Tubulointerstitial Disease

**FIGURE 10-6 (Continued)**
The EDTA–lead mobilization test was normal in normotensive subjects with normal renal function and in patients with chronic renal failure (I) of well-known origin (V). (Adapted from Sanchez-Fructuoso and coworkers [4].)

**FIGURE 10-7**
Decrease in renal function after 25-year exposure to cadmium (Cd). In workers exposed to cadmium for an average time of 25 years, a progressive decrease in renal function occurs during a 5-year follow-up period, despite removal from cadmium exposure 10 years earlier. On average, the glomerular filtration rate was shown to be decreased to 31 mL/min/1.73 m² after 5 years instead of the expected age-related value of 5 mL/min/1.73 m². (Adapted from Roels and coworkers [5].)

**FIGURE 10-8**
Tubular markers in cadmium workers. Impairment of renal proximal tubular epithelium induced by cadmium can be documented by an increase in urinary excretion of urinary neutral endopeptidase 24.11 (NEP), an enzyme of the proximal tubule brush borders, as well as by an increase in microproteinuria: Clara cell protein (CC16), retinol-binding protein (RBP) and β₂-microglobulin (β₂-m). The data were obtained from 106 healthy persons working in cadmium smelting plants. These markers could be used for the screening of cadmium workers. (Adapted from Nortier and coworkers [6].)
Toxic Nephropathies

Lithium nephropathy

**LITHIUM NEPHROTOXICITY**

- Reversible polyuria and polydipsia
- Persistent nephrogenic diabetes insipidus
- Incomplete distal tubular acidosis
- Chronic renal failure (chronic interstitial fibrosis)

**FIGURE 10-9**
Lithium acts both distally and proximally to antidiuretic hormone-induced generation of cyclic adenosine monophosphatase. Polyuria and polydipsia can occur in up to 40% of patients on lithium therapy and are considered harmless and reversible. However, nephrogenic diabetes insipidus may persist months after lithium has been discontinued [7]. Lithium also induces an impairment of distal urinary acidification. Chronic renal failure secondary to chronic interstitial fibrosis may appear in up to 21% of patients on maintenance lithium therapy for more than 15 years [8]. However, these observations are still a matter of debate [7].

**FIGURE 10-10** (see Color Plate)
Lithium nephropathy. A 22-year-old female patient was on maintenance lithium therapy (lithium carbonate 750 mg/d) for 5 years. She presented with polyuria (6500 mL/d) and moderate renal failure (creatinine clearance, 60 mL/min). Proteinuria was not present, and the urinary sediment was unremarkable. A renal biopsy showed focal interstitial fibrosis with scarce inflammatory cell infiltrate, tubular atrophy, and characteristic dilated tubule (microcyst formation). Half of the glomeruli (not shown) were sclerotic. (Magnification × 125, periodic acid-Schiff reaction.)

Germanium nephropathy

**CIRCUMSTANCES OF CHRONIC RENAL FAILURE SECONDARY TO GERMANIUM SUPPLEMENTS**

- Ge-dioxyde elixir, food additives, or capsules (used to improve health in normal persons [Japan])
- Ge-lactate-citrate (used to rebuild the immune system) in patients with HIV infection (Switzerland)
- Ge-lactate-citrate (used to improve health) in patients with cancer (the Netherlands)
- Ge-dioxyde elixir (used to restore health) in patients with chronic hepatitis (Japan)

**FIGURE 10-11**
Germanium (atomic number, 32; atomic weight, 72.59) is contained in soil, plants, and animals as a trace metal. It is widely used in the industrial fields because of its semiconductive capacity. The increased use of natural remedies and trace elements to protect, improve, or restore the health has lead regular supplementation with germanium salts either through food addition or by the means of elixirs and capsules. The chronic supplementation by germanium salts was at the origin of the development of chronic renal failure secondary to a tubulointerstitial nephritis [9–12].
**FIGURE 10-12**
Light microscopy of renal tissue in a patient with chronic renal failure secondary to the chronic intake of germanium, showing focal tubular atrophy and focal interstitial lymphocyte infiltration. A, Hematoxylin and eosin stain. (Magnification × 162.)

Renal tubular epithelial cells show numerous dark small inclusions. B, Periodic acid–Schiff reaction. (Magnification, × 350). (From Hess and coworkers [12]; with permission.)

**Exposure to Analgesics**

**FIGURE 10-13**
Analgesic nephropathy and papillary necrosis. The characteristic feature of analgesic nephropathy is the papillary necrosis process that begins with swollen papillae and continues with fornical erosion, detachment, and calcification of necrotic papillae.

**FIGURE 10-14**
Pathology of analgesic nephropathy. Nephrectomy showing a kidney reduced in size with necrosed and calcified papillae.