

The influence of orally administered short chain fatty acids on intestinal histopathological changes and intensity of *Trichinella spiralis* infection in mice

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ABSTRACT: The influence of short chain fatty acids (SCFA) on histopathological changes in the small intestine and the intensity of invasion of *T. spiralis* in mice were investigated in this study. The animals were infected with doses of 500 and 250 *T. spiralis* larvae per mouse. A SCFA solution containing acetic, propionic and butyric acid (30 : 15 : 20mM) was administered orally to the mice starting from the 5th day before infection to the 20th day after infection (day). Fragments of the jejunum collected during dissection on the 7th and 10th day were used to prepare specimens to assess the histopathological changes. In the infected animals, the intestinal trichinellae were counted on the 7th and 10th day, while on the 42nd day the muscle larvae number were determined. The strongest host reaction in the intestine was observed on the 7th day at a dose of *T. spiralis* 500 larvae, and on the 10th day at a dose of 250 larvae. Numerous inflammatory infiltrations, strong shortening of the intestinal villi, extension of the intestinal crypts, and the lowest ratio of the villi length to the intestinal crypts depth were observed. The ratio was 1.3 ± 0.3 on the 7th day at a dose of 500 larvae, and on the 10th day, at dose of 250 larvae the ratio reached 1.5 ± 0.5 . Both values differed significantly from the control group: 3.3 ± 0.5 ($P < 0.01$). Administration of SCFA to the animals infected with *T. spiralis* caused remission of local histopathological changes resulting from the presence of the parasite in the small intestine after the mentioned periods. This manifested as limited villi shortening and reduced deepening of intestinal crypts. At the higher infectious dose, in animals receiving the acid solution, on the 7th day the intestinal villi were considerably longer ($356 \mu\text{m} \pm 35$) than in the group infected with *T. spiralis* but not treated with the acids ($279 \mu\text{m} \pm 57$; $P < 0.01$). At a lower dose of parasites, on the 10th day these values were $339 \mu\text{m} \pm 88$ and $306 \mu\text{m} \pm 47$ respectively and the observed differences were not statistically significant. The solution of SCFA also caused a decrease in the numbers of mature parasites in the intestine and the muscle larvae at a dose of 500 larvae/mouse. In animals receiving the SCFA, $24\,050 \pm 10\,415$ larvae were observed in muscles, while in the infected mice, which did not receive the acids, $32\,875 \pm 16\,762$ larvae were detected ($P < 0.05$). An increase in the intensity of infection accelerated the rate of host reaction to the presence of *T. spiralis* in the intestines (self-cure). To summarize, the administered solution of short chain fatty acids alleviated the formation of histopathological changes in the intestine in response to the parasite's presence, and lowered the intensity of *T. spiralis* invasion after infection with a higher dose of larvae.

Keywords: trichinellosis; SCFA; intestinal morphology; mouse

Short chain fatty acids (SCFA) are the most important end products of the fermentation conducted by microorganisms in the gastrointestinal tract. They result from the decomposition of carbohydrates originating mainly from plant cells: cellulose, pectin, starch, and other dextrans and soluble carbohydrates, and also from the bacte-

rial decomposition of proteins. The concentration of the end products of bacterial fermentation in the caecum, especially ammonia and SCFA, reflects the activity of the intestinal microflora, which conditions the normal processes occurring in this section of the gastrointestinal tract (Bergman, 1990).

In the gastrointestinal tract, the most numerous produced SCFA are: acetate, propionate and butyrate, which after absorption are used as energy sources for primary metabolism, animal growth, and lipogenesis. SCFA affect the intestinal mucosa in various manners. They increase intercellular pH, and modulate sodium absorption and chloride excretion. They stimulate the release of mucins, and increase the blood flow in the mucosa (Engelhardt et al., 1998; Sellin, 1999). Inhibition of the growth of pathogenic bacteria in the large intestine, including *E. coli* (Byrne and Dankert, 1979), as well as anti-inflammatory properties has been described for SCFA (Rotstein, 1993; Cavaglieri et al., 2003). The joint interaction of three acids: acetic, propionic, and butyric, with the intestinal epithelium stimulates normal intestinal crypt cells to proliferate, while butyric acid alone inhibits the growth of the colon cancer cell lines by induction of apoptosis (Chiou et al., 1994; Engelhardt et al., 1998). The main influence of SCFA on inflammatory processes lies in their effect on lymphocyte and cytokine production. Butyrate production inhibits the proliferation of lymphocytes and IL-2 and IFN- γ while propionate partially prevents this inhibitory effect of butyrate. Also, both acids increase IFN- γ and IL-10 production (Cavaglieri et al., 2003).

Such properties of SCFA can modulate the immunological processes during *T. spiralis* intestinal infection. In the mature stadium, the nematodes are present in the epithelial layer of the host small intestine. Structural, cellular, and physiological changes in the intestine resulting from their presence are the reason for the immunological response manifested as acute inflammation (Garside et al., 2000; Khan and Collins, 2004; Dehlawi et al., 2006).

In the intestinal phase of trichinellosis, the “self-cure” phenomenon plays an important role. It occurs as a result of a rapid expulsion of the parasites from the gastrointestinal tract. The early phase of the intestinal phase of trichinellosis is characterized by accumulation of inflammatory cells (mainly mast cells), eosinophils, Th1 and Th2 lymphocytes responses, production of IgE antibodies, and release of mediators and cytokines (Grencis et al., 1991; Finkelman et al., 1997; Piekarska, 2004). It is known that faster expulsion of the mature forms of *T. spiralis* from the intestines can be connected with the production of IL-2, IL-3, and IFN- γ . IL-5 contributes to slower removal of trichinellae from the intestine (Kelly et al., 1991; Mink et al., 1994). An increase in chemokine expression in the mouse intestinal epithelium enhances the

recruitment of neutrophil granulocytes and lymphocytes to the intestine (Kostro et al., 2000). Since SCFA alter chemokine expression in enterocytes (Sanderson, 2004), they can also play a role in the anti-parasite response.

In the intestinal phase of *T. spiralis*, a decrease in SCFA production and change in their relative levels has been described (Mista et al., 2005). The influence of parasitic infection on the fermentation pattern and SCFA levels has been also confirmed in ascariasis in sheeps (Varadyova et al., 2001). The effect of fermentation products on the intestinal phase of *T. spiralis* could be an example of the interaction between the saprophytic intestinal microflora and the parasite.

The aim of the study was to show the intestinal changes resulting from the inflammatory processes caused by the parasites, and to determine the effect of SCFA administration on these processes, by observing the histopathological changes, counting the number of mature parasites in the intestinal trichinellosis, and the number of larvae in muscles.

MATERIAL AND METHODS

The material for the research consisted of 117 CFW inbred mice at ages of around three months, weighing around 20 g. 96 mice were infected *per os* with *T. spiralis* T1 (ISS1820) larvae. 48 mice were infected with a dose of 500 larvae/mouse, while the remaining 48 were administered a dose of 250 larvae/mouse. There were six experimental groups:

C – healthy mice (7)

S – healthy mice receiving SCFA (14)

T 500 – mice infected with *T. spiralis* at dose of 500 larvae (24)

TS 500 – mice infected with *T. spiralis* at dose of 500 larvae, and receiving SCFA (24)

T 250 – mice infected with *T. spiralis* at dose of 250 larvae (24)

TS 250 – mice infected with *T. spiralis* at dose of 250 larvae, and receiving SCFA (24)

During the whole time of the experiment, all animals were maintained under identical conditions. SCFA solution was administered with drinking water from the 5th day before infection to the 20th day of infection. The molar concentrations of the following acids: acetic, propionic, and butyric, in the dosed solutions were 30, 15, and 20mM, respectively.

Table 1. The number of adult trichinellae in the jejunum on the 7th and 10th days after infection

Group	T 500	TS 500	T 250	TS 250
7 th day	121.6 ± 38.3	79.8 ± 30.3	33.1 ± 10.6	29.6 ± 39.4
10 th day	3.4 ± 2.8	3.7 ± 2.6	20.0 ± 16.8	16.8 ± 20.6

Results are expressed as the mean ± SD of 7 animals

T = *T. spiralis*-infected mice, TS = SCFA-administered mice and infected with *T. spiralis*

On the 7th and 10th day of infection, after slaughtering seven animals in each group, tissue samples from their jejunum were collected. After fixation in a neutralized 8% formaldehyde water solution, four thick paraffin sections were stained with hematoxylin and eosin (H & E). Cellular infiltration intensity, the shape and size of villi and intestinal crypts, as well as the presence of goblet cells were assessed. The analysis of the intestinal villi and crypts was conducted using the Photomicroscope-Axiophot, and the computer program MultiScan Base V 8.08. Parasitological studies of the intestines were performed to determine the invasion intensity on the 7th and 10th days after infection. On the 42nd day, 10 animals from each group were slaughtered in order to establish the number of muscle larvae using the digestion method (Kozar and Kozar, 1972).

The results were analysed using one-way ANOVA and STATISTICA 8.0 software. The significance of the differences was confirmed by the multiple comparison Tukey's test for $P < 0.05$ and $P < 0.01$. Obtained results are presented in Tables 1–3 as the mean values and standard deviations.

RESULTS AND DISCUSSION

In the parasitological studies conducted in this experiment, the observed differences in the number of parasites related only to the animals infected with the dose of 500 larvae/mouse. On the 7th day, a lower number of parasites in the small intestine of the infected mice which received SCFA (TS 500) was observed in comparison with the infected mice which did not receive the acid solution (T 500). However, the differences were not confirmed statistically (Table 1). In above-mentioned groups, on the 10th day only single adult parasites were observed in the intestine. This observation points to the “self-cure” phenomena. Significant differences were confirmed in the number of muscle larvae on the 42nd day. In the animals of the TS 500 group,

the number of larvae was smaller in comparison to the T 500 group (Table 2).

Based on results mentioned above, it can be supposed that administration of the SCFA resulted in decreased numbers of newborn *T. spiralis* larvae in the intestines of mice infected with the higher dose of *T. spiralis*. The reason for this might have been direct interaction of SCFA with the parasite or (which seems to be more likely) interaction of the SCFA with the mucosa and the intestinal environment. This could have resulted in changes which prevented the females from giving birth to larvae or the larvae from surviving. Changes in local microflora composition caused by the SCFA administration may have importance because previous studies showed a significant role for intestinal microflora in determining the invasive capacity of *T. spiralis* in mice (Przyjalkowski et al., 1969, 1983).

At a dose of 250 larvae/mouse no differences in the intensification of *T. spiralis* intestinal infection were observed among the groups. However, in comparison to the groups in which mice received the higher dose of *T. spiralis*, significantly lower numbers of parasites in the intestines was observed on the 7th day (Table 2). On the 10th day, at this dose, the number of *T. spiralis* in the intestine decreased only slightly. Thus, the “self-cure” phenomena occurred later than in those mice which received the 500 larvae dose. The number of muscle larvae on the 42nd day was similar in both infected groups

Table 2. The number of muscle larvae per mouse on the 42nd day after infection

Group	T	TS
500 larvae/mouse	32 875 ± 16 762 ^a	24 050 ± 10 415 ^b
250 larvae/mouse	18 542 ± 17 967	17 000 ± 13 875

Results are expressed as the mean ± SD of 10 animals

T = *T. spiralis*-infected mice, TS = SCFA-administered mice and infected with *T. spiralis*

^{ab}significant differences at $P < 0.05$

Table 3. The lengths of intestinal villi and crypts in experimental trichinellosis in mice (μm)

Group	C	S	T 500	TS 500	T 250	TS 250
7 th day						
Villi	465 \pm 13 ^A	456 \pm 36 ^A	279 \pm 57 ^B	356 \pm 35 ^C	316 \pm 31 ^{BC}	326 \pm 46 ^{BC}
Crypts	143 \pm 27 ^A	135 \pm 22 ^{Aa}	230 \pm 46 ^{Bc}	208 \pm 22 ^B	188 \pm 43 ^{bc}	177 \pm 23 ^{ab}
v/c	3.3 \pm 0.5 ^A	3.5 \pm 0.7 ^A	1.3 \pm 0.3 ^B	1.8 \pm 0.4 ^B	1.8 \pm 0.5 ^B	1.9 \pm 0.4 ^B
10 th day						
Villi	465 \pm 13 ^{Aa}	462 \pm 55 ^A	385 \pm 49 ^b	388 \pm 45 ^b	306 \pm 47 ^B	339 \pm 88 ^B
Crypts	143 \pm 27 ^{Aab}	143 \pm 25 ^{Aa}	192 \pm 18 ^B	186 \pm 9 ^c	214 \pm 40 ^B	180 \pm 25 ^{bc}
v/c	3.3 \pm 0.5 ^A	3.4 \pm 0.7 ^A	2.1 \pm 0.3 ^B	2.1 \pm 0.1 ^B	1.5 \pm 0.5 ^B	1.9 \pm 0.6 ^B

Results are expressed as the mean \pm SD of 7 animals

C = the control group, S = the group of animals that received SCFA solution, T = *T. spiralis* infected mice,

TS = SCFA-administered mice and infected with *T. spiralis*

500, 250 = the number of larvae/mouse

v/c = the villus to crypt height ratio

^{abc}significant differences at $P < 0.05$

^{ABC}significant differences at $P < 0.01$

(T 250 and TS 250). These results suggest that the magnitude of the host's reaction to the presence of parasites in the intestines increases together with the increase in invasion intensity. The influence of SCFA on intestinal trichinellosis is stronger with the higher number of parasites.

An effect of SCFA administration on parasite invasions in the intestine was also described by Petkevicius et al. (2004). Infusion of SCFA and lactic acid into the caecum had a strong anti-parasitic effect in the case of *Oesophagostomum dentatum*, manifesting in a decreased number of eggs, mature forms, and a lowered fertility of females. Similar effects were obtained during intestinal parasitoses in pigs after administering fodder containing highly fermentable carbohydrates (i.a. inulin), which decompose in the large intestine resulting in high levels of SCFA. Decreased numbers and fertility of *Oesophagostomum dentatum* and *Trichuris suis* have been observed in the large intestine (Petkevicius et al., 2003, 2007). Lower numbers of parasites in the intestines of animals fed with highly fermentable carbohydrates in comparison to animals receiving fodder supplemented with resistant carbohydrates was also observed by Thomsen et al. (2005, 2006). Considering the influence of carbohydrates contained in the fodder on the survival of intestinal nematodes, it seems that the type of dietary carbohydrates plays a crucial role. Fermentable carbohydrates cause an increase in the

intensity of bacterial fermentation in the intestines. This leads to the elevated production of SCFA, the inhibiting influence of which on the survival and breeding of the nematodes, has been demonstrated (Petkevicius et al., 2004).

The results of the present study also confirm the inhibitory effect of the products of bacterial fermentation in intestines on the survival and fertility of nematodes. The diminished numbers of parasites after oral administration of SCFA allows us to speculate that parasitoses of the gastrointestinal tract are influenced by the activity of saprophytic bacteria present in the intestines, as well as a number of factors, which influence local microflora (e.g. feeding of the animals), especially the carbohydrate profile of the feed. A change of the environment in the intestines, which takes place along with the accumulation of large amounts of organic acids, may play a significant role in this model (Petkevicius et al., 2004; Petkevicius, 2007).

The influence of SCFA on histopathological changes in the jejunum was also observed in this study. In control animals, long intestinal villi with regular, finger-like shape, and oligocellular mesenchymal stroma, as well as shallow intestinal crypts were observed. Goblet cells were sparse within the villi, and moderately numerous in the intestinal glands (Figure 1). Administration of the SCFA solution to healthy animals caused sparse inflammatory infiltrations in the stroma of the intestinal villi

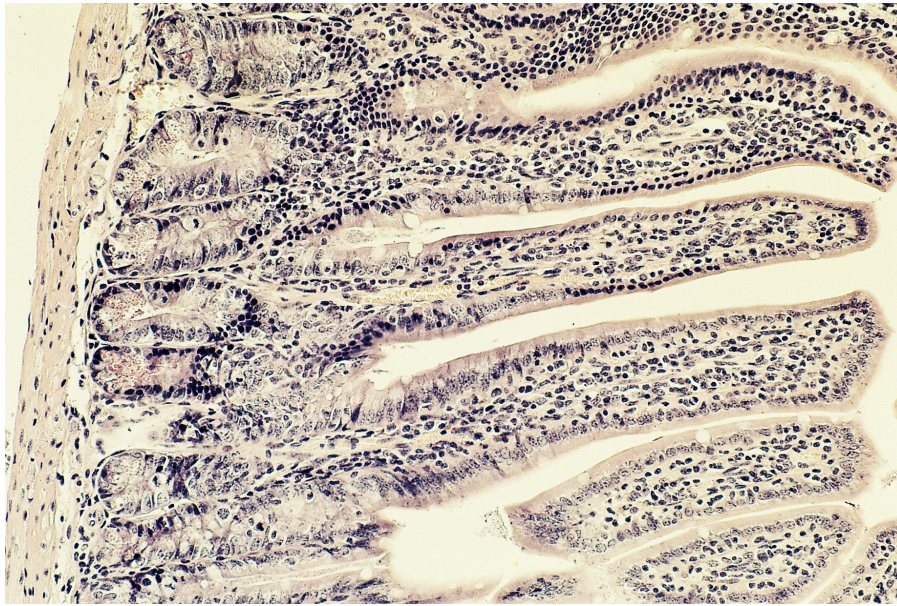


Figure 1. Cross-section of a healthy mouse's jejunum. High, narrow intestinal villi with a small number of goblet cells and oligocellular mesenchymal stroma; shallow intestinal crypts are visible. HE, magnification 200×

and mild hyperaemia on the 7th day (Figure 2). In animals infected with both doses of parasites, the intestinal villi were shortened, leaf-shaped, and the intestinal crypts were greatly developed (Figure 3). In the lamina propria of mucosa on the whole length of the intestinal villi, dilatation of blood vessels and numerous inflammatory infiltrations, even as deep as the muscularis mucosa, were seen. Abundant eosinophils were present in the infiltrations. Single

T. spiralis cross sections were visible. The changes were most pronounced on the 7th day at the dose of 500 larvae/mouse, while on the 10th day they were most intense at a dose of 250 larvae/mouse. At the above-mentioned time periods, the strongest shortening of the intestinal villi was observed in both groups infected with *T. spiralis*, and which did not receive the SCFA (T 500 and T 250) (Table 1). In all infected groups, numerous goblet cells were

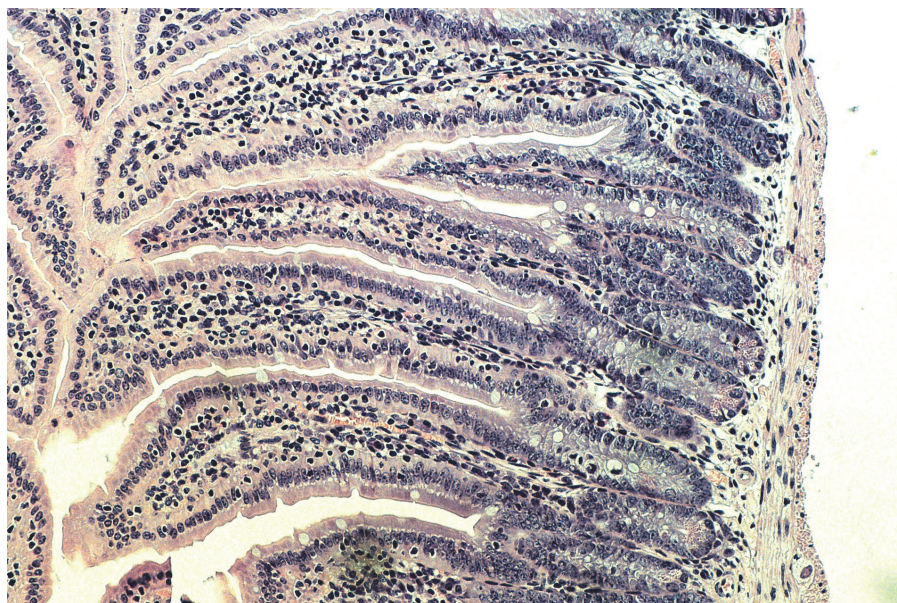


Figure 2. The jejunum of an animal that received the SCFA solution for 13 days (on the 7th day of the experiment). Long intestinal villi and shallow crypts, sparse inflammatory infiltrations in the stroma. HE, magnification 200×

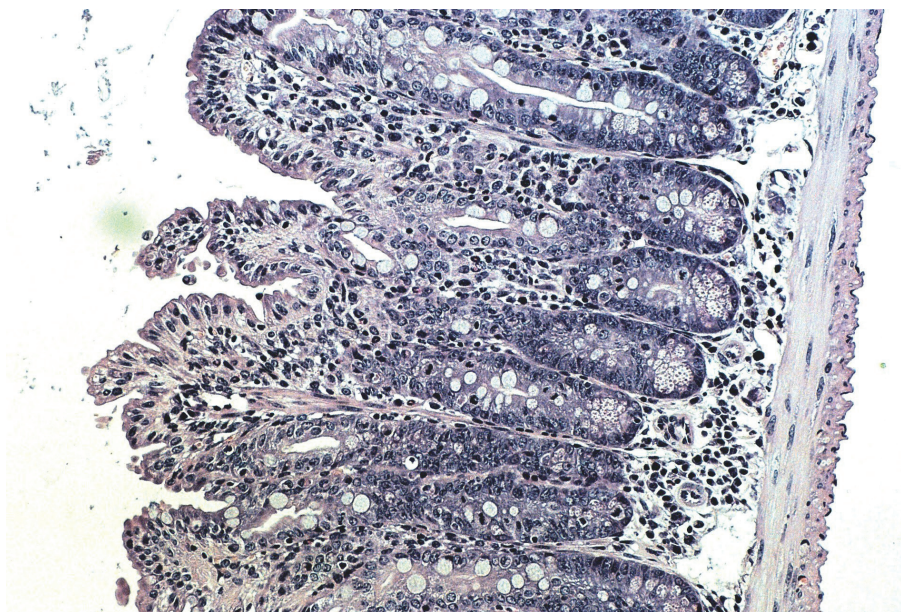


Figure 3. Jejunum of a *T. spiralis*-infected mouse on the 7th day. Shortened and leaf-shaped intestinal villi with a large number of goblet cells, and overgrown intestinal crypts are noticeable. The dilatation of blood vessels and numerous inflammatory infiltrations with abundant eosinophils are present in the lamina propria of the mucosa. HE, magnification 200×

observed. On the 7th day at the higher dose of the parasite, these cells were most abundant in the middle and lower regions of the intestinal villi and in the crypts (Figure 3).

Increases in the number of goblet cells have been described as phenomena which accompany the invasion of multiple nematodes species, including *T. spiralis* (Ishikawa et al., 1997; Khan et al., 2001; Sagar et al., 2004). During the invasion of *Nippostrongylus brasiliensis* qualitative changes in mucus composition have also been observed in these cells (Koninkx et al., 1988; Ishikawa et al., 1993). Th2 cells play the main role in the development of goblet cells during intestinal trichinellosis (Ishikawa et al., 1997). The greater number and increased activity of mucus-producing cells suggests that nematode invasions remain under the immunological control of the organism (Khan et al., 1995; Khan, 2008). Beside the mucus, the intestinal goblet cells also produce TFF3 (trefoil factor), which helps to prevent disturbances in the mucosa and improves regeneration (Dehlawi et al., 2006). Moreover, according to researches, in the intestines of Specific Pathogen Free (SPF) animals, goblet cells are less numerous than in conventional animals. This indicates the participation of saprophytic bacteria in mucus production. Increases in SCFA concentrations resulting from the activity of

these bacteria could be correlated with increases in mucus production (Theodoropoulos et al., 2005). In this study, no such dependence has been confirmed. Indeed, the addition of dietary fibre is the main stimulus for increases in mucus production in the intestine; however, it is still believed that the produced short chain fatty acids can participate in the process (Montagne et al., 2003).

Shortening and deformation of the intestinal villi, loss of the microvilli of the enterocytes and development of the crypts are typical symptoms accompanying the infection of intestinal nematodes. Administration of the SCFA solution in our study caused changes in villi length and crypt depth in mice infected with *T. spiralis*. SCFA reduced the shortening of villi and deepening of the intestinal crypts at the time periods when the biggest changes caused by the parasite were observed, i.e., in mice infected with 500 larvae on the 7th day and in mice infected with 250 larvae on the 10th day (Figure 4, Table 3). In animals infected and receiving acids solutions (TS group) at these time points, smaller cellular infiltrations than in the infected (T) group have been observed. It allows us to suppose that administration of the SCFA contributes to alleviating the symptoms of the *T. spiralis* intestinal phase.

Beside the length of the intestinal villi and the depth of crypts in particular experimental groups,

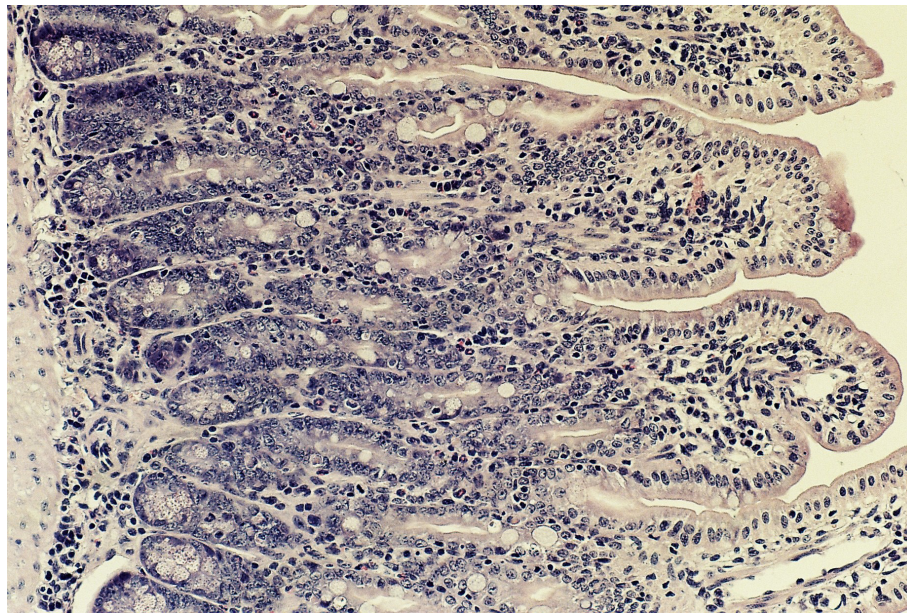


Figure 4. The jejunum of an SCFA-administered mouse infected with *T. spiralis* on the 7th day. The hypertrophy of intestinal crypts with villi shortening and deformation are less prominent than formerly (Figure 3). Inflammatory infiltration in the lamina propria with numerous eosinophils and a large number of goblet cells are present. HE, magnification 200×

their mutual proportions were also compared (v/c index). At both doses of *T. spiralis*, shortened villi and increased depths of the crypts were observed in the infected animals, thus the v/c index value decreased. On the 7th day, the index reached the lowest value in the T 500 group. In the T 250 group, the index was at its lowest level on the 10th day (Table 1). These data allow to conclude that a higher dose of the parasite results in earlier morphological changes in the intestine, and earlier epithelial regeneration (on the 10th day at the dose of 500 larvae, longer villi and shorter crypts were observed than those observed on the 7th day).

A greater invasive dose of *T. spiralis* (500 larvae/mouse) caused earlier intensification of changes (shortening of the villi and extension of the crypts) and quicker host reactions (cellular infiltrations, “self-cure”) in comparison with the lower dose (250 larvae/mouse). Also, a stronger effect of the SCFA in the intestine (manifested mainly by less intensive shortening of the intestinal villi), which might have contributed to lowered parasite number, was observed earlier at the higher dose of *T. spiralis* (on the 7th day). After infection with the lower dose of larvae, the immunological response, as well as the influence of SCFA on changes in the intestines, were observed later, i.e., on the 10th day. This probably could not have limited too greatly

the transfer of larvae to the blood system, and in effect could not have influenced the muscle phase of the invasion.

A reduced shortening of the intestinal villi during trichinellosis was also observed in mice infected with *Lactobacillus casei*, which produce lactic acid (Bautista-Garfias et al., 1999). In the study of Petkevicius et al. (2003) cited above, the lower number of parasites in the large intestines in pigs after administration of highly fermentable dietary carbohydrates was accompanied by changes in the structure of intestinal mucosa. The diet did not result in any morphological changes in healthy animals, while in animals infected with *Oesophagostomum dentatum* it influenced the mucus composition, epithelial cell proliferation, and the structure of large intestinal crypts, resulting mainly in a reduction in their volume. Similarly, Thomsen et al. (2006) observed a smaller depth of the large intestinal crypts during *Trichuris suis* infection in pigs fed with fermentable carbohydrates in comparison to infected pigs fed with resistant carbohydrates. In studies with germ-free rats it was shown that the influence of fermentable dietary fibres on epithelial cell proliferation requires the presence of intestinal microflora (Goodlad et al., 1989; Montagne et al. 2003). This might indicate that the trophic effect of fibre is connected with

the activity of its bacterial decomposition products, mainly the SCFA. In contrast to earlier articles, where a stimulating effect of SCFA on a epithelial cell proliferation was described (Sakata, 1987), in the above-cited studies of Thomsen et al. (2006), no influence of SCFA on mitotic counts in the intestinal crypts were observed. This result is reproduced by the present study, where no differences in intestinal villi length between mice from groups C and S have been confirmed. A conclusion can be drawn that the influence of SCFA on the intestinal epithelium manifests itself mainly during pathological conditions.

Similarly, according to the studies of Ramos et al. (1997, 1999), orally administered SCFA reduced the inflammation of mucosa in the small and large intestines in mice. It resulted in faster regeneration of the epithelium, a reduction in inflammatory infiltration cells, and elongation of the intestinal villi in comparison to the animals that did not receive the acid solution. The impact of SCFA was independent of endogenous production of short-chain fatty acids. In healthy animals, no influence of SCFA on the intestinal mucosa has been observed. The trophic effect of SCFA on damaged mucosa suggests that their administration might be beneficial not only during parasitic invasions, but also during such diseases as ulcerative intestine inflammation or colon cancer (Kim, 1998).

Short-chain fatty acids produced during microbiological fermentation also act in the large intestine. Studies have demonstrated that gastric and rectal instillation of SCFA stimulated epithelial cell proliferation in rat jejunum and ileum. The increase in proliferation was significantly higher with rectal instillation than gastric instillation (Ichikawa et al., 2002). Previous studies have also demonstrated the effect of SCFA on distal sections of the intestine (Sakata, 1987). A trophic effect in rodent small intestines was also observed with intravenous infusion of SCFA (Koruda et al., 1990). SCFA are rapidly absorbed by intestinal mucous membranes and their effects on distal sections of the alimentary tract may be explained by mediation of the autonomic nervous and cardiovascular system (Reilly et al., 1993; Frankel et al., 1994; Ichikawa et al., 2002). The effect of SCFA on intestinal mucous membranes may proceed through stimulation of the production of regulatory peptides of the alimentary tract. It was observed that the trophic effect of colonically-infused SCFA on the mucous membrane of rat jejunum proceeded

partially through the intestinal gastrin (Reilly et al., 1995). Reilly et al. (1995) suggested that an autonomic nerve impulse generated under the influence of colonic instillation of SCFA is directed to the central nervous system where the response is released in the form of a nerve or hormone signal. Enteroendocrine cells start producing gastrin under the influence of this signal. Numerous studies have demonstrated a stimulating effect of SCFA and dietary fibre on the secretion of glucagon-like peptide 2 (GLP-2) produced by L cells in the ileum and colon. The trophic effect of GLP-2 relies on increases in proliferation in crypt cells and apoptosis suppression in intestinal mucosa. The effect of GLP-2 infusion on the depth of the crypts as well as the height of the intestinal villi in the ileum and jejunum were demonstrated in parenterally fed pigs (Burrin et al., 2000). This mechanism plays a role in the adaptation of intestines for the absorption of solid food after weaning as well as during adaptation of the organism after resection of the intestine (Burrin et al., 2003). SCFA can also act on the proliferation of enterocytes through modulation of blood flow or through direct action on genes regulating cell proliferation (Blottiere et al., 2003). The impact of SCFA on GLP-2 production and expression of genes responsible for proliferation of enterocytes in the small intestine was observed in rats (Tappenden and McBurney, 1998; Tappenden et al., 1998), whereas a protective effect of SCFA on damaged mucosa of the small intestine was shown in mice (Ramos et al., 1999). The effect of GLP-2 on increases in proliferation and decreases in apoptosis in the epithelium of the small intestines of mice was also observed (Tsai et al., 1997). Reimer and McBurney (1996) and Reimer et al. (1997) showed the impact of dietary fibre on the increase in GLP-2 secretion in rodents. Based on the mechanisms of SCFA action in the intestine, the effect of SCFA on the morphology of the small intestine can occur with oral instillation and may also result from increased microbiological fermentation in the large intestine.

In summary, during intensive *T. spiralis* infection (about 500 larvae per mouse), an orally administered solution of short chain fatty acids caused decreases in numbers of mature nematodes in the intestines and larvae in muscles. The effect was not visible with a lower infectious dose (about 250 larvae). More intensive infection accelerated the rate of the host's reaction to the presence of adult parasites in the intestines – the so-called “self-cure ef-

fect". Moreover, higher invasive doses resulted in the greatest shortening of the intestinal villi and crypt development on the 7th day. The lower dose caused this change on the 10th day. Administration of SCFA to the animals infected with *T. spiralis* alleviated the local histopathological changes caused by the parasite in the small intestine, and manifested mainly in less-intensive shortening of the villi and deepening of the intestinal crypts. Such results support a role for short chain fatty acids in influencing the course of trichinellosis in mice and should be followed by further investigation in order to clarify these mechanisms.

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