Examples of emerging virus diseases in salmonid aquaculture

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Abstract
Aquaculture can offer close to ideal environments for the spread of infectious diseases. Owing to high-density monoculture of hosts, numerous possible routes of transmission and suboptimal protection by available vaccination for several viral diseases, viruses may thrive in modern salmonid aquaculture. Furthermore, infectious diseases do not respect national boundaries and they can have detrimental effects both on the production and on the export of aquaculture products. Effective vaccines are available for only a limited number of serious fish viral diseases, leaving expensive compulsory stamping-out eradication as the official approach. If fish health authorities do not have an efficient risk management procedure, outbreaks may become epizootics. The key to control viral epidemics is to block the transmission of infection. This requires knowledge about reservoirs, susceptibility of infection for the different species of fish, the pattern of shedding of virus and survival of viral infectivity outside the host. The development of highly effective vaccines offers another way of preventing and controlling future risks.

Keywords: salmonids, virus infection, ISA, PD, HSMI

Introduction
An infectious disease in fish aquaculture can be called emerging when its incidence significantly increases in a given time, place and population. A disease can be emerging in one particular geographical area and can be endemic or sporadic in other areas. To emerge, the disease has to be introduced to the area and the fish must be exposed. To introduce an infectious disease implies that the causative agent is introduced. The large amount of susceptible hosts in aquaculture can confer selective advantages for viruses with efficient transmission, i.e. viruses that replicate fast and to high levels and with efficient shedding, properties that may be correlated with disease-causing ability. The history of modern aquaculture indicates that farmed fish are susceptible to new and emerging diseases, and factors like fish density and suboptimal environment are important in this respect. But the possibility of recognizing and characterizing diseases is much better for farmed than wild fish.

The presence of an infectious virus is necessary to cause disease, but additional factors may also be necessary for clinical disease to occur. There are variants of agents, of which some are more prone than others to cause disease, i.e. variations in virulence. Of the host factors influencing the outcome of virus infections are aspects like species, age, nutritional status, stress, hormonal conditions, other clinical and subclinical infections and diseases, genetic determinants, etc. Properties of the virus like virulence, infectious dose and routes of transmission are factors that are important determinants of whether a disease will emerge or remain sporadic. Environmental factors like density, oxygen saturation, salinity, temperature, treatment and stress, and management factors like segregation of generations, ‘all in/all out’ are also important for the outcome of an infection. There are many commonly used interventions and improvements of management procedures like prompt removal of moribund and dead fish and/or removal of infected populations; fallowing; disinfection of eggs; regulation of well boat traffic; surveillance of the
fish population; disposal of carcasses, by-products and waste; control of vectors; and decontamination strategies. Interventions used for the host itself can be vaccination, genetic selection or the use of less susceptible species. There are cases where the host and environmental factor are of less or no importance for the emergence of a disease, like the viral haemorrhagic septicaemia outbreaks in wild fish in the Great Lakes area in United States/Canada. But in general, a disease may be emerging in one geographical area and may be either endemic or sporadic in others due to some or a combination of several of the above-mentioned factors.

In Norwegian farming of salmonids, the diseases pancreas disease (PD) and heart- and skeletal muscle inflammation (HSMI) are both regarded as emerging. The incidence of PD has increased from less than 10 to more than hundred annually during the last decade. Heart- and skeletal muscle inflammation was recognized as a disease entity in 1999, and in and 2007 and 2008, about 150 outbreaks were recorded each year. The number of outbreaks of infectious salmon anaemia (ISA) in Norway has been more stable in the last few years, but in the Faeroes, Canada, United States and Chile, ISA has been on the rise and fall, i.e. it has been an emerging disease for a period of time. These three diseases are therefore described very briefly.

**PD**

Pancreas disease is caused by infection with SAV. Currently, there are six known subtypes of SAV. The SAV2 subtype is the cause of sleeping disease in rainbow trout, mainly found in central Europe, while SAV3 is the only subtype found in Norway (Hodneland, Bratland, Christie, Endresen & Nylund 2005). Clinical signs of PD-affected fish populations are lack of appetite, lethargy, faecal casts and increased mortality (Mcvicar 1987; McLoughlin, Nelson, McCormick, Rowley & Bryson 2002). Fish may be spiralling or swimming in a circular motion or may lie still at the bottom of the cage. For a recent review of salmonid alphavirus (SAV) infections, see McLoughlin & Graham 2007.

Why is PD emerging in some areas and not in others? Pancreas disease is enzootic in Irish salmon farming (Rodger & Mitchell 2007), but emerging in Norwegian salmon farming. In Norway, the bulk of PD outbreaks occurs between April and September, but outbreaks are recorded all through the year.

The virus infectivity can withstand more than 2 months in sterile sea water at low temperatures, which implies that horizontal transmission between adjacent farms can occur directly or indirectly (Graham, Staples, Wilson, Jewhurst, Cherry, Gordon & Rowley 2007). This suggests that a reservoir of infection in the sea water environment can build up and be present long after outbreaks. A possible occurrence of vertical transmission is not decided.

Sea lice may possibly act as vectors of infection, as they are found to be able to carry SAV (Karlsen, Hodneland, Endresen & Nylund 2005), implying that sea lice control is beneficiary. Improved management like synchronized falling, segregation of generations, restrictions on movement, improved surveillance and vaccination have recently been introduced in Norway and tentatively yield optimistic results. Such improved management would also reduce the infection pressure of subclinical infections with other organisms that may infect the salmon and perhaps influence the outcome of a SAV infection. There is strong evidence of a high level of acquired life-long (production-long) immunity to PD as outbreaks have not been reported to occur more than once in the same population of fish (Houghton 1994), implying that vaccination would be protective for the fish.

**HSMI**

Heart and skeletal muscle inflammation is a transmissible disease in farmed Atlantic salmon, assumed to be caused by a reo virus (Palacios, Lovoll, Tengs, Hornig, Hutchison, Hui, Kongtorp, Savji, Bussetti, Solovyov, Kristoffersen, Celone, Street, Trifonov, Hirschberg, Rabadan, Egholm, Rimstad & Lipkin 2010; Kongtorp, Kjerstad, Guttvik, Taksdal & Falk 2004). The disease normally affects salmon in the period 5–9 months after sea transfer. Although both HSMI and PD are present in some geographical areas in Norway, HSMI is more prevalent in the middle and the northern part of the Norwegian coast, while PD is present further south and almost absent in the northern parts. Whether this indicates that temperature is an important factor for disease development or the presence of virus reservoirs or other environmental factors, etc is unknown. The risk factors and causes of introduction of HSMI in the field are largely not described, but it has been shown recently that movement of fish during the seawater phase is a significant risk of spreading HSMI to new locations (Kongtorp & Taksdal 2009). A study that followed a natural HSMI
outbreak showed that cardiac changes may be observed several months before the clinical outbreak, suggesting a slow disease development and the presence of virus for a long duration of time (Kongtorp, Halse, Taksdal & Falk 2006).

**ISA**

Infectious salmon anaemia was first found in Norway in 1984 in Atlantic salmon (Thorud & Djupvik 1988). Field outbreaks of the disease have only been detected in farmed Atlantic salmon. Fish are severely anaemic in the terminal stage, hence the name of the disease. The ISA epidemic in Norway peaked in around 1990, when ISA was detected annually in more than 80 fish farms, and this prompted the national fish health authorities to implement various bio-security actions. In the last decennium, ISA has become endemic in Norway, with a number of annual outbreaks of 3–20, while the salmon production has increased at least 7-fold after the ISA epidemic peaked. In Scotland, Canada, United States and the Faeroes, the disease is not present as of 2008; however, the ISA situation in Chile has many similarities to that of Norway in the early 1990s.

Atlantic salmon is considered to be the only species in which ISA occurs naturally, although it has been reported from Coho salmon (Kibenge, Garate Johnson, Arriagada, Kibenge & Wadowska 2001). The ISA virus (ISAV) can replicate in several other species; these species may thus be important as carriers of virus and may possibly function as reservoirs (Nylund & Jakobsen 1990; Nylund, Kvenseth, Krossoy & Hodneland 1997; Snow, Raynard, Bruno, van Nieuwstadt, Olesen, Lovold & Wallace 2001). Available data suggest that ISAV may remain infective for a long time outside its host (Nylund, Hovland, Hodneland, Nilsen & Lovik 1994; Rimstad & Mjaaland 2002). The virus is stable in the pH range 5–9 (Falk, Namork, Rimstad, Mjaaland & Dannevig 1997); five cycles of freezing and thawing do not reduce infectivity. Infectivity of tissue preparations is retained for at least 48 h at 0 °C, 24 h at 10 °C and 12 h at 15 °C (Torgersen 1997).

Because water is the natural environment for ISAV, attempts have been made to estimate the viral survival time in water (Rimstad & Mjaaland 2002). Water is not a constant unit, but varies with factors such as temperature, ultraviolet radiation, content of bacterial and enzymatic activities, organic material, etc. The effect of these factors is difficult to estimate, but not necessarily negative for the virus infectivity. Ultra-violet radiation is effectively stopped in water, and organic material may be protective for virus survival. The ISAV has a glycosylated surface and accordingly is easily attached to different particulate material, which could affect virus survival as well as spread.

Water-borne transmission has been demonstrated in cohabitation experiments, indicating that it is important for the spread of ISA, and then notably by horizontal spreading between nearby infected farms (Thorud & Djupvik 1988). The virus may be shed into the water from infected hosts by various routes and by waste from dead fish (Totland, Hjeltnes & Flood 1996). The most likely route of viral entry is through the gills, through skin injuries, eye or through ingestion (Rimstad, Falk, Mikalsen & Teig 1999). The importance of gills as a port of entry is also indicated by the supposed non-virulent HPR0 variant that is reportedly mainly detected in the gills (Anonymous 2005).

The ISAV has been detected by real-time RT-PCR in fertilized eggs from brood fish with clinical ISA (Softeland 2005) and in smolt production sites (Devold, Karlsen & Nylund 2006). However, it is not known whether such findings indicate that an infective virus can be transmitted to the next generation through sexual products. Other studies could not find transmission of virus through fertilized eggs from ISAV-positive brood stock to the offspring, and no transmission was observed after injection of materials from fertilized eggs into parr (Melville & Griffiths 1999). However, that study was conducted at a time when the existence of non-virulent forms of ISAV (HPR0) was unknown. In Norway, field evidence is not supportive of significant vertical transmission of the disease. However, the ISAV found in Chilean aquaculture from 2007 and onwards is genetically highly similar to currently circulating European ISAV; thus, introduction from Europe to Chile through transport of biological material is likely to have occurred, indicating that vertical transmission is a possible route for introduction (Vike S, Nylund & Nylund 2009).

Currently available vaccines against ISA are based on inactivated whole virus. Such vaccines have been used in Canada, United States, Faroe Islands, in restricted areas of Norway and, from 2009, in Chile. Evaluation of the efficacy of the vaccines in the field situation has so far not been published.

**References**


