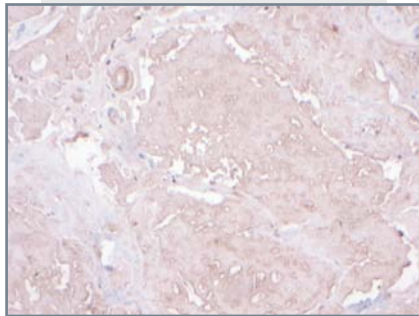


7

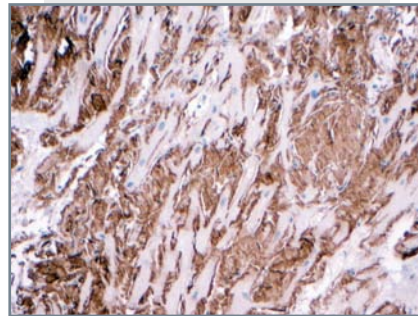
The term 'amyloid' was first employed by Rudolph Virchow in 1854 to describe deposits in human tissues. Thought to be 'starch-like', it has been learned that amyloid is actually composed predominantly of proteinaceous material. Amyloidoses differ in the protein precursor that undergoes aggregation to form the beta pleated sheets which yield the congophilic material called amyloid. These different amyloids differ in the target organs involved and in their clinical features. To date, at least 28 different proteins have been identified as causative agents of amyloid diseases, ranging from localized cerebral amyloidosis in neurodegenerative conditions such as Alzheimer's and Creutzfeldt-Jakob diseases, to systemic amyloidoses such as immunoglobulin (Ig) monoclonal light chain amyloidosis (AL) and transthyretin (ATTR) amyloidosis.

The identification of amyloid generally begins with a Congo red stain, which should be performed on an 8 micron tissue section. A positive test is defined as the presence of dichroic birefringence observed with crossed polarizing filters.

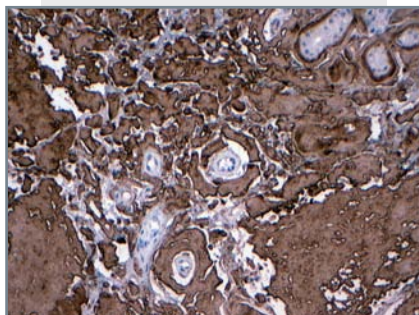
Correct subclassification of amyloid is essential, as amyloid can be treatable and different treatment regimens are applied to different amyloid diseases. IHC can be employed to subclassify amyloids into those composed of AA protein, immunoglobulin light chains, transthyretin (prealbumin), beta amyloid and keratin, among others. The use of IHC requires experience and understanding of the often 'sticky' nature of amyloid proteins, and the ability to distinguish between specific and nonspecific signal. In general, only strong signals are considered positive, and correct interpretation of amyloid immunostains requires considerable experience and expertise.



*Kappa*

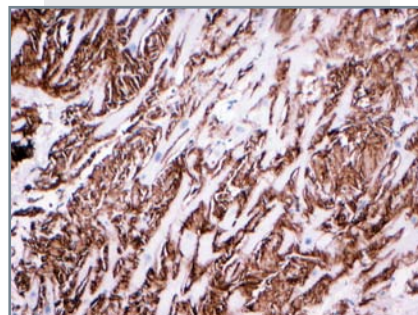


*Amyloid P*



*Lambda*

*Soft tissue light chain (AL) amyloid deposits identified with antibodies to lambda light chains by IHC*



*Transthyretin*

*Cardiac transthyretin (ATTR) amyloid deposits identified with antibodies to amyloid P (a component of all amyloid subtypes) and transthyretin*