Diffusion against convection

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I read with great interest the recent paper entitled "Convective washout reduces antidiarrheal efficacy of enterocyte surface–targeted antisecretory drugs" by Jin et al. (2013) in the February 2013 issue of the Journal. In this paper, the influence on drug diffusion of adverse fluid convection was modeled by solving a diffusion convection equation with appropriate boundary conditions. In effect, the paper models the likelihood that solute can travel from the mucosal surface to the crypts in the face of adverse fluid secretion.

The concept of normal intestinal secretion from the enterocytes has been advocated many times, but its existence and function have periodically been questioned, as early as the late nineteenth century (Hoppe-Seyler, 1879). The need for luminally directed movement of fluid specifically to flush material or harmful bacteria away from the mucosal surface was advocated by Pavlov (1897) as itself confirming the existence of fluid secretion as a normally occurring physiological event. Although it can also be argued that secretion has no obvious normal physiological function (Lucas, 2010), the concept of an antibacterial purpose to secretion arises often (Barrett and Keely, 2000), as well as a putative need for secretion to transport in a timely way crypt cell products to the tips of the villi. Despite this, there are very few published solutions to this diffusion–convection problem, and the present authors are to be commended for providing one.

If their input values are accepted, it seems clear that normal secretion rates close to those observed in extreme cases of cholera (Fig. 2 of Jin et al., 2013) would be required to keep the mucosal surface free of bacteria. This is evident when the diffusion coefficient for bacteria is taken into account, as this can be of the order of 10^{-5} cm^2 sec^{-1} (Kiørboe et al., 2002) for some bacteria. At rates of fluid velocity that are allegedly normal, i.e., required by the premise that the small intestine normally secretes one liter of fluid per day, the Péclet number is likely to be far less than that assumed by the authors and insufficient to keep bacteria off the mucosal surface. The argument for normally occurring rates of secretion having a hygienic function seems fatally undermined by the calculations provided by the authors.

However, a concern that should be expressed is that the theoretical values selected by the authors may vary by an order of magnitude from real values. On the question of what constitutes reasonable values for convection and diffusion in the crypts, it may be that the authors have overestimated the velocity of convection and underestimated the diffusion coefficient within the crypts. In their Table 1 of baseline parameters, the diffusion coefficient in the crypt/villus region is estimated to be one tenth of the value in the intestinal lumen and implies that free diffusion does not occur within the fluid between the villi because of the presence of mucus. There is no doubt that viscosity is increased by mucus, but it is unlikely that diffusion is reduced to the extent that the authors assume. Using bovine mucus at a concentration of 10%, which had an extremely high viscosity, the reduction in the diffusion coefficient was estimated to be only 30% (Lucas, 1984), which meant that the diffusion coefficient was 70% of the normal value in aqueous solution. This could be higher with the concentrations of mucus that occur physiologically within the inter-villus space. In set agar as opposed to mucus in the flowing state, no reduction in diffusion coefficients is found (Schantz and Lauffer, 1962); hence, the selection by the authors of a diffusion coefficient that is one tenth of normal would need to be justified.

Accordingly, it would be interesting to know how the authors' calculations might change when the diffusion coefficient within the cryptal and inter-villus space is assumed to equal the value in aqueous solution and also when rates of secretion are not set to the extremely high value that occurs in cases of cholera.

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