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Mechanism of Eosinophilia

X. Evidence for Immunologic Specificity of the Stimulus[1] (37989)

RONALD S. WALLS,[2] DAVID A. BASS,[3] AND PAUL B. BEESON

Nuffield Department of Clinical Medicine, University of Oxford, Oxford, England, OX2 6HE

Previous reports from this laboratory have provided evidence that the phenomenon of increased eosinophil production has characteristics of an immunologic reaction. There is a delay of two or more days until it can be detected (1); eosinophilia can be transferred adoptively with thoracic duct lymphocytes (2); the response does not take place in animals deprived of thymus-processed lymphocytes (3), and it can be prevented by administration of agents which suppress other forms of immunologic reaction (4). A further characteristic is that the eosinophilia is greater after a second challenge than after the first (4, 5).

Examination of immunologic specificity in the eosinophil response has been delayed because of lack of agents which will reliably induce eosinophilia after a single challenge. We have previously employed one test system—intravenous injection of muscle stage larvae of *Trichinella spiralis*. This parasite is of a size suitable for intravenous injection, yet large enough to be arrested in the pulmonary circulation. There it provokes a local inflammatory reaction with a predictable stimulus to marrow eosinophil production and corresponding blood eosinophilia. We have recently reported that a similar eosinophilic response can be elicited by intravenous injection of dextran in the form of beads (6). This has permitted us to compare injections by two different agents from the standpoint of specificity in inducing a "secondary" eosinophil response.

Materials and Methods. Experimental animals. The same parasite-free outbred Wistar and inbred Agus strains of rats were employed as in previous experiments (6).

Administration of substances stimulating eosinophilia. Trichinella spiralis, in a dose of 5000 intact muscle stage larvae, or 5×10^4 "G 200 superfine" Sephadex beads were employed as eosinophilic stimuli. They were administered by intravenous injection as described before (1, 6). The interval between successive injections was four weeks.

Methods for performing eosinophil counts and statistical analysis have been published (1). The eosinophil responses of groups were compared by applying Student's t test to the means of the mean counts for individual days from 4 through 8 or 9.

Results. Peripheral blood eosinophil counts after intravenous larvae in Wistar rats are shown in Fig. 1 and Table I. The response in unsensitized animals resembles that described before (1). In rats previously injected with Sephadex the response is similar ($P > .95$). A second injection of *Trichinella* larvae, on the other hand, produces an augmented response when compared with a single injection ($P < .02$) or with an injection in rats previously given Sephadex ($P < .05$).

In the converse experiment Agus rats

[1] Supported by a grant from the Medical Research Council.

[2] Recipient of C. J. Adams Travelling Fellowship. Present address: Department of Medicine, University of Cape Town, Observatory, Cape, South Africa.

[3] Present address: Department of Medicine, Johns Hopkins Hospital, 601 N. Broadway, Baltimore, MD 21205.

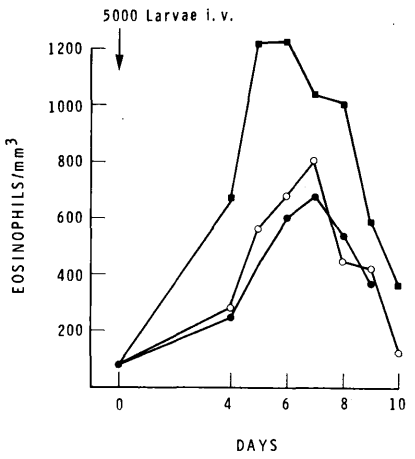

FIG. 1. Peripheral blood eosinophils following intravenous injection of 5000 *Trichinella* larvae in unsensitized Wistar rats (●—●) and in those previously injected with *Trichinella* larvae (■—■) or with Sephadex (○—○).

were injected with Sephadex beads, either initially or after prior challenge with larvae or Sephadex. The result is shown in Table II. A previous injection with *Trichinella* larvae did not affect significantly the subsequent eosinophil response to Sephadex beads ($P > .40$). However, a second injection of Sephadex produced a greater response than a single injection ($P < .02$) or than one following a previous injection of larvae ($P < .05$).

Discussion. We interpret these findings as support for the concept that induction of eosinophilia is an immunologic phenomenon. There appears to be a memory for prior experience with antigen since greater production of eosinophils follows second challenge with the same agent but not with a different one. Whether this discrimination is as fine as that exhibited in the antibody response cannot be determined because of lack of suitable test materials. Certainly these results show little evidence of cross-reactivity between one homogeneous antigenic moiety, dextran, and the varied antigens present in the parasite body.

This apparent specificity in the eosinophil response is not unexpected on the basis of clinical experience. The eosinophilias that occasionally develop during administration

TABLE I. Peripheral Blood Eosinophil Counts Following Intravenous *Trichinella* Larvae.

Previous intravenous injection	Number of rats	Peripheral blood eosinophils/mm³ Mean of the mean responses for days 4–9 ± 1 S.E.M.[a]	Difference from response in unsensitized rats	Difference from response in rats given 2 injections of larvae
Nil	12	480 ± 64	—	$P < .02$
Sephadex	8	522 ± 85	$P > .95$	$P < .05$
Larvae	8	957 ± 111	$P < .02$	—

[a] S.E.M. = Standard error of mean.

TABLE II. Peripheral Blood Eosinophil Counts Following Intravenous Sephadex Beads.

Previous intravenous injection	Number of rats	Peripheral blood eosinophils/mm³ Mean of the mean responses for days 4–8 ± 1 S.E.M.	Difference from responses in unsensitized rats	Difference from response in rats given 2 injections of Sephadex
Nil	15	332 ± 5	—	$P < .02$
Larvae	11	379 ± 20	$P > .40$	$P < .05$
Sephadex	14	487 ± 23	$P < .02$	—

of drugs seem not to apply to other pharmacologic agents being given at the same time. This also appears generally true of the eosinophilias that accompany allergic reactions involving skin or mucous surfaces.

The present findings should not be interpreted as indicating that eosinophils exhibit immunologic specificity in fulfilling their function which, indeed, still remains to be elucidated. We prefer to believe that specificity resides in the *stimulus* to eosinopoiesis, probably during the induction phase of the reaction involving thymus-processed lymphocytes (2, 3).

Summary. Study of the eosinophil response to a single injection of two different agents indicated that there is specificity in the induction of eosinophilia.

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