ANALYSIS

How the gut expels parasites: new clues

Intestinal epithelium acts as a natural barrier against invading pathogens. New research on how parasites affect intestinal epithelial-cell proliferation and what controls cell proliferation may provide a basis for new treatments of gastrointestinal infections.

The mystery of worm expulsion

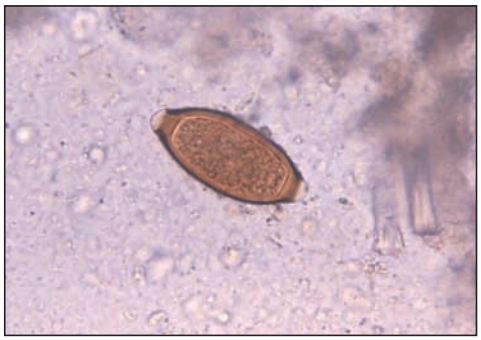
Parasitic infections of the gastrointestinal tract are common. *Trichuris trichiura* (whipworm) is prevalent in the developing world, especially in rural areas where sanitation is poor. Trichuriasis afflicts 500–600 million people worldwide.[1] Although most people with whipworms are asymptomatic, school-age children are particularly prone to heavy infection and can present acutely with dysentery and anemia. Chronic infections can lead to malnutrition, growth retardation and rectal prolapse.

For years, researchers have been investigating why worms are expelled from some patients but cause chronic infections in others. New research by Cliffe and colleagues[2] adds to our understanding of the intestinal mechanism by which parasites are expelled.

The epithelial lining of the intestine undergoes a continual process of renewal wherein the cells proliferate, differentiate and die at a certain rate. Cliffe's group has postulated that the turnover of these intestinal cells might act as an "epithelial escalator," with the rate of cell turnover being related to the rate of parasite expulsion.

To test this idea, Cliffe and colleagues observed mice of 2 strains known respectively to be resistant and susceptible to trichuriasis. After infection, the authors monitored proliferation rates of cecal epithelial cells. Although the cells increased in both strains of mice, they found that cell proliferation in the resistant mice was twice that in the susceptible strain. After 35 days, proliferation rates in the 2 strains had reached similar levels, but mice of the susceptible strain remained infected with worms. Moreover, the authors showed that cell turnover is likely mediated by the immune system: they found that the cytokine interleukin-3 increased the rate of turnover, whereas CXCL10, a chemokine, decreased it.

These findings point to epithelial homeostasis as a novel and important mechanism for controlling nematode infections in the intestine. As the authors note, the intestinal hyperplasia seen in response to worms is also observed with many other pathogens, making modulation of epithelial homeostasis a potential target for therapy development.



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An egg from the nematode *Trichuris trichiura*.

Further investigation into the role of epithelial homeostasis in the immune response is therefore warranted, in the hope that it will broaden our understanding of how to eradicate the organism from infected patients. — *David Secko*, Vancouver

References

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2. Cliffe LJ, Humphreys NE, Lane TE, Potten CS, Booth C, Grencis RK. Accelerated intestinal epithelial cell turnover: a new mechanism of parasite expulsion. *Science* 2005;308(5727): 1463-5.

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