Microbiology Comment provides a platform for readers of **Microbiology** to communicate their personal observations and opinions in a more informal way than through the submission of papers.

Most of us feel, from time to time, that other authors have not acknowledged the work of our own or other groups or have omitted to interpret important aspects of their own data. Perhaps we have observations that, although not sufficient to merit a full paper, add a further dimension to one published by others. In other instances we may have a useful piece of methodology that we would like to share.

The Editors hope that readers will take full advantage of this section and use it to raise matters that hitherto have been confined to a limited audience.

Jon Saunders, Editor-in-Chief

***Escherichia coli* STb toxin and prostaglandin production**

Enterotoxigenic *Escherichia coli* cause diarrhoeal disease in humans and animals by elaboration of exotoxins which are divided into two groups based on thermal stability. The heat-labile (LT) and the heat-stable STa enterotoxins have been investigated in detail and much is known about their mechanisms of action and cellular targets. On the other hand, studies to determine the mechanism of action of *E. coli* STb (heat-stable) toxin are still required to elucidate precisely the way(s) in which it acts on intestinal tissues.

In spite of only rare studies conducted on the subject, some important facts have begun to emerge. A first study done by Greenberg *et al.* (2), using heat-treated (65°C, 30 min) STb culture filtrates, investigated the central pathway(s) triggered by STb. They were the first to observe a stimulation (8-fold) of the intestinal secretion of prostaglandin E₂ (PGE₂) in response to the administered toxin. STb had an early onset of action (30 min in the weaned pig loop assay) that resulted in intestinal PGE₂ secretion. At the same time, it was shown that STb stimulated secretion

through a cyclic-nucleotide-independent pathway. This early report thus indicated that STb was acting differently from LT and STa. Surprisingly, these observations were only recently confirmed. In fact, Hitotsubashi *et al.* (5), using purified toxin, confirmed that STb did not alter cyclic GMP nor cyclic AMP levels in intestinal mucosal cells. As a result of STb action, the level of PGE₂ increased and prostaglandin inhibitors such as aspirin and indomethacin significantly reduced the response to STb. Reduction of fluid secretion brought about by cyclooxygenase inhibitors has also been observed by us, using the rat loop assay as the animal model (J. D. Dubreuil & A. Letellier, unpublished observations).

Later, Fujii *et al.* (1) established that the quantity of PGE₂ produced by intestinal cells was directly related to the quantity of toxin administered to the mouse. Furthermore, the quantity of PGE₂ also correlated with the volume of fluid released into the intestinal lumen. Since then, two other groups have also reported that PGE₂ and 5-hydroxytryptamine (serotonin), are released into the luminal fluid as a result of STb action (3, 7). Peterson & Whipp (7), when comparing the secretory effects of cholera toxin (CT), STa and STb in the pig intestinal loop model, observed that combining maximal doses of STa and STb and of CT and STb yielded additive fluid accumulation. Together these experiments confirmed that the mechanism of action of STb enterotoxin is distinct from STa and CT, although CT as well as STb stimulated the release of PGE₂ and serotonin.

To summarize, results indicate that STb *in vivo* causes a dose-dependent increase in luminal PGE₂ and serotonin which are known secretagogues. As cyclooxygenase inhibitors diminish fluid secretion by STb, stimulation of arachidonic acid metabolism in intestinal epithelial cells is clearly established. On the other hand, PGE₂ is known to stimulate intestinal adenylate cyclase, resulting in the formation of cAMP (6). For STb, this rise in cyclic nucleotides that subsequently result in chloride secretion has not been observed. Thus, serotonin could mediate the remaining secretory effect observed for STb. In fact, at least part of PGE₂ seems to be produced in response to serotonin receptor stimulation as ketanserin, a receptor antagonist of serotonin, reduced the level of PGE₂ observed.

Receptor stimulation could be coupled to the activation of phosphoinositide turnover and/or activation of phospholipase A₂. In the gut, PGE₂ and serotonin promote intestinal secretion by apparently independent mechanisms, yet the release of serotonin and the synthesis of PGE₂ may be coupled events. Overall, PGE₂ formation appears to arise through both serotonin-dependent and serotonin-independent pathways (3). As we know that PGE₂ abolishes neutral sodium chloride absorption and increases electrogenic chloride ion secretion, it is quite puzzling to relate bicarbonate secretion and the absence of chloride observed in an Ussing chamber in response to STb (8).

From another point of view, being aware that PGE₂ has a direct effect on smooth muscle cells, its production in response to STb could be responsible for the spontaneous motility observed in the mouse ileum. As expected from this implication, papaverine, which is known to cause relaxation of smooth muscle, had an inhibitory effect on STb (4).

In conclusion, although some secretion mediators have been clearly shown to be produced in response to STb toxin, the intricacy of their role in the production of diarrhoeal disease still demands some additional studies.

J. Daniel Dubreuil

► GUIDELINES

Communications should be in the form of letters and should be brief and to the point. A single small Table or Figure may be included, as may a limited number of references (cited in the text by numbers, and listed in alphabetical order at the end of the letter). A short title (fewer than 50 characters) should be provided.

Approval for publication rests with the Editor-in-Chief, who reserves the right to edit letters and/or to make a brief reply. Other interested persons may also be invited to reply. The Editors of **Microbiology** do not necessarily agree with the views expressed in **Microbiology Comment**.

Contributions should be addressed to the Editor-in-Chief via the Editorial Office.

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