activation by an infectious event. On the other hand, T-cell dysfunction had been reported to play a role in the pathogenesis of MN [10]. Though the association between HLA-B51-related SNSpA and MN could be by chance, there might be a common pathogenetic mechanism caused by T-cell function in both SpA and MN. In the present case, the combination therapy including CSA was very efficient to improve proteinuria and arthralgia. We suspect that this could support our hypothesis.

We report the first case of HLA-B51-related SNSpA associated with MN. HLA-B51 is much more common in the Japanese population than HLA-B27 [5]. HLA-B51-related SNSpA might be included in uSpA and there might be more frequent cases with this condition than we thought, especially in the Asian region. We propose that one should consider HLA-B51-related SNSpA as one of differential diagnoses in Japanese patients with SpA and/or MN.

**Rheumatology key message**

- HLA-B51-related SpA should be considered as one of the differential diagnoses in Japanese patients with SpA and/or MN.

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**References**


**Comment on: Clinical utility of ANA measured by ELISA compared with ANA measured by immunofluorescence**

Sir, We read with interest the recently published study by Maguire et al. [1] on the clinical utility of ANA testing in a real-world rheumatology setting. By comparing IIF microscopy with ELISA, they reached the conclusion that ELISA is the preferable method. This subject has been a matter of debate for many years [2, 3]. The opinion of Maguire et al. is based in their finding that sera from 169 (14%) patients, out of 1239 analysed during a 12-month period, tested IF-positive but ELISA-negative. This result did not relate to self-reported symptoms suspect of SLE or any other systemic inflammatory disease compared with age- and sex-matched controls testing ANA-negative with both IF and ELISA. However, we have a few objections to the study design. First and foremost, regarding ANA as a criterion for SLE. The 1982 ACR classification states that ‘an abnormal titer of antinuclear antibody by IF or an equivalent technique’ is required [4]. As shown in many studies, IF and ELISA are not equivalent regarding ANA results. Thus, at present, only IF-ANA qualifies as an ACR classification criterion, but solely when it exceeds the cut-off limit for an abnormal antibody titre, i.e. in practice at a serum level higher than the 95th percentile in healthy blood donor material. Maguire et al. screened for IF-ANA at a serum dilution of 1:40. Assuming that their IF test was performed with up-to-date equipment, screening for ANA at this high serum concentration will undoubtedly result in a huge number of positive reactions below abnormal titre [5, 6]. On the other hand, with an appropriate cut-off level for IF-ANA, the analysis is likely to result in a point prevalence of ANA far <95% among patients with established SLE [7]. A caveat regarding the IF-ANA test used by Maguire et al. is that the secondary antibody in their diagnostic kit was achieved using whole human IgG molecules rather than IgG-Fc fragments. Thus, the
fluorochrome-labelled detection antibody may recognize not only IgG, but also light chains of other immunoglobulin isotypes, potentially capturing also IgM class ANA, which is more common than IgG-ANA among healthy blood donors [8]. Based upon more than 3000 serum samples sent for routine ANA testing, although not scrutinizing the clinical rationale to perform the test, we came to the conclusion that IgG class-specific IF-ANA must remain the gold standard for ANA screening (using proper cut-off limits), at least as long as the present ACR classification criteria are in use [5]. In their paper, Maguire et al. do not state the proportion of ELISA-positive sera testing IF-ANA negative. In our hands, this is a bigger problem than the reverse. Nevertheless, in addition to IF microscopy using HEp-2 or -2000 cells as nuclear antigen substrates, we advocate the use of supplementary antigen-specific assays (e.g., ELISA) in order not to miss out patients positive for anti-SSA/Ro60 antibodies!

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Comment on: Clinical utility of ANA measured by ELISA compared with ANA measured by immunofluorescence: reply

Sir, We thank Skogh and Dahle [1] for their interest in our study [2] and welcome the opportunity to reply. Their principal objection is our use of a 1-in-40 serum dilution to screen for IF-ANA. The screening dilution used in IF-ANA is a compromise between sensitivity and specificity. A lower dilution gives greater sensitivity for detecting significant autoantibodies and a higher dilution gives greater specificity. In practice, a dilution of 1-in-40 has been recommended for greatest sensitivity [3] and is commonly used (at least in the UK). It should be noted, however, that this is just the first stage of a multi-step testing strategy. Any positive results are further tested for anti-DNA and ENA antibodies that are more disease specific. Thus, the overall approach gives good sensitivity and specificity.

Our study investigated whether ELISA-ANA-negative and IF-ANA-positive patients were different. It is certainly true that had we screened for IF-ANA at a higher dilution, we might have identified a different group of patients. We have, therefore, re-analysed the data for those patients who were negative in the ELISA-ANA but positive in the IF-ANA at a dilution of 1-in-160 or greater. This dilution has been reported to be the 95th percentile for healthy individuals [3]. There are fewer patients to analyse in this group; however, again no differences were found in reported symptoms between the two groups (Table 1).

Skogh and Dahle made two further observations about our study. They comment that the second antibody we used may have recognized IgM and IgA ANA, but in fact we used gamma chain-specific rabbit anti-human IgG (product code F202; Dako, Glostrup, Denmark), which does not recognize IgA or IgM. They also pointed out that we did not state what proportion of ELISA-positive sera was IF-ANA negative. Of 1302 samples received from rheumatology clinics, 103 (7.9%) were positive by ELISA and negative by IF (at a dilution of 1-in-40), whereas 201 (15.4%) were negative by ELISA and positive by IF. In addition, 186 (14.2%) were positive by both techniques and 812 (62.4%) were negative by both techniques. This indicates that, in our experience, IF-positive ELISA-negative subjects are more common than IF-negative ELISA-positive subjects. Since ELISA is the newly introduced technique, we were keen to document whether patients...