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Longevity and Biological Ageing: Enhancing Health into Advanced Age



SESSION 11

Dr. Felice Gersh

The Gut Microbiome and the Autonomic Nervous System:
An Essential Link to Longevity in Women

2:00-2:45pm

An event by:  Nutritional Medicine Institute

Platinum sponsors:   regenerus labs



The Gut Microbiome & the Autonomic Nervous System: An Essential Link to Longevity in Women

Felice Gersh, MD

Medical Director

Integrative Medical Group of Irvine

Consultative Faculty

Fellowship in Integrative Medicine

University of Arizona School of Medicine

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Overview



- **Become better acquainted with the multiple physiological actions of the Vagus nerve, especially involving mood**
- **Explore the ways the autonomic nervous system interacts with estradiol and the gut microbiome – in reproductive and menopausal aged women**
- **Acquire an integrative approach to improving health in your women patients – involving vagal tone, gut health, and hormone therapy**

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Women's Optimal Health
=
Optimized Hormones
=
Optimal Gut Microbiome
=
**Optimal Function of the
Autonomic Nervous System**

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Prime Directive of Life:

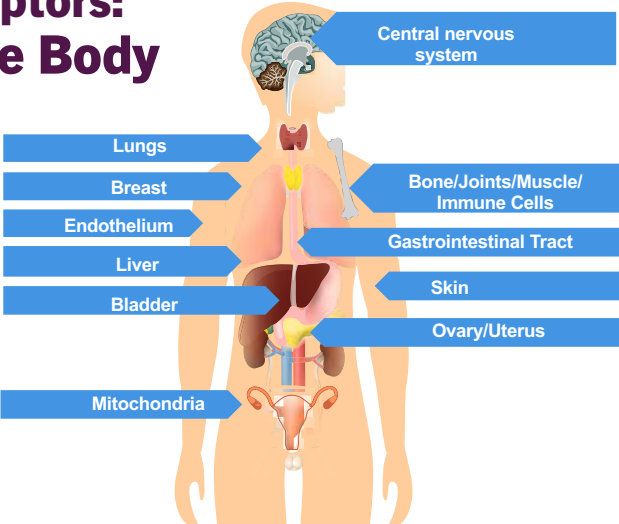
*Reproduction and survival
and then to repeat the process*

...

*It is all about the process of making
and raising babies!*

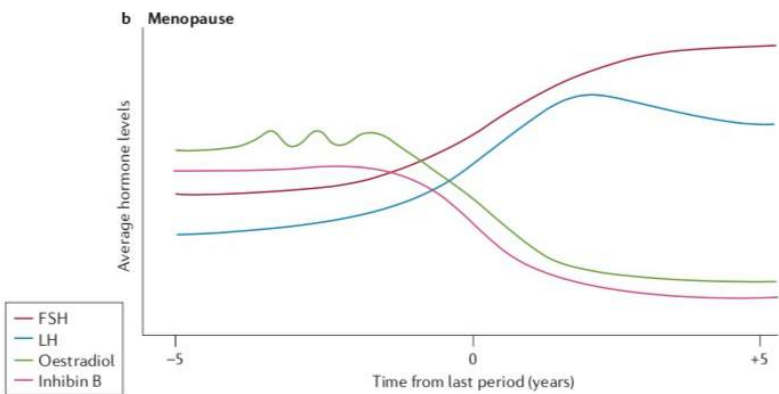
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Estrogen Receptors: Throughout the Body



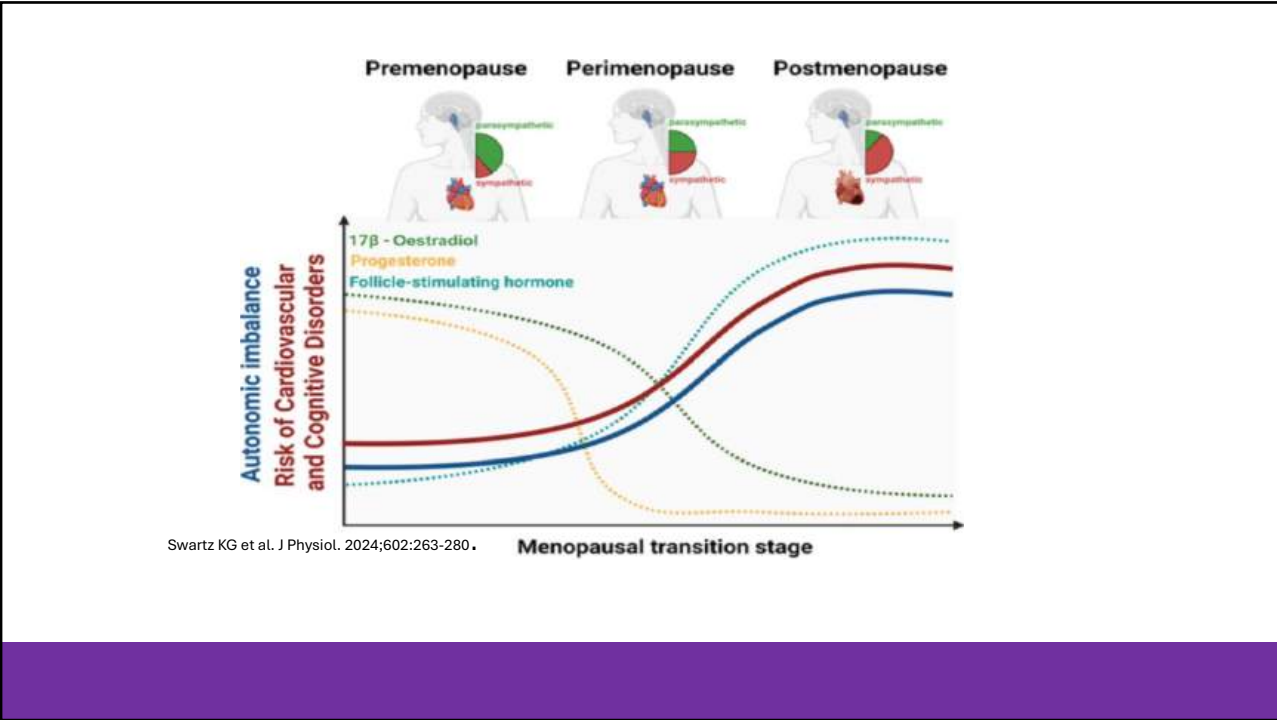
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Fluctuations in Hormones: Related to Menopause & Menopausal Transition



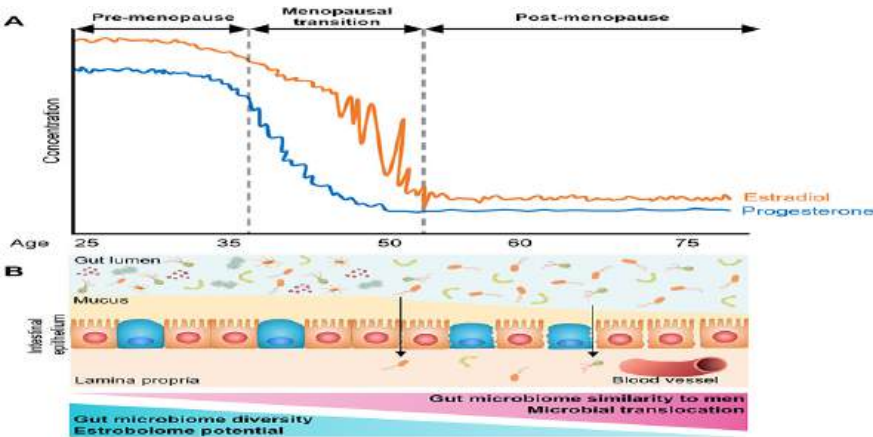
Davis, S., Lambrinoudaki, I., Lumsden, M. et al. Menopause. *Nat Rev Dis Primers* 1, 15004 (2015).

8



9

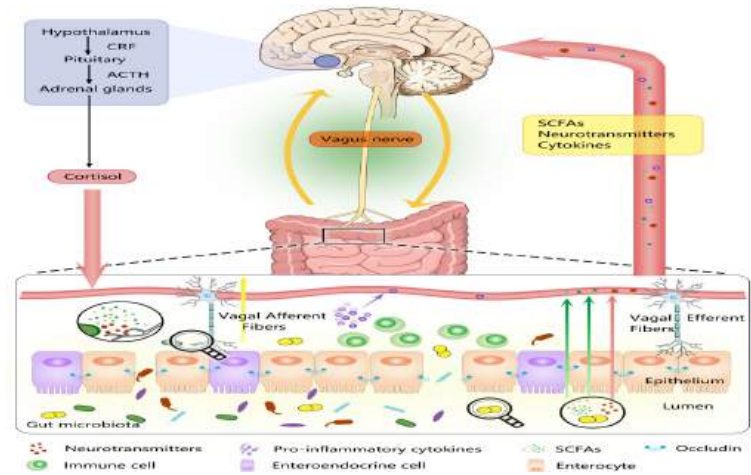
Gut Microbiome and Hormone Levels



Peters BA, Santoro N, Kaplan RC, Qi Q. Spotlight on the Gut Microbiome in Menopause: Current Insights. *Int J Womens Health*. 2022;14:1059-1072

10

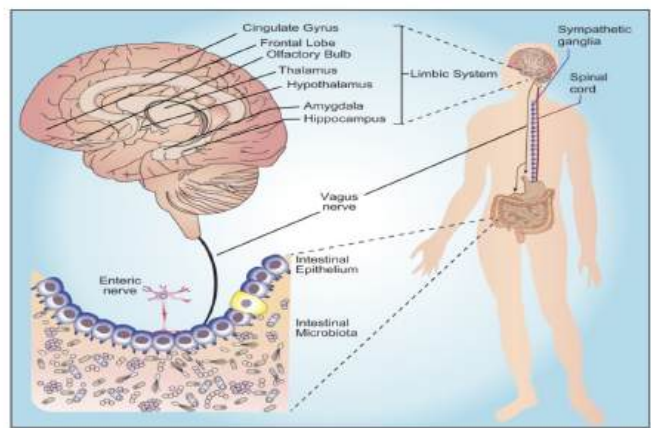
Autonomic Nervous System & Gut Microbiome



Han et al. Vagus Nerve and Underlying Impact on the Gut Microbiota-Brain Axis in Behavior and Neurodegenerative Diseases. J Inflamm Res. 2023-6230; 15: 6213-6230

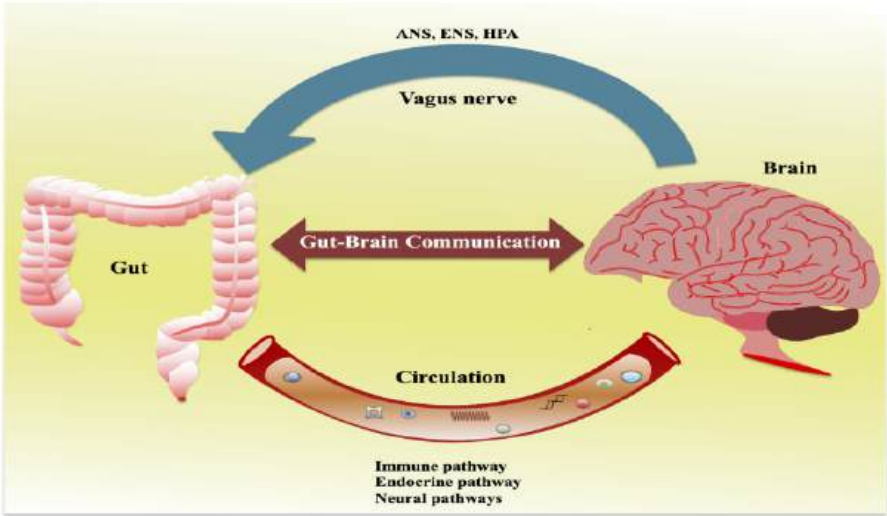
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Microbiota-Gut-Brain-Autonomic Nervous System Axis



Cryan JF et al. The Microbiota-Gut-Brain Axis. Physiological Reviews. 2019 online

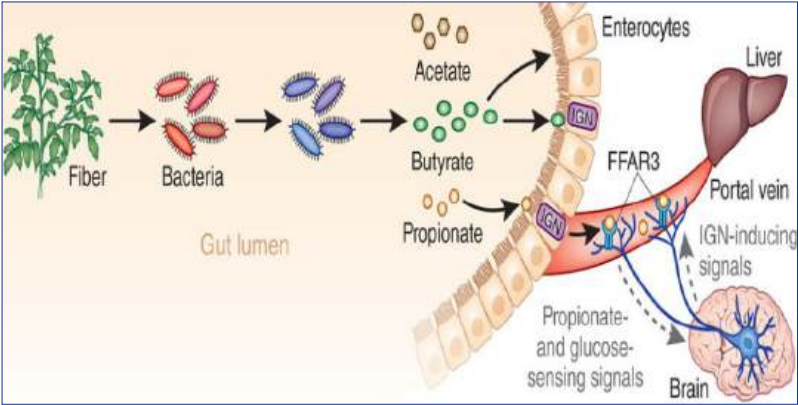
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Suganya K, Koo BS. Gut-Brain Axis: Role of Gut Microbiota on Neurological Disorders and How Probiotics/Prebiotics Beneficially Modulate Microbial and Immune Pathways to Improve Brain Functions. *Int J Mol Sci.* 2020 Oct 13;21(20):7551.

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Linking Microbiome & Short Chain Fatty Acids to Brain Health



Nature Biotechnology. 2014; 32, 243–245

14

The diagram illustrates the pathways of vagal afferent neurons in the Central Nervous System (CNS). The Vagal Afferent Neuron (VAN) receives input from the Ovary (via Estradiol) and the Gastrointestinal (GI) tract. The VAN projects to the Nucleus Tractus Solitarius (NTS) in the CNS. The NTS then projects to the Parabrachial Nucleus (PBN), which in turn projects to the Mid-brain. The diagram also shows a Paracrine Pathway from the GI tract to the NTS and a Hormonal Pathway from the GI tract to the Mid-brain.

Circulating estradiol that secreted from ovary acting on both VAN and the nuclei located in the CNS modulates the responsiveness to gastrointestinal satiety signals

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Estradiol Modulates the Autonomic Nervous System

Clinical and Experimental Pharmacology and Physiology (2007) 34, 827–832

doi: 10.1111/j.1440-1681.2007.04663.x

BRIEF REVIEW

ROLE OF OESTROGEN IN THE CENTRAL REGULATION OF AUTONOMIC FUNCTION

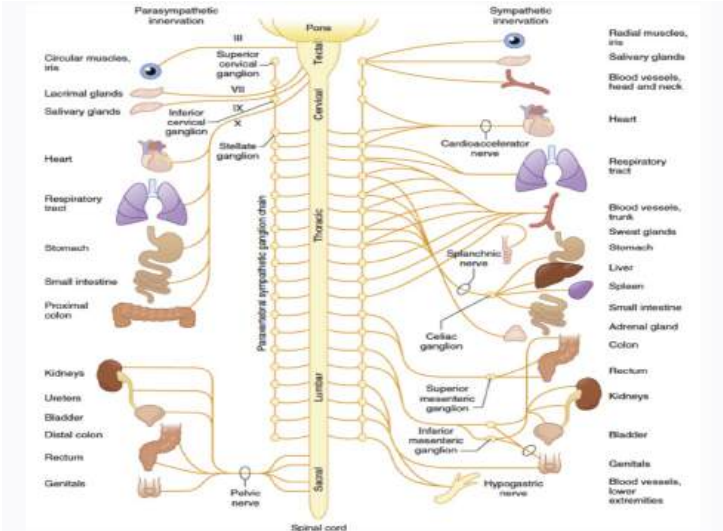
TM Saleh and BJ Connell

Department of Biomedical Science, Atlantic Veterinary College and The Prince Edward Island Health Research Institute, University of Prince Edward Island, Charlottetown, Prince Edward Island, Canada

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The Autonomic Nervous System



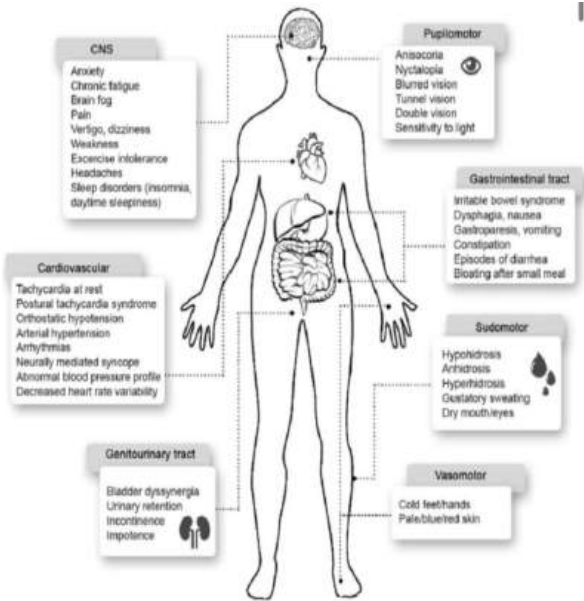
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Autonomic dysfunction and chronic disease

Nov 2018 · [British Medical Bulletin](#) 128(1)
DOI: [10.1093/bmb/ldy036](#)

 Pawel Zalewski ·  Joanna Słomko ·
 Monika Zawadka-Kunikowska

The Dysautonomia Project



Menopause is associated with decreased heart rate variability, which is due to reduced parasympathetic or increased sympathetic outflow to the heart. Acute myocardial infarction may be accompanied by decreased heart rate variability. The causes of autonomic dysfunction in postmenopausal women may be multi-factorial *i.e.*, dyslipidemia, increased body fat percentage, aging and loss of female sex hormones. The cardiac vagotonic and sympatholytic effects of estrogen can explain, at least in part, why premenopausal women compared with postmenopausal women have a lower coronary heart disease incidence and mortality rate.

REVIEW ARTICLE
Year : 2012 | **Volume :** 5 | **Issue :**
1 | Page : 4-9
Menopause and autonomic control of heart
Arunima Chaudhuri, Nirmala G Borade
Department of Physiology, Dr. D. Y. Patil Medical College, Pune,
Maharashtra, India

Autonomic Neuroscience

Volume 187, January 2015, Pages 27-35

Review

Sympathetic regulation of estradiol secretion from the ovary

Sae Uchida  

Show more 

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<https://doi.org/10.1016/j.autneu.2014.10.023> 

Get rights and content 

Highlights

- Autonomic innervation of rat ovary
- Role of autonomic regulation of ovarian function

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Brain Research Bulletin

Volume 165, December 2020, Pages 129-138

Roles of the cholinergic system and vagal innervation in the regulation of GnRH secretion and ovulation: Experimental evidence

Elizabeth Vieyra-Valdez ^{a, b}  ... Leticia Morales-Ledesma ^a

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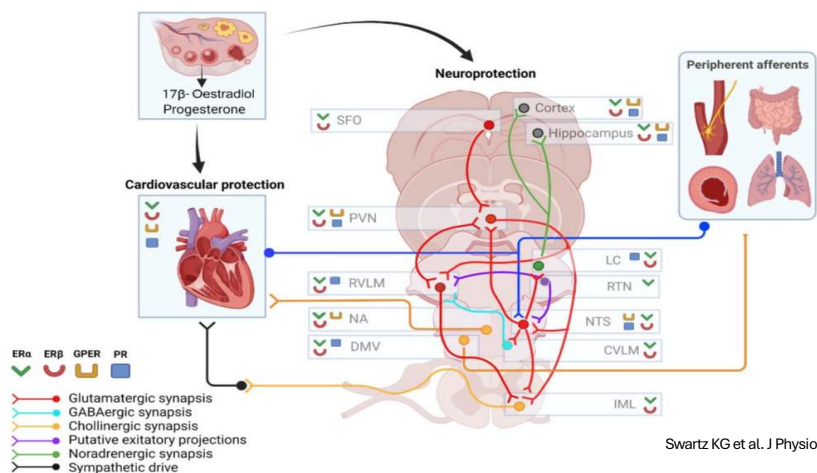
Figure 2. Oestrogen and progesterone signalling in main areas of autonomic sympathetic control

Oestrogen, a female gonadal hormone, exerts regulatory effects on autonomic neural pathways via oestrogen receptor signalling, contributing to cardioprotection and neuroprotection throughout reproductive years. Brain slices reveal the neural connections in the autonomic nervous system control network. The nucleus tractus solitarius (NTS) communicates with pre-sympathetic neurons in the paraventricular nucleus (PVN) through glutamate synapses. Additionally, the NTS directly stimulates the intermediolateral nucleus (IML) and indirectly inhibits the rostral ventrolateral medulla (RVLM) by sending glutamate signals to the caudal ventrolateral medulla (CVLM) via GABAergic neurons. Small pre-autonomic neurons of the PVN reciprocally connect to the RVLM and project signals to the IML. There are potential connections between the RVLM and central chemoreceptors in the retrotrapezoid nucleus (RTN), which are proposed to be relevant in sympathetic-mediated disorders. The RVLM also communicates with the IML via glutamate. Sensory circumventricular organs such as the subfornical organ (SFO) lack a blood–brain barrier, are well-vascularized, and respond to peripheral signals to regulate CNS activity. The SFO connects with the PVN through glutamate and plays a significant role in modulating sympathetic activity in response to peripheral hormones and inflammation in health and disease. In addition, the NTS sends excitatory projections to the locus coeruleus (LC), main source of brain norepinephrine, which regulates executive functions and learning and memory functions in cortex and hippocampus, respectively.

Swartz KG et al. J Physiol. 2024;602:263-280

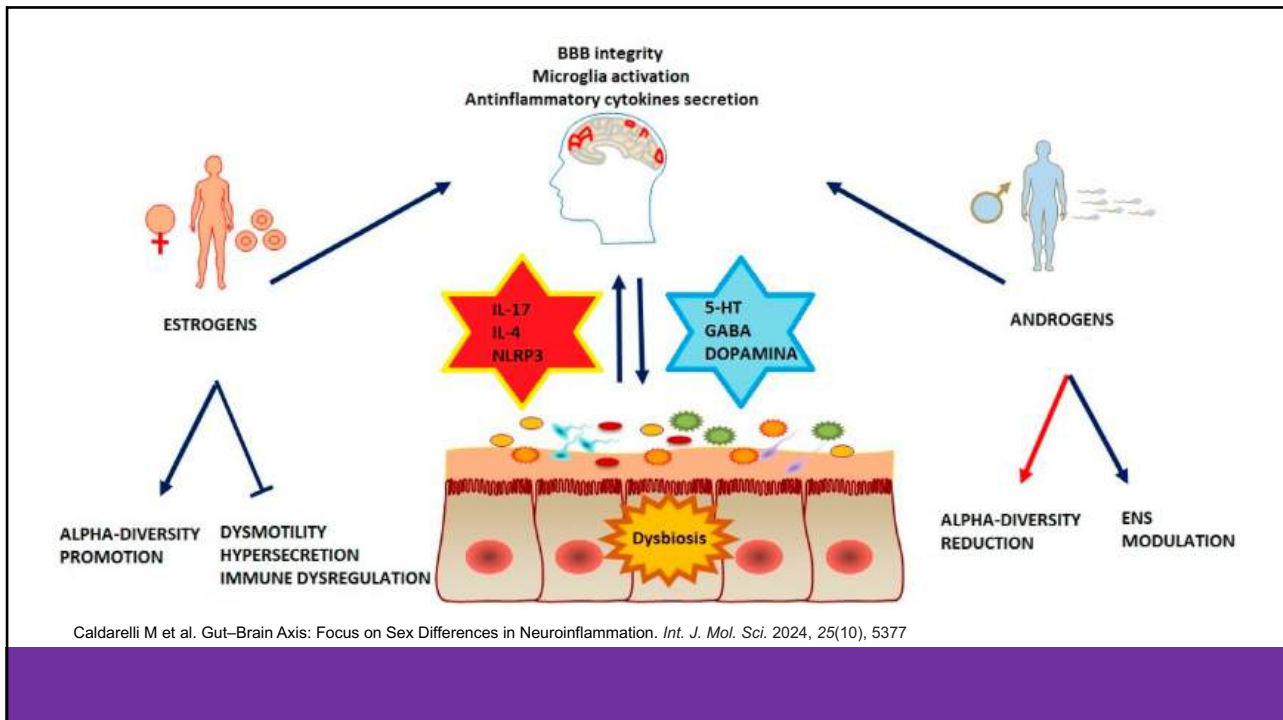
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Estrogen and Progesterone Signaling in Main Areas of Autonomic Sympathetic Control



Swartz KG et al. J Physiol. 2024;602:263-280

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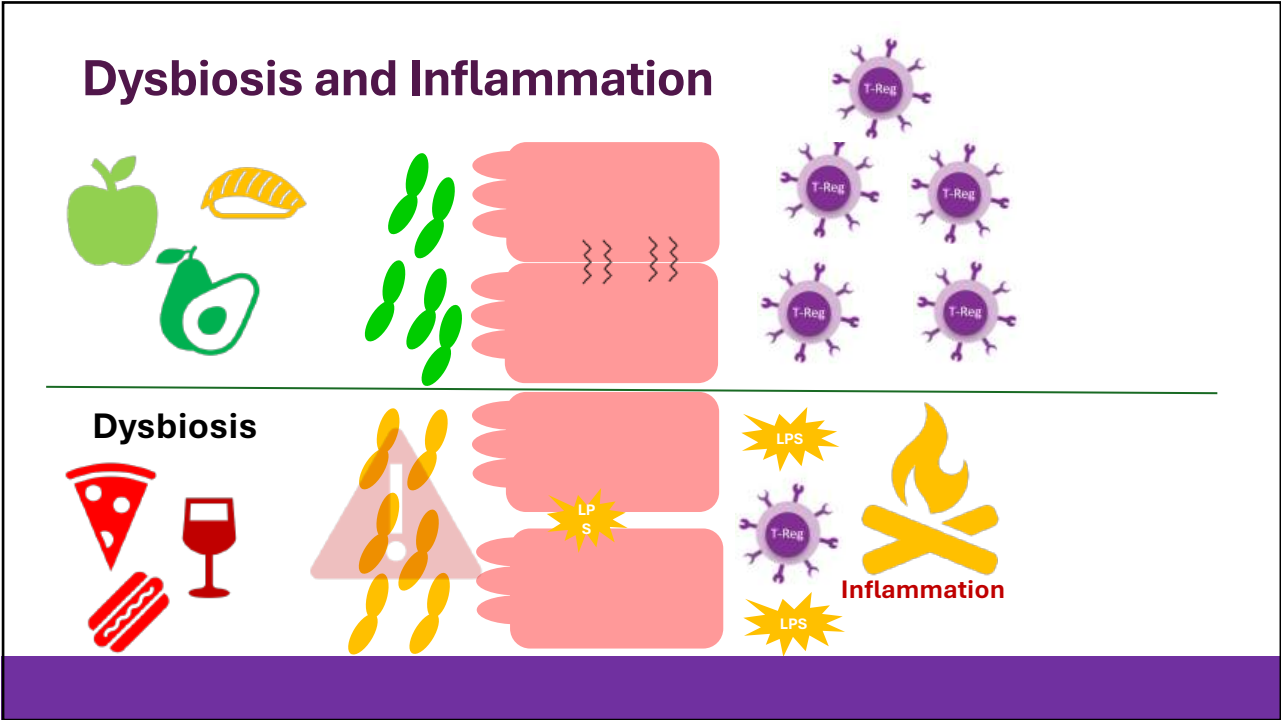
Dysbiosis and Menopause

- **Lower microbial diversity and altered phylogenetic composition**
- **Alterations in markers of gut barrier function and endotoxemia**
- **Increase in LPS producing bacteria and serum LBP levels**

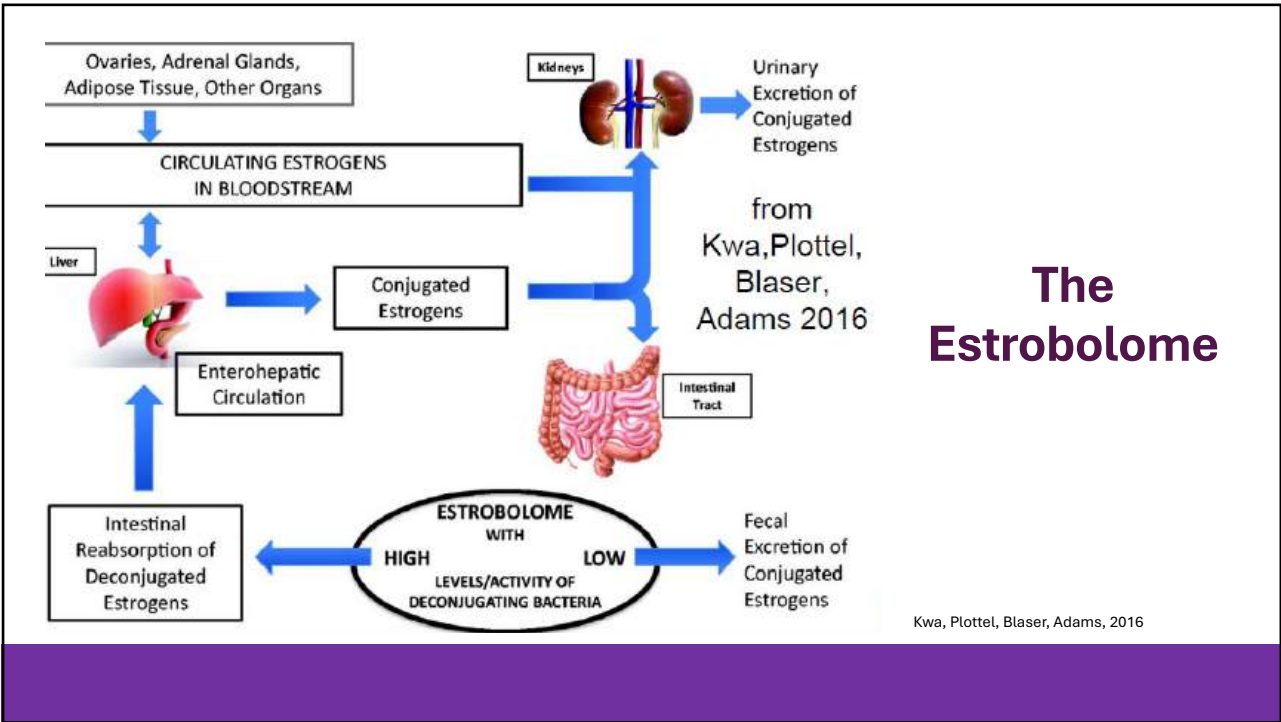
Peters BA, Santoro N, Kaplan RC, Qi Q. Spotlight on the Gut Microbiome in Menopause: Current Insights. *Int J Womens Health.* 2022;14:1059-1072

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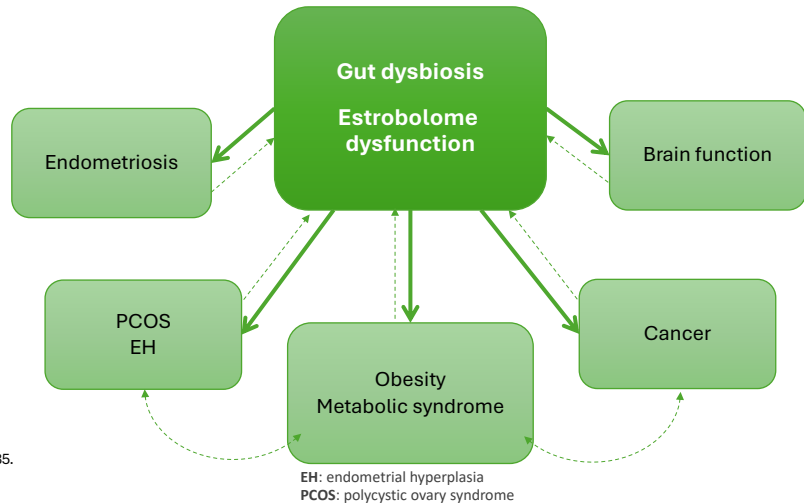
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Impact of Estrobolome Alteration

- **Estrobolome:** a unique segment of the gut microbiome capable of metabolizing and modulating estrogen
- **Dysbiosis impacts the estrobolome,** which may lead to a wide range of disease states

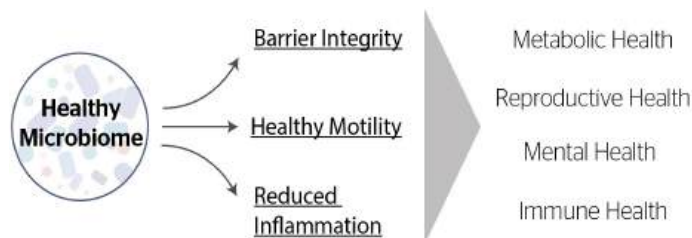


Plottel CS et al. *Cell Host Microbe*. 2011;10(4):324-335.
Baker JM et al. *Maturitas*. 2017;103:45-53.

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Healthy Microbiome: Supports all Systems

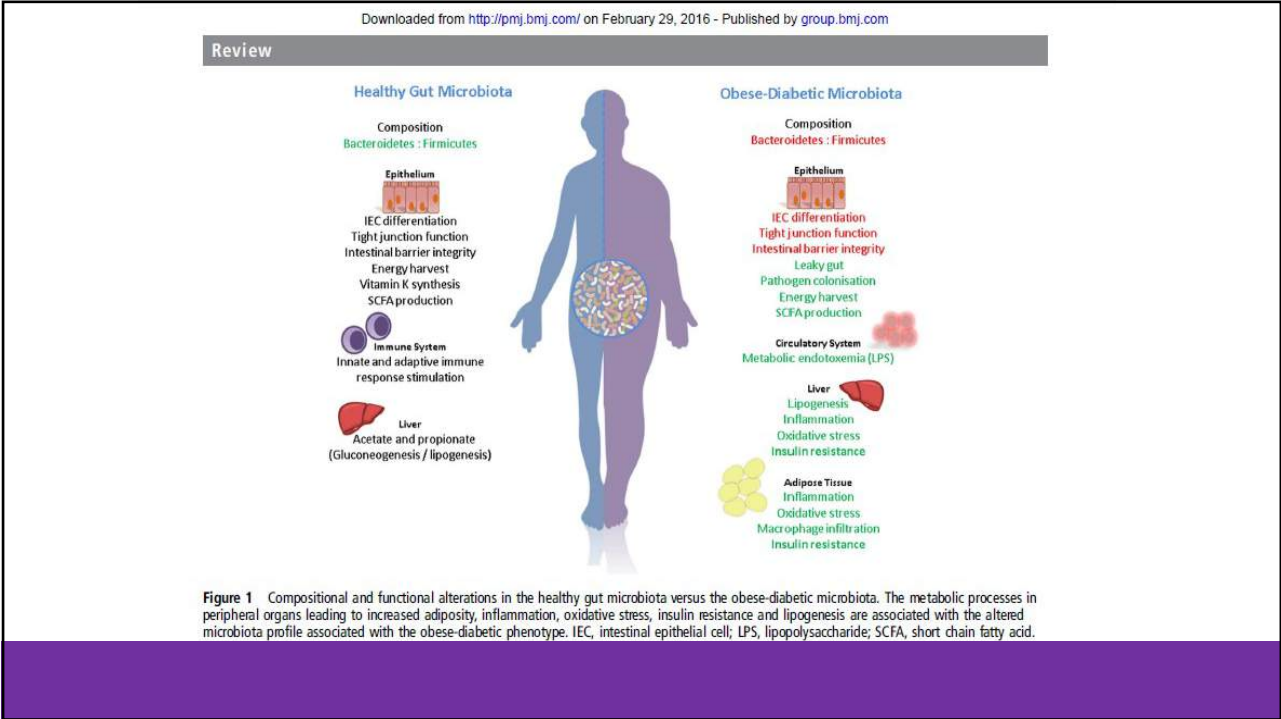
1. Immune activity
2. Hormone elimination
3. GI integrity
4. Metabolic health



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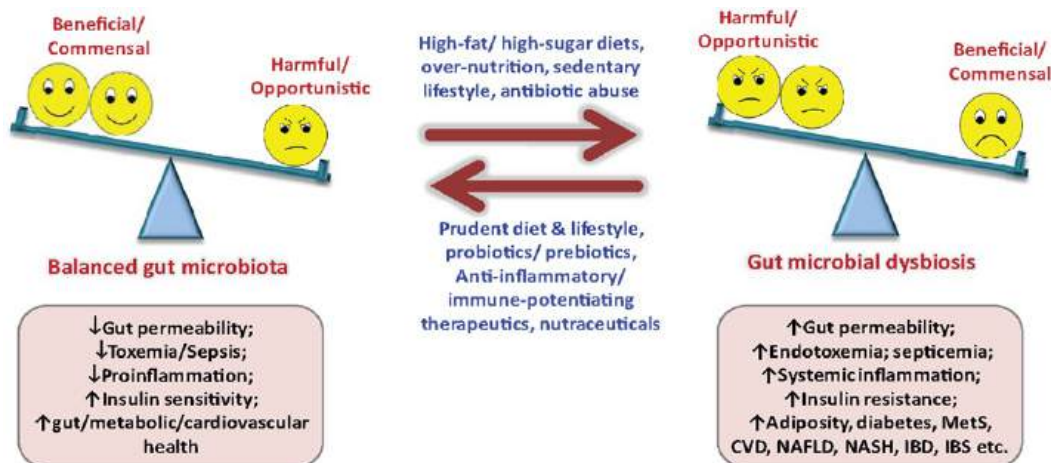
The **microbiome** is among the most important and modifiable underlying factors of **digestive health and overall wellness**

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Work to Achieve a Healthy Gut Microbiome



“Importance of balanced nutrition and gut microbiota, and consequences of gut dysbiosis. MetS, metabolic syndrome; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; CVD, cardiovascular diseases.”

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New Ways to View Food

- Food as information
- Food as medicine
- Food as a hormone
- Food as nourishment for our gut microbiota



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Feed the Gut

- Eat mostly plants & lots of fiber—**HIGH COMPLEX CARBOHYDRATES**
- Eat organic, raw, minimally processed foods—the colors of the rainbow
- Limit sugar, fat, salt
- Avoid alcohol, antibiotics from agriculture, artificial sweeteners, dairy, emulsifiers, gluten
- Take a daily probiotic
- Reboot—eat vegan for 6 months
- Get some great cookbooks



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Nitric Oxide Vegetable Listing

Highest



Moderate

- Kale
- Swiss Chard
- Arugula
- Spinach
- Chicory
- Wild Radish
- Bok Choy
- Beet
- Chinese Cabbage



- Beet Root Juice
- Lettuce
- Cabbage
- Mustard Greens
- Cauliflower
- Parsley
- Kohlrabi
- Carrot
- Broccoli

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Complex Carbohydrates (70% of diet)



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Best Diet to Nourish the Microbiome EXTREMELY HIGH FIBER

INCLUDE	• Complex carbohydrates (70%) whole-grains, all varieties of vegetables, beans, legumes, etc. • Healthy fats from nuts, seeds, olives Add Omega 3 supplement • Natural fiber and prebiotic rich foods • Probiotic rich foods • Green leafy vegetables and root vegetables
LIMIT	• Protein (approximately 12%)
AVOID	• Initially, no protein from animals, dairy, or eggs • NO Sugar and refined carbohydrates • NO Alcohol • AVOID ANY Food intolerances

Fallucca et al. 2014
Candela et al. 2016

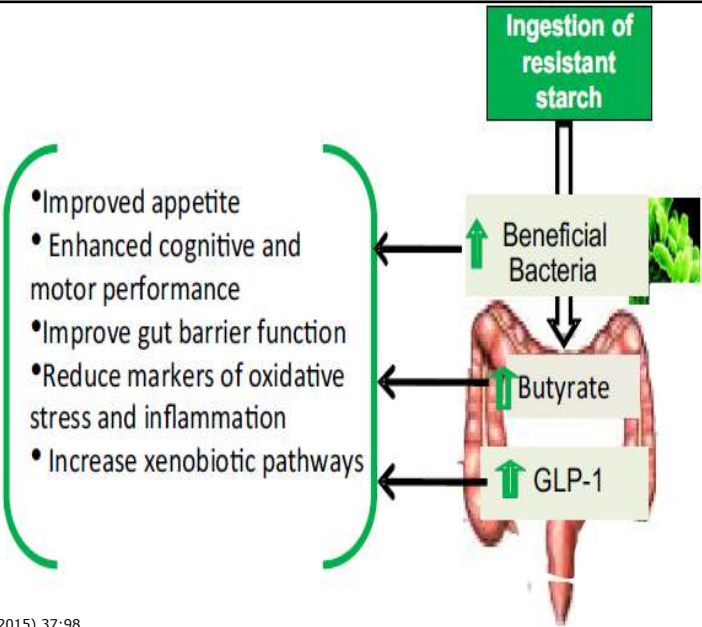
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Diversity of Microbiome Requires Dietary Diversity



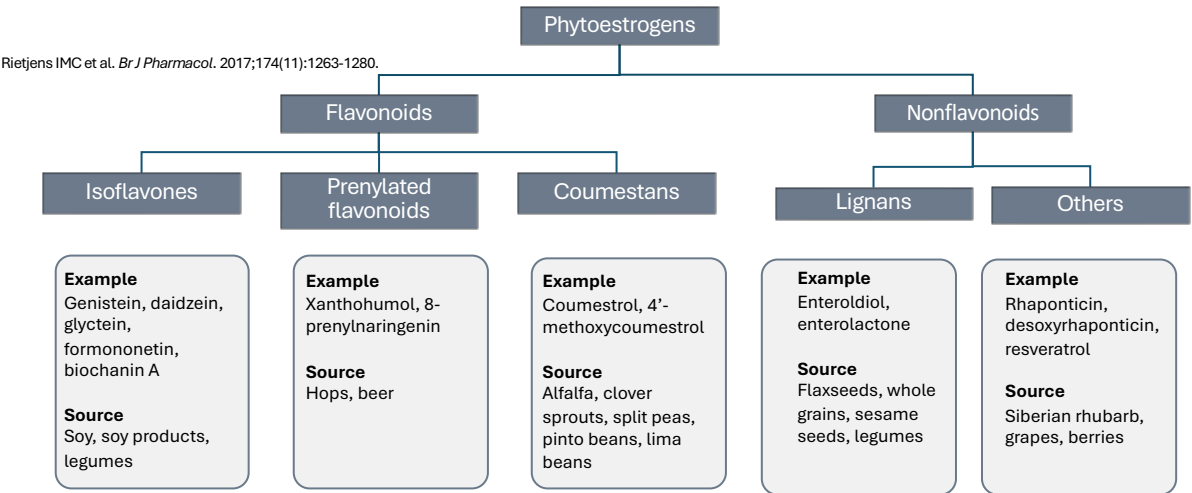
Molecular Metab 2016;1-4

Fig. 1 Proposed mechanisms of HAS and Improved healthspan. Ingestion of high-amylose starches increases beneficial microbiota and stimulates the production of butyrate and increases GLP-1 release from the gut



Keenan, M., Marco, M., Ingram, D., Martin, R. AGE (2015) 37;98

Phytoestrogens—Estrogen-Like Phytochemicals



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Hormetic Effects of Dietary Phytonutrients

- Small amounts have profound effects
- Hormone like action
- Metabolic support
- Polyphenols help shape and support the microbiome.
- Many polyphenols are metabolized by colonic bacteria into bioactive metabolites
- Mediates cell signaling pathways
- Supports growth of beneficial bacteria
- Can compete with non-beneficial bacteria and support microbial balance

Santino A, Scarano A, Santis S, et al. *Curr Pharm Des.* 2017
Etcheberry U et al. *J Agri and Food Chem* 2013; 61:9517-9533

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Phytoestrogens

After menopause, phytoestrogens and lignans support:

- **Gut health**
- **Menopausal comfort**
- **Cognitive health**
- **Cardiovascular and metabolic health**
- **Cellular health**
- **And more...**



Rietjens IM, Louisse J, Beekmann K. Br J Pharmacol. 2016 Oct 9.

Singha KK, Mridulaa D, Rehala J, Barnwala P. C Review Food Scie & Nutri. 2011. 51(3); 210-222.

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Polyphenol Dietary Sources:

Dr. Gersh's Favorites!

- **Pomegranates**
- **Berries**
- **Red Grapes**
- **Apples**
- **Cocoa**
- **Nuts and Seeds**
- **Soy**



Ettxeberria U et al. J Agri and Food Chem 2013; 61:9517-9533

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Probiotics vs. Prebiotics

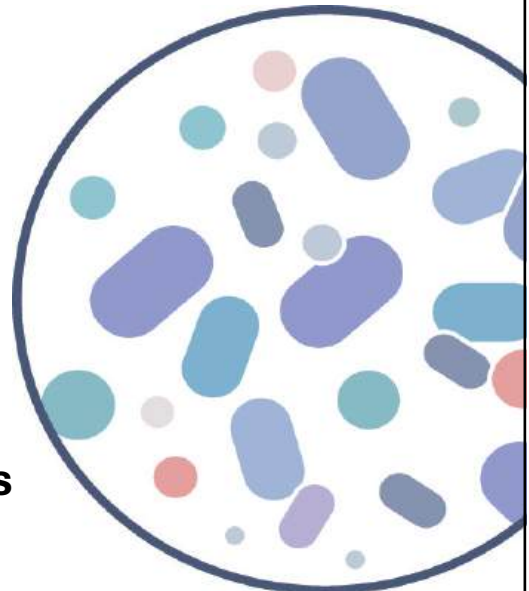
- **Probiotics**
 - Live microorganisms
- **Prebiotics**
 - Non-digestible ingredients that feed colonic bacteria
 - Beneficially affect the host by selectively stimulating the growth and activity of one or a limited number of bacteria in the colon

Gibson GR et al. J Nutr 1995; 125: 1401-1412

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Benefits of Probiotics

- Immune
- G.I.
- Cardiovascular
- Detoxification
- Vaginal health
- Synthesize essential vitamins
- Mood



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- Chai
- Cinnamon
- Chamomile
- Green
- Hibiscus
- Spearmint
- Tulsi
- Lemon grass
- Ginger
- Oolong
- English Breakfast
- Earl Grey

Some Favorite Teas



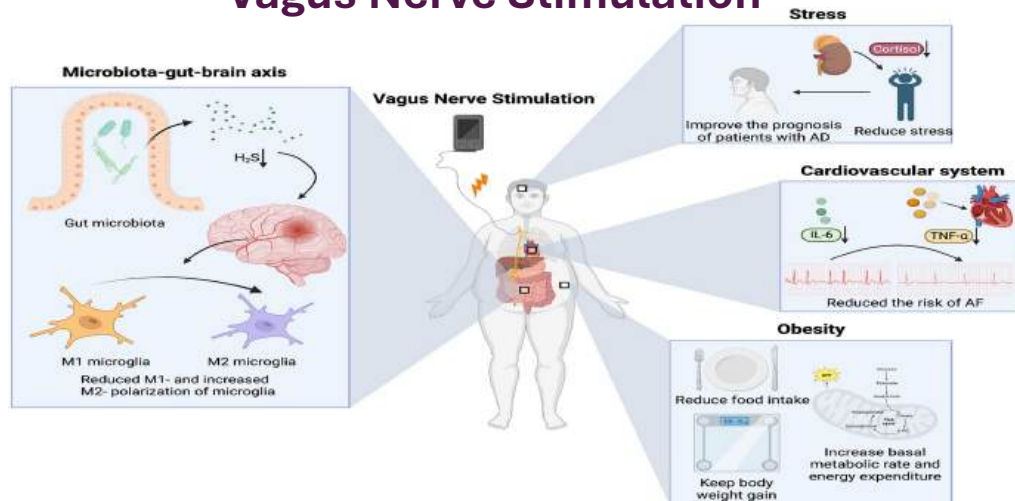
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Support for Gut and Liver Health

- | | |
|-----------------------|---|
| • L glutamine | • Resveratrol |
| • Aloe vera | • Curcumin |
| • Chlorella | • Green tea |
| • Psyllium fiber | • Garlic |
| • Flaxseed | • Omega-3 |
| • Probiotics | • Polyphenols: blueberries, raspberries |
| • Amino acids | • Ellagic acid / Urolithin A |
| • Sulforaphane, DIM | • Quercetin |
| • Calcium D glucarate | • Black ginger |
| • Milk thistle | • N-acetylcysteine (NAC) |
| | • Essential vitamins/minerals |
| | • Zinc Carnosine |

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Vagus Nerve Stimulation



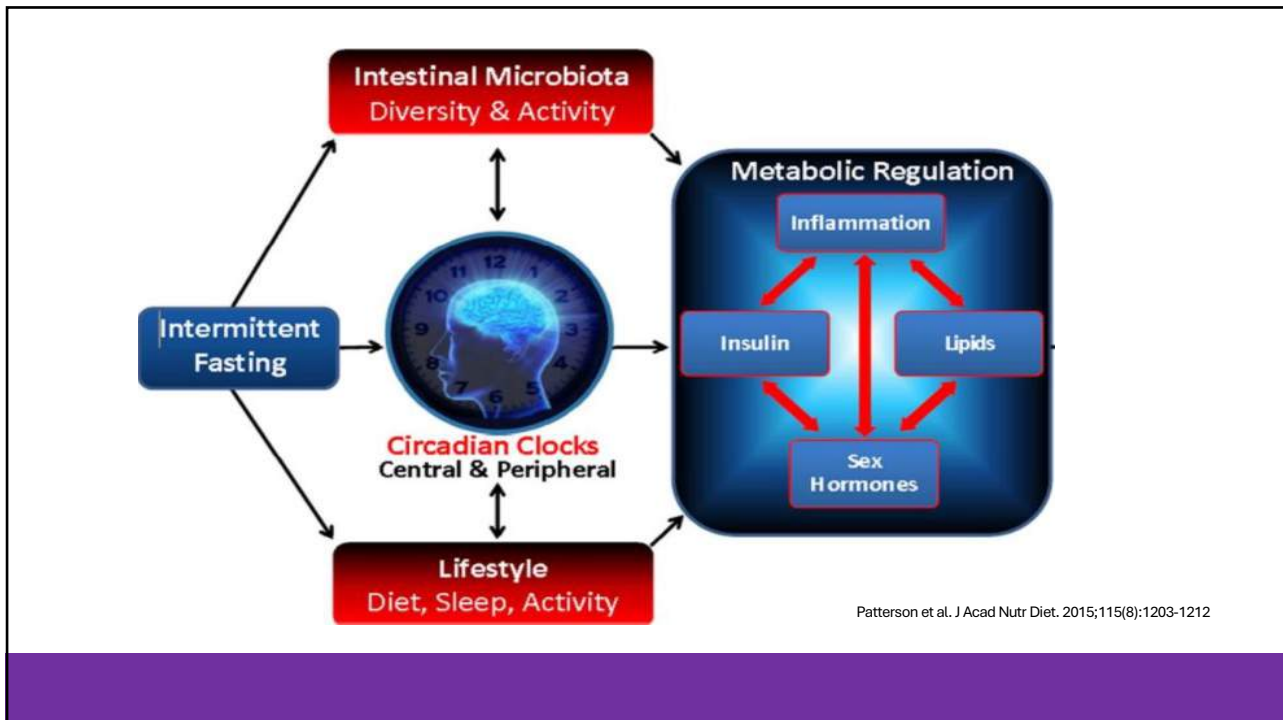
Jin, Z., Dong, J., Wang, Y. *et al.* Exploring the potential of vagus nerve stimulation in treating brain diseases: a review of immunologic benefits and neuroprotective efficacy. *Eur J Med Res* 28, 444 (2023).

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Vagus Nerve Stimulation

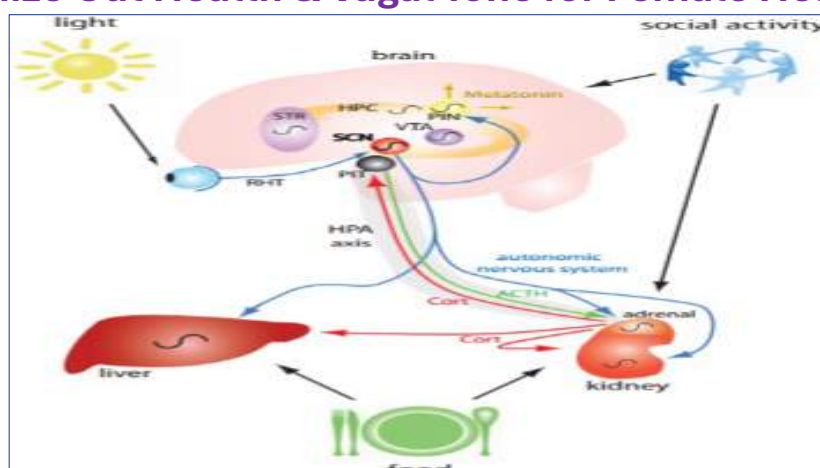
- Vagus Nerve Stimulator
- Laughter yoga
- Guided meditation & biofeedback - heart rate variability
- Meditation
- Breathwork
- Singing and chanting
- Gargling
- Cold plunges
- Acupuncture
- Massage
- Essential oils
- Gut Microbiome support: Probiotics & Prebiotics
- Support Circadian Rhythm
- Adrenal adaptogens
- Omega 3
- Exercise
- Socializing

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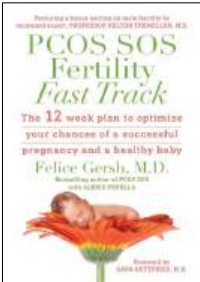
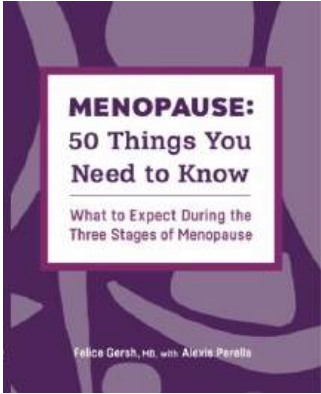
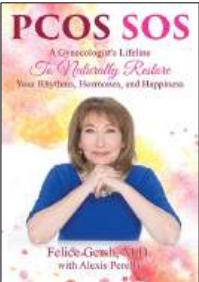
Incorporate All Efficacious Modalities: Optimize Gut Health & Vagal Tone for Female Health



Behav Neurosci 128(3) pp 326-43. 2014.pdf

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Thank you!





Let's keep in touch!

 @FeliceGershMD
 @dr.felicegersh
 @felicegershmd

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NMI SUMMIT 2026

Longevity and Biological Ageing: Enhancing Health into Advanced Age

Saturday 10th October

Featuring Dr. Felice Gersh, Professor Kostas Tsintzas, Dr. Denise Furness, and Dr. Jeffrey Bland.



An event by:  Nutritional Medicine Institute

Platinum sponsors:   regenerus labs

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