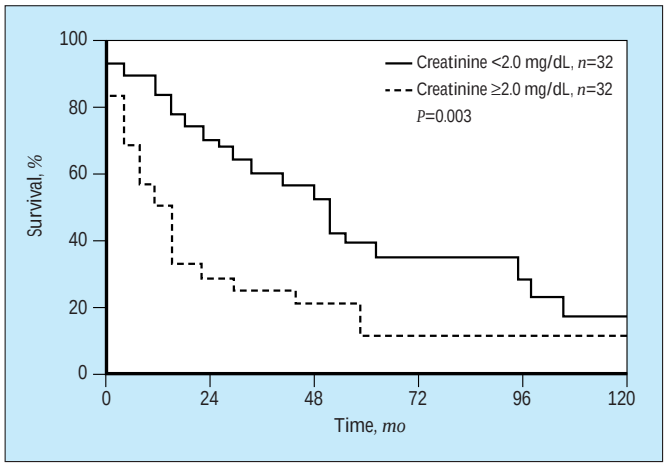

FIGURE 3-45
Association between serum creatinine levels and survival in patients with secondary amyloidosis. A serum creatinine value of 2 mg/dL or more was associated with a shorter survival than was a value of less than 2 mg/dL. (*From* Gertz and Kyle [16]; with permission.)

Familial Amyloidosis

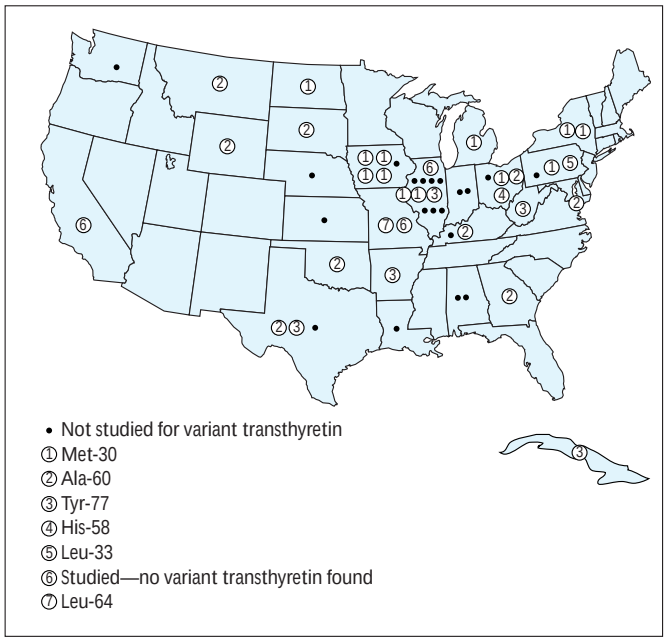

FIGURE 3-46
Wide geographic distribution of familial amyloidosis. Familial or hereditary amyloidosis has an autosomal dominant pattern of inheritance. It accounts for 3.5% of our cases of amyloidosis. In our practice, the geographic distribution is wide and not associated with clustering. Frequently, a family history of amyloidosis was not obtained until after amyloidosis was diagnosed [17]. More than 50 transthyretin mutations have been recognized [18]. (*Adapted from* Gertz et al. [17]; with permission.)

CLASSIFICATION OF FAMILIAL AMYLOIDOSIS

Classification	Major protein component
Neuropathic: Portugal, Japan, Sweden, and other countries	Transthyretin (prealbumin)
Cardiopathic: Denmark and Appalachia in the United States	Transthyretin (prealbumin)
Nephropathic: familial Mediterranean fever	Protein A

FIGURE 3-47

Classification of familial amyloidosis. Clinically, familial amyloidosis can be classified most easily as neuropathic, cardiopathic, or nephropathic. The neuropathic form is characterized by a sensorimotor peripheral neuropathy beginning in the lower extremities. Disturbances of bladder and gastrointestinal function are common. Late onset may occur with the development of symptoms in the seventh or eighth decade of life. The nephropathic form is most often caused by familial Mediterranean fever. This form affects persons of Mediterranean descent and is characterized by recurrent episodes of fever and abdominal pain that begin in childhood.

Familial amyloidosis involving the kidneys has been reported by Ostertag [19] and others [20–22]. Families with apolipoprotein A1 mutation, as well as mutations in the fibrinogen α-chain gene, have been recognized. On presentation, patients with renal involvement exhibit hypertension and mild renal insufficiency that progresses to end-stage renal failure. The amyloid deposits have mutations in the fibrinogen α-chain gene. This form of amyloidosis is autosomal dominant. No peripheral neuropathy develops, and the onset of renal disease occurs in the fifth to seventh decades of life. The mutation consists of the substitution of glutamic acid for valine at position 526 of the fibrinogen chain. A mutation in fibrinogen has been described at position 554 [23,24]. A rare form of inherited secondary amyloidosis produces nephropathy, deafness, and urticaria. This form has been referred to as the Muckle-Wells syndrome [25]. (*Adapted from* Kyle and Gertz [26].)

Dialysis-Associated Amyloidosis

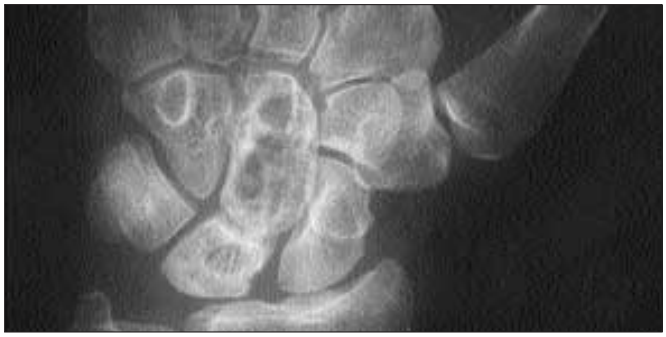

FIGURE 3-48

Radiograph showing carpal tunnel syndrome in a patient with dialysis-associated amyloidosis. Long-term hemodialysis often results in carpal tunnel syndrome with pain involving the shoulders, hands, wrists, hips, and knees. Cystic radiolucencies are common in the carpal bones. Pathologic fractures have occurred from large amyloid deposits. The major component of the amyloid is β_2-microglobulin. (*From* Gertz and Kyle [3]; with permission.)

RATE OF AMYLOIDOSIS (β_2-MICROGLOBULIN) WITH DIALYSIS

Years of dialysis	Patients with amyloidosis, %
10	20
15	30–50
>20	80–100

FIGURE 3-49

Amyloidosis (β_2-microglobulin) with dialysis. The duration of dialysis is directly associated with the incidence of amyloidosis. Dialysis-associated amyloidosis will develop in more than 80% of patients after 20 years of dialysis. It occurs with both hemodialysis and peritoneal dialysis. The amyloid deposition is systemic; however, involvement of visceral organs is usually modest [27,28]. Renal transplantation often leads to dramatic improvement in joint symptoms. A β_2-microglobulin–absorbent column may be useful in therapy [29].

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