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Review of sympathectomy for relief of hypertension

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A Review of Sympathectomy for Relief of Hypertension

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I

Introduction

To practice therapeutic or corrective medicine in surgery, medicine, psychiatry, or any of the other fields, it is necessary to determine the cause or etiology of the process that is producing dysfunction. To understand dysfunction, it is necessary that experiments be conducted and surveys made to establish a better understanding of disease and to ascertain the fundamental reasons for its peculiar behavior.

Although we have only limited knowledge of the etiology of hypertension at the present time, nevertheless experimental work has been attempted along this line, and findings have been made which are of some value in our endeavor to find the cause of high blood pressure. Once the etiology is determined, therapeutic correctiveness and prevention can be established, so that better medicine can be practiced in saving man from this pathological and physiological menace.

II

Physiology of Blood Pressure

In order to understand dysfunction, it is deemed necessary to give a brief summary of the normal mechanisms which control the behavior of the circulatory system. First, there are several factors by which blood pressure is maintained: (1) viscosity of the blood; (2) cardiac output; (3) elasticity of the blood vessels; (4) venous return, in which gravity, muscular activity, and negative pressures are important elements; and (5) peripheral resistance (8). Any abnormality of one or of a combination of two or more of these factors will either lessen or increase blood pressure to produce so-called "hypotension" or "hypertension", which exist in varying degrees of severity, depending upon the intensity of the abnormality.

Two extrinsic body mechanisms whose functions are not thoroughly understood and which influence blood pressure, are the endocrine glands (hormones) and the autonomic nervous system (55). Experimental study has largely been directed toward an elucidation of function of the endocrine and autonomic systems alone, with one another, or with the rest of the organism. So far, only a partial knowledge of the physiology of these

systems has been mastered, which explains why hypertension presents such a great problem, especially when the pathological basis for this condition is unknown.

III

Experimental Work on Blood Pressure

In 1927, Major and Weber (54) proposed that a retention of guanidine was the basis for hypertension. This theory, however, was disproved in later years by several workers, who based their conclusions on two main factors: (1) that too large an amount of guanidine was injected into the experimental animal, and (2) that the reliability of the chemical methods employed was questionable.

Another suggestion was presented by certain German scientists, who maintained that an increase in the blood cholesterol level was an etiological factor in hypertension. Some years later, however, as in the case of guanidine, it was shown that hypercholesteremia is the result, rather than the cause of changes in the cardio-vascular system in arterial hypertension.

Further experimentation along this line has resulted in a variety of theories concerning the etiology of high blood pressure. German workers claimed that a change in the potassium-calcium ratio produced elevated blood pressure, a conjecture which was later disproved by Weinstein and Weiss (76). Peptone was suggested as a causative agent in hypertension, but this idea was

confuted by Jackson (50). Scott, Wood, and Guerrant (44) found that administrations of high protein diet and urea (intravenously or orally) to normal and hypertensive dogs failed to produce a consistent rise or fall in systolic or diastolic blood pressure.

According to various pathological studies (52) (57), a few cases of hypertension are produced by a certain number of the adrenal tumors, and as soon as the tumors are removed surgically, the blood pressures immediately drop. In the Cushing syndrome, besides adiposity, amenorrhea, sexual impotents, hirsutism, and other endocrine abnormalities, hypertension is a related condition; arteriosclerosis and cardiac hypertrophy are also closely associated with the disease (52).

It has been shown that elevation of blood pressure induced by stimulation of the hypothalamus continues for some time after the end of the stimulation. This reaction is probably due to persistent vasoconstriction and cardiac acceleration, and possibly may be caused by persistent secretion of adrenalin after the cessation of stimulation (39).

Further experiments were performed by Page and his co-workers, who produced renal hypertension in dogs.

These research workers elevated the blood pressures of the experimental animals to 240/160 mmhg. for four months; hypophysectomies were then performed, and the blood pressures descended to 150/100 mmhg. within twenty days. No such responses were observed in normal dogs. These results were ascribed to one of two factors: (1) lack of secretions of the adrenal and thyroid glands, or (2) reduction in the responsiveness of blood vessels to chemical stimuli arising in the ischemic kidney (62). Page also carried out similar experimental work on rats (58), with the same results as those found on dogs. Hypersecretion of epinephrine was claimed to be a causative factor in high blood pressure (66). This was later disproven, and it was shown that continuous intravenous injection of epinephrine caused death in dogs, due to gastro-intestinal immotility and carbohydrate mal-metabolism (65).

The role which the nervous system plays in the etiology of hypertension will now be briefly discussed, with special emphasis on past experimental work along this line. Peet and his helpers (63) believed that the renal nerves produced a renal vessel constriction, which was partially due to the sympathetic impulses, and that release could be obtained from a sympathectomy.

Opposite views, however, were polled by Prinzmetal and Wilson (64), by Page (60), and by Goldblatt and his co-workers (41).

Grimson (43) found that by performing a bilateral resection of the carotid sinus and modulator nerve to the aorta, an enduring hypertension could be produced in experimental animals. I was unable to discover whether or not a hypoactivity of these sites produced hypertension basically. However, Grimson (43) went on to report that splanchnic area denervation did not appreciably alter a normal dog's blood pressure or the hypertensive response, produced by a section of the buffer or depressor nerves from the carotid sinus, heart, and aortic arch.

Cannon and Rosenbleuth (67) performed a brain resection on a dog and found two points which, upon stimulation, produced a respective rise and fall in blood pressure; their experimental animal was sympathectomized and bilaterally vagi-severed. These men concluded that, "The dilator fibers in the dorsal roots of the spinal column are probably the efferent paths of the response to stimulation of the depressor points of the vasomotor reflex and of dilator impulses responsible for the fall of blood pressure attending

struggle" (67).

Bradford (10) showed that the greatest power of nervous control lay between the tenth to the thirteenth thoracic level vertebrae. In an article published in January, 1936, regarding elaborate experimental work, Prinzmetal, Myron, and Wilson (64) showed that elevation of blood pressure in essential hypertension is not localized to the splanchnic area, but that vasospasms of arterioles are generalized throughout the body. Page and Heuer (61) have demonstrated that abdominal vessel compensation is lost in hypertension.

Some experimental work has been performed to further substantiate the finding of general vasospasms and to explain the behavior of the peripheral vessel mechanism. Cannon, Dale and Richards, Grand and Bland, and others, each group doing experimental work on different animals, have shown that, following their denervation in peripheral structures, vessels seem to possess an intrinsic tone of their own, and that, when severed (nerves to vessels), there is a fairly rapid restoration of initial arteriole tone, with the vessels still displaying sensitivity to adrenalin (13) (14). Likewise, the external temperature of the skin has little to do with influencing "essential hypertension" (75).

Until the time of Goldblatt's famous discovery of the "ischemic kidney" and its relationship to high blood pressure, a revelation which resulted in the establishment of the humoral theory on hypertension, a number of experimental findings were made which had an essential bearing on the subject. Even as early as 1908 and 1909, lab work was performed by Janeway (51) and Carrel (15) which showed that a reduction of renal substance by coagulation necrosis, due to ligation of branches of the renal artery, produced a slight rise in blood pressure.

Bilateral nephrectomies have been performed, with the observed result being either a slight or no rise in blood pressure (17). Along this same line, partial nephrectomies have been carried out on rats, with a great elevation of blood pressure as the result (18) (69). Unilateral nephrectomy with partial removal, plus coagulation necrosis of the remaining kidney, was attempted in dogs, and a slight to moderate, temporary elevation of blood pressure was obtained (16) (33).

Clinical work, observation, and survey have shown that bilateral obstruction of the ureters produces high blood pressure (12). Nephrotoxic substances have been injected into experimental animals, and the general

conclusion was either no elevation or a slight, temporary rise in blood pressure (31) (6) (70). Hartman and his associates have irradiated the kidneys with roentgen-rays and have been able to produce a moderate rise in blood pressure of the dog (46). Renal infarction has also been produced in experimental animals for the study of blood pressure, but no gratifying results have thus been obtained (16) (5).

Complete constriction of both renal veins has been attempted in dogs, and a moderate to temporary elevation of blood pressure was obtained (7), resulting in terminal uremia and death (37). It was recently discovered that partial occlusion of the renal veins produced a mild, transitory, experimental hypertension (37).

In 1934, Goldblatt and his co-workers produced hypertension by partial compression of the renal arteries by means of the so-called "Goldblatt clamp" (41) (42). This resulted in an ischemia in the end organs, which produced a vasoconstrictor (pressor) substance, called renin. In turn, renin combined with a material in the blood plasma, termed renin-activator, to form angiotonin, which exerted its constrictor action on the minute systemic vessels of the periphery (8).

Harrison, Blalock, and Mason have taken kidney extracts from normal and hypertensive dogs, and have injected these extracts into rats. They observed that greater pressor effect was elicited from the extract of the hypertensive animal (45).

Page and his assistants were able to produce renal hypertension without a pathological ischemia, by placing a parchment membrane or sac around the kidney, this having a tendency to form a thickened hull around the parenchyma. These workers concluded that the pulse-pressure to the kidney was reduced and that this, in turn, stimulated the outpouring of renin (53) (20) (59).

Experimental sympathectomies were performed on seven dogs, whose renal arteries had been compressed. These operations did not prevent the development of hypertension (35), showing that kidney and splanchnic nerve innervation has little to do with relieving experimental hypertension.

The same author, however, refutes the assumption formerly made, by observing that experiments conducted on dogs are entirely different from observations and clinical work done on human beings. He bases his assertion on the fact that animals do not ordinarily assume

an erect position and that, therefore, their splanchnic, visceral innervations have fewer demands placed upon them than do those of human beings (19). It has also been postulated, in various other ways, that experimental animals and humans are not built alike and that, therefore, their reactions differ. Furthermore, experiments carried on in healthy animals do not set up the same conditions that are present in the diseased tissues of humans (71). These points are presented in order that the reader may realize the necessity of exercising his own sense of evaluation and judgment before he accepts any issue, either clinical or experimental, in medicine.

Other experiments with the kidney have been attempted for the production of hypertension. Dradstedt and Geer tried to produce high blood pressure by bilaterally transplanting ureters into the large intestine, but this attempt failed (32). Transplantation of kidney tissue to various regions of the body, with compensatory blood supply supplemented and then curtailed, has produced increased systolic and diastolic pressures, showing that the formation of renin is independent of nervous innervation (8) and that the kidney is in some way related to hypertension.

Emotional instability and allergies and infections have been named as possible causes of hypertension; but little experimental work has been conducted along these lines, and the claims are based mostly on clinical survey (77). Exactly what role the psychic factor plays is an intangible quality, because this topic leads us into a discussion of what constitutes personality and what factors compose its architecture. This highly controversial subject has been analyzed by practically all psychologists and psychiatrists, none of whom has yet been able to form a concrete definition of the term which would be acceptable to the rest of the medical profession as a whole. Of one thing, however, we are certain, and that is the fact that heredity contributes to the cause of hypertension (48), although to what extent and in what tendencies we do not know.

Most clinical pathologists and urologists agree that various types of kidney pathology (chronic glomerular nephritis, pyelonephritis, urinary obstruction (enlarged prostate, and so on), renal tumor, and amyloid, polycystic, hypoplastic (52), and eclamptic kidneys (29)), will produce varying grades of hypertension.

IV

Clinical Discussion

We have presented a brief survey of what has been accomplished experimentally and observed pathologically to determine the etiology of hypertension. It is now advisable, therefore, that we turn our minds to the clinical phases of this menace and attempt to portray our material from the standpoint of the men whose efforts are devoted to the practical side of medicine.

Because hypertension, as I have previously stated, is a relative disease, and because it frequently is referred to as a symptom or pathology of function, rather than of structure (25), let us view the damage which it produces each year and attempt to ascertain its mortality rate. The Metropolitan Life Insurance Company of New York maintains that four times as many deaths result from cardio-vascular-renal disease, of which essential hypertension is the prime cause, as from cancer (68). As compared with tuberculosis and diabetes, there are twenty times more deaths from hypertension and its complications (30) than from the two formerly named diseases. Fifteen per cent of all deaths of persons past the age of fifty years are caused by hypertension and related conditions (1),

which cause approximately 500,000, or one-half million, deaths per year (1).

Like kidney diseases (9), hypertension is classified in a rather vague manner, which makes it extremely difficult to define it in an acceptable way. For this reason, I believe that it is necessary that I mention those classifications which I have found throughout my readings.

Adson and Allen (1), of the Mayo Clinic, claim that there is, first, an essential hypertension, the cause of which is unknown, and that eighty-five per cent of all persons with high blood pressure have this type. They then proceed to break down this primary type into four different grades, which are measured and determined by eye background readings. The second, or miscellaneous, group is divided into several parts, whereby hypertension is considered more as a sign or symptom than as an entity in itself. The subdivisions in this group are, as follows: (1) coarctation of the aorta, (2) glomerular nephritis, (3) tumor of suprarenal gland, (4) hyperthyroidism, (5) generalized arteriosclerosis, (6) traumatic arteriovenous fistula, and (7) aortic heart disease.

Rutledge's (68) classification is similar in

principle to Adson and Allen's. However, he adds the following divisions to his second group: (1) pituitary basophilic adenoma, (2) toxemia of pregnancy, (3) lead poisoning, and (4) infections.

Another worthy consideration of nomenclature is that of Steele and Shroeder (72), who divided hypertension into four groupings, with subdivisions under each main heading. An outline of their system of nomenclature follows.

Hypertension.

A. Renal.
   1. Parenchymal glomerular nephritis.
   2. Pyelonephritis.
   3. Urinary obstructions.
   4. Renal tumor.
   5. Amyloid kidney.
   6. Polycystic kidney.
   7. Hypoplastic kidney.
   8. Eclamptic kidney.

B. Vascular.
   1. Arteriosclerosis.
   2. Buerger's disease.
   3. Periarteritis nodosa.
   4. Renal infarcts.

5. Lupus erythematosus.
6. Lead poisoning.
7. Coarctation of aorta.

C. Nervous.

1. Brain tumor causing increased cranial pressure.
2. Diseases of brain stem.
3. Psychic disturbances.

D. Endocrine.

1. Pituitary basophilic adenoma.
2. Adrenal tumor.
3. Hyperthyroidism.
4. Ovarian tumor.
5. Menopause.
6. Obesity.

I was unable to determine which of the above classifications was best for acceptance. I have, therefore, presented all three forms of nomenclature, the composite of which includes practically all conditions in which hypertension plays some role.

Now that we have established an introduction for our discussion, our next problem concerns the questions, "What cases are desirable for surgery, or are all hypertensions to be considered as candidates for sympathectomies? If not, which ones shall we include in this

category?"

Before we get into an involved examination of this topic, let us undertake to define the condition which was so rudely neglected in the discussion of our clinical analysis. "Essential hypertension is a disorder of one or more etiological factors, in which the blood pressure is over one-hundred-sixty millimeters systolic and ninety millimeters diastolic, with exacerbation and remission which ultimately result in pathologic changes in one or more of the cardio-vascular-renal systems--notably, arteriosclerosis of vessels, cardiac hypertrophy, nephrosclerosis, and ocular vessel disease, the degree and speed of which depends on the age of the individual and the height of the blood pressure" (28). Implications are that in the early phases of the disease, as was previously stated, we have a pathology of function, and in the latter phases, one of structure.

The primary aim of sympathectomy is early diagnosis of essential hypertension, in order to halt high blood pressure before the media layer of the arteries and arterioles has begun to thicken. This is measured by determining the amount of fluctuation or fixation in pressure which is present (21) (34) (22).

Flexibility of vessels is usually found in the younger individual; therefore, sympathectomies should

be performed early. Crile and Crile (27) think that in cases concerning people with complaints of headache, nervousness, weakness, palpitation, dizziness, dyspnea, and arteriole changes, it is advisable to operate (celiac ganglionectomy). Just how much change is observed is a relative and a disputed point; what we are most interested in is the degree of flexibility of the vascular system.

This vascular flexibility is measured by several different methods. One of these is the cold pressor test (49). Another consists of the use of a sedative, preferably sodium amytal, which is administered in three or more doses every half hour, in quantities of three grains per dose, plus restriction to bed. The blood pressure is taken at short and equal intervals of time and is charted accordingly (68). Other useful drugs which serve the same purpose are sodium nitrate, which is given in six doses of one-half hour, and sodium pentathal (five per cent solution), which is administered intravenously in the form of light anesthesia, with measurement of blood pressure being made intermittently and then graphed (68). Men at the Mayo Clinic have even suggested that the patient take a warm bath and that his blood pressure then be recorded; if a momentary

decrease is noted, the selection of this candidate is favorable (4).

Besides the indications and tests mentioned above, it is important that we know some of the contra indications for sympathectomies. One of these is a hypertensive heart, which is associated with cardiac decompensation or coronary occlusion (23). Likewise, an inverted T wave, which is usually recorded with these conditions, brings forth comments for no surgery (56). History of stroke, kidney pathology, and eye ground changes, if marked, indicate a bad prognosis. A patient with generalized arteriosclerosis is also classified as a poor selection for treatment by sympathectomy, as was previously pointed out. Our aim is to get patients whose blood pressures are able to fluctuate, a condition usually found in the younger individual; hence, it is generally agreed that sympathectomies are of the greatest aid to the younger group.

Throughout the United States, various clinics have adopted different types of surgical techniques. One of these is the subdiaphragmatic operation with celiac ganglionectomy. This method, perfected by Crile at the Cleveland Clinic, seems to be quite successful, according to the statistical report (26).

Another technique is the rhizotomy or anterior horn root resection, in which the preganglionic fibers, rather than the postganglionic ones, are divided. This operation is performed from the sixth dorsal thoracic to the second lumbar level, and it is carried out in two stages, (1) exposure of the dura, and (2) opening the dura and severing the nerve roots. This is quite an effective operation. Its use, however, is questioned because of its following undesirable qualities: (1) it has a high mortality rate, (2) it is time-consuming to perform, and (3) there is possible danger to the cord, with a resulting multiple sclerosis (47).

A bilateral supradiaphragmatic operation consists of a splanchnicectomy and a lower dorsal ganglionectomy. This, according to Peet and his co-workers (63), offers the best prognosis of any form of therapy yet reported. Figures used in his article to illustrate this fact give us very favorable results.

Smithwick and his group in Boston (73) have compromised upon the various procedures previously presented and have created the transdiaphragmatic operation. This is performed by means of a hockey stick incision, giving us exposure from the ninth dorsal to the second lumbar level. Resections are then done as anatomical

structures permit. The operation is performed at two different periods of time, each side respectively. At the time of operation it is possible for the surgeon to observe the adrenal gland and the kidney for possible pathology.

The principles in medical management of a hypertensive patient are based upon several factors. These include (1) bed rest, (2) reduction of diet, (3) irradication of foci of infections, (4) sedation, and (5) a depressant drug, such as potassium thiocyanate (78), under careful control.

The main purposes of sympathectomies are to disconnect the arterioles from the vasomotor centers, thus inducing a state of decreased tonicity, or to produce a decreased vasoconstriction and an increased flow of blood through the kidneys (3). Smithwick (73) says, "The aim in surgery is to produce relaxation of a large portion of the arteriole bed, namely, the lower extremities and the splanchnic region." Another postulation is that when extensive anterior nerve root resection is performed, there is a reduction of abdominal pressure. This causes paralysis of the abdominal muscles, thereby decreasing intra-abdominal pressure and permitting the visceral vessels more chance of dilation (61) (11).

Curious individuals would wonder what end results were obtained from the various surgical procedures for the relief of this menace and whether or not there was any abnormal physiology observed in other regions of the body. Relief was reported for the general symptoms of headache, fatigue, dizziness, nervousness, and palpitation and pain in the chest (24) (47), qualities which can be determined by no one except the patient; this is also true for gall bladder trouble, goiter, peptic ulcer, and other diseases too numerous to mention. Sympathectomy is usually followed by a temporary drop in blood pressure, which lasts for varying lengths of time, and by a temporary tachycardia (3), which eventually disappears. Surgery also results in improvement in such conditions as papilloedema, angiospasm, exudates, and hemorrhage; eye ground improvements and decrease of retinitis have also been reported to have resulted from this type of surgery (38) (80).

There is another criterion by which we measure the success of sympathetic ganglion removal or anterior nerve root resection. Besides cutting down the incidence of dysfunction and abnormal pathology to the vital organs, the heart, brain, and kidneys, patients in the early stages of essential hypertension have, as

a whole, benefited from sympathectomy. However, in cases where the operation was quite extensive (rhizotomy) or was extremely risky, some unfavorable signs have appeared postoperatively, such as abdominal cramps, backache, areas of hyperesthesia in the flank and extremities, and light headedness. The Mayo Clinic records the following sequelae of extensive sympathectomy: sweating feet and legs, loss of ejaculatory power, paralysis of the muscles of the urogenital trigone, sterility in the male, some small and large bowel disturbances, and tachycardia, especially upon exertion (2). Whenever the splanchnic nerves which innervate the kidney are resected clinically, no impairment of function appears (36).

The aims of surgery may be summarized as follows: to decrease blood pressure, to provide symptomatic relief for the patient, and to prolong the patient's life expectancy. After considering all of the material herein presented, I was unable to make a definite evaluation of sympathectomies, since this form of treatment is still in a highly experimental stage (47). I would advise the performance of this operation, however, in selected cases similar to those which I have mentioned in my thesis.

V

Summary

1. In my introduction, I briefly outlined the physiology of blood pressure and vaguely discussed factors which are potential causes of hypertension or which are closely associated with this condition.

2. I next attempted to review significant physiological experiments which have been performed in this field and gave the results and validity of each, arriving at the conclusion that "neurogenic" and "humoral" factors, associated with renal physiopathology, are two elements in body economics which are responsible for or related to hypertension. The most recent work carried out by Page and his associates reveals that a decrease in pulse pressure, as well as renal ischemia, will produce an elevated blood pressure.

3. My next concern was a clinical discussion, which included the incidence of hypertension, the classification of hypertension, and the selection of patients for sympathectomies, with emphasis being placed on flexibility of the vascular system and on the age of the patient. Various surgical techniques and the rationale of sympathectomy were also considered in this section.

4. It may be concluded that the sympathectomy is still in the experimental stage and that it applies, on the whole, to cases similar to those selected ones which were cited in this thesis.

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