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# Review of Adaptation and Histopathological Changes of the Fish Respiratory System to Parasites and Diseases

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**ABSTRACT**

The respiratory system of fish is particularly susceptible to parasitic infections and diseases that can cause significant histopathological changes. This article discusses the adaptation of fish's respiratory system to environmental stresses caused by parasites and pathogens, as well as the histopathological changes that occur in response to infection. Some of the major changes observed include hyperplasia, hypertrophy, necrosis, and edema of the tissues in the gills, which can affect the respiratory function of the fish. In addition, granuloma formation and increased mucus production were also noted as adaptive responses to parasitic infections. Although some histopathological changes can improve the fish's body defenses, the tissue damage that occurs as a result of chronic infections can lead to serious impaired respiratory function and decrease the survival of fish. Understanding the mechanisms of adaptation and histopathological changes is very important for fish health management, especially in aquaculture, in order to reduce the negative impact of diseases and increase fish productivity.

## INTRODUCTION

Fish are members of the poikilothermic vertebrates or cold-blooded animals that live in water and breathe with gills. Fish have a wide variety of species spread around the world with a total of more than 27,000 species (Andalia et al., 2022). In terms of taxonomy, fish belong to a paraphyletic group whose kinship is still debated. In general, fish are classified as jawless fish or the Agnatha class of which 75 species include lampreys and hagfish, upper cartilaginous fish of the Chondrichthyes class, 800 species including sharks and rays and the rest are classified as hard-boned or true bony fish, class Osteichthyes.

Fish physiology itself includes various processes, namely, osmoregulation, circulatory system, respiratory system, bioenergetic and metabolism, digestion, sensory organs, nervous system, endocrine and reproductive system (Fujaya, 1999). In the respiratory system of fish, the most important organ is the gills. Gill belongs to a type of fish (pisces). The gills are in the form of thin pink sheets and are always in a moist state. The outermost part of the gills is directly related to water, while the inner part is closely related to the blood capillaries. Each gill sheet is made up of a pair of filaments and each filament contains many thin layers called lamellas. In the gill filament there are blood vessels that have many capillaries so that they allow $O_2$ to diffuse in and C $O_2$ to diffuse out. The gills in true bony fish are covered by a gill cap called the operculum, whereas the gills in cartilaginous fish are not covered by the operculum. Therefore, the need for oxygen in water must be maintained because a lack of oxygen will cause the biota we maintain to compete with each other to meet their oxygen needs, resulting in stress up to total death (Maudina & Diamahesa 2023).

In its function, the gills not only function as a respiratory apparatus but also as a means of excretion of salts, food filters, ion exchange devices and osmoregulators. In the respiratory system of fish, there are also additional aids, for example a maze. Labyrinths function to store $O_2$ reserves so that fish can survive environmental conditions that lack $O_2$. Examples of fish that have a maze are snakehead fish and catfish. To store $O_2$ reserves, in addition to the labyrinth, the fish have swimming bubbles located near the back. One of the fish's adjustments to the environment is to regulate the balance of water and salt in their body tissues, because some aquatic vertebrate animals contain salts with different concentrations from their environmental media (Dahril *et al*., 2017). The impact of parasites and diseases on fish health extends beyond immediate respiratory issues, often leading to a cascade of physiological stress responses that can compromise their overall well-being. For instance, chronic infections can weaken the immune system, making fish more susceptible to secondary infections and environmental stressors (Novotny *et al*., 2021).

Additionally, the presence of parasitic infestations, such as those caused by protozoa or helminths, has been shown to affect not only the respiratory efficiency but also growth rates and reproductive success in various species (Khair *et al*., 2023). This interconnectedness highlights the importance of monitoring fish populations for early signs of disease and implementing effective management practices to mitigate these risks, ensuring both ecological balance and sustainable fisheries. The piscine respiratory system is represented by gills as mentioned in this paper, and Gill diseases are extremely common and may be caused by a large variety of etiologic agents, such as viruses, bacteria, fungi, and parasites.

This review aims to examine the adaptations made by the fish's respiratory system in the face of stress from parasites and diseases, as well as to outline the various histopathological changes that occur in response to infection or disorder. By understanding the mechanisms of adaptation and tissue changes in the respiratory system, it is hoped that this information can provide useful insights in efforts to diagnose, prevent, and manage fish health, especially in the aquaculture environment.

## RESULTS AND DISCUSSION

### Fish Respiratory System

There are two phases in the respiratory system of fish, including:

a. **Fish Inspiration Phase**

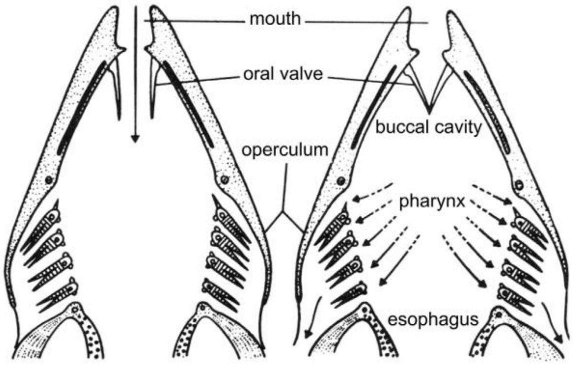


Figure 1. Illustration of zebrafish respiration (Jonz, 2020)

The movement of the gill cap to the side and the membrane of the gill cap remains attached to the body resulting in the oral cavity increasing in size, on the contrary, the gap behind the gill is closed. As a result, the air pressure in the oral cavity is less than the outside air pressure. The mouth gap opens so that there is a flow of water into the oral cavity (Cartner *et al*., 2022)

**b. Fish Evaporation Phase**

Once water enters the oral cavity, the mouth gap closes. The gills return to their original position followed by the opening of the gill slit. The water in the mouth flows through the gill fissures and touches the gill sheets. In this place, respiratory air exchange occurs. The blood releases $CO_2$ into the water and binds the $O_2$ from the water. In the inspiration phase, $O_2$ and water enter the gills, then $O_2$ is bound by blood capillaries to be carried to the tissue that needs it. On the other hand, in the expiratory phase, $CO_2$ carried by the blood from the tissues will end up in the gills, and from the gills it is excreted out of the body (Cartner *et al*., 2022).

**Respiratory Mechanism of Chondrichthyes**

In the Chondrichthyes group, it is divided into 3 types, namely a type of shark, stingray, and chimaeras. Each of these types has quite different breathing mechanisms. The breathing mechanism in sharks, water is taken in through its mouth and expelled through the gill slits located on the side of its body. Almost the same mechanism as Osteichthyes, but sharks use a ram ventilation mechanism. This mechanism works by keeping the shark's mouth open and always swimming to drain water from the mouth and get it out into the gill gap. Therefore, some sharks that have this breathing mechanism do not stop swimming or they will run out of $O_2$ and cause death. For the stingray, it does not take water from its mouth, but through the spiral which is on its head, precisely behind its eyes. Water is drained from above and expelled through a total of five gill slits in the lower part of its body located near the mouth (Schultz 2004). In a type of Chimaeras, there is a slight difference from sharks and stingrays, where Chimaeras only have one gill slit and are covered with operculum (Helfman *et al*., 2009).

**Mechanism of Osteichthyes**

$O_2$ gas is taken from water-soluble $O_2$ gas through gills by diffusion. From the gills, $O_2$ is transported through blood vessels to all tissues of the body. From the body's tissues, $CO_2$ gas is transported by the blood to the heart. From the heart to the gills to carry out gas exchange. This process occurs continuously and repeatedly. Osteichthyes breathe by opening their mouths to take in water to be drained by the muscles attached to the operculum towards the gills. The blood flow in the gills flows in the opposite direction of the water flow which is useful for binding $O_2$. In some types of Osteichthyes can filter approximately 85% of the content from the water that flows through its gills (Umazewa *et al*., 2012).

**Lampreys Mechanism**

Lampreys have 7 pairs of ventilation holes on the side of their body in which there are gill sacs containing blood capillaries. Lamprey inhales water from the hole which is then placed in the available gill sacs. In the gill sac, there is binding of $O_2$ levels in water by blood capillaries. After the binding of $O_2$ levels, the water is discharged back through the same ventilation hole (Schultz, 2004).

**Respiratory Aids in Fish**

Breathing apparatus in fish consists of various structures that allow them to obtain oxygen from water. One of them is the labyrinth, which is an extension of the gills at the top with folds that form irregular cavities. Fish such as catfish (*Clarias batrachus*) and cork (*Channa striata*) have a maze that functions to store oxygen reserves for use when in an environment with low oxygen levels. Some fish, such as betta fish (*Betta* sp.), are also able to take in oxygen directly from the atmosphere using labyrinths, similar to lung function in humans.

In addition to the labyrinth, some species of fish such as catfish, carp, and tilapia have additional structures called arborescenes, which are shaped like coral flowers and function to help breathing in environments with low oxygen levels. Fish that live in the tropics, such as cork (*Channa striata*), also have additional structures called diverticula in the pharyngeal region, which support their respiratory function in oxygen-restricted conditions.

Some fish also use swimming bubbles as a breathing aid. These bubbles function to regulate the buoyancy of the fish so that they do not need to continue swimming to stay in a certain position in the water. Fish such as carp (*Cyprinus carpio*) and tawes fish (*Puntius javanicus*) have swimming bubbles that vary in shape, which help the fish regulate their depth and position in the water. In lunged fish, as in the Dipnoi group, the swimming bubbles function similarly to the lungs, storing oxygen for respiration (Campbell, 2003).

**Respiratory System Vulnerability**

The respiratory system of fish, which is mainly made up of gills, has a high susceptibility to various external factors due to its position in direct contact with the surrounding environment. As the main organ for gas exchange, the gills function to filter oxygen from water and remove carbon dioxide. However, this process also means that the gills are always in direct contact with water which can contain various pathogenic microorganisms or pollutants. Direct exposure to the external environment makes gills a major entry point for harmful parasites and microorganisms. Different types of parasites, such as protozoa and worms, can infect the gills, cause damage to tissues and interfere with the respiratory function of the fish. In addition, bacteria and viruses contained in the water can also attack the gills, causing infections that lead to inflammation, swelling, or even tissue necrosis. This vulnerability is exacerbated by other factors such as poor water quality, high fish population density, and the stress that fish experience. When fish are in poor environmental conditions, their respiratory system becomes more susceptible to infections and disturbances. Therefore, maintaining good water quality and minimizing exposure to pathogens is essential to prevent damage to the fish's respiratory system. (Hamilton *et al.,* 2017).

Moreover, the respiratory vulnerability of fish is exacerbated by environmental stressors such as poor water quality and overcrowding, which can lead to increased susceptibility to infections. For instance, studies have shown that high population density in aquatic environments significantly correlates with higher rates of respiratory diseases among fish populations ($p=0.000$, $OR=15.000$) (Raenti et al., 2019). Additionally, factors like inadequate ventilation within aquaculture systems can create hypoxic conditions, further compromising the health of these organisms. As a result, it becomes imperative for aquaculture practitioners to implement effective management practices aimed at improving water quality and reducing crowding, thereby enhancing the overall resilience of fish against respiratory infections and parasitic diseases.

### Parasites And Diseases That Attack the Respiratory System Of Fish

Parasites that attack the respiratory system of fish can be of different types, including protozoa and worms. One example of protozoa that is often found in fish is Ichthyophthirius multifiliis, which causes "white spot disease" (Nugraheni et al. 2019). These protozoa can attach to the gills of fish, disrupt gas exchange and cause inflammation. In addition to protozoa, worms such as Dactylogyrus spp. can also infect the gills of fish, causing irritation to the gill tissue and interfering with the respiratory function of fish (Shamsi et al. 2009). Morphology of Dactylogyrus sp. has a dorsoventral and bilaterally symmetrical body shape as can be seen in the Figure 2.

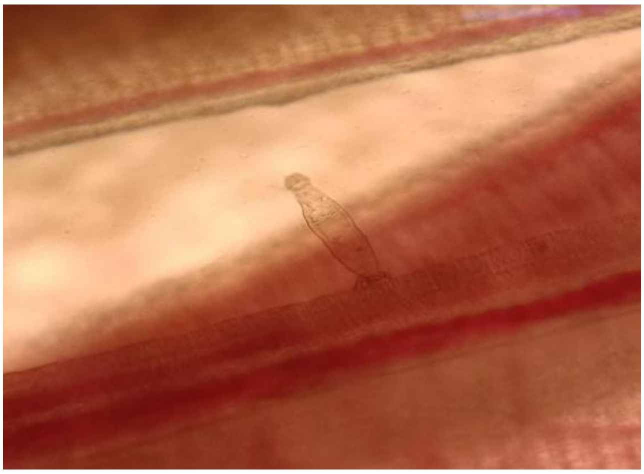

Figure 2. Tilapia gills exposed to the parasite *Dactylogyrus* sp. 400X magnification (Mora *et al*., 2022)

In addition to parasites, bacterial and fungal infections are also common causes of disorders in the respiratory system of fish. One of the bacteria that often causes infections in fish is *Flavobacterium columnare*, which can infect the gills and skin of fish, causing inflammation and tissue necrosis (LaFrentz *et al.,* 2018). Fungal and viral infections are also common, especially in poorly maintained environments, which can worsen the respiratory conditions of fish and increase their susceptibility to other infections.

The clinical impact of parasitic infections and these diseases can be seen through external symptoms such as inflammation of the gills, swelling, and hyperplasia (increased cell count) in the gill tissue. Other symptoms include discoloration of the gills and excess mucus accumulation. In addition, impaired respiratory function is a major impact faced by infected fish, which can lead to difficulty breathing, decreased oxygen levels in the body, and even death if not treated immediately.

### Histopathological Changes in The Respiratory System

#### General Histopathological Reactions

The histological structure of gills in fish varies by species, but in general they have the same components (Hughes, 1984). In the gill filament there are several lamellas, namely primary lamellas and secondary lamellas. Gill filaments also contain blood vessels with many capillaries, which allows the process of diffusion of oxygen in and carbon dioxide out. The primary lamellae is located perpendicular to the secondary lamellae and serves as the primary place of gas exchange. In the middle of the primary lamellae is the central venous sinus, which is a large duct containing erythrocytes. The primary lamellar consists of cartilage wrapped in the perichondrium, with the epithelium arranged in several layers of cells, including monocyte cells, mucocyte cells, and epithelial cells that are similar to the secondary lamellae.

Secondary lamellae, according to Lagler *et al*. (1977), are transverse sheet shaped and have an outer wall consisting of a layer of flattened epithelial cells. This epithelial sheath is surrounded by a medial vascular layer consisting of woven blood capillaries originating from the efferent branchialis artery. Secondary lamellae play an important role in gas exchange as well as the regulation of water and electrolyte balance. Inside there are pillar cells that are polyedral and function as a barrier between epithelial cells and blood capillaries. These pillar cells are modified endothelial cells and have a polymorphic nucleus, as explained by Wilson & Laurent (2002).

In addition, secondary lamellae also contain mucous cells and chloride cells, which are located in the peripheral part along the primary and secondary lamellae. Mucous cells, which are oval in shape, produce mucus in the form of glycoproteins that are alkaline or neutral. This mucus serves as protection, reduces friction, fights pathogens, and facilitates the exchange of ions, gases, and water. These cells are very important in maintaining gas exchange functions and osmotic balance in fish, as explained by Irianto (2005) and Susanah (2011).

**Histopathological Changes in Fish Gills as Indicators of Environmental Stress**

Hyperplasia and Hypertrophy of Gill Lamellae and Necrosis and Tissue Edema

The histopathological changes in fish gills, particularly hyperplasia, hypertrophy, necrosis, and tissue edema, are critical indicators of environmental stressors, particularly heavy metal exposure and pollution. These alterations can significantly impact fish health and serve as biomarkers for assessing water quality. The following sections detail these changes and their implications.

Hyperplasia and hypertrophy are common histopathological responses observed in fish gill tissues under environmental stress. Hyperplasia refers to the increased proliferation of cells in gill tissues, often manifesting as interlamellar cell hyperplasia, which is a response to stressors like cadmium exposure (Gulzar *et al*., 2023). On the other hand, hypertrophy involves the enlargement of gill epithelial cells, leading to structural changes such as lamellar fusion and deformation, as observed in various fish species (Marinović *et al*., 2021; Batista *et al*., 2018). These alterations in gill structure can negatively impact respiratory function, highlighting the importance of monitoring environmental stressors in aquatic ecosystems.

Necrosis refers to the death of cells in gill tissues, often occurring due to severe environmental stress. For example, necrosis has been observed in the gills of fish from polluted areas, indicating significant tissue damage (Shahid *et al*., 2021). This condition can severely impair the respiratory function of fish, as damaged gill cells are unable to perform gas exchange effectively, potentially leading to broader health issues for the fish. Alongside necrosis, tissue edema can also occur in gill tissues, which manifests as fluid accumulation. Edema is often seen in combination with hyperplasia and hypertrophy and indicates inflammation and compromised gill function (Gulzar *et al*., 2023; Batista *et al*., 2018).

While these histopathological changes are crucial for understanding the health of fish, it is important to note that not all environmental stressors lead to severe alterations. Some fish species exhibit resilience, showing minimal histological changes despite exposure to pollutants. This suggests a complex interaction between species, exposure levels, and environmental conditions, where certain species may be better equipped to cope with stress, thus minimizing the extent of tissue damage (Marinović *et al*., 2021).

**Granuloma Formation and Epithelial Damage**

Granuloma formation and epithelial damage are significant consequences of chronic bacterial infections, particularly in conditions like Chronic Granulomatous Disease (CGD). Granulomas arise as a protective response to persistent pathogens, while epithelial damage can result from direct pathogen invasion or immune-mediated injury. The following sections elaborate on these effects. Granulomas are organized aggregates of immune cells, primarily mononuclear phagocytes, that form in response to chronic inflammation or infection (Kaye, 2004). In chronic granulomatous disease (CGD), the inability of phagocytes to effectively kill certain bacteria and fungi leads to recurrent infections and subsequent granuloma formation in various organs, including the lungs and gastrointestinal tract (Arnold & Heimall, 2021; Nemade & Shinde, 2021). These granulomas can cause significant tissue remodeling, potentially leading to complications such as abscess formation and fibrosis, which further disrupt organ function (Fayyaz *et al*., 2020).

Certain pathogens can directly damage epithelial cells, leading to inflammation and ulceration, and in chronic granulomatous disease (CGD), recurrent infections with catalase-positive organisms can exacerbate this damage (Nemade & Shinde, 2021). The inflammatory response associated with granuloma formation can also contribute to epithelial injury, as the immune response may inadvertently harm surrounding tissues (Ying *et al*., 2012). While granuloma formation serves as a protective mechanism, it can also lead to chronic inflammation and tissue damage, highlighting the complex interplay between host defense and pathology. Understanding these dynamics is crucial for developing targeted therapies for conditions like CGD.

**Adaptation of The Respiratory System to Parasites and Diseases**

The adaptation of the respiratory system to parasites and diseases involves various physiological and morphological changes, as well as inherent limitations. These adaptations are crucial for enhancing host defense mechanisms against parasitic infections, particularly in the context of respiratory involvement.

**Physiological Adaptations**

In response to parasitic infections, the respiratory system often increases mucus production as a protective mechanism, creating a barrier to reduce pathogen contact and facilitate clearance (Sharpe et al., 2018). Additionally, infected hosts may experience decreased metabolic activity, which helps conserve energy and allows for a more efficient immune response against the invading parasites. These physiological changes highlight the body's adaptive responses to combat parasitic infections while maintaining immune function.

**Morphological Adaptations**

In response to chronic infections, the lamellae in the respiratory tract may thicken, providing additional structural support and protection against mechanical damage caused by parasites (Oliveira *et al*., 2023). Additionally, following injury from parasitic invasion, tissue proliferation often occurs to cover damaged areas, aiding in the restoration of respiratory function (Oliveira *et al*., 2023). These adaptive changes in the respiratory tissues help the host cope with the damage caused by parasites while maintaining the integrity and function of the respiratory system.

**Limitations of Adaptation**

Severe infections can cause permanent disruption to the lung architecture, leading to irreversible changes that result in chronic respiratory issues (Oliveira *et al*., 2023). In aquatic environments, parasitic infections can significantly impair fish health, affecting their growth and survival rates due to compromised respiratory function. These impacts highlight the importance of maintaining healthy respiratory systems in fish to ensure their well-being and survival in the face of parasitic threats. While these adaptations are vital for host survival, they can also lead to long-term health consequences, highlighting the complex interplay between host defenses and parasitic strategies. Understanding these dynamics is essential for developing effective treatment and prevention strategies.

**Implications for Fish Health Management Histopathological**

Diagnosis plays a crucial role in the early detection of infections in aquaculture, guiding effective treatment strategies. By examining tissue samples, pathologists can identify unique morphological features of infectious agents and assess the host's response, which is vital for managing fish health (Rolon, 2023). This diagnostic approach not only aids in recognizing infections but also informs treatment decisions, ultimately enhancing fish welfare and productivity.

Histopathological diagnosis plays a crucial role in the early detection of infections, enabling rapid identification and preventing widespread outbreaks. By providing an accurate diagnosis, histopathology also guides the selection of appropriate pharmacological therapies, which significantly improves recovery rates in affected fish (Rolon, 2023). This diagnostic tool is essential for effective disease management and the overall health of fish populations.

Parasite and disease control strategies involve maintaining optimal water quality to reduce stress and susceptibility to infections in aquatic organisms (Oladosu *et al*., 2023). In addition, pharmacological and biological prevention methods, such as antiparasitic medications and biological controls, are essential for effectively managing infections and ensuring the health of fish populations (Islam *et al*., 2024). These combined approaches are crucial for maintaining a healthy aquatic environment and preventing the spread of diseases. In aquaculture, maintaining healthy fish populations is crucial for enhancing fish productivity, as it leads to increased growth rates and improved marketability (Rahmati-Holasoo *et al*., 2023). Additionally, effective health management practices contribute to the overall welfare of farmed fish, ensuring their well-being and reducing the risk of disease outbreaks (Islam *et al*., 2024). These factors are essential for achieving sustainable and profitable aquaculture operations. Conversely, while histopathological methods are invaluable, reliance solely on these techniques may overlook the benefits of integrating advanced technologies like IoT and machine learning for proactive disease management in aquaculture (Islam *et al*., 2024).

## CONCLUSION

In conclusion, the respiratory system of fish, especially the gills, is particularly susceptible to parasitic infections and diseases due to direct exposure to the external environment. Although fish have adaptive mechanisms such as increased mucus production and thickening of gill lamellae in response to infection, histopathological changes such hypertrophy, and tissue necrosis persist, indicating a disturbance in respiratory function. Parasites such *as Ichthyophthirius multifiliis* and *Dactylogyrus* spp., as well as bacterial and fungal infections, can damage gill tissue and interfere with the fish's ability to breathe, which has an impact on the overall health of the fish. Therefore, understanding these histopathological adaptations and changes is essential in disease prevention and treatment, as well as in the management of fish health, especially in a growing aquaculture environment.

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