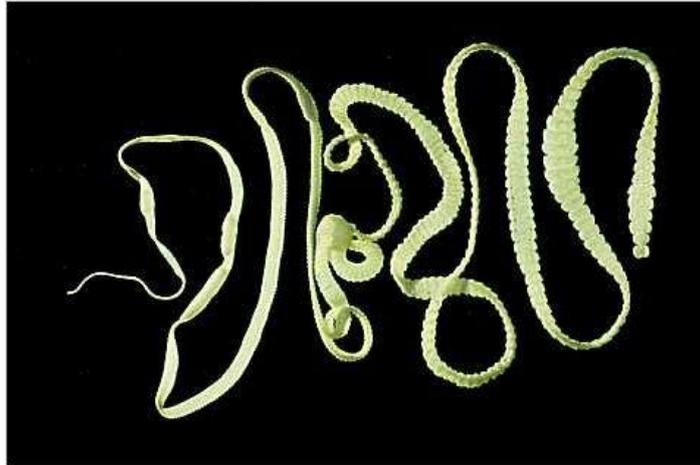


British Society for Parasitology – Journal Club article:



Therapeutic helminths may harm as well as heal...

Incidence of autoimmune disorders such as inflammatory bowel disease and rheumatoid arthritis (RA) in the developed world has risen over the last forty years. The 'hygiene hypothesis' proposes that this is linked to decreased exposure to the infectious organisms we have evolved and adapted to interact with at an immunological level- a result of improved public health and sanitation, antibiotics and vaccinations.

Our missing helminths appear critical to this; a number of studies suggest that concomitant infection with certain species of worms can result in modulation and alleviation of some or all of the symptoms associated with autoimmune disease – suggesting that once those infections kept these disorders in check. It seems helminths can act as powerful immune modulators which could hypothetically be utilised to treat patients – a concept known as 'helminthic therapy'.

However, a recent publication by Graepel *et al.*, in the *International Journal for Parasitology* offers a word of caution for therapeutic exploitation of helminths. The authors argue that infection with the cestode *Hymenolepis diminuta* in Balb/C mice contributed to worsening of joint inflammation and pain in a polyarthritic model of arthritis (the K/BxN arthritrogenic serum model) which captures many of the features of RA. This was in contrast to previous work which had shown that *H. diminuta* infection, when given prophylactically or therapeutically, significantly protected from or alleviated the symptoms of Freund's complete adjuvant (FCA) -induced monoarthritis (a less useful model for comparison with RA).

But why the difference? The researchers discovered that under conditions of the K/BxN model, infection with *H. diminuta* led to higher levels of inflammatory innate immune cell infiltration into arthritic joints. In addition, infection resulted in mast cell activation and elevated levels of C5a- a pro-inflammatory component of the complement pathway. This is

important, as both mast cell and C5a activation are required elements for successful induction of polyarthritis in the K/BxN model. Therefore, they may have exacerbated polyarthritic symptoms via an additive effect during infection. Neither is enhanced in *H. diminuta* infected animals with concomitant FCA-monoarthritis, suggesting an explanation for the benevolence of infection in that setting.

Helminth parasites could become wildly useful tools in battling autoimmune disease; some genera such as *Trichuris* are already being trialled in humans for their therapeutic effects. However, this study gives us food for thought when considering the importance of fully characterising the immunological response to individual helminth species, and being aware of how that might interact with the immunological etiology of a targeted disease.

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Full Reference:

Graepel, R., Leug, G., Wang, A., Villemaine, M., Jirik, F.R., Sharkey, K.A., et al. 2013. Murine autoimmune arthritis is exaggerated by infection with the rat tapeworm *Hymenolepis diminuta*. *International Journal for Parasitology*. doi: 10.1016/j.ijpara.2013.02.006. [Epub ahead of print]

Image:

Adult *H.diminuta* from rat intestine. Image courtesy of Micrographia

(<http://www.micrographia.com/specbiol/helminth/platyhel/cest0100/hymenol0.htm>)