**DEVELOPING DIAGNOSTIC CRITERIA IN WALDENSTRÖM'S MACROGLOBULINAEMIA.**

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**There are currently no universally accepted diagnostic criteria for Waldenström's macroglobulinaemia (WM). The majority of clinical studies accept the presence of an IgM paraprotein in the context of an apparently indolent lymphoproliferative disorder as sufficient evidence for a diagnosis of WM. This is unsatisfactory and criteria incorporating clinical, morphological, immunophenotypic and ultimately genotypic parameters are required for the accurate diagnosis of WM.**

**The secretion of an IgM paraprotein per se is not synonymous with a diagnosis of WM as they are demonstrable in all subtypes of mature B-cell lymphoma as well as MGUS. It has also been suggested that the paraprotein concentration is useful in differentiating WM from other lymphoproliferative disorders. Indeed paraprotein concentrations tend to be higher in WM but there is considerable overlap such that it is not possible to define a paraprotein concentration, which consistently distinguishes WM from MGUS and other lymphoproliferative disorders. It is also interesting to note that many of the classical clinical features such as hyperviscosity syndrome appear to be relatively rare and these should not therefore be used as disease defining features.**

**WM is characterized by bone marrow infiltration by small lymphocytes showing a variable degree of plasmacytoid / plasma cell differentiation. The pattern of infiltration is usually diffuse or interstitial. A purely paratrabecular pattern of infiltration is rare and follicular lymphoma requires specific exclusion in such cases.**

**It is clear that immunophenotypic criteria are needed. In our analysis of 111 patients we found that the majority of patients were characterized by the following immunophenotype: CD5-CD10-CD19+CD20+CD23-CD79b+. All cases expressed surface IgM and the majority appeared to express IgD by flow cytometry although this is not usually demonstrable by immunohistochemistry. The plasma cell component was almost invariably CD138+ while CD27, CD52 and bcl-2 were expressed in virtually all cases.**

**I would therefore suggest the following diagnostic criteria for WM: bone marrow infiltration by small lymphocytes in a non-paratrabecular distribution, IgM paraprotein of any concentration and a sIgM+CD5-CD10-CD19+CD20+CD23-CD79+ immunophenotype.**