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Electrolyte Transport in Piglets Infected With Transmissible Gastroenteritis Virus
Stimulation by Verapamil and Clonidine

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The effects of clonidine, an α-adrenergic agonist, and verapamil, a Ca\(^{2+}\) channel blocker, on Na\(^{+}\) and Cl\(^{-}\) absorption were studied in stripped jejunal mucosa from control and transmissible-gastroenteritis-virus-infected piglets. All infected piglets developed severe diarrhea 18–24 hours after oral inoculation. Jejunum from infected animals, as compared with control jejunum, had decreased mucosal-to-serosal, serosal-to-mucosal, and net Na\(^{+}\) and Cl\(^{-}\) fluxes. Clonidine and verapamil caused a decrease in short-circuit current and stimulation of Na\(^{+}\) and Cl\(^{-}\) absorption in control jejunum. In infected piglets, although the jejunum exhibited severe villus atrophy, both drugs stimulated Na\(^{+}\) and Cl\(^{-}\) absorption in control jejunum. In infected piglets, although the jejunum exhibited severe villus atrophy, both drugs stimulated Na\(^{+}\) and Cl\(^{-}\) absorption in control jejunum. In contrast, n-glucose stimulated Na\(^{+}\) absorption, and the decrease in short-circuit current caused by verapamil and clonidine, were decreased in transmissible-gastroenteritis-infected jejunum. Such pharmacological stimulation of Na\(^{+}\) and Cl\(^{-}\) absorption might be useful in the management and treatment of certain viral diarrheal diseases.

Abbreviations used in this paper: [Ca\(^{2+}\)], intracellular Ca\(^{2+}\) concentration; G, conductance; Isc, short-circuit current; PD, potential difference; TGE, transmissible gastroenteritis.
ing intracellular levels of calcium, but it may also be due to an as yet unidentified action that mimics the effects of decreased $[\text{Ca}^{2+}]$, (9–11).

Neonatal piglets are highly susceptible to a variety of viral and bacterial enteric infections that result in severe diarrhea. In addition, neonatal, conventional, specific pathogen-free, and gnotobiotic piglets have been used as animal models for the study of human viral enteritis that also affects children (12–15). In this study, we describe the effects of verapamil and clonidine on electrolyte transport in the small intestine of normal piglets, and of piglets with severe villus atrophy from transmissible gastroenteritis (TGE) caused by a coronavirus infection.

**Materials and Methods**

**Animals**

Conventional crossbred healthy 2–5-day-old piglets were obtained from a commercial herd. Piglets were removed from the sow, kept in isolation for 24–48 hours before any use, and fed a commercial diet (SPF Lac, New York, NY) supplemented with gentamicin, 0.5 mg/mL (TechAmerica Group, Inc., Elwood, KS). A total of 11 control uninfected and 12 TGE-virus-infected piglets were used in these studies.

**Virus Infection**

A virulent strain of porcine TGE coronavirus, obtained from the University of Nebraska (Lincoln, NE) (16), was used as a 1:10 bacteria-free suspension of fecal material collected from an experimentally infected gnotobiotic piglet. Piglets were orally infected with 1.0 mL of the viral suspension and were killed 48 hours later at the peak of severe diarrhea and villus atrophy that occurred in all test animals. Control piglets were kept uninfected (in a pathogen-free facility) for 48 hours before the experiments. Segments of jejunum, adjacent to all of the segments used in the electrolyte transport studies, were fixed with 10% buffered formalin and processed for histological evaluation by conventional procedures (17).

**In Vitro Electrolyte Transport**

Active jejunal electrolyte transport was measured by the Ussing chamber-voltage clamp technique according to the method described by Donowitz and Asarkof (5) for use in rabbits. Piglets were killed with an overdose of sodium pentobarbital. Jejunal intestinal mucosa was removed and stripped from its underlying muscle, mounted between two lucite modified Ussing chambers with an aperture of 1.13 cm$^2$, oxygenated, and maintained at 37°C. Both the serosal and mucosal bathing fluids, respectively, were warmed to 37°C. Both the serosal and mucosal surfaces were bathed in Ringer's-HCO$_3$ buffer composed of [mmol/L] of Na$^+$, 140; K$^+$, 5.2; Mg$^{2+}$, 1.2; Ca$^{2+}$, 1.2; Cl$^-$, 119.8; HCO$_3^-$, 25; HPO$_4^{2-}$, 2.4; H$_2$PO$_4^-$, 0.4; pH 7.4, and with 95% O$_2$–5% CO$_2$. Glucose (10 mmol/L) and mannitol (10 mmol/L) were added to the serosal and mucosal bathing fluids, respectively, at the time of mounting the tissue. Transmural potential difference (PD), short-circuit current (Isc) and conductance (G) were measured. An automatic voltage clamp, corrected for fluid resistance between the PD sensing bridges, provided continuous short-circuiting of the tissue. The major transport measurement reported in this paper is the Isc, which is equivalent to the electrical sum of all electrogenic ion transport processes occurring simultaneously. Unidirectional fluxes of $^{22}$Na and $^{36}$Cl were also measured 20–100 minutes after the addition of isotopes on tissues matched to differ in conductance by not more than 25%. In these experiments two 20 minute flux periods were measured before the addition of any drug, then verapamil or clonidine were added to the serosal side and three 20 minute flux periods were determined. Fluxes from untreated tissue were also measured for time controls. The effects of the two drugs were evaluated in both normal (n = 5) and virus-infected piglets (n = 4 for studying the effects of verapamil and n = 5 for clonidine). Nine of the 10 animals studied were paired with respect to the two drug treatments. In the ion flux experiments, a negative sign (−) indicates net secretion and a positive sign (+) indicates net absorption.

Statistical analyses were performed with Student's t test for paired and unpaired data. All results are expressed as means ± SE.

**Materials**

$[^{22}\text{Na}]{\text{NaCl}}$ and $[^{36}\text{Cl}]\text{HCl}$ were obtained from Amersham, Arlington Heights, IL. Verapamil and clonidine were purchased from Sigma Chemical Co., St. Louis, MO.

**Results**

**Virus Infection**

Control uninfected piglets remained healthy during their isolation period until death. All TGE-virus-infected piglets developed severe diarrhea within 18–24 hours after oral inoculation. Jejunal samples from all test animals used in the in vitro tests had severe villus atrophy as verified by microscopic examination at the time of selection of jejunal samples for use in the Ussing chambers, and as confirmed by histopathology (Figure 1) in adjacent segments.

**Basal Short-Circuit Current and Electrolyte Transport in Control and Virus-Infected Piglets**

For comparison of Isc and transport in control and infected tissues, the data in Tables 1 and 2 have been combined and are as follows. Basal Isc in infected piglets was not significantly different than the basal values in control piglets (0.3 ± 0.3 μEq · cm$^{-2}$ · h$^{-1}$ in infected vs. 0.6 ± 0.4 μEq · cm$^{-2}$ · h$^{-1}$ in controls). However, infected jejunum had significantly different Na$^+$ mucosal-to-serosal fluxes (0.9 ± 0.9 μEq · cm$^{-2}$ · h$^{-1}$ in infected tissues vs. 17.6 ± 2.4


Figure 1. Histological sections of jejunum adjacent to segments used for Isc measurement from a control (A) (original magnification ×65) and from a TGE virus infected piglet (B) (original magnification ×65) using H&E stain showing the loss of villi. C. Further magnification (340×) of a portion of B indicated by the arrow shows that the surface epithelial cells are totally destroyed.

μEq cm⁻² h⁻¹ in control tissues; P < 0.01; Na⁺ serosal-to-mucosal fluxes (8.5 ± 0.7 μEq cm⁻² h⁻¹ in infected tissues vs. 14.5 ± 2.1 μEq cm⁻² h⁻¹ in control tissues; P < 0.05); net Na⁺ fluxes (−1.6 ± 0.7 μEq cm⁻² h⁻¹ in infected tissues vs. 3.2 ± 0.3 μEq cm⁻² h⁻¹ in controls; P < 0.01); Cl⁻ mucosal-to-serosal fluxes (3.2 ± 0.8 μEq cm⁻² h⁻¹ in infected tissues vs. 10.0 ± 1.5 μEq cm⁻² h⁻¹ in controls; P < 0.01);

Table 1. Effects of Verapamil on Short-Circuit Current and Ileal Na⁺ and Cl⁻ Transport in Control and Virus-Infected Piglets

| Conditions                           | n  | Isc | j⁺ₛₘ | j⁻ₛₘ | j⁺ₘₛ | j⁻ₘₛ | j⁺ₘₑ | j⁻ₘₑ | j⁺ₑₘ | j⁻ₑₘ |
|--------------------------------------|----|-----|------|------|------|------|------|------|------|------|
| Control—untreated (t = 0–40 min)     | 5  | 0.6 ± 0.3 | 17.3 ± 2.5 | 11.5 ± 1.9 | 2.8 ± 0.0 | 0.6 ± 1.5 | 6.7 ± 1.7 | 2.0 ± 1.0 |
| Period A                             |    |       |      |      |      |      |      |      |      |      |
| Verapamil (10 μmol/L) (t = 40–100 min)| -1.2 ± 0.4 | 20.4 ± 1.8 | 15.9 ± 1.2 | 4.5 ± 1.2 | 12.7 ± 1.1 | 8.1 ± 1.1 | 4.6 ± 1.2 |
| Period B                             |    |       |      |      |      |      |      |      |      |      |
| P                                    | -1.7 ± 0.1 | 3.1 ± 1.4 | 1.4 ± 1.3 | 1.7 ± 0.4 | 3.1 ± 1.9 | 1.4 ± 1.6 | 1.7 ± 0.6 | <0.05 | NS   | NS   | NS   | <0.05 |
| Period B–A                          |    |       |      |      |      |      |      |      |      |      |
| Untreated infected (t = 0–40 min)    | 4  | 0.5 ± 0.1 | 7.7 ± 1.3 | 8.6 ± 0.9 | -1.1 ± 0.5 | 4.2 ± 1.0 | 3.3 ± 1.2 | 0.9 ± 0.8 |
| Period A                            |    |       |      |      |      |      |      |      |      |      |
| Verapamil (10 μmol/L) (t = 40–100 min)| -0.1 ± 0.1 | 9.4 ± 1.2 | 8.7 ± 1.3 | 0.8 ± 1.2 | 5.7 ± 1.7 | 3.9 ± 2.0 | 1.8 ± 1.4 |
| Period B                            |    |       |      |      |      |      |      |      |      |      |
| P⁺                                  | -0.6 ± 0.1 | 1.7 ± 0.4 | -0.2 ± 0.7 | 1.9 ± 0.3 | 1.5 ± 1.0 | 0.6 ± 1.0 | 0.9 ± 0.7 |
| P⁻                                  | <0.05 | <0.05 | NS | <0.01 | NS | NS | NS | NS |
| Period B–A                          |    |       |      |      |      |      |      |      |      |      |

NOTE: Values are means ± SE; n, number of animals studied. In the experiments, isotopes were added at time 0. In period A, flux measurements were taken between 0 and 20 minutes and between 20 and 40 minutes after adding isotope. Verapamil was added at 40 minutes. In period B, flux measurements were taken between 40 and 60 minutes, 60 and 80 minutes, and 80 and 100 minutes. Units are μEq cm⁻² h⁻¹ for fluxes and Isc.

J, flux; ms, mucosal to serosal; sm, serosal to mucosal.

* Differences between periods A and B (paired t test).

* Differences between effects of verapamil on control and infected jejunum (unpaired t test).
Table 2. Effects of Clonidine on Short-Circuit Current and Ileal Na⁺ and Cl⁻ Transport in Control and Virus-Infected Piglets

| Conditions                        | n  | Isc   | J⁺ₘ₄ | J⁻ₘ₄ | J⁺ₘ₅ | J⁻ₘ₅ | J⁺ₘ₆ | J⁻ₘ₆ |
|-----------------------------------|----|-------|------|------|------|------|------|------|
| Control—untreated (t = 0–40 min)  | 5  | 0.8 ± 0.4 | 17.9 ± 2.4 | 14.4 ± 2.2 | 3.5 ± 0.5 | 10.3 ± 1.7 | 7.4 ± 1.3 | 2.9 ± 1.1 |
| Clonidine (3 μmol/L)              |    |       |      |      |      |      |      |      |
| (t = 40–100 min)                  |    | -1.1 ± 0.5 | 22.0 ± 1.6 | 16.6 ± 1.9 | 5.4 ± 0.4 | 14.5 ± 1.2 | 8.3 ± 1.4 | 6.2 ± 1.8 |
| Period A                          |    | -1.9 ± 0.2 | 4.1 ± 1.0 | 2.2 ± 0.4 | 1.9 ± 0.8 | 4.2 ± 1.0 | 0.9 ± 0.6 | 3.3 ± 1.2 |
| Δ                                 |    | <0.05   | <0.01 | <0.01 | <0.02 | <0.01 | NS   | <0.05 |
| P                                 |    |         |       |       |       |       |      |      |
| Period B-A                       |    | -0.8 ± 1.0 | 4.3 ± 0.7 | 3.3 ± 1.2 | 1.0 ± 1.0 |     |      |      |
| Period B                         |    | -0.8 ± 0.2 | 1.6 ± 0.5 | 0.4 ± 0.6 | 1.2 ± 0.1 | 1.7 ± 0.4 | -1.3 ± 1.1 | 3.0 ± 1.0 |
| Unweighted infected (t = 0–40 min)| 5  | 0.3 ± 0.2 | 6.6 ± 0.8 | 8.6 ± 2.3 | -2.0 ± 1.1 | 2.6 ± 0.7 | 4.6 ± 1.5 | -2.0 ± 1.4 |
| Clonidine (3 μmol/L)              |    | -0.1 ± 0.1 | 8.2 ± 0.8 | 9.0 ± 0.8 | -0.8 ± 1.0 | 4.3 ± 0.7 | 3.3 ± 1.2 | 1.0 ± 1.0 |
| (t = 40–100 min)                  |    | -0.4 ± 0.2 | 1.6 ± 0.5 | 0.4 ± 0.6 | 1.2 ± 0.1 | 1.7 ± 0.4 | -1.3 ± 1.1 | 3.0 ± 1.0 |
| Period B-A                       |    | <0.05   | <0.02 | NS   | <0.001 | <0.01 | NS   | <0.05 |
| P                                 |    |         |       |       |       |       |      |      |
| Period B-A                       |    | <0.005  | 0.06  | <0.05 | NS   | <0.05 | NS   | NS   |

NOTE. Values are means ± SE; n, number of animals studied. In the experiments, isotopes were added at time 0. In period A flux measurements were taken between 0 and 20 minutes and between 20 and 40 minutes after adding isotope. Clonidine was added at 40 minutes. In period B, flux measurements were taken between 40 and 60 minutes, 60 and 80 minutes, and 80 and 100 minutes. Units are μEq cm⁻² h⁻¹ for fluxes and Isc.

J, flux; ms, mucosal to serosal; sm, serosal to mucosal.

* Differences between periods A and B (paired t test).

b Differences between effects of clonidine on control and infected jejunum (unpaired t test).

and net Cl⁻ fluxes (-0.8 ± 1.0 μEq cm⁻² h⁻¹ in infected tissues vs. 2.9 ± 0.9 μEq cm⁻² h⁻¹ in controls; P < 0.05). Cl⁻ serosal-to-mucosal fluxes in infected piglets were not significantly different than those in controls (3.9 ± 1.1 μEq cm⁻² h⁻¹ in infected vs. 7.1 ± 1.5 μEq cm⁻² h⁻¹ in control piglets).

Effects of Verapamil and Clonidine on Short-Circuit Current and Electrolyte Transport in Control and Virus-Infected Piglets

Figure 2 and Table 1 and Figure 3 and Table 2 show the effects of 10 μmol/L verapamil and 3 μmol clonidine, respectively, on Isc and Na⁺ and Cl⁻ fluxes in control and infected jejunum. Verapamil and clonidine both decreased Isc in control and virus-infected piglets. The decrease in Isc (measured 20 minutes after drug addition) caused by verapamil (ΔIsc = -25.8 ± 2.0 μA/cm²; starting Isc = 23.6 ± 4.6 μA/cm²; n = 7; Figure 2) or clonidine (ΔIsc = -19.8 ± 1.5 μA/cm²; starting Isc = 18.5 ± 4.4 μA/cm²; n = 8; Figure 3) in infected tissue, was significantly smaller (P < 0.02 in both cases) than the effect of either drug on Isc in control tissue. In control tissue the decrease in Isc caused by verapamil was 51.5 ± 3.0 μA/cm² (n = 9) (starting Isc = 47.3 ± 6.9 μA/cm²), and the decrease in Isc caused by clonidine was 46.2 ± 2.6 μA/cm² (n = 9; starting Isc = 44.1 ± 6.5 μA/cm²). The reduced response to verapamil or clonidine in the infected piglet might be explained by the reduced surface area of the tissue exposed to the drugs (Figure 1) caused by the loss of mature enterocytes. Potential difference values were significantly decreased in control jejunum from -2.6 ± 0.4 mV (n = 10) to -0.1 ± 0.2 mV (n = 5; P ≤ 0.01) after the addition of verapamil, and to -0.5 ± 0.1 mV (n = 5; P ≤ 0.01)

Figure 2. Effect of 3 μmol/L verapamil on Isc in control (Δ; n = 9) and infected (Δ; n = 7) piglets. The points shown are means ± SE. The starting Isc was 47.3 ± 6.9 for the control tissues and 23.6 ± 4.6 for the infected tissues.
The starting Isc was 44.1 ± 8.5 for the control tissues and 18.5 ± 2 October 1991. P I

Verapamil, and to -29.0 ± 6.6 mS and infected (A; n = 8) piglets. The points shown are means ± SE.

Increased from -22.9 ± 2.7 mS in control or virus-infected jejum by the addition of either drug. In normal tissue, G values increased from -22.9 ± 2.7 mS · cm⁻² (n = 10) to -27.2 ± 6.3 mS · cm⁻² (n = 5) after the addition of verapamil, and to -29.0 ± 6.6 mS · cm⁻² (n = 5) after the addition of clonidine. In infected tissue, G values increased from -12.7 ± 1.7 mS · cm⁻² (n = 9) to -10.3 ± 4.0 mS · cm⁻² (n = 4) after the addition of verapamil, and to -12.2 ± 5.2 mS · cm⁻² (n = 5) after the addition of clonidine.

The decrease in Isc, caused by verapamil and clonidine, correlated with increased Na⁺ and Cl⁻ absorption (Tables 1 and 2). Verapamil caused significant increases in net Na⁺ and Cl⁻ absorption in control jejum (Table 1). This increase in absorption is caused by increases in the mucosal-to-serosal Na⁺ and Cl⁻ fluxes. In virus-infected jejum, verapamil caused a significant increase in Na⁺ absorption but only a slight, nonsignificant increase in net Cl⁻ absorption; these changes were also caused by increases in the mucosal-to-serosal Na⁺ and Cl⁻ fluxes. The magnitude of the increases in net Na⁺ and Cl⁻ fluxes and mucosal-to-serosal fluxes were similar in control and infected tissues.

Clonidine also significantly increased net Na⁺ and Cl⁻ absorption (Table 2). The increase in Na⁺ and Cl⁻ absorption caused by clonidine was mainly because of an increase in ion movement from the mucosal-to-

Figure 3. Effect of 0.3 µmol/L clonidine on Isc in control (A: n = 9) and infected (A; n = 8) piglets. The points shown are means ± SE.

The starting Isc was 44.1 ± 6.5 for the control tissues and 18.5 ± 4.4 for the infected tissues.

In separate studies, the maximum increase in Isc was determined in response to 10 mmol/L glucose added to the mucosal surface.Glucose-stimulated Isc (assumed to be Na⁺ transport) was significantly decreased in infected tissue as compared to controls; ∆Isc caused by the addition of mucosal glucose in infected jejum was 13.6 ± 5.1 µA/cm² (n = 11) vs. 72.5 ± 10.2 µA/cm² in control tissue (n = 12; P < 0.005).

Discussion

The search for antisecretory drugs for the therapeutic management of bacterial diarrheas mediated by enterotoxins, particularly cholera, has gained attention during recent years (18). This has not been the case to the same extent with viral diarrheal diseases in which electrolyte and water disturbances are not thought to be associated with enterotoxins, but rather with the loss of mature absorptive enterocytes and their replacement by immature cryptlike cells (2-4). Approaches for the potential treatment of neonatal intestinal viral infections have followed immunological and nonimmunological lines, the latter including the use of protease inhibitors or glycoproteins blockers (19). The TGE virus is known to infect the mature enterocytes lining the intestinal villi of jejunum and ileum of young piglets. After infected enterocytes are shed, they are replaced by cells migrating from the crypts at an accelerated rate (2,3,20,21). Davidson et al (22) have suggested that the defective epithelial function after human rotavirus infection is primarily caused by retarded differentiation of the uninfected migrating enterocytes. These enterocytes, isolated from atrophied villi during acute diarrhea, had an enzymatic profile typical of crypt cells, being rich in thymidine kinase and low in sucrose activities. The current study examines several aspects of the Na⁺ absorptive processes in the jejunum of TGE-infected animals. Mucosal-to-serosal Na⁺ and Cl⁻ fluxes (Tables 1 and 2), serosal-to-mucosal Na⁺ and Cl⁻ fluxes and net Na⁺ and Cl⁻ fluxes as well as glucose-dependent Na⁺ absorption were all decreased in jejunum from TGE-virus–infected animals.

It was found previously (7-11), that verapamil and clonidine increase Na⁺ and Cl⁻ absorption in rabbit
ileum. In the present study, verapamil and clonidine not only stimulate Na\(^+\) and Cl\(^-\) absorption in the jejunum of normal piglets, but also in the jejunum of TGE-virus-infected piglets. Surprisingly, the magnitudes of the verapamil- and clonidine-induced increases in Na\(^+\) and Cl\(^-\) absorption were similar in normal and virus-infected jejunum. These data are notable because it has been thought that the luminal membrane NaCl cotransport system may be absent in piglet jejunum after infection with TGE virus (23). The evidence for this was the lack of 5'-cyclic adenosine monophosphate (cAMP)-mediated or furosemide-mediated antiabsorptive effects. One possible explanation for the discrepancy may lie in the fact that our results demonstrate stimulation of absorption, and such stimulation may be necessary before antiabsorptive effects can occur. Alternatively, the piglets used in the two studies differed considerably in age (4–7 days vs. 17 days).

Glucose-stimulated Na\(^+\) transport in the small intestine has been shown to be defective in TGE-infected animals (24) because of the absence of the high-affinity D-glucose carriers (25). This defect in Na-D-glucose transport was confirmed in the current study in which n-glucose-stimulated Na\(^+\) absorption was markedly reduced in TGE-infected tissue when compared with normal tissue. Oral rehydration therapy is effectively used in the treatment of viral diarrheal diseases in children, further confirming that the defect in glucose-dependent Na\(^+\) transport is only partial (26,27). Thus, these different Na\(^+\) absorptive processes, which are present in small intestinal Na\(^+\) absorbing epithelial cells, were affected differently in TGE-infected jejunum. n-Glucose carriers have been shown, with antibodies raised to the purified Na-D-glucose carrier, to be present predominantly in the villus tips, whereas the location at which neutral NaCl absorption takes place is unknown. These results are consistent with neutral NaCl absorption being present throughout the villi, whereas the Na-D-glucose transporter is found predominantly in the villus tips, the site of the most severe histological damage in TGE diarrhea.

Histological observations in this study, showing severe villus atrophy and replacement of the intestinal mucosa by flat cuboidal immature intestinal cells present in the affected jejunal sections, support the conclusion that verapamil and clonidine induce Na\(^+\) and Cl\(^-\) absorption either in some remaining mature villus enterocytes not killed by the virus, in the immature villus cells, in crypt cells that are capable of absorbing Na\(^+\) and Cl\(^-\), or in all three of these cell types. Which of these possibilities is correct awaits identification of the location of the neutral NaCl absorptive process. Earlier studies in somewhat older piglets have shown that at the height of diarrhea, the epithelium consists predominantly of immature cells that have migrated to the villi in a relatively undifferentiated state (21,23,24). As mentioned earlier, these cells were not able to generate cAMP-mediated or furosemide-mediated antiabsorptive effects, but only serve as the site for cAMP-mediated anion secretion, suggesting the absence of neutral NaCl cotransporters in these cells. The mucosa of the infected tissue was shown to be composed of cells closely resembling those occurring in normal crypts, in that they have similar enzyme activities (23). In addition to the effects on Na\(^+\) absorption, another transport process was significantly affected in TGE-infected jejunum. The process is that represented by the verapamil- and clonidine-induced decrease in Isc. Initially, it was thought that this process represented inhibition of bicarbonate secretion; however, it has recently become obvious that a decrease in Isc in this setting can represent several transport processes involved in hydrogen ion transport (28). These current studies do not shed light on the nature of this transport process but do suggest that whatever that process, it is probably localized to the same cells which are responsible for D-glucose-stimulated Na\(^+\) absorption and are likely to be the jejunal villus tip cells.

The fact that under the conditions of the study, verapamil and clonidine caused an increase in Na\(^+\) and Cl\(^-\) absorption in jejunal segments of TGE-virus-infected piglets, opens the possibility of using drugs to pharmacologically stimulate NaCl absorption, especially those which lower intracellular Ca\(^{2+}\), for the management of diarrheal diseases. Clinical trials to evaluate the effectiveness of these and similar drugs in piglets might be valuable to veterinary medicine. It might be also important to test the efficacy and safety of these drugs in humans, because the piglet disease bears many similarities to human rotavirus enteritis (12–15).

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