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).
- Age, gender, and pregnancy influence susceptibility to T. gondii infection in mice (Johnson et al. 1995, Thouvenin et al. 1997, Walker et al. 1997).

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 is able to induce transient immune down-regulation (Channon & Kasper 1996, Denkers et al. 1996, Khan et al. 1996)
- 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).
- CD4+ and CD8+ T lymphocytes appear to act in concert to prevent reactivation of chronic T. gondii infection (Brown & McLeod 1990, Araujo 1991, Gazzinelli et al. 1992c).
- 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).
- Cytokine levels are elevated in infected humans and in murine models of toxoplasmosis. Overview about immunopathology of T. gondii infection: Beaman et al. 1992, Gazzinelli et al. 1993, Subauste & Remington 1993, Hunter & Remington 1994, Hunter et al. 1994b.
- 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, Gazinelli et al. 1992b, Sher et al. 1993, Hunter et al. 1995a,

1995b, Roberts et al. 1996, Bessieres et al. 1997, Neyer et al. 1997, Deckert-Schluter et al. 1998, Jebbari et al. 1998).

- 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 typhimurium 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

Alexander J, Scharton-Kersten TM, Yap G, et al. (1997) Mechanisms of innate resistance to Toxoplasma gondii infection. Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences 352, 1355-1359

Araujo FG (1991) Depletion of L3T4+ (CD4+) T lymphocytes prevents development of resistance to Toxoplasma gondii in mice. Infection and Immunity 59, 1614-1619

Araujo FG, Williams DM, Grumet FC, et al. (1976) Strain-dependent differences in murine susceptibility to toxoplasma. Infection and Immunity 13, 1528-1530

Beaman MH, WongSY, Remington JS (1992) Cytokines, Toxoplasma and intracellular parasitism. Immunological Reviews 127, 97-117

Bessieres MH, Swierczynski B, Cassaing S, et al. (1997) Role of IFN-g, TNF-a, IL4 and IL10 in the regulation of experimental Toxoplasma gondii infection. Journal of Eukaryotic Microbiology 44, 87S

Blackwell JM, Roberts CW, Alexander J (1993) Influence of genes within the MHC on mortality and brain cyst development in mice infected with Toxoplasma gondii: kinetics of immune regulation in BALB H-2 congenic mice. Parasite Immunology 15, 317-324

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

Buxton D (1980) Experimental infection of athymic mice with Toxoplasma gondii. Journal of Medical Microbiology 13, 307-311

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

Deckert-Schluter M, Bluethmann H, Rang A, et al. (1998) Crucial role of TNF receptor type 1 (p55), but not of TNF receptor type 2 (p75), in murine toxoplasmosis. Journal of Immunology 160, 3427-3436

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

Denkers EY, Gazzinelli RT (1998) Regulation and function of T-cell-mediated immunity during Toxoplasma gondii infection. Clinical Microbiology Reviews 11, 569-588

Dubey JP (1994) Toxoplasmosis. Journal of the American Veterinary Medical Association 205, 1593-1598

Dubey JP, Frenkel JK (1973) Experimental Toxoplasma infection in mice with strains producing oocysts. Journal of Parasitology 59, 505-512

Ferguson DJ, Graham DI, Hutchinson WM (1991) Pathological changes in the brains of mice infected with Toxoplasma gondii: a histological, imunocytochemical and ultrastructural study. International Journal of Experimental Pathology 72, 463-474

Ferguson DJ, Hutchinson WM (1987) The host-parasite relationship of Toxoplasma gondii in the brains of chronically infected mice. Virchows Archiv. A, Pathological Anatomy and Histopathology 411, 39-43

Fernando MA (1982) Pathology and pathogenicity. In: The biology of the coccidia (Long PL, ed). Baltimore: University Park Press, pp 287-327

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 Immunity 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

Goetz L, Pomeroy C (1996) Impact of prophylactic ganciclovir on bronchoalveolar lavage lymphocyte numbers and phenotypes in murine cytomegalovirus-induced reactivation of Toxoplasma pneumonia. Journal of Laboratory and Clinical Medicine 128, 384-391

Hauser WE, Sharma SD, Remington JS (1982) Natural killer cells induced by acute and chronic Toxoplasma infection. Cellular Immunology 69, 330-346

Hay J, Hair DM, Graham DI (1984) Localization of brain damage in mice following Toxoplasma infection. Annals of Tropical Medicine and Parasitology 78, 657-659

Hisaeda H, Sakai T, Ishikawa H, et al. (1997) Heat shock protein 65 induced by gamma-delta T cells prevents apoptosis of macrophages and contributes to host defense in mice infected with Toxoplasma gondii. Journal of Immunology 159, 2375-2381

Hunter CA, Bermudez L, Beernink H, et al. (1995a) Transforming growth factor-b inhibits interleukin-12 induced production of interferon-g by natural killer cells: a role for transforming growth factor-b in the regulation of T cell-independent resistance to Toxoplasma gondii. European Journal of Immunology 25, 994-1000

Hunter CA, Chizzonite R, Remington JS (1995b) IL-1b is required for IL-12 to induce production of IFN-g 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, Remington JS (1994) Immunopathogenesis of toxoplasmic encephalitis. Journal of Infectious Diseases 170, 1057-1067

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

Hunter CA, Subauste C, Remington JS (1994b) The role of cytokines in toxoplasmosis. Biotherapy 7, 237-247

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

Johnson LL, Gibson GW, Sayles PC (1995) Preimmune resistance to Toxoplasma gondii in aged and young adult mice. Journal of Parasitology 81, 894-899

Johnson LL, Sayles PC (1997) Interleukin-12, dendritic cells, and the initiation of host-protective mechanisms against Toxoplasma gondii. Journal of Experimental Medicine 186, 1799-1802

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

Jones TC, Erb P (1985) H-2-complex-linked resistance in murine toxoplasmosis. Journal of Infectious Diseases 151, 739-740

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

Kittas S, Kittas C, Paizi-Biza P, et al. (1984) A histological and immunohistochemical study of the changes induced in the brains of white mice by infection with Toxoplasma gondii. British Journal of Experimental Pathology 65, 67-74

Luder CG, Lang T, Beuerle B, et al. (1998) Down-regulation of MHC class II molecules and inability to up-regulate class I molecules in murine macrophages after infection with Toxoplasma gondii. Clinical and Experimental Immunology 112, 308-316

Nash PB, Purner MB, Leon RP, et al. (1998) Toxoplasma gondii-infected cells are resistant to multiple inducers of apoptosis. Journal of Immunology 160, 1824-1830

Neyer LE, Grunig G, Fort M, et al. (1997) Role of interleukin-10 in regulation of T-cell-dependent and T-cell-independent mechanisms of resistance to Toxoplasma gondii. Infection and Immunity 65, 1675-1682

Nguyen TD, Bigaignon G, Van Broeck J, et al. (1998) Acute and chronic phases of T. gondii infection in mice modulate the host immune responses. Infection and Immunity 66, 2991-2995

Orellana MA, Suzuki Y, Araujo FG, et al. (1991) Role of beta interferon in resistance to Toxoplasma gondii infection. Infection and Immunity 59, 3287-3290

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

Sasaki S, Miyagami T, Suzuki N (1981). Study on experimental toxoplasmic meningoencephalomyelitis. Its infectious route and lesions in CNS. Zentralblatt für Bakteriologie, Mikrobiologie und Hygiene. Serie A 250, 167-172

Scharton-Kersten TM, Yap G, Magram J, et al. (1997) Inducible nitric oxide is essential for host control of persistent but not acute infection with the intracellular pathogen Toxoplasma gondii. Journal of Experimental Medicine 185, 1261-1273

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

Stahl W, Dias JA, Turek G, et al. (1995a) Etiology of ovarian dysfunction in chronic murine toxoplasmosis. Parasitology Research 81, 109-113

Stahl W, Kaneda Y (1998) Aetiology of thyroidal dysfunction in murine toxoplasmosis. Parasitology 117, 223-227

Stahl W, Kaneda Y, Tanabe M, et al. (1995b) Uterine atrophy in chronic murine toxoplasmosis due to ovarian dysfunction. Parasitology Research 81, 114-120

Starec M, Sinet M, Kodym P, et al. (1997) The effect of drugs on the mortality of mice inoculated with Friend leukaemia virus or Toxoplasma gondii. Physiological Research 46, 107-111

Subauste CS, Remington JS (1993) Immunity to Toxoplasma gondii. Current Opinion in Immunology 5, 532-537

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

Suzuki Y, Conley FK, Remington JS (1989) Importance of endogeneous IFN-g for prevention of toxoplasmic encephalitis in mice. Journal of Immunology 143, 2045-2050

Suzuki, Y, Joh K, Orellana MA, et al. (1991) A gene(s) within the H-2D region determine development of toxoplasmic encephalitis in mice. Immunology 74, 732-739

Thouvenin M, Candolfi E, Villard O, et al. (1997) Immune response in a murine model of congenital toxoplasmosis: increased susceptibility of pregnant mice and transplacental passage of Toxoplasma gondii are type 2-dependent. Parasitologia 39, 279-283

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

Watanabe H, Suzuki Y, Makino M, et al. (1993) Toxoplasma gondii: Induction of toxoplasmic encephalitis in mice with chronic infection by inoculation of a murine leukemia virus inducing immunodeficiency. Experimental Parasitology 76, 39-45

Williams DM, Grumet FC, Remington JS (1978) Genetic control of murine resistance to Toxoplasma gondii. Infection and Immunity 19, 416-420

Wing EJ, Boehmer SM, Christner LK (1983) Toxoplasma gondii: decreased resistance to intracellular bacteria in mice. Experimental Parasitology 56, 1-8

Wong SY, Remington JS (1993) Biology of Toxoplasma gondii. AIDS 7, 299-316

Author: G. Pohlmeyer / M. Mähler