THE IMMUNOLOGY OF THE HOST-PARASITE RELATIONSHIP IN *Taenia solium* CYSTICERCOSIS: IMPLICATIONS FOR PREVENTION AND THERAPY

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

INTRODUCTION

Cysticercosis is a parasitic disease that results from ingestion of the microscopic eggs of the *Taenia solium* tapeworm. These eggs contaminate the environment in endemic areas and pigs which ingest them become intermediate hosts for the parasite by developing pea sized *T. solium* larvae in their tissues, a condition called porcine cysticercosis. 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 develop into adult tapeworms which can grow up to 8 m in length. These intestinal tapeworms produce eggs which are released into the environment in the feces, 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 because the larval and adult parasites must survive without killing their hosts and without being destroyed by host immune responses. The evolution of the parasite would be expected to select parasites which most efficiently parasitize pig tissues and human intestines and which cause minimal disease in these hosts.

The principal significance of the *T. solium* parasite is, however, its ability to infect human tissues as an 'accidental' intermediate host; when humans in-

[1] *University of Cambridge Medical School, Cambridge, England, UK.*

[2] *The Cysticercosis Working Group in Perú, Coordination Board: Robert H. Gilman, Armando E. González, Héctor H. García, Manuela Verástegui, Víctor C.W. Tsang.*

gest microscopic *T. solium* eggs, they develop cysticercosis. Human cysticercosis is, therefore, caught from humans with tapeworms and 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 Peru[2] and Mexico.[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 does not have persistent tolerance for the larval stage of the parasite and the resultant immune recognition and inflammation may contribute greatly to the pathogenesis of human cysticercosis.

THE IMMUNOLOGY OF ASYMPTOMATIC CYSTICERCOSIS

The pig is the natural intermediate host for *T. solium* larvae and multiple cysticerci may survive within pig tissues. In some endemic regions, examination of pigs tongues for palpable living larvae before purchase has been routine practice 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 (reviewed by Gemmell *et al*, 1988[4]). Living cysticerci may occasionally cause disease through local pressure effects or by obstructing the flow of cerebrospinal fluid, despite the absence of a host inflammatory response. In contrast, symptomatic cysticercosis is usually associated with inflammation around one or more degenerating cysticerci.

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 in different ways, 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. Imaging studies with radio-labeled antibodies have also demonstrated that these circulating anticysticercus antibodies have access to the surface of cysticerci.[5] Furthermore, sero-epidemiological studies in endemic regions have revealed a similar rate of antibody positivity in healthy people to the prevalence of asymptomatic cysticercosis suggested by autopsy series.[2]

T. solium larvae therefore usually survive within pig and human tissues without causing symptomatic inflammation, despite the presence of circulating antibodies. Our understanding of the complex mechanisms employed by helminths to prevent immune-mediated destruction is increasing rapidly (reviewed by Maizels *et al*, 1993[6]) and several of the mechanisms employed by cysticerci have been elucidated and are discussed below.

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'. Distinct immunological characteristics of the central nervous system compared with other tissues include: 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 (reviewed by Fabry *et al*, 1994[7]) and the resistance of the brain parenchyma to leukocyte diapedesis.[8] Recent evidence also suggests that inflammatory cell apoptosis is up-regulated in these sites.[9] Although we are not aware of systematic studies of the number of cysticerci in human brain compared with non-neurological tissues, in our experience peripheral, mainly muscular cysticerci are far more numerous than those in the central nervous system. The apparent predilection of cysticerci for the brain may, therefore, 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[10] and chemotherapeutic challenge or death of cysticerci is rapidly followed by intense inflammatory cell infiltration.[11]

Antigenic shifts. Concomitant immunity describes protection against newly invading larvae in hosts harboring an established worm infection. This may result from changes or 'shifts' in the antigens expressed by parasites as they develop through different stages of their life-cycle. Hence, adult larvae may be able to counteract those immune effector mechanisms that kill immature forms. Concomitant immunity has not been demonstrated in *T. solium* cysticercosis. However, animals may harbor vaccine-derived *T. saginata* and *T. hydatigena* larvae despite having acquired resistance to further egg challenge. This mechanism may explain the lack of overwhelming cysticercosis in hyperendemic regions since animals may only be able to acquire cysticercosis for 1 or 2 weeks after primary exposure to the parasite. Thereafter, the animal may be resistant to re-infection despite the survival of viable cysticerci resulting from the primary infection.[4]

Molecular mimicry. Parasites may evade immune recognition by synthesizing host-like antigenic determinants. Willms *et al*[12] detected immunoglobulin G (IgG) on the surface of *T. solium* cysticerci by immuno-electron microscopy, but after purification this IgG showed no specificity for antigens on the cysticercus. The possibility that it was synthesized by the parasite was tested *in vitro* by translation of parasite-derived messenger-RNA. One of the protein products was precipitable with rabbit anti-pig IgG, providing evidence that the cysticercus itself synthesized host-mimicking antigens. The occurrence of homologous genome sequences in host and parasite may explain the selectivity of cestodes for particular hosts, for example *T. solium* for pigs and humans.

Masking of cysticercal antigens by host immunoglobulins. The presence of host antibodies in fresh cysticerci obtained from human surgery has been compared with the antibodies present in patient's serum and cerebrospinal fluid (CSF). Although circulating human IgG was present with the same frequency as IgG on the surface of the parasite, IgM, IgA and IgE were present only on the surface of the parasite and could not be detected in the serum or CSF. Furthermore, *T. solium* cysticerci have recently been shown to express an Fc receptor for IgG. These results, reviewed by Flisser,[13] are consistent with the hypothesis that cysticerci are masked by host immunoglobulins, although the importance of this possible mechanism of immune evasion has not been established.

Modulation of host immunity. Some evidence suggests that *T. solium* cysticerci may not only 'hide from' the host immune system, but they may also actively suppress host immunity. A secretion product of living cysticerci, anti-

gen B, has been shown to bind to and inhibit C1q, the first component of the complement cascade.[14] As yet unidentified secretory products of cysticerci also have a suppressive effect on cultured human lymphocytes stimulated with phytohaemagglutinin.[15] Similarly, viable cysticerci implanted into the peritoneal cavity of mice release factors which depress rather than enhance lymphocyte reactivity.[12] Mice infected with *T. crassiceps* larvae also had suppressed cell-mediated immunity. Furthermore, there was evidence of up-regulated Th2 and down-regulated Th1 type T-lymphocytes in the vicinity of infecting larvae.[16] Further elucidation of the mechanisms by which living larvae suppress local immune responses may allow more specific and effective anti-inflammatory therapy to be administered during cestocidal therapy.

THE IMMUNOPATHOLOGY OF SYMPTOMATIC CYSTICERCOSIS

T. solium larvae commonly live within humans as accidental intermediate hosts for many years without causing symptoms or significant inflammation. However, the principal importance of the parasite is the symptomatic disease which results from failure of this immune tolerance when one or more cysticerci degenerate within the brain. The association between cysticercal degeneration and the onset of symptoms is suggested by the contrasting radioimaging studies of asymptomatic and symptomatic intracerebral lesions, findings at excision biopsy and autopsy. However, more compelling evidence is provided by the time-course of human infections and the transient adverse effects of cestocidal therapy, both of which are discussed below.

THE TIME COURSE OF HUMAN CYSTICERCOSIS

A study of 450 British soldiers who acquired cysticercosis whilst stationed in India[17] provided information concerning the time course of disease. Few soldiers returned from India with epilepsy, the majority developed seizures 2-8 years after infection. The longest interval between infection with cysticercosis and appearance of symptoms was 30 years. This is remarkable because studies in pigs and humans have shown that cysticerci take only 60-70 days to reach maturity after infection.[18] Symptoms therefore developed years after the infecting larvae had reached full size. To explain this, it was proposed that a biologic objective of cysticerci while in the tissues of the intermediate host is to remain quiescent and that the death of the parasite liberates toxins, causing cerebral irritation.[19] Alternatively, the death of cysticerci may end ac-

tive immune evasion by the parasite, allowing immunologically mediated inflammation to develop and cause symptoms. The absence of seizures or other neurological signs in cysticercotic pigs, in contrast to humans with cysticercosis, may be explained by the fact that pigs are usually slaughtered in their first year of life, before cysticerci degenerate and cause inflammation. Alternatively, *T. solium* larvae may be better able to evade immune recognition in the pig compared with human tissues because of the evolutionary pressures discussed in the introduction.

THE IMMUNE RESPONSE TO TREATMENT OF CYSTICERCOSIS

Studies of the experimental treatment of 'asymptomatic' cysticercotic pigs showed that while parasites had little macroscopic or histopathological evidence of damage prior to treatment, cestocidal therapy with praziquantel led to accumulation of eosinophils around cysticerci, followed by lymphocytes and macrophages which appeared to phagocytose cysticercal material and cell debris. The macroscopic disappearance of killed cysticerci took 2 months.[13] We have observed similar macroscopic and radio-imaging disappearance of cysticerci following cestocidal therapy. This rarely precipitated the death of heavily infected pigs.

A single low dose of the cestocidal drug praziquantel given to humans to treat intestinal parasitosis may cause sufficient damage to latent asymptomatic cysticerci that inflammation and epilepsy result, providing evidence for active immune evasion or suppression by living cysticerci.[20] Full dose cestocidal therapy administered for the empirical therapy of human neurocysticercosis has rarely precipitated overwhelming, fatal cerebral inflammation when the human brain has contained many cysticerci (e.g. Wadia, 1988[21]). An immunological study of neurocysticercosis patients treated with praziquantel (without major adverse effects) reported elevated soluble interleukin-2 (IL-2) in the CSF suggesting a Th1-type immune response to therapy.[22] This contrasts with the Th2-type immune response found in an animal model of viable cysticerci.[16] These findings are consistent with the hypothesis that living cysticerci facilitate immune evasion by inducing a Th2-type immune response until the death of the larval parasite allows Th1-mediated inflammation to develop.

THE IMMUNE RESPONSE IN SYMPTOMATIC CYSTICERCOSIS

The reason that untreated cysticerci eventually degenerate in human tissues is not known but it has been proposed that death of the parasite may

simply occur at the end of its natural life-expectancy. Alternative possibilities include cumulative damage from chronic host inflammation, or alterations in host tolerance for encysted parasites following re-infection or the ingestion of parasite antigens.[23] The human tissue response to a degenerating cysticercus is granulomatous, consisting of plasma cells, lymphocytes, eosinophils and macrophages enclosed in a network of connective tissue. In later stages, host cells penetrate the remnants of the parasite. After 1-2 months, a glial or connective tissue scar remains, which may then calcify.[4]

This relatively benign natural history is often reported from Southern India where, in some hospitals, patients with epilepsy resulting from degeneration of a solitary parenchymal cysticercus are treated symptomatically. Inflammation and the resultant symptoms may resolve despite the lack of active intervention.[24,25] In contrast, one or more degenerating cysticerci may cause chronic, progressive granulomatous inflammation which may prove fatal despite steroid and or surgical therapy; a clinical syndrome which appears to be more common in South America. There have been reports of neurocysticercosis dependant upon chronic steroid therapy to suppress inflammation. At autopsy, these have revealed only the remnants of degenerated cysticerci surrounded by granulomatous inflammation. It is not clear whether variations in the parasite or the host response explain these variable clinical syndromes.

Our ongoing research suggests that patients with symptomatic human cysticercosis, compared with controls, have elevated concentrations of eosinophil-selective mediators but not T-cell and neutrophil chemokines. It is not yet known whether these cytokines mediate principally helpful immune responses or inflammatory injury. The presence of eosinophil chemo-attractants is consistent with the role of eosinophils in immunity to helminths. In one series of neurocysticercosis patients, eosinophils were found in over 57% of inflammatory CSF samples.[26] It is noteworthy that ablation of the eosinophil chemokine IL-5 was associated with more severe intracranial disease in a murine model of *Angiostrongylus cantonensis* infection, consistent with a protective effect of eosinophils in this parasitic infection of the brain.[27]

IMPLICATIONS FOR CYSTICERCOSIS THERAPY

If it is not simply the presence of living *T. solium* larvae, but rather their death, that causes inflammation and symptoms in the majority of cases of human neurocysticercosis, then what is the role of cestocidal treatment?

Praziquantel and albendazole both kill *T. solium* larvae and have become widely used for treating human neurocysticercosis. Although they may accelerate radiological resolution of cerebral cysticerci, this is associated with some morbidity and rarely mortality. Since epidemiological research has shown that the natural history of asymptomatic neurocysticercosis is most commonly benign and hospital based studies suggest that symptomatic inflammation often signifies the start of cysticercal degeneration, cestocidal therapy may be expected to have limited therapeutic value in human neurocysticercosis.

The management of human neurocysticercosis is considered in detail elsewhere in this volume but our understanding of the immunopathogenesis of neurocysticercosis makes it unsurprising that recent randomized, placebo controlled trials have shown no clinical benefit of cestocidal therapy over steroid therapy alone[25,28] and have focused attention on the methodology of earlier studies.[29]

IMMUNE PROCESSES IN CYSTICERCOSIS PREVENTION AND CONTROL

Cysticercosis is a disease of poverty and social under-development. Human cysticercosis may be prevented by provision of sanitation and treatment of tapeworm carriers. The parasite life-cycle may also be broken by enforcing meat inspection, adequately freezing/cooking pork or by large scale commercial pig rearing which denies pigs access to human feces. Such improvements in public health and animal husbandry have led to the virtual eradication of human and porcine cysticercosis in wealthy countries but these measures are not currently practicable in many developing regions.[4]

VACCINATION TO PREVENT CYSTICERCOSIS

Human vaccination to prevent cysticercosis has not been widely considered as an appropriate intervention in endemic regions because little is known about the immunology of human cysticercosis and symptomatic cysticercosis is greatly under-diagnosed.[2] It has been suggested that cysticercosis occurs with greater than expected frequency in immunologically deficient children[30] but this uncontrolled observation may reflect a chance association or diagnostic bias rather than an effect of immunodeficiency on susceptibility. Cysticercosis has not been noted to be common in immunosuppressed or immunodeficient adults.[31]

In common with most other human cestodes, protective immunity against the adult tapeworm has not been demonstrated and adult tapeworm carriage does not appear to protect against cysticercosis. However, there is evidence in experimental animal models that the immune response in the definitive host can reject tapeworms or cause them to destrobilate.[4]

Vaccination of pigs to prevent porcine cysticercosis has been proposed as a strategy to improve animal health, meat yield and to break the parasite life-cycle, potentially preventing human disease. Molinari[32] showed that vaccination of healthy pigs with cysticercal antigens caused partial protection against the subsequent development of porcine cysticercosis. Likewise, immunization of pigs with excretory-secretory products of *T. solium* oncospheres caused a decrease in the number of cysticerci which developed from subsequent challenge infection.[24] Similar protective vaccination has been developed for other *Taenia* species.[33,34] Oral vaccination against *T. solium* has not been attempted. Prophylactic vaccination may not be practicable in areas where cysticercosis is common because in these regions pigs typically roam freely and are reared by individual families on a subsistence basis.[4]

IMMUNOTHERAPY FOR PORCINE CYSTICERCOSIS

In contrast to preventive measures which are difficult to apply in endemic regions, an inexpensive treatment for porcine cysticercosis may be of practical value in the poorer areas where the disease is most common. Such a treatment may be sought after and used by owners of infected pigs if it improved animal health, meat yield and especially if it caused the degeneration of cysticerci that are easily visible in infected 'measly' pork, halving its value.[1] Immunotherapy for porcine cysticercosis may, therefore, be a cost-effective way of breaking the life cycle of the parasite, preventing human as well as animal disease and it may have the advantage of protecting against re-infection. Our group is investigating treatments for porcine cysticercosis with drug therapy[35] and immunotherapy.[23]

Cysticerci may be destroyed by immunological processes. Herbert and Oberg[36] infected nine pigs with cysticercosis at the age of two months and re-infected four of these pigs two months later. Paradoxically, autopsy revealed significantly fewer cysticerci in the pigs that had been infected twice, suggesting that re-infection accelerated cysticercus degeneration and absorption. Similarly, re-infection of cows infected with *T. saginata* and of sheep infected with *T. hydatigena* caused degeneration of established cysticerci.[37-39]

Molinari, Meza and Tato[40] reported that immunotherapy caused the resolution of cysticercosis in two pigs and this immunotherapy was then evaluated in a field trial.[41] The prevalence of cysticercosis fell significantly in two villages where pigs were vaccinated repeatedly. However, there was no control group and cysticercosis was diagnosed by tongue palpation only. Seven cysticercotic pigs given immunotherapy were studied in more detail and 73% of cysts excised from them failed to evaginate compared with 5% in seven untreated cysticercotic pigs.

These encouraging results led us to further investigate the effect of immunotherapy on porcine cysticercosis in a prospective, randomized, controlled and blinded study.[23] This study confirmed that when pigs naturally infected with *T. solium* cysticercosis were inoculated with cysticercal antigen, the viability of cysticerci was significantly reduced. The percentage of cysticerci that showed no evidence of viability was more than doubled in the group of pigs given crude antigen and most of these animals developed new electro-immuno transfer blot bands suggesting an antibody response to the immunotherapy. However, all of the pigs remained macroscopically heavily infected and most of the cysticerci in the majority of the treated animals appeared viable for causing human disease.

The statistically significant effect of immunotherapy on parasite viability illustrates the active nature of the host-parasite interaction and the potential for manipulating this relationship in the prevention and treatment of this infection.

CONCLUSIONS

T. solium has evolved to survive within pig tissues and the human bowel without causing morbidity sufficient to impair host reproduction, but there has been no such evolutionary pressure to limit pathology when the larval stage of the parasite accidentally infects human tissues. Little is known about the immunology of adult tapeworm infections in the human bowel but some of the mechanisms by which tapeworm larvae survive within human tissues have been established. Manipulation of this host-parasite relationship may provide an opportunity for controlling the parasite.

Symptomatic human neurocysticercosis most commonly results from break-down of host tolerance associated with death of the infecting larval parasite. The resultant inflammation may be asymptomatic, transiently symptomatic, chronic or fatal. Neurocysticercosis may be treated with

anticonvulsants and anti-inflammatory drugs. The addition of cestocidal therapy is unlikely to affect the course of the disease once cysticerci are degenerating or destroyed. Research is in progress to clarify the value and safety of using cestocidal drugs to kill cysticerci in patients with epilepsy or those with asymptomatic cysticercosis. This is likely to depend upon the number and location of cysticerci. Increased understanding of the immunopathogenesis of symptomatic neurocysticercosis may allow improved and more specific anti-inflammatory therapy in this common neurological disease.

ACKNOWLEDGEMENTS

Dr. Carlton Evans gratefully acknowledges the editorial assistance of Tapasree Goswami and financial support from: TEMCO, Rhone-Poulenc PLC, The Fox Memorial Trust, the British Medical Research Council and Trinity College, Cambridge, England.

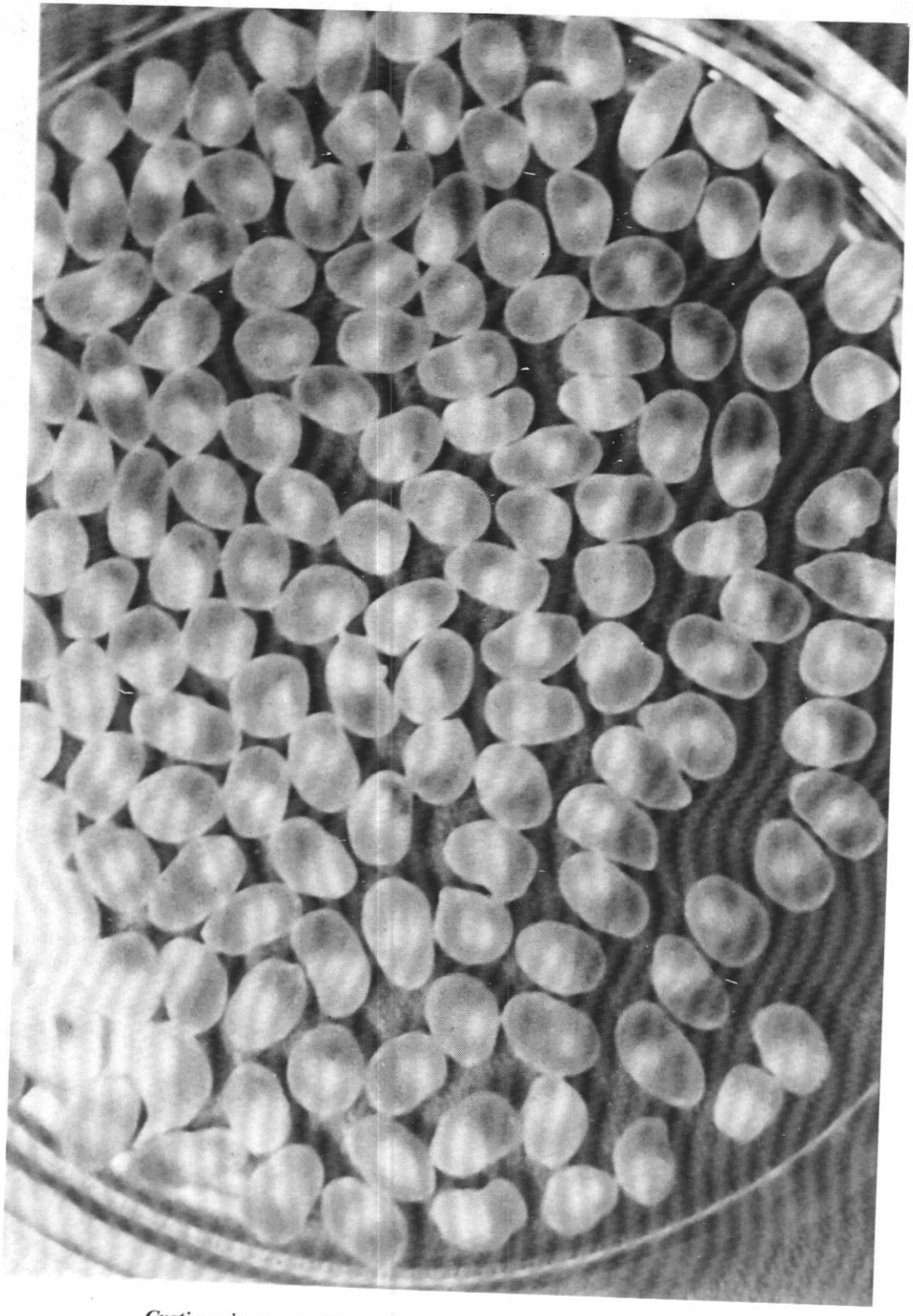
REFERENCES

1. Gonzalez AE, Cama V, Gilman RH, Tsang VC, Pilcher JB, Chavera A, *et al.* Prevalence and comparison of serologic assays, necropsy, and tongue examination for the diagnosis of porcine cysticercosis in Peru. *American Journal of Tropical Medicine and Hygiene* 1990; 43: 194-9.
2. García HH, Martinez M, Gilman RH, Herrera G, Tsang VCW, Pilcher JB, *et al.* Diagnosis of cysticercosis in endemic regions. *Lancet* 1991; 338: 549-51.
3. Flisser A. Neurocysticercosis in Mexico. *Parasitology Today* 1988; 4: 131-7.
4. Gemmell M, Matyas Z, Pawlowsky Z, Soulsby EJL (Eds.) *Guidelines for surveillance and control of Taeniasis/cysticercosis.* VPH/83.49. Geneva: World Health Organization, 1983: 1-207.
5. Skromne-Kadlubik G, Celis C, Ferez A. Cysticercosis of the nervous system: diagnosis by means of specific radioimmunoscan. *Annals of Neurology* 1977; 2: 343-4.
6. Maizels RM, Bundy DAP, Selkirk ME, Smith DF, Anderson RM. Immunological modulation and evasion by helminth parasites in human population. *Nature* 1993; 365: 797-805.
7. Fabry Z, Raine CS, Hart MN. Nervous tissue as an immune compartment: the dialect of the immune response in the CNS. *Immunology Today* 1994; 15: 218-24.
8. Anderson PB, Perry H, Gordon S. Intracerebral injection of proinflammatory cytokines or leukocyte chemotaxins induces minimal myelomonocytic cell recruitment to the parenchyma of the central nervous system. *Journal of Experimental Medicine* 1992; 176: 255-9.
9. Streilein JW. Unravelling immune privilege. *Science* 1995; 270: 1158-9.

10. Willms K, Arcos L. *T. solium:* host serum proteins on the cysticercus surface identified by ultrastructural immunoenzyme technique. *Experimental Parasitology* 1977; 43: 396-406.
11. Rickard MD, Williams JF. Hydatidosis and cysticercosis. Immune mechanisms and immunization against infection. *Advances in Parasitology* 1982; 21: 229-96.
12. Willms K, Merchant MT, Arcos L, Sealey M, Diaz S, de Leon LD. Immunopathology of cysticercosis. In: Larralde C, Willms K, Oritz-Oritz L, Sela M (Eds.) *Molecules, Cells & Parasites in Immunology*. New York: Academic Press; 1980: 145-62.
13. Flisser A. Taeniasis and cysticercosis due to *T. solium*. In: Tsieh Sun (Ed.) *Progress in Clinical Parasitology*. Florida: CRC Press Inc; 1994: 77-116.
14. Laclette JP, Shoemaker CB, Richter D, Arcos L, Pante N, Cohen C, *et al.* Paramyosin inhibits complement C1. *Journal of Immunology* 1992; 148: 124-8.
15. Molinari JL, Tato P, Reynosa OA, Cazares JML. Depressive effect of a *T. solium* cysticercus factor on cultured human lymphocytes stimulated with phytohemaglutinin. *Annals of Tropical Medicine and Parasitology* 1990; 84: 205-8.
16. Villa OF, Kuhn RE. Mice infected with the larvae of *Taenia crassiceps* exhibit a Th2-like immune response with concomitant anergy and downregulation of Th1-associated phenomena. *Parasitology* 1996; 112: 561-70.
17. Dixon HBF, Lipscomb FM. Cysticercosis: an analysis and follow-up of 450 cases. *Medical Research Council Special Report. London. Her Majesty's Stationary Office* 1961; 299: 1-58.
18. Grove DI. *A History of Human Helminthology.* Oxon: CAB Intl; 1990: 355-83.
19. MacArthur WP. Cysticercosis of the brain. *British Medical Journal* 1935; ii: 1229.
20. Johnson RB. Potential hazard of mass praziquantel use. *American Journal of Medicine* 1986; 80: A88.
21. Wadia N, Desai S, Bhatt M. Disseminated cysticercosis. New observations, including CT scan findings and experience with treatment by praziquantel. *Brain* 1988; 111: 597-614
22. Rolfs AF, Muhlschlegel R, Jansen-Rocsseck AR, Martins EA, Bedaque WM, Tamburus L, *et al.* Clinical and immunologic follow-up study of patients with neurocysticercosis after treatment with praziquantel. *Neurology.* 1995; 45: 532-8.
23. Evans CAW, Gonzalez AE, Gilman RH, Verastegui M, Garcia HH, Chavera A, *et al.* Immunotherapy for porcine cysticercosis: implications for prevention of human disease. *American Journal of Tropical Medicine and Hygiene* 1997; 56: 33-7.
24. Pathak KML, Gaur SMS. Immunization of pigs with culture antigens of *T. solium. Veterinary Parasitology* 1980; 34: 353-6.
25. Padma MV, Behari M, Misra MK, Ahuja GK. Albendazole in neurocysticercosis. *National Medical Journal of India* 1995; 8: 255-8.
26. Sotelo J, Guerrero V, Rubio F. Neurocysticercosis: a new classification based on active and inactive forms. A study of 753 cases. *Archives of Internal Medicine* 1985; 145: 442-5.
27. Sasaki O, Suguya H, Ishida K, Yoshimura K. Ablation of eosinophils with anti-IL-5 antibody enhances the survival of intracranial worms of *Angiostrongylus canteonensis* in the mouse. *Parasite Immunology* 1993; 15: 349-54.
28. Carpio A, Santillan F, Leon P, Flores C, Hauser A. Is the course of neurocysticercosis

modified by treatment with antihelminthic agents? *Archives of Internal Medicine* 1995; 155: 1982-8.

29. Kramer LD. Antihelminthic therapy for neurocysticercosis. *Archives of Neurology* 1990; 47: 1059-60.
30. Flisser A. Discussion. In: Flisser A, Willms K, Laclette JP, Larralde C, Ridaura C, Beltran F (Eds.) *Cysticercosis: Present state of Knowledge and perspectives.* New York: Academic Press; 1982: 611.
31. Soto-Hernandez JL, Ostrosky-Zeichner L, Tavera C, Gomez-Avina A. Neurocysticercosis and HIV infection. Report of two cases and a review. *Surgical Neurology* 1996; 45: 57-61.
32. Molinari JL, Meza R, Suarez B, Palacios S, Tato P. *T. solium*: immunity in hogs to the cysticercus. *Experimental Parasitology* 1983; 55: 340-57.
33. Flisser A, Perez-Montfort R, Larralde C. The immunology of human and animal cysticercosis: a review. *Bulletin of the World Health Organization* 1979; 57: 839-56.
34. Johnson KS, Harrison GBL, Lightowlers MW, O'Hoy KL, Cougle WG, Dempster RP, *et al.* Vaccination against ovine cysticercosis using a defined recombinant antigen. *Nature* 1989; 338: 585-7.
35. Gonzales AE, Garcia HH, Gilman RH, Gavidia CM, Tsang VCW, Bernal T, *et al.* Effective, single dose treatment of porcine cysticercosis with oxfendazole. *American Journal of Tropical Medicine and Hygiene* 1996; 54: 391-4.
36. Herbert IV, Oberg C. Cysticercosis in pigs due to infection with *T. solium*, Linneaus 1758. In: Soulsby EJL (Ed.) *Parasitic Zoonoses, Clinical and Experimental Studies.* London: Academic Press; 1974: 187-95.
37. Gallie GJ, Sewell MMH. The survival of *Cysticercus bovis* in resistant calves. *Veterinary Record* 1972; 91: 481-2.
38. Sewell MMH, Gallie GJ. Immunological studies on experimental infections with the larval stage of *T. saginata.* In: Soulsby EJL (Ed.) *Parasitic Zoonoses, Clinical and Experimental Studies.* London: Academic Press, 1974.
39. Gemmell MA. Hydatidosis and cysticercosis. III. Induced resistance to the larval phase. *Australian Veterinarian Journal* 1970; 46: 366-9.
40. Molinari JL, Meza R, Tato P. *T. solium*: cell reactions to the larva (*Cysticercus cellulosae*) in naturally parasitised, immunized hogs. *Experimental Parasitology* 1983; 56: 327-38.
41. Molinari JL, Soto R, Tato D, Rodriguez D, Retana A, Sepulveda J, *et al.* Immunization against porcine cysticercosis in an endemic area in Mexico: a field and laboratory study. *American Journal of Tropical Medicine and Hygiene* 1993; 49: 502-12.



Cysticerci extracted from pig muscle (Photo Dr. H. Escalante).