ESSENTIAL VASCULAR HYPERTENSION

JOSEPH H. BARACH, M.D.
PITTSBURGH

Vascular hypertension, according to our present day conception, is found in one group of individuals who have demonstrable pathologic lesions. These lesions when discovered are usually of the atherosclerotic type. The greatest damage caused by these lesions occurs in the brain, in the heart and in the kidneys.

Vascular hypertension occurs in another group of individuals in whom all the diagnostic methods of today fail to reveal which organ is at fault. This type of case has been designated essential vascular hypertension.

Since the etiology of hypertension is an unsolved problem, it is our duty to continue its discussion. This paper deals with some etiologic factors in the life history of these patients, and above all is an attempt to show there is a continuity in this disease, from the early to the later life of the individual. Essential vascular hypertension is not a spontaneous occurrence. During the last three years, a number of illuminating and interesting discussions from the standpoint of the clinician and pathologist have appeared in the American literature. Among them is that of Moschcowitz,[1] Ringer,[2] Hopkins,[3] Riesman,[4] Piersol [5] and Mosenthal.[6]

Moschcowitz, in 1919, after a complete review of the literature and his own careful studies, concludes, first of all, that essential vascular hypertension is not the result of arteriosclerosis or nephritis; and, secondly, that arteriosclerosis itself may be the product of a persistent hypertension or of the same cause which brings on hypertension. In adopting these views, he accepts the position of Clifford Allbutt.[7] Ringer,[2] in 1921, stated his belief that every case of hypertension is potentially nephritic. Allbutt, in 1903, described the group in which hypertension is the primary disease and nephritis secondary. Hopkins,[3] in 1919, described a type of hypertension developing in women at the time of menopause. Riesman,[4] in the same year, described a type of hypertension occurring in women, based on some endocrine disturbance, not improbably arising in the ovary and occurring about the time of menopause. Pawinski,[8] in 1905, described the hypertension as well as the hypotension which occurs in women at the menopause.

We may well say, then, that the best views of today are also the views of from fifteen to twenty years ago. This standstill in the knowledge of a disease, the etiology of which is admittedly unknown, is, to say the least, not satisfactory. It is of interest to note that, so far as the ultimate etiologic factors are concerned, Ringer,[2] in a discussion of nephritis, adopts the views of Professor Stockard of Cornell that every person dies from the disease with which he is born. Having a predisposition which plays the greater rôle, infections and exposure are but the precipitating factors of the disease.

Moschcowitz [9] considers the direct etiology of hypertension unknown; and he gives a vivid description of a type of individual in whom hypertension is likely to occur. Christian [10] considers essential hyptertension as having probably a variety of causes: remote infections, endocrine disturbance, disturbances due to the menopause, ovarian activity, thyroid activity, arteriosclerosis, nephritis, nervous disturbance, overeating and poisons.

Surveying the present day knowledge of this disease, which is based on a large number of accurate observations, I believe that we are nearer a satisfactory explanation of the development of hypertension than we seem to be at first glance. The fact that our views of today are not contradictory to those of fifteen to twenty years ago is in reality not so much an evidence of failure of a better understanding as it is an evidence of the accuracy of observation by the workers of those days. The work done since then becomes in a large measure corroborative evidence.

The observations to be detailed here deal with a combination of three factors which I believe play an important part in the etiology of essential vascular hypertension. These factors are hereditary tendency, the infections, and disturbances in the endocrine functions, as we know them today.

While I would not minimize the importance of other factors in the production of hypertension, this discussion will be limited to that group in which the triad mentioned is predominant.

HEREDITY

The factor of heredity is perhaps the predominant one in the hypertension group. In going over a list of forty patients in this group whom I have had under observation for a long time and whose records are complete in this respect, there were two instances only in which a positive history of cardiovascular disease was lacking in the immediate family. By immediate family, I mean brother, sister, parent and offspring.

In about half of these forty cases, my observations were made on brothers and sisters, and in the others on parent and offspring.

In some instances, the observations were made on three generations, all showing distinct cardiovascular inferiority. We may well look on heredity as the dominant predisposing factor.

ACUTE INFECTIONS

In surveying the preceding history of all cases in this group, the infections both acute and chronic occupy a prominent place. The parts played by infection and by hereditary influence are not easily differentiated. One frequently observes a greater susceptibility to infection in children of parents who suffered from chronic infections. Such children develop the throat infections and show a lowered vasomotor tone. When one is careful as to the anamnesis of his patients, he will be much impressed by the fact that, while some individuals have suffered nearly all of the acute infections, there are many who have escaped most of them, this being due not to mere chance but to an inherited immunity.

Table 1 corroborates the findings of many observers as to the occurrence of previous infections. It is based on the history of sixty-eight cases of vascular hypertension. The etiologic importance of infections in that class of cases in which hypertension occurs has been

1. Moschcowitz, Eli: Am. J. M. Sc. **158**: 668 (Nov.) 1919; Hypertension with Minimal Renal Lesions, J. A. M. A. **77**: 1075 (Oct. 1) 1921.
2. Ringer, A. I.: Am. J. M. Sc. **161**: 798 (June) 1921.
3. Hopkins, A. H.: Am. J. M. Sc. **157**: 826 (June) 1919.
4. Riesman, David: Hypertension in Women, J. A. M. A. **73**: 330 (Aug. 2) 1919.
5. Piersol, G. M.: M. Clin. N. A. **5**: 705 (Nov.) 1921.
6. Mosenthal, H. O.: M. Clin. N. A. **5**: 1139-1160 (Jan.) 1922.
7. Allbutt, Clifford: Med. & Chir. Soc. **86**: 1903; Brit. M. J., Oct. 20, 1906; Diseases of the Arteries Including Ongina Pectoris, London, 1915.
8. Pawinski, J.: Rev. de méd. **25**: 125-219, 1905.
9. Moschcowitz, Eli: Footnote 1, first reference.
10. Christian, H. A., and Mackenzie, James: The Oxford Medicine, 1920.

pointed out for many years by Allbutt,[11] Ophüls,[12] Jores,[13] Thayer,[14] Adami,[15], Klotz [16] and others. While those convalescent from acute infectious diseases seem to recover without visible after-effects, their subsequent history indicates that these diseases are not without remote sequelae. In a previous communication,[17] on the etiology of cardiovascular affections, a definite relationship was established between cardiac involvement and a preexisting typhoid fever, tonsillitis, diphtheria, pneumonia and rheumatism. It is perfectly obvious that a similar relationship can exist here.

TABLE 1.—HISTORY IN SIXTY-EIGHT CASES OF VASCULAR HYPERTENSION

	No. of Cases
Typhoid	28
Tonsillitis (recurring)	15
Scarlet fever	9
Diphtheria	8
Rheumatic fever	5
Malaria	5
Syphilis	3

CHRONIC INFECTIONS

The long-continued infections surmounted by acute exacerbations are without a doubt also responsible for remote effects. In discussing the effects of chronic infection, I shall bring evidences to bear showing a continuity in the disease process, which begins early and continues through life, going through the period of childhood, adolescence and middle life, and altering the individual both physically and mentally.

TABLE 2.—SYMPTOMS IN TONSIL-THYROID SYNDROME (ARRANGED ACCORDING TO FREQUENCY)

Chronic tonsillitis (hypertropic)	Obesity
Tonsillar node	Tendency to sterility
Thyroid gland enlarged (colloid or adenomatous goiter)	Hands moist, cold, cyanotic
Leukopenia, lymphocytosis	Hypersensitive to cold
Complexion pasty and sallow	Blood pressure low, pulse slow
Low basal metabolism	Tongue thickened and tooth marked
Skin dry, hair dry	Speech thick and voice coarse
Breast, excessive development	Puffiness of eyes, eyelids swollen in morning
Menstrual function disturbed	Alopecia, nails brittle
Subcutaneous tissue thickened	Neuralgias

ENDOCRINE DISTURBANCES

On account of involvement of the endocrines, the clinical picture manifests itself differently in the sexes. I shall, therefore, discuss them under the headings of female and male.

In the Female.—Up to Middle Life: In a previous communication,[18], there were reported a series of twenty-five cases of chronic tonsillar and throat infections, with large thyroid glands and typical manifestations of dysthyroidism. The patients ranged from 15 to 35 years of age. All had large diseased tonsils and infected cervical glands; nearly all had large thyroids (colloid or adenomatous goiter), obesity, menstrual disorders, subnormal basal metabolism and such physical and mental disturbances as characterize definitely the state of hypothyroidism. They presented a picture of chronic infection associated with endocrine disturbances.

How this is manifested clinically is illustrated by the following case:

Mrs. A., who had a fatal case of hyperthyroidism, and whose sister had exophthalmic goiter, had two daughters: one, now 20, had diseased tonsils removed at the age of 3, and at the present time was in normal good health; the other, aged 16, had large tonsils, enlarged cervical lymphatic glands, a very large colloid or adenomatous goiter, low basal metabolism, leukopenia and low blood pressure and pulse.

Whether chronic infection impoverishes the organism of iodin, and this leads to colloid or adenomatous goiter, cannot be answered to the satisfaction of all at this time. Marine believes that this is precisely what does occur. That chronic infection and dysthyroidism is capable of and does set up profound constitutional disturbances is to be seen in the life history of these individuals. Of twenty-nine patients in the tonsil-thyroid series, twenty-two were married. Of these, eight were sterile, ten had but one child, four had two, and none had more than two children.

TABLE 3.—REPRODUCTION IN TONSIL-THYROID CASES

Total number of patients	29
Married	22
No children	8
1 child	10
2 children	4
3 children or more	0
7 unmarried past the age of 30	

After Middle Life: On reviewing the history of a series of thirty-five cases of essential hypertension in women after middle life, I was much impressed with the reproductive history. After all, the ability to reproduce is a strong evidence of the normality of the female. In these thirty-five cases, as is shown in Table 4, reproduction is at a very low level, indicating a constitutional disturbance.

These thirty-five cases of vascular hypertension presented distinct evidences of what we recognize clinically as dysthyroidism. About half of them presented evidences of hypothyroidism; while the other half showed some indications of hyperthyroidism. The observations in this class of cases have not extended over a sufficient length of time to justify one in saying that they go through both stages of thyroid activity. I have at present quite a number of female patients who received prolonged courses of medical treatment for goiter, ten or twenty years ago, and who now suffer from vascular hypertension. Plummer estimates that it is seventeen and one-half years from the time of the colloid goiter to the hyperthyroidism.

TABLE 4.—REPRODUCTION IN THIRTY-FIVE WOMEN WITH VASCULAR HYPERTENSION

Married	30
No children	12
Premature births	2*
One child	5
Two children	6
Three children	3
More than three	2
	30

* Nonsyphilitic.

In comparing the two groups described above, the married women of the tonsil-thyroid group and the married ones in the essential vascular hypertension

11. Allbutt, Clifford: Footnote 7, first reference.
12. Ophüls, William: Subacute and Chronic Nephritis as Found in One Thousand Unselected Necropsies, Arch. Int. Med. **9**: 156 (Feb.) 1912; Etiology and Development of Nephritis, J. A. M. A. **69**: 1223 (Oct. 13) 1917.
13. Jores, L.: Deutsch. Arch. f. klin. Med. **94**: 1, 1908.
14. Thayer, W. S.: Southern M. J. **10**: 367 (May) 1917.
15. Adami: Brit. M. J., Dec. 22, 1906.
16. Klotz: Am. J. Med., December, 1919.
17. Barach, J. H.: Etiology of Cardiovascular Affections, J. A. M. A. **76**: 1211 (April 30) 1921.
18. Barach, J. H.: Tonsil-Thyroid Syndrome in the Female, New York M. J. **114**: 648 (Dec. 7) 1921.

group, we find points of striking similarity. In the first group, there is a history of chronic infection followed by evidences of dysthyroidism and disturbances of other endocrine functions sufficient to cause a reduction in fertility. In the second, we find the history of a severe acute infectious disease or a chronic infection. In this group, evidences of dysthyroidism are also present; half of them have symptoms suggesting hypothyroidism, while the other half shows evidences of hyperthyroidism. Both groups have in common the history of a preceding infection, endocrine disturbances and a tendency to sterility. In the younger group, it is not manifest; in the patients beyond middle life, essential vascular hypertension is present. Perhaps when more is known about the involuntary nervous system, we may be better able to classify some of the bizarre endocrine disturbances.

TABLE 5.—NEUROCIRCULATORY ASTHENIA (EFFORT SYNDROME)

Delicacy in childhood	Fainting, giddiness
Weakness	Headache
Fatigue	Tremor of hands and legs
Early exhaustion	Sweating of hands, axilla, feet
Precordial pain	Cyanosis of extremities
Palpitation	Blood pressure elevation, temporary
Pulse acceleration	Preference for light work
Extrasystole	

In the Male.—Whereas, in the female, chronic tonsillar and upper respiratory infections as described produce a picture of dysthyroidism, in the male, as indicated in a previous communication,[18] the result is entirely different.

Chronic tonsillar and upper respiratory infection in the male is found associated with the clinical picture of neurocirculatory asthenia, or effort syndrome. I was much impressed by this fact when I found a brother and sister of nearly the same age having diseased tonsils. In that case, the girl will show dysthyroidism of the type described, while the boy will present a typical case of neurocirculatory asthenia. This divergence in the pathologic physiology of a disease is of great interest. Here, it accounts for the fact that in goiter clinics there are ten times as many female as male patients.

Neurocirculatory asthenia, or effort syndrome, is essentially a disease of civillian life. Its discovery by the army officer was for one purpose only; to insure such an individual against exposure to physical or nervous strain. The individual with this syndrome is a constitutional inferior. As seen in these cases, neurocirculatory asthenia occurs in a person who is the product of a bad heredity plus severe or oft-repeated infection. This type of patient finds his way to the cardiac clinics and, in their present nomenclature, his case is classified as "potential cardiovascular," which is entirely correct. The syndrome in these male patients is unmistakable. When they are not exposed to undue strain, the symptoms complained of are mainly subjective, and of varying degrees of severity. They show an inability to perform arduous labor, and they are breathless after sustained physical effort. The most frequent symptoms are precordial pain, dizziness, profuse perspiration, cyanosis, and sweating of the extremities, and there are other evidences of an inefficient circulatory system.

For a time, this class of patients was considered as suffering from hyperthyroidism; but this seems to have been disproved. Nevertheless, they do show evidences of some endocrine or autonomic disturbance.

That infection plays a prominent antecedent rôle in neurocirculatory asthenia is believed by many observers. Swan,[19] in a series of ninety cases, found a demonstrable infection present in 87 per cent.

Thomas Lewis,[20] whose studies of effort syndrome (neurocirculatory asthenia) in recent years were the first and also the most complete, places infection of one kind or another as the dominant factor. Of 558 patients, about 80 per cent. had suffered from severe infection.

In youth and early adult life, vascular tension in persons with neurocirculatory asthenia is about normal. There is a constant tendency, however, for the blood pressure to go high under physical and nervous stimuli. This was pointed out by Sir James McKenzie and R. M. Wilson.

Patients giving a history of neurocirculatory asthenia when young and of hypertension in middle life constitute, in my experience, the larger proportion of the essential vascular hypertension group. This group of cases serves as a connecting link between the infections of early life, which are followed by neurocirculatory asthenia, and the hypertension of later life, which is preceded by neurocirculatory asthenia.

Neurocirculatory asthenia occurs most typically in the first three decades. During middle life, when the patient's nutrition and general well-being is at its height, the neurocirculatory asthenia as a whole may be masked.

During this phase, we find the man who, although very delicate in youth, has put on considerable weight, has to all appearances improved in health, and has taken a great hold on his occupation working at it with vigor and force. The work of his choice is seldom physical. It is mental energy that he expends so lavishly. He avoids effort and exertion, not because of a perverted mental attitude but because of a physical incapacity for that effort. This is the type of person whom we find with essential vascular hypertension after middle life. As I see him, he is the type whom Moschcowitz[9] describes as the candidate for hypertension:

> The patients are overweight, sometimes obese. Physically, these people are tense and irritable. Their interest outside their business is desultory. In their leisure hours, they play cards, sit in the theater, read the newspaper, or rehearse the business activities of the day. It is the picture of the tired business man. He eats well, drinks alcohol and takes no exercise. He is successful, he may be said to die of success. He has an incapacity for play, he is physically old.

TABLE 6.—ARTERIAL HYPERTENSION (100 CASES)

	Females	Males
Essential hypertension	33	25
Nephritis with hypertension	14	16
Cardiovascular lesion with hypertension	3	9
	50	50

A careful study of the life history of this individual reveals the fact that he suffered from neurocirculatory asthenia in his youth. Because of his effort syndrome, he finds escape from the physical hardships of life by using his brain. He submerges himself in work. The particular type described by Moschcowitz is the product of a metropolis. The same person, with local coloring, is seen in the provincial atmospheres and in the country.

19. Swan, J. M.: Analysis of Ninety Cases of Functional Disease in Soldiers, Arch. Int. Med. **28**: 586 (Nov.) 1921.
20. Lewis, Thomas: The Soldier's Heart and the Effort Syndrome, New York, Paul B. Hoeber, 1919, p. 33.

Occasionally, we find him taking exercise for his health. Once he discovers the stimulation and exhilaration which comes with exercise, and overcomes to a certain extent his innate dislike for it, he frequently becomes a "nut" on his hobby. In a little while, however, he will have applied so much of his mental intensity to the sport that he defeats the very object of it, thus reestablishing the former vicious circle, and hurrying on the vascular hypertension, which is awaiting him.

Such is the road leading to essential vascular hypertension in the male: heredity, severe acute or chronic infection, and disturbance in the endocrines or autonomic vascular control producing that circulatory disturbance known as neurocirculatory asthenia.

DIFFERENTIAL DIAGNOSIS

The relative frequency of this type of hypertension is well illustrated in Table 6, which is based on the last 100 unselected cases in my private practice.

The predominance of essential hypertension among women and of the vascular type in men is noteworthy. Of the thirty-three females, all but three belong distinctly to the dysthyroid group. Among the males, of twenty-five cases of essential hypertension, all but six belonged definitely to the neurocirculatory asthenia type.

The grouping of these patients cannot be accurately made without a complete survey of the life history, as well as a careful consideration of all the clinical evidences in the case. Of the fifty-eight cases of essential vascular hypertension, forty-nine conformed completely to the course of the disease as described.

In the segregation of nephritis and essential hypertension it is of great importance that it be carefully done, with clinical acumen and judgment. The mere presence of albuminuria is no criterion; nor is cylindruria or nocturnal polyuria. Many times I have seen these three disappear after hypertension was reduced and a normal circulation reestablished. Fixation of specific gravity, of urea and salt elimination, permanent nocturnal polyuria, low phenolsulphonepthalein elimination and such clinical evidences as edema are decisive. Biochemical examination of the blood, one or more times in almost every one of these cases, was the least helpful toward a reasonably early diagnosis of nephritis. Aside from the blood pressure readings, the diagnosis of nephritis depends on positive findings; while the diagnosis of essential vascular hypertension depends more on the absence of those findings.

COURSE AND SEQUELAE OF ESSENTIAL HYPERTENSION

Essential vascular hypertension is not a spontaneous occurrence. It may be discovered unexpectedly, but it does not come on suddenly. Vascular hypertension occurs for brief periods as a physiologic response, for many years before it becomes permanently established. Once arterial hypertension is permanently established, it continues for a variable time. Prognosis in essential vascular hypertension is a hazardous undertaking on the part of the physician. The life of the individual with vascular hypertension does not depend on the degree of hypertension: it will be determined by the organ inferiority of that individual. This organ inferiority manifests itself by a decompensation or "break" in the heart, in the kidneys, or in the brain. Which organ will suffer decompensation first is determined by an inherited tendency and by the remote effects of previous infections [17] and injury. A person who has suffered a severe course of typhoid fever or meningitis with severe delirium, or has undergone a terrific mental strain, will show cerebral decompensation. A person who has had pneumonia, rheumatic fever or diphtheria, during which the myocardium was injured, will have a cardiac decompensation. The one who has had severe scarlet fever, repeated tonsillar infections or exposure with renal complications will, when the time comes, show renal failure, with all of its manifestations.

SUMMARY

1. The conception of some of the early writers as to the etiology of essential vascular hypertension is corroborated by the evidences of today.

2. There are three prominent factors in the etiology of most of the cases of essential vascular hypertension: heredity, infection and endocrine disturbance.

3. These factors affect the male and the female differently. In the male, cases of essential hypertension give a history of an inherited tendency, systemic infection, neurocirculatory asthenia and vascular hypertension after middle life. In the female, there is a history of heredity, infection and endocrine disturbances involving the thyroid and generative system; and there is a tendency to dysthyroidism, sterility and vascular hypertension at the menopause and thereafter.

4. The course and sequelae of essential vascular hypertension will be determined by the organ inferiority of the individual. The organ inferiority is determined by heredity, previous infection and strain.

Jenkins Building.

A BIOLOGIC MECHANISM OF HUMAN ISOHEMAGGLUTINATION

THE CONSTITUTION OF THE BLOOD GROUPS AND THE INHERITANCE OF THE AGGLUTINOGENS

MANUEL G. GICHNER, M.D.
BALTIMORE

In his two communications on the medicolegal application of the blood groups, Buchanan [1] casts serious doubt on the present structure of knowledge concerning the mechanism of human isohemagglutination and the transmission in heredity of this function of the blood, and questions hypotheses that have long stood unchallenged. We are therefore called on to reexamine these hypotheses and to test their validity against observable phenomena.

CONSTITUTION OF THE BLOOD GROUPS

It is generally admitted, certainly by all the parties to the present controversy, that human individuals, classified with reference to the agglutinating power of their blood serum toward human red blood cells and the agglutinability of their red blood cells by human serums, fall into four groups. The following classification and description of the groups, adopted by the joint committee reporting in THE JOURNAL,[2] will be followed in the present discussion:

Group I. The serum agglutinates the cells of Groups II, III and IV. The cells are agglutinated by no serum.

Group II. The serum agglutinates the cells of Groups III and IV. The cells are agglutinated by the serums of Groups I and III.

1. Buchanan, J. A.: Medicolegal Application of the Blood Group, J. A. M. A. **78**: 89 (Jan. 14) 1922; **79**: 180 (July 15) 1922.
2. Isohemagglutination, J. A. M. A. **76**: 130 (Jan. 8) 1921.