5 ml. of sterile water. Unlike mechlorethamine, solution remains stable for 3 hours. By above reasons it is all right if it is administered over 2 hours in an intravenous infusion as its pharmacological activity is not affected. Moreover, cyclophosphamide is added to the same solution wherein dexamethasone is present and it is advisable to administer it over 2-4 hours to avoid the adverse effects associated with pulse steroid therapy.

2. Prevention of cyclophosphamide induced sterile hemorrhagic cystitis

The rationale behind the additional infusion of 500 ml of 5% dextrose on the day of intravenous cyclophosphamide is to wash out any retained drug in the urinary tract to prevent urinary complications of cyclophosphamide. We have made this a part of the protocol so that adequate hydration become a fixed routine on the day of administration of cyclophosphamide. We chose 5% dextrose to the normal saline to avoid the sodium load. This was well accepted by the patients and none of our patients had any complications associated with such an administration. Adequate oral supplementation of fluids definitely will suffice. However, such instruction which cannot be incorporated in protocol are frequently neglected / over looked.

The use of MESNA in these patients is an accepted practice. However studies have shown that subclinical renal toxicity has been observed in children receiving ifosfamide, which is an oxazophosphorine like cyclophosphamide, despite MESNA administration and that administration of MESNA does not eliminate the need for adequate hydration and careful observation of the patient.

3. The early morning administration of steroids to avoid HPA axis suppression is only relevant when short or intermediate acting corticosteroids are used for therapy. In pulse therapy for pemphigus, we are administering high dose of dexamethasone which is a long acting corticosteroid, (action for 24 to 36 hours). Hence, irrespective of the time of administration, the drug is in circulation for the whole day. More importantly it is administered only for 3 days in a month. Adrenal suppression occurs only when corticosteroids are administered for more than 2 weeks which is not the case in pulse therapy for pemphigus.

P. Narasimha Rao, T. S. S. Laxmi
Dept. of Dermatology, Osmania Hospital & Osmania Medical College, Hyderabad.

Address for correspondence: Dr. P Narasimha Rao
B-48, Income Tax Colony, Mehdipatnam, Hyderabad - 500 028, India. E-mail: dermarao@hotmail.com

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Response by Dr. Ramam

Sir,

The suggestions made by Gandhi et al will have to be considered by centers administering pulse therapy and implemented if considered beneficial and feasible. It would be ideal to compare the proposed changes to the original schedule in a randomised, controlled trial. Carefully kept records will be needed to document the
time to remission, the duration of remission with treatment and the relapse-free period after stopping therapy: outcomes of importance to patients and dermatologists alike. I would like to make a comment on the utility of immunofluorescence testing in determining the length of treatment. There are few situations where indirect immunofluorescence (IIF) testing is of any significant diagnostic value in pemphigus. Its role in predicting prognosis is also limited. Direct immunofluorescence (DIF) testing fares better in predicting relapse-free remissions but is not reliable enough to be useful in everyday clinical practice. ELISA for antibodies to desmoglein 3 and desmoglein 1 is a relatively new test and time will tell if it will have much application in prognosis though this appears unlikely from previous experience with IIF. For the present, it appears that we will have to continue our search for reliable predictors of the response to treatment.

M. Ramam
Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi - 110029.

Address for correspondence: Department of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi - 110 029. Email: mramam@hotmail.com

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Response by Dr. Pasricha

Sir,

This is to thank Dr. Navin Modi and Dr. Gandhi et al for their comments/suggestions on the articles on pulse therapy in pemphigus published in the IJDVL.1,2,3,4

My response to the comments is as follows:

1. The duration of infusion of dexamethasone between 1 to 2 hours has been found to be safe. In case the infusion is more rapid it can produce some disturbances in the heart rate, while if it is too slow it may not produce the peak levels as produced by the 2-hour infusion. The same is true of the oral pulse.

2. Use of azathioprine or methotrexate at Hyderabad is a welcome modification5 and deserves to be assessed further.

3. The suggestion to use cyclophosphamide pulses instead of daily cyclophosphamide4 needs to be evaluated to see if it will produce equal or better results. I feel the patients would prefer to swallow a tablet daily rather than have a drip. Cyclophosphamide toxicity among our patients is already negligible because our patients drink a lot of water. In an occasional patient who develops toxicity, MESNA and other measures may be used. I am not in favor of using too many drugs as a routine in every patient.

4. Should one depend upon the results of direct immunofluorescence (DIF) and indirect immunofluorescence (IIF) to decide the duration of phase II and phase III? This needs to be assessed. Most of our patients show negative or low titers at the end of phase III, but I have also found positive DIF/IIF even 5 years post-treatment even when there had been no clinical relapse. I find it very difficult to assess which patient requires more treatment and which one requires less. Neither the percentage of body area of involvement at the start of the treatment nor the IIF titer seem to have any bearing on the promptness of the recovery in each case.

5. Shortening the duration of phase II and phase III seems to lead to a higher rate of relapse as also the administration of the pulses at irregular intervals rather than the exact 28 day cycles.

6. I feel the use of immunoablative high dose of cyclophosphamide is more risky and would not like to use it.

In conclusion, every worker has a right to modify the original regimen and any regimen which produces