INTRODUCTION

In discussing immunology with an audience interested in immunotoxicology it may be useful to focus on a specific problem such as contact dermatitis while recognizing that factors similar in principle but differing in detail will apply to other immunological diseases such as asthma. Because this is not a formal review many of the references are based on work with which I am closely familiar from which further references to the literature may be found. To begin with it may help to consider a particular manifestation and then to see how our experimental knowledge of contact sensitivity bears on this.

Nickel dermatitis is a common disease and is acquired by contact with nickel mainly through costume jewellery and earrings (sleepers) which contain nickel. Nickel has the chemical reactivity which is a common feature of contact sensitizers. It dissolves under slightly acid conditions in sweat and its salts have a high affinity for a number of proteins including albumin (Dolovich et al, 1984) which has a metal binding site and for C3b, B in which bivalent nickel can replace magnesium and actually generates an unusually stable C3 convertase (Fishelson et al, 1983). This interaction with protein is due to the ability of nickel to form coordination compounds with the amino groups of lysine and the N terminal amino acids and the imino group of histidine.

It is not clear why the immune system regards nickel as a good contact sensitizer. However the ability of nickel sulphate to cause blast transformation in unimmunized animals and newborn humans (Al Tawil et al, 1981; Nordlind, 1983) raises the question whether it has a direct effect on macrophages and other antigen presenting cells and causes them to release IL-1 (see below).

Nickel dermatitis poses several problems

a) If nickel were a new agent, could its ability to sensitize be predicted and would there be a serious alternative to testing in man?

b) Is the incidence of nickel dermatitis a direct reflection of the level of exposure or are there individual factors which explain why under similar environmental conditions some individuals have no lesions, other minors lesions around the point of exposure while yet others have intermittent or chronic eczema of the hands (Hansen et al, 1982)?

c) What is the mechanism of the skin lesion?
MECHANISM OF THE CONTACT SENSITIVITY REACTION

The classical view is that following exposure to antigen, proliferation occurs in the regional lymph nodes and gives rise to effector cells. These effector cells leave the lymph node and circulate in the blood and move to the skin test site as the result of the minor degree of inflammation caused by challenge. There is argument whether there is any antigen specificity in this arrival, i.e. whether cells clonally committed to the antigen show greater arrival than other cells. The lymphocytes then interact with antigen, probably on the surface of antigen presenting cells which provide class II major histocompatibility products (MHC) which are otherwise known as transplantation antigens. The lymphocytes then release various lymphokines which cause the local inflammation and in particular lead to the further influx of cells and to fibrin deposition in the more severe lesions.

Recently it has been realized that basophils enter some lesions in the guinea pig and man. It is thought that a subset of lymphocytes and in some situations circulating antibody is responsible, see Mitchell and Askenase, (1982). However in general antibody only plays a subsidiary role in augmenting certain delayed hypersensitivity (but not apparently contact sensitivity) skin reactions, while the essential reaction is transferred by T lymphocytes (Asherson, 1967).

Askenase and his coworkers have described a further mechanism which probably serves to amplify the contact sensitivity reaction (Askenase et al, 1983; Askenase and Loveren, 1983). Mice with established contact sensitivity have T lymphocytes which liberate an antigen specific T cell factor. This factor is reminiscent of IgE in that it arms mast cells. These then release mediators, of which serotonin may be the main one, which increase the permeability of the local capillaries to protein and to cells. The increased permeability then facilitates the passage of the classical effector T cells which liberate lymphokines and are responsible for the bulk of the reaction. It is not yet critically clear whether these two functions are due to different sets of T lymphocytes.

CONTROL OF THE SIZE AND DURATION OF THE CONTACT SENSITIVITY REACTION

Generalities

Some of the main factors which influence contact sensitivity are listed in table 1. It is outside the scope of this article to discuss physiological and pharmacological factors such as skin permeability and the dermal equivalent of the bronchial hyperreactivity seen in asthma, although these are clearly important and skin permeability in particular will influence the dose of antigen received by an individual. This increase in permeability may explain in part the greater ease with which contact dermatitis is induced when agents are applied to damaged skin and the adverse effect of irritants