

and vascular abnormalities may also be present in advanced stages of these diseases.

Tubulointerstitial nephritis can be acute or chronic. *Acute tubulointerstitial nephritis* has a rapid clinical onset and is characterized histologically by interstitial edema, often accompanied by leukocytic infiltration of the interstitium and tubules, and tubular injury. In *chronic interstitial nephritis* there is infiltration with predominantly mononuclear leukocytes, prominent interstitial fibrosis, and widespread tubular atrophy. Morphologic features that are helpful in separating acute from chronic tubulointerstitial nephritis include edema and, when present, eosinophils and neutrophils in the acute form, while fibrosis and tubular atrophy characterize the chronic form.

These conditions are distinguished clinically from the glomerular diseases by the following hallmarks:

- Absence of nephritic or nephrotic syndrome
- The presence of defects in tubular function. The latter may be subtle and include impaired ability to concentrate urine, evidenced clinically by polyuria or nocturia; salt wasting; diminished ability to excrete acids (metabolic acidosis); and isolated defects in tubular reabsorption or secretion. Advanced forms, however, may be difficult to distinguish clinically from other causes of renal insufficiency.

Specific conditions are listed in Table 20-8 and are discussed elsewhere in this book. This section deals principally with pyelonephritis and interstitial diseases induced by drugs.

Pyelonephritis and Urinary Tract Infection

Pyelonephritis is one of the most common diseases of the kidney and is defined as inflammation affecting the tubules, interstitium, and renal pelvis. It occurs in two forms. *Acute pyelonephritis* is generally caused by bacterial infection and is associated with urinary tract infection. *Chronic pyelonephritis* is a more complex disorder; bacterial infection plays a dominant role, but other factors (vesicoureteral reflux, obstruction) predispose to repeat episodes of acute pyelonephritis.

Pyelonephritis is a serious complication of *urinary tract infections* that affect the bladder (cystitis), the kidneys and their collecting systems (pyelonephritis), or both. Bacterial infections of the lower urinary tract may be asymptomatic (asymptomatic bacteriuria) and often remain localized to the bladder without the development of renal infection. However, lower urinary tract infection can potentially spread to the kidney.

Etiology and Pathogenesis. More than 85% of cases of urinary tract infection are caused by the gram-negative bacilli that are normal inhabitants of the intestinal tract. For most urinary tract infections, the infecting organisms are derived from the patient's own fecal flora. By far the most common is *Escherichia coli*, followed by *Proteus*, *Klebsiella*, and *Enterobacter*. *Streptococcus faecalis*, also of enteric origin, staphylococci, and virtually every other bacterial and fungal agent can also cause lower urinary tract and renal infection. Mycobacterial and fungal organisms induce caseating and non-caseating granulomatous inflammation, respectively. In immunocompromised persons,

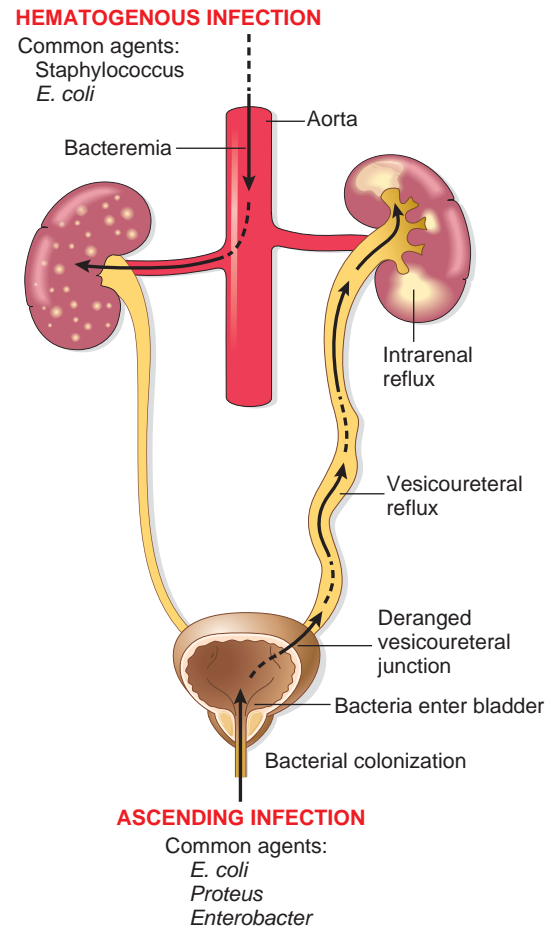


Figure 20-25 Schematic representation of pathways of renal infection. Hematogenous infection results from bacteremic spread. More common is ascending infection, which results from a combination of urinary bladder infection, vesicoureteral reflux, and intrarenal reflux.

particularly those with transplanted organs, viruses such as *polyomavirus*, *cytomegalovirus*, and *adenovirus* can also be a cause of renal infection.

There are two routes by which bacteria can reach the kidneys: (1) through the bloodstream (hematogenous infection) and (2) from the lower urinary tract (ascending infection) (Fig. 20-25). The hematogenous route is less common and results from seeding of the kidneys by bacteria from distant foci in the course of septicemia or localized infections such as infective endocarditis. Hematogenous infection is more likely to occur in the presence of ureteral obstruction, and in debilitated patients. Typically, in patients receiving immunosuppressive therapy, nonenteric organisms, such as staphylococci and certain fungi and viruses, are involved.

Ascending infection is the most common cause of clinical pyelonephritis. Normal human bladder and bladder urine are sterile; therefore, a number of steps must occur for renal infection to occur:

- The first step in ascending infection is the *colonization of the distal urethra and introitus* (in the female) by coliform bacteria. This colonization is influenced by the degree of bacterial adherence to urethral mucosal epithelial, as discussed in Chapter 8, which involves adhesive