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THE SURGICAL TREATMENT
OF
ESSENTIAL HYPERTENSION
BY
SYMPATHECTOMY

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INTRODUCTION

This paper is an attempt to place the surgical treatment of essential hypertension on a rational basis. The inadequacy of the current medical treatment deems it necessary that a new and better treatment be forwarded. Although one realizes that the surgical treatment is obviously not the final answer to the problem, an attempt will be made to explain the efficacy of sympathectomy in selected cases.

Cardiovascular-renal disease kills one-half million people annually in the United States. That is four times as many deaths as are attributed to cancer (1). Apparently, hypertension accounts for from one-half to three-fourths of all deaths referable to cardiovascular-renal disease and thus is two to three times as deadly as cancer (2) (3). About a fourth of all deaths of individuals past 50 years of age is referable to hypertension (4).

PHYSIOLOGY OF HYPERTENSION

Hypertension is merely a clinical sign which occurs in a large number of diseases. Its manifestations are numerous. It may be temporary or permanent, stationary or progressive, benign or malignant, obviously secondary to the underlying disease, or frequently, mysteriously primary. An elevation of the actual blood pressure may be due to increased blood volume, increased peripheral resistance, increased blood viscosity, increased cardiac output, or any combination of these four factors. It must be noted that cardiac output and peripheral resistance, in addition, are subject to control by the sympathetic nervous system and in part by the circulating hormones.

Of the many types of high blood pressure, the most important one is essential benign hypertension. In its early stages it has been found that the cardiac output, blood volume, and blood viscosity are normal. Thus, it is agreed that the chief disturbance of the pressure is a result of increased peripheral resistance. Physiologists have shown that constriction of the splanchnic arterioles will cause a marked elevation of systemic blood pressure. This, of course, they reasoned, was due to the increase in the peripheral resistance. The pathologists, in turn, lent support to this view by demonstrating striking lesions of the splanchnic

arterioles in autopsies on hypertensives. It was only natural to assume that this splanchnic vasoconstriction was probably produced by overactivity of the sympathetic nervous system.

Prinzmetal and Wilson (5) pointed out that if this selective vasoconstriction were limited to the splanchnic area alone there should be a shunt of the blood to other regions such as muscles and skin where according to the hypothesis, the arteriolar tone is still normal. Their observations did not bear out this hypothesis, for they found the arteriolar tension in the forearm was normal in hypertensive individuals. Stead and Kunkel (6) verified the results by showing a normal blood flow in the cerebral vessels.

In hypertensive patients the arteriolar responses to local heat, local cold, the metabolites of exercise, body warming, body chilling, epinephrine, pituitrin, histamine, and tyramine are essentially normal. Stead and Kunkel (6) observed that hypertension neither diminished nor accentuated the vasodilatation produced by exercise of the forearm muscles. They also noticed that sensory stimuli such as noise, pinching and deep breathing produced vasoconstriction in the hand and foot quantitatively and qualitatively similar to that occurring in normal subjects. Steele and Kirk (7) found no differences in the skin temperatures on normal and

hypertensive patients. Prinzmetal and Wilson (5) found no differences in the normal and hypertensive patients as regards blood flow when acid metabolites accumulated.

The question arises--is this increased arteriolar tone due to abnormal activity of the vasoconstrictive center? Experimentally it has been shown that when vasoconstrictor impulses were abolished to an entire extremity by anesthetizing the paravertebral sympathetic ganglia in the hypertensive and normal individual the increase in blood flow was essentially the same.

From the above evidence authorities are inclined to agree with Wiggers (8) who believes that essential hypertension is basically due to unknown humoral agents which "probably causes contraction of the muscular elements throughout the vascular system".

The probable importance of unidentified humoral agents has been stressed so much that it is well to recall that vasoconstriction of nervous origin may be superimposed periodically upon this presumed basal and constant arteriolar hypotonus just as is the case in transient physiological elevations of blood pressure in normal individuals. Significant reduction of blood pressure occurs in many patients during physical and mental rest. The frequent association of essential hypertension with continuous nervous tension and emotional stress and anxiety, indicates that though the fundamental

abnormality may be humoral in origin, the sympathetic nervous system can still accentuate the grade of hypertension and accelerate its advance.

Taking the evidence as a whole, one is able to make a few generalizations. The circulatory system in essential hypertension seems to differ from the normal chiefly in the basal level at which arteriolar tone is, so to speak, set by a mechanism which is apparently humoral in type. Many normal stimuli seem to raise or lower arteriolar tone temporarily and locally without at any time influencing detectably this underlying set of the vascular system. Despite this set, naturally occurring and powerful dilator substances, such as those resulting from exercise and temporary ischemia, increase blood flow physiologically in hypertensive subjects. They cannot, however, produce a blood flow greater than normal because they are apparently unable to irradiate the persistent and uniform tonus which appears to be the constant companion of benign hypertension and related types of chronic elevation in man.

Investigators interested in hypertension have always pointed an accusing finger at the kidney. Moritz and Oldt (9) found the kidney to be the only organ in which arteriolar sclerosis is almost invariably associated with hypertension. Blackman (10) described the frequency with which renal arteries are blocked partially

by atherosclerosis. Cohn, Schroeder, and Steele (11) have demonstrated the great frequency of renal abnormalities by intravenous pyelography in patients with so-called hypertension. Goldblatt, in his classical works, has shown the relationship of renal ischemia to hypertension (12). All this is very interesting, but in man what produces the first abnormality of renal blood flow, which once began, perpetuates itself in a vicious cycle? From here on, the evidence concerning the cause is greatly circumstantial and theoretical.

Theoretically, there are several possibilities when one considers in what manner the blood may be modified in passing through a presumably ischemic kidney.

1. The failure to discharge into the blood stream a depressor or anti-pressor substance.
2. The pressor substance may be liberated from an ischemic kidney.
3. The failure to remove a pressor substance or its precursor from the blood stream.

To begin with, the urine of hypertensive patients contains less depressor substance than that of the normal subjects. This observation was confirmed by Elliot and Nuzum (13) in 1934 but the injection of the depressor substance in purified form had no effect on human hypertension.

With respect to the possible pressor substances, Tigerstedt and Bergman (14) found that saline extracts of kidney tissue contained a protein-like pressor substance which they called "rennin". Landis, Montgomery and Sparkman (15) demonstrated that in striking contrast to other pressor substances such as epinephrine, these purified kidney extracts elevate blood pressure without reducing peripheral blood flow. Kapp, Friedland and Landis (16) found that rabbits made hypertensive by a partial clamping of the renal artery had normal skin temperature during body warming. The injection of rennin in these already hypertensive animals elevated blood pressure still further without reducing skin temperature or blood flow during the entire pressor response. Prinzmetal and Friedman (17) have reported that extracts from kidneys of patients who have died from high blood pressure raise the blood pressure of dogs to a greater average amount than extracts prepared from the kidneys of other persons who have died from other causes. However, the results of other such experiments have been highly controversial and the results obtained do not afford convincing evidence for or against the humoral renal origin of hypertension.

One must now consider the third possibility, that normal tissue in some way neutralizes, destroys or excretes the substance responsible for hypertension.

Williams and Harrison (18) report that an anti-pressor substance, extracted from the kidney tissue, may reduce for days the hypertension of man and animals. Page and Helmer (19) have presented evidence to show that rennin itself is not pressor but combines in the circulating blood with rennin-activator to produce angiotonin which in combination again with a different activator finally produces vasoconstriction and elevates blood pressure. Furthermore, Page, Helmer, Kohlstaedt, Fouts, and Corcoran (20) have found that extracts of kidney, muscle and lung contain an antipressor substance which neutralizes the rennin-angiotonin activator system and reduces hypertension strikingly in animals and moderately in man.

In conclusion, it can be said that the sustained blood pressure in man can only be described fully by that chemist, physiologist or clinician who identifies in blood some abnormality which is uniformly associated with the hypertensive state in man, or who presents an entirely new concept which explains away a web of circumstantial and indirect evidence which at present makes the humoral hypothesis seem most logical.

THEORY OF TREATMENT

As has been stated in the opening paragraph, sympathectomy can in no sense be regarded as a cure for hypertensive disease since it does not remove the cause. Surgical denervation of the splanchnic area in the treatment of essential hypertension aims at reducing the peripheral resistance in a large area. It is obvious that the effectiveness of the operation depends upon how much the blood pressure level is directly proportional to the vasoconstriction of sympathetic origin. Since it is probable that in hypertensive patients excessive vasoconstriction is generalized, denervation of the splanchnic area at best can cause release from constriction in that area alone; persistence of the pressor substance would maintain constriction of the arterioles outside the splanchnic area. Berwald and Devine (21) maintain that there are secondary effects of this vasodilatation that are of import. There is an increase in blood supply to the kidneys and an increase in intrarenal pulse pressure and thus a decrease in the renal pressor substance. There is a postural fall in blood pressure which follows sympathectomy but usually disappears over a period of months or a few years. There is a decrease in the amount of adrenalin secreted as a result of excitement, fear, and other vasomotor stimuli.

SURGICAL PROCEDURES

There is a wide variance in the surgical approach, however, the aims are practically the same. Complete operation aims at bilateral resection of the sympathetic chain and its ganglia from D9 to either L1 or L2 inclusive, and avulsion of the greater splanchnic nerves.

The varieties of operations used have been of several types dependent of the clinic where performed.

1. The supradiaphragmatic splanchnic nerve section and lower dorsal sympathetic ganglionectomy has been advocated by Peet (22). In this operation, one interrupts the splanchnic nerves above the diaphragm and excises the ninth to twelfth sympathetic ganglion. The operation does not permit the examination of the kidney and adrenal gland or interruption of the lumbar sympathetic nerves.

2. Infradiaphragmatic splanchnic nerve section is advocated by Craig (23). The splanchnic nerves are severed below the diaphragm, together with a small portion of celiac plexus. In addition, the first and second lumbar ganglia are removed. Regeneration of the splanchnic nerves is difficult to prevent after this operation. In obese patients who have a retroperitoneal lymphadenopathy, the identification of all the splanchnic trunks may be difficult. Finally, branches that are

given off toward the periaortic plexus from the splanchnic nerves and the sympathetic chain above the diaphragm are missed at operation.

3. Smithwick (24) devised a transdiaphragmatic splanchnic nerve section that supposedly combines the advantages and eliminates the disadvantages of the two previous operations. It is a complete resection of the major splanchnic nerve, removing it from the fifth dorsal root down to its entrance into the celiac ganglion. In addition, the sympathetic ganglionated trunk is removed from the ninth dorsal to below the first or occasionally the second lumbar ganglion. In order to obtain this exposure, the diaphragm may be incised and sutured. Through this approach, the renal artery, pelvis, ureter, renal parenchyma, and adrenal glands may be inspected and palpated.

4. Another operation is described by Huer and Glenn (25)--the anterior root section or extensive rhizotomy. It consists of division of the anterior nerve roots of the spinal cord from the sixth dorsal to second lumbar vertebrae. It is a very complete operation inasmuch as all the sympathetic fibers carrying vasoconstrictor impulses to the splanchnic area are eliminated. This procedure differs from the preceding in that the preganglionic fibers are divided instead of the postganglionic rami. The operation is usually performed

in two stages. The first consists of exposure of the dura by laminectomy. The second consists of the opening of the dura and division of the nerve roots. This operation is very difficult and not without danger because of the possibility of damage to the cord or transverse myelitis.

CLASSIFICATION OF HYPERTENSION

There is a great need for a standardized criterion of signs and symptoms on which cases are selected for the operation and from which evaluations are made. The most suitable classification we have to date is that given by Wagner and Keith (26). Hypertensives are divided into four groups depending mostly on the severity of eye ground changes. Because the arterioles throughout the organs of the body seem to be the chief point of attack and can be readily visualized only in the retina, the findings obtained by the ophthalmoscope are very important.

Group 1. Patients who have only mild narrowing (increased tonus) or sclerosis of the retinal arterioles. There must be good retinal, cerebral, cardiac and renal function.

Group 2. Patients who have a moderate to marked sclerosis of the retinal arterioles, characterized especially by generalized and localized irregular narrowing of the arterioles. There must be good retinal, cerebral, cardiac and renal function.

Group 3. Patients who have a combination of sclerotic and spastic lesions in the arterioles and a superimposed cotton-wool patches, who have hemorrhagic areas in the retina but whose optic discs are not edematous. There is evidence of dysfunction of one or of

several organs belonging to the arterial system.

Group 4. Patients who have a combination of sclerotic and spastic lesions in the arterioles with a superimposed cotton-wool patches and hemorrhagic areas in the retina, plus a measurable edema of the optic discs. They are definite functional failures because of interference in the blood supply to the retina, brain, heart and kidneys.

Keith, Wagener, and Barker (27) have shown that the mortality in hypertension, groups 1 and 2, is 30 and 40 per cent, respectively, in four years from the time of diagnosis. For a similar period, the mortality of hypertension, group 3 is 78 per cent, and in group 4 it is 98 per cent. Among subjects who have systolic blood pressures of about 170 mm. of mercury, the relation of actual mortality to expected mortality is as 219.6 to 100. Among those patients whose systolic blood pressure exceeds 200 mm. of mercury the actual mortality is to the expected as 827.5 is to 100 (4) (28). For individuals more than 40 years of age, systolic pressure ranging from 35 to 44 mm. in excess of normal increases the expected mortality two and one-half times. Such a slight increase in blood pressure as that represented by the figures 170 to 174, systolic, and 106, diastolic, increases the expected mortality two and one-half times (29).

Not all clinicians use this classification in their studies on the effect of sympathectomy on hypertension, thus it is increasingly difficult to evaluate their results. However, we find that many use eye-grounds as one of their prognostic signs. On this basis and others, I present the following discussion of the work done on this subject by well known and recognized clinics.

CLINICAL REPORTS

Probably no other group of men has contributed more to research in this field than those of the Mayo Clinic. Among these we find such names as Craig, Allen, Adson, and Rowntree.

The first case presented by the Mayo Clinic was by Rowntree and Adson (30) and the case report written up in the Journal of the American Medical Association in September of 1925. Their case:

History: A 33 year old male admitted to Mayo Clinic complaining of blurring of vision, headache, and some nausea and vomiting.

Examination: Systolic blood pressure was 230 and diastolic 130. Ophthalmoscopic examination revealed slight edema of the discs, cotton-wool exudates, hemorrhages involving particularly the left macular region, and a general reduction in the size and caliber of the retinal arteries. There was a slight albuminuria and the phenolsulphonophthalein output in two hours was 70 per cent. The dilution and concentration tests of renal function showed variations in specific gravity of the urine from 1.006 to 1.024, or a slight diminution in dilution capacity. The diagnosis was "early malignant hypertension". "The case seemed to fall into the group 2 described last year by Wagner and Keith (31) in which eyeground changes are definite, while the cardiac and renal functions are practically unimpaired"--(Group 3).

Operation and Results: They removed the ganglions with the rami and all branches and trunks of the second, third and fourth lumbar segments of the sympathetic chain through a midline excision.

"The postoperative course was excellent. At first the subjective improvement was striking. The blood pressure level was distinctly lowered at least for the two weeks following operation. The headaches which had previously occasioned such great distress, entirely disappeared, and recurred but once during the first month and then only for a short time. His vision improved markedly. . . No change was noted in volume

or composition of the urine; certainly the efficiency of the kidney was in no way impaired."

"While the patient was getting up and about, the blood pressure gradually mounted. He now responded well to nitrites and hypertension baths, exhibiting marked improvement over his former condition. At six months he reports recurrence of hypertension (systolic blood pressure, 220, and diastolic, 120), but otherwise the patient is in good health. However, the period elapsing is entirely too short to admit of conclusions as to the effectiveness of this procedure. The case is reported at this time merely to call attention to the possibilities of abdominal sympathetic neurectomy and to the interesting changes observed subsequent to the operation."

Adson and Brown (32) in a report in 1934 make this statement concerning the above discussed case:

"In 1925 Rowntree and one of us (Adson) reported a case of malignant hypertension in which treatment was bilateral sympathetic lumbar ganglionectomy and trunk resection, which included second, third, and fourth lumbar sympathetic ganglions and the intervening trunks. The results on the blood pressure and ultimate outcome were not significant. It was apparent that the operation did not denervate sufficient arteries to change the systemic arterial pressure and that a more extensive operation was needed. One of us (Adson) suggested and performed an extensive rhizotomy (anterior nerve root section) in order to include all sympathetic innervation below the diaphragm and to include the motor innervation of the abdominal muscles."

The extensive rhizotomy was performed on a woman aged 29, with a blood pressure of 228 systolic and 156 diastolic and belonging to group 3. The patient showed a severe form of progressive essential hypertension. Organic changes in the retinal arterioles and active retinitis were present. The life expectancy is less than 3 years according to Keith (33).

Depressor effects were probably due to loss in

vasomotor control of the splanchnic and peripheral arteries below the diaphragm and in lowering of intra-abdominal pressure by paralyzing the abdominal muscles.

Immediate results included a decrease in systolic and diastolic pressure with a greater decrease of the systolic; decrease in retinitis; and no changes in kidney function.

A longer time is necessary before the remote results will be evident, however, the author states, "The favorable results of the operation in so severe a form of hypertension are more encouraging and its further use for younger patients with severe progressive forms of essential hypertension seems justifiable."

In 1933 Craig and Brown (34) of the Mayo Clinic, issued another preliminary report to show, first, absence of untoward effects of unilateral and bilateral resection of the splanchnic nerves, and secondly, in the most severe cases of hypertension in which organic narrowing of the arterioles was advanced, removal of the central control of the splanchnic arteries did not restore the blood pressure to normal levels. The responses in blood pressure to stimulation were not materially changed. A sufficient amount of the arterial bed remained under neurogenic influences, or the

hypertrophy of the musculature of the arterioles was too advanced; or the existence of renal insufficiency may have nullified the blood pressure lowering effects of the operation. They found that in the less severe forms of hypertension with minimal degrees of hypertrophy of the arterioles and in which the vaso-motor factor seems paramount, there are significant reductions in the levels and responses of the systolic blood pressures. The removal of the left splanchnic nerves seems more effective than the removal of the right. They conclude that in some progressive forms of essential hypertension among young adults with abnormal fluctuations in blood pressure and minimal grades of hypertrophy of the musculature of the arterioles the advantage of this operation should not be ignored.

Following these promising preliminary reports the clinic began to pursue a more vigorous course. Adson (35) classified hypertension using as a basis the rate of progress and severity of symptoms.

BENIGN:

1. Age of onset is forty to fifty-five years of age.
2. The form pursues a slowly progressive course.
3. Life expectancy is ten to fifteen years.
4. Maximal blood pressures in mercury are systolic-200 and diastolic--140.

EARLY MALIGNANT:

1. Age of onset is eighteen to fifty years of age.
2. The form pursues a moderately progressive course.
3. Life expectancy is three to four years.

4. Maximal blood pressures are systolic--250 and diastolic--160.
5. Signs of irreparable cardiac, coronary, and renal disease.
6. Spasm of retinal arteries with hemorrhages.

MALIGNANT:

1. Age of onset is eighteen to fifty years.
2. Course is rapidly progressive.
3. Life expectancy is eighteen months.
4. Maximal blood pressures are systolic--310 and diastolic 190.
5. Spasm of retinal arteries, retinal hemorrhages.
6. Cardiovascular and nephritic disease.

At first, the operation of choice was complete rhizotomy and extensive splanchnic section. Numerous post-operative sequelae developed.

After complete rhizotomy (36) there is a loss of sweating function of the feet, legs, and lower part of the abdomen up to the transverse line situated about 1 to 2 inches above the umbilicus. Paralysis of the ejaculatory powers and muscles of the urogenital triangle is similar to that following neurectomy of the presacral nerves. It deprives the large and small bowel and bladder of sympathetic innervation, but does not appear to increase frequency of urinary or fecal evacuation. There are no changes whatsoever in the genital system.

The effects of splanchnic section and removal of the first and second lumbar ganglia are similar to those obtained by rhizotomy except that the level of sweating and sebaceous loss and increase in surface temperature occur at a lower level than that obtained by rhizotomy.

Pre-operative studies consist of at least twenty-four consecutive hourly determinations of the values for the blood pressure so that determinations of the maximal blood pressure, the minimal blood pressure, and the mean or average blood pressure is made. Post-operative studies are of the same type.

Pre-operative prediction of the effects on pressure of neurosurgical treatment was introduced by the Mayo Clinic in 1936 (37). Anesthesia induced by intravenous injection of a solution of pentothal sodium in sufficient amounts to cause a maximal increase in the temperature of the skin of the toes is a safe procedure if the drug is administered expertly. The blood pressure resulting from this procedure constitutes an accurate reflection of that resulting from the neurosurgical method described. Pre-operative prediction of the immediate effects of operation on the blood pressure can therefore be made safely and accurately. Incomplete studies indicate that prediction can usually be based on the effect on the blood pressure of the oral administration of sodium amytal in amounts of three grains hourly for three doses. Inhalation of amyl nitrite may also affect the blood pressure in much the same way as neurosurgery. The lowest systolic and the lowest diastolic pressures determined during the study, regardless of whether they are observed

at the same time, are considered the "pre-operative prediction values".

The response of blood pressure to immersion of the hand in ice water (30) gives important information as it indicates the degree of increase of the blood pressure following other stimuli such as fright, anger, and nervous tension. Thus, it may be desirable to operate on patients who have hypertension, group 1, provided immersion of the patients hand in cold water invokes a high degree of hypertension.

Pre-operative selection of cases is also based on the degree and duration of subjective symptoms of which headache, nervousness, and pain in the left side of the thorax occur in a high percentage of cases.

The results of operation were grouped as follows:

1. Failures--where changes in blood pressure were only slight and transient.
2. Temporary--blood pressures were significantly lower following operation than they were pre-operatively but returned to approximately the pre-operative level either between the time of dismissal of the patient from the hospital and the first subsequent record of their blood pressures which was from two to eight months.
3. Fair--significant post-operative prolonged reduction in both systolic and diastolic phases of blood pressure, not approaching normal levels.

4. Good--greatly reduced blood pressure although not all in the range of normal.

A report by Adson and Craig (36) in 1935 on the results of the various operative procedures used indicate that splanchnic section with removal of first and second lumbar ganglia and partial section of suprarenal glands was the operation of choice. This was based on a survey of 45 cases.

| TYPE OF OPERATION | CASES | GOOD | FAIR | FAILURES | DEATHS |
|---|-------|------|------|----------|--------|
| Extensive rhizotomy | 27 | 13 | 6 | 6 | 2 |
| Splanchnic section with removal of first lumbar ganglion. | 7 | 2 | 1 | 4 | 0 |
| Splanchnic section with removal of first and second lumbar ganglia and partial section of suprarenal gland. | 7 | 5 | 2 | 0 | 0 |
| Miscellaneous | 4 | | | 4 | 0 |
| TOTAL | 45 | 20 | 9 | 14. | 2 |

Later, however, these men chose subdiaphragmatic sympathetic denervation as the operation of choice.

According to Adson and Craig (39) mortality is practically negligible. The fact that post-operative

relief of symptoms and that of hypertension have not run parallel courses confuses the issue of a true evaluation of results. This might be explained by the fact that where the relief of symptoms exceeds the lowering of the blood pressure there is a tendency for the blood pressure level to become more stable.

Results based on retinal changes indicate:

1. Patients with a detectable sclerosis received good or fair results in 83 per cent of cases.
2. Sclerosis of grade 1 or 2 received good or fair results in 22 per cent of the cases.
3. Sclerosis of grade 3 showed good or fair results in 22 per cent of the cases.
4. Those cases with advanced hypertension, with organic arterial disease, are very little benefited by operation.

Symptomatic relief for headache, nervousness, and pain in the left side of the thorax occurred in a large percentage of cases either transiently or over fairly long periods of time.

Adson (35) in 1939 found that operation diminishes the response of blood pressure to immersion of a hand in ice water; operation usually relieves symptoms whether the blood pressure is greatly reduced or not (80 per cent being benefited clinically); the heart may decrease in size and inverted T waves of an electro-

cardiogram may become upright; retinitis and spasm of retinal arteries may be diminished or disappear; albuminuria may decrease and renal function improved; the basal metabolic rate may be decreased. Blood pressure was not materially reduced in 45 per cent of the cases.

Post-operative results in 224 cases after using subdiaphragmatic resection of the splanchnic nerves with resection of the celiac ganglion and resection of the lumbar sympathetic trunk, including the first and second lumbar ganglia on both sides, was presented by Allen and Adson of the Mayo Clinic (40).

They found that results of operation can be predicted with reasonable certainty by observing the response of the blood pressure to rest and sleep, to the injection of sodium amytal, and to injection of pentothal sodium. When poor results of operation are predicted as a conclusion of these tests, the operative results are almost uniformly unfavorable. When good results are anticipated, some patients do not receive as much benefit from operation as was expected.

There have been no operative deaths in a series of 300 cases.

Clinical symptoms invariably disappear with reduction of blood pressure, but in a number of instances the patient continues to be free from symptoms even

though there has been a gradual return of elevated blood pressures. (This is similar the results of venesection.)

Several collateral results of sympathectomy that have been enumerated but not discussed were two definite phenomena that develop in the cardiovascular system following resection of the splanchnic nerve and lumbar ganglia. Both have to do with the influence of gravity on the blood volume in the denervated area. The first is when the patient assumes an upright position, there is a marked fall in blood pressure. The second is tachycardia that is aggravated by exertion.

From the large number of cases studied, Craig and Adson (39) (40), and Adson and Allen (39), have reached the following conclusions:

1. In general, it can be said that the patient will probably get good results when diastolic pressure drops to 110 or below as a result of rest, administration of sodium amytal, or injection of pentothal sodium. When the sclerosis of the retinal arteries is absent or slight. Probabilities of a good result are small in the presence of advanced sclerosis of the retinal arteries, when the maximal diastolic pressure exceeds 150, when the diastolic pressure does not decrease to less than 120 as a result of the above tests. In the group between these extremes is a large number of patients in

which the result of sympathectomy cannot be accurately predicted.

2. Most patients who have hypertension group 1 do not require surgical treatment. Surgical treatment is advisable for patients who have hypertension group 2 or 3, if the hypertension is known to be progressive and if the function of the heart and kidneys is good. Hypertension group 4 does not respond satisfactorily to surgical treatment because of its advancement.

3. Often the relief of symptoms is out of proportion to the fall in blood pressure.

4. Rapidly progressive hypertension seems to respond less favorably than slowly progressive hypertension does.

5. Blood pressure results in 74 per cent of group 3 and 100 per cent in group 4 are reported as temporary or poor.

6. Numerous sequelae develop post-operatively but are unimportant.

About the same time the Mayo Clinic began their extensive work, George Crile (41) made this observation during his work with denervation of the adrenal glands,

"It is very interesting that we get a very good result in cases of essential hypertension on young adults. The operation does not bring the blood pressure down to the normal level but it does bring the blood pressure down to a lower level and it stabilizes at that level. The rise in systolic pressure in excitement does not occur so that accident of hemorrhage

is avoided. In this group the blood pressure is more or less stabilized, but denervation does nothing at all in advanced cases of hypertension."

He also noted (42) that in the course of the denervation of the adrenal glands and division of the splanchnic, when the sympathetic nerves are manipulated there is a rise in the blood pressure, both systolic and diastolic--sometimes to such a height that it cannot be measured with a manometer. On the other hand if the field is first flooded with novocaine there is no rise but rather a dramatic fall in the blood pressure. The adrenal sympathetic complex, thus, is the only tissue in the body which, when manipulated, can specifically affect the blood pressure.

Unlike the Mayo Clinic, Crile did not have any definite criteria upon which he selected his patients for operation, rather, he believed (43) that the determination of operability of the case depends in large part upon the experience of the operator and to a lesser degree upon laboratory findings. The clinical results being judged by:

1. Examination of the eyegrounds, the heart, the kidney function, and the blood pressure of the patient.
2. Knowledge as to whether or not the patient is able to go back to his usual occupation; whether or not the headaches, the dizziness, the failing vision, the precordial pain, the heart consciousness, and physical

disability have diminished or disappeared.

As a result of experience (44) he has selected celiac ganglionectomy with denervation of the adrenal glands as the procedure of choice. Symptomatically and its effects upon the blood pressure, the operation yields the most encouraging results, in his estimation. He emphasizes the fact that results obtained are dependent upon the amount of sclerosis present since the sclerosis is irreversible. Thus calendar age has very little to do with indications for operation and the effectiveness of operation. He makes this statement:

(45) "The physiologic age, not the calendar age is what counts. There is a certain stage in hypertension in which there is an irreversible condition due to sclerosis alone. Of course, as the individual grows older, the blood pressure tends to rise secondary to advancing sclerosis, this is termed the cardiovascular age. In a case where there is extensive sclerosis present the blood pressure may fall after celiac ganglionectomy, but the extent to which it will fall is limited by the cardiovascular age of the patient."

This author found it justifiable to operate in cases of cerebral accident where there has been no deterioration of brain tissues or in cases of glomerulonephritis secondary to hypertension and a urea clearance above 50.

The author (46) by 1939 had performed 476 operations on the adrenal sympathetic system in 285 patients. These have included 325 celiac ganglionectomies in 199 patients. In this series, 35 cases were operated on two or more years prior to the publishing of this

information, from these cases conclusions have been drawn concerning the effect on blood pressure. The average decrease has been 39/20. The extent:

| PRESSURE REDUCED | SYSTOLIC | DIASTOLIC |
|------------------|----------|-----------|
| 20 pts. or more | 78.6 % | 57.1 % |
| 30 " " " | 5.7 % | 35.7 % |
| 40 " " " | 42.9 % | 14.3 % |
| 50 " " " | 21.4 % | 7.1 % |
| 75 " " " | 7.1 % | |

Among the patients who left the hospital prior to 1940, Crile noticed that 33 per cent died at varying periods. It is generally accepted that approximately 60 per cent of unoperated patients with essential hypertension die from cardiac failure. In his series of cases treated by surgery, only 11.8 per cent died from cardiac failure, and there has not been a single cardiac death in the hospital following operation.

It has been his experience that a patient experiences a feeling of relief from the driving force within himself. The urge for work and the internal strain, the pressure in the chest, the headaches, the extreme restlessness, the wakefulness--all of these symptoms were partially or completely relieved in 88 per cent of his patients even when the blood pressure

is not decreased. This observation conforms closely to that of Adson et al.

He states,

"In the long run the value of any surgical procedure and medical measure is told by the patient himself. If the patient is able to return to his former occupation, if he is relieved of his subjective symptoms, then that determines, and that only, the value of the operation."

Although Crile was not as exacting as his fellow workers in his selection of patients, he received very good results in his series of cases. For this reason his work cannot be overlooked. It is impossible to evaluate accurately or compare his findings, but we can conclude from his exhaustive work that the operative treatment of essential hypertension is valuable where the patients do not have markedly sclerotic arterioles.

A very extensive and exhaustive work was done by Peet and coworkers (22). They published results in 350 consecutive cases of essential hypertension treated by bilateral supradiaphragmatic splanchnicectomy and lower dorsal ganglionectomy. Their efforts were very painstaking and accurate, consequently, they adhered to the following principles.

1. The surgical procedure must be utilized in a large number of cases and must remain identical in all cases.
2. Selection of cases must be based on constant

criteria fully investigated in each case before operation.

3. Post-operative results must be judged by the same criteria in an identical manner and on as many occasions as possible.

4. All cases in which operation was performed must be included in results.

5. The trial must extend over a sufficiently long period of time to eliminate mere temporary effect of the operative procedure.

The requirements for selection of patients for the operation are based on a few simple requirements. Preferably the patient is not over fifty years of age, but several exceptions have been made to this rule. The renal function must be adequate as indicated by an urea clearance of more than 40 per cent of normal and a urine concentration above 1.012. No patient with a blood nonprotein nitrogen of more than 45 mg. per hundred cubic centimeters is accepted. The heart must be compensated and the general physical status of the patient adequate to withstand a major operative procedure. Patients with a systolic blood pressure under 200 mm. of mercury are usually advised to not have the operation unless they have had an adequate trial of conservative medical treatment.

A summary of the results of splachnicectomy

with percentage of cases studied showing improvement (from nine months to seven years after operation) is presented by Peet et al.

| BLOOD PRESSURE | PER CENT |
|--|----------|
| Reduced to normal ----- | 11.7 |
| Markedly reduced (not to normal) ----- | 7.6 |
| Total cases significantly reduced ----- | 51.4 |
| GENERAL DISABILITY | |
| Symptoms improved ----- | 86.6 |
| Complete recovery from incapacity ----- | 55.5 |
| Total improved from incapacitation ----- | 81.3 |
| EYEGROUNDS | |
| Disappearance of papilledema ----- | 73.8 |
| Total cases with improvement ----- | 69.4 |
| HEART | |
| Heart size diminished ----- | 64.0 |
| Electrocardiogram improved ----- | 53.4 |
| RENAL FUNCTIONS | |
| Urea clearance improved ----- | 52.2 |
| Urine concentration improved ----- | 44.8 |

From these results it must be concluded that sympathectomy is of value in the treatment of essential hypertension.

An interesting study was made by P. Foa, N. Foa, and Peet (47) on the relationship of arteriolar lesions in hypertension. An estimation of the prognostic value of muscle biopsy was made. The ratio of the thickness of the wall to the diameter of the lumen (W/L) of the arterioles in skeletal muscle was computed from data obtained by direct measurement of the blood vessels in biopsy material. Three hundred and fifty consecutive cases of essential hypertension were studied. All of the patients were submitted to supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglion-

ectomy and followed nine months to seven years after the operation. The degree of thickening of the arteriolar wall was compared to the severity of other signs and symptoms and to the therapeutic results. Patients with more severe thickening of the arteriolar walls had more severe symptoms, showed poorer therapeutic results and greater mortality. The correlation is particularly significant between arteriolosclerosis and other evidence of damage to the vascular system, such as the elevation of the blood pressure. The results show that the determination of W/L in skeletal muscle adds very significant information to the clinical and pathological picture of hypertension. It is important in the prognosis of the disease. The results are in agreement with the hypothesis that the surgical treatment of hypertension gives better results when hypertension is due to spasm of the arterioles or to a mild reversible degree of hypertrophy of the muscle fibers of the media and not when severe anatomical lesions have transformed the majority of the arterioles into narrow and rigid tubes.

In 1941, Peet and Woods (48) made a comparison of mortality following operation with that of the Wagener-Keith medically treated control series--a study of 75 cases from five to seven years after operation.

A factor that cannot be controlled in a comparison

of these two series is the selection of cases. Presumably the patients of Wagener and Keith were unselected and consecutive. Peet's patients were, by necessity, selected in that they were in sufficiently good physical condition to permit operation. Briefly the criteria for selection of patients were:

1. All patients had essential hypertension.
2. All patients were under 60 years and preferably 50 years.
3. Renal function must be such that nonprotein nitrogen of the blood is under 45 mg. per cent. Urine concentration above 1.012 and urea clearance at least 40 per cent of normal.
4. A compensated heart.

Wagener and Keith did their work on a series of 219 patients whereas Peet and Woods had a consecutive series of 76 patients.

Comparison was based on the funduscopic groupings of Keith's original classification and their relationship to survival rate. The results were very interesting.

1. In group 4, 99 per cent of the control series were dead in five years, whereas 66.5 per cent were dead in the surgically treated cases in the same time.
2. In group 3, 80 per cent of those treated medically died within five years, whereas only 36 per

cent of the surgically treated patients died in the same time.

3. In group 2, the results are approximately the same--about 50 per cent of the patients died in five years.

4. In group 1, the mortality for the medical control series was 30 per cent, contrasted with no deaths in the surgical group.

It is obvious from the statements made by the Mayo Clinic group that the results in their studies are not directly comparable to those in Peet's series because of the lower average blood pressure levels and the lesser severity of retinal changes in their cases.

Comparison of mortality rates of the two sexes reveals a higher death incidence among males (95 per cent in the Wagener-Keith control series; 61 per cent in the surgical series) than among females (Wagener-Keith 88 per cent; Peet 42 per cent).

Rapidly progressive hypertension seems to respond more favorably than slowly progressive hypertension does in the experiences of Peet et. al.

The classical work of these three groups of men has added much to the treatment of essential hypertension. Their contemporaries have added very little.

De Takats, Heyer, and Keeton (49) published the

results of the various types of operation on a series of 24 patients. The patients had adequate follow-up records, by which is meant that they were re-examined at intervals of two to three months. There were 4 patients with supradiaphragmatic, 15 with infradiaphragmatic and 5 with transdiaphragmatic splanchnic nerve section. There was no surgical mortality. It is believed that at least two readily recognizable factors influence results. One is the type of operation performed and the other the stage of the disease in which the operation is undertaken. Of the splanchnic nerve sections, the supradiaphragmatic and infradiaphragmatic operation yielded such doubtful results that they were discontinued. The transdiaphragmatic total splanchnic nerve section has given excellent results in patients with grade 1 and grade 2 hypertension and produced considerable subjective relief in one patient with grade 3 hypertension. In one patient with malignant nephrosclerosis it failed.

Contraindications to surgical treatment of hypertension are the presence of grade 4 hypertension, cardiac decompensation, nitrogenous retention, severe atherosclerosis of larger vessels and age over 50 years.

Another report was issued by Bordley, Galston, and Dandy of Johns Hopkins (50) following the surgical treatment of 12 patients diagnosed "essential hypertension".

"Ten of these have been followed for three to seven years since operation. Two died shortly after operation. Ten of the patients were from 28 to 40 years of age and two were 50 years old at the time of operation.

"The sole criterion for operation was the presence of incapacitating symptoms. In three patients, a supradiaphragmatic splanchnicectomy (Peet operation) and in nine, an infradiaphragmatic splanchnicectomy (Adson-Craig operation) was performed. The Peet operation was carried out at first, but was supplanted by the Adson-Craig operation because the latter permits exploration of the kidneys and adrenal glands and interruption of a large part of the sympathetic supply of the thighs and legs in addition to that of the splanchnic area."

They observed:

1. Relief from symptoms referable to hypertension occurred in nine of the twelve patients shortly after operation. In five of these patients it was associated with a lowering of arterial pressure and in the remaining four, it occurred in the absence of changes in hemodynamics.

2. In four cases the symptoms returned when the arterial pressure rose to pre-operative levels. One other patient remained without complaints for 4 years even though the arterial pressure returned to the pre-operative hypertensive levels in less than 2 years and he had exhibited evidence of progression of cardiovascular and renal disease.

3. Of the three patients who did not obtain symptomatic relief, the first had a cerebral vascular accident 2 months prior to operation; the second died

of a cerebral accident 5 weeks following operation and the third died 22 hours after the second stage of an infradiaphragmatic splanchnicectomy.

4. The levels of arterial pressure was lowered for 6 to 18 months in four of the nine patients treated by infradiaphragmatic operation (Adson-Craig) and for 4 years in one of the three patients treated by the subdiaphragmatic operation (Peet).

5. In two patients abnormal findings in the heart and eyegrounds regressed during the period of lowered arterial pressure and returned after the arterial pressure rose again.

6. Regeneration of the arterial pressure to pre-operative hypertensive levels was not associated with regeneration of the sympathetic nerves supplying the lower extremities which were severed during the Adson-Craig operation.

Apparently the only contemporary organized evaluation of sympathectomy in cases of essential hypertension is given by Hinton (51) who based his results on the selection of patients by the Keith-Wagener criteria. He found:

1. Cases falling in groups 1 and 2 show gratifying results with an essentially zero mortality.

2. Cases which belong in group 3 and 4 are frequently seen and they are not the ideal type for the

best end results, but they may be entitled to the benefit of surgery after careful clinical study.

3. In spite of the various tests, it is difficult if not impossible to forecast the end results of a thoracolumbar sympathectomy.

Thoracolumbar sympathectomy has produced reversible changes in kidney function as demonstrated by blood chemistry findings. Papilledema resulting in blindness has been relieved with return of normal vision. Patients totally disabled over long periods of time, one to four years, have been restored to normal earning capacity.

He states that cases in group 4 who have been disabled over long periods must not be considered hopeless as excellent results are often obtained by operation.

No evidence of any relationship between the length of known duration of hypertension and the end results of sympathectomy have been found.

Berwald and Devine (21) contributed some of the latest work on the surgical treatment of hypertension. Their criteria for operation was as follows:

1. Age 50 or under, however, if the patient is over this age and has elastic vessels and a good response to tests, he is not denied the operation.

2. Sodium nitrite test--1/2 grain of the drug is

given every half hour for six doses, and blood pressure is recorded every half hour for five hours under absolute rest and quiet. If diastolic pressure is reduced 20 mm. of mercury or more, chances are that 64 per cent will have a good final result.

3. Sodium amytal test follows the same pattern as above except that 3 grains of the drug are given every hour for three doses. If diastolic pressure is reduced 20 mm. of mercury or more, chances are that 64 per cent will have a good final result.

The lowering of the systolic blood pressure is a less accurate criterion.

Patients with advanced cardiac and renal damage are refused operation and also obese individuals.

The authors studied the results of 29 patients. The pre-operative blood pressure average was 244/127 and the average post-operative blood pressure 9.8 months following sympathectomy was 166/112. The average reduction in systolic pressure was 78 mm. of mercury and the average diastolic reduction was 15 mm. The average systolic drop under sodium nitrite and sodium amytal was 42.7 mm., and the average diastolic drop was 18.2 mm. They considered a good result when drop in systolic blood pressure is 50 mm. or more and diastolic drop of 20 mm. or more.

No evidence of any relationship between the length

of known duration of hypertension and the end results of sympathectomy was seen. Subjective results in the 29 patients show--15 greatly improved, 9 moderately improved, 1 slightly improved, 2 not improved. That is, over 92.5 per cent of patients felt subjectively improved as a result of their operation. The mortality from operation is practically nil, especially with the subdiaphragmatic approach.

CONCLUSIONS

1. Four types of operations have been used extensively with varying results.

(a) The subdiaphragmatic splanchnic nerve section advocated by the Mayo Clinic has shown gratifying results. It enables the surgeon to examine the kidney and adrenal glands.

(b) The supradiaphragmatic splanchnic nerve section as used by Peet has shown good results. The operation does not permit the examination of the kidney and the adrenal gland and cannot interrupt the lumbar splanchnic nerves.

(c) Crile used celiac ganglionectomy with denervation of the adrenal glands. The operation is not very extensive and the results are a trifle ambiguous.

(d) The recent innovation of transdiaphragmatic splanchnic nerve section as introduced by Smithwick in 1940 has not received enough trial to predict its efficacy but preliminary reports are promising. Apparently it combines the advantages and eliminates the disadvantages of the three previous operations.

2. The criteria used for selection of cases for operation have varied a great deal but in general it is based on several established tests and facts.

(a) Response of blood pressure to pentothal sodium anesthesia, sodium amytal, or sleep.

(b) If the function of the heart and kidneys are good and the disease is known to be progressive.

(c) The general physical status of the patient must be adequate to withstand a major operative procedure.

3. The results have been somewhat variable but in general it can be said that the results of sympathectomy are inversely proportional to the degree of arteriolar sclerosis as seen in the retinal vessels.

It has been uniformly agreed that patients show a

relief of symptoms out of proportion to the fall in blood pressure, and in many cases, though the physical signs return, the symptoms remain mild.

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