Increased Tissue Conductance and Ion Transport in Guinea Pig Ileum After Exposure to *Staphylococcus aureus* Delta-Toxin In Vitro

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Prior studies had shown that *Staphylococcus aureus* delta-toxin was able to inhibit water absorption in guinea pig ileum and to elevate the cyclic AMP content of this tissue, but was unable to elicit certain cyclic AMP-mediated changes in Y-1 adrenal or Chinese hamster ovary cells. Because water movement passively follows the net movement of electrolytes in the gut, this study investigated the effect of delta-toxin on ion transport in guinea pig ileum maintained in vitro. The transmural potential difference (PD) of guinea pig ileum was measured and nullified with an automatic voltage clamp. The short circuit flowing under these conditions ($I_w$) was measured, and the conductance was calculated ($I_w/PD$). Unidirectional $^{22}$Na⁺ and $^{36}$Cl⁻ fluxes were measured. In a glucose-free Ringer solution, delta-toxin caused an immediate spike in PD and $I_w$, and the extent and duration of the spike generally increased with increasing toxin concentration. The conductance of ileum was increased by delta-toxin, and this effect on conductance could be blocked by lecithin, a known inhibitor of delta-toxin. Tissue in the presence of glucose did not exhibit a spike in PD or $I_w$ when exposed to delta-toxin. In a glucose-free medium, delta-toxin caused a 1.5- to 2.5-fold increase in both the unidirectional absorption and secretion of Na⁺ and Cl⁻, whereas the net secretion of Na⁺ increased above basal levels. The observation that delta-toxin causes a prompt increase in intestinal ion flux lends credence to the concept that the elevation in cellular cyclic AMP, which occurs later, is a secondary response to the toxin. The rapid increase in ion flux may reflect the ability of delta-toxin to augment intercellular movement of ions across the mucosa rather than the stimulation of transcellular processes.

Staphylococcal enteritis is a diarrheal disease occasionally seen in individuals treated with broad-spectrum antibiotics. We recently suggested that delta-toxin, a nonantigenic peptide produced by most strains of *Staphylococcus aureus*, may be involved in the pathogenesis of this disease. This suggestion was based on the observation that delta-toxin caused a prompt inhibition of water absorption in rabbit and guinea pig small intestines (7) and a delayed elevation in the cyclic AMP (cAMP) content of guinea pig ileum in vitro (8). Because water passively follows the net movement of ions, the purpose of this study was to determine the effect of delta-toxin on electrolyte transport in guinea pig ileum in vitro.

To investigate ion transport in the gut, the normally occurring transmural potential difference (PD) must be nullified by application of an opposing potential across the tissue (15). The current flowing under these short-circuited conditions, designated $I_{sc}$, is a measure of the net flow of all actively transported ions. Furthermore, under such conditions a specific radioiso- tope may be added to the serosal or mucosal side of the intestine, and the ion flux can be measured without interference from a gradient-induced potential.

**MATERIALS AND METHODS**

**Toxin.** Delta-toxin was prepared and assayed as previously described (6). In this study only the soluble form of delta-toxin with a specific activity of approximately 100 50% hemolytic doses (HD₅₀) per mg was used. One hemolytic unit is equivalent to 10 μg of toxin.

**Perfusing solution.** Perfusion was conducted with a Ringer solution having the following composition (in millimoles per liter): Na⁺, 140; K⁺, 10; Ca²⁺, 1.25; Mg²⁺, 1.1; Cl⁻, 123.7; HCO₃⁻, 25; and H₂PO₄⁻, 2.0. The pH of the solution after equilibration with 95% O₂ + 5% CO₂ was 7.35 to 7.45. When desiring to add lecithin to the solution, Ca²⁺ and Mg²⁺ were omitted to prevent precipitation of the phospholipid.

**Preparation of tissues.** Guinea pigs, weighing 500...
to 900 g and allowed food and water ad libitum, were killed by a blow to the head. The ileum was delivered through a midline incision and cut near the ileocecal valve and again about 20 cm proximally. Segments were rinsed clean of luminal contents by flushing with warm oxygenated Ringer solution delivered through a 50-cm³ syringe with a blunted needle, then cut into 2- to 3-cm sections free of obvious lymph nodes. The sections were opened along the mesenteric border and pinned over a conical-shaped Lucite half-chamber. Care was taken to avoid unnecessary stretching of the tissue or contact with the mucosal surface. Because of the difficulty in stripping guinea pig ileum, the muscularis was not removed. A second half-chamber was fitted over the first, and the entire chamber was clamped together and attached to a glass perfusion apparatus designed for ion transport studies (M. R. A. Corp., Boston, Mass.). The temperature of the tissue and bathing solution was maintained at 37°C by circulating warm water through a jacket surrounding the perfusing apparatus. The perfusing solution was continuously gassed with a water-saturated mixture of 95% O₂ + 5% CO₂. From each animal, four tissues (chambers) were prepared and simultaneously maintained.

Electrical measurements. The transmural PD of chamber-mounted ileum was detected by using matched calomel electrodes (Fisher Scientific Co., no. 13-639-51) immersed in saturated KCl and connected to the Lucite chambers via polyethylene 280 tubing filled with Ringer solution solidified with 2% agar. PD was measured and nullified (“shorted”) by delivering an opposing potential through Ag-AgCl₂ electrodes immersed in saturated KCl and connected to the lucite chamber via Ringer-agar bridges. An automatic voltage clamp, designed essentially according to Rothe et al. (12), was used for generation of the counter potential and measurement of the Iₑ. A positive PD indicated a serosal potential higher than the mucosal potential, and the sign of the Iₑ corresponded to the direction of current (+, mucosa to serosa; −, serosa to mucosa). The clamp gave direct digital readings of the PD and the Iₑ. The instrument corrected the Iₑ for the combined electrode-bridge junction potentials and also corrected for the potential drop due to fluid resistance between the PD-measuring bridge tips and the tissue surfaces. The device was capable of clamping in the range of ±20 mV of the open-circuit potential. Tissue conductance (G), an electrical indicator of the relative ease of ionic movement, was calculated by dividing Iₑ by open-circuit PD.

Experimental design. At zero time, 1 ml of siliccone antifom (Dowex C), diluted 1:50 in Ringer solution, was added to both sides of each tissue to prevent foaming after toxin was added. After 15 min for equilibration, four base line measurements of Iₑ and PD were recorded for each tissue at 2-min intervals. Tissues whose average base line conductance exceeded 2 standard deviations from the mean for the animal were excluded from subsequent data tabulation. Various doses of delta-toxin in 1 ml of Ringer solution were added to the mucosal side of tissues immediately after the fourth base line measurement (23 min). An equal volume of Ringer solution without toxin was added to the serosal side of the chamber and to both sides of control tissues. Delta-toxin in the concentrations used had no effect on the osmolarity of the salt solution (275 mosmol) as measured on an Advanced Hi-Precision osmometer, no. 3149. After toxin addition, electrical readings were obtained at 1- to 5-min intervals. After 45 min (22 min after toxin addition), glucose, at a final concentration of 10 mM, was added to both sides of each chamber. The glucose was added to determine tissue viability which was registered as a spike in Iₑ and PD. Electrical readings were continued at 2-min intervals until the experiment was terminated at 55 min. Variance of intramural base line electrical measurements was as great as the interanimal variance, so base line electrical data from control tissues and tissues subsequently exposed to toxin were pooled. In some cases tissues were pre-treated with 500 µg of chromatographically pure egg lecithin per ml (5) before exposure to delta-toxin.

The effect of glucose on the ability of tissue to respond to various doses of delta-toxin was examined by maintaining tissues in Ringer solution containing 10 mM glucose. Delta-toxin was added as usual (after 23 min), but no additional glucose was added at 45 min. These experiments were continued for a total period of 1.75 h.

Radioisotope fluxes and calculations. The method for measuring ²²Na and ³¹Cl fluxes was a modification of the method of Field et al. (2). ²²Na and ³¹Cl, both obtained in the form of NaCl from Amer sham/Searle, were diluted in Ringer solution. A 10-μCi amount of each isotope contained in 1 ml was added to the mucosal side in two chambers and to the serosal side in the other two chambers. After a 15-min period to permit establishment of a steady-state isotope flux, four successive 1-ml samples were removed at 10-min intervals from both sides of each chamber. A second series of samples were similarly obtained after the addition of either delta-toxin or Ringer solution. In the control group of tissues, 4 ml of Ringer solution was added to both the mucosal and serosal side of each chamber (at 46 min) to replace fluid volume previously removed for sampling. In the other group, the Ringer solution for the mucosal side contained delta-toxin. After allowing 15 min for equilibration, 1-ml samples were removed from both sides of the chambers at 10-min intervals (60, 70, 80, and 90 min) after original time of isotope addition. ²²Na was assayed in a well-type gamma counter. The combined radioactivity of ²²Na and ³¹Cl was then determined in a liquid scintillation counter with P.B.S. solubilizer (Amer sham/Searle) as a scintillation cocktail. Because the energy of the beta-emission spectrum for ²²Na and ³¹Cl is approximately the same, the relative efficiency of the two nuclide counters was determined by counting standards of ²²Na on each instrument. ²²Na sample activity as measured with the gamma counter was multiplied by the relative efficiency factor, and the value was subtracted from the total beta counts obtained with the liquid scintillation counter. This yielded total radioactivity for ³¹Cl, which emits beta radiation only. The counts for the four samples from the labeled side of each chamber were averaged to determine specific activity of each isotope.

Unidirectional Na⁺ and Cl⁻ fluxes were determined
according to the following formula: \( \mu \text{eq of Na}^+ \) or \( \text{Cl}^- \) \( h^{-1} \cdot \text{cm}^{-2} = \left( \frac{\left( C_2 - C_1 \right) \left( \mu \text{eq} \right) (V)(60)}{[(C_1)(t)(A)]} \right) \), where \( C_2 \) = count on samples from unlabeled side at time 2; \( C_1 \) = count on samples from unlabeled side at time 1; \( \mu \text{eq} = \text{concentration of measured element in } \mu \text{eq/ml} \). 

The flux values obtained over the three 10-min intervals before toxin addition were averaged to provide a base line for comparisons. Symbols used to express unidirectional flux in the absorptive direction (mucosa to serosa) were \( J_{\text{Na}}^\text{m} \) or \( J_{\text{Cl}}^\text{m} \), whereas symbols representing unidirectional secretory flux (serosa to mucosa) were \( J_{\text{Na}}^\text{s} \) or \( J_{\text{Cl}}^\text{s} \). The net Na (\( J_{\text{Na}}^\text{n} \)) and net Cl (\( J_{\text{Cl}}^\text{n} \)) fluxes were calculated as the difference between oppositely directed unidirectional fluxes on paired tissues. Pairing was based on tissue conductance values. All unidirectional fluxes were expressed as positive numbers; net fluxes were designated as positive when in the absorptive direction and negative when in the secretory direction. Unidirectional flux measurements from control or toxin-treated tissues were pooled.

Electrical measurements were made at 1-min intervals for a 6-min period after the addition of delta-toxin and at 5-min intervals during the second flux period (60 to 90 min). The average \( I_c \) for each 30-min flux period was determined for each tissue, and the average value for tissues in the same group (controls or toxin treated) was calculated. Net ionic movements were calculated based on Faraday's law of electrolysis. This was done by multiplying the average microampere values (\( I_{\text{MC}} \)) by 0.0093 to convert to \( \mu \text{eq h}^{-1} \cdot \text{cm}^{-2} \) (the units used for Na and Cl flux).

The residual ion flux (\( J_{\text{IR}} \)), as defined by Field et al. (2), was calculated as the difference: \( \mu \text{eq} \text{RT} = (J_{\text{IR}}^\text{m} + J_{\text{IR}}^\text{s}) \), where \( \mu \text{eq} \text{RT} \) was the total ion flux derived from \( I_c \) as above.

**RESULTS**

**Effect of delta-toxin on PD, \( I_c \), and G.** Concentrations of delta-toxin ranging from 1 to 100 HD50/ml of bathing solution were assessed for their effect on the electrical (PD, \( I_c \), and G) responsiveness of guinea pig ileum. The actual amount of toxin bound to ileum was indeterminable. However, with a starting concentration of 100 HD50/ml, 60% of the hemolytic activity of the delta-toxin was detectable in solution at the completion of an experiment, and with an original concentration of 50 HD50/ml, 47% of the activity was still present. The number of tissue preparations exposed to each concentration of toxin ranged from 4 to 23 (average was 6) and were obtained from 3 to 21 animals. The effects of toxin on potential difference and \( I_c \) were analyzed as the change from a 21-min base line reading. Student's \( t \) test was used to assess differences between control and toxin-treated tissues.

The effect of delta-toxin on the potential across guinea pig ileum is shown in Fig. 1A and B. Toxin in concentrations as low as 2.5 HD50/ml caused a significant spike in PD within 1 min after toxin addition, but the effect was transitory. At 50 HD50/ml the potential increased rapidly and remained significantly elevated for the 21-min period of observation. Conversely, 100 HD50/ml caused an immediate and sustained decrease in the transmural potential as compared with controls. Delta-toxin significantly decreased the magnitude of the glucose-mediated spike in potential at concentrations as low as 2.5 HD50/ml.

Delta-toxin in concentrations as low as 2.5 HD50/ml caused a prompt spike in \( I_c \) (Fig. 2A and B). The increase in current was sustained for at least 5 min at toxin concentrations of 10 HD50/ml or greater, and at 50 HD50/ml the elevation in current persisted for the 21-min period of observation. At 21 min the \( I_c \) in tissues treated with 100 HD50/ml was significantly decreased. In contrast to the effect of delta-toxin on the glucose-mediated spike in potential, delta-toxin did not significantly alter the glucose-mediated spike in \( I_c \).

Delta-toxin caused a pronounced increase in the conductance (\( G \)) of ileum at concentrations of 25, 50, and 100 HD50/ml (Fig. 3), although the effect occurred sooner with 100 HD50 of toxin per ml. The conductance of tissue treated with 50 HD50 of toxin per ml increased when glucose was added at 45 min (Fig. 3). Because conductance is a calculated value (\( I_c/\text{PD} \)), this surge in conductance reflects a relatively greater increase in \( I_c/\text{PD} \) than PD. The conductance of control tissue remains the same after addition of glucose, indicating an equal surge in \( I_c/\text{PD} \) and PD. Because glucose, when added at 45 min, did not cause as great an increase in \( I_c/\text{PD} \) for tissue treated with 100 HD50 of toxin per ml as that for tissue treated with 50 HD50 of toxin per ml (Fig. 2B), no surge in conductance was seen. Lecithin was able to block the increase in conductance caused by delta-toxin, but by itself itself did not change in G values (data not shown).

The effects of delta-toxin were also studied with tissues bathed in Ringer solution containing 10 mM glucose. Control tissues exhibited a similar basal conductance, but in the presence of glucose both the PD and \( I_c \) were increased over values previously noted in the absence of glucose. In the presence of glucose, delta-toxin did not elicit a spike in transmural potential (Fig. 4), but at higher concentrations of toxin the potential was significantly decreased as compared with controls. These changes were no longer significant after 96 min, possibly reflecting tissue deterioration. Although delta-toxin did not...
cause a spike in $I_{sc}$, at 50 and 100 HD$_{50}$/ml, the short-circuit current eventually increased significantly over that of control tissues (Fig. 5). Consequently, the conductance was also significantly increased in tissues treated with 50 or 100 HD$_{50}$ of toxin per ml in the presence of glucose (Fig. 6), but the response was delayed as compared with that of tissues in the glucose-free medium.

**Ion fluxes.** Delta-toxin caused a significant increase in both Na$^+$ and Cl$^-$ unidirectional fluxes. There was a decrease in the $\mu$eq$_T$ of control tissues during the second flux period, but there was no decrease in the $\mu$eq$_T$ of toxin-treated tissues (Table 1). Although delta-toxin caused an initial significant increase in unidirectional Na$^+$ and Cl$^-$ absorption, by 45 min the ion fluxes...
Fig. 2. (A) Effect of S. aureus delta-toxin on the short-circuit current ($I_{sc}$) in guinea pig ileum. The $I_{sc}$ is expressed as microampere change from the 21-min base line value. Each point represents the average derived from 6 to 23 tissues. For clarity the responses to higher doses of toxin are shown separately in (B), but the control values are the same as in (A). At 1 min post-toxin addition, all $I_{sc}$ values for tissues treated with 2.5, 5.0, 10, 25, 50 and 100 HD$_{50}$ of toxin per ml are significantly higher than controls ($P < 0.05$).

Fluxes had returned to nearly base line values (Fig. 7A and 8A). The increase in unidirectional ion secretion produced by delta-toxin, however, was still pronounced after 45 min (Fig. 7B and 8B).

Delta-toxin caused a net Na$^+$ secretion and possibly a net Cl$^-$ secretion, but the values of the latter did not reach the levels normally considered significant (Table 2). Delta-toxin also reversed the direction of average residual net flux, but due to a large variance the results did not attain statistical significance.
Fig. 3. Effect of delta-toxin on the conductance of guinea pig ileum. Each point represents the average of 6 to 23 tissues. The conductance values for tissues treated with 1.0, 2.5, or 5.0 HD_{50} of delta-toxin per ml were similar to those of controls and are not shown. The conductance value at 44 min for tissues treated with 100 HD_{50}/ml was 584 mmho. From 5 to 28 min after toxin addition, the conductance values of tissues treated with 25, 50, and 100 HD_{50} of toxin per ml are significantly higher than controls (P < 0.025).

DISCUSSION

Previous studies had shown delta-toxin capable of inhibiting water absorption in rabbit and guinea pig intestine (7) and of increasing the cAMP content of guinea pig ileum (8). Although delta-toxin caused an almost immediate inhibition of water absorption, the increase in cAMP occurred only after a 1-h lag. Moreover, delta-toxin apparently did not elevate intracellular cAMP in the same manner as did cholera toxin, because delta-toxin was unable to evoke certain cAMP-mediated changes in Chinese hamster ovary or Y-1 adrenal cells (9). The purpose of our present investigation was to determine what toxin-induced changes in ion flux, if any, might be responsible for inhibition of water absorption. Because most of our previous studies were done with guinea pig intestine, we elected to continue the use of this species. Because of the pronounced lag before delta-toxin increased cAMP levels, the time periods employed for ion flux study appeared unlikely to reflect changes resulting from elevations in cAMP content of guinea pig ileum.

The mammalian small intestine is characterized by extremely high transepithelial conductance [I_{se}/(PD \times 1,000)] ranging from 10 mmho/cm² for unstripped rabbit and rat ileum to approximately 25 mmho/cm² for stripped preparations of rabbit ileum and unstripped rat jejunum (13). Our preparations of unstripped guinea pig ileum had an average conductance of 24 mmho/cm² as compared with the value of 18 mmho/cm² reported by Powell et al. for stripped preparations of guinea pig ileum (10). These high transepithelial conductances apparently result not from leaky cell membranes, but rather from high-conductance intercellular spaces (4). Indeed, Frizzell and Schultz (3) present evidence that at least 85% of transmural conductance in rabbit ileum can be attributed to ions moving through this intercellular pathway; thus, appar-
**Fig. 4.** Effect of delta-toxin on transmural potential of guinea pig ileum in presence of 10 mM glucose. PD is expressed as change in millivolts from the 21-min base line. Each point represents the average from four to eight tissues. From 5 to 21 min after toxin addition, the PD values for tissues treated with 50 and 100 HD₅₀ of toxin per ml are significantly lower than controls (P < 0.005).

**Fig. 5.** Effect of delta-toxin on Iₛₑ in guinea pig ileum in presence of 10 mM glucose. Short-circuit current is expressed as change in microamperes from the 21-min base line value. Each point represents the average from four to eight tissues. The average value at 96 min for tissue treated with 100 HD₅₀ of delta-toxin per ml was 527 μA. From 5 to 96 min after addition of 50 HD₅₀ of toxin per ml, the Iₛₑ values are significantly higher than control values (P = 0.05). From 21 to 96 min after addition of 100 HD₅₀ of toxin per ml, the Iₛₑ values are significantly higher than control values (P < 0.05).
ent only 15% of the conductance is transcellular.

The guinea pig ileum differs from rabbit ileum in its secretory nature (11). Based on their experimental observations, Powell et al. proposed a model for the mechanism of electrolyte secretion (10). The key features of the model involve an absorptive pump which would carry out active transport of Na\(^+\) from the mucosal to serosal solution and a secretory pump which would cause active transport of anion from serosal to mucosal solution. The absorptive pump would be primarily responsible for the electrical properties of the tissue (PD and \(I_c\)), would be sensitive to ouabain (a cardiac glycoside capable of inhibiting Na\(^+\)-K\(^+\) adenosine triphosphatase), and would be located at the basal or lateral borders of the epithelial cells. The location of the ouabain-sensitive adenosine-triphosphatase was suggested by Schultz and Zalusky, who noted that ouabain could only negate the \(I_c\) when added to the serosal but not the mucosal side of rabbit ileum (14). The secretory system would be a neutral Na\(^+\) anion (Cl\(^-\) or HCO\(_3\)\(^-\)) pump not contributing to the electrical properties of the tissue and having a location that could not be determined a priori.

These transport mechanisms suggest at least three possible explanations for the marked effect of delta-toxin on conductance, ion transport, and \(I_c\). First, delta-toxin could cause denudation of villi, thus resulting in increased conductance and ion transport. Secondly, delta-toxin could specifically stimulate the absorptive and secretory pumps suggested by Powell et al. Thirdly, delta-toxin could preferentially enhance the intercellular transport shunt by disrupting tight junctions. Any combination of interpretations is also possible.

Tissue destruction by delta-toxin with loss of villi tips is certainly a reality (8), but several considerations argue against denudation of villi as the sole mechanism involved. Only doses of delta-toxin as great as 1.0 mg/ml (100 HD\(_{50}\)/ml) were able to cause epithelial loss within 30 min of exposure to toxin (8). Although tissue destruction could account for the aberrant electrical responses seen with tissues exposed to 100 HD\(_{50}\) of delta-toxin per ml, it would be a less satisfactory explanation for other effects seen with smaller doses. In addition, no concentration of delta-toxin was able to inhibit significantly the increase in short-circuit current exhibited by tissues after exposure to glucose, a response
which is a manifestation of an increase in active Na⁺ absorption (1). Furthermore, tissue destruction cannot account for the immediate spike in the transmural potential and in the \( I_c \) as seen with a concentration of 2.5 HD₃₀ or more of delta-toxin per ml in the absence of glucose. Finally, the return of ion fluxes to normal levels 45 min after exposure of tissue to 25 HD₃₀ of delta-toxin per ml would not be likely if tissue destruction had occurred.

There is some evidence for the specific stimulation of both the absorptive and secretory pumps suggested by Powell et al. The immediate spike in PD and \( I_c \) when tissues were exposed to 2.5 HD₃₀ or more of delta-toxin per ml suggests a surge in Na⁺ transport from mucosa to serosa or anion secretion (10, 14). It is interesting that the spike in PD was absent in tissues maintained in the presence of 10 mM glucose and that delta-toxin inhibited the glucose-initiated increase in PD in a dose-related manner. Although glucose and delta-toxin might both affect the same Na⁺ absorptive pump, this suggestion does not entirely agree with our findings because delta-toxin was unable to block the tissue \( I_c \) response to glucose. A study of ion fluxes in the presence of glucose, however, might reveal that delta-toxin does not increase the absorption of Na⁺ and Cl⁻.

The unidirectional increases in \( J_{\text{Na}}^b \) and \( J_{\text{Cl}}^b \) suggest a stimulation of the secretory pump. Our previous studies (8) indicated that ileal cAMP levels did not increase until more than 1 h after exposure to delta-toxin; therefore, stimulation of adenyl cyclase with a subsequent increase in cellular cAMP does not offer a reasonable explanation for the rapid increase in Cl⁻ secretion. The possibility that the reverse is true seems more tenable. Perhaps delta-toxin, by stimulating the secretory pump, secondarily causes an elevation of cellular cAMP. This could explain why delta-toxin was unable to effect certain cAMP-mediated changes in Y-1 adrenal and Chinese hamster ovary cells. Whether delta-toxin elevates intracellular cAMP by the more conventional mechanisms such as stimulation of epithelial adenyl cyclase or the inhibition of phosphodiesterase has not been determined, but studies along these lines are worthy of pursuit.

The possibility that delta-toxin may increase conductance by an effect on an intercellular shunt is both tenable and novel. Assuming no denudation of villi, the magnitude of the effect of delta-toxin on tissue conductance suggests an increase in intercellular movement because transcellular transport appears to account for only a small fraction of the electrical conductance (3). It may be that the delta-toxin-induced
Fig. 7. Effect of S. aureus delta-toxin on Na⁺ transport in guinea pig ileum. (A) Flux in the mucosa to serosa direction ($J_{ms}^{Na}$); (B) serosa to mucosa flux ($J_{sm}^{Na}$). Each point (± standard error) represents the mean Na⁺ flux derived from 10 to 14 tissues during the 10-min period indicated. The final concentration of delta-toxin was 25 HD₅₀/ml.
DELTA TOXIN ON $J_{ms}^cI$ IN GUINEA PIG ILEUM MEAN±SE

$\mu$Eq hr$^{-1}$ cm$^{-2}$

MINUTES

RINGER'S ADDED

TOXIN ADDED

DELTA TOXIN ON $J_{sm}^cI$ IN GUINEA PIG ILEUM MEAN±SE

$\mu$Eq hr$^{-1}$ cm$^{-2}$

MINUTES

RINGER'S ADDED

TOXIN ADDED
increase in vascular permeability in guinea pig skin, as reported previously (8), is a reflection of an increase in intercellular leakage. The question might be answered by comparing the transport of various sized labeled markers in delta-toxin-treated and control tissues. If delta-toxin increases intercellular transport, it could provide a unique model for further study.

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LITERATURE CITED


FIG. 8. Effect of S. aureus delta-toxin on Cl⁻ transport in guinea pig ileum. (A) Flux in the mucosa to serosa (J_{mu}^-) direction; (B) serosa to mucosa flux (J_{sm}^-). Each point (± standard error) represents the mean Cl⁻ flux derived from 7 to 13 tissues during the 10-min period indicated. The final concentration of delta-toxin was 25 HD_{50}/ml.