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REVIEW

Emerging flavobacterial infections in fish: A review

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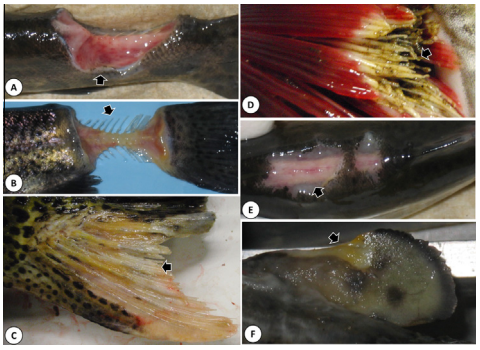
GRAPHICAL ABSTRACT



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ABSTRACT

Flavobacterial diseases in fish are caused by multiple bacterial species within the family Flavobacteriaceae and are responsible for devastating losses in wild and farmed fish stocks around the world. In addition to directly imposing negative economic and ecological effects, flavobacterial disease outbreaks are also notoriously difficult to prevent and control despite nearly 100 years of scientific research. The emergence of recent reports linking previously uncharacterized flavobacteria to systemic infections and mortality events in fish stocks of Europe, South America, Asia, Africa, and North America is also of major concern and has highlighted some of the difficulties surrounding the diagnosis and chemotherapeutic treat-

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ment of flavobacterial fish diseases. Herein, we provide a review of the literature that focuses on *Flavobacterium* and *Chryseobacterium* spp. and emphasizes those associated with fish.

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Introduction

Flavobacterial diseases were first reported by Davis in 1922 and have since been recognized as a serious threat to wild and propagated fish stocks alike. Originally, these diseases were attributed to three bacteria within the family Flavobacteriaceae [1]; namely, *Flavobacterium psychrophilum*, the etiological agent of bacterial cold water disease and rainbow trout fry syndrome [2,3]; *Flavobacterium columnare*, the causative agent of columnaris disease [4,5]; and *Flavobacterium branchiophilum*, the putative agent of bacterial gill disease [5,6]. Others have reported additional *Flavobacterium* spp. associated with diseased fish, including *Flavobacterium johnsoniae* [7], *Flavobacterium succinicans* [8], *Flavobacterium hydatis* [9], as well as other uncharacterized yellow-pigmented bacteria (Austin and Austin [10] and references therein). In acute flavobacteriosis, cumulative mortality upwards of 70% can occur among affected fish stocks, while survivors may suffer poor growth and spinal abnormalities (reviewed in Austin and Austin [10]). In subacute and chronic infections, flavobacteriosis elicits lingering mortalities that can lead to continuous economic losses [11]. Taxonomy and speciation of this family has undergone many revisions; therefore, throughout this review, the most currently recognized terminology of genera and species will be used.

With the recent advances in molecular biology and biotechnology, several novel genera within the family Flavobacteriaceae (e.g., *Chryseobacterium*, *Elizabethkingia*, *Tenacibaculum*, and *Ornithobacterium*) have emerged that encompass pathogens of fish, amphibians, reptiles, birds, and mammals, including humans [1]. Among these, *Tenacibaculum* spp. are important pathogens of marine fishes that have been reviewed elsewhere [12,13] and will not be discussed further herein. Rather, this review predominantly focuses on the genera *Flavobacterium* and *Chryseobacterium*, within which multiple novel species have been described over the last decade in association with diseased fishes from around the world [14–26].

History of flavobacterial diseases in fish

In the process of studying protozoan parasites at the U.S. Fisheries biological station in Fairport, Iowa, Davis [27] observed multiple fish mortality events during the summers of 1917–1919 that he associated with an unidentified bacterium. The affected fish, which included buffalofish (*Ictiobus bubalus*), sunfish (*Leopomis* spp.), common carp (*Cyprinus carpio*), largemouth and smallmouth bass (*Micropterus salmoides* and *Micropterus dolomieu*), crappie (*Pomixis* spp.), warmouth (*Leopomis gulcosus*), yellow perch (*Perca flavescens*), white bass (*Morone chrysops*), brook trout (*Salvelinus fontinalis*), bluntnose minnow (*Pimephalus notatus*), channel catfish (*Ictalurus punctatus*), and bullhead catfish (*Ameiurus* spp.), were cultured in aquaria and earthen ponds. Davis [27] noted that affected fish displayed "dirty-white or yellowish areas" on the body, whereby lesions developed and caused death within 24–72 h. Fins (especially the caudal fin) were eroded and, in more severe cases, only "mere stubs" remained. There was also necrosis of the gills visible as white patches that spread rapidly, causing death. The author also observed mortalities in wild fishes of the Mississippi River associated with this bacterium. Although he was unable to isolate the bacterium in any of these outbreaks, he observed large numbers of long, slender, flexible rods associated with the necrotic lesions of the skin and gills of affected fish that formed "column-like masses"; thus, he named the bacterium *Bacillus columnaris*. Two decades later, Ordal and Rucker [28] successfully isolated the yellow-pigmented bacterium and named it *Chondrococcus columnaris* due to its association with cartilage and what they characterized as the production of fruiting bodies and microcysts. However, Garnjobst [29] showed that *C. columnaris* did not produce such structures and reclassified the bacterium within the genus *Cytophaga*, as *Cytophaga columnaris*. While agreement on the negative impacts this bacterium had on fish stocks was well accepted, as evidenced by its inclusion in the list of notifiable fish diseases outlined in the British Diseases of Fish Act of 1937 [10], the disagreement on its taxonomy continued when it was provisionally placed into the genus *Flexibacter* [30,31]. Extensive molecular and phylogenetic studies by Bernardet et al. [32] placed the bacterium in the genus *Flavobacterium* as *F. columnare*, where it has remained to the present day and is recognized as the etiologic agent of columnaris disease.