HYPERTENSIVE DISEASE

Diagnosis and Treatment

BY

Sibley W. Hoobler, M.D.

ASSOCIATE PROFESSOR OF INTERNAL MEDICINE, UNIVERSITY OF MICHIGAN MEDICAL SCHOOL; DIRECTOR OF HYPERTENSION UNIT, UNIVERSITY OF MICHIGAN HOSPITAL

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Preface

Although the cause of essential hypertension is still a mystery, it is now possible to bring about effective reduction in the blood pressure level by appropriate treatment. Survival rates following sympathectomy, as well as daily experiences in the practical management of the disease, demonstrate that in the main blood pressure reduction is beneficial rather than harmful as once was thought. Three factors are primary in determining the survival of the patient with hypertension: (1) the height of the blood pressure, (2) the duration of its elevation, and (3) the vulnerability of the arterial system to the morbid process. Successful treatment has a dimension of time as well as magnitude.

The effective use of procedures for bringing the blood pressure temporarily under control is widespread in the United States today, but methods to maintain blood pressure reduction and to assess vascular vulnerability in this disease are little understood. This book is intended to bring to medical practitioners knowledge of those procedures that have been developed in special clinics for the treatment of hypertension. It is based largely on the author's ten years of experience as Director of the Hypertension Unit at the University of Michigan Hospital. All phases of patient management are included whether the treatment is given at home, at the office, or in the hospital.

The first two sections of the book describe criteria for the recognition of secondary forms of hypertension and give recommendations for the treatment of those types susceptible to cure. The three sections that follow are devoted to the diagnosis and treatment of primary hypertension and its complications and include a thorough discussion of the principles underlying treatment. Specific treatment regimens designed to reduce the blood pressure are considered, giving the pharmacodynamics, advantages, and disadvantages of particular therapeutic agents, as well as

discussing operative procedures and other methods of treatment. The twelve Appendixes contain precise details and techniques for tests and for treatment, including the handling of hypertensive emergencies. This section was designed to be of maximum aid to the physician for quick reference. Specific instructions are given for the choice of patient, drug dosage, contraindications and side effects, and total patient management. Throughout the text of the book case histories have been incorporated to emphasize the clinical viewpoint.

The management of patients with hypertension has entered a phase not unlike that which confronted the physician when insulin first became available for diabetes. Success in treatment requires a high degree of understanding and co-operation on the part of patient and physician. The practical difficulties in the way of long-term management should be looked upon as a challenge to devise more convenient and logical techniques for using available drugs. It is hoped that this book, with its clinical emphasis, will be of assistance to the physician in the effective treatment of his patients with hypertensive disease.

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S. W. H.

Ann Arbor

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SECTION I

SECONDARY HYPERTENSION SUSCEPTIBLE TO CURE

CHAPTER 1

"Curable" Renal Hypertension

Immediately following Doctor Goldblatt's epochal report of the production of experimental renal hypertension in the dog by partially clamping one or both renal arteries (Goldblatt, 1934), physicians began to identify the apparent clinical counterpart, and in cases of unilateral renal disease, nephrectomy was advised. Disappointment over the frequent failure of this procedure to lower the blood pressure led to a period of skepticism, but two recent reviews leave little doubt that in the properly selected case a permanent cure can be effected (Smith, 1956; Thompson, 1957). The diagnosis of this condition has been made with greater frequency since it has been recognized that aortography might reveal renal vascular lesions not suspected from intravenous pyelograms (Poutasse, 1956a).

In the dog, clamping one renal artery leads to transient hypertension that can be made permanent only by contralateral renal artery constriction or nephrectomy. In the rat, obstructing the blood supply to one kidney often leads to sustained hypertension. Removal of this kidney restores normotension as long as the contralateral kidney is free of hypertensive vascular disease (Byrom, 1949). In man as in the rat, partial obstruction of one renal artery may give rise to sustained hypertension, and removal of the kidney or of the arterial obstruction has relieved hypertension that has been present for as long as 6 years (Poutasse, 1956a; Margolin, 1957). On the other hand, hypertension from a unilateral renal lesion may produce sufficient

vascular damage in the contralateral kidney to perpetuate the hypertension after removal of the initially offending kidney. Even in the presence of considerable impairment of contralateral renal function, however, reduction of the blood pressure by removing the abnormally perfused kidney may, over a period of many months, result in gradual improvement of the contralateral kidney with restoration of normal renal function (Imber, 1955).

In man, a great variety of curable renal lesions has been described, but in general they may be placed in four categories:

1. Obstructive lesions of the renal vessels
2. Old, healed pyelonephritis
3. Obstruction of the ureters on one or both sides
4. Lesions causing shrinkage or interference with the renal capsule (Wilms tumor, renal hematoma, irradiation of the kidney, etc.)

CLINICAL FEATURES OF HYPERTENSION OF CURABLE RENAL ORIGIN

The clinical aspects of *obstructive arterial lesions* are well reviewed by Margolin, Merrill, and Harrison (1957). Such a lesion may be suspected when there is a record of the sudden onset of extreme polyuria or dysuria, when albuminuria is prominent, or when one kidney is smaller than the other. When a sudden severe rise in the blood pressure occurs in a patient who was known to be normotensive in the previous two or three years, and especially when this patient is without a family history of hypertension, a curable renal vascular lesion is to be suspected. Perera (1952) maintains that since essential hypertension always develops before the later years of life, renal hypertension is to be suspected when an elderly person with a previous history of normal blood pressure experiences the sudden onset of marked hypertension. Finally, total vascular obstruction with consequent renal infarction may lead to elevation of the blood pressure, as in the case reported by Howard (1954) in which the occlusion caused severe back pain and was followed by hypertension.

When there is a history of *pyelonephritis* or other urinary tract infection, one should consider the possibility of a curable renal lesion. Although the disease is often bilateral, intravenous and

retrograde pyelograms may be necessary to establish this fact. Severe hypertension caused by a unilateral healed pyelonephritis is frequently unaccompanied by a characteristic history and is detected only by pyelographic studies.

Obstructive lesions of the ureters are an exceptional cause of hypertension. Total complete obstruction of one or both ureters rapidly results in pressure atrophy of the kidney without elevation of the blood pressure. Partial obstruction, if it develops gradually, may cause hypertension and be found without oliguria or anuria, either because the obstruction is unilateral or because a high intrapelvic pressure may force urine past a bilateral obstruction. Such a syndrome has been seen in a few cases in our clinic, once as a result of ureteral obstruction following extensive x-ray therapy to the pelvic region, once following carcinomatous infiltration of the ureter, and once in a young man with a congenital urethral valve. A most interesting case in which this mechanism may have been involved has been described by Dr. Reed Nesbit (1958). The patient was a young girl with vesico-ureteral backflow evident on cystograms. The child was able to go for as long as 24 hours without voiding because of the large capacity of the bladder, ureter, and kidney pelvis. When she was trained to void regularly at 2-hour intervals, the ureteral reflux disappeared and the hypertension subsided. Although the relationship between hypertension and renal disease in this case is more doubtful than in the others cited, these scattered experiences indicate the importance of investigating the renal excretory system in obscure cases of severe and unusual hypertension.

In the varied forms of hypertension secondary to unilateral renal disease, there are no unusual *physical findings,* except that the blood pressure elevation may vary from mild to severe, is usually rapidly progressive, and commonly is associated with marked retinopathy. Smithwick (1957) has reported that a reduction in blood pressure on assuming the erect posture is common in renal hypertension.

Routine *laboratory findings* are not diagnostic, although a tendency to leukocytosis has been described (Margolin, 1957). The urine may be entirely normal or, if polyuria and nocturia are the complaints, the urine concentrating ability may be impaired.

Albuminuria and signs of infection may or may not occur. The renal function varies from near normal to the range of azotemia.

SPECIAL DIAGNOSTIC PROCEDURES

Intravenous pyelograms are required in severe hypertension to exclude a unilateral renal origin (Table 1). They should be performed in all cases of recent onset in which the disease is definitely established. When the hypertension is of long duration, the question is often raised whether it is worthwhile to perform pyelograms since chronic renal hypertension rarely responds to nephrectomy. However, previously mild hypertension may have been aggravated by the more recent development of a curable renal vascular lesion. Furthermore, since some cases of more than 5 years' duration have been reported to be cured by nephrectomy (Margolin, 1957), it is not impossible that pyelography may lead to the discovery of a curable renal lesion even in cases of prolonged hypertension.

When hypertension is accompanied by renal excretory insufficiency, pyelography is useless since the kidneys will not visualize. If a unilateral renal lesion had initiated the hypertension in such a case, it may be argued that the contralateral kidney has become so diseased as to render the condition irreversible even following removal of the originally involved kidney. Occasionally, however, special studies are advisable in hypertension accompanied by azotemia. When there is a possibility that the unilateral renal lesion was of very recent origin as in the case described by Imber (1955), or when bilateral obstructive uropathy is a possibility, certain renal investigations may be justified. Abdominal x-rays may indicate the size of the kidneys or the presence of ureteral calculi or other cause of obstruction. Aortograms are generally contraindicated by the danger of aggravating the renal insufficiency. Retrograde investigations are dangerous and should be avoided unless there is real likelihood of making a diagnosis that can lead to successful treatment.

Intravenous pyelograms may reveal distortion or displacement of one kidney, or provide evidence of decreased size or of absence of visualization on one side. The x-ray findings most likely to be significant, in order of descending importance, are: (1) a

TABLE 1. "CURABLE" UNILATERAL RENAL HYPERTENSION—DIAGNOSTIC FEATURES

Clinical features	*Pathological aspects*	*I.V. Pyelograms*	*Aortograms indicated*
Recent onset of severe hypertension	Renal artery obstruction	Not always diagnostic	Yes
Hypertension with papilledema in elderly patients	Arteriosclerotic renal obstruction	Not always diagnostic	Yes
Hypertension after back pain or hematuria	Renal infarction	Not always diagnostic	Yes
All children with severe hypertension	Varied	Not always diagnostic	Yes
Chronic severe hypertension	Old chronic unilateral pyelonephritis	Nonvisualization or very small kidney	No, retrograde pyelograms first choice
	or		
	Renal artery obstruction, or infarction	Kidney size somewhat reduced or poorly visualized	Yes
	or		
	Hydronephrosis from aberrant renal artery or calculous obstruction	Hydronephrosis or ureteral abnormality	No, retrograde pyelograms

In azotemia or hypertension exceeding 5 years, cure is improbable. (See text for details.)

renal shadow less than 80 per cent of the size of its counterpart, (2) nonvisualization on one side, (3) delayed or distinctly reduced excretion of contrast medium on one side, and (4) evidence suggesting unilateral hydronephrosis or pyelonephritis.

In certain situations pyelograms will appear to be normal despite the presence of a partial unilateral renal arterial obstruction causing hypertension. This follows from the fact that a pyelogram shows only very grossly the excreted radiopaque medium, and the density of the shadow is further dependent on urine flow, ureteral peristalsis, overlying intestinal shadows, and other factors. These may influence the comparative renal density far more than a partial reduction in the inflow of blood. Since the kidney excretes in a single circulation all contrast medium that perfuses it, it is evident that a dense excretory shadow can rapidly appear even when blood flow to one kidney is deficient.

If further study seems indicated, *retrograde pyelography* may be considered. When one kidney is not visualized on intravenous pyelograms, agenesis must be excluded. Failure to find a ureteral orifice on retrograde cystoscopic examination is most helpful in this situation. However, this procedure should be withheld unless the hypertension is serious, in which case appropriate antibiotic premedication should be carried out to prevent possible infection of the single kidney. If the ureters can be entered, retrograde pyelograms are the best means for demonstrating obstructive uropathy or an old pyelonephritis. Vascular lesions, however, are less likely to be demonstrated by this procedure. When retrograde examination is performed, the renal function of each kidney should be determined separately and with the greatest possible accuracy. Unfortunately, random variations in urine flow and leakage around the catheter often make it difficult to be certain of comparative renal function on the two sides. However, the appearance time of an indicator such as phenolsulfonphthalein or indigo carmine, when urine flow has been accelerated by a high fluid intake, may indicate comparative renal functions. Similarly, the sodium and creatinine concentrations of ureteral urine are also independent of leakage around the catheters. This examination has recently been advocated for identifying a unilateral arterial obstruction on the basis of the fact that in a kidney with reduced renal arterial pressure, sodium reabsorption is increased (Howard, 1954). However, this pro-

cedure appears less reliable than aortography in identifying vascular obstructive lesions (Dustan, 1957).

Aortography is generally more useful than retrograde pyelography as a diagnostic technique. The indications for this examination are outlined in Table 1. The procedure carries some risk, however, and should not be performed unless the hypertension is severe enough to justify nephrectomy should a lesion be found. This criterion applies even more forcibly when renal failure is actual or impending. The procedure will not ordinarily distinguish between renal agenesis and an old atrophic pyelonephritis. For this purpose retrograde studies are preferable. Aortography is useful in studying those patients with severe hypertension of recent onset who have apparently normal intravenous pyelograms, and in investigating further all those with borderline pyelographic abnormalities, in whom the hypertension is severe enough to justify nephrectomy if a unilateral lesion were found.

Renograms, in which renal uptake of I^{131} labeled Diodrast is compared by external counting over both kidneys, has also proved useful in identifying cases of renal ischemia (Winter, 1957).

Needle biopsy of the kidney has been of great investigative and occasional therapeutic value in locating a pyelonephritic lesion that is causing hypertension but is not reflected in urinary findings (Kark, 1955). Such lesions are usually bilateral. The area may be missed by the needle; consequently, a negative biopsy report does not exclude pyelonephritis. The procedure is not likely to influence the physician's treatment frequently enough to justify its routine use in identifying a renal lesion possibly causing hypertension.

TREATMENT OF UNILATERAL RENAL LESIONS

Treatment for such renal lesions as have been described above usually consists in nephrectomy or replacing the obstructed renal artery with a vascular graft. The former is preferred when the kidney reveals very poor function; the latter is useful when good renal function is present, the surgeon is skillful, and the obstruction is not too close to the aorta. The use of vascular transplants as reported by Poutasse (1956) is particularly valuable, since