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Evaluation of sympathectomy for hypertension

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AN EVALUATION OF SYMPATHECTOMY FOR HYPERTENSION

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INTRODUCTION

Hypertension with its resulting cardiovascuarl disease is generally recognized today as the most important disorder of man. Responsible for more deaths annually than another human disease, it is also frequently responsible for premature disability (1).

In any evaluation of the therapy of essential hypertension, effect on the subjective symptoms, renal, cardiac, and cerebral areas, as well as the blood pressure, should be included.

To evaluate sympathectomy in the treatment of hypertension, evidence will be presented as to its effects on these manifestations.

Excluded from this discussion are the well defined causes of hypertension, such as coarctation of the aorta, unilateral renal disease, pheochromocytoma, corticoadrenaly tumors, and the full-blown Cushing's syndrome. This leaves the large group of patients affected by hypertensive cardiovascular disease, for which the etiology has not been determined definitely. There has been much investigation into the cause of hypertension which has resulted in some generally accepted principles.

It is now evident that many factors participate in the maintenance of blood pressure and that the whole complex may be deranged in some instances, two or more factors in most cases (2).

Because the vascular tone is the most important factor, changes in cardiac output in blood volume or loss of depression tone are of relatively little importance in experimental or clinical hypertension (2).

Peripheral resistance is calculated by dividing arterial pressure by cardiac output, and is regularly increased in hypertension. Most of the resistance, normally and in hypertension, is in the arteriolar segment. Relatively small changes in caliber cause marked changes in resistance (2). Such decreases in lumen of the arterioles may be caused by an abnormal control or reflex vasoconstrictive tone via the sympathetic nervous system, by humoral vasoconstrictors traveling in the blood stream or by disease of the arterioles (3).

Smithwick believes that the original elevation of blood pressure is most frequently neurogenic and that as a consequence, widespread vascular disease may result and perhaps a humoral vasoconstrictor substance as well. Also, that in the great majority of patients with continued hypertension the central vasoconstrictor outflow is not only intermittently increased but is also continually excessive. He believes that the purpose of sympathectomy is to modify the intermittent responses as well as to decrease the continuous outflow (1).

It is believed by Smithwick that the immediate purpose of all sympathectomies is similar, namely, to denervate a large vascular area (the splanchnic bed) in an effort to decrease the

peripheral resistance to blood flow. Grimson (3) and Poppen (4) agree with this essentially, differing only to what extent the operation should be carried.

Peet (4) and his associates believe that the prime factor in the perpetuation of the hypertensive state is the physiologic Goldblatt (4) "clamp" effect upon the efferent vascular bed to the kidney. The "clamp" is induced by vasopressor stimuli arising in the hypothalmus, which system responds in this fashion to pertinent stimuli either exogenous or endogenous in origin. Sympathectomy removes the clamp (4).

The true mechanism by which sympathectomy effects hypertensives awaits further investigation.

Any study of hypertension or its therapy is very difficult due to the great variability of the course of the disease in different individuals. Although there is controversy over the natural history of this disorder, Smithwick (5) has advanced a plausable sequence of events.

It seems highly probable that in the pre-hypertensive stage the blood pressure is unusually variable within a normal range. At this time, the phenomenon of hyperactivity as evidenced by an unusual blood pressure response to emotion or physical activity probably exists. Such individuals were classified as hyperreactors. If followed for long periods of time, such individuals appear to be much more likely to develop hypertension than those

who do not hyper-react. There is evidence that this characteristic is inherited. Thus, it seems apparent that a predisposition to the development of hypertension exists in many cases.

With the passage of time, probably many years as a rule, the blood pressure becomes intermittently elevated. Thus, when the patient is emotionally stimulated or is responding to physical activity, the physician finds the blood pressure elevated. At first, it may fall promptly to normal after a short rest period in the horizontal position. Under these circumstances the hypertension may be regarded as transient. Later it may require hours, days, or weeks of rest for spontaneous reversal to take place.

It is, therefore, apparent that when hypertension becomes persistent and cardiovascular disease begins to make its appearance the question of therapy should be considered. In the last analysis the merits of any form of therapy for this disorder will be judged by its effect upon the rate of progress of cardiovascular disease and upon life expectancy. The fact that the stage of persistent hypertension, with the rare exception referred to, is the beginning of the crucial phase of this disorder cannot be overemphasized. This cannot be detected by ambulatory blood pressure reading. The patient must be placed at bed rest. Smithwick employs a period of forty-eight hours of bed rest to differentiate between persistent and transient hypertension. Evidence of cardiovascular disease is rarely present in the stage of intermittent or transient hypertension and rarely absent in the stage of persistent hypertension.

Evidence of cardiovascular damage varying from slight to marked is present in over 95 per cent of patients. From this point on, theprognosis becomes quite different and varies according to the amount of cardiovascular damage which exists when the patient is first seen and the severity of the hypertension as judged by the resting diastolic blood pressure level. The prognosis for males is poorer than for females. Once hypertensive patients develop cardiovascular changes, these changes are progressive in nature. The rate of progress of cardiovascular disease varies greatly.

It is of interest and of great clinical importance to be aware of the manner in which hypertension develops in man. This is so not only from the viewpoint of theories of origin but also from the viewpdnt of prognosis. So long as hypertension is spontaneously reversible in response to short periods of rest, cardiovascular disease is rarely in evidence and the prognosis is excellent. Occasional male patients develop cardiovascular changes of consequence in the stage of transient hypertension. This is rarely the case in females. It is undoubtedly true that most hypertensive patients remain in thestage of intermittent hypertension for many years. Since most physicians do not differentiate between intermittent hypertension and persistent hypertension, they may gather the impression that hypertension may be a relatively benign disorder.

Classification of Hypertensives.--In order to study hypertensive patients and have a better insight into the prognosis of the individual patient, various authors have proposed different grading systems or classifications. These are listed below and will be referred to by the name of their originators throughout the paper.

Keith, Wagener, and Barker (6) of the Mayo Clinic were the first to recognize the fact that the prognosis for a hypertensive patient varies according to the status of his cardiovascular system when first examined. In an outstanding communication, they showed that the prognosis varied according to the changes noted on examination of the eyegrounds. A series of 219 cases was divided into four groups according to eyeground changes, and the mortality and survival rates for each group were calculated after a five to nine year period had elapsed. The patients in Group I had mild narrowing or sclerosis of the retinal arteries. Those in Group II had moderate to marked sclerosis of the retinal arteries, characterized especially by exaggeration of the arterial reflex and arteriovenous compression. Group III contained patients with angiospastic retinitis, characterized especially by edema, cotton-wool exudate, and hemorrhages in the retina, superimposed on a combination of sclerotic and spastic lesions in the arteries. If measurable edema of the optic disks was added to this picture, the case was placed in Group IV.

Palmer (7) modified Kieth, Wagner, and Barker's classification as follows:

Grade I: Variable hypertension, 150 to 200 mm. systolic and 100 to 120 diastolic, 23 per cent falling to normal levels (140 systolic and 90 diastolic or less) with rest or sedatives, occasionally under stress going above the limits noted; no changes or minimal changes in fundi as represented by narrowing of arterioles; minimal or no changes in heart or kidneys. This is early or mild hypertension.

Grade II: Variable hypertension, 170 to 250 mm systolic and 110 to 130 diastolic, usually at the lower levels, occasionally even lower, but falling to normal with rest or a sedative in 11 per cent, the fundi showing arteriovenous compression with widening of the light reflex, narrowing and caliber changes in the arterioles; the heart showing a slight enlargement or prominence in the region of the left ventricle by roentgen examination; the urine showing no change or slight grades of albuminuria and minimal numbers of formed elements in the sediment; the renal function being normal or slightly impaired by concentration and intravenous phenosulfonphthalein tests. This is moderate hypertension.

Grade III: Variable, but usually upward, hypertension, almost always over 170 mm systolic and 110 mm diastolic but observed normal levels in 8 per cent; the fundi showing arteriovenous compression, caliber changes in arterioles, wide light reflex, often exudates or hemorrhages; the heart often enlarged commonly

with sumptoms of anginal failure; the urine often showing albumin and casts; renal function often impaired, but actual failure (uremia) unusual; cerebral accidents sometimes occur. This is late benign hypertension, frequently of many years standing.

Grade IV: Blood pressure, especially the diastolic, usually decidedly high although exceptionally normal blood pressure levels may be observed; difficulties often of recent onset in a patient almost always under 50, often under 40 years of age, the cardinal sign being edema of the optic disks with or without exudate and hemorrhage; cardiac enlargement and congestive heart failure may be present; renal impairment and failure are common. This is malignant hypertension.

Peet (8) classified his patients into 6 groups:

(1) Early, mild hypertension. These patients were entirely asymptomatic, had normal or grade 1 fundi, and showed no evidence of cardiac or renal involvement.

(2) Symptoms predominate. All patients in this group complained of symptoms and had abnormal fundi, but displayed no evidences of cardiac, cerebral, or renal impairment.

(3) Organic heart disease is predominant. In each case, the diagnosis of heart disease was confirmed either by a definitely abnormal electrocardiogram or a teleroentgenogram showing cardiac enlargement, or by both.

(4) Cerebrovascular disease is predominant. Each patient in this group had one or more previous cerebral accidents.

(5) Impaired renal function ispredominant. Each patient showed diminished concentrating ability and urea clearance values.

(6) Malignant hypertension. These patients had severe neuroretinitis with definite papilledema of 1 diopter or more, and displayed a rapidly progressive, downhill course.

Hammarstrom (22) modified Keith, Wagner andBarker's groups as follows:

Group 1 contained patients with uncomplicated hypertensive cardiovascular disease. Group 2 includes those with marked subjective symptoms but without signs of myocardial damage. They may show left axis deviation in the electrocardiogram, and/or a relative enlargement of the left ventricle if the heart volume is within normal limits according to teleroentgenography. The retinal changes in the patients in their second group are classified as Group 1 or 2 according to Keith and Wagner. Group 3 includes those with the same eyeground changes or, in addition, retinal hemorrhages with or without signs of thrombosis of the retinal vessels. Patients in Group 3 further show one or more of the following signs of cardiovascular damage; negative T, in the electrocardiogram, heart volume above the predicted normal (500 ml. per square meter of body surface in men, and 450 ml. per square meter in women, or the transverse diameter of the heart greater than one-half the inner thoracic diameter), residual

damage after cerebral insult, and constant albuminuria. In Group 4 they include all hypertensive patients with definite retinal exudates and/or papillary protrusion, since they found the life expectancy to be about the same if the pa ients in this group did or did not have papillary protrusion.

Smithwick's (9) latest classification is designed to control as many of the variable factors as possible, in an attempt to make the patient material in each group as comparable as possible. Following a careful study of the cardiovascular system as a whole, a numerical value is assigned to various factors which have a bearing on prognosis. These are summarized in Table I. The numerical values for each factor present are totaled and this gives the numerical grade for the patient. If the numerical grade is less than 4, the patient will be in Group 1 or 2. If the numerical grade is 4 or more, the patient will be in Group 3 or 4. The additional factors which determine the exact group of the patient are given in Table II.

Table I -- Numerical Value of Various Factors
Which Influence Prognosis

	Numerical Value of Each Factor
Cerebrovascular Accident without or with minor residual . .	
Abnormal ECG	
Enlarged heart	
Impending failure	
P.S.P.* less than 25% in 15 min., or less than 60% in 2 hr.	1
Age 50 or over	
Mild angina	
Cerebrovascular accident, with residual + ...	
Frank congestive failure, moderate angina	
P.S.P.* less than 20% in 15 min.	2
Unsatisfactory response to sedation	
P.S.P.* less than 15% in 15 min.	3
Nitrogen retention	4

* Phenolsulfonphthalein.
\+ Cerebral deterioration or definite involvement of arm and/or leg.

Table II -- Classification of Hypertensive Patients

Group	Criteria for Grouping: Numerical Grade	Criteria for Grouping: Other Factors
1	Less than 4	Eyegrounds Grade 0 or 1 No changes in cerebral, cardiac, or renal areas
2	Less than 4	Eyegrounds Grade 0 or 1, with changes in cerebral, cardiac, and/or renal areas; eyegrounds Grade 2, 3, or 4, with or without changes in cerebral, cardiac, or renal areas.
3	4 or more	Resting diastolic level below 140 mm; changes are present in cerebral, cardiac, and/or renal areas, but they do not include the following: (a) Cerebrovascular accident with marked residual (b) Frank congestive failure (c) P. S. P. below 15% in 15 min., associated with a poor response to sedation.
4	4 or more	Resting diastolic blood pressure below 140 mm combined with one or more of the following: (a) Cerebrovascular accident with marked residual (b) Frank congestive failure (c) P. S. P. below 15% in 15 min. combined with a poor response to sedation. Patients with a resting diastolic level of 140 mm or more.

METHODS OF OPERATION

Bruning (10), Pende (10) and Danielopolu (10) were apparently thefirst to propose neurosurgical treatment of hypertension. Bruning observed in 1923 that the blood pressure of a patient with angina pectoris regularly rose in association with anginal attacks. After cervical sympathectomy the patient obtained relief from pain and also from the hypertensive crisis. This experience caused Bruning to discuss the possibility of lowering the blood pressure in patients with essential hypertension by resection of the splanchnic nerve. Adson (10) appears to have been the first to perform a sympathectomy in hypertension. At the suggestion of Rowntree, he carried out in 1925 bilateral lumbar ganglionectomy in another patient with malignant hypertension.

After Cannon's studies on complete sympathectomy in animals (2, 10) neurosurgical treatment of hypertension was employed to an increasing extent during the 1930s.

Bilateral section of the lower thoracic and upper lumbar anterior spinal nerve roots was performed in hypertensives during the 1930s (10). Adson, Brown and Craig, who introduced but later abandoned this method of operation, describe it "as a rather formidable procedure"(10). Its effect on blood pressure is no more obvious than the one achieved by splanchnicectomy and the risk of complications and sequelae is greater than a splanchnic resection and ganglionectomies. Hyndman et al (10) report that anterior chordotomy reduces blood pressure to normal levels in women with benign hypertension but does not influence the pressure in men

with advanced hypertension. In patients whose blood pressure fell after operation, it began to rise after four to six months.

Crile (10) operated on a great number of hypertensives by means of bilateral celiac ganglionectomy and splanchnic section. The method has been criticized as being post-ganglionic sympathectomy (11) and has no been applied in recent years.

Subdiaphragmatic sympathectomy was introduced in 1932 by McCraig (10). This operation, mainly performed at the Mayo Clinic, consists of bilateral subdiaphragmatic splanchnic resection including a portion of the celiac ganglion and the two upper lumbar ganglia. It has sometimes been combined with renal decapsulation and renal grafts (10). Subdiaphragmatic sympathectomy in hypertensives gives less favorable results than supra- and trans-diaphragmatic sympathectomy. At the Mayo Clinic they have in recent years proceeded to dorsolumbar sympathectomy according to Smithwick.

Heuer and Glen (3) employed three types of operation. 1) Anterior root section. 2) Supradiaphragmatic splanchnic resection. 3) Subdiaphragmatic splanchnicectomy and ganglionectomy L 1 & 2. They urged continuation of surgical therapy on an experimental basis employing more complete operations such as that of Smithwick.

There are at present three surgical methods in widest use in the neurosurgical treatment of hypertension. In all these three methods more or less complete splanchnicectomy is performed including dorsal or dorsolumbar ganglionectomies of varying extent.

By the supradiaphragmatic operation, Peet's operation (8), the 11th rib is resected, then the supradiaphragmatic part of the

splanchnic nerves is removed including the sympathetic chain from Th: 9 to Th: 12 inclusive. The operation is performed on both sides, usually in one stage.

Grimson et al (13) performed "complete" sympathectomy in several stages. Besides the resections performed according to Smithwick (see below) the whole thoracic ganglion chain was removed, including the stellate ganglion.

Smithwick (1) removes the lower thoracic chain to include the eighth ganglion in all instances, and occasionally the seventh or the sixth.. It is fel that the portion of the dissection which lies above the ninth ganglion adds little or nothing to the completeness of the splanchnic denervation but may be an additional safeguard against regeneration. The second and at times the third lumbar ganglia are also removed particularly if the postural blood pressure reflex is unusually active.

THERAPEUTIC RESULTS OF SYMPATHECTOMY

Effect of Sympathectomy on Blood Pressure

There is a variance of opinion as to the importance of blood pressure levels in a study of sympathectomy in hypertension. Palmer (7) has stated that "common sense and clinical and scientific hypothesis as well hold that the unfavorable progress and end of patients with hypertension is related to the height of the blood pressure. Not the only test but an important test of any therapeutic procedure in continued arterial hypertension is the effect on the level of the blood pressure. Since it has been observed

that most patients with essential hypertension have well defined spontaneous lowering of the blood pressure and that a considerable number have normal blood pressure levels transiently (23 per cent of early benign cases, 11 per cent of moderate cases, 8 per cent of advanced cases and even 8 per cent of malignant cases), the duration of the hypotensive effect and a fall to normal or near normal are important criteria for critical evaluation".

Smithwick in 1949 (5) stated that the lowering of basal blood pressure levels varies considerably from patient to patient, both in magnitude and duration. Most discussions of the value of surgery in the treatment of hypertensive cardiovascular disease have revolved about its effect upon blood pressure levels. It is now apparent that patients may be improved for years from the view point of the cardiovascular system and relief of symptoms, and may also have their life expectancy increased significantly when the effect of operation upon blood pressure levels is significant but temporary, or in other cases in which the basal levels are never significantly lowered.

Goldring and Chasis, (13) studying the effect of sympathectomy on blood pressure note that in view of the great sponatneous variability of blood pressure levels and the many variables involved in its maintenance, they find it impossible to define significance in terms of blood pressure change. Furthermore, in view of their opinion that there is no relationship between level of the blood pressure and severity of hypertensive disease, they believe

it may be misleading to categorize the effect of sympathectomy on the blood pressure level as good, fair, and poor. Goldring and Chasis are of the opinion that an effect on blood pressure level is significant only when the blood pressure falls into the average normal range and persists in that range for at least one year. In none of their patients has this result been achieved.

The effects of sympathectomy on blood pressure in ten large series of patients containing a total of 1513 patients is listed in Table III.

The Smithwick operation (11), or a modification thereof, was used in all series except Peet's (8) where supradiaphragmatic splanchnicectomy and Grimson's (3) paravertebral sympathectomy were done. The percentages listed in the "normal" column are those patients with a blood pressure of 150/100 or diastolic pressure below 100 with the exception of Ray's series (16) where "near normal" patients were also included. Those percentages listed under moderate lowering had a lowering of diastolic pressure of 20 mm Hg or more Smithwick (14) (19), Hinton (20); 25 mm or more Thorpe (15) and Peet (8); or else the criteria is given in the chart. Listed under significant are those patients whose diastolic blood pressure was lowered 10-19 mm Hg. Smithwick (14) (19); lowered 15-25 mm Hg., Peet (8) and Thorpe (15); or according to the criteria listed.

Although these series are not strictly comparable, they give a general overall picture of the effects on blood pressure by

TABLE III

Source	No Pts	Group N.	I	II	III	IV	Time Observed	% of Pts With decrease in blood pressure: Normal	Moderate Lowering	Significant Lowering	Same Worse Dead
Smith-wick (14)	100	12	67	68	70	39	1-5 yrs.	35	29	20	16
	100						5-9 yrs.	21	13	13	53
Thorpe (15)	500	18	96	81	251	54	0-6 yrs. mean 35.5 mo.	9.8	17.2	29.2	43.8
Peet (8)	251	Living Pts.					5-11 yrs.	20.3	26.2	35.5	18
	437	Complete series								47	53
Ray (16)	300	15	51	141	40	44	1-6 yrs.	29.8	Good 31.6	Fair 17.8	20.8
Hinton, Lord (17)	152	-	-	-	-	-	6 mos.-3 yrs.	-	53	-	47
Fish-berg (18)	119	-	-	-	-	-	13-72 mos.	22	Diastolic Pressure Lowered 25% or more 32		46
Smith-wick (19)	500	-	-	-	-	-	1-12 yrs.	36		31	33
Hinton (20)	164	-	-	-	-	-	1 year	57 Below 110 Diastolic		Above 110 Diastolic 43	
Poppen & Lemmon (21)	100	-	72	19	9	-	1½-4 yrs.	-	Good 47	Fair 24	29
Grimson (3)	41	-	4	18	7	9	18-76 mos	25.5	49		25.5

sympathectomy. It appears that operation lowers the blood pressure significantly in a majority of the cases.

By comparing the figures in Smithwicks (14) first series it can be seen that the results obtained in the first 5 years after operation are not completely maintained during the second 5 years. Smithwick (19) in a series of 307 patients compared at 1 year and 5 year intervals noted that 57% of the patients maintained lower diastolic levels all at the 5 year period. This tendency for the results of sympathectomy to become less favorable has been noted by other workers (22) (7).

EFFECT OF SYMPATHECTOMY ON ELECTROCARDIOGRAM AND HEART SIZE

Effect on Electrocardiogram of Sympathectomy in Hypertension

The ECG in hypertensive patients is often improved by their being confined to bed. Consequently, the changes in the ECG observed directly after sympathectomy may be due to the rest in bed.

Improvements in the ECG following drop in blood pressure after sympathectomy in hypertension have been reported by several authors. (10, 19, 20, 23) Peet and Isberg (8) have examined the ECG before and 5 to 11 years after supradiaphragmatic sympathectomy in 141 patients with hypertension. Before operation 84 showed a normal ECG in this group 74 presented an unchanged and 6 an unfavorably changed ECG at the follow-up examination. A pathological ECG was found in 57 patients before operation, 30 of whom showed improvement, 24 showed an unchanged ECG, and 3 showed unfavorable changes.

In 1948 Isberg and Peet (24) reported on 384 patients with arterial hypertension treated surgically by bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy. Sixty per cent of the patients with hypertensive heart disease were still living 5 to 12 years after their operation. Of the hypertensive patients with normal hearts, 93% were still

living 5 to 12 years after operation. Of the patients still alive, 41% of those with abnormal pre-operative electrocardiograms recently showed significant improvement in their tracings 5 or more years after operation.

De Takats et al (25) give illustrative instances of improvement and normalization of ECGs after sympathectomy in hypertension. White et al (37) published a study of the ECGs from 87 of Smithwick's patients obtained before and 2 days to 40 months after transdiaphragmatic sympathectomy. They found that the incidence of change varied little with the length of time after operation. In their study improvement of unfavorable changes in the T-wave in Lead I or in the electrical axis correspond to an elevation of at least 1 mm in the T-wave, and a shift of at least 15 degrees in the axis. The T-wave in Lead I improved in 47% of their series. The axis improved in 30%, shifted more to the left in 13%, and remained unchanged in 57%. The ECG as a whole improved in 57%, became worse in 13%, and remained unchanged in 30%. In the patients studied by White et al (37) the chances of improvement of the ECG after sympathectomy increased with increasing retinal changes, diastolic pressure and depression of the T-wave in Lead I. They found no positive correlation between post-operative ECG findings and pre-operative heart size, known duration of the hypertension, symptoms of functional disorder of the heart, age of the patient, or degree of arteriolar changes as found in renal biopsies at operation.

Bridges et al (38) extended the investigation of the ECG in hypertensive patients to comprise 144 of Smithwick's patients who had been observed for at least one year after lumbodorsal sympathectomy. Analysis of the limb leads gave the following data: 55.5 per cent of the ECGs had been normal before operation. There was a progressive improvement in the abnormal ECGs after sympathectomy, shown by the fact that 67 per cent of the total series were normal two weeks after operation and 78.5 per cent at the end of the first year after operation. Shifts of the electrical axis toward the right by more than 10 degrees were found in 34.1 per cent of the cases after the lapse of one year. A decrease in the amplitude of R I by more than 3 mm was found in 31.2 per cent of the cases two weeks after operation, and in 41.7 per cent after one year. The sum of R I and S I showed a decrease in 63.4 and 72.3 per cent after similar periods of observation. The T-waves in Leads I and II were abnormal pre-operatively in 75 per cent. One year after operation, the T I was found to be normal in 86.1 per cent and T II in 90.9 per cent. In the cases where the T-waves in Leads I and II were normal pre-operatively there was an average increase of 1 mm from the preoperative to the one-year post-operative reading. Chest leads were normal before operation in 50 per cent of the patients, and one year after sympathectomy these leads were normal in 65 per cent.

Investigations into the ECG before sympathectomy and at varying intervals after the operation all go to show that a pathologic ECG has improved in more than half of the patients and become worse in less than 15 per cent. (10)

As there often is a regression of the T, S-T changes after sympathectomy in hypertension, there is reason to conclude, like White et al (37)that inverted T-waves in hypertension are in themselves indications for sympathectomy rather than contra-indications.

Effect of Sympathectomy on Heart Size

Peet and Isberg (8) studied the effect of supradiaphragmatic sympathectomy on the heart size of 128 patients as examined before and 5 to 11 years after operation. In 80 cases the heart size was normal before operation. In 73 of these no significant post-operative change was observed and in 7 there was an increase in the heart size. Forty-eight patients had an enlargement amounting to 18 per cent or more of the normal heart size before operation. In 25 patients there was a significant decrease, in 21 no significant change and in 2 patients an increase in the heart size. The authors do not mention the criteria for a change in the heart size.

In 1948 Isberg and Peet (24) reported on 384 patients. Sixty per cent of the patients with hypertensive disease were still living

5 to 12 years after their operation.

Forty-four per cent of those with pre-operative cardio-enlargement showed significant decrease in heart size.

In Rays (16) entire series of 300 patients, roentgenograms of the heart before operation were judged normal in 29 per cent, slightly to moderately enlarged in 56 per cent, and markedly enlarged in 15 per cent. In patients who had any degree of cardiac decompensation, measurements of the heart for purposes of comparison were determined only after compensation had taken place.

Comparisons between roentgenograms taken before and one or more years after operation were made in 150 cases. Among the patients with normal heart size and configuration before operation there was no change from normal in 83.6 per cent, decrease in size in 9.6 per cent, and increase in size in 6.8 per cent. Among the patients with slight to moderate increase in cardiac size before operation there was no change in 50.2 per cent, significant decrease in size in 37.9 per cent and increase in size in 11.9 per cent. Among the patients with markedly enlarged hearts before operation, there was no change in 46.1 per cent and significant decrease in size in 53.9 per cent. Decrease in the degree of tortuosity of the aorta after operation was a rather common occurrence.

It can be concluded from the above studies that sympathectomy significantly improves the ECG and decreases the heart size in approximately 50 per cent of the cases. There is also evidence that

sympathectomy may aid in the prevention of these abnormal changes for the patients with normal ECG's and heart size before operation.

EFFECT OF SYMPATHECTOMY ON HYPERTENSIVE EYE-GROUND CHANGES

In Peet's series, the eye-grounds were examined before and 5 to 11 years after supradiaphragmatic sympathectomy in 146 cases. (8) In a group of 88 patients with angiospastic retinitis with or without hemorrhages and exudate before operation, the retinal conditions were improved in 82 per cent, unchanged in 17 per cent and worse in 1 per cent. In a group of 17 patients with malignant hypertension and papillary edema, all were alive and presented improved eye-grounds. In 44 patients with normal eye-grounds or sclerosis of the retinal vessels before operation, the retinal changes grew worse in three patients only.

On the 1500 patients which Peet (26) followed 5 to 12 years after splanchnicectomy the funduscopic findings in cases that showed, before operation, angiospastic retinitis with or without hemorrhages or exudates now show absence of angiospasm, hemorrhages, or exudates in 82 per cent.

In Peet and Isberg's(27) study of 143 cases of malignant hypertension the survival rate was 21.6 per cent for a 5 year period. All living patients receiving a funduscopic examination 5 years and more after operation showed no evidence of papilledema.

Of 120 patients of Smithwicks series (19) in whom the retinal area was examined 40.7 per cent showed improvement. Thirty-seven and two-tenths per cent showed no change and 20 per cent were worse. These patients were all followed 5 to 7 years after operation.

In studying the effect of sympathectomy on eye grounds, Ray (16) found of the 291 patients who survived the operation, funduscopic examinations in 95 per cent post-operatively permit a comparison with the pre-operative findings. Alterations in the funduscopic appearance of the eye grounds of those in Groups I and II has been difficult to evaluate. In some cases there has perhaps been an improvement in the appearance of the arterioles, but more significant is the fact that with a single exception none has developed hemorrhages, exudates, or edema. In patients with Group III or IV eye ground changes who have lived six months or more after operation, the hemorrhages, exudates, and edema have disappeared regardless of the effect of the operation on blood pressure. Some who have since died had a recurrence of hemorrhages and edema, but the incidence is not known.

In high thoracolumbar resections carried out at the Lahey Clinic in Boston, Evans (28) found that hemorrhagic exudative fundi in group III had showed satisfactory reversion to lower groups, 36 of 44 showing a loss of hemorrhage and exudate. Five out of eight patients in Group IV had complete cure of choked disks, hemorrhage and exudate. Three patients who were almost blind left the hospital able to read.

In 119 patients with severe essential hypertension selected for sympathectomy by Fishberg (18) retinopathy was found in 17 patients. The retinopathy was cleared in 12 of the 17 patients. The retinopathy may disappear after operation without fall in blood pressure. Fishberg suggests that the reason why cephalic manifestations (headache and retinopathy) of hypertension are the most favorably affected is that sympathectomy results in a redistribution of the cardiac output with a smaller fraction going to the cephalic portions of the body. The results of sympathectomy offer evidence that rise in pressure in the minute vessels of the brain and retina is of great importance in the pathogenesis of hypertensive headache and retinopathy.

Several authors report a decrease in degree or disappearance of exudates and hemorrhages together with a diminution in the spastic constriction of the retinal arterioles in hypertensive patients after sympathectomy (4, 7, 10, 15, 20, 21) Where papillary edema had led to blindness, the vision became normal when the retinopathy regressed after sympathectomy (20) Sclerotic retinal changes are not influenced by sympathectomy (10)

Regression of hypertensive retinopathy after sympathectomy must be evaluated against the possibility of a spontaneous regression.

In essential hypertension retinopathy may subside or disappear, when the blood pressure falls during prolonged rest. Goldring and Chasis (13) draw attention to the fact that hypertensive disease is often characterized by acute episodes, and appearance of retinal

hemorrhages, extreme narrowing of the arterioles due to spasm and new areas of retinal degeneration. "It is not uncommon for this acute phase to last for weeks and then to subside gradually and spontaneously. These changes are indistinguishable from those appearing in the accelerated phase of hypertensive disease. It is with this possibility in mind that one must accept with caution reports of regression following sympathectomy. Spontaneous regression of retinal hemorrhages and areas of degeneration is a common event in the course of prolonged hypertensive disease" (13).

It seems probable that spontaneous regression of retinopathy occurs in a relatively small number of cases of essential hypertension and chronic nephritis, even if it might be "a common event" with the few who live for a longer time after the onset of retinopathy.

The regularity with which regression of retinopathy appears after sympathectomy contradicts the view that the coincidence between operation and improvement is incidental only.

It may be said that regression or complete disappearance of retinopathy occurs in a large majority of the patients undergoing sympathectomy. This may occur without significant drop in blood pressure.

EFFECT OF SYMPATHECTOMY ON SUBJECTIVE SYMPTOMS

One of the earliest benefits of sympathectomy to be discovered was that the operation was capable of giving subjective relief (36).

Allen and Adson (1) have followed 224 patients three months to five years after subdiaphragmatic sympathectomy. The effect on blood pressure is in 31 per cent of the patients characterized as good or fair and in 69 per cent as temporary or poor. Improvement of headache was obtained in 94 per cent of the former and in 79 per cent of the latter group. Improvement of dizziness and tiredness is stated to be attained equally often in both groups. Relief of thoracic pain and shortness of breath were obtained in 72 and 65 per cent in the group with post-operative drop in blood pressure and in 59 and 54 per cent of the remainder.

At Peets Clinic (26) bilateral subdiaphragmatic splanchnicectomy has been done on more than 1500 patients. The majority of patients have been followed for one to twelve years since the operation. Symptomatic relief has been striking. Excruciating headaches, usually sub-occipital, nervousness and irritability, insomnia and distressing palpitation have been greatly relieved or completely eradicated in 86% of the patients still living. This percentage of improvement has persisted almost unchanged over post-operative periods of 5 to 12 years. Such symptomatic relief is not necessarily dependent on a significant lowering of the blood pressure or the improvement of cardiac or renal function.

Rogers and Palmer (29)reviewed the records of 1,072 patients to compare the effects of medical and surgical treatments of hypertension. Relief of headache and throbbing of the head by dorsolumbar sympathectomy is nearly 100% while general symptomatic relief by medical means varies from 90% in grade I to 46% proportion with malignant grade IV hypertension.

Ray (16)states that improvement in symptoms after the immediate effects of the operation have worn off is so common that there is temptation to give too much importance to them as an indication for operation or as evidence of beneficial effects of operation. For example, headache which was present in significant degree in about half the patients before operation was with few exceptions abolished or greatly lessened even in those who had little or no lowering of their blood pressure.

In a critical report on sympathectomy Goldring and Chasis (13) admitted that with few exceptions symptomatic relief has been striking in the sympathectomized patients. This had been just as striking in patients in whom the blood pressure level was unaffected as in those in whom lowering of blood pressure occurred. In common with general experience, prolonged relief from hypertensive headache occurred regularly. Goldring and Chasis have been impressed with the degree of rehabilitation following sympathectomy. However, in their experience, relief from headache and return to gainful occupation just as frequently followed various forms of

non-operative treatment; which leads them to believe that unexplained spontaneous alterations or simple reassurance play a large, if not exclusive, part in symptomatic relief following sympathectomy.

In 119 patients studied by Fishberg (18) worthwhile symptomatic improvement occurred in 59 per cent. Headache was the symptom most often relieved.

Smithwick (19) studied the records of 263 surgically treated patients with malignant or essential hypertension and found, with regard to symptoms, over 90 per cent of the patients who have so far been interviewed 5 to 9 years post-operatively are improved in this respect.

Chris (30) in 35 patients followed 2 to 51 months, average 18 months after transpleural sympathectomy, revealed that only 25 of the patients had maintained a significant fall in blood pressure but that 66 per cent of them had been relieved of incapacitating symptoms and had returned to work.

Hinton and Lord (17) have followed up 150 patients for more than six months after Smithwick's operation. Seventy-six per cent of the cases were subjectively improved and 81 per cent had improvement of one objective symptom. Thirty-one cases were followed for 18 months. Twenty-four of these (77 per cent) were subjectively improved and 28 cases objectively improved.

Peet and Isberg, Hinton and Lord have not mentioned the number of patients who had subjective symptoms pre-operatively,

but it is probable that the greater percentage of objective over subjective improvement is due to the fact that some patients presented no subjective symptoms before operation.

Several authors, who have described the effect of neurosurgical treatment in hypertensive patients, have emphasized that the operations produced relief or disappearance of subjective symptoms, especially of headache, in a great number of the patients even though the blood pressure was not significantly lowered (1, 3, 7, 8, 15, 21).

It is obviously not wise to evaluate the therapeutic effect chiefly on the basis of a subjective improvement. Both confinement to bed and a "non-specific" major operation often result in the disappearance of subjective symptoms for a longer or shorter time. The importance of suggestion must not be underrated. Finally, hypertensive symptoms often show a tendency to appear and disappear periodically, especially in benign hypertension.

The points of view mentioned above have often been maintained, when the results of neurosurgical treatment of hypertension have been criticized and it has been stressed that there is no reason to draw any conclusions from the improvement of subjective symptoms (13) Against this can be stated that headache especially has often been a constant symptom of long duration before sympathectomy and that it has been absent for several years after operation. Also , the large number of patients that have been relieved of subjective symptoms for long periods of time would indicate that

this is the result of the surgical intervention and not just coincidental, or due to the psychological effect of an operation.

EFFECT OF SYMPATHECTOMY ON RENAL FUNCTION

Peet and Isberg (8) examined the renal concentration ability of 117 hypertensive patients before, and 5 to 11 years after, supradiaphragmatic sympathectomy. Of 62 patients with normal function the concentration ability remained unchanged in 51, and was lower in 11 patients. Of 55 patients with impaired function before operation, the ability was insignificantly improved in 20, unchanged in 29 and worse in 6 patients.

In a more recent report Peet and Isberg (26) believed that the renal function following splanchnicectomy has shown definite improvement both in water concentrating ability and in urea clearance.

A comparison between renal state before and one to five years after transdiaphragmatic sympathectomy in Smithwick's series showed a great percentage of post-operative improvements (39).The majority of patients had a pathological renal state before operation. After sympathectomy, albuminuria disappeared in 40 of 90 patients and the sediment improved in 32 of 49 who had pathological sediment before operation. Capacity to excrete phenolphthalein improved in 26 of 33 patients with reduced excretory capacity before operation. Urine concentration tests showed improvement in 18 of 20 patients with pre-operatively reduced ability. Deterioration of renal state occurred in isolated cases only.

In 1948 Smithwick (19) reported on 263 patients with malignant or essential hypertension who were treated by his surgical technic. Of 114 patients followed 5 to 9 years, in whom the renal vascular region was examined, 28.9 per cent showed improvement. Sixty-one and three-tenths per cent showed no change and 9.8 per cent were worse.

DeTakats et al (31) noticed that urea clearance improved after sympathectomy in hypertensive patients without retinopathy, when the operation caused a fall in blood pressure.

There are no findings to support the assumption that renal function is unfavorably influenced by a fall in blood pressure during the late course after a sympathectomy. Contrarily, the drop in blood pressure may check a deterioration and even produce an improvement of the renal state, which before operation was not too depressed.

Various investigators, who performed diodrast and insulin clearances before and after sympathectomy in hypertension, found as a rule, no significant changes in renal blood flow and filtration rate after the operation (10).

COMPLICATIONS OF SYMPATHECTOMY

The complications of sympathectomy were best described by DeTakats in 1949 (32). He has divided the complications into those resulting from physiologic changes following sympathectomy, the complications of section of the splanchnic nerves per se, and the technical complications of section of the splanchnic nerves.

Physiologic Changes Following Sympathectomy

These are perhaps not true complications in the usual sense, but are unavoidable changes in bodily physiology as a result of sympathectomy. Thus, these changes should be explained pre-operatively to the patient or else he will interpret them as being complications of the surgical procedure.

Postural Hypotension--Among the side effects, postural hypotension with its associated symptoms is the cause of most complaints. It appears that post-operative postural hypotension is necessary to the achievement of a satisfactory reduction in blood pressure. These patients may show temporary dizziness, fainting and lack of mental acuity post-operatively.

Substernal Fluttering and Breathlessness-- A majority of patients will note a sensation of substernal fluttering or breathlessness early in their post-operative course, though not to a degree that might suggest anginal pain. Before many weeks or months have elapsed, however, this notable degree of hypotension

will disappear, but some degree of postural hypotension may persist for years but not to the point at which it is uncomfortable.

Hyperhydrosis--Hyperhydrosis of the non-denervated portions of the body may be discomforting for the patients. This, too, is most severe during the immediate postoperative period and either gradually diminishes or loses significance in the eyes of the patients.

Accentuation of the Vasomotor Tonus--Compensatory accentuation of the vasomotor tonus of the non-denervated portions of the body may be manifested by notable alterations in the vascular supply of the upper part of the trunk and the upper extremities. The observation of some patients subjected to sympathectomy will disclose cold, bluish-white, mottled extremities, which will suggest the presence of cutis marmorata, acrocyanosis, or even Raynaud's disease, though actually this is merely a manifestation of varying degrees of compensatory vasoconstriction in response to homeostatic demands.

Derangement of Sexual Functions--This is a matter of importance to the younger hypertensive men. Despite numerous references in the literature to the fact that the removal of the first and second lumbar ganglions bilaterally will produce loss of libido, failure of ejaculation and even sterility, this has not been uniformly the case in deTakat's (32) experience or in that of Poppen and Lemmon (21). It seems probable that other factors are often involved when impotence does occur. Erection has rarely been influenced; ejaculatory ability has more often been adversely affected. Sympathectomy has no adverse effect on the female genital tract.

Motor and Sensory Dysfunction--Motor or sensory dysfunction of a large portion of the intestinal tract might be anticipated as a result of its sympathetic denervation to a large degree. Post-operative abdominal discomfort and distension have not been rare. Distension and decreased intestinal motility is the reverse of what might be expected since the sympathetic supply to the bowel is largely inhibitory and the action of the now unopposed vagus is predominantly motor and secretory; however, the degeneration of the residual pre-ganglionic fibers might so stimulate the celiac ganglion cells that their post-ganglionic fibers might produce a transitory inhibitory effect on visceral motility. A subsequent increase in gastric motility and secretion might cause the development of recurrence of gastric or duodenal ulcers.

Elimination of Visceral Pain--Surgical removal of the visceral sympathetic nerve supply may so modify or abolish normal visceral sensation that thepresence of ulcer or its complications, the acute manifestations of gallbladder, renal or pancreatic disease or, equally important, the development of malignant disease may be completely masked or misinterpreted until its late stages, when involvement of somatic nerves or systemic manifestations become evident.

The Complications of Section of the Splanchnic Nerve Per Se

A hypertensive patient is not normal, and since this is so, it is natural that there should be certain complications peculiar to, or more frequently encountered in the surgical care of such patients.

Cardiac Complications--Although it has been recognized for

several years that patients with hypertension subjected to sympathectomy usually obtain notable subjective relief from previous cardiac complaints and that objective improvement as evidenced by electrocardiographic changes and diminution of the size of the heart is frequent, this is not uniformly the situation. The improvements which are noted are due to a lightening of the cardiac load which follows the decrease in the peripheral resistance of the now dilated vascular bed. This is not only desirable but is usually essential to a satisfactory operative result. Still, early in the post-operative period a rapid shifting of the circulating blood volume may so diminish venous return that cardiac failure may be precipitated unless adequate care is rapidly instituted. It is also conceivable that a temporary reduction in coronary blood flow combined with changes in blood coaguability in the post-operative period might predispose to the production of coronary thrombosis.

Cerebral Complications--Several examples of disturbed cerebral functions have been encountered, These are of a localizing nature following sympathectomy which would appear to be explicable on a basis of decreased cerebral blood flow due either to relative cerebral anoxia or to small foci of cerebral thrombosis precipitated by surgical intervention.

The Technical Complications of Section of the Splanchnic Nerves

If proper selection of cases has been employed, technical complications will account for most of the morbidity encountered after sympathectomy.

Shock--Shock should be a rare occurrence in any planned surgical procedure if proper precautions are taken. Particularly in hypertensive patients, prolonged periods of hypotension are undesirable, not only because of the ease with which patients go into profound shock but also because of the increased dangers of the effect of hypoxia on the already damaged cerebral and cardiac systems.

Pulmonary Complications--Hydrothorax, hemothorax, pneumothorax, and atelectasis were encountered in 23 per cent of the cases, but were rarely a problem. Pulmonary complications may be the result of certain technical errors or oversights. Great care should be taken to avoid damage to the pleura. Good pre-operative and post-operative care with early ambulation are essential as is good anesthesia and anesthetic technic.

Neuralgia--Neuralgia is a familiar complication and may be exceedingly troublesome. Intercostal neuralgia is most frequent and may be minimized if care is exercised not to damage the nerve. Fortunately, within two to three months the neuralgia has disappeared.

Myalgia--Myalgia of the sacrospinalis or psoas muscle groups is usually the result of injury produced while attempting to obtain satisfactory exposure of the lumbar sympathetic chain. Management of the myalgia presents a problem similar to that mentioned in connection with neuralgia though, fortunately, the symptoms are usually somewhat less severe and less persistent.

Injury to the Thoracic Duct--Injury to the thoracic duct in the course of sympathectomy did not occur in deTakat's experience,

though conceivably this duct might be mistaken for the major splanchnic nerve and sectioned if proper identification werenot made.

Operative Mortality

The post-operative morbidity rate of sympathectomy for hypertension was below 10 per cent and the mortality rate below 1 per cent.

Severe, prolonged, and intractable myalgia and neuralgia occurred post-operatively in 13 per cent of the cases despite extreme care and are the major cause of complaint on the part of the patients. Hydrothorax, hemothorax, pneumothorax, and atelectasis were encountered in 23 per cent of deTakat's cases but were rarely a problem.

Sympathectomy is of definite benefit in the treatment of hypertension, but the benefits must be weighed carefully against the inherent disadvantages, possible complications, and at times uncertain results which will be encountered in any large group of even carefully selected cases.

In 1940 a report was issued from the Mayo Clinic by Allen and Adson (1) on subdiaphragmatic sympathectomy of 300 hypertensive patients without operative mortality. In 1946 Peet (8) after bilateral supra-diaphragmatic sympathectomy of 578 patients reported an operative mortality of 3.6 per cent, whereas Smithwick (33) in 1944 after bilateral transdiaphragmatic sympathectomy of 378 patients obtained an operative mortality of 3.4 per cent. Peet's and Smithwick's materials include a greater number of patients with malignant and advanced hypertensive disease than the series of patients operated onby Allen and Adson. After having made a more rigorous selection of patients,

Smithwick operated on 169 consecutive patients without fatalities. In 1946 he reported an operative mortality rate of 2.2 per cent in more than 600 patients operated on from 1940 to 1945 (

THE EFFECT OF SYMPATHECTOMY ON THE PROGNOSIS IN HYPERTENSION

Various investigations into prognosis in hypertension can be summarized as follows:

It becomes less favorable with rising blood pressure.

It is worse for men than for women and worse in juvenile hypertension than in hypertension occurring in higher age groups.

Cardiac disease, cerebral hemorrhage, and uremia are the predominant causes of death in hypertension. Heart symptoms in the form of angina pectoris, cardiac decompensation and enlargement, and electrocardiographic changes are prognostically unfavorable. Impaired renal function is a serious prognostic sign. Hypertensive encephalopathy has beenplaced on a par with malignant hypertension from a prognostic point of view (10). Retinopathy in hypertension is a prognostically unfavorable symptom, the serious import of which is further enhanced in the presence of papillary edema.

"A man is as old as his arteries." In cases of hypertension it is rather the degree of arteriosclerosis that decides the prognosis. Keith, Wagener and Barker (6) and Peet et al (8) have performed biopsies from intercostal musculature in

hypertensive patients. A positive correlation was obtained between the degree of arteriolosclerosis in muscle specimens and the late mortality rate, both in the non-operated series of Keith et al and in the hypertensive patients of Peet et al followed-up after supradiaphragmatic sympathectomy.

Keith and Wagener (6) recorded the mortality rate after 5 to 9 years in 219 medically treated hypertensive patients classified into 4 goups. Out of 146 patients with malignant hypertension (group IV) 79 per cent died within a year, 88 per cent within two and 94 per cent within three years. One patient only, a woman, lived for more than four years. Out of 37 patients in group III, 35 per cent died within a year, 67 per cent within two and 78 per cent within three years.

When comparing the mortality rate of Keith and Wagener's material with that of hypertensive patients subjected to supradiaphragmatic sympathectomy in Peet's series, the operated cases with retinopathy have a lower mortality rate. In group III of Peet's material 21 out of 33 patients and in group IV 8 out of 24 were alive four years after sympathectomy. A later investigation showed that 21 out of 112 patients with malignant hypertension were alive 5 to 11 years after sympathectomy (8). A comparison with Keith and Wagener's material shows that sympathectomy has increased the chance that a patient with malignant hypertension may live for more than five years from less than 1 to 19 percent.

With regard to Group III, too, the prognosis is decidedly better in Peet's material; he also includes, however, patients with retinal angiospasm without hemorrhages or exudate in this group. In groups I and II no significant difference in mortality rate is obtained between Keith and Wagener's and Peet's material, each of which has less than 40 cases in these two groups.

Thorpe and his coworkers reported (15) observations on 500 patients with hypertension who were subjected to a bilateral thoracolumbar sympathectomy. The mean period of observation was about 3 years. In the follow-up study 22% were found to have died. The results of the operation were excellent or good in 27%, fair in 29%, poor in 12% and unknown in 10%. Comparison of the survival curves of this group with a comparable medically treated group a t the end of average period of 3 years shows no statistically significant difference in groups 1, 2, and 3. In group 4, however, a significantly higher survival rate is apparent in the group operated on. These groups are those of Palmer and associates.

P. D. White et al (40) after a 3 year follow-up of 50 sympathectomized patients found that the result was excellent or good in 11, fair with definite, though not decided, improvement in 11, and in 5 instances there was little or no change, 11 were worse and 12 patients were dead. In contrast, in 50 controls, only 1 patient continued to be in good condition, 4 were unchanged and 41 were worse or dead. The sympathectomized hypertensive patients with serious cardiovascular complications showed in a follow-up analysis a considerably better status both in mortality and morbidity

than did the non-sympathectomized persons. This is a more impressive evidence of the beneficial effect of this therapeutic measure in certain cases than is the usual method of studying the effect on blood pressure alone in cases in which important complications do not exist.

In 1950 Hammarstrom and Bechgaard (22) presented a series of 251 operated patients that had been followed two to eight years. the non-operated control series was selected according to the same rules as the patients operated on and followed up 2 to 10 years. They were collected from about 130,000 records from various hospitals in Denmark and Sweden.

Patients with cardiac decompensation at rest, auricular fibrillation, myocardial infarct, or renal insufficiency were not included in the non-operated series. A few patients in the operated series had cardiac insufficiency and were compensated with digitalis before operation. All of them died, mostly within a year after operation. The mortality rates for their two series are summarized in the table below.

Table IV. -- Comparison of Prognosis in 435 Unoperated Hypertensive Patients Followed 2 to 10 years, with that in 251 Hypertensive Patients Followed 2 to 8 years after Sympathectomy. (Hammarstrom and Bechgaard, 1950)

		Unoperated			Operated		
Group	Sex	No. Cases	No. Deaths	Mortality (%)	No. Cases	No. Deaths	Mortality (%)
2	m	42	9	21.4	29	4	13.8
		122	21	17.2	58	0	0.0
	TOTAL	164	30	18.3	87	4	4.6
3	m	83	57	68.7	35	9	25.7
	f	94	44	46.8	50	8	16.0
	TOTAL	177	101	57.1	85	17	20.0
4	m	69	68	98.7	38	18	47.3
		25	24	96.2	41	16	38.9
		94	92	97.8	79	34	43.0

Smithwick (9) in his latest communication discusses the effect of thoracolumbar splanchnicectomy on the mortality and survival rates of the first 892 patients in his series of 3,000 patients referred to him for consideration for surgical treatment. They were seen during the years of 1938 to 1946 inclusive, and have been followed at least four and at most 12 years.

He includes a table (below) of mortality among hypertensive patients not treated surgically.

Table V. -- Mortality Among Hypertensive Patients Not Treated Surgically.

	Number of Cases	Time Followed (Yr)	Mortality (%)
Janeway (1913)	244	5-10	81
Blackford, Bowers, and Baker (1930)	202	5-11	50
Keith, Wagener, and Barker (1939)	219	5-9	91
Rasmussen and Boe (1945)	100	6	52
Bechgaard (1946)	1,038		
Palmer, Loofbourow, and Doering (1948)	430	8-av.	61
Perera (1948)	250	12 av.	17
Hammarstrom and Bechgaard (1950)	435	2-10	51

A study of these data indicates that the mortality rate for the different groups of patients varies tremendously, from 17 to 91%. While the duration of follow-up also varies, it is apparent that this is not an adequate explanation for the marked difference in mortality rates. A detailed study of these rports as well as of Smithwick's own material indicates that the amount of cardiovascular disease which exists when the patient is first seen is extremely important for prognosis.

Smithwick (9) studied the mortality rates for the 219 cases of Keith, Wagener, and Barker and a similar group of 192 patients referred to him but not operated on. See Table VI.

He found them comparable and for this reason and in order to obtain a larger control series to compare with a similar number of consecutive cases treated surgically, these two control series have been combined, and the mortality rates are compared

Table VI. -- Mortality Rates for Nonsurgically Treated Hypertensive Patients Grouped according to Criteria of Keith, Wagener, and Barker

	Nonsurgical Series (K., W., and B.)					Nonsurgical Series (Smithwick)				
Group	No. of Cases	No. of Deaths at 5 yr.	Mortality at 5 yrs. (%)	No. of Deaths 5-10 yr.	Mortality at 5-10 yr. (%)	No. of Cases	No. of Deaths at 5 yr.	Mortality at 5 yr. (%)	No. of Deaths 5-10 yr.	Mortality at 5-10 yrs. (%)
1	10	3	30.0	4	40.0	59	18	30.5	22	37.0
2	26	12	46.3	17	65.4	53	22	41.5	23	43.5
3	37	30	81.0	34	92.0	52	37	71.0	41	79.0
	146	145	99.4	145	99.4	28	28	100.0	28	100.0
Totals	219	190	87.0	200	91.2	192	105	55.0	114	99.5

Table VII. -- Mortality Rates for 411 Nonsurgically and 538 Surgically Treated Hypertensive Patients Grouped According to Criteria of Keith, Wagener, and Barker

	Nonsurgical Series (K., W., and B. plus Smithwick)					Surgical Series (Smithwick)				
Group	No. of Cases	No. of Deaths at 5 yr.	Mortality at 5 yrs. (%)	No. of Deaths 5-10 yr.	Mortality 5-10 yr. (%)	No. of Cases	No. of Deaths at 5 Yr.	Mortality at 5 yr. (%)	No. of Deaths 5-12 yr.	Mortality 5-12 yr. (%)
1	69	21	30.4	26	37.6	165	17	10.3	25	15.1
2.	79	34	43.0	40	50.5	142	24	16.9	37	26.0
3	89	67	75.4	75	84.5	154	53	34.5	69	45.0
4.	174	178	99.5	173	99.5	77	38	49.5	43	56.0
Totals	411	295	72.0	314	77.0	538	132	24.6	174	32.4

with those for the surgical series in Table VII. All the control patients, as well as those treated surgically, were followed for a minimal period of five years and a maximal period of 12 years. A study of the data in Table VII indicates that the mortality rate for each of the four groups is significantly lower in the surgical series. It is quite clear that surgical therapy has significantly prolonged the life expectancy of these patients.

During the years 1940 to 1946, inclusive, 296 patients were referred to Smithwick (9) for study who were not operated on. During the years 1938 to 1944, inclusive, 596 patients were referred for study and were operated on. At that time, no satisfactory criteria for operation were available. These 892 patients were studied in a similar fashion, and operation was suggested to them as offering a reasonable or a slight chance for a worthwhile result according to the status of their cardiovascular systems when first studied. The majority of the patients elected to be operated on. Those who decided to follow a medical regimen make up the control series. All cases in both series have been followed for a minimal period of four years and a maximal period of 12 years.

Table VIII. -- Mortality Rates for Nonsurgically and Surgically Treated Hypertensive Patients Grouped According to Smithwick Criteria

	Nonsurgical Series (Smithwick)					Surgical Series (Smithwick)				
Group	No. of Cases	No. of Deaths at 4 yr.	Mortality at 4 yr. (%)	No. of Deaths 4-10 yr	Mortality at 4-10 yrs. (%)	No. of Cases	No. of Deaths at 4 yr	Mortality at 4 yr. (%)	No. of Deaths at 4-12	Mortality at 4-12 yr. (%)
1	59	6	10	8	14	60	2	3	4	7
2	115	38	33	42	37	325	39	12	70	22
3	59	34	58	42	71	115	22	19	39	34
	63	55	87	57	90	96	50	52	63	65
Totals	296	133	45	149	51	596	113	19	176	30

The mortality rates for the control series are compared with those of the operated series in Table VIII. A study of this table indicates that, with the exception of the cases in Group 1 the mortality rates for the surgical cases have been reduced significantly. The cases in Group 1 have persistently elevated blood pressure, with minimal or no eyeground changes and no abnormalities in the cerebral, cardiac, or renal areas. Those in the other groups have increasing amounts of cardiovascular disease.

If patients are arranged into four groups according to Smithwick's criteria, outlined in Talbes I and II, it is clear that the prognosis for cases in Groups 2, 3, and 4 has been significantly improved by thoracolumbar splanchnicectomy (Table VIII). These patients had cardiovascular changes ranging from slight to severe. Todate, while the mortality rate is lower for Group 1 cases treated surgically than for the control series, the difference has not as yet become statistically significant. It is expected that it will become so with a longer period of observation. Severe kidney damage, as indicated by persistent evidence of nitrogen retention, is the one finding which positively contraindicates splanchnicectomy in the more advanced stages of cardiovascular disease. The great majorityof the patients treated surgically, as well as the controls, were middle-aged. Approximagely 90 per cent were under 50, and 80 per cent were between 20 and 49 years of age.

The findings which have been presented indicate quite clearly that the prognosis for patients with hypertensive cardiovascular disease significantly improves after thoracolumbar splanchnicectomy. To date, the best results, when judged both by their significance in comparison with control cases as well as by the evenutal mortality rates, have been obtained in cases falling into Groups 2 and 3 (Smithwick classification) and groups 3 and 4 (Hammarstrom's classification).

Smithwick (9) emphasized that the control data available has to do with the outlook for hypertensive patients treated by so-called conventional medical measures. It does not take into consideration the long range outlook for hypertensive patients treated by more recently developed diets and drugs. Whether these measures, such as severe and prolonged dietary restrictions, particularly of salt intake, will materially influence the long range prognosis will not be known for years. In the meantime, it seems proper to recommend surgery where it appears to have been most effective. It also seems probable that the best results in the long run will be obtained by those patients who have the benefit of both surgery and medicine. It is becoming obvious that surgery should not be reserved as a last resort.

The Selection of Patients for Sympathectomy

In the early series of patients sympathectomized for hypertension, no criteria were used for the selection of patients. With the passage of time it became evident that if satisfactory results were to be obtained, a method of selection would have to be formulated. Earlier, the selection of patients was in direct contrast to the indiscriminate method previously used. Sympathectomy was urged for those with relatively mild hypertensive disease without complications (3). More recently, the value of sympathectomy in the more severe types of hypertension has become apparent. This is especially true of malignant hypertension. Peet's work with this type of hypertension has increased the 5 year survival rate from a rare occurrence to a 19-21 per cent survival rate (27) As more patients with this disorder are operated on earlier in the course of their disease, this percentage should rise.

At first, special tests were advocated to select the candidates for operation that would most likely benefit from the procedure. The amytal test, nitrite test, spinal and caudal anesthesia, cold pressor tests, Valsalva maneuver and other procedures affecting blood pressure were advocated as methods to use for selection of patients. (10) Although reliance on any of these tests as indications for sympathectomy has not been borne out, they have proved their worth as aids in the over-all evaluation of the patient as a candidate for sympathectomy.

A valuable by-product of the search for a method to select patients for sympathectomy has been the development of grading systems

as an aid to prognosis of this variable disease. I am sure a better insight into the natural history, as well as an improved knowledge of the etiology involved in hypertension have also been derived from the study of patients for this therapeutic procedure.

Keith, Wagner, and Barker (6) were the first to recognize the value of eyeground changes in the prognosis of hypertension. Most of the workers that have proposed methods of grading have incorporated or based their grading on the work of Keith, Wagner, and Barker. The only unfortunate thing that has come of this outstanding communication is that it has been used too frequently as a control for the comparison of operated and non-operated series. It is far too top heavy with patients having malignant hypertension (146 out of 219 patients) to be used for comparison of hypertensive patients with anything but malignant hypertension.

The method of selection of patients that has evolved from the study of the problem is generally as follows.

The patient is given a thorough hypertensive work-up. All known causes of hypertension are eliminated. The blood pressure, eyegrounds, cardiac, renal and cerebral areas are evaluated. Each author has his own particular method of evaluating the hypertensive but selection from the following procedures is usually used.

In addition to a history and physical, these procedures are done: The person's pschi is evaluated to see if the patient is psychologically able to benefit from the operation or if encephalopathy is present. The eyegrounds are examined and classified into 4 groups

based on the method of Keith, Wagner andBarker.

The cardiac status is evaluated by teleorentgenograms, electrocardiograms, and exercise tolerance tests as needed.

Renal status is studied by urinalysis, concentration and dilution tests, phenolsulfonphthalein excretion, urea clearance, NPN and IV pyelograms.

Blood work, including cbc, sedimentation rate, smears, hemoglobin, serum protein, chlorides, and cholesterol, type, Rh factor, sugar, and serology are done.

The blood pressure is evaluated by cold pressor, postural and sedation tests, bed rest, pressor response to CO_2, breath holding, exhaling, exhaling with a closed glottis and other tests affecting vasomotor tonus.

Etamon and Diabenamine are sometimes used.

A neurologic examination is carried outin persons who have suffered a cerebral vascular accident and appropriate procedures done.

DeTakats estimates the participation of the cortico-adrenal mechanism by the use of the insulin tolerance and epinephrine eosinophilia.(34)

The selection of the patient is an individual problem and the pros and cons in each case should be weighed carefully. The actual selection is a process of exclusion. The patients who have no contraindications to sympathectomy are selected.

In general, the contraindication may be summarized as follows:

The patient should not be over 55 years of age unless his physiologic age appears much younger than his chronological age.

The best results are obtained in those under 50 and out of their teens.

Poor renal function is an absolute contraindication to sympathectomy, especially if there is nitrogen retention. I think it is most generally agreed that nothing more than a slight impairment of renal function should be allowed in persons selected for sympathectomy.

Marked cardiac changes such as actual or impending failure or coronary occlusion within the last 6 months are among the contraindications. Congestive failure need not be a contraindication if it can be well controlled by medical means if the other vascular areas show little relative impairment. Angina and tachycardia are not considered contraindications if the sympathectomy includes the cardiac accelerator and anginal pain pathways. Auricular fibrillation, heart block, gallop rhythm are contraindications, as is an enlarged heart over 50% of normal.

Hypertensive encephalopathy, severe psychosis are not amenable to sympathedtomy. Cerebral vascular accidents after recovery from the acute phase without marked residual are not considered contraindications per se.

Eye ground changes other than arteriosclerosis are not considered contraindications. Patients with grade 4 fundi whould be operated before cardiac or renal function become impaired. Once non-protein nitrogen retention appears, the results of sympathectomy are poor.

Patients with arteriosclerotic hypertension with a high pulse pressure, a fixed diastolic level and general arteriosclerotic changes are not considered for sympathectomy. This, of course, applies to

other known causes of hypertension.

It has not yet been established that patients with mild hypertension without symptoms or complications are benefited by this operation, thus they should be watched along with patients with intermittent and "benign" hypertension for signs of progression to the more advanced stages of the disease before operation is suggested.

The methods of selection by different authors are reviewed below.

Smithwisk (9) urges sympathectomy in his groups 2 and 3 and suggests that surgery may be employed in group 4 cases, but because the eventual mortality rate is still very high in spite of thoracolumbar splanchnicectomy, it would seem much wiser to utilize surgical therapy earlier in the disease if it is to be considered at all. Until it has been established statistically whethereor not surgery is beneficial in his group I patients, sympathectomy is utilized in his patients who are notdoing well on medical therapy, or who for one reason or another cannot follow a medical regimen. Surgery is also given serious consideration in group I patients who are young and have high resting diastolic levels, 110 mm or more. In any case, they should be followed closely for evidence of the development of cardiovascular disease.

DeTAkats in his latest communication (34) used these indications for splanchnicectomy. In the cases discussed, three distinct indications for operation have consistently been employed. An intermittent hypertension that can be reduced to normal by bed rest or by barbiturates may be watched expectantly, but, at the appearance of the

earliest sign of vascular damage in the retina, heart, or kidney, sympathectomy should be undertaken for two reasons. In the first place, the patient has demonstrated his vascular vulnerability, which varies according to sex, heredity, environment, and possible dietary factors. In the second place, the operation in this stage is highly efficient in arresting the progress of vascular damage and in reducing the blood pressure to a normal level.

The second indication is the condition of a middle-aged hypertensive patient who shows diffuse vascular damage and whose moderately elevated diastolic pressure of 100 to 110 mm. Hg. shows a consistent rise in spite of medical management. Such a patient has irreversible arteriosclerosis and his diastolic pressure cannot be lowered below 100 to 110 mm. Hg. His prognosis will depend on the extent of renovascular damage and on the many uncontrollable factors that initiate vascular accidents in the brain and heart. Nevertheless, lowering of the diastolic pressure and the lessening of the sudden rises of pressure that occur with exertion, undue emotion, cold, and posture change, give such a patient better chance for survival than if the hypertension is not treated.

The third indication is hypertension in the rapidly progressive pre-malignant phase or, should one believe in a malignant phase with papilledema, when the diastolic pressure is fixed but no advanced renal damage has occurred. In such patients the operation may be life-saving, but the extent of the operation must be correlated with the

severity of the disease so that in this stage more extensive procedures are in order.

The fourth indication is intractable headache resulting from hypertensive encephalopathy in patients with advanced renal damage. This palliative procedure is a limited one stage operation that is equivalent to a continuous venesection in diverting blood from the cerebral and retinal areas and aiding cerebral compensation. The fourth indication has been recognized very seldom as valid, but this situation does occur occasionally.

Certain limitations of sympathectomy for hypertension can be established. Hypertension in the adolescent, latent hypertension with increased vascular reactivity, and intermittent hypertension without vascular damage have not been included among surgical indications. Arteriosclerotic hypertension with little or no progression is distinctly a medical problem. Advanced essential hypertension with irreversible damage that is mostly renal does not respond favorably to sympathectomy. (34)

Thorpe (15) and his co-workers reported their observations on 500 patients with sympathectomy. While grading hypertensive patients according to the method of Keith, Wagner and Barker (6) , they found frequent disparity between the vascular changes in the fundi and those present in other organs. They, therefore, employed the four group classification of Palmer (7) and associates which considers damage to other organs as well.

They concluded that the group 4 patients were the only patients that had a significantly higher survival rate than their medical control groups.

They considered the following conditions to be absolute contra-indications to sympathectomy: 1) intractable cardiac failure, 2) renal insufficiency that presents a pre-operative blood urea nitrogen level in excess of 20 mg per cent, 3) mental confusion, 4) CVA or myocardial infarct less than 6 months before operation, 5) serious psychiatric disturbance at any previous period, e.g., manic depressive psychosis and severe psychoneurosis.

Hinton (35) used the following method for selection of his patients.

Four organs are considered in making selection of patients: eyes, brain, heart, and kidneys, the rating 0 to plus 4 being used, according to the extent of disease in each organ. Operation is indicated in all cases in which there is no contraindication and for patients with persistent hypertension associated with minimal changes in any one of the four systems. Contraindications to thora-columbar sympathectomy are: 1) renal disease, 4 plus; 2) 4 plus cardiac disease in which congestive failure is unremitting or if coronary occlusion occurs within 3 months; 3) 4 plus cerebral disease if confusion exists or if a stroke occurs within 3 months; 4) if there are two 4 pluses other than the eyes; 5) if the total plus count equals 11 or more.

In selecting his 300 patients for thoracolumbar sympathectomy, Ray (16) used these indications for operation. During the period

covered by this investigation, all patients under the age of 50 years shown to have a sustained significant elevation of blood pressure, presumably of the essential type, were considered for operation. Exceptions were made for some in the fifties whose physiological status appeared to be younger than their actual age. Ninety-two per cent had a resting diastolic pressure of 110 or over after rest in the hospital. Included were a small group of ten cases presumed to have essential hypertension but subsequently found variously to have glomerulonephritis, periarteritis, polycystic kidney, and pituitary-corticoadrenal syndrome.

Patients with serious functional damage of the brain, heart or kidneys were excluded from operation. More specifically, patients considered to have encephalopathy as evidenced by confused states, delirium, stupor, and signs of recent multiple vascular accidents were thought unfit for operation. Heart block, cardiac decompensation or fibrillation that did not respond promptly to digitalis, and clinically identifiable coronary occlusion were taken as specific contraindications to operation.

Impaired renal function of significant degree was usually reflected in all renal function tests, but a blood urea nitrogen which remained over 20 mg per 100 cc after medical treatment was with few exceptions taken to be a contraindication to operation.

Most patients with psychosis, fixed neuroses, or marked anxiety states were excluded, chiefly because the symptoms for which they

sought relief are not usually benefited by the operation, although the blood pressure in a few was significantly reduced.

But even though certain findings constitute contraindications to operation, and others diminish the likelihood of success, the surgeon must often decide on the basis of his individual evaluation of the patient whether an operation is warranted and this applied in the selection of a number of the patients with borderline conditions in this series.

The efforts to determine by special tests or deductive reasoning exactly which patients will get the hoped-for results from operation have thus far been only partially successful. It is too much to expect that any operation can be wholly satisfactory, and a mistake to limit its use to the patients with only the best prospect for benefit. Perhaps non-surgical methods of treatment will prove to be sufficient or as good in some patients but it is folly to ignore the serious nature of hypertension and disregard sympathectomy because it is an operation. In some patients the progress of the disease is slow and never reaches the advanced stages, but too often what is on one day considered to be a "benign, uncomplicated hypertension" is on the next day disastrously complicated by a cerebral vascular accident or a coronary thrombosis.

SUMMARY

A theory of the natural course of hypertension is included.

The methods of operation are presented. No attempt was made to evaluate which technic is the most beneficial.

The therapeutic value of sympathectomy on hypertension was evaluated by studying the effects of theoperation on blood pressure, ECG's and heart size, eye ground changes, relief of subjective symptoms, renal function, and prognosis. This was done by reviewing the large number of series of patients appearing in the literature.

The selection of patients was discussed as well as the grading of patients for purposes of evaluating prognosis.

CONCLUSIONS

The following conclusions may be drawn from the preceding reviews of the literature.

1. Sympathectomy has a favorable effect on blood pressure in a significant number of cases. With the passage of time, the blood pressure levels return toward pre-operative values.
2. Improvement in ECG and decrease in heart size are seen in a significant number of patients operated on, however, splanchnicectomy does not influence the course of the disease in these patients having cardiac enlargement greater than 50% above predicted normal or marked changes in ECG.

3. Reversion to normal or regression of eye ground changes, especially grades3 and 4, is seen in a majority of the patients following sympathectomy.

4. Sympathectomy has a favorable effect on subjective symptoms in a large majority of patients.

5. It is doubtful if sympathectomy affects renal function to a significant degree. There is no evidence to support the idea that renal function is impaired by the procedure.

6. The favorable effect on the heart, eye grounds, relief of symptoms and mortality is seen in patients following sympathectomy who have not had a significant lowering of blood pressure or else just a temporary lowering.

7. Prognosis is significantly improved by adequate sympathectomy in patients with hypertensive cardiovascular disease graded as group 2 and 3, according to Smithwick, or 3 and 4 according to Hammarstrom in properly selected cases.

8. Prognosis is improved for patients with malignant hypertension by Peet's operation if the patients are operated on before renal or cardiac function is markedly impaired.

The future of sympathectomy probably will depend on whether or not a medical treatment is developed which will give better results than this form of treatment. One of the drawbacks to sympathectomy that has been mentioned is the fact that too few patients are eligible for the operation. It is possible that this might be corrected by

careful observation of patients with hypertension and prompt surgical intervention when the indications arise.

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