Letters

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Recommendations for the recognition, diagnosis, and management of long COVID

The British Society for Allergy and Clinical Immunology (BSACI) would like to respond to the article by Nurek *et al*.[1] We appreciate this is a growing area of interest, and that further research is needed, but we feel that this article makes conclusions that are not supported by evidence, and which has the potential to trigger unnecessary referrals to allergy and immunology clinics, which are already facing huge pressures.

In Box 1, described as *'Known examples of conditions associated with long COVID'*, included are *'Mast cell activation, including urticaria, angioedema, and histamine intolerance'*, along with *'New-onset allergies and anaphylaxis'*. It has been recognised that SARS-CoV-2 infection can be associated with urticaria and angioedema,[2] as is the case with many infections,[3] but there is no evidence to suggest that acute infection or long COVID causes new allergic sensitisation or manifestations of allergic or atopic diseases including anaphylaxis. Similarly, it is not clear that urticaria itself is increased in long COVID, after the initial phase of infection. The term 'histamine intolerance' can be misleading in that there is no clear evidence to support a role for ingested histamine in chronic urticaria, a well-recognised auto-immune disorder.[4,5]

The authors draw parallels between the symptoms of 'mast cell activation syndrome (MCAS)' and those of long COVID, and suggest that this diagnosis should be considered in patients with a broad range of symptoms. They acknowledge as do we that MCAS is a controversial area with no clear diagnostic criteria. An association between autonomic dysfunction and mast cell disorders is suggested, although in fact this remains unproven and based predominantly on symptom reporting.[6] They then offer recommendations for treatment including low-histamine diets, antihistamines, and montelukast, and suggest referral to immunology or allergy specialists. No evidence is provided to support the use of low-histamine diets, or an association between MCAS and long COVID. This is an interesting area for further research, but the evidence is not there for this to be put forward as a recommendation to family doctors.

We understand that the article represents the lived experience of a number of doctors dealing with long COVID, and is an attempt to shed light on possible mechanisms and treatment approaches. However, the casual reader may assume the recommendations carry the same weight as for instance a National Institute for Health and Care Excellence (NICE) guideline.

We are concerned that no specialists in the field of allergy or immunology were involved in the publication. We do not feel that referral of patients with non-specific symptoms to allergy/immunology clinics is appropriate, unless there is a clear clinical question requiring assessment of a possible specific allergic trigger.

NICE has published detailed guidance for investigation and management of long COVID.[7] Scottish Intercollegiate Guidelines Network (SIGN) guidelines also include specific advice on management of urticaria and angioedema in the context of long COVID, which emphasises that no different management strategies are required.[8] Considerable investment has been made by NHS England into long COVID services, which are now starting to develop across the UK.[9] We would encourage family doctors to use the published NICE and SIGN guidance when assessing patients and to use approved referral pathways.

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Author response

In their letter, the British Society for Allergy and Clinical Immunology (BSACI) criticise our suggestions on the role of mast cells in managing long COVID based on lack of evidence, and the risk of triggering unnecessary referrals to immunology and allergy clinics.

Our paper was written over a year ago, before long COVID clinics and in the face of an urgent need to bridge the gap between evidence-based practice and clinical experience in the face of a widening health emergency. Given the slow pace of research, we are no further on in 'NICE-standard' evidence, yet we now have 1.7 million people with long COVID, half of whom with symptoms for over a year and over a million with their working lives significantly impacted.[1] For GPs to sit back and take the stance of the BSACI would be a gross failure to meet the needs of our patients. Our recommendations on treating urticaria do not step beyond the Scottish Intercollegiate Guidelines Network guidance cited, except in considering it reasonable to extend the symptomatic scope of treatment. Referral in severe cases of angioedema or anaphylaxis is within current guidance.

Ongoing research in long COVID