ANTIEOSINOPHIL SERUM AND THE KINETICS OF EOSINOPHILIA IN *SCHISTOSOMIASIS MANSONI**

By ADEL A. F. MAHMOUD, KENNETH S. WARREN, AND RICHARD C. GRAHAM, JR.

(From the Divisions of Geographic Medicine and Infectious Diseases, Department of Medicine, Case Western Reserve University and University Hospitals, Cleveland, Ohio 44106)

Although eosinophilia is a hallmark of helminth infections, the function of the eosinophil granulocyte remains unknown. The recent development of a monospecific rabbit antimouse antieosinophil serum (AES)[1] in our laboratories (1) has provided a unique tool by which the roles of eosinophils may be elucidated. Using a murine model of schistosomiasis, the most important helminth infection of man (2), the kinetics of eosinophilia in the peripheral blood, bone marrow, and tissue lesions was carefully established; this was followed by an examination of the effects of AES on these reactions.

In previous studies of the eosinophilia in schistosomiasis in mice the animals were hyperinfected, and mortality was high in the acute stages of infection (3, 4). Mice exposed to relatively low numbers of cercariae, however, will survive for at least a year despite the development of mild to moderate hepatosplenic disease (5, 6). The kinetics of eosinophilia in the peripheral blood and bone marrow was studied, therefore, in mice exposed to three different intensities of infection and the responses were followed for as long as 20 wk.

The effect of *Schistosoma mansoni* eggs on eosinophilia in the blood, bone marrow and granulomatous lesions was then examined by injecting isolated purified eggs into mice singly and multiply by various routes. While the host response was dependent on the route of injection, primary and anamnestic secondary reactions were seen after successive intravenous injections. Administration of AES under these conditions profoundly suppressed peripheral eosinophilia, induced a marked increase in eosinophil precursors in the bone marrow, and ablated eosinophils from the tissue lesions, considerably reducing their size.

Materials and Methods

Animals. Young adult female mice of the CF-1 strain (18–22 g in body weight) obtained from Carworth Farms, Inc. were used in these experiments.

Eosinophilia in Naturally Infected Mice. Groups of mice were infected by the subcutaneous injection of 10, 50, or 200 cercariae of the Puerto Rican strain of *S. mansoni* as described by Peters and Warren (7). The worm burden in each of the experimental groups was assessed by perfusion of 10 mice 8 wk after infection (8). Eosinophil counts on five animals in each group were done weekly for the first 6 wk after infection and then at 2-wk intervals.

* This study was supported by U.S. Public Health Service grants AI 08163 and AM 11308, and grants from The Rockefeller Foundation, the Edna McConnell Clark Foundation, and the Fannie E. Rippel Foundation.

[1] *Abbreviations used in this paper:* AES, antieosinophil serum; NRS, normal rabbit serum.

Peripheral Eosinophil Counts. Blood was obtained from the retro-orbital plexus using a microhematocrit tube. Absolute eosinophil counts were made using Discomb's fluid as diluent (1). Fresh fluid was prepared each week and cell counts were performed in bright line counting chambers at 400 × magnification. After confirmation of a diurnal fluctuation in peripheral blood eosinophil counts in control mice, blood samples were all taken approximately at 12:00 noon.

Bone Marrow Counts. The total nucleated cell and absolute eosinophil counts in the bone marrow were done by a modification of the method described by van Furth and Cohn (9). Both femurs of the mice were removed and carefully cleaned of attached muscle. The bones were cut at both ends in the region of the metaphyses, and the bone marrow flushed out with 2 ml of Hanks' balanced salt solution injected through a 26 gauge needle. The cell suspension was dispersed by repeated gentle aspiration in a pipette. The total white cell count was determined by a Coulter counter, and absolute eosinophil counts were performed as described above. The bone marrow eosinophil counts thus obtained included all cells that had eosinophilic granules. As both femurs have been found to contain 11.8% of the total body bone marrow (10), the total number of eosinophil precursors and bone marrow eosinophils in the animals could be computed.

Eosinophilia in Mice Injected with S. mansoni Eggs. *S. mansoni* eggs were isolated from the livers of mice infected for 8 wk, counted, and their viability assessed by hatching (11). A standard dose of 1,500 eggs suspended in 0.5 ml of physiological saline was used in all of the experiments. Eggs were injected by three different routes (subcutaneous, intraperitoneal, or intravenous) into groups of 10 mice each. The peripheral eosinophil count was determined every other day for 8 days, half of each group being bled each time. A second injection of 1,500 eggs was given 8 days later at the same or a different site, and the peripheral eosinophil counts were followed for an additional 8 days. Since the blood volume of a 20 g mouse has been determined to be about 2.54 ml (12), the total number of eosinophils per mouse could be calculated.

Bone marrow eosinophil counts were determined in groups of animals after primary and secondary intravenous (i.v.) egg injections, the latter preceded by i.v. or intraperitoneal (i.p.) injections. At 2-day intervals randomly selected subgroups of five mice from each group were killed, and the total nucleated cells and eosinophils in both femurs were determined.

Eosinophil migration into the granulomatous lesions around the intravenously injected eggs in the lungs was monitored in unsensitized and i.p. sensitized mice. After the i.v. injections of eggs, groups of four to five mice were anesthetized and the lungs removed (13) at 12-h intervals for 4 days and then at 8 days. The lungs were fixed in formalin, embedded in paraffin, and sections were stained by Archer's modification of the Leishman stain (14), which specifically identifies eosinophils. Additional sections were stained with hematoxylin and eosin for identification of the other cellular components of the granulomas.

Effect of Antieosinophil Serum. Monospecific rabbit antimouse eosinophil serum (AES) was prepared as described previously (1). Three groups of mice injected intravenously with 1,500 *S. mansoni* eggs were used: (*a*) unsensitized, (*b*) i.v. sensitized and (*c*) i.p. sensitized mice. These groups were subdivided into control animals which received normal rabbit serum (NRS) and experimental animals which received AES. Beginning 6 days before egg injection the sera were administered intraperitoneally in 0.25 ml doses every other day throughout the course of the experiments. Peripheral as well as bone marrow eosinophilia was estimated as described above in groups of five mice at each time interval. In addition, the fine structure of the bone marrow cells was studied by electron microscopy. Bone marrow cells were obtained from femurs of NRS- and AES-treated mice 4 days after the primary egg injection. The cells were washed twice in Hanks' balanced salt solution and fixed in 0.7% formaldehyde, 0.95% glutaraldehyde in 0.05 M phosphate buffer, pH 7.4 at 4°C for 1 h. The cells were then exposed to 1% osmium tetroxide in 0.05 M phosphate buffer, pH 7.4, and embedded in agar (15). Blocks of agar-embedded cells were dehydrated in ethanol and propylene oxide and embedded in Epon-Araldite by standard techniques. Sections were stained sequentially with uranyl acetate and lead citrate and examined in an AEI EM-68 electron microscope (AEI Scientific Apparatus Inc., Elmsford, N.Y.). All recognizable eosinophilic cells were photographed for later evaluation and staging. Differential counts of eosinophilic bone marrow cells were made using the criteria described by Bainton and Farquhar (16).

The presence of eosinophils in the lung granulomas around the schistosome eggs was monitored in unsensitized and i.p. sensitized mice treated with NRS or AES as described above. In addition,

in each experimental group (six mice) the mean area of approximately 100 8-day granulomas was measured using a πMC particle measurement computer (Millipore Corp., Bedford, Mass.) as previously described (17).

Results

Eosinophilia in Naturally Infected Animals. At 8 wk of infection total worm recovery equaled 46–55% of the 10, 50, or 200 cercariae used for infection (Table I). The average worm burdens in the three experimental groups were 5, 24, and 111.

The mean eosinophil count in the peripheral blood of normal mice at 12:00 noon was 78 ± 12/mm^3; the comparable values in the three groups exposed to different numbers of cercariae are illustrated in Fig. 1. At 3 wk of infection the mice exposed to 50 and 200 cercariae showed significant but low and transient increases in their mean peripheral eosinophil counts. From 8 wk on, marked eosinophilic responses occurred which differed with the cercarial exposures. Animals exposed to 10 cercariae developed a prolonged moderate eosinophilia

TABLE I

Worm Recovery 8 Wk After the Subcutaneous Injection of Different Numbers of Cercariae to Groups of 10 Mice

Cercarial exposure no.	Worm recovery				Worm recovery
	Males	Females	Pairs	Total	
	Mean ± SE		*Mean ± SE*		%
10	1.4 ± 0.3	0.3 ± 0.2	1.6 ± 0.3	4.6 ± 0.7	46
50	2.5 ± 0.5	0.3 ± 0.2	10.8 ± 0.6	24.3 ± 1.4	49
200	15.4 ± 2.8	3.3 ± 1.1	46.0 ± 3.4	110.6 ± 6.1	55

which plateaued between 10 and 16 wk at about 500 eosinophils/mm^3. The eosinophil level began to decline at 18 wk and reached 208 ± 18/mm^3 at 20 wk. The highest level of peripheral eosinophils (820 ± 120/mm^3) was seen in the 50 cercariae-exposed mice, but these animals began to die at 12 wk, mortality being virtually complete by 14 wk. Animals exposed to 200 cercariae showed a moderate peak of eosinophilia at 8 wk (388 ± 45/mm^3), but mortality began at that time and the remaining mice showed a decline in eosinophilia before they all succumbed by 11 wk.

In the bone marrow of our normal mice the total number of eosinophils and eosinophil-precursors as identified by Discomb's fluid varied from 6.8 to 10.2 × 10^6 cells/mouse. The changes in the bone marrow cells in the animals with schistosomiasis were similar to those of the peripheral eosinophils (Fig. 1), and demonstrates two distinct phases of eosinophilia during the course of schistosomiasis. The early phase occurred in all three infected groups, but in the group with the lowest worm burden (five worms/mouse) the increase in eosinopoiesis was not reflected in the peripheral blood counts. Due to mortality in the more heavily infected animals the course of the second wave of eosinophilia in the bone marrow could be studied fully only in the lightly infected animals. In the mice exposed to 10 cercariae the total number of eosinophils plateaued at 47–51

$\times 10^6$ cells/mouse from the 10th to the 16th wk of infection and declined thereafter to 33 and 21 $\times 10^6$ cells/mouse at 18 and 20 wk. Animals exposed to 50 or 200 cercariae showed increasing levels of bone marrow eosinophils 6 and 8 wk after infection. While the rise was sustained in the 50 cercariae-infected group until 12 wk when the animals began to die, the steep rise in the 200 cercariae group at 8 wk was followed by a sharp decline before their death shortly after 10 wk.

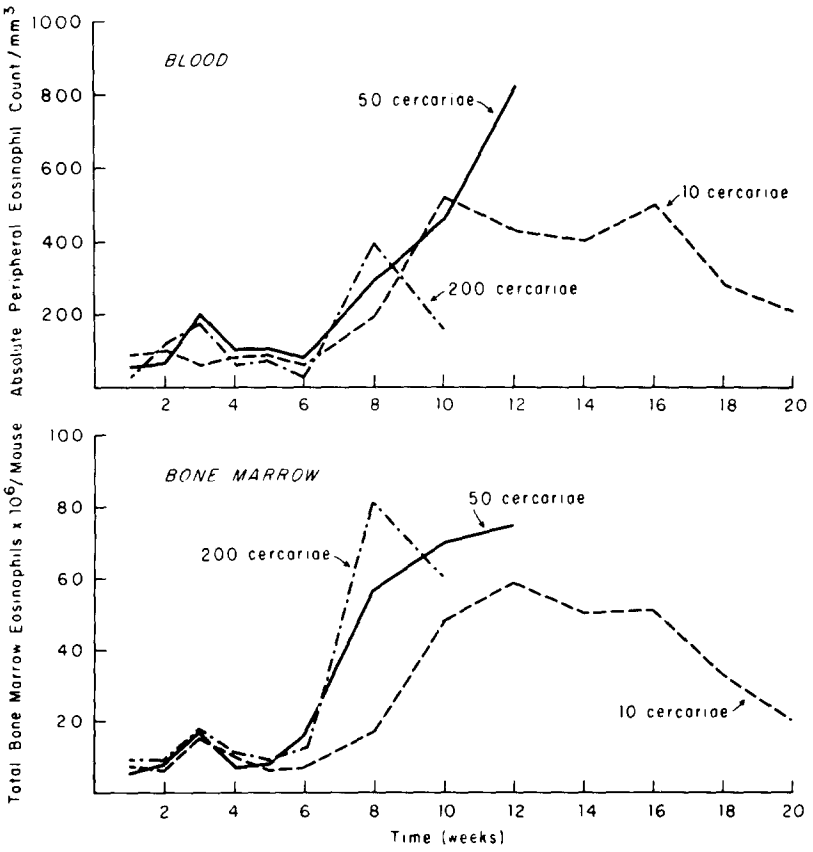

FIG. 1. Mean absolute peripheral blood eosinophil counts and total bone marrow eosinophils in mice exposed to 10, 50, and 200 cercariae of *S. mansoni*. Mortality prevented the follow up of the more heavily infected animals.

Effect of Egg Injections. Since the major peripheral eosinophilic response in naturally infected animals occurred soon after the onset of egg production by the schistosomes, the effect of injecting purified suspensions of eggs at different sites in normal mice was examined (Fig. 2). When injected i.p. neither the first nor the second injection of eggs evoked an eosinophilia. Primary i.v. injection of eggs, however, resulted in a peripheral eosinophil response which peaked at 4 days at 0.5 $\times 10^6$ total eosinophils/mouse and subsided by 8 days. A second intravenous injection of eggs elicited an accelerated augmented reaction that peaked at day 2 at 0.8 $\times 10^6$ total eosinophils/mouse. In contrast, a second i.v.

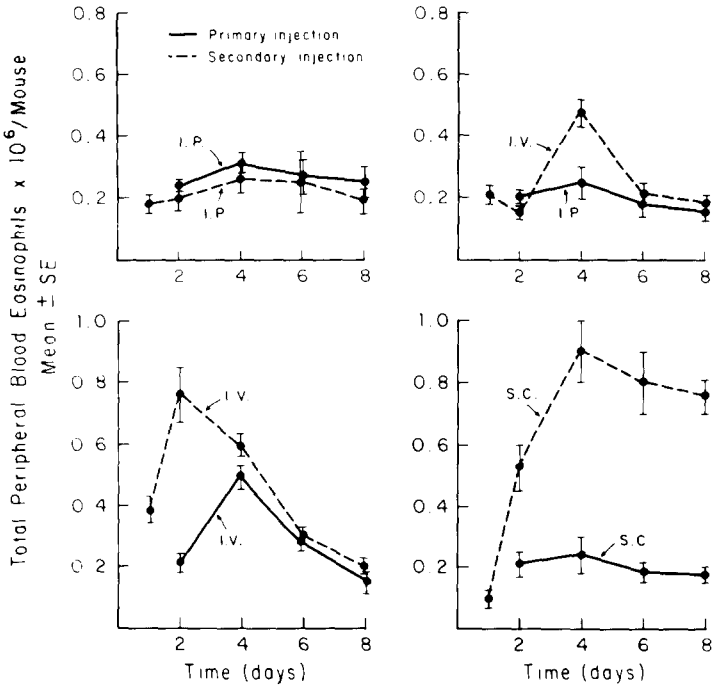

FIG. 2. Mean total peripheral blood eosinophils in groups of mice injected at different sites with purified *S. mansoni* eggs.

TABLE II

Total Nucleated Cell and Eosinophil Counts in the Bone Marrow 2, 4, 6, and 8 Days After the Intravenous Injection of 1,500 Purified S. mansoni Eggs into Unsensitized Mice and those Sensitized by a Prior Injection of Eggs

Experimental group*	Mean bone marrow cell counts × 10^6 ± SE							
	2 days		4 days		6 days		8 days	
	Total cells	Eos.	Total cells	Eos.	Total cells	Eos.	Total cells	Eos.
Unsensitized	356 ± 19	26 ± 4	346 ± 21	32 ± 4	329 ± 21	25 ± 6	354 ± 12	23 ± 5
Sensitized (1,500 eggs i.v., 8 days previously)	294 ± 15	66 ± 9	334 ± 29	92 ± 5	341 ± 20	73 ± 9	305 ± 15	68 ± 7
Sensitized (1,500 eggs i.p., 8 days previously)	322 ± 31	12 ± 3	315 ± 26	23 ± 6	298 ± 14	37 ± 5	359 ± 19	54 ± 8

* Groups of five mice.

injection after a primary i.p. injection elicited only a primary reponse. Using the s.c. route, the first egg injection had no effect on the eosinophil count, but the second induced marked and relatively prolonged eosinophilia with counts ranging between 0.5 and 0.8 × 10^6 total eosinophils/mouse from 2 to 8 days.

The total nucleated and eosinophil cell counts in the bone marrow after the different egg injection regimens are shown in Table II. No change in the total nucleated cells was seen after any of the injection regimens. On the other hand,

the eosinophil cell counts showed a considerable increase which was maximal at 4 days, and was most prominent in the i.v. sensitized group. While the counts of animals that received a primary egg injection returned to normal levels at 8 days, significant eosinophilia ($P < 0.01$) was still present at that time in both sensitized groups.

Examination of the initial inflammatory response to *S. mansoni* eggs injected into the pulmonary microvasculature of unsensitized mice revealed no reaction whatsoever from 0 to 48 h and minimal inflammation at 60 h. By 72 h definite mononuclear infiltrates were seen; by 96 h the reaction was larger and eosinophils were first seen in the lesions. On day 8 the granulomas were greatly increased in size and eosinophils constituted approximately 25–50% of the cells. In animals sensitized by an i.p. injection of eggs 8 days before their i.v. injection, no cellular reaction was observed at 6, 12 and 18 h, but by 24 h both mononuclear cells and eosinophils were seen around the eggs. The reaction rapidly increased in size, with eosinophils constituting about 25% and 50% of the cells at days 2 and 8 respectively.

Effect of AES. AES treatment of mice injected intravenously with schistosome eggs resulted in a drastic reduction in the peripheral eosinophil response, while NRS had no effect (Fig. 3). Even in animals which had received a secondary egg injection, AES treatment maintained eosinophil counts at less than 10% of the peak levels seen in NRS-treated animals (Figs. 4, 5).

In contrast, the bone marrow counts 4 days after egg injection revealed a moderate increase in eosinophils in NRS-treated animals which was markedly increased in the AES-treated group ($P< 0.001$). This difference was maintained at 6 and 8 days. Neither of the antisera, however, had a significant effect on the total nucleated cells of the bone marrow.

Electron microscopy of bone marrow cells obtained from serum-treated animals 4 days after primary egg injection revealed the majority of eosinophilic cells from both experimental groups to be myelocytes (Table III, Fig. 6). Band and segmented eosinophils (Fig. 7) were not observed in bone marrows from AES-treated mice, although such cells were encountered in marrows from mice in the other two groups. Eosinophil precursors in bone marrows of AES-treated mice displayed no detectable structural abnormalities.

8 days after the injection of schistosome eggs into the pulmonary microvasculature of NRS-treated mice, eosinophils constituted 25–50% of the cells in the granulomas. In AES-treated animals, however, no eosinophils were seen in the lung granulomas at either 4 or 8 days. At the latter time period the mean granuloma area around the eggs was markedly reduced in AES-treated mice in comparison with NRS-treated controls ($P < 0.001$) (Table IV), the area of inflammation being less than 1/3 of the control values (Fig. 8). Similarly, AES treatment resulted in complete absence of eosinophils in the larger lesions seen in the i.p. sensitized mice; consequently the granulomas were less than 1/2 the size of those in the control animals.

Discussion

Schistosomiasis is a widespread infection of man and animals which is frequently associated with peripheral eosinophilia as well as large numbers of

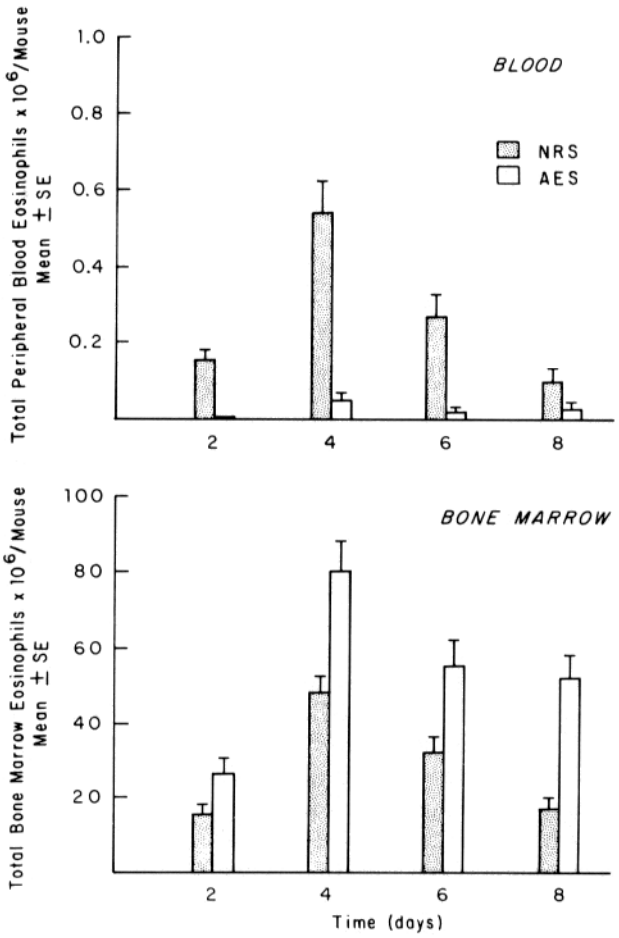

FIG. 3. Effects of NRS and AES administration on total peripheral blood and bone marrow eosinophils after a primary i.v. injection of *S. mansoni* eggs.

eosinophils in the granulomatous lesions developing around parasite eggs trapped in the tissues. While there are several reports describing the eosinophilia seen in experimental and human schistosomiasis, there are no detailed data on the kinetics of eosinophils in relation to the intensity and duration of infection. Previous experimental investigations have all been terminated at 10–12 wk by the death of heavily infected animals (3, 4). In the present study peripheral and bone marrow eosinophilia was quantitated during the course of schistosomiasis mansoni of low, moderate, and heavy intensities. Eosinophils increased in the peripheral blood and bone marrow of infected animals in two distinct waves. The first, which occurred 3 wk after exposure to cercariae, was relatively minor and was seen in the peripheral blood only in the mice with the heavier worm burdens; eosinophilia occurred in the bone marrow, however, at all three levels of infection. During this early stage of the infection the schistosomula are in the process of migrating from the lungs to the liver (18). Similar

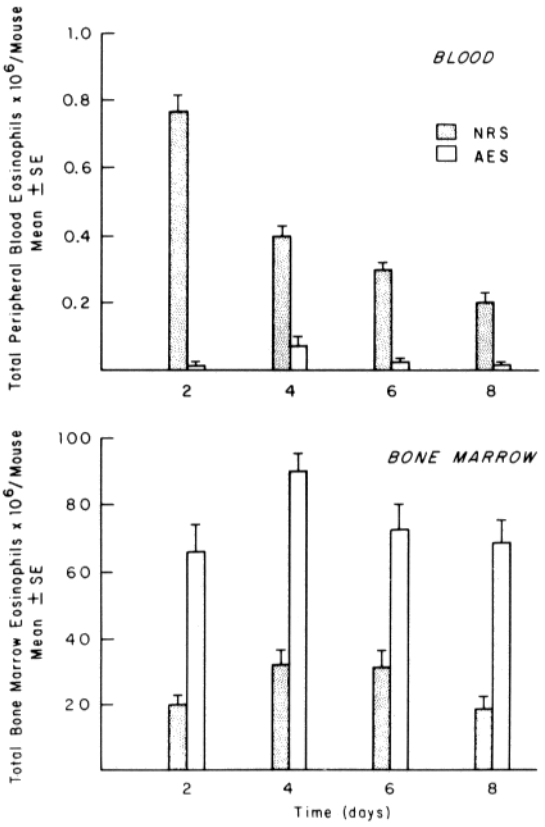

FIG. 4. Effects of NRS and AES administration on total peripheral blood and bone marrow eosinophils after a secondary i.v. injection of *S. mansoni* eggs (preceded by primary i.v. injection).

increases in peripheral eosinophil counts have been demonstrated during the migratory phases of other helminthiases such as hookworm infection, ascariasis, and strongyloidiasis (19, 20). While there is no explanation as yet for this wave of eosinophilia in schistosomiasis, it is interesting to note that by the time the schistosomula had all migrated into the intrahepatic portal venules, the peripheral as well as the bone marrow eosinophil counts dropped to normal.

Later in the course of infection a second major wave of eosinophilia occurred coincident with the appearance of mature antigen-secreting schistosome eggs in the host tissues. The heavy infections (111 worms/animal) were associated with a moderate eosinophil response which fell before the death of the animals. Maximum stimulation of eosinopoiesis, as manifested by the number of circulating eosinophils, was seen in the mice with moderate worm burdens (24 worms/animal); these mice also succumbed to the infection. Most of the mice with an average of five worms did not die, however, enabling the eosinophilia to be followed for 20 wk. Eosinophil counts were maximal by 10 wk, plateaued until 16 wk, and then declined at 18 and 20 wk. The development of peripheral eosinophilia coincident with egg deposition and maturation in the host tissues

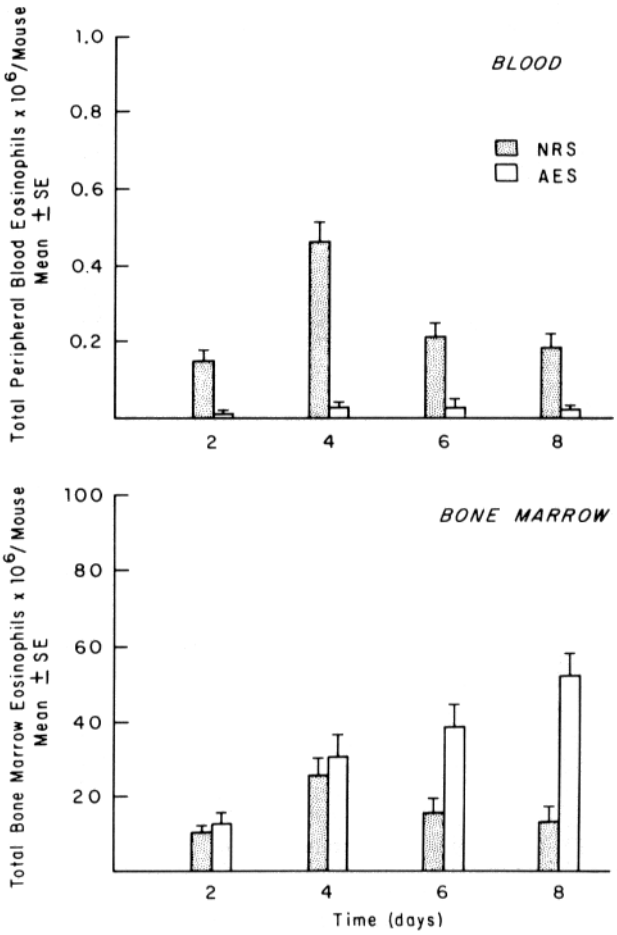

FIG. 5. Effects of NRS and AES administration on total peripheral blood and bone marrow eosinophils after a secondary i.v. injection of *S. mansoni* eggs (preceded by a primary i.p. injection).

TABLE III

Differential Counts of Bone Marrow Eosinophilic Cells Performed on Electron Micrographs of Normal Mice and Those Injected Intravenously with 1,500 S. mansoni Eggs During NRS Treatment and AES Treatment

Experimental group	Total eosinophilic cells counted	Promyelocytes	Myelocytes	Metamyelocytes	Bands and segmented
		%		%	
Control (2 mice)	37	2.7	83.8	5.4	8.1
Egg injected + NRS (5 mice)	65	0	72.3	21.5	6.2
Egg injected + AES (7 mice)	125	4.0	74.4	21.6	0

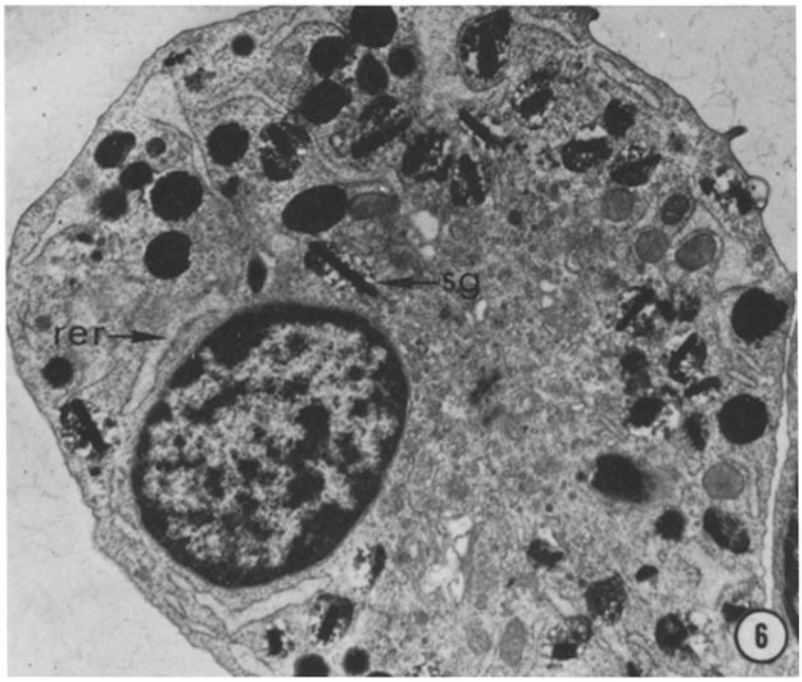

FIG. 6. Electron micrograph of an eosinophil myelocyte obtained from the bone marrow 4 days after i.v. injection of *S. mansoni* eggs into an AES-treated mouse. Relative nuclear immaturity is indicated by multiple small chromatin aggregates scattered throughout the nucleus. Cytoplasmic immaturity is indicated by the flocculent nature of the material surrounding the crystalloids in the specific granules (*sg*) and by the many profiles of rough endoplasmic reticulum (*rer*). × 10,000.

may be related to the presence of large numbers of eosinophils in the granulomatous lesions. Colley (21) has demonstrated that lymphoid cells from *S. mansoni*-infected animals produce a lymphokine eosinophil stimulation promotor (ESP), which is also secreted by isolated liver granulomas on incubation in vitro with soluble egg antigens (D. Colley, personal communication; Pelley et al., work in progress).

The role of the schistosome eggs in stimulating eosinophilia was then studied in a manner similar to the investigations of Basten et al. (22) with *Trichinella* larvae, with the addition of quantitative examination of the bone marrow and the pulmonary lesions. After the i.v. injection of the eggs there was eosinopoiesis in the bone marrow, eosinophilia in the peripheral blood, and the gathering of eosinophils around eggs deposited in the lungs. Several aspects of this reaction resembled the *Trichinella* model: the eosinophilia manifested itself after a delay period and was dependent on the site of the egg injection. Eosinophils appeared in the lung lesions of unsensitized animals 4 days after the egg injection while in sensitized animals they were found around the eggs within 24 h. As the granulomas increased in size, eosinophils became the most prominent cells in the lesions.

Since Basten et al. (23) were able to show that the eosinophilia induced by

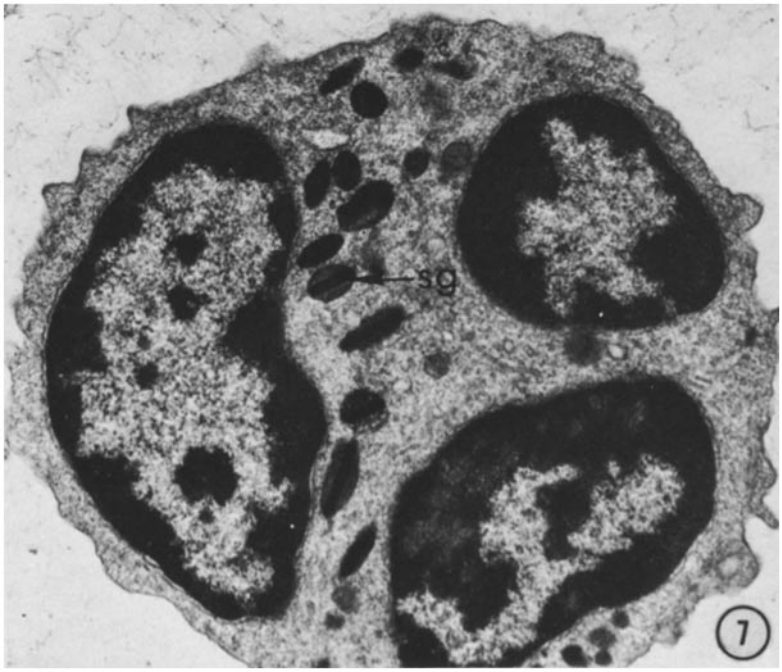

FIG. 7. Electron micrograph of a mature eosinophil obtained from the bone marrow 4 days after i.v. injection of *S. mansoni* eggs into an NRS-treated mouse. Nuclear maturity is indicated by the large, peripherally located chromatin aggregates. Cytoplasmic maturity is indicated by the condensed material surrounding the crystalloids in the specific granules (*sg*), and by the absence of rough endoplasmic reticulum. × 10,000.

TABLE IV

Mean Granuloma Area 8 Days After the Intravenous Injection of S. mansoni Eggs into the Pulmonary Microvasculature of NRS- and AES-Treated Mice

	Mean granuloma area × 10^3 μm^2 ± SE	
	Unsensitized	Sensitized*
NRS-treated	22.9 ± 1.5	44.8 ± 4.9
AES-treated	8.9 ± 0.7	19.0 ± 2.0

* These mice received an intraperitoneal injection of *S. mansoni* eggs 8 days before the intravenous injection of eggs.

Trichinella larvae injected into the lung microvasculature was essentially a cell-mediated reaction, it is important to note that on the basis of anamnesis, specificity and cell transfer the schistosome egg granuloma has also been found to be largely a delayed hypersensitivity response (13). This reaction has also been correlated with other forms of delayed hypersensitivity both in vivo and in vitro (24, 25). In the present study the major wave of bone marrow and peripheral eosinophilia in *S. mansoni* infected mice coincided with the onset of egg

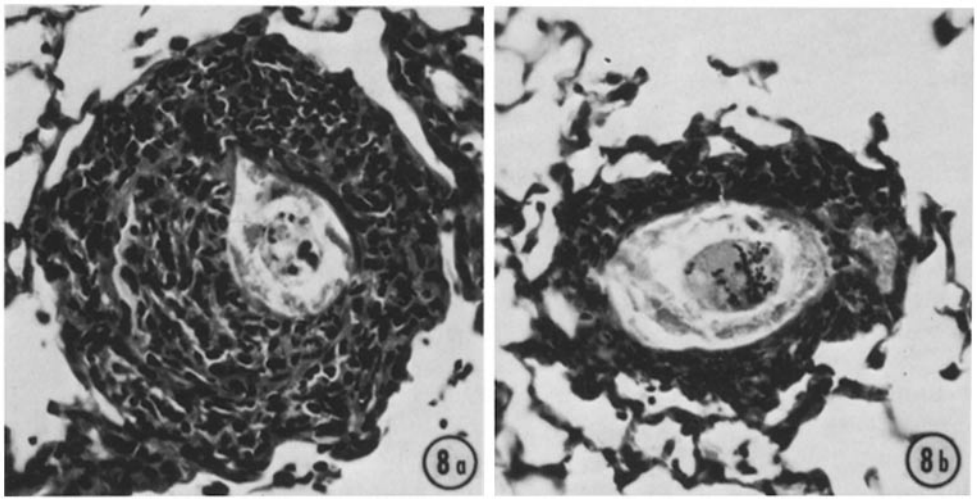

FIG. 8. Granulomas representative of the mean areas of lesions around *S. mansoni* eggs 8 days after their injection into (*a*) NRS-treated and (*b*) AES-treated animals. Hematoxylin and eosin stain. × 360.

deposition and granuloma formation. Furthermore, when eggs were injected into the pulmonary vessels of uninfected animals, anamnestic eosinophil responses were observed on secondary exposure. Finally, it had previously been demonstrated that depletion of T lymphocytes in mice infected with *S. mansoni* suppressed both granuloma formation around schistosome eggs and eosinophilia (26). Recent studies in chronically infected animals have shown the modulation of granulomatous hypersensitivity and cellular responses to soluble schistosome egg antigens, including delayed foot pad swelling and production of macrophage migration inhibitory factor by spleen cells maintained in vitro (27). The waning of eosinophilia 18 and 20 wk after infection appears to be related to this general modulation of cell-mediated responses to schistosome egg antigens.

The effect of AES on this complex series of reactions which involves an immunologic stimulus to eosinophils in the tissues followed by both peripheral and bone marrow eosinophilia was then investigated. Previously, we reported that a single injection of AES virtually eliminated the peripheral eosinophilia in animals infected with *S. mansoni;* it also markedly reduced the number of peritoneal eosinophils obtainable from normal mice repeatedly injected intraperitoneally with saline (1). Studies now in progress on eosinophilia in mice infected with *Trichinella spiralis* have demonstrated virtual elimination of peripheral eosinophils with the AES raised against cells obtained from mice with schistosomiasis. In the present study we have chosen to concentrate on the effect of AES on the eosinophil responses after egg injection. This is a reproducible system that allows simultaneous quantitation of the responses in the peripheral blood, bone marrow, and the granulomatous lesions. While AES aborted the peripheral eosinophilia after both primary and secondary egg injections, it induced a marked increase in eosinophilic bone marrow cells. On electron microscopy, however, this increase was found to be due wholly to the immature

eosinophil metamyelocytes and myelocytes, as the relatively mature band and segmented eosinophils were completely eliminated. Thus, AES is not only cell-specific but has specificity for the stage of maturity of the cells. Comparable results have been recorded in guinea pigs treated with antineutrophil serum: the mature cells were destroyed but there was a proliferation of their precursors in the bone marrow (28). The recent development of monospecific antisera to human eosinophils, basophils, neutrophils, and myeloblasts has revealed similar specificity with respect to the stage of maturity of the cells (29, 30).

The schistosome egg granuloma has been shown to be the principal factor in the pathogenesis of hepatosplenic schistosomiasis (31). The eggs alone do not significantly impede liver blood flow but the avascular granulomas, which may be 100 times the volume of the egg alone, obstruct the portal circulation (32), leading to portal hypertension and the development of portal systemic collateral circulation. In the present study AES not only aborted peripheral eosinophilia, but eliminated eosinophils from the lung granulomas which were consequently much decreased in size. Absence of eosinophils from the lesions resulted in granuloma volumes of less than $^1/_{10}$ those seen in control animals. As reduction in granuloma size by a variety of immunosuppressive means is associated with a significant reduction in the development of hepatosplenic disease (33, 34), it is probable that elimination of the eosinophils from the granulomas, which greatly reduces their size, will be beneficial to the host.

Summary

Mice were exposed to different intensities of infection with *Schistosoma mansoni* (10, 50, or 200 cercariae) and the kinetics of peripheral and bone marrow eosinophilia was followed for as long as 20 wk. When the schistosomula (immature worms) were migrating from the lungs to the liver there was a mild, transient eosinophilia, but soon after the onset of egg laying by the schistosomes, a major and prolonged increase in eosinophils occurred. This was terminated in the heavier infections by the death of the animals, but showed a spontaneous decline beginning at 18 wk in the lightly infected mice. The effect of *S. mansoni* eggs on eosinophilia in the blood, bone marrow, and granulomatous lesions was then examined by injecting schistosome eggs into mice intraperitoneally, subcutaneously, and intravenously. While the host response was dependent on the route by which eggs were administered, primary peripheral and bone marrow responses were seen on intravenous injection, and secondary responses occurred on intravenous and subcutaneous injection. In unsensitized and egg-sensitized mice, eosinophils were first seen around eggs injected into the pulmonary microvasculature at 96 and 24 h respectively. When the granulomas were maximal in size eosinophils made up at least 50% of the lesions. Administration of antieosinophil serum profoundly suppressed eosinophils in the peripheral blood, eliminated mature eosinophils and markedly increased eosinophil precursors in the bone marrow, and ablated eosinophils from the tissue lesions, considerably reducing their area.

The authors wish to acknowledge the expert technical assistance of Pierre Peters, Earlene Moss, and George Makohin.

Received for publication 7 April 1975.

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