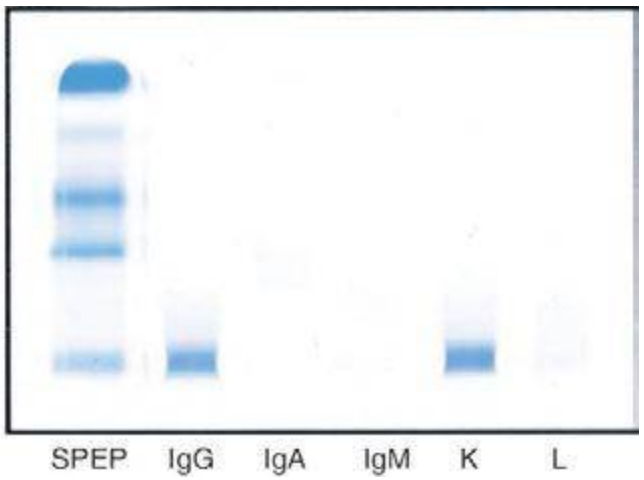

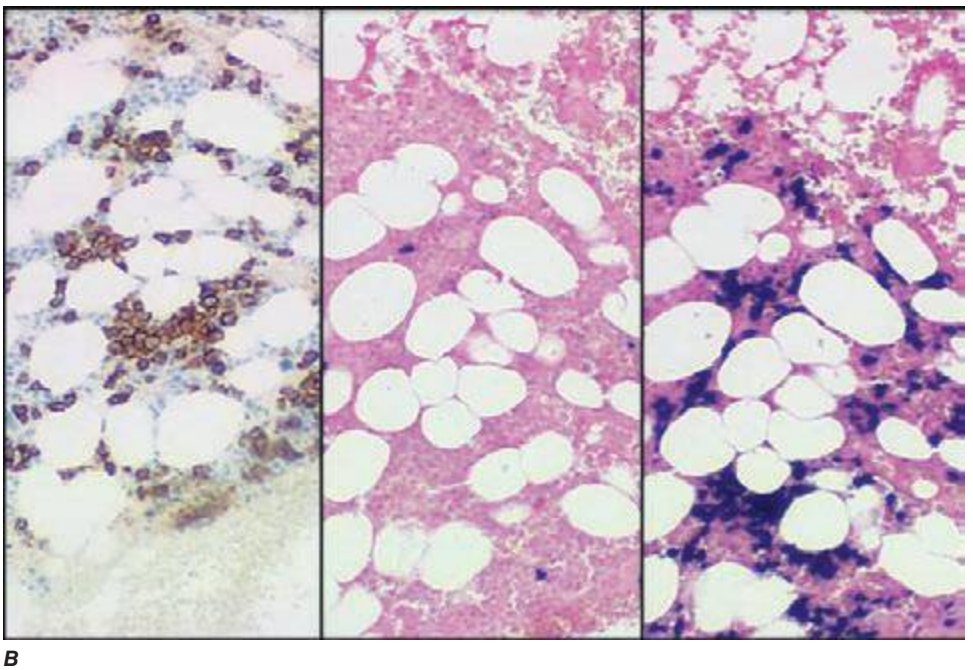

FIGURE 137-3 **Laboratory features of AL amyloidosis.** ***A.*** Serum immunofixation electrophoresis reveals an IgGκ monoclonal protein in this example; serum protein electrophoresis is often normal. ***B.*** Bone-marrow biopsy sections stained by immunohistochemistry with antibody to CD138 (syndecan, highly expressed on plasma cells) (*left*) or by in situ hybridization with fluorescein-tagged probes (Ventana Medical Systems) binding to κ mRNA (*center*) and λ mRNA (*right*) in plasma cells. *(Photomicrograph courtesy of C. O'Hara; with permission.)*

clonal bone-marrow plasma cells, using approaches employed for multiple myeloma. Treatment with oral melphalan and prednisone can decrease the plasma cell burden but rarely leads to complete hematologic remission, meaningful organ responses, or improved survival and is no longer widely used. The substitution of dexamethasone for prednisone produces a higher response rate and more durable remissions, although dexamethasone is not always well tolerated by patients with significant edema or cardiac disease. High-dose IV melphalan followed by autologous stem cell transplantation (HDM/SCT) produces complete hematologic responses in ~40% of treated patients, as determined by loss of clonal plasma cells in the bone marrow and disappearance of the monoclonal LC, as determined by SIFE/UIFE and free LC quantitation. Hematologic responses can be followed in the subsequent 6–12 months as improvements in organ function and quality of life. Hematologic responses appear to be more durable after HDM/SCT than in multiple myeloma, with remissions continuing in some patients beyond 15 years without additional treatment. Unfortunately, only about half of AL amyloidosis patients are suitable for aggressive treatment, and, even at specialized treatment centers, transplantation-related mortality rates are higher than those for other hematologic diseases because of impaired organ function. Amyloid cardiomyopathy, poor nutritional and performance status, and multiorgan disease contribute to excess morbidity and mortality. A bleeding diathesis resulting from adsorption of clotting factor X to amyloid fibrils also increases mortality rates; however, this syndrome occurs in only 5–10% of patients. A randomized multicenter trial conducted in France compared oral melphalan and dexamethasone with HDM/SCT and failed to show a benefit of dose-intensive treatment, although the transplantation-related mortality rate in this study was very high. It has become clear that careful selection of patients and expert peritransplantation management are essential in reducing transplantation-related mortality.

For patients with impaired cardiac function or arrhythmias due to amyloid involvement of the myocardium, the median survival period is only ~6 months without treatment. In these patients, cardiac transplantation can be performed and followed by HDM/SCT to eliminate the noxious clone and prevent amyloid deposition in the transplanted heart or other organs.

Novel anti–plasma cell agents have been investigated for treatment of plasma cell diseases. The immunomodulators thalidomide, lenalidomide, and pomalidomide display activity; dosing may need