Gut Lactase Activity: Decrease During *Salmonella Typhimurium* Infection in Mice[1] (35436)

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In infants, intolerance to lactose and occasionally other disaccharides has been observed frequently in association with, or immediately after, episodes of acute diarrhea (1). Isolation of pathogens during this event has been disappointing; nevertheless, it has been inferred that bacterial and/or viral gastroenteritis may contribute in some manner to disaccharide intolerance (1, 2). In studies concerned with experimental salmonellosis in mice, gut disaccharidases, particularly lactase, were affected during infection. This finding is the subject of this report.

Materials and Methods. Six-week-old Carworth Farms CFl female mice, were used since it was possible to establish the infection orally with a relatively small inoculum in these, but not in the other strains tested. Mice initially weighing approximately 18 g were housed individually at 70 ± 1° and fed a 20% protein diet, described by Schaedler and Dubos (3). It was dispensed in powdered form in feeding tubes (4), which enabled an estimate of the daily food consumption during the course of these studies. Mice were fed this diet for 3-week intervals then given an LD_{50} dose of *Salmonella typhimurium* (TmW), (10^5 organisms/0.5 ml of saline) via a polyethylene gavage. Organisms were grown in Trypticase soy broth at 37° for 24 hr, and suspended in saline to the LD_{50} dose. Bacterial counts were performed routinely on all challenge doses. Isolation and identification of *S. typhimurium* (TmW) from infected animals was carried out using selenite-F enrichment media, S S, brilliant green, eosin methylene blue, and Kligler's iron agars, and specific typing sera.

Results. Typical disease distribution pattern obtained in 60 mice, 28 days following oral challenge, with *S. typhimurium* (TmW) was as follows: of the 50% which survived approximately 29% were still infected at the time the study was terminated. In these, salmonellae were recovered from liver, spleen, and cecal content. An additional 8% were carriers, from which salmonellae were recovered from the cecal content only. Noninfected survivors—devoid of salmonellae in either organ or stool culture—comprised the remaining 13%. In these studies mice which succumbed to infection generally did so within the first week to 10 days. Thus, the remaining time period presumably reflected healing, and correlated morphologically with repair of the GI tract.

Disaccharidase activities were determined prior to and during the course of salmonella infection on three separate occasions. At intervals varying from 1 to 28 days after infection, mice were selected at random and killed by cervical dislocation. A midline abdominal incision was made and the small bowel was flushed *in situ* with ice-cold saline. The entire small bowel stripped of its mesentery during the process of removal, was opened longitudinally along the line of mesenteric attachment. After washing thoroughly in ice-cold saline, the gut was blotted, weighed, and homogenized in 7 vol of ice-cold saline. Disaccharidase activities were measured according to Dahlqvist (5) and protein determinations according to Lowry and associates (6).

Table I lists the gut weight and gut protein in control and infected animals following challenge with the LD_{50} dose of *S. typhimurium* (TmW). An insignificant de-

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TABLE I. Gut Weight and Gut Protein in Mice After Oral Challenge with LD_{50} Dose of *S. typhimurium* (TmW).

Days:	1	7	10	14	21	28
No. of mice/group:[a]	12	12	12	11	10	13
			Gut wt (g)			
Control	1.08 ± 0.09[b]	1.11 ± 0.09	1.08 ± 0.05	1.09 ± 0.07	1.17 ± 0.07	1.22 ± 0.66
Infected	1.09 ± 0.05	0.88 ± 0.04	0.91 ± 0.06	0.97 ± 0.05	1.09 ± 0.06	1.14 ± 0.05
			Gut protein (mg)			
Control	179 ± 11[b]	195 ± 20	192 ± 14	194 ± 13	207 ± 15	222 ± 12
Infected	184 ± 10	151 ± 41	158 ± 14	162 ± 13	194 ± 13	205 ± 11

[a] The number of mice used were the same in both control and infected groups.
[b] Mean ± SEM.

crease in gut weight ($p>0.04$)[2] and in gut total protein ($p>0.05$)[2] was observed between 7 to 10 days post-challenge. Sucrase and maltase activities, both total and specific, paralleled these alterations in gut weight and gut protein; no significant differences were noted between control and infected mice. Lactase activity (Fig. 1), however, was significantly decreased by 7 days; and by 10 days both total and specific lactase activities were reduced to 42 and 50%, respectively, of noninfected control values ($p<0.01$).[2] Repair of the gastrointestinal tract, as assessed enzymatically, occurred by the 14th day; and by 28 days, specific and total activities were similar to control values.

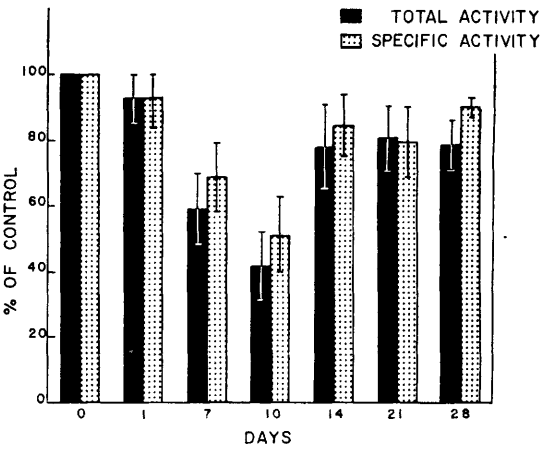

FIG. 1. Gut lactase activity in mice fed 20% protein diet and challenged with LD_{50} *S. typhimurium* (TmW).

Discussion. These studies demonstrated a decrease in intestinal lactase activity during experimental salmonellosis in the mouse. Since sucrase and maltase activities remained unchanged during the course of infection, it is unlikely that decreased lactase activity merely reflected reduced dietary intake during the acute stage of illness. For similar reasons, the findings could not be due to an increased rate of epithelial cell turnover (7) with cellular extrusion occurring prior to cellular maturation, or to a decrease in the total number of gut mucosal epithelial cells. An effect of the organisms or products thereof was more likely—either directly on gut metabolism (8) or indirectly, as the vasculature of the gut was compromised (9) during infection. Thus, impaired protein synthesis in general or an increased rate of protein degradation, may occur briefly during passage of the organism through the mucosal epithelial cell or multiplication of the organism in the gut lamina propria. This is compatible with the observation of a decrease in gut protein 7 to 10 days following challenge. While this finding *per se* was not significant, it was not surprising. The marked inflammatory response within the gut lamina propria seen histologically in the present study and previously by Takeuchi and Sprinz (9), in the guinea pig challenged with salmonellae, would tend to obscure any decrease in protein endogenous to the mucosal epithelium.

Generalized effects on protein synthesis would be reflected by a decreased level of disaccharidases at this time. During the pro-

[2] Paired *t* test.

cess of gut repair, sucrase and maltase activities would return to preinfection levels rapidly, since both respond to nonspecific carbohydrate induction in less than 24 hr in rats (10, 11) and humans (12). Lactase, however, is not as readily induced. In the rat, at least, a minimum of 7 days is required (13) to increase the activity over preinduction levels. Thus, the decreased lactase activity observed during enteric infection may not represent a specific effect on lactase activity *per se,* but may reflect a slower response in lactase synthesis during the repair process. Whether repeated insults of this nature would contribute to permanently decreased lactase activity warrants additional consideration.

Summary. Six-week-old CFl female mice were challenged *per os* with an LD_{50} dose of *S. typhimurium* (TmW). Following infection, small bowel disaccharidase activities were determined in surviving animals at varying time intervals over a 28-day period. Maltase and sucrase activities were not significantly altered. However, gut lactase activity, specific and total, was reduced approximately 50%, 7 to 10 days postinfection and returned to normal levels 21 to 28 days postinfection.

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