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Title:
Malaria parasites in the intestine – inflammation & intestinal permeability in *Plasmodium chabaudi* AS infected mice.

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CONTENT:

Background:
Mild gastrointestinal symptoms can be observed during *Plasmodium spp* infection with reports of increased intestinal permeability during *P. falciparum* infection. Malaria-induced enteritis may provide an opportunity for pathogenic intestinal bacteria to breach the intestinal mucosa, resulting in life-threatening bacteraemia.

Methods:
To begin to define intestinal pathology during a mild/resolving malaria infection, C57BL/6J mice were inoculated (i.p.) with recently mosquito-transmitted *P.chabaudi* AS (PcAS). At schizogony, intestinal tissues were collected for qPCR analysis and immunohistochemistry for immune mediators and malaria parasites. Inflammatory proteins were measured in plasma and faeces and intestinal permeability was assessed by measurement of FITC-dextran in plasma 1 hour after oral administration.

Results:
Parasitaemia peaked at 0.5-3.5% at days 7-9 and resolved by day 14, with mice experiencing significant and transient anaemia but no weight loss. Plasma IFN-ɣ was significantly elevated at day 7, with raised IL-10 concentrations on subsequent days. qRT-PCR of the intestine revealed a significant increase in transcripts for *ifng* and *cxcl10* on days 7 to 11, respectively, along with parasite 18S rRNA. Histological analysis revealed parasites within blood vessels of both the submucosa and intestinal villi and evidence of mild crypt hyperplasia. In faeces, the inflammatory marker lactoferrin was raised on days 9 and 11. FITC-dextran in plasma (evidence of increased intestinal permeability) was detected on days 9 and 11, and was significantly positively correlated with peripheral parasitemia and faecal lactoferrin.

Conclusions:
Using a relevant model, we have found that mild, acute malaria infection is associated with intestinal inflammation and increased intestinal permeability. This model can now be used to explore the mechanisms of parasite-induced intestinal inflammation and to assess the impact of increased intestinal permeability on translocation of pathogenic enterobacteria.

Keywords:
plasmodium, intestinal permeability, gastroenteritis