the arterial musculature as an initiating process on an inherent labile vascular system, states Stieglitz (58). Kylin believes hyperirritability of the sympathetic nervous system is the basic condition in primary hypertension, emotional stress being an "inciting cause". Koenigsberger and others report vasospasm a chief factor at the outset, preceding demonstrable significant arteriolar disease (42). Interference with the vasomotor system is a primary cause whether due to a circulating toxic substance or a disturbance of the sympathetic nervous system, according to Keith (45). Granger subscribes to heredity and vasomotor hyperirritability (33). Patek and Weiss speak of a barrage of the vasomotor system by sympathetic nerve impulses causing a spasm, which narrows the arteriolar lumen (55).

Yater presents the following interesting side thought: "The fact that the arterioles of the heart and lungs, whose sub-
jection to vasomotor control is undoubtedly slight, because they are such vital organs, unlike other viscera, escape in great measure the process of hypertrophy of their musculature which occurs elsewhere, is additional evidence in support of the vasoconstriction theory of essential hypertension." (17).

Riesman remarks that essential hypertension has all the earmarks of being dependent on a vasoconstriction, a functional change affecting especially arterioles, the precapillary vessels, which, for their size, have the largest amount of muscular tissue in their walls; it may be said the process is more pronounced in the renal vessels (25).

Fish and Palmer have shown high blood pressure readings in adolescence are more liable to permanent hypertension ten years later, assuming that essential hypertension, in general, because of its early variability, begins as a purely functional disorder of vasomotor origin. This is by no means a justifiable deduction, for an early or partial sclerosis of the vascular bed might just as well produce an unstable hypertension as might functional disturbances contends King. He continues: "It seems established that a certain type of individual, who is liable to changes in blood pressure, is liable to develop permanent hypertension. These merely form a group within a group of permanent hypertension cases. To explain all cases of essential hypertension by assuming previous vasomotor or functional disturbances, seems quite inadequate but cannot be explained further (3). Kylin avers the etiology does not become clear by considering it
as a disturbance in the vegetative system - different disturbances can bring on the symptom of vasolability with a rise of blood pressure (79).

A certain tension of the arterioles is necessary for everyone to maintain an adequate constant flow of blood. The sympathetic nervous system, declares Bain, is unlikely to be concerned, as it is reserved for rapid changes called for by external stimuli (19).

Craig and Brown were able to lower blood pressure with success in patients in whom the vasomotor factor was paramount - there was little arteriolar involvement, by sectioning the splanchnic nerves; especially effective when sectioned on the left. This would be a prophylactic measure of some merit (47). In experimental animals, the additional removal of one of the suprarenals further reduced blood pressure; this was from another earlier series by Craig and Brown (40).

Brown (39) continues, "To assume that essential hypertension has a peripheral origin, it would be necessary to postulate abnormal behavior of the reactor mechanisms, a hyper-reactive musculature in the arterioles, or that the sympathetic nerve endings in the arteries are at fault, or that an excessive response on the part of the pressor hormones is present. The evidence at hand, although incomplete, favors the central origin of the widespread vasoconstriction".

"Although it is known that the vegetative nervous system plays an important role in the regulation of blood pressure,
practically nothing is known of its state in essential hypertension" concludes Fishberg (57).

The time to dispense with the term essential hypertension has not yet come and it still must serve a useful purpose as a confession of ignorance.

A man with persistent hypertension who can learn to stop thinking or praying for an hour after lunch and can prop his feet above his head, smoke a pipe and doze, will arrest the progress of his hypertension. To arrest the disease is all we can hope to do, and if the average age when it is first seen be near the normal span of 58, with ten years of the happiest period of his life ahead of him, provided he can be taught to carefully discipline his thoughts and daily life, we should be content, happily agree to handle arterial hypertension and give up the search for a specific drug, so that harmful medication may be curtailed (1).

Osler has been cited as saying that "a moderate hypertension may be a blessing because it leads to a more sane and leisurely manner of life".

"Although we must confess our inability to change constitutional peculiarities, we can in a measure control environments and can assist in the living of better balanced lives. A judicious optimism on the part of the physician will play a
large part in meeting this problem." (76).

It is apparent that a great mass of literature on this subject, only a very minor fraction of which has been presented here, has been put before the profession. Few, if any, theories meet with universal approval and the matter is still an open question.

Most men believe increased peripheral resistance to be the immediate cause, but the underlying factor of the etiology is debatable. Whether it is of peripheral or central origin, of kidney disease, of pressor substance presence, or of "constitutional inadequacy" is not definitely known. That the so-called "inciting causes", such as gluttony, hyperthyroidism, emotion, etc, merely precipitate the latent inherent tendency to essential hypertension, is a theory adhered to by a great many recent observers. Perhaps such recent work, as that of Gillespie (84), will prove to be open sesame of this now theoretical question.
Case Report

Julia E., 82, f., white, was seen by me, while on University of Nebraska Dispensary Out-call Service. The chief complaint was occipital morning headaches of two years duration, and dyspnea. Past infectious history was negative. The Wassermann was not taken. Family history was negative.

Physical examination revealed a negative heart, perhaps slightly enlarged to the left, and an accentuated A2 sound over aortic area, and an inflamed throat of moderate degree. Her blood pressure readings, in late afternoon, ranged from 195 to 210 systolic, and diastolic varied, but little, around 100. Arteriosclerosis in the radial arteries was quite apparent - eyeground examination was not done. Hypertrophic arthritis in knee and phalangeal joints was marked.

Relief was obtained with acetylsalicylic acid gr. X, on arising in the morning, for three weeks, and then became inadequate. Magnesium sulphate gms. 1½, twice weekly, has since given complete relief of headache and alleviated the dyspnea to great extent. Systolic readings were reduced 20 mm.
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