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ESSENTIAL OR PRIMARY HYPERTENSION

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Table of Contents

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I. Introduction

"Persistently elevated arterial pressure with associated morbid changes of the vascular tree is probably responsible, directly or indirectly, for more disability and death than any other single pathological condition, including cancer and tuberculosis." (#40) Approximately 140,000 deaths in the United States in 1934 were due wholly or in part to a sustained high blood pressure. (#16)

Thus we find this subject a very pertinent medical question of today. Now that blood pressure measurements have become routine in the examination of patients and of applicants for life insurance, the frequency of the existence of high blood pressure, especially in persons of middle age, has become, not only among the medical practitioners but also among the laity, a matter of common knowledge. They also know of the consequences of this condition and are very apprehensive. They need much in the way of reassurance and that burden rests upon our shoulders, so we can well delve deeper into the study of this problem. Much has been written upon this subject so brevity in discussion is essential.

Essential hypertension, primary hypertension, hyperpiesia, arterial hypertension (synonyms) is a con-

dition occuring in middle or later life, especially between the ages of 40 to 60 years, though some cases are in the 10 to 20 year group. (#7) McCloud in his article (#24) quotes statistics obtained from three other authors and illustrated the causes of death with this condition.

	Heart Disease	Apoplexy	Uremia	Intercurrent Disease
Bell	60%	19.3%	8.5%	11.7%
Christian	32%	25 %	4.5%	37.5%
Granger	52%	31 %	5.5%	11 %

There is little difference in the incidence in sexes, there being some predominance in the males. In one series the ratio was 1.4 males to 1 female (#7) while in another series there were 48 males to 33 females. (#22) Factors tending to raise the mormal blood pressure are age, climate, increasing temperature, emotions, work, pregnancy, obesity, and fever. In general they are minor factors and not of consideration here.

Historically, although the circulation was described by William Harvey in a qualitative way, it was not until 1906 that blood pressure instruments were perfected to be used by the average physician. (#24) Life insurance companies recognized their value and hastened their use. It was not until 1918 that the value of the diastolic reading was recognized.

II. Definition.

3.

"Essential hypertension is a definite clinical entity in which, as the term suggests, increased blood pressure is the primary or essential finding. The pathologic changes which take place in various structures, notably the brain, kidney, and heart, are later developments produced by hypertension. The maintainence of adequate kidney function in this disease is one of its most characteristic features and serves to differentiate it from hypertension secondary to true nephritis." (#18) Mosenthal brings out the point that it is a persistant and increasing elevation in both systolic and diastolic blood pressure (#27), but it is generally agreed that it is classed as a raised blood pressure, the normal being generally given as 120/80 for a person 20 years old with an average increase of 2 mm. Hg. systolic and 1 mm. Hg. diastolic for every 5 years up to the age of 60 years. (#7) Bell and Clawsen also condider anyone having a systolic pressure of 150 mm. Hg. or over as a case of essential hypertension.

Kernohan and Keith have made the following clinical classification:

I. Mild benign hypertension shows a diastolic under 115 mm. Hg.; no impairment of heart or kidney.

II. Severe benign hypertension shows a diastolic over 115 mm. Hg. with evidence of impairment of vital organs and often with changes in the retina.

III. Malignant hypertension shows the diastolic pressure 130 to 150 mm. or higher, perhaps with marked impairment of vital organs with special changes in the

4.

retinal vessels.

There is the one point to be emphasized and that is primary or essential hypertension is not secondary or produced by a predeeding kidney lesion. (#7) Fishberg in his article (#17) adds the words "clinically nor anatomically evolved from the kidney" to exclude those cases that show a contracted kidney at the post mortem table. Although etiologically we can put no blame on the kidneys, we always find arteriolosclerosis there and some degree of renal involvement as the process goes on. Barker (#6) states that he believes that these separate phases of renal and arteriosclerosis are merely factors along a progressive line of degeneration.

Arteriosclerosis and hypertension are frequently associated, but it is important to remember that the prevailing opinion is that arteriosclerosis when associated with hypertension is an effect rather than a cause. (#18)

III. Etiology

The etiology of essential hypertension is as yet unproven. We have a great many ideas about it, which in turn proves that we cannot point to anything definitely and so gather in a mass of material from which to take the best. The cause of this condition is so important because therapeusis cannot well be practiced until we can remove the cause. Data has accumulated

much in the last few years and Dr. Weiss (#41) has an excellent recent article concerning this subject. He divides the line of approach up into the following groups: (1) the role of circulating substances, including hormones; (2) the influence of the nervous system; (3) the reactivity of the vascular system and mechanical factors; (4) infections and allergy; and (5) constitutional factors.

We shall consider them in the above order for the sake of routine.

(1) The role of circulating chemical substances in arterial hypertension:

This approach to the etiology of hypertension is perhaps the most obvious, particularly since examples of hormones with a vasoconstrictor effect are available.

Guanidine has been proposed as a causative factor but Jackson in a communication to Weiss (#41) was unable to show any conclusive results.

Cholesterol has been found experimentally to rise in hypertension, but Weinstein and Weiss (#39) concluded the rise was the result rather than the cause.

Potassium-calcium Ratio has been studied but Steiglitz (#36) found in his study that hypocalcemia is not a factor in the hypertension of pregnancy. Elevation of the ratio of potassium-calcium ratio was found to be the result of circulatory failure. (#49)

Proteins have been found experimentally to cause arteriosclerosis of rabbits but this is not a part of

the disease picture in man and has therefore been
discredited. (#39)

Epinephrine has aroused considerable study be-
cause of its pressor effect. Philpot (#33) suggested
hyperadrenalemia as responsible for at least a cer-
tain type of hypertension. However, Curtiss and
others (#11) found no increased pressor effect in the
blood of hypertensive patients. It should be remem-
bered also that many negative findings in post-mortem
examinations of hyperplasia and adenoma of the cortex
of the adrenal gland are not reported. Cases of se-
vere and fluctuating hypertension in the tumors of the
adrenal gland (#31) are not sufficiently well under-
stood to be decided upon.

The pituitary theory of the origin of hypertension
has aroused much interest lately by the contributions
of Cushing. (#12, #13) In describing the syndrome of
basophilic adenoma, he has called attention to the fact
that arterial hypertension is frequently present. Not
only is there insufficient work along this line but in
view of the association of basophilic adenoma with bod-
ily changes involving different types of tissues, the
interrelation between basophilic adenoma and hyperten-
sion is open to a number of other explanations than
the effect of circulating pituitrin.

Thyrotoxicosis has been studied (#37) but there
seems to be no direct relationship to hypertension.

Vasoconstrictor substances of undetermined nature
have been seriously considered and much work done.

7.

Weiss (#41) was able to demonstrate a pressor sub-
stance in the blood and in the urine of normal sub-
jects, as well as in patients with hypertension.
Also this vasopressor substance had no relation to the
degree or to the type of hypertension. He found the
most powerful vasopressor substances were extracted
from the urine of normal subjects.

Alcohol and tobacco have been absolved as a part
in the etiology from a lack of any evidence to support
them. (#37) The fact that a study of the sex inci-
dence in a large group of cases (#34) showed a greater
incidence in females would tend to rule out alcohol
and tobacco.

Lead has been investigated and found a hyperten-
sion with sclerosis of the vascular system (#19) in
chronic lead poisoning, but this would account for
only a small fraction of the cases of hypertension.

Thus to summarize the results of many years of
investigation about the etiologic role of circulating
vasoconstrictor substances, there is nothing to sup-
port this theory except in those few cases where lead
is responsible.

(3) The role of the nervous system in the causa-
tion of hypertension:

The significant role of the nervous mechanism in
the regulation of blood pressure is well known. It
controls by means of sympathetic and parasympathetic
nerves. It has been suggested that hypoactivity of
the carotid sinus and other depressor reflexes might

8.

be responsible for arterial hypertension. However, studies on man have not found evidence to support this view and so it should be further studied. (#41)

The second possibility, namely that of an increased pressor nervous mechanism or sympathetic nerve action, is based on more evidence. Patek and Weiss (#33) found the influence of the sympathetic nervous system was more pronounced and that of the parasympathetic less so in patients with hypertension than in control subjects with normal cardiovascular systems. Bordley and Baker (#8) claimed an ischemia resulting from arteriosclerosis of the medullary centers is a factor, but Cutter's study (#14) casts much doubt on this idea, and we must remember there is greater ischemia in many conditions unassociated with hypertension.

Emotional stress as a factor influencing blood pressure has been much discussed. Whether vascular diseases with arterial hypertension are really modern diseases is quite doubtful. Apoplexy, heart failure of non-valvular origin, and uremia have always been common clinical manifestations, and hypertension occurs frequently among the population of quiet, farming villages. However, in a comparative analysis of a group of patients with essential hypertension and with normal cardiovascular systems, overexcitability, impulsiveness and a tendency to worry was more frequently present in the hypertensive group. (#32) Although psychic trauma and conflicts, as well as abnormal sensitivity of the psyche, play a role in essential

9.

hypertension, personality and emotional factors alone are not adequate in the explanation of even a single type of hypertension. This contention is also sup- ported by the fact that emotional psychoses bear no relationship to the level of the blood pressure. (#41) Barker (#6) also lays considerable stress on the psychic wear and tear on the vascular system.

(3) The reactivity of the vascular system and mechanical factors:

One mechanism in the development of a narrowed arteriolar system, namely, increased nervous tonus, has already been discussed. A second possibility, namely, a primary cellular or mechanical origin, also deserves careful consideration. Clinical and postmortem experiences reveal variations in the arterial lumen in different subjects. In advancing age there is progressive accumulation of intercellular cement substances, loss of elasticity of tissues, arteriosclerotic and other involutionary changes which are all included in the collective term of "changes of senescence." These changes result in the shrinkage of the lumen of the small arterial vessels and in a secondary progressive rise in blood pressure. A moderate degree of progressive rise is thus an expression of physiologic senescence. In persons thus with congenitally hypoplastic arterial systems or with increased severity of degenerative changes an increased arteriolar resistance also develops. Increased peripheral resistance plays a role in arterial hypertension is shown by cases of

10.

of obesity in which the hypertension may completely disappear with reduction of body weight; and in the fact that there is a sudden rise in the incidence of hypertension with the age of onset of involutionary changes in the body in each sex.

Wiggers (#43) claims that there is a progressive loss of elasticity and of the propulsive action of the aorta and other large vessels, but this should be further investigated.

Viscosity of the blood is largely discredited as a factor even though it is in Nesfield's opinion. (#28)

Local diseases of the kidney and urinary passages do tend to cause arterial hypertension, but the causes are not known. (#41)

(4) The role of infections and vascular allergy:

Evidence that infections play a direct etiologic role in the majority of instances of hypertension is lacking, but clinical observations, on the other hand, furnish ample evidence indicating an indirect etiologic role for infections. There is not a single type of infectious agent which is regularly associated with hypertension. The majority of infections associated with hypertension first produce kidney lesions, and hypertension then develops as a secondary manifestation.

Syphilis is not an etiological factor. (#32)

Diabetes mellitus appears to be a contributary cause in some cases of hypertension. (#7)

Allergy was given a part as a contributor to the etiology of hypertension by Waldbott (#38), but it is better to consider it an associative thing until more

11.

work is done.

(5) Constitution and arterial hypertension:

With all of the foregoing discussion, it seems as inevitable to have one more factor and that is the one of heredity. Daily clinical experience, also, suggests that among patients with pronounced hypertension all types of bodily habitus occur with approximately the same frequency. It is suggestive, then, that an understanding of the inherited anatomic and functional characteristics of the nervous and vascular systems rather than the bodily habitus will eventually bring the solution. It is known that the vascular and nervous systems are particularly apt to transmit constitutional stigmata. O'Hare with others (#30) elicited a family history of vascular disease in 68% of a group of patients with arterial hypertension. Ayman (#4) gave additional information. The fact that a hereditary history cannot be obtained in a higher percentage of cases is natural, and does not invalidate the significant role of the constitution; for a hereditary history is but partial and rather crude evidence of hereditary constitution. (#41)

Etiological Summary:

Weiss (#41) thus appreciates that arterial hypertension is not a disease entity but a bodily state of multiple etiology. The transition from a normal to a hypertensive state is very gradual. In the majority of instances of hypertension we are dealing with but a moderate accentuation of the physiologic factors.

Experience , on the other hand, has taught us that
patients with markedly elevated blood pressure fre-
quently exhibit functional and structural disturbances
of various organs; hence the clinical emphasis on the
problem of hypertension is justified.

In the study of the etiology of arterial hyper-
tension evidence today is available indicating that
the role of inheritance and constitutional predisposi-
tion are represented mainly be inherited and at times
acquired local irritability of the minute vessels, hy-
perirritability of the sympathetic vasomotor centers,
and hypoplastic development of the vascular system.
Among the secondary factors acting on such constitu-
tionally susceptible nervous and vascular systems are
emotional stress, physiologic changes of involution
and senescence, obesity, certain types of infections,
and reflexes, particularly from the kidney, and a few
exogenous chemical substances. The relative role of
these factors varies considerably. The present evi-
dence indicates that in the great majority of instances
involutionary and senescent changes are active in the
constitutionally predispesed individuals.

Thus the etiology varies and as Stieglitz states
(#37) "it was not the last straw that broke the camel's
back, according to the fable, but the last straw plus
all the rest of the previous load, and that load may
have been almost anything."

IV. Pathology

A brief rudimentary discussion of the physiology
of blood pressure is necessary to better understand
the underlying pathology. (#43) By blood pressure is
meant the lateral pressure exerted on the walls of the
vessels by the contained blood. It varies as the pro-
duct of the cardiac output and the peripheral resis-
tance. There are no heart changes in our study of
hypertension and so we have left the influencing fac-
tor of the peripheral resistance. It in turn is de-
pendent upon the factors of (1) the fluid viscosity;
(2) the size of the lumen of the tube; and (3) the vel-
ocity of the flow. In essential hypertension we con-
sider we have no alteration of the blood or its rate
of flow, and consequently we have left only the factor
of the size of the lumen of the tube. The reson the
greater resistance lies in the arterioles rather than
in the capillaries is because the rapidly moving fluid
meets much more resistance than the slowly moving flu-
id. The arterioles are under the influence of the
vasomotor center located in the medulla in the floor
of the fourth ventricle and are caused to respond by
the sympathetics and parasympathetics.

In studying the pathology of this condition, the
significant findings have mainly been in the arterioles.
Fishberg (#17) in 1925 reported findings in a series of
72 cases coming to necropsy. He found arteriolosole-
rosis occurs most frequently and most markedly in the
kidney and so his description is of the typical lesion

in that organ. In the afferent arterioles, the first
change noted is a deposition of so-called hyaline sub-
stance directly under the endothelium. The hyperplas-
tic elastic tissue undergoes regressive changes with
the appearance of lipoid and hyaline substance and
reactive proliferation of the neighboring connective
tissue, gradually resulting in marked narrowing of the
lumen which may slowly go on to complete obliteration.
There is a gradual and progressive degenerative atrophy
of the medial muscle with replacement fibrosis. These
lesions appeared in the kidney in every case, the spleen-
ic in two-thirds of the cases, the pancreatic in about
half, the hepatic in less than a third, and the cerebral
in about one-fifth. The arterioles of the skeletal
muscles, skin, and gastro-intestinal tract were rarely
involved and then to only an insignificant extent.
However, he concludes that the anatomic changes in the
kidney cannot be reconciled with the theory that essen-
tial hypertension is due to a disorder of renal func-
tion.

In 1938 Keith, Wagener, and Kernohan (#33) made a
study of 81 cases with special reference to the retinal
picture. However, in 7 cases they were able to make a
careful study of the pathology and found that the most
outstanding thing was the diffuseness of the lesions
and the degree of involvement of the smaller arteries
and arterioles, while the larger arteries and the cap-
illaries are comparatively free from change. The
changes in the arterioles are different from those ob-

15.

served in the arteries of old persons: there is marked
hyperplasia of the intima and hypertrophy of the media
and internal elastic lamina in contrast to the degen-
erative changes in senile arteriosclerosis with their
deposit#s of lipoids, fatty acid and calcium in the
intima and fragmentation but little hypertrophy of the
internal elastic lamina. Again in senile arterioscle-
rosis the smaller arteries and arterioles do not mani-
fest the extensive intimal hyperplasia and the marked
narrowing of the lumina which is so definitely shown
in these cases of malignant hypertension. The most
important and constant feature of these cases is the
extreme diffuseness of the lesion; not a single organ
or tissue escapes, and even the vessels of the gastro-
intestinal tract and the skeletal muscles are equally
severely involved. Sometimes the kidney, the heart,
or the brain is more severely injured, but not any
organ escapes.

In 1929 a very intensive study of the pathologi-
cal picture was made by Kernohan, Anderson, and Keith
(#23) in a run of 53 cases. They had conceived the
idea from the work in the preceeding reference here
that biopsy material from a superficial muscle in am-
bulatory cases of hypertension might show early histol-
ogic changes in the smaller arteries. Muscle tissue
was chosen because it composes about 35 to 40 per cent
of the body and thus an assumption that there is a
widespread lesion of the arterioles could be readily
proved or disproved. They examined the arterioles in

small pieces of muscle taken by biopsy from the pectoralis major. The most pronounced and most constant change observed in the vessels was in the media, which was definitely hypertrophied, and there was an increase in the nuclear elements of this tissue. There was no fibrosis or increase in connective tissue; the entire change was due to proliferation of muscle. There was also hypertrophy of the internal elastic lamina. In the intima the change was widely varied, but the most common modification was proliferation of the lining endothelial cells. This sometimes was accompanied by proliferation of the subendothelial tissue, and when both changes were present the vessel was almost occluded. Complete occlusion was the rule. It does not seem logical, they think, to assume that any vasomotor spasm could bring about proliferation of the lining endothelial cells, although it might possibly produce some hypertrophy of the media. The fundamental changes occuring in these vessels were hypertrophy of the media and proliferation of the intima. There was no degeneration , nor any change that could be attributed to senile retrogression.

They classified the types of hypertension into benign, severely benign, or early malignant, and malignant hypertension. In benign hypertension there may be no lesions in the peripheral arterioles or there may be moderate ones. Their data, obtained at biopsy, was in harmony with the long retention of adequate retinal, cardiac and renal function and with the stationary or

17.

slow progression of the general condition. In the severe benign or early malignant hypertension, the clinical observations indicate more serious involvement. In spite of the clinical evidences of diffuse involvement, and a corresponding marked pathologic change in the peripheral arterioles that often is present, many of these patients still had remarkably good retinal, cardiac, and renal function. Such results suggest that either the lesion in the arteriole, although marked, has been of shorter duration, or better compensation has taken place. In their cases of malignant hypertension there was a definite retinitis. In such cases there was almost invariably a marked thickening of the wall and narrowing of the lumen of the arteriole in the muscles. The clinical course was rapidly progressive. So they considered there were good reasons for considering malignant hypertension as the terminal stage of the severe benign or early malignant type. They did some nice work in the study of the relation of the vessel wall to the lumen and so the results of the work were that in a lesion of the arterioles of voluntary muscle, the chief pathological changes were hypertrophy of the media, proliferation of the intima and marked reduction in the ratio of wall to lumen.

Keith, Barker, and Kernohan in 1931 (#21) concluded in addition that the changes do occur in skeletal muscle more often in cases of severe hypertension, but the changes are not proportional to the duration, height, or fixation of the blood pressure, and also

when present with clinical manifestations, the ulti-
mate prognosis is serious.

V. Pathogenesis

The development of the pathological changes is
not well understood because we are not sure of our
etiological foundation, but McCloud (#24) in his clas-
sical article has given a very good interpretation to
the arteriolar changes as he believed it to be.

Step 1--There occurs an irritation to the arteri-
oles by almost anything (toxins, protein excess, bac-
terial poisons, condiments, vasomotor hypertonia, etc.)
which results, ofcourse, in

Step 2--Increased tonus or spasticity of the
smooth muscle of the mesial layer of 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 con-
tinuation of the original irritation, the spasticity
becomes even more marked.

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

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

Such hyperirritability is also seen in the nervous
mechanism. We all become cranky, fussy, irritable when
very tired. With such a lowered threshold, mild irri-

tation or stimulation leads to an exaggerated response
of more spasticity.

Thus a _vicious_ _circle_ is set up: Steps 4-5-6-4-5-
6-4-etc. This is called "The perpetuating factor in
hypertension," as it continues to operate, although the
original source of irritation in Step 1 **has ceased to**
exist. It is also termed "The **vicious** circle of fatigue

Step 7--If fatigue continues to _exhaustion_, the
muscle cells degenerate, die and fail. Thus simulta-
neously with the activity 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 proliferated to sup-
port the crumbling framework of the vascular wall as a
scaffolding to protect it. Eventually the greater por-
tion of the arteriolar medial muscle is replaced and
the final stage is

Step 9--Up to Step 7 the processes are reversible
biologically; fatigue may be relieved by rest, hyper-
trophy may subside. Beyond Step 7, with fibrotic re-
placement of _exhausted_ muscle, the processes are irre-
versible and _not_ amendable to therapy. Characteristic,
ofcourse, of the spastic early phases is the variabil-
ity of the diastolic tension; inversely, after fibrosis
occurs, diastolic tension is fixed and rigid. There-
fore, we may use the variability of the diastolic ten-
sion as an index to the degree of permanent change; the

more variable the diastolic tension is, the _less_ the
actual sclerosis.

Ofcourse, all of these processes are slow and
gradual; taking years to develop. Probably in various
structures various phases of this procession occur
simultaneously, and there is _no_ sharp transition be-
tween the steps.

VI. _Symptomatology._

The symptomatology is a very variable factor.
Many cases of essential hypertension are picked up in
a life insurance examination and so are consequently
unaware of their condition and have no complaints re-
ferable to it. However, many patients do come in with
definite complaints and these are summarized by Rise-
man and Weiss (#35) from a series of 1,090 ambulatory
cases who were not suffering from the accidents or com-
plications of this condition seen in the majority of
patients with hypertension who enter hospital wards.
These cases are made up of 389 men and 801 women. The
systolic pressure was 160 mm. Hg. or above in 90 per
cent of instances; the diastolic pressure was 100 mm.
Hg. or above in 64.5 per cent of the cases. The symp-
toms with percentage occurrence were as follows:

1. _Headaches_ (43.3 per cent of cases) were usually
steady and noted mostly early morning or evening.

2. _Dizziness_ (40.3 per cent) occurred mainly by
change of position and immediately after rising in the
morning and after retiring at night.

3. Somatic aches and pains (38.7 per cent) were distressing both to the patient and to the examiner. The pains were of various sorts, but usually vague and indescribable and changed locations, and so on. No explanation for them was found, physiotherapy giving temporary relief.

4. Dyspnea on exertion (27.7 per cent) was the only main cardiac symptom recorded and yet there was not enough evidence to justify a diagnosis of myocardial insufficiency.

5. Nocturia (25.9 percent) is another symptom not well explained as there was no sign of renal damage in any of these cases.

6. "Nervousness" (13.2 per cent) included a tendency to worry, to become easily upset, emotionally unstable, and introvertive.

7. Palpitation of the heart (13.1 percent) in a small percentage of cases.

8. Tinnitus (11.8 per cent) was bilateral usually, steady and continuous, and very distressing to the patient.

9. Weakness (11.6 per cent) usually includes both an increased ease to fatigue and also a subjective sense of weakness or loss of muscle power, especially the legs.

Many other symptoms are mentioned, but they occur of but 5 per cent or less frequency--as insomnia, epistaxis, precardial pain, numbness and tingling, edema, spots before the eyes, hot flashes, cramps, nausea, vomiting, blurred vision, and so on. 129 patients had

no symptoms whatsoever. Almost all of the symptoms of patients with arterial hypertension are referable to a disturbance of the central nervous system and are expressions of a disordered vasomotor system.

In the vast majority of cases, symptoms and signs of serious involvement of the three organs vitally concerned with this condition usually develop--namely, the heart, brain, and kidneys. (#7)

The indications of cardiac disease are dyspnea, edema, cardiac pains of various kinds, cyanosis, palpitation, enlargement of the heart, and murmurs. Death may occur suddenly from coronary occlusion.

The symptoms referable to the brain are headaches, dizziness, nervousness, nocturia, fainting, irritability loss of memory, and transient or permanent paralysis.

The evidences of renal damage are usually high blood pressure, severe retinal changes, progressive renal insufficiency (as indicated by laboratory tests), albuminuria and casts, and terminally clinical signs of uremia. Albuminuria alone is not evidence of serious renal disease, since it may be due to passive congestion or to temporary ischemia of the kidneys.

As a rule the symptoms are predominently referable to one of these organs.

VII. Diagnosis

By virtue of the definition of this condition, the diagnosis rests primarily upon blood pressure readings by means of a sphygmomanometer, the systolic usually being where the sounds first come in and the diastolic

where the sound changes from sharp and clear to soft
and muffled or where it completely disappears, the
average difference between the two being 4 mm. Hg.---
the former usually being used. (#34)

As we have explained in the preceeding, the symp-
toms may aid in the diagnosis, but are sometimes ab-
sent and so the diagnosis must be made by blood pres-
sure and additional signs. Normal blood pressure is
around 120 systolic and 80 diastolic for a person 20
years old (#7) and then with a gradual progressive
rise with age up to around 140 systolic and 86 diastolic
Bell and Clawson (#7) called all cases with a persis-
tent systolic blood pressure of 150 mm. Hg. or over,
of unknown etiology, as cases of essential hyperten-
sion. Usually, however, most authors take the diastolic
reading as the important one and if it is over 90 under
40 years of age or over 95 over 40 years of age, it
will show an increased mortality and a diastolic of 100
mm. Hg. at any age is pathologic and certainly classed
as an essential hypertension. That the diastolic ten-
sion is the least fluctuating of the two readings is
given by most authors, but Ayman shows marked varia-
tions in the readings. (#3) The essential point here
in diagnosis is a persistently high or rising blood
pressure above the limits of normal.

A valuable aid in identifying the hypertensive
state is by the aid of the opthalmoscope. This aid
is found mainly in the more severe states and gives
a bad prognosis. The early cases do not show any

marked changes. Keith, Wagener, and Kernohan (#22)
reported a series of 81 cases of the early and later
malignant types and all except one case had consistent
eye findings. The vision is surprisingly good. The
type of retinitis and not its severity is characteris-
tic. Edema of the discs is a striking feature in all
the cases and is often disproportionate to the other
retinal changes. All grades of retinitis, from the
mildest to the most severe, run a characteristic course
which may be divided into four stages. The first with
hyperemia and mild edema of the disc and few superficial
hemorrhagic areas and cotton-wool exudates are present.
The second, edema of the disc and retina becomes more
marked and spreads into the macular region and peri-
phery, the hemorrhagic areas and cotton-wool exudates
become more numerous and are found farther away from
the disc. In the third stage, edema begins to recede
from the peripheral part of the retina and small spots
of pigment are seen instead. Punctate hemorrhages be-
gin to outnumber the cotton-wool exudates. In the
fourth stage, the disc has become definitely pale.
Atrophy has replaced edema of the retina and only a
few residual punctate exudates may remain, usually in
the macular region. The first stage is the shortest
and the third stage is the longest and most frequently
observed, it being only a matter of months for the
progression. The average length of life after diag-
nosis for this series was eight months.

Ernstene and Snyder (#15) have experimented and

found useful for diagnosis in essential hypertension the injection of a small quantity of histamine dihydrochloride into the forearm skin. They found a marked reduction in the size of the flare in patients with hypertension of the intermediary and malignant types. They recommend it as a valuable diagnostic aid.

Reference is made in Brown and Craig's article (#9) that experimental evidence is found indicating an abnormal vasomotor response to the application of a standard amount of a cold stimulus. This is apparent years before any rise in blood pressure and again is a valuable diagnostic aid.

VIII. Prognosis

Prognosis for a disease of the qualifications which this one possesses is a very individual thing. The group mortality and morbidity is definitely increased in cases of hypertension. (#34) Vascular disease destroys a very large number of people in or past the fourth decade of life. (#37)

Etiology is important in the prognosis because it is with the success that we can remove or alleviate it that we can modify the course of the disease. If the family history is especially predisposing, we can again not hope for very much. Definite constitutional factors in the etiology, such as heriditary vasomotor instability, obesity, poor neuromuscular control, inherent thyroid instability, affect the prognosis adversely. Specific infections, however, can be more

26.

definitely treated and influenced.

With increasing age there is probably an increasing incidence of arterial hypertension and so consequently an increasing mortality rate, but the younger the age with the onset the more malignant the condition tends to be. The amount of arteriolar sclerosis and the opthalmological findings give a good prognosis as to the future duration.

The most fundamental factor in the prognosis is the extent to which the pathogenesis has gone. If it is early, complete recovery may be hoped for, but after irreversible changes have set in, palliative relief is all that can be hoped for. The variability of the diastolic pressure is given by most men as to an estimate of the amount of arteriolar sclerosis. Stieglitz (#37) estimates this by comparing the average pressure of the patient to when he has inhaled 5 minims (ampule) of amyl nitrite.

The and result of this condition has already been pointed out; namely, that the mortality is chiefly in failure of the cardiac, cerebral, and kidney units. Thus it is necessary to measure and evaluate them in considering the prognosis. (#35)

Malignant hypertension can be distinguished from the benign form by the persistently high blood pressure and the rapid course. It may arise apparently out of the dark in the young, but frequently it is a later stage of the benign type. (#33) It has a rapid course, the average length of life after diagnosis was eight

months in one series of cases. (#23)

IX. Treatment

Therapy directed toward a subject of such varied etiology must necessarily be wide in its scope to attempt to cover all sides. The chief object in therapy is a gradual reduction of the excessive arterial tension to the optimal levels for the individual patient. This does not mean the theoretical normal because years of body readjustment and habituation to higher levels of arterial tension may make a moderate hypertension imperative for normal physiologic existence. The second objective is sparing the heart and this is evident with the realization that the chief cause of death is cardiac failure.

The first principle in treatment is to remove the etiological source if at all possible. This necessitates a careful study of the patient and his background. (#37)

The greatest aid we can give any patient is that of rest and so it is here. Mental and physical rest must be secured. Mental rest must be secured by making the patient shift some of his responsibilities and inquiring into his home condition and habits. Physical rest must be curtailed and a few of the principles are those of 1 to 2 hours rest after lunch every day, a full night's rest, and rest in bed over the week-ends if necessary. Rest is the cardinal treatment in this condition.

Drugs are a great aid in medicine and the same applies here. They are mainly effective as an adjuvant to rest and those much used along this line are phenobarbital and the bromides. Other drugs advocated are magnesium sulphate, opiates, iodides, hepatic extracts, sulphocyanates, and calcium. They are mostly of no proven worth. (#37)

Of the drugs there are three more that deserve mention. Bismuth subnitrate (#37) is advocated by Stieglitz as a most excellent therapeutic measure, explaining that by its slow breakdown in the intestinal canal into the nitrites there is a prolonged vasodilator action, the bismuth radicals not being absorbed. However, in a recent study (#10) it was not found to be of any value so it is of doubtful therapeutic worth. Digitalis is the drug of time honored value and should certainly be used continuously at the first signs or symptoms of an impaired circulation are noted. The nitrite vasodilators are of value in vascular crises for temporary use.

, Dietary management is necessary. Fats and carbohydrates give rise to obesity. Mosenthal (#37) found an increased blood pressure in 78 percent of people who were 30 per cent or more overweight. Regardless of our views on the relationship of obesity and hypertension, they both place a load on the heart and this is the greatest danger to the hypertensive. Thus we must give a well rounded diet and gradually reduce to an optimal level. The protein amount has no effect even

even though it supposedly has--the artic explorers and eskimos with their high protein diet not having an increased incidence--the important factor is to give the amount necessary for maintainence.

Fluids may be taken in amounts up to 6 liters per day with no influence on blood pressure and so as the average daily intake is around 1.5 to 3 liters, they may be freely encouraged if no cardiac or renal failure signs are present. (#27)

Salt restriction does not lower blood pressure but it has a distinctly advantageous effect on cardiac complications of palpitation, dyspnea, angina pectoris, edema, and anasarca. The cleansing of the intestinal tract by excessive purgation and irritation has found its advocates here as well as in other conditions. Alverez and his co-workers (#3) have shown that constipation and so-called intestinal autointoxication do not have any relation to hypertension, but this does not mean to neglect the bowels. (#37)

In the way of physical means of treatment, venesection is an old much-used means and is effective and desired in cases of vascular crises before apoplexy and cardiac failure. It, however, produces a secondary anemia and so should be used with wisdom. (#37)

Baths at body temperature are good to aid in body relaxation. Do not send a patient to another climate for rest if he would worry about the financial strain and so secure no rest.

Massage is good for terminal cases but it is not

greatly used.

Diathermy and light radiation are of doubtful value.

X-Ray and radium seem to give temporary relief or drop in blood pressure but are not for long continued use until further study. (#20)

Some newer therapeutic procedures have been devised, but must be further investigated. Ayman used Theelin (crystaline ovarian hormone) in treating patient on the basis of correlating endocrine and arterial functions, but his efforts were not successful. (#5)

Brown and Craig (#9) and Adson and Brown (#1) have done recent work in denervating the splanchnic area and suprarenal glands of their sympathetic nervous control and obtained a good reduction in blood pressure with but little effect on the patient. This is a specially good form of treatment in young adults with the malignant form.

X. Conclusions

1. High blood pressure appears to depend chiefly upon a narrowing of the lumina of the arterioles in the precapillary areas.

2. The arterial narrowing is at first functional, due to hypertonus of the arterial musculature, though later it is also partly organic, due to arteriolar sclerosis.

3. The actual causes of the persistent arteriolar hypertonus and of the organic arteriolar sclerosis are

as yet unknown. The relations to chronic renal disease, to atherosclerosis in general, to exogenous and endogenous poisons, to infectious processes, to the "wear and tear" of life, to abnormal metabolic states, to endocrine disorders, and to certain types of constitutional make-up have been much discussed.

4. The different types of the disease seem to be related to each other in a progressive way--arising from the same fundamental process.

5. When recognized early, much can be done in treatment, if not in curing, to at least prolonging for a long and useful life.

6. In the later stages, much can be done to relieve symptoms and give comfort to the patient, but it is much better to face reality than to attempt meddlesome therapy.

7. The chief prophylaxis against this condition is to get ourselves well-born, from an unblemished family stock and then lead a life of temperance and well regulated activity.

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