



Fig. 2 Evolution of concepts regarding the proton barrier function of gastric mucus. **(A)** Prior to the 1990s, asymmetric transport of protons was assumed, with secreted acid freely traversing the layer by an unknown mechanism, whereas diffusion of back-diffusing acid was retarded by mucus to some extent. **(B)** After 1990, the concept of viscous fingering of secreted acid was supported by newly published data. A transgel pH gradient was also firmly supported by the available data. **(C)** With the advent of direct, non-invasive *in vivo* measurement of mucus pH, the most plausible explanation of the available data is that secreted acid freely crosses the mucus gel by simple diffusion. The modest retardation of proton diffusion through mucus damps rapid changes of luminal pH at the epithelial surface in order to enable the timely activation of intrinsic epithelial homeostatic mechanisms. Juxtamucosal pH is determined by luminal pH such that bicarbonate secretion predominates with pH3 luminal contents, whereas acidic secretion predominates when luminal pH is raised to 5.

Conclusions

Gastric mucus presents only a modest permeability barrier to acid diffusion. This characteristic enables secreted acid to freely traverse the mucus layer without specialized mechanisms such as tunnels or viscous fingers. Conversely, although mucus is not rate-limiting for proton back-diffusion, it appears to play an important role in damping rapid changes of luminal pH, providing time for activation of cellular homeostatic mechanisms. Recent non-invasive measurements of mucus pH *in vivo* strongly suggest that mucus pH is set simply by the pH of the fluid entering the layer. Figure 2 summarizes the evolution of the understanding of the barrier function of gastric mucus.

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