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THE IMMUNOLOGY OF TAENIASIS/CYSTICERCOSIS: IMPLICATIONS FOR PREVENTION AND TREATMENT

Carlton Evans [1] and the Cysticercosis Working Group in Peru [2]

INTRODUCTION

Cysticercosis is a parasitic disease that results from ingestion of *Taenia solium* tapeworm eggs. These microscopic eggs contaminate the environment in endemic areas and when pigs ingest them porcine cysticercosis develops. Porcine cysticercosis is the presence of pea sized *T. solium* larvae in pig tissues, making the pig the intermediate host for the parasite larvae. Pigs usually remain healthy despite this parasitosis, but their meat is greatly reduced in value. In the Andean region of Peru up to 50% of pigs have cysticercosis, contributing to economic hardship and malnutrition.[1]

When humans eat infected pork the *T. solium* larvae hatch out in the bowel where they may grow into adult tapeworms, growing up to 13 m in length. These tapeworms produce further eggs which are released into the environment in the faeces, completing the parasite life-cycle. Humans are therefore the natural definitive host to the adult tapeworm.

Infection of pig tissues with *T. solium* larvae and of the human bowel with adult tapeworms constitute the natural life-cycle which is essential for the continuing existence of the parasite in communities. This propagation depends upon evasion or modulation of host immunity: the larval and adult parasites must survive within their hosts without being destroyed by immune responses and without killing their hosts. The evolution of the parasite has selected parasites which most efficiently parasitize pigs and humans with minimal host disease.

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However, the principal significance of the *T. solium* parasite is its ability to infect humans as an 'accidental' intermediate host: when humans accidentally ingest microscopic *T. solium* eggs they develop cysticercosis. Cysticercosis is therefore caught from humans with tapeworms, not from pigs. The presence of *T. solium* larvae in human tissues is an important cause of neurological disability and mortality in many developing countries including 0.5 to 4% of people in Perú' and México.[3] This human cysticercosis is a 'dead end' for the parasite and there has therefore been no evolutionary pressure for the *T. solium* larvae to evade immune recognition in human tissues. The human host is not tolerant of the larval stage of the parasite and the resultant immune recognition and inflammation may contribute greatly to the pathogenesis of human cysticercosis.

IMMUNOLOGY OF ASYMPTOMATIC CYSTICERCOSIS

The pig is the usual intermediate host for the *T. solium* larvae and tolerates living cysticerci well. In some endemic regions examination of the pig's tongue for palpable living larvae has been routine practice before purchase since biblical times, because this reliably diagnoses cysticercosis.[1] The usual absence of apparent illness in infected pigs is remarkable considering that thousands of cysticerci are often found at autopsy, scattered throughout neurological and other tissues.

In humans, autopsies of victims of warfare and road traffic accidents have revealed that a large proportion (typically 80%) of neurocysticercosis infections are asymptomatic, discovered incidentally at necropsy.[4] Living cysticerci may occasionally cause disease through local pressure effects or by obstructing the flow of cerebro-spinal fluid, despite the absence of a host inflammatory response. Asymptomatic human cysticercosis may be diagnosed serologically or by biopsying subcutaneous lesions. Although circulating anticysticercus antibodies have access to the surface of cysticerci, as illustrated by imaging studies with radio-labelled antibodies,[5] hundreds of eight mm cysticerci may live within human tissues, evading immune destruction and symptomatic inflammation.

The immune response to cysticerci has been studied mainly because of the need for a diagnostic blood test. Although the literature is confused by numerous serologic tests evaluated with varying degrees of scientific rigor, it is clear that virtually all cases of symptomatic cysticercosis are associated with a detectable humoral immune response, the exception being a minority of

single-cyst infections. Furthermore, sero-epidemiological studies in endemic regions have revealed a similar rate of antibody positivity in healthy people to the prevalence of asymptomatic cysticercosis in autopsy series.[2]

How do *T. solium* larvae survive within pig and human tissues without causing symptomatic inflammation in the majority of cases, despite the presence of circulating antibodies and evidence of cell mediated immunity? Our understanding of the complex mechanisms employed by helminths to prevent immune-mediated destruction is increasing rapidly[6] and several of the mechanisms employed by cysticerci have been elucidated.[7]

MECHANISMS OF IMMUNE MODULATION BY CYSTICERCI

Sequestration. After a brief period of migration, *T. solium* larvae lodge in host tissues and form cysticerci. The site at which they settle and the nature of their relationship to the encapsulating host may contribute to sequestration of the parasites from immune attack. The unequal distribution of cysticerci throughout body tissues does not mirror regional blood flow but may result from selective invasion by the parasite or differential survival and encystment of larvae in different tissues.

In humans, cysticerci occur commonly within the brain, spinal cord and eye, all of which may be considered to be 'immunologically privileged sites'. The central nervous system differs from other tissues in: the presence of the blood brain barrier which prevents conventional lymphocyte recirculation; the inducible rather than constitutive expression of major histocompatibility class I and II molecules; and the presence of specialized cells that execute immunological effector functions. These features may explain the unique interaction between the central nervous and immune systems[8] and the resistance of the brain parenchyma to leukocyte diapedesis.[9] Recent evidence also suggests that inflammatory cell apoptosis is up-regulated in these sites.[10] However, we are not aware of systematic study of the number of cysticerci in human brain compared with non-neurological tissues and the apparent predilection for the brain may simply reflect the severe symptoms which result from lesions in this organ.

The firm, fibrous encapsulation which surrounds some cysticerci, particularly in non-neurological tissues, is unlikely to form a physical barrier to immunity since humoral factors do gain access to the internal fluids of cysticerci[11] and chemotherapeutic challenge or death of cysticerci is followed by immediate intense inflammatory cell infiltration.[12]