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COUNTER-INSURGENTS OF THE BLUE REVOLUTION? PARASITES AND DISEASES AFFECTING AQUACULTURE AND SCIENCE

Reginald B. Blaylock and Stephen A. Bullard*

Department of Coastal Sciences, Gulf Coast Research Laboratory, University of Southern Mississippi, 703 East Beach Drive, Ocean Springs, Mississippi 39564. Correspondence should be sent to: *reg.blaylock@usm.edu*

ABSTRACT: Aquaculture is the fastest-growing segment of food production and is expected to supply a growing portion of animal protein for consumption by humans. Because industrial aquaculture developed only recently compared to industrial agriculture, its development occurred within the context of a growing environmental awareness and acknowledgment of environmental issues associated with industrial farming. As such, parasites and diseases have become central criticisms of commercial aquaculture. This focus on parasites and diseases, however, has created a nexus of opportunities for research that has facilitated considerable scientific advances in the fields of parasitology and aquaculture. This paper reviews *Myxobolus cerebralis*, *Lepeophtheirus salmonis*, white spot syndrome virus, and assorted flatworms as select marquee aquaculture pathogens, summarizes the status of the diseases caused by each and their impacts on aquaculture, and highlights some of the significant contributions these pathogens have made to the science of parasitology and aquaculture.

The cultivation of organisms in water (aquaculture) represents 0.6% of the world's gross domestic product (agriculture = 9 billion tons/yr; aquaculture = 60 million tons/yr) but approximately 3.6% of the animal protein consumed by humans (Boyd et al., 2013). Asian nations (China, Vietnam, Thailand) account for about 90% of aquaculture production (FAO, 2010; Boyd et al., 2013, and references therein). Aquaculture production in the United States is in its infancy and clearly not keeping pace with rapidly advancing technologies and the scale of aquaculture production in other nations.

Since beginning in China 4,000 yr ago, aquaculture has been largely a subsistence activity. The forerunner technologies of modern aquaculture were conceived in the mid-1800s, and in the mid-twentieth century, advanced techniques helped supplement stagnating capture fisheries (Boyd et al., 2013). Beginning in the mid-1900s, as a result of advances in hatchery technology and declines of some wild fish stocks, industrial aquaculture began in earnest. By 2008, aquaculture had become a major industrial complex responsible for producing >$100 billion of product and directly supporting over 11 million jobs worldwide; aquaculture is now the fastest-growing segment of food production (FAO, 2010). Combined with the resurgence of interest in science-based stock enhancement in the late 1990s to support the multimillion dollar recreational fishing industry, modern aquaculture has become a major economic engine. Worldwide, about half of fisheries products come from aquaculture (FAO, 2010). Wild fisheries production, of which the United States is a significant contributor, has been stable since the late 1980s (Boyd et al., 2013) and is not expected to increase significantly in the future, because approximately 90% of known fisheries resources are either overexploited, fully exploited, depleted, or recovering (FAO, 2010). The United States is a major exporter of agricultural products but a minor producer of aquaculture products (of which a trivial amount is exported); however, the United States is a major importer. Approximately 80% of the seafood consumed by Americans is imported, and the annual seafood trade deficit approaches $10 billion.

Boyd et al. (2013, p. 15) stated that, "Aquaculture is an old endeavor dating back thousands of years, but it came of age in the midst of the current era of environmental awakening and is embroiled in the sustainability controversy." Although the world's population would have failed to reach the current level without industrial agriculture ("Green Revolution"), aquaculture ("Blue Revolution"), and advances in control of human diseases (also intimately linked to water resource uses), the worldwide success and proliferation of agriculture and aquaculture have come at a price. Environmentalist non-governmental organizations (eNGOs; sensu Boyd et al., 2013) underscore concern about the environmental footprint of aquaculture. Traditional agriculture has been criticized for failure to protect the environment, genetic pollution, inhumane treatment of animals, introduction of invasive species, and spread of disease(s). Aquaculture has garnered many of the same criticisms, but it is unusual in several aspects. First, commercial aquaculture is a young industry. Other food production industries were well established before the advent of commercial aquaculture, and the problems associated with the development of those industries were well known as aquaculture began to expand. Second, aquaculture coexists with wild fisheries both geographically and economically. No other commercial food production industry competes with, or shares the market with, wild product. Third, whereas other commercial food production industries are based on single-species models, the "aquaculture industry" represents the culture of an ever-growing roster of fishes, shellfishes, and plant species. Finally, aquaculture happens in water, a shared resource that is difficult to contain or delineate into parcels and that is governed by the public trust doctrine. The combination of these characteristics has placed aquaculture in a unique position that has created considerable controversy as the industry's growth has coincided with increasing interest in sustainability and environmental stewardship.

While the environmental and genetic concerns with respect to agriculture and aquaculture are not trivial, issues related to diseases and parasites are of particular importance, as evidenced by the existence of the veterinary medical industry. Indeed, the development of disease-resistant crop varieties facilitated the growth of industrial agriculture (Borlaug, 1983). Similarly, parasites and infectious diseases are a primary bottleneck that constrains the "Blue Revolution" (Subasinghe et al., 1998). Diseases and parasites have been relocated along with animals, and new diseases have emerged and spread amongst wild and cultured animals. Despite the lack of quantitative evidence, the role of aquaculture in harboring and spreading disease in the

* Aquatic Parasitology Laboratory, School of Fisheries, Aquaculture, and Aquatic Sciences, Auburn University, Auburn, Alabama 36849.
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aquatic environment has become one of the main arguments against the development of a robust domestic aquaculture industry in the United States.

The notion of disease is not simple but can be simply defined. Perhaps the simplest of definitions is "deviation from normal." Another definition is "an extreme of the host–parasite relationship marked by the presence of a lesion (gross, histological, physiological, behavioral) and/or mortality of the infected host." The likelihood and severity of disease are often directly correlated with the intensity of the infection (i.e., the number of individuals of a parasite species infecting the individual host) and analogous to the dose of a toxin. For example, a captive fish infected by a multitude of parasites is of concern to husbandry staff, who likely will treat the infection because of the intuitive likelihood that the fish will become sick, die, or act as a reservoir host, facilitating infection of its tank mates. On the other hand, and perhaps erroneously, parasitologists seldom consider duration of exposure (length of time the pathogen and host interact) as predictive of the likelihood of disease.

More generally, little information is available on how often, and under what conditions, protozoans, metazoans, bacteria, or viruses weaken or kill their aquatic hosts in nature. Observing sick or dead fish in the ocean is challenging or unlikely, considering weakened hosts are likely consumed by predators before death, quickly consumed by scavengers, or simply out of reach in the vast space and depth of the ocean. Perhaps this explains why there are so few reports of wild mortalities of fishes attributable to infectious disease and virtually none for the majority of ecto- and endoparasite taxa that routinely associate with fishes (see examples in Bakke et al. [2007] and Bullard and Overstreet [2008]). In some cases, these disease outbreaks result from several unusual events acting in synergy (e.g., presence of an introduced/non-native pathogen and/or host, sudden meteorological changes/anomalies [rapid warming or cooling], and an anthropogenic concentration of susceptible hosts [Bakke et al., 2007; Bullard and Overstreet, 2008]). Parasitic diseases in culture, on the other hand, are easily observed. Thus, aquaculture (apart from the translocation of diseases) is assumed to facilitate disease. As such, the growth of aquaculture has allowed significant research into the occurrence of myriad parasites and diseases, and it will continue to do so as new fish species are brought into culture along with their diseases. Indeed, several books and reviews provide thorough accounts of parasites and diseases with significant biological or economic impacts on aquaculture (e.g., Woo, 1995; Plumb, 1999; Scholz, 1999; Woo and Bruno, 1999; Kent, 2000; Austin and Austin, 2007; Eiras et al., 2008; Woo and Buchmann, 2012; Lafferty et al., 2014).

Herein, we highlight select marquee aquaculture pathogens, summarize the status of the disease and its impact on aquaculture, and review the significant contributions these pathogens have made to the science of parasitology and aquaculture. Our choices and coverage are necessarily limited by space constraints. Bacterial pathogens and other disease agents are well-known primary actors in the initiation of diseases across all organisms in all aquaculture settings, but we do not and cannot address all categories of pathogens. Rather, we have chosen examples across the spectrum of taxa, including *Myxobolus cerebralis*, *Lepeophtheirus salmonis*, white spot syndrome virus (a non-traditional parasite), and assorted flatworms, which provide a nexus from which to evaluate some significant scientific advances facilitated by parasites and diseases. Finally, we elucidate a potential path forward for both the science of parasitology and aquaculture.

WHIRLING DISEASE

Myxobolus cerebralis, the causative agent of whirling disease in salmonid fishes, is a myxozoan parasite first identified in Germany in 1893 apparently benignly infecting native brown trout (*Salmo trutta*). In 1903, rainbow trout (*Oncorhynchus mykiss*) and brook trout (*Salvelinus fontinalis*) imported as eggs from the United States experienced inflammatory, granulomatous lesions throughout the cranium and vertebral column that resulted in skeletal abnormalities, abnormal swimming behavior, and extensive mortality. The disease spread quickly, aided particularly in the post–World War II era by massive transfaunation of live rainbow trout (Hoffman, 1970). By 1950, most of Central Europe was involved. By the 1970s, the parasite had spread to an additional 18 Central and Northern European countries, the USSR, Lebanon, the United States, Morocco, South Africa, and New Zealand. In the United States, the infection was first detected in Pennsylvania in 1956. Since then, the disease has spread to 25 states, primarily in the northeast and Rocky Mountain west (Bartholomew and Reno, 2002; Hallett and Bartholomew, 2012). In Europe, the disease was primarily a hatchery issue affecting non-native salmonids. Outside of Europe, as the parasite spread to wild, susceptible populations, some populations were devastated. As a result of the perceived economic and biological threat, this parasite facilitated research that has resulted in significant advances in our understanding of its life history and ecology/epidemiology, with implications for public policy.

Life history

By the time the spread was in progress, scientists understood that the disease was associated with sediments. Schaperclaus (1931) cautioned against disturbing sediments. Beginning in the 1930s, the prevailing wisdom was that spores were released from dead fish, aged in mud for 3–6 mo, which then were ingested (Hoffman and Putz, 1969; Bartholomew and Reno, 2002). It was not clear how spores were released from the mud, but several researchers between the 1930s and 1970s had examined ideas on transmission. Schaperclaus (1931) argued that horizontal transmission was unlikely. O'Grodnick (1975) demonstrated that the parasite was not vertically transmitted. Throughout the 1960s and 1970s, there was disagreement over whether or not myxosporean spores were directly infective to fish. Some researchers (e.g., Hoffman and Putz, 1969; Uspenskaya, 1978) claimed success in direct transmission experiments. Others (e.g., Schafer, 1968; Molnar, 1979) reported failure (for summary, see Kent et al., 1993). Several investigators had proposed the idea of an alternative host (Schaperclaus, 1931; Schafer, 1968; Sanders et al., 1970), but none had been found. During this same period, knowledge of a group of related parasites in oligochaetes called actinosporeans was progressing. Like the myxosporeans, the life cycle and transmission mechanism of actinosporeans were unknown, and direct worm to worm transmission had not been demonstrated (Marques, 1984).

In the early 1980s, a series of papers by Markiw and Wolf (Markiw and Wolf, 1983; Wolf and Markiw, 1984) demonstrated conclusively that spores of *M. cerebralis* did not produce infection

when ingested by salmonids. They also reported that a tubificid oligochaete was required as an alternative host. Markiw and Wolf's discovery (later confirmed by El-Matbouli and Hoffman [1989] and Hedrick et al. [1989]) that representatives of 2 entirely different classes of organisms actually represent different life history stages of a single organism transformed our knowledge of an entire phylum of organisms. In 1994, after 14 myxosporean genera had been shown to share similar life cycles requiring an actinosporean in an oligochaete, Kent et al. (1994) suppressed the Class Actinosporea and all families within it as part of the Myxosporea, a single class in the Phylum Myxozoa. Subsequent debates have focused on the validity of the phylum itself, but that is beyond the scope of this paper.

Ecology/epidemiology

The new knowledge of the life cycle brought into focus many of the observations accumulated during the 80-yr history of the disease and provided a potential means for investigating the biology and ecology of the organism. Although there was originally much debate about the source (i.e., spillover from brown trout in which it was benign or transfer from marine fish used as food in hatcheries), spread through movement of infected fish or fish tissue can be documented (see Bartholomew and Reno, 2002). The rapid spread also suggested that several or concurrent introductions may have occurred (Hnath, 1996). Monitoring the spread of the infection in the United States had produced a number of interesting findings (reviewed in Bartholomew and Reno, 2002).

The presence of the parasite in hatcheries does not necessarily translate into spread in the wild. At least 5 states that report presence in hatcheries suggest no evidence of the parasite in wild populations. In some cases, documented stocking of infected fish produced no infections in the wild. In other cases, even though the infection spread to the wild, removing the source of infection (closing of the infected hatchery) resulted in a decrease in prevalence in the wild. Likewise, presence in the wild does not necessarily mean disease. In Europe, even though the organism was widespread, the disease was mostly a hatchery phenomenon attributed to the concentrated presence of fry. California, for example, has had the parasite since the mid- to late-1960s but reports little impact on wild populations (Modin, 1998). Colorado and Montana have reported substantial (90%) decreases in rainbow trout populations (Walker and Nehring, 1995; Vincent, 1996).

In light of these observations, scientists began to hypothesize about the factors that might facilitate the maintenance or spread of an infection. Over 30 yr, methodical research has elucidated much about the host/environment/pathogen relationship in systems affected by this parasite. Water temperature appears to be a primary determinant of impact. As with any organism, *M. cerebralis* and its hosts require a certain range of temperature (10–15 C). Deviation from this range affects the development rate of the parasite in the hosts, the pattern of shedding from the oligochaete host (i.e., the number of actinospores available), and the timing of the overlap of the 2 hosts to facilitate transmission (reviewed in Hallett and Bartholomew, 2012). Actinospores are buoyant and carried in the current; thus, increased flow decreases the number of actinospores available in a given area for transmission and results in decreased severity of infection. Myxospores, on the other hand, settle. However, high flow might carry those myxospores away from an environment conducive to transmission (Bartholomew et al., 2005; Hallett and Bartholomew, 2008). Although tubificid worms are widespread in their distribution, they tend to be less common in areas of high water flow and more common in areas of low flow and high sedimentation (Krueger et al., 2006; Hallett and Bartholomew, 2008).

Factors attributable to the hosts include the characteristics and composition of the fish community. Complex communities with multiple species of salmonids may be more likely to maintain the infection, but species less affected by the disease, such as brown trout, may produce fewer myxospores per given dose of actinospores than rainbow trout (Hedrick et al., 1999). The number of young salmonids with unossified bone is correlated with severity of disease (Bartholomew et al., 2005). Susceptibility of the hosts also is an important determinant. Almost all salmonids are capable of sustaining the infection, but rainbow trout and several subspecies of cutthroat trout (*Oncorhynchus clarki*) appear to be the most susceptible. Brook trout show somewhat reduced susceptibility. Atlantic salmon (*Salmo salar*), brown trout, several species of anadromous Pacific salmon, and Arctic grayling are somewhat to highly resistant (see table 8.2 in Hallett and Bartholomew, 2012). A quantitative trait locus that controls 50–86% of the variation in resistance has been identified (Baerwald et al., 2011). Some populations of oligochaetes have shown resistance (Beauchamp et al., 2002, 2005). Where susceptible fish species have experienced reduced populations, fish community structure has shifted as resistant species have filled the niches (Granath et al., 2007). As the fish community shifts, the transmission rate may change as more resistant fish shed fewer myxospores. Variability in the susceptibility of the tubificids has been noted as well (Krueger et al., 2006).

Pathogen-associated factors include dose and virulence. Although other factors can influence the availability of spores in the environment, dose in and of itself is an important determinant of infection. Severity of disease is positively correlated with dose (Hallett and Bartholomew, 2008). A more virulent pathogen may induce disease from a smaller dose than one of low virulence. Bartholomew et al. (2005) reported no differences in virulence among geographically diverse isolates. Early genetic studies (Andree et al., 1999; Whipps et al., 2004) showed little genetic variation among isolates, but recent work (Lodh et al., 2012) that included increased sample sizes and geographic range suggests there is variation and perhaps multiple introductions of the parasite to North America.

Policy and practice

Prior to, and during, the original outbreak of whirling disease, fish health was an inexact science. Several diseases, including whirling disease, manifested as vaguely similar symptoms, and diagnosis of whirling disease was possible only through physical observation of spores. Even observation of the spores was of limited value due to the lack of knowledge of the life history. Although the parasite continued to be a problem in Europe throughout the 1950s and 1960s, observations had led to strategies to accomplish some degree of management and control. These strategies included switching from earthen ponds to synthetic rearing vessels based on the observation that the disease

appeared to be associated with sediments, the separation of juvenile fish from adults based on the observation that juveniles with unossified bone were more susceptible to disease, and the use of independent well or spring water supplies for juvenile rearing based on the observation that it was an infectious agent in surface waters. As the parasite spread beyond European hatcheries and concern over the spread of the disease grew, fish health practitioners mobilized to respond to what was one of the earliest worldwide fish health emergencies. Unfortunately, what had been learned did not prohibit the shipment of live salmonids. Hoffman (1968) was one of the first to provide standardized detailed methods for detecting the parasite, which included instructions on how to process head tissue to reveal the presence of spores. The ability to accurately assess the presence or absence of the parasite led to efforts to restrict movement of fish. In some cases, depopulation orders were given in efforts to control the parasite after introduction (Bartholomew and Reno, 2002).

In 1968, the issue of whirling disease helped to develop the concept of a reportable disease that would disqualify import of an aquatic organism. The first national fish disease law in the United States (Code of Federal Regulations, Title 50, Section 13.7) was passed in 1968 with the intent of preventing the import of certain fish diseases, including whirling disease. To meet the criteria for importation, salmonids and salmonid eggs had to be certified as free of the pathogens in question. To be certified free of whirling disease, fish for importation had to be from sources free of the disease for the lifetime of the fish, eggs and sperm had to come from sources free of infection for 1 yr, and any incubation must have been done in water free of *M. cerebralis*–positive fish (Bartholomew and Reno, 2002). Issues surrounding whirling disease and a few other fish pathogens led to the establishment of the Fish Health Section of the American Fisheries Society in 1972 and subsequent founding of the Fish Health Blue Book in 1975, which set official standards for detection and identification of specific fish pathogens.

Whirling disease also presents an opportunity for the future because much remains to be done to achieve control. Drugs have been of little benefit, but they provide an opportunity for research. As the parasite is firmly established in many places, control must incorporate the vast knowledge of ecology and epidemiology achieved over the years and focus on mitigating the effects of the disease. Risk assessment models (i.e., Bartholomew et al., 2005) and epidemic modeling can be used to predict the likelihood of introduction and establishment given a certain set of variables at a given location.

SEA LICE

Although approximately 600 species comprising 37 genera of caligid copepods (Order Siphonostomatoida) parasitize marine fishes (Ahyong et al., 2011), *Lepeophtheirus salmonis*, more commonly known as the sea (or salmon) louse, which parasitizes salmonid fishes in the Northern Hemisphere, is perhaps the most well known because it accounts for up to $500 million in economic losses annually (Costello et al., 2004; Costello, 2009). *Lepeophtheirus salmonis* has a typical caligid life cycle consisting of 5 phases and 10 stages, including 2 free-swimming naupliar stages, one free-swimming infective copepodid stage, four attached chalimus stages, 2 mobile but host-associated pre-adult stages, and a mobile, but host-associated, adult stage (Kabata, 1972; Johnson and Albright, 1992). The organism is stenohaline and adapted to the life cycle of anadromous salmonids that transit through estuarine areas in high concentrations and overlap with multiple species and/or generations, where the transmission of the infective stages occurs before the adults enter freshwater and the smolts depart for the open ocean. Parasitic stages feed on the mucus, skin, and blood of the host (Burka et al., 2012).

Unlike traditional agriculture in which animals are contained in farms with no wild counterparts, salmon aquaculture typically involves net pens in which salmon are held in cages suspended in coastal waters or the open ocean, where they are surrounded by wild fishes. The continuous presence of large numbers of farmed salmon interacting with wild animals and the environment additionally created the perception that salmon farming provided ideal conditions for disease transmission and environmental degradation, which resulted in conflicts among the salmon farming industry, government, and eNGOs. As a result, the sea louse–salmon system has been instructive in the scientific understanding of key aspects of parasite and host biology as well as the role of science in a modern media-based society.

Host and parasite biology

Although the parasite has been known for more than 100 yr, detailed studies of the parasite's morphology, life history, and ecology were accomplished only after the parasite emerged as a serious pathogen in aquaculture. Burka et al. (2012), Torrissen et al. (2013), and references therein, describe the general biology of the sea louse. The work also has elucidated some issues relevant to the host–parasite interaction. The parasite releases trypsin and prostaglandins, which aid in the digestion of host tissue and down regulation of the host immune response (Fast et al., 2005; Wagner et al., 2008). Depending on the intensity of infection, the parasite elicits a stress response in the host due to the fluid and tissue loss at the feeding site. The stress response includes cortisol release, which modulates the host immune response and may result in increased susceptibility to other diseases. Subclinical sequelae include changes in blood glucose, electrolytes, reduced hematocrit, and reduced swimming performance (Johnson and Albright, 1992; Ross et al., 2000). Not all hosts are equally susceptible (see Burka et al., 2012). Resistant hosts typically mount strong localized and systemic hyperplastic and inflammatory responses that include neutrophil infiltration and result in either shedding of the lice or tolerance of high parasite numbers. In susceptible hosts, immune processes are down regulated by the presence of the parasite (Fast et al., 2006a, 2006b). In addition to interspecific differences in resistance, heritable intraspecific differences have been identified, but the markers identifying the resistance are poorly understood (reviewed in Torrissen et al., 2013).

Ecology/epidemiology

The need to understand, predict, and control the impacts of sea lice has driven the collection of large-scale ecological data sets that have provided the opportunity to understand more about the population dynamics and epidemiology of sea lice than perhaps any other aquatic pathogen. Sea lice are common on wild adult fish, although the intensity of infection can be low (Nagasawa, 2001; Jackson et al., 2013). As the adult fish return to estuaries and freshwater, where they experience elevated temperatures and a significant concentration of fish, sea lice proliferate. Under

normal circumstances, the parasite is rarely problematic. Fish typically move through the estuary into freshwater, where the parasites are shed. If fish experience low water flow and/or high temperatures that impede their passage into freshwater, the population of sea lice builds and produces significant lesions that expose underlying muscle and bone and result in osmotic imbalances that induce morbidity and mortality (Johnson et al., 1996). In Europe, sea lice infestation increases in the spring as wild salmon return to the coast. The size of adult females reaches a maximum (and most fecund), and the parasite population structure also shifts toward younger chalimus (and presumably copepodid) stages, indicating significant transmission in inshore waters (Torrissen et al., 2013). In British Columbia, consistent patterns in increases or decreases in lice infestation have been elusive due to the more or less continuous presence of large populations of 6 species of wild anadromous salmonids. Clearly, returning adult salmon commonly carry lice, but pink and chum salmon appear to carry more (Nagasawa, 1987; Torrissen et al., 2013). In addition, the same body of water may concurrently support different species returning at different times, different runs within the same species returning at different times, and a year-round resident population of some species. Additionally, other non-salmonid species, such as the three-spined stickleback, have been shown to carry some level of *L. salmonis* (Jones et al., 2006). The result may be a more or less continuous pool of infectious material, the importance of which may vary in individual localities under specific external circumstances.

Both wild and farmed salmon in coastal systems are subject to a variety of natural and anthropogenic forces, such as temperature, current, and salinity. Copepodids move toward light and congregate near the surface at the boundary of freshwater and saltwater. To the extent that these boundaries can be moved by wind or current, copepodids can be caught in eddies and gyres and either maintained or transported to areas not predicted under normal conditions (Costello, 2009). Complex models using this information to predict transmission and population growth have been constructed (Brooks, 2005; Krkošek et al., 2005); however, consistent fit with actual data has been debated.

Torrissen et al. (2013) reviewed the many studies that demonstrate the positive relationship between host density and sea lice population growth. However, the relative importance of wild versus farmed fish in maintenance and/or increase of sea lice populations is hotly debated. Epizootics of sea lice in wild populations have been reported (Huntsman, 1918; White, 1940, 1942; Gilhousen, 1989; Johnson et al., 1996). Several studies have attempted to link the disease in farms to effects on wild populations (reviewed in Torrissen et al., 2013). Krkošek et al. (2007) predicted the collapse of a pink salmon population in the Broughton Archipelago, British Columbia, as a result of sea lice acquired by juveniles as they outmigrated past salmon farms. Price et al. (2010) argued that sea lice infection levels in wild fish in British Columbia were primarily related to the biomass of farmed salmon in the area. Krkošek et al. (2013) compared survival in parasiticide-treated and non-treated Atlantic salmon following release as smolts and return as adults and estimated that sea lice accounted for a 39% loss of wild adult salmon recruitment in the northeast Atlantic. Other studies in Europe have shown little, or only moderate, effects (Jackson et al., 2011; Gargan et al., 2012). It is clear, however, that the predictions of imminent collapse of pink salmon populations in the Broughton Archipelago have not occurred. Returns have remained at or above the historical average (Brooks and Stucchi, 2006), and the population of pink salmon in the area in question actually increased in the years following the prediction (Brooks and Jones, 2008). Marty et al. (2010) reported no effect of farmed salmon on productivity of wild salmon, either in terms of sea lice numbers or farm production numbers, and Jones and Beamish (2012) showed no relationship between sea lice infection and biomass of farmed salmon or proximity to salmon farms. The issue continues to inspire debate.

Policy and practice

As stated eloquently by Paul Greenberg in *Four Fish: The Future of the Last Wild Food*, fish are our last wild food and, therefore, have deeply rooted cultural significance. Moreover, one of the trademarks of Western Civilization, the public trust doctrine, has enshrined in our laws the idea that not only are fisheries a shared resource, but that the government has the responsibility to manage and maintain the fisheries for the good of all. In the latter half of the 20th century, however, political scandals such as Watergate in the United States and scientific scandals such as the collapse of the cod fishery in the North Atlantic have eroded the public's trust in government. In addition, the perhaps well-intentioned commingling of commercial aquaculture with traditional fisheries in regulatory agencies responsible for the stewardship of natural resources has challenged the assumption of an independent, impartial government agency. The emergence of open-access media (i.e., cable news and the internet), which occurred at about the same time, provided a mechanism by which to foment and air these challenges to traditional authority. The issue of *L. salmonis* as a disease arose at a volatile time in the evolution of our current media-based society and, therefore, has informed our modern view of the relationships among science, government, and the public.

By the 1990s, salmon farming had clearly created jobs and economic activity, but, perhaps because of early missteps, it had also created the perception that fish farming negatively impacts wild stocks, damages the environment, and displaces commercial and recreational anglers (see Robson, 2006), thereby interfering with the deeply rooted historical cultural connection with wild fisheries. In Europe, the growth of salmon farming coincided with a precipitous decline in the wild salmon fishery, and by the early 1990s, there were claims that sea lice from salmon farms were killing wild fish (Tully et al., 1993a, 1993b). The development of salmon farming in British Columbia began in the 1980s and occurred in the context of what had already occurred in Europe with respect to salmon farming, a burgeoning environmental movement, and the growing mistrust of government and industry. So, as adeptly reviewed in Bocking (2011), in the early 2000s, when sea lice appeared in wild salmon in the Broughton Archipelago, an area recently occupied by salmon farms, the wariness among the industry, the government, and eNGOs devolved into open conflict. The combination of the lack of existing information on the sea lice issue at the time and normal scientific uncertainty put government and industry in a difficult position. Established science organizations (i.e., government agencies) required time to mobilize in order to address the issue, but the delay allowed other scientists to define the issue and perpetuated the perception that neither the government nor

industry was interested in responding (or were actively colluding in a cover-up). Into the void stepped a cadre of activists and eNGOs who saw the media as a tool with which to use the veneer of science to advance their deeply held convictions. Along with sympathetic, mostly well-intentioned scientists, both loosely and officially associated with this faction, a research community was formed to counter the perceived government shortcomings. In a blistering series of papers between 2005 and 2012, scientists from both sides published data-heavy papers and roundly criticized one another for their failures in analysis and interpretation. Scientists, the media, and the public failed, however, to put the research into the proper perspective. As Bocking (2011) keenly notes, the 2 sides were actually asking different, but quite legitimate, questions. Government and industry tended to be asking questions at a resource-wide scale, while "independent" scientists often asked questions at local scales. Thus, given the complexity of the system and normal scientific uncertainty, the fact that 2 seemingly similar studies could legitimately come to completely different conclusions due to the difference in ecological scale was lost on myopic scientists and a mostly scientifically ill-equipped media and public (Bocking, 2011).

The shared appreciation of potential risk to both wild and farmed salmon has motivated researchers to take a precautionary approach to limit exposure to sea lice. Most authorities now actively monitor sea lice levels and accept some threshold sea lice density, above which a series of actions, typically parasiticidal treatments, is initiated to reduce the number of lice. Other actions include adjusting the production cycle to avoid peak populations of lice, separating farms at distances that do not facilitate the interchange of lice, periodic fallowing, single-generation stocking, and fish health monitoring programs. The issue has further stimulated molecular advances such as sequencing the entire genome of sea lice, identifying candidate antigens for vaccines, and creating functional genomics approaches that seek to control the population through immunity and reproductive manipulation (reviewed in Torrissen et al., 2013). Progress in reconciling the seemingly disparate findings among studies also has been accomplished. The province of British Columbia founded the Pacific Salmon Forum, which brings together representatives from the public, government, industry, and academia for regular meetings to develop scientific consensus on salmon farming. Rogers et al. (2013) brought together the research efforts of representatives from both sides to bridge the research gap between the groups in an effort to build a mathematical model for the dynamics of sea lice in the Broughton Archipelago designed to facilitate suppression of sea lice on wild salmon.

WHITE SPOT SYNDROME VIRUS

Shrimp is the most valuable aquaculture commodity in the world, worth over US$10 billion per year. However, since the large-scale commercialization and intensification of shrimp farming in the 1970s, outbreaks of a variety of diseases have made disease a major impediment to the growth of shrimp aquaculture (Lotz, 1997). Indeed, China, traditionally the world's leading aquaculture producer, lost almost its entire shrimp farming industry to viral diseases in the early 1990s (Lotz, 1997). Although early mortality syndrome, a recently emerging disease caused by the bacterium *Vibrio parahemolyticus*, is causing significant losses (Tran et al., 2013), white spot syndrome virus (WSSV), which emerged in Taiwan in 1992 and quickly spread around the world in association with shrimp farming, has been the most historically significant of the shrimp pathogens and has cost the economies of several Asian, Central, and South American countries over US$8 billion since 1992 (Escobedo-Bonilla et al., 2008; Escobedo-Bonilla, 2011; Dutta et al., 2013). WSSV is an enveloped, non-occluded, bacilliform dsDNA virus of the family Nimaviridae, genus *Whispovirus*. It is one of the largest known animal viruses with a genome of 300 kbp and a size of 120–150 × 270–290 nm (Liu et al., 2009; Escobedo-Bonilla, 2011). The virus infects a broad range of hosts, including almost all decapod crustaceans and possibly a few other arthropods (Escobedo-Bonilla et al., 2008; Liu et al., 2009).

Although viruses have exacted a huge economic toll on an important food production industry, veterinary science has no arsenal of treatments or vaccines for use in invertebrate animals. This is due in part to our comparatively limited knowledge of invertebrate immunity. Extensive work has shown invertebrates to have innate immunity, but nothing homologous to B-cells, T-cells, or the major histocompatibility complex, the key components of vertebrate acquired, specific immunity. Further, crustaceans (and all arthropods) lack all the typical anti-viral immune components characteristic of vertebrates such as interferon, natural killer cells, antibodies, and cytotoxic T-cells. Thus, fundamental questions about how arthropods deal with pathogens remained until recently. Kurtz and Franz (2003) and Kurtz (2005) showed that arthropod immune systems were capable of some level of specificity and memory. Dong et al. (2006) demonstrated that mosquitoes produce highly diverse splice forms of a neuronal signaling molecule to match specific pathogens, which could account for a type of specific, acquired immunity. Nevertheless, despite advances in understanding invertebrate interactions with bacterial and fungal pathogens in species of scientific importance such as mosquitoes and fruit flies, shrimp defenses, particularly with respect to viruses, remained largely unexplored. Within the last several years, however, studies on shrimp viruses such as WSSV have contributed significantly to our understanding of immunity in crustaceans and other invertebrates. In the remainder of this section, we will briefly focus on some examples of how shrimp viruses have contributed to our understanding of some of the important steps in crustacean immunity. Readers are directed to several recent reviews of invertebrate and crustacean immunity, such as Liu et al. (2009), Soderhall (2010), and Hauton (2012), for details.

Pathogen recognition

Historically, invertebrate immunity has been viewed as non-specific and mediated through a variety of pattern recognition proteins (PRPs). Crustaceans possess a variety of general PRPs such as lipopolysaccharide- and β-glucan binding proteins as well as lectin-like proteins (Hauton, 2012). Other specific receptors in penaeid shrimps, such as YRP65, and GTPases, such as PmRab7 and PjRab, have been shown to bind viruses or envelop proteins to perhaps create receptor complexes or mediate phagocytosis (Yi et al., 2004; Wu et al., 2008; Liu et al., 2009). Homologues of Toll receptors/triggers and Janus kinase/signal transducer and activator of transcription (JAK/STAT), which are signaling molecules in vertebrate immunity, are known in shrimp, but their precise roles in the immune response are unknown because some studies

in penaeid shrimps have not supported predictions based on our understanding of vertebrate Toll and JAK/STAT activity (Liu et al., 2007; Chen et al., 2008; Liu et al., 2009; Wang et al., 2010; Hauton, 2012).

The discovery of Down syndrome cell adhesion molecules (DSCAMS) as an advanced pathogen-recognition system has transformed our view of invertebrate immunity. DSCAMS are transmembrane proteins with significant structural and sequence homology to the immunoglobulin (Ig) superfamily of cell-adhesion molecules. Long known as signaling mechanisms in neuronal development, the discovery that DSCAMS were present in almost all arthropod tissues, and the fact that their absence resulted in immune dysfunction (Watson et al., 2005), changed the views on invertebrate immunity. DSCAM receptors consist of 10 Ig-like domains and 6 fibrinogen-like domains. Three of the Ig-like domains (2, 3, and 7) can undergo post-transcriptional alternative splicing to produce thousands of different isoforms. Typical membrane-bound forms have been identified from a wide range of arthropods (Hauton, 2012; Hung et al., 2013), including shrimps. Secreted forms (i.e., produced by cleavage from the membrane), which share the domain architecture of the membrane-bound forms, are also known (Hung et al., 2013). While the precise nature of the interaction between pathogens and DSCAMS is unknown, experimental evidence from penaeid shrimp has shown that the sequence in DSCAM domains is altered by specific pathogens and that DSCAMS can accurately identify specific bacteria to which the shrimp has been previously exposed, differentiate among categories of bacteria, and selectively bind to known pathogens as opposed to opportunistic or experimentally induced infections (Watthanasurorot et al., 2011; Hung et al., 2013). Although it cannot yet be generalized to all shrimp species, DSCAMS in 2 commercially important species (*Litopenaeus vannamei* and *Penaeus monodon*) are unique in that they lack transmembrane domains and cytoplasmic tails, and they possess unusually complex membrane-bound forms (Hung et al., 2013). Further, research has shown that the tailless forms are expressed within the cell and secreted from the cells via vesicles.

Pathogen processing

Pathogen recognition triggers a cascade of events, including the degranulation of semi-granular and granular hemocytes. Degranulation activates a number of general defense mechanisms, including the prophenoloxidase (PPO) system, which, while not directly relevant to WSSV defense (Wang and Zhang, 2008), results in multiple downstream effects such as melanization, opsonization, phagocytosis, and encapsulation, which are mediated by various chemicals, some of which are known to be active against WSSV (Hauton, 2012). Studies of penaeid shrimp responses to WSSV have contributed to the identification of a number of proteins and genes that are up regulated in response to viral infection (summarized in table 1 in Liu et al., 2009). Research has also shown that silencing of many of these genes or proteins increases mortality from the virus, but the effect may be somewhat species specific (Liu et al., 2009).

Exposure to foreign RNA sequences activates RNA interference (RNAi), an anti-viral mechanism common in a variety of plant and animals, including marine shrimp (reviewed in Liu et al., 2009). RNAi processes dsRNA into smaller pieces that can then be incorporated into a silencing complex that binds to the homologous mRNA to prevent replication. RNAi studies with WSSV and/or genes from it have shown that even though it may be a short-term transient effect, WSSV replication can be slowed in vitro, and mortality from WSSV can be delayed or reduced in vivo (reviewed in Escobedo-Bonilla, 2011). Perhaps the most instructive uses of RNAi with marine shrimp viruses have been in using RNAi to silence particular genes that encode known proteins or enzymes and evaluating the resulting effects on mortality following infection. Silencing of Toll, rr2, and caspase-3 demonstrated no effect on mortality induced by WSSV, while silencing of shrimp Rab7 inhibited viral infections (Escobedo-Bonilla, 2011). RNAi technology is inspiring investigation of its use as a "vaccine." Some experimental injections of RNAi molecules have shown promising results in reducing mortality, and the ability to produce quantities of RNAi in bacteria for administration through feed has been demonstrated (reviewed in Escobedo-Bonilla, 2011). Thus, studies in preventing WSSV mortalities may serve to advance development of tools to address infectious diseases in both human and animal medicine.

Viruses are known triggers of apoptosis, or programmed cell death. Several viruses such as WSSV have been shown to increase DNA fragmentation in cells, a proxy for impending apoptosis, as the infection progresses (Sahtout et al., 2001; Wongprasert et al., 2003; Liu et al., 2009). As a result, some have considered apoptosis to be an important host strategy for controlling the spread of viruses (Aubert and Jerome, 2003; Liu et al., 2009). Others consider apoptosis a critical part of the process of spreading viruses (Teodoro and Branton, 1997). Studies with shrimp viruses, however, are equivocal. Chayaburakul et al. (2005) has suggested that apoptosis of lymphoid cells in *P. monodon* is an important mechanism for controlling infectious hematopoietic hypodermal necrosis virus. Wang and Zhang (2008) found that inhibition of apoptosis increased the number of WSSV copies and mortality in *Marsupenaeus japonicus*. Inhibition of caspase-3, a key gene in apoptosis, reduced mortality only in low doses of WSSV (Rijiravanich et al., 2008). As such, although shrimp viruses such as WSSV are helping elucidate the regulation of apoptosis, the role of apoptosis in immunity is unresolved.

FLATWORMS

Although myxozoans and sea lice arguably have had the most demonstrable and substantive impact on disease and the perception of metazoan diseases in finfish aquaculture, the depth and breadth of literature treating other parasitic infections in marine and freshwater culture settings are growing rapidly (Benz and Bullard, 2004; Hayward, 2005; Whittington, 2005; Bullard and Overstreet, 2008; Whittington and Chisholm, 2008). Some settings may have no effect on these disease aspects or even act to reduce flatworm prevalence of infection (e.g., in the case of some parasites that have complex, multiple-host life cycles that are disrupted in closed recirculating systems wherein a monoculture is maintained). Although not treated by us herein, perhaps the best examples of these sorts of epidemiological modifications that exacerbate disease outbreaks in marine and freshwater culture settings are sourced from studies of bacterial pathogen–fish relationships (Plumb, 1999; Austin and Austin, 2007). Overall, in fact, disease occurrence has helped shape how and when fishes are harvested.

It is important to note that despite their demonstrated ability to negatively impact fish culture facilities (for food production and stock enhancement), by and large, and with exception of *Gyrodactylus salaris*, flatworms are not notifiable pathogens, and none has garnered the international reputation as an alarming pathogen in the transport of live fish stock, frozen or fresh seafood, or as a pathogen of an ornamental fish species in international trade or shipment of live fish. Rather than interpret that apparent lack of concern in regulatory function as an indication that these parasites are benign or of little or no concern to the health and well-being of captive fishes and wild fish populations, we think that, simply, fundamental awareness of these pathogens and a codified means of monitoring their translocation across borders and their presence/absence in transported fish (live or dead) have lagged behind that of other livestock species in agriculture. This "lagging behind" of the aquaculture industry regarding best management practices, biosecurity, and product consistency is typical, but in stark contrast to the present state of those matters within the swine, poultry, and beef agriculture industries, for example, which are vertically integrated, federally regulated, and adhere to stringent quality standards for the marketed product. The United States in particular is being outcompeted in the aquaculture realm.

Ectoparasitic and endoparasitic flatworms have demonstrably impacted aquaculture of marine and freshwater fishes (Bullard and Overstreet, 2002, 2008; Cribb, 2005; Hayward, 2005; Ogawa, 2005; Whittington, 2005; Bakke et al., 2007; Whittington and Chisholm, 2008). This "impact" includes killing fish outright or devaluing the harvested product. Good examples of pathogenic flatworms in aquaculture include those infecting the skin and gill of fishes (Monogenoidea, also referred to as "monogenetic trematodes," "monogenes," and "monogeneans") and particular endoparasitic flukes (Digenea) that exploit cultured fishes collectively as intermediate and definitive hosts. Diseases associated with flatworm infections are typically regarded as acute when present and are marked by a rapid increase in intensity, subsequently culminating in host death, wasting, or recovery (Bullard and Overstreet, 2008). Although it is not uncommon to read that "secondary infections of opportunistic pathogens," comprising bacteria, viruses, or fungi, are presumed to be acting in synergy with an initial parasitic infection, seldom are strains cultured and subjected to Koch's postulates. Damage to skin associated with intense ectoparasitic infections (e.g., obliteration of epidermis, necrosis/hydropic degeneration of dermis, spongiosis of somatic muscle) poses an immediate threat to the integrity (flesh quality) of underlying somatic musculature, which is typically the product being harvested and sold. As such, even if the pathogen or its associated infection does not kill the fish outright, the lesion that results from an intense infection can aesthetically foul and devalue product, thereby affecting the farmer's bottom line. Similarly, the chronic effects of sub-clinical flatworm infections in fishes have been little studied, but they may have significant cumulative/collective economic impacts on yield (dress-out percentage, filet yield) and food conversion rates. These flatworms generally cause reduced growth performance, and, in extreme cases with high-intensity infections, mortality or preemptive stock destruction results. Infected hosts exhibit demonstrable immunological responses but typically do not show gross signs of disease despite being infected (Bullard and Overstreet, 2008; Whittington and Chisholm, 2008). Very little has been reported about antibody response(s) or the immunological detail(s) of ectoparasite– and endoparasite–host relationships among fishes at liberty in the ocean.

Regarding digeneans, although not treated herein with depth, the fish blood flukes (Digenea: Aporocotylidae) are a good example of an obscure group of flatworms becoming more prominent as pathogens in connection with the growing offshore/marine cage culture of particular high-value fishes (e.g., tunas [*Thunnus* spp.] and amberjacks [*Seriola* spp.]) in the southwest Pacific Ocean and Mediterranean Sea (Bullard and Overstreet, 2008). Unlike monogenoids, digeneans undergo asexual reproduction in an intermediate host (typically a mollusc) before infecting a vertebrate host, which may become a second intermediate host or the definitive host. Marine and freshwater fish blood flukes use bivalves and polychaetes or gastropods (Orélis-Ribeiro et al., 2014), respectively, and if susceptible invertebrate and fish hosts are in close proximity to each other, heavy infections in the cultured fish can result. Fish blood fluke infections are of concern within intensive systems (Bullard and Overstreet, 2002, 2008; Hardy-Smith et al., 2012; Ishimaru et al., 2013), and the intensity of research activities focused on these flatworms in aquaculture has greatly increased our knowledge of their biology and life cycles. Orélis-Ribeiro et al. (2014) asserted that the tuna blood fluke *Cardicola forsteri*, which matures in commercially prized southern bluefin tuna (*Thunnus maccoyii*), is now among the most extensively studied marine fish trematode. These flukes are relatively unique because they can harm the fish host as adults by blocking blood vessels and asphyxiating the host, as eggs, which destroy or block gill epithelia and vessels, or as miracidia, which hatch from eggs within gill epithelium and bore through the gill epithelium (Bullard and Overstreet, 2002, 2008). Other examples of digeneans that act as economically impactful pathogens in aquaculture are sourced from earthen pond aquaculture (extensive culture) of channel catfish, *Ictalurus punctatus*, the most economically important aquaculture fish species in the United States. Cercariae and metacercariae, not adults, cause direct harm to fish. These stages are associated with bacterial infections or otherwise devalue the cultured product and lead to economic losses to the industry (see Overstreet et al., 2002; Overstreet and Curran, 2004). Members of Bolbophoridae, Clinostomidae, Diplostomidae, Neodiplostomidae, and Strigeidae are identified as pathogens or potential pathogens of freshwater fishes in extensive culture systems (see Bullard and Overstreet [2008] for an overview of their life cycles and associated diseases).

The general biology and life history attributes of monogenoids have been reviewed extensively and recently (Ernst et al., 2002; Benz and Bullard, 2004; Hayward, 2005; Whittington, 2005; Bakke et al., 2007; Whittington and Chisholm, 2008). Monogenoids are the non-segmented relatives of the tapeworms (Cestoda). Most are ectoparasites of epidermis (gill and olfactory surfaces, body surface), but some are true endoparasite specialists that infect blood (heart), rectal gland, urinary bladder, and gastrointestinal tract of vertebrates; many species fit the widely accepted definition of being mesoparasitic (embedding a portion of their body within a host tissue). Unlike cestodes, however, monogenoids have direct life cycles, not requiring an intermediate host (although a few can exploit paratenic hosts, such as crustaceans or fishes, for dispersal) (Bullard et al., 2000a; Benz and Bullard, 2004; Hayward, 2005; Whittington, 2005; Whitting-

ton and Chisholm, 2008). Adult worms copulate with themselves or another worm, produce eggs singly (but egg production can be continuous), and eject an egg that sinks or floats and contains a ciliated or non-ciliated larva (oncomiracidium) that is infective to the same or another host individual. As such, these flatworms can rapidly develop large populations on captive hosts, leading to disease outbreaks. These generalities will become less predictive as more detailed studies are published on specific life history details for freshwater and marine monogenoids; several striking examples of this template life cycle already exist. The most obvious exceptions are species of *Gyrodactylus*, which are viviparous (see below; Cone, 1995; Kearn, 1998; Bakke et al., 2007). The literature holds many casual reports of other gill- and skin-infecting monogenoids that have been blamed as primary pathogens of cultured fishes. Perhaps as a result, husbandry personnel are concerned with, and routinely treat for, infections. This occurs despite a general lack of definitive evidence that infections by most flatworm species kill or harm their host, even when infections are intense. Some anecdotal evidence suggests that therapeutic exposure may cause more insult to the infected fish than direct exposure to the parasite.

A noteworthy observation is that aquaculture practices (for food production or stock enhancement) have reportedly introduced ectoparasitic flatworms pathogenic to wild fish populations: (1) *Nitzschia sturionis* infecting stellate sturgeon (*Acipenser stellatus*) that moved from the Caspian Sea to the Aral Sea caused an epizootic on ship sturgeon (*Acipenser nudiventris*) (see Zholdasova, 1997; Whittington and Chisholm, 2003; taken from Whittington and Chisholm, 2008); (2) *Neobendenia girellae* reportedly infiltrated Japanese marine aquaculture putatively by infected fingerling *Seriola dumerili* being moved from Hainan to Hong Kong (Ogawa et al., 1995); and (3) *Pseudodactylogyrus anguillae* and *Pseudodactylogyrus bini* were introduced into North America and Europe from Asia by imported *Anguilla japonica* and now infect *Anguilla rostrata* and *Anguilla*, respectively (Hayward et al., 2001).

Neobenedenia melleni is a morphologically perplexing species that is not taxonomically resolved, probably comprising a species complex. It has purportedly low host specificity, infecting >100 fish species (Whittington and Horton, 1996; Bullard et al., 2000b, 2003). It is a virulent and highly pathogenic parasite of fishes in high-density recirculating culture systems, public aquaria, and the pet trade, wherein probably many lethal infections go unreported. As such, it is difficult to estimate the impact of this flatworm on quarantine protocols in the display and pet aquarium trade. This species is widely viewed as constraining the further development of marine aquaculture of bony fishes in sea cages (Whittington and Chisholm, 2008, and references therein). There is also growing recognition that this species may be a threat as an exotic invasive pathogen of fishes in culture systems and nearby endemic fish populations, given its apparent low level of host specificity. It was first reported in Australian waters in 2001 (Deveney et al., 2001) during an epizootic of barramundi, *Lates calcarifer*. The pet trade has likely transported strains of *N. melleni* across oceans, given that fishes sourced from different ocean basins are mixed by sharing water, and therefore parasites. This species, or a morphologically similar species, has been associated with outbreaks on *Oreochromis mossambicus* in Hawaii (Kaneko et al., 1988), cultured amberjack in Japan (Ogawa et al., 1995), barramundi in Australia (Deveney et al., 2001), red snapper (*Lutjanus campechanus*) and tripletail (*Lobotes surinamensis*) in recirculating culture systems in Mississippi (Bullard, pers. obs.), and cobia *Rachycentron canadum* in Brazil (Kerber et al., 2011; Moreira et al., 2013). Ogawa et al. (1995) indicated that *N. melleni* was imported into Japan by unregulated import of fry of greater amberjack, *S. dumerili*, from Hong Kong and Hainan, China.

Benedenia seriolae is another devastating, economically impactful pathogen, which has affected the viability of culturing amberjacks (*Seriola* spp.) since the 1960s (Ernst et al., 2005). It has an egg that can disperse great distances and with oceanic currents, which makes placement (relative to oceanic currents) and separation of sea cages critical in curbing spread of infections (Chambers and Ernst, 2005). Cages positioned in a line or row likely enhance transmission of the parasite, but if cages are laid out in a line perpendicular to the current, then transmission of *B. seriolae* is likely decreased. Costs to treat infections can be 20% of total fish production costs (Ernst et al., 2005). Infections constrain fish species stocked, stocking density, size of cage, and the design of sea cages. Ernst et al. (2005) predicted that the expansion of amberjack culture outside of the western Pacific Ocean will likely reveal similar disease management problems.

Gyrodactylus salaris is perhaps the most economically impactful ectoparasitic flatworm of fish. It is the only notifiable flatworm disease listed by the Office International des Epizooties (OIE) (World Organization for Animal Health) and the only metazoan fish parasite listed in the *Manual of Diagnostic Tests for Aquatic Animals*. In 1983, *G. salaris* was recognized as a notifiable disease in Norway, and in 2002, it was classified as a "significant fish disease" by the OIE. Bakke et al. (2007) provided an in-depth review of the biology, disease history, treatment, and social/political ramifications of infections by *Gyrodactylus* spp., especially particular strains of *G. salaris*. Mitigation and management of the disease associated with *G. salaris* in Norway alone were estimated at US$450–500M cumulatively over a 30+ yr period (Bakke et al., 2007). *Gyrodactylus salaris* was introduced as a result of aquaculture activities and now impacts the management of wild fish stocks, demonstrating a relationship between aquaculture and wild capture fisheries. It was introduced on Atlantic salmon, *Salmo salar*, and possibly other hosts (Bakke et al., 2007) in Norway during the 1970s, during which time the first outbreaks of disease in farmed and wild salmon populations were noticed. The culprit parasite was introduced from the Baltic region into eastern Atlantic stocks of salmon that lacked endogenous resistance to the parasite (Bakke et al., 2007). Spread of *G. salaris* throughout rivers and hatcheries in Norway was facilitated by translocation of infected fish (Malmberg, 1993; Whittington and Chisholm, 2008). Since 1975, fishes in 46 of 379 salmon rivers and cultured in 39 farms have been infected by *G. salaris*. In an effort to protect wild salmon stocks, rotenone (non-specific, highly toxic to fish and air-breathing aquatic invertebrates) has been widely used to kill *G. salaris*. Despite the acute impact of the toxin on river fishes and invertebrates, 28 of 46 (61%) impacted Norwegian rivers were treated between 1981 and 2003 to control *G. salaris*. Dispersal from river to river was typically by infected fish moving through an estuary and into another river (brackish water dispersal, 24 rivers), but federal fish hatcheries also directly transmitted infections from hatcheries to rivers in several instances (9 rivers). In 1984, *G. salaris* infections killed the equivalent of 25% of the total salmon catch (Egidius et al., 1991; Bakke et al., 2007), reducing the riverine density of

salmon parr and adults by 85% (Johnsen et al., 1999; Johnsen and Jensen, 2003), and exterminating salmon in several rivers while threatening populations in many others. Drastic measures have been implemented in Norway to protect Atlantic salmon from *Gyrodactylus* infections, including rotenone, as well as acidified aluminum treatments of entire river courses and extreme biosecurity measures for reducing the probability of reintroduction of *G. salaris* into treated rivers (Bakke et al., 2007). Artificial barriers, selective breeding of disease-resistant fish families, and combinations of control strategies (integrated control measures) also have been discussed and implemented variously.

CONCLUSIONS

Aquaculture and parasitology (or more broadly, the study of diseases) have benefited from one another over the years. The relationship has facilitated some significant advances in our understanding of both hosts and pathogens. We appreciate the opportunity to highlight a few of them. As aquaculture production is expected to rise considerably in the future to support both the increased human population and the increased per capita fish consumption due to the health benefits of fish, this relationship is likely to continue. Moreover, as aquaculture grows, new diseases, new issues, and new opportunities will emerge. Parasitologists with experience in taxonomy, bioengineering, physiology, molecular biology, economics, natural history, and systematics will be key players as best management practices are optimized and implemented by the aquaculture industry. Much remains to be learned, but the foundation for continued study is strong. We urge scientists in all fields to consider the opportunities for study afforded by aquaculture systems.

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