Studies on Flare and Rash Phenomena in Guinea-Pigs

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Summary. Both in men and animals flaring-up of existing or already healed dermatitis is rather common. Flare reactions especially seem to occur after systemic administration of allergen. The reactions are sometimes associated with the development of a generalized erythema (rash).

In this paper a description is given of the attempts performed to identify the components capable of eliciting flare and rash phenomena in guinea-pigs with contact hypersensitivity to DNCB. Intravenous injection of 300 mg DNBSO$_3$Na provoked in 16 of 18 adult guinea-pigs flares at one week old contact reaction sites combined with a generalized erythema; both phenomena were maximal after about 6 h. Neither mixtures of DNP-amino acids or DNP-conjugates with guinea-pig serum protein were found capable of producing similar symptoms. On the other hand, injection of less than 200 mg of a low molecular weight fraction (obtained by column chromatography on Sephadey of a mixture of DNBSO$_3$Na and guinea-pig serum incubated during 1 h at 37°C) did provoke flare and rash phenomena. Ten mg of K$_2$Cr$_2$O$_7$ proved to elicit the particular symptoms as well.

Introduction

In a recent review [3] it was concluded that flare and rash phenomena are rather common both in men and animals with a strong contact allergy to simple chemicals. Flaring of existing or already healed dermatitis...
seems to occur especially after systemic administration of allergen (injection, ingestion or inhalation), sometimes after patch testing or during desensitization treatments (poison ivy); in these cases exacerbations may be observed at sites where no direct skin contact with the allergen has taken place [3]. Flare reactions may occur also in areas which were the site of an active dermatitis one or more years earlier (Ni-dermatitis). The flare phenomena sometimes are associated with the development of a generalized erythema (rash). It has been shown that also in animals (guinea-pigs) flaring of old sites of contact dermatitis may occur, especially after intravenous injection of allergen [1,3,5,6].

Frey, De Weck and Geleick [1] studied these phenomena more closely. Flaring of sites of previous contact reactions to 2, 4-dinitrochlorobenzene (DNCB) was observed in hypersensitive guinea-pigs who had been given an intravenous injection of dinitrobenzene-sulfonate (DNBSO\textsubscript{3}Na). In these experiments the flares occurred maximally 48–72 h after the injection, usually associated with a generalized erythema appearing after 5 h. The erythema occurred regularly in highly sensitized animals but was not seen in animals with a low degree of contact sensitivity.

Similarly, Polák and Turk [5] could provoke exacerbations of old test sites in guinea-pigs sensitized to K\textsubscript{2}Cr\textsubscript{2}O\textsubscript{7} or BeF\textsubscript{2} by intravenous injection of the allergen. Twenty mg bichromate (per kg body weight) leads within 6 h to flaring of old test sites in animals with a high grade of contact sensitivity. A generalized dermatitis had been observed in 30\% of the animals. They found that the flare reactions could be blocked by an antiserum to the "lymph-node-permeability factor". Histologically the flares showed an infiltration with polymorphonuclear leukocytes.

In contrast, Jansen and Bleumink [3] observed that flares, provoked in guinea-pigs hypersensitive to DNCB, showed a marked infiltration with lymphocytes and dilated vessels. The reactions could not be inhibited by pretreatment of the animals with heparin, antihistamins or \textepsilon\-amino-caproic acid. These contradictory results acted as a stimulus to look further into the mechanism of the flare and rash phenomena in guinea-pigs with a contact hypersensitivity to DNCB.

Materials and Methods

Materials and Chemical Methods

Sodium-2,4-dinitrobenzenesulfonate was purchased from Eastman Organic Chemicals (Rochester, N.Y.) and recrystallized three times from water, 2,4-dinitrophenyl-amino acids were obtained from Mann Research Laboratories (New York), 2,4-dinitrophenol from Fluka AG (Switzerland) and 2,4-dinitrochlorobenzene from Merck AG (Darmstadt). Some DNP-amino-acids (\textepsilon\-N\text-N\text-DNP-L-arginine HCl, DNP-DL-serine, \textepsilon\-DNP-L-lysine-HCl, DNP-D-methionine sulphoxide and DNP-