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REVIEW PAPER

The impact of disease on the sustainability of aquaculture

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Abstract

The rapid expansion in aquacultural production in the years since the end of the Second World War has been matched by increases in the incidence and severity of disease. Thus, the number of diseases has increased together with losses. However, there has been a growing awareness of the need for and implementation of effective disease control strategies, i.e. to implement effective biosecurity procedures. Attention has focused on site location, water flow, diet and effective management procedures. The latter includes use of sensible hygiene and disinfection policies, movement restrictions and slaughter in the case of the most serious diseases. Advances have been made with combating disease from the initial emphasis on chemotherapy with inhibitory compounds including antibiotics to more modern prophylaxis procedures involving vaccines, non-specific immunostimulants, pre- and probiotics, bacteriophages and medicinal plant products. Challenges remain, but there is evidence of great ingenuity in aquaculture research to overcome obstacles for a sustainable future.

Introduction

Sustainability is a fairly imprecise term, but generally reflects the ability of human beings to co-exist on the planet in harmony with the environment, and by making decisions to mitigate against adverse effects, such as caused by pollution and climate change. In the case of aquaculture, there has been steady growth of the activity in the years since the end of the Second World War. Indeed, since 1970, annual growth has been estimated at 7.5% so that by 2018, the total production worldwide was 114.5 million tonnes with a value of US $263.6 billion (FAO, 2022). The projection is that, compared to 2016, aquaculture production will increase by 28.1%, 37.2% and 46.3% in developed, developing and underdeveloped countries by 2030, respectively (FAO, 2018). There has been a real *Blue Revolution*. Aquaculture is important for nutrition and national economies, providing high quality protein for the rapidly increasing human population, and generating employment for rural communities where other opportunities are rare or do not exist at all (Massa et al., 2021). However, there are issues including the availability of suitable sites with adequate supplies of clean water, the provision of high-quality feed (for carnivorous fish, this depends on the supply of trash fish for the protein source), problems with pollution, and disease (Asche et al., 2022). Recirculation may be an option particularly for locations where water supplies are limited (Ahmed & Turchini, 2021). Certainly, there needs to be consideration of the impact of aquaculture on other aquatic activities, such as tourism (Galparsoro et al., 2020). Fortunately, software models are available, which integrate environmental, geographical, physical and social information, i.e. Geographic Information Systems, to assist with siting that reduce impact of the aquaculture facility on the surrounding area (e.g. Puniwai et al., 2014; Falconer et al., 2020).

Disease is a way of life for all multicellular species on the planet – from plants to fish to terrestrial mammals. In terms of aquaculture, there is inevitably a large number of individuals, usually of the same species, i.e. monocultures, within confined spaces in an aqueous medium that enables the rapid proliferation and spread of pathogens. Thus, the aquaculture environment is unfortunately ideal for the transmission and spread of disease (Austin & Austin, 2016). According to the World Bank, the aquaculture industry loses ~US $6 billion, i.e. ~2% of the total production annually, of which disease is a significant factor.

Common Features of Aquaculture

In addition to containing a large number of individuals within confined spaces, farmed species are often in close proximity with native populations of the same or different species, and thus there are opportunities for the microfloras to move from one host to another through water. In short, there is the potential for the movement of pathogens between wild and farmed species, and the environment (Peeler, 2010). This situation may be exacerbated when species, which are exotic to an area, are introduced and farmed, and acquire pathogens from native animals (Gortázar et al., 2007). The introduced species may be completely or partially sensitive to the diseases of wild populations, which could lead to high levels of clinical disease and mortalities than recorded in native animals. Moreover, if two or more aquaculture facilities are located close to each other on the same water course, the effluent from one is effectively the inflow to the second site. Thus, there is the potential for the spread of disease from one site to the next. In this scenario, there is the likelihood of the rapid spread of disease between sites. This situation will be exacerbated by the vagaries of hygiene and the aquatic environment, such as poor water flow and hypoxia, the presence of pollutants (including uneaten food and faeces, and the build-up of nitrogenous compounds) and indigenous organisms, some of which may be pathogenic, and the prolonged presence of corpses around otherwise healthy stock. The outcome may well be detrimental to the health of the farmed species, and necessitate measures to manage disease, i.e. biosecurity procedures, which are essential to prevent the development and spread of disease in aquaculture (Delphino et al., 2022). In short, this is Confucianism in practice (Badanta et al., 2022).

What Is A Disease?

There are many definitions of disease. An example taken from the British Medical Journal states that "A disease is the sum of the abnormal phenomena displayed by a group of living organisms in association with a common characteristic or set of characteristics by which they differ from the norm of their species in such a way as to place them in a biological disadvantage" (Campbell et al., 1979). The causes centre on abiotic and biotic factors, with the former referring to non-biological situations, such as pollutants, and the latter pathogens. There is a long list of pathogens associated with disease of aquatic animals, and include bacteria, fungi/parasites and viruses (Table 1). New pathogens are regularly reported in the literature, such as:

- a distro-like virus identified from *Procambarus clarkia* with "Black May" disease (Huang et al., 2020),
- a pilchard orthomyxovirus that was linked to salmon orthomyxoviral necrosis, which was newly recognised in Atlantic salmon (Godwin et al., 2020),
- a newly described amoeba, *Vannella mustalahtiana,* which was associated with rainbow trout nodular disease (Kudryavtsev et al., 2022).

Table 1. Pathogens and parasites of importance to aquaculture (based on Austin & Austin, 2016; Austin & Crumlish, 2023).

Pathogen	Disease	Affected Host	Occurrence
Bacteria			
Aeromonas spp. (motile)	Motile aeromonas septicaemia, fin/tail rot	Many freshwater fish species	Worldwide
A. salmonicida	Furunculosis, carp erythrodermatitis	Salmonids, carp	Europe, North and South America, Japan
Allivibrio salmonicida	Coldwater vibriosis	Atlantic salmon	Norway, North America
Candidatus spp.	Epitheliocycstis	Many fish species	Many countries
Edwardsiella spp.	Enteric septicaemia of catfish	Many fish species	Japan, USA, Vietnam
Flavobacterium columnare	Columnaris	Many freshwater fish species	Extensive
F. psychrophilum	Rainbow trout fry syndrome, coldwater disease	Rainbow trout	Europe, USA
Francisella noatunensis	Francisellosis	Atlantic salmon, tilapia	North and South America, Europe
Lactococcus garvieae	Lactococcosis	Many fish species	Extensive
Moritella viscosa	Winter ulcer disease	Atlantic salmon	Iceland, Norway
Mycobacterium spp.	Mycobacteriosis	Many fish species	Worldwide
Photobacterium damselae subsp. *damselae*	Photobacteriosis	Many marine fish species	Mediterranean countries, Asia
P. damselae subsp. *piscicida*	Pasteurellosis, pseudotuberculosis	Many marine fish species	Mediterranean countries
Piscirickettsia salmonis	Coho salmon syndrome	*Salmo* spp.	Chile, North America, Europe
Renibacterium salmoninarum	Bacterial kidney disease	Trout	Europe, North and South America, Japan
Streptococcus spp.	Streptococcosis	Many fish species	Extensive
Tenacibaculum maritimum	Gill disease	Many marine fish species	Mediterranean countries
Vibrio anguillarum	Vibriosis	Most marine fish species	Worldwide
V. harveyi	Luminous vibriosis	Shrimp	Asia, South America
V. parahaemolyticus	Acute hepatopancreatic necrosis disease, shrimp vibriosis	Shrimp	Asia, North America
V. vulnificus	Septicaemia	Eels, bivalves	Europe, Japan, North America
Yersinia ruckeri	Enteric redmouth	Rainbow trout	
Viruses			
Infectious hypodermal and haematopoietic necrosis virus	Infectious hypodermal and haematopoietic necrosis	Shrimp	Asia, Central and South America, Pacific Islands, Middle East
Infectious haematopoietic necrosis virus	Infectious haematopoietic necrosis	Trout	Europe, North America
Infectious salmon anaemia virus	Infectious salmon anaemia	Atlantic salmon	Chile, Europe, North America

Koi herpes virus	Koi herpes virus disease	Carp	Asia, Europe
Spring viraemia of carp virus	Spring viraemia of carp	Carp	Asia, Europe, North and South America
Taura syndrome virus	Taura syndrome	Shrimp	Asia, North and South America
Viral haemorrhagic septicaemia virus	Viral haemorrhagic septicaemia	Many fish species	Asia, Europe, North America
White spot syndrome virus	White spot syndrome	Shrimp	America, Asia, Middle East
Parasites			
Aphanomyces invadans	Epizootic ulcerative syndrome	Many freshwater fish species	Africa, Asia, Australia and North America
Lepeophtheirus salmonis	Sea lice	Atlantic salmon	Europe
Neoparamoeba perurans	Amoebic gill disease	Atlantic salmon	Australia, Scotland
Saprolegnia spp.	Saprolegniasis	Many freshwater fish species	Worldwide

It should be emphasized that disease need not be caused by a single species of pathogen, but may involve one of more bacterial taxon with parasites and/or viruses. The organisms may act together or sequentially; one may be the primary pathogen, and another a secondary invader of already diseased tissue (Austin & Austin, 2016). Also, well established pathogens may be linked to new disease conditions, an example of which is *V. parahaemolyticus*, the causal agent of vibriosis in penaeids. This pathogen has been recognised to be involved in the newly described white faeces syndrome and acute hepatopancreatic necrosis in shrimp (AHPND; notably *Penaeus monodon* and *Litopenaeus vannamei*) farmed in South East Asia (e.g. Ahmed et al., 2022). In this case, pathogenic cultures of *V. parahaemolyticus* had acquired plasmids encoding lethal toxins, PirA/PirB, that led to rapid mortalities among infected shrimp (Ahmed et al., 2022).

Disease Stressors

The development of disease often reflects the presence of stressors of which there are numerous possibilities capable of adversely affecting the host leading to the development of disease. Possibilities include handling leading to abrasions, overcrowding in which the stocking density is too high leading to accumulation of faecal material and aggression whereby finfish may be observed to attack each other leading to the development of wounds. These may produce entry points for pathogens. Poor water flow, which may occur when nets/cages become fouled, allows the build-up of waste material and microbial communities in the immediate vicinity of farmed stock. Water may transmit chemical pollutants (including terrestrial agricultural runoff) and/or sewage contaminants to the aquaculture facility (Sun et al., 2022). In addition, there may be adverse effects caused by poor aeration/oxygen levels and suboptimum temperatures, such as may occur as a result of global warming (Hassan et al., 2021; Teffer et al., 2022). In one example, microplastic particles, which result from the degradation of plastic waste, were considered to cause damage to the hepatopancreas and immunosuppression, and thus adversely affect the health of crustaceans, especially shrimp (Niemcharoen et al., 2022; Sun et al., 2022).

Consideration needs to be given to problems associated with inadequate nutrition, including feed contaminated with micro-organisms [notably fungi] and their toxins, such as aflatoxins, fumonisins, ochratoxins, trichothecenes and zearalenone, the presence of which may reflect inappropriate storage practices (Oliveira & Vasconcelos, 2020).

Issues with Disease Diagnosis

It is appropriate to recall the ages old adage: “Seek, and thou shall find” [from the King James translation of Matthew 7:7]. This sums up the often-stilted approach whereby diagnosticians emphasize isolation and identification of the causal agent, whereas such detailed information does not necessarily help with devising effective control measures. In particular, a full diagnosis leading to the precise identity of a pathogen may lead to a delay before appropriate control measures are adopted. It is personal experience that the visual signs that may be indicative of the disease, such as fin or tail rot, may be largely overlooked in the quest for recovery of the pathogen(s). Notwithstanding, diagnosis has progressed from a purely descriptive phase, to histology, to culturing of the bacterial, viral and fungal pathogens, phenotyping of the isolates (Austin & Austin, 2016), to serology (e.g. Kumas & Tanrikul, 2022), molecular techniques, including use of the polymerase chain reaction (PCR) and novel methods, such as MALDI-TOF-MS, flow cytometry, and nanotechnology (Fig 1; e.g. Fernandez-Alvarez et al., 2019; Li et al., 2020; Nasr-Eldahan et al., 2021; Johny et al., 2022; Ma et al., 2022). Commonly, a combination of histology, culturing, serology and/or molecular methods may be used by diagnosticians to achieve identification of the pathogen (e.g. Mitchell & Goodwin, 1999). Overall, there has been a progression in terms of sensitivity, specificity and speed from a dependence on culturing to diagnosis directly from diseased tissue.

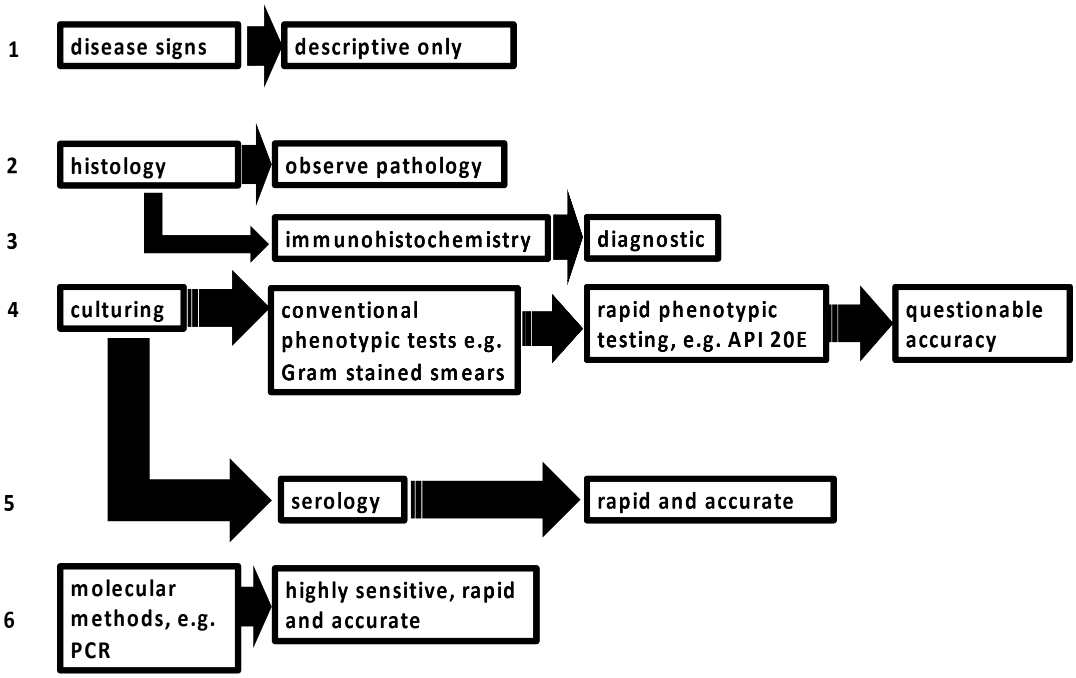

Figure 1. Six stages of diagnosis from description of disease signs, histology, immunohistochemistry, culturing, serology to molecular biology.

Histology has made a valuable contribution to the pathology of aquatic organisms insofar as the microscopic examination of thin sections stained with haemotoxylin and eosin, or the Grams or Ziehl-Neelsen method (the latter for acid-fast bacteria notably *Mycobacterium*) has enabled the visualization of diseased tissues and revealed the presence of pathogens (Wada et al., 1991). However, histology is fairly slow, and generally permits the observation of only large number of pathogens; small number of microbial cells are likely to be missed (Kent et al., 2013).

The problem with culturing is that a diversity of media and incubation regimes are needed; some pathogens are very fastidious requiring complex media and prolonged incubation conditions without which recovery (to produce visible growth) is unlikely. Examples of such fastidious organisms include *Mycobacterium*, *Nocardia* and *Renibacterium salmoninarum*, the latter of which may need up to 16 weeks on serum and cysteine-containing medium to enable clearly visible colonies to develop (Austin and Austin, 2016). Then, identification of the pure cultures relied on morphological and biochemical tests, which were slow and often of dubious accuracy, and use of diagnostic schemes most of which had been developed for human rather than fish pathogens (Austin and Austin, 2016). Rapid biochemical tests, e.g. API 20E, API 20NE and Biolog-GN, became available commercially, and have been invaluable in saving the time of media preparation. However, there is a bias in the data bases used for identification to medically important bacteria, which grow at 37 ºC within 48 h rather than the lower temperatures and longer times required for most fish pathogens. This may lead to misidentification of the fish pathogens (Austin & Austin, 2016).

Serology, such as agglutination reactions, immunofluorescence, and the enzyme linked immunosorbant assays (ELISA) improved the speed, accuracy and sensitivity of diagnoses especially with the development and availability of highly specific monoclonal antibodies (Adams et al., 1995; Austin and Austin, 2016; Li et al., 2021). Moreover, some methods, such as the ELISA, could be used directly on tissue samples without the need for prior culturing (Li et al., 2021). As an example of sensitivity and specificity, Li et al. (2021) reported that an ELISA developed for Koi herpes virus (KHV) detected 1.56 ng/ml of KHV but did not cross reaction with carp oedema virus, frog virus 3, grass carp reovirus or spring viraemia of carp virus.

Molecular methods, such as DNA microarrays, PCR (including nested-, quantitative- real time- multiplex- and droplet digital PCR), loop-mediated isothermal amplification (LAMP) and nucleotide sequencing, permitted the simultaneous identification and differentiation of extremely small numbers/quantities of multiple pathogens or their subcellular components also without the need for culturing (Ma et al., 2022; Abdelsalam et al., 2023). For example, a multiflex-PCR permitted the simultaneous recognition and differentiation of three pathogens, i.e. *Streptococcus agalactiae*, *S. iniae* and *Staphylococcus aureus* (Diyie et al., 2022). Recently, a droplet digital PCR (ddPCR) detected 2 ± 0.37 copies/μl DNA sample of largemouth bass ranavirus but did not react with Chinese giant salamander iridovirus or cyprinid herpesvirus II. Moreover, during the diagnosis of 50 largemouth bass, 43 positives were identified by ddPCR, but only 34 positives by quantitative PCR (Jiang et al., 2022). Certainly, molecular approaches are highly sensitive and specific, and are capable of detecting extremely low numbers of pathogens or their subcellular components. However, the relevance of positive results in the absence of clinical disease needs to be questioned. Does positivity reflect only the presence of intact, viable potentially pathogenic cells or could incomplete, senescent, dormant or non-viable entities be recorded? This has relevance in terms of determining the significance of the diagnoses to the management of the disease. Also, there is concern about false positives. For example, endogenous viral elements of *Penaeus stylirostris* densovirus in the host genome occurs randomly, and could result in false positives because current systems target only small nucleotide sequences of the virus (Arunrut et al., 2019).

There has been a tendency for diagnosticians to focus on finding and reporting single species of pathogenic organisms associated with disease. It is speculative how often infections caused by two or more organisms are missed. These co-infections could lead to enhanced disease severity and increased mortalities (Wise et al., 2021). For example:

- the causal agent of ichthyophthiriasis (= white spot disease), *Ichthyophthirius multifilii*, has been recovered with *Aeromonas hydrophila* in co-infections in septicaemic striped catfish (*Pangasianodon hypophthalmus*) (Kumar et al., 2022c),
- infectious pancreatic necrosis virus and *Yersinia ruckeri* were found together as a co-infection in rainbow trout (*Oncorhynchus mykiss*) (Pajdak-Czaus et al., 2021).

This shortcoming in diagnostics by which co-infections are not properly recognized could have serious implications for the adoption of appropriate disease control methods.

Impact of Disease

Apart from mortalities and the cost of disease mitigation measures (= treatments), there is the added impact on the economy in terms of employment, debt accumulation, the supply chain (e.g. reduced need for feed, wasted feed], process and retail). As an example of impact, there was a large-scale disease problem with Atlantic salmon (*Salmo salar*) production in Scotland with the harvest reduced by >10% from 40.5 x 10^3 tonnes in 1991 to 36.1 x 10^3 tonnes a year later with the cause of mortalities identified as furunculosis and sea lice (Munro & Gauld, 1996). Disposal of 4.4 x 10^3 tonnes of fish which died over a comparatively short period of time would have been a major task. Moreover during the late 1990s, infectious salmon anaemia (ISA) reduced the harvest of Atlantic salmon in Scotland. However, the Scottish experience did not match the monumental losses in the Chilean aquaculture industry (Lagno et al., 2019). Thus, there was a significant outbreak of ISA when total salmonid production and especially valuable exports declined from 2008 to 2010 by 33.3% and 29.6%, respectively (Asche et al., 2009). Furthermore in 2021, Chile reported annual losses of >11% worth US$700 million largely attributed to salmon rickettsial syndrome with resulting increased costs for chemotherapy (Flores-Kossack et al., 2020). The impact in Chile was highlighted by the employment issues when approximately half of the workers (notably those in rural area without other means of employment), i.e. ~25,000, were laid off.

Asia has experienced heavy losses in farmed shrimp (especially *Penaeus monodon* and *Litopenaeus vannamei*). AHPND was recognized initially in 2010 in China and Vietnam, spreading extensively throughout Southeast Asia, and thence to North and South America. AHPND was largely responsible for estimated combined losses between 2010 and 2016 in China, Malaysia, Mexico, Thailand and Vietnam of >US$44 billion. This amount included the impact on exports and reduced feed sales. Also, there was the adverse sociological effect on processing plants, income (debt) to local communities including the result of unemployment, investment opportunities, and the cost of disease control procedures (Tang & Bondad-Reantaso, 2019).

An additional problem concerns the reduced economic value of visible diseased stock. This would be compounded by poor feed conversion leading to adverse growth rates and thus increased production costs. The impact on the public perception of aquaculture is an aspect which is difficult to quantify. If a disease has relevance to human health then restrictions on sales could be another concern.

The influence of climate change/global warming and its impact on disease/pathogens is a largely unknown factor. The overall effects of climate change on aquaculture are likely to centre on extreme weather conditions, precipitation (= very heavy rain/snow/hail), flooding, changes to dissolved oxygen levels, salinity and temperature (Reid et al., 2019). Arguably, higher temperatures would affect the physiology of farmed animals and pathogens (Cascarano et al., 2021). The resulting stress may lead to greater susceptibility of animals to disease leading to higher levels of clinical disease and mortalities. Unlike their wild counterparts, farmed animals would be unable to move to more acceptable water temperatures. Then, there is the impact of higher temperatures on pathogen virulence. This aspect may well be addressed by the advances in whole genome sequencing, which could be instrumental in understanding the reasons for the change in pathogen virulence, the emergence of new diseases, and the impact on aquaculture (Bayliss et al., 2017).

Source of Pathogens

Pathogens will occur as part of the microflora of animals and plants, water and sediment. For example, *V. harveyi* and *V. parahaemolyticus* have been recovered from marine invertebrates including hard-shelled mussel (*Mytilus coruscus*), Mediterranean mussels (*Mytilus galloprovincialis*) and grooved carpet shells (*Ruditapes decussatus*) (e.g. Lamon et al., 2019; Hossain et al., 2020). The marine copepod parasite, *Lernanthropus kroyeri*, harboured *V. anguillarum* as determined by the loop mediated isothermal amplification method (Yildiz & Otgucuoglu, 2021). Therefore, many pathogens are in direct contact with the host even in the absence of disease. Also, *Mycobacterium* has been recovered from aquatic invertebrates (Davidovich et al., 2020). *Aeromonas salmonicida*, which causes furunculosis in salmonids and ulceration in cyprinids and marine flatfish, may exist in a carrier state within apparently healthy fish (Austin & Austin, 2016). Progression to clinical disease follows stress, such as immunosuppression (Austin & Austin, 2016). Once an infection cycle is initiated, disease spread will occur within the immediate area and thence to other sites on the same water course.

Pathogens may be acquired from the aquatic environment, either from the water or from other aquatic inhabitants or from sewage. For example, *Aeromonas salmonicida* has been found in sewage communities with micro-plastics possibly acting as carriers for the pathogen (Lai et al., 2022). Vibrios are part of the normal microflora of the marine environment, and provide a ready inocula to initiate disease cycles in aquaculture (e.g. Sampaio et al., 2022).

Disease Control / Mitigation

The principle that “Prevention is better than cure” [attributed to the Dutch philosopher Desiderius Erasmus in around 1500] is fundamental to modern health care. For aquaculture, it means that prophylaxis is preferable to reliance on therapy. However, in some cases damaged / diseased animals heal spontaneously with or without evidence of physical damage, which could impact on saleability. In the majority of situations, positive action is needed to mitigate against the effects of disease, starting with effective legislation, good lines of communication between producers, government and those involved with disease surveillance, consideration of socio-economic and ecological conditions, certified disease-free stock, “good” husbandry and site management practices, including effective hygiene, e.g. cleanliness of the site, water treatment (if feasible) and the adoption of meaningful sanitary standards (Garza et al., 2019; Ina-Salwany et al., 2019; Hinchliffe et al., 2021). Consideration could be given to genetic improvement of stock especially where evidence points to resistance against disease, such as adopted by the shrimp industry in Asia in the aftermath of AHPND (Tang & Bondad-Reantaso., 2019). The concept of increasing resistance by selective breeding was discussed initially by Embody & Hayford (1925) in connection with controlling furunculosis in brook trout (*Salvelinus fontinalis*). More recently, resistance to columnaris (causal agent = *Flavobacterium columnare*) was considered to be an ideal candidate for genetic improvement of stock by selective breeding of rainbow trout from among survivors of natural disease outbreaks (Fraslin et al., 2022). Similarly, increasing resistance of Atlantic salmon to furunculosis, infectious pancreatic necrosis and infectious salmon anaemia, and rainbow trout to eye fluke (*Diplostomum pseudospathaceum*) has been researched (Drangsholt et al., 2011; Karami et al., 2022). A genetic approach to disease control was appropriate for managing scuticociliatosis in large yellow croaker (*Larimichthys crocea*) because other control methods were not available. Again, natural populations of fish were examined from which disease resistance linked to the nuclear factor (NF)-kappa B signaling pathway was identified (Zhang et al., 2022). This approach is especially relevant for areas where particular diseases are endemic and resistance stock would greatly reduce the likelihood of mortalities (Austin and Austin, 2016). In short, there is definitely a role for genetics and genomics in controlling aquacultural diseases (Sciuto et al., 2022).

Disease control options have developed from therapy with use of antibiotics and other antimicrobial compounds, which garnered interest and widespread use in the years after World War II, to prophylactic approaches. Gutsell (1946) may be credited with the pioneering work on the use of antimicrobial compounds in aquaculture by recognising the effectiveness of sulphonamides for the control of furunculosis in trout. Other inhibitory agents followed, quickly, including oxytetracyline (Snieszko & Griffin, 1951) and chloramphenicol (Wold, 1950), with the former becoming the most widely used antibiotic in aquaculture. For example, in Norway, use of oxytetracycline peaked at just under 50 tonnes in 1987, but has declined ever since (Veterinaerinstituttet, 2016). However, there is widespread concern about the use of antibiotics in all nonmedical situations with concerns focused on problems of the development and spread of antibiotic resistance, especially by R-plasmids (Aoki et al., 1971), and tissue residues (e.g. Mohan et al., 2019; Dawood et al., 2021; Kumar et al., 2022b). Immunoprophylaxis was considered to be an answer to the concerns of therapy. Duff (1942) made a promising start by inactivating a culture of *A. salmonicida* with chloroform, and protected cutthroat trout (*Salmo clarkii*) against furunculosis. However, to date, only a comparatively few vaccines have reached the marketplace (e.g. Mondal & Thomas, 2022). Instead, attention has focused on alternative approaches including non-specific immunostimulants, such as astaxanthin, chitosan, ß-1,3 glucan, lipopolysaccharide and vitamin C (e.g. Mohan et al., 2019; Eldessouki et al., 2022; Ghafarifarsani et al., 2022; Kumar et al., 2022a), bacteriophages (Luo et al., 2018; Xu et al., 2021), probiotics (Ishthiaq et al., 2021; Austin and Sharifuzzaman, 2022; Chattaraj et al., 2022), prebiotics (Yilmaz et al., 2022), synbiotics (Yilmaz et al., 2022) and medicinal plant products and their secondary metabolites, namely the essential oils, e.g. garlic (*Allium sativum*) and turmeric oil (Nikl et al., 1993; Nya & Austin, 2009; Dawood et al,. 2021; Kumar et al., 2022b; Liao et al., 2022). Garlic, in doses of 0.5 and 1.0 g/100 g of feed led to improved growth, immunomodulation and greatly reduced mortalities (Relative Percent Survival = 95%) of rainbow trout after challenging with *A. hydrophila* (Nya & Austin, 2009). It is notable that many publications have focused on the benefit of ß-1,3 glucans in preventing disease (e.g. Yano et al., 1989; Matsuyama et al., 1992; Chen & Ainsworth, 1992). A form of biological control has been adopted successfully in the Faroe Islands, Ireland, Norway and Scotland for the control of sea lice, *Lepeophtheirus salmonis*, in Atlantic salmon. Thus, cleaner fish (notably corkwing wrasse, *Symphodus melops*) have seen added to the Atlantic salmon facilities to consume the parasites (Gentry et al., 2020; Gonzalez & de Boer, 2021). Probiotics and medicinal plant products have found extensive interest in Asia as feed supplements. Research has pointed to improved appetite and growth performance, immunomodulation, and reduced disease and mortalities among fish after administration (Austin and Sharifuzzaman, 2022; Liao et al., 2022).

For some diseases, e.g. *Renibacterium salmoninarum* which is the causal agent of bacterial kidney disease (BKD) in salmonids, the presence is regarded as serious enough to warrant movement restrictions to prevent spread, i.e. stock must remain on the infected sites, and not transferred to other facilities (e.g. Hall et al., 2014). However, some countries, of which Iceland is a prime example, have adopted a slaughter policy for BKD with killing of infected Atlantic salmon broodstock leading to an overall reduction in the incidence of disease (Gudmundsdóttir et al., 2000). Initially, the incidence of BKD was ~35% on two ranch sites, but a few years after adopting the slaughter programme, the incidence was reduced to <2% (Gudmundsdóttir et al., 2000). Slaughter is the fate awaiting fish infected with infectious haematopoietic necrosis and viral haemorrhagic septicaemia, which are notifiable diseases and listed by the World Organisation for Animal Health. Thus, after euthanasia, the animals would be incinerated or buried in lime, and the site(s) disinfected and kept fallow until proven to be disease-free by surveillance (e.g. Hoferer et al., 2019).

Risk to Human Health

There is a risk that some aquaculture pathogens could be transferred to humans with the resultant adverse publicity for the industry. Fortunately, the evidence of zoonoses is limited, and includes *Aeromonas hydrophila*, *Edwardsiella tarda*, *Erysipelothrix rhusiopathiae*, *Mycobacterium marinum*, *Photobacterium damselae*, *Streptococcus iniae*, *Vibrio parahaemolyticus* and *V. vulnificus* (Lehane & Rawlin, 2000; Haenen et al., 2013). *V. parahaemolyticus* and *V. vulnificus* have been identified in cooked and raw shellfish (Padovan et al., 2020; Ding et al., 2022). Transfer to humans particularly in the case of *V. parahaemolyticus* and *V. vulnificus* may be via wounds or orally on food leading to gastro-intestinal disease often with watery diarrhoea (Austin, 2010). *V. vulnificus* has been associated with septicaemia resulting from contamination of wounds with seawater, or the ingestion of raw shellfish, particularly oysters (Carmona-Salido et al., 2021).

Conclusions

Aquaculture has increased rapidly in many countries during the years after the Second World War, and has become an important food source for many people especially in developing countries. Also, the economic value of luxury products including caviar and smoked salmon should not be overlooked. However, disease may have a profound effect on the success and sustainability of aquacultural practices. Yet, innovation has provided some answers by way of increasingly rapid, sensitive and specific disease diagnostic systems, and control measures to replace the reliance on therapy by antibiotics and other inhibitory chemicals. Undoubtedly, global environmental change will impact adversely on agriculture, including aquaculture, and this is another challenge that needs to be resolved. For the present, the aquaculture industry may mitigate against some of the adverse effects of disease by:

- giving serious consideration to site selection, avoiding obviously polluted areas, the proximity to other aquaculture facilities, and/or areas of poor water supply.
- considering the needs of other users of the aquatic environment to avoid conflict and adverse publicity.
- making a sensible choice of the species/strain to be farmed, if possible using stock recognised to be resistant to diseases known to be in the general area of the facility.
- ensuring effective site management including the adoption of realistic stocking levels with good water supplies. Often, by producing less the output is increased as there will be less mortalities.
- arranging the training of staff to familiarise them with all the aquaculture operations, including the need for surveillance such that unhealthy situations may be recognised quickly, and remedial action taken.
- using supplementary air/oxygen as necessary, as anoxia is harmful to farmed stock.
- using nutritious feed stored in dry conditions that is not contaminated with microbial populations, especially fungi, and/or their toxins.
- adopting a sensible disinfection policy especially for nets, vehicles used to transport farmed stock, protective footwear and disinfectant foot baths, and size grading machinery.
- encompassing sensible disease control strategies, emphasising prophylaxis procedures, including vaccines, nonspecific immunostimulants, dietary supplements, bacteriophages, prebiotics, probiotics and medicinal plant products.
- if feasible removing biofouling communities, i.e. algae and slime, from the surfaces of fish tanks, thus improving water flow and discouraging the build-up of biofouling communities, which may harbour potential pathogens.
- quickly removing dead animals from the tanks/cages/ponds to reduce the risk of transfer to healthy stocks. These mortalities need to be disposed of hygienically, such as by incineration, ensiling or burying in quick lime.

Let us hope that human ingenuity will prevail, and conquer the diseases that affect aquaculture. There is confidence that new approaches to disease management will be developed in the future with direct applicability for aquaculture.

Ethical approval

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

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