

### Winter Challenges: How To Reduce The Impact Of Respiratory Diseases.

Swine respiratory disease in the U.S. Midwest show seasonal trends, with higher prevalence during winter.

## Introduction

As the winter season sets in, low temperatures bring not just a chill to the air but also an increased risk of respiratory diseases in pigs. These colder conditions create an environment where common infectious agents like Swine Influenza Virus (SIV), Porcine Reproductive and Respiratory Syndrome Virus (PRRSV), and Mycoplasma hyopneumoniae (Mhp) thrive, putting pigs, most significantly post-weaning, at a heightened risk of illness and mortality. The previously mentioned pathogens trigger excessive production of reactive oxygen species (ROS), overwhelming the natural antioxidant defenses of pigs, disrupting the balance of pro-oxidants and antioxidants in the body. This oxidative stress damages cellular components, weakens the immune response, and contributes to systemic inflammation, complicating recovery. Understanding the challenges pigs face following infection enables the implementation of targeted interventions to mitigate and preserve health.

This TechTalk explores the mechanisms by which respiratory diseases trigger oxidative stress in pigs, the consequences on morbidity and mortality, and the efficacy of interventions, particularly water-soluble vitamin and micronutrients supplementation, in mitigating these effects.

# Mechanisms of oxidative stress:

After infections occur, oxidative stress is indeed a consequence of the immune response. During inflammation, immune cells release reactive oxygen species (ROS), which can lead to oxidative stress by exceeding the body's antioxidant defenses. This oxidative burst is crucial for pathogen elimination but can also damage surrounding tissues, creating a cycle of inflammation and further oxidative stress. Additionally, oxidative stress can activate signaling pathways that enhance inflammatory responses, linking the two processes tightly together. Thus, oxidative stress and immune response are interdependent mechanisms in various diseases. Research indicates that all of these agents significantly increase ROS levels in infected pigs, resulting in oxidative damage to lipids, proteins, and DNA.

## **Oxidative Stress Triggers:**

- Reactive Oxygen Species (ROS) Production: after infections cells start producing NADPH oxidase (a critical enzyme complex whose main function is to produce ROS), contributing to oxidative stress and respiratory tissues injury.
- Innate Immune Response: The respiratory infectious agents stimulate a strong innate immune response, enhancing pro-oxidation processes and increasing the expression of cytokines and interferon-stimulated genes.
- Co-Infections: Co-infection with other pathogens like Mycoplasma hyopneumoniae can exacerbate oxidative stress, leading to more severe disease outcomes.
- Gene Regulation: Infection with SIV affects genetic pathways related to immune and inflammatory responses, further promoting oxidative stress (4). Mhp infection alters the expression of genes involved in redox homeostasis and antioxidant defense, such as those regulated by the transcription factor NRF2. This response is linked to the pathogen's ability to produce hydrogen peroxide, a cytotoxic agent (5).

- Mitochondrial Dysfunction: PRRSv and Mhp enhance mitochondrial calcium uptake from the endoplasmic reticulum, resulting in mitochondrial ROS release, which exacerbates oxidative stress (6).
- Inflammatory Response: these agents induce a strong inflammatory response, further contributing to oxidative stress and tissue damage (10).

## **Vitamins Roles:**

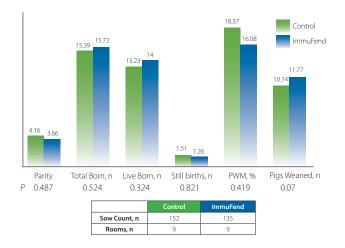
Vitamins A, C, D and E help neutralize ROS, protect cell membranes, and maintain immune function. During viral infections or bacterial challenges like Mhp, supplementing sows and pigs with antioxidants enhances their ability to respond to pathogens effectively. Benefits include improved immune response, reduced inflammation, faster recovery, reduction of mortality rates, improvement of feed efficiency, and shortening of recovery times.

- <u>Vitamin A</u> plays a significant role in respiratory health, particularly maintaining the integrity of the respiratory epithelium and supporting immune function.
- <u>Vitamin C</u> acts as an antioxidant protecting against inflammation.
- <u>Vitamin D</u> supports immune cell function and reduces respiratory infection, combined with Zinc, it enhances immune response and may reduce the duration of clinical signs.
- <u>Vitamin E</u> has demonstrated efficacy in reducing oxidative damage and improving recovery from viral infections like SIV and PRRS.

## **Timely Interventions:**

Combating oxidative stress is key to improving pig health and survival.

ImmuFend<sup>®</sup> is a specific combination of water-soluble vitamins and micronutrients. Such a combination can enhance the effect of individual ingredients through a concept known as nutrient synergy, which occurs when nutrients work together to improve absorption and effectiveness, resulting in greater health benefits than when consumed alone. Nutrient synergy, where vitamins and minerals work together, can enhance benefits such as improved immune functions, reducing post weaning mortality.

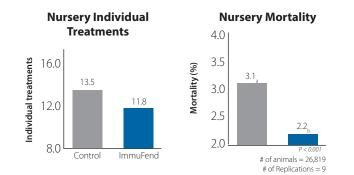


#### **Prevention in Breeding Herds:**

Sows supplemented with ImmuFend had an improvement on key performance indicators such as pigs born alive, stillbirths, preweaning mortality and pigs weaned per sow.

#### Intervention During Outbreaks:

Timing interventions a few days before the anticipated highest incidence of clinical signs, should have a positive impact. A strategic, cost-effective solution lies in supplementing with ImmuFend. the best moment to deliver it thru the water would be immediately after weaning. This timing aligns with the onset of respiratory symptoms, the decline in maternal antibodies, and the different additive stress factors associated with weaning. This early intervention can help bolster the pigs' antioxidant defenses, potentially reducing the severity of respiratory diseases and improving overall health outcomes.



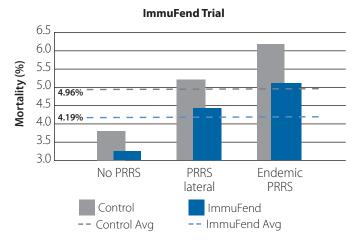
In a study at a large Midwest swine producer, weaned pigs, approximately 20 days old were given ImmuFend immediately after placement. ImmuFend was administered for at least 5 days. A reduction in mortality was demonstrated (P < 0.001).

#### **Nutritional Support in Nurseries and Grow-Finish**

Ongoing antioxidant supplementation minimizes the impact of chronic stressors like subclinical infections or environmental challenges. If pigs are challenged with SIV and/or Mhp two weeks after weaning, it would be optimal to deliver antioxidants in the water starting around one week after weaning. This timing allows the antioxidants to potentially mitigate oxidative stress before the challenge occurs. Administering antioxidants prior to the expected challenge can help enhance the pigs' antioxidant defenses, potentially reducing the impact of oxidative stress associated with Mhp infection. This approach aligns with strategies that aim to prepare pigs for anticipated stressors and infections.

#### **Cost-Effectiveness**

In a study involving 141,045 pigs conducted by a large Midwest swine production system, ImmuFend demonstrated an overall reduction in nursery mortality from 4.96 to 4.19% -- a 15.5% decrease (*P* < 0.0001)



The cost of ImmuFend supplementation is minimal compared to the potential losses incurred from disease outbreaks. The ROI from the previous mentioned studies were between 4.03:1 and 6.51:1 in PRRS flow vs non PRRS flow systems.

## **Conclusion:**

Respiratory challenges in swine herds demand a proactive approach to health management. By addressing oxidative stress with strategic interventions, like ImmuFend, producers can mitigate the devastating effects of viral and bacterial pathogens, especially during the cold weather, safeguarding herd performance and profitability.

#### References

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4. Ramos Gonzalez et al. Neurología 39 (2024) 292-301. 5. Kunst et al 2023.



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<sup>1.</sup> Deblanc et al. (2013). Veterinary Microbiology 162 (2013) 643-65 Pre-infection of pigs with Mycoplasma hyopneumoniae induces oxidative stress that influences outcomes of a subsequent infection with a swine influenza virus of H1N1 subtype

<sup>2.</sup> Sgarbanti et al. Current Topics in Medicinal Chemistry, 2014, Vol. 14, No. 22. Intracellular Redox State as Target for Anti-Influenza Therapy