REFERENCES

BAKER, D.J. (1983) Generalized pruritus as the presenting feature of bullous pemphigoid. *British Journal of Dermatology*, **109**, 237.

BINGHAM, E.A., BURROWS, D. & SANDFORD, J.C. (1984) Prolonged pruritus and bullous pemphigoid. *Clinical and Experimental Dermatology*, **9**, 564.

LEVER, W.F. (1979) Pemphigus and pemphigoid. *Journal of the American Academy of Dermatology*, **1**, 2.

MACDONALD, K.J.S. & RAFFLE, E.J. (1984) Ritodrine therapy associated with remission of pemphigoid gestationis. *British Journal of Dermatology*, **111**, 630.

PACIUCCI, P.A. & HOLLAND, J.F. (1984) Hypothesis AIDS:AAIDS (Acquired Autoimmune Immunodeficiency Syndrome)? *Aids Research*, **1**, 149.

SAURAT, J.H., DIDIERJEAN, L., CALS-CADORET, F. *et al* (1978) Pemphigoide papuleuse. *Annales de Dermatologie et de Vénéréologie (Paris)*, **105**, 973.

SHAFER, R.W., OFFIT, K., MACRIS, N.T. *et al.* (1985) Possible risk of steroid administration in patients at risk for AIDS. *Lancet*, **I**, 934.

ZOLLA-PAZNER, S. (1984) B cells in the pathogenesis of AIDS. *Immunology Today*, **5**, 289.

Reply

MADAM, The therapeutic effect of the beta-mimetic drug ritodrine in our patient with pemphigoid gestationis (herpes gestationis) (*British Journal of Dermatology*, 1984, **111**, 630) was striking, although its *modus operandi* was unclear. We were interested to know whether others had observed a similar effect in herpes gestationis but had not considered a therapeutic trial of this drug in other bullous diseases. The report by Levy *et al.*. of its value in suppressing bullous pemphigoid in a patient with AIDS-related complex is extremely interesting and it is, in fact, the only feed-back we have had on this topic. We agree that further evaluation of the clinical and pharmacological effect of ritodrine in pemphigoid and other bullous diseases is called for.

Department of Dermatology,
Ninewells Hospital,
Dundee DD1 955,
Scotland

K.MACDONALD
E.J.RAFFLE

The human skin blanching assay—use and abuse

MADAM, The standard method employed by pharmacologists to study relative potency is to compare equipotent concentrations. This is normally done by preparing dose-response curves and comparing either the maximal response or the concentrations required to produce a half maximimal effect. The assay of corticosteroid potency using the blanching test advocated by Haigh *et al.* (*British Journal of Dermatology*, 1985, **113**, 502) is qualitative and may only be used as a rank order test. There is no *a priori* evidence that the use of a non-parametric 'area under the curve' assay is more reliable than measurement at a single specified time.

Using a simple all or none end-point, McKenzie (1962) was able to use the blanching test to study the dose-response relationship in a manner that eliminated observer bias as far as possible. The dose-response relationship has also been measured objectively using colchicine-arrested mitotic rate measurements (Marks, Pongsehirun & Saylan, 1973) and suppression of irritant-induced epidermal thickening (Barnes *et al.*, 1975). Other methods that may provide quantitative information on corticosteroid-induced effects are measurements of dermal thickness using ultrasound and of skin blood flow.

The blanching test is difficult to interpret since the degree of pallor depends on factors such as ambient temperature and may be obscured by changes in skin colour induced by ointment bases (Burdick, Poulsen & Place, 1970; Coldman & Lockerbie, 1971; Woodford & Barry, 1973). Furthermore, the method is

subjective and can only, at best, be used to establish a rank order of potency. Since the blanching test was first introduced, standards of drug assay have improved and the blanching test should no longer be accepted as adequate except as a preliminary crude assay.

The Royal Free Hospital,
Hampstead,
London NW3 2QG, U.K.

P.M.GAYLARDE

REFERENCES

BARNES, H., GAYLARDE, P.M., BROCK, A.P. & SARKANY, I. (1975) An improved method of assessing topical corticosteroid activity. *British Journal of Dermatology*, **92**, 459.

BURDICK, K.H., POULSEN, B. & PLACE, V.A. (1970) Extemporaneous formulation of corticosteroids for topical usage. *Journal of the American Medical Association*, **211**, 462.

COLDMAN, M.F. & LOCKERBIE, L. (1971) Placebo ointment response in the blanching test. *British Journal of Dermatology*, **85**, 398.

MARKS, R., PONGSEHIRUN, D. & SAYLAN, T. (1973) A method for the assay of topical corticosteroids. *British Journal of Dermatology*, **88**, 69.

MCKENZIE, A.W. (1962) Percutaneous absorption of steroids. *Archives of Dermatology*, **86**, 611.

WOODFORD, R. & BARRY, B.W. (1973) The placebo response to white soft paraffin propylene glycol in the skin blanching test. *British Journal of Dermatology*, **89**, 53.

Reply

MADAM, Whilst we are in agreement with Dr Gaylarde's comment that there is a base induced blanching response in human skin, this normally occurs for only 1–2 h after the removal of the corticosteroid formulation. As we pointed out in our original letter, this is one of our objections to conclusions drawn from single readings of blanching made 1 h after removal of the residual topical formulation.

It is a well established fact that a response-time profile, from which the area under the curve value is determined, provides complete characterization of the observed phenomenon. Considering that the profiles of two topical corticosteroid formulations may be coincident at certain time intervals while deviating substantially at others, the use of a single point assessment may result in an invalid conclusion.

We accept that the human skin blanching assay is subjective in that a visual determination of blanching is made. It should be noted, however, that workers in Germany (Altmeyer & Krumney, 1978) and England (Feather *et al.*, 1982), who have developed quantitative instrumental reflectance methods for measuring skin colour at the site of blanching, have shown a very close correlation between visual and instrumental determinations of the intensity of skin pallor.

We disgree strongly with Dr Gaylarde's statement that the blanching assay should no longer be accepted as adequate. While the simple all or none end point used by McKenzie (1962) may well be considered a preliminary crude assay, considerable research has been performed since that time utilizing and refining this assay in keeping with the general trends of improvement in drug analysis methods. Comprehensive studies by Barry and Woodford (1978) have shown that, provided the protocol of the method is strictly adhered to by experienced workers, the blanching assay is sensitive, accurate and reproducible.

Finally, we would like to assure Dr Gaylarde that we do not advocate the use of the human skin blanching assay. There are several other *in vivo* methods for determining corticosteroid activity which will provide equally meaningful results. What we *are* advocating is that if the human skin blanching assay is going to be used, then it should be used properly.

School of Pharmaceutical Sciences,
Rhodes University,
Grahamstown,
6140 South Africa

J.M.HAIGH
I.KANFER
E.MEYER
E.SMITH