Using the Western blot method with an epidermal extract as substrate it was found that normal human serum contains a large number of antibodies which, using this method, react with epidermal antigens. A similar observation was made using normal human serum in an indirect immunofluorescence system with normal human skin as substrate.[7]

Some of the lines seen on Western blot disappear when the serum is adsorbed onto a culturable micro-organism. This might indicate extensive sharing of antigenic determinants between epidermis and micro-organisms.

In view of the above observations it is possible to speculate that a number of the immune dermatoses could be brought about or be maintained by environmental micro-organisms.

REFERENCES

1 Damian RT. Molecular mimicry: antigen sharing by parasite and host and its consequences. *Am Nat* 1964; **98:** 129–56.

2 Cunningham MW, Hall NK, Krisher KK *et al.* A study of anti-group A streptococcal monoclonal antibodies cross-reactive with myosin. *J Immunol* 1986; **136:** 293–8.

3 Holoshitz J, Drucker I, Yaretzky A *et al.* T-Lymphocytes of rheumatoid arthritis patients show augmented reactivity to a fraction of mycobacteria cross-reactive with cartilage. Lancet 1986; **ii:** 305–9.

4 Stefansson K, Dieperink ME, Richman DP *et al.* Sharing of antigenic determinants between the nicotine acetylcholine receptor and proteins in *Escherichia coli*, *Proteus vulgaris* and *Klebsiella pneumoniae*. *N Eng J Med* 1985; **312:** 221–5.

5 Acosta AM, Sadigursky M, Santos-Buch CA. Anti-striated muscle antibody produced by *Trypanosoma cruzi*. *Proc Soc Exp Biol Med* 1983; **172:** 364–9.

6 Wood JN, Hudson L, Jessell TM *et al.* A monoclonal antibody defining antigenic determinants on subpopulations of mammalian neurons and *Trypanosoma cruzi* parasites. *Nature* 1982; **296:** 34–8.

7 Van Joost Th. Serum antibodies with affinity to the cytoplasm of epidermal basal cells. In: *Immunopathology of the skin* (Beutner EH, ed), 2nd Edn. Chichesters: John Wiley 1979; 473–88.

The role of T lymphocytes in the pathogenesis of psoriasis

E.P.Prens, K.Benner* and Th.van Joost

*Departments of Dermatology, Venereology and *Immunology, University Hospital, Rotterdam*

The aetiology of psoriasis remains obscure, but there are two main hypotheses as regards its pathogenesis:[1] the epidermal hyperplasia is primary and the dermal inflammatory changes are secondary; the epidermal hyperplasia is secondary. The first hypothesis was supported by studies performed by Van Scott and co-workers.[2] Their results appeared to support the hypothesis that psoriasis is a genetically determined condition inherent to keratinocytes and this resulted in research into the proliferative properties (cell cycle time), the course of cell differentiation (keratin markers) and the aberrant metabolism (cAMP and cGMP contents) of the 'psoriatic' keratinocyte. The findings included the results that keratinocytes from psoriasis lesions produce increased amounts of the mediators of inflammation, particularly leukotriene B_4 (LTB_4) and 12-hydroxyeicosatetraenoic acid (12HETE), which are also chemotactic factors for myeloid cells and would explain the presence of cells of the non-specific immune system. (PMNs, monocytes) in the inflammatory infiltrate.

The second hypothesis postulates that the epidermal lesions in psoriasis are secondary to a primary immunological inflammation in the skin. When monoclonal antibodies (MAb) became available the immunopathology of psoriasis was studied further and it was found that the inflammatory infiltrate in the earliest lesions consisted mainly of $CD4^+$ (inducer/helper) T lymphocytes and monocytes, whereas polymorphonuclear cells were absent. Moreover, T lymphocytes were also present in the epidermis where they were arranged closely to HLA-DR^+ dendritic cells. Such an immunohistological pattern might also be consistent with a type IV allergic reaction. The efficacy of cyclosporin A in psoriasis indicated an involvement of T lymphocytes in maintaining activity and that they play a key role in the pathogenesis of psoriasis.[3-7] T lymphocytes from patients with psoriasis were stimulated to proliferate by autologous epidermal cells. This reaction was described as the mixed epidermal cell–T lymphocyte reaction (MECLR). We have confirmed this reaction and investigated the role of epidermal and peripheral blood antigen-presenting cells in the process. In our *in vitro* system the strength of the autologous MECLR proved to be dependent on the dose of epidermal cells administered. The autologous MECLR proved to be a HLA-DR-restricted process. This reaction was induced, not by peripheral blood antigen-presenting cells but by epidermal cells. In the autologous MECLR the epidermal Langerhans cell did not play the crucial role as observed in allergic contact reactions, as elimination of these cells from the epidermal cell suspension led to merely a slight decrease in the proliferative response. Elimination of the other HLA-DR^+ cells from the epidermal cell suspension led to a virtually complete inhibition of the response. The above results were used to produce a pathogenetic model in which both hypotheses function. HLA-DR^+ dendritic epidermal cells present the 'psoriasis antigen' to T lymphocytes. T lymphocytes become activated in the dermis, proliferate and produce lymphokines (e.g. IL-2 and IFN-γ). In response to the locally produced cytokines, keratinocytes and/or fibroblasts are likewise activated and proliferate. Due to genetically determined factors, these keratinocytes and/or fibroblasts show an increased response to cytokines produced by T lymphocytes. The production of an autocrine growth factor is thereby induced in keratinocytes and/or fibroblasts. Alternatively, there is no negative feedback system for T lymphocyte-induced proliferation in the psoriatic keratinocytes and/or fibroblasts. The two original hypotheses are suggested to be interdependent.

REFERENCES

1 Zachariae H. Epidemiology and genetics. In: *Textbook of Psoriasis.* (Mier PD and Van de Kerckhof PCM, eds), Edinburgh: Churchill Livingstone 1986; 4–12.

2 Van Scott EJ, Ekel TM. Kinetics of hyperplasia in psoriasis. *Arch Dermatol* 1963; **88:** 373–81.

3 Fry L. Psoriasis. *Br J Dermatol* 1988; **119:** 445–61.

4 Van Joost Th, Heule F, Stolz E *et al.* Short-term use of cyclosporin A in severe psoriasis. *Br J Dermatol* 1988; **114:** 615–20.

5 Bos JD. The pathomechanisms of psoriasis; the skin immune system and cyclosporin. *Br J Dermatol* 1988; **118:** 141–55.

6 Valdimarsson H, Baker BS, Jonsdittir I *et al.* Psoriasis: a disease of abnormal keratinocyte proliferation induced by T lymphocytes. *Immunology Today* 1986; **7:** 256–9.

7 Gottlieb AB. Immunologic mechanisms in psoriasis. *J Am Acad* Dermatol 1988; **18:** 1376–80.