Sensitization, Inhibition and Immunological Tolerance to Simple Chemical Compounds in Guinea Pigs

J.R.		Frey ^a
A.L.		de Weck ^b
H.		Geleick ^a

^aDepartment of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., Basle; Department of Dermatology, Inselspital, University of Bern, Bern (Switzerland)

Authors' address: Dr. J. R. Frey and Dr. H. Geleick, Department of Experimental Medicine, F. Hoffmann-La Roche & Co., Ltd., Basle, and Dr. A. L. de Weck, Department of Dermatology, Inselspital, University of Bern, Bern (Switzerland)

Epicutaneous contact or intradermal injection with compounds such as 2–4 dinitrochlorobenzene (DNCB) will provoke in guinea pigs both delayed and immediate type hypersensitivities. In sensitive guinea pigs, partial or total inhibition of the contact reaction can be achieved by intravenous injection of DNCB or the cross-reacting dinitrobenzene sulfonate (DNBSO₃) which probably form conjugates in vivo. This inhibition is specific but temporary.

According to the quantitative relationships existing between the dose of hapten injection and the original hypersensitivity level of the animals, various effects can be observed, such as partial or complete inhibition, generalized delayed-type dermatitis and flare up of older test sites. These different effects are best explained by considering direct interaction between specific lymphoid cells and antigen (conjugate) molecules as a prerequisite for the development of allergic delayed-type inflammation.

By investigating the inhibiting effect of different haptens, hapten-amino acid and hapten-protein conjugates of the dinitrophenyl system, one may gain some information about the specificity of the contact reaction to DNCB. It is apparent that contact or injection of DNCB induces an immunological response of wide inhomogeneity, due to several types of antigenic conjugates formed in vivo. The role of circulating antibodies in delayed type contact reactions is not yet fully clear, but cannot be denied as summarily as it used to be.

Adult guinea pigs become tolerant to DNCB if, previous to the sensitizing contact, they are injected intravenously with DNBSO₃. The

* Will be published in extenso in the Journal of Investigative Dermatology and in International Archives of Allergy and Applied Immunology.

26

Frey, deWeck and Geleick

state of unresponsiveness obtained is dependent upon the time elapsed between the injection of DNBSO₃ and the sensitizing contact as well as upon the dose of DNBSO₃ administered.

Accordingly, complete or partial tolerance may be achieved. When DNBSO₃ is given twice, 4 and 2 weeks before sensitization, 100% of the animals become tolerant.

This tolerance is specific as in double sensitized animals the reaction against a second hapten remains uninfluenced. Furthermore, the tolerance is of long duration (38 weeks) as demonstrated by subsequent testing. Without repeated testing (first test performed 2 months after sensitizing

attempt) the animals are still tolerant. The tolerance is independent of circulating anti-dinitrophenyl (DNP) antibodies. Such antibodies are not found in tolerant animals and their deliberate induction by DNP-protein conjugates does not affect the state of unresponsiveness to DNCB contact. The tolerance can not be terminated nor induced by a second sensitization performed with Freund's adjuvant.

The tolerance studies were also performed with Neoarsphenamine (NEO). Adult guinea pigs can be sensitized by one intradermal injection of this compound and respond later to the same dose with a tuberculinlike reaction. When NEO is injected previously by the intravenous route, a permanent and specific tolerance is achieved.

Already sensitized animals can be rendered permanently tolerant when an intravenous injection of NEO is followed 6 or 12 hours later by an intradermal one. When an interval of 1 or 3 days has elapsed between the intravenous and the intradermal injections, only part of the animals become tolerant, and no tolerance is achieved when the interval lasts 7 or 14 days.

I. In animals sensitized to DNCB

the intravenous injection of DNBSO₃ followed 6 hours later by a test elicits only a temporary inhibition and not a long lasting tolerance as with NEO. The different behaviour of these haptens may be due to their different elimination rates but also to different effects on the immune response. It must be stressed that the immunologic reaction to NEO we succeeded in repressing in tuberculin-like

while in the experiments with DNCB a contact dermatitis is dealt with.