Corresponding author:
Dr. Jignaben Krunal Padhiyar,
Department of Dermatology, Venereology and Leprology, GCS Medical College Hospital and Research Centre, Ahmedabad, Gujarat, India.
dr.jignapadhiyar@gmail.com

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Response to a reader's query on CD19+ B cell as predictor of relapse in pemphigus vulgaris

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Sir,

We thank the authors[1] for their interest in our article 'Identification of clinical and immunological factors associated with clinical relapse of pemphigus vulgaris in remission.'[2]

We understand that 40 may be a small control sample size to derive the normal value, and that sampling a larger number of normal individuals would have been better. We agree that use of a normative data from Indian population of over 1000 subjects would be useful. However, the journal that published the data of 1000 healthy Indians is indexed by Web of Science, Current Contents, Geobase, Chemical Abstracts, IndMed, and Scopus and not indexed in PubMed. Hence, we missed the reference to this article.[3] We appreciate the authors' efforts in finding it out.

However, since we were interested in not just the frequency of CD19+B cells but also the CD19+CD27+ memory B cells (which is lacking in the study referred to), we would still have to study the same age and sex-matched normal control subjects for comparison of CD19+CD27+B cells. The purpose of this analysis was not to project these data as a reference for normal healthy control subjects of North India, but only for comparative analysis of the study subjects in question. Moreover, since the blood samples of controls and subjects with pemphigus vulgaris were stained with the same lot and clone of the antibodies and were analyzed on the same flow cytometry platform, we were able to ensure assay uniformity. Additionally, practical difficulties such as willingness to participate despite not having the disease in question and financial constrains in respect to study funding are some important considerations in this type of study.

The controls were age and gender matched individuals with other dermatological diseases attending our outpatient department. One qualified as a control if s(he) did not have any recent infectious disease or autoimmune disease including pemphigus.

We agree with the authors that: 'Peripheral CD19+ B cell count being significantly influenced by steroid use and steroid withdrawal and rituximab being the most potent and total CD19+ B lymphocyte depleter among all the previous treatment', and that is why rituximab induces remission for a longer time. Other treatments also have effects on CD19+ B cells. The objective of the study was to see repopulation of CD19+ B cells and subsequent effects, not to study depletion of B cells with a particular treatment that is assumed to have had happened since the patients were in remission when they were included in the study.

To have clinical relapse, first step is immunological reactivation in the form of B-cell repopulation. There is no other known source of immunoglobulins. In other words, it can be assumed that B-cell repopulation must occur irrespective

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of treatment modality employed preceding clinical relapse in a prototype IgG-mediated disease such as pemphigus. Yes, this is an assumption and it may be an endeavor of scientific community to establish in a future research.

The authors also mention: 'During discussion of results, author has compared their findings with one published by Albers *et al*.; study referred by author was strictly limited to B cell repopulation after rituximab therapy.' We had considerable difficulty in understanding context of their reference to this study. We studied B-cell repopulation along with other parameters and we think that it is logical and prudent to do additional things.

We agree to the authors' suggestion: 'Analysis of patient previously treated with rituximab vis a vis other treatment modalities and baseline CD19+ B cell count among them and subsequent trend in both the groups would have thrown more light on this very interesting aspect of relapse in pemphigus vulgaris.' However, the number of patients required in each treatment group and thus overall number of pemphigus patients in remission (who are willing to follow-up periodically for a long time when they do not have a clinical disease) is likely to be very high to have meaningful statistical result and thus practically difficult. This shall definitely give a better understanding of achievement of remission.

We also agree to the suggestion: 'Pilot study on CD19+ B cell behavior with various treatment modalities may also help understand this immunological marker in pemphigus.' The authors also mention: 'No other treatment like steroid, azathioprine, DCP are known to thoroughly deplete B cell from circulation as rituximab.' If the latter statement is based on scientifically established fact, the pilot study as suggested in the first statement is perhaps not required, but can still be done if there is uncertainty regarding the latter.

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Conflicts of interest
There are no conflicts of interest.

Ankur Guliani, Dipankar De, Sanjeev Handa, Rahul Mahajan, Naresh Sachdeva[1], Bishan Das Radotra[2], Kamal Kishore[3]

Departments of Dermatology, Venereology and Leprology, [1]Endocrinology (Immunology Division), [2]Histopathology and [3]Biostatistics, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding author:
Dr. Dipankar De,
Department of Dermatology, Venereology and Leprology, Postgraduate Institute of Medical Education and Research, Sector 12, Chandigarh, India.
dr_dipankar_de@yahoo.in

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