Epidemiology of marine gill diseases in Atlantic salmon (Salmo salar) aquaculture: a review

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Received 29 October 2019; accepted 9 March 2020.

Abstract
Gill disease of farmed Atlantic salmon (Salmo salar) in the marine environment has emerged as a significant problem for the salmon aquaculture industry. Different types of marine salmon gill disease reported include amoebic gill disease (AGD), parasitic gill disease, viral gill disease, bacterial gill disease, zooplankton (cnidarian nematocyst)-associated gill disease, harmful algal gill disease and chemical/toxin-associated gill disease. The term ‘multifactorial gill disease’ is used when multiple distinguishable types of disease (as opposed to an obvious single primary type) are present. When gill disease is non-specific, it is referred to as ‘complex gill disease’ (CGD) or ‘complex gill disorder’. These two terms are often used interchangeably and are overlapping. The significance of many infectious and non-infectious agents that may be associated with CGD is often unclear. In this review, we summarise aspects of the different types of gill disease that are relevant to the epidemiology of gill disease and of CGD in particular. We also tabulate simultaneously occurring putative pathogens to explore the multifactorial nature of gill disease.

Key words: Atlantic salmon, complex gill disease (CGD), marine gill disease, proliferative gill disease (PGD), proliferative gill inflammation (PGI).

Introduction
Gill disease of farmed Atlantic salmon (Salmo salar) refers to conditions in which gill pathologies are observed. Affected fish may display clinical signs of compromised respiratory function, and mortality rates may be increased (Mitchell & Rodger 2011). In the European salmon-producing countries like Norway, Scotland and Ireland, gill disease of salmon in the marine environment has become one of the most significant health challenges for the salmon aquaculture industry (Rodger 2007; Matthews et al. 2013; Hjeltnes et al. 2017; Scottish Government 2018b).

Marine gill disease in farmed salmon can be classified by aetiology-based subtypes. There are currently seven distinguishable types that refer to infection by one principal causal agent or insult: (i) amoebic gill disease (AGD), (ii) parasitic gill disease, (iii) viral gill disease, (iv) bacterial gill disease, (v) zooplankton (cnidarian nematocyst)-associated gill disease, (vi) harmful algal gill disease and (vii) chemical/toxin-associated gill disease (Rodger 2007). Amoebic gill disease has been categorised separately from other parasitic gill disease because of its significance and well described distinctive pathology. These types require complete investigation for accurate diagnosis, to include histopathology, clinical signs, history, gross gill observations, parasitology, water samples and molecular test results.

When some, or all, of these seven types are observed simultaneously and there is no obvious primary causal agent, the subtype is referred to as ‘multifactorial gill disease’ (CGD). This term is used when disease is non-specific and is defined as the simultaneous occurrence of one or more of the seven types of disease (Rodger 2007). The term CGD is often used interchangeably with ‘complex gill disease’ (CGD).

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interchangeably and are overlapping. An example of CGD can be found in Figure 1.

The epidemiology of CGD, particularly regarding the influence of various pathogens, environmental contributors and the role of some management practices, is not well understood. This review is intended to provide an up-to-date overview of infectious and non-infectious agents involved with gill disease, with a particular focus on factors relevant to the investigation of the epidemiology of gill disease in general, and CGD more specifically, in farmed Atlantic salmon. We provide an overview of CGD, and separately the seven types of gill disease listed above to provide as much distinction as possible, though these types may often occur simultaneously in multifactorial or complex gill disease cases. Where known, we have included descriptions and nomenclature of pathogens/agents putatively associated with gill disease, the effects of the pathogens/agents, information on the temporal and geographical distribution of forms of gill disease, clinical signs of disease, risk factors for disease, treatment options and a selection of additional reviews for further information. We have also tabulated the simultaneously occurring agents and pathogens to review the multifactorial-aspect of gill disease.

**Complex gill disease and related syndromes**

Complex gill disease encompasses syndromes referred to as ‘proliferative gill inflammation’ (PGI) and ‘proliferative gill disease’ (PGD; Herrero et al. 2018). PGI is a pathology-based diagnosis first described in Norway, in which gills present a combination of the following four histopathological changes: lamellar vascular changes, inflammation, cell death and epithelial cell hyperplasia (Kvellestad et al. 2005). In addition to these histopathological changes, additional signs include grossly pale gills, increased mucus and the presence of epitheliocysts in gill tissue (Steinum et al. 2010; Nylund et al. 2011). PGD has been present since at least the 1980s in Norway (Kvellestad et al. 2005).

In Scotland and Ireland, gill conditions similar to PGI have been reported (Mitchell & Rodger 2011; Rodger & Mitchell 2013) which have been called PGD in the past (Matthews et al. 2013). PGD has been used as a non-specific term derived from examination of gross lesions in the salmon gill in the field (Herrero et al. 2018), and also as a general descriptive term for gill disorders that include proliferative changes in the gill epithelium (Nylund et al. 2008). The term ‘proliferative gill disease’ is also used for specific conditions in other species, for example, the leading parasitic disease for farm-raised channel catfish (*Ictalurus punctatus*) in the United States of America (Bosworth et al. 2003; Beecham et al. 2010). CGD is increasingly commonly diagnosed in Atlantic salmon where proliferative-type gill disease is observed associated with exposure to one or more agents. Because CGD encompasses PGI and PGD, but is an emerging term, we have included information on PGI and PGD in this ‘complex gill disease’ part of the review where appropriate.

Proliferative-type gill disease in salmon can result in elevated mortality rates, reduced growth rates, runting and reduced food conversion efficiency (Kvellestad et al. 2005; Rodger et al. 2011b). PGI affects farmed salmon during the seawater production phase (Kvellestad et al. 2005; Steinum et al. 2009). It remains to be conclusively shown whether there is an association between gill disease in the marine environment and prior experiences encountered by salmon during the freshwater phase of production. Examples of putative pathogens that are encountered in both environments are *Candidatus Clavochlamydia salmonicola* (Mitchell et al. 2010), described in the bacterial gill disease section and salmon gill pox virus (Gjessing et al. 2017), described in the viral gill disease section.

The aetiology of CGD is unclear. The non-specific pathology may be a chronic end-stage pathology following insult(s) and challenge(s) or a cascade of such events (Gjessing et al. 2017). A number of putative pathogens have been detected in proliferative-type gill disease (Table 1). The significance of many of the agents and insults remains to be determined (Mitchell & Rodger 2011; Rodger et al. 2011a; Herrero et al. 2018), such as those associated with the formation of epitheliocysts (Kvellestad et al. 2005; Steinum et al. 2008, 2009, 2010; Mitchell et al. 2013). Other unidentified bacteria have also been detected in salmon with gill disease (Steinum et al. 2009). Parasites detected in cases of gill disease include *Neoparamoeba perurans* (Nylund et al. 2008, 2011; Steinum et al. 2008; Gjessing et al. 2019), *Desmozoon lepeophtherii* (Steinum et al. 2010; Nylund et al. 2011; Matthews et al. 2013; Gjessing et al. 2019), *Ichthyobodo* spp. (Kvellestad et al. 2005; Nylund et al. 2010), *Ichthyobodo* spp. (Kvellestad et al. 2005; Nylund et al. 2010).
Table 1 Cross tabulation of different terms of gill disease (pathological changes consistent with), bacteriological agents, parasites, viruses and jellyfish associated with gill disease co-occurring in one fish as described in literature.

| Gill disease | Gill disease | Bacterial |
|--------------|--------------|-----------|
| | CUD/ multifactorial gill disease | PGD | PGI | Epitheliocysts | Ca. Psychrophilus salmonis | Ca. Branchiomonas cyrтокола | Ca. Syngnathidium salmonis | Ca. Clavochlamydia salmonicola | Penaeobacter penaei | Penaeobacter penaei | Penaeodiscus penaei | Penaeodiscus penaei | Penaeodiscus penaei | Non-specified or other bacteria |
| CUD/ multifactorial gill disease | - | - | - | - | - | - | - | - | - | - | - | - | - |
| PGD | - | - | - | - | - | - | - | - | - | - | - | - | - |
| PGI | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Epitheliocysts | - | - | - | - | - | - | - | - | - | - | - | - | - |
| -Ca. Piscichlamydia salmonis | Gjessing et al. 2019 | Nyland et al. 2008 | Mitchell et al. 2013, Steimun et al. 2009, Steimun et al. 2009 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 | Gjessing et al. 2017, Mitchell et al. 2013, Nyland et al. 2015 |
| -Ca. Branchiomonas cyrтокола | Gjessing et al. 2019 | - | Mitchell et al. 2013 | - | - | - | - | - | - | - | - | - | - |
| -Ca. Syngnathidium salmonis | Gjessing et al. 2019 | - | Mitchell et al. 2013 | - | - | - | - | - | - | - | - | - | - |
| -Ca. Clavochlamydia salmonicola | Gjessing et al. 2019 | - | Mitchell et al. 2013 | - | - | - | - | - | - | - | - | - | - |
| Tenuicellicraceum maritimum | - | - | - | - | Rodger et al. 2011b | - | - | - | - | - | - | - | - |
| Tenuicellicraceum spp | - | - | - | - | Rodger et al. 2011b | - | - | - | - | - | - | - | - |
| Verruca stercoraria | - | - | - | - | Rodger et al. 2011b | - | - | - | - | - | - | - | - |
| Non-specified or other bacteria | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |

Marine gill diseases in Atlantic salmon
| Table 1 (continued) |
|---------------------|
| **Parasites**       |
| **Jellyfish**       |
| **AVS**             |
| **Viral**           |
| **SGP**             |
| **AVP**             |
| **Dexamenon**       |
| **Amoebida (AGD)**  |
| **Costia (echinopodo spp.)** |
| **Amoeba (salt, AGD)** |
| **Dermocystid**     |
| **Pericladia**      |
| **Paracodium**      |
| **Saprolegnia**     |
| **Non-specified, other** |
| **ASPV**            |
| **SCV**             |
| **SVA**             |

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| C | Gill disease | Bacterial |
|---|---|---|
| | CCO | multicausal gill disease | PCD | PGI | Encephalitozoon | C. piscidea pseudobranchicola | C. salmonis | C. synchirion | C. synchirion salmonis | Tenacibaculum finmarkense | Tenacibaculum maritimum | Tenacibaculum faeurnum | Yersinia ruckeri | Non-specified or other bacteria |
| Costia (Ichthyobodo spp.) | - | - | - | - | Gjessing et al. 2017 | - | - | Gjessing et al. 2017 | - | - | Rodger et al. 2011b | - | - | - |
| Amoeba (salt; AGD) | Gjessing et al. 2008 | Nyland et al. 2008 | Nyland et al. 2011 | Steinman et al. 2008 | Gjessing et al. 2017 | Gjessing et al. 2017 | Steinman et al. 2015 | Gjessing et al. 2017 | Steinman et al. 2015 | Nyland et al. 2018 | Downes et al. 2018a | Powell et al. 2005 | Rodger et al. 2011b | Valdengro et al. 2015 | Adams et al. 2004 |
| Dascococcus (leperithecium) | Gjessing et al. 2013 | Matthews et al. 2013 | Nyland et al. 2011 | Steinman et al. 2010 | Wells et al. 2017 | Gjessing et al. 2019 | Nyland et al. 2011 | Gjessing et al. 2019 | Nyland et al. 2011 | Gjessing et al. 2019 | Nyland et al. 2011 | - | - | - | Wells et al. 2017 |
| Trichodina | - | - | - | - | Kvellestad et al. 2005 | Mitchell et al. 2013 | Nyland et al. 2011 | Garsett et al. 2018 | - | - | - | Rodger et al. 2011b | - | Garsett et al. 2018 |
| Parvicapsula pseudobranchiola | - | - | - | - | Nyland et al. 2011 | - | - | - | - | - | - | - | - | - |
| Saprolegnia | - | - | - | - | Nyland et al. 2011 | - | - | - | - | - | - | - | - | - |
| Non-specified, other parasites, or fungi | - | - | - | - | Nyland et al. 2011 | - | - | - | - | - | - | - | Rodger et al. 2011b | - | - |
| ASPV | - | - | - | - | Kvellestad et al. 2005 | Steinman et al. 2010 | Fridl et al. 2004 | Kvellestad et al. 2003 | Kvellestad et al. 2005 | - | - | - | - | - | - |
| SGPV | Gjessing et al. 2017 | Nyland et al. 2008 | Nyland et al. 2011 | Steinman et al. 2015 | Garsett et al. 2018 | Steinman et al. 2015 | Gjessing et al. 2019 | Steinman et al. 2015 | Downes et al. 2018a | Steinman et al. 2015 | Nyland et al. 2011 | - | - | - | Garsett et al. 2018, Gjessing et al. 2017 |
| SA V | - | - | - | - | Nyland et al. 2011 | - | - | - | - | - | - | - | - | - |
| Jellyfish | - | - | - | - | Nyland et al. 2011 | - | - | - | - | - | - | - | - | - | Delannoy et al. 2011, Ferguson et al. 2010, Marcos-Lopez et al. 2016, Rodger et al. 2011b, Rume et al. 2013, Smidt et al. 2017 | - | - | - |

Cross tabulation of different terms of gill disease (pathological changes consistent with), bacteriological agents, parasites, viruses and jellyfish associated with gill disease co-occurring in one fish as described in literature. Note: only marine samples were taken into account. Different tests were used in the different studies, and not every study tested for the same/all agents and diseases. Absence of detection does not exclude co-existence.
†Disappeared after 4-6 weeks in marine environment.
et al. 2011), Trichodina (Kvellestad et al. 2005; Nylund et al. 2011; Mitchell et al. 2013), Parvicapsula pseudobranchicola (Nylund et al. 2011) and others (Nylund et al. 2011). Detected viruses include Atlantic salmon paramyxovirus (ASPV) (Kvellestad et al. 2005; Steinum et al. 2010), salmon gill poxvirus (SGPV) (Nylund et al. 2008, 2011; Gjessing et al. 2017; Gjessing et al. 2019) and salmon alphavirus (SAV) (Nylund et al. 2011). For reviews of infectious and non-infectious agents that can affect salmonid gills, see Mitchell and Rodger (2011) and Rodger et al. (2011a).

Often, multiple putative pathogens occur simultaneously in CGD cases, which are shown in Table 1. Variation in coinfections makes histopathological diagnosis of CGD highly complex (Gjessing et al. 2019). The relationship between CGD and some of the associated pathogens has been described as dose-dependent, but complex (Steinum et al. 2010; Mitchell et al. 2013; Gunnarsson et al. 2017; Downes et al. 2018a). For example, epitheliocysts were inconsistently observed in PGI-positive cases (Mitchell et al. 2013) and were found in lesser quantities in non-PGI cases (Steinum et al. 2010), and there were signs of a dose-dependent relation between severity of PGI cases and epitheliocysts (Mitchell et al. 2013). This suggests that they are unlikely to be the primary cause of PGI, but might contribute to the severity of the condition, or be proliferating opportunistically as a secondary result of the effects of another pathogenic agent.

In addition to the presence of putative pathogens, a number of other potential risk factors for CGD have been proposed. One major type of risk factor may be environmental insult to the gills, such as exposure to harmful phytoplankton, gelatinous zooplankton species in the water column or biofouling organisms dislodged into pens during in situ net washing (Rodger et al. 2011a; Bloecher et al. 2018; Kintner & Brierley 2019). Bath treatments involving the use of chemotherapeutants such as formalin (Speare et al. 1997) or hydrogen peroxide (Kiener & Black 1997; Rodger et al. 2011a) can be directly damaging to gills or may exacerbate existing gill conditions and may represent a risk factor for the development of CGD. Infectious organisms that cause gill pathology, such as the hyperplastic response of the gill to the presence of N. perurans in AGD (Adams et al. 2004), can be risk factors. Other factors that have been suggested to affect incidence and severity of proliferative-type gill disease include salmon genetic strain, environmental conditions (such as water eutrophication and pollution), nutritional deficits (reviewed by Rodger et al. 2011a), concurrent health issues and husbandry practices, such as use of lice-skirts, frequency of handling and the use of mechanical deousing systems.

The occurrence of CGD appears to have a seasonal pattern, with signs occurring mainly at the end of summer to early winter in Norway and Scotland (Kvellestad et al. 2005; Matthews et al. 2013), though there have been cases in May reported from Norway (Nylund et al. 2011), summer in Ireland (Rodger et al. 2011b) and as early as March/April in Scotland (Chris G.G. Matthews, pers. comm., 2019). In Norway, proliferative-type gill disease mainly occurs in western Norway (Nylund et al. 2011), which suggests that geographic location may play a role. Within specific regions, certain sites are perceived to be more prone than other sites (Chris G.G. Matthews, pers. comm., 2019).

Treatment strategies that have been used in cases with CGD include supplemental oxygenation or aeration within sea pens, treatment with freshwater baths, installation of short tarpaulin skirts or booms (in an attempt to exclude surface harmful algae or jellyfish blooms), provision of functional feeds purported to boost immune function or promote healing and in rare circumstances a course of oral broad-spectrum antibiotics (Rodger et al. 2011b). It has been suggested that vaccination might become a viable treatment strategy if specific bacteria or viruses can be confirmed as playing critical roles in the aetiology of CGD in farmed Atlantic salmon (Koppang et al. 2015).

Specific types of marine salmonid gill disease

Amoebic gill disease

Arguably, the most significant infectious agent contributing to proliferative gill diseases of farmed Atlantic salmon globally is the marine amoeboid amoebo N. perurans, which is associated with AGD (Crosbie et al. 2012). AGD has emerged as a distinct and significant health challenge since 2011 in marine salmon farms in Europe. AGD can lead to high mortalities, reportedly reaching up to 82% (Steinum et al. 2008) and significant morbidity. Changes occurring in the gill as a result of infection with N. perurans can lead to compromised gas exchange and ion regulation across the gills, potentially affecting appetite, growth and overall survival (Hvas et al. 2017). AGD has had a large impact on the aquaculture industry in Tasmania since 1984 (Taylor et al. 2009). The disease has since been reported in Atlantic salmon from all major producing countries (Oldham et al. 2016): Ireland in 1995 (Rodger & McArdle, 1996; Downes et al. 2018b), Scotland and Norway in 2006 (Steinum et al. 2008; Young et al. 2008), Chile in 2007 (Bustos et al. 2011) and western Canada in 2016 (ICES, 2016). Species other than Atlantic salmon can be affected by AGD, such as coho salmon (Oncorhynchus kisutch), rainbow trout (Oncorhynchus mykiss), chinook salmon (Oncorhynchus tschawytscha), turbot (Scophthalmus maximus), ayu (Plecoglossus altivelis) and halibut (Hippoglossus hippoglossus) (Jansson & Vennerstrom 2014; Rodger 2019). AGD has also been found in fish species used as biological parasite control in farmed Atlantic salmon including lumpsucker (Cyclopterus
Cyclopterus lumpus) and wrasse (Labridae spp) (Oldham et al. 2016; Haugland et al. 2017; Hellebø et al. 2017).

Neoparamoeba perurans is also referred to as Paramoeba perurans (Young et al. 2008; Nowak & Archibald, 2018). It has been suggested that Paramoeba and Neoparamoeba should be merged into a single genus prioritising the name Paramoeba (Feehan et al. 2013), but this has not been commonly accepted because taxonomic conclusions were based on single-gene trees with low number of Paramoebidae (Young et al. 2014; Volkova & Kudryavtsev, 2017). Other amoeba, including P. branchiphila, P. pemaquidensis/ N. pemaquidensis and Nolandella spp., have been observed from gills of fish with AGD using culture and PCR techniques. In these studies, N. perurans appeared to be the primary pathogen, and the role of the other amoeba remained unclear (Kent et al. 1988; Dyková & Novoa, 2001; Morrison et al. 2005; Vincent et al. 2007; English et al. 2019a; English et al. 2019b).

The first observed clinical signs of AGD are often a reduction in appetite, lethargy and altered swimming behaviour such as fish swimming close to the surface. As disease progresses, clinical signs observed can include respiratory distress, progressing to death of affected individuals in severe cases. Gross gill appearance includes multifocal pale lesions on the gill surface or raised white mucoid spots and plaques (Adams et al. 2004), as shown in Figure 2.

Several systems have been developed to score AGD severity based on gross observations of gills of anaesthetised fish. Adams et al. (2004) use a system with scores 0–3 based on number of affected hemibranchs. Adams and Nowak (2004) use the terms ‘clear’, ‘faint spots’, ‘spots’ and ‘patches’ based on translucent appearance and quantity of spots. A system of scores 0–5 based on white patches or scarring and percentage gill coverage, used by Taylor et al. (2009), has been commonly adopted by industry in Norway (Hellebo et al. 2017) and other European countries.

Presumptive diagnosis of AGD is based on clinical signs and the microscopic observation of typical amoeba on wet gill smears. The presence of N. perurans can be confirmed using polymerase chain reaction (PCR), which does not require the destruction of the fish host (Downes et al. 2017, 2018b), or destructively by histology, in which observed abnormalities are epithelial hyperplasia, lamellar fusion, inflammation, cell death, presence of interlamellar vesicles and presence of amoeba (Adams et al. 2004; Mitchell & Rodger, 2011).

Environmental risk factors for AGD are high salinity (Clark & Nowak, 1999), proximity to an infected site and elevated temperatures (Douglas-Helders et al. 2001). Described husbandry risk factors include high stocking density (Crosbie et al. 2010) and local crowding, which can be five times the stocking density at times and might be reduced by the use of lights (Wright et al. 2015, 2017).

Biofouling, which are the diverse assemblage of flora and fauna formed by successive growth of organisms on solid surfaces exposed to the marine environment (Tan et al. 2002) may be a risk factor for AGD, (Tan et al. 2002). However in another study, biofouling did not affect AGD prevalence, but fewer net changes, which could mean more growth of biofouling on nets, was a risk factor (Clark & Nowak 1999). Microbial dysbiosis, which is disturbance or imbalance of the microbiome, may also contribute to AGD (Nowak & Archibald 2018).

The genetics of fish stocks can also affect AGD. Hybrid fish such as Atlantic salmon x brown trout (Salmo trutta) have been shown to be more resistant to AGD. Furthermore, genetic selection can reduce the number of AGD treatments needed (Taylor et al. 2014; Maynard et al. 2016).

Cleaner fish (i.e. fish of other species cohabited with salmon to remove sea lice) of the species Cyclopterus lumpus and Labrus bergylta (or ballan wrasse) can develop AGD from N. perurans (Karlsbakk et al. 2013; H. Rodger in Oldham et al. (2016)). It was suggested that cleaner fish are more tolerant to N. perurans with a slower developing pathology compared with Atlantic salmon and may therefore act as a carriers, transmitting the amoeba to salmon (Haugland et al. 2017).

Freshwater bathing is the main treatment of choice against AGD. It has to be repeatedly applied, because it alleviates but does not eliminate AGD (Parsons et al. 2001; Clark et al. 2003), at least in part due to the continued presence of amoeba in the environment. Disadvantages of this method include its labour intensity and its expense. The treatment has been reported to remove 86% of live amoeba (Clark et al. 2003), but can be variable, which might be due, for example, to hardness and chemical composition of the freshwater used (Powell et al. 2015). Other treatments, such as the use of hydrogen peroxide, are being applied or developed (Powell et al. 2015). There is some evidence of resistance of Atlantic salmon against repeated infestations by N. perurans (Vincent et al. 2006; Taylor et al. 2009), but an effective vaccine has not been developed (Valdenegro-Vega et al. 2015). Restricting or minimising movement of fish and overall good hygienic standards have been recommended as preventive measures.

Amoebic gill disease has been detected in CGD, PGD and PGI cases (Nylund et al. 2008, 2011; Steinum et al. 2008; Gjessing et al. 2019). It has been detected simultaneously with the parasites D. lepeophtherii (Steinum et al. 2015; Downes et al. 2018a; Gjessing et al. 2019), and Trichodina sp. (Rodger & McArdle 1996; Rodger et al. 2011b) and Scotnicociliatia (Dyková et al. 2010). It has also been found alongside salmon gill pox virus (SGPV; Nylund et al. 2008; Gjessing et al. 2015, 2017, 2019; Hvas et al. 2017; Downes et al. 2018a) and damage due to the jellyfish
Desmozoon lepeophtherii (syn. Paranucleospora theridion) Desmozoon lepeophtherii, less frequently referred to as Paranucleospora theridion (Freeman & Sommerville, 2011), is a microsporidian that was discovered in sea lice in Scotland in 2000 (Freeman 2002). AGD has been detected simultaneously with Yersina ruckeri (Valdenegro-Vega et al. 2014) and Tenacibaculum maritimum (Powell et al. 2005; Rodger et al. 2011b; Downes et al. 2018a). However, in an experimental trial involving AGD-affected fish which were subsequently infected with T. maritimum, no evidence of interaction (e.g. predisposal) was observed (Powell et al. 2005). AGD has also been detected simultaneous to other or non-specific bacteria species (Adams et al. 2004). See Table 1 for an overview.

Reviews that focus on AGD include Mitchell and Rodger (2011) and Oldham et al. (2016).

Other forms of parasitic gill disease

Apart from amoeba, many other parasite species have been identified in marine salmon gills diagnosed with CGD or proliferative-type gill disease, as shown in Table 1. The parasites described here are putative pathogens sometimes associated with CGD.

Desmozoon lepeophtherii (syn. Paranucleospora theridion) Desmozoon lepeophtherii may have been present for much longer in these populations: it has recently been identified, for example, in samples collected in 1995 in Ireland (Downes et al. 2018b). In salmon, the parasite infects different cell types such as gill and skin epithelial cells, blood vessel endothelial cells, polymorphonuclear leucocytes and macrophage-like cells (Nylund et al. 2010; Weli et al. 2017). The transmission route of the parasite has not been fully elucidated, but it has been suggested that the microsporidian spores possibly infect the salmon gills first and then spreads to other tissues and organs (Nylund et al. 2010; Sveen et al. 2012). It is likely that the sea lice would ingest the parasite spores whilst feeding on the epithelial cells of the skin of infected salmon (Sveen et al. 2012). The sea lice may not be essential for infection of salmon (Sveen et al. 2012).

Desmozoon lepeophtherii occurs in apparently healthy fish, but is reportedly more abundant in diseased or compromised fish, such as fish diagnosed with PGI (Steinum et al. 2010) and fish with a low condition factor (Gunnarsson et al. 2017). Reports about associations between disease and D. lepeophtherii are scarce. Matthews et al. (2013) showed that D. lepeophtherii appeared to be acting as a causative agent associated with distinct pathology, but it could not be definitively concluded that D. lepeophtherii was the true primary pathogen. A dose dependency with disease was described by Steinum et al. (2010), in which study higher D. lepeophtherii densities were associated with PGI fish compared with non-PIG fish. Weli et al. (2017) describe the progression of D. lepeophtherii disease in a farm in Norway with severe gill disease, poor growth and mortalities. It has not been established whether the abundant presence of D. lepeophtherii is causative to pathology.

Histopathological changes observed in gills and attributed to D. lepeophtherii include hyperplasia and hypertrophy associated with presence of developmental stages or the degeneration of D. lepeophtherii (Nylund et al. 2011). An initial acute pathology in gills is necrosis and can be a direct result of D. lepeophtherii, but the chronic proliferative and inflammatory stage might be a result of a fish host response (Weli et al. 2017). Fish with high levels of D. lepeophtherii have also been reported with non-specific histopathological changes in kidney, spleen, gut, exocrine pancreas, somatic muscle and heart (Freeman 2002; Nylund et al. 2010, 2011), but it is unknown if those changes are associated with or due to the presence of D. lepeophtherii. In addition to histopathology, molecular methods are also used to detect D. lepeophtherii (Nylund et al. 2010).

Desmozoon lepeophtherii was detected in PGD and PGI cases (Nylund et al. 2011; Matthews et al. 2013; Steinum et al. 2015; Gjessing et al. 2019), and in combination with other pathogens, such as epitheliocysts (Weli et al. 2017) and associated bacteria (Nylund et al. 2011; Steinum et al. 2015; Downes et al. 2018a; Gjessing et al. 2019). Also, Figure 2 Severe amoebic gill disease (AGD) lesions.
T. maritimum (Downes et al. 2018a) and other non-specificified bacteria (Weli et al. 2017) were found alongside D. lepeophthereii. Others are N. perurans (Steinum et al. 2015; Downes et al. 2018a; Gjessing et al. 2019), Trichodina spp. (Weli et al. 2017) salmonid alphavirus (SAV; Nylund et al. 2011; Gunnarsson et al. 2017) and salmonid gill pox-virus (SGPV; Nylund et al. 2011; Downes et al. 2018a; Gjessing et al. 2019). See Table 1.

There is a paucity of described risk factors for presence of D. lepeophthereii in salmon gills. As for other microспорidians, a temperature of about 10°C or higher may be essential for propagation and the subsequent production of spores, in order to establish a systemic infection (Sveen et al. 2012). Probably due to the effect of temperature, infection appears to be seasonal. In a study by Gunnarsson et al. (2017), D. lepeophthereii densities were higher in salmon sampled in autumn of the first year at sea, compared with other seasons of the first year at sea, and in a study by Sveen et al. (2012), D. lepeophthereii infections were similar, but different for fish transferred when the water temperature was already low as these fish did not develop systemic infections in their first winter. Another effect of temperature could be the geographic region, as D. lepeophthereii infections were more intense and abundant in Western Norway compared with Northern Norway (Nylund et al. 2011).

**Viral gill disease**

Whilst there are a number of viruses that may be detected in gills, such as salmonid alphavirus (SAV), two viruses in particular have been associated with marine salmonid gill disease: Atlantic salmon paramyxovirus (ASPV) and salmon gill pox virus (SGPV).

**Atlantic salmon paramyxovirus**

Atlantic salmon paramyxovirus (ASPV) was first identified and described in Norway in 2003 (Kvellestad et al. 2003). It has been suggested that ASPV might be a contributor for PGD in conjunction with other pathogens and that the slow *in vitro* replication rate of ASPV may explain the long duration of the PGD outbreaks on fish farms (Kvellestad et al. 2005). However, challenge experiments did not result in any mortality or pathology (Fridell 2003 in (Nylund et al. 2008)). Another suggested association between ASPV and disease is that it may cause disease if fish are weakened or stressed (Fridell 2003), but recent studies have shown an inconsistent association between the virus and PGD outbreaks (Steinum et al. 2010; Nylund et al. 2011).

Atlantic salmon paramyxovirus was detected in PGD cases (Kvellestad et al. 2005; Steinum et al. 2010), and simultaneous to epitheliocysts (Kvellestad et al. 2003; Fridell 2003; Kvellestad et al. 2005), but correlation between ASPV and epitheliocysts was not expected because none, one, or both were detected in the same fish (Kvellestad et al. 2005). See Table 1.

**Salmon gill pox virus**

Salmon gill pox virus (SGPV) was first reported in Atlantic salmon at a freshwater site in Norway (Nylund et al. 2006 (in Norwegian) in Nylund et al. (2008)) and has since been reported from Canada (ICES 2016), Faroe Islands (Nolsøe et al. (2015) in Gjessing et al. (2016)), Scotland (Rodger, pers. comm. in Gjessing et al. (2016)) and Ireland using samples from as early as 1995 (Downes et al. 2018b), in fresh and salt water. SGPV has also been detected in wild salmonids (Garseth et al. 2018).

Salmon gill pox virus has been associated with high levels of acute mortality during the freshwater phase of salmon growth. Impact of SGPV is reportedly most pronounced during smoltification (Gjessing et al. 2017) and in fry stages (Chris G.G. Matthews, pers. comm., 2019). The virus may be involved with disease during the entire seawater cycle as well, as it was found 67 weeks after seawater transfer (Downes et al. 2018a).

A typical histopathological sign of SGPV is apoptosis of gill epithelial cells, but because this is not always observed. A molecular test for SGPV is considered essential to reliably indicate its presence (Gjessing et al. 2017). Some fish that tested positive by histology and PCR for SGPV had abnormalities in spleen, liver, heart and pyloric ceca (Gjessing et al. 2015). At present, recommendations around control of SGPV focus on maintaining best practice husbandry and biosecurity procedures. The effects of an outbreak can be minimised through cessation of feeding, increasing dissolved oxygen levels and avoidance of stress (Gjessing et al. 2016).

Molecular techniques have revealed that SGPV is widely distributed and occurs often in combination with other agents, which may mean that it forms part of the multifactorial pathology of CGD (Gjessing et al. 2017). However, SGPV has been inconsistently observed in fish with gill disease (Nylund et al. 2011) and has been detected from apparently healthy fish (Gjessing et al. 2017). SGPV disrupts the epithelial barrier and compromises innate immunity. In a multifactorial pathology such as suggested for CGD, SGPV may aid opportunistic infections by other organisms by facilitating insult, and it may precede and exacerbate the development of AGD (Gjessing et al. 2017).

Salmon gill pox virus has been found in fish with CGD, PGD and PGI (Nylund et al. 2008, 2011; Gjessing et al. 2017; Gjessing et al. 2019). It has also been detected simultaneously with epitheliocysts and epitheliocyst-forming bacteria (Nylund et al. 2008; Gjessing et al. 2017, 2019; Garseth et al. 2018; Downes et al. 2018a), T. maritimum
(Downes et al. 2018a) and other unspecified bacteria (Gjessing et al. 2017; Garseth et al. 2018). Parasites and fungi detected simultaneously with SGPV include N. perurans (Nylund et al. 2008; Gjessing et al. 2015, 2017, 2019; Hvas et al. 2017; Downes et al. 2018a), D. lepeophtherii (Nylund et al. 2011; Downes et al. 2018a; Gjessing et al. 2019), Ichthyobodo spp. (Gjessing et al. 2017; Garseth et al. 2018), Trichodina sp. (Garseth et al. 2018), Saprolegnia sp. (Gjessing et al. 2017; Garseth et al. 2018), among others (Garseth et al. 2018). See Table 1.

For a review of fish poxviruses see Gjessing et al. (2016).

Bacterial gill disease

The bacteria described here are associated with proliferative-type gill diseases in marine salmon. They are generally considered to be secondary invaders or opportunists.

Epitheliocysts

Epitheliocysts, that is disease due to epitheliocysts, is a condition in which fish gills, and less commonly skin epithelial cells, present with cytoplasmic membrane-bound inclusions (epitheliocysts) which contain bacteria, many of which remain to be characterised (Mitchell et al. 2013). The bacteria can be observed late in the infection when they have formed their characteristic cysts (Kvellestad et al. 2005). Epitheliocysts has been described in over 50 fish species around the globe, in fresh and salt water (Fryer & Lannan 1994; Nowak & LaPatra 2006). The discussion here will be restricted to salmonids and with respect to CGD.

Epitheliocysts in salmonid gills has been detected in Ireland (Downes et al. 2018b), Norway (Draghi et al. 2004; Mitchell et al. 2013), Scotland (Rodger & Mitchell 2013) and Tasmania (Nowak & LaPatra 2006). The presence of epitheliocysts often is not associated with clinical disease in farmed salmon, as it has been observed in apparently healthy fish (Mitchell et al. 2010). However, epitheliocysts have been suspected to play a role in some cases of CGD where mortality rates reached up to 100% (Nylund et al. 1998). If associated with disease or mortality, the condition is also referred to as a hyper infection (Nowak & LaPatra 2006). Epitheliocysts are not present in all CGD cases (Mitchell & Rodger 2011; Matthews et al. 2013).

To date, at least four agents have been identified that lead to epitheliocystis in Atlantic salmon in Norway and Ireland in a marine environment: Candidatus Piscichlamydia salmonis, Ca. Branchiomonas cysticola, Ca. Sygnamidia salmonis and Ca. Clavochlamydia salmonicola. Sometimes several of these agents may be detected simultaneously, for example Ca. Piscichlamydia salmonis and Ca. Branchiomonas cysticola (Mitchell et al. 2013; Steinum et al. 2015).

Candidatus Piscichlamydia salmonis, a bacterium identified from salt- and freshwater, was proposed to have been responsible for epitheliocystis in marine farmed Atlantic salmon in Norway and Ireland in 1999 and 2000 (Draghi et al. 2004). No direct correlation could be found, however, between the pathogen and gill disease (Steinum et al. 2010; Mitchell & Rodger 2011). Furthermore, chlamydia-like organisms might be opportunistic rather than primary pathogens (Horn 2008), indicating there may be other primary pathogen(s) or agent(s) involved.

One such possible primary pathogen is the beta-proteobacterium Ca. Branchiomonas cysticola (Toenshoff et al. 2012). It has been detected in a wide range of samples from Norway and Ireland and is considered common in European salmon aquaculture (Mitchell et al. 2013). The presence of this organism, which like Ca. Piscichlamydia salmonis is found in salt- and freshwater salmon (Mitchell et al. 2013; Wiik-Nielsen et al. 2017), has been shown to be quantitatively correlated with pathological changes consistent with CGD, but it has also been frequently found in fish without apparent gill pathology. During freshwater infection trials, in which the water of infected fish was used as a source of waterborne infection for a population of naïve juvenile Atlantic salmon, Ca. B. cysticola infections were associated with gill epithelial cell proliferation and subepithelial inflammation (Wiik-Nielsen et al. 2017). In a study looking at the histopathology of co-infections in Atlantic salmon obtained from salt water, necrosis in hyperplastic lesions, pustules and necrosis of subepithelial cells were specific changes that appeared to be associated with Ca. B. cysticola infection (Gjessing et al. 2019). Both these findings suggest that histological lesions other than only the formation of cysts in the epithelial cells may occur in gills infected by the bacteria. Unfortunately, the high prevalence of Ca. B. cysticola in healthy fish has hindered understanding its role in CGD.

A third reported bacterial agent is Ca. Sygnamidia salmonis. This is another member of the Chlamydiaceae, which has been isolated from a farm with fish diagnosed with gill disease and elevated mortality rates (Nylund et al. 2015). Correlation with the severity of pathology was not reported, and it is unknown if this organism causes epitheliocystis in apparently healthy fish, since only diseased fish were used in the study. It has been shown capable of replicating in N. perurans (Nylund et al. 2018).

The fourth reported agent is Ca. Clavochlamydia salmonicola (Karlsen et al. 2008). This is a Chlamydiaceae associated with freshwater epitheliocystis. It has not been shown to be associated with pathological changes such as epithelial hyperplasia in most fish. A study of the occurrence of Ca. Clavochlamydia salmonicola reported that the agent could no longer be observed 4–6 weeks after fish were transferred to marine pens (Mitchell et al. 2013).
Depending on severity of infection, histopathological changes of gills of fish with epitheliocystis can be consistent with CGD: these include a proliferative hyperplasia with hypertrophy, inflammation and necrosis (Nowak & Clark, 1999). Additionally, gills have characteristic cysts, which can be observed macroscopically in some instances as white to yellow cysts. Molecular tests have been developed for all mentioned agents: Ca. P. salmonis (Rueane et al. 2013), Ca. B. cysticola (Toenshoff et al. 2012; Mitchell et al. 2013), Ca. S. salmonis (Nylund et al. 2015) and Ca. C. salmonicola (Mitchell et al. 2010).

Other bacteria that have been detected simultaneously with epitheliocystis are T. maritimum (Rodger et al. 2011b; Downes et al. 2018a), and unidentified bacteria (Steinum et al. 2009; Garseth et al. 2018). Co-occurring parasites include Ichthyobodo spp. (Gjessing et al. 2017), N. perurans (Steinum et al. 2015; Gjessing et al. 2017, 2019; Nylund et al. 2018; Downes et al. 2018a), D. lepeophtherii (Nylund et al. 2011; Steinum et al. 2015; Welii et al. 2017; Downes et al. 2018a; Gjessing et al. 2019) and Trichodina spp. (Garseth et al. 2018). Viruses that have been simultaneously detected with epitheliocystis include ASPV (Kvellestad et al. 2003; Fridell 2003; Kvellestad et al. 2005), though there was no correlation observed (Kvellestad et al. 2005); and SGPV (Nylund et al. 2008; Gjessing et al. 2017, 2019; Garseth et al. 2018; Downes et al. 2018a). See Table 1.

Little is known about risk factors for epitheliocystis. High stocking densities and high nutrient levels in the water may affect presence (Woo & Bruno 2014). It has been suggested that the season might be important, but neither water salinity nor age of the fish appear to be risk factors (Nowak & Clark, 2005), though there was no correlation observed (Kvellestad et al. 2005); and SGPV (Nylund et al. 2008; Gjessing et al. 2017, 2019; Garseth et al. 2018; Downes et al. 2018a). See Table 1.

Fish infected with T. maritimum may be lethargic, anorexic (Handlinger et al. 1997) and have an increased respiratory rate. They can have erosions and haemorrhages within and around the oral cavity, scale loss, ulcerative skin lesions, frayed fins and tail rot. A typical yellow margin might be present around these lesions (Smage et al. 2017), see Figure 3, which can be the portal of entry for other bacterial or parasitic agents (Toranzo et al. 2005). Lesions in the gills, which are not always present, can consist of focal areas of necrosis, and erosion in connective tissue associated with filamentous bacterial mats on lamellae, which looks like ‘gill rot’. Free ends of one to several primary lamellae can be eroded. Gills may have increased mucus, or an acute inflammation, which could indicate another insult, such as jellyfish exposure (Handlinger et al. 1997; Mitchell & Rodger 2011). Tenacibaculum may also be involved in the pathogenesis of ‘winter ulcers’, a condition of which Mortierella viscosa is considered an important factor (Olsen et al. 2011).

Risk factors for tenacibaculosis are high water temperatures, usually over 15°C (Toranzo et al. 2005; Downes et al. 2018a), but possibly lower, depending on the bacterial strain (Frisch et al. 2017). The bacteria often colonise epithelia secondary to other insults, such as infection with D. lepeophtherii (Weli et al. 2017) or injuries caused by harmful zooplankton and jellyfish (Rodger et al. 2011a). Younger fish are at greater risk (Toranzo et al. 2005). T. maritimum is usually outcompeted in seawater by other bacterial species and might need to remain attached to a substrate or animal surface (Avendaño-Herrera et al. 2006a). Such a substrate might be a host or vector for this bacteria, such as the jellyfish species Phialella quadrata (Ferguson et al. 2010), P. noctiluca (Delannoy et al. 2011) and Muggiae atlantica (Fringuelli et al. 2012), the sea louse

T. maritimum is an opportunistic bacterium that is commonly found on gill tissue of both healthy and diseased fish (Fringuelli et al. 2012). Though high levels were associated with gill disease (Ruane et al. 2013), it is unknown whether this association implies causality of T. maritimum for gill disease, the other way around, or an entirely different type of association. Gills might not be the most important route for infection of this opportunistic pathogen as it also affects other organs (Avendaño-Herrera et al. 2006b). The pathogen has been reported in many different fish species in Japan, Europe, Australia, USA, Chile and Canada, and for reviews see Toranzo et al. (2005), Avendaño-Herrera et al. (2006b) and Frisch et al. (2017). Other Tenacibaculum spp. have been identified as salmonid pathogens that cause similar disease symptoms, including as T. finnmarkense (Smage et al. 2016a, 2017) and T. dicentrarchi (Avendaño-Herrera et al. 2016). It has been suggested multiple Tenacibaculum spp. colonise the surface of Atlantic salmon (Karlsen et al. 2017).

Tenacibaculosis/flexibacteriosis
This salt water ulcerative disease has been given many different names, such as ‘salt water columnaris disease’, ‘gill ing bacterial disease of sea fish’, ‘bacterial stomatitis’, ‘eroded mouth syndrome’ and ‘black patch necrosis’ (reviewed by Avendaño-Herrera et al. (2006b)). This Gram-negative filamentous bacterium responsible for the disease is currently known as Tenacibaculum maritimum, after having previously been described as Flexibacter marinus, Flexibacter maritimus and Cytophaga marina (reviewed by Suzuki et al. (2001) and Avendaño-Herrera et al. (2006b)).
Lepeophtheirus salmonis (Barker et al. 2009), and the cleaner fish Cyclopterus lumpus L (Småge et al. 2016b). Other risk factors include high salinities, stress, elevated ammonia and physical or toxic insults (Mitchell & Rodger 2011). In a study in Norway, recently transferred smolts were more affected by tenacibaculosis than smolts that had been in the salt water longer (Småge et al. 2017). This may be because smolts that have just transferred to salt water have reduced resilience due to changes in their microbiota as a result of the change in conditions (Lokesh & Kiron 2016), pressure on osmoregulatory control and elevated stress levels as a result of the transfer process (Iversen et al. 2005).

Definitive diagnosis can be based on microbiological methods (Toranzo et al. 2005), and on PCR (Avendaño-Herrera et al. 2006b; Fringuelli et al. 2012). Treatment is through antibiotics (Morrison & Saksida 2013), improved environment or removal of the primary stressor or insult.

The presence of T. maritimum could not be statistically associated with increased gill scores (Fringuelli et al. 2012). It has been observed simultaneously with epitheliocysts (Rodger et al. 2011b; Downes et al. 2018a), the parasites Ichthyobodo spp, Trichodina, D. lepeophtherii (Rodger et al. 2011b; Downes et al. 2018a), the virus SGPV (Downes et al. 2018a) and jellyfish (Ferguson et al. 2010; Delannoy et al. 2011; Rodger et al. 2011b; Ruane et al. 2013; Marcos-Lopez et al. 2016). T. maritimum was observed simultaneously with N. perurans (Powell et al. 2005; Rodger et al. 2011b; Downes et al. 2018a), but there was no evidence of interactions between them (Powell et al. 2005). See Table 1.

For a review, see Avendaño-Herrera et al. (2006b).

Zooplankton (cnidarian nematocyst)-associated gill disease

Gelatinous zooplankton (referred to hereafter as jellyfish) occur in oceans worldwide and can be associated with high mortality rates in open-pen salmonid aquaculture. Examples include a study in Ireland in which 70% of mortality of all fish was due to occasional bloom events (Ruane et al. 2013; Marcos-Lopez et al. 2016), and a study in Scotland which found that around 60% of all fish mortalities due to plankton between 1999 and 2005 were associated with jellyfish (Scottish Government 2018a). Jellyfish abundance has been correlated to daily mortality rates with a lag of one to seven days (Baxter et al. 2011a), and blooms can lead to increased operational cost and insurance fees (Lucas et al. 2014).

Most zooplankton-associated gill disease is due to stings of free-living jellyfish. Cnidarian jellyfish have stinging cells which contain nematocysts that can cause mechanical and toxic insults to the fish gills and epithelia (Marcos-Lopez et al. 2016). In open net pens such as used in salmon aquaculture, small and transparent cnidarian jellyfish enter the fish pens intact, whereas larger jellyfish are broken up against the net mesh (Marcos-Lopez et al. 2016). Both of these cases can lead to nematocyst damage. Additionally, avoidance behaviour of the fish, such as excessive jumping, may result in more mechanical damage (Bämstedt et al. 1998). It has been proposed that jellyfish may serve as reservoirs or vectors for pathogens such as Tenacibaculum spp. (Ferguson et al. 2010; Fringuelli et al. 2012; Småge et al. 2017), which can cause disease in the fish.

Sessile jellyfish, hydrozoans, can foul aquaculture structures so that water flow and quality is reduced. To counter this, nets can be cleaned using pressure washers, but fish in cages have been observed to exhibit avoidance behaviour from the dense clouds of debris that come off the nets during the cleaning process. Experimental challenges showed that this debris can cause pathological changes in the gills, such as epithelial sloughing, necrosis and haemorrhaging (Baxter et al. 2012; Bloecher et al. 2018).

Clinical signs associated with presence of or damage caused by jellyfish include lethargic behaviour, fish swimming high in the water column close to the water surface and increased jumping behaviour (Marcos-Lopez et al. 2016). Sometimes zooplankton can still be seen in the gills both macroscopically and microscopically. Macroscopic signs include skin erosions, scale loss, swollen or haemorrhagic lesions on the skin with ulcers, see Figure 3. Microscopically, the gill damage observed can consist of hyperplasia, lamellar fusion, occasional presence of giant cells and bullae-like formations at the edges of filaments in chronic lesions with necrosis, haemorrhages, congestion,

Figure 3 Zooplankton damage from Muggiaea atlantica with erosion of gill rakers and Tenacibaculum sp. colonisation of damaged tissue obvious as yellowish colouration on damaged tissue.
infiltration, oedema, lamellar epithelium sloughing and loss of tissue inflammation (Baxter et al. 2011a, 2011b; Ruane et al. 2013; Marcos-Lopez et al. 2016). Microscopic and/or macroscopic signs are not always observed during a jellyfish bloom (Småge et al. 2017). A yellow-brown colour associated with skin and gill lesions from jellyfish could indicate aggregations of Tenacibaculum sp. (Rodger et al. 2011a; Marcos-Lopez et al. 2016).

Risk factors for jellyfish blooms are warm weather (Marcos-Lopez et al. 2016), and there is some evidence that processes like overfishing, eutrophication, climate change, translocations and habitat modification may lead to more jellyfish blooms (Richardson et al. 2009). Fish have been treated with antibiotic, such as oxytetracycline in some cases in the past, after a jellyfish encounter to reduce the impact of secondary bacterial infections (Marcos-Lopez et al. 2016).

Jellyfish damage has been observed simultaneously with T. maritimum (Ferguson et al. 2010; Delannoy et al. 2011; Rodger et al. 2011b; Ruane et al. 2013; Marcos-Lopez et al. 2016) and T. finmarkense (Småge et al. 2017). See Table 1.

For a review on this topic, see Purcell et al. (2013).

Harmful algal gill disease

Many species of phytoplankton occur in fresh and salt water. Any phytoplankton species that may have a deleterious effect on other aquatic species or humans (including economic damage) is referred to as harmful (Kralberg et al. 2010). Harmful algae blooms (HABs) have been responsible for gill damage and salmon mortality around the world (Rodger et al. 2011a). Several mechanisms can lead to gill damage and mortality. Clogging and abrasion of gill structures can lead to excessive mucus production, which can lead to oxygen deprivation and thus suffocation of the fish (Bruno et al. 1989; Kent et al. 1995). Photosynthesis and respiration of phytoplankton populations associated with HABs can lead to both oxygen depletion and oxygen supersaturation during a major bloom event (Jones & Rhodes 1994; Hishida et al. 1998). Toxins produced by algae can cause damage to gills or other organs and cause morbidity and mortality (Chang et al. 1990). Lastly, phytoplankton may attach to benthic substrate and cause increased biofouling (Kaatvedt et al. 1991). Clinical signs of HABs are decreased feeding rate, avoidance behaviour such as maintaining a particular position in the water column and respiratory distress behaviour such as gasping at the surface, increased ventilatory effort and respiration rate and gathering in areas of higher oxygen like facing into the incoming current (Treasurer et al. 2003; Rodger et al. 2011a). Furthermore, irritation of the gills due to HABs can lead to bleeding gills, petechiae on gills and increased mucus production on the gills (Rodger et al. 2011a).

Associated pathology in gills depends on the type of interaction between the different algae species and gill tissue. It includes severe necrosis and sloughing with separation of secondary gill lamellae and hyperplasia (Bruno et al. 1989). There can also be oedema at the base of the secondary lamellae, inflammation (Kent et al. 1995) and vascular changes (Chang et al. 1990). Other organs, such as the liver, can also be affected (Treasurer et al. 2003; Mitchell & Rodger 2007).

Mitigation methods against HABs have been reviewed by Rensel and Whyte (2004) and include adjusting feeding and other husbandry practices during the bloom, airlift pumping of deep water into the cages, oxygenation and aeration, moving or submerging cages, using alternatives to seawater cages such as onshore tanks, treating the water (e.g. through adding clay), using live cage bioassays nearby a production site as early indicators and to test virulence of HABs, early harvest and using freshwater to lower salinity and reduce energy costs of osmoregulation.

For reviews, see Rensel and Whyte (2004) and Rodger et al. (2011a).

Chemical/toxin-associated gill disease

Eutrophication around coastal areas can lead to an increase of harmful compounds in the water, for example (waste) products of forestry, agriculture, industry or sewage systems (Rodger et al. 2011a). Very little is known about the effect of such compounds on fish gills in salt water, which may be different to the effects on gills of fish in fresh water (Mallatt 1985). Also chemicals from treatments, such as hydrogen peroxide, may affect gills (Kiemer & Black 1997; Adams et al. 2012). The effects that water quality in freshwater has on the marine survival of salmon remains to be determined for many parameters, metals and chemicals such as pH, carbon dioxide and formalin (Kroglund et al. 2007).

Discussion and Conclusions

An increase in prevalence of marine gill disease and associated financial losses led to an increase in research on putative aetiological factors of CGD over the last decade. This resulted in an increase in monitoring, mapping and our understanding of marine gill diseases, but has not led to a full understanding of the role of the different putative components of the aetiology of CGD.

Complex gill disease is frequently associated with multiple putative pathogens. Table 1 lists pairs of putative pathogens that occurred simultaneously, and more often than not more than two pathogens occur in one sample. In
addition, perhaps the aetiology of CGD involves more than these putative pathogens and is similar to other multifactorial diseases where disease response is not only determined by infectious agents, but also by synergic effects between infectious agents, environment, management and the immune status of the animals (Lorenz et al. 2011; Herrero et al. 2018). An example of a possible complex association between CGD and management is the employment of cleaner fish to control sea lice, which requires a smaller mesh size (Kent 1992), which may in turn affect abundance, species richness, and species composition of biofouling organisms (Bloecher et al. 2018), which in turn may affect gill health. In future studies of CGD, it is therefore important to not only investigate the relation between CGD and putative aetiological agents, but also between CGD and other factors such as management strategies and interactions between the different putative components of the aetiology of CGD.

Areas for continued study

Studying the transmission of putative pathogens between fish and the effect of interactions between pathogens is a challenge. This review and accompanying tables show that many different pathogens may be involved with CGD, and they occur in many different combinations. Although some pathogens listed may not be primary pathogens, they may exacerbate CGD. Controlled laboratory trials with these putative pathogens are currently not possible, because most of the pathogens have not been cultured successfully. An uncontrolled laboratory trial, such as described in a study by Wiik-Nielsen et al. (2017) in which freshwater salmon that were naturally infected with putative pathogens for CGD in the field and were imported into the laboratory and used in cohabitation experiments may currently be the only way to study transmission of putative pathogens. However, this method cannot be standardised as there is no control over infection levels and types of putative pathogens in the infected fish imported from a field situation. It may therefore on the one hand be important to identify key players in the aetiology of CGD and develop systems that allow for controlled trials, but on the other hand considering the system as a black box and focusing on mitigation of risk factors in farm management systems.

One of the key challenges in any study of CGD is the need for a clear case definition. The different terms that have been used to describe marine gill disease have led to confusion and make it difficult to compare between studies and areas. CGD as currently used, includes most other pathologies (Herrero et al. 2018; Noguera et al. 2019), but its boundaries are not well defined. A clear case definition would allow for a systematic estimation of prevalences across the salmon industry in different areas and countries and could aid epidemiological studies such as risk-factor analyses.

There is a need for comprehensive epidemiological studies that take into account the different putative components of CGD. Research regarding individual components, such as putative pathogens and environmental factors, has provided increased knowledge and understand of their associations with marine gill disease. With this knowledge came awareness and increased surveillance for putative components for CGD. As a result of this knowledge and increased monitoring, a next step may be to attempt understanding the possibly complex interactions between such components. Two such studies were launched in 2018, when salmon producers in Scotland and Norway engaged in industry wide, inclusive epidemiological projects on marine gill health in farmed salmon (FHF 2019; SAIC 2019).

It is unclear why CGD has emerged as a significant health problem, as many of the putative pathogens associated with CGD have been shown to be present for years retrospectively. The answer may lay in other components that may be part of a multifactorial aetiology for CGD, which have changed over the last decade. For example, the industry saw many changes in management strategies stimulated by the need to be sustainable and profitable, such as further intensification, changes in diet ingredients, changes in genetic factors (Ellis et al. 2016) and technological advances (Føre et al. 2018). Also, natural processes, such as the climate, have not remained constant, and temperatures have been rising. As a result of changes occurring simultaneously in the different putative components for CGD, it is challenging to retrospectively pinpoint why CGD has emerged as a significant fish health problem.

Looking to the future, it may not be possible to eliminate CGD entirely, similar to the current state of sea lice and AGD. Mitigation efforts may need to focus on control of CGD to proportions that are acceptable from both an animal welfare and animal production standpoint. Current research efforts are improving our knowledge and may help to better understand CGD.

Acknowledgements

This work was partly supported by the Scottish Aquaculture Innovation Centre grant SL_2017_07.

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