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Reprint of ‘Diseases in marine invertebrates associated with mariculture and commercial fisheries’

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Abstract

Diseases in marine invertebrates are increasing in both frequency and intensity around the globe. Diseases in individuals which offer some commercial value are often well documented and subsequently well studied in comparison to those wild groups offering little commercial gain. This is particularly the case with those associated with mariculture or the commercial fisheries. Specifically, these include many Holothuroidea, and numerous crustacea and mollusca species. Pathogens/parasites consisting of both prokaryotes and eukaryotes from all groups have been associated with diseases from such organisms, including bacteria, viruses, fungi and protozoa. Viral pathogens in particular, appear to be an increasingly important group and research into this group will likely highlight a larger number of diseases and pathogens being described in the near future. Interestingly, although there are countless examples of the spread of disease usually associated with transportation of specific infected hosts for development of aquaculture practices, this process appears to be continuing with no real sign of effective management and mitigation strategies being implicated. Notably, even in well developed countries such as the UK and the US, even though live animal trade may be well managed, the transport of frozen food appears to be less well so and as evidence suggests, even these to have the potential to transmit pathogens when used as a food source for example.

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1. Introduction

Globally, documented cases of disease outbreaks are increasing in both frequency and intensity in many marine taxa (Burge et al., 2014; Harvell et al., 2004). These recent increases in disease outbreaks (Ward and Lafferty, 2004) may be caused by either the introduction of new pathogens or changes within the environment (Burge et al., 2014; Harvell et al., 2004). Although there are many recorded disease outbreaks in invertebrates, here, we are only focusing on those diseases associated with mariculture and other commercially important marine species. We will also focus on the potential of spread of certain well documented pathogens, through specific pathways such as the transportation of commercially important species from country to country, a result which inadvertently often includes the transfer of specific pathogens capable of infecting native populations of similar species. The three most commonly cultured phyla or subphyla include that of Echinodermata, Crustacea and Mollusca. The World Organisation for Animal Health (Office International des Epizooties (OIE)) currently lists notifiable diseases for only the two latter groups, crustaceans and molluscs, as these are arguably the most important invertebrates on a commercial basis. However, Holothuroidea (i.e. sea cucumbers) are increasing in popularity throughout many areas of the globe and likely warrant being added to OIE’s list of notifiable diseases in the not too distant future.

The ability to assess the effects that disease may have on wild fisheries in terms of production losses is far more challenging than in farmed stocks. Therefore, as a result, there is limited information available on the pathogens and disease of echinoderms, crustaceans and molluscs, and this has led to a deficit in knowledge on causes of mortalities within the wild populations. Furthermore, recent work has also highlighted a difference in pathogens present in juvenile and adult populations of wild organisms (Bateman et al., 2011). Such data is important in understanding the potential for disease to cause ‘silent mortalities’ (i.e. unobserved) in commercially exploited stocks. This data, also highlights that the ability to accurately assess the effect disease may have in terms of production losses in the wild is far more challenging than in a farmed environment (Stentiford et al., 2012). In this respect an emerging disease within wild fisheries may be more difficult to identify and classify when compared to the farmed stocks. In this review, we are not listing all known diseases for the three main commercially important phyla/sub-phyla and/or class (echinoderms, crustaceans and molluscs), but instead focus on those which likely pose a major threat and/or are infecting large populations of both wild and farmed organisms around the world. We have therefore opted to split the review into sections outlined by major pathogenic and/or parasite causal agents.

1.1. Phylum: Echinodermata — Class Holothuroidea

The impacts of disease on numerous echinoderm species have been relatively well documented over previous years and have in some cases provided compelling examples of major shifts in ecosystem state and cascading community effects following disease-induced die-offs in wild systems (Uthicke et al., 2009). In addition to the fact that such outbreaks in the wild can illicit dramatic changes to whole ecosystems, the increase in mariculture for certain species particular those from the class Holothuroidea (sea cucumbers) has further exacerbated the need to understand diseases in this phylum. Recent improvements in artificial breeding techniques of sea cucumbers around the world — with ~90,000 tonnes of sea cucumber (live weight) being harvested throughout China, rearing currently results in over 1–2 billion seeds being produced with ~90,000 tonnes of sea cucumber (live weight) being harvested every year. Such rapid expansion and intensification of sea cucumber farming have subsequently led to the occurrence of various diseases, causing serious economic losses and becoming one of the limiting factors in the sustainable development of this industry. Although, little research has been conducted on these diseases so far, it is clear that in the next few years the causes and consequences of outbreaks in this group of organisms need to be understood for commercial practices to continue unabated.

1.1.1. Viral diseases in Holothuroidea

1.1.1.1. Acute peristome edema disease (APED). Agent: To date, although there have been no definitive results, the most likely candidates for pathogenesis appear to be viruses.

Hosts affected: Cultured sea cucumbers in particular Apostichopus japonicus (Wang et al., 2007).

Clinical signs and pathology: Diseased individuals first show edema in their peristomes, the tentacles cannot retract completely and adhesion capacities are weakened. This latter ailment results in disease individuals dropping to the bottom of the ponds. Grazing rate and activity decrease and upwards of 80% eviscerate (i.e. eject their internal organs). About 2–3 days later, small white lesions usually appear on the surface of the skin and gradually expand, and increased mucus secretion is often noticed over large areas of the body wall. About 5–6 days after occurrence of the first symptoms the sea cucumbers die, with mortality often in excess of 90% (Wang et al., 2005a). Virus-like particles (VLPs) have been found associated within the epithelium of the intestine of diseased individuals (Wang et al., 2007). Transmission electron microscopic examinations showed that the virions are spherical, 80–100 nm in diameter, and composed of a helical nucleocapsid within an envelope with surface projections. Detailed studies on the morphogenesis of these viruses found many characteristics previously described for other coronaviruses (Wang et al., 2007). Virus particles were found to be congregated, and always formed a virus vesicle with an encircling membrane (Wang et al., 2007). The most obvious cellular pathologic feature appears to be large granular areas of cytoplasm, relatively devoid of organelles. Tubular structures within virus-containing vesicles, nucleocapsid inclusions, and double-membrane vesicles are also routinely found in the cytopathic cells. Furthermore, in support of a viral pathogen being the causal agent for this disease, no rickettsia, chlamydia, bacteria, or other parasitic organisms have been seen to be associated with any of the diseased tissues sampled (Wang et al., 2007). Furthermore, these VLPs are only present in diseased individuals and absent in healthy animals. However, no infection trials have been conducted to date. Therefore, further evidence is required to prove that these VLPs are the aetiological agent. Interestingly, the same VLPs have also been observed in diseased larvae (30 days old). This latter finding suggests that the disease may be transmitted vertically from parents, which may have severe implications for transportation of brood stock from pond to pond.

Epidemiology: First reported in cultured sea cucumbers along the Shandong and Liaoning province coasts in China in 2004, it has now caused a significant number of deaths in cultured sea cucumbers throughout China.

Diagnosis and/or treatment: Based on disease signs only at the current time.

1.1.1.2. Stomach atrophy syndrome (SAS). Agent: An unknown virus approximately 75–200 nm in diameter (Deng et al. 2008).

Hosts affected: A. japonicus.

Clinical signs and pathology: The stomach of diseased larvae can be observed to shrink gradually exhibiting thick, rough and distorted walls. Virus-like particles have been observed only in diseased individuals, these are predominantly spherical or hexagonal with a well-defined envelope, and exhibit dense core structures (Yin-Geng et al., 2005). Sizes range from 75 to 200 nm in diameter. The VLPs have also been found in the gonad, body wall, alimentary canals and the
respiratory trees of corresponding parents suggesting akin to APED (above), a possible route for vertical transmission of this pathogen. Further examination of larvae by electron microscopic observations showed that the virus affects mainly the connective tissue cells and epithelial cells (Yin-Geng et al., 2005).

Epidemiology: In 2006, SAS was first observed in A. japonicus throughout the Liaoning area (Yin-Geng et al., 2005). SAS affects mainly larvae, approximately 1–7 days after hatching (Deng et al., 2008).

Diagnosis and/or treatment: Based on disease signs only at the current time.

1.1.2. Bacteria diseases in Holothuroidea

1.1.2.1. Skin ulceration disease (SUD) aka bacterial ulceration syndrome (BUS) aka acute peristome tumescence (APT). Agent: Numerous bacterial pathogens have been proposed (Deng et al., 2009; Lu et al., 2015; Ma et al., 2006; Wang et al., 2005a; Wang et al., 2007; Zhang et al., 2006). Commonly members of the genus Vibrio are isolated from diseased lesions, including Vibrio cyclitrophicus, Vibrio splendidus, Vibrio harveyi, Vibrio tasmaniensis, Vibrio tapetis, and Vibrio alginolyticus (Deng et al., 2009; Ma et al., 2006; Wang et al., 2005a; Wang et al., 2007; Zhang et al., 2006, 2015). However others such as a Photobacterium sp. (Deng et al. 2008; 2009), Pseudomonas nigrifaciens (Deng et al., 2009; Wang et al., 2005a), Aeromonas salmona and Aeromonas media (Wang et al., 2007), a Pseudoalteromonas sp. and Pseudoalteromonas tetraodonis (Liu et al., 2010) and a Marinomonas dokdonensis (Deng et al. 2009; Ma et al., 2006) have also been implicated to play some role. The latter pathological agent, has been described under one of the alternative names associated with disease, APT (Deng et al., 2009; Ma et al., 2006). Inoculation experiments have been fulfilled for a few of these candidate pathogens including the Pseudoalteromonas sp., P. tetraodonis (Liu et al., 2010) and V. splendidus (Lu et al., 2015), suggesting that at the very least these three play a significant role in the disease aetiology. Furthermore, phage therapy has been used to treat this disease targeting V. alginolyticus (Zhang et al., 2015) again suggesting a role for this bacterium.

In addition, like many marine diseases, researchers are only recently searching for viruses associated with these diseases. Indeed, two distinct virus like particles have now been observed associated with the disease lesions (Wang et al., 2005a; Wang et al., 2007). These include, a spherical virus with a diameter of 80–100 nm and a spherical virus with a nucleocapsid and diameter of 120–250 nm (Wang et al., 2005a; Wang et al., 2007). The latter of the two has been named, skin ulceration and peristome tumescence syndrome virus (SUPTSV) (Liu et al., 2010). Crude experimental inoculation trials, which included the addition of filtered tissue extracts (i.e. supposedly only containing viruses) to otherwise healthy individuals elicited similar disease signs, suggesting that the proposed virus does indeed play an important role in disease onset. Interestingly, the disease signs produced from the bacterial pathogens and viral pathogen, although resulting in the same overall pathology had certain differences. For example, inoculation with the bacterial pathogens included ulcer spots on the dorsal skin and abdominal parapodia, followed by an increase in the number and merging of ulcer spots and a decrease or loss of tentacle activity. In comparison symptoms caused by inoculation of the viral pathogen included an initial decrease in tentacle activity or loss of activity all together, peristome tumescence and the decay of dorsal papillate podia and peristome, along with abdominal ulceration. These differences suggest that the virus first affects the function of cells in tentacles and peristome, whereas bacteria initially cause ulceration of the skin. Finally, its worthy of note here that unidentified platyhelmints are often observed in diseased tissue and they are thought to cause heavy damage to the skin. The size of the worms is variable, normally ranging from 50 to 130 mm. Histological observations demonstrate that there is an abundance of worms in the tissues of the lesion area. They occupy a large space within the tissues and cause topical necrosis and scattering of the musculature (Wang et al., 2005a; Wang et al., 2007). However, exactly how these worms fit into the overall pathology of this disease remains unknown.

Hosts affected: Numerous sea cucumber species including: Juvenile Holothuria scabra, A. japonicus and Isostichopus fuscus (Mercier et al., 2005; Yin-Geng et al., 2005). Clinical signs and pathology: Due to its wide spread distribution, numerous names have been proposed for what some say is likely the same disease. However there are slight differences in the way the disease often manifests itself, suggesting that there may actually be multiple diseases currently under this one banner. For example in Australia and Madagascar, white lesions are observed to appear near the cloacal orifice and extends over the whole body, whilst in China, the white lesions have been noted to occur on any part of the body, begin canking and then extend over the whole body surface (Mercier et al., 2005; Yin-Geng et al., 2005). This disease usually results in chronic mortalities, with cumulative rates reported of 30–50%. Generally, infected individuals die within 3–15 days of the first clinical signs being observed. Skin ulceration begins with the appearance of small white patches (ca. 1 mm in diameter), which enlarge and eventually expose the underlying muscle and spicules. Yet, the mesothelium, the muscles and the internal organs remain unaffected. Padia inside lesions are often totally destroyed. Juveniles have been reported to show less motivation once they have contracted the disease and become translucent (Mercier et al., 2005; Yin-Geng et al., 2005). Scanning electron micrographs show two distinct ‘zones’ associated with this disease. The first, where the epidermis and cuticle are totally destroyed and where disorganized connective tissue is exposed has been referred to as the ‘effective zone’ and appears to be colonised by numerous different types of microorganisms. The second ‘zone’ is the border line area of infection, a few tens of micrometres wide where the surface is again colonised by a mix of microorganisms and where patches of degrading epidermis are mixed with degrading, exposed connective tissue. In the ‘affected zone’, collagen fibres run in all directions, breaking off from each other and ossicles, some of which appear highly degraded, are exposed to the external medium.

Epidemiology: Skin Ulceration Disease was first described by (Becker et al., 2004) affecting juvenile H. scabra reared in the hatchery of Toliara, Madagascar. Since then, the same disease has been found in numerous species of cultured sea cucumbers in Australia, New Caledonia, Ecuador and China.

Diagnosis and/or treatment: Based on disease signs only at the current time. However preventive measures have been suggested for this disease and include many general husbandry practices such as: (1) good hatchery management operations; (2) disinfection of tanks, plates and tools before use; (3) removal of excess food, faeces and other organic matter; and (4) provision of high quality water. Furthermore, the disease can be treated with antibiotics (3–5 ppm) such as Ofloxacin, Terramycin, Acheomycin, Levofloxacin hydrochloride, Cefobid, Doxycycline, Novobiocin and Sulphanilamides. This latter treatment suggestion may favour the roles of the bacteria as primary pathogens, over that of the viruses.

1.1.2.2. Stomach ulceration symptom (SUS). Agent: Reportedly associated with pathogenic bacteria.

Hosts affected: The disease is known to target the larvae, with the auricularia being notoriously susceptible to the infection. The mortality of affected larvae has been shown to rise up to 90% in certain instances.
Clinical signs and pathology: Stomach walls of the diseased juveniles appear thick, rough, and visibly atrophic (Liu et al., 2002). The ulceration of the stomach usually results in reduced growth and a lower metamorphosis rate. The disease often leads to mortality during the metamorphosis from the auricularia to the doliolaria stage.

Epidemiology: Stomach Ulceration Symptom (SUS) has been shown to have strong linkages with increases in temperature, occurring more commonly during the warmer summer months. The disease is also often triggered by feeding with unsuitable feeds and when the animals are kept in high stocking densities (Liu et al., 2002; Zhang and Liu, 1998).

Diagnosis and/or treatment: Based on disease signs only at the current time. Interestingly, although no specific pathogens have been identified, numerous treatments have been suggested, including using appropriate feeds from the onset (i.e. marine yeast) or treating with antibiotics such as penicillin or streptomycin, in the range of 3–5 ppm (Zhang and Liu, 1998). Similar to SUD, described above, finding a successful treatment for such diseases can aid in the identification of pathological agents. In this instance as antibiotics succeed in stopping the disease (again, similar to SUD), the most likely causal agents appear to be bacterial.

1.1.2.3. Viscera rejection syndrome (VRS). Agent: To date only, two bacterial isolates have been implicated in this disease: Arthrobacter protophormiae, and Staphylococcus equorum compared to the 12 in SUD (see above). However, as antibiotics rarely have a significant effect on treatment of this disease, these bacteria may actually turn out to be secondary causal agents or alternatively opportunistic pathogens. Again similar to SUD a virus has also been implicated in this disease, although little information is available with regard to morphology, structure etc. However, one study has shown that exposure to media containing this virus results in mortality of upwards of 90–100% of individuals infected (Deng et al., 2009).

Hosts affected: Various sea cucumber species.

Clinical signs and pathology: First identified in 2004, viscera rejection syndrome (VRS) usually starts with only a few infected individuals at the bottom of ponds, but the disease often spreads quickly. After 2–3 days, the viscera are ejected out of the body and the sea cucumbers succumb shortly afterwards. More than 50% of hatcheries have been known to exhibit this disease, with more than 90% mortality in some areas. Previously VRS was characterised in the same disease group as SUD (see above), however Deng et al. (2009) argued that due to substantial differences in pathology, these diseases should be classed as separate diseases/syndromes. There are four main reasons which led Deng and colleagues to suggest a separation of these diseases. Primarily, sea cucumbers suffering from SUD rarely exhibit signs of viscera ejection but do exhibit peristome edema expanding to the whole body. A second reason for this proposed separation of diseases is that after desiccation of infected individuals the majority of those with SUD (over 90%) had satiation intestines in coelom. In comparison, those with VRS (again upwards of 90% of infected individuals) had no intestines within their coeloms. Furthermore, both diseases show differences in their mortality rates and have different methods proposed for prevention. SUD for example has been shown to be treatable with antibiotics (slowing the spread), with mortality usually around 50%. In contrast VRS shows high infectivity, rapid spread, little response to antibiotic treatment and usually 80–100% mortality. Finally, although no definitive causal agents have been proposed for either disease state, the general consensus over the causal agents seems to differ between diseases.

Epidemiology: There is currently, very limited information on the spread of this disease.

Diagnosis and/or treatment: Based on disease signs only at the current time.

1.1.2.4. Rotting edges symptom (RES). Agent: Only one dominant bacterium (Vibrio lentus), has been highlighted as the likely causal agent in this disease (Zhang et al., 2010).

Hosts affected: Again, this disease predominantly occurs during the auricularia stages of development of many different sea cucumber species, with mortality being recorded as high as 90% in certain cases (Zhang et al., 2010).

Clinical signs and pathology: This symptom was first detected in commercial sea cucumber hatcheries in the Shandong Province in China. Compared with healthy larvae, diseased individuals exhibit a darkening of the body edges, giving this disease its name. These individuals then undergo autoysis and the body completely disintegrates within 2 days of initial signs. If metamorphosis is achieved, the pentactae are weak and the survival rate is significantly lower than healthy individuals. Infected larvae show a dark purple discolouration when stained with haematoxylin and eosin. Cells appear inflamed and often infiltrate the spheroplasts. The epithelial tissues appear ulcerated with epithelial cell necrosis. No obvious pathological changes have yet to be observed in the internal organs, apart from shedding of the gastric mucosal cells from the epithelial cells. Early ulceration also often occurs on the skin.

Epidemiology: To date, there is limited information on the spread of this disease.

Diagnosis and/or treatment: Based on disease signs only at the current time. Treatment with antibiotics including deomycin appears to cure this disease and again suggests that bacteria are the likely causal agents (Zhang et al., 2010).

1.1.2.5. Off-plate syndrome (OPS). Agent: Three dominant rod shaped gram-negative bacteria have been isolated from specimens collected from different hatcheries, all of which are thought to come from the genus Vibrio (Zhang et al., 2009).

Hosts affected: Shown to occur in settled juveniles (normally on PVC plates) of many different species. OPS causes significant mortality of juveniles metamorphosing from the doliolaria to the pentactula stage, with rates often reaching 100% (Zhang et al., 2009).

Clinical signs and pathology: The affected juveniles shrink and gradually lose the ability to remain attached onto the available substrate, hence the name of this disease. Subsequently, the epidermis of infected individuals usually disappears, however in more extreme cases the whole body can dissolve with the autolysing process. In such cases, the spicules can be found on the bottom of the infected tanks as they drop from the dissolved carcasses.

Epidemiology: Limited information on the spread of this disease.

Diagnosis and/or treatment: Based on disease signs at the current time.

1.1.3. Parasitic infestations in Holothuroidea

Agent: Many different protozoa have been described to be associated with holothurios yet these are often disregarded as commensals (Snyder, 1980). Although there are no specific described diseases associated with protozoa, infections do often manifest themselves. Infected individuals often appear weak and sluggish but rarely show any conspicuous lesions, hence why names have most likely not been assigned. That said, one species worthy of note, Diplodina gonadipertha, infests the
gonads of *Cucumaria frondosa* and could partially destroy the gonads completely (Djakonov, 1923). A result which would obviously have knock on effects in brood stocks. Furthermore, diseases caused by Platyhelminthes have been shown to infect both aestivated juveniles (larger than 1 cm) and adults of many different sea cucumber species. However, similar to protozoa (above), no specific disease states have been named. Numerous umagillids for example have been shown to ingest intestinal host tissue (similar to that observed with protozoan parasites).

Hosts affected: Many sea cucumber species.

Clinical signs and pathology: Such infestations have been recorded as being very high, with instances of upwards of 200 flatworms for example being observed within a single individual. Infestation by turbellarian egg capsules in particular have been recorded in over 70% of inspected individuals, with numbers being in excess of 10,000 in some instances. The majority of infestations usually manifest themselves in the form of small internal wounds with no lethality, however in rare instances high mortality has been noted (over 90%) within one month for example.

Epidemiology: Limited information as no specific names have been described linked to these parasites.

Diagnosis and/or treatment: Based on disease signs only at the current time.

1.1.4. Fungal disease

Agent: Although, no fungal pathogens have been definitively described for sea cucumbers, two have been described based on morphology alone. One is large with branched hyphae and macroconidia that contain more than 8 spores, whilst the second species is thin, with straight hyphae and small sporangium (Yin-Geng et al., 2005).

Hosts affected: Many sea cucumber species.

Clinical signs and pathology: Although fungal diseases have not been reported to cause widespread death, they will result in an unhealthy appearance and poor quality of the final product. The papillae of the sea cucumbers become white during the early stage of fungal infections. With large areas of the body wall often appearing bluish white as the skin is eroded by the fungi. Unlike bacterial infections, there is no obvious mucus around the lesions. In some cases, the whole body surface becomes discoloured and transparent; the body wall becomes thinner and the affected individuals develop edema. Histopathological observations have shown that fungal hyphae and spores can be detected in the muscular tissues, indicating that these fungi can invade the body wall and grow deep into the body tissues (Yin-Geng et al., 2005). Connective fibre tissue has also been reported to turn necrotic and disintegrate during heavy infections.

Epidemiology: Fungal diseases frequently occur in sea cucumbers during summer months. Both juveniles and adults have been shown to be infected, yet larvae appear to be unaffected to date.

Diagnosis and/or treatment: Based on disease signs only at the current time.

1.1.5. Predatory copepods

Agent: The main causal agent in these incidences is the predatory copepod, from the genus *Microsetella* (Liu et al., 2002; Zhang and Liu, 1998).

Hosts affected: Many sea cucumber species.

Clinical signs and pathology: In the presence of high numbers of copepods, the abundance of juveniles decrease acutely within 1 or 2 days. Usually, these predatory copepods will attack juveniles smaller than 5 cm, and often cause high mortalities. Juveniles often have lesions on their body and become weak. Eventually, the juveniles die off, the body walls dissolve and the spicules disseminate on the bottom of the rearing tanks.

Epidemiology: Summer often marks the peak of copepod reproduction as the larvae of sea cucumbers develop into juvenile stages. Normally, the rearing conditions for juveniles are favourable for the growth and reproduction of this parasite. At temperatures between 15 and 25 °C, one adult copepod can produce 90 individuals in 20 days. Generally, the mature female can produce new oocysts within a few minutes following the release of an initial batch. The copepods compete for food and space, as well as bite the young sea cucumber juveniles.

Diagnosis and/or treatment: Based on disease signs only at the current time. However, the use of Chlorophos has been proposed as the best option to control the problem. A dosage from 2 to 3 ppm has been shown to be effective; at this concentration all copepods can be killed in 2 h without harming the sea cucumber juveniles (Liu et al., 2002; Zhang and Liu, 1998).

1.2. Sub-Phylum: Crustacea

Several diseases pose significant threats to many different crustaceans, in both the wild and within post-capture holding facilities (Shield, 2011b; Stentiford and Neil, 2011). Annual production of farmed and captured crustaceans exceeds 10 M metric tonnes with a first sale value of $40bn, with the sector being dominated by farmed tropical marine shrimp. Strikingly, current estimates predict that up to 40% of total shrimp production is lost annually (~$3bn) and this loss is mainly accredited to disease. The World Organisation for Animal Health (Office International des Epizooties (OIE)) currently lists 8 notifiable crustacean diseases, 6 of which are viral in origin, 1 bacterial and 1 protistan. Three of the viral diseases in particular are also listed within European legislation, EC Council Directive 2006/88/EC. Although viral pathogens appear to exert the most significant constraints on the growth and survival of crustacea under culture conditions, protozoan pathogens appear to elicit the greatest detriment effects in wild populations, and affect the marketability of products harvested from these hosts (Stentiford et al., 2012).

1.2.1. Viral diseases in crustaceans

1.2.1.1. White spot syndrome virus (WSSV). Agent: White spot disease (WSD) is caused by the white spot syndrome virus (WSSV) and is probably the most extensively studied crustacean virus to date. This is primarily due to the devastating effect it has had on the shrimp farming industry, with cumulative losses exceeding $10bn since 1993 (Stentiford et al., 2012). WSSV was originally classified as an unassigned member of the Baculoviridae family. However, it was quickly reclassified to be from a new genus *Whisposivirus* in the family *Nimiviridae* and was named White Spot Syndrome Virus 1 by the ICTV (Mayo, 2002). To date, WSSV 1 is currently the only member of this new genus.

Hosts affected: The virus appears to be non-specific, with all decapod and non-decapod crustaceans being listed as susceptible. To date, more than 98 species of arthropods have been reported as hosts or carriers of WSSV, either from culture facilities, the wild or experimental infection (Sánchez-Paz, 2010). From the 98 susceptible species, Stentiford et al. (2009) identified 67 which were eligible to be described as susceptible using the European Food Standard Agency (EFSA) principles. However, although all these species are susceptible, they have recently been found to vary in their levels of susceptibility (Bateman et al., 2012a).
Research is also concentrating on potential vectors of this disease, which may be facilitating the spread. Numerous aquatic organisms such as rotifers (Yan et al., 2004), bivalves, polychaete worms (Vijayan et al., 2005), non-decapod crustaceans such as Artemia sp. and copepods have all been reported as potential vectors (Stentiford et al., 2009). Although, the viruses have been shown to accumulate in these vectors in large viable numbers, there has been no evidence of replication within these hosts meaning they are currently classed as only being ‘mechanical’ vectors (Chang et al., 2002; Lo et al., 1996; Yan et al., 2004).

Clinical signs and pathology: The name of the disease refers to the clinical signs that have been reported in some (but not all) species of shrimp. White spots, associated with a calcium deposit, appear on the inner surface of the cuticle. WSSV infects all tissues of mesodermal and ectodermal origin, such as gills, lymphoid organ, mid-gut but especially cuticular epithelium and sub-cuticular connective tissues. Virions are ovoid or ellipsoidal and consist of an electron dense nucleocapsid, with a tight fitting capsid layer, surrounded by a loose-fitting trilaminar envelope. Virions measure 120–150 nm in diameter and 270–290 nm in length and in some cases a tail like projection can be seen extending from one end. WSSV virions possess a very distinctive capsid layer giving the DNA core a cross-hatched or striated appearance (Wu et al., 2005).

Epidemiology: The virus was originally discovered in 1991 in Penaeus japonicus in China and Taipei, and was shown to spread rapidly throughout Asia and then to America (Shengli et al., 1995; Stentiford et al., 2009). Due to this rapid spread, and the isolation and identification by numerous independent laboratories, the virus was referred to by a variety of different names; however it was agreed that these infections are actually all caused by the same agent and the name White Spot Syndrome Virus was adopted (Joseph et al., 2015). WSD is listed as an OIE notifiable disease and as a non-exotic disease within Europe, EC Council Directive 2006/88/EC. Although not officially reported (i.e. in scientific publications), outbreaks of WSD have been observed in shrimp farms in Southern Europe, and these reports provided the basis that WSD should be classified as a non-exotic disease to Europe. However, the prevalence and spread of this virus throughout Europe remain unclear; with the last known/reported outbreak of the disease being in 2001 on a shrimp farm in Italy (Stentiford and Lightner, 2011).

Interestingly and also alarmingly, a recent study investigated the viability of WSSV in supermarket commodity shrimp which were imported into the UK (Bateman et al., 2012b). Unsurprisingly, the shrimp in the supermarkets harboured viable viral particles which were transmissible to live penaeid shrimp. Furthermore, WSSV was also successfully transmitted to Homarus gammarus, which were fed on these infected supermarket-derived shrimp, suggesting a possible pathway for WSSV to infect other species such as lobsters and highlighting a pathway for this disease to infect European crustacean stocks in the future (Bateman et al., 2012a). Finally, anecdotal evidence also suggests that some anglers are using commodity product as bait. As commodity product is not covered or controlled by existing legislation, we suggest that this practice needs to be investigated and regulated, as there is the potential for spread of pathogens such as WSSV in this way.

Diagnosis and/or treatment: Clear pathological signs and PCR of the virus.

1.2.1.2. Taura syndrome. Agent: The causal agent, Taura syndrome virus (TSV), is currently classified by the ICTV as an unassigned species in the family Dicistroviridae, from the order Picornavirales. To date, at least four genetic variants have been identified and it is likely that more will be assigned in the near future. Similarly to WSSV, TSV is listed as an OIE notifiable disease and as an exotic disease within Europe, EC Council Directive 2006/88/EC.

Hosts affected: The principal host for TSV is Litopenaeus vannamei, although the susceptible host range of TSV is thought to include most farmed marine shrimp species. However, susceptibility has been shown to vary between species and virulence also varies for the different strains of the virus. The virus mainly affects small shrimp at the nursery or during the grow-out phase in shrimp production, within 4–40 days after stocking, although larger shrimp have been shown to become affected in some instances (Lightner et al., 2012). To date, other crustaceans including freshwater shrimp and crabs appear to be resistant to the disease but may also be potential carriers. Certain species of birds and the water-boatman, Trichocorixa reticulata have been proposed as possible mechanical vectors (Brock, 1997) which are capable of transporting the disease from pond to pond, therefore making control of this disease very difficult. The focal origin of the TSV panzootic and absence of evidence of infection prior to the first outbreak suggest that, as for WSSV, penaeid shrimp are not likely to be the natural host and this remains unidentified to date.

Clinical signs and pathology: There are three main stages of the infection, acute, transition and chronic. Mortalities in the acute phase can be as high as 95%, but surviving shrimp remain infected and have been shown to carry the virus for the rest of their life. Therefore, these survivors act as a potential source of virus transmission between stocks. TSV causes necrosis of cuticular epithelium, haemopoietic tissues and the antennal gland, infected cells are rounded with pyknotic nuclei. The lymphoid organ itself is not infected but lymphoid organ spheroids (LOS) develop during infection. Virions are non-enveloped, icosahedral in shape and measure 32 nm.

Epidemiology: First documented in L. vannamei in Ecuador in 1992 (Lightner and Redman, 1998), The disease is named after the Taura River where the disease was first identified, however it was initially thought to be caused by a toxin (Hasson et al., 1995). The disease spread rapidly throughout shrimp farming regions in Central and South America and in 1998, it was detected in Taiwan and has now spread throughout much of Asia (Tu et al., 1999). The rapid spread of this virus, similar to that of WSSV, has been attributed to the international trade in live shrimp (Walker and Winton, 2010).

Diagnosis and/or treatment: Clear pathological signs and PCR of the virus.

1.2.1.3. Yellow head disease (YHD). Agent: Yellow head disease (YHD) is caused by the yellow head virus (YHV). To date, there are six known genotypes in the yellow head complex, however only YHV (genotype 1) has been shown to be the causal agent of YHD. Interestingly, gill-associated virus (GAV) is designated as genotype 2 and along with four of the other known genotypes (genotypes 3–6) are commonly associated with healthy Penaeus monodon in East Africa, Asia and Australia and are rarely or never associated with disease outbreaks (Walker and Winton, 2010). Furthermore, despite this variance in pathogenicity, all the genotypes in the yellow head complex are currently classified by the ICTV as a single species (gill-associated virus), from the genus Okavirus, family Roniviridae, order Nodivirales (OIE, 2013). This is mainly because there is strong evidence of genetic recombination between the different genotypes (Wijegoonawardane et al., 2009). Again similar to WSSV and TSV, YHD is listed as an OIE notifiable disease and as an exotic disease within Europe, EC Council Directive 2006/88/EC.

Hosts affected: YHD mainly affects black tiger shrimps (P. monodon), however many other penaeid and palinomon shrimp species have also been shown to be susceptible to experimental infection with YHV or GAV. P. monodon appears to be the natural host, yellow-head complex
viruses are detected rarely in other penaeid shrimp species (Walker and Winton, 2010).

Clinical signs and pathology: YHD is characterised by high rapid mortality and was named after the gross appearance of yellowing of the cephalothorax and general bleaching of body colour in some affected shrimp. YHD causes necrosis of ectodermal and mesodermal tissues such as cuticular epithelium, haemocytes, haemopoietic tissue, gills and connective tissues. YHV also affects the lymphoid organ, stromal matrix cells that comprise the tubules become infected leading to loss of tubular structure, and tubules appear degenerate. Virions measure 200 nm and appear rod-shaped with prominent projections at surface.

Epidemiology: YHD first emerged in P. monodon in Central Thailand in 1990 and has since been reported in most major shrimp farming countries in Asia, including India, Indonesia, Malaysia, the Philippines, Sri Lanka, Vietnam and Taiwan (Boonyaratpalin et al., 1993). However, there is also a recent unconfirmed report that YHD is also present in farmed Peneaus vannamei and Peneaus stylirostris in Mexico, showing again that transportation of stock likely spreads these pathogens around the globe. Although, it must be noted that there are no official confirmed reports of this virus causing disease outbreaks in shrimp farms in the Americas at the time of writing (Lightner, 2011).

Diagnosis and/or treatment: Clear pathological signs and PCR of the virus.

1.2.1.4. Peneaus stylirostris brevidensovirus (PstDNV). Agent: Infectious Hypodermal and Haemato poetic Necrosis Virus (IHHNV) was first described by Lightner et al. (1983) from a disease outbreak in cultured P. stylirostris in the Americas. IHHNV has been renamed as P. stylirostris brevidensovirus (PstDNV), from the genus Brevidensovirus and in the family Parvoviridae, although this listing has not been completely accepted by the ICTV (Kaufmann et al., 2010; Shike et al., 2000). The original name of this virus was given to describe the principal lesions observed and is still often referred to as IHHNV by many researchers as this is how it is commonly known. This viral infection remains an OIE notifiable disease since the original discovery of PstDNV in 1983.

Hosts affected: Multiple penaeid species appear to be susceptible to the virus and have been shown to carry the virus, however, the severity of infection and mortality rate often differs between species, with P. stylirostris for example appearing most susceptible (Bell and Lightner, 1984).

Clinical signs and pathology: In addition to necrosis, the virus was also found to cause stunted growth and deformities called by another disease name, runt deformity syndrome (RDS) in P. vannamei and P. monodon (Bell and Lightner, 1984; Primavera and Quinito, 2000). Typical signs of PstDNV in these species were shown to develop after indirect exposure via contaminated water or direct feeding of infected P. stylirostris carcasses. PstDNV infects the haematopoietic tissue, nervous tissue, gills, gonad, connective tissues and antennal gland. Hypertrophied nuclei containing eosinophilic inclusion bodies can usually be seen distributed throughout the tissues. Virions are non-enveloped, icosahedral in shape and measure 20–22 nm.

Epidemiology: The disease has caused substantial economic losses in shrimp farming in infected areas (Wyban, 1992). Three distinct genotypes of PstDNV have now been identified (Tang and Lightner, 2002, 2006; Tang et al., 2003). Type 1 from the Americas and East Asia, Type 2 from South-East Asia and Type 3 from East Africa, India, Australia and the western Indo-Pacific region. Types 1 and 2 are infectious to penaeids, whilst Type 3 appears to not be infectious to P. vannamei and/or P. monodon (Tang and Lightner, 2002, 2006; Tang et al., 2003). Non-infectious inserts of the partial PstDNV genome into the shrimp genome have been discovered in P. monodon which were sampled in East Africa and Australia (Krabetsvse et al., 2004; Tang and Lightner, 2006).

Diagnosis and/or treatment: Clear pathological signs together with a modified PCR method which was developed to detect the infectious type (Tang et al., 2007). False positives were found to occur under standard PCR conditions.

1.2.1.5. Infectious myonecrosis virus (IMNV). Agent: Infectious myonecrosis virus (IMNV) is the most recently emerging of the major viral diseases of marine shrimp. IMNV although still un-described is thought to be most closely related to members of the family Totiviridae, and belonging to the genus Giardiavirus. Interestingly, the only other known members of this family infect yeasts and protozoa.

Hosts affected: Litopenaeus vannamei late PL, juveniles and sub-adults, experimentally infected Litopenaeus stylirostris and P. monodon.

Clinical signs and pathology: Shrimp with the acute form of the disease display various degrees of skeletal muscle necrosis, which is visible as an opaque, whitish discolouration of the abdomen. IMNV causes significant disease and mortalities in juvenile and sub-adult pond reared stocks of L. vannamei and has been responsible for millions of dollars in losses in the affected regions. Surviving shrimp progress to a chronic phase with persistent low-level mortalities. Virions are non-enveloped, icosahedral in shape and measure ~40 nm.

Epidemiology: It first appeared in farmed white Pacific shrimp, L. vannamei at Pernambuco in Brazil in 2002 and has subsequently spread throughout coastal regions of north-east Brazil and more recently to Indonesia, Thailand and the Hainan Province in China (Walker and Winton, 2010). The original source of infection is unknown but the trans-continental spread has almost certainly been due to the voluminous trade in L. vannamei. Although, to date several other farmed marine shrimp species have been reported to be susceptible to infection by IMNV, only L. vannamei has shown pathological signs. The increasingly common practice in parts of Asia of co-cultivation of L. vannamei and the black tiger shrimp (P. monodon) is likely to present opportunities for adaptation and further spread of this disease.

Diagnosis and/or treatment: Clear pathological signs and PCR of the virus.

1.2.1.6. Panulirus argus virus (PaV1). Agent: Panulirus argus virus 1 (PaV-1) was the first description of a viral infection in lobsters (Shields and Behringer, 2004). Although, given a name, the exact classification of this virus still remains to be resolved.

Hosts affected: The infection was initially observed in juvenile P. argus.

Clinical signs and pathology: Juveniles appear lethargic, displaying milky haemolymph, which does not clot and infected individuals sometimes exhibit a discoloured, heavily fouled carapace. PaV1 has been shown to be transmitted to juvenile lobsters via inoculation, ingestion of diseased tissue and through close contact with infected individuals. The virus has also been shown to be transmitted via the water over small distances although contact and waterborne transmission were shown to be the least efficient methods (Butler et al., 2008). This ease of transmission is worrying and highlights the likely instances of more cases being reported in the near future.

Interestingly, juveniles with light infections and adult lobsters do not appear to show any obvious external signs of infection. It is only upon histological investigation whereby researchers can observe nuclear hypertrophy with Cowdry-type A viral inclusions in infected haemocytes.
In heavily infected individuals, virtually all the hosts haemocytes and semi-granulocytes are destroyed, the granulocytes however appear to not be affected. Furthermore, fixed phagocytes, blood vessels and surrounding connective tissues appear necrotic and often destroyed in these heavily infected individuals. Li et al. (2008a) and Li et al. (2008b) showed that the infection initially infects the fixed phagocytes and the connective tissues within the hepatopancreas. In heavily infected lobsters virally infected cells have also been found in the spongy connective tissues surrounding most organs (Li et al., 2008a). Histological evidence has also suggested that the prevalence of the virus is highest (−16%) among crevice-dwelling juveniles measuring 15–20 mm carapace length. This has been shown to decline to 5% once they reach 35–45 mm CL and is virtually undetectable in adults (<1%). Virions are icosahedral in shape and measure approximately 182 nm. Envelopes possess an electron lucent inner layer and an electron dense outer layer on which there are possible projections when located extracellularly.

Epidemiology: PaV1 was first shown to be present throughout the Florida Keys, and infections have since been found in Belize, Mexico and the US Virgin Islands, so it is thought to be widespread throughout the Caribbean (Butler et al., 2008). Prevalence of PaV1 is usually highest among the smallest juveniles and has been shown to decline with increasing lobster size (Behringer et al., 2011). Early benthic juveniles appear to be highly susceptible; with field experiments indicating that prevalence in wild populations exceeded 50% in focal outbreaks (Butler et al., 2008).

Diagnosis and/or treatment: Clear pathological signs and PCR of the virus.

1.2.1.7. Sighs disease (SD). Agent: The condition has been found to be caused by a ronivirus infection of the connective tissues and was named Eriocheir sinensis ronivirus (EsRV).

Hosts affected: Chinese mitten crabs (Eriocheir sinensis) are an economically important species in China and have been extensively cultured in recent years. As demand increased over the years, the culture practices were developed and in conjunction with this step up in production, outbreaks of disease suddenly increased. A viral infection specifically associated with E. sinensis was one of these diseases and named ‘sighs disease’ (Zhang and Bonami, 2007).

Clinical signs and pathology: The disease is named after the sounds which can be heard at night when affected crabs release a slow extrusion of bubbles reminiscent of a sigh. The disease is also known as black gill syndrome (BGS), due to the discolouration seen within the gills (dark grey or partly black colouration, usually at the tips of the gill filaments). Signs of infection can be noted in the, connective tissues of gills, hepatopancreas (HP), heart and gut. Infected cells display pale to anorexic, are slow growing and display a ‘corkscrew’ swimming behaviour. They show a significant atrophy of the hepatopancreas (HP) which often becomes yellowish or white within the HP connective tissue capsule. The HP does not squash easily between thumb and finger and black spots or streaks are sometimes visible. Other signs of the disease include a soft, generally darker shell, motting of the carapace and moribund shrimp sink to the bottom of the ponds. Mortalities have been shown to reach as much as 100% in severely affected ponds.

Epidemiology: The condition was first reported in China in 2009; then subsequently spread to Vietnam, Malaysia and Thailand (FAO, 2013). Furthermore, and akin to many of the viral diseases reviewed above, EMS/AHPND has also recently been reported in Mexico (Nunan et al., 2014). It now causes annual losses of more than US$1 billion.

Diagnosis and/or treatment: The current practice after an outbreak has occurred is to disinfect the ponds to try to remove any potential pathogens or their carriers, however a recent study by De Schryver et al. (2014) suggests that this practice may do more harm than good. Upon restocking, the increase in nutrient availability, decreased microbial community and consequent lack of competition may favour fast growing bacteria, such is the case with the genus Vibrio. The authors go on to suggest that microbial management practices may be the best solution to control this disease (De Schryver et al., 2014). The development of diagnostic tests for rapid detection of the EMS/AHPNS pathogen is ongoing, which will enable improved management of hatcheries and ponds, and help lead to a long-term solution for this disease. This will also enable a better evaluation of risks associated with importation of frozen shrimp or other products from countries affected by EMS/AHPND. In fact, some countries have already implemented policies that restrict the importation of frozen shrimp or other products from EMS/AHPND-affected countries. However, research currently indicates that EMS/AHPND does not survive cooking or freezing, and repeated attempts to transmit the disease using frozen tissue have so far been unsuccessful (Lightner et al., 2012). Therefore, frozen shrimp are likely to pose a low risk for contamination of wild shrimp or the environment because EMS/AHPND-infected shrimp are typically very small and do not enter international commerce, so although this disease is damaging and worthy of note in this review, the potential for spread to other countries should be relatively limited.

1.2.2. Bacterial diseases in Crustacea

1.2.2.1. Early mortality syndrome/acute hepatopancreatic necrosis disease (EMS/AHPND). Agent: EMS/AHPND is caused by a bacterial agent, which has been shown to be transmitted orally. The causative agent is reported to be a pathogenic Vibrio belonging to the Harveyi clade, presumably Vibrio parahealmonolyticus. The Vibrio is also thought to be infected by a virus known as a phage, which causes the release of a potent toxin (Tran et al., 2013), a result which causes the particular signs of the disease. A similar phenomenon occurs in the human disease cholera, where a phage makes the Vibrio cholerae bacterium capable of producing a toxin that causes cholera’s life-threatening diarrhoea. To date, it remains unclear as to whether or not all incidences of EMS/AHPND are caused by one or more strains of V. parahaemolyticus. The Vibrio has been shown to colonize the shrimp’s gastrointestinal tract and produces a toxin that causes tissue destruction and dysfunction of the hepatopancreas.

Hosts affected: EMS/AHPND outbreaks typically affect the post-larvae of both black tiger shrimp (Litopenaeus monodon) and white Pacific shrimp (L. vannamei), appearing within 20–30 days after initial stocking.

Clinical signs and pathology: Diseased shrimp become lethargic and anorexic, are slow growing and display a ‘corkscrew’ swimming behaviour. They show a significant atrophy of the hepatopancreas (HP) which often becomes yellowish or white within the HP connective tissue capsule. The HP does not squash easily between thumb and finger and black spots or streaks are sometimes visible. Other signs of the disease include a soft, generally darker shell, motting of the carapace and moribund shrimp sink to the bottom of the ponds. Mortalities have been shown to reach as much as 100% in severely affected ponds.

Epidemiology: The condition was first reported in China in 2009; then subsequently spread to Vietnam, Malaysia and Thailand (FAO, 2013). Furthermore, and akin to many of the viral diseases reviewed above, EMS/AHPND has also recently been reported in Mexico (Nunan et al., 2014). It now causes annual losses of more than US$1 billion.

Diagnosis and/or treatment: The current practice after an outbreak has occurred is to disinfect the ponds to try to remove any potential pathogens or their carriers, however a recent study by De Schryver et al. (2014) suggests that this practice may do more harm than good. Upon restocking, the increase in nutrient availability, decreased microbial community and consequent lack of competition may favour fast growing bacteria, such is the case with the genus Vibrio. The authors go on to suggest that microbial management practices may be the best solution to control this disease (De Schryver et al., 2014). The development of diagnostic tests for rapid detection of the EMS/AHPNS pathogen is ongoing, which will enable improved management of hatcheries and ponds, and help lead to a long-term solution for this disease. This will also enable a better evaluation of risks associated with importation of frozen shrimp or other products from countries affected by EMS/AHPND. In fact, some countries have already implemented policies that restrict the importation of frozen shrimp or other products from EMS/AHPND-affected countries. However, research currently indicates that EMS/AHPND does not survive cooking or freezing, and repeated attempts to transmit the disease using frozen tissue have so far been unsuccessful (Lightner et al., 2012). Therefore, frozen shrimp are likely to pose a low risk for contamination of wild shrimp or the environment because EMS/AHPND-infected shrimp are typically very small and do not enter international commerce, so although this disease is damaging and worthy of note in this review, the potential for spread to other countries should be relatively limited.

1.2.2.2. Milky haemolymph disease of spiny lobsters (MHD-SL). Agent: The condition is thought to be caused by a rickettsia-like bacteria.

Hosts affected: It has been shown to infect multiple spiny lobsters (Panulirus spp. especially Panulirus ornatus, Panulirus homarus and
Panulirus stimpsoni) from tropical regions but the condition has only been reported in Vietnam to date. The condition affects younger lobsters (juveniles approximately 3 months old) and appears to be a similar disease to that reported in other crustacean species (Nunan et al., 2010) such as Carcinus maenas (Eddy et al., 2007) and L. monodon (Nunan et al., 2010).

Clinical signs and pathology: The bacterium causes the haemolymph of infected lobsters to appear milky white and lose the ability to form clots. Onset of the disease is relatively rapid, with affected lobsters becoming lethargic and showing signs of the milky haemolymph within 3–5 days. Furthermore, the lobsters die soon after clinical signs become apparent.

Epidemiology: The disease emerged in Vietnam in 2007 (Shields, 2011a) and has caused massive economic losses, with farmers suffering high losses (up to 60%) and failed crops causing between US$10 and 30K in losses.

Diagnosis and/or treatment: Diagnostic tests have been developed and the disease is under consideration for listing as a notifiable disease by the OIE.

1.2.2.3. Necrotising hepatopancreatitis (NHP). Agent: Necrotising hepatopancreatitis (NHP) is another OIE notifiable disease caused by infection with a Gram-negative, pleomorphic intracytoplasmic rod shaped rickettsial like organism which is a member of the α subclass of proteobacteria, yet remains unclassified (Frelier et al., 1993; Lightner and Redman, 1998; Loy et al., 1996). Genetic analysis of the pathogenic agent from outbreaks in North and South America suggests that the isolates are either identical or very closely related subspecies (Loy et al., 1996).

Hosts affected: Most penaeid species can be infected with NHP, infections in L vannamei appear most severe where the intracellular bacterium can cause acute epizootics and mass mortality (>90%). Juvenile, broodstock and sub-adult life stages are the most severely affected (OIE, 2013).

Clinical signs and pathology: The disease has four distinct phases; initial, acute, transition and chronic. In the initial and chronic stages of the disease, molecular and antibody diagnostic techniques are necessary to confirm infection as there are no pathognomonic lesions. In the acute and transition phase, disease pathognomonic lesions are typically present in histological sections of the hepatopancreas (Vincent et al. 2004).

Epidemiology: The bacterium has been detected in the Western hemisphere in both wild and cultured penaeid shrimp and is commonly found in cultured penaeid shrimp in Belize, Brazil, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, United States of America, and Venezuela, highlighting the current and global extent of the issue. Natural transmission of NHP has been shown to occur via the practice of cannibalism, however cohabitation and dissemination of NHP via the water column is also thought to play a part (Frelier et al., 1993). Similar to many of the diseases highlighted in this review, outbreaks of the disease are often preceded by prolonged periods of high water temperature (approximately 30 °C) and salinity (up to 40 parts per thousand [ppt]) (OIE, 2013).

Diagnosis and/or treatment: The use of antibiotics has been suggested as the best treatment for NHP which is currently available, particularly if the disease is detected in the initial phase (OIE, 2013).

1.2.2.4. Gaffkaemia. Agent: Gaffkaemia or red tailed disease is a fatal systemic bacterial disease. First reported in 1947 (Stewart, 1975) the pathogen has been identified as the gram positive coccus Aerococcus viridians var. homari.

Hosts affected: First identified infecting the American lobster Homarus americanus. Similar to many diseases in this group, it has been particularly well studied due to the disease impacting on stocks of such a commercially viable species. Although, predominantly associated with H. americanus, the pathogen has been recorded in low prevalence in other crustacean species in the wild such as Libinia emarginata, Carcinus maenas, Cancer borealis, Cancer irroratus and Peneaus aztecs (Alderman, 1996). Furthermore, experimentally, the disease has been transferable to Panulirus interruptus, Pandalus platyceros, Cancer irroratus, Cancer magister, Geryon quinquedens, Chionoecetes opilio and Callinectes sapidus (Alderman, 1996). The diverse number of species this pathogen has been associated with clearly shows the dramatic influence epidemics of this disease can have on the crustacean populations and the whole ecosystem in general. Enzootics in both wild populations and captive animals are relatively common off the American/Canadian coast line and reports have occurred in cultured lobsters in California, however prevalence was reportedly low (Stewart, 1975). Despite the high number of species which have been shown to be susceptible to this disease, the pathogen had not been reported to be present in European waters until relatively recently. In 2011, the press reported the capture of an American lobster off the coast of Devon, Southern UK (Stebbing et al., 2012a). The lobster caught, had blue bands around its claws, indicative of being caught and tossed overboard by a passing ship. This lobster tested positive for Gaffkaemia and this spread real concern of the possibility that European lobsters H. americanus could have been exposed to this devastating disease.

Since this first report, and a further positive outbreak in a European lobster holding facility in South Wales, a base line survey was conducted to test the presence or absence of the disease in wild populations of H. americanus around the east coast of England and Wales (Stebbing et al., 2012b). Results showed that although Gaffkaemia was detected in wild populations, its prevalence was low (positive in ~1% of those tested). Pulsed-field gel electrophoresis conducted on the strains of A. viridians var. homari collected from the UK wild lobsters, those in the Welsh holding facility and examples from the USA and Canada showed that the isolates were identical, supporting the theory that this pathogen has been introduced into the UK, likely with the release of American lobsters, H. americanus. Although the increase in H. americanus in UK waters is of great concern and has the potential to cause a pandemic of Gaffkaemia, there are reports that there was a previous outbreak in England in the 1960s, although this is difficult to confirm (Stebbing et al., 2012b). To date, however no other European crustaceans have been tested for the presence of this pathogen and future studies should focus on assessing the extent of the problem in European waters.

Clinical signs and pathology: Infections occur when the bacteria gain entry through breaks in the exoskeleton. Eventually, large numbers of cocci, often arranged in chains or tetrads, are visible in the haemolymph (Steenbergen et al., 1978). The disease gets its common name, ‘red tail’, from the dark orange discoloration of the ventral abdomen of affected lobsters. This is the haemolymph seen through the thin ventral arthrodermal membranes. The red discoloration comes from astaxanthin, acarothenoid pigment, which is exported to the blood during times of stress.

Epidemiology: The bacterium has been detected in the Western hemisphere in both wild and cultured penaeid shrimp and is commonly found in cultured penaeid shrimp in Belize, Brazil, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Peru, United States of America, and Venezuela, highlighting the current and global extent of the issue. Similar to many marine diseases, it has been proposed that A. viridians var. homari is temperature-dependent.
with strains lying dormant when lobsters are held at temperatures as low as 1 °C whilst warming to only 3 °C can cause the signs of classical disease (Steenbergen et al., 1978). Generally diseased lobsters are found in waters ranging from 10 to 16 °C, interestingly above temperatures of 22 °C, virulence of *A. viridans var. homari* has been shown to reduce significantly (Steenbergen et al., 1978).

Diagnosis and/or treatment: Bacteriology and PCR.

1.2.2.5. Epizootic shell disease (ESD). Agent: Despite its devastating potential, the pathogen has only just been identified as the bacterium *Aquimarina homaria* (Quinn et al., 2012). However, there is the strong possibility that this bacterium is not the only causal agent, with other co-infecting pathogens and conditions (environmental or physiological) confounding a simple cause–effect relationship (Castro et al., 2012).

Hosts affected: American lobsters (*H. americanus*).

Clinical signs and pathology: Many infected individuals display deep shell lesions, sometimes covering most of their carapace (Castro et al., 2006) a result which renders them unmarketable. The cuticle is eroded by bacteria growing horizontally into the endocuticle.

Epidemiology: East coast of North America, in particular Long Island Sound. In 2011, an epizootic outbreak caused such a decimation of the population of American lobsters that the fishery was recommended to be closed. Although the disease has subsided, to a degree, ESD prevalence remains relatively high but varies temporally and geographically between 10 and 40% (Castro and Somers, 2012). Similarly to Gaffkaemia, ESD has also recently been reported in *H. gammarus* populations off the coast of Norway and within public aquaria. Although little research has been conducted on these European diseased lobsters, it is hypothesised that the pathogen (again similar to that for Gaffkaemia) has been transported over with their American cousins (Jørstad et al., 2011) and there is a very high potential that a similar epidemic (to that recorded in the East Atlantic) could occur in European waters.

Diagnosis and/or treatment: Pathology and PCR.

1.2.3. Prokaryotic crustacean diseases

1.2.3.1. *Spiroplasma*. Agent: *Spiroplasma* is a relatively new pathogen occurring predominantly in farmed crabs (Nunan et al., 2004, 2005). *Spiroplasmas* belong to a unique genus of the family *Spiroplasmataceae* and members of this genus are some of the smallest prokaryotes in the world. Although only recently identified as a cause for concern in the marine environment, *Spiroplasmas* are not new to science and were first identified in 1973 associated with terrestrial plants and animals (Williamson and Whitcomb, 1975). In 2003, the first study showed the isolation of a novel *Spiroplasma* in the marine environment and was associated with the now widely distributed Chinese mitten crab, *E. sinensis*. Since the initial discovery in *E. sinensis*, other spiroplasma-caused diseases have been identified in freshwater crayfish, *Procambarus clarkii*, (Wang et al., 2005b) and in shrimp such as the white Pacific shrimp, *P. vannamei* (Nunan et al., 2004) and *Rimicaris exoculata* (Zbinden and Cambon-Bonavita, 2003), highlighting the likeliness of more cases being confirmed in the coming years. However, despite the pathogen being described in 2003, it took a further seven years before the pathogen was actually named, *Spiroplasma eriocheiris* (Wang et al., 2011).

Hosts affected: Numerous species of crabs, shrimps and crayfish.

Clinical signs and pathology: Little is known about the specific signs caused by these pathogens. One named disease caused by *Spiroplasmas* is known as tremors disease (TD) (Wang et al., 2011). Although the proposed pathogen (*S. eriocheiris*) was only identified in 2003, TD was initially recorded in 1994, with mortalities in populations ranging from between 70 and 100% (Wei, 1999).

Epidemiology: Now, pathogens from this novel genus are being found throughout the world, for example cultured shrimps (*P. vannamei*) in Colombian farms have just been described as showing similar disease signs which have been accredited to a further species of *Spiroplasma, S. penaei* (Nunan et al., 2005). These studies indicate that spiroplasmas have a wide distribution in the aquatic environment and may be serious threats to crustaceans, especially those in cultured ponds.

Diagnosis and/or treatment: Pathology and PCR.

1.2.4. Protistan crustacean diseases

1.2.4.1. *Paramikrocytos canceri*. Agent: Initially this infection was thought to be caused by a haplosporidian, however phylogenetic analysis robustly grouped the parasite as a sister (68% similar) to *Mikrocytos mackini*, causative agent of Denman Island disease in oysters. The pathogen has now been described as belonging to a new taxon, *Paramikrocytos canceri* n.gen. et n. sp. on the basis of its phylogenetic affinity to the genus *Mikrocytos*, its difference in host range, and its ability to form plasmodia (Hartikainen et al., 2014).

Hosts affected: The pathogen has only been observed in juvenile life stages of the edible crab, *Cancer pagurus*, and to date has not been observed within adult populations. Juvenile crabs have shown high prevalence (27%) for the pathogen with peaks (at 80% prevalence) occurring in March (Bateman et al., 2011). The fact that the parasite is only observed in juvenile life stages may indicate that the parasite is causing mortality within these infected crabs, hence removing them from the population. If this is the case, the disease could likely have a devastating impact upon the fishery and further work is urgently needed to investigate the effect this parasite may have upon edible crab populations around the UK.

Clinical signs and pathology: There does not appear to be any visible signs of infection externally, however upon dissection the parasite can be observed infecting the antennal gland (bladder) of the edible crab causing the organ to become massively hypertrophied, distinctly yellow coloured and gelatinous in appearance. Histology of infected individuals has revealed massive proliferation of both the major lateral lobes of the antennal gland and the bladder, in the regions next to the hepatopancreatic lobes. Uninucleate and multicellular parasitic plasmoidal stages have also been found to be distributed throughout the epithelial cells of the infected glandular tubules. Electron microscopy confirmed that infection of these epithelial cells occurred with unicellular parasite stages developing to multicellular plasmodia.

Epidemiology: First discovered in juvenile edible crabs (*C. pagurus*) sampled originally from the shoreline in Weymouth, UK (Bateman et al., 2011). A similar parasite has also recently been reported in edible crabs from South Wales (Thrupp et al., 2013). Mikrocytid specific primers have now been utilised to screen invertebrate tissues and environmental DNA (eDNA) samples from marine, freshwater and soil environments from the UK, continental Europe, South Africa, Panama and Borneo. To date, *P. canceri* has not been detected in any of the environmental samples, however it was detected in a range of shoreline invertebrates, demonstrating that these newly recognised parasites are common, diverse and widespread. Therefore, they should be considered when assessing risks of aquaculture activities, invasive species spread and movements of ballast water and sediments with associated invertebrates (Hartikainen et al., 2014).
Diagnosis and/or treatment: Pathology and PCR.

1.2.4.2. Hematodinium species. Agent: Hematodinium species are dinoflagellate parasites with broad host specificity.

Hosts affected: Shown to infect more than 35 crustacean host species (Pagenkopp Lohan et al., 2011; Small, 2012). Specifically, devastating impacts have been recorded for numerous crab populations worldwide (Small, 2012), as infections are more often than not fatal. There have been various disease names associated with this parasite, which is due to the various characteristics of the disease in each species. These include: bitter crab disease (in Chionoecetes spp.) (Meyers et al., 1987), pink crab disease (in Cancer pagurus) (Stentiford et al., 2002), milky disease (in Portunus trituberculatus, Scylla serrata) (Eddy et al., 2007; Li et al., 2008b), yellow water disease (in S. serrata) (Xu et al., 2007) and milky shrimp disease (in Exopalaemon carinicauda) (Xu et al., 2010). This condition causes massive losses to wild crustacean populations and associated fisheries (Small, 2012) and has recently been associated with losses in cultured crabs and shrimp in China, with losses of up to 100% having been reported in these farms. The now increasingly common practice of rearing several different species in the same pond (known as polyculture) is likely a significant contributing factor towards transmission of the parasite between species and the occurrence of Hematodinium infections within E. carinicauda has obvious implications for the culture of other economically important shrimp species (Small, 2012). Following the emergence of Hematodinium in aquaculture in China (Xu et al., 2007, 2010; Li et al., 2008b), Small (2012) proposed that Hematodinium meets the criteria for listing as an emerging aquatic animal disease and suggested that the listing of this disease should be considered by the OIE.

Clinical signs and pathology: Grossly affected hosts are lethargic and often present a hyperpigmented or ‘cooked’ appearance of the host carapace and appendages. Advanced infections can usually be characterised by the appearance of white or cream coloured haemolymph due to the high numbers of parasites being present. The parasite causes a biochemical alteration of the crab meat causing them to become bitter tasting and hence unmarketable which causes significant commercial losses.

Epidemiology: Three genotypes have been identified infecting hosts from different geographical locations: the English Channel, east coast of the United States and Gulf of Mexico, and eastern China. Identification of Hematodinium species appears to be largely dependent upon geographical location, rather than host species. However it is important to note that this is not exclusive, as both Hematodinium species can be found infecting multiple species from same location in the English Channel.

Diagnosis and/or treatment: Pathology and PCR.

1.3. Phylum: Mollusca

Similar to crustacea, there are many diseases which pose significant threats to commercially important mollusk species both farmed and in the wild. Aquacultured shellfish include various oyster, mussel and clam species. These bivalves are filter and/or deposit feeders, which rely on ambient primary production rather than inputs of fish or other feed. As such, shellfish aquaculture is generally perceived as benign or even beneficial in some cases. Depending on the species and local conditions, bivalve molluscs are either grown on beaches, on longlines, or suspended from rafts and harvested by hand or by dredging. Over-fishing and poaching have reduced wild populations of many commercially important species such as abalones to the brink of extinction and increased farming activity is proposed as a measure to reduce wild collections and ultimately conserve wild stocks. However, as with other farming practices, increased densities of mollusca in these farms often result in disease outbreaks and the pathogens effectively cultured in these packed conditions can easily affect wild stocks as well.

1.3.1. Viral diseases in mollusca

1.3.1.1. Pacific oyster mortality syndrome (POMS). Agent: The cause of the mortalities appears to be from a microvariant of Type 1 Osterid Herpes virus (OsHV-1 µVar) (Segarra et al., 2010). OsHV-1 is a member of the family Herpesviridae known to infect a variety of different oysters, clams and scallop species (Farley et al., 1972). Recently, it was proposed to include OsHV-1 in the newly created family Malacoherpesviridae in the order Herpesvirales (Davison et al., 2009). The Ostreid Herpes virus variant, OsHV-1 µvar, is defined on the basis of partial sequence data exhibiting a systematic deletion of 12 base pairs in ORF 4 of the genome in comparison with OsHV-1 (GenBank # AY509253) (Renault et al., 2014).

Hosts affected: Most commonly the Pacific oyster, Crassostrea gigas, however the disease has been recorded to infect numerous other species as well. Interestingly, a few species are however starting to show levels of resistance to this virus with the most recent being the Black-lip pearl oyster (Tan et al., 2015) and the Pacific oyster (Pernet et al., 2015).

Clinical signs and pathology: Interestingly, prior to death there are no visibly identifiable gross pathological lesions. However upon histological analysis, a high viral load can be seen causing multifocal to coalescing ulceration with attenuation of the epithelium and pyknotic nuclei throughout the connective tissue (Renault and Novoa, 2004).

Epidemiology: Horizontal transmission has been shown to play a role in spreading the disease from infected adults to larvae and subsequently the spat, however vertical transmission may also play a role in transmission, yet this remains to be demonstrated. As is becoming a common theme throughout this review, prevalence of this disease has been associated with increases in average sea surface temperatures and overcrowding (Sauvage et al., 2009). To date, this condition has been recorded throughout much of Europe and especially in France and around Ireland. Mortality associated with OsHV-1 is primarily observed among oysters less than one year of age, although all ages of oysters have been recorded as contracting the disease at some point. A harmonised approach has also now been implemented between EU member states with regard to managing and mitigating the spread of this disease, particularly focusing at trying to keep the virus from UK waters (Murray et al., 2012), which at the time of writing show only a few isolated cases of infection (Murray et al., 2012). Given the economic importance of oyster aquaculture in many European countries, the EU Commission Regulation n. 175/2010 was enacted in March 2010 to identify the presence of OsHV-1 µvar associated with mortality in oysters in order to reduce the spread of the virus to uninfected regions. According to the regulation, disease control measures must be implemented which include the establishment of containment areas and the restriction of movement from these areas if OsHV-1 µvar and accompanying mortality is identified. In addition to affecting the Pacific oyster in Europe, reports of POMS have also been made in two estuaries in New South Wales, Australia (Paul-Pont et al., 2014) highlighting another potential problem area which needs to be monitored and managed to mitigate further spread.

Diagnosis and/or treatment: Pathology and PCR. However, very recently challenge experiments, involving the inoculation of oysters with OsHV-1 µvar at both high and low levels showed that infected oysters exhibited an increase in glycolysis and voltage-dependent anion channel (VDAC) accumulation, which reflects the ‘Warburg effect’, first reported in cancer cells and more recently in shrimps infected with other types of viruses (Corporeau et al., 2014; Su et al., 2014).
These latest results should allow the identification of potential biomarkers of disease resistance which will aid in the development of antiviral measures.

1.3.1.2. Abalone viral ganglioneuritis (AVG). Agent: Abalone herpesvirus (AbHV) has been tentatively assigned as the second member of the Malacoherpesviridae, following comparisons between AbHV and OsHV-1 that showed similarities of 19 to 53% over some common coding regions (Savin et al., 2010). AVG is currently another OIE notifiable disease.

Hosts affected: Susceptible species are listed as the greenlip abalone (Haliotis laevigata), the blacklip abalone (Haliotis rubra), the diversicolor abalone (Haliotis diversicolor) and hybrids of greenlip and blacklips (OIE, 2013).

Clinical signs and pathology: Affected abalone exhibit a distinct curling of the foot when infected. Most die within 1–2 days of showing this sign. Ganglioneuritis has been observed in sections of neural tissue by light microscopy and confirmation of the presence of AbHV can be obtained by quantitative polymerase chain reaction (qPCR) and/or in situ hybridisation (Corbeil et al., 2010). In on-farm epizootics, cumulative mortality has been recorded in all age classes and has been known to reach in excess of 90%. In experimental trials, 100% mortality has been shown to occur within 5 days post-exposure. The major histopathological lesion identified in abalone affected with AVG is ganglioneuritis (i.e. inflammation which is confined to the neural tissue). The cerebral, pleuropedal and buccal ganglia can also be affected as well as the cerebral commissure and associated peripheral nerves (Hooper et al., 2007).

Epidemiology: To date, the condition has been reported in Australia and Taiwan and causes mortalities of up to 90% in all size classes of animals. Due to the high prevalence of this disease occurring in multiple species and the increasing number of aquaculture farms being developed around the world for this group, the chance of spread of this disease is significantly high and we are therefore likely to see an increase in reports of this disease.

Diagnosis and/or treatment: Due to the typical curling of the foot (see above), false positives of this infection are therefore rare based on pathology alone. However, as there are currently no effective anti-viral treatments, preventive measures should always be taken. These consist of implementing high levels of on-farm and live-holding facility biosecurity and regional movement restrictions. Following an on-farm outbreak, the destruction of infected stock, disinfection of water and equipment, and fallowing procedures appear to be effective at preventing reinfection.

1.3.2. Bacteria diseases in mollusca

1.3.2.1. Vibriosis. Agent: Among several pathogens thought to be involved in these mortalities, the gamma-proteobacterium Vibrio aestuarianus, is frequently isolated from adult moribund oysters (Labreuche et al., 2006). Furthermore, isolated cultures of V. aestuarianus have been shown to induce similar disease pathologies in inoculation trials under controlled laboratory conditions. Alarmingly, prevalence of this pathogen in certain populations appears to be increasing. In 2012 for example, V. aestuarianus was detected in 100% of moribund adults tested, whereas only a few individuals tested positive in 2009 and 2010 (Wendling et al., 2014). Interestingly, all oysters which tested positive in 2012 had isolates which matched those from French oysters (Wendling et al., 2014). Furthermore the virulence of specific isolates also appears to be increasing, with this particular French isolate being particularly pathogenic (Wendling et al., 2014). Similarly, isolates of V. aestuarianus from infected oysters in Ireland have shown to induce very high mortalities of otherwise healthy C. gigas within only a few days of inoculation. However, despite this apparent increase in virulence, there is no evidence to suggest that new strains are responsible for the current outbreaks and future research should focus on assessing the environmental conditions that could potentially favour this apparent increase in virulence.

Hosts affected: Primarily the Pacific oyster (C. gigas) in Europe, however some clam species have also been described with this disease.

Clinical signs and pathology: V. aestuarianus causes necrosis of the adductor muscle and epithelial atrophy within the digestive gland. Organisms which contract this disease often exhibit setting and a decrease in larval motility. Furthermore adults suffer sudden mortalities. In oysters, progressive growth of the bacterium can be seen along the mantle and into the visceral mass. Velar deformation occurs without tissue invasion and immobility and progressive visceral atrophy often occur. In clams, entry of the pathogen appears to occur via the oesophagus.

Epidemiology: Occurs in Europe and the west coast of North America.

Diagnosis and/or treatment: Pathology and PCR. Once disease signs become obvious it is often too late for any treatment. However various antibiotics such as chloramphenicol, polymyxin B, erythromycin and neomycin can be used in an attempt to control the infection.

1.3.2.2. Withers syndrome. Agent: This OIE notifiable disease is caused by Xenohaliotis californiensis (Friedman et al. 2002; Haaker et al. 1992). The rickettsial bacterium infects the gastrointestinal epithelia of wild and farmed abalones, particularly Haliotis spp. There is limited information available on strain variations of this bacterium, however it is thought that X. californiensis may be infected with a phage highlighting a similar mode of pathogenesis as that which occurs in early mortality syndrome/acute hepatopancreatic necrosis disease in crustaceans (Friedman and Crosson, unpublished).

Hosts affected: Infects members of the genus Haliotis. Susceptibility is known to vary between species, but can cause upwards of 100% mortality in some (e.g. the white abalone, Haliotis soresnensi). All post-larval life stages have been shown to be susceptible to this condition but disease is typically observed in animals less than 1 year old and often in farms rather than the wild (OIE, 2013).

Clinical signs and pathology: Gross signs of disease include pedal atrophy, mottled digestive gland and weakness and lethargy. Infection is characterised by intracytoplasmic bacterial inclusions within the oesophagus, intestine and epithelia of the digestive gland.

Epidemiology: The disease occurs along the south-west coast of North America, infected abalones have been reported to have been transported to other areas and as such the geographical range is thought to be extensive in areas where Haliotis rufescens are cultured. Interestingly, infections have been shown to persist for long periods without any evidence of disease when the host is maintained in cool conditions, and the disease only manifests itself at elevated water temperatures (those above 18 °C).

Diagnosis and/or treatment: The bacterium can be detected in tissue squashes stained with propidium iodide, microscopic examination of stained tissue sections, PCR or in situ hybridization. Candidatus Xenohaliotis californiensis can be differentiated from other closely related alpha-Proteobacteria by its unique 16S rDNA sequence. The bacterium is not cultivable on synthetic media or in fish cell lines (e.g. CHSE-214) and may be controlled by tetracyclines (oxytetracycline) but not...
by chloramphenicol, clarithromycin or sarafloxacin (Friedman et al., 2000). Recently a new methodology has been designed to simplify detection of this pathogen in abalone (Cruz-Flores et al., 2015). Vacuoles can be visualized by staining with nucleic acid fluorochrome and their identity confirmed utilising the combined techniques of laser capture microdissection and PCR.

1.3.3. Eukaryotic molluscan diseases

1.3.3.1. Marteiliosis (Aber disease/QX disease). Agent: Marteiliosis is caused by the paramyxean protist pathogen Marteilia refringens. Currently three types, O, M and C have been defined based on the basis of the presence or absence of a restriction fragment in the ITS-1 region of the genome. Interestingly, both O and M appear to be generally specific to either oysters or mussels, with type M more often detected in mussels and type O in flat oysters. However, co-infection has also been shown to exist. When such co-infection occurs, it does however appear to be restricted to those areas where the prevalence of the disease is significantly higher. Type C, in contrast is predominantly associated with mass mortalities of cockles in Delta del Ebro (Carrasco et al., 2013) and Galicia (Villalba et al., 2014) in Spain. Although classed under the same disease name, this latter type has been subsequently named Marteilia cochlilia. Although very little is known about this more recently described type, mixed infections of all three have been shown to occur in rare cases.

The life cycles of both Marteilia species are not completely known, however it appears to involve at least one intermediate host. Multiple taxa of zooplankton in the same areas as the oysters, mussels and cockles are likely to play important roles at different stages of the life cycle, along with at least two copepods from the genus Paracartia, P. latisetosa and P. grani (Audemard et al., 2002). In the latter instances, Marteilia have been shown to be transmitted from infected oysters and infected mussels to healthy copepods. Mature sporangia of M. refringens have recently been observed in spring and autumn in mussels suggestive that the parasite has two cycles per year and that the mussels release the parasites from spring to autumn. In conjunction, M. refringens has also been detected in P. grani copepodid stages between June and November strengthening the hypothesis of the transmission of the parasites from copepods to mussels. In addition, in-situ end labelling showed that the Marteilia were present within the digestive tracts and gonads of the 3rd copepodid stages (Arzul et al., 2014). As stated above, very little is really known about these pathogens, but as they appear to use multiple hosts in different parts of their lifecycle, management and mitigation of this disease will be difficult to say the least.

Hosts affected: Shown to infect the flat oyster, Ostrea edulis, and two mussel species: Mytilus edulis and Mytilus galloprovincialis (Murray et al., 2012). It is listed as an OIE notifiable disease. QX disease is the term used to describe this pathology for the Sydney rock oyster, Saccostrea glomerata.

Clinical signs and pathology: Basically these pathogens have various effects on their hosts via two major target systems, digestive and reproductive. For an in-depth review on this disease we refer you to Berthe et al. (2004). Severe infections often cause loss of condition as a consequence of reduced energy acquisition. The parasite may also interfere with the digestion of host tissues by certain enzymes the parasite secretes. To become systemic, resulting in significant destruction of epithelia and connective tissues. This destruction is thought to be primarily caused by the digestion of host tissues by certain enzymes the parasite secretes.

Epidemiology: Wide geographic presence occurring from the Pacific Islands through Australia, Southeast Asia, to Europe and to Uruguay (Cho and Park, 2010). In addition, P. olseni has been shown to infect the Eastern oyster (Crassostrea virginica), Pacific oyster (C. gigas), suminoue oyster (Crassostrea ariakensis), mangrove oyster (Crassostrea rhizophorae), Cortez oyster (Crassostrea cortezensis), softshell clam (Mya arenaria) and Baltic macoma (Macoma balitica) (OIE, 2013). P. olseni, in particular has a wide geographical presence, occurring from the Pacific Islands through Australia, Southeast Asia, to Europe and to Uruguay (Cho and Park, 2010). In addition, P. olseni has been shown to infect an equally large number of hosts (clams, oysters, cockles, and abalones).

Clinical signs and pathology: Affected oysters are typically thin, pale and ‘wasted’ in appearance, as tissues are overrun by the explosively proliferating parasites. Uninucleate trophozoites of 2 to 10 μm develop into multinucleate ‘rosette’ forms (15 μm) that rupture to release more uninucleate trophozoites. This process occurs most rapidly and causes the greatest mortality during the warmer months of the year. Infections usually remain in the gut epithelium but have often been seen to become systemic, resulting in significant destruction of epithelia and connective tissues. This destruction is thought to be primarily caused by the digestion of host tissues by certain enzymes the parasite secretes.

Epidemiology: Wide geographic presence occurring from the Pacific Islands through Australia, Southeast Asia, to Europe and to Uruguay (Cho and Park, 2010). In addition to severely affecting wild populations, this disease has been shown to occur in farms. However outbreaks can be reduced by culturing oysters in waters with salinity below 12 to 15 ppt (Cook et al., 1998). In the wild, season salinities, around 12 ppt, appear favorable for supporting full dermo disease outbreaks, so in theory areas most at risk from these disease outbreaks can be identified by local salinity patterns (Cook et al., 1998). Perkinsus proliferates at temperatures higher than 20 °C and in warm, southern waters ‘dermo’ has been recorded as decimating up to 50% of oyster beds each year (Cook et al., 1998). The parasites are transmitted directly between individual oysters, primarily when the oysters are in advanced stages of infection, die and then disintegrate. New infections are acquired as oysters feed, the parasite infecting its hosts through the gut epithelium. Interestingly, it has been reported that most serious outbreaks occur during drought years, so as climate change is predicted to increase periods of draught in many areas of the globe, increases in this disease may also likely occur. Areas such as in the gulf of Mexico are also likely to see increases
in this disease, as dermo has been linked to the El Nino-Southern Oscillation (ENSO) cycle (Cook et al., 1998), with serious outbreaks regularly following the arrival of warm, dry, La Nina climatic conditions.

Interestingly, it has been proposed that P. olseni, has recently been introduced into Florida and infections in giant clams has been documented. It had only previously been associated with clams in Vietnam and it has been hypothesised that the parasite has been transported to Florida by the aquarium trade. Furthermore, a recent study has highlighted that certain Perkinsus species are sympatric and have been shown to occur within close proximity to each other (Fernández-Boo et al., 2014). The same study also highlighted that Perkinsus cheaspeaki (a parasite previously only detected in North America) was present in France (Fernández-Boo et al., 2014). This latter study highlights the real possibility that the rest of Europe may begin to show outbreaks of dermo in a variety of species of clams, oysters, cockles, and abalones.

Diagnosis and/or treatment: Currently based on the pathology and epidemiology of diseased individuals. However, the effect of dermo disease in aquaculture can be minimized by culturing oysters in waters where the salinity is below 12 to 15 ppt (Cook et al., 1998). However, prospects for successful culture in waters of higher salinity are improving with the development of fast-growing, relatively disease-resistant, domesticated oyster strains.

1.3.4.2. Bonamiosis in oysters. Agent: The genus Bonamia includes small-size (2–3 μm) unicellulate protozoan parasites also called microcells (Carnegie and Cochenne-Lauvoir, 2004).

Hosts affected: Two of these microcells are thought to be of particular concern, including Bonamia ostreae, which affects populations of the European flat oyster O. edulis and Bonamia exitiosa which infects Ostrea chilensis from New Zealand and Ostrea angasi from Australia. Both species cause diseases which are listed as notifiable by the OIE. Other known species of the genus are Bonamia roughleyi infecting Saccostrea commercialis from Australia and Bonamia perspora described in Ostreola equestris from North Carolina, USA. However, at the current time both these two species are thought to not be of high enough risk warranting notifiable status by the OIE.

Clinical signs and pathology: Although, we seem to be getting a better understanding of the diversity of Bonamia species (see above), their mode of pathogenesis remains largely unknown. We are, however, beginning to understand how certain species may play specific roles. For example, B. ostreae appears to mainly infect the haemocytes of infected oysters and transmission appears to be direct from infected to naive oysters. The parasites enter through epithelia from pallial organs including the gills. Once they have passed the epithelium barrier, they are internalized within haemocytes which in turn contribute to the spread of the parasite in all the other organs. Multiplication of B. ostreae occurs inside the haemocytes and is associated with a decrease of esterases and production of reactive oxygen species. Furthermore, the modulation of apoptosis and decrease of phagocytosis has been also proposed as being important mechanisms related to resistance to these parasites (Engelsma et al., 2014). B. ostreae, affects the granular blood cells (haemocytes) of the host. Lesions occur in the connective tissue of the gills, mantle and digestive gland. The parasite multiplies by binary fission. Ten or more parasites have been observed within an infected haemocyte. More rarely, during the terminal stages of the disease, a larger plasmodial form can occur, this contains between 3 and 5 nuclei.

Epidemiology: To date, oysters such as O. chilensis in Chile, O. puella in Argentina, C. ariakensis in North Carolina, and O. stentina in Tunisia have shown no presence of any Bonamia species (Hill et al., 2014). However, in 2007, B. exitiosa was detected in Spain (Ramilo et al., 2014) and in the Adriatic Sea in Italy (Nardi et al., 2010) in samples of O. edulis which led credence to the theory that Bonamia have a global distribution already and questions were asked with regard to this parasite impact on European flat oyster populations (Narcisi et al., 2011). Importantly, as both parasites; B. exitiosa and B. ostreae have been shown to occur in the same locations and sometimes even in the same individuals, specific diagnostic tools are urgently needed to understand the spread of these parasites and improve our understanding of specific infections (Murray et al., 2012).

Diagnosis and/or treatment: Diagnosis of infected oysters is made by histological or cytological examination and molecular techniques. There is no known treatment for Bonamiosis and therefore the only effective measure is to prevent the introduction of the disease. Principally, methods of oyster health surveillance will allow for the limitation of the spread. Furthermore, the use of predictive models of disease progression in infected areas could help to improve stock management and minimize the impact of these particular parasites (Engelsma et al., 2014). Moreover, with respect to aquaculture practices, the development of resistant animals has been suggested and may help to revive specific production. In this context, studies are currently being undertaken to understand how B. ostreae interacts with O. edulis.

1.3.4.3. Denman Island Disease. Agent: Mikrocytos mackini is the final pathogen we will deal with here in this review and again causes another OIE notifiable disease, known as Denman Island Disease.

Hosts affected: The disease causes mortalities in several economically important oyster species (C. gigas, C. virginica, O. edulis, O. lurida).

Clinical signs and pathology: Infected oysters display yellow/green pustules within the mantle tissues, labial palps and adductor muscle. Histologically, the microcell parasite appears morphologically similar to the Bonamia sp. (mentioned above) and can be identified within the cytoplasm of vesicular connective tissues and the muscle fibres. Areas of haemocyte infiltration within the mantle, labial palps and adductor muscle have also shown the presence of the parasite. The parasites are often associated with intense inflammatory reaction around the site of infection.

Epidemiology: Reports of this disease have occurred along the west coast of North America and Canada (OIE, 2013). The disease usually affects oysters when water temperatures are cooler; below 10 °C (Hervio et al. 1996). All life stages of the oyster appear to be susceptible, with mortalities reaching up to 40%. Although the life cycle outside the host is currently unknown, the disease has been transmitted experimentally under laboratory conditions by cohabitation or by intramuscular inoculation of purified parasites.

Furthermore, a novel Mikrocytos infection has been recently recorded in the UK (Hartikainen et al., 2014). In fact the causative agent was initially suspected to be that of M. mackini due to the similarities in gross pathology to that of Denman Island Disease. Pacific oysters (Crassostrea gigas) were shown to suffer mortality events with upwards of 20% of animals reportedly being lost. Infected individuals were seen to be gaping and were thin and watery, with green pustules observed on the adductor muscle and on the surface of the mantle tissue. Furthermore, histology revealed the presence of microcell parasites throughout the cytoplasm of vesicular connective tissues and within the fibres of the adductor muscle. However, diagnostic tests for M. mackini came back negative and sequencing revealed that it was only 79% similar to M. mackini. Hartikainen et al. (2014) was the first to describe this recent outbreak and highlighted that it is the first time that a Mikrocytos infection has been described infecting Pacific oysters in Europe. This recent discovery therefore represents a new potential threat to the molluscan industries throughout Europe.

Diagnosis and/or treatment: Due to the risk of spread, a diagnostic test has been designed in the attempts to screen oysters and prevent any further spread (OIE, 2013). A combined approach of both PCR and
fluorescent in situ hybridization (FISH) would give the greatest chance of detecting this pathogen in hosts. For primers and protocols see Carnegie et al. (2003) and Meyer et al. (2005). Interestingly, this latter study showed that only 70% of the positive oysters diagnosed with these techniques were found infected via the normal histological procedure, highlighting the importance of well validated diagnosis techniques. Finally, it is worthy of note that a very closely related parasite, initially identified in C. gigas has also been found causing a similar pathology to Denman Island Disease in O. lurida in Canada. This has now been named as a new species from the same genus, Mikrocytos boweri sp. nov. (Hartikainen et al., 2014).

2. Conclusion

This review highlights the importance and strikingly large numbers of diseases prevalent in three main commercially important marine invertebrate phyla/sub-phyla and/or class. We highlight a dramatic skew in the knowledge available between different phyla, particularly associated with the level of importance these groups are given based on their importance in aquaculture and as a sustainable food source. Specifically, species in the sub phylum Crustacea and the phylum Mollusca are extensively studied in contrast to Holothuroidea, although there remains a large amount of unknowns with regard to specific diseases and parasites/pathogens even in these two groups. Interestingly, especially with regard to mariculture, researchers appear to be well advanced with regard to viral work for both Crustacea and Mollusca. Even with regard to bacterial induced diseases, the discovery of how phages interact with the proposed pathogens, highlights the importance viruses play not just in disease but also with regard to healthy systems. Finally, and more importantly, this review highlights the very real risk of the continued spread of specific pathogens around the globe. This is likely to occur either via the introduction of the hosts (during set up of different aquaculture practices for example) or alternatively via the transmission of the pathogen’s hosts (by transport in the ballast waters of ships or through the aquarium trade). Despite the well documented cases of disease spread, it is surprising that we appear to not be able to learn from these past mistakes and are continuing the transport diseased individuals or vectors around the globe. Specifically a call for more control appears to be needed, implemented in the movement of live individuals and also frozen food to attempt to seriously minimize further spread of novel pathogens and those already described.

As far as prevention and treatment of outbreaks are concerned, this review highlights that there is very little information available to draw on. Therefore, we can only suggest that the best strategy to minimize stocks contracting disease at the current time should be robust management. For example, broodstocks used for reproduction should be healthy without any signs of pathogens which will avoid vertical infections occurring. Stocking density should be adapted to the environmental conditions, culture method and experience – overcrowded conditions would lower resistance to diseases. Individuals should be fed with high quality diets that are supplemented with necessary elements including vitamins and minerals. Water quality should be maintained by keeping an optimum stocking density, avoiding over feeding and increasing water exchange rates whilst monitoring the water quality on a daily basis. All equipment and tools should be disinfected before use or before transfer from one tank to another and excess food, faeces and other organic wastes should be siphoned and removed as quickly as possible. Finally, if a disease is detected, actions and effective measures should be taken and moribund individuals should be removed from the tanks and be properly disposed. As a last resort antibiotics should only be used when the causative pathogen(s) have been confirmed (see above for which diseases this relates to). Although the above will assist in reducing disease spread in mariculture, they do not relate to spread in wild populations, yet any improvements which can occur in aquaculture husbandry may reduce the risk to wild populations and limit the spread into these environments as well.

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