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SIR—In developing countries, the immunogenicity of orally administered vaccines is often substantially lower than in industrialised countries.[1] Proposed explanations for this phenomenon include direct interference between vaccine strains and concurrent wild-type infections with other enteric pathogens, which are far more common in developing countries, or non-specific interference through the induction of interferon or other immunomodulators.[1,2] However, a much higher prevalence of diarrhoea with concomitant destruction of the intestinal mucosa and reduced gastrointestinal transit time is also believed to have a prominent role.[1] The importance of addressing this problem is further underscored by the focus of the Children's Vaccine Initiative on the development of effective orally administered preparations.[2]

One simple method of improving the immunogenicity of oral vaccines might be the concurrent administration of oral rehydration solution (ORS), a simple, inexpensive, and universally available treatment for diarrhoea, which consists of sugar, electrolytes, and water.[3] Because of its substantial effect on water absorption in the small bowel, the use of ORS could result in a net flow of vaccine towards the intestinal mucosa, thus facilitating delivery of antigens from the intestinal lumen to M-cells and other gut-associated lymphoid tissue.[2,3] Rice-ORS might be especially useful as an adjuvant for oral immunisation, since it appears to increase intestinal absorption of water and reduce gastrointestinal transit time more effectively than sugar-based formulations.[4] Because of its slight alkalinity (pH 8–9), rice-ORS may also be more likely to preserve the integrity of vaccines upon exposure to gastric acid, and could potentially mitigate the need for coadministration of bicarbonate solution or other buffers which are often required for oral vaccinations. Formulations that also contain glutamine might be especially attractive as an adjuvant for rotavirus vaccines, given the role of glutamine as an energy source for the intestinal mucosa and its effectiveness in enhancing intestinal absorption of water and electrolytes in experimental rotavirus infections in piglets.[5]

We believe that the use of ORS as an adjuvant should be explored on the basis of its theoretical potential for improving the immunogenicity of orally administered vaccines, simplicity of administration, low cost, universal availability, and unparalleled record of safety. Although the effectiveness of such an approach may be more apparent in populations in whom diarrhoeal illness is endemic and in individuals, notably children, whose intestinal absorption may be chronically impaired from recurrent infection (even in the absence of overt diarrhoea), it may also prove beneficial when the intestinal flora and architecture are normal. The potential for ORS to improve the absorption or adsorption of other orally administered pharmaceuticals should also be examined.

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