Management of Moderately Severe Arterial Hypertension

By Irvine H. Page, M.D.

I SHALL review with you the course of a patient with the aim of demonstrating our approach to the treatment of severe essential hypertension. We are a long way from knowing all the answers; indeed we must admit that many of the basic mechanisms which sustain and regulate normal arterial pressure are obscure; still, interest in and knowledge of the arterial hypertension has grown astonishingly in the past 15 years.

Dr. Piette, would you present an abstract of the patient's history?

Dr. Piette: This 52 year old man has been in good health most of his life. His mother died at 64 years of heart failure and his father at 69 of a stroke. When he was 22, a college health examiner told him his blood pressure was slightly elevated on one occasion, but not sufficiently to cause any concern. He passed several life insurance examinations; on two of these occasions he was asked to return for recheck of blood pressure. The last time was 15 years ago. His blood pressure was found to be definitely elevated six years ago during a routine company physical examination. He had no symptoms and he gave it no thought. About three years ago he experienced occasional morning headaches; two years ago these became regularly recurrent. Some nine months ago he noted shortness of breath on slight exertion and, more recently, that he slept best when supported by two or three pillows. About three months ago, his ankles became swollen during hot weather. He has had nosebleeds on two or three occasions and twice in the past three months episodes of transient weakness of the right arm and difficulty in forming words.

He is an active, successful businessman. He seems socially and domestically well adjusted. He gives the impression of having a proper self-confidence and ability to express his feelings. He is not unduly depressed or concerned by what has happened, but is intent on a definitive resolution of his problem.

Dr. Page: You will notice that this man's story is almost monotonously familiar. In fact, that is the reason it is brought up for discussion. I realize it would be more dramatic to present some unusual situation, some rarity, such as pheochromocytoma, because of our more satisfactory understanding of its nature and treatment. But that is not our main problem. It is the commonplace and the familiar which is also the obscure; this we must constantly try to illumine.

The first point to be established is whether or not we can identify a single cause of this man's hypertensive disease. Glomerulonephritis, pyelonephritis, pheochromocytoma, coarctation of the aorta and many rarer causes should be considered (in women, of course, toxemia of pregnancy should also be considered). These are classified and tabulated for ready reference on page 25 of that excellent text, Hypertension: Its Diagnosis and Treatment (second edition).

Dr. Taylor: The most commonly overlooked of these is pyelonephritis. This simply should not be; prompt and proper treatment with antibiotics and antibacterials should eliminate this as a cause of hypertensive disease. I have become almost a missionary for this point of view; still, hardly a week passes without my seeing one or more victims of this sort of neglect.

From the Research Division of the Cleveland Clinic Foundation, and the Frank E. Banta Educational Institute, Cleveland, Ohio.
A PHYSICIAN: Dr. Taylor, do you perform excretory urography regularly in order to exclude unilateral renal disease and polycystic kidneys?

DR. TAYLOR: We routinely perform excretory urography not so much for the detection of rare pheochromocytomas—which urograms rarely define—and unilateral renal disease, but as an indication of renal tubular function.

Now, in this man's case, this question does not seem to arise. Rather, the urgent problem is to relieve the damage his hypertension has caused before spending his time and ours in looking for causes we may never find, or in trying this or that obscure means of lowering his pressure. I take it that he is already on a low-salt diet, has been digitalized and is being weighed daily.

DR. CORCORAN: This man's disease was until recently asymptomatic. He comes now for the relief of symptoms caused by hypertensive vascular disease; this disease results in large measure from persistent elevation of arterial pressure. Consequently, the lowering of pressure to a reasonable level is a paramount issue; any other treatment is a stop-gap merely.

DR. PAGE: You both think, then, that there is still some future for those who want to specialize in cardiovascular disease? There is always geriatrics, just in case, and the more hypertension you cure, the more geriatrics there will be.

The heredity in this patient favors the diagnosis of essential hypertension, and it is rather strongly weighted against him. But notice that both parents lived fairly long lives, despite manifest vascular disease. I think it makes a difference and it is always a relief to hear that the family is relatively long lived in spite of the occurrence of vascular disease in both parents.

I won't dwell on the many interesting problems associated with the social and economic aspects of hypertension. Suffice it to say at the moment that at long last some statisticians and insurance companies have had the good grace to allow people to die of essential and malignant hypertension rather than piecemeal from uremia, apoplexy, "nephritis" or heart failure. I feel sure that this failure to recognize the nature of the disease is one of the many reasons why hypertension has been such a difficult disease "to sell" to physicians and the laity.

A PHYSICIAN: Dr. Page, you use the words "essential hypertension and malignant hypertension" as if they were separate diseases. Will you clarify this?

DR. PAGE: I suppose "malignant hypertension" should rather be called the "malignant syndrome" because it appears under such a variety of circumstances. But the term malignant hypertension is so widely used, I doubt if anything we say is going to change it. Widespread necrotizing arteriolitis is the characteristic pathologic picture, and this is associated with marked diastolic hypertension. The syndrome usually is added to pre-existing hypertension of varied origin and usually of long duration. There are patients, though, in whom the arterial disease and the hypertension start almost simultaneously. To be more specific, the malignant syndrome is probably not a separate disease but something added to the existing hypertension.

The fact that slight transient hypertension was discovered when this patient was 22 brings up an interesting and often delicate problem. When slight transient hypertension is found, should the diagnosis of essential hypertension be made? What do you think, Dr. Corcoran?

DR. CORCORAN: I certainly do not think an unequivocal diagnosis should be made. There is seldom any hurry about making a final diagnosis in this disease. You may recall that when we were at the Rockefeller Institute Hospital we examined a number of lads from the Brooklyn Navy Yard because of transient hypertension. A good many years later some had developed severe hypertension, but many of them were perfectly normal. It is from those with labile hypertension that the majority of the full-blown cases come, but it by no means follows that all persons with transient elevations of blood pressure will develop the disease. The family history should influence this decision.

DR. TAYLOR: The time of incipiency is
when the physician must be most alert in recognizing and treating whatever disease may be the cause of hypertension. There is no excuse for allowing anyone to go for years with recurrent "cystitis" until irremediable renal disease results in severe hypertension. "Principis obsta; sero medicina paratur."

A Physician: Dr. Page, do you always consider the possibility of coarctation of the aorta? How do you exclude it?

Dr. Page: The diagnosis of coarctation of the aorta will rarely be missed if the femoral and pedal arteries are palpated at physical examination. Measurement of femoral blood pressure is desirable but this requires special cuffs for the sphygmomanometer. Even if the diagnosis were missed in the physical examination it should be picked up in the x-ray film by discovering notching of the ribs and absence or smallness of the aortic knob.

Before we get far afield in this discussion, we should consider whether this patient really has essential hypertension or not. The history is in its favor. Physical examination shows the arterioles in the eyegrounds to be sclerosed and constricted; there is arteriovenous compression and a few scattered hemorrhages are seen as well. But there is no papilledema; nor are there exudates, retinal edema or showers of hemorrhages, which are some of the findings which go to make the diagnosis of malignant hypertension. These fundus photographs will help you visualize the disturbance (fig. 1).

The episodes of transient weakness, aphasia, severe nuchal headache which the patient described, point to cerebrovascular disease. The shadow of the heart is enlarged on the x-ray film and the electrocardiogram shows both left ventricular preponderance and the strain pattern. Since the patient has already had bouts suggestive of cardiac failure, these observations fit in with what might be expected. Renal function was moderately reduced as shown by the reduced ability to concentrate urine. We use the Addis concentration test at the Clinic, which as you may know, has a lower limit of normal of 1.024 to 1.026. The best this patient could do was 1.018. The estimate of renal blood flow from the para-aminohippurate (PAH) plasma clearance showed 640 ml. per minute. There were demonstrated also cylinduria (100,000 casts), proteinuria, hematuria (2,100,000 red cells in 12 hour urine specimen). Dr. Corcoran always gives us new ideas about renal function, even after all these years.

Dr. Corcoran: That's harder to do every day. I have the impression that every tenth medical graduate is given a bottle of para-aminohippurate, a trained dog or patient, two catheters (one venous, one urethral) and a corner in the laboratory along with his diploma.

As concerns this man, he demonstrates what Dr. Taylor and I speak of as the cerebrorenal polarity of hypertensive disease; this is a high-flown way of saying that most people with advanced cerebrovascular disease have good kidneys, and that most with highly nephrosclerotic kidneys retain their brains.

Of course this man does have active nephrosclerosis, as is indicated by the sediment count; but the advantage to him of his relatively good renal function is that, in general, those who retain such function retain also the capacity to respond to appropriate hypotensive regimes in greater degree and for longer periods than those in whom advanced renal disease imposes what may be secondary and relatively irremediable hypertensive mechanisms.

A Physician: From a practical standpoint, Dr. Page, could we get enough information about renal function from determination of the blood urea or the blood urea nitrogen?

Dr. Page: I think not. Retention of urinary excretory products is a late manifestation of renal disease. It is the progress of the vascular disease in the kidneys that we wish to follow and this can only be done with the more discrete tests of kidney function.

The participation of adrenal cortical function in hypertension is still most controversial. The problem arises first from George Crile's concepts of adrenal function as expressed in his books on anoci-association and on man as an adaptive mechanism. Later some of us found that adrenal cortical function is essential to the maintenance of renal hypertension in dogs and Selye produced hypertension by giving desoxycorticosterone to uninephrectomized, salt-fed rats. Selye then developed the
concept that hypertension is a disease of adaptation, in which adrenal dysfunction is an arresting hypertensive disease and of lowering arterial pressure. But many are not convinced

Fig. 1. Examples of the various stages of hypertension as reflected in the eyegrounds.
in this field as an example of recondite pharmacology and most of the hypotheses as thinner than air. Dr. Harriet Dustan has done some work in this field and I would like to know her views on this healthy dichotomy of opinion.

Dr. Dustan: I don't know the answer. I doubt that anyone knows enough to be as categorical as most are. What we have found is that some people with hypertension do show increased outputs of formaldehydegenic corticoid. That is the fact. The rest is opinion. We think this is due to an abnormality in the mode of corticoid excretion possibly consequent to renal damage and not a result of hypercorticoidism. Of course, desoxycorticosterone hypertension is a factor too, and so is the hypertension in Cushing's syndrome; the opposition to Selye's concept of "mineralocorticoid secretion" on the basis that no such corticosteroid could be demonstrated is having a hard time these past weeks with Simpson and Tais' demonstration of such a material in cortical extract and adrenal venous blood. The problem is still vexed by its methodology; obviously, a sufficient hypocorticoidism should remit hypertension in most instances, clinical or experimental; our scant clinical experience with adrenalectomy indicates this; but it also demonstrates that the operation is hardly worthwhile in the presence of advanced renal disease, and, in my view, hardly justifiable except as a last resort. Consequently, it will not have a place in the treatment of hypertension unless and until adrenogenic non-Cushing's hypertoners can somehow be segregated from the essential hypertensions.

Dr. Page: I am going to assume, and I trust in this clinic with complete justification, that all the proper examinations have been made to rule out the ascertainable causes of hypertension, such as coarctation and pheochromocytoma. Never forget that the obvious is the easy thing to miss—and that must be obvious too.

A Physician: Dr. Page, do you routinely do a screening test for pheochromocytoma? I understand such hypertension may masquerade almost precisely as essential hypertension. Inasmuch as it can be cured by operation in most instances, is it not wise always to do such a test?

Dr. Page: Yes, indeed, we screen all patients for pheochromocytoma.

We can, therefore, make the diagnosis of severe essential hypertension in the patient who is being discussed, but what are we to do about it? Not more than 15 years ago there just wasn't much you could do about it. Today I am convinced that a lot can be done, but it takes a lot of doing by both patient and physician to accomplish a substantial benefit to the patient.

The first problem is to determine how rapidly the vascular disease is advancing; are we trying to put out a fire in the wastebasket or one in a dry forest in a high wind? Both started the same way—a cigarette—but the results differ appallingly.

A Physician: Dr. Page, before you take up treatment, would someone explain the strain pattern and its significance in hypertension?

Dr. Page: Dr. Taylor, you don't speak in public too harshly of the electrocardiogram, so will you answer the question?

Dr. Taylor: The strain pattern, which consists of left axis deviation plus inversion of the T waves and depression of the S-T segments, is probably in fact due to strain since it occurs so characteristically in the presence of arterial hypertension, regardless of its mechanism. Further, it is the electrocardiographic change which is so often reverted toward or to normal when arterial pressure is reduced.

Dr. Page: The simplest way to determine rate of progress is to select several reasonably objective criteria such as heart size, renal blood flow, examination of the eyegrounds, and to repeat the observation over periods of months, or at intervals determined by the rate at which vascular disease seems to be progressing. In a word, drastic disease justifies drastic treatment. Now having decided that this man has a fairly rapidly progressive severe essential hypertension, what are we to do for him? Obviously, the simpler measures such as rest and sedatives alone would be insufficient, although I believe more firmly than ever that some reorganization of the patient's life and a sound education in the nature of the disease is the beginning of
treatment of all chronic diseases. It is ignorance that breeds fear and fear augments the hypertension. Unfortunately, from my point of view, there are those who believe the less the patient knows the better.

A careful explanation of hypertension, and what the patient may expect, is in my experience never resented and usually deeply appreciated. I have felt strongly enough about it to write a small manual for the patient, not the physician, so that he may refresh his memory from time to time on the things most physicians would like him to know. To lose the benefit of this educational process is to lose one of the most reliable methods of lowering arterial pressure.

But education and the abolition of fear do not suffice. We must, therefore, consider diet, the ganglion blocking agents, hydrazinophthalazine (Apresoline), thiocyanate and nitroprusside, and finally sympathectomy. There is much talk regarding methods of selection of patients for each of these treatments. It is constantly stressed that patients should be selected "properly." Indeed, they should, but how? Despite the long list of suggested tests none of them have proved valuable in selection of patients for treatment. It is a great pity that this is so, because raising the successful outcome from an average of 20 to 30 per cent to 90 to 100 per cent would more than justify almost any of the current treatments.

Our patient is required by his work to do much traveling and for that reason only a very easily prepared, drastic low-salt diet would be of any use. The rice diet is the simplest and from the gastronomic point of view the one most awful to contemplate. Whether he is willing to live on such restricted fare only time will tell. I think it fair to say that few physicians are able to prescribe the diet with the confidence and enthusiasm of its originator, and much is lost in this failure. On the other hand, most of us do not believe in it that much either. If the patient lived at home, I am sure I would want him on a varied diet containing not more than 200 mg. of sodium as determined by the urinary excretion of sodium. This would be especially desirable if heart failure were impending, as it is in this patient. It would, then, seem best to request the company for which he works to transfer him from a travelling to an office job so that he could follow a diet which can be constructed with the aid of one of the new manuals, such as that issued by the American Heart Association, which allows enough variety to insure the patient's remaining on it for many months and perhaps years. The proper training in the use of diets is difficult: it is just as well that this is so, thus preventing automatically much

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Fig. 2. The electrocardiogram shows left ventricular preponderance and the strain pattern RS-T depressed in leads I, aVL and V₅. T inverted in I, II, aVF and V₅.

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of the damage that careless dieting can engender. A change in a life long pattern is a big step in a patient's life. Remember that it might be your own.

A PHYSICIAN: I am a bit confused about low sodium diets. Some physicians seem to feel that restriction of sodium to 500 mg. a day is as useful as restriction of sodium in the diet to 200 mg. a day. The 500 mg. diet is of course a good deal easier for the patient.

DR. PAGE: While the 500 mg. sodium diet is much easier to prepare, our results show that the more rigid restriction is necessary if the most in blood pressure lowering is to be gotten out of the diet. With any low salt diet it must be recognized that the limits of error with many patients are great, so that a 500 mg. diet may mean anything from 300 to 1000 mg. Low-salt diets are in most cases an ordeal and if they are to be used, should be employed to achieve the greatest benefit. The patient, his wife, and the physician have to work at it! For those of you who feel the urge to prescribe low-salt diets lightly, I suggest you try the prescription yourself first.

A PHYSICIAN: Are the diets you speak of really practical?

DR. PAGE: Yes and no. Most of the "low-salt" diets aren't low-salt at all, hence they merely impose hardship and no advantages accrue from their use. The American Heart Association will shortly issue a low-salt cookbook which is practical and excellent. Thurman Rice has written a good one on the same subject. Salt-poor meats as well as bread, fish, and other foods are now on the market, so that things are becoming much simpler. Sodium-free condiments add much to the palatability of these diets.

The salt substitutes are always controversial. At the Clinic we offer them but find most patients prefer to do without them. Unfortunately, the best of the lot from the point of view of taste were those containing lithium chloride.

A PHYSICIAN: Would you mention some of the salt substitutes which may be used without getting into trouble such as that which occurred from the use of lithium chloride?

DR. PAGE: I believe Neocortesal, Cosal and Diasal are the most popular. As you wisely point out, lithium caused us lots of trouble and it took us some time to find out why some of our patients on low salt diets were not doing well. It was an interesting experience but left me with a healthy respect for nature's way of doing business and for the need of penetrating studies before a drug or food substitute is sold.

DR. CORCORAN: Don't you think the urinary sodium should be measured at varying intervals? Not more than two or three out of 10 outpatients are able to keep their urine sodium constantly below the desired limit, and sometimes not from any fault of their own. Of course most patients at some time or another fool themselves as well as the doctor. Who could have thought a patient would get enough sodium from toothpaste or from chocolate bars to put her well above the 200 mg. sodium limit?

DR. DUSTAN: You haven't mentioned the dangers of these diets. There are some, you know! Extreme depletion of sodium, with weakness, nausea, vomiting and complete circulatory collapse, may occur, especially in hot weather, or after a large mercury-induced diuresis. The patient should be warned of it. It often takes longer to replace the sodium than one would think. A day or two may be required to restore depleted sodium to normal.

DR. PAGE: Unfortunately, time is moving on. The next problem I want to discuss briefly is the ganglion blocking agents such as tetra-ethylammonium chloride (TEAC) hexamethonium and Pendimid. TEAC has been largely dropped in the treatment of hypertension because its action is much too transient. But it is still actively studied in the laboratory because of its unusual and fascinating properties.

Hexamethonium (Bistrium-Squibb) is a drug which has been introduced and quite extensively studied by English physiologists and clinicians, notably Ing and Barlow, along with Paton and Zaimis. Dr. Smirk of New Zealand, who not too long ago paid us such a delightful visit, has been most active in its study.

Hexamethonium blocks the transmission of impulses through both sympathetic and para-
sympathetic ganglia, but not completely. It is by no means a "total nervous blockade." Those impulses which adjust the caliber of vessels when the patient stands up are completely blocked. Thus, orthostatic hypotension is the most outstanding action of the drug. Since both sympathetic and parasympathetic ganglia are paralyzed, a variety of side effects result, such as stuffy nose, dry mouth, dilated pupils, inability to empty the bladder, and other symptoms. By far the most disturbing are the gastrointestinal upsets which more often than not follow both oral and parenteral injection. These may end in a disabling paralytic ileus unless promptly recognized.

Dr. Corcoran: I think it should be stressed at this point that both orthostatic hypotension and the gastrointestinal effects are dangerous. The patient must be very carefully instructed in order to avoid serious accidents.

Dr. Taylor: This has not been sufficiently appreciated by most physicians. A barrage of premature newspaper and magazine publicity, aided and abetted by some physicians, has misled both public and physicians into believing that at last we have the answer and that it is a simple one.

Dr. Page: I liked what one magazine called the drug—"Dangerous Hex." The premature and immoderate publicity given this drug has led many to believe that hexamethonium is a simply-administered, life-saving drug. In the first place, taken by mouth, its absorption is very irregular and the drug itself may cause even more irregularity. Not only may gastrointestinal complaints be very severe but, unless carefully controlled, the constitutional effects often become a threat to life. The usual initial dose is 125 mg, four times a day before meals. This is to be increased slowly until a total dosage of 3 to 4 Gm. per day is reached. We have seen so much difficulty from the oral use of hexamethonium that our enthusiasm for its use is small.

Some idea of how much the patient is receiving is gained by giving the drug parenterally. I think that a patient, intelligent and understanding wife is a prerequisite to successful use of parenteral hexamethonium. She must take blood pressure readings regularly and constantly adjust the dose according to need.

The development of tolerance is a very serious handicap. We have many patients in our clinic who become almost completely refractory to the drug after several months, with return of arterial pressure to the pre-treatment levels. A few days without the drug usually restores responsiveness but the dosage must again be adjusted. There are many patients who simply do not respond to hexamethonium with a fall in average pressure. This is a point which seems to be widely forgotten, if it was ever known.

Bladder symptoms, constipation, and other effects are often distressing. We use Urecholine (5 to 10 mg, four times a day) or Myastenol (2.5 to 5 mg, three times a day) to aid in their correction.

Since hexamethonium is largely excreted by filtration through the kidneys, reduced renal function is another indication for great care in its use.

It is hardly any secret that we have viewed the widespread use of this drug, even under carefully controlled circumstance, with some dismay. Certainly it, along with other drugs, is useful in the treatment of emergencies of hypertensive patients but how much of a place it will have in day to day treatment I am not so certain as others. It is a pity that in this country the results of weeks or at most months of study have been published as though they were adequate evidence on which to evaluate the drug.

A Physician: Would you give more of the details of your method of treatment with hexamethonium administered parenterally? What is the beginning dosage? How rapidly does one increase the amount? How often each day should it be given? Do you consider that in general the use of hexamethonium is the best method of treatment of hypertension?

Dr. Page: We think it better not to give any hard and fast rules for the dosage of hexamethonium. When it is to be started parenterally, enough is given by infusion to reduce the supine pressure to the desired level. This is the starting dose given usually
every 12 hours. It may have to be raised rapidly.

The drug is given two to three times daily by subcutaneous injection or orally three to four times. It is a dangerous drug if only for the orthostatic hypotension it produces. The amount required varies over a period of weeks and months so that constant readjustment is necessary if a really satisfactory supine blood pressure level is to be achieved. I have noticed that many practitioners are using such small amounts that no side effects occur, nor is there any really significant fall in arterial pressure.

We are currently investigating another blocking agent, Pendiomid. So far our results suggest that it has only slightly less marked parasympathetic side effects while lowering arterial pressure. Like hexamethonium, when taken carelessly, it can produce dangerous collapse.

Summing up, then, I believe the ganglion blocking agents to be of great theoretic interest and of some practical value in treatment. But these drugs are dangerous and unusually difficult to regulate. After more than two years study we are not convinced that the long term results will compare favorably with those obtained by careful treatment with the drug in the first few months. Therefore a current belief that hexamethonium is alone a practical treatment of hypertensive patients seems an exaggeration. There are many other aspects of the blocking agents that are of interest but our time is running out. The second drug to be considered is hydrazinophthalazine, or Apresoline. Perhaps Dr. Taylor will discuss its use.

Dr. Taylor: There is increasing evidence that Apresoline blocks one of the pressor mechanisms believed to participate in many patients with essential hypertension. Further, since 60 per cent of our hypertensive patients respond at least somewhat favorably, we feel that most patients with advancing vascular disease and hypertension should have a trial with this drug. We define an adequate trial as a period of at least eight weeks during which the patient receives 200 mg. four times a day. To minimize the unpleasant side reactions, which are transiently present in 70 per cent of patients, dosage is increased slowly from 25 mg. four times a day to the higher levels. The patient's distress can be made more tolerable by reassurance that symptoms are usually not permanent. Antihistaminic drugs, analgesics and sedatives also are helpful.

Among patients with evidence of hypertensive or arteriosclerotic heart disease, restriction of dietary sodium, digitalis and gradual reduction of blood pressure will guard against congestive failure and coronary insufficiency.

A Physician: Dr. Taylor, would you give me some more specific information about the use of antihistaminic drugs, analgesics and sedatives? There seems to be a general feeling that Apresoline cannot be taken by a substantial proportion of patients.

Dr. Taylor: We use Benadryl in 25 to 50 mg. amounts, or Pyribenzamine in 50 mg. doses, with each dose of Apresoline. When fever, joint pains and muscle aches occur, aspirin (0.6 to 1.0 Gm.) is given with the Apresoline. Phenobarbital 32 to 50 mg. seems to modify favorably the gastrointestinal symptoms. What you mean by a "substantial number" not being able to take Apresoline depends on the criteria selected for intolerance. Seventy per cent of those who take the drug have some side reactions but less than 10 per cent find them intolerable. Another 10 per cent continue to have mild symptoms but not severe enough to prevent continuing treatment. The 30 per cent of patients who have no symptoms and the remainder who become adjusted to the drugs hardly constitutes a "substantial proportion" of patients who cannot tolerate Apresoline.

A Physician: Dr. Taylor, you have not said anything about the use of the veratrum preparations, such as Veriloid and protoveratrine, nor have you mentioned potassium sulfocyanate. Would you give us your opinion about these preparations?

Dr. Taylor: There is much evidence from our laboratory that veratrum alkaloids elicit hypotension by a mechanism somewhat similar to that of Apresoline. Unfortunately, the nausea producing and therapeutic doses are so
close that it is only in the exceptional patient
that significant, long lasting reduction of
arterial pressure is achieved. In our series of
several hundred patients, only three could take
the drug in amounts sufficient to lower average
blood pressure and not induce vomiting. The
long term results also have not been especially
encouraging. Our experience with proto-
veratrine is that the results do not differ
greatly from those of Veriloid itself.

A Physician: Dr. Page, would you give us
your opinion about the use of thiocyanate, and
sodium nitroprusside. I believe you introduced
the latter drug several years ago.

Dr. Page: As I have pointed out many
times, thiocyanate often is a sovereign drug
for treatment of intractable hypertensive head-
aches. Treatment may be started with an
initial intravenous dose of 1.5 Gm. of the
sodium salt and then the blood level kept at
from 3 to 5 mg. by oral thiocyanate when
headache alone is being treated. If the hypo-
tensive effect is also desired then the level in
the blood should be raised to 8 to 12 mg. per
100 ml. It is essential that the amount in the
blood be measured at regular intervals if the
drug is to be used. Guessing the blood level is
courting disaster!

Sodium nitroprusside is slowly converted in
the blood to thiocyanate, hence the dosage can
be followed by blood thiocyanate determina-
tions. For the best results, we try to attain
levels of 12 to 15 mg. per 100 ml. For acute
episodes of encephalopathy, or great rises in
arterial pressure, it may be given by intra-
venous drip, the amount given depending on
the level of pressure desired. It is given orally
in capsules (30 mg. four times a day) and in
some patients average arterial pressure is
reduced when other drugs have failed. It is
another drug which requires much more study
and chemical modification to determine if it
can or cannot be improved.

And lastly, lumbodorsal sympathectomy
should be considered. Though it is an old
treatment relative to the rush and trouble of
modern research, it has been used for only
some 20 years. Some of you remember the
bitterness with which most of this early work
was greeted. Some of it was bad work, but not
all of it. I think we should not forget the
part played by the team of Alfred Adson, now
deceased, and Edgar Allen. They were the
pioneers and shared their early meager knowl-
edge freely with the rest of us. While we no
longer do many sympathectomies at the
Clinic, still my opinion is that the operation is
often very valuable. Dr. Corcoran, who has
been so long associated with this work, has
held some strong views on sympathectomy and
will be glad, I am sure, to present them to you.
Incidentally, I should point out that his
measurements of renal blood flow before and
after sympathectomy were the first to be done,
and showed that renal ischemia was not
relieved by the operation. Even when, for one
reason or another, a pre-existing ischemia was
abolished, there was no obligatory fall in
blood pressure.

Dr. Corcoran: Those few measurements
indicated that lumbodorsal sympathectomy
did not necessarily increase renal blood flow or
relieve "renal ischemia." Many measurements
have confirmed this. However, one should not
overlook the occasional patient in whom
sympathectomy has greatly relieved hyper-
tension, remitted the progress of nephrosclero-
sis and resulted in decreased renal vascular
resistance.

As you suggested earlier, Dr. Page, the
problem is basically one of selection. When
once we find a means of detecting the 10 per
cent who will respond dramatically and
persistently to the operation, it will be a great
day for patients and surgeons alike. Until
then, both are bound to meet disappointments;
surgeons are congenital optimists, so they are
the less affected; the internists see the disap-
pointing results.

As a generalization then, until such means
are found, the operation can only be justified
in very special situations, largely because with
diet, Apresoline and methionium we have
available means of treatment which are less
expensive, less traumatic, more certain. There
is also the possibility that other still better
nonsurgical procedures will come out of the
laboratories into the clinics.

Your and Dr. McCubbin’s proposed mode of
selection for sympathectomy by demonstration
of repetitive deep depressor responses to tetrathylammonium chloride has unfortunately never been adequately tested. I wish someone would do that. But, as I suggest, with the means now available for the relief of hypertension, I doubt that we would be justified in advising sympathectomy for this reason alone.

A Physician: Dr. Page, one of the most difficult decisions concerns the type of treatment one will use when a patient with hypertension comes under his care. Do you have any ideas about the kind of patients whose blood pressure will respond most satisfactorily to a specific medication or do you have to determine the response by trial? I think it would help those of us who have not had the great experience that you and your associates have had in the treatment of hypertension if you would outline your plans of treatment for the patient whose case history was presented earlier in this conference.

Dr. Page: You have touched on one of the most important problems in the field of hypertension. I know of no method short of trial to select those patients who will respond to a particular treatment. Think what it would mean if a 95 per cent success was achieved after proper selection for sympathectomy. This is one of the more important practical reasons why the various mechanisms of this clinical mosaic need be understood.

The best we can now do is to determine the rate at which vascular disease is advancing and then decide whether a more or less drastic regimen is to be recommended. In the particular patient presented this morning, we would first put him on a low-salt diet, then give Apresoline. If he failed to respond to the latter, hexamethonium would be tried and lastly, sympathectomy.

I think you will all realize that both from the diagnostic and the therapeutic viewpoint, advances have been made in the past decade. The old nihilistic approach has given way to a wave of optimism, and, I am glad to say, investigation of high order. But there is still much to be done, and we had all best get on with it by less talk and more work.
Management of Moderately Severe Arterial Hypertension
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