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Response to: 'Antisynthetase syndrome or what else? Different perspectives indicate the need for new classification criteria' by Cavagna *et al*

We thank Cavagna *et al*[1] for their thoughtful analysis relating to our recent publication.[2] Several important points are raised, many of which we also referred to. It is of great interest and reassurance that the demographics and clinical features of antisynthetase syndrome (ASS) are broadly similar between the AENEAS (American and European NEtwork of Anti-Synthetase syndrome) and EuroMyositis cohorts. Clearly the frequency of interstitial lung disease and arthritis differs due to the sources of case ascertainment. This highlights the importance when evaluating the natural history and demographics of a disease presenting with heterogeneity that one must use more than one source of case ascertainment.

The paradigm of classification of the idiopathic inflammatory myopathies (IIM), particularly with regard to ASS, is a subject of much debate. This reflects our developing understanding of these disorders and the growing agreement regarding the importance of autoantibody status in determining a phenotype. One unanswered question relates to the heterogeneity within the ASS spectrum and the underlying mechanisms that explain why certain antisynthetase antibodies (ASAs) are associated with certain clinical phenotypes. We also agree that if the shift towards disease definition according to clinicoserological syndrome is to continue, harmonisation of antibody testing methodologies is required. However, exceptions are required for patients displaying typical clinical features of ASS, but without a detectable ASAs, in some cases almost certainly the consequence of the presence of a hitherto unrecognised antibody or the limitations of current antibody testing methodologies.

To develop a well-rounded knowledge of ASS, future collaboration across multiple disease specialities is vital. Together with other groups such as the International Myositis Assessment and Clinical Studies Group (https://www.niehs.nih.gov/research/resources/imacs/index.cfm) and the European Reference Network for Rare Diseases, future standardised classification criteria will be developed. We agree that the presence of skeletal muscle inflammation should not be a prerequisite for the diagnosis of ASS and that labelling such patients as having an IIM is becoming less intuitive. More accurate clinicoserological criteria will allow more homogeneous participant groups in research studies, and in the future allow for more targeted therapies.

We look forward to broadening the existing collaboration between our groups, facilitated through the recently awarded Foundation for Research in Rheumatology grant (http://www.foreum.org/prg_13_myositis_transition.cfm). It is only with such collaborative efforts that we can advance our search for a more accurate diagnosis and better treatment options in the future.

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