

environmental sources shaped by local hydrodynamics and farm layout. Laboratory and epidemiological evidence support a role for particles and biofouling communities (e.g., plankton, fouled oysters on equipment) in transporting OsHV-1 and other pathogens, though successful transmission via fouling organisms appears rare and complex (Fuhrmann et al., 2021).

5.3 Risks associated with seedstock circulation and inter-regional transmission

Network analyses of French oyster farming show highly dynamic, heterogeneous transfer patterns among farm categories and growing sites, with seasonal peaks in movements and specific sites acting as high-risk hubs for becoming infected or transmitting disease (Coralie et al., 2016). Spatial epidemiology of OsHV-1 shows mortality starting in dense farming areas and spreading kilometres outward, consistent with animal movements and waterborne export from seedstock hotspots, while connectivity to farms is a strong mortality risk factor for both juveniles and adults (Gangnery et al., 2019). Historically, large-scale imports of Pacific oyster stock into Europe in response to disease crises created a positive feedback loop between introductions of non-native species (including pathogens) and further stocking, with continuing vector activity inferred over decades. More broadly, anthropogenic vector analysis identifies movements of live growing stock and culture substrates as among the highest-risk vectors in shellfish aquaculture networks, logistically difficult to manage but central to disease spread pathways across regions (Lovett et al., 2024).

6 Host Immune Response and Pathophysiological Mechanisms

6.1 Innate immune system and changes in disease-resistance responses

The oyster innate immune system relies on circulating haemocytes and a highly expanded repertoire of recognition and effector genes, enabling pathogen detection, phagocytosis, oxidative killing, antimicrobial peptide production and apoptosis (Wang et al., 2018). During bacterial or viral outbreaks, these defences can be subverted; for example, *Vibrio aestuarianus* deregulates hemocyte oxidative metabolism, impairing cellular functions and survival (De Lorgeril et al., 2018). Disease resistance varies strongly among families and life stages. Resistant oysters show higher basal expression of stress and antiviral pathway genes (TLR-NF κ B, JAK-STAT, STING-RLR), supporting more robust responses to Pacific oyster mortality syndrome (POMS). In contrast, susceptible juveniles in field outbreaks sense pathogens and activate receptors and signaling, but fail to induce key antimicrobial, apoptotic and redox-homeostasis genes, leading to microbial overgrowth and high mortality.

6.2 Characteristics of tissue damage and metabolic disorders

Complex pathogenesis is well illustrated in POMS, where OsHV-1 μ Var first infects haemocytes, inducing an immunocompromised state that permits secondary bacterial invasion and fatal bacteraemia (Destoumieux-Garzón et al., 2024). Histopathological observations in experimental infections show invasion of connective tissues by opportunistic bacteria during dysbiosis, consistent with systemic sepsis as a terminal lesion pattern. (Delisle et al., 2022; Destoumieux-Garzón et al., 2024) Metabolic reprogramming is another key feature of pathophysiology. During intense OsHV-1 replication, oysters show increased glycolysis and altered mitochondrial porin (VDAC) levels, resembling a “Warburg effect” that redirects energy metabolism. Other pathogens induce broad metabolic and cellular stress responses; *Vibrio coralliilyticus* infection in larvae reduces feeding, mobilizes energy reserves, remodels fatty acids, and activates antioxidant and heat-shock defences alongside immune pathways.

6.3 Mechanisms of gut and microbial community imbalance

Oysters host tissue-specific, dynamic microbiota that differ from surrounding seawater and are shaped by both environment and host genetics. In healthy states, this microbiota contributes to immune education and homeostasis; antimicrobial peptides help fine-tune microbial communities (Destoumieux-Garzón et al., 2024). Under stress or disturbance, rare phylotypes are lost, overall diversity declines, and the coupling between host genetics and microbiome composition breaks down, suggesting stress-driven community destabilization (Lokmer et al., 2016). Dysbiosis is now recognized as central to major syndromes such as POMS and environmentally driven mass mortalities. In POMS, OsHV-1-induced immune suppression leads to microbiota destabilization, replacement of commensals by virulent communities, and spill-over of opportunistic bacteria into tissues, amplifying disease