The enteric phase of a primary nematode infection is associated with structural and functional changes in the intestinal mucosa (25). In addition, studies from our and other laboratories (4, 6, 38, 41, 45) have shown that Trichinella spiralis infection also induces changes in the deeper neuromuscular layers of the intestine, accompanied by accelerated intestinal transit. Because the increased propulsion is observed in extrinsically denervated gut segments (1), the changes in propulsive activity must reflect changes in those components of the motility apparatus that are intrinsic to the bowel wall, thus implicating enteric nerves and muscle.

Previous studies (9, 13, 46) have demonstrated that these changes in intestinal physiology are influenced by the immune response of the host to the invading parasite. We have postulated that the increased propulsive activity is due to a recruitment of the intestinal motor system by the host immune response, enabling it to act as an extension of the immune system in evicting the parasite from the gut. In the rat, both worm expulsion and increased tension generation by intestinal muscle are attenuated in the absence of functioning T lymphocytes (46), suggesting a common immunologic mechanism. We have continued to pursue this investigation in the mouse, to exploit a broader range of investigative tools. In our first study in the mouse (41), we showed that T. spiralis infection was accompanied by increased tension development by intestinal muscle. Interestingly, we showed that the magnitude of this increase was greater in mouse strains that evicted the parasite rapidly (e.g., NIH Swiss) (2, 41) compared with that seen in mice that evicted the parasite slowly and incompletely, such as the B10.BR strain (41). These observations strengthened the association between worm expulsion and changes in muscle contractility and prompted a closer evaluation of this relationship and underlying immunologic mechanisms.

The present study was undertaken to investigate the time course of changes in muscle contraction in relation to worm expulsion in the mouse and to determine the extent to which contractility changes are mediated by T cells. The previous study in rats examined only one time point postinfection (PI) and left open the possibility that other immunologic or inflammatory mechanisms may contribute to enhanced muscle contractility within the overall time frame of primary infection by this nematode parasite.

The results from this study identify two distinct components of increased contractility in the mouse intestine after T. spiralis infection. There is an early phase that occurs rapidly, within 6 days of infection, followed by a smaller sustained phase that persists for up to 21 days. In athymic and SCID mice, the early phase is delayed several days and the sustained phase is reduced in magnitude. This attenuated profile of muscle contractility is accompanied by a delay in worm expulsion. Reconstitution of T cell function in athymic mice is accompanied by restoration of the profile of muscle contraction seen in euthymic mice and by faster worm expulsion. These results suggest that both the timing and magnitude of muscle changes are important in worm expulsion and that there are both T cell-dependent and -independent mechanisms that underlie the enhanced contractility of intestinal smooth muscle in this model.

MATERIALS AND METHODS

Mice. Athymic (nu/nu) BALB/c mice as well as their heterozygous (nu/+) euthymic littermates were purchased...
from the National Cancer Institute (Frederick, MD), whereas CB.17 SCID/beige mice, which are congenic with BALB/c mice, were bred and kept in the animal facilities of McMaster University (Hamilton, Ontario, Canada). For these experiments, male mice, aged 4–6 mo (to be age matched to T lymphocyte-reconstituted mice), were used. Mice were kept in sterilized and filter-isolated cages, under specific pathogen-free (SPF) conditions, in groups of four to five in positive-pressure rooms with a constant ambient temperature and photoperiod (14:10-h light-dark cycle). All experiments were approved by the Animal Care Committee at McMaster University and were conducted in accordance with the guidelines of the Canadian Council on Animal Care.

Trichinella infection. Mice were infected by administration via gavage of 0.1 ml of PBS containing ~375 T. spiralis larvae. Athymic, euthymic, and reconstituted mice were infected together, with the same larval preparation to minimize differences. SCID/beige mice were infected in separate experiments along with euthymic BALB/c mice, which were tested as controls to ensure that the infections were successful. The larvae were obtained from rodents 30–90 days PI using a modification of the technique described by Castro and Fairbairn (5). The T. spiralis parasites used in this study originated in the Department of Zoology at the University of Toronto, and the colony was maintained through serial infections alternating between male Sprague-Dawley rats and male CD1 mice.

Worm counts. Mice were killed by cervical dislocation, and the entire length of the small intestine was then counted, using a modification of the method described by Castro and Fairbairn (5). Briefly, the intestine was opened longitudinally, and the mucosa was separated from the underlying muscularis by scraping with a glass microscope slide and was mixed in 1 ml of PBS. The worms were then counted using a scored petri dish and an inverted microscope and expressed as the number of adult worms recovered per mouse. In accordance with established practices, worm rejection was considered complete when at least 98% of the infective dose had been expelled from the gut (47).

Myeloperoxidase assay. Myeloperoxidase (MPO) is an enzyme contained in the azurophilic granules of neutrophils as well as other myeloid cells and is commonly used as an index of neutrophil infiltration and inflammation (32). MPO was measured using a modified version of an assay as previously described (49). After the mice were killed, samples of the jejunum (50–100 mg) ~4 cm distal to the ligament of Treitz were removed for MPO measurement. The samples were snap frozen in liquid nitrogen and stored at ~70°C. The activity of MPO is reported as units of MPO per milligram of wet tissue where a unit of MPO is defined as the quantity of enzyme able to convert 1 µmol of hydrogen peroxide to water in 1 min at room temperature.

T lymphocyte reconstitution. Euthymic BALB/c mice, 6–10 wk old, were killed by cervical dislocation. Their spleens were removed aseptically, placed in RPMI medium with 10% fetal bovine serum, cut into small pieces, and crushed between two sterile glass slides. Once a single cell suspension was generated, the cells were placed in covered culture dishes in a 37°C incubator and incubated for 2 h. Then nonadherent cells were removed and spun down over Ficoll-Hypaque (Pharmacia, Sweden) for 20 min at 1,500 rpm. Theuffy coat of mononuclear cells was collected, washed twice with RPMI medium, and then pelleted through centrifugation and resuspended in a small volume of PBS. The cells were then counted and analyzed for viability using trypan blue exclusion, and 30,000,000 viable cells were injected intravenously into the tail vein of recipient athymic mice (6–10 wk of age). The reconstituted athymic mice were then left for 2–3 mo, allowing sufficient time for the repopulation of their T lymphocyte complement.

Determination of lymphocyte reconstitution by FACS analysis. To confirm the immunodeficiency of the SCID/beige and athymic mice and to assess the success of T lymphocyte reconstitution, SCID/beige mice, athymic and euthymic BALB/c mice, as well as T cell-reconstituted athymic mice (2–3 mo after reconstitution), were euthanized, and their spleens were removed and prepared for FACS analysis. The isolated mononuclear cells were then stained and analyzed by fluorescence-activated cell sorting (FACS) (FACS-Scan flow cytometer, Becton Dickinson, Mountain View, CA) with a specific biotinylated monoclonal antibody to CD3 (2C11), followed by streptavidin-phycocerythrin (Becton Dickinson). Cells were then fixed in 0.1% paraformaldehyde and analyzed on a FACSScan. Data analysis was performed using PCl/ysis software (Becton Dickinson).

Measurement of muscle contraction. The preparation of sections of jejunal longitudinal muscle for muscle contractility analysis and the analysis of the length-tension relationship have been described previously (41). In brief, the jejunum was removed and placed in oxygenated (95% O2, 5% CO2) Krebs solution, and 1-cm segments of whole gut were cut from the jejunum, beginning at the ligament of Treitz and proceeding distally. The lumen of each segment was flushed with Krebs buffer, before the insertion of short (2–3 mm) lengths of Silastic tubing (0.065 OD, 0.030 ID) (Dow Corning, Midland, MI) into the open ends of the gut segments. Tubing was then tied in place with surgical silk. The insertion of the tubing was found to maintain patency of the gut segments over the course of the experiments. Segments were then hung in the longitudinal axis and attached at one end to a Grass FT03C force transducer (Quincy, MA), and responses were recorded on a Grass 7D polygraph. Tissues were equilibrated for 30 min at 37°C in Krebs solution, oxygenated with 95%O2-5%CO2 before starting the experiment. Experiments were then conducted to examine the length-tension characteristics of the muscle before and after infection. Segments were stretched by applying tension equivalent to 0–1,250 mg of force transducer (375 T. spiralis larvae). Initial experiments indicated that this tension range was sufficient to determine the maximal responsiveness of both control and inflamed tissues at this carbachol concentration. Tissues were then rinsed twice and equilibrated at the next tension level in fresh Krebs for 15 min, before the next addition of carbachol. At the end of each experiment, tissue segments were removed, blotted, and weighed. The degree of applied tension or stretch producing the maximum response to carbachol was identified as the optimal tension (T0), and the tissue length at this tension was then used to calculate the cross-sectional area of the tissue.

Data presentation and statistical analysis. Responses to carbachol were recorded from tracings, followed by the calculation of contractile activity, which were expressed as milligrams of tension per cross-sectional area, as described previously (37). For each mouse, the mean tension was calculated from at least three segments. The results comparing euthymic, athymic, and reconstituted mice were pooled from three separate infections, all of which gave similar results, while the SCID mouse data are from an additional two infections, which were similar and were also pooled. Results are expressed as means ± SE; n refers to the number of mice tested. Statistical significance was calculated using the Student’s t-test for comparison of two means or ANOVA for the compari-
son of three or more means. Multiple comparisons were performed using the Newman-Keuls multiple comparison test. \( P < 0.05 \) was considered significant.

**RESULTS**

Euthymic BALB/c mice: muscle contraction. During the course of a *T. spiralis* infection, euthymic BALB/c mice developed a significant increase in isometric tension development by jejunal longitudinal smooth muscle. The data shown represent the contractile response to a submaximally effective concentration of carbachol (1 \( \mu \text{M} \)) at each time point PI. As shown in Fig. 1A, in BALB/c mice there are two components of this contractile response to carbachol. There is an early phase that is rapid in onset and occurs by day 6 PI, which is also the time point of maximum contraction. Subsequently, the magnitude of the contractile response decreases. The second component is the sustained phase of increased contraction that persists until at least day 21 PI. This biphasic contractile profile is seen in other immunocompetent *T. spiralis*-infected mice, such as the NIH Swiss strain (41).

T cell-deficient athymic BALB/c mice: muscle contraction. In contrast to the pattern seen with euthymic mice, the rapid phase of contraction was delayed in onset until day 8 PI in athymic BALB/c mice and did not peak until day 12 PI (see Fig. 1B). In addition, the sustained phase of contraction was significantly smaller in magnitude than that seen in euthymic BALB/c mice, with the tension generated at day 14 PI and thereafter not significantly different from control.

T cell-deficient CB.17 SCID/beige mice: muscle contraction. The pattern of increased isometric tension development by longitudinal muscle from infected SCID/beige mice is also shown in Fig. 1B and is similar to that seen in infected athymic mice. The peak component of increased contraction was delayed until day 12 PI. The increased contraction was not well sustained, so that by day 21 PI, values were not different from those of uninfected SCID/beige mice.

T cell-reconstituted athymic BALB/c mice: muscle contraction. T cell reconstitution of athymic mice resulted in restoration of a profile of contraction similar to that seen in euthymic BALB/c mice. The onset of the
early phase of contraction occurred by day 6 PI, compared with day 10 PI in athymic mice, and the sustained phase of contraction persisted from day 8 until at least day 21 PI when its magnitude was significantly greater than that seen in athymic mice on day 21 (compare Fig. 1, B and C). Similar to infected euthymic mice, tension generated by reconstituted mice on day 21 PI was also significantly greater than that generated by uninfected mice.

Evaluation of T cell deficiency and T cell reconstitution. As depicted in Fig. 2, <1.0% of the splenic cells recovered from SCID/beige mice and only 3.0% of the mononuclear population recovered from the spleen of athymic BALB/c mice were CD3 positive, consistent with their deficiency in the generation of T lymphocytes (20, 29). The small number of positive cells seen in SCID mice likely represents only background, since SCID mice are considered to be almost completely deficient in T cell function. In contrast, euthymic BALB/c mice possessed a greater number of CD3-positive splenic cells (12.2%) and reconstituted mice were found to possess an even greater portion of CD3-positive splenic cells (17.1%) than euthymic mice, reaching as high as 25% of the cell population (not shown). This confirms the successful reconstitution of T lymphocytes in the mononuclear cell-injected athymic mice.

MPO activity in SCID, euthymic, athymic, and reconstituted mice. In contrast to the differences observed in muscle contraction between euthymic and athymic mice during infection, maximum MPO activity levels were not significantly different between infected euthymic and athymic mice (7.9 ± 1.5 vs. 8.9 ± 2.6 U/mg tissue, respectively). However, the onset of maximum MPO activity was advanced by 2 days in the athymic mice (day 8 PI) compared with the euthymic mice (day 10 PI), as shown in Fig. 3. MPO was significantly elevated over control values on days 8–12 in euthymic BALB/c mice and on days 6–16 in athymic BALB/c mice. MPO activity returned to normal levels by day 16 in euthymic mice and on day 21 in infected athymic animals.

Reconstituted athymic infected mice also developed an increase in MPO activity with levels of 7.1 ± 1.3 U/mg tissue found on day 10 PI (not shown). Interestingly, no increase in MPO activity was found during T. spiralis infection in SCID/beige mice, indicating either a requirement for T and B cells in the recruitment of

![Fig. 2. Fluorescence-activated cell sorter analysis of mononuclear cells isolated from spleens of euthymic (A), athymic (B), and T cell-reconstituted athymic BALB/c (C), as well as SCID/beige mice (D). Cells were stained with biotinylated anti-CD3 monoclonal antibody followed by streptavidin-conjugated phycoerythrin. Profiles of CD3 staining are displayed as histograms, after gating on small lymphoid cells. Nos. in histograms represent % of small lymphoid cells that were CD3 positive. M1, marker 1.](http://ajpgi.physiology.org/Downloaded from http://ajpgi.physiology.org/)
neutrophils to the infected gut or possible effects of the beige mutation. Recovery of parasites from gut in euthymic, athymic and T-cell reconstituted mice. During infection of BALB/c mice, there appeared to be an early component that determined the survival of T. spiralis larvae to adulthood. Only 50% of the larvae gavaged into euthymic mice survived to be counted on day 4 PI, compared with 90–100% in athymic mice (see Fig. 4). The larvae that survived to adulthood in the euthymic mice were then expelled between days 10 and 21 PI, with complete expulsion obtained by day 21 PI. In contrast, worm expulsion was slower and occurred in two phases in athymic mice, with the first phase of eviction occurring between days 8 and 10 PI, when approximately one-third of the worm burden was expelled. This first phase of expulsion corresponded with the transient increase in muscle contraction seen in this strain (see Fig. 1B). After this phase, worm numbers remained stable until day 16 PI, after which the athymic mice started to expel the remaining parasites. In contrast to euthymic mice, expulsion was incomplete in athymic mice on day 21 PI, with a smaller but significant number of worms (43 ± 11) remaining in the intestine on day 21 PI. This represented 11.5% of the total original infective load. Intestinal worm numbers were also determined 21 days after infection in SCID/beige mice. Similar to athymic mice, worm expulsion was incomplete in these animals with 32 ± 13 adult T. spiralis worms recovered on day 21 PI. This again shows a role for T lymphocytes in the successful expulsion of a T. spiralis infection.

T-cell reconstitution of athymic mice changed the survival curve of gavaged larvae to one that was intermediate (70%) between euthymic and athymic mice. The pattern of worm expulsion in reconstituted mice was also changed, becoming significantly more rapid than that found in unreconstituted athymic mice. Significantly fewer worms were recovered from reconstituted mice than unreconstituted athymic mice on days 6, 8, 10, 16, and 21 PI. Expulsion continued to completion by day 21 PI in the reconstituted mice, compared with the small but significant parasite load that remained in the gut of athymic mice on day 21 PI. However, worm expulsion from reconstituted mice did not quite reach that seen in euthymic mice, since reconstituted mice retained significantly more worms than euthymic mice on day 16 PI.

DISCUSSION

This study builds on previous work showing that in the rat the increased tension development by intestinal muscle on day 6 after T. spiralis infection was T cell dependent (46). The present study not only confirms that finding in mice but also identifies T cell-independent components of contraction and, importantly, addresses the temporal relationship between worm expulsion and both T cell-dependent and -independent components of intestinal muscle contraction.

The hypothesis that T cells play a role in altering muscle function was based on and supported by several studies (21, 30). Including the finding that the phenomenon of worm expulsion after primary infection by T. spiralis is, at least in part, dependent on T lymphocytes. Furthermore, we have shown (27) that activation of T cells in vivo, using an anti-CD3 antibody, leads to accelerated intestinal transit as well as increased tension generation by intestinal smooth muscle, demonstrable in vitro. We have also previously demonstrated that T cells infiltrate the muscularis externa during T. spiralis infection (11) and that intestinal muscle cells increase T cell survival by reducing apoptosis (19). In addition, muscle cells have been shown to interact directly with T cells in the context of major histocompatibility complex class II-linked antigen presentation (14,
T. spiralis mice PI. MPO activity was similar in the three groups of BALB/c inflammatory response to the infection as maximum contraction was increased. These changes cannot be constituted athymics and euthymics were abrogated. In particular, the onset of peak contraction was accelerated, component of contraction was lower in magnitude than that seen in euthymic mice, suggesting a partial dependency inhibited the infiltration of neutrophils into the gastrointestinal tract by a neural mechanism after administration of IL-4 to mice. Taken together, these findings suggest that the interactions between muscle and T cells are bidirectional and complex but may in fact result in the augmentation of the contractile properties of muscle. With respect to the changes seen in the inflamed intestine, it is of potential relevance to recall that T lymphocytes have also been implicated in the genesis of airways muscle hyperresponsiveness in a murine model of asthma.

However, we also chose to examine the role of T cells in the modulation of murine intestinal muscle in this study, based on the discovery that SCID and athymic mice, which lack functional T lymphocytes (20, 29), developed increased tension generation by intestinal muscle during infection, implying that the T cell dependency found previously in the rat could not be confidently extrapolated to the mouse. This may reflect differences in the pathological regulation of murine vs. rat intestinal smooth muscle or the limited number of time points tested in the T. spiralis-infected rat, since McKay et al. (24) have shown that limited changes in intestinal epithelial function can occur in nematode-infected athymic rats. In either case, the presence of altered muscle function in the T cell-deficient mice indicated that the pathological regulation of intestinal smooth muscle function may be more complex than simple dependence on a single cell type. Our results show that in the infected athymic and SCID/beige mouse, the peak increase of muscle contraction was delayed in onset and that the subsequent sustained component of contraction was lower in magnitude than that seen in euthymic mice, suggesting a partial dependence on T lymphocytes. After reconstitution of T cell populations, as verified by flow cytometry, most of the differences in the profile of contraction between nonreconstituted athymics and euthymics were abrogated. In particular, the onset of peak contraction was accelerated and the magnitude of the sustained level of contraction was increased. These changes cannot be ascribed to differences in the magnitude of the acute inflammatory response to the infection as maximum MPO activity was similar in the three groups of BALB/c mice PI.

Interestingly, SCID/beige mice showed no increase in MPO activity during the course of T. spiralis infection. This may indicate that their extreme immunodeficiency inhibited the infiltration of neutrophils into the gut (confirmed by histology); however, this may also involve the beige mutation that results in an abnormal structure and function in some granulated cell types, including neutrophils and natural killer (NK) cells (35). No studies to date have characterized whether MPO activity is affected by this mutation. Although it is possible that this mutation may play a role in the neutrophilic response to T. spiralis infection, it likely plays no role in worm expulsion, since several studies have shown that the beige mutation had no impact on the expulsion of nematode infections (36) or the anti-parasite activity of inflammatory cells in vitro (18). Nor is it likely that the beige gene or a deficiency in NK cells plays a role in the changes in muscle function during infection, since athymic mice develop a similar timing and magnitude of increased muscle contraction to that seen in the SCID/beige mouse, yet athymic mice are known to have a heightened NK cell activity (28). However, the development of muscle dysfunction in SCID/beige mice, in the absence of an increase in MPO, does confirm previous speculation (6, 46) that neutrophils play no role in the pathological regulation of intestinal muscle function.

While the elaboration of IL-4, or other mediators, by T cells may reflect at least part of the mechanism underlying increased tension development by muscle, our results indicate that T cells are not the sole determinants of increased tension development in this model, as significant contractile changes were observed in nonreconstituted infected athymic and SCID mice. Therefore, other possibilities also need to be considered. Parasitic infection can induce an eosinophilia in athymic mice (37), and mucosal mast cells, which are present in T cell-deficient mice, have been shown to release T helper cell type 2 cytokines, including IL-4 (26). Thus the cellular locus of action of this or other mediators on muscle contractility requires further elucidation. Studies in nematode-infected rats have revealed several loci of change in the intestinal muscle cell, including suppression of Na+-K+-ATPase, altered calcium handling (45), and an increased actin content (50). Because corticosteroid treatment completely abolished the increased tension development in the T. spiralis-infected rat (22) and mouse (Collins et al., unpublished data), the changes that persist in the absence of T cells presumably still reflect host factors rather than a direct effect of the parasite. Currently, our investigation is focusing on the roles of macrophages, eosinophils, and mast cells (42, 44), in the context of other mechanisms that might underlie muscle changes. An intriguing observation is the persistent increase in tension generation evident at day 21 PI in BALB/c mice, when worms have already been expelled and the inflammatory response resolved. In the NIH Swiss strain, this persistent increase in tension development was evident 6 wk after infection (2). It is highly unlikely that inflammatory cells sustain this persistent change as the tissue was histologically normal. We have postulated a smooth muscle origin for the factors that sustain this persistently increased tension generation, as previous studies (6) have shown that muscle cells can elaborate arachidonic acid metabolites as well as cytokines. Autocrine regulation of such factors is a putative mechanism to explain altered muscle function.
in the absence of lymphocytes or other immune or inflammatory cells in the muscle layer at these late time points PI (6).

A major goal of this study was also to evaluate the changes in muscle contraction and worm expulsion at various time points in our experimental paradigms. Our results suggest that the two parameters are related. In euthymic mice, the peak increase in tension generation by muscle occurred within 6 days PI, however, tension generation was sustained above control levels over the following 15 days, during which time the infection was completely expelled. In contrast, in athymic mice, the peak increase in tension development occurred at days 10–12 PI when about one-third of the parasites were evicted. Tension generation then fell to a lower level than observed in euthymic mice and was accompanied by a slow evocation of the remaining two-thirds of the worm burden, with >11% of the original worm burden remaining by day 21 PI. In successfully reconstituted athymic mice, the peak increase in tension generation occurred by day 6 PI and the worms were completely evicted between days 10–21 PI when tension generation was sustained at a level equal to or higher than that seen in euthymic mice. Thus the initial peak increase in tension development may be required to initiate worm expulsion and the sustained component may assist in the expulsion of the remaining parasites over a longer time frame. The higher level of sustained tension development seen in reconstituted mice may have been necessary to eliminate the larger initial worm burden seen on day 4 PI in reconstituted mice (70% of the initial dose) compared with that seen in euthymic mice (50% of the initial dose), or may be the result of the increased number of T cells recovered from reconstituted mice, compared with normal euthymic mice (see Fig. 2).

Our results suggest a relationship between the timing and the magnitude of the increased tension development by muscle in this model and the eviction of the parasite from the gut. This is supported by other studies, including our recent report (41) in which we found a positive correlation between the ability of certain mouse strains to expel the parasite and the tension generated by intestinal muscle during infection. In that study, NIH Swiss mice, which are efficient in expelling the parasite, also developed the greatest increase in tension generation, whereas the B10.BR mouse, which is very inefficient in its ability to expel the parasite so that they can develop chronic infections (3), had a smaller and delayed increase in tension development. Further evidence for a role for motor activity in worm expulsion comes from studies utilizing the W/W^v mouse strain which lacks both the c-kit receptor and mast cells. In the W/W^v mouse, expulsion of the nematode parasite Nippostrongylus brasiliensis was markedly delayed after primary infection, but this delay could not be corrected by restoring mast cell populations after bone marrow reconstitution (17). Because the W/W^v mouse also lacks the interstitial cells of Cajal (ICC), which control slow wave and propulsive activity in the gut (16), the delayed expulsion of the parasite most likely reflects altered motility. In addition, an earlier study (38) demonstrated that opiate-induced inhibition of gut motility resulted in delayed expulsion of T. spiralis from mice. Together, these results invoke intestinal motility as an important determinant of successful worm expulsion from the gut. Because increased propulsive activity was demonstrated in extrinsically denervated gut segments during nematode infection (1), cells, similar to smooth muscle, which are intrinsic to the gut wall are important in determining propulsive motor activity. Taken together, these studies also provide indirect support for a major conclusion of the present study, that increased tension generation by intestinal smooth muscle and the efficient expulsion of the parasite from the gut contraction are linked.

A role for increased propulsive motor activity in the expulsion of enteric infections has also been suggested by Urban et al. (40) and this is supported indirectly by the demonstrations of altered motility in a number of enteric infections, including bacteria (31), protozoa (8), and nematode parasites (1, 6, 38, 41, 45). Changes in motility likely combine with other mechanisms, including increased fluid secretion (48), to expel parasites from the gut (6), rendering the intestine an inhospitable environment for the parasite, leading to both decreased fecundity and the expulsion of the parasite (40). The involvement of lymphocytes in the generation of altered muscle contraction also has bearing on noninfective gastrointestinal diseases associated with altered motility, such as inflammatory bowel disease (34) and pseudoobstruction (23, 33). In Crohn’s disease, lymphocytes have been demonstrated in the muscle layers (10), and massive lymphoid infiltration of the neuromuscular layers has been found in patients with certain types of acquired pseudoobstruction (23, 33). These observations thus extend the relevance of our study beyond that of enteric infections. Furthermore, these results indicate a more complex pathogenesis for altered intestinal muscle function than was previously suspected.

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