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TISSUE AND BLOOD EOSINOPHILIA  
IN MAST CELL-DEFICIENT SI/SI<sup>d</sup> MICE  
INFECTED WITH *TRICHINELLA SPIRALIS*<sup>1</sup>

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The influence of mast cell-deficiency on the gut, muscle and blood eosinophilia in SI/SI<sup>d</sup> mice infected with *Trichinella spiralis* was examined. In mast cell-deficient SI/SI<sup>d</sup> mice, eosinophilia in the peripheral blood, small intestine and muscles was observed in primary and tertiary infections. But the time courses of tissue eosinophilia in SI/SI<sup>d</sup> mice and normal littermates were somewhat different. Although tissue eosinophilia was a partially mast cell-dependent phenomenon, the mast cell was not central to eosinophilia. Also, the mast cell did not appear to play a role in blood eosinophilia.

Key words: eosinophilia, mast cell, SI/SI<sup>d</sup> mice, *Trichinella spiralis*

INTRODUCTION

Tissue and peripheral blood eosinophilia is a striking and consistent response to helminth infection. Also, eosinophils play a role in limiting the deleterious effect of helminth infection; phagocytosis of immune complexes and ability to mediate antibody-dependent damage to larvae<sup>14</sup>. *Trichinella*-infection induces a profound tissue and blood eosinophilia. Peripheral blood eosinophilia reflects an increase in eosinopoiesis or an alteration in eosinophil dynamic, whereas tissue eosinophilia may reflect both an increase in eosinopoiesis and a local chemotactic effect. Tissue and blood eosinophilia have been shown to be thymus-dependent in *T. spiralis* infection.<sup>13</sup> Mast cells produce substances which have a strong chemotactic attraction for eosinophils, such as the eosinophil chemotactic factor of anaphylaxis (ECF-A), a family of intermediate molecular weight peptides, histamine and certain oxidative metabolites of arachidonic acid.<sup>14</sup> It has been shown that in anti-basophil serum treated guinea pigs the number of eosinophils as well as basophils is reduced at tick feeding sites. Therefore, the

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present study was undertaken to determine the role of mast cells in eosinophilia. In adult SI/SI<sup>d</sup> mice, connective tissue and mucosal mast cells accounted for less than 1% of the cells observed in +/+mice<sup>5, 9)</sup> This study was done by counting the eosinophil numbers in the blood, small intestine and muscle of *T. spiralis*-infected mast cell-deficient SI/SI<sup>d</sup> mice.

#### MATERIALS AND METHODS

Male WCB6F<sub>1</sub>-SI/SI<sup>d</sup> (WC-SI/+ × C57BL/6J-SI<sup>d</sup>/+) mice and their normal male littermates (SI/+, SI<sup>d</sup>/+ and +/+) were obtained from the Jackson Laboratory, Bar Harbor, Maine, USA. The mice used in this study were more than 100 days old.

The strain of *T. spiralis* used was originally isolated in 1968 from a polar bear, *Thalarctos maritimus*, at Maruyama Zoo, Sapporo, Japan, and had been maintained in our laboratory. The infective muscle larvae were obtained from infected mice after conventional digestion with HCl and pepsin for about 2 hours.<sup>8)</sup>

In order to examine the course of primary infection, each mouse infected orally with 400 infective muscle larvae, and to examine the course of tertiary infection, two times of infection with 100 infective muscle larvae were carried out 7 and 3 weeks before the challenge infection with 400 infective muscle larvae.

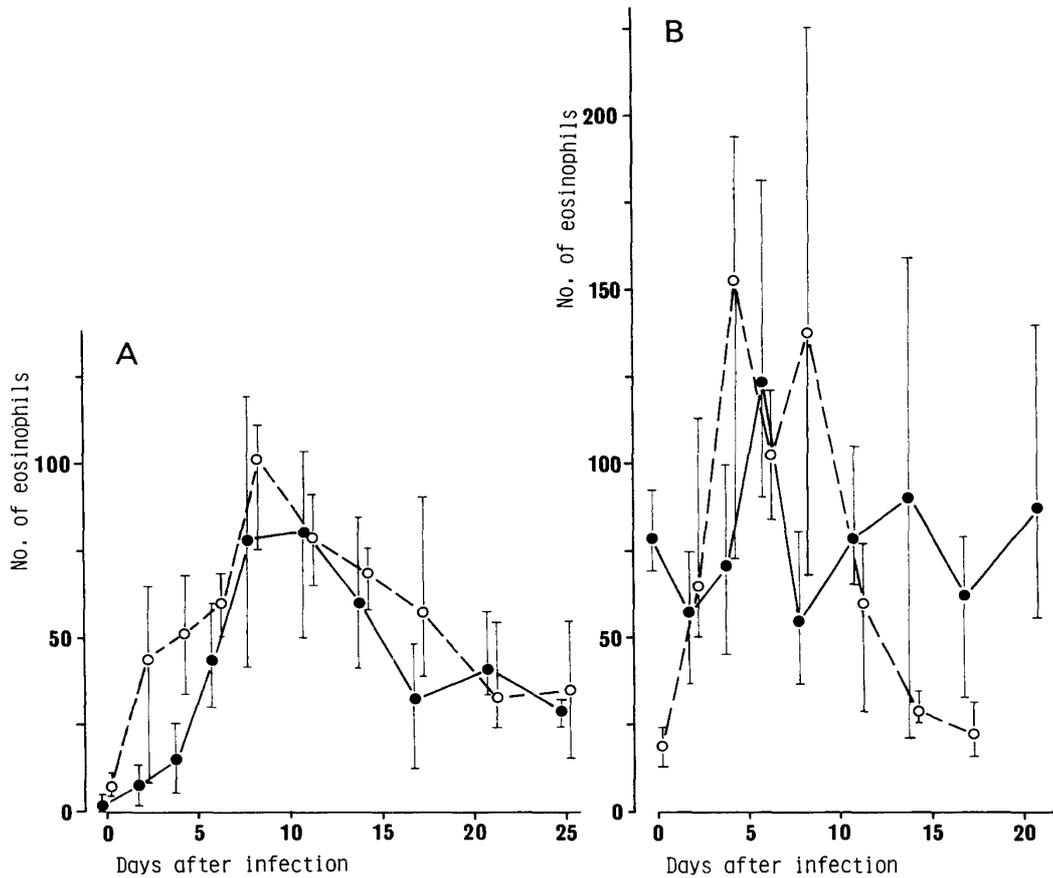
For histological examination, mice were killed under anaesthesia by bleeding the femoral artery. A 1cm piece of jejeunum, which was approximately 8–10cm distal to the pyloric sphincter of the stomach was removed. The tongue, diaphragm and abdominal muscles were also removed. Tissues were fixed in 10% formalin, dehydrated in ethanol, cleared in xylene, embedded in paraffin wax, and sectioned to 6 μm thickness. The paraffin sections were stained by a modified Dominici stain.<sup>8)</sup> The number of eosinophils in the small intestine was enumerated based upon observation of 5 eye-fields of 200 μm × 200 μm square each.

Blood samples were collected from the femoral artery. Eosinophil counts were made using blood film stained with Giemsa's stain. Percentage of eosinophils was determined based upon observation of at least 200 white blood cells per smear.

#### RESULTS

As shown in figure 1, eosinophilia in the small intestine of SI/SI<sup>d</sup> mice was observed. In primary infection, the number of eosinophils in SI/SI<sup>d</sup> mice increased later than that in normal littermates, and the peak response of SI/SI<sup>d</sup> mice was observed on Days 9–12, the same as that of normal littermates. In normal littermates with tertiary infection, the increase in number of eosinophils in the small intestine was faster and stronger than that with primary infection, and the response had subsided by Day 15 after tertiary infection. In SI/SI<sup>d</sup> mice with tertiary infection, eosinophilia in the small intestine was observed on Day 0, the peak response was on Day 7 and the response did not subside by Day 20. Eosinophilia in the muscles of SI/SI<sup>d</sup> mice was

FIGURE 1 Eosinophil response to *Trichinella spiralis* in small intestine

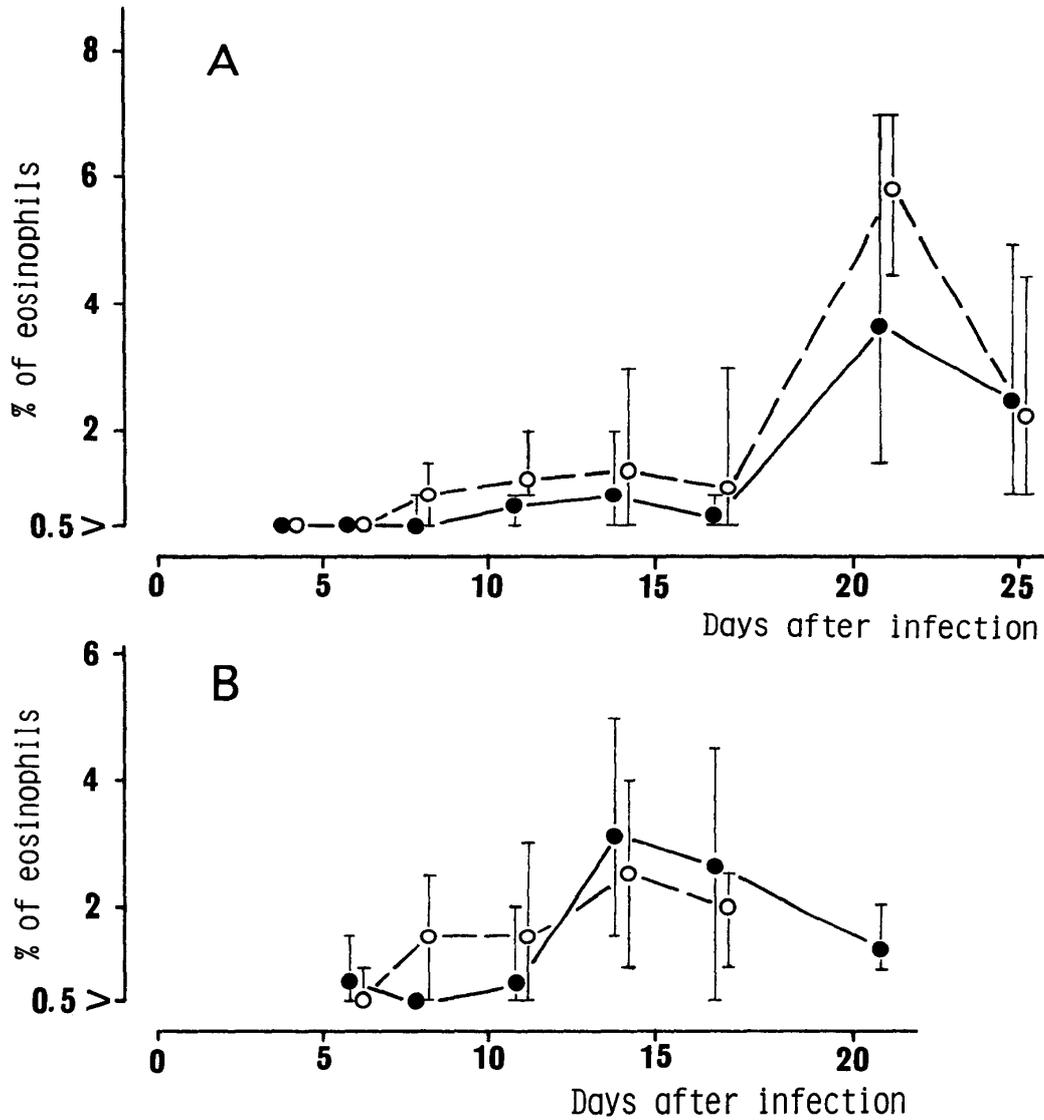


WCB6F<sub>1</sub>-SI/SI<sup>d</sup> mice (●) and their normal littermates (○) after primary (A) and tertiary (B) infections. Mean ± range of eosinophils counted in 5 eye-fields (200 μm × 200 μm each) per mouse. 3-4 mice per day.

TABLE 1 Eosinophil response in muscles (tongue, diaphragm and abdominal wall) of WCB6F<sub>1</sub> (SI/SI<sup>d</sup>, SI/+, SI<sup>d</sup>/+ and +/+) mice infected with *Trichinella spiralis*

STRAIN	DAYS AFTER INFECTION						
	0	3	5	10	14	22	40
SI/SI <sup>d</sup>	-*	-	-	-	-	++	+++
SI/+	-	-	-	-	+++	+++	+~+++
SI <sup>d</sup> /+	-	-	-	-	+~+++	+++	+++
+/+	-	-	-	±~+	+~+++	+++	++

\* - to +++ = semi-quantitative evaluation of eosinophil reaction; (- = no; ± = weak; + = little; ++ = moderate; +++ = strong reaction) groups of 2-3 mice

FIGURE 2 *Eosinophil response to T. spiralis in peripheral blood*

WCB6F<sub>1</sub>-SI/SI<sup>d</sup> mice (●) and their normal littermate (○) after primary (A) and tertiary (B) infections. Mean ± range of percentages of eosinophils. 3-4 mice per day.

observed as shown in table 1. The increase in number of eosinophils in muscles of SI/SI<sup>d</sup> mice was later than that of normal littermates. Peripheral blood eosinophilia was also observed in the SI/SI<sup>d</sup> mice as in the normal littermates (figure 2).

## DISCUSSION

Gut eosinophilia of normal mice in tertiary infection subsided faster than that in primary infection. This discrepancy in timing between primary and tertiary infections was related to a difference in expulsion time of adult worms.<sup>5)</sup> Although the worms alone were not chemotactic for eosinophils,<sup>15)</sup> eosinophils were attracted by metabolic products of *T. spiralis* in the presence of immune serum. Furthermore, the surface of the larvae and the adults of *T. spiralis* activated complements<sup>10)</sup> and the release of C567 and C5a may also be involved in eosinophil chemotaxis.

SI/SI<sup>d</sup> mice showed gut eosinophilia for a longer time than did the normal mice. This may be related to a delayed expulsion of adult worms<sup>5)</sup> and mast cell deficiency. Mast cells increase in number<sup>5,13)</sup> and play a role in the removal of *T. spiralis* antigens, which combine with antibody and attract eosinophils. Released mast cell granules may bind with antigens, and are followed by the uptake of their antigen complexes by phagocytic cells.<sup>7)</sup> Intact mast cells may also take up antigens.<sup>11)</sup> Gut and muscle eosinophilias in SI/SI<sup>d</sup> mice were observed later than that in normal mice, suggesting a partial mast cell-dependence of tissue eosinophilia. However, mast cells are not central to tissue eosinophilia in mice infected with *T. spiralis*. It can be either proposed that delayed increase of tissue eosinophilia of SI/SI<sup>d</sup> mice reflects a generalized deficiency in the microenvironment of hematopoiesis,<sup>9)</sup> or that very few mast cells are enough to mediate an eosinophil response in SI/SI<sup>d</sup> mice.

Accelerated eosinophilopoiesis, which may be an important factor of peripheral blood eosinophilia, has been shown to be primarily mediated by thymus-derived or dependent lymphocytes.<sup>1)</sup> Eosinophil growth stimulating factor has been demonstrated to be similar to or identical to eosinophilopoietin, a partially characterized *in vivo* stimulator of bone marrow eosinophil production.<sup>3)</sup> However, eosinophilia is not exclusively under T-cell control.<sup>12)</sup> It has been shown that daily treatment with Promethazine (an antihistamine reagent) brought about a rapid drop in blood eosinophil numbers to normal values in *T. spiralis*-infected rats.<sup>4)</sup> In our investigation, mast cells did not appear to play a role in peripheral blood eosinophilia of mice infected with *T. spiralis*.

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