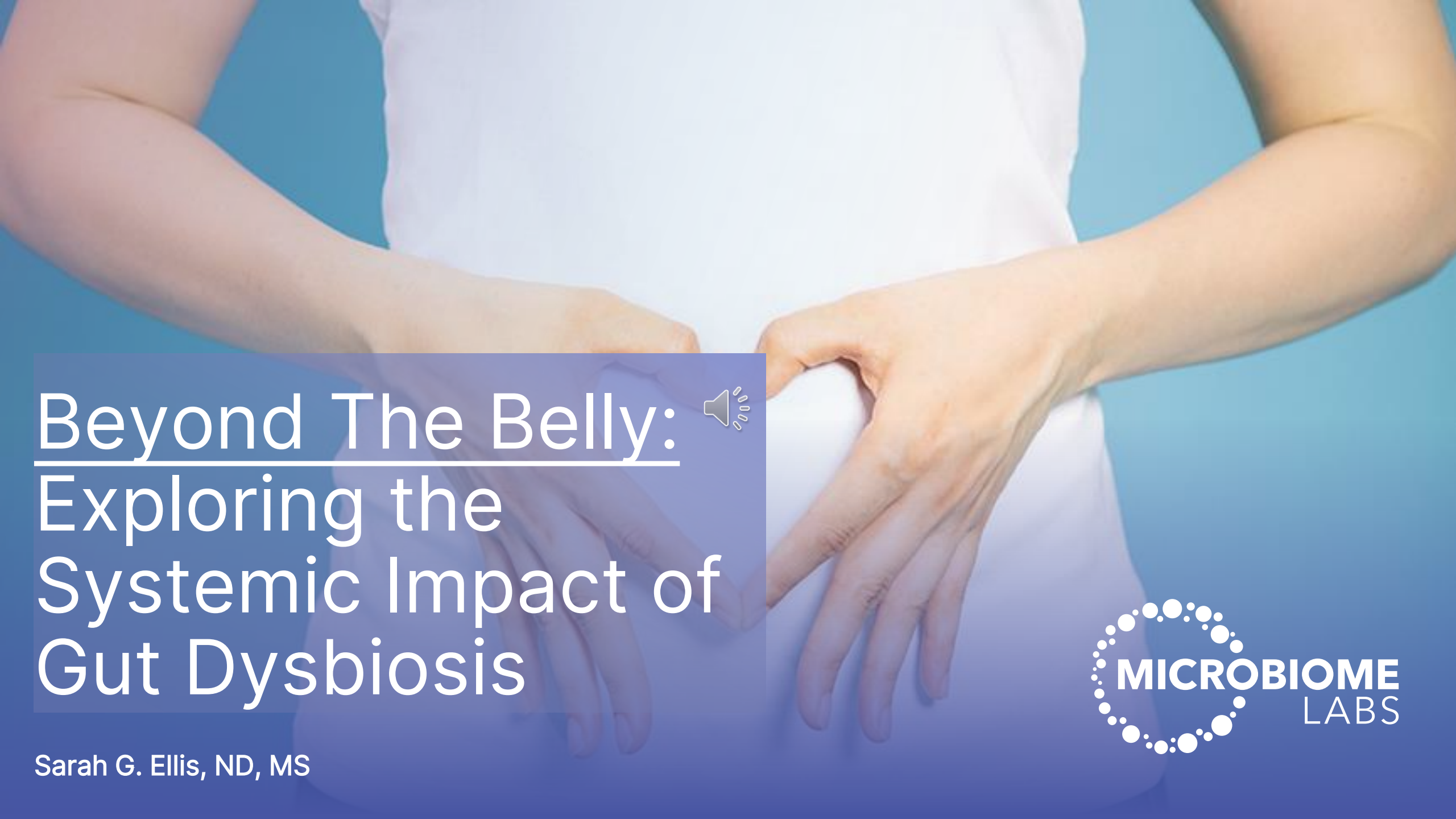


Beyond The Belly: Exploring the Systemic Impact of Gut Dysbiosis

MICROBIOME LABS

Sarah G. Ellis, ND, MS

Agenda

- Brief Overview of Gut Dysbiosis
- Differences between a Healthy vs Leaky Gut
- The Impact of Gut Dysbiosis on Overall Health
- Dysbiosis & The Gut-Brain Axis
- Dysbiosis & The Gut-Heart Axis
- Dysbiosis & The Gut-Lung Axis
- Dysbiosis & The Gut-Endocrine Axis
- Dysbiosis & The Gut-Immune Axis
- Dysbiosis & The Gut-Genitourinary Axis
- Summary

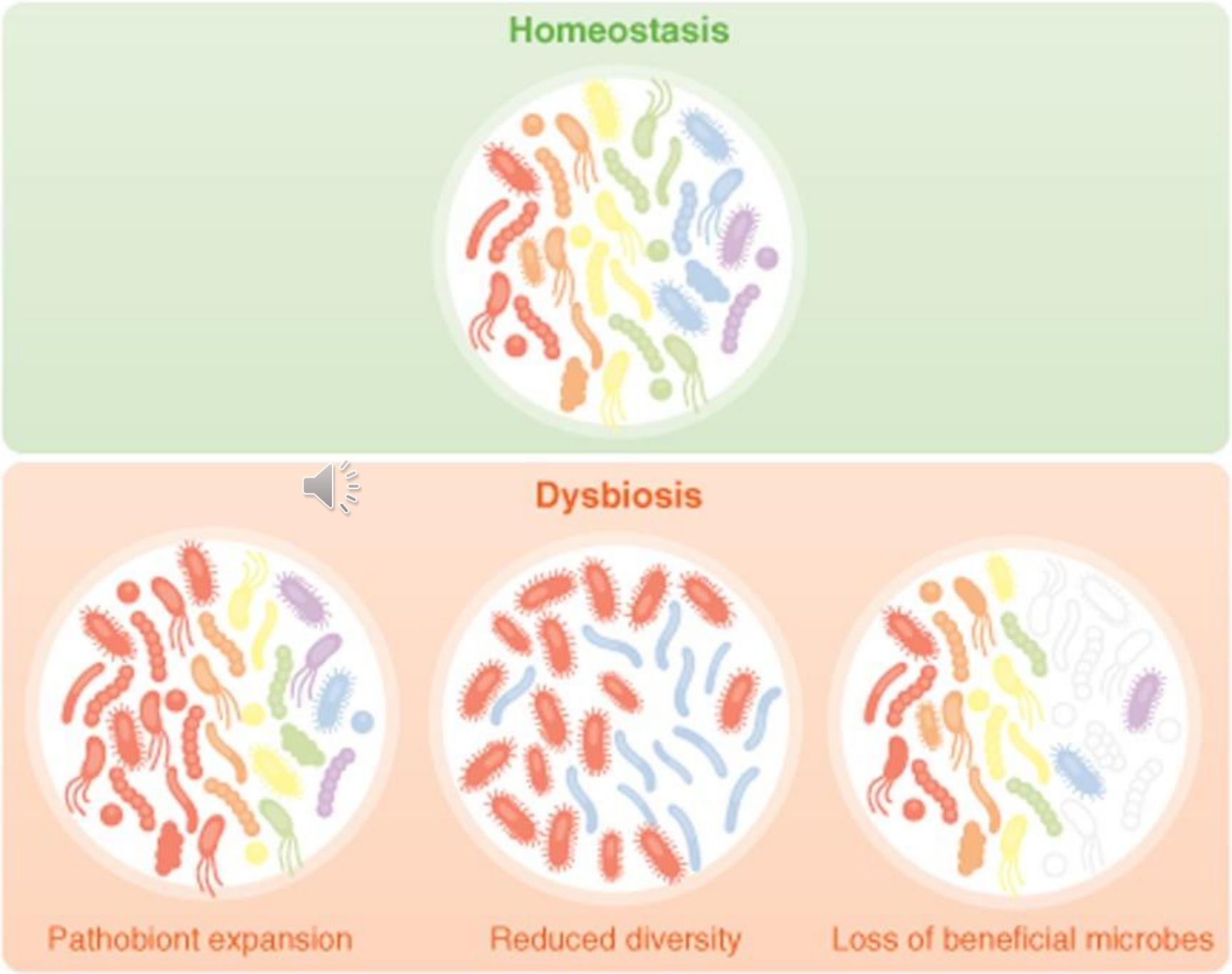
MICROBIOME LABS

Overview of Gut Dysbiosis

Dysbiosis can be defined as a reduction in microbial diversity and a combination of the loss of beneficial bacteria and a rise in pathobionts.

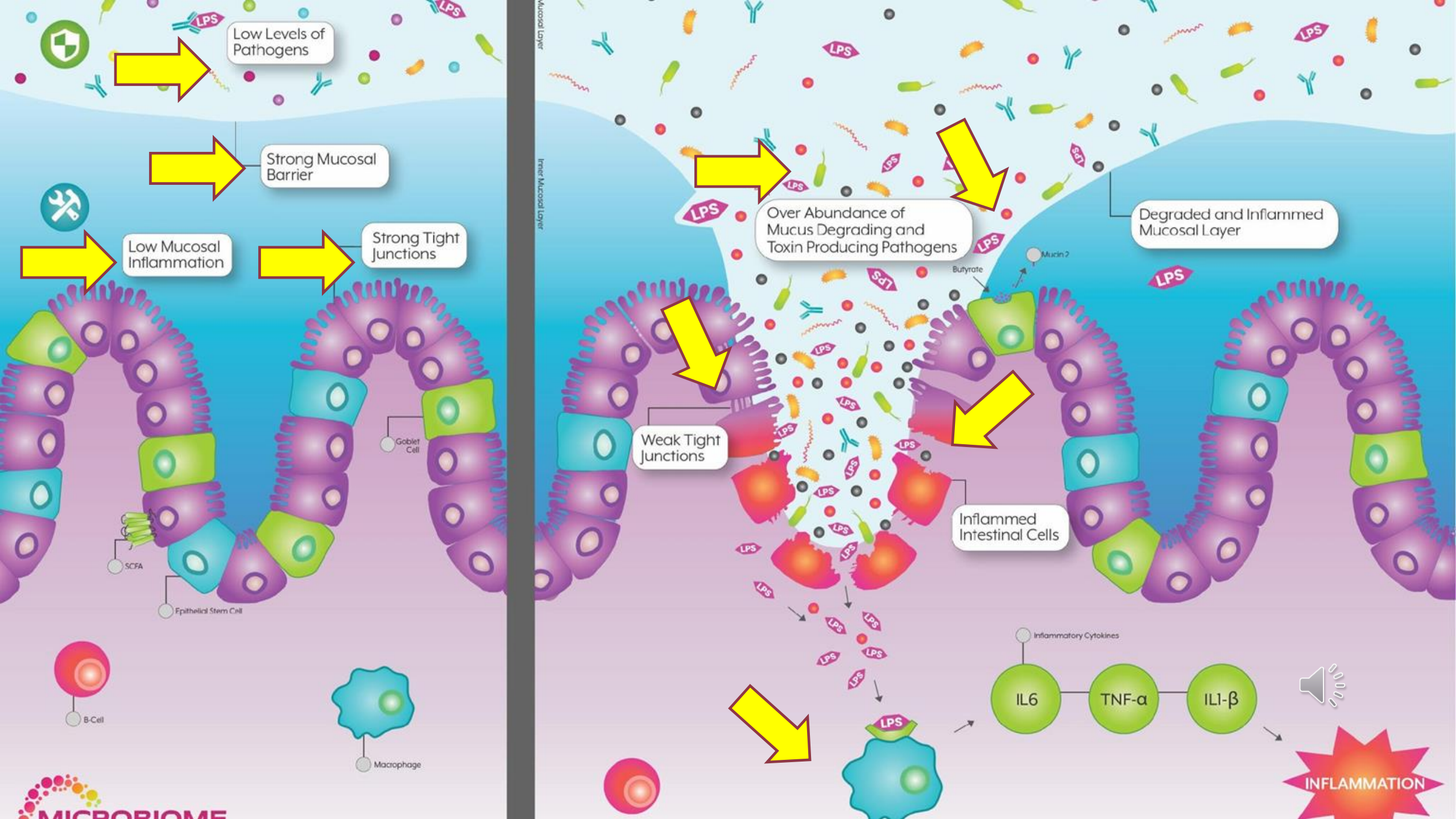
Signs of Dysbiosis on a Stool Test:

- Decreased alpha & beta diversity
- Decreased keystone species
- Decreased production of beneficial by-products
- Increased pathobionts
- Increased production of harmful by-products
- Increased inflammation



Dysbiosis risk factors

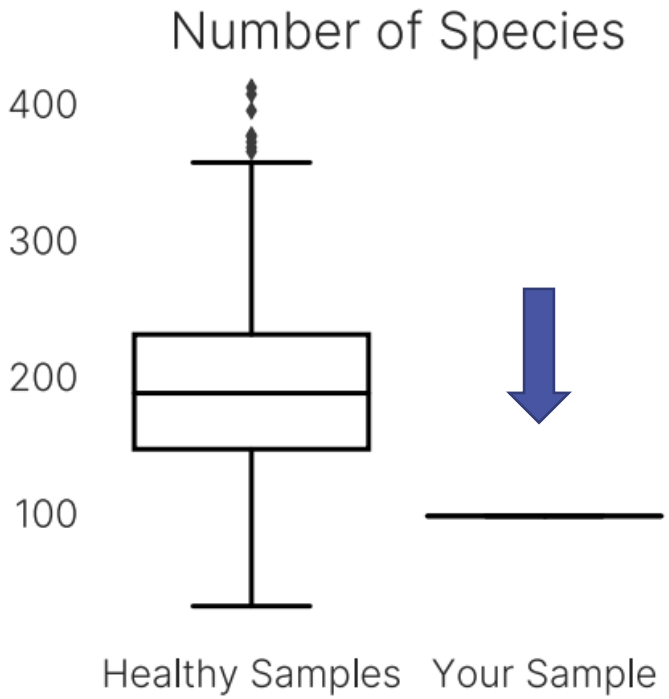
- Prescription Antibiotics
- Natural Antimicrobials
- Pesticides
- Infections
- Excessive Alcohol Intake
- Smoking
- Stress
- Lack of Sleep
- Intense Exercise
- Standard American Diet/Saturated Fats


Low Levels of Pathogens
Strong Mucosal Barrier
Low Mucosal Inflammation
Strong Tight Junctions
Goblet Cell
SCFA
Epithelial Stem Cell
B-Cell
Macrophage
Outer Mucosal Layer
Inner Mucosal Layer
Over Abundance of Mucus Degrading and Toxin Producing Pathogens
Degraded and Inflammed Mucosal Layer
Mucin 2
Butyrate
Weak Tight Junctions
Inflammed Intestinal Cells
Inflammatory Cytokines
IL6
TNF-α
IL1-β
INFLAMMATION
LPS

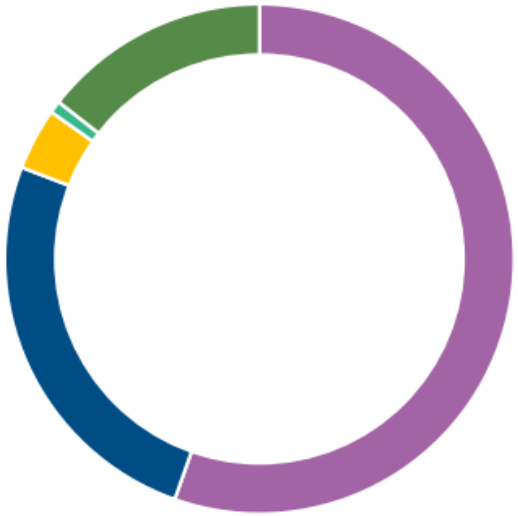
Dysbiosis risk factors alter the core microbiome

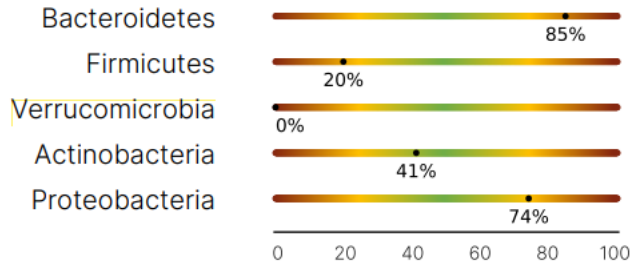
Alpha Diversity

Number of species in the gut microbiome: **98**
Your Alpha Diversity was found to be: **6.18**



Phylum Level Your Sample





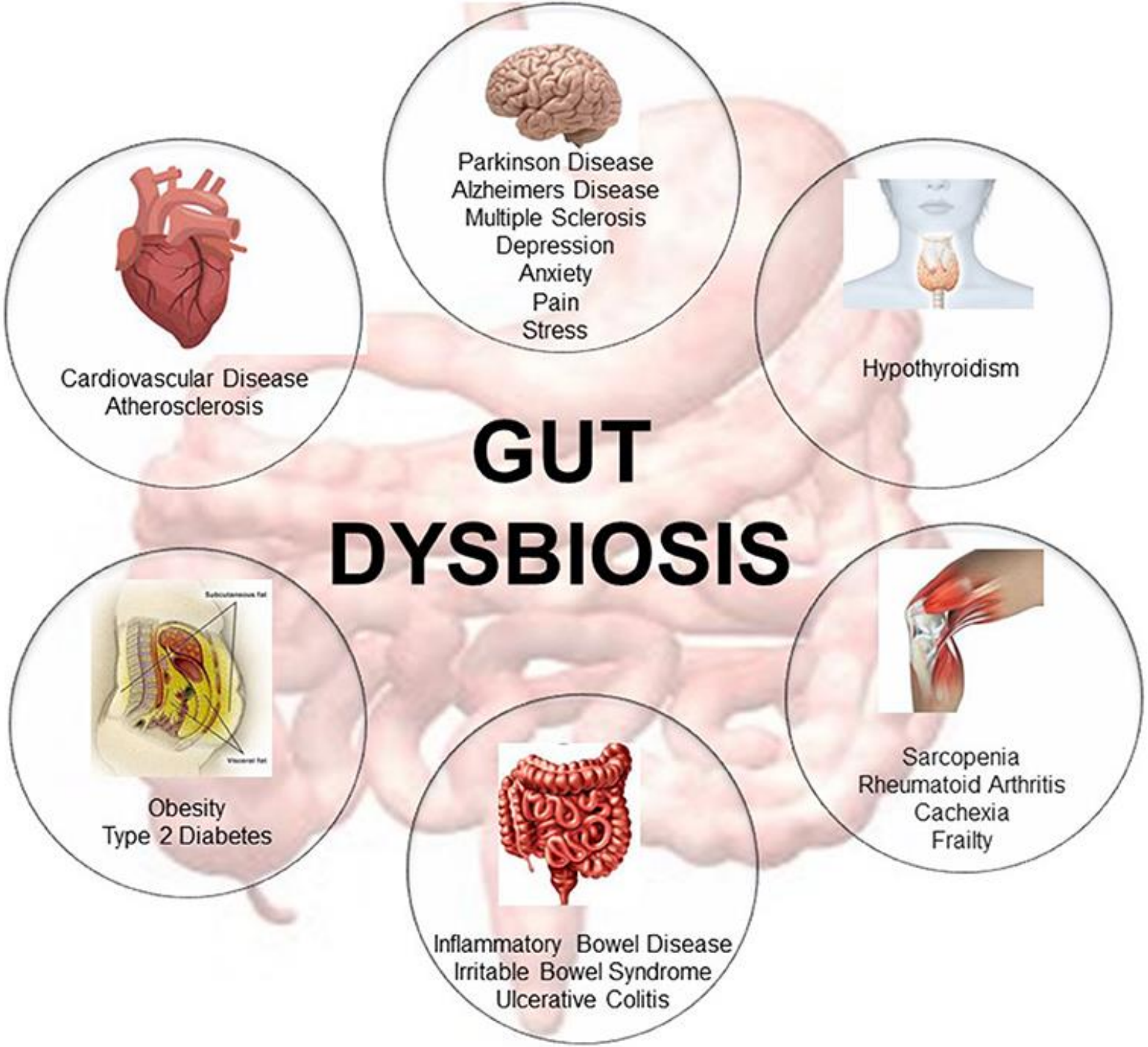
- Bacteroidetes 55.40%
- Firmicutes 25.45%
- Proteobacteria 3.92%
- Actinobacteria 0.78%
- Others 14.45%

MICROBIOME LABS

Bacterial contributions of a healthy Gut vs Dysbiotic Gut

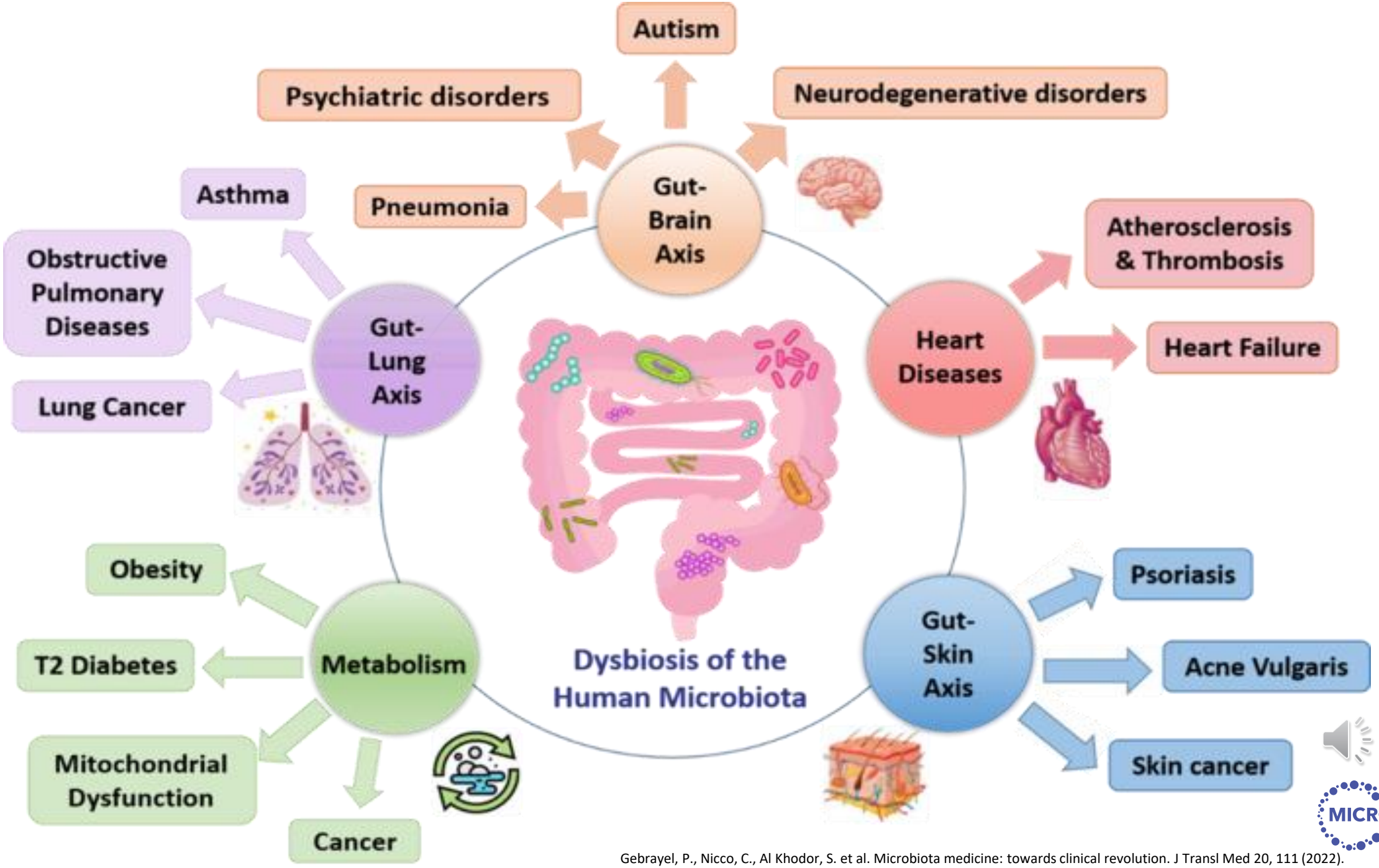
Commensals	Opportunistic/Pathogenic
Short-Chain Fatty Acids	Ammonia
Vitamins	Hydrogen Sulfide
Antioxidants	Methane
Neurotransmitters	Toxins and virulence factors
Optimize the gut pH	Lipopolysaccharide (LPS)

MICROBIOME LABS

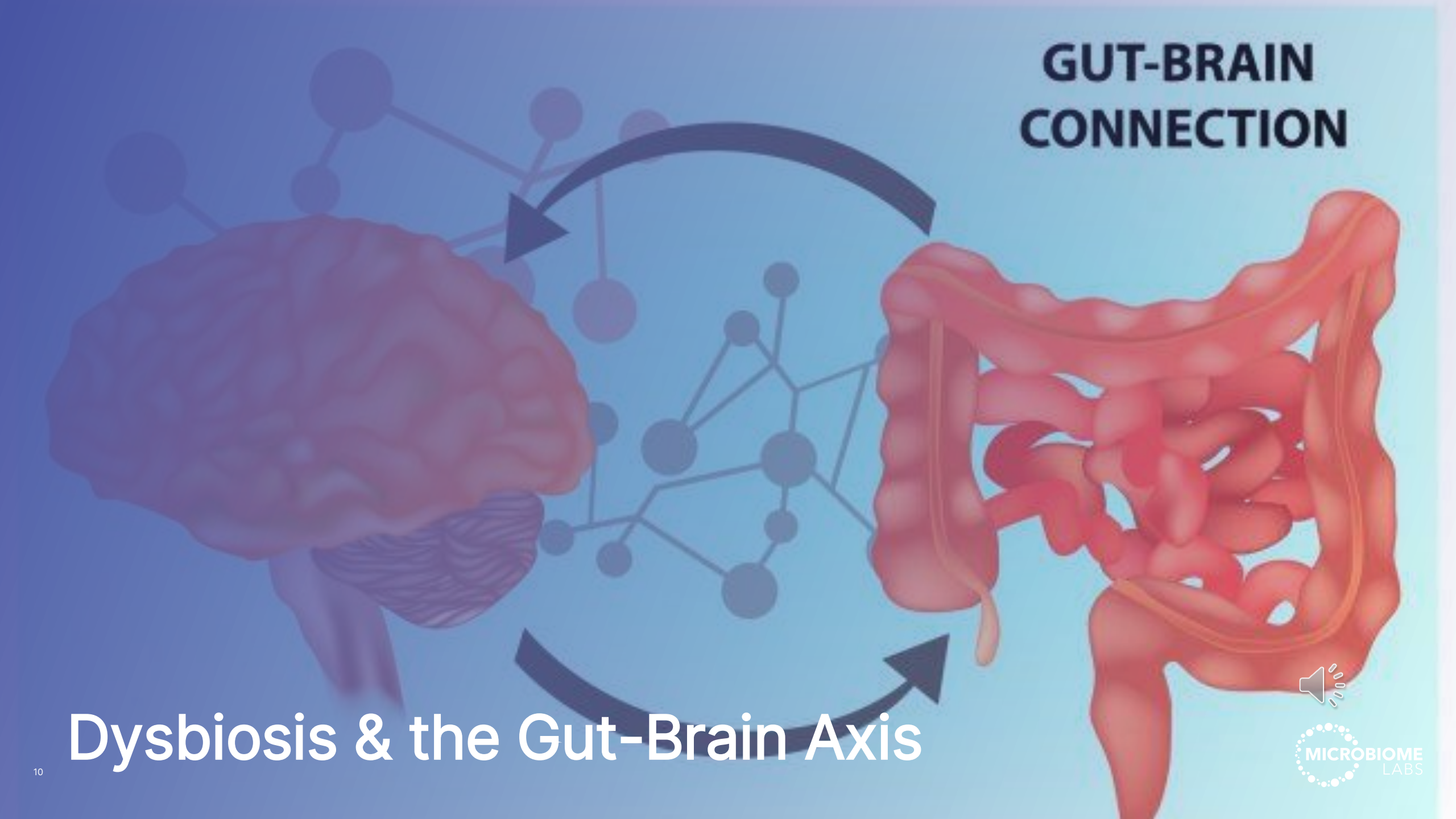


MICROBIOME IMPACT

- Metabolic dysfunction
- Autoimmunity
- Skin conditions
- Nervous system disorders
- Hormone balance
- Liver health and function
- Anxiety and depression



Gebrayel, P., Nicco, C., Al Khodor, S. et al. Microbiota medicine: towards clinical revolution. J Transl Med 20, 111 (2022). https://doi.org/10.1186/s12967-022-03296-9



Dysbiosis & the Gut-Brain Axis

MICROBIOME LABS

The Enteric Nervous System

There are *a lot* of neurons in the ENS

There are more neurons in the gut (>100 million) than there are in the entire spinal cord.

The Brain in Your Gut

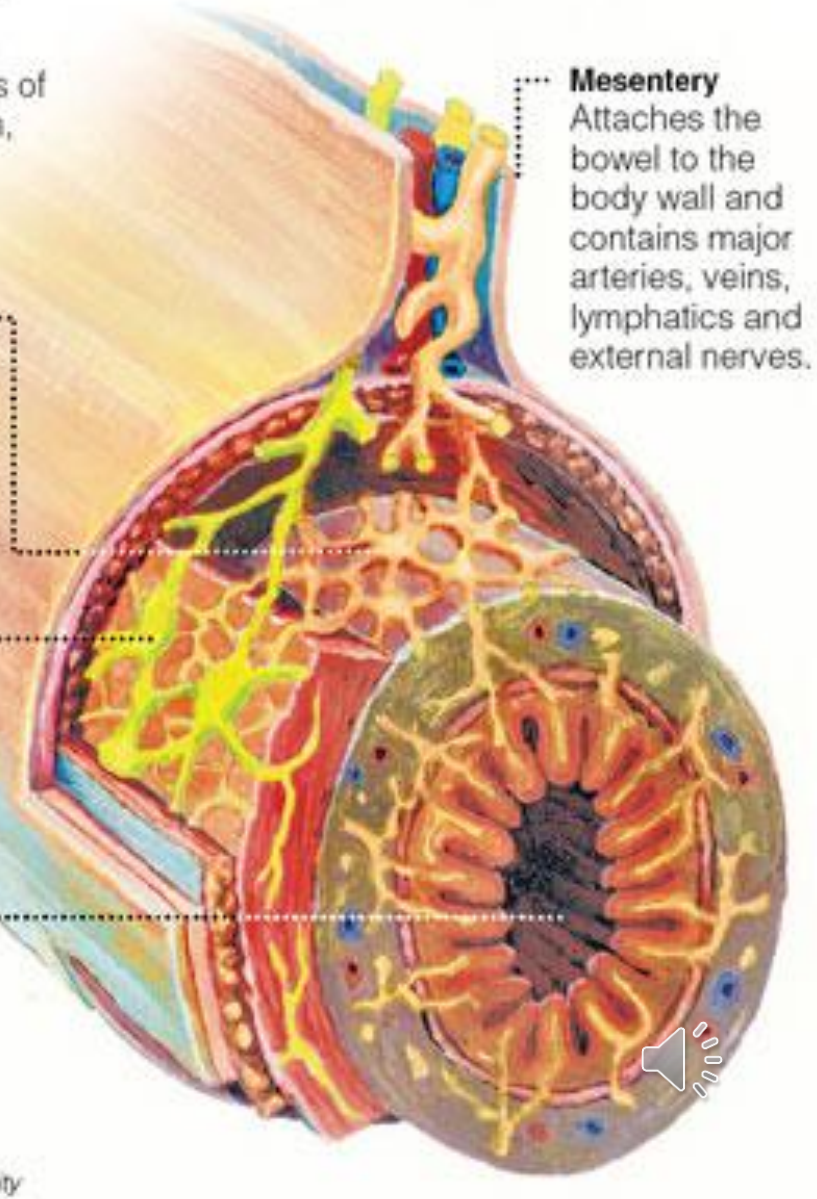
The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

SMALL INTESTINE CROSS SECTION

Submucosal plexus Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

Myenteric plexus Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

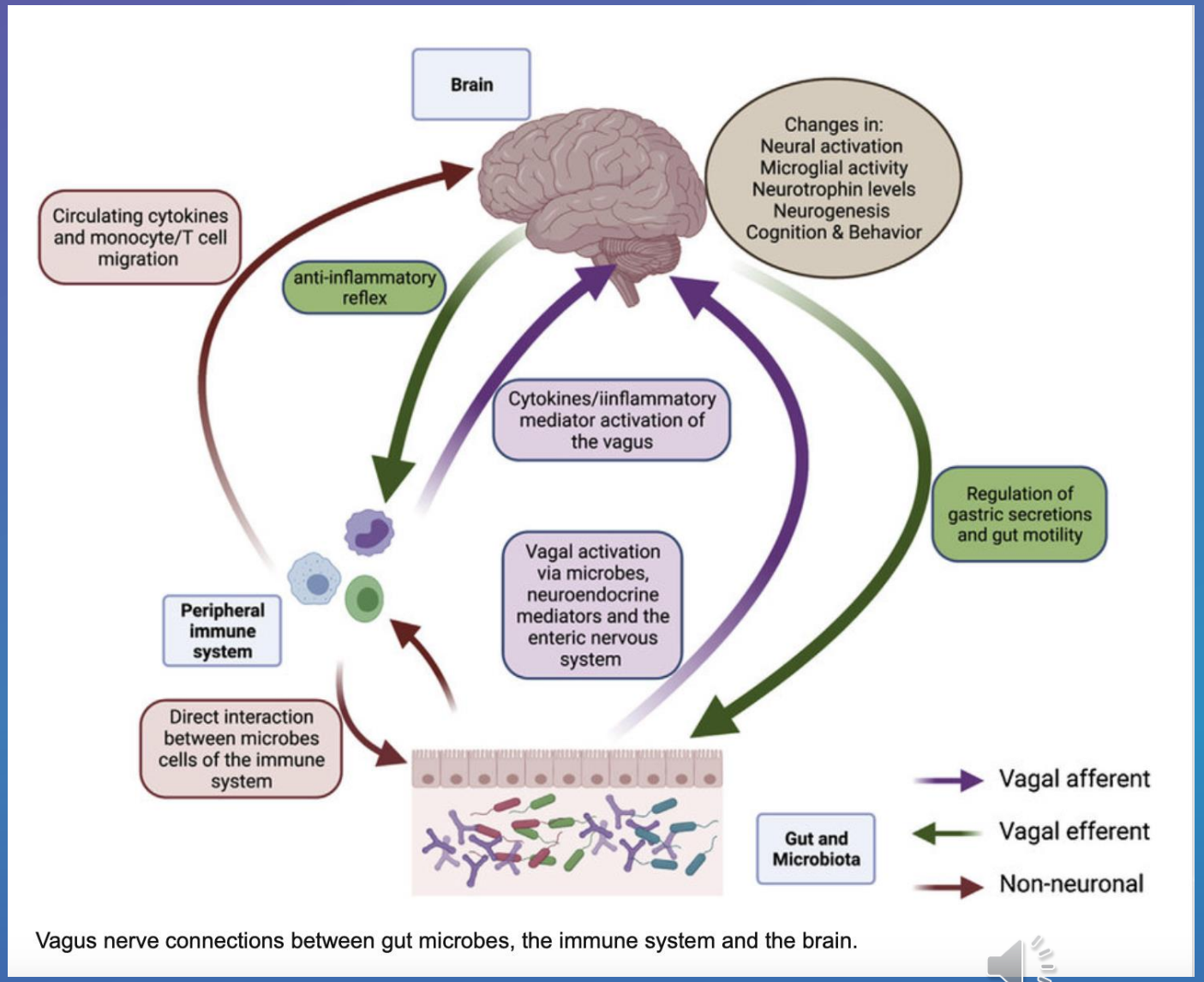
Lumen No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.



Source: Dr. Michael D. Gershon, Columbia University

The Vagus Nerve

- Gut-Brain Axis: Bidirectional communication between the gut and the brain; regulates GI homeostasis and connects emotional/ cognitive areas of the brain with gut functions
  - Vagus Nerve, brain, spinal cord
  - Endocrine system (HPA axis)
  - Immune system
  - Gut microbiome
- Enteric nervous system (ENS): more nerves than the spine and produces more than 30 neurotransmitters
- Hormones and peptides released by ENS into the blood can cross the blood brain barrier (BBB), like ghrelin, and act with the vagus nerve
- Afferent = Gut to Brain signal (90% of signals)
- Efferent= Brain to Gut signal (10% of signals)



Vagus nerve connections between gut microbes, the immune system and the brain.

The Vagus Nerve

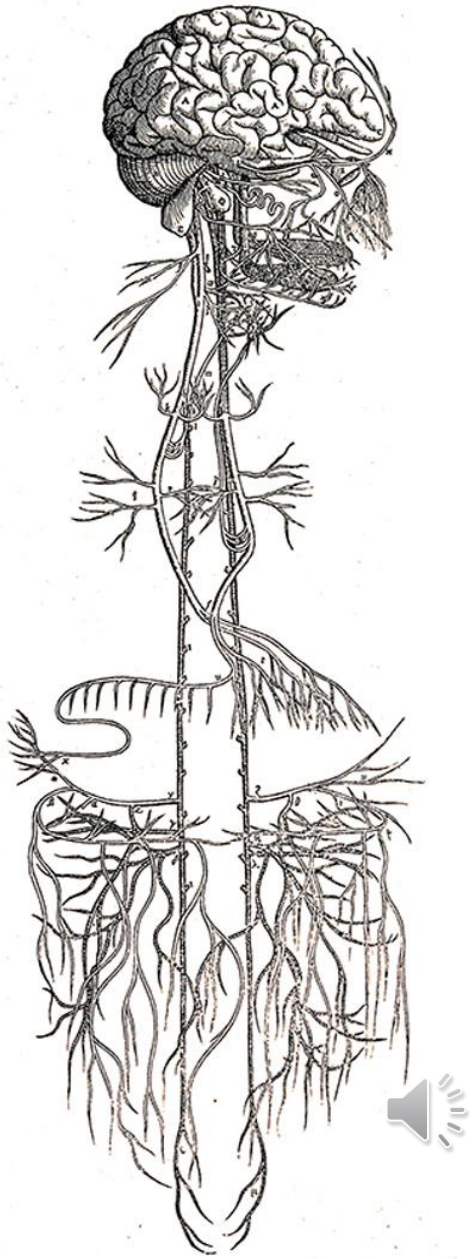
The vagus nerve is the 10th cranial nerve and the fastest and most direct route that connects the gut and the brain.

Its name is derived from the Latin for wandering, due to its extensive innervation, which allows collection of information from different visceral organs

- **Neck:** innervates pharynx and larynx (swallowing)
- **Chest/thorax:** parasympathetic supply to the heart (reduces heart rate)
- **Intestines:** regulates contraction of smooth muscles and glandular secretions; innervates the muscular and mucosal layers of the gut (lamina propria)
- **GI vagal afferents:** receptors in the esophagus, stomach, and proximal small intestine, and sensory endings in the liver and pancreas

Responsible for:

- Regulating internal organ functions (digestion, heart rate, and respiratory rate)
- Vasomotor activity, and certain reflex actions (coughing, sneezing, swallowing, and vomiting)



The Rise of Functional Gastrointestinal Disorders (FGIDs)

Defined as a group of disorders characterized by a constellation of chronic GI symptoms:

Abdominal pain
Dysphagia
Dyspepsia
Diarrhea
Constipation
Bloating

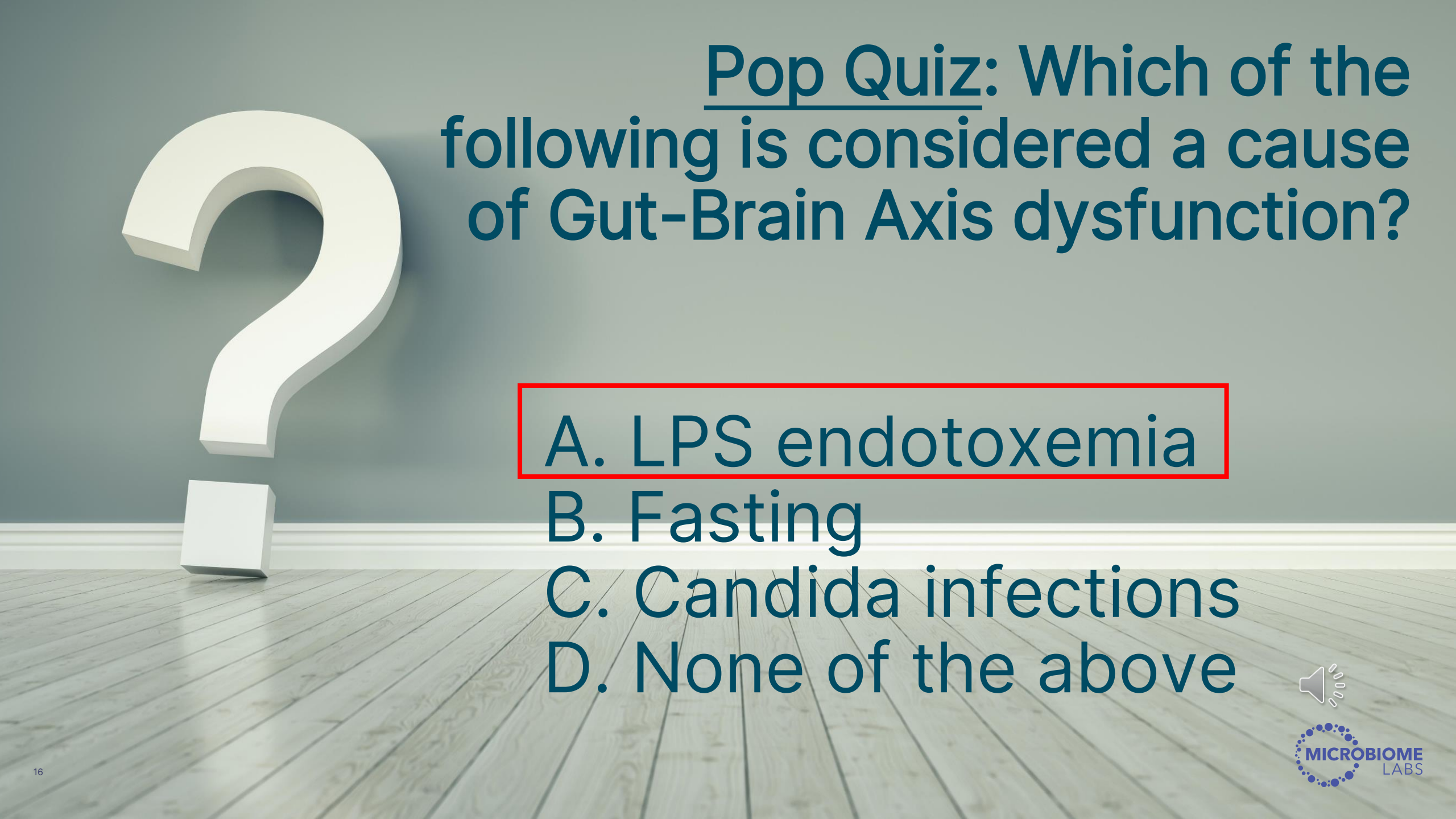
These conditions arise due to alterations in gut-brain communication.

They account for over 30% of gastroenterology outpatient visits and are often associated with chronic pain (FM) and other functional syndromes (CFS, etc.).

According to the ROME IV classification system there are *33 adult disorders and 20 pediatric disorders*

Including:
Functional dysphagia
Functional heartburn
Functional Dyspepsia
Rumination syndrome
Irritable Bowel Syndrome (IBS)
Functional constipation/diarrhea
Fecal incontinence

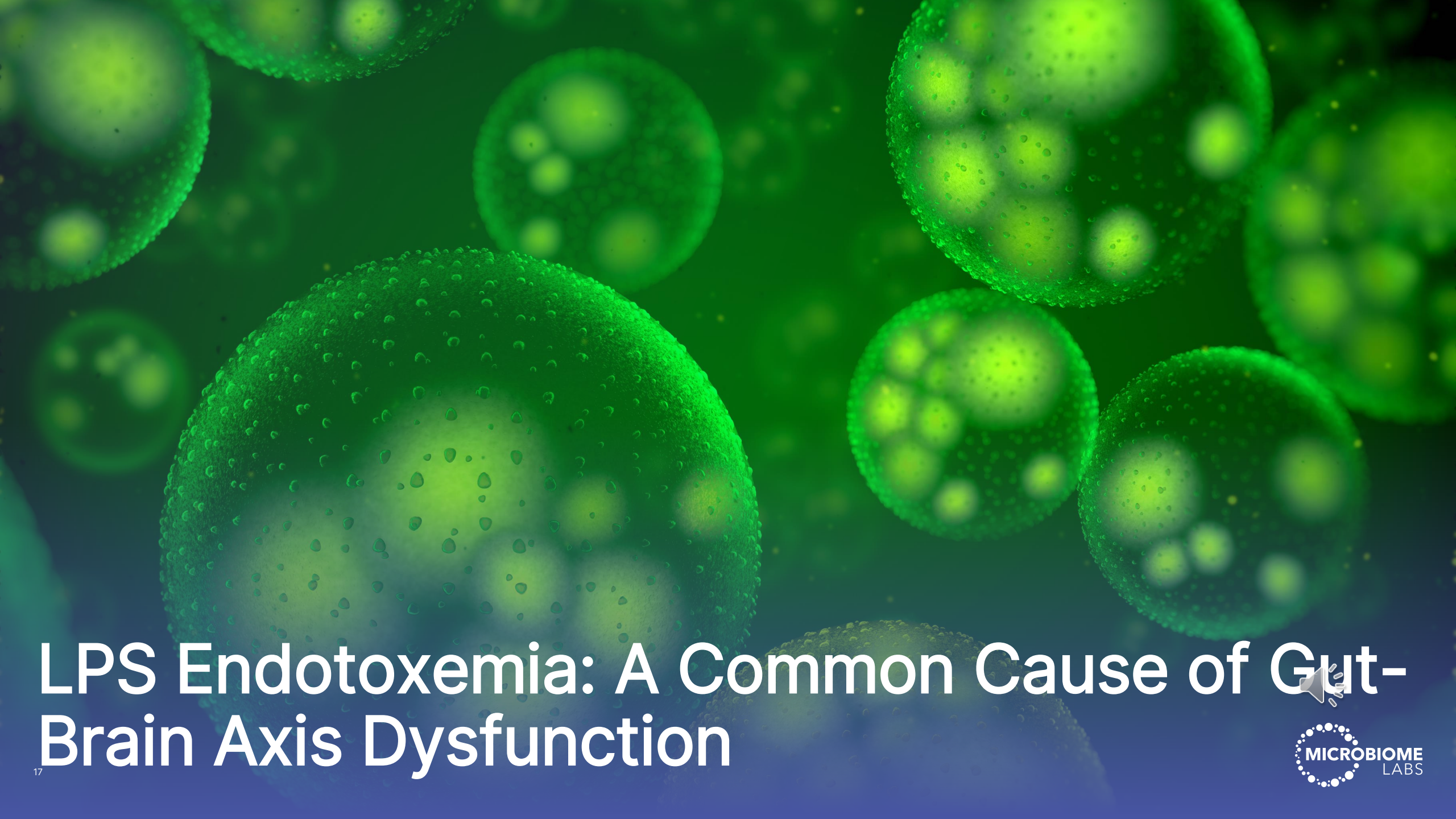
MICROBIOME LABS



Pop Quiz: Which of the following is considered a cause of Gut-Brain Axis dysfunction?

A. LPS endotoxemia
B. Fasting
C. Candida infections
D. None of the above

MICROBIOME LABS



LPS Endotoxemia: A Common Cause of Gut-Brain Axis Dysfunction

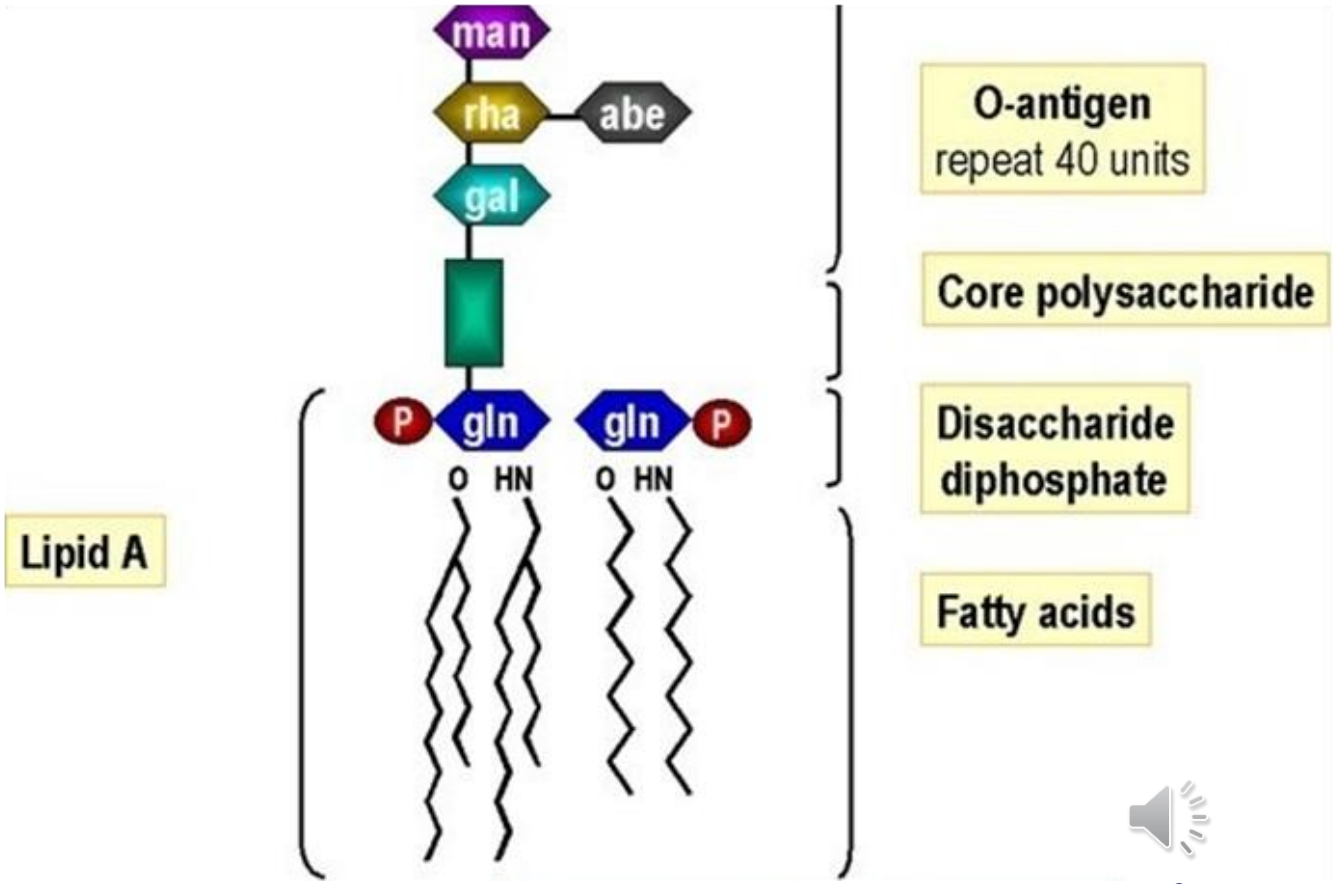
MICROBIOME LABS

LPS Endotoxin Driven Inflammation

LPS Basics:
- Endotoxin by gram negative bacteria
- Gram (-) bacteria make up 50-60% of the bacteria in our microbiome.
- When it is *inside of* the bacteria it doesn't cause harm.

The Problem:
- When the bacteria die, they release LPS into the lumen
- if it seeps out of a leaky gut with weakened tight junctions and enters circulation *the first place it goes to is the brain*.

In the brain it can wreak havoc.....



MICROBIOME LABS

The gut-brain barrier in major depression: Intestinal mucosal dysfunction with an increased translocation of LPS from gram negative enterobacteria (leaky gut) plays a role in the inflammatory pathophysiology of depression

Michael MAES [1], Marta KUBERA [2] and Jean-Claude LEUNIS [3]

1. MCare4U Outpatient Clinics, Belgium;
2. Department of Experimental Neuroendocrinology, Institute of Pharmacology, Polish Academy of Sciences, Krakow, Poland;
3. Laboratory Ategis, Waver, Belgium.

Correspondence to: Prof. Dr. M.Maes, M.D., Ph.D. Director: M-Care4U Outpatient Clinics, Olmenlaan 9, 2610 Antwerp, Belgium. TEL: +32-3-4809282 FAX: +32-3-2889185 www.michaelmaes.com E-MAIL: crc.mh@telenet.be

Submitted: 2008-01-06 *Accepted: 2008-01-27* *Published online: 2008-02-22*

Key words: **major depression; chronic fatigue syndrome; inflammation; enterobacteria; leaky gut; gut permeability; cytokines; LPS; oxidative stress**

Neuroendocrinol Lett 2008; **29**(1):117–124 **PMID:** 18283240 NEL290108A12

Abstract

There is now evidence that major depression (MDD) is accompanied by an activation of the inflammatory response system (IRS) and that pro-inflammatory cytokines and lipopolysacharide (LPS) may induce depressive symptoms.
The aim of the present study was to examine whether an increased gastrointestinal permeability with an increased translocation of LPS from gram negative bacteria

ORIGINAL AR

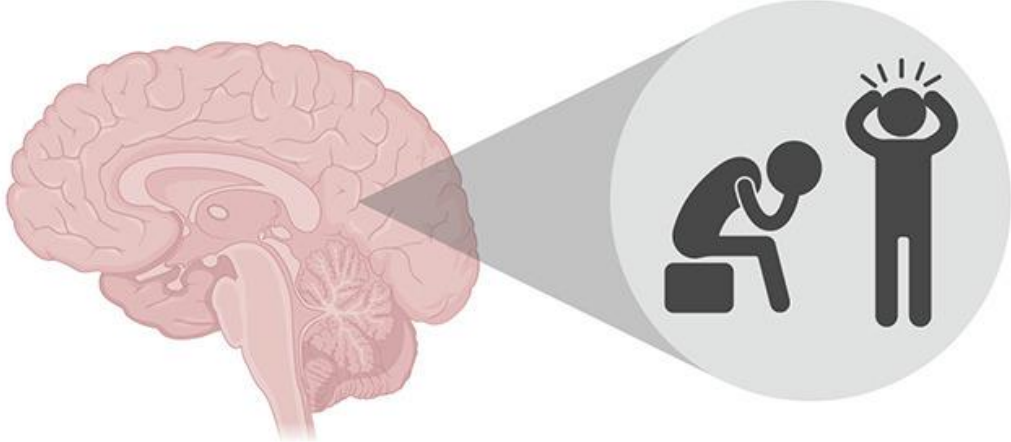
Results
Anxiety & Depression

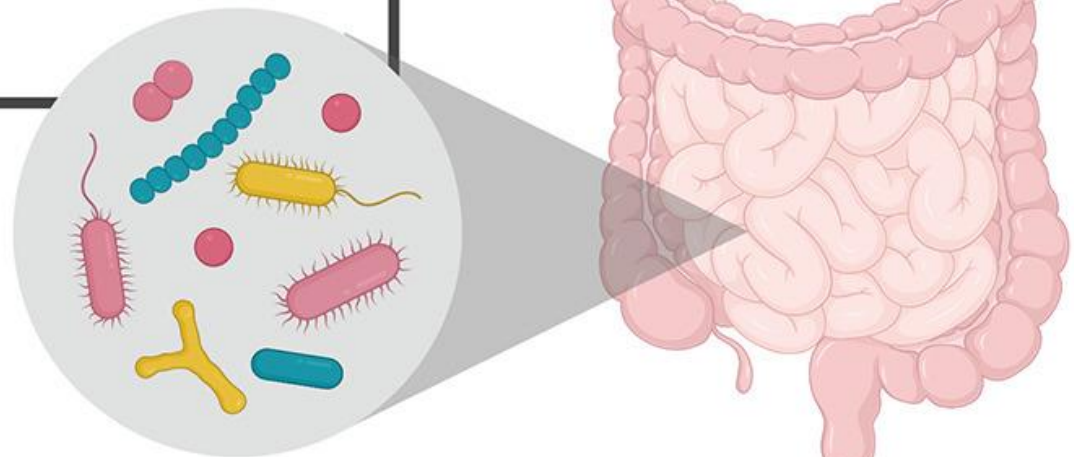
Short-chain fatty acid producers

(*Faecalibacterium* spp., *Coprococcus*)

Taxa associated with inflammation

(Enterobacterales, *Enterobacteriaceae*, *Desulfovibrio)*





Confounders Requiring Further Investigation

- Diet
- Psychiatric medication
- Clinical stratification criteria
- Sex

frontiers in Immunology

PERSPECTIVE
published: 04 September 2017
doi: 10.3389/fimmu.2017.01064

Microbiome-Derived Lipopolysaccharide Enriched in the Perinuclear Region of Alzheimer's Disease Brain

*Yuhai Zhao[1,2], Lin Cong[1,3], Vivian Jaber[1] and Walter J. Lukiw[1,4,5]**

[1]Neuroscience Center, Louisiana State University School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, United States, [2]Department of Anatomy and Cell Biology, Louisiana State University School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, United States, [3]Department of Neurology, Shengjing Hospital, China Medical University, Heping District, Shenyang, China, [4]Department of Neurology, Louisiana State University School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, United States, [5]Department of Ophthalmology, Louisiana State University School of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA, United States

OPEN ACCESS

Edited by:
Wesley H. Brooks, University of South Florida, United States

Reviewed by:
Ai-Ling Lin, University of Kentucky, United States
Abdul Sadiq, University of Malakand, Pakistan

***Correspondence:**
Walter J. Lukiw

Abundant clinical, epidemiological, imaging, genetic, molecular, and pathophysiological data together indicate that there occur an unusual inflammatory reaction and a disruption of the innate-immune signaling system in Alzheimer's disease (AD) brain. Despite many years of intense study, the origin and molecular mechanics of these AD-relevant pathogenic signals are still not well understood. Here, we provide evidence that an intensely pro-inflammatory bacterial lipopolysaccharide (LPS), part of a complex mixture of pro-inflammatory neurotoxins arising from abundant Gram-negative bacilli of the human gastrointestinal (GI) tract, are abundant in AD-affected brain neocortex and hippocampus. For the first time, we provide evidence that LPS immunohistochemical signals appear to aggregate in clumps in the parenchyma in control brains, and in AD, about 75% of anti-LPS signals were clustered around

"According to this conceptualization, the inflammatory response increases gut permeability and exposure to endotoxins or other bacterial products and induces α-synuclein aggregations, which in turn propagate to the CNS via the vagus nerve."

JMD
https://doi.org/10.14802/jmd.18067 / J Mov Disord 2019;12(2):67-83
pISSN 2005-940X / eISSN 2093-4939

REVIEW ARTICLE

Altered Gut Microbiome and Intestinal Pathology in Parkinson's Disease

Han-Lin Chiang,[1] Chin-Hsien Lin[2]

[1]Department of Neurology, Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan
[2]Department of Neurology, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan

ABSTRACT

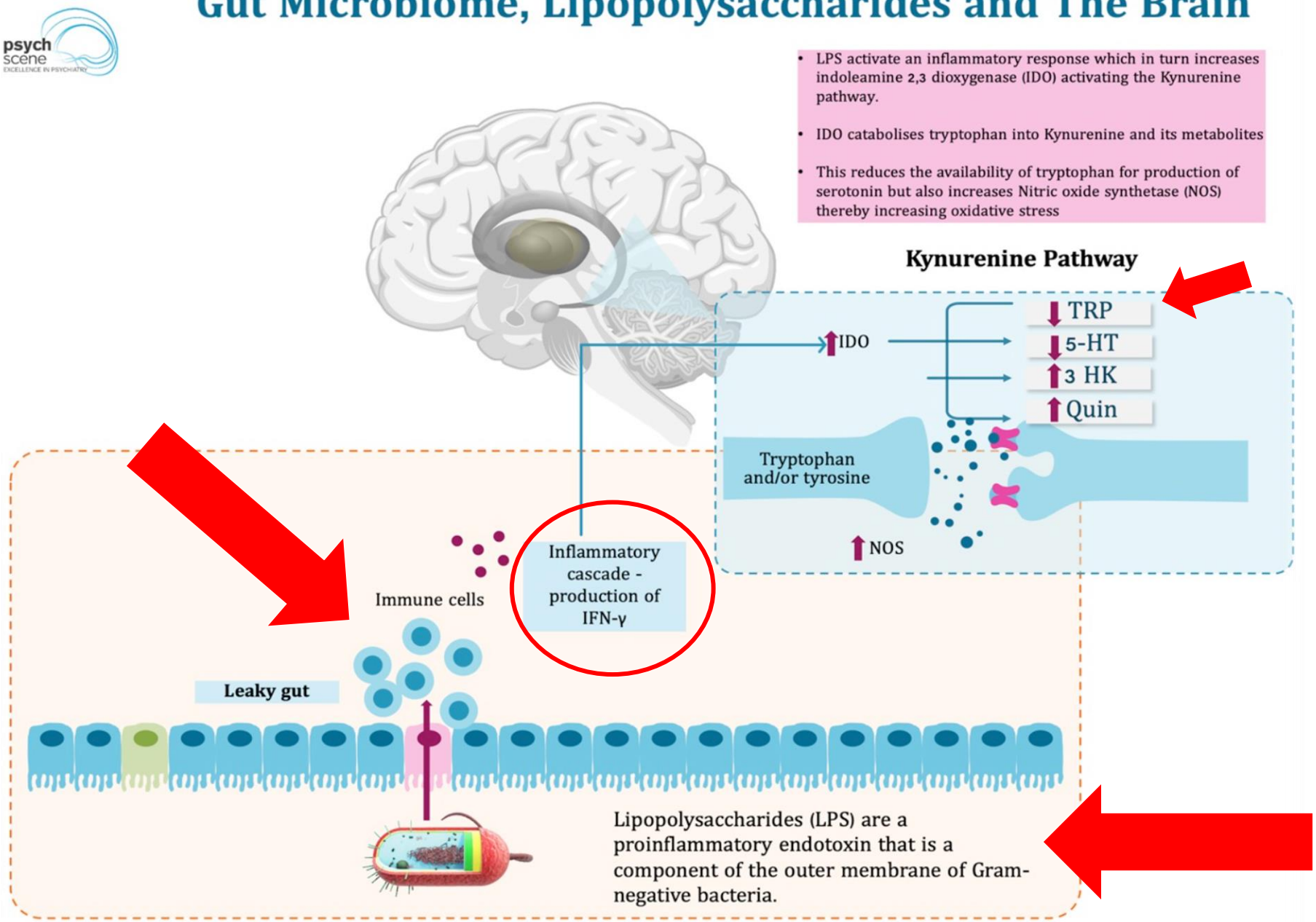
Parkinson's disease (PD) is a common neurodegenerative disorder arising from an interplay between genetic and environmental risk factors. Studies have suggested that the pathological hallmarks of intraneuronal α-synuclein aggregations may start from the olfactory bulb and the enteric nervous system of the gut and later propagate to the brain via the olfactory tract and the vagus nerve. This hypothesis correlates well with clinical symptoms, such as constipation, that may develop up to 20 years before the onset of PD motor symptoms. Recent interest in the gut–brain axis has led to vigorous research into the gastrointestinal pathology and gut microbiota changes in patients with PD. In this review, we provide current clinical and pathological evidence of gut involvement in PD by summarizing the changes in gut microbiota composition and gut inflammation associated with its pathogenesis.

Key Words Microbiome; Gut inflammation; Gut–brain axis; Parkinson's disease.

Parkinson's disease (PD) is a common neurodegenerative disorder arising from the interplay between genetic and environmental factors. In addition to the well-known motor symptoms of bradykinesia, rigidity, rest tremor, and postural instability, PD also involves various nonmotor symptoms, including constipation in PD pathogenesis.[6]

Findings from several subsequent studies are in line with Braak's hypothesis, although there are some conflicting results. Bowel inflammation triggered by rotenone, immune activation by *Escherichia coli* (*E. coli*)-producing amyloid protein curli or bacteri-

Gut Microbiome, Lipopolysaccharides and The Brain



- LPS induces an inflammatory response, which increases IDO.
- IDO is an enzyme that turns tryptophan into kynurenine & its toxic metabolites
- This reduces the availability of tryptophan to produce other important hormones & neurotransmitters

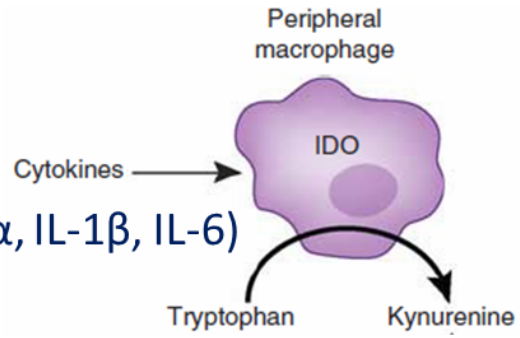
Reus G et al., Kynurenine pathway dysfunction in the pathophysiology and treatment of depression: evidences from animal and human studies. J Psychiatr Res. 2016;68:316-328
Liu L and Zhu G. Gut-brain axis and mood disorder. Front Psychiatry. 2018;9:223.

HIOMT: hydroxyindole-O-methyltrasferase
IDO: indolamine-2,3-dioxygenase
KAT: kynurenine aminotransferase
KMO: kynurenine 3-monooxygenase
KYNU: kynureninase
SNAT: serotonin-N-acetyltransferase
TPH: tryptophan hydroxylase

Diet

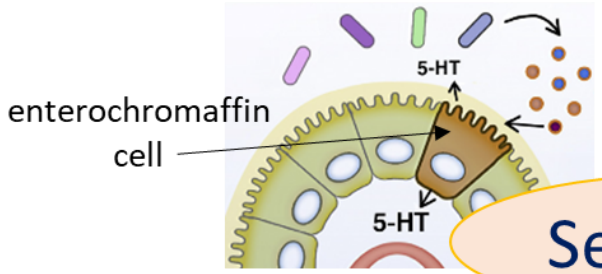
Microbiota

Inflammation
(IFN-α, INF-γ, TNF-α, IL-1β, IL-6)



Tryptophan

Stress
(HPA axis, cortisol)



TPH

IDO

Serotonin

Kynurenine

SNAT; HIOMT

KAT

KMO; KYNU

Melatonin

Kynurenic acid

Quinolinic acid

- Sleep
- Circadian rhythm
- Positive outlook
- Resiliency to stress
- Good memory

Neuroprotective pathway

Neurotoxic pathway

- depressed mood
- irritability
- ↓ resistance to stress
- poor sleep
- ↓ concentration

MICROBIOME LABS

Gut-Heart Axis

Gut-Heart Axis

Dysbiosis plays critical role in development of chronic disease, including CVD

Several studies have highlighted the cross-talk between nutrition, the microbiome, intestinal permeability, and the immune responses that affect cardiac homeostasis or promote CVD

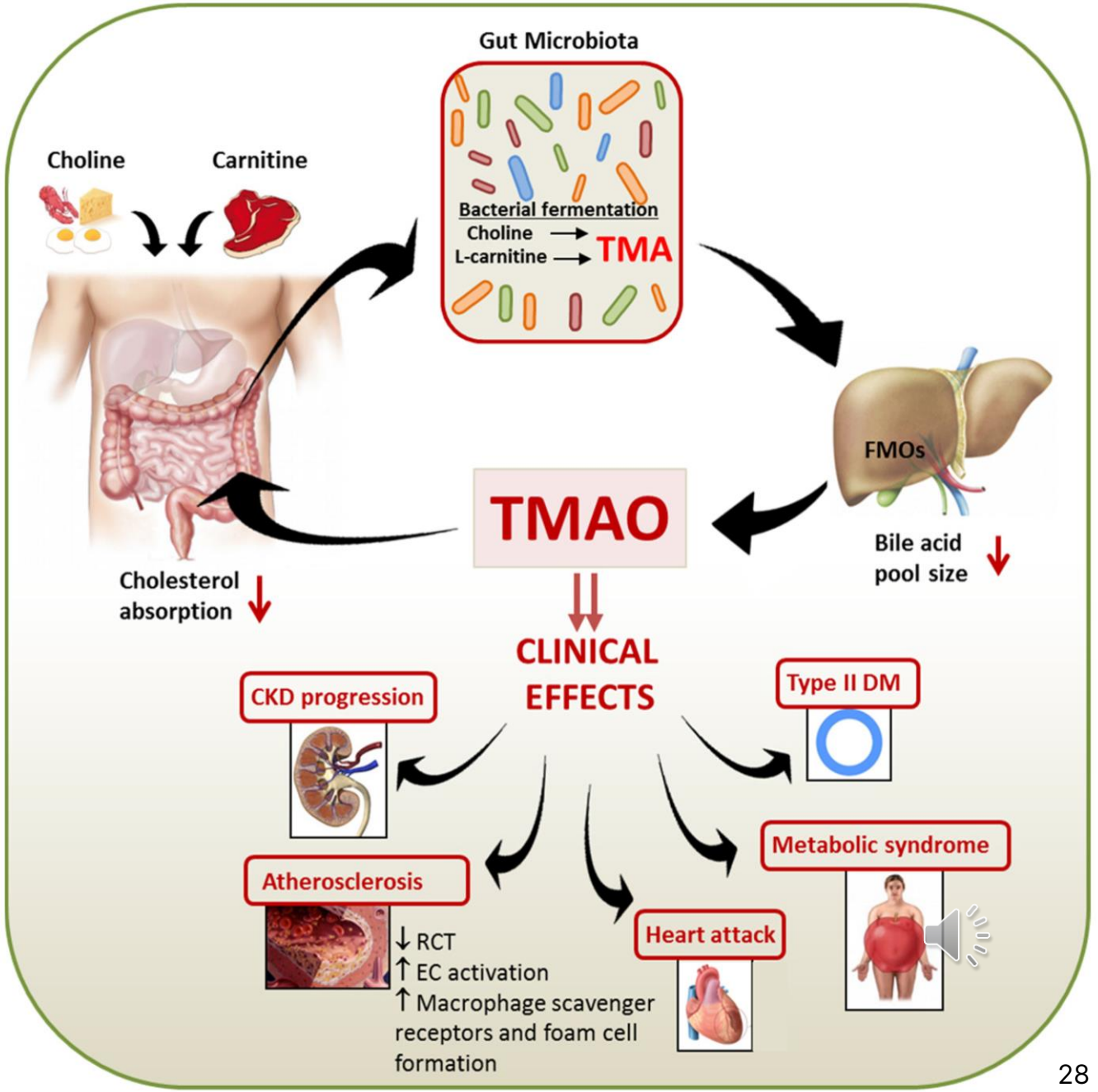
Several microbial metabolites have been identified as impacting the development of cardiovascular disease

TMA, LPS, bile acids, serotonin, SCFAs

MICROBIOME LABS

Trimethylamine N-oxide (TMAO)

- Trimethylamine (TMA) is produced by the gut microbiome from lecithin (phosphatidylcholine), choline, and L-carnitine rich foods
- Commonly found in red meat, full fat dairy, eggs, fish
- Trimethylamine N-oxide (TMAO)
- Biomarker known for its proatherogenic effects → positively correlated with early atherosclerosis
- TMAO role in atherosclerosis
- Inflammation, cholesterol metabolism and thrombosis
- A meta-analysis of 19 studies showed higher plasma TMAO levels linked to increased risk of cardiovascular events like stroke, MI, death
- Higher microbial diversity has been shown to decrease TMAO



Dysbiosis in Cardiovascular Disease

2017 study analyzed stool samples from 218 people with ACVD and 187 healthy controls.

The gut microbiome of patients with atherosclerotic cardiovascular disease showed the following patterns:

- Overabundant amounts of Enterobacteriaceae (E. coli, Klebsiella) and Streptococcus spp.
- Depletion of butyrate producing bacteria like Faecalibacterium prausnitzii)
- Presence of inflammatory metabolites & toxins like TMA/TMAO, H2S, histamine, & LPS
- Reduced fermentation of dietary fiber
- Reduced SCFA production

Bacterial DNA has been found in atherosclerotic plaques

novozymes

Types of CVDs	Changes in the gut microbiota	Involvement of gut microbiota metabolites	Mechanism
Coronary atherosclerosis	Increased *Streptococcus*; Increased *Roche*; Increased *Ruminococcus*; Increased *Clostridium*.	TMAO	Cholesterol metabolism ↓; Foam cells ↑.
			Promote the activation of NF-κB; IL-18 ↑; IL-1β ↑.
		BAs	Cholesterol increase ↑; Reduce the risk of atherosclerosis.
		LPS	Foam cells ↑; Cholesterol ↑.
HTN	Increased *Prevotella*; Increased *Bifidobacterium*; Increased *Lactobacillus*.	SCFAs	Knock out of Olfr78 and GPR41, lead to high blood pressure.
		Propionate	Adjust Th17 and lower blood pressure.
HF	Increased *Candida*; Decreased *Faecalibacterium*.	BAs	Regulate the calcium ion concentration.
		SCFAs	Disrupt the intestinal barrier; Promote the translocation of endotoxins into the blood.
		TMAO	Ca^{2+} ↑; Myocardial fibers ↑.
			Induce T-tubule network damage and calcium processing dysfunction.
			Activate NLRP3.

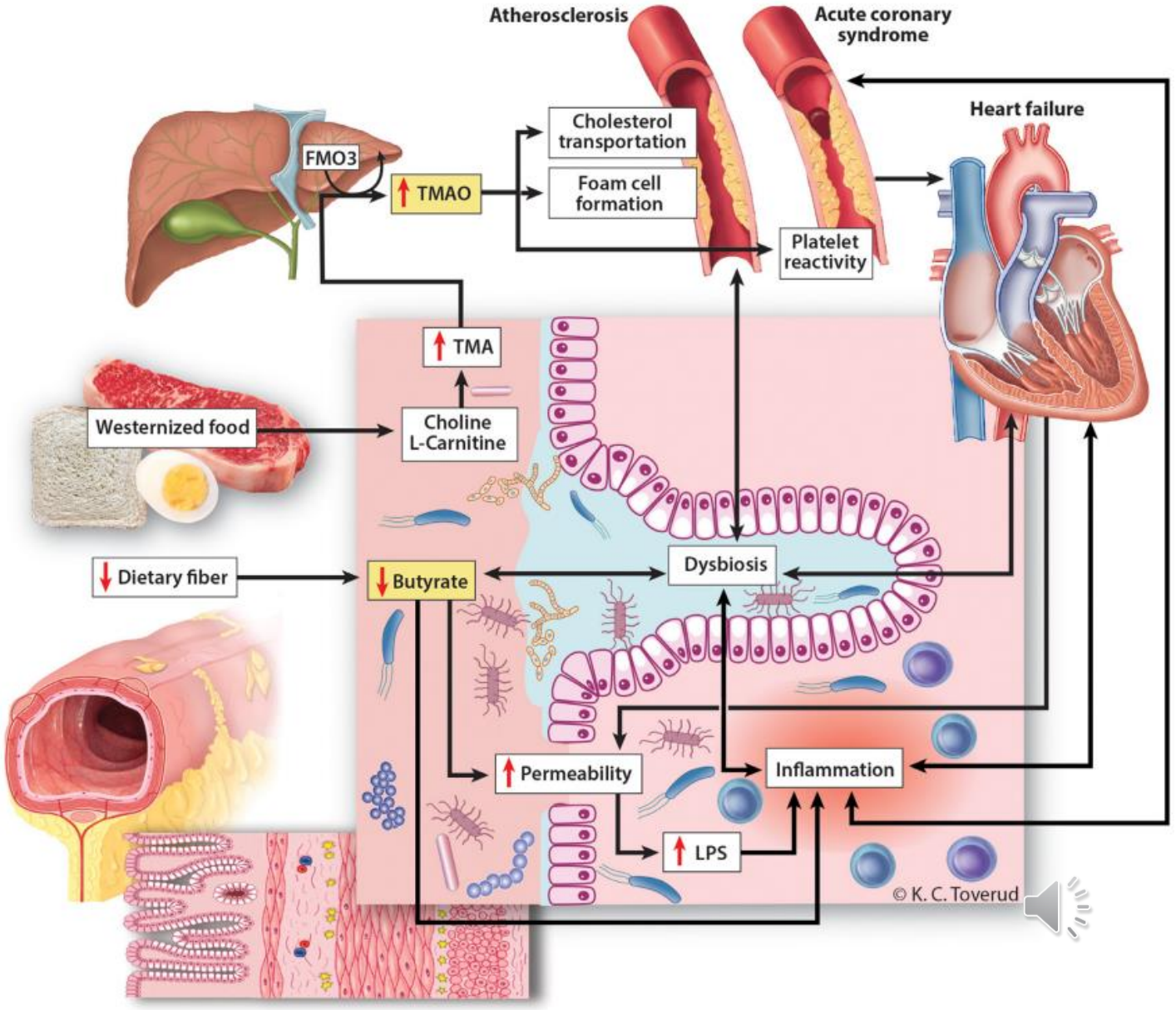
CVDs: Cardiovascular diseases; HTN: Hypertension; HF: Heart failure; TMAO: Trimethylamine-N-oxide; BAs: Bile acids; LPS: Lipopolysaccharide; SCFAs: Short-chain fatty acids.

Dysbiosis in Coronary Artery Disease

2019 clinical study showed that the gut microbial composition and metabolites changed significantly with CAD severity.

The gut microbiome of patients with CAD showed the following patterns:

- Increased abundance of proteobacteria (Klebsiella, Streptococcus, etc.)
- Increased production of toxic metabolites
- Decreased SCFA production, particularly low butyrate

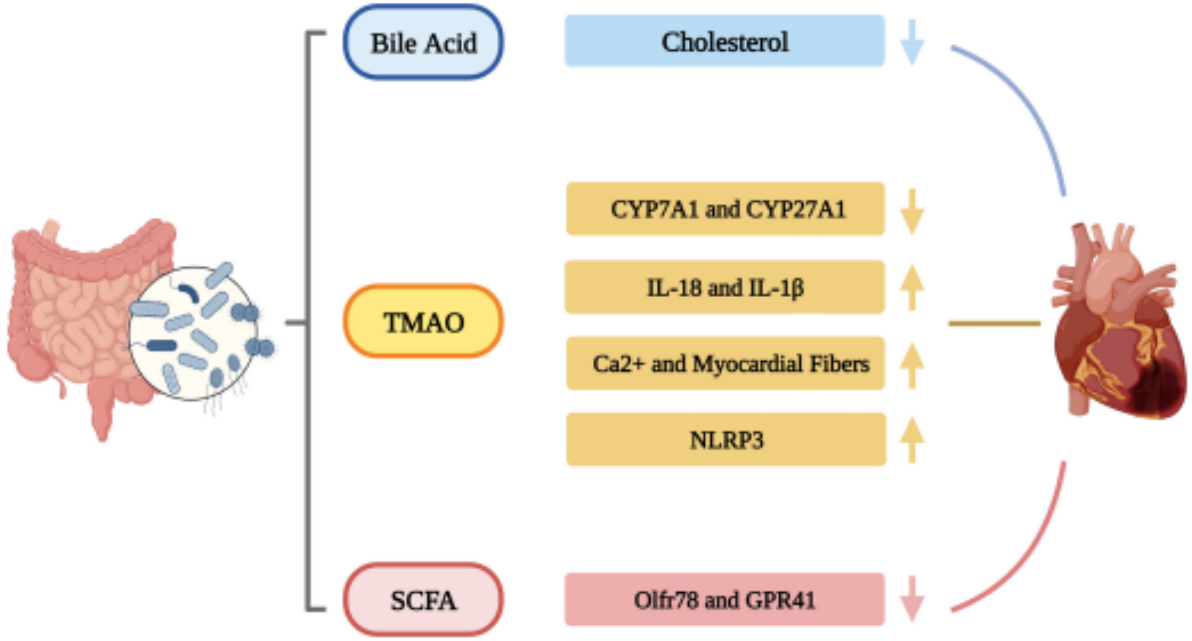


Dysbiosis in Hypertension

HTN is the most common risk factor associated with cardiovascular disease.

The gut microbiome has been shown to play a role in blood pressure regulation. Compared to healthy individuals, those with HTN tend to have a microbiome with:

- Reduce alpha & beta diversity
- Increased abundance of the Prevotella genus
- Imbalances in the abundance of Bifidobacterium, Lactobacillus, Streptococcus, & E. coli can make neurotransmitters that can impact the ANS, vascular tone, etc.
- Elevated TMAO is positively associated with HTN
- Reduced SCFA production



Fecal microbiota transplantation from hypertensive patients can increase the blood pressure of germ-free mice.

novozymes

Gut Dysbiosis & The Lungs

Gut Dysbiosis & The Lungs
Asthma

Dysbiosis and subsequent dysregulation of microbiota-related immunological processes affect the onset of the disease, its clinical characteristics, and responses to treatment.

Immunity
Review

The Role of Lung and Gut Microbiota in the Pathology of Asthma

Weronika Barcik,[1,2] Rozlyn C.T. Boutin,[1,2] Milena Sokolowska,[4,5] and B. Brett Finlay[1,2,3,*]
[1]Department of Microbiology and Immunology, University of British Columbia, Vancouver, BC, Canada
[2]Michael Smith Laboratories, University of British Columbia, Vancouver, BC, Canada
[3]Department of Biochemistry and Molecular Biology, University of British Columbia, Vancouver, BC, Canada
[4]Swiss Institute of Allergy and Asthma Research, University of Zurich, Davos, Switzerland
[5]Christine Kühne - Center for Allergy Research and Education (CK-CARE), Davos, Switzerland
*Correspondence: bfinlay@interchange.ubc.ca
https://doi.org/10.1016/j.immuni.2020.01.007

Asthma is a common chronic respiratory disease affecting more than 300 million people worldwide. features of asthma and its immunological and molecular etiology vary significantly among patients. Ar

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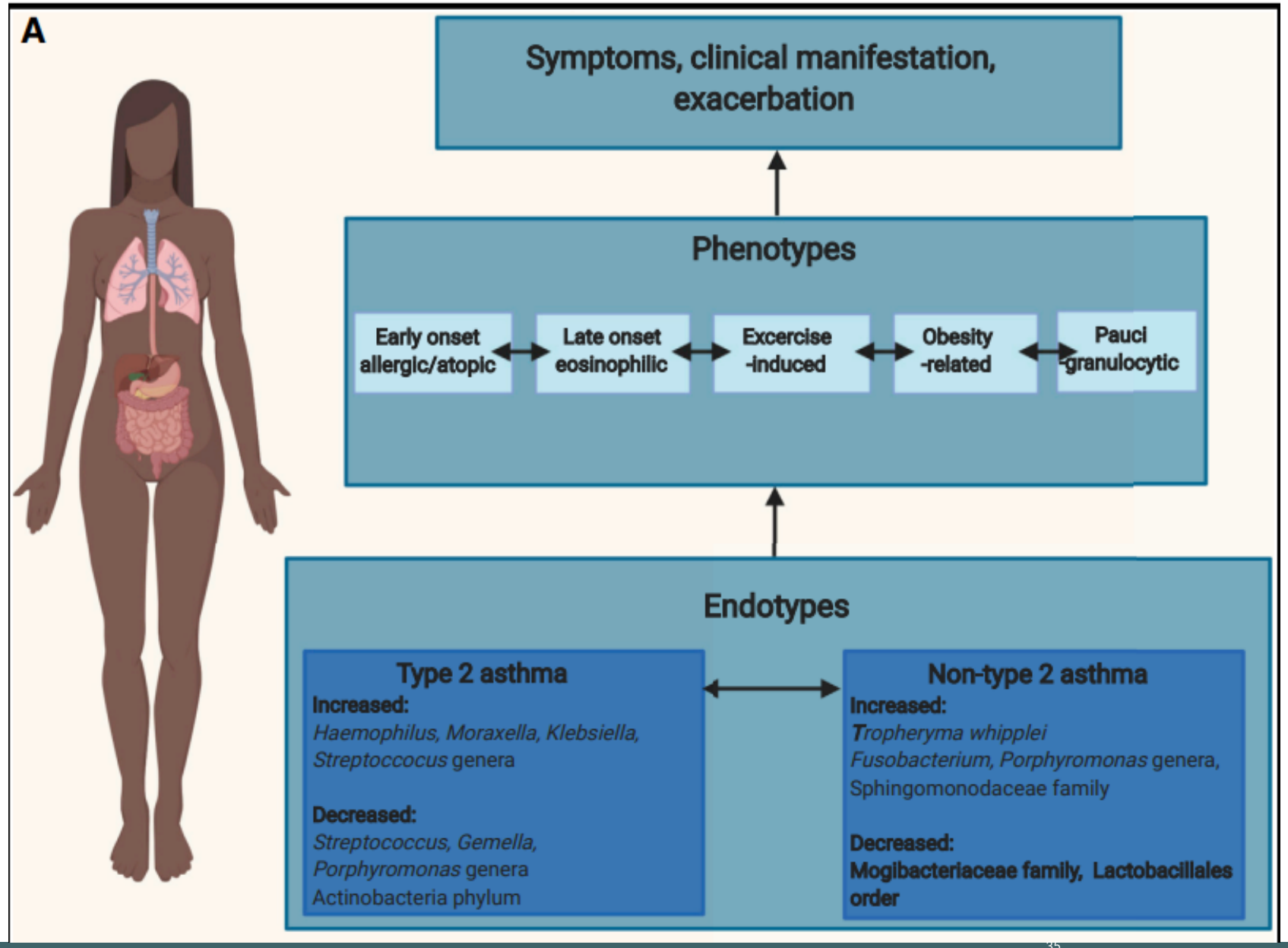
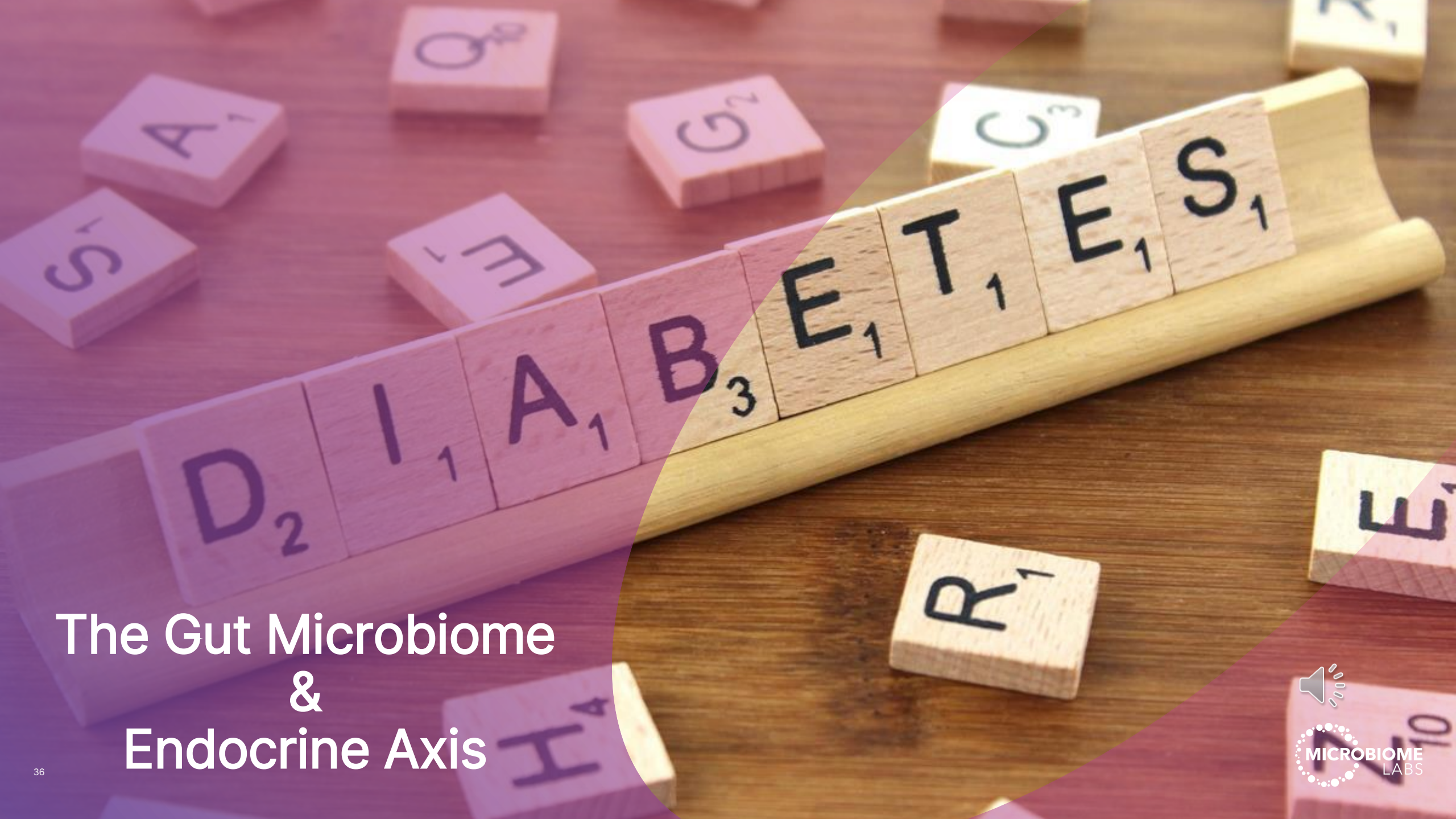

A
Symptoms, clinical manifestation, exacerbation
Phenotypes
Early onset allergic/atopic
Late onset eosinophilic
Excercise -induced
Obesity -related
Pauci -granulocytic
Endotypes
Type 2 asthma
Increased:
Haemophilus, Moraxella, Klebsiella, Streptoccocus genera
Decreased:
Streptococcus, Gemella, Porphyromonas genera
Actinobacteria phylum
Non-type 2 asthma
Increased:
Tropheryma whipplei
Fusobacterium, Porphyromonas genera,
Sphingomonodaceae family
Decreased:
Mogibacteriaceae family, Lactobacillales order



The Gut Microbiome & Endocrine Axis

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Type 2 Diabetics Are More Likely to Have Gut Dysbiosis

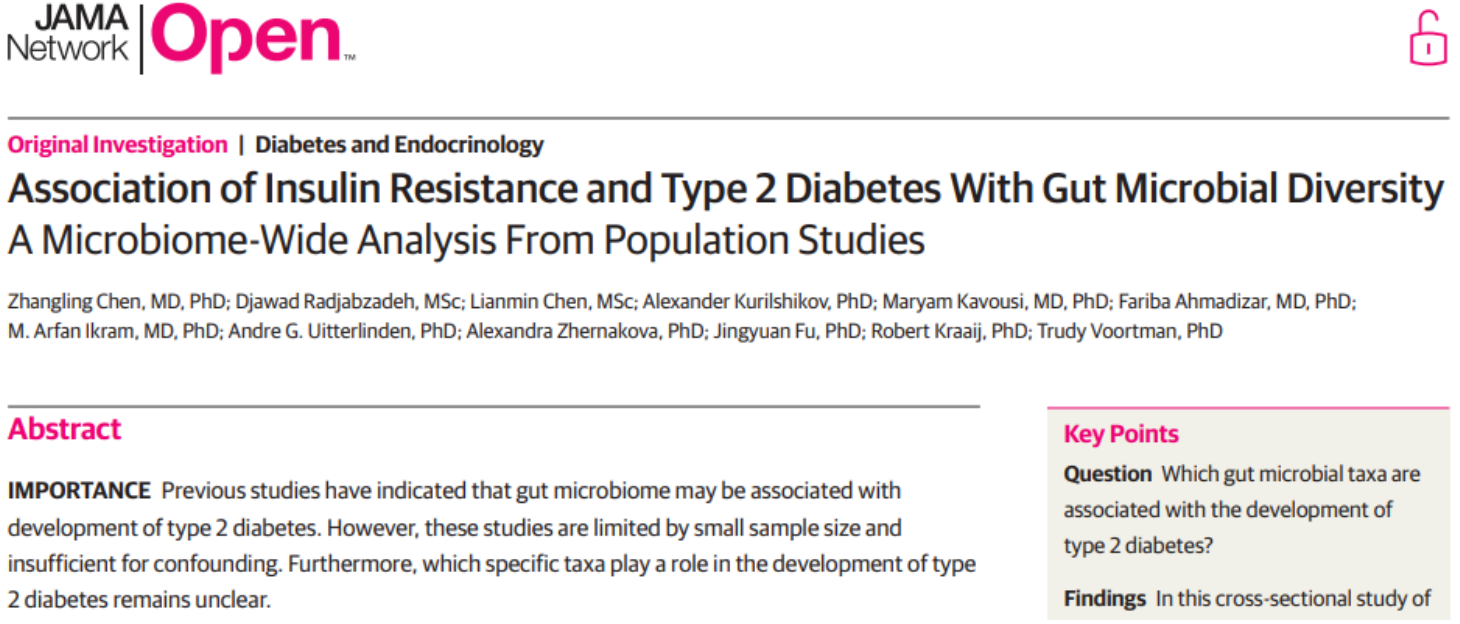
The gut microbiome not only helps regulate our hunger & satiety hormones, but it can also impact insulin release & sensitivity.

Several studies have highlighted the connection between the gut microbiota and glucose dysregulation.

Lactobacillus fermentum, L. plantarum, L. casei Roseburia intestinalis, Akkermansia mucinophila, and B. fragilis have been shown to improve glucose metabolism & insulin sensitivity while suppressing pro-inflammatory cytokines.

Metformin, the first-line pharmacotherapy for type 2 diabetes, has been shown to act primarily in the gut and alters the composition of the gut microbiota.

- It increases butyrate production
- Increases propionate production
- Increased levels of Akkermansia muciniphila



JAMA Network | Open

Original Investigation | Diabetes and Endocrinology

Association of Insulin Resistance and Type 2 Diabetes With Gut Microbial Diversity
A Microbiome-Wide Analysis From Population Studies

Zhangling Chen, MD, PhD; Djawad Radjabzadeh, MSc; Lianmin Chen, MSc; Alexander Kurilshikov, PhD; Maryam Kavousi, MD, PhD; Fariba Ahmadizar, MD, PhD; M. Arfan Ikram, MD, PhD; Andre G. Uitterlinden, PhD; Alexandra Zhernakova, PhD; Jingyuan Fu, PhD; Robert Kraaij, PhD; Trudy Voortman, PhD

Abstract

IMPORTANCE Previous studies have indicated that gut microbiome may be associated with development of type 2 diabetes. However, these studies are limited by small sample size and insufficient for confounding. Furthermore, which specific taxa play a role in the development of type 2 diabetes remains unclear.

Key Points

Question Which gut microbial taxa are associated with the development of type 2 diabetes?

Findings In this cross-sectional study of

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Metformin Acts on The Gut & Alters Microbial Composition

Open Access Review

The Relationship between the Gut Microbiome and Metformin as a Key for Treating Type 2 Diabetes Mellitus

by Chae Bin Lee [1], Soon Uk Chae [1], Seong Jun Jo [1], Ui Min Jerng [2] and Soo Kyung Bae [1,*]

[1] College of Pharmacy and Integrated Research Institute of Pharmaceutical Sciences, The Catholic University of Korea, Bucheon 14662, Korea

[2] Department of Internal Medicine, College of Korean Medicine, Sangji University, Wonju 26339, Korea

[*] Author to whom correspondence should be addressed.

Int. J. Mol. Sci. **2021**, *22*(7), 3566; **https://doi.org/10.3390/ijms22073566**

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- At the phylum level, the abundance of Firmicutes in T2DM patients was lower than that in the control group
- Proteobacteria were more abundant than in the control group.
- Roseburia, a butyrate-producing bacterium, was less abundant in the T2DM patients [27,29,30,32].
- The abundance of Gram-negative bacteria, which can stimulate the immune system like TLRs, was increased in T2DM patients.
- T2DM patients often had low alpha diversity

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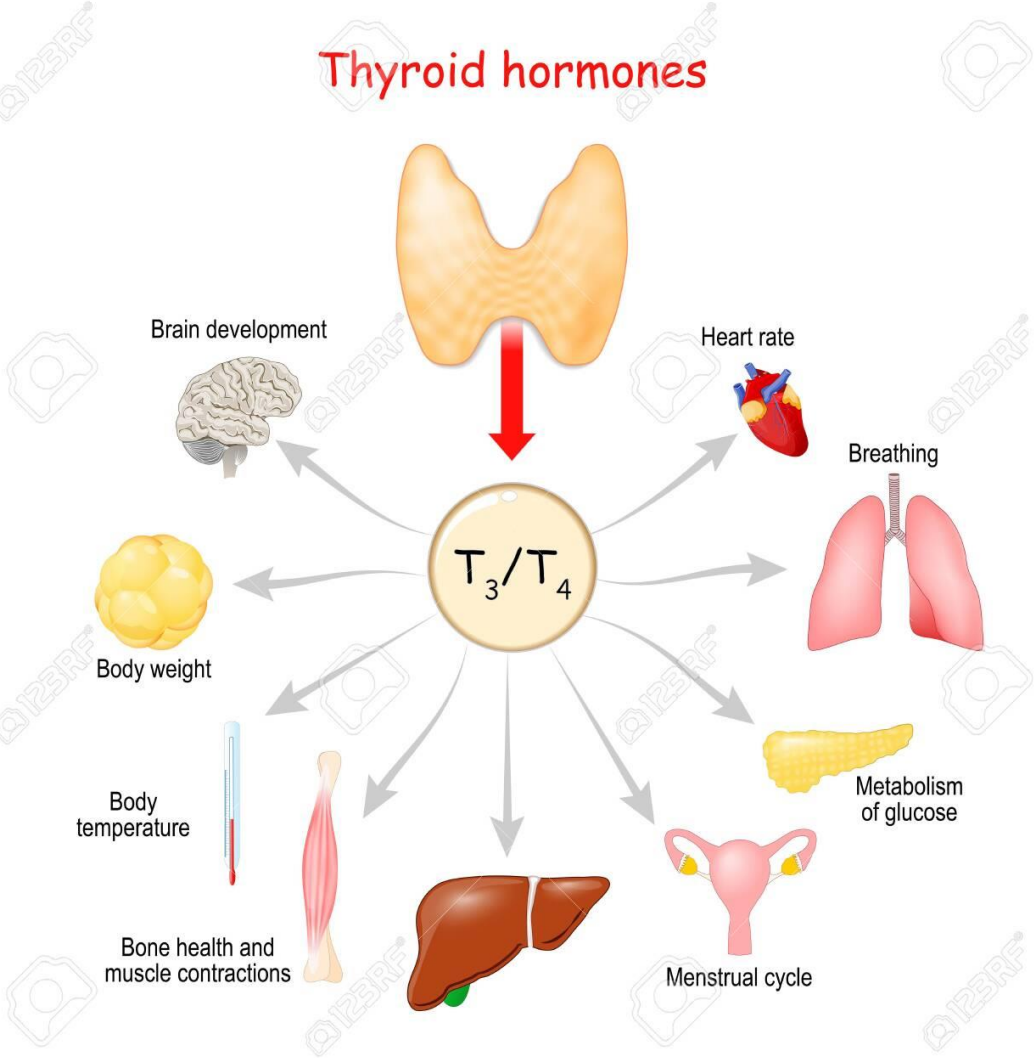
Thyroid

The gut is a target organ for our thyroid hormones:

- Thyroxine (T4)
- Triiodothyronine (T3)

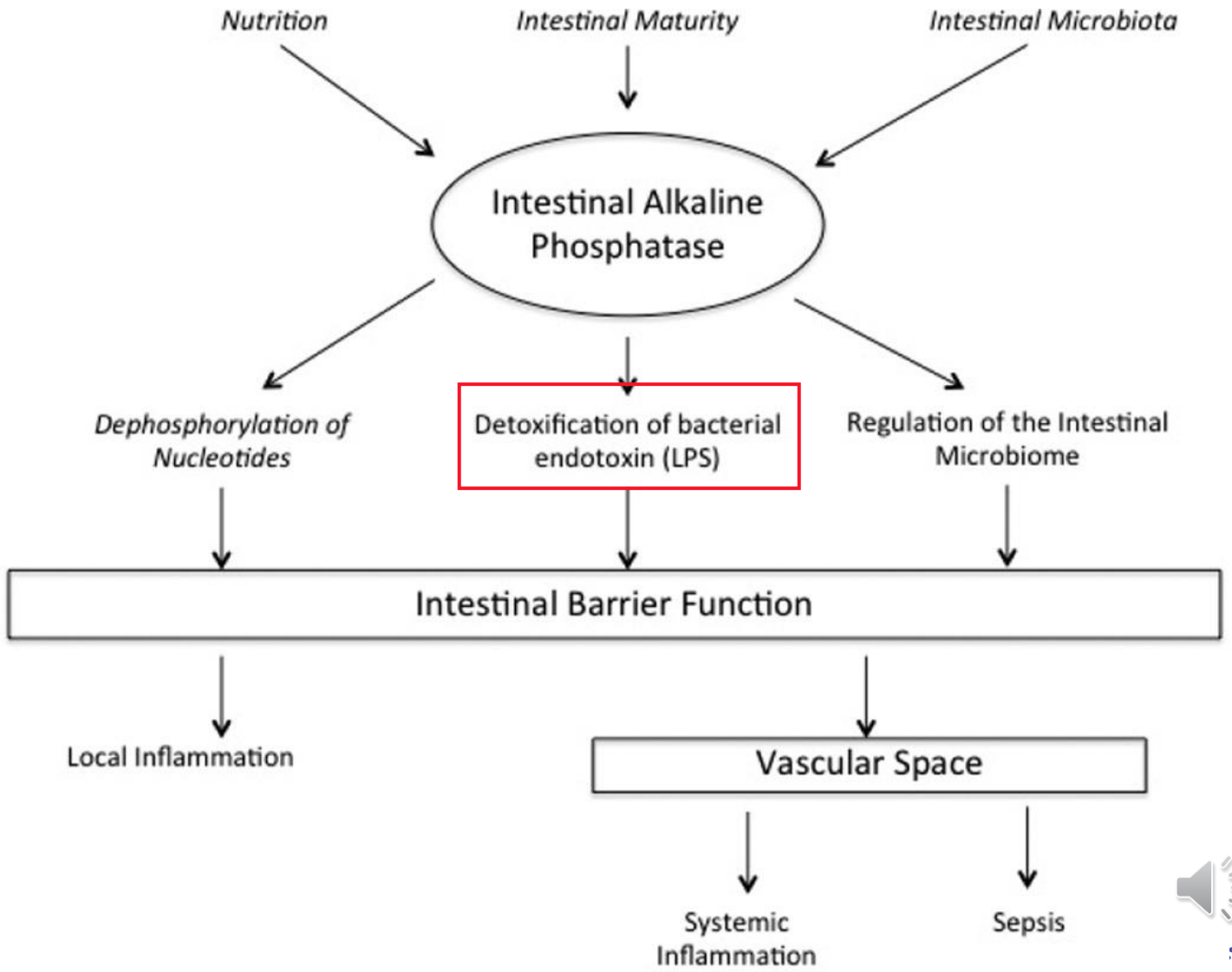
Thyroid hormone receptors are expressed on the surface of intestinal epithelial cells.

Disruption in the microbial composition is associated with Hashimoto's Thyroiditis, Grave's Disease, and Grave's Orbitopathy(9).



Intestinal Alkaline Phosphatase (IAP)

- A brush-border enzyme that is primarily expressed on the duodenum.
- IAP works to dephosphorylate LPS which prevents it from translocating into circulation.
- The IAP gene is a T3-responsive gene which directly links its expression to thyroid hormone levels.
- Animal models discovered decreased IAP gene transcription in hypothyroid rats.
- IAP knock-out zebrafish were more susceptible to LPS toxicity(9).



Microbial Patterns in Autoimmune Thyroid Disease

Bacterial Strains Associated with Decreased Expression of TPOAb & TRAb

Bacteroides

Dorea spp.

Faecalibacterium prausnitzii

Bacterial Strains Associated with Increased Expression of TPOAb & TRAb

likely due to molecular mimicry

Blautia spp.

Lactobacillus spp.

Alistipes spp.

Ruminococcus spp.

Bacterial Strains seen in patients with Hashimoto's

Lachnoclostridium

Bilophila wadsworthia

Klebsiella pneumoniae

Fenneman AC, Bruinstroop E, Nieuwdorp M, van der Spek AH, Boelen A. A Comprehensive Review of Thyroid Hormone Metabolism in the Gut and Its Clinical Implications. Thyroid. 2023 Jan;33(1):32-44. doi: 10.1089/thy.2022.0491. Epub 2023 Jan 6. Erratum in: Thyroid. 2023 Apr;33(4):534. PMID: 36322786.

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The Gut Microbiome & Immune Axis

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Dysbiosis of gut microbiota has been shown to be related to various alterations of the immune system.

Gut commensal bacteria have vital roles in the establishment of a regular innate immune system.

In turn, dysbiosis of gut microbiota might cause the alteration of the innate immune system, and vice versa.

REVIEW article

Front. Immunol., 21 February 2020

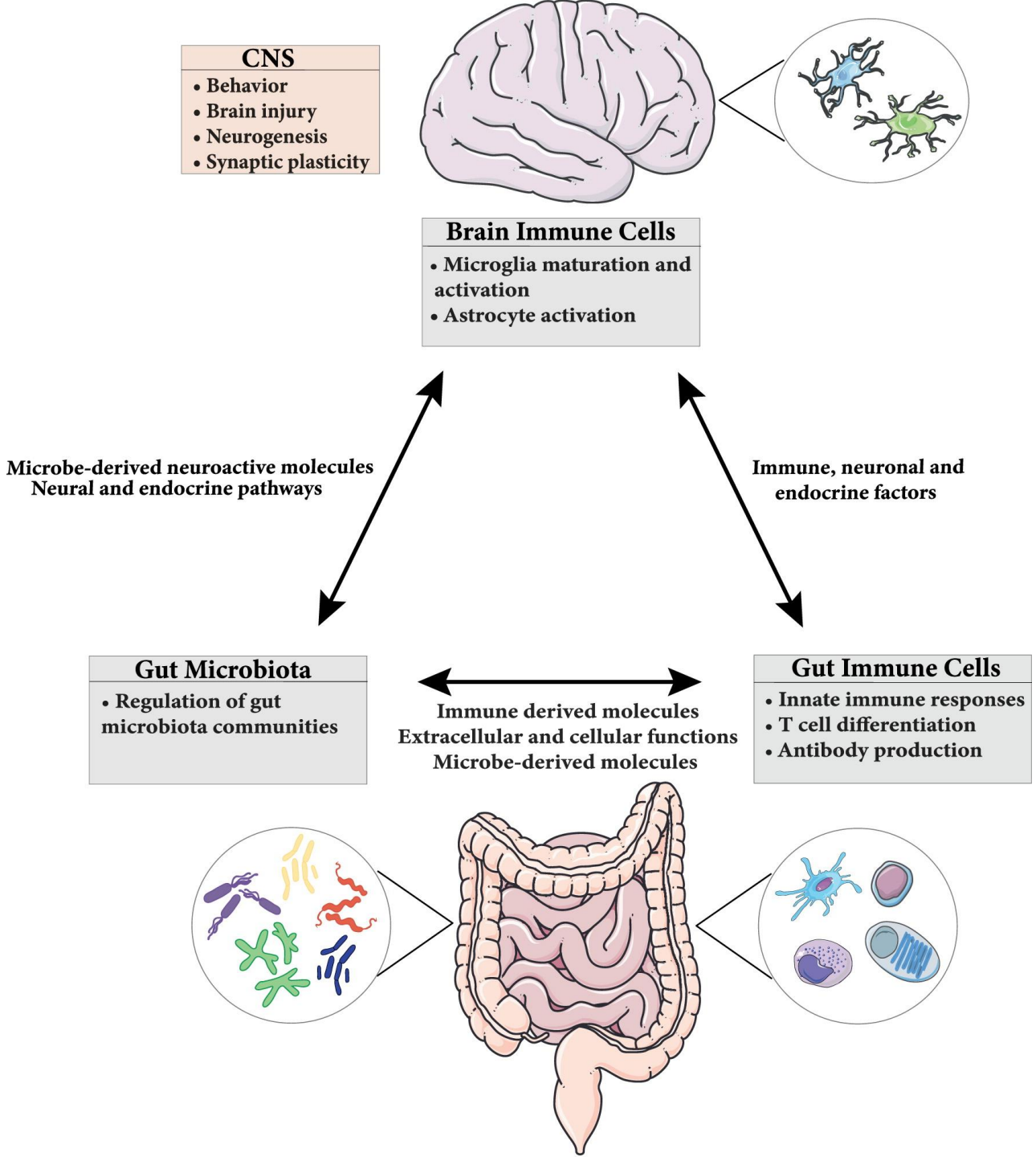
Sec. Autoimmune and Autoinflammatory Disorders

Volume 11 - 2020 | https://doi.org/10.3389/fimmu.2020.00282

Crosstalk Between Gut Microbiota and Innate Immunity and Its Implication in Autoimmune Diseases


Yuhao Jiao[1,2] Li Wu[3,4,5]

Nicholas D. Huntington[6*] Xuan Zhang[1,7*]



Microbiota colonization in the GI tract during early life affects the development of T cell populations into different types of T helper cells (Th) including: Th1, Th2, and Th17 or into regulatory T cells (Tregs)

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Gut Microbiome & Genitourinary Axis

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Intro to the Vaginal Microbiome

- Unlike the gut microbiome, we do **not** want high diversity in the vaginal microbiome.
- The vaginal microbiome has a high abundance of lactobacillus species
- A healthy vaginal pH should be between 3.8 – 4.5
- Four most dominant lactobacillus species found in the vaginal microbiome:
    1. L. crispatus
    2. L. gasseri
    3. L. jensenii
    4. L. iners (may be associated with dysbiosis)

Intro to the Vaginal Microbiome

Lactobacillus is Critical for a Healthy Vaginal Microbiome:

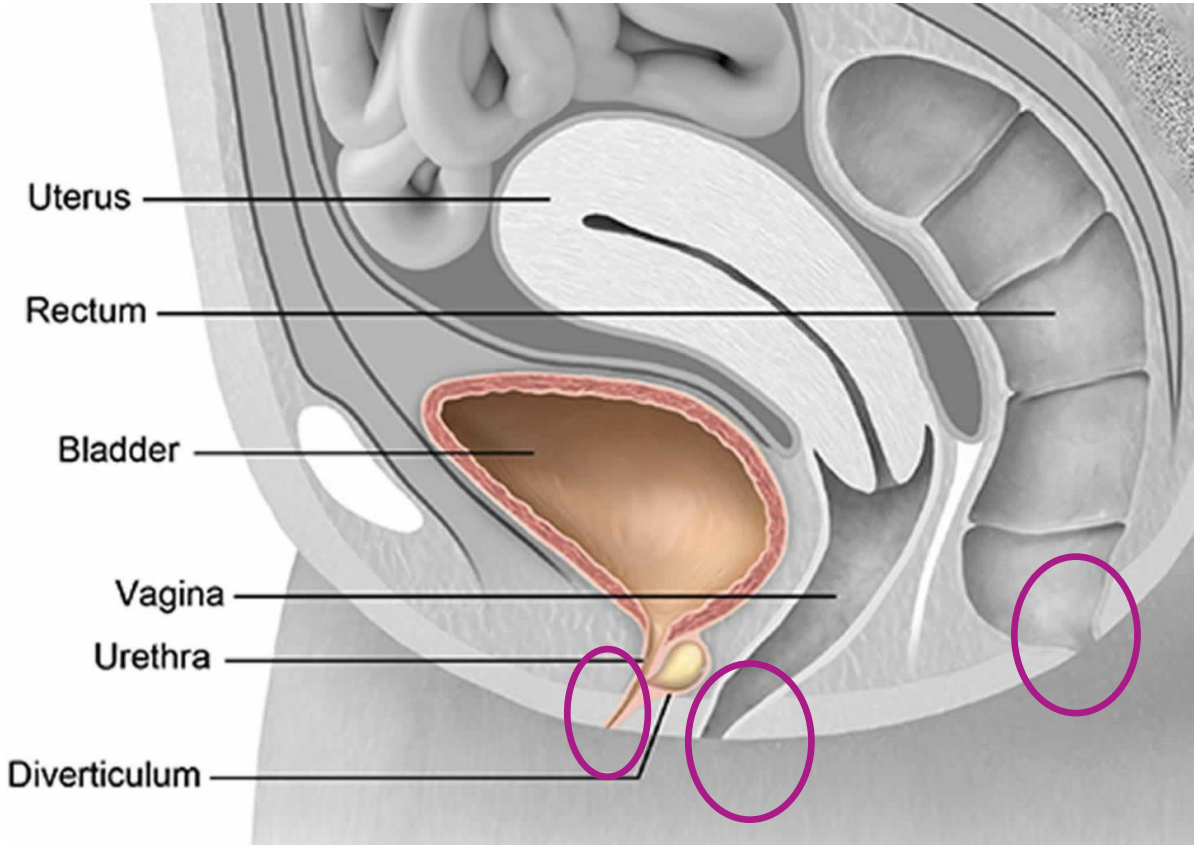
- Lowers pathogen abundance by producing lactate, bacteriocins, and hydrogen peroxide
- Inhibits adherence of pathogens by producing biosurfactants that compete with attachment sites or by coaggregation with the pathogen, which allows the pathogen to be swept away by the host's body fluid

Intro to the Vaginal Microbiome

Vaginal Microbiome is Impacted by:

1. Age and hormones
2. Sexual habits
3. Medications
4. Use of vaginal products
5. Diet
6. Stress
7. Tobacco use
8. *Gut microbiome*

Gut-Vaginal Microbiome Crosstalk

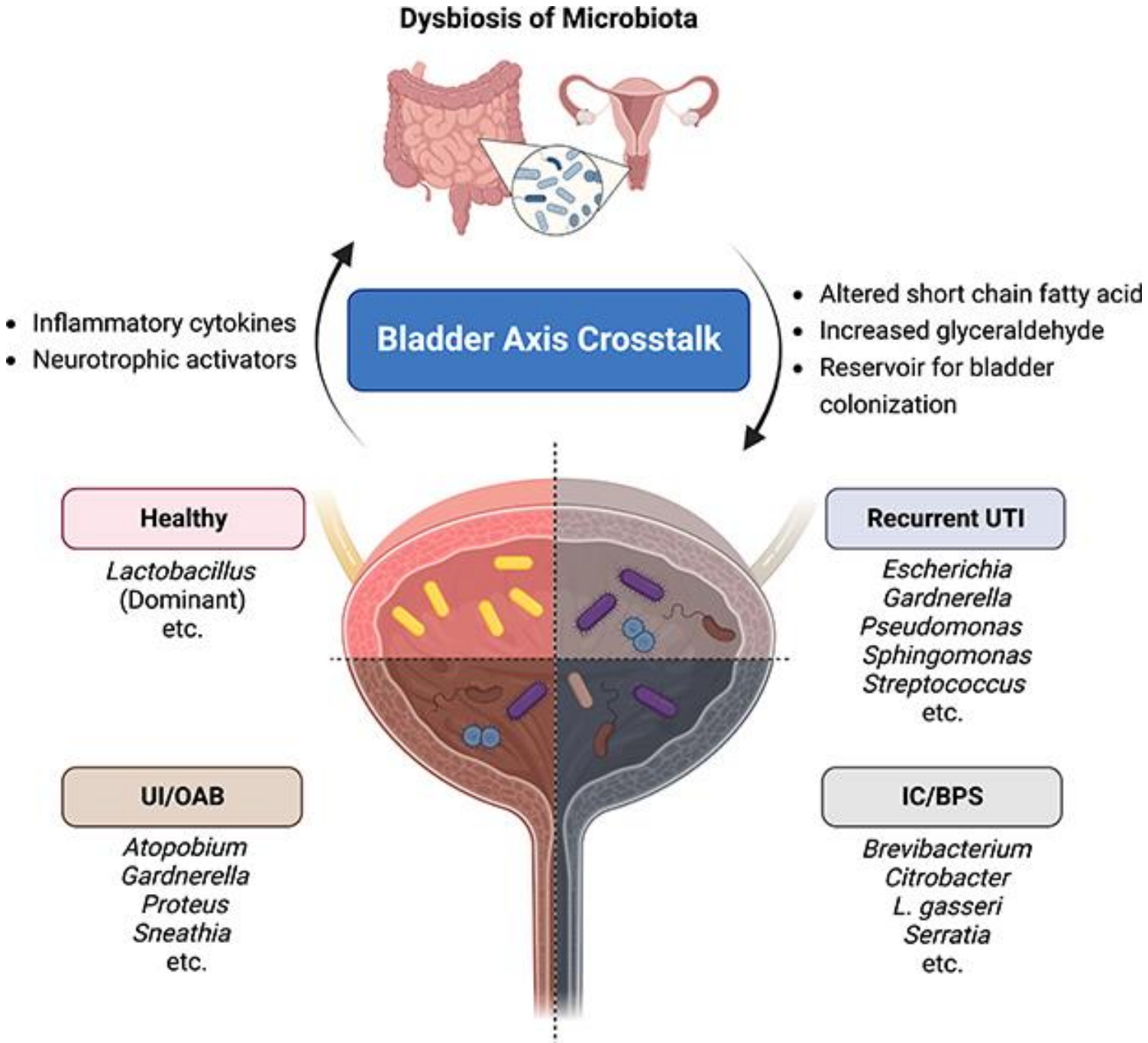


- Linked through the close proximity of the vagina to the anus and the translocation of species after being shed in the feces
- Due to the close proximity of the urethra to the vagina, the vaginal microbiome can also play a role in the development of UTI's

Link to the Gut Microbiome

- Women with BV-associated bacteria in stool reported higher incidence of BV:
  - Gardnerella vaginalis
  - Prevotella bivia
  - Atopobium vaginae
  - Mycoplasma hominis
- Gut probiotics containing lactic acid producing bacteria (like Bacillus spores) can maintain the vaginal pH and obstruct the growth of pathogenic bacteria
- By inhibiting the growth of unfriendly bacteria like E. coli, gut probiotic Bacillus spores promote vaginal microbiome health
- Women with higher concentrations of L. crispatus in stool where more likely to have healthy vaginal microbial composition

Marrazzo, et al. Extravaginal Reservoirs of Vaginal Bacteria as Risk Factors for Incident Bacterial Vaginosis. *The Journal of Infectious Disease.* 2012; 205(10): 1580–1588



Dysbiosis of the urinary microbiome may be directly associated with disorders of the urinary tract such as UTI, IC, urinary incontinence (UI), and BPS.

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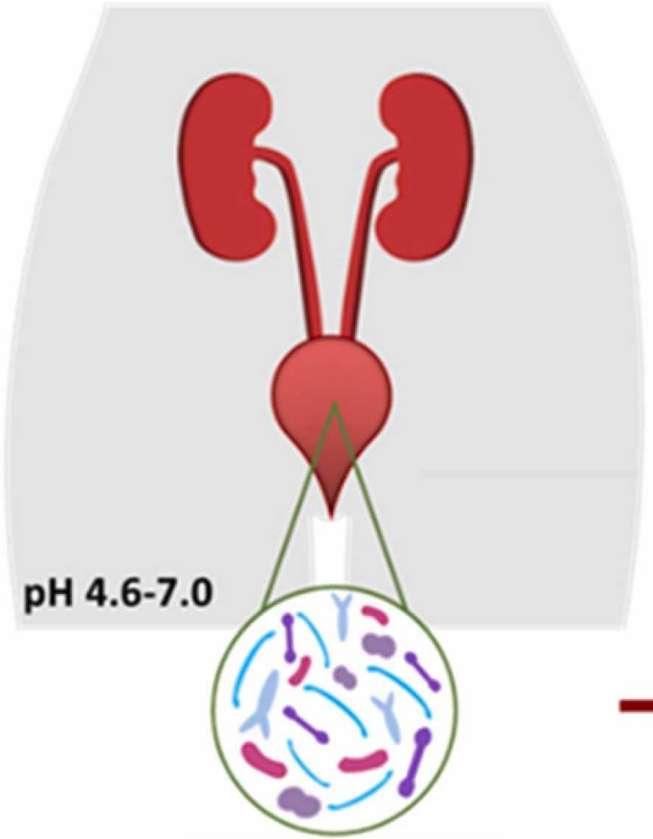
Urinary Microbiome

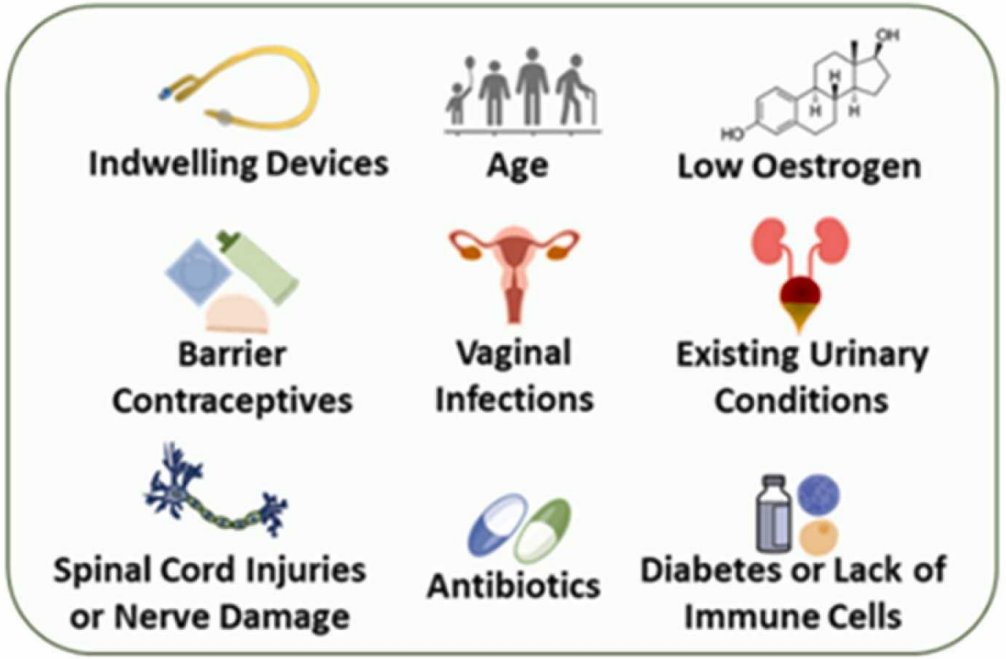
(A) Healthy State



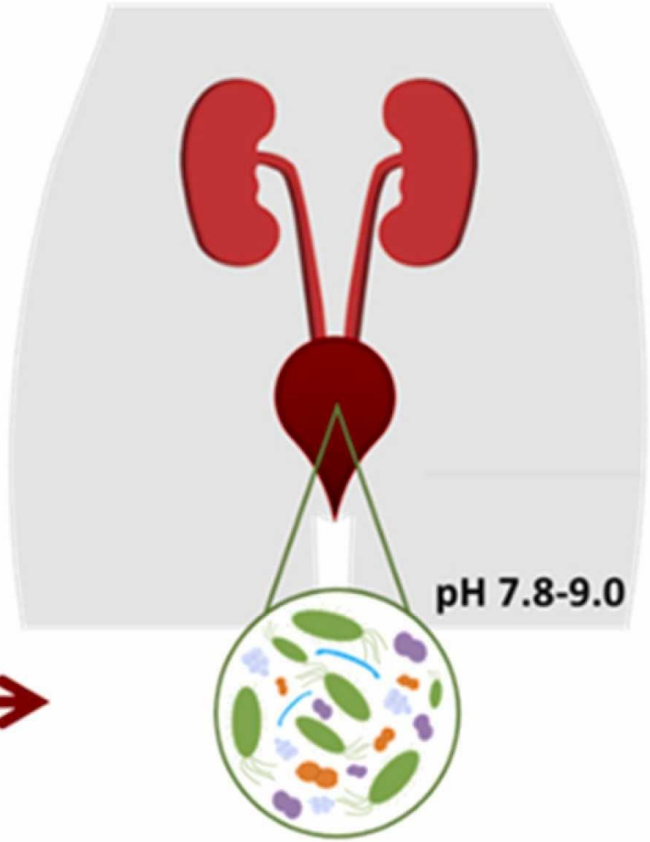
pH 4.6-7.0

Lactobacillus ↑
Prevotella
Corynebacterium
Gardnerella
Shigella

(B) Risk Factors



(C) UTI



pH 7.8-9.0

E. coli
Enterococcus
Staphylococcus
Gardnerella
Lactobacillus ↓

Summary:

Dysbiosis is an imbalance between beneficial and harmful bacteria

This microbial imbalance impacts all areas of our health

Gut dysbiosis has been associated with:

- Anxiety
- Depression
- Alzheimer's and Parkinson's disease
- Asthma
- Type 2 diabetes
- Autoimmune disease
- Urinary tract infections

- Restoring gut homeostasis is critical for supporting overall health and reducing chronic disease.

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Thank you
for your attention

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