BBA Report

BBA 71068

Intestinal transmural electrical activity: Selective effects of mucosal and serosal anaerobiosis

R. DAVID BAKER, MALCOLM J. WALL★ and JO LLU LONG

Department of Physiology, University of Texas Medical Branch, Galveston, Texas 77550 (U.S.A.)

(Received December 11th, 1970)

SUMMARY

We have found that when actively transported organic solutes are not present, potential difference (PD) and short-circuit current (I_{sc}) across rat small intestine are much more dependent upon oxygen in the serosal solution than in the mucosal solution. However, the electrical response to an actively transported sugar is more sensitive to mucosal O_2 than to serosal O_2.

Flat sheets of upper jejunum from unfasted male rats derived from the Sprague–Dawley strain were clamped between Lucite chambers. To each side were added 3.0 ml of Krebs–Ringer–bicarbonate solution (pH 7.4). Mixing was accomplished by the bubble-lift method. Each side was gassed with either 5% CO_2 in O_2 or 5% CO_2 in N_2. Open-circuit potential difference (PD) was recorded most of the time during each experiment from agar–KCl bridges connected to calomel electrodes; I_{sc} and transmural resistance (R_m) were determined at frequent intervals using customary techniques.

Fig.1 shows results from a typical control experiment in which mucosal and serosal solutions were both oxygenated the entire time. After about 10 min the electrical parameters usually became fairly stable. Fig.2 illustrates that (1) mucosal anaerobiosis, at least over a period of several minutes, had no obvious effect on PD and I_{sc}; (2) serosal anaerobiosis promptly reduced PD and I_{sc} even though the mucosal side was oxygenated; (3) PD and I_{sc} were quickly restored when the serosal solution was re-oxygenated.

Fig.3 shows another sample experiment that supports the above conclusions. Qualitatively similar results have been observed in over 40 additional experiments. However, there have been occasional experiments in which mucosal O_2 partially main-

Abbreviations: PD, potential difference; I_{sc}, short-circuit current; R_m; transmural resistance.

★Present address: Clinical Physiology Section, Marquette School of Medicine, Milwaukee, Wisc., U.S.A.

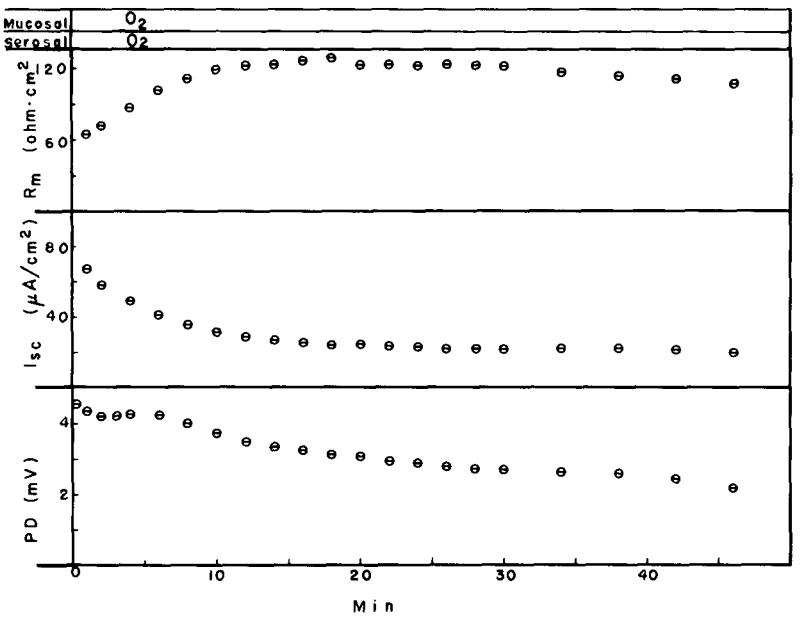

Fig.1. Data from a typical control experiment using a flat sheet of rat jejunum incubated in Krebs–Ringer bicarbonate solution (pH 7.4) at 37°; no organic solute was present. The mucosal and serosal solutions were both oxygenated (95% O_2, 5% CO_2) throughout the experiment, as indicated at the top of the figure Note that I_{SC} falls and R_m rises for about the first 10 min and then both become fairly stable.

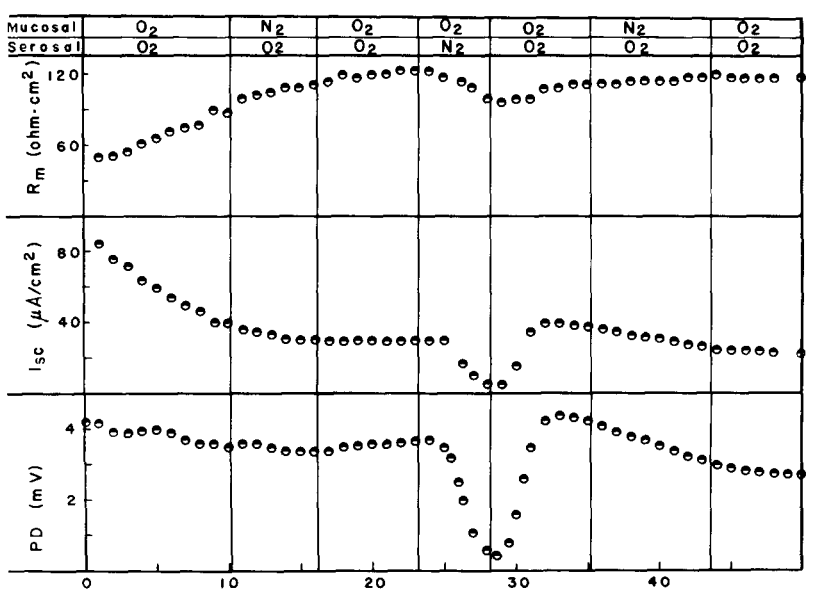

Fig.2. Effects of mucosal or serosal anaerobiosis on a flat sheet of rat jejunum. No organic solute was present. Data are from one experiment; these results were typical of many other experiments, except that the change in R_m during serosal anaerobiosis was not usually observed.

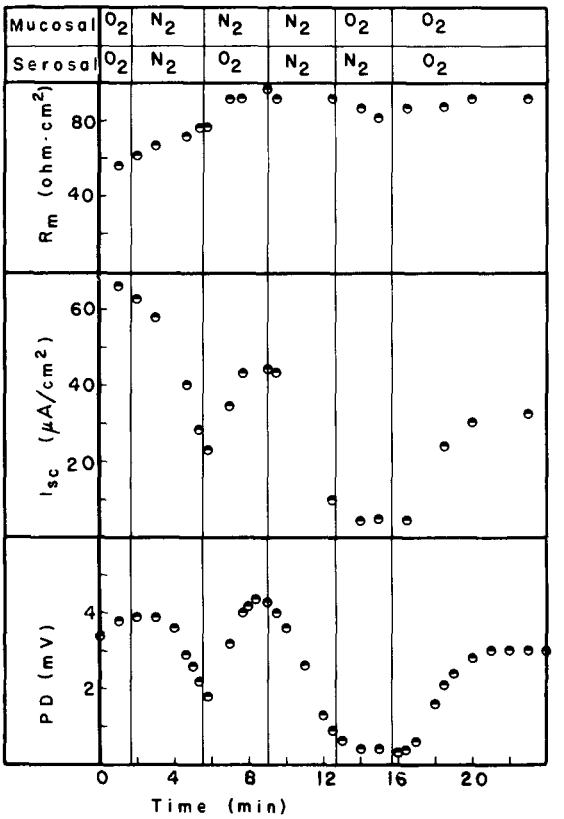

Fig.3. Data from another experiment with rat jejunum, demonstrating the ability of serosal, but not mucosal, oxygenation to restore PD and I_{sc} following bouts of anaerobiosis.

tained PD and I_{sc} even when the serosal side was anaerobic. In spite of this inconsistency, it is quite clear that PD and I_{sc} are far more dependent upon serosal O_2 than upon mucosal O_2. Mucosal O_2 is usually not necessary and is almost never sufficient in itself to support PD and I_{sc}. Serosal O_2 is practically always necessary and is usually sufficient to support PD and I_{sc}. Similar results have often been obtained with hamster jejunum, but the responses have been somewhat less consistent than with rats.

Qualitatively similar effects on PD have been obtained using a different technique in which serosal solution was circulated through a cannulated segment of everted rat or hamster jejunum by a bubble lift. The segment was immersed in mucosal solution in a test tube. Again, some inconsistency was found, but, in general, the results confirmed those with flat sheets of jejunum. Some of these results with hamsters are shown in Fig.4. This figure also shows the effect of transferring the segment to a new mucosal solution containing 10 mM D-galactose. The electrogenic effect of galactose was maintained in spite of serosal anaerobiosis, but was severely reduced by mucosal anaerobiosis.

Since basal transmural electrical activity (*i.e.* without organic solute) and galactose-

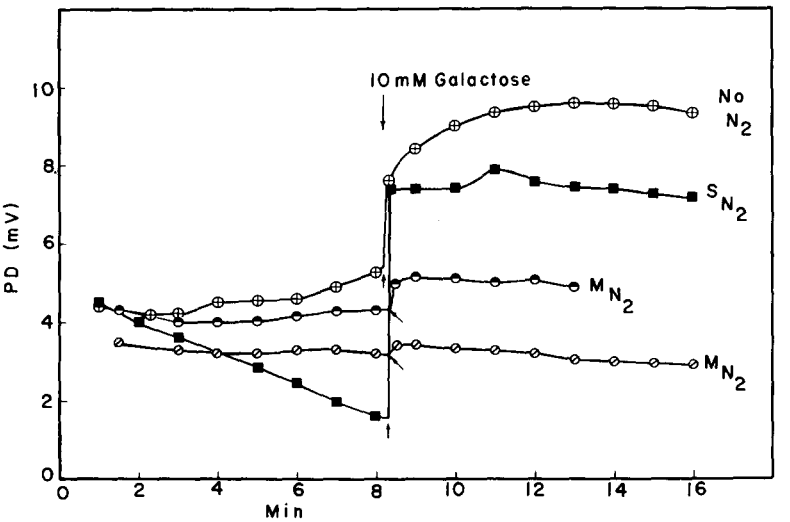

Fig.4. Results of four experiments with everted segments of hamster jejunum. Serosal solution (3.0 ml) was circulated and gassed by a bubble lift; mucosal solution (12.0 ml) was gassed in a test tube. Three different gassing combinations were employed: (1) O_2 on both sides (no N_2); (2) O_2 on mucosal side, N_2 on serosal side (S_{N_2}); (3) O_2 on serosal side, N_2 on mucosal side (M_{N_2}). O_2 and N_2 always contained 5% CO_2. At the arrows, the segments were transferred to new mucosal solutions containing 10.0 mM D-galactose.

induced electrical activity can be turned on and off selectively, they behave, at least partially, as separate and independent processes. The galactose-induced increments in PD and I_{sc} are not merely caused by augmenting the process responsible for basal activity. It is no surprise to find that both electrical processes require oxidative metabolism, but the present results imply that basal activity and galactose-induced activity require different sources of oxidative metabolism. We can surmise that two different pools of mitochondria are involved, one fed with O_2 more readily from the serosal solution, and the other fed more readily from the mucosal solution. Presumably, *in vivo,* both pools are adequately supplied with O_2 from the blood.

We have also determined that uphill transport of galactose across everted segments of hamster jejunum is entirely dependent upon mucosal O_2; it is influenced little or not at all by serosal anaerobiosis, but is completely blocked by mucosal anaerobiosis. Probably the same pool of mitochondria that supports the electrogenic effect of galactose also supports uphill transport of galactose.

We will speculate on the location of these mitochondrial pools. The one supporting basal electrical activity might be in the basal end of the villous epithelial cells, and the one supporting galactose-induced electrical activity and galactose transport might be in the apical end of these same cells. If these locations are correct, possible inconsistency with the Na^+-gradient hypothesis, as commonly formulated[1], should be considered.

Alternatively, perhaps the mitochondrial pool supporting galactose-induced electrical activity and galactose transport is in the villous epithelial cells, and the

pool supporting basal electrical activity is in the crypt epithelial cells (which, of course, are closer to the serosal solution). Location of the latter pool in the crypts would require revision of current ideas regarding the origin of basal electrical activity[2]. Obviously, both of these alternatives introduce interesting problems; at present we do not favor either one over the other.

Finally, we should consider why O_2 from either side does not keep all mitochondria adequately supplied. Evidently, the rate of O_2 diffusion into the tissue from either side cannot match the potential rate of O_2 utilization by the tissue, so that more distally located mitochondria cannot be adequately supplied. We have repeatedly noticed that contractions of the smooth muscle and electrical slow waves that originate in longitudinal muscle (see ref. 3) are abolished by serosal anaerobiosis; mucosal O_2 cannot support this activity, so at least we can be sure that adequate O_2 cannot diffuse all the way from the mucosal solution to the longitudinal muscle.

We wish to acknowledge that the possibility of this selective effect was originally suggested to R.D. Baker by Dr. John F. Quay (The Lilly Research Laboratories, Indianapolis, Ind.). This work was supported by U.S. Public Health Service Grant AM-05778. M.J. Wall received a Predoctoral Fellowship from the James W. McLaughlin Fellowship Fund for Infection and Immunity.

REFERENCES

1 S.G. Schultz and P.F. Curran, *Physiol. Rev.*, 50 (1970) 637.
2 S.G. Schultz and P.F. Curran, in C.F. Code, *Handbook of Physiology*, Section 6, *Alimentary Canal*, Vol. III, *Intestinal Absorption*, American Physiological Society, Washington, D.C., 1968, p. 1245.
3 R.D. Baker, *Am. J. Surg.*, 117 (1969) 781.