Do human digestive physicochemical parameters contribute to children higher susceptibility to cryptosporidiosis ?

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Title: Do human digestive physicochemical parameters contribute to children higher susceptibility to cryptosporidiosis ?

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Abstract:

Background. *Cryptosporidium parvum* is responsible for a zoonotic disease affecting both human health and livestock. The parasite infects its host through the oral route and develops in ileal epithelial cells, leading to acute and sometimes lethal diarrhoea. The severity of cryptosporidiosis is closely related to the immune status of its host, young ruminants, infants, and immunocompromised individuals being more susceptible. However, the impact of the gastrointestinal route the parasite takes before reaching its site of infection on the severity of the disease, has never been investigated.

Materials & Methods. The *in vitro* computer-controlled TNO gastrointestinal model (TIM) was used for a comparative study of *C. parvum* survival and virulence under adult and child digestive conditions. Parasite survival and excystation kinetics in the *in vitro* digestive tract were determined by flow cytometry analysis while virulence was assessed after reinoculation of sporozoites onto HCT-8 cells. A luciferase reporter gene was also used to follow sporozoite activity throughout the digestive process. A global transcriptome analysis by RNA-Seq will be performed to identify differentially expressed parasite genes.

Results. Preliminary data show that the excystation rate is almost maximal in the duodenal compartment, one hour after the beginning of digestion in the TIM. However, a higher amount of parasites reaches the distal ileal compartment while protected in their oocyst shell upon simulation of child compared to adult digestive conditions. After three hours of digestion, the luciferase activity expressed by released sporozoites is significantly higher in the distal intestinal compartments of child compared to adult.

Conclusions. Differences in digestive physicochemical parameters may partially explain why children are more susceptible to cryptosporidiosis than adults. This study is the first one exploring the impact of various digestive conditions on *Cryptosporidium* using a sophisticated gastrointestinal model.