

## *Trypanosoma musculi* Infections in Normocomplementemic, C5-Deficient, and C3-Depleted Mice

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The role of complement in host resistance to infection with *Trypanosoma musculi* was studied in normal, C5-deficient, and C3-depleted mice. Infections in normocomplementemic strains (CBA and B10.D2/n) were generally similar to those in strains genetically deficient in C5 (A and B10.D2/o). There were no differences in inhibition of reproduction, duration of infection, persistence of parasites in the kidneys, or resistance to reinfection. However, peak parasitemias in B10.D2/o mice were slightly greater than in B10.D2/n mice. In addition, B10.D2/o mice had slightly decreased serum levels of C1 early in the course of infection and of C3 early during the elimination of adult forms. These components were unchanged or increased in infections of B10.D2/n. Depletion of C3 and late-acting components in B10.D2/n mice by treatment with cobra venom factor during the reproductive stage of infection resulted in an increase of reproductive forms before the apparent development of ablative immunity as well as slightly greater peak parasitemias when compared with those of untreated controls. Cobra venom factor treatment of B10.D2/o mice during the reproductive stage did not alter the course of infection. Cobra venom factor treatment of C3H mice during the adult stage prolonged infections by interfering with parasite elimination. It is concluded that complement-mediated lysis is not involved in control of *T. musculi*. It is not clear whether a C3-dependent function such as phagocytosis may facilitate elimination of the parasites. The major difference in degree of parasitemias among the various strains of mice studied is due to genetic factors rather than the levels of C3, C5, or late-acting complement components.

*Trypanosoma musculi* produces a characteristic self-limiting infection in mice (17). Early in the infection, there is a period of rapid parasite multiplication and numerical increase. The reproductive rate then gradually declines, the parasitemia stabilizes temporarily at a plateau level, and the nonreproducing (adult) forms are gradually eliminated from the peripheral blood. Infective dividing forms, however, are known to persist in the vasa recta capillaries of the kidneys for at least 1 year (24). Conversion of the reproducing parasites to a population of monomorphic adults results from the action of two serological factors: a thymus-dependent ablastin, which inhibits reproduction; and a thymus-independent trypanocidal antibody, which removes newly formed parasites (16, 22). The exact mechanisms by which the parasites are eliminated have yet to be resolved. Taliaferro (16) believed that infections were terminated by the agglutinating and complement-dependent lytic activities of trypanocidal antibodies. Targett and Viens, however, favor a

cell-mediated mechanism as the means by which the adult forms that escape the initial trypanocidal antibody are eliminated (19, 21, 23).

In this study we examined the role of complement in host control of *T. musculi* by comparing infections in normocomplementemic, C5-deficient, and C3-depleted mice. Infections in normocomplementemic and C5-deficient mice were generally similar, demonstrating that complement-mediated lysis is not essential for elimination of the trypanosomes. C3 depletion by treatment with cobra venom factor (CoF) during the reproductive stage did not alter the course of infection. However, CoF treatment of C3H mice during the adult stage caused a reduced rate of parasite elimination and slightly prolonged infections. C1 and C3 levels were slightly decreased during infections of B10.D2/o mice but not in B10.D2/n mice.

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### MATERIALS AND METHODS

**Experimental animals.** Male mice 1.5 to 3.5 months of age were used. C5-deficient strains (A/Jax and B10.D2/o) and normocomplementemic strains (CBA/HT-6, C3H/Bi, and B10.D2/n) were obtained from the University of Minnesota Mouse Colony, Minneapolis, Minn. (15). Outbred albino mice originally obtained from the Department of Zoology, University of Minnesota, were raised in this laboratory. In each study, the animals were initially divided into experimental groups of five mice each on the basis of weight so that the mean weights of all groups within a study were similar. Mean preinfection weights of the mice in all studies ranged from 18.5 to 23.0 g.

**Maintenance of parasite and infection of experimental animals.** *T. muscili*, originally isolated by D. R. Lincicome and maintained as a laboratory strain by P. A. D'Alesandro, was routinely maintained in this laboratory in outbred mice by syringe passage of infected blood transferred on day 10 of infection. Before infection of experimental animals, the trypanosomes were passaged once through the strain under study with two exceptions. Outbred mice served as the source of parasites for the comparison of infections in A and CBA strains, whereas B10.D2/n mice were used as donors in the comparison of B10.D2/n and B10.D2/o strains. Donor mice were exsanguinated at 6 to 12 days of infection from the retro-orbital plexus by using a Pasteur pipette rinsed with heparin (1,000 U/ml). Trypanosomes were separated from the blood by a method described previously (4) for the isolation of *T. cruzi*. The parasites were washed five or six times with 50 volumes of 0.9% NaCl-5% dextrose, resuspended in 1 ml of the diluent, and counted by using a hemacytometer. The trypanosome suspensions were adjusted to the desired concentration and injected intraperitoneally. Infecting doses were  $1 \times 10^5$  to  $6 \times 10^5$  *T. muscili* in all experiments except the study of CoF-treated C3H mice, in which a dose of  $9 \times 10^6$  trypanosomes was used. Uninfected controls received an equivalent volume of sterile 0.9% NaCl-5% dextrose.

**Course of infection.** Numbers of parasites in tail vein blood samples were determined every 2 or 3 days by hemacytometer counts or by examination of 50 wet-film microscopic fields (10 $\times$  ocular and 40 $\times$  objective) during periods of low parasitemia. For hemacytometer counts, blood samples were diluted in erythrocyte diluting pipettes with 1% Formalin-0.9% NaCl containing 10% Giemsa stain. Percentages of reproductive forms (epimastigotes, small trypomastigotes, and actual dividing forms) were determined by examination of 100 to 500 trypanosomes on Giemsa-stained smears. Blood samples were always obtained between 9 and 11 a.m.

**CoF treatment.** CoF obtained from Cordis Laboratories, Miami, Fla., was used to achieve in vivo depletion of C3 and late-acting components (6). B10.D2/n and B10.D2/o mice received CoF intravenously in the tail veins in two doses of 5 U each 6 h apart on day 0 prior to intraperitoneal infection with

*T. muscili*. An additional 2.5 U was given intravenously to the B10.D2/n mice on days 4, 6, and 8. The B10.D2/o mice received additional intraperitoneal injections of 5 U daily from day 5 to 11 and 10 U every other day from day 12 to 18. C3H mice received 10 U of CoF intraperitoneally on days 8, 9, and 15 after infection. Controls received an equivalent volume of sterile diluent.

**Examination of recovered mice for persistence of *T. muscili*.** Blood samples were obtained from 13 mice that had recovered from *T. muscili* infections 9 to 12 months earlier, and wet films were examined for the presence of trypanosomes. The animals were then sacrificed, and both kidneys were removed. Impression smears were made of each kidney and stained with Giemsa stain. One-half of each kidney was fixed in 10% buffered Formalin, processed, and stained with hematoxylin and eosin or with Giemsa stain for histological examination. The second half of each kidney was cut finely with scissors and then gently homogenized in 1 ml of sterile 0.9% NaCl. The homogenates were examined directly by phase contrast for the presence of parasites, and 0.6 ml of the material was inoculated intraperitoneally into clean 5-week-old male C3H mice. Blood from the C3H mice was examined for parasites every 2 to 4 days after inoculation for a period of 2 weeks.

**Samples for complement determinations.** Mice were bled from the retro-orbital plexus 5 days before and every 4 days after infection. One heparinized capillary tube (Fisher Scientific Co., Pittsburgh, Pa.) containing approximately 100  $\mu$ l of blood was obtained from each mouse at each bleeding. After centrifugation for 5 min in an International Microcapillary Centrifuge, model MB, the plasma was removed and stored at -70°C until used.

**Complement determinations.** Plasma C3 levels were determined by the radial immunodiffusion method of Mancini et al. (12), with rabbit anti-mouse C3 at a 1:6 dilution. Titers were expressed as a percentage of a pooled normal mouse plasma standard obtained from mice of the same strain as used experimentally. C1 was titrated hemolytically (20) by using EAC4<sup>hu</sup> (hu refers to C4 derived from human serum) (3) and 40% of the reactant volumes described in the published procedure. To compare levels of C1 and C3 during infections, the titers are expressed as percentages of preinfection values in Table 4.

**Anti-mouse C3.** Rabbit antiserum to mouse C3 was prepared by a modification of a published method (13). An 80-mg amount of zymosan (Mann Research Laboratories, Rutherford, N.J.) was processed, incubated with 4 ml of B10.D2/n mouse serum, and washed as described previously. The zymosan-complement complex was suspended in 3 ml of 0.9% NaCl and mixed with 3 ml of complete Freund adjuvant. A 3-ml volume of the mixture was used to immunize each of two rabbits in the footpads, intramuscularly, and subcutaneously. The antiserum obtained 1 month after immunization was absorbed of contaminating antibodies with an insolubilized mouse serum protein fraction and tested for monospecificity as previously described for anti-rat C3 (10).

**Statistical analyses.** Student's *t* test was used to

determine statistical significance. Values of *P* less than 0.05 were considered significant.

**RESULTS**

**Course of infection in normocomplementemic and C5-deficient mice.** In one experiment, CBA (normocomplementemic) and A (C5-deficient) strains were infected with  $3 \times 10^5$  trypanosomes. The resultant parasitemias are illustrated in Fig. 1. There were no significant differences between the two strains in onset of patency (2 to 4 days based on wet-film examination [results not shown]), number of parasites, time of peak parasitemia (11 to 13 days), or duration of infection (20 to 22 days). CBA strain mice exhibited consistently higher percentages of reproductive forms, with a significant difference occurring on day 12 (Table 1, experiment

1). The CBA strain, therefore, appears to have a slightly greater susceptibility to *T. muscui* infection than the A strain.

Infections were also compared in the congenic B10.D2/n (normocomplementemic) and B10.D2/o (C5-deficient) strains (15). The parasitemias seen in Fig. 1 were initiated with an inoculum of  $6 \times 10^5$  *T. muscui*. Although there was a slightly greater parasitemia in the B10.D2/o mice on day 9 at the peak of infection ( $P < 0.05$ ), no other significant differences were observed. Inhibition of reproduction (Table 1, experiment 2) and elimination of parasites (Fig. 1) occurred as efficiently in both strains, and infections were terminated in 17 to 22 days. It was also noted that both B10.D2 strains supported lower parasitemias than either the A or CBA strain in spite of receiving a larger infecting dose.

**Infections in CoF-treated mice.** CoF was used to study the effects of complement depletion (C3 and late-acting components) during various stages of infection with *T. muscui*. The effect of depletion during the reproductive stage of infection was studied in B10.D2/n and B10.D2/o mice. The parasitemias of treated B10.D2/n mice initially infected with  $2 \times 10^5$  trypanosomes were compared with those of untreated, infected controls (Fig. 2A). C3 levels in the treated group decreased from a mean preinfection value of 89% of the standard ( $\pm 5$ , standard error [SE]) to 16% ( $\pm 4$  SE) on day 4 but recovered to 70% ( $\pm 17$  SE) by day 8 and 90% ( $\pm 11$  SE) by day 12. Although the course of infection was similar in both groups, there were significantly more reproductive forms in the CoF-treated group on day 4 (Table 2, experiment 1), which probably contributed to the slightly greater parasitemia ( $P < 0.05$ ) on day 8. Other differences were not significant. Inhibition of reproduction was complete in both groups by day 12 or 14, and infections were terminated by day 22. In an effort to prolong the state of complement depletion, B10.D2/o mice were treated with CoF before infection

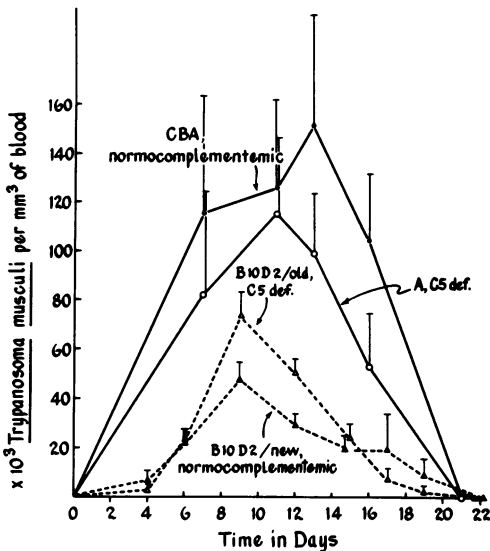


FIG. 1. Comparison of parasitemias in C5-deficient (B10.D2/o and A/J) and normocomplementemic (B10.D2/n and CBA) mice infected with *T. muscui*. Points represent mean values of four or five mice in each group.

TABLE 1. Reproductive activity of *T. muscui* in C5-deficient and normocomplementemic mice

Day of infection	Reproductive forms <sup>a</sup> (%)			
	Expt 1		Expt 2	
	CBA	A	B10.D2/n	B10.D2/o
4			15.1 ± 4.2	14.0 ± 1.9
6	17.5 ± 5.3	8.1 ± 1.6	4.5 ± 1.4	2.2 ± 1.5
10	2.5 ± 0.4	0.8 ± 0.2	0.4 ± 0.1	0.7 ± 0.4
12	2.1 ± 0.7 <sup>b</sup>	0.1 ± 0.1	0	0
14	0	0		

<sup>a</sup> Mean ± SE of five infected mice per group.  
<sup>b</sup> *P* < 0.05 as compared with that of A strain.

with  $10^5$  *T. muscoli*, and treatment was continued at 1- to 2-day intervals throughout the infection. On this schedule of treatment, C3 levels were decreased from a mean preinfection value of 80% of standard ( $\pm 8$  SE) to 10% ( $\pm 1$  SE) on day 4. Titers had returned to 83% ( $\pm 7$  SE) by day 8 in spite of further CoF treatment. There were no significant differences in the course of infection (Fig. 2B) or the inhibition of

reproduction (Table 2, experiment 2) between the treated mice and untreated controls. It is possible that the continuous administration of CoF had an adverse effect on the trypanosomes, resulting in the slightly lower peak parasitemias in the treated mice. These differences were not statistically significant.

In an attempt to accentuate any effect of C3 depletion during the adult stage of infection in a strain highly susceptible to *T. muscoli*, normocomplementemic C3H mice were heavily infected with  $9 \times 10^6$  *T. muscoli*. On day 8 of infection, the mice were randomly divided into two groups; at this time there was no significant difference in C3 levels between the groups. One group was then treated with CoF as indicated in Materials and Methods. C3 levels were decreased from the day-8 level of 64% of standard ( $\pm 3$  SE) to 6% ( $\pm 3$  SE) on day 12 and 10% ( $\pm 4$  SE) on day 17. C3 levels in the untreated group were 74% ( $\pm 7$  SE) on day 8, 64% ( $\pm 23$  SE) on day 12 and 69% ( $\pm 13$  SE) on day 17. The reproductive activity was not modified by the CoF treatment (Table 2, experiment 3). The untreated mice eliminated the parasites and terminated the infections quickly and efficiently (Table 3). In this group, only 40% of the mice were positive for parasites in peripheral blood on day 17, and by day 19 all were negative. In contrast, parasite elimination was delayed in the CoF-treated group during the period of C3 depletion, resulting in slightly prolonged infections, with all mice in this group remaining positive through day 19.

**Plasma complement levels in infected mice.** C1 and C3 levels were measured in infected normocomplementemic and C5-deficient mice and compared with the levels in uninfected controls bled on the same schedule. C1 hemolytic activity in the infected B10.D2/n mice was unaffected during the early period of infection and increased significantly during the terminal stages (Table 4). C3 activity showed an initial

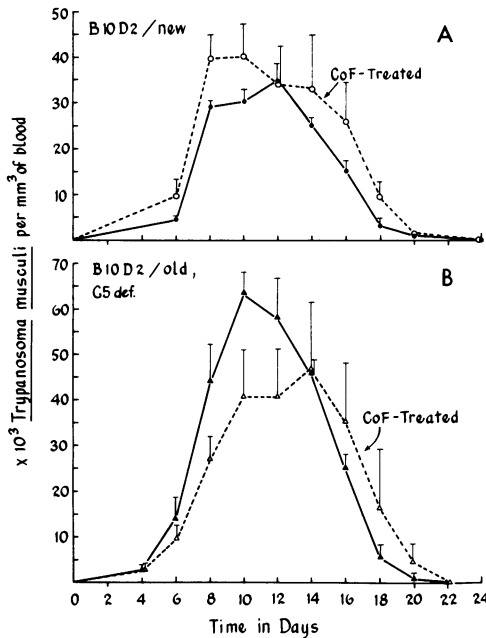


FIG. 2. Influence of CoF treatment of mice on the course of infection with *T. muscoli*. (A) Normocomplementemic B10.D2/n mice: untreated controls (●) and experimentals (○) treated with CoF on days 0, 4, 6, and 8. (B) C5-deficient B10.D2/o mice: untreated controls (▲) and experimentals (△) treated with CoF on day 0, every day from day 5 to 11, and every 2 days from day 12 to 18. Points represent mean values of five animals in each group.

TABLE 2. Reproductive activity of *T. muscoli* in untreated and CoF-treated C5-deficient and normocomplementemic mice

Day of infection	Reproductive forms <sup>a</sup> (%)					
	Expt 1: B10.D2/n		Expt 2: B10.D2/o		Expt 3: C3H	
	Untreated	Treated	Untreated	Treated	Untreated	Treated
4	25.8 $\pm$ 1.9	40.5 $\pm$ 2.6 <sup>b</sup>	10.4 $\pm$ 1.2	10.8 $\pm$ 2.3	20.3 $\pm$ 1.7	19.8 $\pm$ 2.3
6	12.0 $\pm$ 1.8	14.7 $\pm$ 5.5	3.9 $\pm$ 0.2	4.0 $\pm$ 0.9	6.2 $\pm$ 1.5	4.9 $\pm$ 1.1
8	1.6 $\pm$ 0.3	2.2 $\pm$ 0.8	0.9 $\pm$ 0.2	1.0 $\pm$ 0.4	1.4 $\pm$ 0.5	0.9 $\pm$ 0.3
10	0.4 $\pm$ 0.1	0.3 $\pm$ 0.1	0.6 $\pm$ 0.1	0.5 $\pm$ 0.1	0.4 $\pm$ 0.1	0.4 $\pm$ 0.1
12	0	0.4 $\pm$ 0.1	0	0	0.6 $\pm$ 0.2	1.1 $\pm$ 0.5
14		0			0	0

<sup>a</sup> Mean  $\pm$  SE of five infected mice per group.

<sup>b</sup>  $P < 0.0025$  as compared with that of untreated B10.D2/n.

significant increase and then returned to normal levels. In the infected B10.D2/o mice, however, C1 levels were significantly reduced on day 4, increased to normal levels during the later stages of infection, and finally reached significantly greater levels than controls after termination of the infections. C3 levels were significantly reduced during the peak parasitemia (days 8 and 12) and then returned to near-normal levels. However, no correlation could be demonstrated between the number of parasites present and the amount of C3 reduction in individual mice.

Persistence of *T. muscui* in kidneys of normocomplementemic and C5-deficient mice. Six B10.D2/n and seven B10.D2/o mice that had previously been infected with  $1 \times 10^5$  to  $6 \times 10^5$  *T. muscui* were examined for parasites 9 or 12 months after elimination of the trypanosomes from the peripheral blood. No trypanosomes were observed in either strain in fresh blood films or kidney homogenates, in kidney impres-

sion smears or histological sections, or on sub-inoculation of kidney homogenates into clean C3H mice.

Challenge infection of recovered normocomplementemic and C5-deficient mice. Four CBA (normocomplementemic) and four A (C5-deficient) mice were challenged intraperitoneally with a dose of  $5 \times 10^5$  *T. muscui* 82 days after infection with  $3 \times 10^5$  parasites. The initial infection lasted for 20 to 22 days (Fig. 1). No parasites were detected in either strain upon examination of fresh blood films at 24, 48, and 96 h after challenge. Trypanosomes were observed in the blood of previously uninfected control mice at 48 h.

DISCUSSION

The results presented in this paper demonstrate that C5 and the late-acting components are not required for control of *T. muscui* infections. The normocomplementemic CBA and C5-deficient A strains had similar courses of infection; there were no differences between the two strains in inhibition of reproduction, rate of parasite elimination, or resistance to reinfection. The congenic B10.D2 strains (normocomplementemic new line and C5-deficient old line) also experienced similar courses of infection as shown previously by Dusanic (7) and in this laboratory (J. A. Jarvinen and A. P. Dalmasso, Abstr. 49th Annu. Meet. Am. Soc. Parasitol., p. 19, 1974). Inhibition of reproduction and elimination of adult forms occurred equally efficiently in both strains, and the deficiency of C5 did not influence the persistence of parasites in the kidneys. In this study, however, we found that peak parasitemias in the old-line mice were slightly higher than in new-line mice. Although complement-mediated immune lysis of *T. muscui* has been demonstrated in vitro

TABLE 3. Effect of CoF treatment<sup>a</sup> on the elimination of *T. muscui* by C3H mice

Day of infection	No. of <i>T. muscui</i> per mm <sup>3</sup> of blood <sup>b</sup>			P value <sup>c</sup>
	Untreated <sup>c</sup>	CoF treated <sup>d</sup>		
10	220,000 ± 42,990	194,500 ± 9,140		>0.25
12	147,500 ± 28,240	192,500 ± 25,200		>0.10
14	124,000 ± 18,100	172,450 ± 15,650		<0.05
17	400 ± 290	64,750 ± 19,940		<0.01
19	0	7,900 ± 5,350		>0.05
25		0		

<sup>a</sup> CoF administered on days 8, 9, and 15.

<sup>b</sup> A mean of 206,500 ± 14,780 *T. muscui*/mm<sup>3</sup> was present in the 10 mice on day 8 prior to separation into experimental groups and treatment with CoF.

<sup>c</sup> Mean ± SE of five untreated mice.

<sup>d</sup> Mean ± SE of five CoF-treated mice.

<sup>e</sup> Student's *t* test.

TABLE 4. Plasma C1 and C3 levels<sup>a</sup> in normocomplementemic (B10.D2/n) and C5-deficient (B10.D2/o) mice infected with *T. muscui* and in uninfected controls

Day of infection	C1 <sup>b</sup>				C3 <sup>c</sup>			
	B10.D2/n		B10.D2/o		B10.D2/n		B10.D2/o	
	Infected	Control	Infected	Control	Infected	Control	Infected	Control
4	77 ± 10	77 ± 10	56 ± 7 <sup>d</sup>	93 ± 9	155 ± 12 <sup>d</sup>	107 ± 10	132 ± 8	117 ± 10
8	101 ± 9	101 ± 11	67 ± 9	77 ± 5	121 ± 8	108 ± 9	104 ± 6 <sup>e</sup>	134 ± 10
12	164 ± 24 <sup>e</sup>	76 ± 13	73 ± 13	81 ± 10	97 ± 12	116 ± 11	85 ± 7 <sup>d</sup>	117 ± 6
16	142 ± 17 <sup>e</sup>	84 ± 12	107 ± 15	71 ± 17	98 ± 10	103 ± 4	111 ± 16	124 ± 7
20	195 ± 24	151 ± 24	105 ± 9	85 ± 14	102 ± 12	99 ± 10	135 ± 17	124 ± 8
24	248 ± 31 <sup>d</sup>	117 ± 3	135 ± 12 <sup>d</sup>	79 ± 4	99 ± 13	100 ± 11	133 ± 3	120 ± 9

<sup>a</sup> Expressed as a percentage of preinfection value ± SE.

<sup>b</sup> Mean ± SE of five infected and five uninfected mice of each strain.

<sup>c</sup> Mean ± SE of 10 infected and 10 uninfected mice of each strain.

<sup>d</sup> *P* < 0.01. Determined by comparison with uninfected controls of the appropriate strain.

<sup>e</sup> *P* < 0.05. Determined by comparison with uninfected controls of the appropriate strain.

(16), we do not believe the small difference in peak parasite numbers between the old- and new-line mice is sufficient to indicate a role for C5 or lysis in control of the infection.

The initial anticomplement effect of CoF is transitory, lasting only 4 to 6 days, and additional doses are rapidly neutralized by anti-CoF antibody (6, 14). Prolonged C3 depletion is therefore not feasible, and any effect of C3 depletion will remain undetected unless it becomes apparent within this short period of time. Nevertheless, C3 depletion of C3H mice during peak parasitemia resulted in a reduced rate of parasite elimination and prolonged infections. B10.D2/n mice depleted of C3 early in infections experienced a greater percentage of reproductive forms prior to the apparent development of ablastic immunity as well as slightly higher peak parasitemias, compared with mice with normal C3 levels. Although C3 depletion of B10.D2/n mice by CoF resulted in modification of the infections, there was no reduction of C1 or C3 serum levels in untreated, infected animals. This discrepancy may be due to increased synthesis of these components as suggested by the occasional finding of elevated levels in infected animals. A moderate reduction of C1 and C3 levels was occasionally observed in infected B10.D2/o mice. At any rate, it is apparent that *T. musculi* infections of mice do not result in a massive complement activation comparable to that seen in rats infected with *T. lewisi* (10), indeed a remarkable discrepancy of two host-parasite associations that have generally been considered quite similar.

Previous investigators have demonstrated the roles of both natural and acquired immunity in the control of *T. musculi*. Mice possess a natural resistance to the reproduction of this parasite, as well as an innate trypanocidal activity (8, 9, 17), both of which limit the parasitemias before the development of acquired immunity. The innate resistance to reproduction is macrophage dependent and is apparently not due solely to any passively transferable serum factor (9, 17). C3-mediated phagocytosis of reproductive forms involving a natural opsonin may be a mechanism of this natural resistance to reproduction. Although we observed a greater percentage of reproductive forms on day 4 in CoF-treated B10.D2/n mice compared with that of untreated animals, a similar effect of CoF treatment was not seen with B10.D2/o mice. Subsequent control of the infection results from the concomitant action of two acquired antibodies: ablastin, which inhibits reproduction, and a trypanocidal antibody, which removes newly formed parasites (16, 18, 22).

These two factors govern the ultimate level of circulating parasites. Ablastin is thymus dependent as indicated by persistent high rates of reproduction in thymectomized mice (22). In these animals, however, the parasitemia was still partially controlled by the thymus-independent trypanocidal antibody. Our experiments indicate that the effects of ablastin and probably the trypanocidal antibody are independent of complement. Termination of the infection by elimination of the adult forms appears to be a thymus-dependent function (19, 22); our results indicate that this process is independent of C5 and late-acting components but do not allow a conclusion in favor or against a role of C3. Passive-transfer studies with immune serum have given equivocal results (16, 19, 21).

Apparently, genetic factors other than those that control complement levels are of greater importance in determining susceptibility to *T. musculi* infection. C3H mice tend to support higher parasitemias than many other strains (P. A. D'Alessandro, personal communication). We have found parasitemias to be heavier in CBA and A strains than in either B10.D2 new- or old-line mice. Similarly, Dusanic (7) has reported higher parasitemias in CFW mice than in B10.D2/n, B10.D2/o, or their parent strain, C57 Bl/10.

The varying influence of complement on the outcome of infections has been demonstrated with other protozoa. Budzko et al. (4) and Kierszenbaum (11) found increased parasitemias and early mortality in mice infected with *T. cruzi* and depleted of C3 with CoF. We have reported similar parasitemias and mortality rates in C5-deficient, C3-depleted, and normocomplementemic mice with acute infections with *T. cruzi* (J. A. Jarvinen and A. P. Dalmasso, Abstr. 51st Annu. Meet. Am. Soc. Parasitol., p. 39, 1976). In another model, we have observed persistent subpatent *T. cruzi* infections in C4-deficient guinea pigs but not in normocomplementemic animals, although there were no differences between the two strains in the acute stage parasitemias (abstract cited above). Although *T. lewisi* infections of rats cause a profound reduction in serum levels of complement components of the classical pathway, complement does not appear to play an important part in the recovery from the infection (10). *Plasmodium berghei* infections followed a similar course in congenic C5-deficient and normocomplementemic mice (25), and depletion of late-acting components by CoF treatment failed to influence simian infections with *P. coatneyi* (2). In addition, C5-deficient

mice had greater resistance to *Toxoplasma gondii* than did mice with normal or elevated complement levels, presumably due to a lessening of inflammatory injury (1). Thus, complement may be beneficial, deleterious, or irrelevant to the outcome of infections with protozoa, depending on the species of parasite as well as the host involved.

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