

Tyzzler's disease: An update of current information

Lela K. Riley, Craig L. Franklin, Reuel R. Hook, Jr. and Cynthia Besch-Williford
Department of Veterinary Pathology
University of Missouri, Columbia, MO

Tyzzler's disease is an enterohepatic disease of animals, caused by an obligate intracellular bacterium. In laboratory animals, severity of the disease may vary from asymptomatic infection to acute clinical disease with high mortality. The biology of the causative organism and the pathogenesis of the disease are not fully understood. The intent of this article is to review currently available knowledge about Tyzzler's disease.

History of Tyzzler's Disease

The disease was named after Ernest Tyzzler who initially described the syndrome in 1917. Tyzzler reported a fatal epizootic of necrotizing hepatitis and hemorrhagic enteritis that resulted in the death of an entire colony of Japanese waltzing mice. He observed gram-negative, pleomorphic, sporeforming, intracellular bacteria adjacent to necrotic hepatic and intestinal lesions and postulated that the bacterium was the causative agent. Since the organism did not correspond with any known bacterial species, Tyzzler named this newly-identified bacterium *Bacillus piliformis*, based strictly on its morphology. For many years, Tyzzler's disease was believed to be restricted to mice until Allen et al. reported the disease in laboratory rabbits in 1965². Since then the

disease has been reported in a wide range of mammalian animal species, including domestic,^{3,4,5,6} wild^{7,8,9,10} and laboratory animals. In laboratory animals, the disease has been found in rats,¹¹ mice,¹ gerbils,^{12,13} hamsters,¹⁴ rabbits,² guinea pigs,¹⁵ and rhesus monkeys.¹⁶ Outbreaks of the disease have occurred world-wide.

Biology

The Tyzzler's bacillus is an unusual organism, unlike any other bacterium described to date. The organism is a gram-negative, intracellular, pleomorphic, sporeforming, motile bacillus. The vegetative form is large, ranging from 8-40 μm in length, and is motile by means of peritrichous flagella (Fig 1). Spores are 0.5 μm wide and 3 μm long and may be found either as terminal endospores within the bacteria or free within host cells.

Recent studies by Duncan and colleagues,¹⁷ in which they sequenced the 16S rRNA of an isolate obtained from a rabbit with Tyzzler's disease, indicated that the organism is more closely related to the *Clostridium* genus than to the *Bacillus* genus. Based on these findings, Duncan et al. proposed that the Tyzzler's bacillus be reclassified as *Clostridium piliforme*. Experiments in our laboratory with seven additional isolates confirmed their findings (unpublished data).

Despite numerous attempts by many investigators, the organism has not been cultured on cell-free medium. In one study alone, over 190 different microbiological media were tested for their ability to support growth of the bacillus.¹⁸ Based on the universal lack of success in culture of the bacterium on cell-free media and the apparent requirement for viable host cells for propagation of the organism,¹⁹ *C. piliforme* is believed to be an obligate intracellular bacterium.

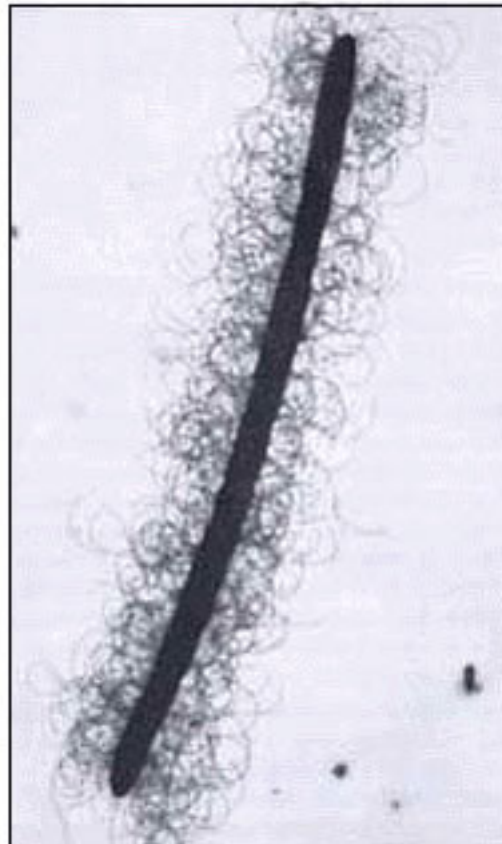


Figure 1. Transmission electron micrograph of *C. piliforme* bacterium. The bacillus is surrounded by large numbers of peritrichous flagella.

[Previous](#) | [Index](#) | [Next](#)

[Back to top of page](#)

Tyzzler's disease: An update of current information

Lela K. Riley, Craig L. Franklin, Reuel R. Hook, Jr. and Cynthia Besch-Williford
 Department of Veterinary Pathology
 University of Missouri, Columbia, MO

(Continued from [page 1](#))

For many years the difficulties in propagation of the Tyzzler's bacillus hampered study of the organism and Tyzzler's disease. Initial investigations required cultivation of the organism in susceptible animals. However, in 1971, Ganaway and colleagues reported successful culture of the bacteria in yolk sacs of embryonated eggs.¹⁹ The organism was subsequently grown on primary cultures of mouse hepatocytes.²⁰ In recent years, the organism has been cultivated on a number of immortal mammalian cell lines, including lines derived from fibroblast, liver and intestinal tissues.^{21, 22, 23} The bacterium has an apparent generation time of 6 hours. Organisms grown in embryonated eggs or mammalian cell culture remain infectious and can cause disease in inoculated laboratory animals with no apparent loss of virulence. Development of techniques for propagation of *C. piliforme* in established mammalian cell culture has permitted more intensive investigation of this organism in recent years.

Organisms designated as *C. piliforme* represent a heterogeneous collection of bacterial isolates that have indistinguishable morphology, but are antigenically distinct. Evidence of diversity among isolates came initially from vaccination studies in mice.^{24, 25, 26} Vaccination was most effective when the challenge isolate of *C. piliforme* was the same as the isolate used for vaccination. Further evidence of differences among *C. piliforme* isolates was demonstrated by agar gel diffusion, complement fixation tests and Western blots.^{21, 23-25} These tests revealed that both conserved and isolate-specific antigens were present in the various *C. piliforme* isolates. Subsequent studies revealed antigenic and size variation among immunodominant flagellin proteins from *C. piliforme* isolates.²⁷

Transmission and Host Susceptibility

Transmission of the organism is believed to occur primarily via ingestion of spores from contaminated feces. Because the vegetative form is particularly labile,²⁸ it is not likely that it plays a major role in natural infections. In contrast, spores are stable and can remain infectious for 1-2 years in contaminated bedding. Thus, it is thought that spores are the primary means of transmission among animals. Experimental studies have documented that spores are shed into feces for 1-2 weeks post-infection and that susceptible animals exposed to contaminated fecal material can develop Tyzzler's disease.^{29, 38, 44} Transplacental transfer has been reported in experimentally-infected mice and immunosuppressed rats, although the relative importance of this mode of transmission in natural infections is not known.^{30,31}

In contrast to other laboratory animals, gerbils are susceptible to infections with isolates from a variety of host species. However, they do not appear to be universally susceptible to infection with all isolates.³⁶ Because of their inherent susceptibility, gerbils have been used extensively in investigations of Tyzzler's disease.

A number of factors may predispose animals to Tyzzler's disease. Stresses such as overcrowding, change in environmental conditions, and immunosuppression may contribute to disease outbreaks in laboratory animals. A high protein diet has also been shown to predispose animals to Tyzzler's disease.³² Disruption of normal flora may contribute to disease susceptibility, since rabbits treated with oral sulfonamide have been reported to break with disease.³³ In addition to species specificity, there is evidence that certain host strains are more susceptible to infection. In studies conducted by Waggle,³⁴ CBA/N and C3.CBA/N mouse strains, which are defective in IgM production, appeared to be more susceptible to infection than were immunocompetent mouse strains. Several pieces of evidence suggest that *C. piliforme* infections may also occur in man: 1) *C. piliforme* infections have been reported in a very broad range of animal species, including rodents, many species of domestic and wild animals, and rhesus monkeys. The occurrence of infections in almost every category of animal species, including rhesus monkeys, a non-human primate physiologically similar to man, implies that *C. piliforme* may also infect man. 2) Studies by Fries using an indirect immunofluorescence assay demonstrated antibodies to *C. piliforme* in 166 of 287 human serum samples.³⁵ In animals, induction of serum antibodies requires infection with viable organisms.³⁶ Extrapolating these data to humans would suggest that antibodies to *C. piliforme* found in humans are the result of active infections, not simple exposure. The inherent difficulties in diagnosis of *C. piliforme* infections may have thus far prevented identification of the disease in man. Further investigations will be needed to document Tyzzler's disease in man; however, it seems reasonable that it may occur.

Host Specificity

C. piliforme isolates are predominately host specific. Host specificity was initially suggested by Fujiwara²³⁻²⁵ and Waggle et al.³⁷ Their findings have been further supported by studies in our laboratory in which well-characterized, antigenically diverse isolates were used to infect rats, mice and hamsters.³⁸ Results of these investigations indicate that isolates are predominately host specific, but some cross-infectivity may occur among animal species, particularly between rats and mice. The molecular mechanism(s) responsible for this host specificity is not known, but it is likely that specific bacterial adhesins or host receptors may control initial events in infection that result in host specificity of isolates.

Pathogenesis

The initial site of infection is the intestinal epithelium with hepatic and cardiac involvement during later stages of the disease. Dissemination of the bacteria is believed to occur via the vasculature. Takagaki and Fujiwara reported that in experimentally infected, cortisone-treated animals, bacteremia occurs in the late stages of the disease.³⁹ Their findings indicated that the number of organisms increased to 10⁶-10⁷ organisms per ml of blood before death.

Like other obligate intracellular pathogens, the ability of *C. piliforme* to cause disease hinges on its ability to invade a host cell and survive within the hostile intracellular environment. In our laboratories the cellular and intracellular events in *C. piliforme* infections have been examined using an in vitro model with a human colon carcinoma cell line, Caco-2.²³ This cell line is particularly applicable because it forms a polarized monolayer with a functional brush border that closely resembles the intestine, the initial site of *C. piliforme* infection. Ultrastructural examination of infected Caco-2 monolayers revealed a putative sequence of events that occur in *C. piliforme* infections (**Fig 2**). Based on these observations, it appears that *C. piliforme* enters the host epithelial cell through the apical surface by a phagocytic-like mechanism. Once inside the cell, the organism rapidly exits the phagosome and replicates within the cytoplasm and nucleus of the host cell. This ability to exit the phagosome is thought to be an important virulence determinant allowing the organism to survive intracellularly and evade host-mediated killing mechanisms. Dissemination of the bacteria appears to occur following lysis of the host cell.

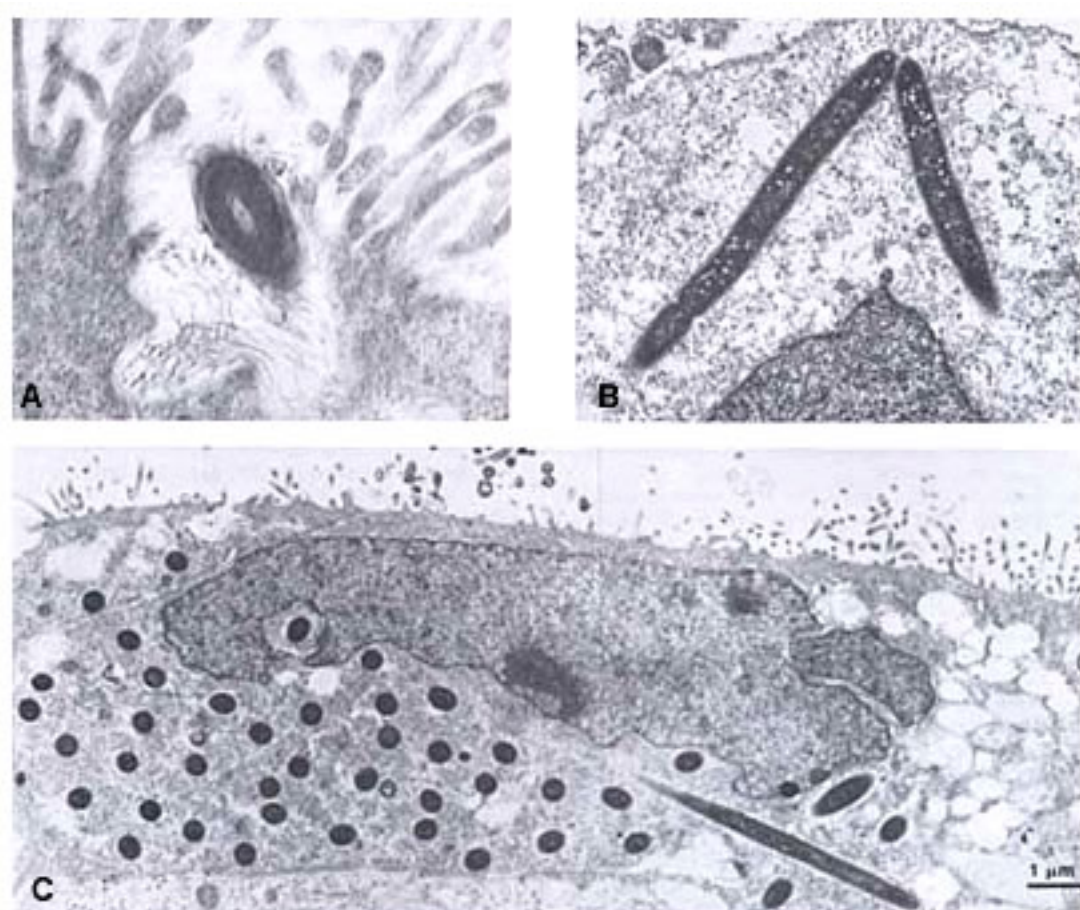


Figure 2. Transmission electron micrographs of Caco-2 mammalian cell monolayers infected with *C. piliforme*. (A) Bacterium invading the apical surface. (B) Bacterium undergoing replication within the cytoplasm of an infected cell. (C) Infected Caco-2 cells containing numerous, intensely-stained intracytoplasmic bacteria.

[Previous](#) | [Index](#) | [Next](#)

[Back to top of page](#)

Tyzzler's disease: An update of current information

Lela K. Riley, Craig L. Franklin, Reuel R. Hook, Jr. and Cynthia Besch-Williford
 Department of Veterinary Pathology
 University of Missouri, Columbia, MO

(Continued)

Virulence determinants of *C. piliforme* are not well defined. Recent studies have shown that certain isolates produce cytotoxins that may function as virulence determinants.⁴⁰ Nine of twelve isolates examined in our laboratories to date produce a high molecular weight, non-protease, temperature sensitive, protein molecule that is cytotoxic for mammalian cells. While the role of toxins in pathogenesis of disease has not been elucidated, preliminary studies indicate that animals infected with toxigenic isolates exhibit strikingly more severe clinical signs and histopathologic lesions and have markedly higher mortality rates than do animals infected with non-toxigenic isolates. Based on these data, it is tempting to speculate that outbreaks with severe clinical disease and high mortality rates may be due to toxigenic isolates, whereas asymptotically-infected animals may be infected with nontoxigenic isolates. While further studies are needed to define the contribution of cytotoxins to pathogenesis of Tyzzler's disease, it is possible that *C. piliforme* toxins, like other bacterial toxins, may play a major role in pathogenesis of the disease.

Clinical Signs

Acute disease is most often observed in suckling or weanling animals, but animals of any age may be affected. Clinical signs of acute disease include rough hair coat, weakness, lethargy, and death. Animals may also experience watery to pasty diarrhea or perianal fecal staining. Megaloileitis has also been correlated with Tyzzler's disease in rats.⁴¹ Onset of clinical signs and death may occur rapidly with mortality rates varying from low to very high. The acute form of the disease appears to be rare in natural infections; however, seemingly healthy animals can apparently harbor a subclinical form of infection which can develop into acute disease when the animal is subjected to stress, such as overcrowding, change in environmental conditions, immunosuppression or other types of experimental manipulations. Severity of *C. piliforme* infections may be dependent on both the isolate and animal species involved. In research facilities, spontaneous outbreaks of clinical Tyzzler's disease are most commonly seen in gerbils, hamsters, guinea pigs and rabbits. Infections in rats and mice often remain asymptomatic.

Pathology

Gross lesions may vary from none to severe and are characteristically found in the liver, lower intestine (ileum, cecum and proximal colon) and less frequently the heart. The most consistent finding is an enlarged liver with multiple gray to white foci scattered throughout the liver (**Fig 3**). Foci may coalesce in severe cases.

While hepatic lesions are a hallmark of Tyzzler's disease, the liver is not always affected. Intestinal lesions are usually evident in acutely infected animals and consist of varying degrees of serosal edema with or without obvious hemorrhage. The small intestine usually contains scant ingesta, whereas the cecum is often filled with abundant watery material. Cardiac lesions consisting of white streaks within the myocardium have been reported in gerbils, hamsters, rabbits, rats and mice.

Histopathologically, lesions of Tyzzler's disease are characterized by necrosis with varying degrees of inflammation in response to the necrosis. Acute hepatic lesions consist of necrotic foci surrounded by minimal, primarily neutrophilic, inflammation (**Fig 4**). As the disease progresses, the inflammatory response may increase but rarely becomes a predominant feature. Chronic foci may become mineralized or fibrotic. Acute lesions of the intestine consist of single cell necrosis of primarily the luminal enterocytes. The lamina propria and submucosa may be edematous and contain a mild neutrophilic infiltrate.

As the lesion progresses, necrosis becomes more extensive and the inflammatory response shifts to lymphocytic. At this stage, necrotic foci may be evident in the intestinal muscular layers especially in the ileum. Healing and repair are evidenced by hyperplasia of the crypt epithelium. Myocardial lesions consist of mild inflammation as associated with small necrotic foci. Histopathologic evidence of encephalitis involving the cerebral cortex and thalamus has been reported in naturally-infected gerbils.⁴²

Because *C. piliforme* organisms stain faintly with hematoxylin and eosin, silver stains, such as Warthin-Starry, Steiner or Dieterle's, are used to enhance detection of these bacteria. In acute to subacute lesions, intracellular bacteria are found in viable cells adjacent to necrotic foci. Bacteria are more difficult to find in chronic repairing lesions. Within the cell, *C. piliforme* are found lying next to each other in a unique, almost pathognomonic, arrangement which has been described as a "bundle of sticks" or "pick up sticks" arrangement (Fig. 4 insert).^{2, 19, 43, 44}



Figure 3. Photograph of gross lesions in a mouse with Tyzzler's disease demonstrating multiple foci of hepatic necrosis.

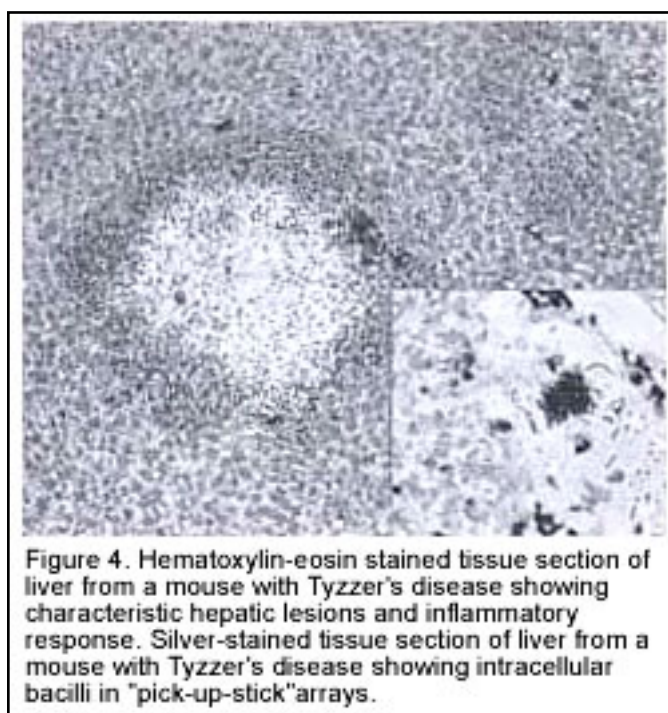


Figure 4. Hematoxylin-eosin stained tissue section of liver from a mouse with Tyzzler's disease showing characteristic hepatic lesions and inflammatory response. Silver-stained tissue section of liver from a mouse with Tyzzler's disease showing intracellular bacilli in "pick-up-stick" arrays.

Tyzzler's disease: An update of current information

Lela K. Riley, Craig L. Franklin, Reuel R. Hook, Jr. and Cynthia Besch-Williford

Department of Veterinary Pathology
University of Missouri, Columbia, MO

(Continued)

Diagnosis

Definitive diagnosis of Tyzzler's disease is often problematic. Diagnosis has traditionally relied on histopathologic evidence of *C. piliforme* infection and is based on the presence of characteristic lesions and the large, intracellular bacteria. While a diagnosis of Tyzzler's disease was once thought to require hepatic involvement, experimental studies have shown that infection of hepatocytes is a transient phenomenon, lasting only 3-7 days. In contrast, intestinal involvement appears to be maintained for a longer period of time, up to 13 days postinfection. Thus, histologic examination of intestinal tissues is critical in establishing a definitive diagnosis.

Since infections can be transient, examination of affected tissue may reveal limited, if any, organisms, which further confounds diagnosis of Tyzzler's disease. In attempts to increase the bacterial numbers, disease provocation regimens, in which immuno suppressive reagents are administered to animals, have been used with mixed success^{32, 45, 46, 47, 48, 49} Based on the limited reliability of these regimens, disease provocation methods appear questionable as convincing diagnostic tools to determine whether animals are free of *C. piliforme*. Alternatively, gerbils, which are uniquely susceptible to Tyzzler's disease, have been used as sentinels to detect *C. piliforme* infections.⁴⁴ While effective in some cases, this strategy is problematic in that gerbils are not susceptible to all strains of *C. piliforme*.³⁸ Serological assays have also been used diagnostically to detect *C. piliforme* infections. Experimental studies have shown that induction of serum antibody to *C. piliforme* requires viable organisms; simple exposure to killed bacteria is insufficient to generate an immune response.³⁸ These findings suggest that the presence of specific serum antibodies to *C. piliforme* indicates that the animals have been infected. In early studies, complement fixation tests were used, but these lacked sensitivity.²⁴⁻²⁶ Subsequently, indirect immunofluorescence assays (IFA) and enzyme-linked immunosorbent assays (ELISAs) were developed using whole organisms or extracts from infected tissues or embryonated eggs.^{50, 51} However, non-specific crossreactivity of antibodies to other organisms often yielded false positive results in these assays. Recent advancement in techniques for propagation of *C. piliforme* in mammalian cell cultures has provided more defined antigen preparations for ELISA testing, which have improved but not eliminated non-specific reactivity. Therefore, careful analysis of the data and comparison of results with known positive controls are needed to appropriately interpret serologic evaluations. More purified and specific antigens will be required to enhance the specificity of ELISA assays and resolve problems associated with nonspecific crossreactivity and false positive results. Until such reagents are developed, definitive diagnosis of subclinical *C. piliforme* infections will remain difficult. At present, there is no adequate confirmatory test. Follow-up testing might include serological examination of cohort animals or histological evaluation following immunosuppression with disease provocation regimens. Recently, a specific monoclonal-based competitive inhibition ELISA has been developed which allows identification of the specific isolate involved in *C. piliforme* infections of laboratory animals.⁵² The ability to delineate the specific isolate may provide a tremendous epidemiological tool for the control and prevention of subsequent disease outbreaks in laboratory animals.

Prevention and Control

Control of Tyzzler's disease is best achieved by preventing entrance of the bacterium into a research colony through strict monitoring of incoming animals and decontamination of food, bedding and water supplies. Since infectious spores are inactivated by heating for 30 minutes at 80 degrees Celsius, routine autoclaving of food, bedding and water should be effective in preventing food-or water-borne Tyzzler's disease. In colonies where Tyzzler's disease is endemic, depopulation is recommended with subsequent repopulation with *C. piliforme*- free animals. Contaminated surfaces can be effectively disinfected by treatment with 0.3% hypochlorite (bleach) for 5 minutes.

Antibiotic treatment of infected animals has yielded variable results. A number of studies have examined various antibiotics for treatment of Tyzzler's disease. Although techniques and evaluation methods varied, tetracycline, oxytetracycline, and penicillin were the most effective antibiotics for alleviation of clinical signs due to *C. piliforme* infection. However, these antibiotics have not been shown to effectively eliminate this bacterium and their use should be restricted to individual or very valuable animals. Antibiotic therapy is not currently recommended for elimination of Tyzzler's disease from an endemically infected colony.

The devastating effect of acute clinical disease and mortalities of laboratory animals on research experiments is obvious. Altered pharmacokinetic responses have been documented in animals recovered from clinical Tyzzler's disease. Other direct effects of Tyzzler's on research have not been documented. However, the pathological effects of the infection on the gastrointestinal tract and liver would suggest that investigations in which these systems are key elements should avoid use of infected animals. Less obvious, but perhaps more detrimental, is the potential effect of subclinical infections on biomedical research. While the effects of asymptomatic infections on the animal physiology remain unknown, subclinical infections may alter the animal physiology, resulting in altered or invalid experimental results.

Summary

Tyzzler's disease is an enterohepatic disease of laboratory animals. The etiologic agent of the disease is a heterogeneous group of sporeforming obligate intracellular bacteria, called *C. piliforme*. Severity of the infection may vary from asymptomatic infection to acute clinical disease with high mortality. Disease manifestations may depend on the animal species and the *C. piliforme* isolate involved. Pathogenesis of the disease is not well-understood. Control of Tyzzler's disease in research colonies is best accomplished by preventing entry of the organism into the facility.

[Previous](#) | [Index](#) | [Next](#)

[Back to top of page](#)

Tyzzer's disease: An update of current information

Lela K. Riley, Craig L. Franklin, Reuel R. Hook, Jr. and Cynthia Besch-Williford
Department of Veterinary Pathology
University of Missouri, Columbia, MO

Literature cited

1. Tyzzer, E.E. 1917. A fatal disease of the Japanese waltzing mouse caused by a spore-bearing bacillus (*Bacillus piliformis* N. sp.). J. Med. Res. 37:307-388.
2. Allen, A.M., J.R. Ganaway, T.D. Moore, and R.F. Kinard. 1965. Tyzzer's disease syndrome in laboratory rabbits. Amer. J. Path. 46:859-882.
3. Swerczek, T., M.W. Crowe, M.E. Prickett, and J.T. Bryans. 1973. Focal bacterial hepatitis in foals: preliminary report. Mod. Vet. Pract. 54:66-67.
4. Qureshi, S.R., W.W. Carlton, and H.J. Olander. 1976. Tyzzer's disease in a dog. J. Am. Vet. Med. Assoc. 168:602-604.
5. Kovatch, R.M., and G. Zebarth. 1973. Naturally occurring Tyzzer's disease in a cat. J. Am. Vet. Assoc. 162:136-138.
6. Webb, D.M., D.D. Harrington, and P.N. Boehm. 1987. *Bacillus piliformis* infection (Tyzzer's disease) in a calf. J. Am. Vet. Assoc. 191:431-434.
7. Canfield, R.J., and W.J. Hartley. 1991. Tyzzer's disease (*Bacillus piliformis*) in Australian marsupials. J. Comp. Pathol. 105:167-173.
8. Stanley, S.M., R.E. Flatt, and G.N. Daniels. 1978. Naturally occurring Tyzzer's disease in the gray fox. J. Am. Vet. Assoc. 173:1173-1174.
9. Marler, R.J., and J.E. Cook. 1976. Tyzzer's disease in two coyotes. J. Am. Vet. Assoc. 169:940-941.
10. Karstad, L., R. Lulis, and D. Wright. 1971. Tyzzer's disease in muskrats. J. Wildl. Dis. 7:96-99.
11. Jonas, A.M., D.H. Percy, and J. Craft. 1979. Tyzzer's disease in the rat. Arch. Pathol. 90:516-528.
12. Carter, G.R., D.L. Whiteneck, and L.A. Julius. 1969. Natural Tyzzer's disease in Mongolian gerbils (*Meriones unguiculatus*). Lab. Anim. Care 19:648-651.
13. White, D.J., and M.M. Waldron. 1969. Naturally-occurring Tyzzer's disease in the gerbil. Vet. Rec. 85:111-114.
14. Zook, B.C., K. Huang, and R.G. Rhorer. 1977. Tyzzer's disease in syrian hamsters. J. Am. Vet. Med. Assoc. 171:833-836.
15. McLeod, C.G., J.L. Stookey, D.G. Harrington, and J.D. White. 1977. Intestinal Tyzzer's disease and spirochetosis in a guinea pig. Vet. Pathol. 14:229-235.
16. Niven, J.S.F. 1968. Tyzzer's disease in laboratory animals. Z. Versuchstierkd. 10:168-174.
17. Duncan, A.J., R.J. Carmen, G.J. Olsen, and K.H. Wilson. 1993. Assignment of the agent of Tyzzer's disease to *Clostridium piliforme* comb. nov. on the basis of 16SrRNA sequence analysis. International J. System. Bacteriol. 43:314-318.
18. Thunert, A. 1984. Is it possible to cultivate the agent of Tyzzer's disease (*Bacillus piliformis*) in cellfree media? Z. Versuchstierk. 26:145-150.
19. Ganaway, J.R., A.M. Allen, and T.D. Moore. 1971. Tyzzer's disease of rabbits: Isolation and propagation of *Bacillus piliformis* (Tyzzler) in embryonated eggs. Infect. Immun. 3 :429-437.
20. Kawamura, S., F. Taguchi, T. Ishida, M. Nakayama, and K. Fujiwara. 1983. Growth of Tyzzler's organism in primary monolayer cultures of adult mouse hepatocytes. J. Gen. Microbiol. 129:277-283.
21. Spencer, T.H., J.R. Ganaway, and K.S. Waggie, 1990. Cultivation of *Bacillus piliformis* (Tyzzler) in mouse fibroblasts (3T3 cells). Vet. Microbiol. 22:291-297.
22. Riley, L.K., C. Besch-Williford, and K.S. Waggie. 1990. Protein and antigenic heterogeneity among isolates of *Bacillus piliformis*. Infect. Immun. 58:1010-1016.
23. Franklin, C.L., D.A. Kinden, R.L. Stogsdill, and L.K. Riley. 1993. In vitro model of adhesion and invasion by *Bacillus piliformis*. Infect. Immun. 61:876-883.
24. Fujiwara, K., A. Yamada, H. Ogawa, and Y. Oshima. 1971. Comparative studies on the Tyzzler's organisms from rats and mice. Jpn. J. Exp. Med. 41:125-133.
25. Fujiwara, K., H. Kurashina, T. Magaribuchi, S. Takenaka, and S. Yokoizuma. 1973. Further observation on the difference between Tyzzler's organisms from mice and those from rats. Jpn. J. Exp. Med. 43:307-315.
26. Fujiwara, K., Y. Takasaki, K. Kubokawa, S. Takenaka, M. Kubo, and K. Sato. 1974. Pathogenic and antigenic properties of the Tyzzler's organisms from feline and hamster cases. Jpn. J. Exp. Med. 44:365-372.
27. Motzel, S.L., and L.K. Riley. 1991. *Bacillus piliformis* flagellar antigens for serodiagnosis of Tyzzler's disease. J. Clin. Microbiol. 29:2566-2570.
28. Cragie, J. 1966. "*Bacillus piliformis*" (Tyzzler) and Tyzzler's disease of the laboratory mouse. II. Mouse pathogenicity of *B. piliformis* grown in embryonated eggs. Proc. Royal Soc. Edinburgh, Sect. B Biol. 165:61-77.
29. Itoh, T., N. Kagiya, and K. Fujiwara. 1988. Production of Tyzzler's disease in rats by ingestion of bacterial spores. Jpn. J. Exp. Med. 59:9-15.
30. Fries, A.S. 1978. Demonstration of antibodies to *Bacillus piliformis* in SPF colonies and experimental transplacental infection by *Bacillus piliformis* in mice. Lab. Anim. 12:23-26.
31. Fries, A.S. 1979. Studies on Tyzzler's disease: transplacental transmission of *Bacillus piliformis* in rats. Lab. Anim. 13:43-46.
32. Maejima, K., K. Fujiwara, Y. Takagaki, M. Naiki, H. Kurashina, and Y. Tajima. 1965. Dietetic effects on experimental Tyzzler's disease. Jpn. J. Exp. Med. 35:1-10.
33. Ganaway, J.R., A.M. Allen, and T.D. Moore. 1971. Tyzzler's disease. Am. J. Pathol. 64:717-730.
34. Waggie, K.S., C.T. Hansen, J.R. Ganaway, and T.S. Spencer. 1981. A study of mouse strain susceptibility to *Bacillus piliformis* (Tyzzler's disease): the association of B-cell function and resistance. Lab. Anim. Sci. 31:139-142.
35. Fries, A.S. 1980. Antibodies to *Bacillus piliformis* (Tyzzler's disease) in sera from man and other species, p. 249-252. In A. Spiegel, S. Erichsen, and H.A. Utrecht (ed.), Animal quality and models in biomedical research: 7th ICLAS Symposium, Utrecht. Gustav Fischer Verlag, New York.
36. Motzel, S.L., and L.K. Riley. 1992. Subclinical infection and transmission of Tyzzler's disease in rats. Lab. Anim. Sci. 42:439-443.
37. Waggie, K.S., L.P. Thornberg, K.J. Grove, and J.E. Wagner. 1987. Lesions of experimentally induced Tyzzler's disease in Syrian hamsters, guinea pigs, mice and rats. Lab. Anim. 21:155-160.
38. Franklin, C.L., S.L. Motzel, L.K. Riley, R.R. Hook, Jr., and C.L. Besch-Williford. Tyzzler's disease: host specificity of *C. piliforme* isolates. Lab. Anim. Sci. (In press.)
39. Takagaki, Y., and K. Fujiwara. 1968. Bacteremia in experimental Tyzzler's disease of mice. Jpn. J. Microbiol. 12:129-143.
40. Riley, L.K., C.J. Caffrey, V.S. Musille, and J.K. Meyer. 1992. Cytotoxicity of *Bacillus piliformis*. J. Med. Microbiol. 37:77-80.
41. Hansen, A.K., F. Dagnaes-Hansen, and K.-E. Mollegaard-Hansen. 1992. Correlation between megaloblastosis and antibodies to *Bacillus piliformis* in laboratory rat colonies. Lab. Anim. Sci. 42:449-453.
42. Veazey, R.S., D.B. Paulsen, and D.O. Schaeffer. 1992. Encephalitis in gerbils due to naturally occurring infection with *Bacillus piliformis* (Tyzzler's disease). Lab. Anim. Sci. 42:516-518.
43. Yokomori, K., N. Okada, Y. Murai, N. Goto, and K. Fujiwara. 1989. Enterohepatitis in mongolian gerbils (*Meriones unguiculatus*) inoculated perorally with Tyzzler's organism (*Bacillus piliformis*). Lab. Anim. Sci. 39:16-20.
44. Waggie, K.S., J.R. Ganaway, J.E. Wagner, and T.H. Spencer. 1984. Experimentally induced Tyzzler's disease in mongolian gerbils (*Meriones unguiculatus*). Lab. Anim. Sci. 34:53-57.
45. Fries, A.A. 1979. Studies on Tyzzler's disease: acquired immunity against infection and activation of infection by immunosuppressive treatment. Lab. Anim. 13:143-147.
46. Gibson, S.V., K.S. Waggie, J.E. Wagner, and J.R. Ganaway. 1987. Diagnosis of subclinical *Bacillus piliformis* infection in a barrier-maintained mouse production colony. Lab. Anim. Sci. 37:786-788.
47. Nakayama, H., S. Oguihara, K. Osaki, W. Toriumi, and K. Fujiwara. 1984. Effect of cyclophosphamide on Tyzzler's disease of mice. Jpn. J. Vet. Sci. 47:81-88.
48. Thunert, A. 1980. Investigations into an antigen causing Tyzzler's disease in mice (*Bacillus piliformis*). Z. Versuchstierk. 22:323-333.
49. Savage, N.L., and W.G. Sheldon. 1973. An epizootic of diarrhea in a rabbit colony. Pathology and bacteriology. Can. J. Comp. Med. 37:313-319.
50. Savage, N.L., and D.H. Lewis. 1972. Application of immunofluorescence to detection of Tyzzler's disease agent (*Bacillus piliformis*) in experimentally infected mice. Am. J. Vet. Res. 33:1007-1011.
51. Waggie, K.S., T.H. Spencer, and J.R. Ganaway. 1987. An enzyme-linked immunosorbent assay for detection of anti *Bacillus piliformis* serum antibody in rabbits. Lab. Anim. Sci. 37: 176-179.
52. Boivin, G.P., R.R. Hook, Jr., and L.K. Riley. 1994. Development of a monoclonal antibody-based competitive inhibition ELISA for detection of *Bacillus piliformis* isolate-specific antibodies in laboratory animals. Lab. Anim. Sci. 44:153-158.

[Previous](#) | [Index](#) | [Next](#)

[Back to top of page](#)