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Title:
Host-parasite interactions and the immunobiology of cestodes

Date:
2016-03-01

Citation:
Mahanty, S. (2016). Host-parasite interactions and the immunobiology of cestodes.
Parasite Immunology, 38 (3), pp.121-123. <https://doi.org/10.1111/pim.12309>.

Persistent Link:
<https://hdl.handle.net/11343/290996>

Received Date : 08-Feb-2016

Accepted Date : 08-Feb-2016

Article type : Commissioned Review or Article

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Editorial: Host-parasite interactions and the immunobiology of cestodes

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This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/pim.12309](https://doi.org/10.1111/pim.12309)

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30 Cestodes, or tapeworms, are a heterogeneous group of parasitic worms that have two
characteristic features: they have flat ribbon-like bodies and they lack an alimentary tract,
requiring them to absorb nutrients directly from their environment. Among the cestodes, adult
worms generally inhabit the gastrointestinal tract, attaching themselves to the mucosa by
means of the scolex, but the larval stages have a wide tissue habitat distribution, with the
35 ability to make their way to many organs. The absence of an alimentary canal differentiates
cestodes from trematodes and nematodes, and likely influences host-parasite interactions and
immune reactions to the parasites. The outer tegument of the body has a dual function serving
not only as a protective barrier but also a metabolically active layer through which essential
nutrients can be absorbed, and waste material transported out of the organism.
40 The adult body consists of a chain of segments or proglottids, which can be immature, mature
or gravid, containing developed uterus packed with eggs. In a sense each tapeworm is
composed of a chain of “individuals”, complete with a set of reproductive organs, with
segments becoming progressively more mature as they grow away from the head or scolex .
Humans can serve both as definitive hosts and intermediate hosts, in which case the larvae fail
45 to develop into adult worms (Table 1).

As a group, the cestodes are medically important parasitic worms since they infect humans and
other mammals worldwide (Table 1). Although precise numbers for the prevalence and impact
of disease attributable to these parasites are not well determined in underdeveloped regions of
50 the world where they are endemic, the two most prevalent cestode species, *Echinococcus* and
Taenia represent major public burdens, infecting an estimated one million (echinococcosis)
and accounting for up to a third of adult onset epilepsy in the areas of transmission
(cysticercosis) (1). However, research on these parasites has been limited and the diseases
have been formally accorded “neglected” tropical disease status by the World Health
55 organization in recognition of their importance as a health burden on the poor (1).

A consequence of the neglect of the burden of cestode infections has been a relative paucity of
published information on host-parasite interactions with cestodes and the factors regulating

inflammatory pathology and protective immunity against these parasites. Although there have
60 been a modest number of reviews of immunological aspects of infections with *Echinococcus*
and *Taenia* spp. in recent years (2-7), the focus in those reviews has been largely on older data.
Many of the older studies either suggested or concluded that immunomodulation associated
with cestodes is similar in nature to that seen in other helminth infections: a T helper (Th) 2
biased immune response that resulted in immunomodulation (2-7). More recent studies have
65 found that the host response is more nuanced, with elements of pro-inflammatory and
immunoregulatory responses at different stages or clinical manifestation of infection (4, 5, 8).
This is not surprising since the parasites are well adapted to their hosts and clearly able to
escape immune attack and destruction over long periods of time; yet as the parasites
degenerate or die, there is a significant amount of inflammation and pathology in affected
70 tissues. The collection of papers in this special issue aims to review recent knowledge of the
immunology of cestode infections, discuss the pathogenesis of disease in humans and explore
applications of the immunological knowledge gained from recent studies to diagnosis and
management of the infections.

75 Peon *et al.* (9) have comprehensively reviewed recent investigations of immune responses to
Taeniids in animal models, and discuss parallels and differences between responses to cestodes
and those reported and now well recognized in nematode and trematode infections. The
review by Gonzales *et al.* (10) discusses the immunopathogenesis of varied clinical
manifestations of cysticercosis, illustrating the key role of inflammation in the pathogenesis of
80 central nervous system dysfunction, and implicating a number of mediators of inflammation,
including TNF- α , chemokines and effectors cells (macrophages and eosinophils) in the
regulation of pathology. A number of proinflammatory mediators, such as substance P have also
be shown to play a potentially direct role in epileptogenesis in the chronic phase of infection. A
next review, by Fleury *et al.* (11) delves into the immune mechanisms operating in the CNS and
85 peripheral circulation that underlie the extraordinary inflammatory pathology of
neurocysticercosis, as revealed by studies in humans. These studies, summarized in the review,
have shown that a mixed proinflammatory and regulatory response is seen in this infection, and

the balance between these two opposing immunological reactions governs the severity of pathology.

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A review by Lightowlers *et al.* (12) explores practical applications of accumulating knowledge about immune responses to *T. solium*. In this review, the authors discuss what they see as the best use of parasitologic, immunological and molecular tests in control programs – in the assessment of success of an intervention strategy. The characteristics of the antibody responses following infection in pigs and humans are considered. The pros and cons of each test are discussed, and the importance of optimizing the sensitivity and specificity of the best tests, detecting antibodies in serum, is highlighted. This will be crucial in the setting of falling prevalence rates. Immunodiagnostic tests should have utility in the assessment of success of control programs, particularly in pigs (the major source of human taeniid infections), which are likely to be targeted in most intervention scenarios. A review of the supporting data is followed by the authors' recommendations for research priorities in investigating future applications of immunological knowledge to disease control and elimination.

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The next three articles focus on *Echinococcus* spp., summarizing and discussing longstanding and recent discoveries related to host responses and parasite determinants of host immunity. Tamarozzi *et al.* (13) discuss recently published work that elucidates the characteristics of anti-parasite humoral and cellular responses in the intermediate hosts (humans). The paper reviews immunological manipulation by the developing larva and cellular and humoral immune evasion mechanisms that have been identified in humans. Diaz *et al.* (14) review our current state of knowledge of *E. granulosus* molecules that interact and regulate immunological responses in the host. They discuss the characteristics of the immunodominant protection-inducing molecule (Eg95) and non-protective molecules that serve as diagnostic antigens (antigens B and 5) and explore the influence of the structure and subcomponents of the antigens on the host immune response.

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In last review Wang and Gottstein (15) turn to *E. multilocularis*, a much less prevalent parasite than *E. granulosus*, but one that causes a far more aggressive infection with features of neoplasia. Wang and Gottstein review current knowledge of innate and adaptive (cellular) responses to the parasite in animal models and human hosts. An interesting finding in the animal studies, and supported by limited data in humans, is the key role of regulatory T cells in down-regulating inflammatory responses that are damaging to the parasite, but also cause host tissue destruction.

The study of the immunobiology of cestodes has made significant progress in the past decade. A renewed focus on these parasites as neglected diseases will likely lead to more attention for research and eradication efforts. It is likely that immunological tools will play key roles in the control and eradication strategy, and a better understanding of the immune responses elucidated by these parasites will be valuable for these efforts. This issue, with a focus on cestodes, brings together a dispersed and seemingly disparate body of literature and is a timely contribution to the research effort.

Acknowledgement

This research was supported in part by the Intramural Research Program of the National Institute of Allergy and Infectious Diseases, NIH.

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Table 1. Major cestode infections of humans

Parasite	Definitive host	Intermediate host	Disease
<i>Diphyllobothrium latum</i> (Fish Tapeworm)	Human, Marine mammals	Fish	Diphyllobothriasis
<i>Dipylidium caninum</i>	Dog	Human	Intestinal infection
<i>Echinococcus granulosus</i>	Canines	Human	Cystic echinococcosis (Hydatid Disease)
<i>Echinococcus multilocularis</i>	Canines	Human	Alveolar echinococcosis
<i>Hymenolepis nana</i> (Dwarf Tapeworm)	Dog	Human	Intestinal infections, neoplasia
<i>Hymenolepis diminuta</i>	Rat	Human	Intestinal infection
<i>Spirometra</i> spp	Frogs, Snakes	Human	Sparganosis
<i>Taenia solium</i> (Pork Tapeworm)	Human	Pig, Human	Intestinal tapeworm (taeniasis) and cysticercosis
<i>Taenia saginata</i> (Beef Tapeworm)	Human	Herbivores	Intestinal tapeworm (taeniasis)
<i>Taenia multiceps</i> or <i>T. serialis</i>	Canines	Human, Sheep, Herbivores	Coenurosis