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

Boerlage, AS; Ashby, Angela; Herrero, Ana ; Reeves, A; Gunn, GJ; Rodger, Hamish D.

Published in:
Reviews in Aquaculture

DOI:
10.1111/raq.12426

First published: 29/05/2020

Document Version
Publisher's PDF, also known as Version of record

REVIEWS IN Aquaculture

Reviews in Aquaculture, 1–20 doi: 10.1111/raq.12426

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

Annette S. Boerlage[1], Angela Ashby[2], Ana Herrero[2,3], Aaron Reeves[1], George J. Gunn[1] and Hamish D. Rodger[4]

1 Epidemiology Research Unit, Department of Veterinary and Animal Science, Northern Faculty, Scotland's Rural College (SRUC), Inverness, UK
2 Fish Vet Group Ltd., Inverness, UK
3 Moredun Research Institute, Pentlands Science Park, Penicuik, UK
4 VAI Consulting, Oranmore, Co. Galway, Ireland

Correspondence
Annette S. Boerlage, Epidemiology Research Unit, Department of Veterinary and Animal Science, Northern Faculty, Scotland's Rural College (SRUC), An Lòchran, 10 Inverness Campus, Inverness, UK. Email: annette.boerlage@sruc.ac.uk

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, consisting of .... (the types of specific gill diseases)'. When principal pathological changes are non-specific, either in combination with, or in the absence of, one or more of the seven distinctive types (including AGD), the type of gill disease is referred to as 'complex gill disease or disorder (CGD)' (Noguera *et al.* 2019). The terms CGD and multifactorial gill disease are often used

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). PGI has been present since at least the 1980s in Norway (Kvellestad *et al.* 2005).

Figure 1 An example of complex gill disease (CGD) lesions in Atlantic salmon.

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

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.

A

Gill disease		Gill disease			Bacterial										
		CGD/ multifactorial gill disease	PGD	PGI	Epitheliocysts	-*Ca.* Piscichlamydia salmonis	-*Ca.* Branchiomonas cysticola	-*Ca.* Sygnamidia salmonis	-*Ca.* Clavochlamydia salmonicola	*Tenacibaculum maritimum*	*Tenacibaculum finmarkense*	*Yersinia ruckeri*	Non-specified or other bacteria
CGD/ multifactorial gill disease													
PGD		-											
PGI†		-	-	Kvellestad *et al.* 2005, Mitchell *et al.* 2013, Steinum *et al.* 2008, Steinum *et al.* 2009, Steinum *et al.* 2010									
Bacterial	Epitheliocysts	-	-										
	-*Ca.* Piscichlamydia salmonis	Gjessing *et al.* 2019	Nylund *et al.* 2008	Mitchell *et al.* 2013, Nylund *et al.* 2011, Steinum *et al.* 2009, Steinum *et al.* 2010	Steinum *et al.* 2010								
	-*Ca.* Branchiomonas cysticola	Gjessing *et al.* 2019	-	Mitchell *et al.* 2013	Gjessing *et al.* 2017, Mitchell *et al.* 2013, Nylund *et al.* 2015	Gjessing *et al.* 2019, Mitchell *et al.* 2013, Steinum *et al.* 2015							
	-*Ca.* Sygnamidia salmonis	-	-	-	Nylund *et al.* 2015	-	-						
	-*Ca.* Clavochlamydia salmonicola	-	-	-	Mitchell *et al.* 2010†	-	-	-					
	Tenacibaculum maritimum	-	-	-	Rodger *et al.* 2011b	-	Downes *et al.* 2018a	-	-				
	Tenacibaculum finmarkense	-	-	-	-	-	-	-	-	-			
	Yersinia ruckeri	-	-	-	-	-	-	-	-	-	-		
	Non-specified or other bacteria	-	-	Steinum *et al.* 2009	Garseth *et al.* 2018	Steinum *et al.* 2009	-	-	-	-	-	-	

Table 1 (continued)

B

		Parasites							Viral			Jellyfish
		Costia (*Ichthyobodo* spp.)	Amoeba(salt; AGD)	*Desmozoon lepeophtherii*	*Trichodina*	*Parvicapsula pseudobranchicola*	*Saprolegnia*	Non-specified or other parasites	ASPV	SGPV	SAV	
Parasites	Costia (*Ichthyobodo* spp.)			-	-	-	-	-	-	Garseth *et al.* 2018, Gjessing *et al.* 2017	-	-
	Amoeba (salt; AGD)			Downes *et al.* 2018a, Gjessing *et al.* 2019, Steinum *et al.* 2015	Rodger & McArdle 1996, Rodger *et al.* 2011b	-	-	Dyková *et al.* 2010	-	Downes *et al.* 2018a, Gjessing *et al.* 2015, Gjessing *et al.* 2017, Gjessing *et al.* 2019, Hvas *et al.* 2017, Nylund *et al.* 2008	-	Marcos-Lopez *et al.* 2016
	Desmozoon lepeophtherii				Weli *et al.* 2017	-	-	-	-	Downes *et al.* 2018a, Gjessing *et al.* 2019, Nylund *et al.* 2011	Nylund *et al.* 2011, Gunnarsson *et al.* 2017	-
	Trichodina					-	-	-	-	Garseth *et al.* 2018	-	-
	Parvicapsula pseudobranchicola						-	-	-	-	-	-
	Saprolegnia							-	-	Garseth *et al.* 2018, Gjessing *et al.* 2017	-	-
	Non-specified, other parasites, or fungi								-	Garseth *et al.* 2018	-	-
Viral	ASPV									-	-	-
	SGPV										-	-
	SAV											-
Jellyfish												

Table 1 (continued)

C		Gill disease			Bacterial								
		CGD/ multifactorial gill disease	PGD	PGI	Epitheliocysts	- *Ca.* Piscichlamydia salmonis	- *Ca.* Branchiomonas cysticola	- *Ca.* Sygnamidia salmonis	- *Ca.* Clavochlamydia salmonicola	*Tenacibaculum maritimum*	*Tenacibaculum finmarkense*	*Yersinia ruckeri*	Non-specified or other bacteria
Parasites	Costia (*Ichthyobodo* spp.)	-	-	Kvellestad *et al.* 2005, Nylund *et al.* 2011	Gjessing *et al.* 2017	-	Gjessing *et al.* 2017	-	-	Rodger *et al.* 2011b	-	-	-
	Amoeba (salt; AGD)	Gjessing *et al.* 2019	Nylund *et al.* 2008	Nylund *et al.* 2011, Steinum *et al.* 2008	Gjessing *et al.* 2017	Gjessing *et al.* 2019, Steinum *et al.* 2015	Downes *et al.* 2018a, Gjessing *et al.* 2017, Gjessing *et al.* 2019, Steinum *et al.* 2015	Nylund *et al.* 2018	-	Downes *et al.* 2018a, Powell et al. 2005, Rodger *et al.* 2011b	-	Valdenegro-Vega *et al.* 2015	Adams *et al.* 2004
	Desmozoon lepeophtherii	Gjessing *et al.* 2019	Matthews *et al.* 2013	Nylund *et al.* 2011, Steinum *et al.* 2010	Weli *et al.* 2017	Gjessing *et al.* 2019, Nylund *et al.* 2011, Steinum *et al.* 2015	Downes *et al.* 2018a, Gjessing *et al.* 2019, Steinum *et al.* 2015	-	-	Downes *et al.* 2018a	-	-	Weli *et al.* 2017
	Trichodina	-	-	Kvellestad *et al.* 2005, Mitchell *et al.* 2013, Nylund *et al.* 2011	Garseth *et al.* 2018	-	-	-	-	Rodger *et al.* 2011b	-	-	Garseth *et al.* 2018
	Parvicapsula pseudobranchicola	-	-	Nylund *et al.* 2011	-	-	-	-	-	-	-	-	-
	Saprolegnia	-	-		-	-	-	-	-	-	-	-	-
	Non-specified, other parasites, or fungi	-	-	Nylund *et al.* 2011	-	-	-	-	-	Rodger *et al.* 2011b	-	-	-
Viral	ASPV	-	-	Kvellestad *et al.* 2005, Steinum *et al.* 2010	Fridell *et al.* 2004, Kvellestad *et al.* 2003, Kvellestad *et al.* 2005	-	-	-	-	-	-	-	-
	SGPV	Gjessing *et al.* 2017, Gjessing *et al.* 2019	Nylund *et al.* 2008	Nylund *et al.* 2011	Garseth *et al.* 2018, Gjessing *et al.* 2017	Gjessing *et al.* 2019, Nylund *et al.* 2008	Downes *et al.* 2018a, Gjessing *et al.* 2017, Gjessing *et al.* 2019	-	-	Downes *et al.* 2018a		-	Garseth *et al.* 2018, Gjessing *et al.* 2017
	SAV	-	-	Nylund *et al.* 2011	-	-	-	-	-	-	-	-	-
Jellyfish		-	-	-	-	-	-	-	-	Delannoy *et al.* 2011, Ferguson *et al.* 2010, Marcos-Lopez *et al.* 2016, Rodger *et al.* 2011b, Ruane *et al.* 2013	Småge *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 co-infections 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 (Kiemer & 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 delousing 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 amphizoic amoeba *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 tshawytscha*), 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*

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 effected 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 (Hellebø *et al.* 2017) and other European countries.

Presumptive diagnosis of AGD is based on clinical signs and the microscopic observation of typical amoebae 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 amoebae 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 *Scuticociliatia* (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

Pelagia noctiluca (Marcos-Lopez *et al.* 2016). It has been observed simultaneously with epitheliocysts (Gjessing *et al.* 2017) and the associated bacteria *Ca.* Piscichlamydia salmonis (Steinum *et al.* 2015; Gjessing *et al.* 2019), *Ca.* Branchiomonas cysticola (Steinum *et al.* 2015; Gjessing *et al.* 2017, 2019; Downes *et al.* 2018a) and *Ca.* Sygnamidia salmonis (Nylund *et al.* 2018). 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-specified 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, 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). It has since been reported from Norway (Nylund *et al.* 2010), Ireland (Ruane *et al.* 2013) and the Pacific coast of North America (Jones *et al.* 2012). *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).

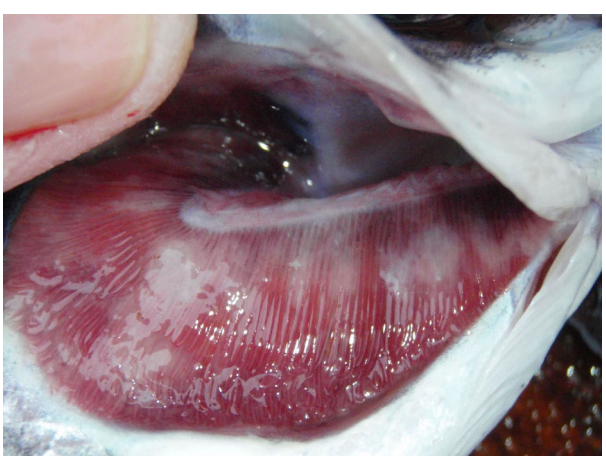

Figure 2 Severe amoebic gill disease (AGD) lesions.

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-PGI 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,

T. maritimum (Downes *et al.* 2018a) and other non-specified bacteria (Weli *et al.* 2017) were found alongside *D. lepeophtherii.* 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 poxvirus (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. lepeophtherii* in salmon gills. As for other microsporidians, 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. lepeophtherii* 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. lepeophtherii* 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. lepeophtherii* 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 PGI in conjunction with other pathogens and that the slow *in vitro* replication rate of ASPV may explain the long duration of the PGI 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 PGI outbreaks (Steinum *et al.* 2010; Nylund *et al.* 2011).

Atlantic salmon paramyxovirus was detected in PGI 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

Epitheliocystis, 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). Epitheliocystis 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.

Epitheliocystis 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 betaproteobacterium *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 *Chlamydiae*, 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 *Chlamydiae* 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 (Ruane *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 *Icthyobodo* 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. lepeoptherii* (Nylund *et al.* 2011; Steinum *et al.* 2015; Weli *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 1999). Cleaner fish of the species *Centrolabrus exoletus*, *Ctenolabrus rupestris*, *Labrus bergylta*, *L. mixtus* and *Symphodus melops* from the west coast of Norway have been found with epitheliocyst-forming *Chlamydia* on the gills, which could mean they act as vectors or reservoir hosts (Steigen *et al.* 2018). However, the *Chlamydiae* observed from the cleaner fish were not detected in salmonids, and it has been suggested that they might not affect salmon (Steigen *et al.* 2018).

Tenacibaculosis/flexibacteriosis

This salt water ulcerative disease has been given many different names, such as 'salt water columnaris disease', 'gliding 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)).

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* (Småge *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).

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 (Småge *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 *Moritella 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 *Muggiaea atlantica* (Fringuelli *et al.* 2012), the sea louse

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 (Båmstedt *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 oxytretracycline 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.

References

Adams MB, Nowak BF (2004) Sequential pathology after initial freshwater bath treatment for amoebic gill disease in cultured Atlantic salmon, *Salmo salar* L. *Journal of Fish Diseases* **27**(3): 163–173.

Adams MB, Ellard K, Nowak BF (2004) Gross pathology and its relationship with histopathology of amoebic gill disease

(AGD) in farmed Atlantic salmon, *Salmo salar* L. *Journal of Fish Diseases* **27**: 151–161.

Adams MB, Crosbie PB, Nowak BF (2012) Preliminary success using hydrogen peroxide to treat Atlantic salmon, *Salmo salar* L., affected with experimentally induced amoebic gill disease (AGD). *Journal of Fish Diseases* **35**: 839–848.

Avendaño-Herrera R, Irgang R, Magariños B, Romalde JL, Toranzo AE (2006a) Use of microcosms to determine the survival of the fish pathogen *Tenacibaculum maritimum* in seawater. *Environmental Microbiology* **8**: 921–928.

Avendaño-Herrera R, Toranzo AE, Magariños B (2006b) Tenacibaculosis infection in marine fish caused by *Tenacibaculum maritimum*: a review. *Diseases of Aquatic Organisms* **71** (3): 255–266.

Avendaño-Herrera R, Irgang R, Sandoval C, Moreno-Lira P, Houel A, Duchaud E *et al.* (2016) Isolation, characterization and virulence potential of *Tenacibaculum dicentrarchi* in salmonid cultures in Chile. *Transboundary and Emerging Diseases* **63**(2): 121–126.

Båmstedt U, Fosså JH, Martinussen MB, Fosshagen A (1998) Mass occurrence of the physonect siphonophore *Apolemia uvaria* (Lesueur) in Norwegian waters. *Sarsia* **83**: 79–85.

Barker DE, Braden LM, Coombs MP, Boyce B (2009) Preliminary studies on the isolation of bacteria from sea lice, *Lepeophtheirus salmonis*, infecting farmed salmon in British Columbia, Canada. *Parasitology Research* **105**: 1173–1177.

Baxter EJ, Rodger HD, McAllen R, Doyle TK (2011a) Gill disorders in marine-farmed salmon: Investigating the role of hydrozoan jellyfish. *Aquaculture Environment Interactions* **1**: 245–257.

Baxter EJ, Sturt MM, Ruane NM, Doyle TK, McAllen R, Harman L *et al.* (2011b) Gill damage to Atlantic Salmon (*Salmo salar*) caused by the common jellyfish (*Aurelia aurita*) under experimental challenge. *PLoS ONE* **6**: 4–9.

Baxter EJ, Sturt MM, Ruane NM, Doyle K, McAllen R, Rodger HD (2012) Biofouling of the hydroid *Ectopleura larynx* on aquaculture nets in Ireland: implications for finfish health. *Fish Veterinary Journal* **13**: 17–29.

Beecham RV, Griffin MJ, LaBarre SB, Wise D, Mauel MJ, Pote LMW *et al.* (2010) The effects of proliferative gill disease on the blood physiology of channel catfish, blue catfish, and channel catfish x blue catfish hybrid fingerlings. *North American Journal of Aquaculture* **72**: 213–218.

Bloecher N, Powell M, Hytterød S, Gjessing M, Wiik-Nielsen J, Mohammad SN *et al.* (2018) Effects of cnidarian biofouling on salmon gill health and development of amoebic gill disease. *PLoS ONE* **13**: 1–18.

Bosworth BG, Wise DJ, Terhune JS, Wolters WR (2003) Family and genetic group effects for resistance to proliferative gill disease in channel catfish, blue catfish and channel catfish × blue catfish backcross hybrids. *Aquaculture Research* **34**: 569–573.

Bruno DW, Dear G, Seaton DD (1989) Mortality associated with phytoplankton blooms among farmed Atlantic salmon, *Salmo salar* L., in Scotland. *Aquaculture* **78**: 217–222.

Bustos PA, Young ND, Rozas MA, Bohle HM, Ildefonso RS, Morrison RN *et al.* (2011) Amoebic gill disease (AGD) in Atlantic salmon (*Salmo salar*) farmed in Chile. *Aquaculture* **310**: 281–288.

Chang FH, Anderson C, Boustead NC (1990) First record of a *Heterosigma* (*Raphidophyceae*) bloom with associated mortality of cage-reared salmon in Big Glory Bay, New Zealand. *New Zealand Journal of Marine and Freshwater Research* **24**: 461–469.

Clark A, Nowak BF (1999) Field investigations of amoebic gill disease in Atlantic salmon, *Salmo salar* L., in Tasmania. *Journal of Fish Diseases* **22**: 433–443.

Clark G, Powell M, Nowak B (2003) Effects of commercial freshwater bathing on reinfection of Atlantic salmon, *Salmo salar*, with Amoebic Gill Disease. *Aquaculture* **219**: 135–142.

Crosbie PBB, Bridle AR, Leef MJ, Nowak BF (2010) Effects of different batches of Neoparamoeba perurans and fish stocking densities on the severity of amoebic gill disease in experimental infection of Atlantic salmon, *Salmo salar* L. *Aquaculture Research* **41**: e505–e516.

Crosbie PBB, Bridle AR, Cadoret K, Nowak BF (2012) *In vitro* cultured *Neoparamoeba perurans* causes amoebic gill disease in Atlantic salmon and fulfils Koch's postulates. *International Journal for Parasitology* **42**: 511–515.

Delannoy CMJ, Houghton JDR, Fleming NEC, Ferguson HW (2011) Mauve stingers (*Pelagia noctiluca*) as carriers of the bacterial fish pathogen *Tenacibaculum maritimum*. *Aquaculture* **311**: 255–257.

Douglas-Helders M, Saksida S, Nowak B (2001) Temperature as a risk factor for outbreaks of amoebic gill disease in farmed Atlantic salmon (*Salmo salar*). *Bulletin of the European Association of Fish Pathologists* **21**: 114–116.

Downes JK, Rigby ML, Taylor RS, Maynard BT, MacCarthy E, O'Connor I *et al.* (2017) Evaluation of non-destructive molecular diagnostics for the detection of *Neoparamoeba perurans*. *Frontiers in Marine Science* **4**: 1–6.

Downes JK, Yatabe T, Marcos-Lopez M, Rodger HD, MacCarthy E, O'Connor I *et al.* (2018a) Investigation of co-infections with pathogens associated with gill disease in Atlantic salmon during an amoebic gill disease outbreak. *Journal of Fish Diseases* **41**: 1217–1227.

Downes JK, Collins EM, Morrissey T, Hickey C, O'Connor I, Rodger HD *et al.* (2018b) Confirmation of *Neoparamoeba perurans* on the gills of Atlantic salmon during the earliest outbreaks of amoebic gill disease in Ireland. *Bulletin of the European Association of Fish Pathologists* **38**: 42–48.

Draghi A, Popov VL, Kahl MM, Stanton JB, Brown CC, Tsongalis GJ *et al.* (2004) Characterization of "*Candidatus* Piscichlamydia salmonis" (Order Chlamydiales), a chlamydia-like bacterium associated with epitheliocystis in farmed Atlantic salmon (*Salmo salar*). *Journal of Clinical Microbiology* **42**: 5286–5297.

Dyková I, Novoa B (2001) Comments on diagnosis of amoebic gill disease (AGD) in turbot, *Scophthalmus maximus*. *Bulletin of the European Association of Fish Pathologists* **21**: 40–44.

Dyková I, Tyml T, Kostka M, Pecková H (2010) Strains of *Uronema marinum* (scuticociliatia) co-isolated with amoebae of the genus Neoparamoeba. *Diseases of Aquatic Organisms* **89**: 71–77.

Ellis T, Turnbull JF, Knowles TG, Lines JA, Auchterlonie NA (2016) Trends during development of Scottish salmon farming: an example of sustainable intensification? *Aquaculture* **458**: 82–99.

English CJ, Swords F, Downes JK, Ruane NM, Botwright NA, Taylor RS *et al.* (2019a) Prevalence of six amoeba species colonising the gills of farmed Atlantic salmon with amoebic gill disease (AGD) using qPCR. *Aquaculture Environment Interactions* **11**: 405–415.

English CJ, Tyml T, Botwright NA, Barnes AC, Wynne JW, Lima PC *et al.* (2019b) A diversity of amoebae colonise the gills of farmed Atlantic salmon (*Salmo salar*) with amoebic gill disease (AGD). *European Journal of Protistology* **67**: 27–45.

Feehan CJ, Johnson-Mackinnon J, Scheibling RE, Lauzon-Guay JS, Simpson AGB (2013) Validating the identity of *Paramoeba invadens*, the causative agent of recurrent mass mortality of sea urchins in Nova Scotia, Canada. *Diseases of Aquatic Organisms* **103**: 209–227.

Ferguson HW, Delannoy CMJ, Hay S, Nicolson J, Sutherland D, Crumlish M (2010) Jellyfish as vectors of bacterial disease for farmed salmon (*Salmo salar*). *Journal of Veterinary Diagnostic Investigation* **22**: 376–82.

FHF (2019) Risikofaktorer, indikatorer og strategisk håndtering av gjellelidelser hos atlantisk laks (GILLRISK). [Cited 4 October 2019.] Available from URL: www.fhf.no/prosjekter/prosjektbasen/901515.

Føre M, Frank K, Norton T, Svendsen E, Alfredsen JA, Dempster T *et al.* (2018) Precision fish farming: a new framework to improve production in aquaculture. *Biosystems Engineering* **173**: 176–193.

Freeman MA (2002) *Potential biological control agents for the salmon louse Lepeophtheirus salmonis (Krøyer, 1837).* PhD thesis. Institute of Aquaculture, University of Stirling, Stirling.

Freeman MA, Sommerville C (2011) Original observations of *Desmozoon lepeophtherii*, a microsporidian hyperparasite infecting the salmon louse *Lepeophtheirus salmonis*, and its subsequent detection by other researchers. *Parasites and Vectors* **4**: 2–5.

Fridell F (2003) *Detection of a paramyxovirus in selected tissues from Salmo salar after experimental challenge*. Master thesis. p 68, Department of Fisheries and Marine Biology, University of Bergen, Norway. (in Norwegian).

Fringuelli E, Savage PD, Gordon A, Baxter EJ, Rodger HD, Graham DA (2012) Development of a quantitative real-time PCR for the detection of *Tenacibaculum maritimum* and its application to field samples. *Journal of Fish Diseases* **35**: 579–590.

Frisch K, Småge SB, Brevik ØJ, Duesund H, Nylund A (2017) Genotyping of *Tenacibaculum maritimum* isolates from farmed Atlantic salmon in Western Canada. *Journal of Fish Diseases* **41**: 131–137.

Fryer JL, Lannan CN (1994) Rickettsial and chlamydial infections of freshwater and marine fishes, bivalves, and crustaceans. *Zoological Studies* **33**: 95–107.

Garseth H, Gjessing MC, Moldal T, Gjevre AG (2018) A survey of salmon gill poxvirus (SGPV) in wild salmonids in Norway. *Journal of Fish Diseases* **41**: 139–145.

Gjessing MC, Yutin N, Tengs T, Senkevich T, Koonin E, Rønning HP *et al.* (2015) Salmon gill poxvirus, the deepest representative of the *Chordopoxvirinae*. *Journal of Virology* **89**: 9348–9367.

Gjessing MC, Weli SC, Dale OB (2016) Poxviruses of fish. In: Kibenge FSB, Godoy MG (eds) *Aquaculture Virology*, pp. 119–125. Academic Press, Oxford.

Gjessing MC, Thoen E, Tengs T, Skotheim SA, Dale OB (2017) Salmon gill poxvirus, a recently characterized infectious agent of multifactorial gill disease in freshwater- and seawater-reared Atlantic salmon. *Journal of Fish Diseases* **40**: 1253–1265.

Gjessing MC, Steinum T, Olsen AB, Lie KI, Tavornpanich S, Colquhoun DJ (2019) Histopathological investigation of complex gill disease in sea farmed Atlantic salmon. *PLoS ONE* **14**: 1–18.

Gunnarsson GS, Blindheim S, Karlsbakk E, Plarre H, Imsland AK, Handeland S *et al.* (2017) *Desmozoon lepeophtherii* (microsporidian) infections and pancreas disease (PD) outbreaks in farmed Atlantic salmon (*Salmo salar* L.). *Aquaculture* **468**: 141–148.

Handlinger J, Soltani M, Percival S (1997) The pathology of *Flexibacter maritimus* in aquaculture species in Tasmania, Australia. *Journal of Fish Diseases* **20**: 159–168.

Haugland GT, Olsen AB, Rønneseth A, Andersen L (2017) Lumpfish (*Cyclopterus lumpus* L.) develop amoebic gill disease (AGD) after experimental challenge with *Paramoeba perurans* and can transfer amoebae to Atlantic salmon (*Salmo salar* L.). *Aquaculture* **478**: 48–55.

Hellebø A, Stene A, Aspehaug V (2017) PCR survey for *Paramoeba perurans* in fauna, environmental samples and fish associated with marine farming sites for Atlantic salmon (*Salmo salar* L.). *Journal of Fish Diseases* **40**: 661–670.

Herrero A, Thompson KD, Ashby A, Rodger HD, Dagleish MP (2018) Complex gill disease: an emerging syndrome in farmed Atlantic salmon (*Salmo salar* L.). *Journal of Comparative Pathology* **163**: 23–28.

Hishida Y, Katoh H, Oda T, Ishimatsu A (1998) Comparison of physiological responses to exposure to *Chattonella marina* in yellowtail, red sea bream and Japanese flounder. *Fisheries Science* **64**: 875–881.

Hjeltnes B, Bornø G, Jansen MD, Haukaas A, Walde C (2017) *The Health Situation in Norwegian Aquaculture 2016*. Norwegian Veterinary Institute, Oslo.

Horn M (2008) *Chlamydiae* as symbionts in eukaryotes. *Annual Review of Microbiology* **62**: 113–131.

Hvas M, Karlsbakk E, Mæhle S, Wright DW, Oppedal F (2017) The gill parasite *Paramoeba perurans* compromises aerobic scope, swimming capacity and ion balance in Atlantic salmon. *Conservation Physiology* **5**: 1–12.

ICES (2016) Interim Report of the Working Group on Pathology and Diseases of Marine Organisms (WGPDMO), 17–20 February 2016. Virginia.

Iversen M, Finstad B, McKinley RS, Eliassen RA, Carlsen KT, Evjen T (2005) Stress responses in Atlantic salmon (*Salmo salar* L.) smolts during commercial well boat transports, and effects on survival after transfer to sea. *Aquaculture* **243**: 373–382.

Jansson E, Vennerstrom P (2014) Infectious diseases of cold-water fish in marine and brackish waters. In: Woo PTK, Bruno DW (eds) *Diseases and Disorders of Finfish in Cage Culture*, 2nd edn, pp. 15–59. CABI International, Wallingford.

Jones JB, Rhodes LL (1994) Suffocation of pilchards (*Sardinops sagax*) by a green microalgal bloom in Wellington harbour, New Zealand. *New Zealand Journal of Marine and Freshwater Research* **28**: 379–383.

Jones SRM, Prosperi-Porta G, Kim E (2012) The diversity of microsporidia in parasitic copepods (*Caligidae: Siphonostomatoida*) in the northeast Pacific ocean with description of *Facilispora margolisi* n. g., n. sp. and a new family *Facilisporidae* n. fam. *Journal of Eukaryotic Microbiology* **59**: 206–217.

Kaatvedt S, Johnsen TM, Aksnes DL, Lie U, Svendse H (1991) Occurrence of the toxic flagellate *Prymnesium parvum* and associated fish mortality in a Norwegian fjord system. *Canadian Journal of Fisheries and Aquatic Sciences* **48**: 2316–2323.

Karlsbakk E, Olsen AB, Einen ACB, Mo TA, Fiksdal IU, Aase H *et al.* (2013) Amoebic gill disease due to Paramoeba perurans in ballan wrasse (*Labrus bergylta*). *Aquaculture* **412–413**: 41–44.

Karlsen M, Nylund A, Watanabe K, Helvik JV, Nylund S, Plarre H (2008) Characterization of "*Candidatus* Clavochlamydia salmonicola": an intracellular bacterium infecting salmonid fish. *Environmental Microbiology* **10**: 208–218.

Karlsen C, Ottem KF, Brevik ØJ, Davey M, Sørum H, Winther-Larsen HC (2017) The environmental and host-associated bacterial microbiota of Arctic seawater-farmed Atlantic salmon with ulcerative disorders. *Journal of Fish Diseases* **40**: 1645–1663.

Kent M (1992) *Diseases of Seawater Netpen-Reared Salmonid Fishes in the Pacific Northwest. Canadian Special Publication of Fisheries and Aquatic Sciences 116.* Department of Fisheries and Oceans, Nanaimo, BC.

Kent M, Sawyer T, Hedrick R (1988) *Paramoeba pemaquidensis (Sarcomastigophora: Paramoebidae)* infestation of the gills of coho salmon *Oncorhynchus kisutch* reared in sea water. *Diseases of Aquatic Organisms* **5**: 163–169.

Kent ML, Whytel JNC, Latrace C (1995) Gill lesions and mortality in seawater pen-reared Atlantic salmon *Salmo salar* associated with a dense bloom of *Skeletonema costatum* and *Thalassiosira* species. *Diseases of Aquatic Organisms* **22**: 77–81.

Kiemer MCB, Black KD (1997) The effects of hydrogen peroxide on the gill tissues of Atlantic salmon, *Salmo salar* L. *Aquaculture* **53**: 181–189.

Kintner A, Brierley AS (2019) Cryptic hydrozoan blooms pose risks to gill health in farmed North Atlantic salmon (*Salmo salar*). *Journal of the Marine Biological Association of the United Kingdom* **99**(2): 539–550.

Koppang EO, Kvellestad A, Fischer U (2015) Fish mucosal immunity. In: Beck BH, Peatman E (eds) *Health in Aquaculture*, pp. 93–133. Academic Press, Oxford.

Kralberg A, Baumann M, Durselen C-D (2010) *Coastal Phytoplankton: Photo Guide for Northern European Seas*. Verlag Dr. Friedrich Pfeil, Munchen.

Kroglund F, Rosseland OB, Teien HC, Salbu B, Kristensenm T, Finstad B (2007) Water quality limits for Atlantic salmon (*Salmo salar* L.) exposed to short term reductions in pH and increased aluminium simulating episodes. *Hydrology and Earth System Sciences Discussions, European Geosciences Union* **4**: 3317–3355.

Kvellestad A, Dannevig BH, Falk K (2003) Isolation and partial characterization of a novel paramyxovirus from the gills of diseased seawater-reared Atlantic salmon (*Salmo salar* L.). *Journal of General Virology* **84**: 2179–2189.

Kvellestad A, Falk K, Nygaard SMR, Flesjå K, Holm JA (2005) Atlantic salmon paramyxovirus (ASPV) infection contributes to proliferative gill inflammation (PGI) in seawater-reared *Salmo salar*. *Diseases of Aquatic Organisms* **67**: 47–54.

Lokesh J, Kiron V (2016) Transition from freshwater to seawater reshapes the skin-associated microbiota of Atlantic salmon. *Scientific Reports* **6**: 1–10.

Lorenz I, Earley B, Gilmore J, Hogan I, Kennedy E, More SJ (2011) Calf health from birth to weaning. III. Housing and management of calf pneumonia. *Irish Veterinary Journal* **64**: 1–9.

Lucas CH, Gelcich S, Uye S-I (2014) Living with jellyfish: management and adaptation strategies. In: Pitt KA, Lucas CH (eds) *Jellyfish Blooms*, pp. 129–152. Springer, Dordrecht.

Mallatt J (1985) Fish gill structural changes induced by toxicants and other irritants: a statistical review. *Canadian Journal of Fisheries and Aquatic Sciences* **42**: 630–648.

Marcos-Lopez M, Mitchell SO, Rodger HD (2016) Pathology and mortality associated with the mauve stinger jellyfish *Pelagia noctiluca* in farmed Atlantic salmon *Salmo salar* L. *Journal of Fish Diseases* **39**: 111–115.

Matthews CGG, Richards RH, Shinn AP, Cox DI (2013) Gill pathology in Scottish farmed Atlantic salmon, *Salmo salar* L., associated with the microsporidian *Desmozoon lepeophtherii* Freeman et Sommerville, 2009. *Journal of Fish Diseases* **36**: 861–869.

Maynard BT, Taylor RS, Kube PD, Cook MT, Elliott NG (2016) Salmonid heterosis for resistance to amoebic gill disease (AGD). *Aquaculture* **451**: 106–112.

Mitchell S, Rodger H (2007) Pathology of wild and cultured fish affected by a *Karenia mikimotoi* bloom in Ireland, 2005. *Bulletin of the European Association of Fish Pathologists* **27**: 39–42.

Mitchell SO, Rodger HD (2011) A review of infectious gill disease in marine salmonid fish. *Journal of Fish Diseases* **34**: 411–432.

Mitchell SO, Steinum T, Rodger H, Holland C, Falk K, Colquhoun DJ (2010) Epitheliocystis in Atlantic salmon, *Salmo salar* L., farmed in fresh water in Ireland is associated with

"*Candidatus* Clavochlamydia salmonicola" infection. *Journal of Fish Diseases* **33**: 665–673.

Mitchell SO, Steinum TM, Toenshoff ER, Kvellestad A, Falk K, Horn M (2013) *Candidatus* Branchiomonas cysticola is a common agent of epitheliocysts in seawater-farmed Atlantic salmon *Salmo salar* in Norway and Ireland. *Diseases of Aquatic Organisms* **103**: 35–43.

Morrison DB, Saksida S (2013) Trends in antimicrobial use in Marine Harvest Canada farmed salmon production in British Columbia (2003–2011). *Canadian Veterinary Journal* **54**: 1160–1163.

Morrison RN, Crosbie PBB, Cook MT, Adams MB, Nowak BF (2005) Cultured gill-derived *Neoparamoeba pemaquidensis* fails to elicit amoebic gill disease (AGD) in Atlantic salmon *Salmo salar*. *Diseases of Aquatic Organisms* **66**: 135–144.

Nolsøe M, Weidmann M, Christiansen DH (2015) *Investigation of the prevalence of salmonid gill pox virus in Faroese freshwater salmonidp Production sites*. Master thesis, University of Stirling, Scotland.

Noguera P, Olsen AB, Hoare J, Lie KI, Poppe TT, Rodger H (2019) Complex gill disorder (CGD): a histopathology workshop report. *Bulletin of the European Association of Fish Pathologists* **39**: 172–176.

Nowak BF, Archibald JM (2018) Opportunistic but lethal: the mystery of Paramoebae. *Trends in Parasitology* **34**: 404–419.

Nowak BF, Clark A (1999) Prevalence of epitheliocystis in Atlantic salmon, *Salmo salar* L., farmed in Tasmania, Australia. *Journal of Fish Diseases* **22**: 73–78.

Nowak BF, LaPatra SE (2006) Epitheliocystis in fish. *Journal of Fish Diseases* **29**: 573–588.

Nylund A, Kvenseth AM, Isdal E (1998) A morphological study of the epitheliocystis agent in farmed Atlantic salmon. *Journal of Aquatic Animal Health* **10**: 43–55.

Nylund A, Watanabe K, Karlsen M, Nylund S, Karlsbakk E, Sæther PA (2006) A new gill disease in salmon—Poxvirus. *Norsk Fiskeoppdrett* **31**: 54–56 (in Norwegian).

Nylund A, Watanabe K, Nylund S, Karlsen M, Sæther PA, Arnesen CE *et al.* (2008) Morphogenesis of salmonid gill poxvirus associated with proliferative gill disease in farmed Atlantic salmon (*Salmo salar*) in Norway. *Archives of Virology* **153**: 1299–1309.

Nylund S, Nylund A, Watanabe K, Arnesen CE, Karlsbakk E (2010) *Paranucleospora theridion* n. gen., n. sp. (Microsporidia, Enterocytozoonidae) with a life cycle in the salmon louse (*Lepeophtheirus salmonis*, Copepoda) and Atlantic Salmon (*Salmo salar*). *Journal of Eukaryotic Microbiology* **57**: 95–114.

Nylund S, Andersen L, Sævareid I, Plarre H, Watanabe K, Arnesen CE *et al.* (2011) Diseases of farmed Atlantic salmon *Salmo salar* associated with infections by the microsporidian *Paranucleospora theridion*. *Diseases of Aquatic Organisms* **94**: 41–57.

Nylund S, Steigen A, Karlsbakk E, Plarre H, Andersen L, Karlsen M *et al.* (2015) Characterization of '*Candidatus* Syngnamydia salmonis' (*Chlamydiales, Simkaniaceae*), a bacterium associated with epitheliocystis in Atlantic salmon (*Salmo salar* L.). *Archives of Microbiology* **197**: 17–25.

Nylund A, Pistone D, Trösse C, Blindheim S, Andersen L, Plarre H (2018) Genotyping of *Candidatus* Syngnamydia salmonis (*Chlamydiales; Simkaniaceae*) co-cultured in *Paramoeba perurans* (*Amoebozoa; Paramoebidae*). *Archives of Microbiology* **200**: 859–867.

Oldham T, Rodger HD, Nowak BF (2016) Incidence and distribution of amoebic gill disease (AGD) – an epidemiological review. *Aquaculture* **457**: 35–42.

Olsen AB, Nilsen H, Sandlund N, Mikkelsen H, Sørum H, Colquhoun DJ (2011) *Tenacibaculum* sp. associated with winter ulcers in sea-reared Atlantic salmon *Salmo salar*. *Diseases of Aquatic Organisms* **94**: 189–199.

Parsons H, Nowak B, Fisk D, Powell M (2001) Effectiveness of commercial freshwater bathing as a treatment against amoebic gill disease in Atlantic salmon. *Aquaculture* **195**: 205–210.

Powell MD, Harris JO, Carson J, Hill JV (2005) Effect of gill abrasion and experimental infection with *Tenacibaculum maritimum* on the respiratory physiology of Atlantic salmon *Salmo salar* affected by amoebic gill disease. *Diseases of Aquatic Organisms* **63**: 169–174.

Powell MD, Reynolds P, Kristensen T (2015) Freshwater treatment of amoebic gill disease and sea-lice in seawater salmon production: Considerations of water chemistry and fish welfare in Norway. *Aquaculture* **448**: 18–28.

Purcell JE, Baxter EJ, Fuentes VL (2013) Jellyfish as products and problems of aquaculture. In: Allan C, Burnell C (eds) *Advances in Aquaculture Hatchery Technology*, 1st edn, pp. 404–430. Woodhead Publishing, Cambridge.

Rensel JE, Whyte JNC (2004) Finfish mariculture and harmful algal blooms. In: Hallegraeff GM, Anderson DM, Cembella AD (eds) *Monographs on Oceanographic Methodology: Manual on Harmful Marine Microalgae*, pp. 693–722. Unesco, Landais.

Richardson AJ, Bakun A, Hays GC, Gibbons MJ (2009) The jellyfish joyride: causes, consequences and management responses to a more gelatinous future. *Trends in Ecology and Evolution* **24**(6): 312–322.

Rodger HD (2007) Gill disorders: an emerging problem for farmed Atlantic salmon (*Salmo salar*) in the marine environment? *Fish Veterinary Journal* **9**: 38–48.

Rodger HD (2019) Amoebic gill disease in farmed halibut (*Hippoglossus hippoglossus*) in the United Kingdom. *Veterinary Record Case Reports* **7**: e000797.

Rodger HD, McArdle JF (1996) An outbreak of amoebic gill disease in Ireland. *Veterinary Record* **139**: 348–349.

Rodger HD, Mitchell SO (2013) Marine gill histopathology workshop. *Bulletin of the European Association of Fish Pathologists* **33**: 35–43.

Rodger HD, Henry L, Mitchell SO (2011a) Non-infectious gill disorders of marine salmonid fish. *Reviews in Fish Biology and Fisheries* **21**: 423–440.

Rodger HD, Murphy K, Mitchell SO, Henry L (2011b) Gill disease in marine farmed Atlantic salmon at four farms in Ireland. *Veterinary Record* **168**: 668.

Ruane N, Rodger H, Mitchell S, Doyle T, Baxter E, Fringuelli E (2013) *GILPAT: An Investigation into Gill Pathologies in*

Marine Reared Finfish. Marine Research Sub-Programme (NDP 2007–2013). Marine Institute, Oranmore.

SAIC (2019) Gill health in Scottish farmed salmon. [Cited 4 October 2019.] Available from URL: www.scottishaquaculture.com/projects/health-and-welfare/details/gill-health-in-scottish-farmed-salmon.

Scottish Government (2018a) *Jellyfish as a Nuisance Species to Aquaculture*. The Scottish Government, Edinburgh.

Scottish Government (2018b) *Marine Scotland Science Scotland's 10 year Farmed Fish Health Framework*. The Scottish Government, Edinburgh.

Småge SB, Brevik ØJ, Duesund H, Ottem KF, Watanabe K, Nylund A (2016a) *Tenacibaculum finnmarkense* sp. nov., a fish pathogenic bacterium of the family *Flavobacteriaceae* isolated from Atlantic salmon. *International Journal of General and Molecular Microbiology* **109**: 273–285.

Småge SB, Frisch K, Brevik ØJ, Watanabe K, Nylund A (2016b) First isolation, identification and characterisation of *Tenacibaculum maritimum* in Norway, isolated from diseased farmed sea lice cleaner fish *Cyclopterus lumpus* L. *Aquaculture* **464**: 178–184.

Småge SB, Brevik ØJ, Frisch K, Watanabe K, Duesund H, Nylund A (2017) Concurrent jellyfish blooms and tenacibaculosis outbreaks in Northern Norwegian Atlantic salmon (*Salmo salar*) farms. *PLoS ONE* **12**: e0187476.

Speare DJ, Arsenault G, MacNair N, Powell MD (1997) Branchial lesions associated with intermittent formalin bath treatment of Atlantic salmon, *Salmo salar* L., and rainbow trout, *Oncorhynchus mykiss* (Walbaum). *Journal of Fish Diseases* **20**: 27–33.

Steigen A, Nylund A, Plarre H, Watanabe K, Karlsbakk E, Brevik Ø (2018) Presence of selected pathogens on the gills of five wrasse species in western Norway. *Diseases of Aquatic Organisms* **128**: 21–35.

Steinum T, Kvellestad A, Rønneberg LB, Nilsen H, Asheim A, Fjell K *et al.* (2008) First cases of amoebic gill disease (AGD) in Norwegian seawater farmed Atlantic salmon, *Salmo salar* L., and phylogeny of the causative amoeba using 18S cDNA sequences. *Journal of Fish Diseases* **31**: 205–214.

Steinum T, Sjåstad K, Falk K, Kvellestad A, Colquhoun DJ (2009) An RT PCR-DGGE survey of gill-associated bacteria in Norwegian seawater-reared Atlantic salmon suffering proliferative gill inflammation. *Aquaculture* **293**: 172–179.

Steinum T, Kvellestad A, Colquhoun DJ, Heum M, Mohammad S, Grontvedt RN *et al.* (2010) Microbial and pathological findings in farmed Atlantic salmon *Salmo salar* with proliferative gill inflammation. *Diseases of Aquatic Organisms* **91**: 201–211.

Steinum TM, Brun E, Colquhoun DJ, Gjessing MC, Lie KL, Olsen AB *et al.* (2015) *Proliferativ gjellebetennelse hos oppdrettslaks i sjøvann – patologi, utvalgte agens og risikofaktorer*. Veterinærinstituttets rapportserie 8-2015. Veterinærinstituttet, Oslo. (In Norwegian, summary and Tables in English).

Suzuki M, Nakagawa Y, Harayama S, Yamamoto S (2001) Phylogenetic analysis and taxonomic study of marine *Cytophaga*-like bacteria: Proposal for *Tenacibaculum* gen. nov. with *Tenacibaculum maritimum* comb. nov. and *Tenacibaculum ovolyticum* comb. nov., and description of *Tenacibaculum mesophilum* sp. nov. and *Tenacibaculum amylolyticum* sp. nov. *International Journal of Systematic and Evolutionary Microbiology* **51**: 1639–1652.

Sveen S, Øverland H, Karlsbakk E, Nylund A (2012) *Paranucleospora theridion* (Microsporidia) infection dynamics in farmed Atlantic salmon *Salmo salar* put to sea in spring and autumn. *Diseases of Aquatic Organisms* **101**: 43–49.

Tan CKF, Nowak BF, Hodson SL (2002) Biofouling as a reservoir of *Neoparamoeba pemaquidensis* (Page, 1970), the causative agent of amoebic gill disease in Atlantic salmon. *Aquaculture* **210**: 49–58.

Taylor RS, Muller WJ, Cook MT, Kube PD, Elliott NG (2009) Gill observations in Atlantic salmon (*Salmo salar*, L.) during repeated amoebic gill disease (AGD) field exposure and survival challenge. *Aquaculture* **290**: 1–8.

Taylor R, Kube PD, Evans B, Elliott N (2014) Genetic variation of handling resilience of Tasmanian Atlantic salmon affected by amoebic gill disease (AGD). In: Herrmesch S, Dominik S (eds) *Breeding Focus 2014 – Improving Resilience*, pp. 101–113. Animal Genetics and Breeding Unit, University of New England, Armidale.

Toenshoff ER, Kvellestad A, Mitchell SO, Steinum T, Falk K, Colquhoun DJ *et al.* (2012) A novel betaproteobacterial agent of gill epitheliocystis in seawater farmed Atlantic salmon (*Salmo salar*). *PLoS ONE* **7**: 1–7.

Toranzo AE, Magariños B, Romalde JL (2005) A review of the main bacterial fish diseases in mariculture systems. *Aquaculture* **246**: 37–61.

Treasurer JW, Hannah F, Cox D (2003) Impact of a phytoplankton bloom on mortalities and feeding response of farmed Atlantic salmon, *Salmo salar*, in west Scotland. *Aquaculture* **218**: 103–113.

Valdenegro-Vega VA, Crosbie P, Bridle A, Leef M, Wilson R, Nowak BF (2014) Differentially expressed proteins in gill and skin mucus of Atlantic salmon (*Salmo salar*) affected by amoebic gill disease. *Fish and Shellfish Immunology* **40**: 69–77.

Valdenegro-Vega VA, Cook M, Crosbie P, Bridle AR, Nowak BF (2015) Vaccination with recombinant protein (r22C03), a putative attachment factor of *Neoparamoeba perurans*, against AGD in Atlantic salmon (*Salmo salar*) and implications of a co-infection with *Yersinia ruckeri*. *Fish and Shellfish Immunology* **44**: 592–602.

Vincent BN, Morrison RN, Nowak BF (2006) Amoebic gill disease (AGD)-affected Atlantic salmon, *Salmo salar* L., are resistant to subsequent AGD challenge. *Journal of Fish Diseases* **29**: 549–559.

Vincent BN, Adams MB, Crosbie PBB, Nowak BF, Morrison RN (2007) Atlantic salmon (*Salmo salar* L.) exposed to cultured gill-derived *Neoparamoeba branchiphila* fail to develop amoebic gill disease (AGD). *Bulletin of the European Association of Fish Pathologists* **27**: 112–115.

Volkova E, Kudryavtsev A (2017) Description of *Neoparamoeba longipodia* n. sp. and a new strain of *Neoparamoeba aestuarina*

(Page, 1970) (*Amoebozoa, Dactylopodida*) from deep-sea habitats. *European Journal of Protistology* **61**: 107–121.

Weli SC, Dale OB, Hansen H, Gjessing MC, Rønneberg LB, Falk K (2017) A case study of *Desmozoon lepeophtherii* infection in farmed Atlantic salmon associated with gill disease, peritonitis, intestinal infection, stunted growth, and increased mortality. *Parasites and Vectors* **10**: 1–13.

Wiik-Nielsen J, Gjessing M, Solheim HT, Litlabø A, Gjevre AG, Kristoffersen AB *et al.* (2017) *Ca.* Branchiomonas cysticola, *Ca.* Piscichlamydia salmonis and salmon gill pox virus transmit horizontally in Atlantic salmon held in fresh water. *Journal of Fish Diseases* **40**: 1387–1394.

Woo PTK, Bruno DW (2014) *Diseases and Disorders of Finfish in Cage Culture*, 2nd edn. CABI International, Wallingford.

Wright DW, Nowak B, Oppedal F, Bridle A, Dempster T (2015) Depth distribution of the amoebic gill disease agent, *Neoparamoeba perurans*, in salmon sea-cages. *Aquaculture Environment Interactions* **7**: 67–74.

Wright DW, Nowak B, Oppedal F, Bridle A, Dempster T (2017) Free-living *Neoparamoeba perurans* depth distribution is mostly uniform in salmon cages, but reshaped by stratification and potentially extreme fish crowding. *Aquaculture Environment Interactions* **9**: 269–279.

Young ND, Dyková I, Snekvik K, Nowak BF, Morrison RN (2008) *Neoparamoeba perurans* is a cosmopolitan aetiological agent of amoebic gill disease. *Diseases of Aquatic Organisms* **78**: 217–223.

Young ND, Dyková I, Crosbie PBB, Wolf M, Morrison RN, Bridle AR *et al.* (2014) Support for the coevolution of *Neoparamoeba* and their endosymbionts, *Perkinsela amoebae*-like organisms. *European Journal of Protistology* **50**: 509–523.