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How Oxidative Stress Drives Hormonal Imbalance, Immune Dysfunction & Inflammation

Lacy Campbell, ND

April 29, 2026

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- **PGY-1:** A Woman's Time, NERC
- **Bio:** I am a first-year naturopathic resident at A Woman's Time in Portland, Oregon, training under the mentorship of Dr. Tori Hudson. Before entering medicine, I worked in zoological animal husbandry and wildlife rehabilitation, a foundation that informs my unique clinical lens rooted in evolutionary medicine, paleopathology, and a One Health framework. I am passionate about translating complex science into practical, patient-centered care and helping individuals feel empowered and at home in their bodies.

The background of the image is a dark, monochromatic marbled paper pattern. It features intricate, swirling, and cellular-like textures in shades of charcoal, black, and dark grey. The patterns resemble organic forms, possibly resembling marbled paper or a microscopic view of certain materials. The overall effect is dense and textured.

Introduction

Why Should We Care About Oxidative Stress?



A dark, grayscale microscopic image of tissue, likely showing cellular structures and possibly some pathological changes. The image is heavily textured with various shades of gray, black, and white, suggesting a complex biological structure. The text "Understanding Oxidative Stress" is overlaid in white, sans-serif font on the left side of the image.

Understanding Oxidative Stress

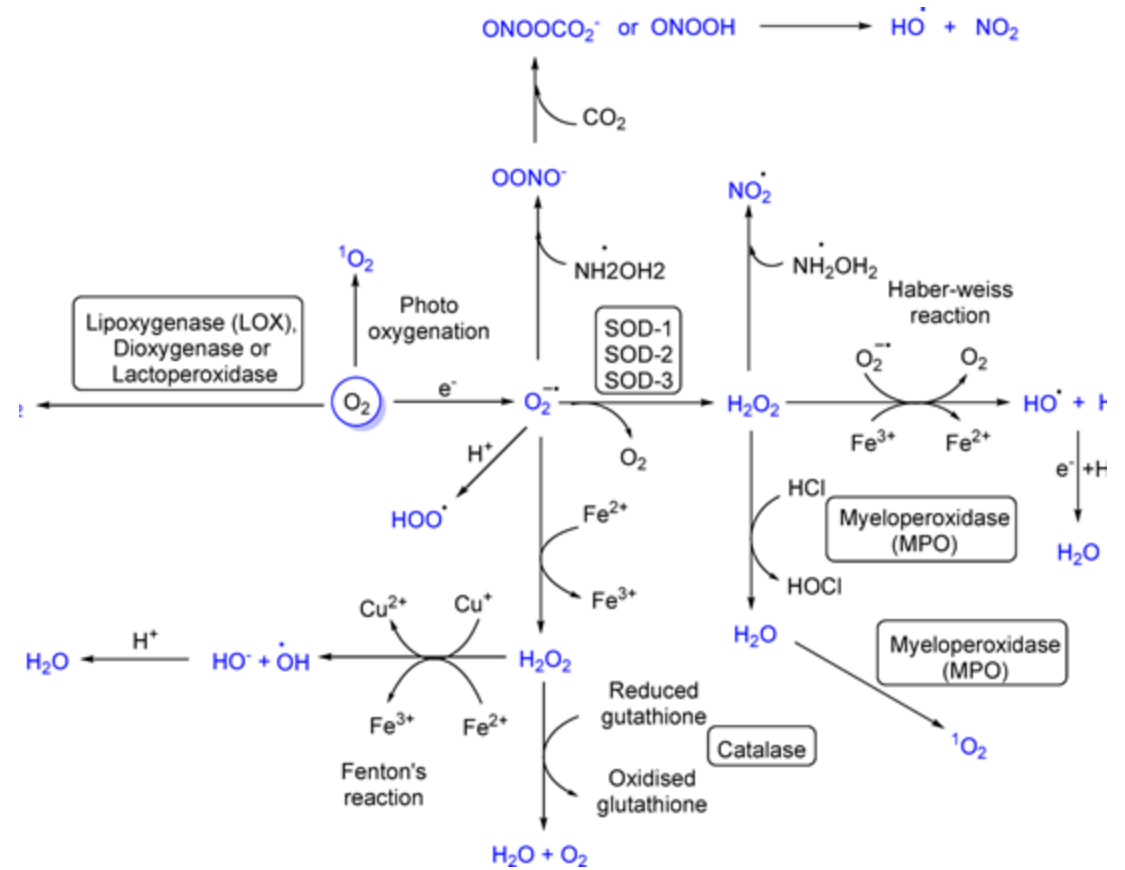
Reactive Oxygen Species (ROS)

Generated through:

- Mitochondrial Respiration
- Immune Activation
- Cellular Metabolism

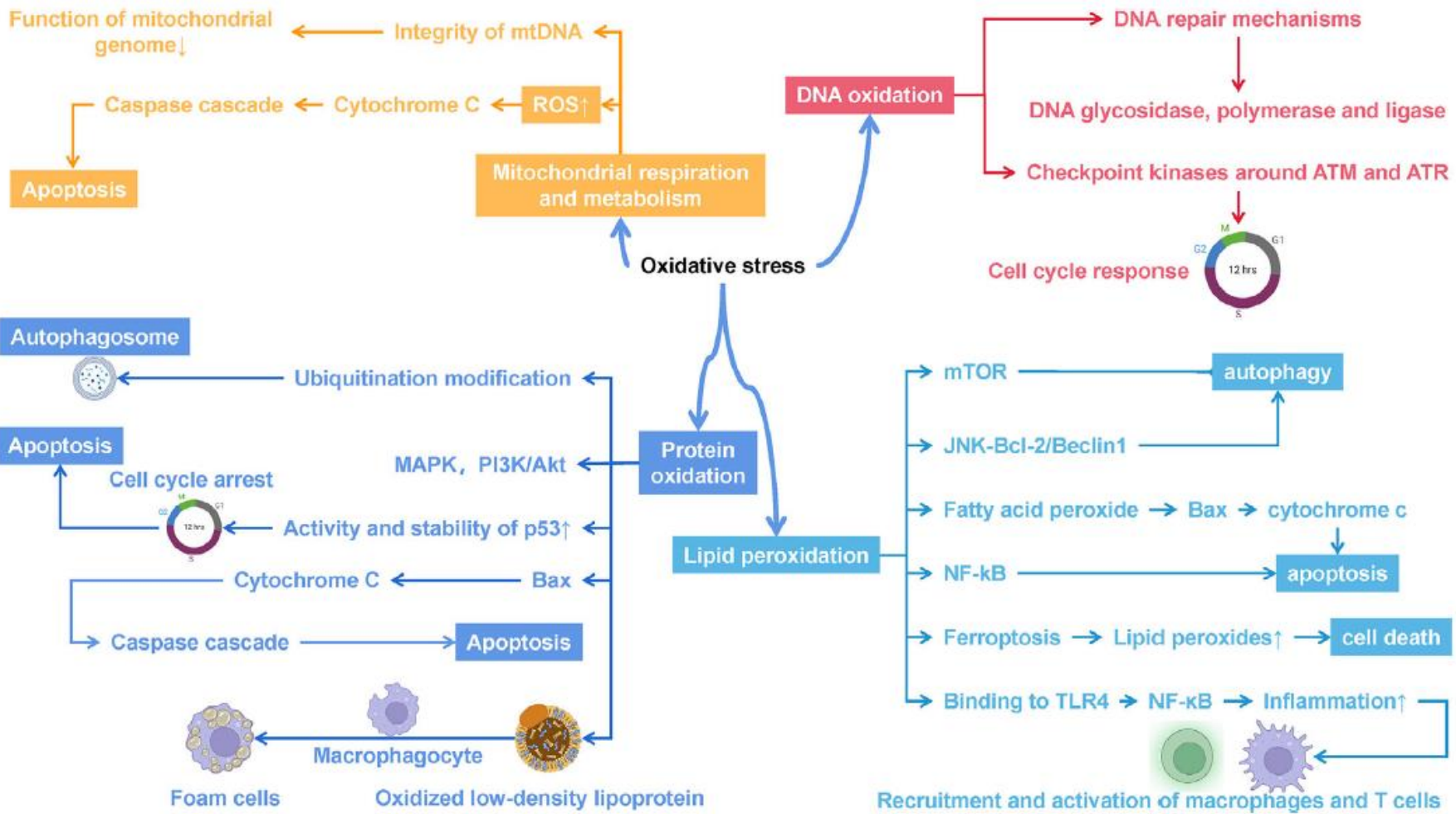
Primary use as signaling molecules

If ROS \gg antioxidant systems = cell damage



Liu S, Liu J, Wang Y, Deng F, Deng Z. Oxidative Stress: Signaling Pathways, Biological Functions, and Disease. MedComm (2020). 2025;6(7):e70268. Published 2025 Jul 1. doi:10.1002/mco2.70268

How We Accumulate Excess ROS

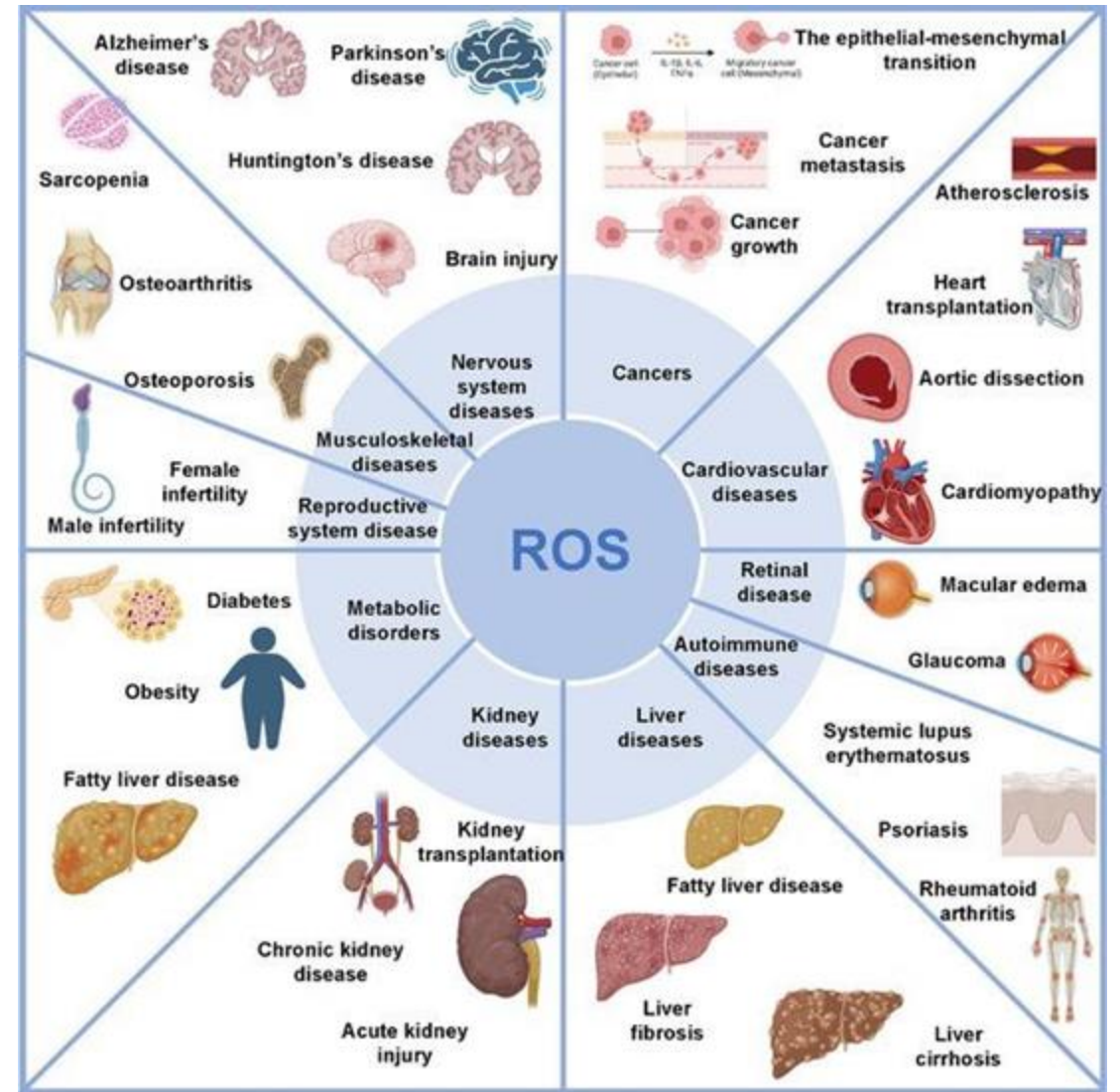


This figure was created with BioRender (<https://biorender.com/>).
 Liu S, Liu J, Wang Y, Deng F, Deng Z. Oxidative Stress: Signaling Pathways, Biological Functions, and Disease. MedComm (2020). 2025;6(7):e70268. Published 2025 Jul 1. doi:10.1002/mco2.70268

ROS-Related Conditions

ROS dysfunction is implicated in:

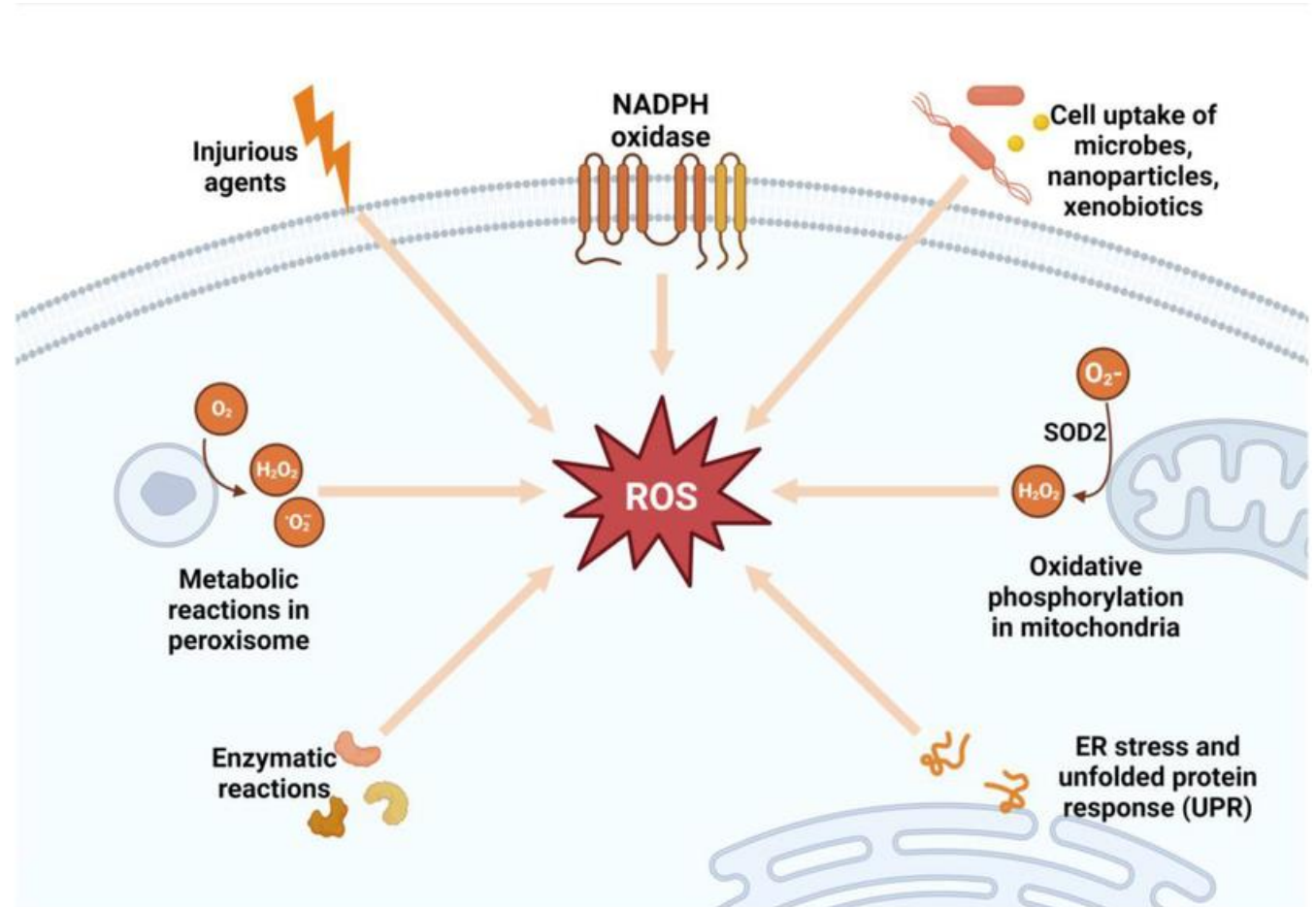
- Cancers
- Cardiovascular diseases
- Retinal Diseases
- Autoimmune Diseases
- Liver Diseases
- Kidney Diseases
- Metabolic Disorders
- Reproductive System Disease
- Musculoskeletal Diseases
- Nervous System Diseases



This figure was created with BioRender (<https://biorender.com/>).
Liu S, Liu J, Wang Y, Deng F, Deng Z. Oxidative Stress: Signaling Pathways, Biological Functions, and Disease. MedComm (2020). 2025;6(7):e70268. Published 2025 Jul 1. doi:10.1002/mco2.70268

Exogenous Triggers of ROS Generation

- Environmental Exposures
- Poor Diet
- Chronic Physiological Stress
- Sedentary Behavior
- Hormonal Changes



Masenga, S. K., Kabwe, L. S., Chakulya, M., & Kirabo, A. (2023). Mechanisms of Oxidative Stress in Metabolic Syndrome. *International Journal of Molecular Sciences*, 24(9), 7898. <https://doi.org/10.3390/ijms24097898>

A grayscale electron micrograph of biological tissue, likely showing cellular injury and an antioxidant response. The image displays a complex network of membranes, including what appears to be the endoplasmic reticulum, and numerous small, dark, electron-dense granules scattered throughout the cytoplasm. The overall texture is highly detailed and granular.

Antioxidant Response and Cellular Injury

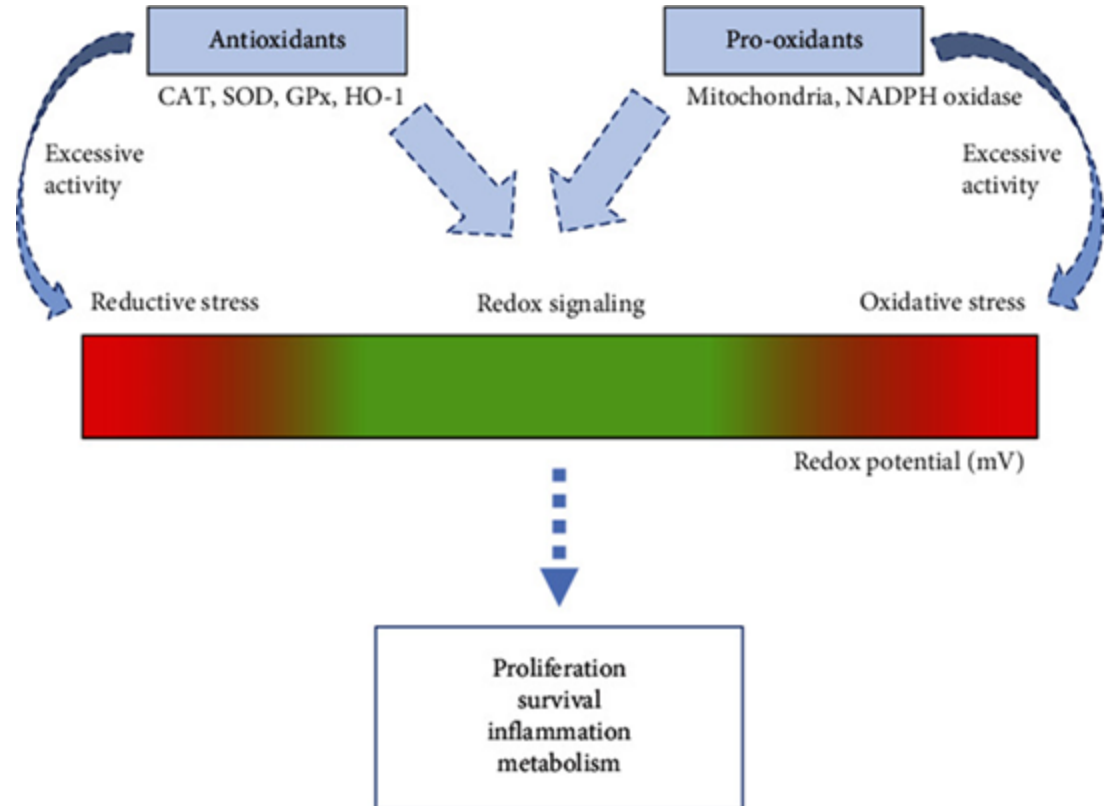
Function of ROS

ROS at optimal levels control cell fate through redox signaling.

Redox signaling controls:

- Cell proliferation
- Cell survival
- Inflammation
- Metabolism

An excess of either pro-oxidant or anti-oxidant stress can cause cell death.



de Almeida AJPO, de Oliveira JCPL, da Silva Pontes LV, et al. ROS: Basic Concepts, Sources, Cellular Signaling, and its Implications in Aging Pathways. *Oxid Med Cell Longev*. 2022;2022:1225578. Published 2022 Oct 19. doi:10.1155/2022/1225578

Antioxidant Response

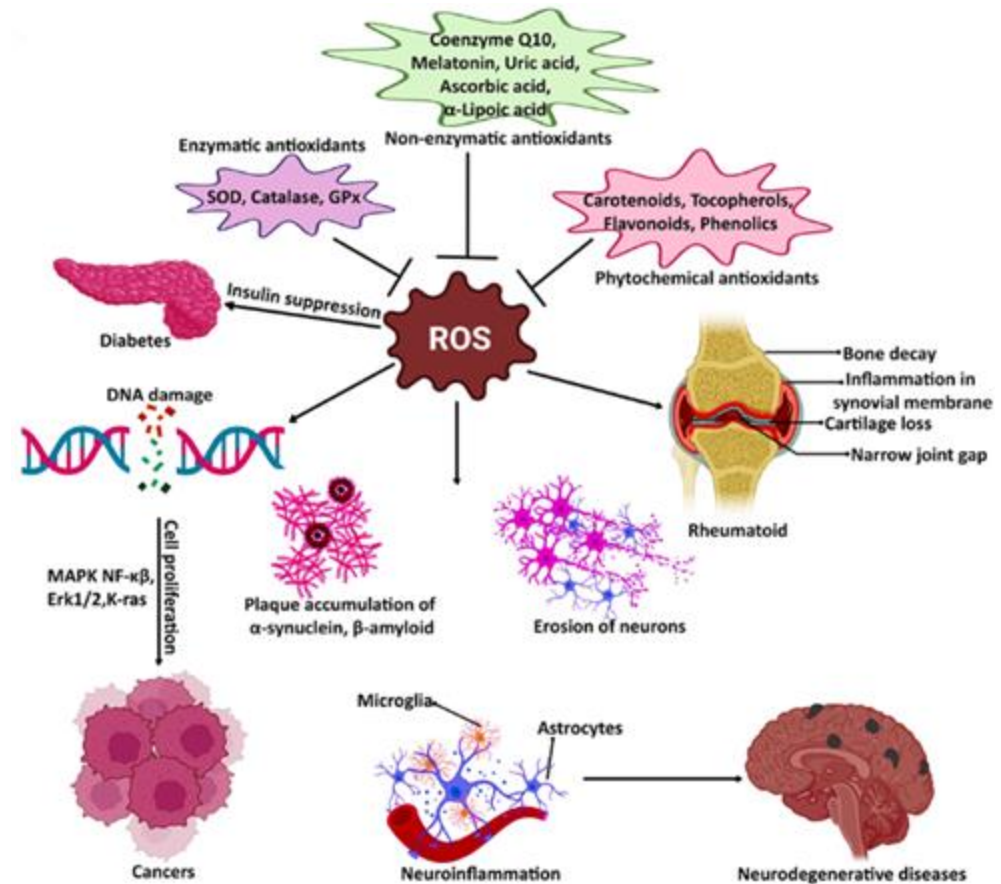
Designed to:

- Neutralize ROS
- Repair oxidative damage

When overwhelmed:

- DNA strand breaks
- Lipid peroxidation
- Protein oxidation
- Mitochondrial injury

Self-perpetuating

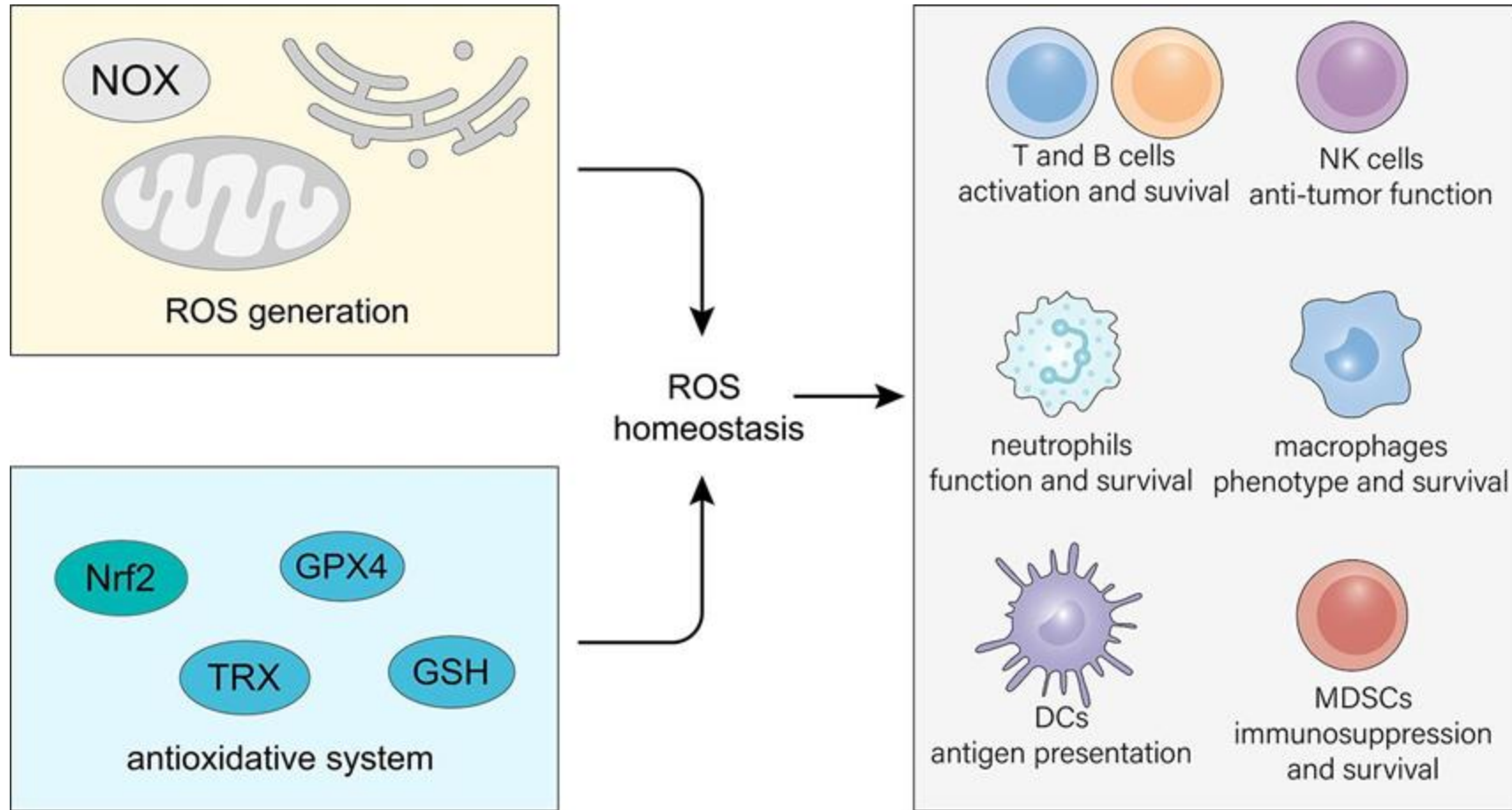


Liu S, Liu J, Wang Y, Deng F, Deng Z. Oxidative Stress: Signaling Pathways, Biological Functions, and Disease. MedComm (2020). 2025;6(7):e70268. Published 2025 Jul 1. doi:10.1002/mco2.70268

A grayscale electron micrograph of biological tissue, showing various cellular structures and organelles. The image is dark and textured, with numerous small, light-colored spots and larger, irregular shapes. The text is overlaid on the left side of the image.

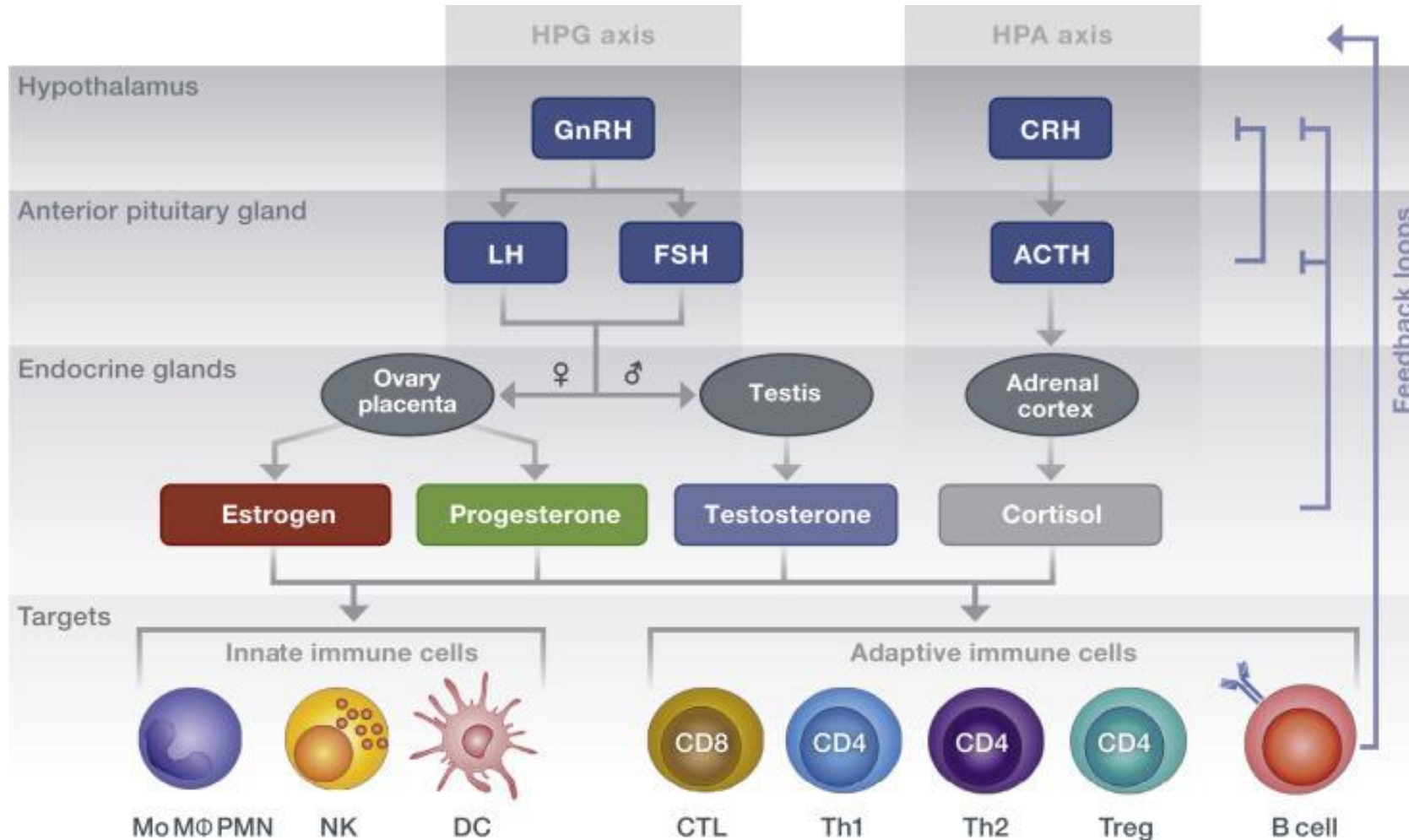
Oxidative Stress and the Immune System

ROS and Immune Signaling



<https://doi.org/10.1016/j.intimp.2023.110069>

Sex Hormones and Immunity



Stelzer IA, Arck PC. Immunity and the Endocrine System. *Encyclopedia of Immunobiology*. 2016;73-85. doi:10.1016/B978-0-12-374279-7.19001-0

A grayscale electron micrograph of biological tissue, showing a complex network of cellular membranes, organelles, and numerous small, dark, electron-dense granules scattered throughout the field. The overall appearance is highly textured and granular, characteristic of a high-magnification view of a cell or tissue section.

Inflammation and Oxidative Stress

Immunology Terms

NF-κB (nuclear factor kappa-B) is a master inflammatory “switch” inside cells. It is a transcription factor, meaning it turns genes on and off.

Important cytokines to know for today:

- **IL-1β (Interleukin-1 beta)**: early inflammatory signal that promotes fever, pain sensitivity, and immune cell activation. Think autoimmune disease, joint inflammation, and chronic pain states.
- **IL-6 (Interleukin-6)**: both acute and long-term inflammation
- **TNF-α (Tumor Necrosis Factor alpha)**: systemic inflammation that promotes immune activation, tissue damage, and insulin resistance.

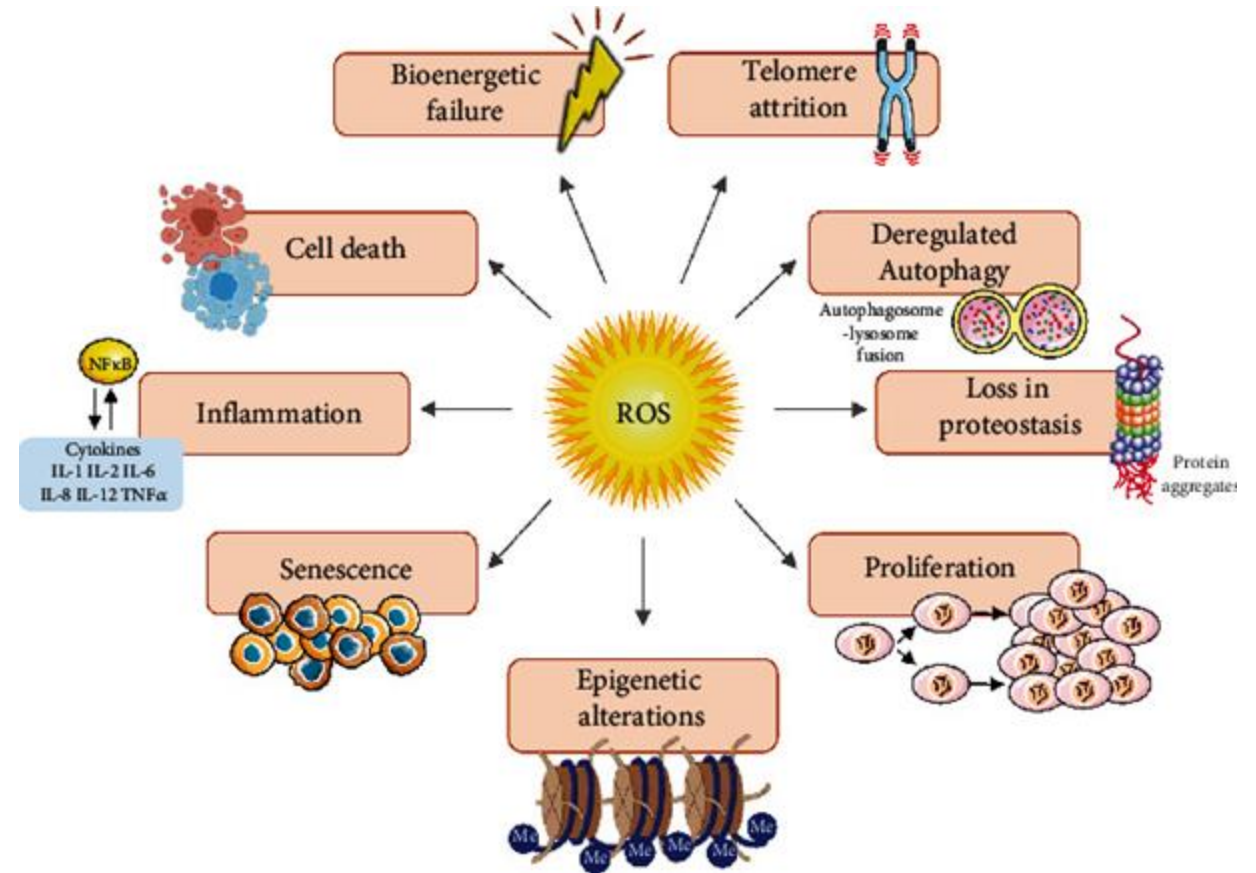
These cytokines increase oxidative stress and interfere with hormone signaling.

oxidative stress → inflammation → hormonal disruption → more oxidative stress

ROS and Aging

ROS activate inflammatory transcription factors such as NF- κ B, which increase production of cytokines including IL-1 β , IL-6, and TNF- α

ROS also plays a role in age related diseases through various mechanisms including inflammation, cell death, bioenergetic failure, telomere attrition, deregulated autophagy, loss in proteostasis, proliferation, epigenetic alterations, and senescence.



de Almeida AJPO, de Oliveira JCPL, da Silva Pontes LV, et al. ROS: Basic Concepts, Sources, Cellular Signaling, and its Implications in Aging Pathways. *Oxid Med Cell Longev*. 2022;2022:1225578. Published 2022 Oct 19. doi:10.1155/2022/1225578

A dark, grayscale microscopic image of tissue, possibly showing cellular structures and a network of fibers. The image is dimly lit, with various shades of gray and black, creating a complex, textured background. The text is overlaid on the left side of the image.

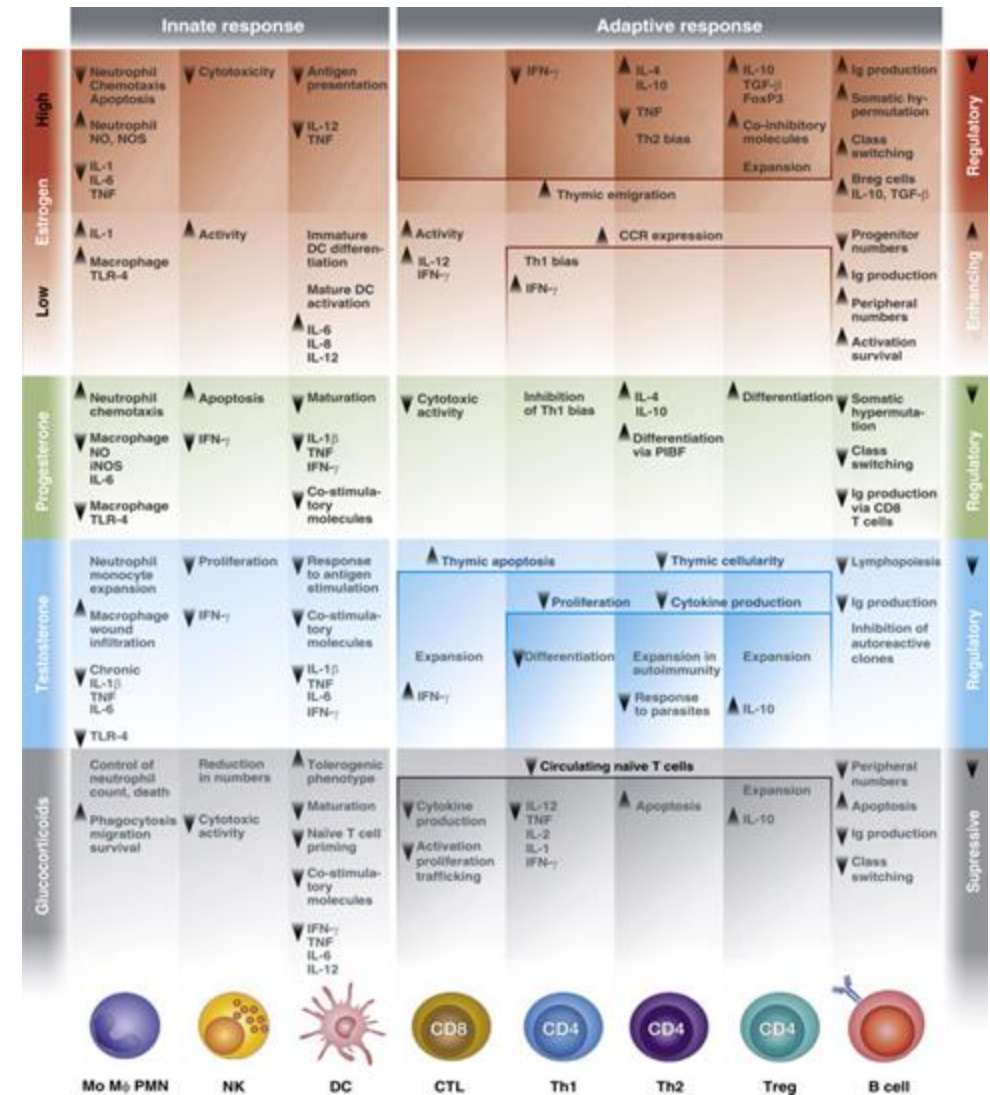
Hormones as Modulators of Immunity, Inflammation, and Oxidative Stress

Steroid Hormones and Innate and Adaptive Immune Response

Effect of steroid hormones on cells of the adaptive and innate immune response.

Arrows indicate stimulation or repression of cytokine secretion and immune cell function as well as increase or decrease of population size.

Bidirectional regulatory loop



Stelzer IA, Arck PC. Immunity and the Endocrine System. *Encyclopedia of Immunobiology*. 2016;73-85. doi:10.1016/B978-0-12-374279-7.19001-0

Hormones and the Immune System

Estrogen

- Immune surveillance
- Antibody response

Progesterone

- Immune tolerance
- Reduces inflammatory signaling

Testosterone

- Immunosuppressive
- Reduces inflammatory cytokines

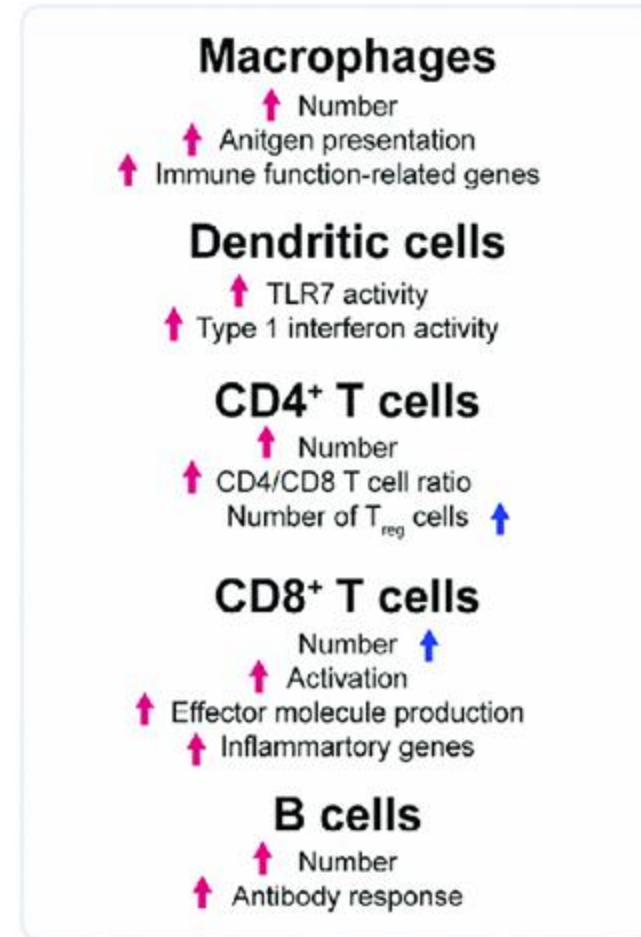
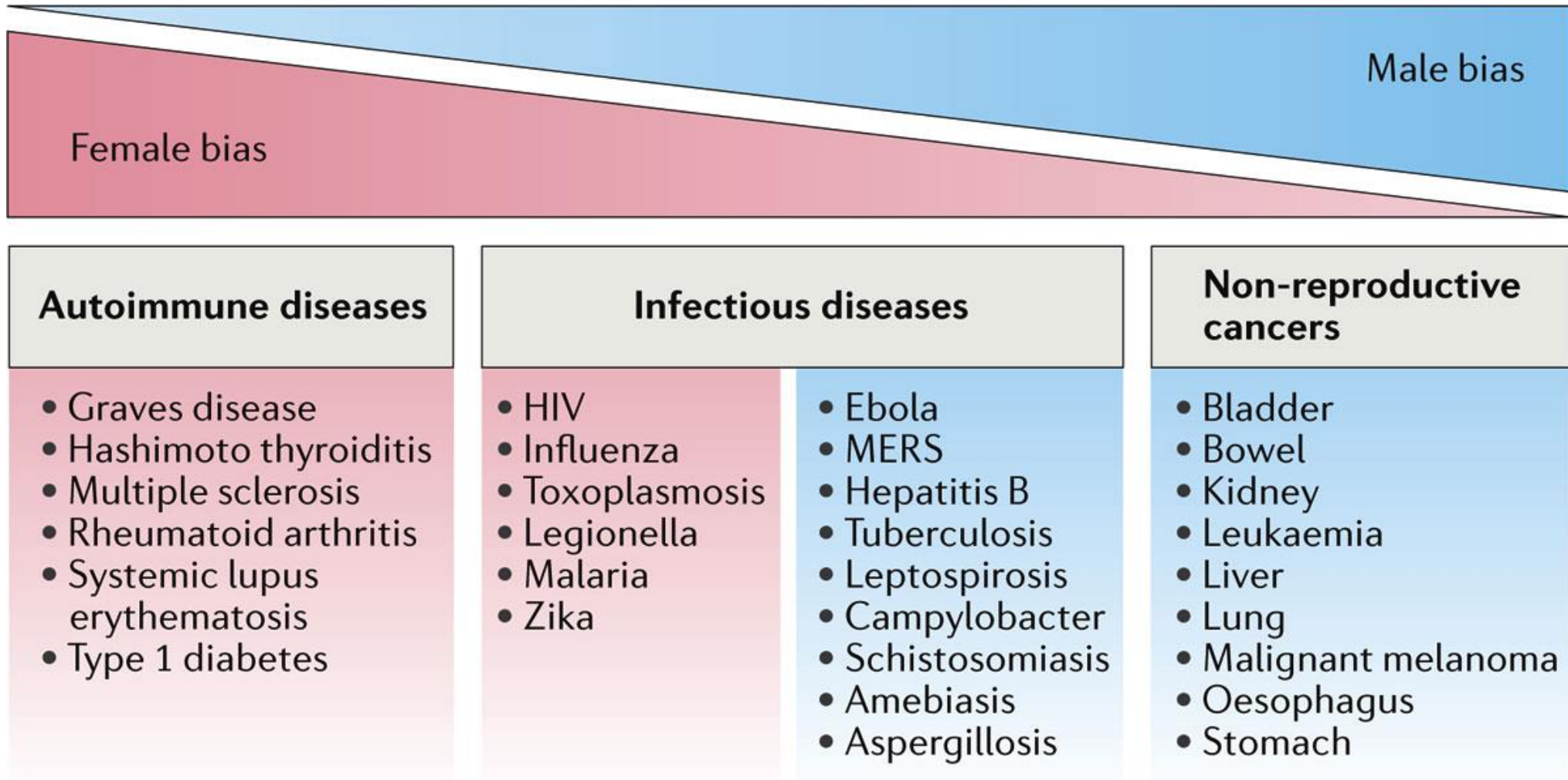


Figure adapted from images created with BioRender.com.

Schafer, Johanna & Xiao, Tong & Kwon, Hyunwoo & Collier, Katharine & Chang, Yuzhou & Abdel-Hafiz, Hany & Bolyard, Chelsea & Chung, Dongjun & Yang, Yuanquan & Sundi, Debasish & Ma, Qin & Theodorescu, Dan & Li, Xue & Li, Zihai. (2022). Sex-Biased Adaptive Immune Regulation in Cancer Development and Therapy. *iScience*. 25. 104717. 10.1016/j.isci.2022.104717.

Hormones Shape Immune Behavior Across Life



Klein, S., Flanagan, K. Sex differences in immune responses. *Nat Rev Immunol* 16, 626–638 (2016). <https://doi.org/10.1038/nri.2016.90>

Nature Reviews | Immunology

Hormones and Oxidative Stress- What Loss of Estrogen Looks Like

Endothelial cells (EC) taken from women showed:

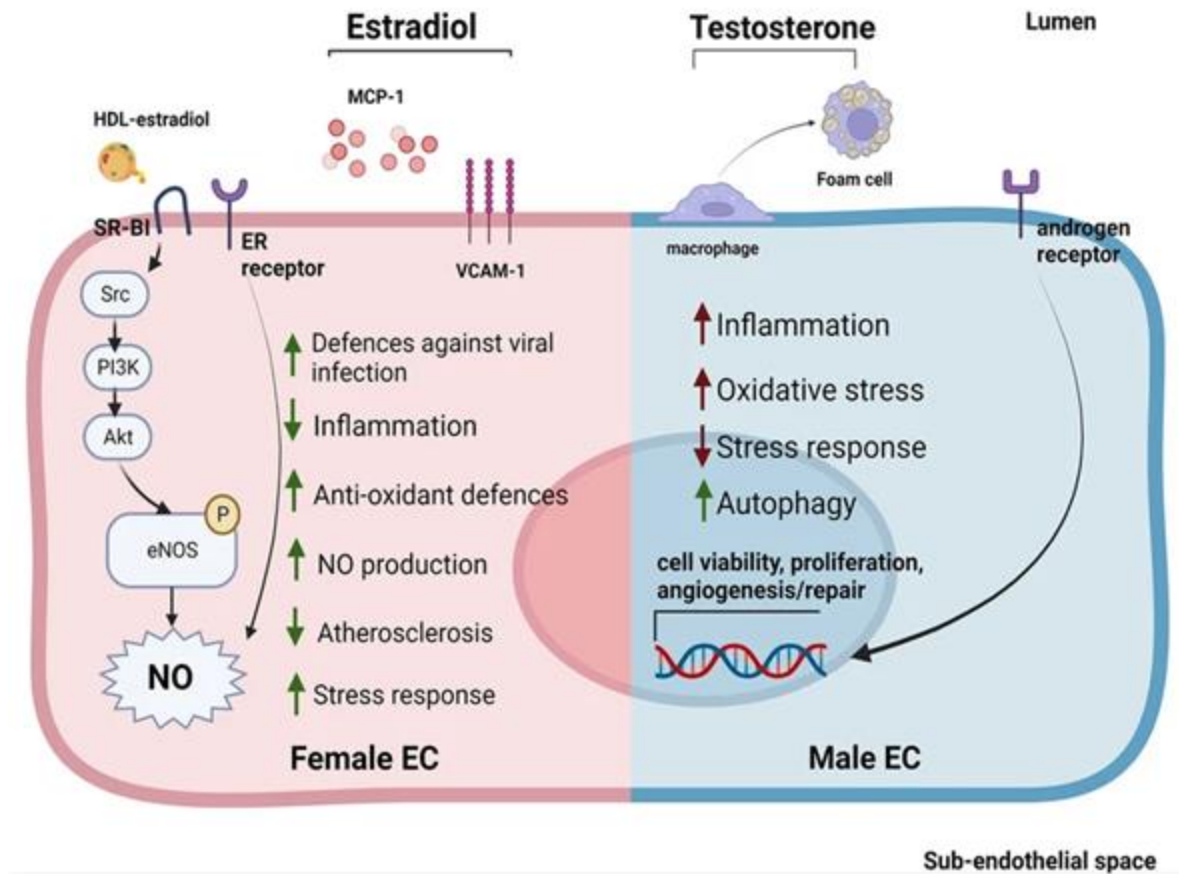
- Reduced response to stress and inflammation
- Increased NO production

In men they found:

- Stronger susceptibility to inflammation and oxidative stress
- Testosterone helps to transform macrophages into foam cells by creating a pro-inflammatory environment

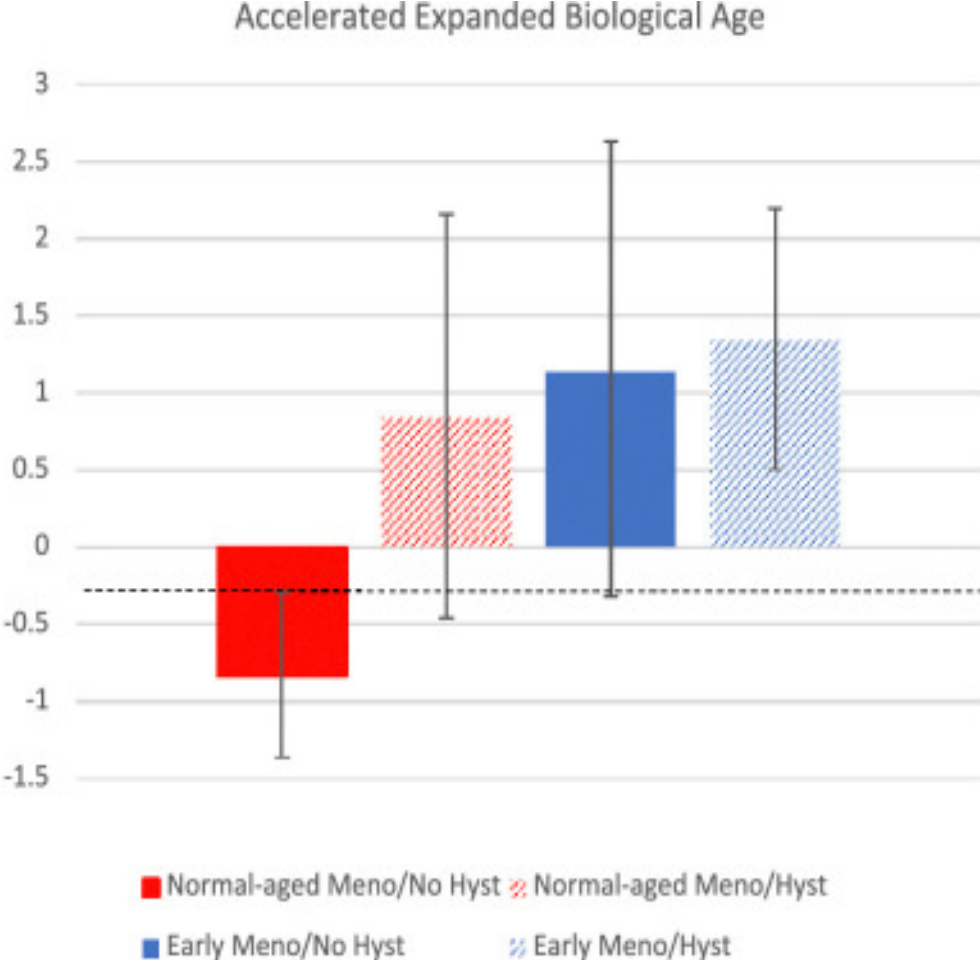
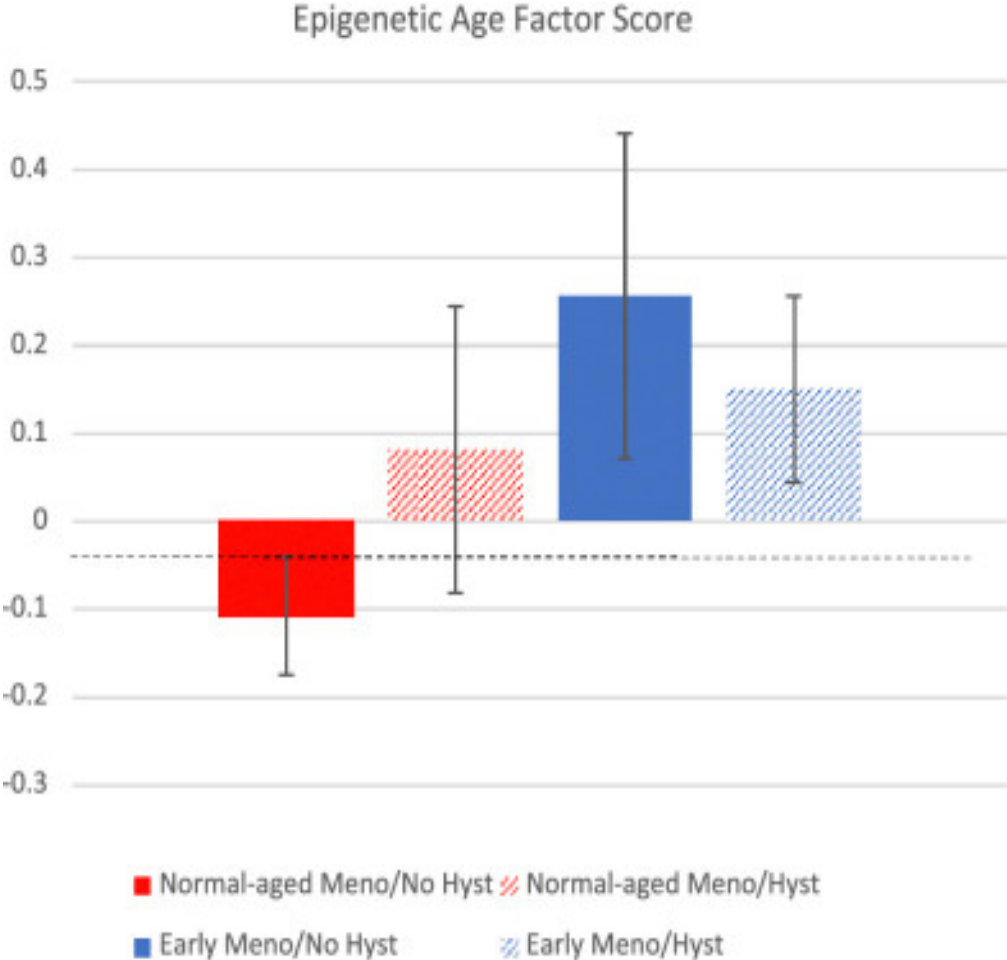
In both:

- Estrogen stimulates NO production through activation of estrogen receptors



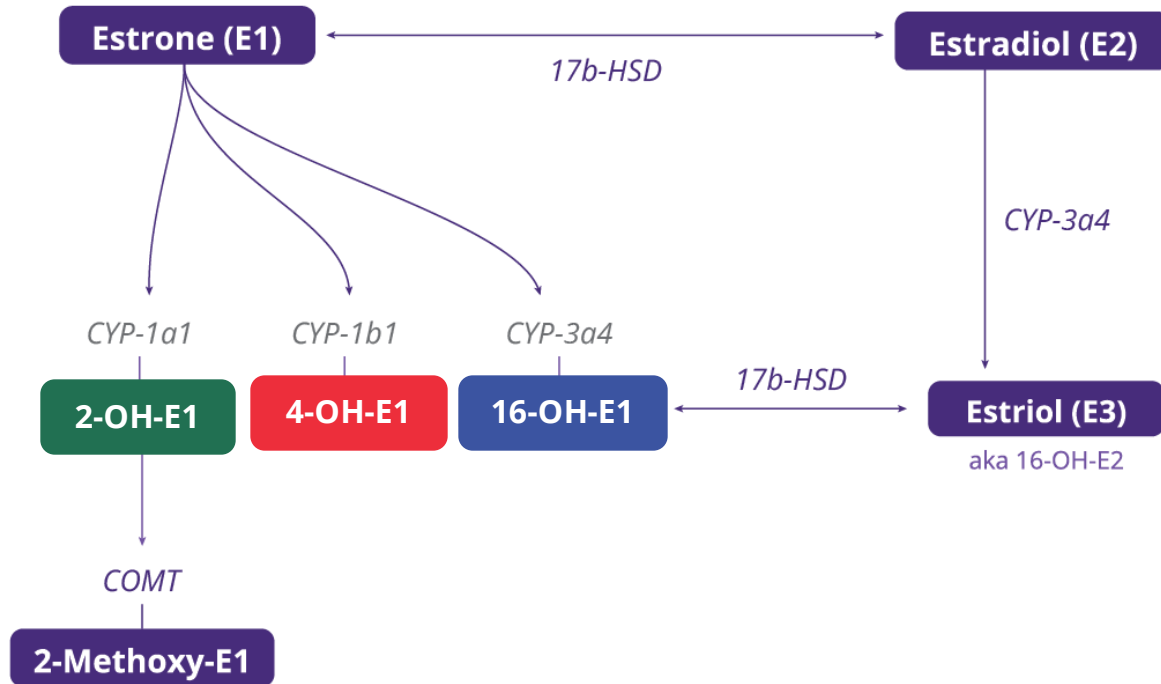
Dietrich, Elisa & Jomard, Anne & Osto, Elena. (2022). OPEN ACCESS EDITED BY. Frontiers in Cardiovascular Medicine. 9. 10.3389/fcvm.2022.989428.

Early Menopause Associated With Faster Aging?



Kim JK, Crimmins EM. Early menopause, hysterectomy, and biological aging: Health and Retirement Study. *Menopause*. 2025;32(8):692-701. Published 2025 Aug 1. doi:10.1097/GME.0000000000002555

Estrogen Metabolism, Oxidation, and Inflammation

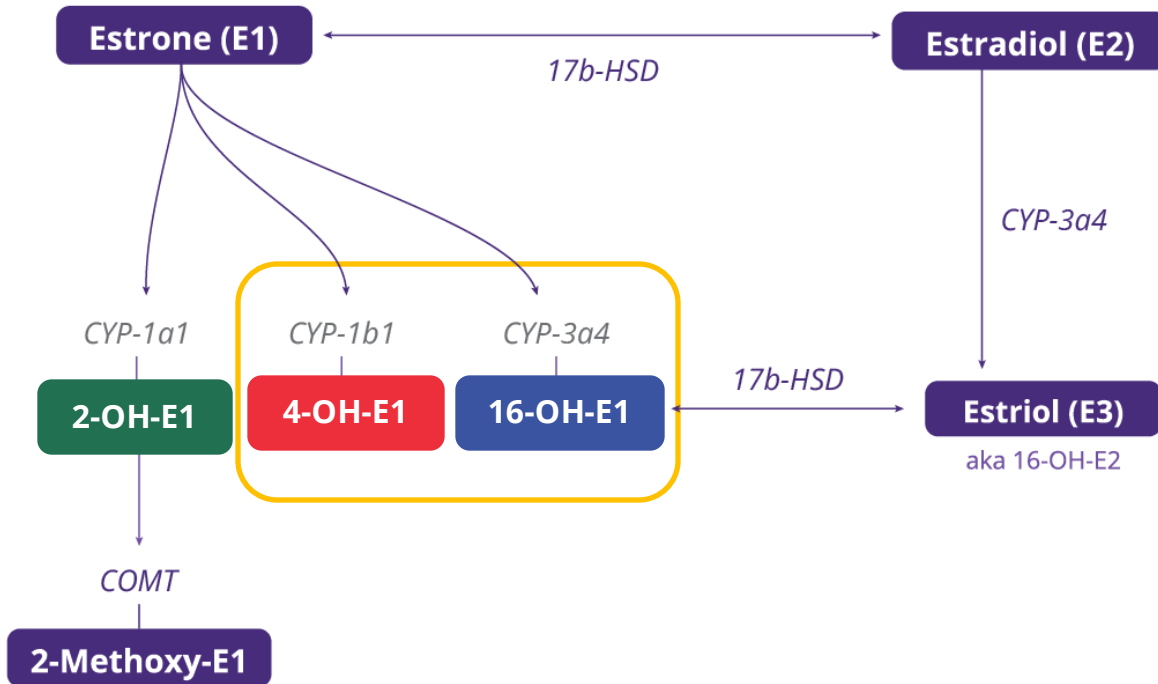


In phase 1, parent estrogens (E1 and E2) are broken down via 3 main pathways.

- **2-OH** is the **most stable** pathway, though it does have some oxidative potential
- **4-OH** is the **genotoxic, oxidative** pathway
- **16-OH** is the **estrogenic, inflammatory** pathway

- **Methylation** neutralizes the oxidative potential of 2-OH and 4-OH metabolites

Estrogen Metabolism, Oxidation, and Inflammation

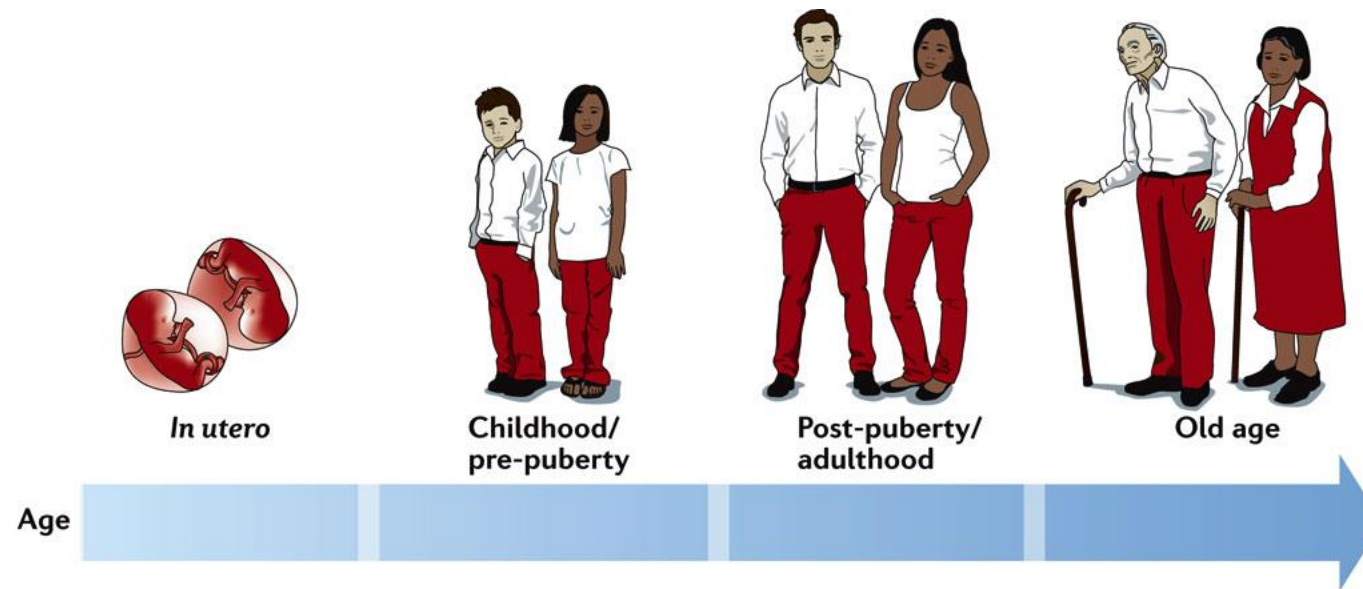


Lifestyle factors that promote of **oxidative** and **inflammatory** estrogen metabolism:

- Pesticide exposure
- Alcohol
- Obesity
- Elevated inflammatory cytokines
- Smoking
- PAHs

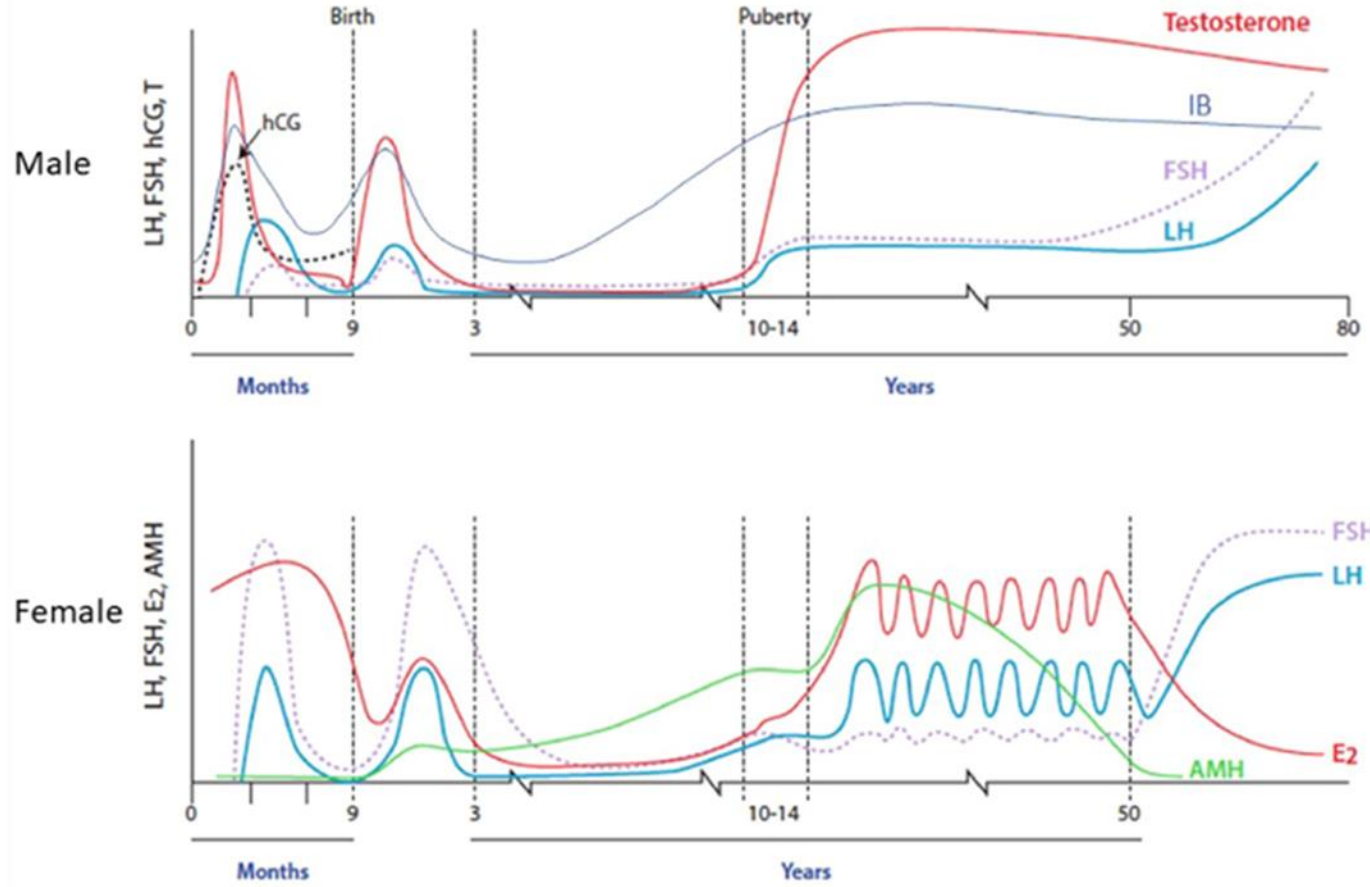
A dark, grayscale microscopic image of tissue, possibly showing cellular structures and a network of fibers. The image is heavily textured and serves as a background for the text.

Immune Function Across Hormonal Life Stages



Innate immunity	<ul style="list-style-type: none"> • Increased inflammatory responses in males 	<ul style="list-style-type: none"> • ↑ Inflammation in males • ↑ NK cells in males 	<ul style="list-style-type: none"> • ↑ Inflammation in females • ↑ NK cells in males 	<ul style="list-style-type: none"> • ↑ Inflammation in males • ↑ IL-10 in females • ↑ NK cells in females
Adaptive immunity	<ul style="list-style-type: none"> • Increased IgE levels in males 	<ul style="list-style-type: none"> • CD4/CD8 ratios and CD4⁺ T cell numbers equal • CD8⁺ T cell numbers equal • IgA levels in males ≥ females • IgM levels in males ≥ females • IgG and IgM levels equal • B cell numbers equal • T_{reg} cell numbers in males ≥ females 	<ul style="list-style-type: none"> • CD4/CD8 ratios and CD4⁺ T cells ↑ in females • CD8⁺ T cells ↑ in males • T cell activation/proliferation ↑ in females • T_{reg} cells ↑ in males • B cells ↑ in females • Immunoglobulins ↑ in females 	<ul style="list-style-type: none"> • CD4/CD8 ratios and CD4⁺ T cells ↑ in females • CD8⁺ T cells ↑ in males • T cell activation/proliferation ↑ in females • T_{reg} cells ↑ in males • B cells ↑ in females • Immunoglobulins ↑ in females

Puberty and Immune Function

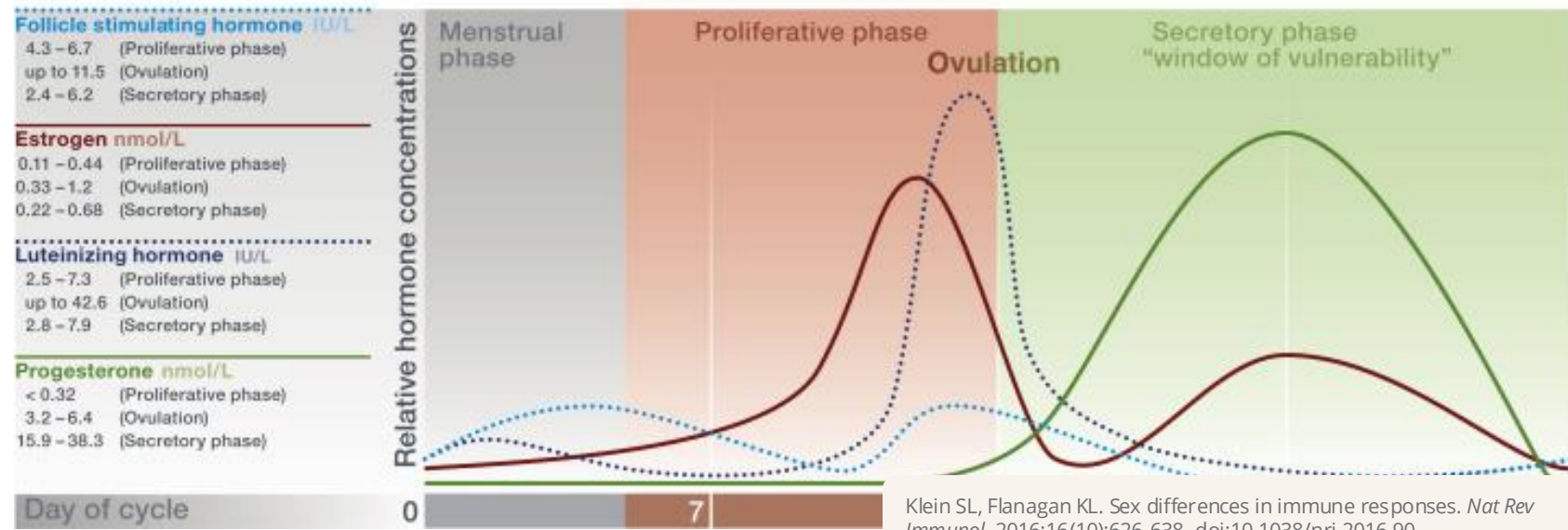
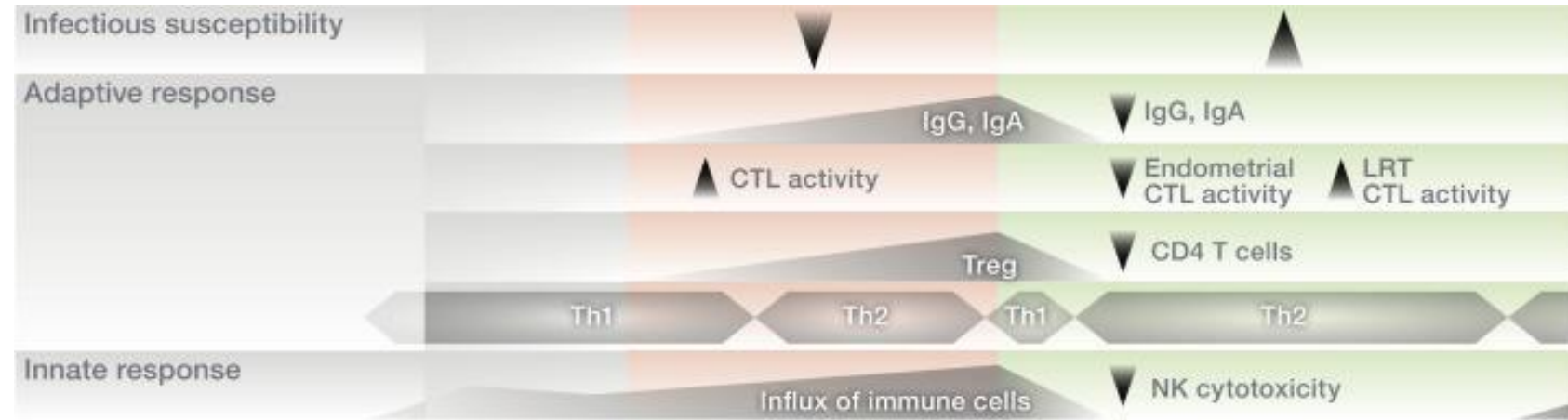


- Hormonal surge reshapes immunity
- Increased sex-based differences
- Shifts in T-cell and B-cell activity
- Changes in infection susceptibility
- Immune-endocrine crosstalk becomes established

Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol.* 2016;16(10):626-638. doi:10.1038/nri.2016.90

Immune Fluctuations Throughout the Menstrual Cycle

- Local immunity is influenced by estrogen and progesterone
- These fluctuations allow fertilization and implantation

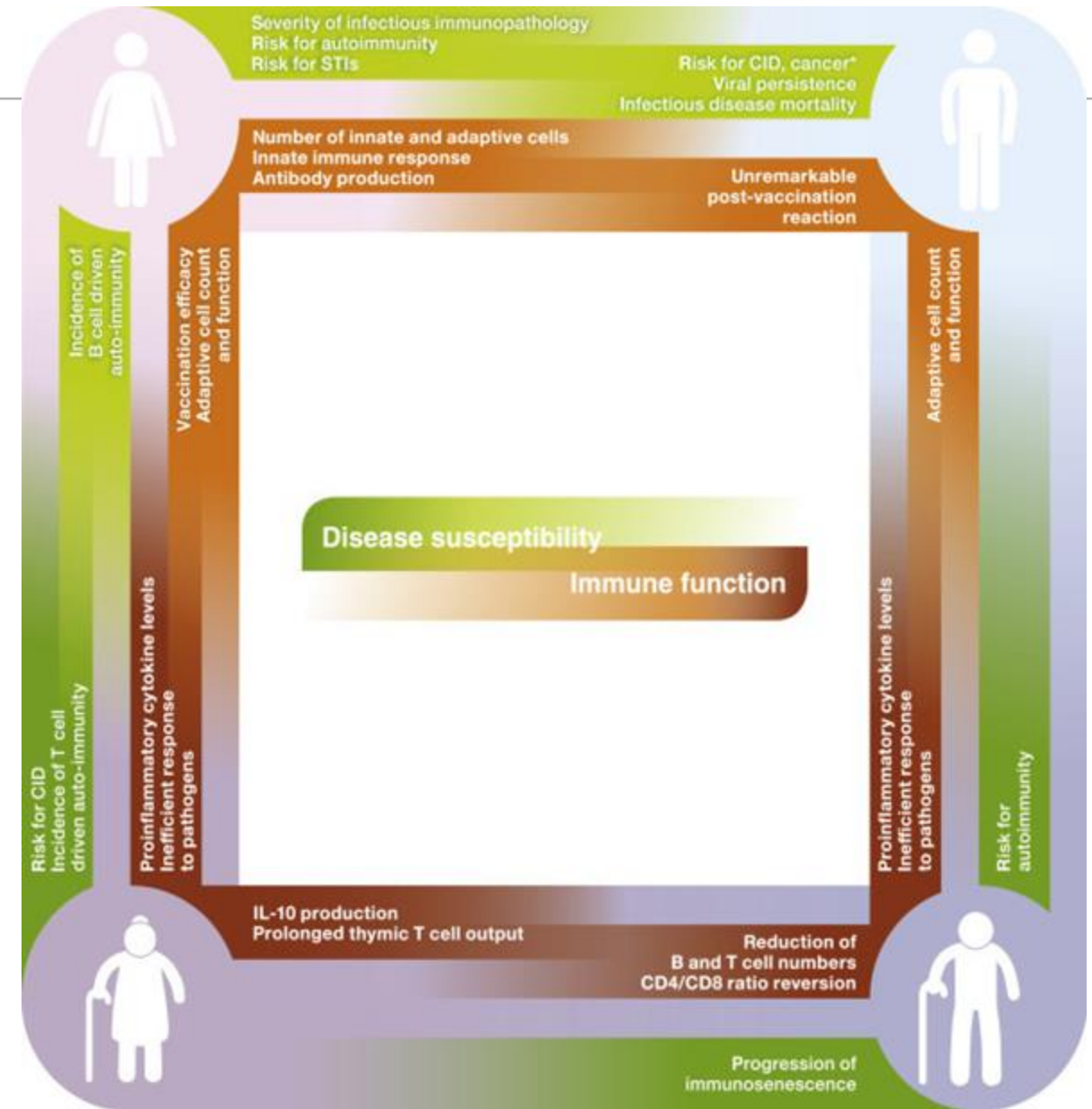


Klein SL, Flanagan KL. Sex differences in immune responses. *Nat Rev Immunol.* 2016;16(10):626-638. doi:10.1038/nri.2016.90

Stelzer IA, Arck PC. Immunity and the Endocrine System. *Encyclopedia of Immunobiology.* 2016;73-85. doi:10.1016/B978-0-12-374279-7.19001-0

Sex, Aging and Immunity

- Reduced levels of testosterone could allow for the increased occurrence of autoimmune diseases seen in aging males
- Decrease in estrogens reduces autoantibody-driven autoimmunity in females, while at the same time enhancing T cell-mediated autoimmune diseases (Straub, 2007).



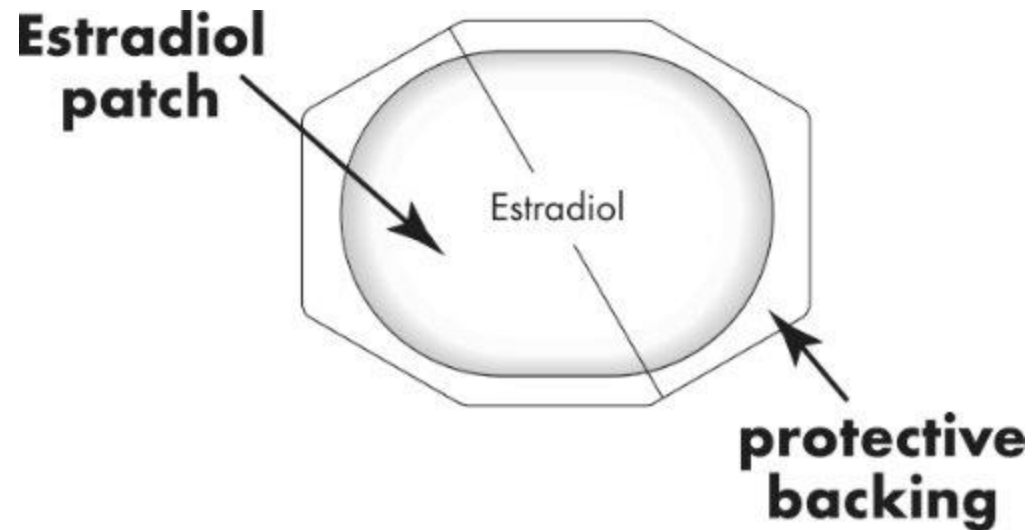
Stelzer IA, Arck PC. Immunity and the Endocrine System. *Encyclopedia of Immunobiology*. 2016;73-85. doi:10.1016/B978-0-12-374279-7.19001-0



Hormone Therapy and Immunity

Benefits of Hormone Therapy

- Menopausal Hormone Therapy (MHT) alleviates most peri and postmenopausal symptoms
- Reduces risk of respiratory infections
- Reduces risk for UTI (vaginal estrogen)
- Mostly reverses age-related immune senescence



Abdi, F., Mobedi, H., Mosaffa, N., Dolatian, M., & Ramezani Tehrani, F. (2016). Effects of hormone replacement therapy on immunological factors in the postmenopausal period. *Climacteric*, 19(3), 234–239. <https://doi.org/10.3109/13697137.2016.1164136>

Potential Drawbacks of Hormone Therapy

- Increased symptoms of SLE
- Possible risk of developing certain autoimmune diseases like SLE or RA
- Women with antiphospholipid antibodies should avoid ORAL MHT due to increased thrombosis risk
- Not all immune changes persist
- Regardless of MHT, postmenopausal women have impaired immune responses



Individualized Risk Assessment

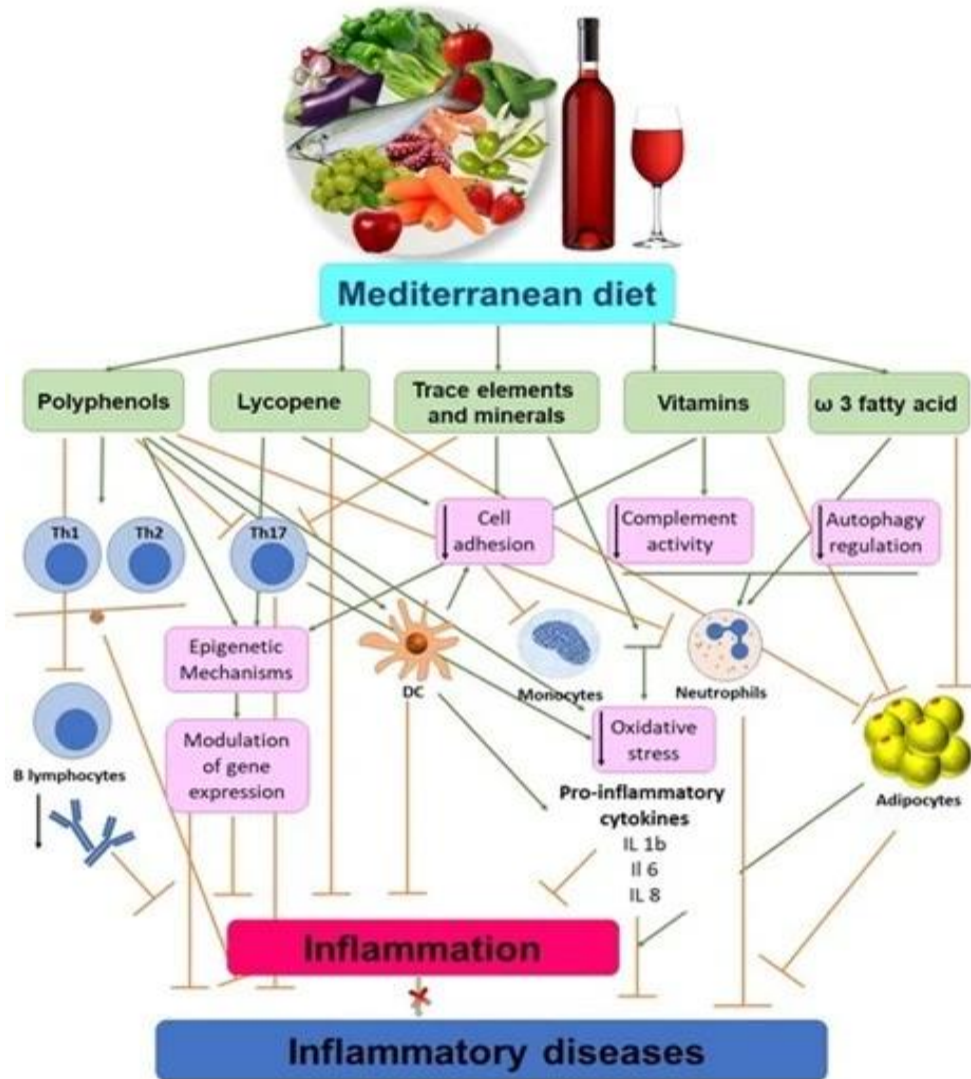
- Timing hypothesis (start within 10 years of LMP or before age 60)
- Transdermal risk << oral
- Risk for autoimmune improvement/exacerbations
- UTI risk decreased
- Hormone therapy is a tool



A dark, grayscale microscopic image of tissue, possibly showing cellular structures and a large, irregularly shaped lesion or area of damage. The text is overlaid on the left side of the image.

Strategies to Reduce Oxidative Stress

Mediterranean Diet



Benefits

- Less processed
- Fiber-rich
- Nutrient and mineral-rich
- Polyphenols
- Omega 3's

Mechanisms

- Reduces inflammatory cytokines
- Reduces oxidative stress
- Regulates complement

Tsigalou C, Konstantinidis T, Paraschaki A, Stavropoulou E, Voidarou C, Bezirtzoglou E. Mediterranean Diet as a Tool to Combat Inflammation and Chronic Diseases. An Overview. Biomedicines. 2020; 8(7):201. <https://doi.org/10.3390/biomedicines8070201>

Supplements

- C- neutralize
- E- neutralize
- NAC- GSH
- ALA- GSH
- CoQ10- energy production
- Polyphenols- calm inflammation



Lifestyle



- Exercise
- Stress Reduction
- Sleep
- Minimizing Toxin Exposure (smoking, alcohol, etc.)

Case Study- Frozen Shoulder

Patient:

- A 49-year-old woman presents with a 4-month history of worsening shoulder stiffness and pain, eventually diagnosed as adhesive capsulitis (frozen shoulder). She reports difficulty reaching overhead, disrupted sleep due to pain, and progressive loss of range of motion. She was told by specialist that she would need steroid injections but wants to avoid them if she can. She is looking for other options.

History & Context:

- Over the past year, she has noticed classic perimenopausal symptoms—irregular cycles, night sweats, increased anxiety, and new joint aches. She also reports increased fatigue and slower recovery after exercise. No prior shoulder injury.

Intervention

After discussing options, she is started on menopausal hormone therapy (MHT) with transdermal estradiol and oral micronized progesterone. The goals include stabilizing hormonal fluctuations, supporting connective tissue health, improving sleep, and reducing systemic inflammation.

She is also offered pain management and progressive stretching exercises with a physical therapist.

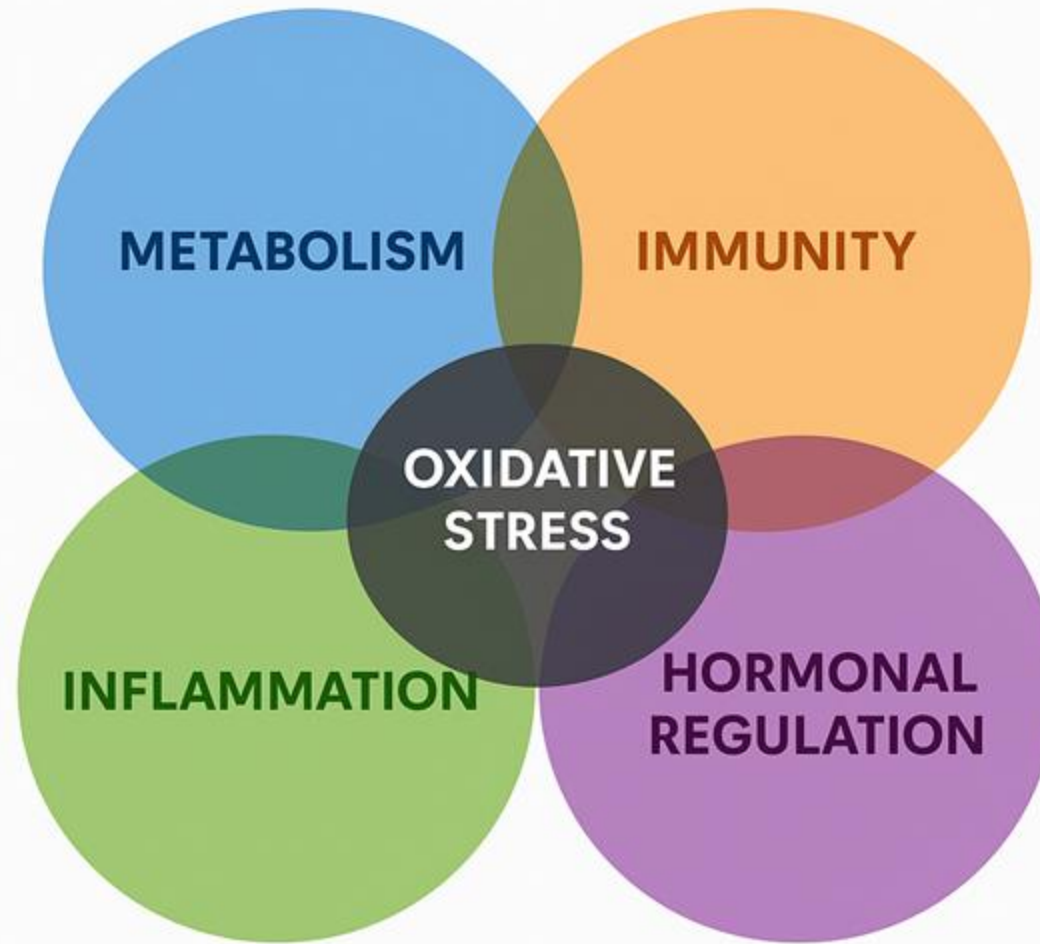


Outcome

After 12 weeks, she reports:

- Improved sleep and energy
- Reduction in global joint stiffness
- Less shoulder pain and better tolerance for physical therapy
- Gradual improvement in range of motion
- Fewer vasomotor symptoms and improved mood stability

Conclusion



Become a Provider Today!

Exclusive hormone education for DUTCH providers



Comprehensive Report



Clinical Support & Education



Peer Reviewed & Validated Research

New DUTCH Providers are eligible for 50% off their first five test kits.

50% off*

*Special offer of 50% off first five test kits is invalid 60 days after new provider registration."

Thank You!

Lacy Campbell, ND

April 29, 2026

dutchwebinars