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Gesellschaft für Versuchstierkunde
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Expert Information

From the Working Group on Hygiene

Implication of infectious agents on results of animal experiments

Oxyuroidea

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Contents

Oxyuroidea

(Syphacia obvelata, Syphacia muris, Aspiculuris tetraptera and other*)*

Background

- *Syphacia (S.) obvelata* was described for the first time by Rudolphi in 1802[1] and by Seurat in 1916.[2]
- *Aspiculuris (A.) tetraptera* was described for the first time in 1821 by Nitzsch[3] and redescribed by Schulz in 1924[4] and 1927.[5]

Prevalence

- The prevalence of pinworms in an infected rodent population depends on age, sex and host immune system.[6]
- Prevalence in laboratory animals in North America and Europe seems to be still high, in 2015 for mice 1.51% and for rats 3.81%.[7]
- Three surveys on prevalence of infections in mice and rats in biomedical research facilities, published in 1998, 2008 and 2018 demonstrated that viral outbreaks are decreasing, whereas the prevalence of parasitic outbreaks remains constant.[8]

Host species

- *S. obvelata*: mainly mouse, also rats, hamsters, gerbils, voles, *Mastomys,* Algerian mice *(Mus spretus)*, and primates, including humans.[9,10]
- *S. muris*: mainly rat, also mouse, Syrian hamster, gerbil, wild rodents.[9,11]
- Experimental transmission of *S. muris* among rats, mice, hamsters, and gerbils is possible.[12]
- *A. tetraptera*: mouse. Other rodents are rarely susceptible. This includes members of the genera *Apodemus, Clethrionomys, Cricetus, Mastomys, Meriones, Microtus, Peromyscus, Rattus* and others.[9]
- *Dentostomella translucida* in gerbils.[13]
- *Passalurus ambiguus* in rabbits, hares, and cotton tail rabbits.[9,14-16]
- *Syphacia mesocriceti* may be the only pinworm species that is native to hamsters.[11]
- *Enterobius vermicularis* in humans, captive chimpanzee, gibbons, and marmosets.[9,17,18]
- Wild non-human primates are rarely infected with helminths but may become infected in captivity.[19]

Properties

Life cycle

Syphacia spp.:

- Direct cycle which requires only 11-15 days. Gravid females deposit their eggs in the perianal region. The eggs become infectious within a few hours after release.[9,18]
- Three possible routes of infection:[9,18]
  1. Direct: by ingestion of embryonated eggs from the perianal region

2. Indirect: by ingestion of embryonated eggs with contaminated food or water
3. Retroinfection: when infective larvae hatch from eggs in the perianal region and the larvae migrate back into the colon through the anus.

A. tetraptera:

- Direct cycle requires 23-25 days. Females lay their eggs in the colon and the eggs leave the host via faecal pellets. The eggs embryonate in the environment and are infective within 5-8 days at 27°C.[9]
- Route of infection: Infection by ingestion of infectious eggs.[9,18]

Susceptibility

- Athymic (*Foxn1^{nu}*) mice have increased susceptibility.[21]
- *Mastomys coucha* is more susceptible than BALB/c mice.[22]
- In rats, the infestation rates of *S. muris* are higher in the WKY strain than in the SHR strain.[23]
- In enzootically infected colonies, weanlings develop the highest parasite loads, males are more heavily parasitized then females.[24]
- *Syphacia* numbers diminish with increasing age of the host[25] and the worm burden decline with age due to activation of the host immune system.[26]
- Increase in resistance to pinworm infection with advancing age of rats.[9,27,28]

Organotropism

- Intestinal tract: *Syphacia* spp. primarily resides within the caecum / rectum, *A. tetraptera* primarily inhabits the colon.[9,18]

Clinical disease

- Subclinical[18,24]
- Pinworms generally are considered to be non- or mildly pathogenic in animals with normal immune system.[15,29,30]
- Symptoms may be poor condition, rough hair coats, reduced growth rate, rectal prolaps.[21,31,32]
- Experimentally with *S. muris* infected animals grow slower than uninfected animals.[33]
- Pinworms of laboratory rodents do generally not cause clinical signs of disease.[9,18,25]

Pathology

- In mice, *A. tetraptera* adult worms can penetrate the colonic wall, thus causing inflammation and a granulomatous reaction in and outside the intestinal wall.[34]
- Rats occasionally may develop focal submucosal granulomas associated with pinworm infection.[11]
- Infection with *Dentostomella translucida* in gerbils was found to be associated with a mild diffuse eosinophilia of the lamina propria of the anterior small intestine[13]. These observations, however, are contradicted by finding a similar eosinophilia in both infected and control animals.[35]
- Heavy parasite loads may lead to catarrhal enteritis, hepatic granulomas and perianal irritation.[9]

Morbidity and mortality

- No data.

Zoonotic potential

- Human infection with *S. obvelata* is uncommon.[9]
- *S. obvelata* was once described to occur in humans[10], but it has no known health significance.[18,25,36]

Interference with research

- Infection with pinworms reduces the occurrence of adjuvant-induced arthritis.[37]
- Animals infected with pinworms are not suitable for growth studies.[27]
- Infection with *S. obvelata* in mice causes a significant reduction of activity in behavioural studies[38], however, infection with *S. muris* in rats does not affect activity levels.[39]

Oncology

- Athymic mice infected with pinworms develop a lymphoproliferative disorder which eventually leads to lymphoma.[40,41]

Teratology

- No data

Infectiology

- Research data support the concept that infection with helminth parasites can reduce the severity of concomitant disease. Infection with helminth parasites has been tried as therapy in inflammatory bowel disease of humans.[42]
- Infection with *S. muris* in Wistar rats induces immunity against subsequent infection with *Echinostoma caproni*. The worm recovery is significantly decreased in rats primarily infected with *S. muris*.[43]

Immunology

- Infection with pinworms alters the humoral response to nonparasitic antigenic stimuli indicating that infection might modulate the immune system.[44]
- Infection with *S. obvelata* induces a proliferation of T- and B-lymphocytes in spleen and lymph nodes and occasional germinal center formation.[28]
- Pinworm infection in neonatal mice causes a strong Th2 response including high levels of interleukin-4 (IL-4) and IL-5 production. This Th2 response ends immediately after pinworm eradication.[45]
- Infection with *S. obvelata* induces a transient Th2-type immune response with elevated IL-4, IL-5, and IL-13 cytokine production and parasite-specific immunoglobulin G1 (IgG1) in BALB/c mice. BALB/c mice deficient in IL-13, IL-4/13, or the IL-4 receptor alpha chain show chronic disease with a >100-fold higher parasite burden, increased gamma interferon production, parasite-specific IgG2b, and a default Th2 response.[46]
- *S. obvelata*-infected mice show altered sensitivity to IL-17.[47]

Toxicology

- No data

Physiology

- In rats, infection with *S. muris* causes impaired transport of water, sodium, and chloride in the intestine.[23,48]
- Infection with *S. obvelata* in mice causes hematopoietic alterations, characterized by increased myelopoiesis and erythropoiesis.[46]
- Somatic extract of *S. muris* adults was examined for proteins with mass spectrometry.[30,39] The largest protein families identified consisted of metabolic enzymes and those involved in the nucleic metabolism and cell cycle.[49]
- Natural *S. obvelata* infection induces significant alterations in murine bone marrow cells manifested at the molecular level. Infection induces sustained phosphorylation of the members of the three major groups of distinctly regulated mitogen-activated protein kinases (MAPKs), the p38, the c-Jun amino-terminal kinase (JNK) and the extracellular signal-regulated kinase (ERK), as well as enhanced expression of mRNA for the inducible nitric oxide synthase (iNOS) in the bone marrow cells. Obviously, *S. obvelata* is able to manipulate signal transduction pathways in the hosts' bone marrow cells.[50]
- Infection with *S. muris* retards the growth of young mice and accelerates the development of their hepatic monooxygenase system.[51]
- Pinworm infection inhibits formation of diabetes in the non-obese diabetic (NOD) mouse.[52]

Cell biology

- No data

Assisted reproductive technology

- No data

Special considerations

- The eggs of pinworms survive for months in the animal room environment.[18,33,53]
- Microscopic destruction on immature but not on mature eggs of *S. muris* by hydrogen peroxide vapour system was detectable. In experiments such eggs seem to be no longer infective in vivo.[54]

Updated by Brunhilde Illgen-Wilcke, Reinach, Schweiz, November 2019

References

1. Rudolphi CA. 1802. Beobachtungen über die Eingeweidewürmer. Wegmanns Archive für Zoologie 2:1-67. [GERMAN]
2. Seurat LG. 1916. Sur les oxyures des mammifères. Comptes-Rendus de la Societé de Biologique de Paris 79:64-68. [FRENCH]
3. Nitzsch CL. 1821. Ascaris. In Ersch: und Gruber (eds) Allg Encycl d Wissensch v Künste. Leipzig, 6:44-49. [GERMAN]
4. Schulz RES. 1924. Oxyuridae of Armenian mice. Reportes Tropical Institute Armenia 2:41-51.
5. Schulz RES. 1927. On the genus Aspiculuris Schulz, 1924, and two new species of it, A. dinniki and A. asiatica from rodents. Ann Trop Med 21:267-275.
6. Baker DG. 1989. Natural pathogens of laboratory mice, rats and rabbits and their effects on research. Clin Microbiol Rev 11(2):231-266.
7. Livingston RS, Besch-Williford CL, Myles MH, Crim M, Riley LK. 2015. Contemporary prevalence of infectious agents of mice and rats in Europe and North America. IDEXX BioResearch.
8. Marx JO, Gaertner DJ, Smith AL. 2017. Results on survey regarding prevalence of adventitial infections in mice and rats at biomedical research. JAALAS 56(5):527-533.
9. Baker DG (ed). 2007. Flynn's Parasites of Laboratory Animals. 2nd ed. Ames: Blackwell Publishing.
10. Riley WA. 1919. A mouse oxyurid, *Syphacia obvelata*, as a parasite of man. J Parasitol 6(2):89-93.
11. Percy DH, Barthold SW (eds). 2001. Pathology of laboratory rodents and rabbits. 2nd ed. Ames: Iowa State University Press.
12. Ross CR, Wagner JE, Wightmen SR, Dill SE. 1980. Experimental transmission of *Syphacia muris* among rats, mice, hamsters and gerbils. Lab Anim Sci 30(1):35-37.
13. Smith GD, Snider TG. 1988. Experimental infection and treatment of *Dentostomella translucida* in the Mongolian gerbil. Lab Anim Sci 38(3):339-340.
14. Wiliams and Wilkins (eds). 1962. Mönning's veterinary helminthology. 5th ed., Baltimore.
15. Levine ND. 1968. Nematode parasites of domestic animals and of man. Minneapolis, Minn.: Burgess Pub Co.
16. Morgan HC, Hawkins PA. 1959. Veterinary helminthology, Minneapolis: Burgess.
17. Ruch TC. 1959. Diseases of laboratory primates. Philadelphia (& London): WB Saunders Co.
18. Flynn RJ. 1973. Parasites of Laboratory Animals.1st ed. Ames, Iowa State University Press, pp.203-320.
19. Hashimoto I, Honjo S. 1966. Survey of helminth parasites in cynomologus monkeys (*Macaca irus*). Jpn J Med Sci Biol 19(4):218.
20. Dix J, Astill J, Whelan G. 2004. Assessment of methods of destruction of Syphacia muris eggs. Lab Anim 38(1):11-16.
21. Jacobson RH, Reed ND. 1974. The thymus dependency of resistance to pinworm infection in mice. J Parasitol 60(6):976-979.
22. Higgins-Opitz SB, Dettman CD, Archer CE, Anderson CB, Becker PJ. 1990. Intestinal parasites of conventionally maintained BALB/c mice and Mastomys coucha and the effects of a concomitant schistosome infection. Lab Anim 24(3):246-252.
23. Lübcke R, Hutcheson FA, Barbezat GO. 1992. Impaired intestinal electrolyte transport in rats infested with the common parasite Syphacia muris. Dig Dis Sci 37(1):60-64..

24. Russell Lindsey J, Boorman GA, Collins MJ Jr, Hsu CK, van Hoosler GL, Wagner JE. 1991. Companion guide to infectious diseases of mice and rats by Committee on infectious diseases of mice and rats. National Research Council, Washington, DC, National Academy Press, pp.61-69.

25. Wescott RB. 1982. Helminths. In: Foster HL, Small JD, Fox JE (eds) The Mouse in Biomedical Research Vol. II: Diseases. 2nd New York: Academic Press, pp.373-384.

26. Prichett-Corning KR, Clifford CB. 2012. Parasitic Infections of Laboratory Mice. In: Hedrich HJ (ed) The Laboratory Mouse. 2nd ed. Academic Press London, pp.503-518.

27. Wagner M. 1988. The effect of infection with the pinworm (*Syphacia muris*) on rat growth. Lab Anim Sci 38(4):476-478.

28. Beattie GM, Baird SM, Lipsick JS, Lannom RA, Kaplan NO. 1981. Induction of T- and B-lymphocyte responses in antigentically stimulated athymic mice. Cancer Res 41(6):2322-2327.

29. Taffs LF. 1976. Pinworm infections in laboratory rodents: a review. Lab Anim 10(1):1-13.

30. Harkness JE, Wagner JE. 1995. Specific diseases and conditions. In: Williams and Wilkins (eds), The Biology and Medicine of Rabbits and Rodents. 4th ed. Baltimore, pp.350-353.

31. Hoag WG. 1961. Oxyuriasis in laboratory mouse colonies. Am J Vet Res 22:150-153.

32. Harwell JF, Boyd DD. 1968. Naturally occurring oxyuriasis in mice. J Am Vet Med Assoc 153(7):950-953.

33. Meade TM, J Watson. 2014. Characterization of rat pinworm (*Syphacia muris*) epidemiology as a means to increase detection and elimination. J Am Assoc Lab Anim Sci 53(6):661-667.

34. Mullink JW. 1970. Pathological effects of oxyuriasis in the laboratory mouse. Lab Anim 4(2):197-201.

35. Berger DM. 1991. Biological characteristics and cycle of *Dentostomella translucida* Schulz and Krepkogorskaja, 1932, in the Mongolian gerbil, *Meriones unguiculatus* (Milne-Edwards). Masters of Science, University of Washington, Seattle.

36. Kellog HS, Wagner JE. 1982. Experimental transmission of *Syphacia obvelata* among mice, rats, hamsters, and gerbils. Lab Anim Sci 32(5):500-501.

37. Pearson DJ, Taylor G. 1975. The influence of the nematode *Syphacia obvelata* on adjuvant arthritis in the rat. Immunology 29(2):391-396.

38. McNair DM, Timmons EH. 1977. Effects of *Aspiculuris tetraptera* and *Syphacia obvelata* on exploratory behaviour of an inbred mouse strain. Lab Anim Sci 27(1):38-42.

39. Webster JP. 1994. The effect of *Toxoplasma gondii* and other parasites on activity levels in wild and hybrid *Rattus norvegicus*. Parasitology 109(Pt 5):583-589.

40. Beattie GM, Baird S, Lannom R, Slimmer S, Jensen FC, Kaplan NO. 1980. Induction of lymphoma in athymic mice: a model for study of the human disease. Proc Natl Acad Sci; 77(8):4971-4974.

41. Baird SM, Beattie GM, Lannom A, Lipsick JS, Jensen FC, Kaplan NO. 1981. Induction of lymphoma in antigenetically stimulated athymic mice. Cancer Res 42(1):198-202.

42. Matisz CE, McDougall JJ, Sharkey KA, McKay DM. 2011. Helminth parasites and the modulation of joint inflammation. J Parasitol Res 2011:942616. doi: 10.1155/2011/942616.

43. Trelis M, Cortés A, Fried B, Marcilla A, Esteban JG, Toledo R. 2013. Protective immunity against *Echinostoma caproni* in rats is induced by *Syphacia muris* infection. Int J Parasitol 43(6):453-463.

44. Sato Y, Ooi H, Nonaka N, Oku Y, Kamiya M. 1995. Antibody production in *Syphacia obvelata* infected mice. J Parasitol 81(4):559-562.

45. Agersbourg SS, Garza KM, Tung KS. 2001. Intestinal parasitism terminates self-tolerance and enhances neonatal induction of autoimmune disease and memory. Eur J Immunol 31(3):851-859.

46. Michels C, Goyal P, Nieuwenhuizen N, Brombacher F. 2006. Infection with *Syphacia obvelata* (pinworm) induces protective Th2 immune responses and influences ovalbumin-induced allergic reactions. Infect Immun 74(10):5926-5932.

47. Bugarski D, Jovčić G, Katić-Radivojević S, Petakov M, Krstić A, Stojanović N, Milenković P. 2006. Hematopoietic changes and altered reactivity to IL-17 in *Syphacia obvelata*-infected mice. Parasitol Int 55(2):91-97.

48. Taylor JR, Lübcke R, Barbezat GO. 1995. Management of *Syphacia muris* infestation in rat colonies. Dig Dis Sc 40(9):1890-1891.

49. Sotilo J, Trelis M, Cortés A, Luz Valero A, Sanchez del Pino MM, Esteban JG, Marcilla A, Toledo R. 2012. Proteomic analysis of the pinworm *Syphacia muris* (*Nematoda: Oxyuridae*), a parasite of laboratory rats. Parasitol Int 61(4):661-664.

50. Ilić V, Krstić A, Katić-Radivojević S, Jovćić G, Milenković P, Bugarski D. 2010. *Syphcia obvelata* modifies mitogen-activated protein kinases and nitric oxide synthases expression in murine bone marrow cells. Parasitol Int 59(1):82-88.

51. Mohn G, Philipp EM. 1981. Effects of *Syphacia muris* and the anthelmintic fenbendazole on the microsomal monooxygenase system in mouse liver. Lab Anim 15(2):89-95.

52. Gale EA. 2002. A missing link in the hygiene hypothesis? Diabetologica 45(4):588-594.

53. Klement P, Augustine JM, Delaney KH, Klement G, Weitz JI. 1996. An oral ivermectin regimen that eradicates pinworms (*Syphacia* spp.) in laboratory rats and mice. Lab Anim Sci 46:286-290.

54. Krause J, Riedesel H. 2002. Elimination of pinworm eggs from caging equipment with vapourised hydrogen peroxide. Report from the Max-Planck-Institute for experimental medicine. American Association for Laboratory Animal Science (AALAS), Ann meeting San Antonio, TX, USA.

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