Toxoplasma gondii
(description for intermediate hosts)

Host species

- Cat (definitive host) (Jones 1973, Wong & Remington 1993)
- All laboratory and domestic animals, birds and humans (intermediate hosts)
- Differential host species susceptibility is reviewed by Innes (1997)

Organotropism

- Central nervous system (Jones 1973, Wong & Remington 1993)
- Muscle and other organs may also be involved.

Clinical disease

- Usually inapparent
- Occasionally neurological symptoms and/or febrile disease

Morbidity and mortality

- Largely depending on the route of infection, parasite strain and dose, and the immunologic state of the host (Dubey & Frenkel 1973, Fernando 1982, Suzuki et al. 1988)
- Clinical disease most likely in young animals or immunocompromised hosts
- Resistance to acute infection and formation of cysts in the brain of mice are genetically controlled (Araujo et al. 1976, Williams et al. 1978).
- Differences in a gene(s) within the H-2D region correlate with resistance or susceptibility to development of Toxoplasma (T.) encephalitis in mice (Jones & Erb 1985, Suzuki et al. 1991, Blackwell et al. 1993).

Zoonotic relevance

- Transmission to humans from other intermediate hosts only by ingestion of uncooked tissues containing T. gondii (Dubey 1994).
Interference with research

**Physiology**

- Mice infected with *T. gondii* exhibit ovarian dysfunction with uterine atrophy and thyroidal dysfunction (decline in serum thyroxine levels), probably due to impaired release of hypothalamic releasing hormones (Stahl et al. 1995a, 1995b, Stahl et al. 1998)

- *T. gondii* infection increases toxicity of some drugs (e.g., neostigmine) (Starec et al. 1997)

**Pathology**

- Central nervous system: organisms intra- or extracellular in the neuropil, within granulomatous encephalitis, glial nodules or perivascular infiltration; occasionally accompanied by meningitis and/or scattered neuronal degeneration; occasionally fibrinoid necrosis of vessel walls in association with microthrombi in the centres of small necrotic foci (Sasaki et al. 1981, Hay et al. 1984, Kittas et al. 1984, Ferguson & Hutchinson 1987, Ferguson et al. 1991).

- Lesions in immunocompromised hosts may lack inflammatory infiltrates and solely consist of small necrotic foci and scattered cysts (Buxton 1980, Johnson 1992)

- Muscle and other organs may be involved with necrotic foci, granulomas and pseudocysts

**Immunology**

- Acute and chronic *T. gondii* infection modulate the immune responses in mice (Nguyen et al. 1998)


- *T. gondii*-infected cells are resistant to multiple inducers of apoptosis (Nash et al. 1998).

- Gamma delta T cells induce expression of heat shock protein 65 in macrophages of mice infected with *T. gondii*, thereby preventing the apoptosis of infected macrophages (Hisaeda et al. 1997).

- Intracellular *T. gondii* interferes with the MHC class I and class II antigen presentation pathway of murine macrophages (Luder et al. 1998).


- NK cell activity and production of IFN-g are increased during the course of *T. gondii* infection in mice; IFN-g plays a critical role in preventing cyst rupture and toxoplasmic encephalitis (Hauser et al. 1982, Suzuki et al. 1989, Sher et al. 1993, Hunter et al. 1994a).


- IL-12 is crucial for the generation of both innate resistance mechanisms during the acute phase of infection and T cell-dependent acquired immunity during the chronic phase (Johnson & Sayles, 1997).

- Various other cytokines, such as IFN-b, IL-1, IL-4, IL-6, IL-10, TGF-b, and TNF-a, are implicated in the pathogenesis of *T. gondii* infection (Chang et al. 1990, Orellana et al. 1991, Gazzinelli et al. 1992b, Sher et al. 1993, Hunter et al. 1995a,

- Inducible nitric oxide is essential for host control of chronic T. gondii infection (Scharton-Kersten et al. 1997).
- Innate resistance mechanisms during T. gondii infection are reviewed by Alexander et al. (1997); T cell-mediated immunity during T. gondii infection is reviewed by Denkers & Gazzinelli (1998).

**Infectiology**

- Macrophage clearance and killing of Listeria monocytogenes and Salmonella typhi-murium are decreased in mice infected with T. gondii (Wing et al. 1983)
- Infection with murine leukemia virus may lead to reactivation of chronic T. gondii infection (Gazzinelli et al. 1992a, Watanabe et al. 1993)
- Infection with murine cytomegalovirus results in reactivation of Toxoplasma pneumonia (Goetz & Pomeroy 1996)
- Mice infected with T. gondii are resistant to proliferation of Cryptococcus neoformans cells in the brain (Aguirre et al. 1996)

**References**

Aguirre KM, Sayles PC, Gibson GW, et al. (1996) Resistance to Cryptococcus neoformans is associated with an inflammatory response to Toxoplasma gondii in the central nervous system of mice. Infection and Immunity 64, 77-82


Brown CR, McLeod R (1990) Class I MHC genes and CD8+ T cells determine cyst number in Toxoplasma gondii infection. Journal of Immunology 145, 3438-3441


Chang HR, Grau GE, Pechere JC (1990) Role of TNF and IL-1 in infection with Toxoplasma gondii. Immunology 69, 33-37

Channon JY, Kasper LH (1996) Toxoplasma gondii-induced immune suppression by human peripheral blood monocytes: role of gamma interferon. Infection and Immunity 64, 1181-1189

Denkers EY, Caspar P, Hieny S, et al. (1996) Toxoplasma gondii infection induces specific nonresponsiveness in lymphocytes bearing the V beta 5 chain of the mouse T cell receptor. Journal of Immunology 156, 1089-1094


Gazzinelli RT, Denkers EY, Sher A (1993) Host resistance to Toxoplasma gondii: model for studying the selective induction of cell-mediated immunity by intracellular parasites. Infectious Agents and Disease 2, 139-149

Gazzinelli RT, Hartley JW, Fredrickson TN, et al. (1992a) Opportunistic infections and retrovirus-induced immunodeficiency: studies of acute and chronic infections with Toxoplasma gondii in mice infected with LP-BM5 Murine Leukemia Viruses. Infection and Immunology 60, 4394-4401

Gazzinelli RT, Oswald IP, Jamos SL, et al. (1992b) IL-10 inhibits parasite killing and nitrogen oxide production by IFN-g activated macrophages. Journal of Immunology 148, 1792-1796

Gazzinelli RT, Xu Y, Hieny S, et al. (1992c) Simultaneous depletion of CD4+ and CD8+ T lymphocytes is required to reactivate chronic infection with Toxoplasma gondii. Journal of Immunology 149, 175-180


Hunter CA, Chizzonite R, Remington JS (1995b) IL-1b is required for IL-12 to induce production of IFN-γ by NK cells. A role for IL-1b in the T cell-independent mechanism of resistance against intracellular pathogens. Journal of Immunology 155, 4347-4354.

Hunter CA, Subauste C, Remington JS (1994a) Production of IFN-g by NK cells from Toxoplasma gondii infected SCID mice: regulation by IL-10, IL-12 and TNF-a. Infection and Immunity 62, 2818-2824


Innes EA (1997). Toxoplasmosis: comparative species susceptibility and host immune response. Comparative Immunology, Microbiology and Infectious Diseases 20, 131-138

Jebbari H, Roberts CW, Ferguson DJ, et al. (1998) A protective role for IL-6 during early infection with Toxoplasma gondii. Parasite Immunology 20, 231-239

Johnson LL (1992) SCID mouse models of acute and relapsing chronic Toxoplasma gondii infections. Infection and Immunity 60, 3719-3724


Jones SR (1973) Toxoplasmosis: a review. Journal of the American Veterinary Medical Association 163, 1038-1042


Khan IA, Matsuura T, Kasper LH (1996) Activation-mediated CD4+ T cell unresponsiveness during acute Toxoplasma gondii infection in mice. International Immunology 8, 887-896


Roberts CW, Ferguson DJ, Jebbari H, et al. (1996) Different roles for interleukin-4 during the course of Toxoplasma gondii infection. Infection and Immunity 64, 897-904


Sher A, Oswald IP, Hieny S, et al. (1993) Toxoplasma gondii induces a T-independent IFN-g response in natural killer cells that requires both adherent accessory cells and tumor necrosis factor-a. Journal of Immunology 150, 3982-3989


Suzuki Y, Conley FK, Remington JS (1988) Differences in virulence and development of encephalitis during chronic infection vary with the strain of Toxoplasma gondii. Journal of Infectious Diseases 159, 790-794


Walker W, Roberts CW, Ferguson DJ, et al. (1997) Innate immunity to Toxoplasma gondii is influenced by gender and is associated with differences in interleukin-12 and gamma interferon production. Infection and Immunity 65, 1119-1121


Author: G. Pohlmeyer / M. Mähler