

# Renovascular Hypertension and Ischemic Nephropathy

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The major issues in approaching patients with renal artery stenosis relate to the role of renal artery stenosis in the management of hypertension, *ie*, “renovascular hypertension,” and to the potential for vascular compromise of renal function, *ie*, “ischemic nephropathy.” Ever since the original Goldblatt experiment in 1934, wherein experimental hypertension was produced by renal artery clamping, countless investigators and clinicians have been intrigued by the relationship between renal artery stenosis and hypertension. Much discussion has focused on the pathophysiology of renovascular hypertension, the renin angiotensin system, diagnostic tests to detect presumed renovascular hypertension, and the relative merits of surgical renal revascularization (SR), percutaneous transluminal renal angioplasty (PTR), and drug therapy in managing patients with renal artery stenosis and hypertension. Hemodynamically significant renal artery stenosis, when bilateral or affecting the artery to a solitary functioning kidney, can also lead to a reduction in kidney function (ischemic nephropathy). This untoward observation may be reversed by interventional maneuvers, *eg*, surgical renal revascularization, PTR, or renal artery stenting. The syndrome of “ischemic renal disease” or “ischemic nephropathy” now looms as an important clinical condition and has attracted the fascination of nephrologists, vascular surgeons, and interventional cardiologists and radiologists.

The detection of renal artery stenosis in a patient with hypertension usually evokes the assumption that the hypertension is due to the renal artery stenosis. However, renal artery stenosis is not synonymous with “renovascular hypertension.” On the basis of autopsy studies and clinical angiographic correlations, high-grade atherosclerotic renal artery stenosis (ASO-RAS) in patients with mild blood pressure elevation or in patients with normal arterial pressure is well recognized. The vast majority of patients with ASO-RAS who have hypertension have essential hypertension, not renovascular hypertension. These hypertensive patients with ASO-RAS are rarely cured of their hypertension by interventional procedures that either bypass or

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dilate the stenotic lesion. Thus, it is critical to distinguish between the anatomic presence of renal artery stenosis, in which a stenotic lesion is present but not necessarily causing hypertension, and the syndrome of renovascular hypertension in which significant arterial stenosis is present and sufficient to produce renal tissue ischemia and initiate a pathophysiologic sequence of events leading to elevated arterial pressure. In the final analysis, proof that a patient has the entity of “renovascular hypertension” rests with the demonstration that the hypertension, presumed to be “renovascular,” can be eliminated or substantially ameliorated following removal of the stenosis by surgical or endovascular intervention, or by removing the kidney distal to the stenosis.

Although the great majority of patients diagnosed as having renovascular hypertension have this syndrome because of main renal artery stenosis, hypertension following unilateral renal trauma,

chronic subcapsular hematoma, and unilateral ureteral obstruction may also be associated with hypertension that is relieved when the affected kidney is removed. These clinical analogues of the experimental Page kidney reflect the syndrome of renovascular hypertension (RVHT), but without main renal artery stenosis. Takayasu’s arteritis and atheroembolic renal disease are additional examples of RVHT without main renal artery stenosis. Accordingly, the anatomic presence of renal artery stenosis should not be equated with renovascular hypertension and the syndrome of RVHT need not reflect renal artery stenosis.

This chapter reviews the types of renal arterial disease associated with RVHT, the pathophysiology of RVHT, clinical features and diagnostic approaches to renal artery stenosis and RVHT, evolving concepts regarding ischemic nephropathy, and management considerations in patients with renal artery stenosis, presumed RVHT, and ischemic renal disease.

### CLASSIFICATION OF RENAL ARTERY DISEASE

| Disease           | Incidence, %* |
|-------------------|---------------|
| Atherosclerosis   | 60–80         |
| Fibrous dysplasia | 20–40         |
| Medial (30%)      |               |
| Perimedial (5%)   |               |
| Intimal (5%)      |               |

\*Percent of renal artery lesions.

**FIGURE 3-1**

Classification of renal artery disease. Two main types of renal arterial lesions form the anatomic basis for renal artery stenosis. Atherosclerotic renal artery disease (ASO-RAD) is the most common cause of renal artery disease, accounting for 60% to 80% of all renal artery lesions. The fibrous dysplasias are the other major category of renal artery disease, and as a group account for 20% to 40% of renal artery lesions. Arterial aneurysm and arteriovenous malformation are rarer types of renal artery disease.



**FIGURE 3-2**

Angiographic examples of atherosclerotic renal artery disease (ASO-RAD). **A**, Aortogram demonstrating severe nonstrial atherosclerotic renal artery disease of the left main renal artery. **B**, Intra-arterial digital subtraction aortogram showing severe proximal right renal artery stenosis (ostial lesion) and moderately severe narrowing of the left renal artery due to atherosclerosis.

Atherosclerotic renal artery disease is typically associated with atherosclerotic changes of the abdominal aorta (see *panel B*). ASO-RAD predominantly affects men and women in the fifth to seventh decades of life but is uncommon in women under the age of 50. Anatomically, the majority of these patients demonstrate atherosclerotic plaques located in the proximal third of the main renal artery. In the majority of cases (70% to 80%), the obstructing lesion is an aortic plaque invading the renal artery ostium (ostial lesion). Twenty to 30 percent of patients with ASO-RAD demonstrate atherosclerotic narrowing 1 to 3 cm beyond the takeoff of the renal artery (nonostial lesion). Nonostial lesions are technically more amenable to percutaneous transluminal renal angioplasty (PTRA) than ostial ASO-RAD lesions, which are technically difficult to dilate and have a high restenosis rate after PTRA. Renal artery stenting has gained wide acceptance for ostial lesions. Endovascular intervention for nonostial lesions includes both PTRA and stents. Surgical renal revascularization is used for both ostial and nonostial ASO-RAD lesions. (From Pohl [1]; with permission.)

## NATURAL HISTORY OF ATHEROSCLEROTIC RENOVASCULAR DISEASE: REPORTS OF SERIAL ANGIOGRAMS

| First author | Year | Months of follow-up, n/n | Patients, n | Progression, n (%) | Total occlusion |
|--------------|------|--------------------------|-------------|--------------------|-----------------|
| Wollenweber  | 1968 | 12/88                    | 30          | 21 (70)            | NA              |
| Meaney       | 1968 | 6/120                    | 39          | 14 (36)            | 3 (8)           |
| Dean         | 1981 | 6/102                    | 35          | 10 (29)            | 4 (11)          |
| Schreiber    | 1984 | 12/60                    | 85          | 37 (44)            | 14 (16)         |
| Tollefson    | 1991 | 15/180                   | 48          | 34 (71)            | 7 (15)          |
| Total        |      |                          | 237         | 116 (49)           | 28 (14)         |

FIGURE 3-3

Natural history of atherosclerotic renovascular disease. Retrospective studies, based on serial renal angiograms, suggest that atherosclerotic renal artery disease (ASO-RAD) is a progressive disorder. This figure summarizes *retrospective* series on the natural history of ASO-RAD. A large series from the Cleveland Clinic in nonoperated patients indicated progression of renal artery obstruction in 44%; progression to total occlusion occurred in 16% of these patients. Reduction in ipsilateral renal size is associated with angiographic evidence of progression in contrast to patients with nonprogressive (angiographically) ASO-RAD.

Zierler and coworkers have prospectively studied the progression of ASO-RAD by sequential duplex ultrasonography. The

cumulative incidence of progression of lesions with less than 60% reduction in lumen diameter progressing to more than 60% reduction in lumen diameter was 30% at 1 year, 44% at 2 years, and 48% at 3 years. Progression to total occlusion occurred only in arteries with a baseline reduction in lumen diameter of more than 60%. The cumulative incidence of progression to total occlusion in patients with baseline stenosis of 60% or greater was 4% at 1 year, 4% at 2 years, and 7% at 3 years. Blood pressure control and serum creatinine were not predictors of progression. The risk of renal parenchymal atrophy over time in kidneys with ASO-RAD has also been described. (*Table adapted from Rimmer and Gennari [2]; with permission.*)

## FREQUENCY AND NATURAL HISTORY OF FIBROUS RENAL ARTERY DISEASES

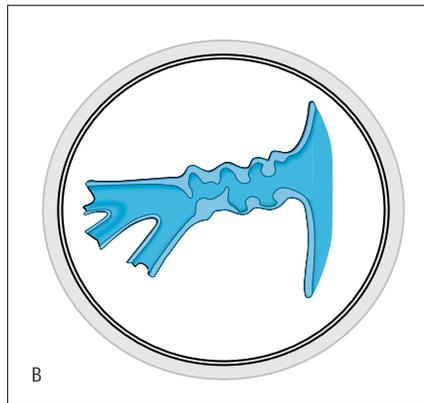
| Lesion                                     | Frequency, %* | Risk of progression | Threat to renal function |
|--|---------------|---------------------|--------------------------|
| Intimal fibroplasia and medial hyperplasia | 10            | ++++                | ++++                     |
| Perimedial fibroplasia                     | 10–25         | ++++                | ++++                     |
| Medial fibroplasia                         | 70–85         | ++                  | —                        |

\*Frequency relates to frequency of only the *fibrous* renal artery diseases.

FIGURE 3-4

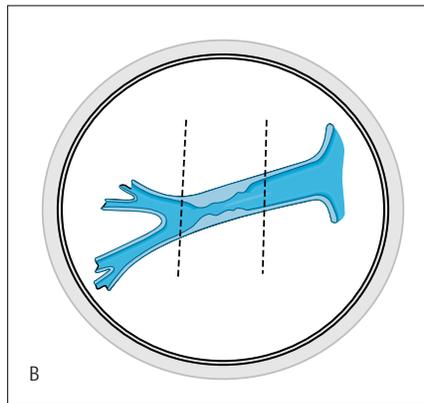
Frequency and natural history of fibrous renal artery diseases. There are four types of fibrous renal artery disease (fibrous dysplasias): medial fibroplasia, perimedial fibroplasia, intimal fibroplasia, and medial hyperplasia. Although the true incidence of these specific types of fibrous renal artery disease is not clearly defined, medial fibroplasia is the most common, estimated to account for 70% to 85% of fibrous renal artery disease. The majority of patients with medial fibroplasia are almost exclusively women who are diagnosed between the ages of 25 to 50 years. Although medial fibroplasia progresses to higher degrees of stenosis in about one third of cases, complete arterial occlusion or ischemic atrophy of the involved kidney is rare. Intervention on this type of fibrosis dysplasia is for relief of hypertension because the threat of progressive medial fibroplasia to renal function is negligible. Perimedial fibroplasia is

the second most common type of fibrous dysplasia, accounting for 10% to 25% of fibrous renal artery lesions. This lesion also occurs predominantly in women, is diagnosed between the ages of 15 and 30, is frequently bilateral and highly stenotic, and may progress to total arterial occlusion. These patients should undergo surgical renal revascularization to relieve hypertension and to avoid loss of renal function. Intimal fibroplasia and medial hyperplasia (usually indistinguishable angiographically) are not common, accounting for only 5% to 10% of fibrous renal artery lesions. Intimal fibroplasia occurs primarily in children and adolescents. Medial hyperplasia is found predominantly in adolescents; angiographically it appears as a smooth linear stenosis that may extend into the primary renal artery branches. Medial hyperplasia, like intimal fibroplasia, is a progressive lesion and is associated with ipsilateral renal atrophy. Surgical renal revascularization is recommended for patients with either intimal fibroplasia or medial hyperplasia to avoid lifelong antihypertensive therapy and to avert renal atrophy.

**FIGURE 3-5**

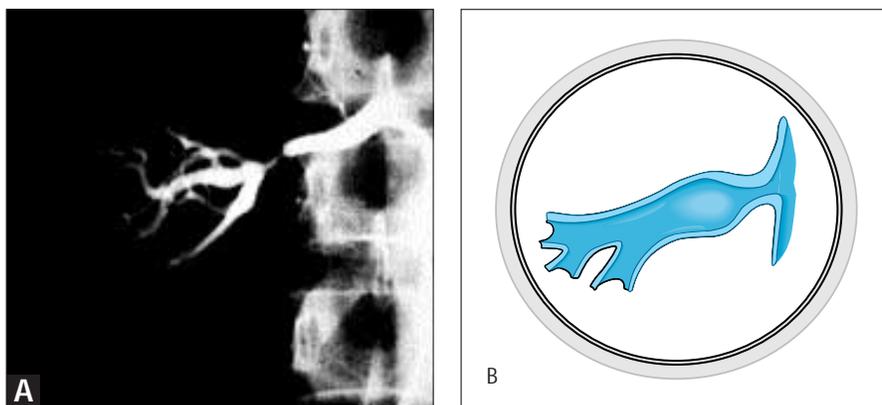
Arteriogram and schematic diagrams of medial fibroplasia. **A**, Right renal arteriogram demonstrating weblike stenosis with interposed segments of dilatation (large beads) typical of medial fibroplasia ("string of beads" lesion). **B**, Schematic diagram of medial fibroplasia.

The lesion of medial fibroplasia characteristically affects the distal half of the main renal artery, frequently extending into the branches, is often bilateral, and angiographically gives the appearance of multiple aneurysms ("string of beads"). Histologically, this beaded lesion is characterized by areas of proliferation of fibroblasts of the media surrounded by fibrous connective tissue (stenosis) alternating with areas of medial thinning (aneurysms). Inspection of the renal angiogram in *panel A* indicates that the width of areas of aneurysmal dilatation is wider than the nonaffected proximal renal artery, an angiographic clue to medial fibroplasia. (*Panel A* from Pohl [1]; with permission.)

**FIGURE 3-6**

Arteriogram and schematic diagram of perimedial fibroplasia. **A**, Selective right renal arteriogram shows a tight stenosis in the mid portion of the renal artery with a small string of beads appearance, typical of perimedial fibroplasia. **B**, Schematic diagram of perimedial fibroplasia.

Perimedial fibroplasia, accounting for 10% to 25% of the fibrous renal artery diseases, is also observed almost exclusively in women. The stenotic lesion occurs in the mid and distal main renal artery or branches and may be bilateral. Angiographically, serial stenoses are observed with small beads, which are smaller in diameter than the unaffected portion of the renal artery. This highly stenotic lesion may progress to total occlusion; collateral blood vessels and renal atrophy on the involved side are frequently observed. Pathologically, the outer layer of the media varies in thickness and is densely fibrotic, producing a severe reduction in lumen diameter (*panel B*). Renal artery dissection and/or thrombosis are common. (*Panel A* from Pohl [1]; with permission.)

**FIGURE 3-7**

Arteriogram and schematic diagram of intimal fibroplasia. **A**, Selective right renal arteriogram demonstrating a localized, highly stenotic, smooth lesion involving the distal renal artery, from intimal fibroplasia. **B**, Schematic diagram of intimal fibroplasia.

Intimal fibroplasia occurs primarily in children and adolescents and angiographically gives the appearance of a localized, highly stenotic, smooth lesion, with post-stenotic dilatation. It may occur in the proximal portion of the renal artery as well as in the mid and distal portions of the renal artery, is progressive, and is occasionally associated with dissection or renal infarction. Pathologically, idiopathic intimal fibroplasia is due to a proliferation of the intimal lining of the arterial wall. Intimal fibroplasia of the renal artery may also occur as an event secondary to atherosclerosis or as a reactive intimal fibroplasia consequent to an inciting event such as prior endarterectomy or balloon angioplasty. (Panel A from Pohl [1]; with permission.)

#### ATHEROSCLEROTIC RENAL ARTERY DISEASE VERSUS MEDIAL FIBROPLASIA

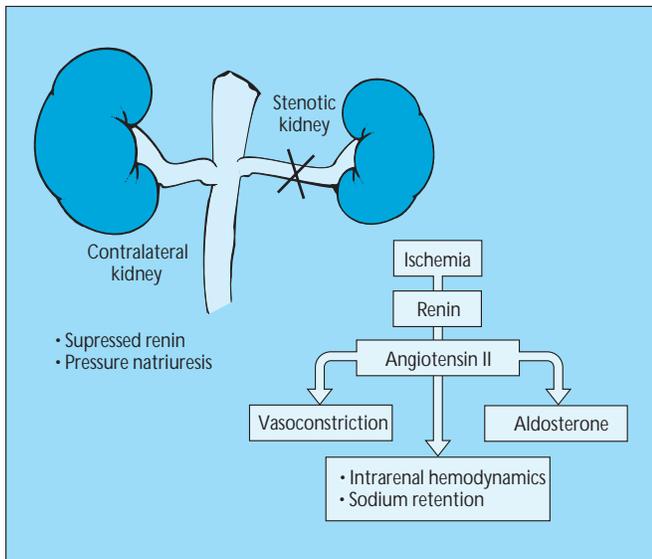
| Atherosclerotic  | Medial fibroplasia   |
|--|--|
| Men and women  | Women  |
| Age >50–55 y   | Age 20–40 y  |
| Total occlusion common   | Total occlusion rare   |
| Ischemic atrophy common  | Ischemic atrophy rare  |
| Surgical intervention or angioplasty:<br>Mediocre cure rates of the hypertension<br>Less amenable to PTRAs | Surgical intervention or angioplasty:<br>Good cure rates of the hypertension<br>More amenable to PTRAs |

**FIGURE 3-8**

A comparison of atherosclerotic renal artery disease and medial fibroplasia. The most common types of renal artery disease (atherosclerotic renal artery disease [ASO-RAD] and medial fibroplasia) are compared here. In general, ASO-RAD is observed in men and women older than 50 to 55 years of age, whereas medial fibroplasia is observed primarily in younger white women. Total occlusion of the renal artery and, hence, atrophy of the

kidney beyond the stenosis are relatively common with ASO-RAD, but ischemic atrophy of the kidney ipsilateral to the medial fibroplasia lesion is rare. Surgical intervention or percutaneous transluminal renal angioplasty (PTRAs) typically produce good cure rates for the hypertension in medial fibroplasia and these lesions are technically quite amenable to PTRAs. In contrast, ASO-RAD is, technically, much less amenable to PTRAs (particularly ostial lesions), and surgical intervention or PTRAs produce mediocre-to-poor cure rates of the hypertension. ASO-RAD and medial fibroplasia may cause hypertension and when the hypertension is cured or markedly improved following intervention, the patient may be viewed as having “renovascular hypertension.” This sequence of events is far more likely to occur in patients with medial fibroplasia than in patients with ASO-RAD. ASO-RAD and medial fibroplasia involve both main renal arteries in approximately 30% to 40% of patients.

## Pathophysiology of Renovascular Hypertension

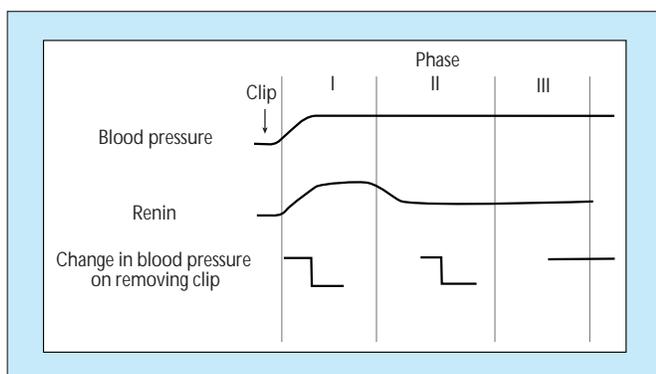


**FIGURE 3-9**

Schematic representation of renovascular hypertension. Renovascular hypertension may be defined as the secondary elevation of blood pressure produced by any of a variety of conditions that interfere with the arterial circulation to kidney tissue and cause renal ischemia. Almost always, renovascular hypertension is caused by obstruction of the renal artery or its branches, and demonstration of causality between the renal artery lesion and the hypertension is essential to this definition.

This diagram shows the classic model of two-kidney, one clip (2K,1C) Goldblatt hypertension, wherein one renal artery is constricted and the contralateral kidney is left intact. In the presence of hemodynamically sufficient unilateral renal artery stenosis, the kidney distal to the stenosis is rendered ischemic, activating the renin-angiotensin system, and producing high levels of angiotensin II, causing a “vasoconstrictor” type of hypertension. Numerous studies have established the causal relationship between angiotensin II-mediated vasoconstriction and hypertension in the early phase of this experimental model. In addition, the high levels of angiotensin II stimulate the adrenal cortex to elaborate larger amounts of aldosterone such that the “stenotic kidney” demonstrates sodium retention. This secondary aldosteronism also produces hypokalemia. The degree of renal artery stenosis necessary to produce hemodynamically significant reductions in perfusion, triggering renal ischemia and activation of the renin-angiotensin system, generally does not occur until a reduction of 80% or more in both lumen diameter and cross-sectional area of the renal artery takes place. Lesser degrees of renal artery constriction do not initiate this sequence of events.

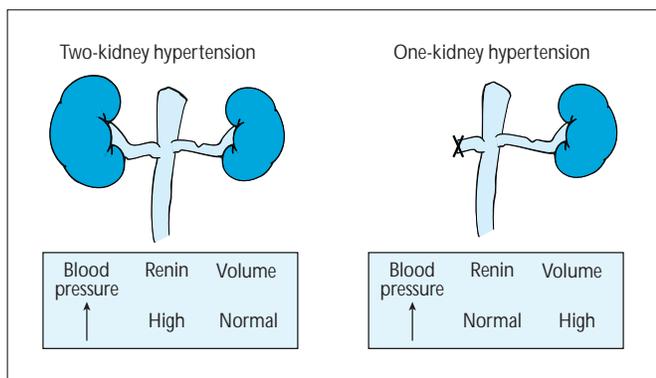
This model of 2K,1C Goldblatt hypertension implies that the contralateral (nonaffected) kidney is present, and that its renal artery is not hemodynamically significantly narrowed. As illustrated, the “contralateral kidney” demonstrates suppressed renin production and undergoes a pressure natriuresis, presumably because of angiotensin II-initiated vasoconstriction and sodium retention, leading to systemic elevation of blood pressure that then results in suppression of renin release and enhanced excretion of sodium (pressure natriuresis) by the “contralateral kidney.”

**FIGURE 3-10**

Sequential phases in two-kidney, one-clip (2K,1C) experimental renovascular hypertension. The schematic representation of renovascular hypertension depicted in Figure 3-9 is an oversimplification. In fact, the course of experimental 2K,1C hypertension may be divided into three sequential phases. In phase I, renal ischemia and activation of the renin-angiotensin system are of fundamental importance, and in this early phase of experimental hypertension, the blood pressure elevation is renin- or angiotensin II-dependent. Acute administration of angiotensin II antagonists, administration of angiotensin-converting enzyme (ACE) inhibitors, removal of the renal artery stenosis (*ie*, removal of the clip in the experimental animal or removal of the “stenotic kidney”) promptly normalizes blood pressure. Several days after renal artery clamping, renin levels fall, but blood pressure remains elevated. This second phase of experimental 2K,1C hypertension may be viewed as a pathophysiologic transition phase that, depending on the experimental model and species, may last from a few days to several weeks. During this transition phase (phase II), salt and water retention are observed as a consequence of the effect of hypoperfusion of the stenotic kidney;

augmented proximal tubular reabsorption of sodium and water and angiotensin II-induced stimulation of aldosterone secretion contribute to this sodium and water retention. In addition, the high levels of angiotensin II stimulate thirst, which further augments expansion of the extracellular fluid volume. The expanded extracellular fluid volume results in a progressive suppression of peripheral renin activity. During this transition phase, the hypertension is still responsive to removal of the unilateral renal artery stenosis, to angiotensin II blockade, or unilateral nephrectomy, although these maneuvers do not normalize the blood pressure as promptly and consistently as in the acute phase.

After several weeks, a chronic phase (phase III) ensues wherein unclipping the renal artery of the experimental animal does not lower the blood pressure. This failure of “unclipping” to lower the blood pressure in this chronic phase (III) of 2K,1C hypertension is due to widespread arteriolar damage to the “contralateral kidney,” consequent to prolonged exposure to high blood pressure and high levels of angiotensin II. In this chronic phase of 2K,1C renovascular hypertension, extracellular fluid volume expansion and systemic vasoconstriction are the main pathophysiologic abnormalities. The pressure natriuresis of the “contralateral kidney” blunts the extracellular fluid volume expansion caused by the “stenotic kidney;” but as the contralateral kidney suffers vascular damage from extended exposure to elevated arterial pressure, its excretory function diminishes and extracellular fluid volume expansion persists. In this third phase of experimental 2K,1C hypertension, acute blockade of the renin-angiotensin system fails to lower blood pressure. Sodium depletion may ameliorate the hypertension but does not normalize it. The clinical surrogate of phase III experimental 2K,1C hypertension is duration of hypertension. Widespread clinical experience indicates that major improvements in blood pressure control or cure of the hypertension following renal revascularization or even removal of the kidney ipsilateral to the renal artery stenosis are rarely observed in patients with a long duration (*ie*, >5 years) of hypertension. (*Adapted from Brown and coworkers [3]; with permission.*)

**FIGURE 3-11**

Schematic representation of two types of experimental hypertension. The discussion so far of the pathophysiology of renovascular hypertension has focused on the two-kidney, one-clip model of renovascular hypertension (“two-kidney hypertension”), wherein the artery to the “contralateral kidney” is patent and the “contralateral” nonaffected kidney is present. Elevated peripheral renin activity, normal plasma volume, and hypokalemia are typically associated with the elevated arterial pressure. There is another type of “renovascular hypertension” known as “one-kidney” hypertension, wherein in the experimental model, one renal artery is constricted and the contralateral kidney is removed. Although there is an initial increase in renin release responsible for the early rise in blood pressure in “one-kidney” hypertension as in “two-kidney” hypertension, the absence of an unclipped contralateral kidney allows for sodium retention early in the course of this one-kidney, one-clip (1K,1C) model. Renin levels are suppressed to normal levels in conjunction with high blood pressure which is maintained by salt and water retention. Thus, extracellular fluid volume expansion is a prime feature of “one-kidney” hypertension.

### A. LESIONS PRODUCING THE SYNDROME OF RENOVASCULAR HYPERTENSION (“TWO-KIDNEY HYPERTENSION”)\*

Unilateral atherosclerotic renal arterial disease  
 Unilateral fibrous renal artery disease  
 Renal artery aneurysm  
 Arterial embolus  
 Arteriovenous fistula (congenital and traumatic)  
 Segmental arterial occlusion (traumatic)  
 Pheochromocytoma compressing renal artery  
 Unilateral perirenal hematoma or subcapsular hematoma (compressing renal parenchyma)

\*Implies contralateral (nonaffected) kidney present.

### B. LESIONS PRODUCING THE SYNDROME OF RENOVASCULAR HYPERTENSION (“ONE-KIDNEY HYPERTENSION”)\*

Stenosis to a solitary functioning kidney  
 Bilateral renal arterial stenosis  
 Aortic coarctation  
 Vasculitis (polyarteritis nodosa and Takayasu's arteritis)  
 Atheroembolic disease

\*Implies total renal mass ischemic.

### STEPS IN MAKING THE DIAGNOSIS OF RENOVASCULAR HYPERTENSION

1. Demonstration of renal arterial stenosis by angiography
2. Determination of pathophysiologic significance of the stenotic lesion
3. Cure of the hypertension by intervention, *ie*, revascularization, percutaneous transluminal angioplasty, nephrectomy

#### FIGURE 3-13

Steps in making the diagnosis of renovascular hypertension (RVHT). With the exception of oral contraceptive use and alcohol ingestion, RVHT is the most common cause of potentially remediable secondary hypertension. RVHT is estimated to occur with a prevalence of 1% to 15%. Some hypertension referral clinics have estimated a prevalence of RVHT as high as 15%, whereas other prevalence data suggest that less than 1% to 2% of the hypertensive population has RVHT.

#### FIGURE 3-12

Lesions producing the syndrome of renovascular hypertension. **A**, Two-kidney hypertension. The most common clinical counterpart to “two-kidney” hypertension is unilateral renal artery stenosis due to either atherosclerotic or fibrous renal artery disease. Unilateral renal trauma, with development of a calcified fibrous capsule surrounding the injured kidney causing compression of the renal parenchyma, may produce renovascular hypertension; this clinical situation is analogous to the experimental Page kidney, wherein cellophane wrapping of one of two kidneys causes hypertension, which is relieved by removal of the wrapped kidney.

**B**, One-kidney hypertension. Clinical counterparts of experimental one-kidney, one-clip (“one kidney”) hypertension include renal artery stenosis to a solitary functioning kidney, bilateral renal arterial stenosis, aortic coarctation, Takayasu's arteritis, fulminant polyarteritis nodosa, atheroembolic renal disease, and renal artery stenosis in a transplanted kidney. In some parts of the world, *eg*, China and India, Takayasu's arteritis is a frequent cause of renovascular hypertension.

Although elderly atherosclerotic hypertensive individuals often have atherosclerotic renal artery disease, their hypertension is usually essential hypertension, not RVHT. On balance, the prevalence of RVHT in the general hypertensive population is probably no more than 2% to 3%. The particular appeal of diagnosing RVHT centers around its potential curability by an interventional maneuver such as surgical revascularization, percutaneous transluminal renal angioplasty (PTRA), or renal artery stenting. Whether or not to use these interventions for the goal of improving blood pressure depends on the likelihood such intervention will improve the blood pressure.

The overwhelming majority of patients with RVHT will have this syndrome because of main renal artery stenosis. Therefore, the first step in making the diagnosis of RVHT is to demonstrate renal artery stenosis by one of several imaging procedures and, eventually, by angiography. The second step in establishing the probability that the renal artery stenosis is instrumental in promoting hypertension is to determine the pathophysiologic significance of the stenotic lesion. Finally, the hypertension, presumed to be renovascular in origin, is proven to be RVHT when the elevated blood pressure is cured or markedly ameliorated by an interventional maneuver such as surgical revascularization, PTRA, renal artery stent, or nephrectomy.

## DIAGNOSIS OF RENAL ARTERIAL STENOSIS

| Clinical clues   | Diagnostic tests                            |
|--|---|
| Age of onset of hypertension <30 y or >55 y  | Duplex ultrasonography                      |
| Abrupt onset of hypertension   | Radionuclide renography                     |
| Acceleration of previously well-controlled hypertension  | Captopril renography                        |
| Hypertension refractory to an appropriate three-drug regimen   | Captopril provocation test                  |
| Accelerated retinopathy  | Intravenous digital subtraction angiography |
| Systolic-diastolic abdominal bruit   | Rapid sequence IVP                          |
| Evidence of generalized atherosclerosis obliterans   | Magnetic resonance angiography              |
| Malignant hypertension   | Spiral CT angiography                       |
| Flash pulmonary edema  | CO <sub>2</sub> angiography                 |
| Acute renal failure with use of angiotensin-converting enzyme inhibitors or angiotensin II receptor-blockers | Conventional (contrast) angiography         |

FIGURE 3-14

Diagnosis of renal artery stenosis. Clinical clues suggesting renal artery stenosis, some of which suggest that the stenosis is the cause of the hypertension, are listed on the left. The well-documented age of onset of hypertension in an individual under the age of 30 or over age 55 years, particularly if the hypertension is severe and requiring three antihypertensive drugs, is a strong clinical clue to renal artery stenosis and predicts that the stenosis is causing the hypertension. The patient with a long history of mild hypertension, easily controlled with one or two drugs, who, particularly in older age, develops severe and refractory hypertension, is likely to have developed atherosclerotic renal artery stenosis as a contributor to underlying

longstanding essential hypertension. Grade III hypertensive retinopathy, malignant hypertension, and flash pulmonary edema all suggest renal artery stenosis with or without renovascular hypertension. The observation of a diastolic bruit in the abdomen of a young white woman suggests fibrous renal artery disease and, further, is a reliable clinical clue that the hypertension will be helped substantially by surgical renal revascularization or percutaneous transluminal renal angioplasty.

The diagnostic tests listed along the right side are used mainly to detect renal artery stenosis (*ie*, the anatomic presence of disease). Captopril renography is also used to predict physiologic significance of the stenotic lesion. The popularity of these diagnostic tests in detecting renal artery stenosis varies from institution to institution; correlations with percent stenosis by comparative angiography are widely variable. A substantial fall in blood pressure following initiation of an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker suggests RVHT. With the exception of a diastolic abdominal bruit and accelerated retinopathy, no clear-cut physical findings definitely discriminate patients with RVHT from the larger pool of patients with essential hypertension.

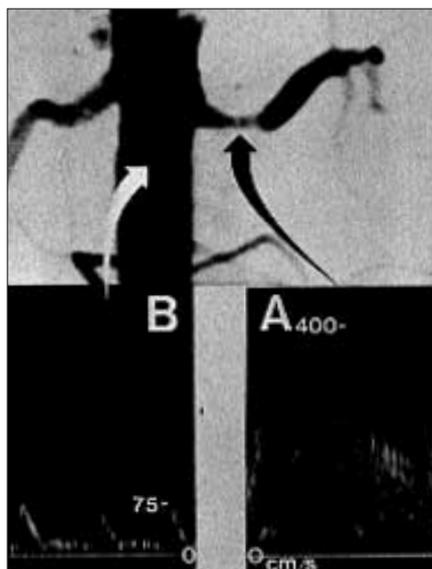


FIGURE 3-15

Renal duplex ultrasound for diagnosis of renal artery stenosis. Duplex ultrasound scanning of the renal arteries is a noninvasive screening test for the detection of renal artery stenosis. It combines direct visualization of the renal arteries (B-mode imaging) with measurement of various hemodynamic factors in the main renal arteries and within the kidney (Doppler), thus providing both an anatomic and functional assessment. Unlike other noninvasive screening tests (*eg*, captopril renography), duplex ultrasonography does not require patients to discontinue any antihypertensive medications before the test. The study should be performed while the patient is fasting. The *white arrow* indicates the aorta and the *black arrow* the left renal artery, which is stenotic. Doppler scans (*bottom*) measure the corresponding peak systolic velocities in the aorta and in the renal artery. The peak systolic velocity in the left renal artery was 400 cm/s, and the peak systolic velocity in the aorta was 75 cm/s. Therefore, the renal-aortic ratio was 5.3, consistent with a 60% to 99% left renal artery stenosis. (*From Hoffman and coworkers [4]; with permission.*)

### COMPARISON OF DUPLEX ULTRASOUND WITH ARTERIOGRAPHY

| Percent stenosis by ultrasound | Percent stenosis by arteriogram |       |       |     |       |
|--------------------------------|---------------------------------|-------|-------|-----|-------|
|                                | 0–59                            | 60–79 | 80–99 | 100 | Total |
| 0–59                           | 62                              | 0     | 1     | 1   | 64    |
| 60–99                          | 1                               | 31    | 67    | 0   | 99    |
| 100                            | 0                               | 1     | 1     | 22  | 24    |
| Total                          | 63                              | 32    | 69    | 23  | 187   |

Sensitivity, 0.98.

Specificity, 0.98.

Positive predictive value, 0.99.

Negative predictive value, 0.97.

### DETERMINATION OF PATHOPHYSIOLOGIC SIGNIFICANCE OF THE STENOTIC LESION

Duration of hypertension <3–5 y

Appearance of lesion on angiogram (>75% stenosis)

Systolic-diastolic bruit in abdomen

Renal vein renin ratio >1.5

Positive captopril provocation test or captopril renogram

Abnormal rapid sequence IVP

Hypokalemia

#### FIGURE 3-17

Determination of pathophysiologic significance of the stenotic lesion. The second step in making the diagnosis of renovascular hypertension (RVHT) is to determine the pathophysiologic significance of the stenotic lesion demonstrated by angiography. The likelihood of cure of the hypertension by an interventional maneuver is greatly enhanced when one or more of the items listed here are present. A positive captopril provocation test, abnormal rapid sequence intravenous pyelogram (IVP), or positive captopril

#### FIGURE 3-16

Comparison of duplex ultrasound with arteriography. A total of 102 consecutive patients with both duplex ultrasound scanning of the renal arteries and renal arteriography were prospectively studied. All patients in this study had difficult-to-control hypertension, unexplained azotemia, or associated peripheral vascular disease, giving them a high pretest likelihood of renovascular hypertension. Sixty-two of 63 arteries that showed less than 60% stenosis by formal arteriography, were identified by duplex ultrasound scanning.

Twenty-two of 23 arteries with total occlusion on arteriography were correctly identified by duplex ultrasound. Thirty-one of 32 arteries with 60% to 79% stenosis using arteriography were identified as having 60% to 99% stenosis on duplex ultrasound and 67 of 69 arteries with 80% to 99% stenosis on arteriography were detected to have 60% to 99% stenosis on ultrasound. A current limitation of duplex ultrasound is the inability to consistently distinguish between more than and less than 80% stenosis (considered to be the magnitude of stenosis required for hemodynamic significance of the lesion). Nevertheless, duplex ultrasound is currently highly sensitive and specific in patients with a high likelihood of renovascular disease in detecting patients with more or less than 60% renal artery stenosis. Accessory renal arteries are difficult to identify by ultrasound and remain a limitation of this test. (*Adapted from Olin and coworkers [5]; with permission.*)

renogram not only suggest the anatomic presence of renal artery stenosis but also imply that the stenosis is instrumental in producing the hypertension. Reductions of lumen diameter of less than 70% to 80% generally do not initiate renal ischemia or activation of the renin angiotensin system; thus, before recommending a renal revascularization procedure, severe renal artery stenosis (>75% reduction in lumen diameter) should be observed on the renal angiogram. A lateralizing renal vein renin ratio (a comparison of renin harvested from the renal vein ipsilateral to the renal artery stenosis with the renin level from renal vein of the contralateral kidney), particularly when renin production from the contralateral kidney is suppressed, suggests that an intervention on the renal artery stenosis will cure or markedly ameliorate the hypertension in about 90% of cases. Conversely, cure or marked improvement in blood pressure following renal revascularization has been reported in nearly 50% of cases in the absence of lateralizing renal vein renins. Hypokalemia, in the absence of diuretic therapy, strongly suggests that the hypertension is renovascular in origin, consequent to secondary aldosteronism. The sensitivity of an IVP in detecting unilateral RVHT is relatively poor (about 75%) and the overall sensitivity in detecting patients with bilateral renal artery disease is only about 60%. Because RVHT has a low prevalence in the general population, a negative IVP provides strong evidence (98% to 99% certainty) against RVHT.

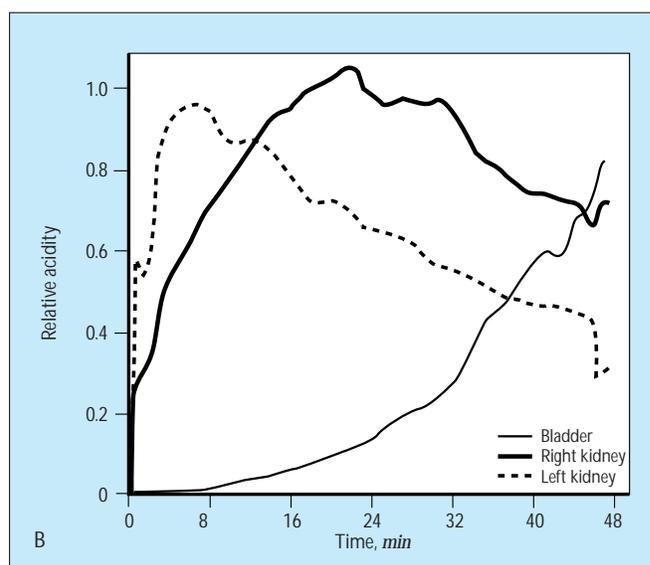
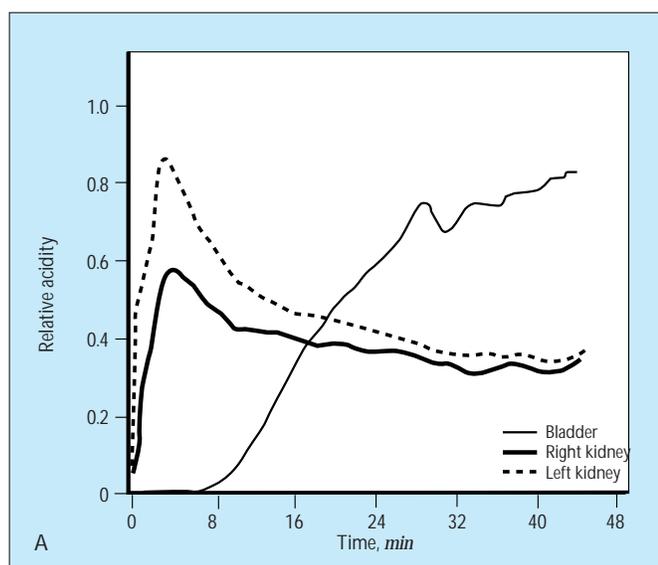
### RENIN CRITERIA FOR CAPTOPRIL TEST THAT DISTINGUISH PATIENTS WITH RVHT FROM THOSE WITH ESSENTIAL HYPERTENSION

Stimulated PRA of 12 ng/mL/h or more  
 Absolute increase in PRA of 10 ng/mL/h or more  
 Percent increase in PRA  
 Increase in PRA of 150% if baseline PRA >3 ng/mL/h  
 Increase in PRA of 400% if baseline PRA <3 ng/mL/h

**FIGURE 3-18**

The captopril test: renin criteria that distinguish patients with renovascular hypertension from those with essential hypertension. The captopril provocation test evolved because the casual measurement of peripheral plasma renin activity (PRA) has been of little

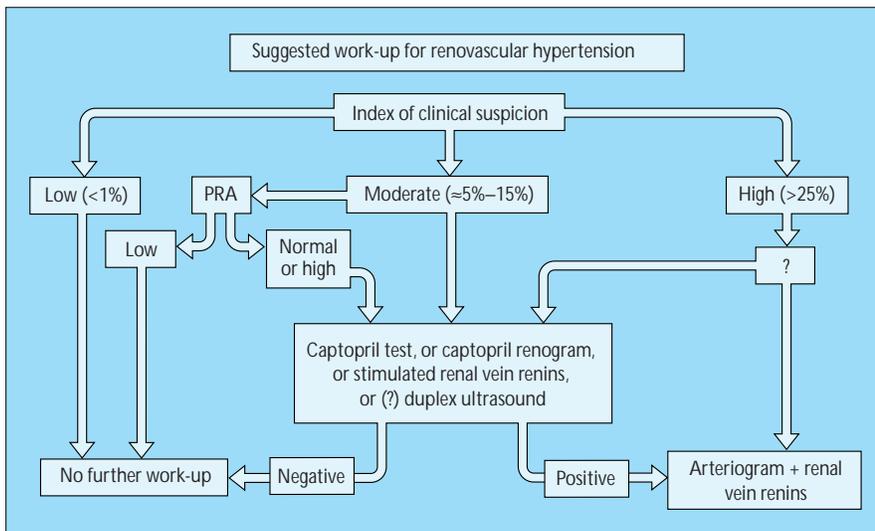
value as a diagnostic screening test for renovascular hypertension (RVHT). The notion that patients with high PRA, even in the face of high urinary sodium excretion, might turn out to have RVHT has not been supported by numerous clinical observations. However, the short-term (60- to 90-minute) response of blood pressure and PRA to an oral dose (25 to 50 mg) of captopril has gained recent popularity as a screening test for presumed RVHT. Preparation of patients for this test is vital; ideally patients should discontinue their antihypertensive medications, maintain a diet adequate in salt, and have good renal function. A baseline blood pressure and PRA are obtained after which captopril is administered; 60 minutes after captopril administration, a "post-captopril" PRA is obtained along with repeat measurements of blood pressure. Early reports with this test indicated a high sensitivity and specificity (95% to 100%) in identifying RVHT if all three of the renin criteria listed here were met. Subsequent reports have not been as encouraging such that the overall sensitivity of this captopril test is only about 70%, with a specificity of approximately 85%. (*Adapted from Muller and coworkers [6]; with permission.*)



**FIGURE 3-19**

Captopril renography. **A**, TcDPTA time-activity curves during baseline. **B**, TcDPTA time-activity curves after captopril administration. These curves represent a captopril renogram in a patient with unilateral left renal artery stenosis. This diagnostic test has been used to screen for renal artery stenosis and to predict renovascular hypertension. Captopril renography appears to be highly sensitive and specific for detecting physiologically significant renal artery stenosis. Scintigrams and time-activity curves should both be analyzed to assess renal perfusion, function, and size. If the renogram following captopril administration is abnormal (*panel B*, demonstrating delayed time to maximal activity and retention of the radionuclide in the right kidney), another renogram may be obtained without captopril for comparison. The diagnosis of renal artery stenosis is based on

asymmetry of renal size and function and on specific, captopril-induced changes in the renogram, including delayed time to maximal activity ( $\geq 11$  minutes), significant asymmetry of the peak of each kidney, marked cortical retention of the radionuclide, and marked reduction in the calculated glomerular filtration rate of the kidney ipsilateral to the stenosis. One must interpret the clinical and renographic data with caution, as protocols are complex and diagnostic criteria are not well standardized. Nevertheless, captopril renography appears to be an improvement over the captopril provocation test, with many reports indicating sensitivity and specificity from 80% to 95% in predicting an improvement in blood pressure following intervention. (*Adapted from Nally and coworkers [7]; with permission.*)



**FIGURE 3-20**

Suggested work-up for renovascular hypertension. Because the prevalence of renovascular hypertension (RVHT) among hypertensive persons in general is approximately 2% or less, widespread screening for renovascular disease is not justified. Despite the proliferation of diagnostic tests

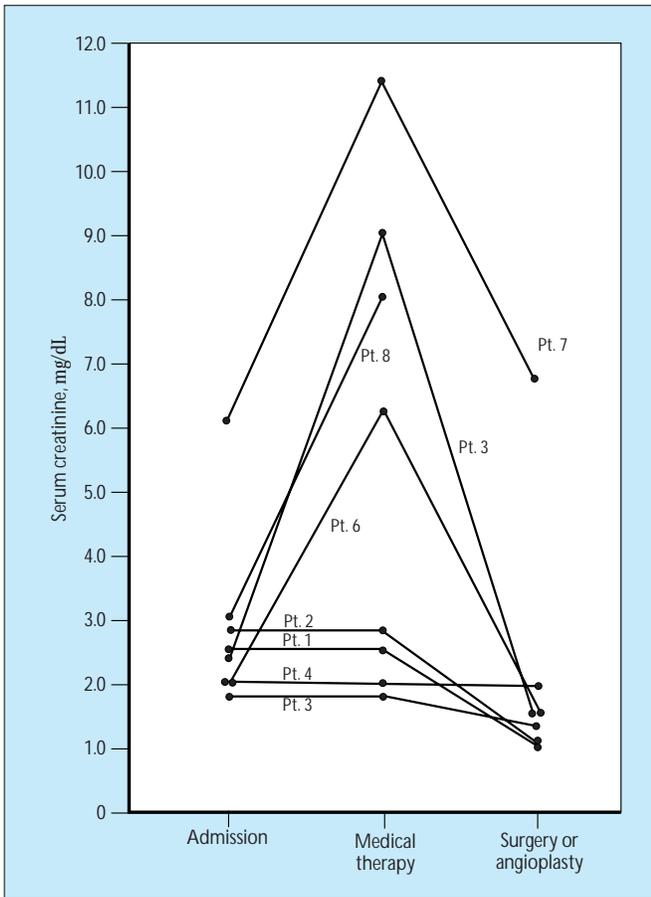
now available to detect renal artery stenosis and several tests designed to predict the physiologic significance of the stenotic lesion, the index of clinical suspicion for RVHT remains the focal point of the work-up for RVHT. A brief duration of moderately severe hypertension is the most important clue directing subsequent work-up for RVHT. If the index of clinical suspicion (see Fig. 3-14) is high, it is reasonable to proceed directly to formal renal arteriography with renal vein renin determination. Alternatively, in patients highly suspected to have RVHT, a captopril renogram followed by a renal arteriogram may be recommended. Strong arguments *against* RVHT include 1) long duration (more than 5 years) of hypertension, 2) old age, 3) generalized atherosclerosis, 4) increased serum creatinine, and 5) a normal serum potassium concentration. For these patients, particularly if the blood pressure is only minimally elevated or easily controlled with one or two antihypertensive medications, further work-up for RVHT is not indicated. (*Adapted from Mann and Pickering [8]; with permission.*)

## Ischemic Nephropathy

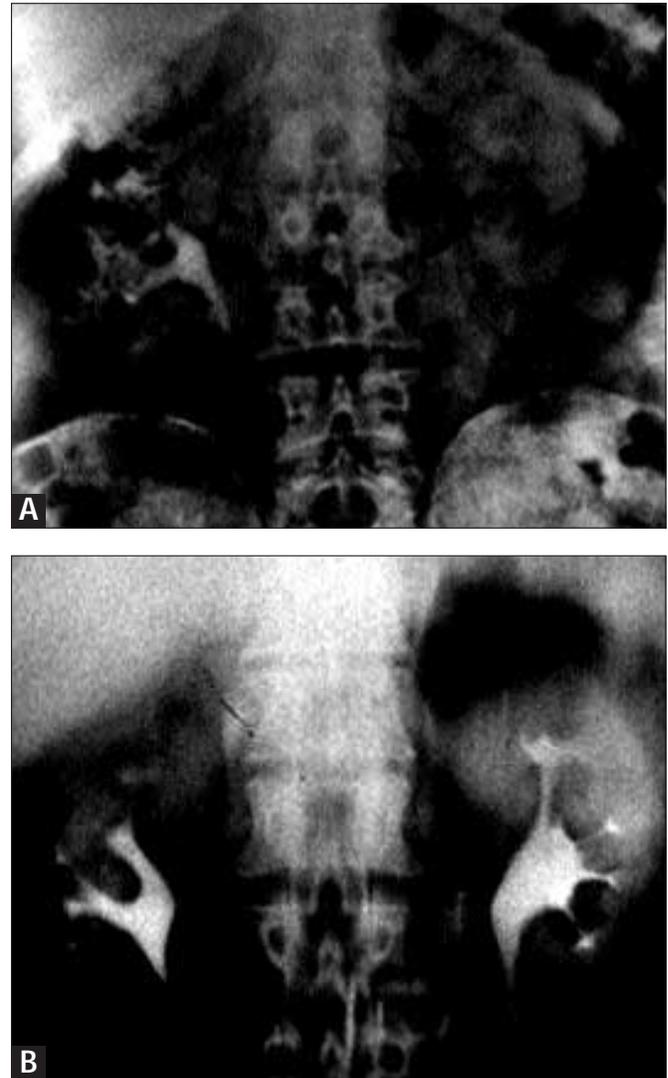


**FIGURE 3-21**

Aortogram in a 62-year-old white woman demonstrating subtotal occlusion of the left main renal artery supplying an atrophic left kidney and high-grade ostial stenosis of the proximal right renal artery from atherosclerosis. This patient presented in 1977 with a recent appearance of hypertension and a blood pressure of 170/115 mm Hg. Three years previously, when diagnosed with polycythemia vera, an IVP was normal. She was followed closely between 1974 and 1977 by her physician and was always normotensive until the hypertension suddenly appeared. A repeat rapid sequence IVP demonstrated a reduction in the size of the left kidney from 14 cm in height (1974) to 11.5 cm in height (1977). The serum creatinine was 2.6 mg/dL. The renal arteriogram shown here indicates high-grade bilateral renal artery stenosis with the left kidney measuring 11.5 cm in height, and the right kidney measuring 14.5 cm in height. Renal vein renins were obtained and lateralized strongly to the smaller left kidney. The blood pressure was well controlled with inderal and chlorthalidone. Right aortorenal reimplantation was undertaken solely to preserve renal function. Postoperatively the serum creatinine fell to 1.5 mg/dL and remained at this level for the next 13 years. Blood pressure continued to require antihypertensive medication, but was controlled to normal levels with inderal and chlorthalidone.

**FIGURE 3-22**

Effects of medical therapy and surgery or angioplasty on serum creatinine levels. This figure describes eight patients hospitalized because of severe hypertension and renal insufficiency. With medical management of the hypertension (antihypertensive drug therapy), four of the eight patients developed substantial worsening of their renal function as measured by serum creatinine; three of these four patients demonstrated improvement following surgery or angioplasty. The other four patients (patients one to four) did not demonstrate a worsening serum creatinine level with medical therapy; but three of these four patients showed improved renal function following surgery or angioplasty. (Adapted from Ying and coworkers [9]; with permission.)

**FIGURE 3-23**

Improved renal function demonstrated by intravenous pyelography following left renal revascularization. **A**, preoperative IVP (5-minute film) in a 65-year-old white man with a 15-year history of hypertension; serum creatinine 2.6 mg/dL. Note poorly functioning left kidney, which measured 11.5 cm in height. **B**, post operative IVP (5-minute film) obtained following left aortorenal saphenous vein bypass grafting to the left kidney. Note the prompt function and increased height (14.0 cm) of the revascularized left kidney versus the preoperative IVP. (From Novick and Pohl [10]; with permission.)

The clinical story of the patient in Figure 3-21, the benefits of surgical renal revascularization or percutaneous transluminal renal angioplasty (Fig. 3-22), and the radiographic evidence of improved renal function after renal revascularization (Fig. 3-23) are examples of ischemic nephropathy. Two definitions of ischemic nephropathy are suggested herein: 1) clinically significant reduction in renal function due to compromise of the renal circulation; and 2) clinically significant reduction in glomerular filtration rate due to hemodynamically significant obstruction to renal blood flow, or renal failure due to renal artery occlusive disease.

### ATHEROSCLEROTIC RENAL ARTERY STENOSIS IN 395 PATIENTS WITH GENERALIZED ATHEROSCLEROSIS OBLITERANS AND IN PATIENTS WITH CORONARY ARTERY DISEASE

|                                 | Patients, n | Percent of patients with >50% stenosis |
|---------------------------------|-------------|--|
| Abdominal aortic aneurysm       | 109         | 38                                     |
| Aorto-occlusive disease         | 21          | 33                                     |
| Lower extremity disease         | 189         | 39*                                    |
| Suspected renal artery stenosis | 76          | 70 <sup>†</sup>                        |
| Coronary artery disease         | 76          | 29 <sup>†</sup>                        |
|                                 | 817         | 20 <sup>‡</sup>                        |

\*50% in diabetic patients.

<sup>†</sup>Data from Vetrovec and coworkers [12].

<sup>‡</sup>Data from Harding [13].

**FIGURE 3-24**

Atherosclerotic renal artery stenosis in patients with generalized atherosclerosis obliterans and in patients with coronary artery disease (CAD). Atherosclerotic renal artery stenosis is common in older patients with and without hypertension simply as a consequence of generalized atherosclerosis obliterans. Approximately 40% of consecutively studied patients undergoing arteriography for routine evaluation of abdominal aortic aneurysm, aorto-occlusive disease, or lower extremity occlusive disease have associated renal artery stenosis (more than 50% unilateral renal artery stenosis) and nearly 30% of patients undergoing coronary angiography may have incidentally detected unilateral renal artery stenosis. Approximately 4% to 13% of patients with CAD or peripheral vascular disease have more than 75% bilateral renal artery stenosis. Correlations of hypercholesterolemia and cigarette smoking with renal artery atherosclerosis are not unequivocally clear, but they probably represent risk factors for renal artery atherosclerosis just as they represent risk factors for atherosclerosis in other vascular beds. (Adapted from Olin and coworkers [11]; with permission.)

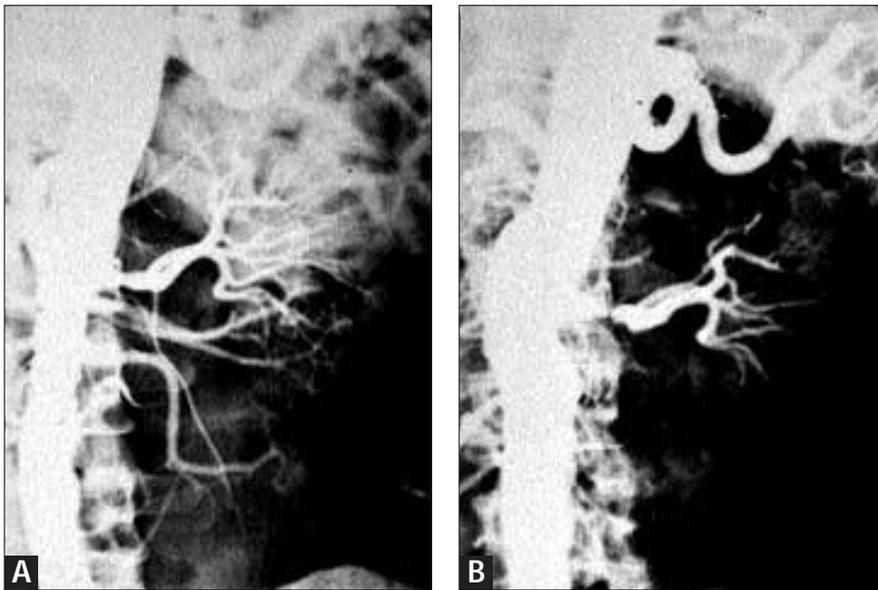
### CLINICAL PRESENTATIONS OF ISCHEMIC RENAL DISEASE

Acute renal failure, frequently precipitated by a reduction in blood pressure (ie, angiotensin-converting enzyme inhibitors plus diuretics)  
 Progressive azotemia in a hypertensive patient with known renal artery stenosis treated medically  
 Progressive azotemia in a patient (usually elderly) with refractory hypertension  
 Unexplained progressive azotemia in an elderly patient  
 Hypertension and azotemia in a renal transplant patient

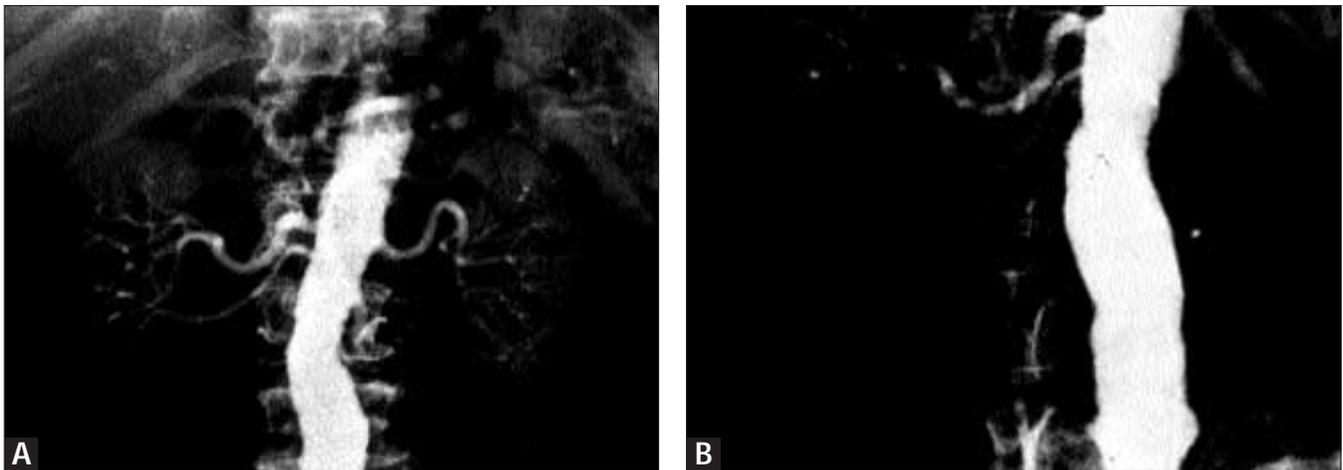
**FIGURE 3-25**

Clinical presentations of ischemic renal disease. The clinical presentation of a patient likely to develop renal failure from atherosclerotic ischemic renal disease is that of an older (more than 50 years) individual demonstrating progressive azotemia in conjunction with antihypertensive drug therapy, risk factors for generalized atherosclerosis obliterans, known renal artery disease, refractory hypertension, and generalized atherosclerosis. Acute renal failure precipitated by a reduction in blood pressure below a "critical perfusion pressure," and particularly with the use of angiotensin converting-enzyme inhibitors (ACEI) or angiotensin II receptor blockers plus diuretics, strongly suggests severe intrarenal ischemia from arteriolar nephrosclerosis and/or severe main renal artery stenosis.

Unexplained progressive azotemia in an elderly patient with clinical signs of vascular disease with minimal proteinuria and a bland urinary sediment also suggest ischemic nephropathy. (Adapted from Jacobson [14]; with permission.)

**FIGURE 3-26**

Mild stenosis (less than 50%) due to atherosclerotic disease of the left main renal artery (*panel A*) that has progressed to high-grade (75% to 99%) stenosis on a later arteriogram (*panel B*). Underlying the concept of renal revascularization for preservation of renal function is the notion that atherosclerotic renal artery disease (ASO-RAD) is a progressive disorder. The sequential angiograms in Figures 3-26 and 3-27 show angiographic progression of ASO-RAD over time. In patients demonstrating progressive renal artery stenosis by serial angiography, a decrease in kidney function as measured by serum creatinine and a decrease in ipsilateral kidney size correlate significantly with progressive occlusive disease. Patients demonstrating more than 75% stenosis of a renal artery are at highest risk for progression to complete occlusion. (From Novick [15]; with permission.)

**FIGURE 3-27**

**A**, Normal right main renal artery and minimal atherosclerotic irregularity of left main renal artery on initial (1974) aortogram.  
**B**, Repeat aortography (1978) showed progression to moderate

stenosis of the right main renal artery (*arrow*) and total occlusion of left main renal artery (*arrow*). (From Schreiber and coworkers [16]; with permission.)

### CLINICAL CLUES TO BILATERAL ATHEROSCLEROTIC RENOVASCULAR DISEASE

Generalized atherosclerosis obliterans  
 Presumed renovascular hypertension  
 Unilateral small kidney  
 Unexplained azotemia  
 Deterioration in renal function with BP reduction and/or ACE inhibitor therapy  
 Flash pulmonary edema

**FIGURE 3-28**

Clinical clues to bilateral atherosclerotic renovascular disease. The patient at highest risk for developing renal insufficiency from renal artery stenosis (ischemic nephropathy) has sufficient arterial stenosis to threaten the entire renal functioning mass. These high-risk patients have high-grade (more than 75%) arterial stenosis to a solitary functioning kidney or high-grade (more than 75%) bilateral renal artery stenosis. Patients with two functioning kidneys with only unilateral renal artery stenosis are not at significant risk for developing renal insufficiency because the

entire renal functioning mass is not threatened by large vessel occlusive disease.

Clinical clues to the high-risk patient are similar to the clinical presentations of ischemic renal disease shown in Figure 3-25. Nearly 75% of adults with a unilateral small kidney have sustained this renal atrophy due to large vessel occlusive disease from atherosclerosis. One third of these patients with a unilateral small kidney have high-grade stenosis of the artery involving the contralateral normal-sized kidney. Flash pulmonary edema is another clue to bilateral renovascular disease or high-grade stenosis involving a solitary functioning kidney. These patients, usually hypertensive and with documented coronary artery disease and underlying hypertensive heart disease, present with the abrupt onset of pulmonary edema. Left ventricular ejection fractions in these patients are not seriously impaired. Flash pulmonary edema is associated with atherosclerotic renal artery disease and may occur with or without severe hypertension.

Renal revascularization to preserve kidney function or to prevent life-threatening flash pulmonary edema may be considered in patients with high-grade arterial stenosis to a solitary kidney or high-grade bilateral renal artery stenosis. Percutaneous transluminal renal angioplasty (PTR), renal artery stenting, or surgical renal revascularization may be employed. Patients with chronic total renal artery occlusion bilaterally or in a solitary functioning kidney are candidates for surgical renal revascularization, but are not candidates (from a technical standpoint) for PTR or renal artery stents.

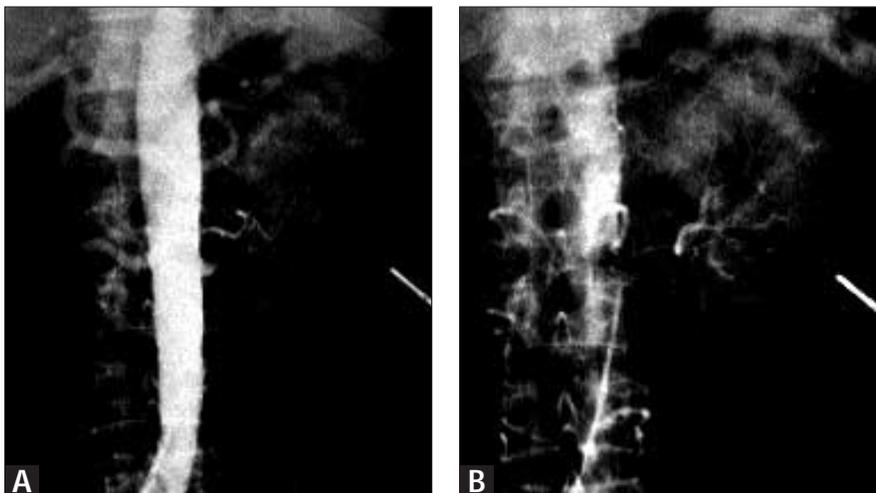
### PREDICTORS OF KIDNEY SALVAGEABILITY

Kidney size >9 cm (laminography)  
 Function on either urogram or renal flow scan  
 Filling of distal renal arteries (by collaterals) angiographically, with total proximal occlusion  
 Glomerular histology on renal biopsy

**FIGURE 3-29**

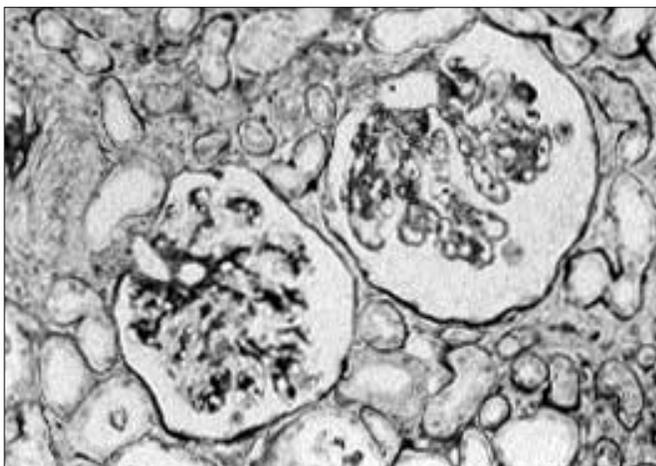
Predictors of kidney salvageability. In evaluating patients as candidates for renal revascularization to preserve or improve renal function, some determination should be made of the

potential for salvable renal function. Clinical clues suggesting renal viability include 1) kidney size greater than 9 cm (pole-to-pole length) by laminography (tomography); 2) some function of the kidney on either urogram or renal flow scan; 3) filling of distal renal arteries (by collaterals) angiographically, when the main renal artery is totally occluded proximally (see Fig. 3-30); and 4) well-preserved glomeruli with minimal interstitial scarring (see Fig. 3-31) on renal biopsy. Patients with moderately severe azotemia, eg, serum creatinine more than 3-4 mg/dL, are likely to have severe renal parenchymal scarring (see Fig. 3-32), which renders improvement in renal function following renal revascularization unlikely. Exceptions to this observation are cases of total main renal artery occlusion wherein kidney viability is maintained via collateral circulation (see Figure 3-30). A kidney biopsy may guide subsequent decision making regarding renal revascularization for the goal of improving kidney function.

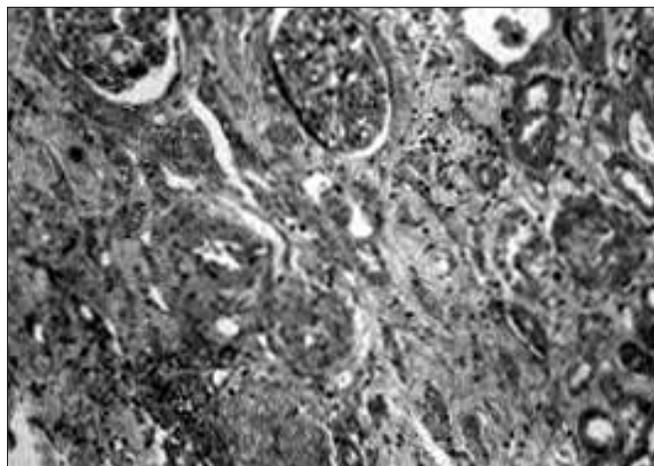


**FIGURE 3-30**

This abdominal aortogram reveals complete occlusion of the left main renal artery (*panel A*) with filling of the distal renal artery branches from collateral supply on delayed films (*panel B*). The observation of collateral circulation when the main renal artery is totally occluded proximally suggests viable renal parenchyma. (From Novick and Pohl [10]; with permission.)

**FIGURE 3-31**

Renal biopsy of a solitary left kidney in a 67-year-old woman who had been anuric and on chronic dialysis for 9 months. The biopsy shows hypoperfused retracted glomeruli consistent with ischemia. There is no evidence of active glomerular proliferation or glomerular sclerosis. Note intact tubular basement membranes and negligible interstitial scarring. Left renal revascularization resulted in recovery of renal function and discontinuance of dialysis with improvement in serum creatinine to 2.0 mg/dL. (From Novick [15]; with permission.)

**FIGURE 3-32**

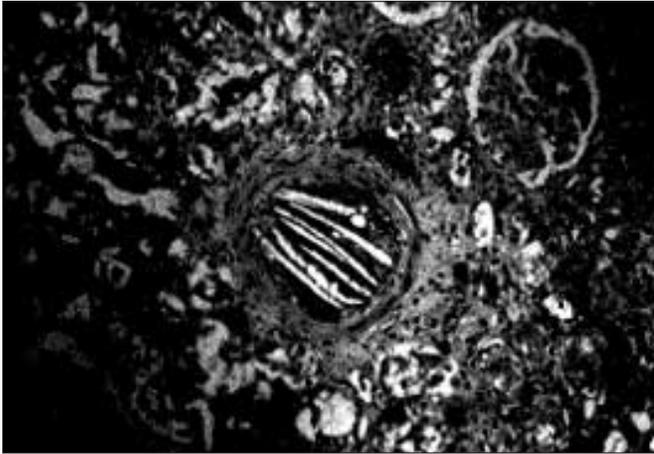
Pathologic specimen of kidney beyond a main renal artery occlusion in a patient with severe bilateral renal artery stenosis and a serum creatinine of 4.5 mg/dL. The biopsy demonstrates glomerular sclerosis, tubular atrophy, and interstitial fibrosis. The magnitude of glomerular and interstitial scarring predict irreversible loss of kidney viability. (From Pohl [1]; with permission.)

**FIGURE 3-33**

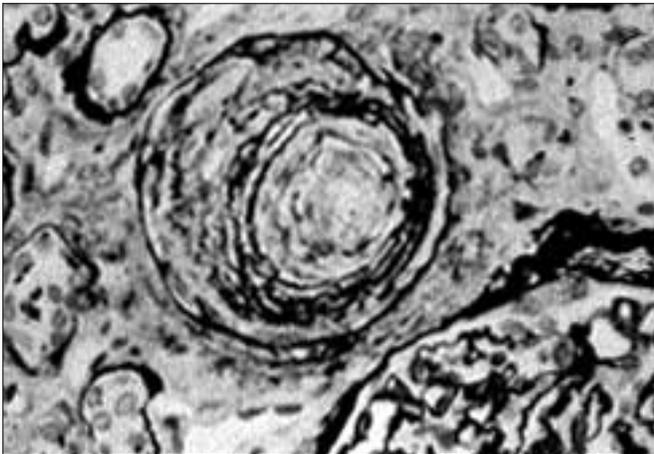
Severe atherosclerosis involving the abdominal aorta, renal, and iliac arteries. This abdominal aortogram demonstrates a ragged aorta, total occlusion of the right main renal artery, and subtotal occlusion of the proximal left main renal artery. Such patients are at high-risk for atheroembolic renal disease following aortography, selective renal arteriography, percutaneous transluminal renal angioplasty, renal artery stenting, or surgical renal revascularization.

**FIGURE 3-34** (see Color Plate)

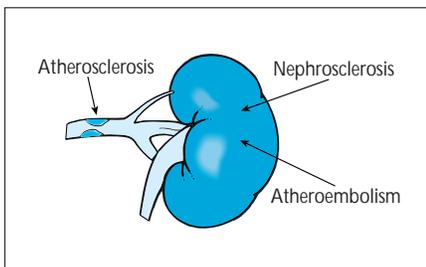
“Purple toe” syndrome reflecting peripheral atheroembolic disease in the patient in Figure 3-33 (ragged aorta), following an abdominal aortogram.

**FIGURE 3-35**

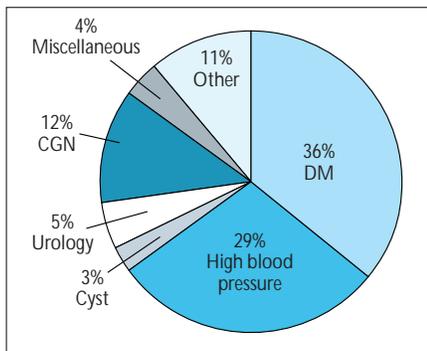
Pathologic specimen of kidney demonstrating atheroembolic renal disease (AERD). Microemboli of atheromatous material are readily identified by the characteristic appearance of cholesterol crystal inclusions that appear in a biconvex needle-shaped form. In routine paraffin-embedded histologic sections, the cholesterol is not seen because the methods used in preparing sections dissolve the crystals; the characteristic biconvex clefts in the glomeruli (or blood vessels) persist, allowing easy identification. Several patterns of renal failure in patients with AERD are recognized: 1) insult (*eg*, abdominal aortogram) leads to end-stage renal disease (ESRD) over weeks to months; 2) insult leads to chronic stable renal insufficiency; 3) multiple insults (repeated angiographic procedures) lead to a step-wise rise in serum creatinine eventuating in end-stage renal failure; and 4) insult leading to ESRD over several weeks to months with recovery of some renal function allowing for discontinuance of dialysis.

**FIGURE 3-36**

Renal biopsy demonstrating severe arteriolar nephrosclerosis. Arteriolar nephrosclerosis is intimately associated with hypertension. The histology of the kidney in arteriolar nephrosclerosis shows considerable variation in intensity and extent of the arteriolar lesions. Thickening of the vessel wall, edema of the smooth muscle cells, hypertrophy of the smooth muscle cells, and hyaline degeneration of the vessel wall may be apparent depending on the severity of the nephrosclerosis. In addition to the vascular lesions of arteriolar nephrosclerosis there are abnormalities of glomeruli, tubules, and interstitial areas that are believed to be secondary to the ischemia that results from arteriolar insufficiency. Arteriolar nephrosclerosis is observed in patients with longstanding hypertension; the more severe the hypertension, the more severe the arteriolar nephrosclerosis. Arteriolar nephrosclerosis may also be seen in elderly normotensive individuals and is frequently observed in elderly patients with generalized atherosclerosis or essential hypertension.

**FIGURE 3-37**

Schematic representation of ischemic nephropathy. Patients with atherosclerotic renal artery disease (ASO-RAD) often have coexisting renal parenchymal disease with varying degrees of nephrosclerosis (small vessel disease) or atheroembolic renal disease. Whether or not the renal insufficiency is solely attributable to renal artery stenosis, nephrosclerosis, or atheroembolic renal disease is difficult to determine. The term “ischemic nephropathy” is more complex than being simply due to atherosclerotic renal artery stenosis. In addition, in the azotemic patient with ASO-RAD, one should exclude other potential or contributing causes of renal insufficiency such as obstructive uropathy, primary glomerular disease (suggested by heavy proteinuria), drug-related renal insufficiency (*eg*, nonsteroidal anti-inflammatory drugs), and uncontrolled blood pressure.

**FIGURE 3-38**

Distribution of endstage renal disease diagnoses. Atherosclerotic renal artery disease (ASO-RAD) has been claimed to contribute to the ESRD population. This diagram from the US Renal Data System Coordinating Center 1994 report indicates that 29% of calendar year 1991 incident patients entered ESRD programs because of “hypertension (HBP).” No renovascular disease diagnosis is listed. Crude estimates of the percentage of patients entering ESRD programs because of ASO-RAD range from 1.7% to 15%. Precise bases for making these estimates are both unclear and confounded by the high likelihood of coexisting arteriolar nephrosclerosis, type II diabetic nephropathy, and atheroembolic renal disease. ASO-RAD as a major contributor to the ESRD population is probably small on a percentage basis, occupying some portion of the ESRD diagnosis “hypertension (HBP).” For dialysis-dependent patients with ASO-RAD, predictors of recovery of renal function following renal revascularization and allowing for discontinuance of dialysis (temporary or permanent) include 1) bilateral (vs unilateral) renal artery stenosis, 2) a relatively fast rate of decline of estimated glomerular filtration rate (less than 6 months) prior to initiation of dialysis; and 3) mild-to-moderate arteriolar nephrosclerosis angiographically.

## Treatment of Renovascular Hypertension and Ischemic Nephropathy

### TREATMENT OPTIONS FOR RENOVASCULAR HYPERTENSION AND ISCHEMIC NEPHROPATHY

Pharmacologic antihypertensive therapy  
 PTRAs  
 Renal artery stents  
 Surgical renal revascularization

**FIGURE 3-39**

Treatment options for renovascular hypertension and ischemic nephropathy. The main goals in the treatment of renovascular hypertension or ischemic nephropathy are to control the blood pressure, to prevent target organ complications, and to avoid the loss of renal function. Although the issue of renal function may be viewed as mutually exclusive from the issue of blood pressure control, uncontrolled hypertension may hasten a decline in renal function, and renal insufficiency may produce worsening hypertension. Even in the presence of excellent blood pressure control, progressive arterial stenosis might worsen renal ischemia and promote renal atrophy and fibrosis. Therapeutic options include pharmacologic antihypertensive therapy, percutaneous transluminal renal angioplasty (PTRAs), renal artery stents, and surgical renal revascularization. Pharmacologic antihypertensive therapy is covered in more detail separately in this Atlas.

### INCREASING COMORBIDITY IN PATIENTS UNDERGOING RENOVASCULAR SURGERY

| Condition               | Comorbidity, % |           |
|-------------------------|----------------|-----------|
|                         | 1970–1980      | 1980–1993 |
| Angina                  | 21.4           | 29.9      |
| Prior MI                | 16.3           | 27.0      |
| CHF                     | 12.2           | 23.7*     |
| Cerebrovascular disease | 11.2           | 24.8*     |
| Diabetes                | 7.1            | 18.1*     |
| Claudication            | 35.7           | 56.4*     |

\* $P < 0.001$ .

**FIGURE 3-40**

Comorbidity in patients undergoing renovascular surgery. Patients presenting for renovascular surgery or endovascular renal revascularization are at high-risk for complications during intervention because of age, and frequently associated coronary, cerebrovascular, or peripheral vascular disease. As the population ages, the percentage of patients being considered for interventional maneuvers on the renal artery has increased significantly. Approximately 30% of patients currently undergoing interventional approaches to renal artery disease have angina, or have had a previous myocardial infarction. Congestive heart failure, cerebrovascular disease (eg, carotid artery stenosis), diabetes mellitus, and claudication are frequent comorbid conditions in these patients. Their aortas are often laden with extensive atherosclerotic plaque (Fig. 3-33), making angiographic investigation or endovascular renal revascularization hazardous. (Adapted from Hallet and coworkers [17]; with permission.)

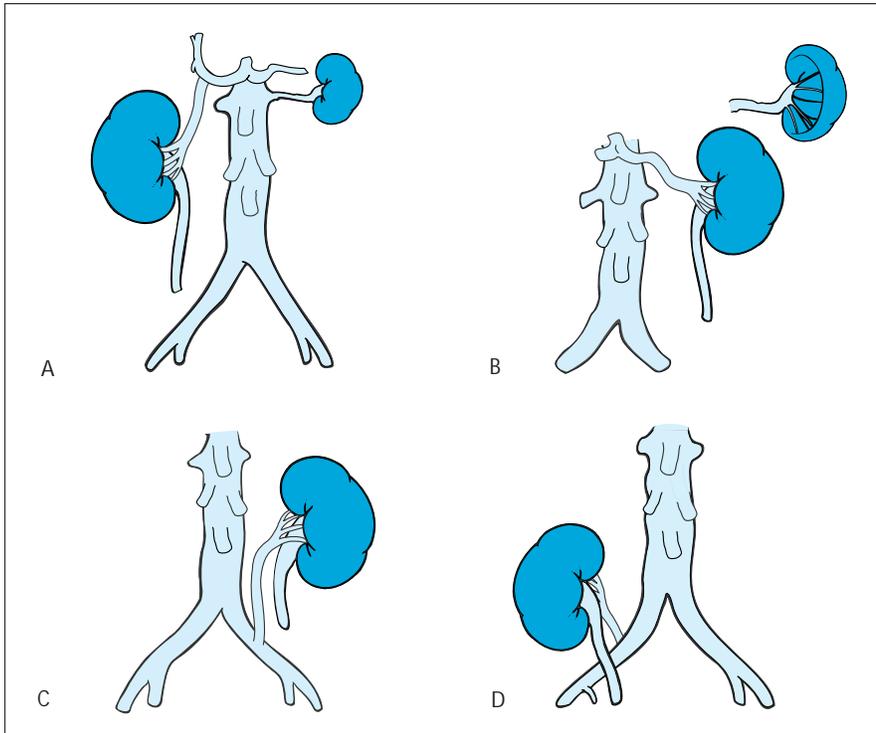
### DIMINISHED OPERATIVE MORBIDITY AND MORTALITY FOLLOWING SURGICAL REVASCULARIZATION FOR ATHEROSCLEROTIC RENOVASCULAR DISEASE

Preoperative screening and correction of coronary and carotid artery disease  
 Avoidance of operation on severely diseased aorta  
 Unilateral revascularization in patients with bilateral renovascular disease

**FIGURE 3-41**

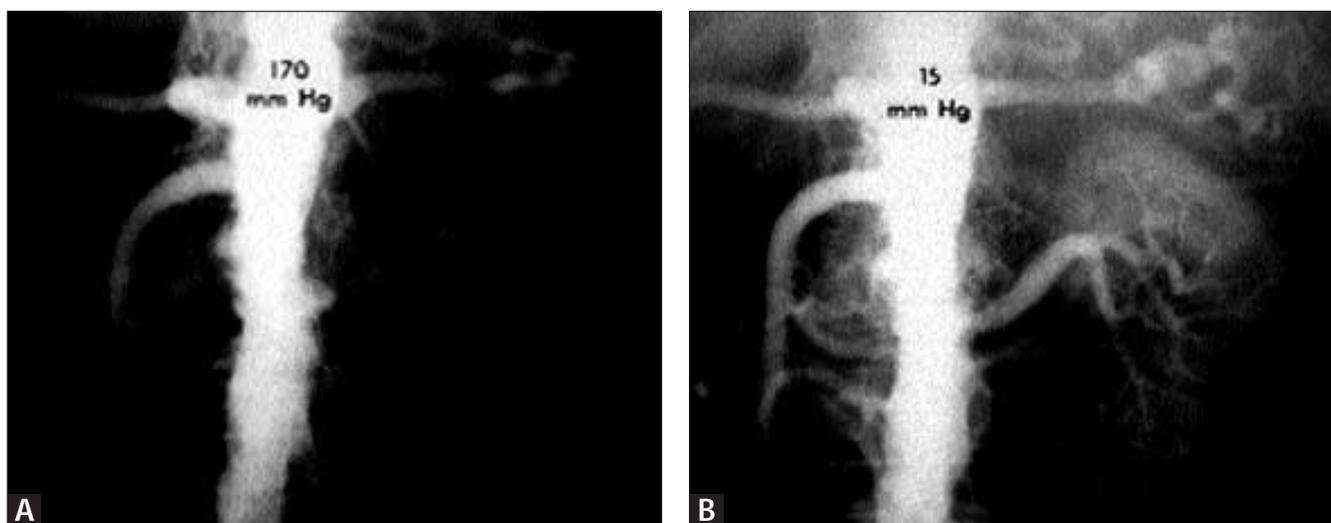
Diminished operative morbidity and mortality following surgical revascularization for atherosclerotic renovascular disease. Operative morbidity and mortality in patients undergoing surgical revascularization have been minimized by selective screening and/or correction of significant coexisting coronary and/or carotid artery disease before undertaking elective surgical renal revascularization for atherosclerotic renal artery disease. Screening tests for carotid artery disease include carotid ultrasound and carotid arteriography. Screening tests for coronary artery disease include thallium stress testing, dipyridamole stress testing, dobutamine echocardiography, and coronary arteriography. Aortorenal

bypass with saphenous vein grafting is a frequently used surgical approach in patients with nondiseased abdominal aortas. Severe atherosclerosis of the abdominal aorta may render an aortorenal bypass or renal endarterectomy technically difficult and potentially hazardous to perform. Effective alternate bypass techniques include splenorenal bypass for left renal revascularization, hepatorenal bypass for right renal revascularization, ileorenal bypass, bench surgery with autotransplantation, and use of the supraceliac or lower thoracic aorta (usually less ravaged by atherosclerosis). Simultaneous aortic replacement and renal revascularization are associated with an increased risk of operative mortality in comparison to renal revascularization alone. Some surgeons advocate unilateral renal revascularization in patients with bilateral renovascular disease.



**FIGURE 3-42**

Schematic diagram of alternate bypass procedures. **A**, Hepatorenal bypass to right kidney. **B**, Splenorenal bypass to left kidney. **C**, Ileorenal bypass to left kidney. **D**, Autotransplantation.

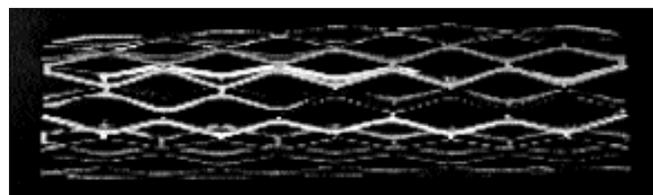
**FIGURE 3-43**

Percutaneous transluminal renal angioplasty (PTRA) of the renal artery. **A**, High-grade (more than 75%) nonostial atherosclerotic stenosis of the left main renal artery in a patient with a solitary functioning kidney (right renal artery totally occluded). Note gradient of 170 mm Hg across the stenotic lesion. **B**, Balloon angioplasty of the left main renal artery was successfully performed with reduction in the gradient across the stenotic lesion from 170 mm Hg pre-PTRA to 15 mm Hg post-PTRA. Repeat aortogram 3 years later demonstrated patency of the left renal artery.

PTRA of the renal artery has emerged as an important interventional modality in the management of patients with renal artery stenosis. PTRA is most successful and should be the initial interventional therapeutic maneuver for patients with the medial fibroplasia type of fibrous renal artery disease (eg, Fig. 3-5A). Excellent technical success rates have also been attained for nonostial atherosclerotic lesions of the main renal artery, as shown here.

**FIGURE 3-44**

High-grade atherosclerotic renal artery stenosis at the ostium of the right main renal artery in a 68-year-old man with a totally occluded left main renal artery. Several attempts at balloon dilatation were unsuccessful. Over the subsequent 10 days, severe renal insufficiency developed (serum creatinine increasing from 2.0 to 12.0 mg/dL) requiring dialysis. Renal function never improved and the patient remained on dialysis.

**FIGURE 3-45**

Palmaz stent, expanded. Because percutaneous transluminal renal angioplasty (PTRA) has suboptimal long-term benefits for atherosclerotic ostial renal artery stenosis, endovascular stenting has gained wide acceptance. Renal artery stenting may be performed at the time of the diagnostic angiogram, or at some time thereafter, depending on the physician's preference and the risk to the patient of repeated angiographic procedures. From a technical standpoint, indications for renal artery stenting include 1) as a primary procedure for ostial atherosclerotic renal artery disease (ASO-RAD), 2) technical difficulties in conjunction with attempted PTRA, 3) post-PTRA dissection, 4) post-PTRA abrupt occlusion, and 5) restenosis following PTRA. It is unclear what the long-term patency and restenosis rates will be for renal artery stenting for ostial disease. Preliminary observations suggest that the 1-year patency rate for stents is approximately twice that for PTRA.

**FIGURE 3-46**

Abdominal aortogram in a 63-year-old male, 6 months following placement of a Palmaz stent. Note wide patency of the left main renal artery.

#### A. SURGICAL REVASCULARIZATION VERSUS PTRA FOR ATHEROSCLEROTIC RENAL ARTERY DISEASE

| Lesion          | Successful PTRA, % | Successful surgical revascularization, % |
|-----------------|--------------------|--|
| Nonostial (20%) | 80–90              | 90                                       |
| Ostial (80%)    | 25–30              | 90                                       |

#### B. SURGICAL REVASCULARIZATION VERSUS PTRA FOR FIBROUS RENAL ARTERY DISEASE

| Lesion       | Successful PTRA, % | Successful surgical revascularization, % |
|--------------|--------------------|--|
| Main (50%)   | 80–90              | 90                                       |
| Branch (50%) | NA                 | 90                                       |

**FIGURE 3-47**

Surgical revascularization vs percutaneous transluminal renal angioplasty (PTRA) for renal artery disease. **A**, Success rates for atherosclerotic renal artery disease (ASO-RAD). **B**, Success rates for fibrous renal artery disease. Success of either PTRA or surgical renal revascularization is viewed in terms of “technical” success and “clinical” success. For PTRA, technical success reflects a lumen patency with less than 50% residual stenosis (*ie*, successful establishment of a patent lumen). For surgical revascularization, technical success is the demonstration of good blood flow to the revascularized kidney determined during surgery, or postoperatively by DPTA renal scan or other immediate postoperative imaging procedures. Technical success with either PTRA or surgical revascularization is rarely defined by postoperative angiography. “Clinical” success may be defined as improved blood pressure or improvement in kidney function, and/or resolution of flash pulmonary edema. Technical and clinical successes do not necessarily occur together because technical success may be apparent, but without improvement in blood pressure or renal function.

The “percent success” for PTRA and surgical revascularization depicted above are estimates, and reflect primarily “technical” success for both nonostial and ostial lesions in ASO-RAD. Technical success rates for surgical revascularization are high, approximating 90%, with little difference in the technical success rates between ostial and nonostial lesions. For PTRA, technical success rates are much higher for nonostial lesions. There is a high rate of restenosis at 1 year ( $\approx 50\%$  to  $70\%$ ) for ostial ASO-RAD, which has promoted the use of renal artery stents for these lesions.

The success rates of surgical renal revascularization and PTRA for stenosis of the main renal artery in fibrous renal artery disease are comparable, approximately 90%. Hypertension is more predictably improved with surgical revascularization and PTRA in fibrous renal artery disease in comparison with ASO-RAD. Technical success rates with surgical renal revascularization are high for branch fibrous renal artery disease, but long-term technical and clinical success rates are not available for PTRA of branch lesions due to fibrous dysplasia. NA—not available. (*Adapted from Pohl [18]; with permission.*)

### COMPLICATIONS OF TRANSLUMINAL ANGIOPLASTY OF THE RENAL ARTERIES

Contrast-induced ARF (mild or severe)  
 Atheroembolic renal failure  
 Rupture of the renal artery  
 Dissection of the renal artery  
 Thrombotic occlusion of the renal artery  
 Occlusion of a branch renal artery  
 Balloon malfunction (may lead to inability to remove balloon)  
 Balloon rupture  
 Puncture site hematoma, hemorrhage, or vessel tear  
 Median nerve compression (axillary approach)  
 Renal artery spasm  
 Mortality ( $\leq 1\%$ )

**FIGURE 3-48**

Complications of transluminal angioplasty of the renal arteries. The more common complications of PTRAs are contrast-induced acute renal failure (ARF) and atheroembolic renal failure. Dissection of the renal artery, occlusion of a branch renal artery, and occasionally thrombotic occlusion of the main renal artery may occur. In experienced hands, rupture of the renal artery is rare. Minor complications relate primarily to the puncture site. When the axillary approach is used (because of severe iliac and lower abdominal aortic atherosclerosis), median nerve compression may transpire. Some of these complications of percutaneous transluminal renal angioplasty, particularly atheroembolic renal failure and/or contrast-induced acute renal failure (ARF) may also be observed with renal artery stent procedures.

### FACTORS TO CONSIDER IN SELECTION OF TREATMENT FOR PATIENTS WITH RENAL ARTERY DISEASE

Is renal artery disease causing hypertension?  
 Severity of hypertension  
 Specific type of renal artery disease and threat to renal function  
 General medical condition of patient  
 Relative efficacy and risk of medical antihypertensive therapy, PTRAs, renal artery stenting, surgical revascularization

**FIGURE 3-49**

Selection of treatment for patients with renal artery disease. In selecting treatment options for patients with renal artery disease, there are several factors to consider: what is the likelihood that the renal artery disease is causing the hypertension? For patients with fibrous renal artery disease the likelihood is high; for patients with atherosclerotic renal artery disease (ASO-RAD), the likelihood for a cure of hypertension is small. The more severe the hypertension, the greater the inclination to intervene with either surgery or balloon angioplasty. For children, adolescents, and younger adults, most of whom will have fibrous renal artery disease, intervention is usually recommended to avoid lifelong antihypertensive therapy. Cardiovascular comorbidity is high for patients with ASO-RAD and appropriate caution in approaching these patients is warranted, weighing the relative efficacy and risk of medical antihypertensive therapy, percutaneous transluminal renal angioplasty (PTRAs), renal artery stenting, and surgical revascularization. Local experience and expertise of the treating physicians must be considered as well in selection of treatment options for these patients.

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