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Letter to the Editor

Not infection with parasitic worms, but rather colonization with therapeutic helminths

The report by Williams and colleagues in the August issue of Immunology Letters [1] describes a case in which a scientist exposed himself/herself to a helminth well-known among the veterinary community, the porcine whipworm. The intention was to observe the effects of exposure to the helminth on the scientist's immune disorder and to monitor the fate of the organisms following that exposure.

The scientist saw improvement in his or her psoriasis, adding yet another anecdote consistent with observations we have made using a socio-medical methodology: Hundreds of people are using helminths to alleviate a variety of inflammatory conditions [2,3]. The collective experiences of these self-treating individuals in concert with a variety of studies using laboratory animal models suggest that the presence of helminths in the ecosystem of the human body is probably necessary to ensure healthy immune function. The working paradigm in the field is that helminths have the potential to alleviate one of the ultimate causes of inflammatory disease in Western society, biota depletion, defined as the loss of biodiversity from the ecosystem of the human body as a result of modern technology [4–6].

The ova of the porcine whipworm, Trichurus suis ova (TSO), were first identified as a promising therapeutic agent more than 10 years ago [7], and rapidly came to be viewed as the most promising helminth for therapeutic use. With no substantial momentum behind the development of any other therapeutic helminth for clinical use, the field suffered more than a catastrophic failure when Ovamed, the owner of the TSO technology, shut down clinical trials in mid-2015 due to a lack of effectiveness.

But failure of a helminth in a clinical trial, more so than failure of a precisely characterized pharmaceutical, is not necessarily a sign that potential is low. Our socio-medical studies [2] suggest that storage of TSO at a pH above 4, the standard used in the Ovamed-sponsored trials, may impede the therapeutic effect of the organisms in humans. Fortunately, Williams used a lower pH formulation (produced in-house using the ParaTech protocol and stored at pH 1; personal communication from co-author Nejsum to William Parker), consistent with the formulation that worked in early trials and that received consistently high marks from individuals self-treating with helminths [2]. Importantly, the Williams et al. study highlights the fact that it is premature to put nails in the coffin of therapeutic TSO.

Helminthic therapy, the use of helminths to treat inflammatory disease, faces a number of hurdles in addition to potential complexities in the formulation of effective helminth preparations [8,9]. Foremost among these hurdles is a public relations crisis. Indeed, our imagination of infection with parasites provides fodder for nightmares and horror films alike, and appears even less palatable than drinking water from a natural source, or living without soap, activities that once provided our pre-industrial ancestors with more than enough helminths to properly exercise and train their immune systems.

Our view is that helminth therapy's public relations crisis can be alleviated in part by a more rigorous adherence to basic definitions in biology. If an organism benefits its host without causing harm, it is by definition a mutualist, not a parasite. By the same token, if it does not cause disease, then it is by definition colonization, not infection and not a burden. We have described the host-helminth relationship as contextual [6]. The same tapeworm that pushes one host over the brink of starvation into death might alleviate multiple sclerosis with no adverse effects in another host, proving itself to be a parasite in one setting and a mutualist in another. Further, the contextual nature of host-symbiont relationships can extend beyond the individual, to the society as a whole. Typical individuals living in a Western society will probably interact with helminths much differently than individuals in a pre-industrial, overly crowded agrarian society, who in turn may relate differently than individuals from a pre-agrarian hunter-gatherer society. The practical implications of this contextual relationship for public health are potentially vast. The same society that once benefited from access to clean drinking water, effectively reducing the number of symbiotic helminths, may now desperately need to domestic the organisms for controlled reintroduction.

As science overcame superstition and fear during the last century, we learned that bacterial symbionts are not all pathogens out to kill us. History is in the throes of repeating itself as we learn the same lesson with our larger intestinal symbionts. Part of that learning process involves changing our view of helminths as burdensome, infectious parasites, realizing that they are some of our most complex and ancient symbionts, whose intricate and nuanced connection with us is influenced not only by our culture, but also by the language we use to describe them.

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