ARTERIAL HYPERTENSION— THIRTY-FOUR YEARS AGO AND NOW

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THIRTY-FOUR years ago many clinicians firmly believed that elevated blood pressure should not be lowered lest a reduced perfusion of the kidneys result in uremia. This dictum bequeathed by Cohnheim provided a useful excuse because there was no means available for lowering arterial pressure. Now thirty-four years later, there are many ways and some are quite satisfactory.

The first clue we had, and this is long forgotten, of the harmlessness of blood pressure reduction was that the urea clearance did not change when arterial pressure was lowered by, of all things, colloidal sulfur. The experiment was crude but it did show that an elevated blood pressure was not necessary or "essential," and that the kidneys possessed a remarkable capacity to readjust to change in perfusion pressure.

Let us hasten to add that we are telling a story of hypertension as two people see it. There are quite evidently other ways.

The next step in our thinking occurred when Dr. E. V. Allen of the Mayo Clinic told one of us that his neurosurgical colleague, Dr. Alfred Adson, had performed an anterior rhizotomy in a hypertensive patient, and the blood pressure had been sharply reduced. Forthwith, at our suggestion, Dr. George Heuer performed such an operation in a patient with malignant hypertension. The reason we selected a patient with the malignant form was that bitter experience showed how hopeless was its prognosis. To our great surprise, the patient survived the "yard-long" laminectomy; retinopathy disappeared; the heart size was reduced; the inverted T waves became upright; and blood pressure came down. This was the first reversal of malignant hypertension ever seen, and to do it we medical people used a surgeon as our journeyman and, as you will see, this was not the last time.

The story of the drug treatment of hypertension is long and tortuous, filled with complications and distress for both patient and physician. At one time we had the dubious distinction of creating a new disease for every new antihypertensive drug. The early use of ganglion-blocking drugs produced patients exhibiting maximum entropy; their world had turned cold and all but lifeless. Sympathetic function was suppressed, which was the mechanism of the antihypertensive effect, but it was the parasympathetic paralysis that was deadening. Patients breathed but their mouths were so dry that food was tasteless. They could not read because near vision was paralyzed, and although distant vision was maintained, few people had television to enjoy. They had atony of the stomach, intestines, and urinary bladder, and were impotent. Many had incapacitating orthostatic hypotension. This was a way of life, but that was about all. However, many patients did not experience such paralyzing side effects, and were relieved of the complications of hypertension.

Hydralazine showed us another method for lowering blood pressure. Reserpine followed, and broadened the approach to the mechanisms of hypertension. Then, chlorothiazide was introduced, and our group first explained the mechanism of the powerful synergistic action of this diuretic with other antihypertensive drugs. This happy circumstance allowed us to reduce antihypertensive drugs to amounts that did not produce the side effects that were so troublesome, but which we had come to accept as inevitable.

So with the passing years, the drugs have become better and we have become more sophisticated in their use. We now feel that good blood pressure control should be the rule, not the exception, and should be accomplished with a minimum of discomfort to the patient and of disruption to his life.

It has been 12 years since our first patients were treated with drugs with some degree of effectiveness. Now, we are finding that drug therapy may be withdrawn after a few years of good control without return of blood pressure to previous hypertensive levels. This beginning suggests that prolonged maintenance of supine blood pressure at normal levels in some people will so alter the regulatory mechanism that they reset at lower levels.

There have been many vastly important investigations into the mechanisms of hypertension, which slowly are providing us with understanding of the disease. Many of these studies have not as yet crystallized into a delineable pattern. It is clear, however, that many of the ingredients of the pattern are already known, though there are certainly more to come. These discoveries are the necessary background on which a field expands. One of the products has already made headlines and concerns the recognition of a form of renal hypertension due to disturbance of the blood supply of the kidneys. All divisions of the Cleveland Clinic have contributed to its understanding.

We now recognize occlusive renal arterial disease as a significant cause of hypertension. The fact that arterial reconstructions or nephrectomy often lowers arterial pressure in patients with such lesions lends a false aura of understanding to this particular type of hypertension, for the recognition has only added another to the list of renal hypertensions but has not explained its mechanism.

Disease of main renal arteries or their primary branch was suspected as a cause of hypertension after Goldblatt showed that renal arterial constriction produced hypertension in the dog. The clinical experience that followed quickly upon this discovery was disheartening, because in only about one quarter of the patients was arterial pressure lowered by nephrectomy. Two reasons are now apparent for these therapeutic failures. One was the inability to visualize renal arteries, and the other was misinterpretation of normal intravenous urograms.

The development of renal angiography as a feasible and safe procedure has been the major methodologic advance in the field of clinical renal hypertension. The impetus for its development came from the reports of Howard and co-workers, which showed that renal arterial stenosis could cause remediable hypertension and

could produce certain urographic abnormalities as well as disparity in function of the two kidneys.

At the present time the final diagnosis rests on renal angiography. However, since this is not a routine test, some guide lines are necessary for selecting patients in whom it should be done. To establish such guides, we recently reviewed the diagnostic features in 139 patients with occlusive renal arterial disease, and compared these with similar aspects in 127 patients thought to have essential hypertension. This analysis showed that urographic abnormalities occurred frequently in renal hypertensive patients, and were the most important indications for renal angiography. Difference in lengths of the two kidneys of one centimeter or greater, and difference in concentration of the radiopaque medium or the latter alone was found in 70 per cent, while such disparities were apparent in only 9 per cent of the essential hypertensive group. Important as these urographic abnormalities are, it must be recognized that patients with renal artery disease may have normal urograms, and that sometimes urographic films are not adequate for evaluation. It is in such patients that certain clinical features assume importance. These are malignant hypertension, sudden onset of hypertension after the age of 35 years, hypertension under the age of 35 years, and hypertension present for more than one year with sudden increase in the severity of vascular disease. These clinical features and urographic signs seem the hallmarks of hypertension associated with renal arterial stenosis for only in 2 of 70 patients in whom they were lacking, and hypertension was the only indication for renal angiography, were such lesions found.

The surgical treatment of this type of hypertension includes a variety of procedures that bypass or remove obstructive arterial segments. Only occasionally is nephrectomy the procedure of choice. The Cleveland Clinic experience with surgical therapy has shown remission of diastolic hypertension in 62 per cent of patients, substantial pressure decreases in 16 per cent, and no change in 22 per cent. The results are promising, but not enough time has passed to give a final evaluation of effectiveness of these operations.

For those individuals with renal arterial stenoses who are not considered subjects for surgical treatment, much can be gained by the use of antihypertensive drugs if hypertension is severe enough to warrant their use. Operations carry a high risk in patients with diffuse atherosclerosis and, therefore, do not seem justified. Further, there are those patients with segmental renal atrophy who are azotemic because of nephrosclerosis in the rest of the renal tissue and, in these, operations cannot be helpful.

To guess, we would suppose that we have traveled in the past 34 years something like a quarter of the length of the road. We can treat hypertension in most cases fairly effectively. We are beginning to find diagnostic criteria for some of the varied types of hypertension. We have some indications of the nature of the "mosaic" that describes the many mechanisms involved, but our knowledge is still fragmentary. We know that some types of hypertension are reversible, but our

understanding of the vascular disease associated with hypertension is abysmally primitive.

It is heartening to think that the course of a modern lifetime can span the formulation and at least partial solution of one of the most important health problems of mankind. It proves that science is a ponderous tool but with a sharp cutting edge.