8 Table Pitfalls in Interpretation of Lab Studies of Sjogren's and SLE

It is a common error that the "tail" (ie. pattern of the ANA) was the dog (ie. the clinical diagnosis).

Often, this diagnostic confusion is based on the titer and pattern of the ANA (anti-nuclear antibody) that is performed during screening. These diagnostic discussions (and often conflicting diagnoses among rheumatologists) must take into account:

1) the ANA titer can differ substantially in different laboratories and in the same laboratory when different methods are used. This is particularly a problem when ELISA methods to detect ANA are used, in comparison to tube dilution titers using immune fluorescent assays on Hep 2 cells. Indeed, a recent New England Journal of Medicine "Clinical Pathologic Discussion Case" had the diagnosis revolve around differences in the method used for testing for ANA(3).

Thus, the same laboratory may give entirely different results on the same patient sample depending on which method is used for the assay(4, 5).

2) the problem of ANA detection is a particular problem for SS patients, since the assays are set up for detection of SLE associated antigens(4, 5). This leads to results such as a negative ANA but a positive SS-A antibody. Since the SS-A is presumably in the nucleus, how can we resolve this inconsistency(6-8). Some antigens in the nucleus (such as fibrillary proteins or chromatin associated) are not well solubilized. Other antigens are destroyed by the extraction or fixation processes.

For example, we used to have a diagnosis called "subacute lupus" where the ANA was negative and the antibody to SS-A was positive. It was subsequently recognized that this paradox was the result of the high "acetone" solubility of the SS-A antigen, which was removed during "overfixation" of commercially available slides(9-12). The "control" sera for the ANA assay is generally selected from SLE patients (often chosen for their high titer to DNA or Sm/RNP) and continued to detect positive antigens even though the SS-A antigen had been leached out. This may lead to a misleading laboratory report that the ANA is negative when the antibody to SS-A/B is positive.

3) The diagnosis of SS or other related disease is defined by their clinical presentations (Tables 2 to 4) and not by the pattern of their ANA. The pattern of ANA (ie. fine speckled or centromere or nucleolar) correlates more closely with the patient's genotype than with their clinical presentation . Thus, ANA and their patterns/specific antibodies are used to confirm a clinical diagnosis rather than used as the basis of a "fishing expedition."
4) Not all patients fit into a nice, neat single category and exhibit overlap

features. This is important in choosing therapies. In some cases, patients may fulfill more than one set of criteria and should be considered an “overlap.”