# Mycoplasma hyopneumoniae and Immunomodulation

To survive in the presence of harmful pathogens, nature has provided living organisms with a specialised built-in tool to protect themselves that science refers to as the immune system (Fig. 1). The immune system is divided into two parts, the innate immune system, and the adaptive immune system.

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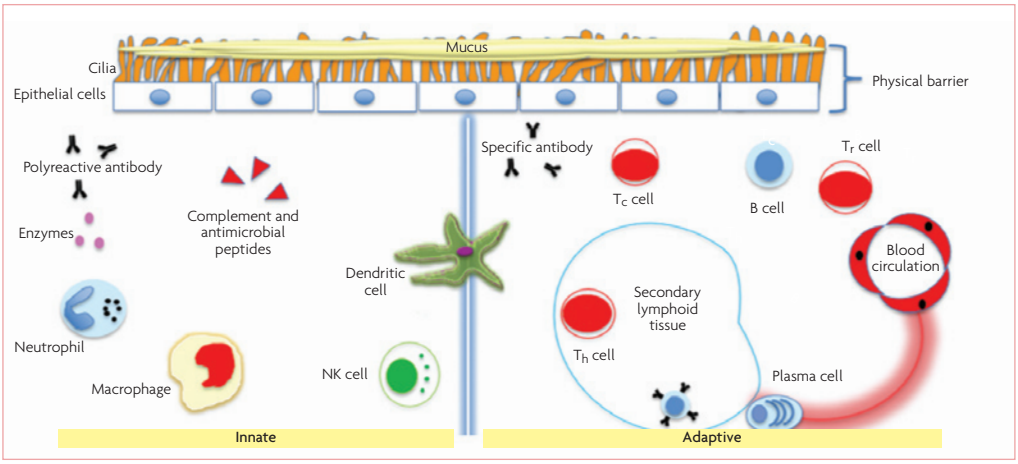


**Fig. 1. The Immune System (Adapted from Day MJ and Schultz RD, 2014).**

The innate immune system is equipped with physical barriers and resident defence cells including macrophages and neutrophils. The adaptive immune system is equipped with T cells and B cells. When a pathogen overwhelms the physical barriers, it triggers the innate immune system to simultaneously activate the resident defence cells to neutralise the pathogen.

The activation of these cells, particularly macrophages and neutrophils, triggers the release of pro-inflammatory cytokines (for example IL-1β, IL-6, IL-8, TNFα), leading to inflammation. While this takes place, the adaptive immune system is also activated by macrophages and dendritic cells presenting fragments of the pathogen to the T cells.

The T cells respond in three ways - destroy the infected cells (cytotoxic T cells), activate the B cells to produce antibodies (T helper cells) and regulate the overall adaptive immune response (T regulatory cells).

These complex and interlinked processes continue until the pathogen is eliminated. Once eliminated, the T cells send signals to switch off the immune system, allowing the body to heal and recover. However, certain bacteria and viruses can overwhelm the immune system, creating a worst-case scenario from which the pig may not recover.

In this scenario, there is excessive release of pro-inflammatory cytokines (cytokine storm), triggering uncontrolled inflammation resulting in inflammation-related tissue damage. Mycoplasma hyopneumoniae as well as Actinobacillus pleuropneumoniae, PRRSV, porcine respiratory coronavirus and PCV2 are swine pathogens capable of altering the immune response to the host animal's detriment.

Mycoplasma hyopneumoniae causes a disease in pigs known as Enzootic Pneumonia. It primarily affects the respiratory tract which clinically manifests as coughing.

The disease is of economic importance as it is associated with reduced average daily gain, decreased feed efficiency and increased medication cost. The disease is estimated to cost $US5.84/pig in finishers in infected herds. It affects pigs of all ages and is commonly seen in finisher pigs. Mycoplasma hyopneumoniae is one of the primary agents of PRDC together with other bacteria and viruses.

It can modulate and/or evade the immune response. Therefore, lung lesions seen when performing necropsies can in part be a result of uncontrolled inflammation because of the ability of this bacteria to alter the immune response.

Along with optimal farm management and vaccination, antibiotics with licensed claims against Mycoplasma hyopneumoniae are commonly needed to control or eliminate the disease. Suitable antibiotics include macrolides, pleuromutilins, fluoroquinolones, lincosamides, tetracyclines, amphenicols and aminoglycosides.

These antibiotics act either by inhibiting or killing bacteria. In addition, a few macrolides, including tylvalosin (Aivlosin/Valosin), have immunomodulatory and anti-inflammatory activity in-vitro.

Immunomodulators are natural or synthetic substances that help regulate or normalise the immune system. In-vitro studies demonstrate that tylvalosin (Aivlosin/Valosin) modulates the release of pro-inflammatory cytokines and reduces the recruitment and activation of inflammatory cells. This study also showed that tylvalosin reduces oxidative stress triggered by PRRSV. Tylvalosin also induces apoptosis and efferocytosis and promotes the secretion of pro-resolution lipid mediators (lipoxin and resolvin) that aid in tissue repair and healing.

In the most recent in-vivo study carried out in piglets challenged with Mycoplasma hyopneumoniae and PRRSV, tylvalosin (Aivlosin/Valosin) eliminated Mycoplasma hyopneumoniae lung infections and reduced both local and systemic pro-inflammatory cytokines. The researchers also noted increased serum IFNα, usually suppressed by PRRSV, in pigs treated with tylvalosin (Aivlosin/Valosin).

These findings indicate that tylvalosin (Aivlosin/Valosin) can improve pig health if used judiciously in operations with coexisting Mycoplasma hyopneumoniae and PRRSV infections.

## Key points

- The immune system is a network of complex and interlinked processes to help the animal survive in the presence of harmful pathogens.
- Some pathogens, including Mycoplasma hyopneumoniae, alter the immune response, causing inflammation-related tissue damage.
- In addition to its antimicrobial effect, immunomodulation is believed to be an important attribute of some macrolide antibiotics in improving clinical outcomes.
- In-vitro, tylvalosin (Aivlosin/Valosin) aids immunomodulation by:
  - Modulating the release of cytokines.
  - Reducing oxidative stress.
  - Modulating recruitment and activation of inflammatory cells.
  - Inducing apoptosis and efferocytosis.
  - Increasing the secretion of pro-resolution lipid mediators.
- In-vivo, tylvalosin (Aivlosin/Valosin) fights respiratory disease by:
  - Reducing Mycoplasma loads from the lungs.
  - Reducing local and systemic proinflammatory cytokines. ■

References are available from the author upon request