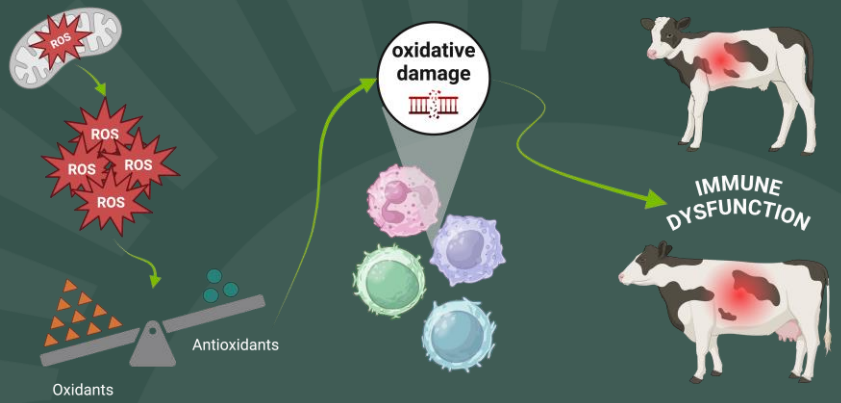
MICHIGAN STATE UNIVERSITY | College of Veterinary Medicine

ABUELO LAB
dairy health | immunology | epidemiology



Mastering Redox Balance for Herd Health

Angel Abuelo DVM, MRes, MS(VetEd), Ph.D.

Diplomate, American Board of Veterinary Practitioners (Dairy Practice)
Diplomate, European College of Bovine Health Management
Associate Diplomate, American College of Veterinary Internal Medicine – Large Animal

VIP SEMINAR

ADISSEO
A Bluestar Company

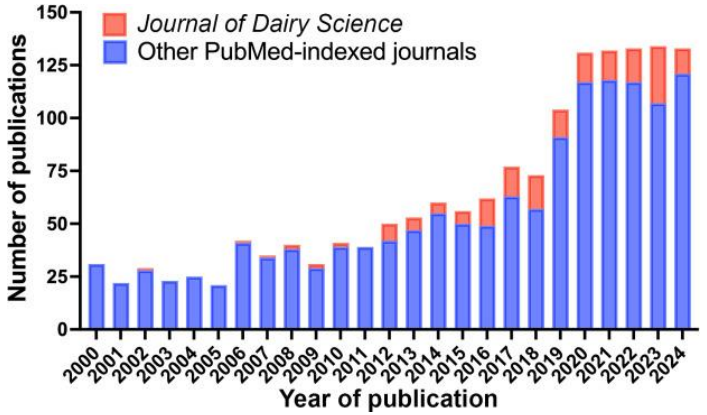
Future-Ready Dairy
From Scientific Insights to Impactful Solutions

Oxidative Stress and Implications for Health

Oxidative Stress

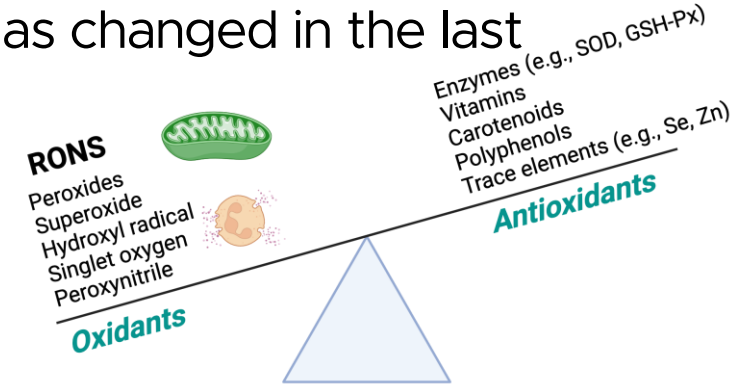
Definition

- Relatively new field in Dairy Science



Abuelo, 2025

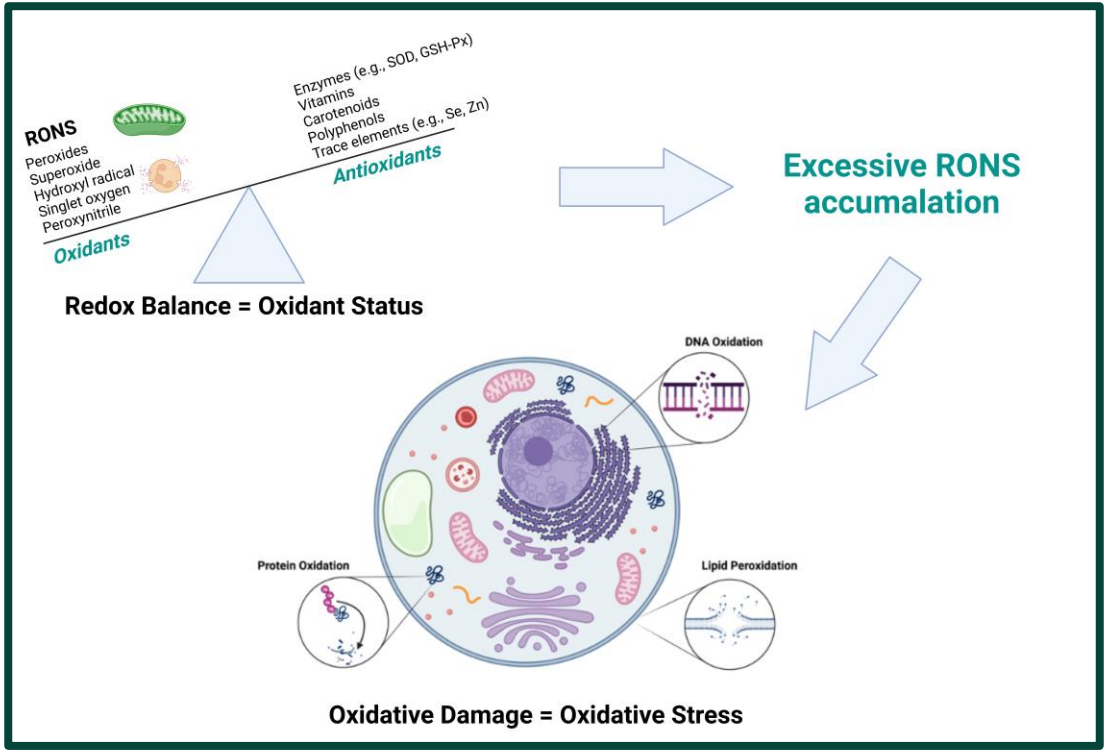
- Definition has changed in the last decades



Redox Balance or Oxidant Status

Oxidative Stress

Definition



Oxidative Stress

Oxidative Stress vs. Oxidant Status

Oxidant Status ≠ Oxidative Stress

- Oxidative damage results from shifts in oxidant status
  - Not all shifts in redox balance result in OS
  - Some ROS are needed for essential functions (e.g., redox signaling)
  - Changes in oxidant status might reflect changes in redox signaling not associated with cell/tissue dysfunction

BIOMARKERS

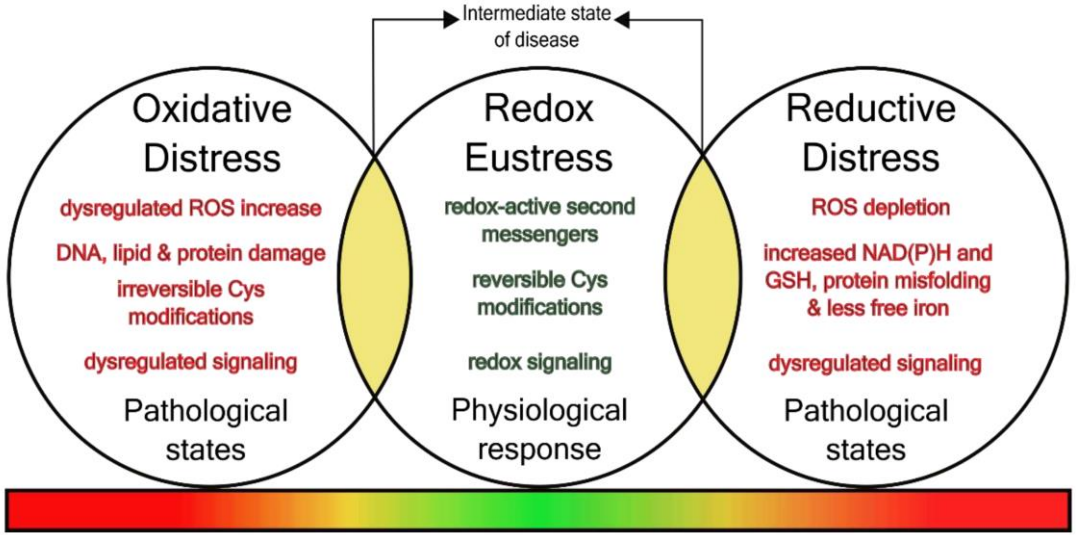
Oxidant Status	Oxidative Stress
ROS/RNS	Isoprostanes
dROMs	Oxylipids
Total antioxidant capacity (TAC)	Advanced oxidation protein products (AOPP)
Individual antioxidants *(not full picture)*	8-Oxo-2′-deoxyguanosine
Oxidant Status index (ROS/TAC)	MDA/TBARS *(insensitive)*

Oxidative Stress

Oxidative Stress vs. Oxidant Status

Oxidant Status ≠ Oxidative Stress

- Excessive antioxidant supply can also lead to stress



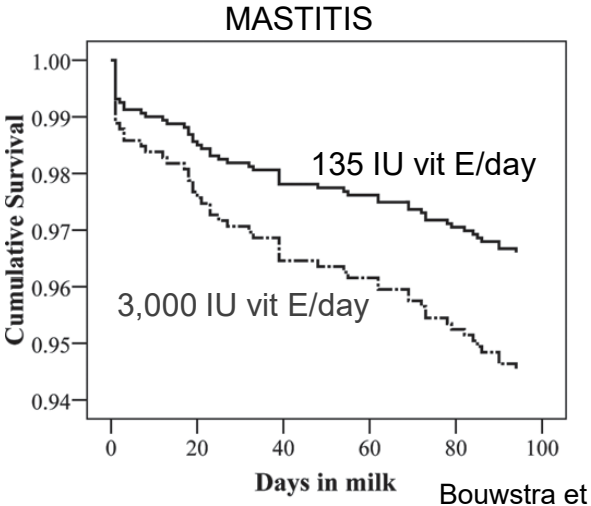
Palacio et al. 2022

Oxidative Stress

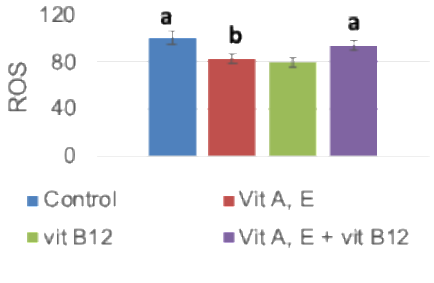
Oxidative Stress vs. Oxidant Status

Oxidant Status ≠ Oxidative Stress

- Excessive antioxidant supply can also lead to stress



Bouwstra et al., 2010



Data from Rizzo et al., 2013

Parenteral supplementation in addition to premix

Oxidative Stress

Advancing Quantification in Dairy Science

- Recommendations:
  - For redox balance, measure both components of the balance

Animal (2013), 7:8, pp 1374–1378 © The Animal Consortium 2013
doi:10.1017/S1751731113000396

animal

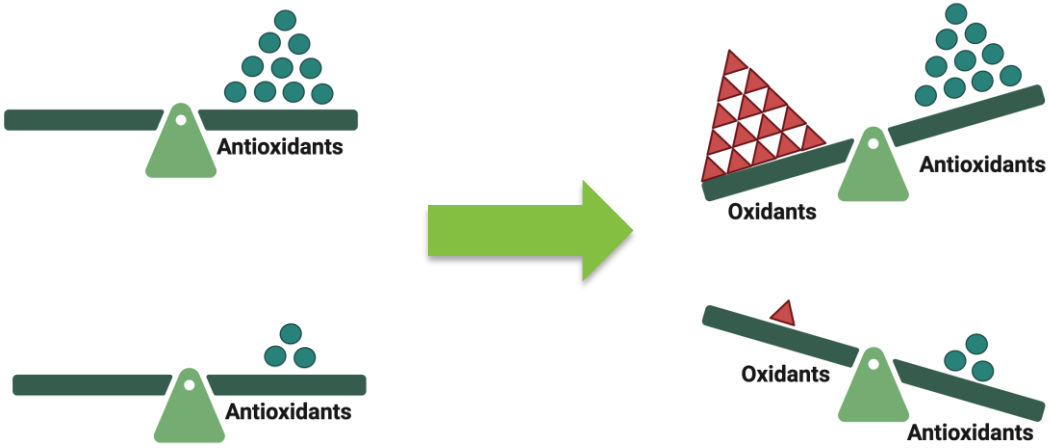
Really oxidant status...

Oxidative stress index (OSi) as a new tool to assess redox status in dairy cattle during the transition period

A. Abuelo†, J. Hernández, J. L. Benedito and C. Castillo

Department of Animal Pathology, College of Veterinary Medicine, University of Santiago de Compostela, Campus Universitario, s/n – 27002 Lugo, Spain

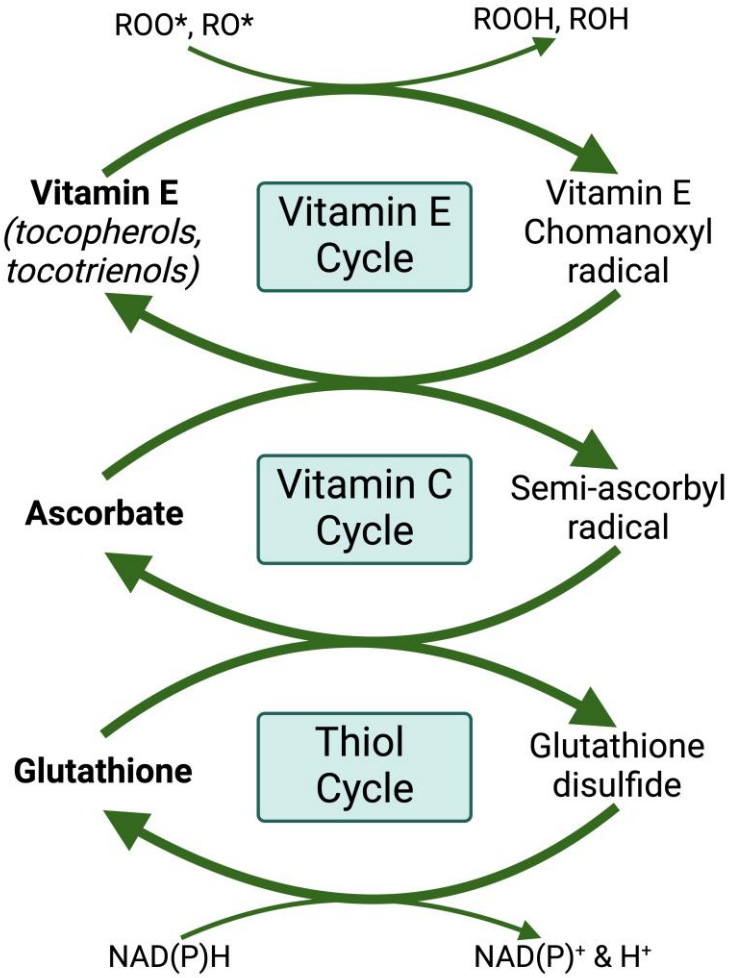
OSi = Oxidants / Antioxidants



Oxidative Stress

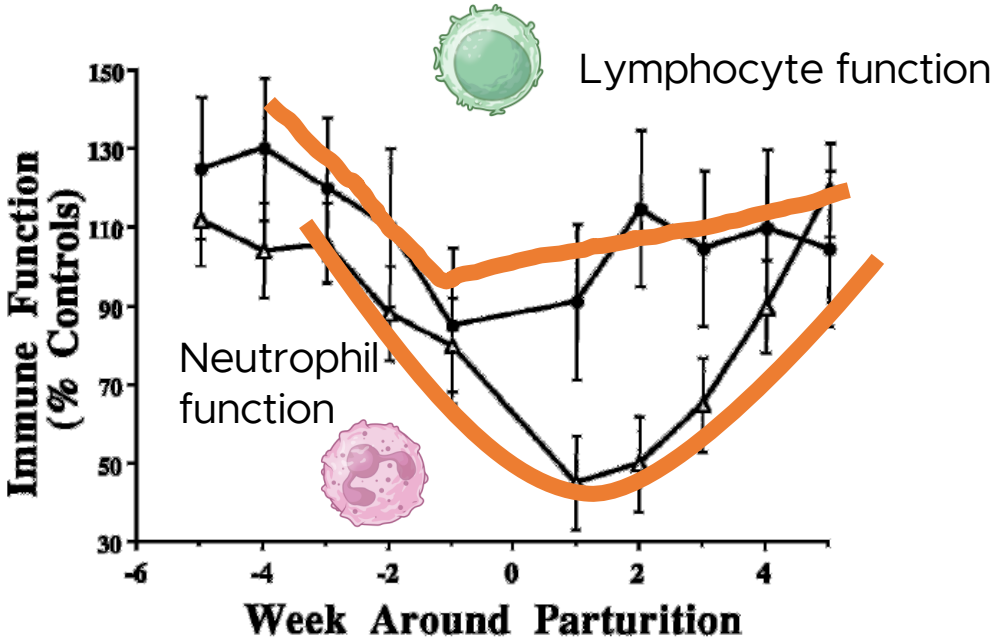
Advancing Quantification in Dairy Science

- Recommendations:
  - For redox balance, measure both components of the balance
  - Measuring single antioxidants does not capture the whole picture



Periparturient Cows

Immune dysfunction



Goff & Horst. J. Dairy Sci., 1997. 80(7): p. 1260-1268.

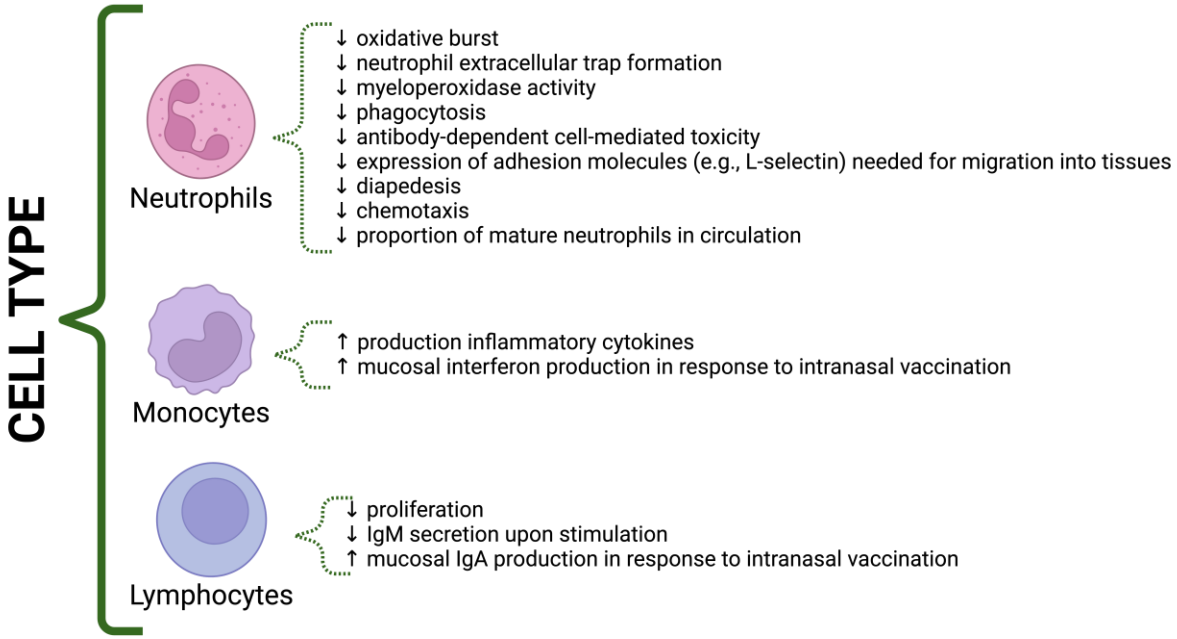
Periparturient Cows

Immune dysfunction

Metabolic Factors at the Crossroads of Periparturient Immunity and Inflammation

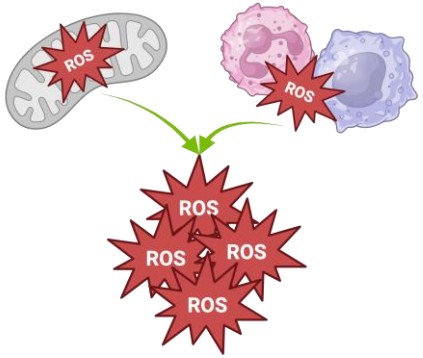
Angel Abuelo, DVM, MRes, MS (Vet Educ), PhD, Dip. DABVP (Dairy Practice), Dip. ECBHM, MRCVS[a],
Sabine Mann, Dr. med. vet., PhD, Dip. ACVPM (Epidemiology), Dip. ECBHM[b,*],
Genaro Andres Contreras, DVM, MS, PhD[a]

Functional Changes

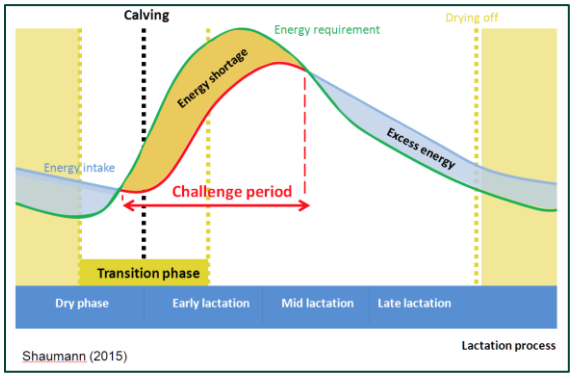


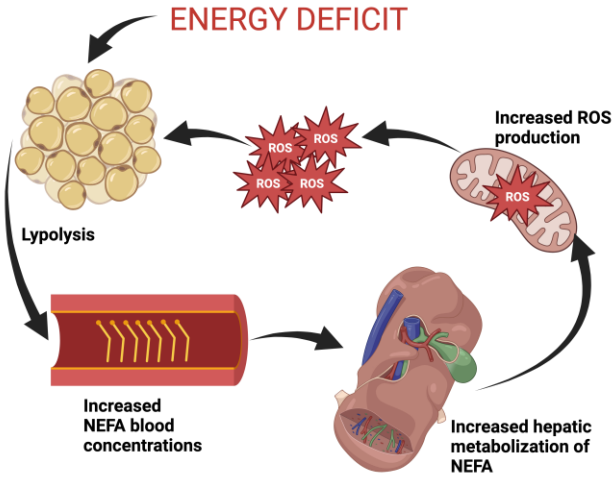
Periparturient Cows

Origin of Oxidative Stress



- Decreased DMI → ↓ antioxidant intake
- Increased metabolic demands → ↑ ROS production
- Increased innate immune responses → ↑ ROS production

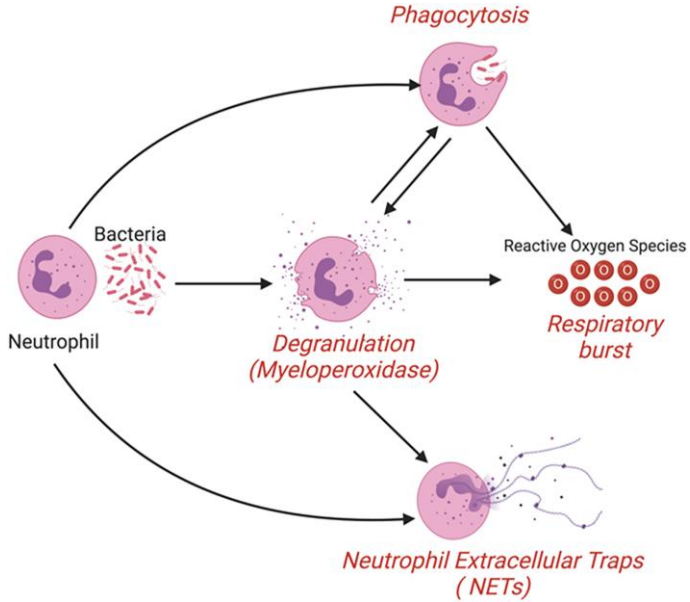




Oxidative Stress and Immune Function

Innate Immunity

- The redox status can alter the immune response at the site of infection
  - Generation of ROS is a pathogen-killing mechanism of phagocytes
    - Excessive ROS accumulation decreases phagocytosis



Oxidative Stress diminishes the functional capabilities of immune cells

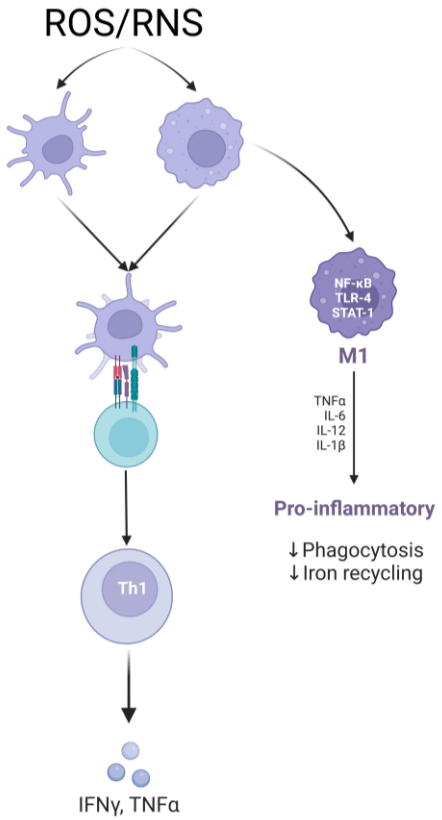
Oxidative Stress and Immune Function

Innate Immunity

ROS can activate antigen-presenting cells

Th1 biased response

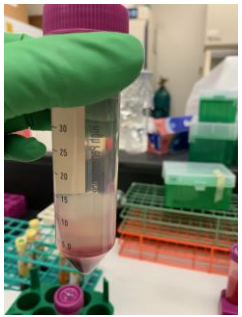
PRO-INFLAMMATORY RESPONSE



Oxidative Stress and Immune Function

Adaptive Immunity

n=6 (3-4d)



12 h

37 C
5% CO_2

- Control (Media)
- AAPH (3 m*M*)
- PMA
- BHV-1
- PMA + AAPH
- BHV-1 + AAPH

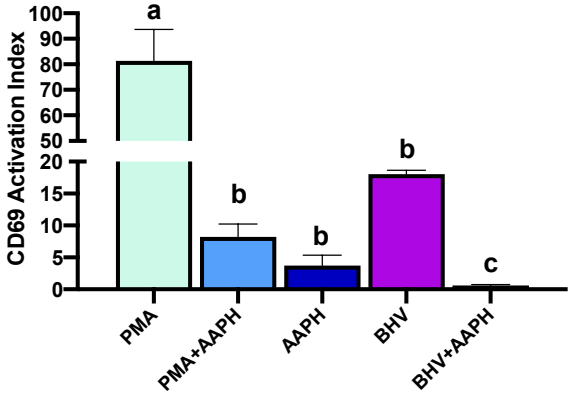
- Lymphocyte activation
- Antigen-specific antibody production
- Cytokine expression

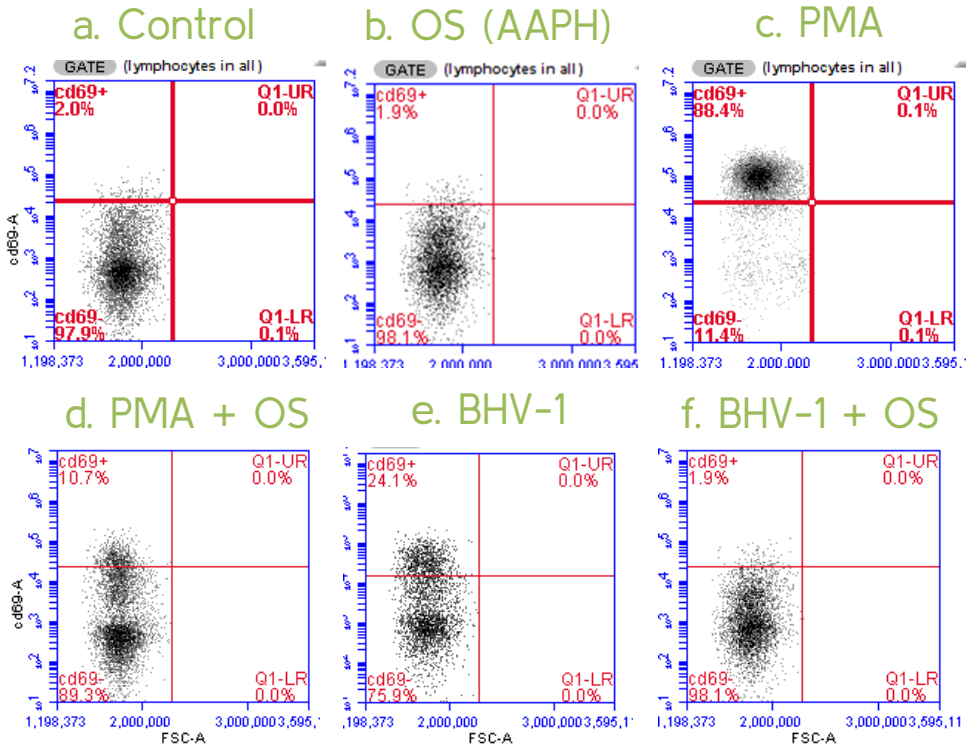
AAPH = 2,2'-Azobis(2-amidinopropane) dihydrochloride
PMA = Phorbol 12-myristate 13-acetate
BHV-1 = Bovine herpesvirus 1

Oxidative Stress and Immune Function

Adaptive Immunity

- *Lymphocyte activation*
  - *CD69 expression*





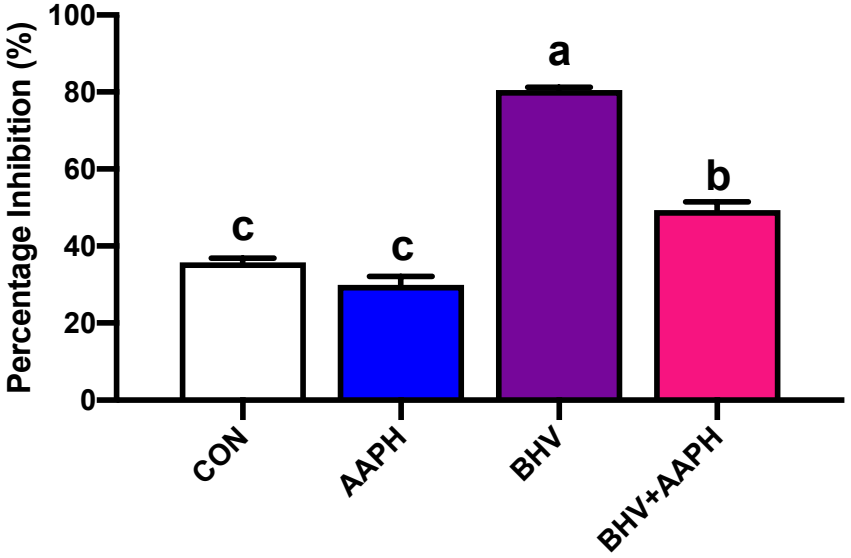
Cuervo et al. 2021

Oxidative Stress and Immune Function

Adaptive Immunity

- *Antibody production*
  - *Anti-BHV-1 IgG ELISA*

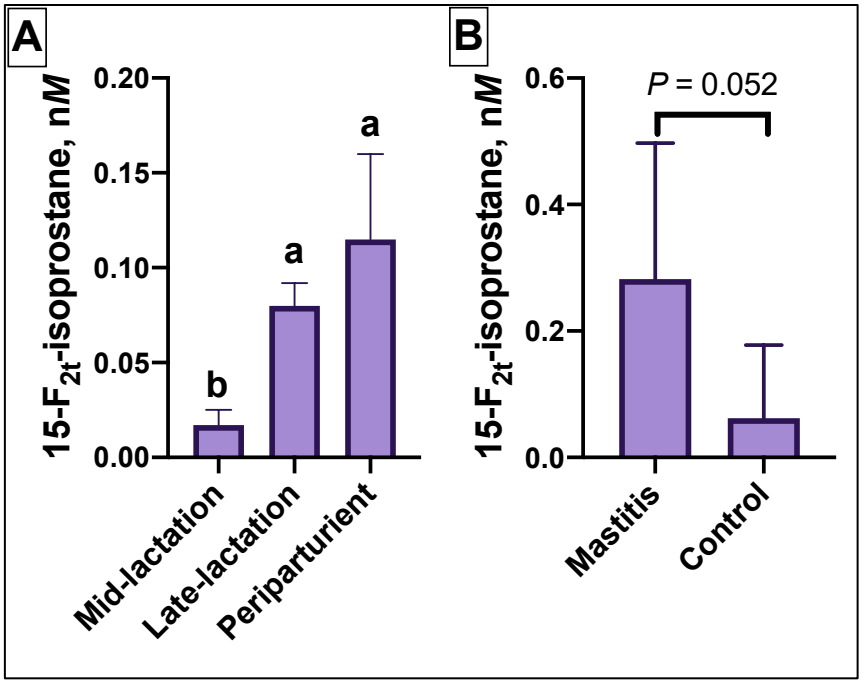
Oxidative Stress compromises critical lymphocyte functions



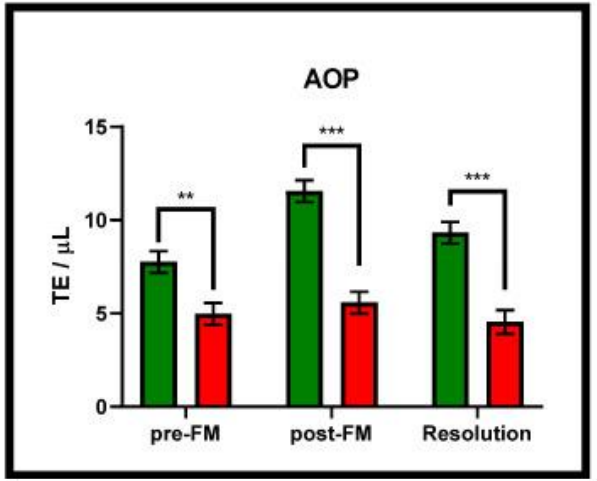
Cuervo et al. 2021

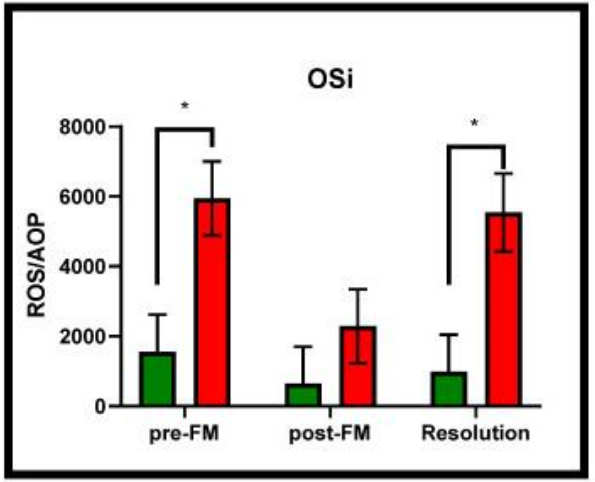
Oxidative Stress Changes

Lactation stage & Disease status



Mavangira et al., 2016; Kuhn et al., 2018



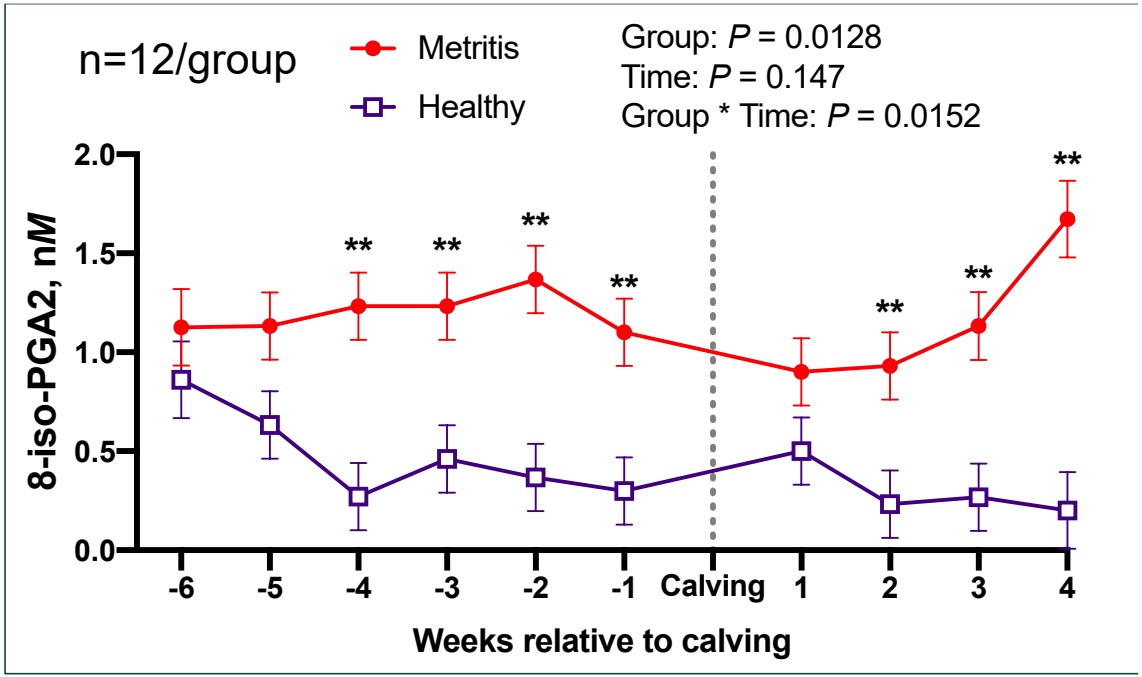


Green = survived
Red= Died or Euthanized

Walker et al., 2022

Oxidative Stress Changes

Oxidative Stress Biomarkers as Disease Predictors



- Critical cut-off points are still lacking! (on-going work)

Oxidative Stress Changes

Oxidative Stress Biomarkers as Immune Modulators

Contents lists available at ScienceDirect

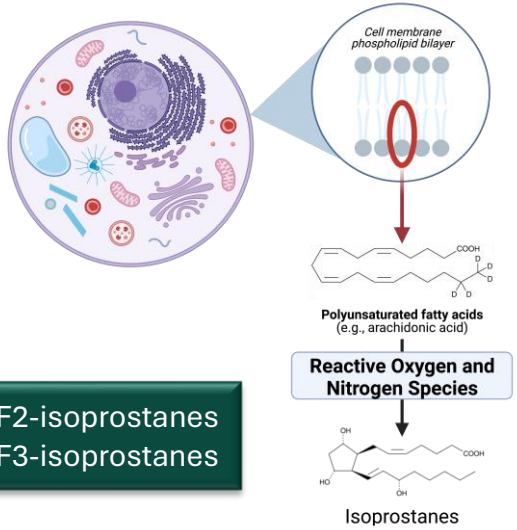
Developmental and Comparative Immunology

journal homepage: www.elsevier.com/locate/devcompimm

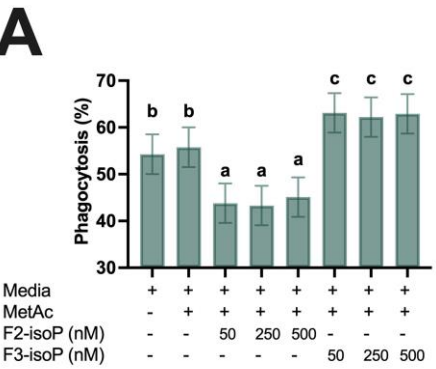
Effect of F-isoprostane class on cow peripheral blood neutrophil microbicidal function in vitro

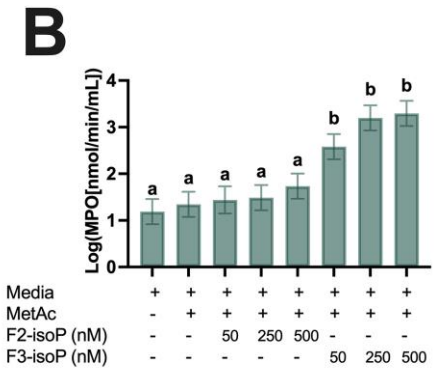
Eric J. Owczarzak, Angel Abuelo*

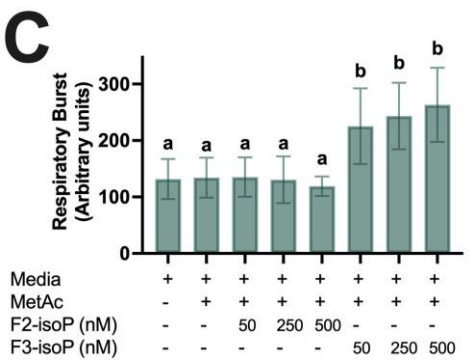
Department of Large Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI, USA

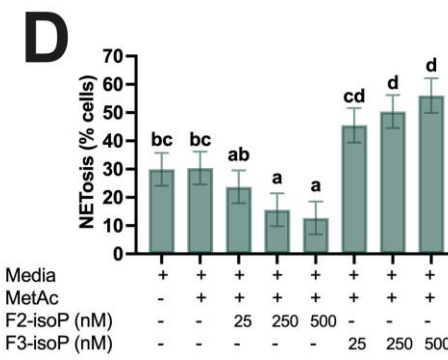


ω-6 → F2-isoprostanes
ω-3 → F3-isoprostanes





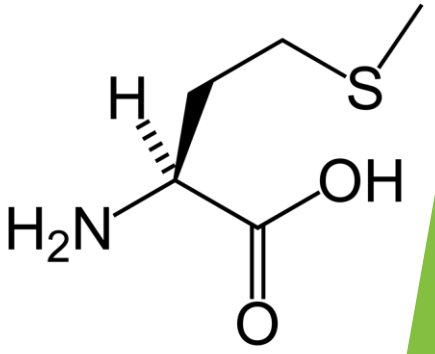




Methionine as an Antioxidant

Methionine

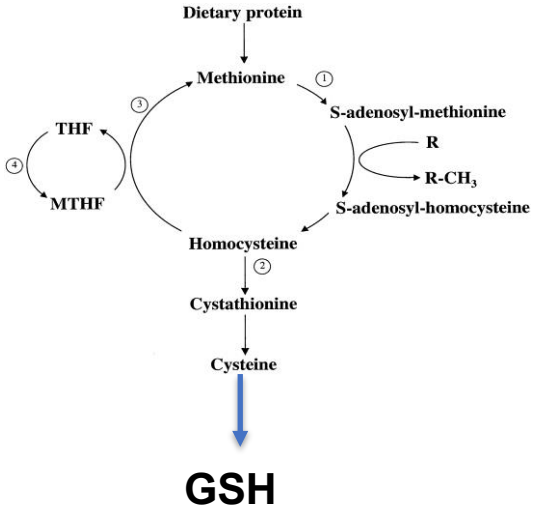
What is Methionine?



- **Essential amino acid**
  - First-limiting amino acid in many dairy rations
- **Precursor for key molecules**
  - cysteine, taurine, glutathione (ANTIOXIDANT)
- **Involved in methylation reactions** (DNA, protein synthesis)

Methionine

Methionine as an Antioxidant



DIRECT ROS SCAVENGING

ROS

Methionine neutralizes reactive oxygen species (ROS) by being oxidized to methionine sulfoxide (MetO), protecting vital protein regions.

INDIRECT ANTIOXIDANT SYNTHESIS

Cys GSH

Serves as a precursor for cysteine and glutathione (GSH), a key antioxidant in cellular redox balance

PROTEIN REGULATION

Met MetO

Reversible Met/MetO cycling acts as a redox-sensitive switch to modulate protein function under oxidative stress

Methionine & Immunity

Antioxidant Defense and Immunity

Glutathione Synthesis Boost

Methionine promotes synthesis of glutathione, enhancing the antioxidant defense in dairy cows.

Reduction of Oxidative Stress

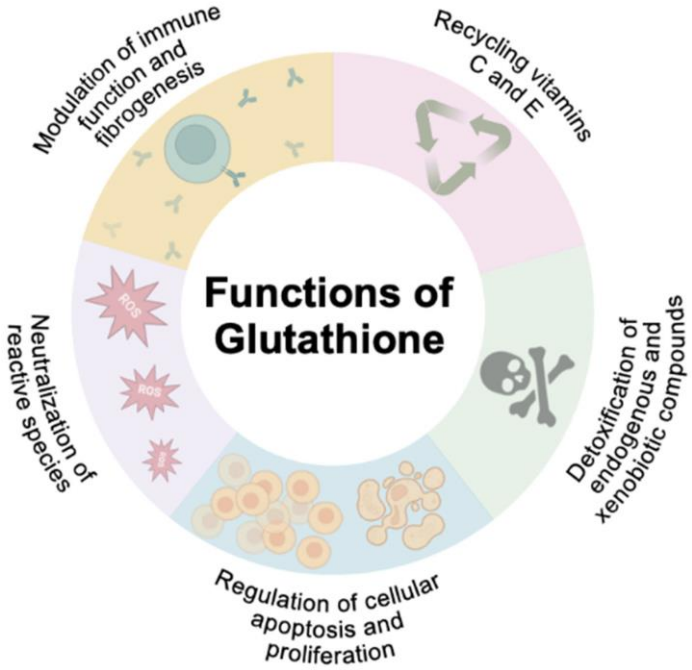
Increased glutathione neutralizes ROS, reducing OS and inflammation.

Lower Inflammatory Markers

Methionine supplementation lowers inflammatory markers like TNF and IL-6 in transition cows.

Improved T-Cell Ratio

Methionine improves CD4+/CD8+ T-cell ratio, indicating a robust adaptive immune response in cows.



Methionine

Documented Effects of Met Supplementation

Increased Milk Yield & Quality

Adequate methionine boosts milk protein and fat levels, enhancing overall product value.

Improved Metabolic Health

Supports optimal liver function and overall metabolic efficiency.

Better Nitrogen Utilization

Enables lower-protein diets, cutting nitrogen waste and reducing environmental impact.

Stronger Immune Defense

Promotes antioxidant production (e.g., glutathione) to lower stress and improve immunity.

Enhanced Fertility

Balanced nutrition with methionine supports reproductive success and herd productivity.

Selenium and Vitamin E

Prevention of Oxidative Stress and Implications for Health

Selenium and Vit. E

Mechanisms of Action and Synergy

Vitamin E Antioxidant Role

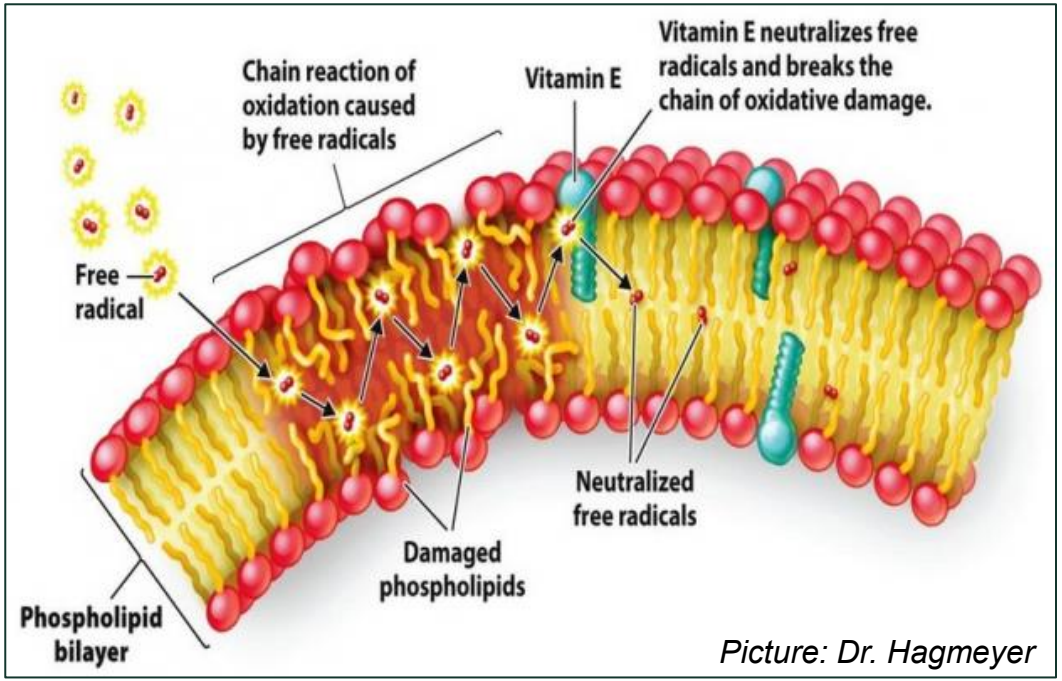
Neutralizes free radicals and protects cell membranes from lipid peroxidation in dairy cattle.

Selenium Detoxification Function

Crucial for selenoproteins that detoxify hydrogen peroxide and lipid peroxides inside cells.

Synergistic Antioxidant Effect

Together, vitamin E and selenium enhance the management of oxidative stress and support immune function in cattle.

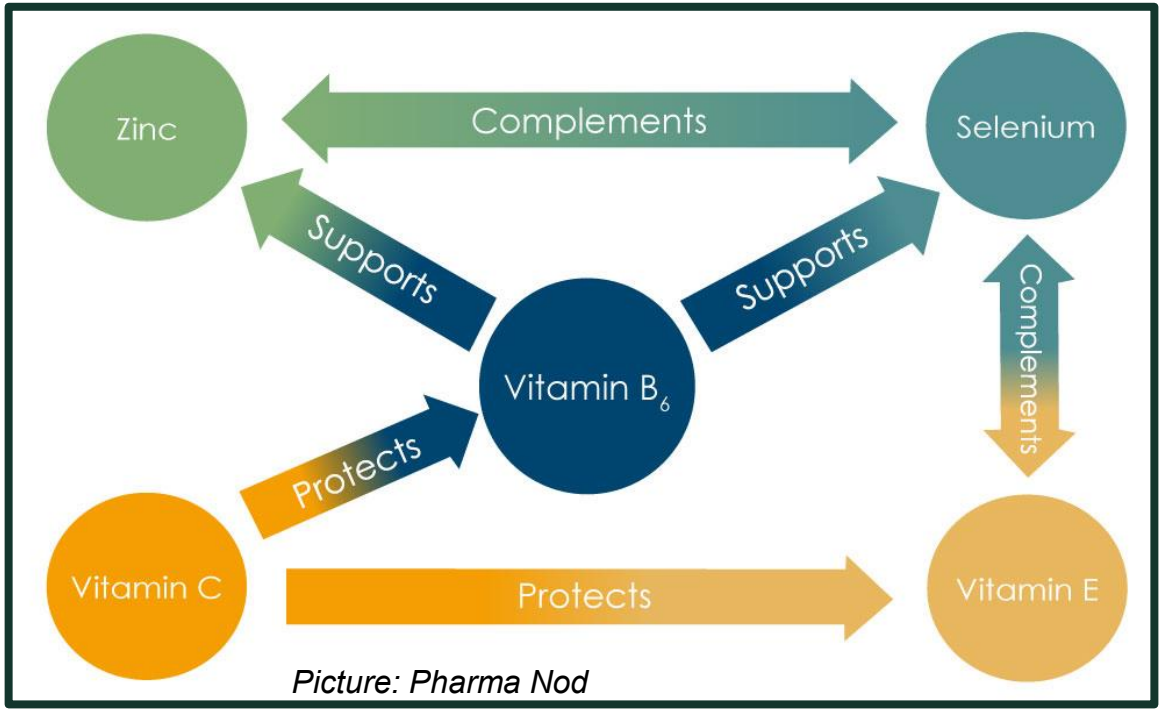


Picture: Dr. Hagmeyer

Selenium and Vit. E

Mechanisms of Action and Synergy

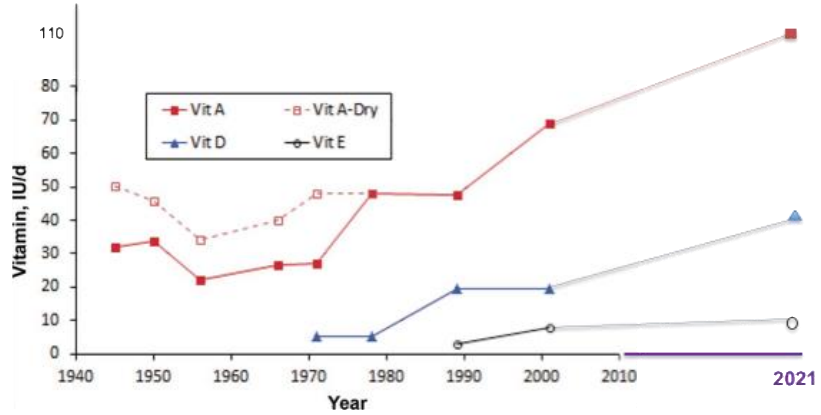
Multiple antioxidants are needed for optimal antioxidant function, given their networks



Picture: Pharma Nod

Selenium and Vit. E

NCR/NASEM Recommendations



Modified from Weiss, *J Dairy Sci* **2017**, *100*, 10045-10060

- Traditionally developed to prevent deficiencies or toxicosis
- Research has shown benefits at higher supplementation rates
- Typical diets 1.5 – 2.5 x NRC

Selenium and Vit. E

Immune Function Enhancement

Neutrophil Activity Enhancement

Vitamin E and selenium enhance neutrophil function, crucial for combating mastitis/metritis pathogens in dairy cattle.

Antioxidant Support Mechanisms

Vitamin E maintains neutrophil membrane integrity; selenium promotes GSH-Px activity for detoxification.

Reduced Inflammatory Markers

Supplementation lowers pro-inflammatory markers like IL-1β, IL-6, and haptoglobin in dairy cattle.

Elevated Antioxidant Enzymes

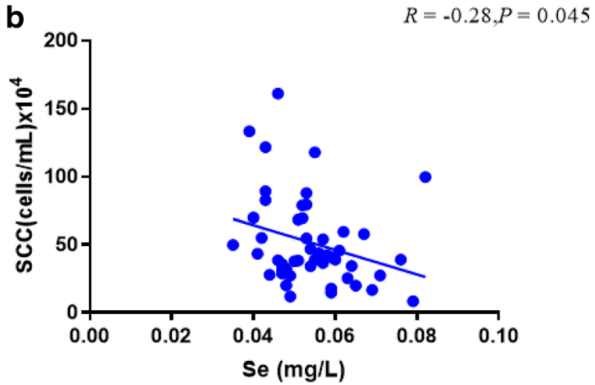
Increased levels of GSH-Px and superoxide dismutase enhance oxidative resilience in cattle.

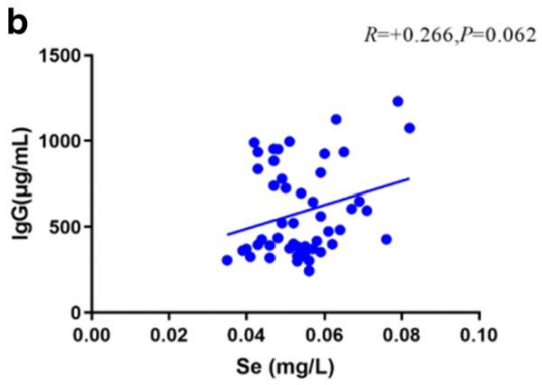
Selenium and Vit. E

Disease Reduction and Economic Benefits

Disease Reduction in Dairy Cattle

Vitamin E and selenium supplementation reduces mastitis, metritis, and ketosis in dairy cows by boosting immunity.





Wang et al., 2020

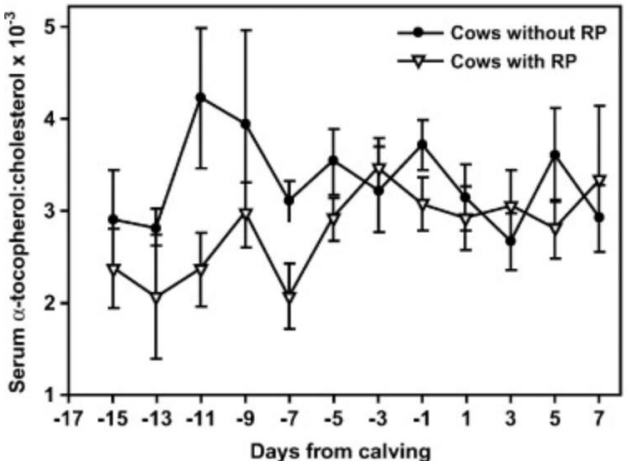
Selenium and Vit. E

Disease Reduction and Economic Benefits

Disease Reduction in Dairy Cattle

Vitamin E and selenium supplementation reduces mastitis, metritis, and ketosis in dairy cows by boosting immunity.

An increase in serum α-tocopherol of 1 μg/mL in the last week prepartum reduced the risk of retained placenta by 20%



LeBlanc et al., 2004

Selenium and Vit. E

Disease Reduction and Economic Benefits

Disease Reduction in Dairy Cattle

Vitamin E and selenium supplementation reduces mastitis, metritis, and ketosis in dairy cows by boosting immunity.

Improved Productivity

Supplemented cows exhibit increased milk yield and better reproductive performance, enhancing overall herd productivity.

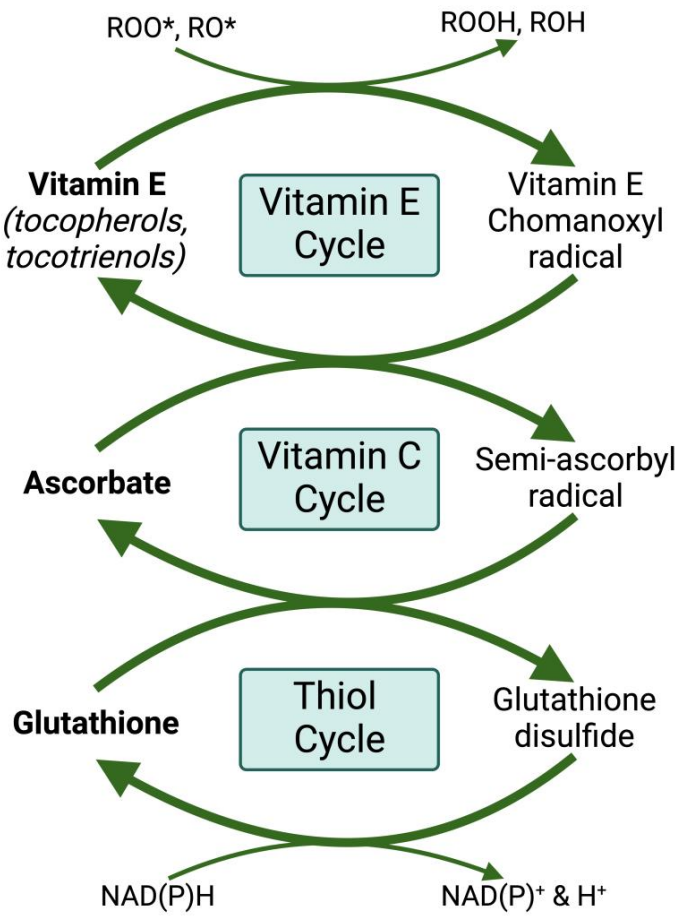
Economic Benefits

The cost of supplementation is offset by higher productivity and reduced veterinary expenses, thereby improving farm profitability.

Selenium and Vit. E

Practical Considerations

- Selenium amount in the diet is restricted to 0.3 ppm (FDA)
  - *Prevention of Se toxicity*
- Need to consider the “synergistic” effect of antioxidants to leverage potential
- Glutathione (made of Methionine) can increase vitamin E effects via recycling pathways



Conclusions (I)

- **Oxidative stress (OS) negatively impacts the innate and adaptive immune responses of transition cattle.**
  - *Links to disease susceptibility and severity*

- **Antioxidant supplementation can ameliorate OS and improve health outcomes.**
  - *Excessive supplementation could be detrimental*

Conclusions (II)

- **Methionine, an essential amino acid, also acts as an antioxidant.**

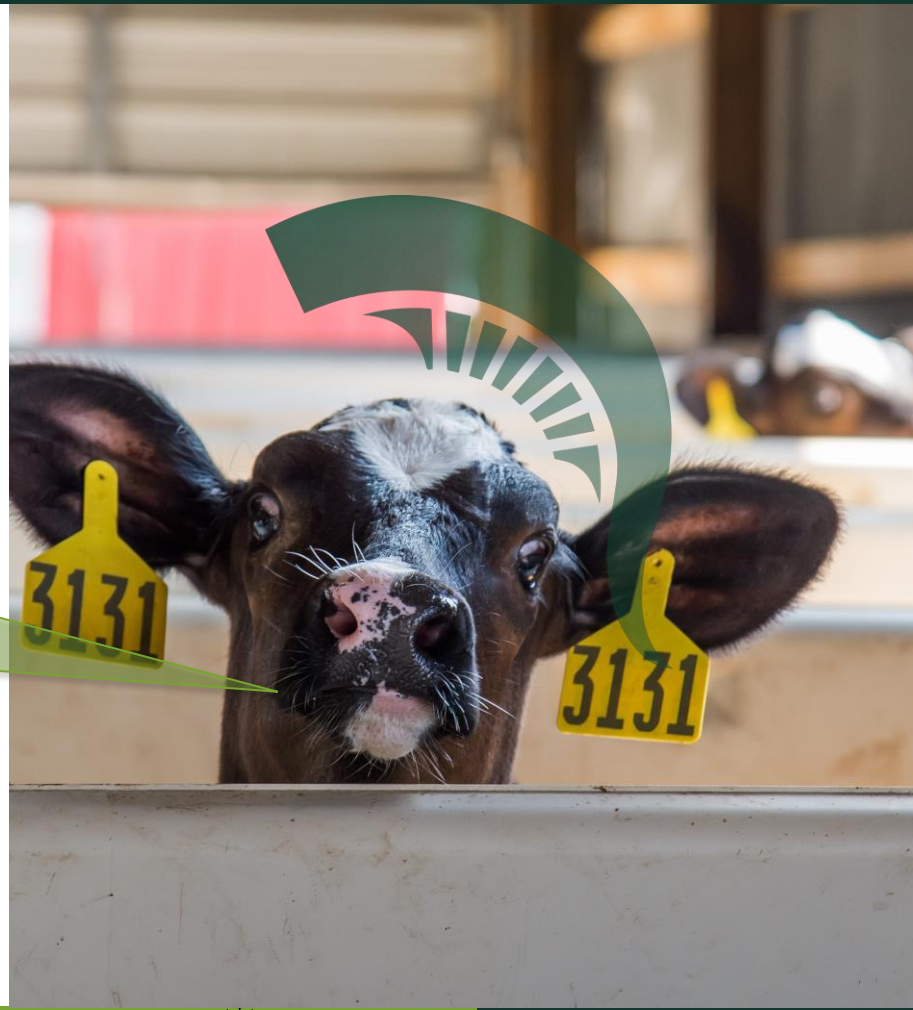
- **Vitamin E & Se are the most commonly used antioxidants in cattle diets**
  - *Documented effects on health and productivity*
  - *The synergistic action of antioxidants cannot be overlooked*

Acknowledgments

My team

Thank you!

Questions?



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