

Thymus Dependence of Tapeworm (*Hymenolepis diminuta*) Elimination from Mice

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Although normal mice eliminated the lumen-dwelling intestinal cestode *Hymenolepis diminuta* by day 21 post-cysticercoid inoculation, congenitally thymus-deficient (nude) mice maintained their worm burdens. Nude mice grafted with thymus glands or injected with thymus cells eliminated their worms.

Hymenolepis diminuta, a noninvasive tapeworm of the small intestine, is maintained in rats for many months. This worm becomes established in mice also, but in mice worms grow for 10 days, then destrobilate, and are eliminated from the host shortly thereafter (2). Although elimination is considered to have an immunological basis (2), the precise mechanism of elimination is uncertain. The availability of congenitally thymus-deficient (nude *nu/nu*) mice (8) allows a critical evaluation of the importance of thymus competence in the elimination of this parasite. We have investigated *H. diminuta* infections in normal and nude mice and in nude mice provided with thymus competence. We present evidence that elimination of *H. diminuta* from mice is a thymus-dependent phenomenon.

Groups of nude mice and their normal littermates, from a line crossed onto the BALB/c strain, were infected by stomach tube with one or three cysticercoids of *H. diminuta* dissected from the flour beetle *Tribolium confusum*. On days 7, 14, and 21 of infection, representative animals from each group were killed and examined for the presence of *H. diminuta*. The results of several experiments (Table 1) show that worms became established by day 7 in both nude and normal mice. In nude mice the prevalence of infection was high throughout the 21 days of observation; in marked contrast, in normal mice the prevalence of infection was greatly reduced by day 14, and by day 21 none of the normal mice examined was positive for *H. diminuta*. Worms recovered on day 21 from nude mice were large, frequently 50 to 70 cm in length, whereas in normal mice worms seldom exceeded 16 cm in length before destrobilation or elimination occurred.

Because thymus deficiency is not the only abnormality of nude mice (1, 7), it was im-

portant to investigate *H. diminuta* infections in nude mice with thymus competence. Thus, nude mice bearing BALB/c thymus gland grafts or injected with BALB/c thymus cells, untreated nude mice, and normal mice each were infected with three cysticercoids; representative animals from each group were examined for the presence of *H. diminuta* on days 7 and 21 of infection. The results (Table 2) show that, unlike nude mice, nude mice with thymus competence can eliminate *H. diminuta*. In this experiment, all mice examined on day 7 were positive for *H. diminuta*. By day 21, all normal mice and nude mice injected with thymus cells had eliminated their worms, and worms were recovered from only 2 of 18 (11%) thymus-grafted nudes. These two positive mice each had one worm; these worms measured 0.5 cm in length and thus were not comparable in size with the worms (50 to 70 cm) recovered on day 21 from the nude mice.

At necropsy, large, histologically normal thymus glands were found under the renal capsules of all thymus-grafted nude mice. Representative animals from the nude, normal, and thymus-grafted nude groups were assayed for immune competence after immunization with the thymus-dependent antigen sheep erythrocytes. Five days after intravenous administration of 10^8 sheep erythrocytes, spleens were assayed for sheep erythrocyte-specific plaque-forming cells (PFC) using the localized hemolysis in gel assay (3). The PFC responses of nude mice and normal mice were 3,495 PFC/spleen and 88,482 PFC/spleen, respectively. Thymus-grafted nude mice responded with 46,875 PFC/spleen. These observations verify that thymus glands were present and functioning in the thymus-grafted nude mice. In this experiment we did not directly appraise the immune capacity of the nude mice injected with

TABLE 1. Development of *H. diminuta* in nude and normal mice^a

No. of mice	No. of cysticercoids/mouse	Duration of infection (days)					
		7		14		21	
		% pos	% rec	% pos	% rec	% pos	% rec
Nude							
11	3	100	92				
9	3			100	85		
6	3					100	96
Normal							
12	3	75	59				
9	3			22	7		
7	3					0	0
Nude							
3	1	100	100				
3	1			100	100		
12	1					83	83
Normal							
1	1	100	100				
4	1			0	0		
9	1					0	0

^a Mice were infected with one or three cysticercoids on day 0; on days 7, 14, and 21, representative animals were killed and their small intestines were examined for the presence of developing worms. Results are expressed as the percentage of mice positive for adult worms after inoculation with cysticercoids (% pos) and as the percentage of cysticercoids recovered as adult worms in mice (% rec).

BALB/c thymus cells; however, in other experiments we (unpublished data) and others (4) have observed that such animals can make thymus-dependent immune responses.

In summary, these data show that elimination of *H. diminuta* from mice requires thymus competence and supports the concept that elimination has an immunological basis (2). The role of the thymus in the elimination process remains to be established. Interestingly, recent work indicates that nude mice fail to produce immunoglobulin E (5) and peripheral blood eosinophilia (6), two events often associated with parasitic infections. Selective reconstitution of nude mice with antibody of known class and activity and/or selected immunologically relevant cell types could prove useful in attempts to elucidate the mechanisms involved in elimination of cestodes from their hosts, a process which to date has remained undefined.

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TABLE 2. Development of *H. diminuta* in nude mice with thymus competence^a

No. of mice	Duration of infection (days)			
	7		21	
	% pos	% rec	% pos	% rec
Nude				
10	100	90		
21			62	44
Nude-TG^b				
6	100	83		
18			11	4
Nude-TC^c				
1	100	67		
6			0	0
Normal				
16	100	71		
32			0	0

^a All mice were infected with three cysticercoids. Results are expressed as in Table 1.

^b At 42 days preinfection, nude mice were grafted with one neonatal BALB/c thymus gland under each renal capsule.

^c At 21 days preinfection, nude mice were injected intravenously with 1.5×10^6 BALB/c thymus cells.

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