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Francisellosis of Atlantic cod (*Gadus morhua* L.)

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Susceptible species

Francisellosis, caused by infection with *Francisella noatunensis*, primarily affects Atlantic cod (*Gadus morhua*) and was first described in Norway in 2004 (Nylund *et al.*, 2006) and 2005 (Olsen *et al.*, 2006). The disease has also been reported affecting Atlantic salmon (*Salmo salar*) in Chile (Birkbeck *et al.*, 2007).

Disease name

Francisellosis.

Aetiological agent

F. noatunensis is recognized as the causative agent of francisellosis in Atlantic cod (Ottem *et al.*, 2009). Bacteria belonging to the genus *Francisella* are Gram-negative, non-motile, aerobic, facultative intracellular organisms belonging to the γ -proteobacteria. *Francisella* sp. are generally biochemically unreactive and the number of phenotypical tests useful for differentiation of the species are few (Colquhoun and Duodo, 2011). Fish pathogenic *Francisella* sp. can be distinguished by their requirement for cysteine in culture media and their inability to grow at temperatures above 35°C (Ottem *et al.*, 2007).

Geographical distribution

The disease has been reported primarily from farmed Atlantic cod in Norway (Nylund *et al.*, 2006; Olsen *et al.*, 2006) and from wild-caught cod from the South coast of Ireland and subsequently reared in a research facility (Ruane *et al.*, 2015). There is also evidence that the bacterium is present in wild Atlantic cod along the west coasts of Sweden and Norway, with a reported prevalence of 6.8% off southwest Norway (Alfjorden *et al.*, 2006; Ottem *et al.*, 2008; Colquhoun and Duodo, 2011). A visceral granulomatous disease in Atlantic cod in the North Sea in the 1980s was also reported to be due to *F. noatunensis* (Zerihun *et al.*, 2011). The disease has also been reported causing mortalities in freshwater farmed Atlantic salmon in Chile (Birkbeck *et al.*, 2007).

Associated environmental conditions

There is little information available on the environmental conditions associated with clinical Francisellosis. Clinical disease has been reported in Atlantic cod at water temperatures above 14°C (Olsen *et al.*, 2006; Ruane *et al.*, 2015) and Ottem *et al.*, (2008) suggested that the differences in disease prevalence in cod farms in the north and south of Norway could be temperature related.

Significance

Francisellosis is a significant health problem for Atlantic cod aquaculture, particularly in Norway which has seen a decline in the number of registered farms from 240 in 2007 to 84 in 2012 (Hjeltne, 2014). As the disease is chronic in nature and highly infectious, the prevalence of infected fish in a population can be high.

Gross clinical signs

Francisellosis is principally a chronic systemic granulomatous inflammatory disease with varying degrees of mortality. The gross signs observed among most host species are similar and include disseminated white nodules of various sizes in liver, spleen and kidney although most tissues and organs may be affected. Splenomegaly and sero-sanguinous ascites has been observed in cod. Microscopic lesions include widespread chronic granulomatous inflammation in all organs, associated with variable numbers of Gram-negative bacteria (Birkbeck *et al.*, 2011).

Control measures and legislation

Francisellosis is not reportable to the OIE but is a List 3 disease in Norway. There is currently no licensed vaccine available for the disease although research on a trial vaccine for francisellosis caused by *F. asiatica* in tilapia, *Oreochromis niloticus* has shown promise (Soto *et al.*, 2011). Due to the intracellular nature of the bacterium, antibiotic treatment has proven difficult and there are no reports of successful antibiotic treatments of francisellosis in Atlantic cod.

Diagnostic methods

The gold standard for diagnosis of francisellosis is culture of the bacterium combined with macroscopic and histological observations of affected tissues (Colquhoun and Duodo, 2011). *F. noatunensis* does not grow on routine, general-purpose agar plates and is also easily outcompeted by other bacteria. Several agars selective for *Francisella* sp. have been published (Birkbeck *et al.*, 2011), the most common being cysteine heart agar supplemented with antibiotics. Immunohistological methods have also been used to diagnose this disease (Jansson *et al.*, 2007). Diagnosis using molecular methods is also common for francisellosis including sequencing of the 16S rRNA gene (Nylund *et al.*, 2006; Olsen *et al.*, 2006), real-time PCR (Ottem *et al.*, 2008) and *in situ* hybridization (Colquhoun and Duodo, 2011).

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Figure 1. Gross clinical appearance of Atlantic cod, *Gadus morhua*, with francisellosis showing characteristic multiple granulomas (white spots) on the liver.



Figure 2. Close up from the caudal part of body cavity of wild Atlantic cod with francisellosis. Multiple granulomas (white spots) are seen in the spleen. Granulomas of various development stages can be observed in a range of organs/tissues: liver, kidney, spleen, skin, heart.

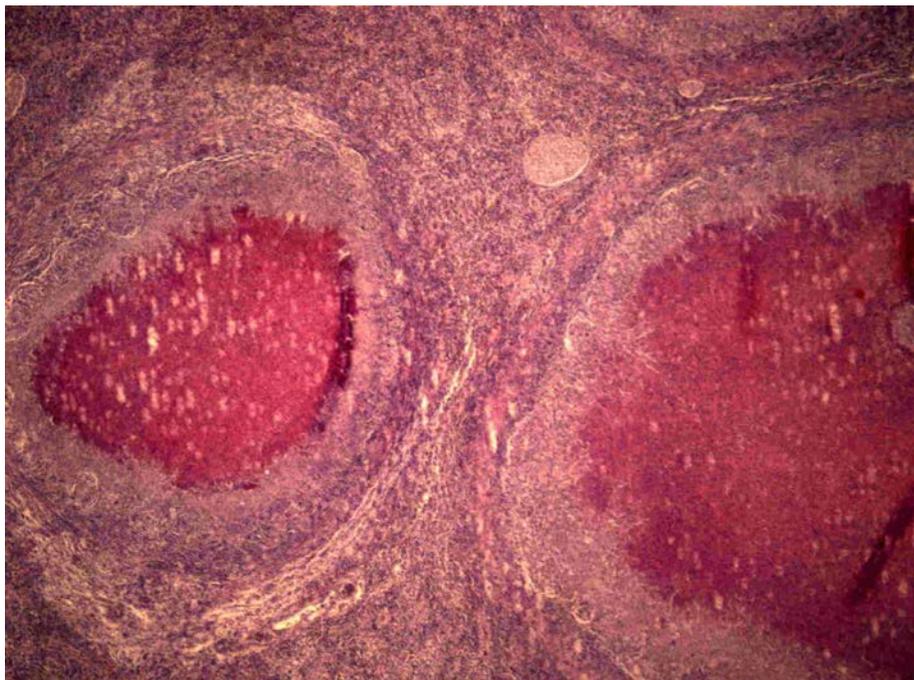


Figure 3. PAS stained section of spleen, low magnification. Two large granulomas in spleen of Atlantic cod.

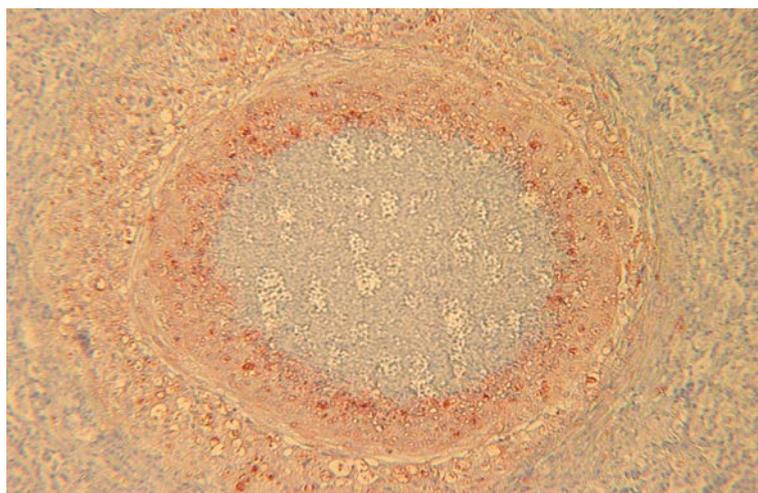


Figure 4. Immunohistology-stained section of spleen, low magnification. The epitheloid cells surround areas with numerous *Francisella* bacteria predominately in vacuoles and in macrophages. There is no *Francisella* bacteria observed in the inner parts of the granuloma.

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