

## Helicobacter species

### Classification

Gram-negative bacteria; spiral, fusiform, or curved; some with flagella

### Family

Helicobacteriaceae

The species currently described in rats and mice are: *H. bilis*, *H. ganmani*, *H. hepaticus*, *H. muridarum*, *H. mastomyrinus*, *H. rappini*, *H. rodentium*, and *H. typhlonius* (mice) and *H. bilis*, *H. muridarum*, *H. rodentium*, *H. trogontum*, and *H. typhlonius* (rats). The *Helicobacter* species associated with clinical disease in rats and mice are primarily *H. bilis* and *H. hepaticus*.

### Affected species

Almost every species of mammal examined appears to have at least one associated *Helicobacter* species.

### Frequency

Common in both wild rodents and laboratory animal facilities.

### Transmission

The usual means of transmission is the fecal-oral route, for example, by ingestion of feces by weanling or naïve animals. *Helicobacter* spp. may be transmitted between animals housed in open-topped cages through the movement of dust and other fomites. Vertical transmission has not been reported. Transmission by tumor transplantation has been reported, although the frequency with which it occurs is moot. Some *Helicobacters* may be zoonotic or anthrozoönotic.

### Clinical Signs and Lesions

*Helicobacter* primarily colonizes the cecum and colon, although some of these species may also colonize the gall bladder and liver. A few less-common species can colonize the stomach, although caution must be exercised in interpreting *Helicobacter* detection in the stomach of coprophagic animals, as the presence of *Helicobacter* nucleic acid does not necessarily indicate

colonization. Most animals that carry *Helicobacter* spp. are asymptomatic. Disease in immunocompetent animals caused by *Helicobacter* is almost exclusively limited to susceptible strains of mice infected with either *H. bilis* or *H. hepaticus*. Immunodeficient animals seem susceptible to disease due to a broader range of *Helicobacter* spp. In susceptible animals, the main clinical sign associated with *Helicobacter* infection is rectal prolapse secondary to typhlitis or typhlocolitis. *Helicobacter*-infected animals can also present with diarrhea. *H. hepaticus* may also be associated with the development of liver and colon cancer in some strains of mice, such as the A/J. On histopathology, typhlocolitis, and hepatitis may be seen. The common rodent *Helicobacter* spp. do not colonize the stomach, so gastritis is not seen.

### Diagnosis

Serologic diagnosis of *Helicobacter* infection is possible. Serology is not commercially available because although the assay is sensitive (after a time delay, to allow for antibody production), it is not specific. It is also not clear whether intestinal colonization with all *Helicobacter* spp. will incite an antibody response. Diagnosis is best accomplished through PCR of fecal material. As fecal material contains PCR inhibitors, which may result in false negative results, proper handling of samples and assay design is important. PCR is available to identify *Helicobacter* as a genus, as well as to speciate infections with *Helicobacter*.

### Interference with Research

Many *Helicobacter* species are not currently associated with disease in immunocompetent mice. The species that are associated with disease seem only to cause disease in susceptible strains. If animals are infected with *H. bilis* or *H. hepaticus*, the inflammatory response in the gut and liver may affect the host response to other stimuli or manipulations. In addition, because the typhlocolitis caused by enterohepatic *Helicobacters* resembles inflammatory bowel disease, it may confound genetic investigation or therapeutic research into digestive diseases. Infection with *Helicobacter*

# technical sheet

*hepaticus* has also been linked to hepatocellular carcinoma in A/J mice, and possible colon carcinoma. Recently, it has been suggested that the inflammatory response to *Helicobacter* could also alter mammary carcinogenesis in mice.

## Prevention and Treatment

*Helicobacter* remains common in laboratory mice. Health monitoring for *Helicobacter* should be performed regularly. However, because the organism so highly sensitive to desiccation, it does not transfer readily from one room to another, nor will it be introduced with feed, bedding, or equipment. Thus, a facility that is *Helicobacter*-free and only imports *Helicobacter*-free mice may only need to monitor annually. Aseptic hysterectomy rederivation with fostering onto clean females or embryo transfer rederivation will remove *Helicobacter* from a colony. *Helicobacter*-free animals may also be generated by fostering pups on clean females shortly after birth (within 24 hours). *Helicobacter* infection may be treated with an antibiotic regimen and treatment diets are available commercially, although these diets may not eradicate infection. Due to the sensitivity of these bacteria to desiccation, environmental decontamination is not required.

## References

Baker, D.G. *Natural Pathogens of Laboratory Animals: Their effects on research*. 385 (ASM Press, Washington, D.C, 2003).

Chichlowski, M. & Hale, L. P. Effects of *Helicobacter* infection on research: the case for eradication of *Helicobacter* from rodent research colonies. *Comp. Med.* **59**, 10-17 (2009).

Fox, J.G., Anderson, L.C., Lowe, F.M. & Quimby, F.W. *Laboratory Animal Medicine*. 2nd ed. 1325 (Academic Press, San Diego, 2002).

Fox, J.G. *et al.* *The Mouse in Biomedical Research: Diseases*. 2nd ed. 756 (Academic Press, New York, 2006).

Goldman, C. G. & Mitchell, H. M. *Helicobacter* spp. other than *Helicobacter pylori*. *Helicobacter* **15 Suppl 1**, 69-75, (2010).

Truett, G. E., Walker, J. A. & Baker, D. G. Eradication of infection with *Helicobacter* spp. by use of neonatal transfer. *Comp. Med.* **50**, 444-451 (2000).

Rossi, G. *et al.* *Helicobacter pylori* infection negatively influences pregnancy outcome in a mouse model. *Helicobacter* **9**, 152-157 (2004).

Scavizzi, F. & Raspa, M. *Helicobacter typhlonius* was detected in the sex organs of three mouse strains but did not transmit vertically. *Lab Anim* **40**, 70-79 (2006).

Whary, M. T. & Fox, J. G. Natural and experimental *Helicobacter* infections. *Comp. Med.* **54**, 128-158 (2004).

Whary, M. T. & Fox, J. G. Detection, eradication, and research implications of *Helicobacter* infections in laboratory rodents. *Lab. Anim.* (NY) **35**, 25-27, 30-26 (2006).