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Review

Viral Pathogens with Economic Impact in Aquaculture

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Abstract

Intensive fish farming provides an increasing part of the human diet and is a major economic resource in many countries. Keeping a large number of animals together increases the risk of disease outbreaks, including viral infections. This paper aims to provide a general overview of up-to-date information on the most common viral pathogens causing serious economic losses in fish farming, with a focus on the main aquaculture farming species grown in our country: common carp (*Cyprinus carpio* Linnaeus, 1758), European catfish (*Silurus glanis* Linnaeus, 1758), pikeperch (*Sander lucioperca* Linnaeus, 1758), rainbow trout (*Oncorhynchus mykiss* Walbaum, 1792), Russian sturgeon (*Acipenser gueldenstaedtii* Brandt and Ratzeburg, 1833), etc. Despite the lack of sustainable antiviral drugs suitable for aquatic environment, fish farming is a fast-growing economic sector that needs well-thought-out combinations of immunostimulants, antiviral drugs and/or vaccination. Good management practices could reduce the number of viral outbreaks or even provide solid protection against viral diseases and could enhance the sustainable growth of fish farming by contributing to the welfare of wild fish populations.

Keywords: fish viral pathogens, fish viral diseases, high mortality, DNA viruses, RNA viruses

Резюме

Интензивното развъждане на риба осигурява все по-голяма част от храната на човечеството и е основен икономически ресурс в много страни. Отглеждането на голям брой животни заедно, увеличава риска от огнища на заболявания, включително вирусни инфекции. Тази статия има за цел да представи обобщен преглед на актуалната информация за най-честите вирусни патогени, причиняващи сериозни икономически загуби в рибовъдството, с акцент върху основните аквакултури, отглеждани в страната ни: обикновен шаран (*Cyprinus carpio* Linnaeus, 1758), европейски сом (*Silurus glanis* Linnaeus, 1758), бяла риба (*Sander lucioperca* Linnaeus, 1758), дъгова пъстърва (*Oncorhynchus mykiss* Walbaum, 1792), руска есетра (*Acipenser gueldenstaedtii* Brandt and Ratzeburg, 1833) и др. Въпреки липсата на устойчиви антивирусни лекарства, подходящи за водна среда, рибовъдството е бързо развиващ се икономически сектор, който показва необходимостта от добре обмислени комбинации от имуностимуланти, антивирусни препарати и/или ваксинация. Добрите практики на управление могат да намалят броя на вирусните огнища или дори да осигурят солидна защита срещу вирусни заболявания и биха могли да увеличат устойчивото развитие на рибовъдния сектор и да сътрудничат за опазване здравето на популациите на дива риба.

Introduction

Fish species are cultured in high stocking density where they become more susceptible to diseases. Fish viral diseases cause mass morbidity and high mortality rate in farmed fish and are very difficult to treat directly in the open environment. Prevention is one of the best control measures against viral infections. Diagnostic methods for detection need to be easy and in time because viruses can be easily transmitted from one culture pond to another through equipment, infected fish/water, birds, or improper management. Viruses are unique and extremely small. Once they have entered the cell, they produce thousands of progenies. The number

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and distribution of fish viral pathogens has grown rapidly (www.ICTV). The World Organization for Animal Health (OIE) has a list of 13 reportable fish diseases and 11 of them are caused by viruses (www.OIE). There are both DNA and RNA viruses, which cause high morbidity and mass mortality of commercially important farmed fish, with significant economic losses (www.FAO).

DNA viruses

Adenoviridae family

Adenoviruses infect a wide range of vertebrate animals including humans, however, there is only one confirmed fish adenovirus (Benko *et al.*, 2002; Davison *et al.*, 2003). Fish adenovirus infection was first described in 1985 in California, where it caused a mortality of up to 50% over a 4-month period in cultured juvenile white sturgeon (*Acipenser transmontanus* Richardson, 1836) (Hedrick *et al*., 1985). The disease is named sturgeon wasting disease (SWD) because of the chronic nature of the infection and by the name of the first infected host (Noga, 2010). The adenovirus identified by electron microscopy was named white sturgeon adenovirus 1 (WSAdV-1) (Harrach *et al*., 2011). External clinical signs include lethargic, anorexic and emaciated infected fish, with no food in the gastrointestinal tract; internal signs showed hypertrophy of the mucosal layer of the gastrointestinal tract and paler liver tissue (Kim and Leong, 1999). Specific agents for control of adenovirus infections had a limited space. It is known that adenoviruses are relatively heat stable and resistant to pH 3-9; they are not sensitive to lipid solvents or alcohol below 50% and are inactivated by 1:1000 concentration of formaldehyde (Nagy, 2016).

Alloherpesviridae family

The International Committee on Taxonomy of Viruses (ICTV) changed the taxonomy of herpesviruses in 2008, and herpesviruses isolated from fish and amphibians previously classified into the family *Herpesviridae* based on their morphology were moved to the new family *Alloherpesviridae* divided into four genera. One of these genera contains the herpesviruses of amphibians and the other three contain herpesviruses of three different fish species (www.ICTV).

Cyprinid herpesvirus 3 (CyHV-3), also called carp interstitial nephritis and gill necrosis virus (CNGV), and *Koi herpesvirus* (KHV) often causes 100% morbidity and over 90% mortality in koi fish (*Cyprinus rubrofuscus* Lacepède, 1803), common carp (*Cyprinus carpio* Linnaeus, 1758) and its hybrids (Hedrick *et al.*, 2000; Haenen *et al*., 2004). CyHV-3 is distributed all over the world except Australia (Hampton and Hyndman, 2019). Infected fish could be recognized by gill lesions, food refusal and lethargy, uncoordinated swimming, respiratory distress, sunken eyes, enormous increase in mucus production causing sandpaper skin and bleeding gills, skin and fins, and gill and skin necrosis and fish death at the least (www.OIE). The virus affects carps from fingerlings to adult fish (Haenen *et al*., 2004). The infection is horizontal, from fish to fish or via infected water/equipment. There is no effective treatment of the disease; some disinfectants show effectiveness against CyHV-3, but their success should be revised because different conditions such as water temperature may affect the result (Bowker *et al*., 2011).

Acipenserid herpesvirus 2 (AciHV-2) has been isolated from different sturgeon species, including Bester hybrids (beluga *Huso huso* Linnaeus, 1758 x sterlet *Acipenser ruthenus* Linnaeus, 1758). The virus caused 100% mortality of Bester fingerlings, and clinical signs included focal epidermal hyperplasia, skin necrosis, multiple skin haemorrhages and integumentary tropism while infecting different organs and tissues (Shchelkunov *et al.*, 2009).

SalHV-1 and SalHV-2 are the principal herpesviruses which cause mass mortality in young salmonid fish. SalHV-1 causes mass mortality of juvenile rainbow trout (*Oncorhynchus mykiss* Walbaum, 1792) but not in other salmonid species. The disease occurs at 6-9°C (Davison, 1998). SalHV-2 was also named *Oncorhynchus masou virus* (OMV) to the first described host (*Oncorhynchus masou* Brevoort, 1856) (Kimura *et al*., 1981). SalHV-2 has a wider host range and occurs at a higher temperature optimum than SalHV-1 (Davison, 1998).

Poxviridae family

The *Poxviridae* family includes numerous viruses that are capable of infecting both invertebrates and vertebrates. Poxviruses are transmitted horizontally from fish to fish, or directly/indirectly via contaminated environment (Fenner *et al.*, 2014). One of the most common fish poxviruses is *Carp edema virus* (CEV), which causes 80-100% mortality of koi carp (*C. rubrofuscus*) and common carp (*C. carpio*) at water temperatures of 15-25°C (Miyazaki *et al*., 2005). Water temperature has a critical role in the disease outbreaks by modulating the fish immune system (Magnadottir, 2010). It has been suggested that in polycultural carp farms, silver carp (*Hypophthalmichthys molitrix* Valenci-

ennes, 1844) and grass carp (*Ctenopharyngodon idella* Valenciennes in Cuvier and Valenciennes, 1844) could be reservoirs of CEV (Lewisch *et al*., 2015). CEV was first recorded in Japan in 1974 (Murakami *et al*., 1976), but since then has spread worldwide (www.OIE), and causes carp edema virus disease (CEVD), also called Koi sleepy disease. Clinical signs of CEVD manifest with typically sleepy behaviour: infected fish gather lethargically or lie on the bottom of the pond; exophthalmos, gill hyperplasia and necrosis, anal ulcerative inflammation.

Iridoviridae family

The host range of the family *Iridoviridae* is restricted to insects and ectothermic vertebrates (Hick *et al*., 2016). Members of the subfamily *Alphairidovirinae* infect bony fish, amphibians and reptiles, and members of the subfamily *Betairidovirinae* mainly infect insects and crustaceans (Chinchar *et al*., 2017). The subfamily *Alphairidovirinae* includes numerous virus species belonging to the genera *Ranavirus*, *Megalocytivirus* and *Lymphocystivirus* (www.ICTV). These viral species cause important diseases with mass mortality, which impacts on the production, conservation and welfare of fish. Ranaviruses are pathogens capable of infecting bony fish, amphibians and reptiles; infections are systemic, involve internal organs, and could lead to high levels of morbidity and mortality (Chinchar *et al*., 2017). Megalocytiviruses infect over 50 marine and freshwater fish species; systemic infections involve multiple internal organs (Chinchar *et al*., 2017). Lymphocystiviruses infect over 100 marine and freshwater fish species; diseased fish have formations of wart-like growths composed of infected cells primarily on the skin, but sometimes on the internal organs. Morbidity could be high but mortality often is low (Chinchar *et al*., 2017).

Pikeperch iridovirus (PPIV) belongs to ranaviruses and has been isolated from European and Chinese amphibians (Darling *et al*., 2004). From fish it was first isolated in Finland in 1995, from apparently healthy pikeperch fingerlings (*Sander lucioperca* Linnaeus, 1758) during routine disease prophylactics (Tapiovaara *et al*., 1998). Wild amphibians were observed in the same ponds with asymptomatic pikeperch (*S. lucioperca*) and induced the possibility of interclass transmission (Tapiovaara *et al*., 1998; Duffus *et al*., 2015). Experimental infection with PPIV did not generate disease in pikeperch (*S. lucioperca*) and rainbow trout (*O. mykiss*) but the virus was found in both hosts, which suggests that these species might act as virus carriers (Jensen *et al*., 2011). It is known that PPIV is capable of crossing host species barriers and can cause mass mortality in juvenile pike (*Esox lucius* Linnaeus, 1758) (Jensen *et al*., 2009) and tadpoles of European common frog (*Rana temporaria* Linnaeus, 1758) (Bayley *et al*., 2013).

Epizootic haemopoietic necrosis virus (EHNV) causes epizootic haematopoietic necrosis (EHN) in rainbow trout (*O. mykiss*), European catfish (*Silurus glanis* Linnaeus, 1758) and redfin perch (*Perca fluviatilis* Linnaeus, 1758) (Ahne *et al*., 1989). The disease could be caused by three similar viruses: *Epizootic haematopoietic necrosis virus* (EHNV), *European sheatfish virus* (ESV), and *European catfish virus* (ECV) (Mavian *et al*., 2012). It could be characterised by mortalities due to necrosis in the liver, spleen, haematopoietic tissue of the kidney and other tissues (Ahne *et al*., 1989; Hedrick *et al*., 1992). The EHNV is restricted exclusively to Australia (www.OIE) but ESV and ECV have been detected among fish in Europe (Ahne *et al*., 1989). Infections with ESV and ECV can cause high morbidity and mortality in European catfish (*S. glanis*) (Ahne *et al*., 1989), while EHNV can be the cause of mass mortality in redfin perch (*P. fluviatilis*) (Whittington and Reddacliff, 1995). All fish ages could be affected by EHNV, but mortality is limited to fingerling and juvenile fish (Whittington *et al*., 2010). The mortality in wild redfin perch (*P. fluviatilis*) populations is up to 95%, but in populations of farmed rainbow trout (*O. mykiss*) it is less than 5% (Whittington *et al*., 2010).

European sheatfish ranavirus (ESV) was the first Ranavirus isolated in Europe, in Germany in 1989 (Ahne *et al*., 1989). ESV causes mortalities of up to 100% in infected European catfish (*S. glanis*) (Ahne *et al*., 1989) and also causes high mortality in pike (*E. lucius*) (Jensen *et al*., 2009), but other species, such as black bullhead catfish (*Ameiurus melas* Rafinesque, 1820) (Gobbo *et al*., 2010) and rainbow trout (*O. mykiss*) (Ariel *et al*., 2010) are apparently not affected although viral particles have been detected.

European catfish virus (ECV) was first isolated from European catfish (*S. glanis*) in Germany in 1989 (Ahne *et al*., 1989). This virus causes high mortality in European catfish (*S. glanis*) and black bullhead catfish (*A. melas*), and other economically important fish species, such as pike (*E. lucius*) and pikeperch (*S. lucioperca*), could also be susceptible (Jensen *et al*., 2009; Jensen *et al*., 2011). ECV causes a disease with non-specific clinical signs, but pathology is characterized by widespread systemic

necrosis which is most noticeable in the haematopoietic tissues (Whittington *et al*., 2010). Infections in European catfish (*S. glanis*) could cause 100% mortality in fingerlings and 10-30% mortality in older fish (Ahne *et al*., 1989).

Acipenser iridovirus-European (AcIV-E) is an important and prevalent sturgeon pathogen in Europe, associated with variable levels of morbidity and mortality of various farmed sturgeon species: beluga (*H. huso*), sterlet (*A. ruthenus*), Russian sturgeon (*Acipenser gueldenstaedtii* von Brandt and Ratzeburg, 1833), Siberian sturgeon (*Acipenser baerii* Brandt, 1869), Adriatic sturgeon (*Acipenser naccarii* Bonaparte, 1836) (Ciulli *et al*., 2016; Bigarré *et al*., 2017; Mugetti *et al*., 2020). AcIV-E is related to other sturgeon viruses found in North America, such as *white sturgeon iridovirus* (WSIV) and *Namao virus* (NV) (Bigarré *et al*., 2017). Mortality after AcIV-E infection varies greatly from 50% to over 90%, depending on the host species, the age of the fish and the presence of other pathogens (Ciulli *et al*., 2016).

Circoviridae family

Viruses of the family *Circoviridae* have been found in birds and pigs, and also detected in fish species (Lőrincz *et al*., 2011). The *circovirus* causing 100% mortality of barbel juveniles (*Barbus barbus* Linnaeus, 1758) is called *barbel circovirus* (BaCV) (Lőrincz *et al*., 2011). *Circovirus* causing high mortality of European catfish (*S. glanis*) of all ages is called *catfish circovirus* (CfCV) (Lőrincz *et al*., 2012), and *circovirus* suspected to cause mortality of European eel (*Anguilla anguilla* Linnaeus, 1758) is called *Eel circovirus* (EeCV) (Doszpoly *et al*., 2014). Clinical signs of the disease are skin lesions, vascular dilations in the skin, inflammation of the gastrointestinal tract, and nuclear fragmentation in the haematopoietic cells. Viral DNA has been detected mostly in the liver, spleen, gills, kidneys and the gonads (Lőrincz *et al*., 2012).

RNA viruses

Rhabdoviridae family

Some of the most common and significant fish viral RNA pathogens are members of the family *Rhabdoviridae* (www.ICTV). They cause losses in wild and farmed freshwater and seawater fish. Rhabdoviruses are widespread in a broad geographic range and could lead either to acute diseases and high mortality or to chronic and asymptomatic infections. Typical clinical signs of the fish diseases caused by rhabdoviruses are acute haemorrhagic septicaemias affecting multiple organs, petechial haemorrhages, accumulation of ascites, darkening and exophthalmia, necrosis of multiple organs (www.OIE). Mortality often is highest in juvenile fish and in some cases could be 100%. Fish that survive infection often show protective immunity. Transmission of fish rhabdoviruses could be horizontal between fish, and vertical from infected adult to its brood and eggs (Kurath and Winton, 2008). Economically, the most important pathogenic rhabdoviruses are spring viraemia of carp virus (SVCV), infectious haematopoietic necrosis virus (IHNV) and viral haemorrhagic septicaemia virus (VHSV), which cause damages to wild and farmed fish populations.

Spring viraemia of carp virus (SVCV) causes disease called spring viraemia of carp (SVC). SVC is reportable to the World Organisation for Animal Health (OIE), but the virus is serologically related to other non-reportable viruses (www.OIE). Hosts include a wide range of cyprinid and non-cyprinid fish species: common carp (*C. carpio*), koi carp (*C. rubrofuscus*), grass carp (*C. idella*), silver carp (*H. molitrix*), crucian carp (*Carassius carassius* Linnaeus, 1758), bighead carp (*Aristichthys nobilis* Richardson, 1845), Prussian carp (*Carassius auratus gibelio* Bloch, 1782), orfe (*Leuciscus idus* Linnaeus, 1758), tench (*Tinca tinca* Linnaeus, 1758), roach (*Rutilus rutilus* Linnaeus, 1758), bream (*Abramis brama* Linnaeus, 1758), emerald shiner (*Notropis atherinoides* Rafinesque, 1818), European catfish (*S. glanis*), black bullhead catfish (*A. melas*), pike (*E. lucius*), rainbow trout (*O. mykiss*), Siberian sturgeon (*A. baerii*); largemouth bass (*Micropterus salmoides* Lacépède, 1802), bluegill sunfish (*Lepomis macrochirus* Rafinesque, 1810), Nile tilapia (*Oreochromis niloticus* Linnaeus, 1758), etc. (Jeremic *et al.*, 2006; Dixon, 2008; Soliman *et al.*, 2008; Basic *et al*., 2009; Cipriano *et al*., 2011; Vicenova *et al*., 2011; Phelps *et al*., 2012). The disease has a wide temperature range, but mortality usually occurs between 5-18°C (Ahne *et al*., 2002). The disease outbreaks are usually above 10°C in spring, following a cold winter. Mortality of common carp (C. *carpio*) may reach 90% at 10-12°C while at 20-22°C there are no mortalities (Ahne, 1980). The clinical signs of SVC are non-specific. Infected fish usually swim slowly and erratically, lose balance and swim on their sides. Two of the most obvious and consistent characteristics are abdominal distension and haemorrhages which occur on the skin, fin bases, eyes and gills, also often observed are skin darkens and exophthalmia. The vents are swollen, inflamed with mucoid casts. The abdomen usually is filled with a

clear fluid, sometimes bloodstained. The spleen is enlarged, most internal organs are oedematous, and adhere to each other and to the peritoneum; petechial haemorrhages may be present in the musculature and the swim bladder (Dixon, 2008).

Infectious haematopoietic necrosis virus (IHNV) was first identified in western North America, but now the pathogen has spread to Europe and Asia (www.OIE). *Infectious haematopoietic necrosis virus* (IHNV) causes infectious haematopoietic necrosis (IHN), a disease notifiable to the OIE and various countries and trading areas, including the European Union (www.OIE). IHNV is an economically important pathogen causing clinical disease and 65-100% mortalities in rainbow trout (*O. mykiss*) (Kasai *et al*., 1993). Clinical signs include skin darkening, pale gills, exophthalmos, petechial haemorrhages, empty gut and ascitic fluid. Also, IHNV has been isolated in a wide variety of species, including Atlantic salmon (*Salmo salar* Linnaeus, 1758), brown trout (*Salmo trutta* Linnaeus, 1758), European eel (*A. anguilla*), Black Sea salmon (*Salmo trutta labrax* Pallas, 1814), pike (*E. lucius*), grayling (*Thymallus thymallus* Linnaeus, 1758), European seabass (*Dicentrarchus labrax* Linnaeus, 1758), etc. in which significant mortality has not been observed (www.OIE).

Viral haemorrhagic septicaemia virus (VHSV) causes a disease called viral haemorrhagic septicaemia (VHS). The VHSV has 4 genotypes, with genotypes I, II, III distributed in Europe, and genotype IV found in North America, the Atlantic Ocean and the Pacific Ocean (www.OIE). Genotype I occur in freshwater rainbow trout (*O. mykiss*) with mortality up to 100%, and also in various wild marine fish species. VHSV has a wide host range, and about 80 fish species are affected by all four genotypes (www.OIE). Transmission is horizontal - the virus is excreted with the urine and reproductive fluids (Eaton *et al*., 1991) or with uptake by gill epithelium (Brudeseth *et al*., 2008). Outside the host, the virus stays infective for a year in filtered fresh water at 4°C (Hawley and Garver, 2008) and at lower temperatures survival is even longer (Parry and Dixon, 1997). An average survival in saltwater at 15°C is 4 days (Hawley and Garver, 2008). The disease occurs at water temperatures 4-15°C (McAllister, 1990), for example, at 10°C mortality of bluegill sunfish (*L. macrochirus*) is 90%, but above 18°C mortality is 0% (Goodwin and Merry, 2011). The most common and typical clinical signs in fish infected with VHSV are haemorrhages, exophthalmos and enlarged abdomens with ascites, but mortality could occur without significant clinical signs. However, petechial haemorrhage in the dorsal musculature is a common sign in infected rainbow trout (*O. mykiss*) (www.OIE). Diseased fish could also have anaemia, a darkened colour, lethargy and abnormal swimming behaviour (www.OIE). Several disinfecting methods could inactivate VHSV in cold freshwater, including UV irradiation, high and low pH, and the use of disinfectants containing iodine complexed with a solubilizing agent (Bovo *et al*., 2005).

Orthomyxoviridae family

The family *Orthomyxoviridae* includes influenza viruses which are capable of infecting all kinds of species (McCauley *et al*., 2012), but infectious for fish are *infectious salmon anaemia virus* (ISAV) and *tilapia lake virus* (TiLV). TiLV caused mass mortality of tilapia (*O. niloticus*) in Israel (Eyngor *et al*., 2014) and Ecuador (Ferguson *et al*., 2014). ISAV is an economically important pathogen in aquaculture. Daily mortality varies between 0.05-0.1%, but accumulated mortality could reach more than 80% over several months (Jones *et al*., 1999). Outside its host ISAV remains infectious for a long time: 5 days in seawater at 20°C and up to 70 days in fresh water at 10°C; also,it has been suggested that in natural conditions it could survive even longer (Tapia *et al*., 2013). The disease caused by ISAV is called infectious salmon anaemia (ISA) and was first observed in farmed Atlantic salmon (*S. salar*) in 1984 in Norway (Thorud and Djupvik, 1988). The OIE confessed the existence of the disease in 1990 and since then it has been an OIE-notifiable disease (www.OIE). ISAV is confirmed in Norway, Scotland, Canada, Faroe Islands, Maine and Chile, where it is thought to be endemic and restricted only to farmed fish (www.OIE). The disease has been found only in salmonid species, e. g. Atlantic salmon (*S. salar*) (EFSA, 2012) and coho salmon (*Oncorhynchus kisutch* Walbaum, 1792) (Kibenge *et al*., 2001). The disease could be either acute form or slowly developing chronic disease (Rimstad *et al*., 2011), depending on the distribution between ponds within the farm, which extends the time from infection to development of the disease (Vagsholm *et al*., 1994; Jarp and Karlsen, 1997). Clinical signs could vary from lack of pathological changes to severe lesions, depending on the viral dose, water temperature, fish age, and immune status. The most typical signs are anaemia and circulatory disturbances. External signs are pale gills, local eyes and skin haemorrhages, exophthalmia, scale oedema, and the internal signs are ascites and haemorrhagic

liver necrosis, renal interstitial haemorrhage and tubular nephrosis (Aamelfot *et al*., 2014).

Nodaviridae family

The family *Nodaviridae* includes RNA viruses of the genus *Betanodavirus* which cause a severe neuropathological fish disease called viral encephalopathy and retinopathy (VER), also known as viral nervous necrosis (VNN). Betanodaviruses are distributed worldwide and represent a major limiting factor for seawater aquaculture, infecting practically all farmed marine fish species (Shetty *et al*., 2012). The disease has been included in the most significant fish viral pathogens because of the host range and the lack of effective prophylactic therapies (www.OIE). The geographic distribution of different betanodaviruses depends on their temperature optimum but the viral activity is independent of water salinity (Furusawa *et al*., 2007). The most common is *viral nervous necrosis virus* (VNNV), which causes clinical disease worldwide (Sakamoto *et al*., 2008; Panzarin *et al*., 2012; Shetty *et al*., 2012); the second is *striped jack nervous necrosis virus* (SJNNV) (Maeno *et al*., 2004; Sakamoto *et al*., 2008), followed by *redspotted grouper nervous necrosis virus* (RGNNV) (Panzarin *et al*., 2012). The disease has been confirmed in 160 fish species belonging to 79 families and 24 orders (www.OIE). The most commonly and severely affected species are: sea bass (*D. labrax*), barramundi (*Lates calcarifer* Bloch, 1790), grouper (*Ephinephelus* spp.), flatfish (*Solea* spp.), turbot (*Scophthalmus maximus* Linnaeus, 1758), olive flounder (*Paralichthys olivaceus* Temminck and Schlegel, 1846), striped jack (*Pseudocaranx dentex* Bloch and Schneider, 1801), jacks (*Trachinotus* spp.), drum (*Umbrina cirrose* Linnaeus, 1758), meagre (*Argyrosomus regius* Asso, 1801), red drum (*Sciaenops ocellatus* Linnaeus, 1766), white weakfish (*Atractoscion nobilis* Ayres, 1860) (www.OIE). An increasing number of outbreaks of VNN have recently been reported in freshwater fish (Pascoli *et al*., 2016). Transmission of the disease is horizontal through direct contact with infected fish, contaminated water or equipment. Clinical signs of the disease include varieties in skin colour, anorexia, lethargy, nervous hyper excitability behaviour caused by lesions in the brain and retina which cause blindness, and typical abnormal swimming behaviour which is characterized by swirling and circular movements that alternate with periods of lethargy (Shetty *et al*., 2012; Vendramin *et al*., 2013). Mortality varies depending on water temperature and fish age but for all ages it is generally over 50% (Maeno *et al*., 2004). Generally, younger fish are more susceptible, and in larvae and juveniles the beginning of the disease could be hyperacute with 80-100% mortality (Maeno *et al*., 2004).

Birnaviridae family

The family *Birnaviridae* includes four genera: *Aquabirnavirus*, *Avibirnavirus*, *Blosnavirus* and *Entomobirnavirus*, which infect vertebrates and invertebrates. Aquabirnaviruses are three species infecting fish, molluscs and crustaceans, and one of them is *infectious pancreatic necrosis virus* (IPNV), which is the model species and causes infectious pancreatic necrosis (IPN) (www.ICTV). IPNV and IPNV-like birnaviruses have been isolated from salmonid species (*S. salar*, *O. mykiss*, etc.) and non-salmonid species (*C. carpio*, *Perca flavescens* Mitchill, 1814, *A. brama*, *E. lucius,* etc.), molluscs, crustaceans and pseudocoelomates (McAllister, 2007). IPN was first detected in Canada in 1940s, later in the USA in 1950s, and in Europe in 1970s, but now is found worldwide among wild and cultured salmonid species (www.OIE). IPN was one of the top three causes of economic losses in the salmonid aquaculture during the 2000-2010, and even today remains an important risk for salmonid farming (www.FAO). There are significant losses caused by mortality and weakness of survivors. The cumulative mortality could increase more than double compared to baseline mortality (Jensen and Kristoffersen, 2015). Susceptibility to IPNV and mortality rate depend on the virus strain, fish species and stage/age, fish physiological condition and genetic fund, environment and management factors (Munro and Midtlyng, 2011). In cultured salmonid species, the infection varies from subclinical with low or no mortality to acute outbreak with high mortality over 75% (Shivappa *et al*., 2005). External clinical signs include darkened skin, exophthalmia, abdominal distention, presence of a mucoid pseudofaecal cast extruding from the vent, skin haemorrhages and haemorrhages at the bases of fins. Infected fish swim in a rotating manner along their longitudinal axis and die within a few hours. Internal signs could include pale liver and spleen, empty or filled with mucus digestive tract, and haemorrhages in the visceral organs (Munro and Midtlyng, 2011). The survivors of outbreaks often carry IPNV for lifetime without any clinical signs and serve as reservoirs of the virus, which is transmitted horizontally through faeces and urine, and vertically through contaminated reproductive products (Roberts and Pearson, 2005).

Togaviridae family

The most common members of the family *Togaviridae* are in the *Alphavirus* genus. The most recent alphaviruses are mosquito-borne, causing diseases in birds, mammals and humans (Strauss and Strauss, 1994). Infections could have different symptoms, such as rashes, gastrointestinal problems, arthritis, muscular inflammation, and even encephalitis (Kuhn, 2007; Steele and Twenhafel, 2010). The only known alphavirus infectious for fish (Powers *et al*., 2001) is *Salmonid alphavirus* (SAV) (Weston *et al*., 2002), also called *Salmon pancreas disease virus* (SPDV) isolated from seawater Atlantic salmon (*S. salar*) (Nelson *et al*., 1995), and also called *sleeping disease virus* (SDV) isolated from freshwater rainbow trout (*O. mykiss*) (Castric *et al*., 1997). The disease caused by the virus has two different names: pancreas disease (PD) and sleeping disease (SD), although they have the same histopathology (Weston *et al*., 2002). The disease is spread worldwide, mostly in farms with Atlantic salmon (*S. salar*) and rainbow trout (*O. mykiss*) (www.OIE). The virus has also been isolated from wild common dab (*Limanda limanda* Linnaeus, 1758), long rough dab (*Hippoglossoides platessoides* Fabricius, 1780), plaice (*Platessa platessa* Linnaeus, 1758), brown trout (*S. trutta*) (Boucher *et al*., 1995; Snow *et al*., 2010; Bruno *et al*., 2014; McCleary *et al*., 2014; Simons *et al*., 2016). Virus transmission is horizontal, from fish to fish, or by equipment (Viljugrein *et al*., 2009). In Europe, the economic impact from SAV is significant: in Norwegian salmon fish farming, losses from SAV retreated only to losses caused by sea lice infestations (Jansen *et al*., 2010). During the outbreak, the mean mortality rate could reach 7% and could last 2-3 months (Jansen *et al*., 2010). Mortality, biomass losses, slow growth rate and decreased fillet quality are the major consequences of the infection (Aunsmo *et al*., 2010). Clinical signs of the disease include a discoloured liver, petechiae on the pyloric caeca and visceral fat, and ascites in the intraperitoneal cavity; intestine could be either empty or filled with yellowish faeces (McLoughlin and Graham, 2007). Damage in the fillet, melanisation and miscoloured areas are other signs that are associated with ongoing or previous SAV infection (Taksdal *et al*., 2012). There are a number of approved vaccines against SAV but although they have been reported to have some positive effects, their efficacy has not been sufficient to eliminate SAV (Bang *et al*., 2012).

Discussion

The distribution of viral diseases is one of the major risks to aquaculture practices. The negative aspects are associated with the viral vectors transmission to cultured fish from open-water fish. This is a matter of global economic importance, especially with the increase of 122% in total food fish consumption from 1990 to 2018, and the increased movement and trade of live aquatic animals and their products across national borders (www. FAO). The Food and Agriculture Organization (FAO) of the United Nations calculated the value of the world exports of fish and fishery products in 2018 to be over 164 billion USD compared to 51.5 billion USD in 1998 (www. FAO), which illustrates the economic impact on international trade. Virus distribution could occur through transport of infected or contaminated live aquatic animals and products/water to new destinations, especially through animals with low external clinical signs of disease or subclinical infections and asymptomatic reservoir hosts (Gaughan, 2002; Vike *et al*., 2009; Rodgers *et al*., 2011).

The most effective ways of preventing fish viral diseases are biosecurity strategies, probably because for a number of viral diseases there are no vaccines or therapeutic substances, or if some vaccines are available, they need to be more cost-effective and appropriate to all fish life stages. Good practices could vary from national and international legislation and standards to the good management practices and prophylactics at the single farm level. Good aquaculture management includes on-site quarantine of new fish materials, routine disinfection of the equipment, reducing fish stress and diseases, prophylactics, etc.

Conclusion

Despite the lack of sustainable antiviral drugs suitable for the aquatic environment, fish farming is a fast-growing economic sector that needs well thought-out combinations of immunostimulants, antiviral drugs and/or vaccination. Good practices and management could decrease the number of viral outbreaks or even provide solid protection against viral diseases, and could enhance the sustainable growth of fish farming by contributing to the welfare of wild fish populations.

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