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HYPERPIESIA
(Essential Hypertension)

SENIOR THESIS

Presented to Faculty of University of Nebraska, College of Medicine as partial fulfillment of the requirements for the Degree of Doctor of Medicine.

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Lawrence Milford Mattison
INTRODUCTION

Hyperpiesia, a disease that kills, directly or indirectly, more people than tuberculosis and cancer combined, certainly needs no apology for its introduction for your consideration.

I shall confine myself to that form of high blood pressure known as hyperpiesis, or essential hypertension, by which we understand an elevation of blood pressure above normal, of unknown origin. 27 26 18 33

DEFINITION

The term hyperpiesis was coined by Sir Clifford Allbutt in 1900 to distinguish cases of high blood pressure in which albumenuria was absent and the kidneys postmortem appeared to be healthy from those grouped under the term chronic interstitial nephritis, in which the kidneys are grossly diseased and high blood pressure is also a constant feature. 13

The term hyperpiesia is generally applied to any condition in which blood pressure is maintained at a level above normal, irrespective of the degree of duration of the elevation. Such use of the term admits of confusion and doubt in the mind of the reader, because of the diversity of conditions included is so comprehensive a term. The fact that careful clinicians continue
to report cases with hypernormal blood pressure, in the absence of either cardiac or nephritic degenerative changes, and since we are able to obtain a permanent and lasting return to normal blood pressure values in certain cases by appropriate treatment and hygiene, it would seem to justify an effort to limit this term to admit the presence of such a clinical entity, having as a prominent symptom, a transitory elevation of systolic pressure; for if we fail to recognize this clinical condition, there will remain an unfilled gap in our clinical conception of cardiovascular and renal pathology.

**Physiology of Blood Pressure**

It is essential, in studying blood pressure, that one should be informed concerning its physiology, for without knowledge of the physiological mechanism which plays such an important role, an intelligent comprehension of the sphygmomanometer is impossible. The human blood pressure system comprises essentially, (1) the heart, (2) the blood-vessels and (3) the vasomotor regulating mechanism. The three are so intimately associated that disturbance of any one is followed by a derangement of the balance existing among the three.

**Heart and Blood Vessels.** As far as the heart and blood-vessels are concerned, blood pressure depends essentially on three factors: (a) the energy of the heart,
(b) the peripheral resistance and (c) the volume of the blood. The first two are of great importance which the last has but a theoretical interest.

**Blood Flow in Arteries.** The vascular tree consists of a finely divided system of elastic tubes, the blood flowing through the arteries, through the capillaries, to the veins, the pressure being highest in the arteries and lowest in the veins. This is designed for the movement of the column of blood, as a fluid must flow from the point of highest pressure to the point of lowest pressure. It is through the activity of the heart that the difference in pressure is maintained. When for any reason, the heart ceases to function the circulation continues, that is, the blood flows, despite the failure of the heart from artery to vein, until the pressure in these two branches of the vascular system has been equalized, at which moment the blood stream comes to a standstill.

Despite the periodic activity of the heart, the blood is sent through the vessels in a continuous current, the reasons being, (1) the resistance offered by the arterioles and capillaries, and (2) the elasticity of the arterial wall. These two physical properties of the vessels prevent stagnation of the blood during diastole, and account for its propulsion during this phase of the cardiac cycle. The elastic property of the arteries is especially concerned, for the vessel being put on the stretch during systole,
stores up this energy to discharge it during diastole, thereby contracting the artery and expelling the blood. One might almost speak of this as an echo of the cardiac systole arising in the arteries.

**Blood Flow in Capillaries and Veins.** By the time the blood arrives at the smaller arteries little is to be seen of the rhythmic activity of the heart, that is, pulsation is generally no longer appreciated, and when the capillaries are reached, there is no pulsation at all (excepting in pathological states), although they do possess the power of contraction. By the time the blood gets to the veins, the force of the cardiac systole is nil, and for the propulsion through this part of the vascular tree, the negative pressure is the thorax and the aspiration of blood by the diastole of the heart are called into play.

Newer researches have demonstrated that certain veins are supplied with constrictor fibers, such as the portal vein, which receives branches from the splanchnic nerves, and it has been suggested, and indeed almost proved, that the systemic veins have a vasomotor control. Just how much influence these vasomotor nerves have in the circulation of blood in the veins is uncertain.

**Resistance of Blood-vessels.** In a system of tubes, such as is represented by the vascular apparatus, the blood exerts equal pressure on all parts of the vessel
wall at a given point, but the pressure varies proportionately with the amount of resistance the blood has to overcome.

Were the circulatory apparatus a rigid, unyielding set of tubes, the pressure would diminish in direct proportion to the distance from the heart. We have said before, that the pressure in a system of tubes depends largely on the amount of resistance which the circulating fluid has to overcome. This resistance does not arise from contact of the fluid with the vessel wall, for the fluid in direct contact with the latter is at rest, and therefore the friction must take place in the blood itself, the degree depending on the viscosity of the fluid. The amount of resistance which a constant uniform viscosity exerts is dependent on the length and diameter of the tube or vessel.

Volume of the Blood. This plays a subordinate role, in the maintenance of blood pressure. The volume of the circulating fluid can be much increased, without any appreciable effect on blood pressure, provided the increase takes place slowly. This is seen experimentally by the injection of physiological salt solution and other substances into animals. Failure thus to raise blood pressure, is due to three factors: (1) the rapid interchange between the vessels and tissues, (2) the automatical dilatation of blood vessels in order to adjust themselves to the increased amount of fluid, and (3) the subsequent
polyuria. The last is the most important, the amount of urine running pari passu with the amount injected.

On the other hand, losses of blood do decrease, if but temporarily, the blood pressure, so that one must, in a dog at least, remove about one-fifth of the total quantity of blood before any great depression of blood pressure is seen. In man the loss of one-half of the amount of blood causes death (3-3.5 percent. of body weight).

Vasomotor Regulating Mechanism. The smooth muscle of the arteries was discovered by Henle, and soon thereafter Stilling and Henle hinted at the pressure of vasomotor nerves whose existence was later proved by Claude Benard in 1852. To schiff, Ludwig and Thiry we are indebted for the proof of the vasomotor centre.

When a nerve which controls the vessels is cut, there will be a suffusion of the area supplied by the vessels under control of this nerve, also an increase of the warmth and size of the part and of the blood pouring from the veins. Stimulation of the same nerve has the opposite effect. Depending on the extent of the vessel's nerve distribution there will be a fall or rise in systemic arterial blood pressure, following severing or stimulation of the nerve respectively.

The vasomotor nerves are distributed in the musculature of the media, and since the muscle fibers are circular in their arrangement, the effect of stimulation is to constrict the lumen of the vessel (vasoconstrictor
nerve). The vasodilator nerves are but little understood. Dilatation of the vessels has been held to be due to the influence of the longitudinal muscle fibers acting in opposition to the circular musculature, but Galty believes that vascular dilatation is due to inhibitory nerves, which oppose the vasoconstrictor fibers. It is supposed by recent investigators that both varieties of nerve fibers are present in the same nerve trunk, and that depending on the quality of the irritant constriction or dilatation is effected. This view has been held by Pal, Stricker, and others to explain the occurrence at one time of vasoconstriction and at another time of vasodilatation, as for instance, in the crises of tabes dorsalis.

Vasomotor Centre. That there is a vasomotor regulating centre has long been proved. When the spinal cord in the region of the cervical portion is severed from the medulla, the blood pressure falls, and when the same region is stimulated there will be a rise in pressure, both phenomena being brought about by dilatation and constriction respectively, of the vessels in the splanchnic field. The seat of the vasomotor centre is in the upper part of the medulla. The centre is automatic in its activity. It is influenced principally by three factors: (1) psychic states, (2) gaseous composition of the blood, and (3) reflexly, by cutaneous influences.
Psychic Influences. The result of psychic influences is seen in pallor from fear, and in flushing, as in shame or anger, although it cannot be denied that there is an associated cardiac participation in these phenomena.

Gaseous Composition of the Blood. Whenever there is dyspnea the blood pressure rises through stimulation of the vasomotor centre, some believe, from the diminished amount of oxygen and others from increased amount of carbon dioxide. If the breath is held, the same phenomenon is observed.

Reflex Influences. Very mild irritants applied to skin, such as blowing on the skin or light contact, cause a rise in blood pressure but strong stimuli are without effect. Certain sensory nerves, which, when stimulated, give rise to increase of blood, have a depressor effect when the stimulus is applied to narcosis. Such a nerve possessing these two properties has been discovered by Ludwig and Cyon (N. depressor). It arises from the vagus and the superior laryngeal nerve and terminates in the heart muscle itself. It is believed that vasodilation and depression of blood pressure follow its stimulation and Langendorff hints at the possible existence of a vasodilator centre.

Spinal and Peripheral Vasomotor Centres. The chief regulating influence of the blood vessels lies in the vasomotor centre, whose duty is to assume charge of all blood vessels. The work of this centre, is, so to speak, apportioned out among lesser vasomotor centres, which regulate the activities of local vascular fields and whose seat is in the thoracic portion of the spinal cord.
seems to be definitely proven, inasmuch as the lowered blood pressure which follows division of the medulla, rises again, and disappears entirely when the spinal cord is destroyed. These spinal centres are excited by dyspneic and reflex stimuli but to a much lesser degree than the medullary centres.

THE HYPERTENSION

In a large majority of patients with hyperpiesia (essential hypertension) who come to the physician with subjective symptoms of the disease, the blood pressure is so definitely elevated that there can be no doubt of the existence of hypertension. Usually, the systolic pressure is well over 160 mm. and the diastolic over 100 mm. However, one occasionally encounters cases in which the systolic pressure is about 160 mm. and the diastolic about 95 mm. in a middle aged person, so that without further observation or the demonstration of cardiac hypertrophy, the existence of actual hypertension is questionable. Such borderline cases are met with particularly during insurance examinations and in the examination of patients for complaints having no relation to hypertension.

The height of the blood pressure varies greatly in different cases. The values encountered most frequently are around 200 mm. systolic and 110 mm. diastolic. However, the systolic pressure may reach almost 300 mm. and extremely rarely exceed it, and the diastolic even surpass 180 mm. In other cases the blood pressure remains
for years around 170 mm. systolic and 95 to 100 mm. dia-
stolic. In some instances the blood pressure rises rapidly or more often slowly but progressively as the patient is watched for years. On the other hand, in very many patients the height of the pressure does not change notably from that found at the first examination, even though it is followed for years.

Both systolic and diastolic pressures are elevated, but not necessarily proportionately. Severe arteriosclerosis of the aorta tends to lower the diastolic pressure so that in old individuals with a very rigid aorta, such pressures as 200/95 mm. are not uncommon.

**ETIOLOGY**

One of the most interesting problems in clinical medi-
cine is the etiology of high blood pressure. At the outset one may say that up to the present no satisfactory solution has yet been arrived at. Increased peripheral resistance in the circulation must be an essential factor in high blood pressure. Take the analogy of a fire hose with a pump at one end and a nozzle at the other, other things being equal, the pressure in the hose will rise proportionately as the diameter of the nozzle is decreased.

In human circulation, things are not quite so simple, as the force of the pump is a variable factor, but the analogy suffices to emphasize the important part played by the increased peripheral resistance. Our difficulties arise
when we come to inquire as to the cause of this. Arteriocapillary fibrosis, increased viscosity of the blood, and hypertonus of the arterial system and of the smaller arterioles in particular have been cited as etiological factors of increased peripheral resistance. 13

Experimentally it has been found that various substances when injected will give rise to hypertonus of the arterial system and a rise in blood pressure.

1. Major and Stevenson found that injections of methyl guanidine, one of the normal excretion products of nitrogenous metabolism, will cause a prolonged and pronounced rise of blood pressure when injected into dogs. 38 They suggested that excessive production or deficient elimination of this substance might be an important factor in the causation of higher blood pressure in man. 13

2. It has been suggested that some toxic substance from cellular disintegration in the kidney might be a cause, but Cash has shown experimentally that extensive necrosis of the kidney from ligation of a vessel does not cause any rise of blood pressure in dogs. 13

Imperfect elimination of various other waste products of nitrogenous metabolism by a diseased kidney has been suggested as a possible cause of high blood pressure.

The term hyperpiesia was coined by Sir Clifford Allbutt in 1900 to distinguish cases of high blood pressure, in which albumenuria was absent and the kidneys postmortem appeared to be healthy, from those grouped under the term
chronic interstitial nephritis, in which the kidneys are grossly diseased and high blood pressure is also a constant feature. At that time the clinical differentiation was not always easy, but since the days of the estimation of the blood urea, it has become possible to draw a sharp line of demarcation between the two groups, and to classify them, as that in which this is nitrogen retention, with a high blood urea, and the hyperpiesia group in which the blood urea content is normal. 13

Many of the symptoms in these two groups are similar and may be attributed to the high blood pressure, e.g., tendency to cerebral hemorrhage, headache, retinitis, respiratory symptoms, such as so-called cardiac asthma and attacks of paroxysmal dyspnea and cheyne Stokes respiration. 13

The subjects of hyperpiesia usually die of cerebral hemorrhage or heart failure, the kidney cases, though they may have a similar termination, die more commonly with symptoms of what has been termed uremia. It is curious that this term, which was coined many years ago, and has been subjected to a good deal of abloquy in the past, because it was proved that urea was not the toxic agent which killed in kidney disease, should now in a way have come to its own; for though urea may not be the toxin which produces the fatal symptoms, excess of urea in the blood is always of serious prognostic significance and one of the most important investigations that can be made from the point of prognosis in renal diseases. 13
The symptoms of what is termed uremia include most of those already mentioned as occurring in hyperpiesia, but the termination by convulsions and coma is rare in simple hyperpiesia and the headache and vomiting are usually more severe in renal cases, and the general aspect of the patient much more toxic. I think one must conclude that there is in addition to the hyperpiesis some toxic substance or substances, not eliminated by the kidney, which play a part in uremia. Moreover, the fact that the blood nitrogen content is normal in simple hyperpiesia, but is greatly increased in cases of uremia, shows there is impaired excretion of nitrogenous waste products, among which may be the unknown toxic substance responsible for some of the symptoms in uremia.

If the nitrogen content of all the known non-protein bodies in the blood, including creatinine, creatine, amino acids, and so on, is estimated, and also the total nitrogen content of the blood, it is found that there is an excess of nitrogen in some combination of unknown constitution. This moiety is increased in all cases of nitrogen retention, and may possibly be the element responsible for the toxic symptoms in uremia, which may present in addition to those due to high blood pressure.

If, then, we exclude retention of nitrogenous waste products as the cause of increased peripheral resistance, what alternatives are left? Hypertonus of the arterial system might be accounted for by undue stimulation of the
vasoconstrictor fibers by impulses from the sympathetic or the vasomotor centre in the medulla. 13

Excessive secretion of pressor substances such as adrenalin or pituitrin have been suggested as possible causes. Experimentally, repeated injections of adrenalin will raise the blood pressure in animals and give rise to aneurisms in rabbits and conversely in Addison's disease destruction of the adrenals is associated with a very low blood pressure. 13

In Grave's disease excessive secretion of the thyroid is responsible for the symptoms so it is conceivable that excessive secretion of adrenalin might be a factor in hyperpiesis, and this theory was advanced by Balty Shaw in his Goulstonian lectures in 1906. 13

No hypertrophy or abnormality of the adrenals, however, has ever been found in cases of hyperpiesis, and Swale Vincent remarks "that the tonic action of the adrenal function is the one held only by physicians, despite the fact that experimental work fails to demonstrate any definite physiological value for the adrenal output". 13

Starling lays stress on the importance of the blood supply to the vasomotor centre in the medulla and suggests that conditions which give rise to an inadequate supply of blood to this centre may be responsible. Stimulation of this centre would result and the general blood pressure raised by its vasoconstrictor action to insure a more
satisfactory blood supply. He submitted that in investigating the causes of hyperpiesis it should be asked how the cause suggested could modify the blood supply to the vasomotor centre.

Granted that stimulation of the vasomotor centre may be responsible for high blood pressure, we are still in the dark as to how this is effected; it seems more probable that a toxin may be responsible for this, rather than a deficient blood supply.

Undue excitability of the nervous system, with excessive response to emotional disturbances reacting on a hypersensitive vasomotor centre has also been suggested in explanation, but there is no definite evidence in support of this.

Prolonged nervous strain, a hard and strenous life, overwork, abuse of alcohol and tobacco, have been incriminated, but hyperpiesis usually sets in early life and is gradually progressive.

It has been found by various observers, who have investigated the blood pressure in children and adolescents, that it is above the normal in about eight to twenty percent of cases. It would be interesting to follow up such cases and to see if the tendency persists, and if so, whether it could be counteracted by any form of treatment.

Unfortunately cases of hyperpiesia, at a rule, only come under medical care when the blood pressure is already
very high and the cardiovascular changes are advanced. 13

Hereditity plays an important part, as the family history of these cases shows, but it gives us no clue as to their etiology. Hereditity is also a factor to be taken into account in kidney diseases. 13

As high blood pressure may exist in association with, or apart from kidney disease, it seems probably that some common cause is responsible for it in both conditions. Imperfect elimination of nitrogenous waste products by the kidney cannot be incriminated, as the kidney is healthy in the one groupe. It is possible that the liver may be at fault, and that as a result a defective metabolism, some toxin gets into the general circulation which unduly stimulates the vasomotor system. 9

While capillary spasm has been indentified with hyperpiesia, a number of clinicians working in the field of allergy hold that a similar mechanism is responsible for certain manifestations of allergy. Vaughn states that "anagiospasm is the characteristic phenomena of anaphylaxis." Although definite proof of this fact is still lacking, Coca and his school have demonstrated that in anaphylaxis the blood contains substances which contract unstriped muscle tissue. 19

Indeed, there are several factors which point to some connection between hyperpiesis and allergy. Migraine is now considered by many as being of allergic origin. On the
other hand, Westphal, O'Hare and others have found that migraine precedes the onset of hyperpiesia for several months or years in about 50 percent of their cases of hyperpiesia. Kaufmann asserts that sensitiveness to heat is an outstanding feature in the history of cases of hyperpiesia. This symptom has also been explained by Duke to be an allergic manifestation. Heredity, another factor which plays a part in some forms of hypertension, is regarded as a foremost clinical citron in allergic diseases. 19

In order to establish clinical proof of the relation between allergy and hyperpiesia, it would be necessary to demonstrate, first, the occurrence of both diseases in more than an incidental number of cases; second, the occurrence of hypertension without kidney involvement in a number of allergic families; and, third, the fact that control of the allergic factor influences the hyperpiesia. 19

Laugstroth 12 thinks hyperpiesia along with some other chronic disease, may be the result of vitamin deficiency and that protective diets will prevent or ameliorate this condition.

In 1924, M. J. McDonald of St. Catherine's, Ontario, 15 first observed clinically the depressor effect of liver extract in the human being. This came about in the course of experiments during the previous year, working on the idea
that the liver was a defense organ with some special influence that might be utilized in the prevention of cancer. His observation that certain liver extracts exerted a notable depressor effect caused him to study, with the extract, 33 cases of clinical hyperpiesia. The results were so encouraging that an intensive study, physiologically and chemically, of liver extracts was begun. An observation by Macdonald was that blood pressure was temporarily lowered after an injection of histamine, whereas a lower pressure effect was maintained for a much longer period by the extract.

Parallel with Macdonald, R. H. Major, 37 of the University of Kansas, was working on the same problem. His researches advanced around quanidine and methylguanidine, and he showed that prolonged pressor effects were brought about by this pressor effect, parallel with the reduction in excessive blood pressure.

The work of Banting which isolated insulin by alcoholic fraction of the pancreas stimulated Harrower 36 to apply this method to other tissues, and in the summer of 1925 he succeeded in preparing an active, stable solution of liver extract by alcoholic fraction. This liver principle he called anabolin, because he considers that it brings about detoxication and lowered blood pressure as an anabolic process in building up amino-acids into urea.
Mosenthal 24, states that there is a very distant heredity tendency associated with hyperpiesis. This has been stressed, apparently with good judgment, as being one of the most important etiological factors. The transmitted predisposition to apoplexy is appreciated in clinical medicine and in fiction. Weity 38 has taken up this subject in a thorough and exhaustive a manner as one may; he proves statistically that hypertension is a familial disease affecting women as well as men. Alvarey, Walgen and Mahoney 24 conclude that hyperpiesia seems to be an inherited peculiarity the appearance of which can be suppressed in women so long as the ovaries function well. Exactly what functional disturbance is inherited is not clear, however, it may be regarded as an established fact that hyperpiesis is proven to be transmitted from one generation to the next. 28

Regarding the cause or causes of hypertension in its restricted sense, these may be summed up in the word "intoxication", although much yet remains to be explained concerning the precise nature of the processes leading to its production. The causes are essentially the same as those producing arteriosclerosis, but differ in that they have acted over a shorter period of time and are probably less active in character. This belief is borne out by the clinical fact that, if permitted to continue, the condition gradually progresses until it imperceptibly merges into and becomes one of true arteriosclerosis.
and cardio-renal disease.

That the adrenals and other members of the chromaffin system play an important role is shown in various ways. Recently Sergent and Cottintat have shown that irradiation of the adrenals in eleven cases of hypertension, in which all known causes of this condition had been eliminated, caused marked improvement.

**PATHOLOGY**

The more one reads the literature of hyperpiesis the more he becomes lost in the conflicting maze of theories regarding the changes it produces in the structure and function of tissues. One finds many conflicting reports. For instance, some observers state that arteriosclerosis is one of the causes of high blood pressure; but it must be determined first whether arteriosclerosis is the cause of high blood pressure or hyperpiesia 24 is the cause of arterial degeneration. Huchard thinks that arteriosclerosis is a cause, while Thoma holds that in an uncomplicated degeneration of the arteries blood pressure does not rise. This means that in cases of arteriosclerosis with hypertension kidney lesions must be ruled out. On the other hand there are many cases of high blood pressure with no arterial degeneration.

We are ignorant 14-10 of the direct cause of hyperpiesis. We know that it is absolutely essential for the brain, with
its vital centres which control the circulation, respiration, etc., to receive an adequate and constant supply of nourishment. Otherwise immediate death would ensue. To insure this prerequisite blood supply, a vasomotor mechanism exists, which is part of the vegetative nervous system, with its centre located in the medulla oblongata, near the respiratory centre, which so regulates the lumen of the bloodvessels of the rest of the body and therefore the blood pressure, and thus supplies the vital cerebral centres with unfailing nourishment under constant pressure. These vital centres have the first call (first mortgage) of the body's blood supply. In other words, the arterioles and perhaps the capillaries of the rest of the body are contracted to direct the stream of blood to the brain and its vital centres. This is the true mechanism of hypertension. 27

Still another author, Vincent Nesfield, believes high blood pressure in the absence of renal disease to be due to an increased viscosity of the blood. He states the increased viscosity is due to an increase of fibrinogen, and probably of all the proteins. The increased quantity of blood protein being due to the inability of the living cells to utilize the proteins offered them. 9-10

William Norris, in his text written as early as 1916, states the term hyperpiesis has been applied to hypertension not due to demonstrable renal, cardiac and arterial disease.
It is suspected that if unchecked this condition may be an antecedent of organic hypertension. In arteriosclerotic conditions the increased blood pressure, at least up to a certain point, subserves a necessary function; in hyperpiesis, so far as we can determine, the pressure increase in addition to being sudden and associated with unpleasant symptoms subserves no useful function.

The first careful pathologic study of the arteries in hypertension made in 1972 by Gull and Sulton who emphasized that although the most profound changes occurred in the renal vessels, the process was not confined to the kidney. It has been maintained that non-nephritic hypertension (hyperpiesia) is secondary to generalized arteriocapillary fibrosis, but the predominant lesions are never-the-less in the renal arterioles. There is also considerable sclerosis in the splanchnic area. Fishberg's recent thorough study of the arterioles and arterial pathology in so called "essential" hypertension has demonstrated in 72 cases that arterioles sclerosis was invariably present. In every instance the minute arterioles of the kidney were effected, the splenic arteries were involved in about 60 percent of the cases, the pancreatic in about 50 percent, the hepatic in about 50 percent and the cerebral in about 20 percent. The smaller vessels of other structures were rarely involved or to a greatly lesser extent. Similar findings have been more recently reported from a series of 420 necropsies in cases of primary hypertension.
Renal arteriolar sclerosis occurred in 97.6 percent of the cases. The afferent glomerular arterioles showed varying degrees of sclerosis in 39 percent. Fishberg concludes that the conception that hyperpiesia is due to the statically increased resistance offered by these organic lesions is untenable. The arteriolar sclerosis is the result of the increased wear and tear from the abnormal intravascular tension and not the cause thereof. Fishberg's findings in the arteriolar lesions in the kidney definitely controvert the older incorrect view that hyperpiesia is due to a disorder of renal function. 11

The main characteristic of the arterial lesion in hyperpiesia as distinguished from that of the decrescent type of arteriosclerosis, has been claimed to be the marked hypertrophy of muscular, elastic and connective tissues. The occurrence of changes in the smooth muscle have been stressed especially. Pal, believing that the increased tone of the arteries plays a part in the production of hyperpiesia, subscribes to this view. Moschcowity finds that in transient cases of hypertension the radial arteries become thickened because of such a muscular hypertrophy, which disappears after the blood pressure has returned to a normal level for a few weeks. 8

Changes in the fundus oculi are nearly always present in hyperpiesia. It is very remarkable to see what different interpretations have been put upon these signs, especially in correlating them with clinical disease. A few
salient facts are worthy of note. O'Hare and Walker claim that every instance of hypertensive disease is associated with retinal arteriosclerosis; they go one step further in their conclusions in believing that arteriosclerosis of the retinal vessels indicates a previous elevation of blood pressure even where this does not exist at the moment; finally, they find that patients with advanced decrescent arteriosclerosis, as evidenced during life in the radial and brachial arteries, may have absolutely normal retinal vessels, provided there is no increase in arterial tension. These statements, I believe, are approximately correct. They lay stress on the frequent association of retinal arteriosclerosis and hypertension. Arteriosclerosis of the retina is described by Martin Coehn as follows:

"The suggestive signs are: (1) uneven caliber and undue tortuosity of the arteries, (2) prominence of its central light streak, (3) light color of the arteries, (4) dilated and tortuous veins."

"The pathognomic signs are: (1) the arteries are decidedly contracted and tortuous, especially the secondary and tertiary branches; (2) white stripes bordering the arteries, or complete obliteration of the lumen, which appearances produce the silver wire aspect; (3) alternate contraction and dilation of veins due to areas of endothelial proliferation and indentation of veins from a varying amount of mechanical pressure when crossed by
hyalinized arteries; the arterial crossing of the veins by the arteries, or vice versa, produce the following effects upon the vein, depending upon the degree of arteriosclerosis: (1) slight flattening, (2) pushing it aside, (3) direct indentation.

**SYMPOMOLOGY**

The symptoms associated with hypertension vary a good deal with the different stages of the malady; since hyperpiesis often exists for months or years, it almost always induces changes in other organs, notably in the arteries of the kidneys, heart and brain. However, the symptoms that are most frequent, even in cases of short duration, are included in the following list: 2-20-24-3

**Headache** — which is most apt to be occipital or vertical in location, often designated by the patient as an ache in the back of the neck, and which is prone to occur in the early hours of the morning, from four to six A.M. It is widely known to the medical profession under the name of the "lead cap" headache 34, a term popularized by Janeway because of its frequent location over the vertex and the sense of pressure associated with it. The headache often disappears completely after the patient has been up for several hours; dizziness is not necessarily an associated symptom.

**Dizziness** — Dizziness is not often troublesome in the earlier months or years of the disease, but in some individuals
it becomes the dominant symptom. It varies in degree from a slight and temporary uncertainty to a condition that makes physical activity impossible. In its milder form it is usually of brief duration - several minutes to several hours - but it sometimes lasts almost without intermission for days or weeks. Fortunately the most severe forms are quite uncommon. 32

**Precordial Pain** -- The precordial pain of hyperpiesia should be clearly distinguished from that known as angina pectoris. The pain now under discussion is almost always precordial rather than substernal and is most frequent at or around the apical region of the heart. 3 It is dull, constant, aching, and usually bears no clear relation to the activity that immediately preceded the onset. It is much more common in those who have considerable cardiac enlargement, and most frequent in those who are suffering from heart failure. 3 - 32 - 24.

**Nervous Symptoms** -- In many patients the manifestations of disturbances in the nervous system outweigh all others. Among the more common might be mentioned insomnia, general nervous irritability, a tendency to mental depression and melancholia, easy fatigability and repeated evidences of transient interference with the cerebral circulation. This last named symptom, while it does not occur exclusively in those suffering from hyperpiesia, is more frequent in such patients. In its commonest and most dramatic form, the pat-
ient appears to have suffered rupture or thrombatic closure of a cerebral artery, with resultant complete or partial paralysis of one or more extremities and often complete aphasia. 7 After a period of several hours all such signs of a cerebral lesion disappear completely, and there is no subsequent residual signs. The episodes are usually explained on the basis of temporary spasm of the cerebral arteries, with subsequent relaxation and restoration of the normal blood flow; this is an attractive and satisfactory explanation if one is able to accept the statement that arteries subsequently shown to be in a state of advanced sclerosis are capable of prolonged spasm. 32

C02 atiC: Pulsation — Bolatin 30 has examined caratid pulses of one hundred and five cases hyperpiesia and found right caratid pulsation occurrence in 30% of cases.

DIAGNOSIS

In the large majority of instances of hyperpiesia, there is little difficulty in establishing the diagnosis, which is immediately obvious when a definitely abnormal elevation of blood pressure is found in a middle-aged or elderly individual. 7 The following four types of cases, which at times present diagnostic difficulties, may be mentioned:

1. It is not uncommon, particularly in women about the time of menopause, to find that the blood pressure fluctuates so considerably from examination to examination that on one
Occasion it is definitely elevated and on another within the normal range. Such cases need considerable observation before coming to a decision. In menopausal women, or those under a nervous strain, these transitory elevations may completely disappear. Much more often, however, the blood pressure ultimately becomes consistently high; in fact, it seems most probable that most such transitory elevations of blood pressure indicate an incipient or abortive form of hyperpiesis. The establishment of cardiac enlargement may aid in establishing the diagnosis of hyperpiesia.

2. In relatively young patients with hyperpiesia, it may be difficult or impossible to decide whether this is due to chronic glomerulo-nephritis or to hyperpiesia, particularly in the malignant phase. The clinical picture of severe hypertension, albuminuria, cylinduria, microscopic hematuria, renal insufficiency, retinal lesions, and no edema other than perhaps cardiac, may be present in either chronic glomerulo-nephritis or hyperpiesia. Of course, a history of acute glomerulo-nephritis or nephritic edema in the past speaks strongly in favor of chronic glomerulo-nephritis. However, such a history is often absent in the latter disease. Extreme hypertension, over 250 mm. systolic and 150 mm. diastolic for more than a transitory period, is decidedly more common in hyperpiesia, particularly in the malignant phase, than in glomerulo-nephritis, though Fishberg 7 reports having seen such tensions in unusual cases of the latter disease. If the
patient is in the twenties, the case is more probably one of chronic glomerulo-nephritis, for hyperpiesia is unusually at this age. When the patient is in the thirties or forties, the differentiation may be impossible in cases presenting the features described above. In the fifties and later, such a case is in all probability one of hyperpiesia.

3. Not uncommonly, one encounters middle-aged or elderly patients with myocardial insufficiency an enlarged heart in the absence of valvular lesions in whom the blood pressure is within normal limits. There are often symptoms or electrocardiographic evidence of myocardial damage due to coronary arteriosclerosis. The question whether or not these patients previously had hyperpiesis may be difficult to decide if there is no history of previous elevation of blood pressure.

In fact, the question whether or not coronary artery disease in itself can cause hypertrophy of the heart is not as yet finally decided. The pressure of retinal arteriosclerosis is strong evidence that hypertension has been present at some time. Impairment of renal function, if the disease of the urinary passages can be ruled out, speaks in the same direction. Sometimes, a rise in blood pressure as the heart improves may reveal the hyperpiesia.

4. In patients with hyperpiesia and urinary obstruction resulting from prostatic enlargement, it may be difficult to decide whether the elevation of blood pressure is due to the urinary obstruction or to hyperpiesia. The course of
events after free urinary drainage has been established will settle the issue, though it is to be remembered that bed-rest can lower hyperpiesia notably. 3

**PROGNOSIS**

Prognosis obviously depends on numerous factors. Life insurance statistics show that taking all hypertensives as a class, the expectancy of life is very much shortened and that, broadly speaking, the mortality increases quite definitely with the actual height of the pressure. 41

On the other hand, it is clinically a fact that hyperpiesis may carry very high pressures for ten to twenty years, whereas clear-cut nephritic hypertensives are apt to die within two years. 41 The Finsen Institute figures for the latter, were 84 percent death within two years, the remainder having all been patients who could alter their mode of life.

The difficulty, of course, arises in determining whether a given case is "hyperpiesia" and whether there are remediable factors-focal infection, gastro-intestinal toxemia, strenous living, endocrine or physic disturbances, etc., which can be corrected. 41

The chief causes of death in hyperpiesia are from the side of the heart and the brain, and not from the kidney as was thought during the period when essential hypertension was included in the concept of chronic interstitial nephritis.
The most common cause of disability and death in hyperpiesia is cardiac failure, next to which in frequency are cerebral vascular accidents, particularly cerebral hemorrhage. Following these are various intercurrent complications, notably diabetes mellitus and infections. Renal failure, (uremia), is the cause of death in only a small proportion of cases of hyperpiesia.

**TREATMENT**

In the present state of knowledge of the cause of hyperpiesia its treatment must be mainly, if not entirely, symptomatic.

**Rest.** Of all the remedies tried, physical and mental rest have appeared to produce the most certain results. 12-24-39 The reason why rest in bed may not only lead to a diminution of the hyperpiesia, but to a cessation of unpleasant symptoms, must be that there is less demand made upon the circulation. That rest does not necessarily bring with it a fall of pressure is also proved, is a known fact because in some cases it actually rises. Although it frequently happens that rest in bed does not materially reduce the hyperpiesis and does not prevent its intensification, yet symptoms, frequently abate. To impose complete rest in bed upon all patients suffering from mere hyperpiesis is unnecessary, 39 for it frequently happens that a subject showing hyperpiesis is particularly actively disposed in mind and body and is quite free from
sawptoms. When rest can be carried out completely, favorable results will be achieved more quickly.

When hyperpiesia has been discovered, as it were by accident, in individuals applying for life insurance, or on medical examination before employment, the medical attendant appealed to for treatment must be guided by circumstances as to whether he should insist upon a prolonged period of complete rest or not. If circumstances will admit of such treatment, and the patient is amenable, there can be no doubt that a period of increased rest is a fitting prelude to a life which in the future must be more easeful. To those who object that the knowledge of the presence of hyperpiesia will cause anxiety to the patient, it must be said in reply that frequently the proper treatment cannot be secured unless the patient is fully informed of all the facts. It goes without saying that particularly nervous subjects should be shielded from too close a knowledge of the numerical measurement of the hyperpiesis, and it must be explained that a temporary variation between readings even of 20 or 30 mm., whether of increase or decrease of hyperpiesis, is immaterial. What is of favorable moment is the steady fall through several weeks to the normal level. Every advantage should be taken of the knowledge that some times hyperpiesia is quite a temporary, and that when the manifestation of hyperpiesia has passed off the patient is relieved of the accompanying symptoms. It is discovered that the hyperpiesis persists even with prolonged
rest in bed, it must be left to the practitioner to decide whether he should, or should not, reveal the fact of the permanent presence of hyperpiesis. It should be pointed out that though there is no knowledge whatsoever of the average duration of life when hyperpiesis has established itself, or what is the average period required for the development of the symptoms when once hyperpiesis is established, there is room for a degree of optimism when it is discovered that the blood pressure is raised. More especially is this the case when it is found that the individual concerned looks healthy and is comparatively or entirely free from symptoms. It is not always wise, in order to secure the obedience of the patient, to point out the risk in cases of accidental or other discovery of hyperpiesis of the occurrence fo apoplexy, hemepligia, etc., because the number of cases to be met with in men and women of about middle age or more must be very considerable, judging at least by the routine examination of patients and candidates for insurance and yet the frequency of apoplexy in such subjects is very small. 24 There can be no doubt whatsoever that when hyperpiesis is found to be associated with anaemia, intense factor of breath, dyspnoea, cardiac embarrassment, dropsy, etc., then rest in bed should be insisted upon; naturally such cases would more readily conform. When a patient appears before the practi- tioner merely revealing hyperpiesis, being in every other
way apparently in good health, it is sufficient to try and secure more rest in the hours not devoted to business: in the winter, arrival at the office an hour later than usual may be helpful; the spending the whole of the week-end, or the greater part of it in bed will help to postpone the development of further symptoms. When the practitioner is in doubt as to whether the patient is suffering from permanent hyperpiesia or not, rest in bed would provide means of clearing up the problem: if the blood pressure becomes normal within four or five days, it may be that the individual is merely suffering from what may be spoken of as the "nervous" form of hyperpiesis, more especially would this be probable if the hyperpiesis were found to be unaccompanied by evidence of cardiac hypertrophy, tortuosity of the arteries, albuminuria, retinal change and the other manifestations met with in the later stages of hyperpiesia. Even if the case prove to be one merely of evanescent hyperpiesis of nervous origin, a more restful life, short of causing great inconvenience to the patient, can do no harm, and may be a means of preventing such evanescent hyperpiesis becoming one of permanent hyperpiesis. 31

For practical purposes the development of left-sided cardiac hypertrophy may be regarded as the "hall-mark" of the permanent or much more prolonged hyperpiesis, i.e. of hyperpiesia. 31
Dieting. Much controversy has centered around this subject of the diet suitable for a hyperpiesic subject: A diet rich in carbohydrates should be avoided in order to reduce flatulence, and a diet rich in extractives should be excluded in those cases in whom the kidneys are gravely disturbed. Should the patient be free from symptoms and merely show the earlier signs of hyperpiesia, it is sufficient to leave the patient to choose his dietary just so long as he selects what may be reasonably called simple foods. It does not seem wise to cut down the protein elements of a diet because the patient is passing albumen; indeed this phenomenon should be a call to supply, if anything, extra protein food. If it is found that headache and dyspeptic manifestations are controllable by a simple diet consisting mainly of milk, or of eggs, or fish in part, there can be no reason on the other hand to insist upon a more richly protein diet. Alcohol, tea and coffee in moderation exercise no harmful effects upon the disease. Seeing that the hyperpiesic subject may be free from any symptoms, and seeing that next to nothing is known of how to control the agencies which are producing hyperpiesis, it seems wrong to insist upon this, that or other extreme forms of dietary. It is more reasonable to leave the patient to his own choice just so long as he exercises a moderation.
Supposing early symptoms have developed which indicate the onset of the more serious complications of hyperpiesis, such as anuria, cardiac defect, dropsy, drowsiness, etc., it is advisable to place the patient upon a rigorous milk dietary, allowing three to four pints a day. This, combined with rest in bed and purgation, leads in some cases to disappearance of the symptoms, and then the future dieting of these patients should be based upon the knowledge that restriction exerts favourable effects. If the above features persist, then a very restricted dietary should be maintained. The dropsy may yield to the use of diuretics such as liq. ammom. acetatis, theobromine, diuretin or theocin. 31

Supposing a case of hyperpiesia has undergone prolonged rest in bed with disappearance of symptoms, if not of hyperpiesis, work may be resumed gradually, and continued with if the symptoms do not recur; but such a patient should be kept steadily under observation. The question must be raised as to what amount of exercise should be allowed to these patients. It is a good maxim to lay down that they should take exercise short of producing such symptoms as cardiac pain and marked, or persistent, dyspnoea. Games involving severe muscular effort should be forbidden, as well as the unnecessary ascent of hills or staircases, or walking against a "head" wind. Exercise must be allowed daily, and walking on the flat for a reasonable distance
should be encouraged. There can be little doubt that when the patient is kept in bed, massage and gentle passive movements must be made use of to replace voluntary exercise. Such treatment does not appear to affect the blood pressure unfavorable to any material extent. With regard to the cutting off of more vigorous exercise and game-playing, no absolute rule can be laid down, because there are some subjects who reveal hyperpiesis and are able to play golf and tennis quite vigorously without any symptoms occurring. Such patients may object to have this amount of exercise restricted and the medical attendant must permit it until unfavorable symptoms arise, or until examination shows the progressive intensification of objective changes. The use of tobacco is permissible. 31

Purgation. The use of Epson salts or Glaubert's salts, taken before breakfast in such quantities as to produce one or two stools a day, is advisable. Intestinal putrefaction should be controlled by the use of calomel in fractional doses of such size as not to cause colic or other symptoms in susceptible subjects: the calomel may be given at night or three times a day after food. 24 This should be a routine treatment, but if symptoms of drowsiness suggestive of impending coma occur, then castor oil should be freely used. 31 - 26

Baths. If the patient relishes tepid warm baths, he should be encouraged to take them regularly. In the same
way it will be found that some patients enjoy Turkish and radiant heat baths, and when this is the case they may be used daily or two or three times a week. The radiant heat bath is a very convenient form, for it can be made use of in the patients own home: it may be found by preliminary trial that unpleasant symptoms like headache may be produced by their use. It would be wrong in such cases to insist upon this method of treatment, for there is no proof that the treatment eliminates the poisons concerned in the disease, or in any way controls the mechanism by which dropsy can be developed. Hot air baths do not lead to the permanent fall of blood pressure. The sole reason for using hot baths is that they relieve some patients from some of their symptoms, 12, notably headaches, though as already mentioned they provoke them in others. It is probably more satisfactory to the patient to live in a well-warmed house; quite possible too cool an atmosphere contributes still further to a maintenance of high blood pressure. 31

**Choice of Climate.** Residence in mild, temperate and warm countries is certainly to be preferred to residence in colder latitudes. But here, again, as so often happens in the discussion of treatment, the temperamental peculiarities of the patient must not be disregarded. Some hyperpiesic subjects, contrary to expectation, feel better in the winter than in the summer. 31
Symptomatic Treatment. Usage alone sanctions the routine prescription of potassium iodide, of potassium nitrate and the various nitro-compounds. The use of such remedies may, however, prove unacceptable to the patient, and it would in such cases be undesirable to insist upon them. It will frequently be found that the nitro-compounds are helpful in relieving the angina-like pains. Headache is often relieved by the use of acetyl-salicylic acid, phenacetin, bromides, etc. Insomnia is only too frequently a serious symptom and should chloral hydrate, the bromides, trional, chloralamide, etc., fail to produce sleep, then paraldehyde, hyoscyne and opium derivatives should not be spared. 31

No sign nor symptom will prove more difficult than those which may be attributed to cardiac failure or defeat. The medical attendant should therefore maintain an open mind as to the use of digitalis and its allies and diuretics. It is true that at first sight the use of digitalis in a case already hyperpiesis seems doomed to failure and worse, but its diuretic effect and its power in certain cases of rendering the heart regular in rhythm may outweigh all theoretical objections. 28 The occurrence of convulsions may require the use of hypodermics of morphia, of venesection or of spinal puncture. If coma threatens and cannot be met by the use of aperients such as croton oil or castor oil, venesection may again be of the greatest use. The well known
efficacy of bleeding by venesection or venepuncture in oedema of the lungs renders this form of treatment the standard one for such conditions. 31

Dropsy or serious effusions cause very considerable difficulty. If they fail to respond — as they often are found to do — to the effects of diuresis and diaphoresis then in the case of pleural effusion and ascites relief may be given by tapping the chest or abdomen. Dropsy of the legs should not be relieved by the use of Southey's tubes, acupuncture or malleolar incisions, for although such methods are immediately efficacious, too often cellu­lities results, despite the most meticulous care taken to prevent it. 3

Asepsis. There can be no doubt that the risk of septic infection in cases of hyperpiesia is a real "bete noire." Every means should be taken to remedy gingivitis, and to prevent septic infection generally, for infection too often is the prelude of the sudden or slow demise of the patient. Should extraction of the teeth become necessary to cure gingivitis, then the extraction should be gradual, only a few teeth being removed at a time. General anaesthetics appear to be well borne by hyperpiesic sub­jects. When once severe anaemia has become established, as a result of infection, it is difficult to remedy it. 3

Life Insurance. As this study has shown, men and women appear to show hyperpiesis which is apparently due to
excitement only. It is therefore unwise to exclude from insurance or to load any individual whom on the occasion of examination for life insurance shows hyperpiesis. If, however, a single reading of high tension is accompanied by signs of cardiac hypertrophy and vascular change, its significance is established. If hyperpiesis is the only discoverable clinical sign, the proposer should have readings taken of the blood pressure before rising after a night's rest, and if possible on more than one occasion. The persistence of a high reading under such circumstances should lead to a loading and (or) shortened period of endowment. The pressure of albumen should in such cases arouse further caution: the urine may be free of albumen if the sample is one passed in the early morning after a night's rest: in such a case no extra apprehension need be felt. If albuminuria can be removed by the cure of septic foci, then the case should be looked on as one of mere hyperpiesis and loaded accordingly. If, however, albumen persists as well as the hyperpiesis, then such a case should be declined, not because the pressure of albumen necessarily indicates kidney disease, for that fallacy has been unmasked, but because albuminuria is some measure of the greater severity of the toxaemia which is causing the hyperpiesis in such a case, or may mean that there is some hidden focus of septic infection. The presence of albuminuric retinitis should remain, as it has
done, an absolute bar to insurance, because even though albuminuria may in such a case be slight or occasional only, retinal change renders the outlook so much more serious. 3

**Syphilis.** If a hyperpiesic patient is the subject of syphilis, radical treatment should be instituted with the object of trying to prevent the weakening of the arterial walls which results from this disease. The risk of rupture of blood vessels, already weakened by syphilis, is greater in the conditions of hyperpiesis than when the blood pressure is normal. 2

**General Anaesthetics.** Those who are the subjects of hyperpiesia appear to stand the effects of general anaesthetics well. 3

**Operation for Glaucoma.** With regard of the operation of iridectomy for glaucoma in a patient also suffering from hyperpiesia, a preliminary rest in bed for a fortnight, with the usual dietetic and medicinal treatment, is worth trying, for it may be successful in reducing the blood pressure, thereby also minimizing the risk of intra-ocular hemorrhage following upon the operation. 3
A Synopsis of
Two Hundred and Two Cases

Over a period of ten years J. M. Blackford, M.D., F.A.C.P., and J. N. Wilkinson, M.D., Seattle, Washington, studied and followed two hundred and two cases of hyperpiesia. These authors report a series obtained by reviewing 10,000 consecutive histories of general examination made before 1925. They took for study all cases whose blood pressure was found definitely high, using cases in which the systolic pressure was reported as 175 plus or the diastolic pressure 100 plus. Cases with readings below these figures were omitted because there is some question as to whether temporary causes, particularly nervous, may occasionally give a reading up to these points. Thus they obtained a consecutive series of hypertension cases, unselected except by the fact that some complaint made them come in for a general examination.

The Blackford & Wilkinson Clinic (64) sees in each decade approximately an equal number of men and women, yet hypertension was found twice as frequently in women (64%) as in men (36%). In each decade between 30 and 70 years the percentage incidence of hypertension (hyperpiesis) in women was approximately double that seen in men. Yet more than half of the women were without hypertensive symptoms, whereas hypertension in men was usually accompanied by symptoms. The large groupe of symptomless
females with hypertension is not seen in cardiovascular clinics or by life insurance companies, and hence is not included in hypertension follow-up studies.

This Seattle clinic has made this follow-up study and report as follows: two hundred and two cases of hypertension were followed. After eight years, one half (50.0%) were dead. The female mortality was 79%. About three-quarters of all deaths resulted from hypertensive disease, usually failure of heart or of cerebral circulation and occasionally nephritis. One quarter of all deaths resulted from other causes.

The remaining 101 cases were followed two years more, when this report was made. The gross mortality at the end of ten year period was 60%, and female mortality 50%, male mortality 82%. No male with marked hypertension still survived after the ten year period. Of 66 females still surviving, 39 (59%) are relatively symptom free, whereas of 13 surviving males 3 (24%) are entirely symptom free. Seven females are still alive in spite of marked hypertension discovered ten years ago.

This clinic reports that of the two hundred and two cases studied for ten years only two instances of recovery to normal blood pressure occurred.

The study of hypertension by the Seattle Clinic 40 caused them to come to the following conclusions:
1. Hypertension is twice as frequently found in women.

2. The mortality rate after ten years is twice greater in men.

3. Hypertension results from a constitutional hypertonicity of the autonomic neurovascular control in large majority of instances and is a compensatory angiospasms in the others.

4. Treatment of uncomplicated hypertension is a matter of mental and physical hygiene rather than drugs.

5. Treatment of late results of hypertension requires skillful use of medical and physical measures, added to psychotherapeutic measures.

6. The physician who is a good and cheerful psychologist will be the most successfully in relieving the symptoms of hyperpiesis.
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