TABLE 137-1 AMYLOID PRECURSOR PROTEINS AND THEIR CLINICAL SYNDROMES

Designation	Precursor	Clinical Syndrome	Clinical Involvement
Systemic Amyloidoses			
AL	Immunoglobulin light chain	Primary or myeloma-associated[a]	Any
AH	Immunoglobulin heavy chain	Rare variant of primary or myeloma-associated	Any
AA	Serum amyloid A protein	Secondary; reactive[b]	Renal, other
$A\beta_2M$	β_2-Microglobulin	Hemodialysis-associated	Synovial tissue, bone
ATTR	Transthyretin	Familial (mutant)	Cardiac, peripheral and autonomic nerves
		Age-related (wild type)	
AApoAI	Apolipoprotein AI	Familial	Hepatic, renal
AApoAII	Apolipoprotein AII	Familial	Renal
AGel	Gelsolin	Familial	Cornea, cranial nerves, skin, renal
AFib	Fibrinogen Aα	Familial	Renal
ALys	Lysozyme	Familial	Renal, hepatic
ALECT2	Leukocyte chemotactic factor 2	Undefined	Renal
Localized Amyloidoses			
Aβ	Amyloid β protein	Alzheimer's disease; Down syndrome	Central nervous system
ACys	Cystatin C	Cerebral amyloid angiopathy	Central nervous system, vascular
APrP	Prion protein	Spongiform encephalopathies	Central nervous system
AIAPP	Islet amyloid polypeptide (amylin)	Diabetes-associated	Pancreas
ACal	Calcitonin	Medullary carcinoma of the thyroid	Thyroid
AANF	Atrial natriuretic factor	Atrial fibrillation	Cardiac atria
APro	Prolactin	Endocrinopathy	Pituitary
ASgl	Semenogelin I	Age-related; incidental autopsy or biopsy finding	Seminal vesicles

[a]Localized AL deposits can occur in skin, conjunctiva, urinary bladder, and the tracheobronchial tree. [b]Secondary to chronic inflammation or infection or to a hereditary periodic fever syndrome such as familial Mediterranean fever.

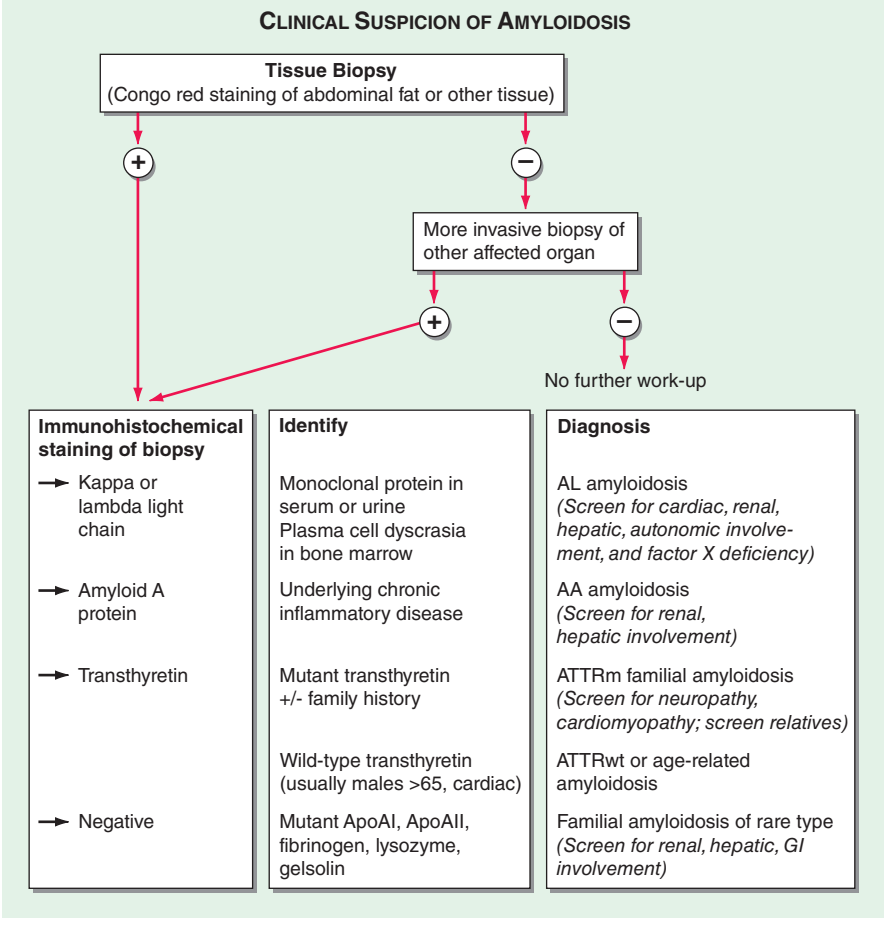

FIGURE 137-1 Algorithm for the diagnosis of amyloidosis and determination of type. Clinical suspicion: unexplained nephropathy, cardiomyopathy, neuropathy, enteropathy, arthropathy, and macroglossia. ApoAI, apolipoprotein AI; ApoAII, apolipoprotein AII; GI, gastrointestinal.

hypoalbuminemia that may be severe; patients with serum albumin levels below 2 g/dL generally have pedal edema or anasarca. Amyloid cardiomyopathy is characterized by concentric ventricular hypertrophy and diastolic dysfunction associated with elevation of brain natriuretic peptide or N-terminal pro–brain natriuretic peptide as well as troponin. These cardiac biomarkers can be used for disease staging, prognostication, and disease activity monitoring in patients with AL amyloidosis. Notably, renal insufficiency can falsely elevate levels of these biomarkers. Recently, biomarkers of cardiac remodeling—i.e., matrix metalloproteinases and tissue inhibitors of metalloproteinases—have been found to be altered in the serum of patients with amyloid cardiomyopathy. Electrocardiographic and echocardiographic features of amyloid cardiomyopathy are described below. Patients with liver involvement, even when advanced, usually develop cholestasis with an elevated alkaline phosphatase concentration but minimal alteration of the aminotransferases and preservation of synthetic function. In AL amyloidosis, endocrine organs may be infiltrated with fibrils, and hypothyroidism, hypoadrenalism, or even hypopituitarism can occur. Although none of these findings is specific for amyloidosis, the presence of abnormalities in multiple organ systems should raise suspicion regarding this diagnosis.

AL AMYLOIDOSIS

Etiology and Incidence AL amyloidosis is most frequently caused by a clonal expansion of bone-marrow plasma cells that secrete a monoclonal immunoglobulin LC depositing as amyloid fibrils in tissues. Whether the clonal plasma