FUNDAMENTAL ASPECTS OF CONTACT SENSITIVITY TO NICKEL

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INTRODUCTION

Contact sensitivity (or allergic contact dermatitis or delayed hypersensitivity to, nickel) is an allergic reaction.

Allergy (also known as hypersensitivity) has been conveniently divided by Gell and Coombs into four different types I-IV. The first three types are "immediates" (types I-II) or semi-delayed (type III): they occur very soon (a few minutes to 2-4 hours) after the attack of an antigen.

Type I or Anaphylaxis: this allergy type includes urticaria, asthma, hay fever, anaphylactic shock (which may lead to death due to insect-wasps in particular-bites), to medications such as penicillin, etc. The allergen or antigen is generally a protein (from pollen for instance) or a polysaccharide. Reaction occurs between this antigen and antibodies, either induced or inherited (known as immunoglobulins) present in the blood.

Type II or Cytotoxic reactions: this includes the hemolytic disease of the newborn, accidents in blood transfusion due to the incompatibility of blood groups, etc. This is again a reaction between an antibody (immunoglobulin) and the attacking antigen (a protein usually).

Type III (also known as Arthus phenomenon): this takes a few hours to show up. The clinical aspects is that of an oedema (swelling of the skin at the site of attack), an erythema (redness of the skin) or even necrosis, allergic vascularitis, glomerulonephritis, etc. Again the antigen is usually a high molecular weight compound.

Contact dermatitis due to nickel belongs to type IV allergy. Type IV includes such important immune phenomena as homograft rejection, autoimmune diseases, and allergic contact dermatitis (ACD). The aggressor is a small molecule (molecular weights usually do not exceed 1000 daltons) called hapten or incomplete antigen. In order to be recognized in the organism, it needs to attach to a carrier molecule (usually a protein), thus forming a complete antigen or allergen. The latter word, allergen, is very often used for small molecular weight compounds which should correctly be named hapten.
It is generally thought that ACD occurs in two distinct phases. In the first contact with the hapten, let us say here with nickel (metal or salt, this will be developed later on) nothing appears at the clinical level. This is the induction phase. What must probably occurs is the following:

The hapten penetrates into the skin, gets bound to a carrier protein molecule in the epidermis, thus forming the complete allergen. This allergen attaches itself to several skin cells and in particular to Langerhans cells, a dendritic cell equipped with HLA receptors (or MHC receptors) and in particular with the \( \text{DR} \) (in man) or \( \text{I} \) (in guinea pigs and mice) antigen which enables this cell to deliver a message to another important cell, a T-lymphocyte. This close contact between the Langerhans cell and the T-lymphocyte, also called "flirt", seems a major event in the induction of sensitization (= induction of allergy).

In a second phase, also known as proliferation phase, the T-cells go to the closest node where they multiply through clonal selection into effector and memory cells. The former will be responsible, through the release into the organism of chemical mediator, lymphokines, for the following clinical events (not apparent in the first contact with the allergen (hapten)): redness (= erythema), swelling (= oedema).

If there is no further contact with the hapten (nickel for instance), there will be no clinical evidence of active sensitization.

In turn if after a few days (the whole process described above takes less than a week), there is a second contact with the allergen (nickel) the same molecular and cellular events take place much faster, and a clinical lesion of the skin (eczema, the combination of erythema, and oedema) shows up. Fortunately, a third subpopulation of T-lymphocytes also appears after a few days: these are called suppressor cells. They are responsible for the decrease of the intensity of the skin reaction. Being sensitized or not is probably due to a delicate balance between suppressor and effector cells.

Cellular events are summarized in Figure 1.

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**Figure 1.**
Summary of cell events

I\(_m\) (mouse) = \( \text{D}_R \) (Man) Major Histocompatibility System antigen; \( \text{L}_T \) = T-Lymphocyte; S = Suppressor cells, M = Memory cells, E = Effector cells