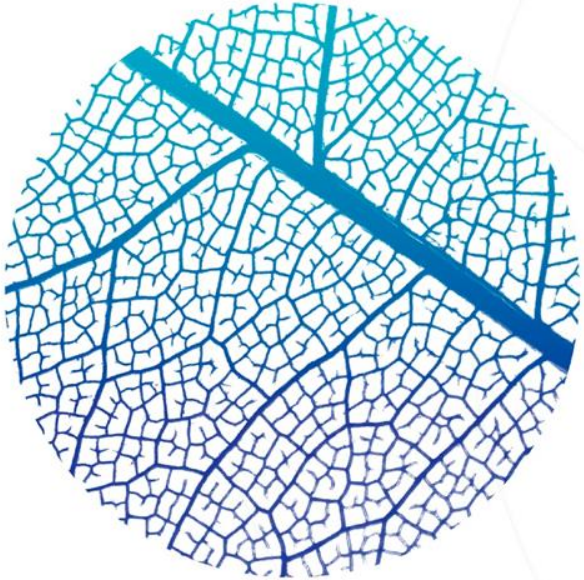


METABOLIC SYNDROME & THE MICROBIOME

CORE THERAPEUTICS FOR A COMMON CONDITION

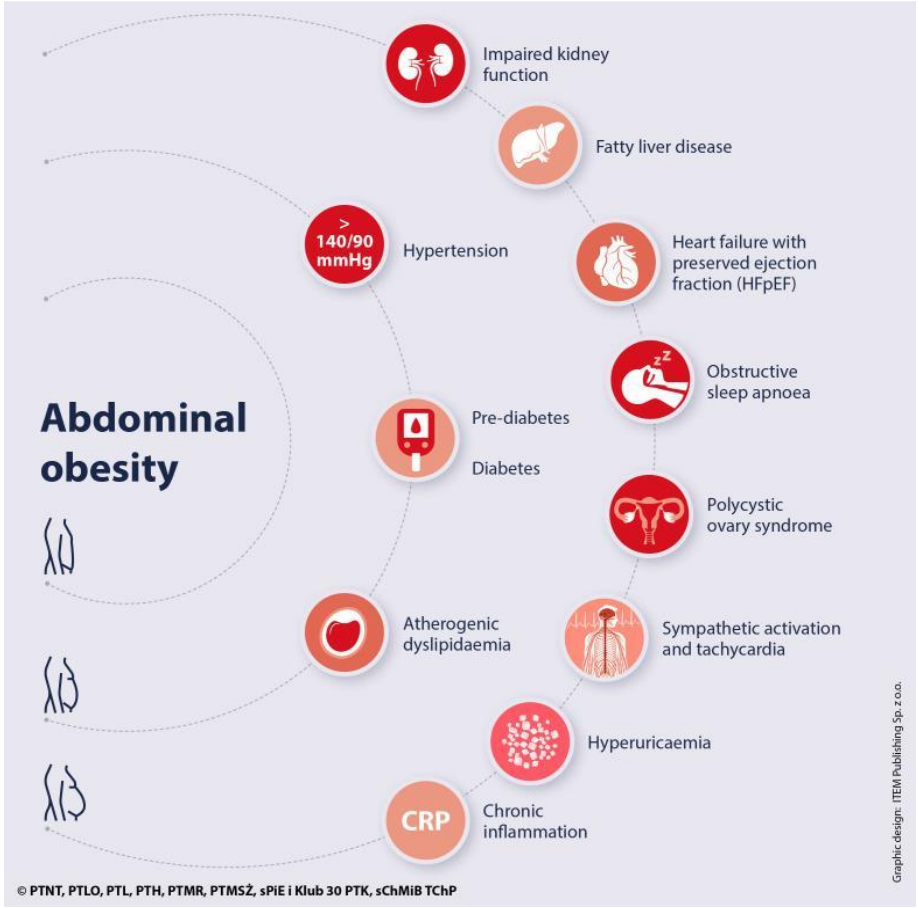
Jocelyn Strand, ND

LEARNING OBJECTIVES

You will come away with a better understanding of:

- Microbes, their metabolites, and how they influence metabolic health
- How the gut microbiome influences gut barrier integrity, satiety and insulin resistance
- Common lab tests that can be used to track the effects of the microbiome on metabolic health
- Novel therapeutic targets that may restore gut microbiome health

METABOLIC DISEASE



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9479724/

MICROBES MATTER MOST

A HEALTHY MICROBIOME BENEFITS THE HOST

- Hydration
- Nutrient synthesis
- Control of epithelial cell proliferation
- Protects against pathogens by a barrier effect
- Houses the immune system
- Immune reserves for systemic defenses
- Production of short-chain fatty acids (SCFAs)

METABOLIC SYNDROME

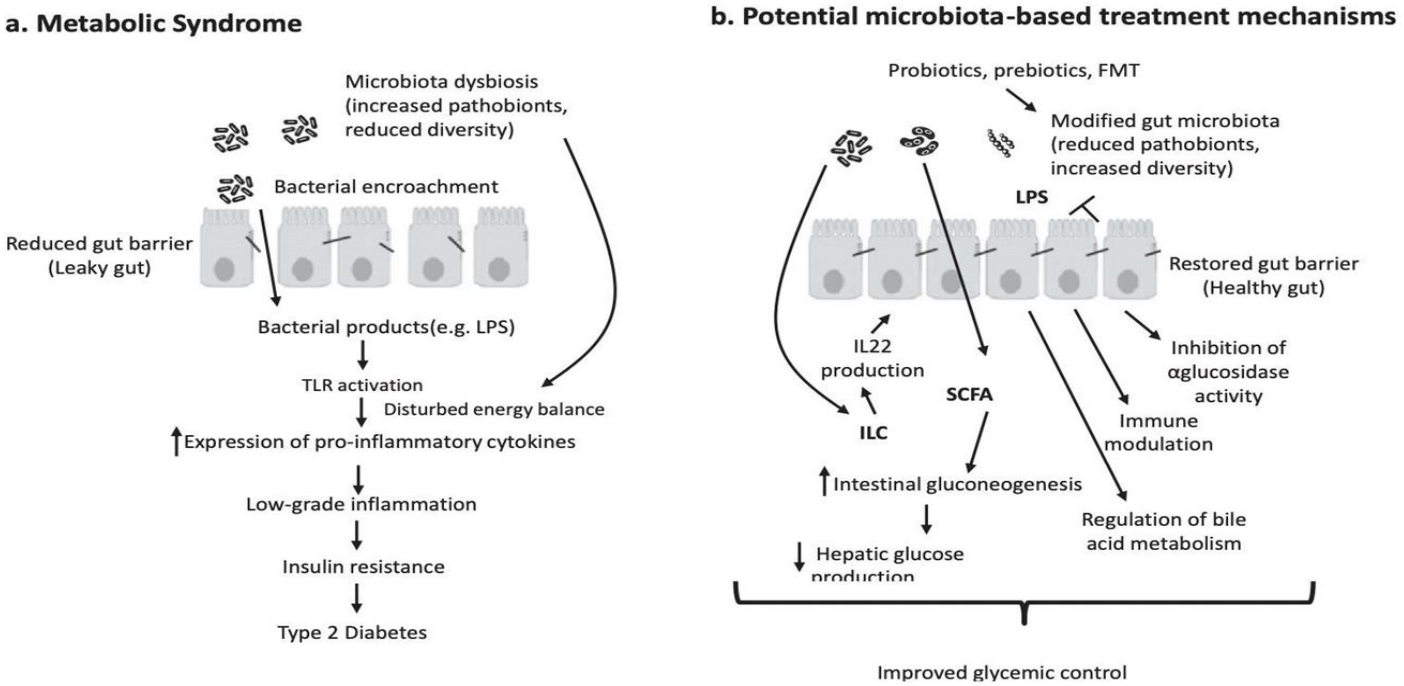


Figure 1. Overview of how a dysbiotic gut microbiota can promote type 2 diabetes (a) and how microbiota-based therapies might treat and/or prevent this disorder (b).

https://pubmed.ncbi.nlm.nih.gov/32005089/

THE MICROBIOME AND THE IMMUNE SYSTEM

Ways that the intestinal microbiome affects systemic immunity:

- Regulation of T cells – the gas and the brakes
- Oral tolerance and immune competence
- Regulation of systemic inflammation
- Production of SCFAs

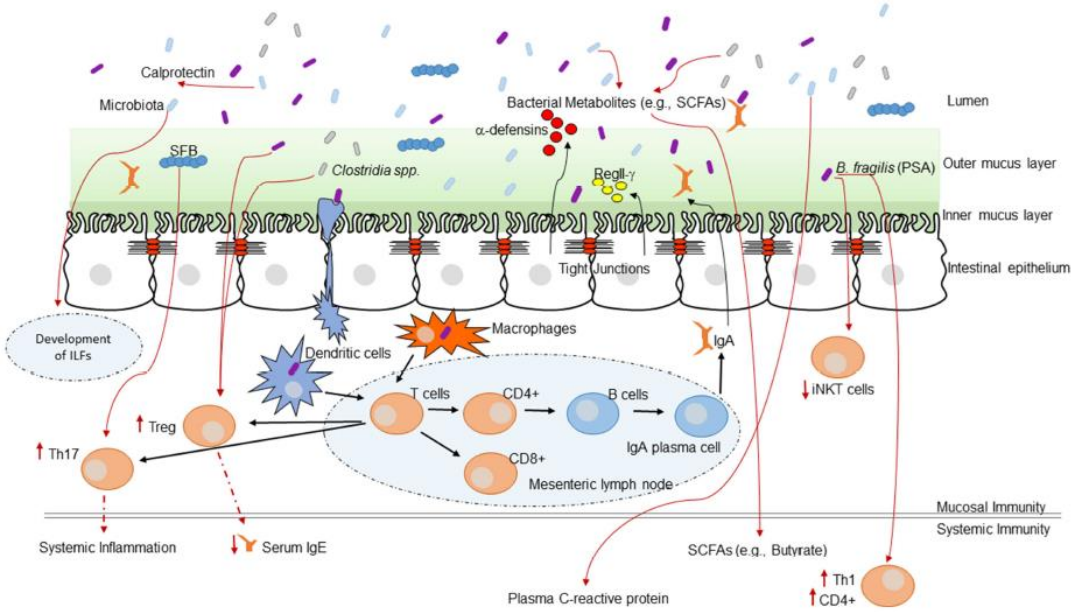
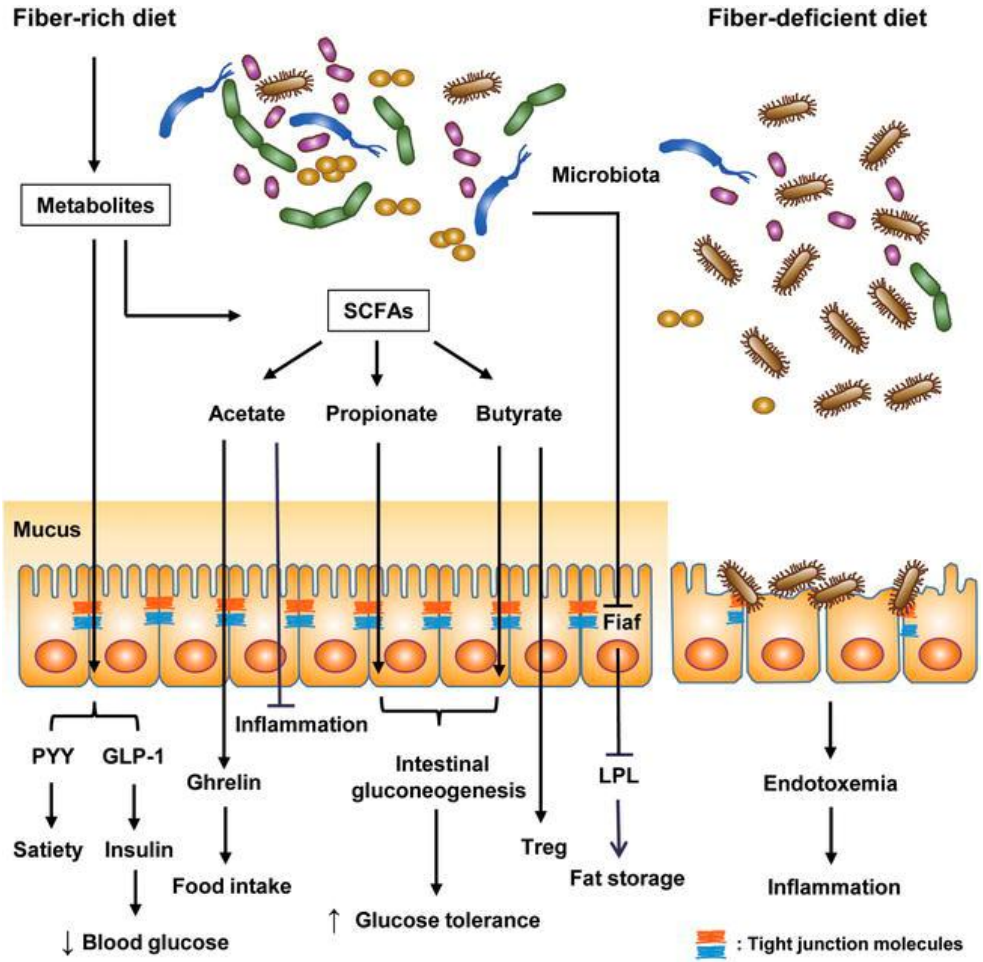


FIGURE 1 | The intestinal microbiota and the host immune system. Interaction between the immune system and the intestinal microbiota. Multiple immune effectors function together to minimize bacterial-epithelial invasion. These include the mucus layer, epithelial antibacterial proteins, and IgA secreted by lamina propria plasma cells. Compartmentalization is accomplished by unique anatomic adaptations that limit commensal bacterial exposure to the immune system. Some microbes are sampled by intestinal DCs. The loaded DCs traffic to the mesenteric lymph nodes through the intestinal lymphatic but do not migrate to distal tissues. This compartmentalizes live bacteria and induction of immune responses to the mucosal immune system. Induced B cells and T cell subsets recirculate through the lymphatic and the bloodstream back to mucosal sites, where B cells differentiate into IgA-secreting plasma cells. Thus, the intestinal microbiota shapes host mucosal as well as systemic immunity. ILFs, isolated lymphoid follicles.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4595839/



https://www.intechopen.com/chapters/73646

SCFAs & INTESTINAL BARRIER FUNCTION

SHORT-CHAIN FATTY ACIDS

- ***Produced by beneficial microorganisms*** through enzymatic conversion and fermentation of undigested dietary residue
- The key mediators for communication between the host and gut microbes
- Metabolites produced by microbes can influence host immunity and metabolism, including promoting T regulatory cell function, reducing risk of inflammatory disease
- Affect gut integrity by decreasing the luminal pH and enhancing absorption of some nutrients, all while directly impacting gut microbiota composition
- ***Exert beneficial effects against intestinal inflammation***

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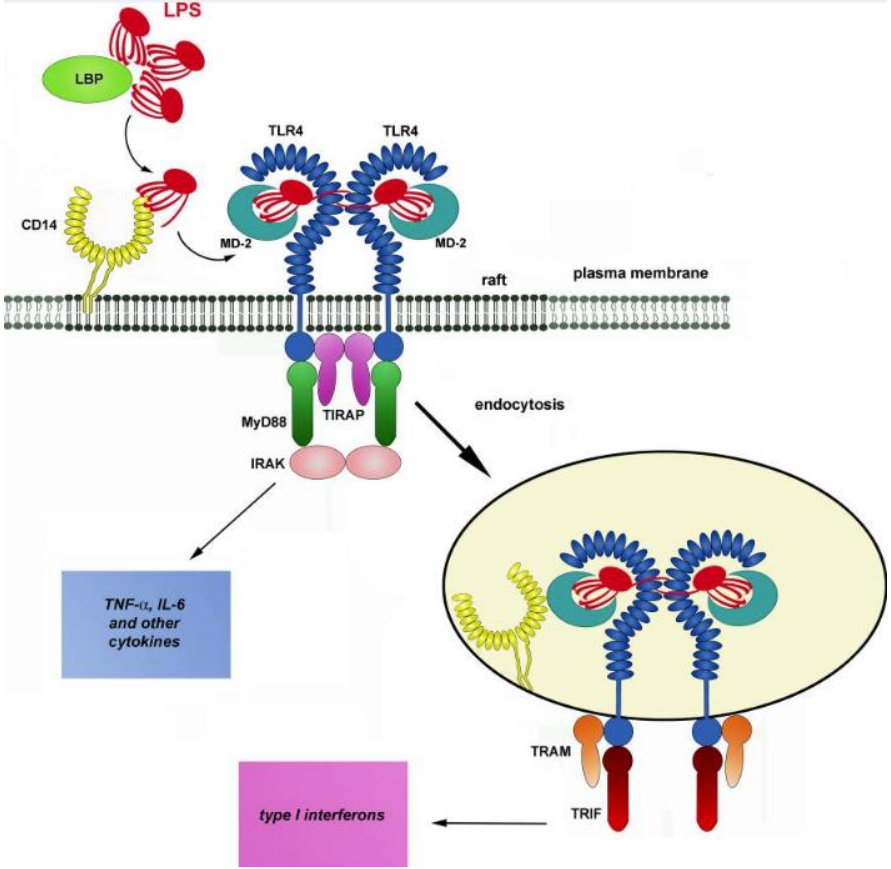
LPS BASICS

- Lipopolysaccharide (LPS) is an endotoxin derived from the outer membrane of gram-negative bacteria
- Detected in the portal venous blood – enters through damaged GI epithelium or chylomicrons
- Present in triglyceride (TG)-rich, very low-density lipoproteins (VLDL) in systemic blood flow
- Dietary and microbial LPS is consistently absorbed through the intestinal epithelia
- A component of biofilms
- Causes immunologic and metabolic disruption

https://www.sciencedirect.com/topics/neuroscience/lipopolysaccharide/pdf

LPS, TLR4, AND INFLAMMATION

- LPS is the most potent immune stimulant known.
- TLR4 is a pattern-recognition receptor – “toll” means “Wow!” in German; so-named because the discovery was so exciting.
- TLR4 receptors have evolved to recognize PAMPS and DAMPS to activate innate and adaptive immunity, and to protect the host.
- TLR4 binding activates NF-Kappa-Beta, increasing proinflammatory cytokines including TNF-alpha and IL-6.



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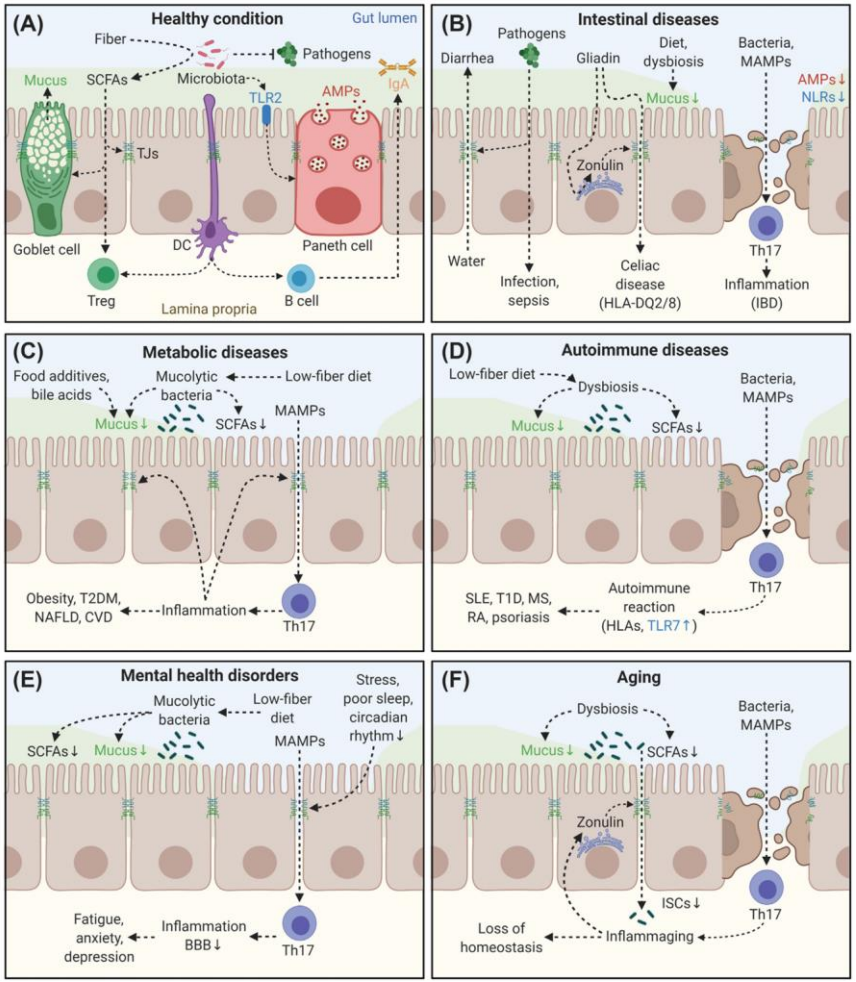
SYSTEMIC INFLUENCES OF THE GASTROINTESTINAL MICROBIOME



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MICROBES AND THE LIVER

LPS AND THE LIVER

Lipopolysaccharides in liver injury: molecular mechanisms of Kupffer cell activation

GRACE L. SU
Medical Service, Department of Veterans Affairs Medical Center and Department of Medicine, University of Michigan, Ann Arbor, Michigan 48109

Su, Grace L. Lipopolysaccharides in liver injury: molecular mechanisms of Kupffer cell activation. *Am J Physiol Gastrointest Liver Physiol* 283: G256–G265, 2002; 10.1152/ajpgi.00550.2001.—Endogenous gut-derived bacterial lipopolysaccharides have been implicated as important cofactors in the pathogenesis of liver injury. However, the molecular mechanisms by
entirely clear. R
such as tumor n
the liver, Kupff
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receptor Toll-lil
The role played

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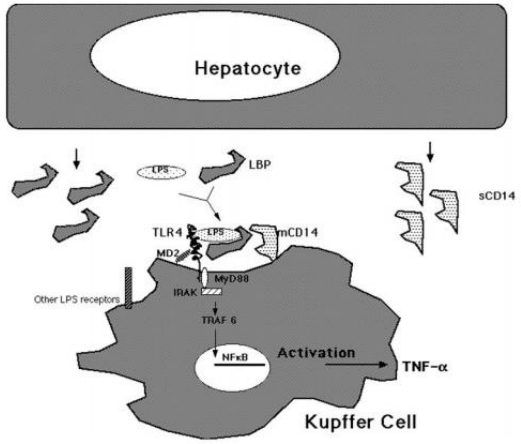

Fig. 1. One pathway of lipopolysaccharide (LPS) signaling in Kupffer cells. LPS in hepatic sinusoids binds to LPS binding protein (LBP) produced by hepatocytes. Binding of LPS to LBP facilitates transfer of LPS to membrane CD14 followed by activation mediated through Toll-like receptor (TLR)4 receptor/MD2. Signaling occurs via MyD88, which associates with interleukin-1 receptor-associated kinase (IRAK) and tumor necrosis factor (TNF)-activated factor 6. This results in translocation of nuclear factor-κB (NF-κB) into the nucleus and production of proinflammatory cytokines. Hepatocytes also produce sCD14, which may alter cellular reactivity to LPS.

https://journals.physiology.org/doi/pdf/10.1152/ajpgi.00550.2001

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BIOFILMS AND TOXICITY

Bhatt *et al. Microb Cell Fact* (2021) 20:72
https://doi.org/10.1186/s12934-021-01556-9

Microbial Cell Factories

REVIEW Open Access

Microbial glycoconjugates in organic pollutant bioremediation: recent advances and applications

Pankaj Bhatt[1,2], Amit Verma[3], Saurabh Gangola[4], Geeta Bhandari[5] and Shaohua Chen[1,2*]

Biofilms are added as inert support and used for the biochemical conversion of pollutants by sorption, particularly heavy metals, hydrocarbons, industrial waste, and wastewater treatment

contaminated the air, soil, and water. Persistent OPs enter
s on living systems. Thus, there is a need to manage the
njugates pave the way for the enhanced degradation of
To date,
which helps to accelerate degradation through microbial metabo
glycoconjugates, their role in biofilm formation, and their applicat
environments.

Keywords: Glycoconjugates, Bioremediation, Biosurfactants, Organic pollutants, Biofilm

Glycoconjugates can have diverse structures, such as glycoproteins, glycopeptides, peptidoglycans, glycolipids, lipopolysaccharides, and glycosides.

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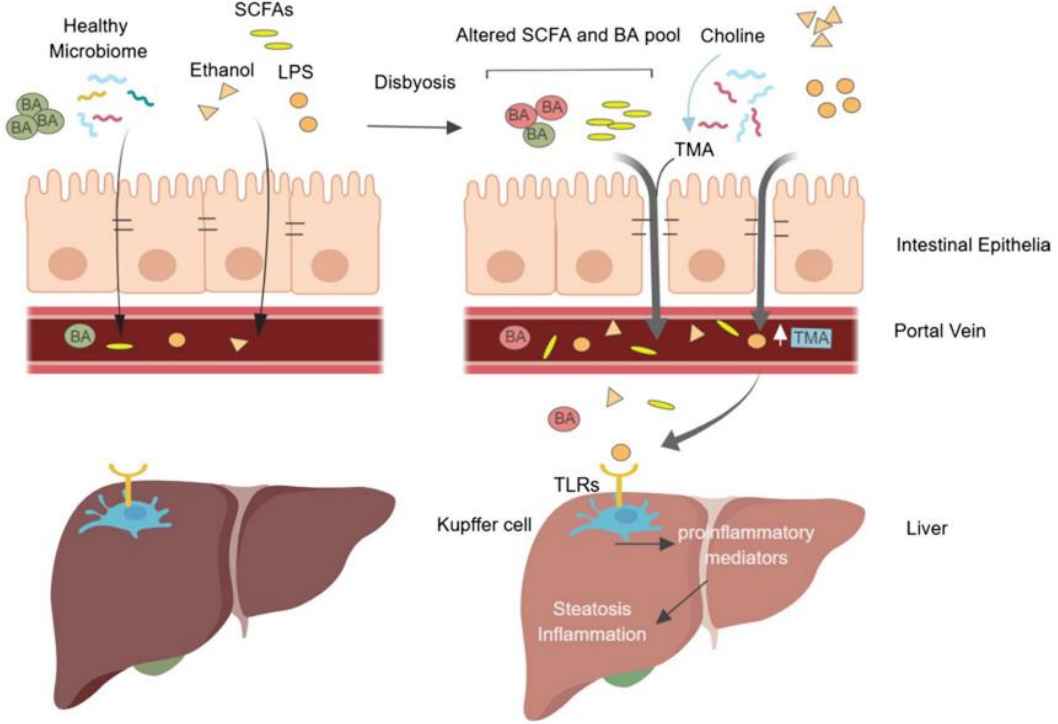
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5715945/pdf/jof-03-00047.pdf

DYSBIOSIS AS A SOURCE OF TOXICITY

- Blood comes from intestines and contains products produced by the microbiome:
  - Phenols
  - Acetaldehyde
  - Ammonia
  - Proinflammatory bacterial components
    - Peptidoglycan
    - LPS
- Immune cells of the liver (lymphocytes, macrophages, dendritic cells, and natural killer cells) respond to DAMPS and PAMPS
- Toll-like receptor binding results in hepatic damage and inflammation



THE MICROBIOME AND THE LIVER

REVIEW

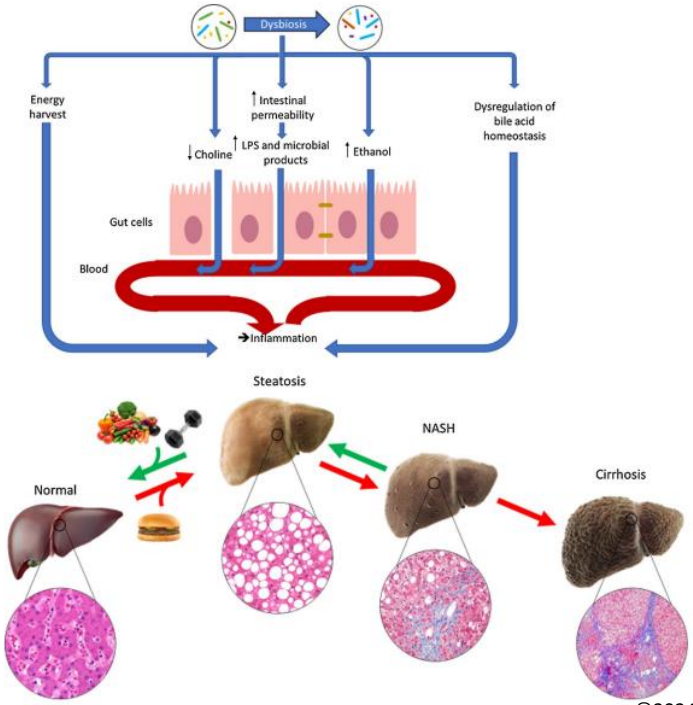
Check for updates

The links between the gut microbiome and non-alcoholic fatty liver disease (NAFLD)

Zahra Safari[1,2] · Philippe Gérard[1]

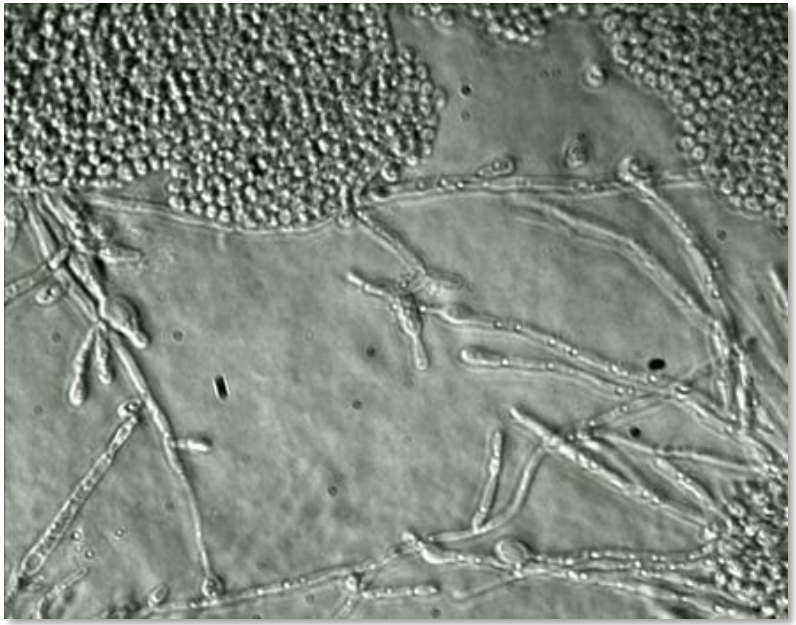
Received: 23 August 2018 / Revised: 11 December 2018 / Accepted: 15 January 2019

NAFLD global prevalence is 24%



SOURCES OF TOXICITY FROM MICROBIAL IMBALANCES

- LPS and other metabolites
- Inflammatory damage to hepatocytes
- Interruption of Gut-Liver Axis
- Loss of protection from SCFAs and GLP-1 activity from metabolites

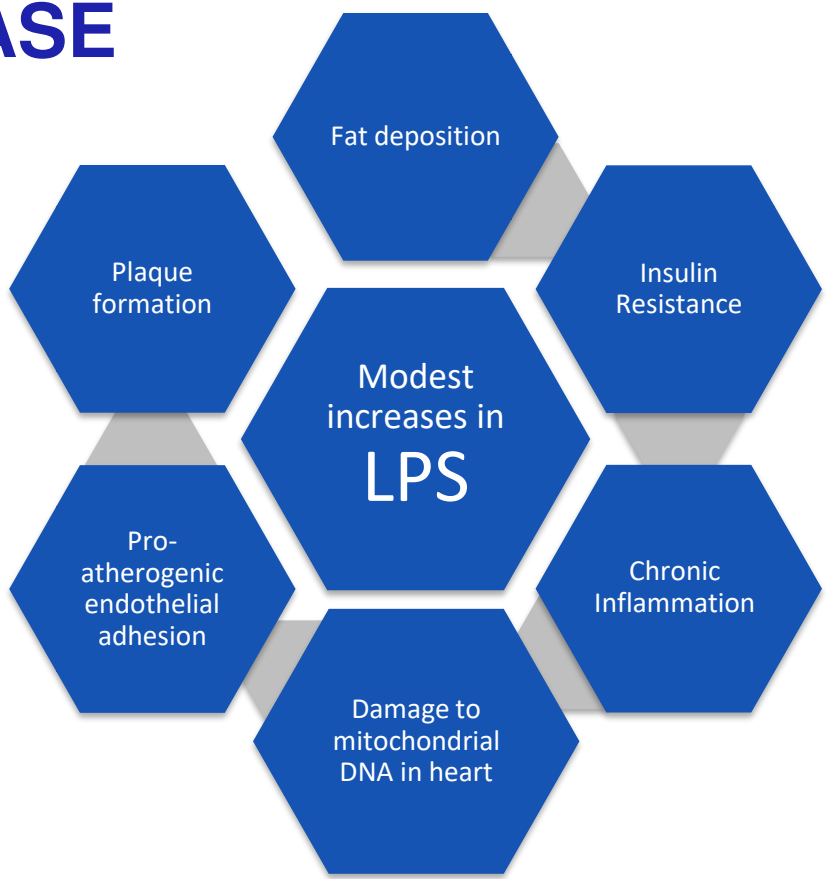


https://www.cancerfightingstrategies.com/images/fungus-and-cancer-candida.jpg

METABOLIC HEALTH AND THE MICROBIOME

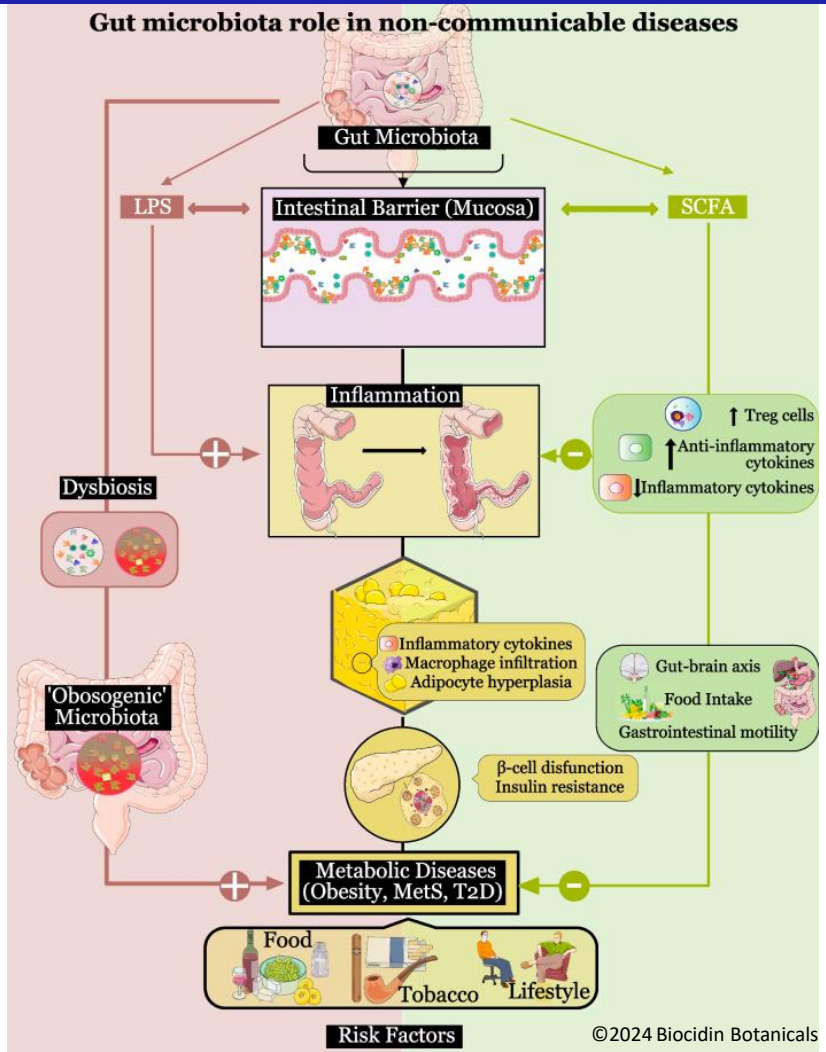
METABOLIC ENDOTOXEMIA AND CARDIOVASCULAR DISEASE

- Defined as a two- to three-fold increase in LPS
- Commonly found in CVD patients

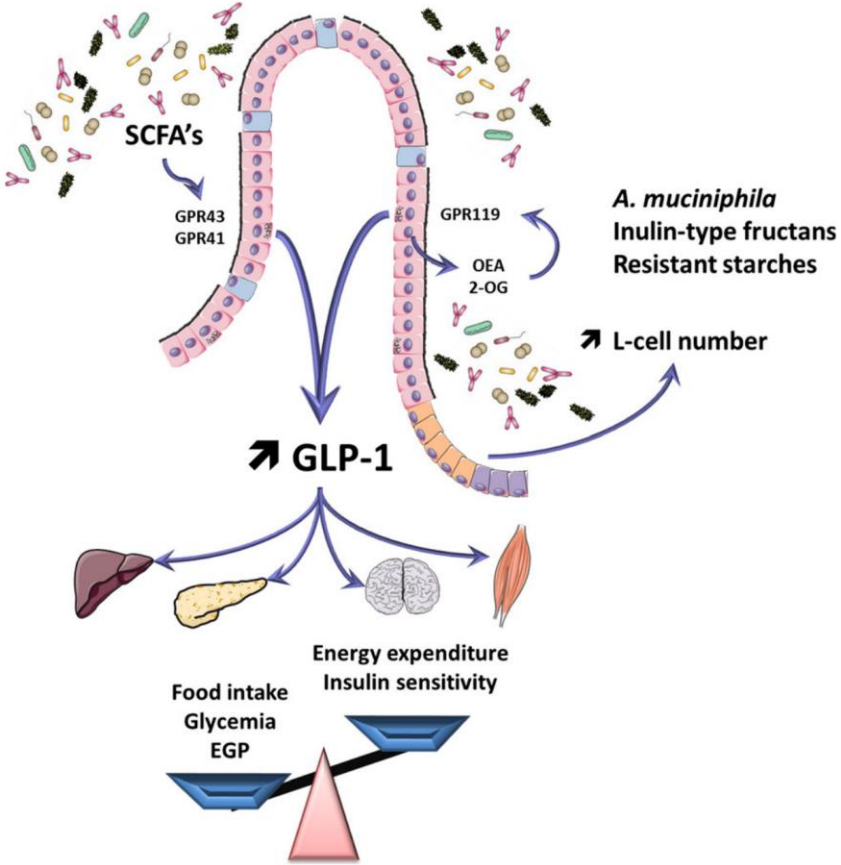


MICROBIOME & METABOLIC DISEASES

- Inflammation regulation by microbiome gets disrupted, leading to:
  - Obesity
  - Metabolic Syndrome
  - Type 2 Diabetes
  - ↑ Cardiovascular Disease



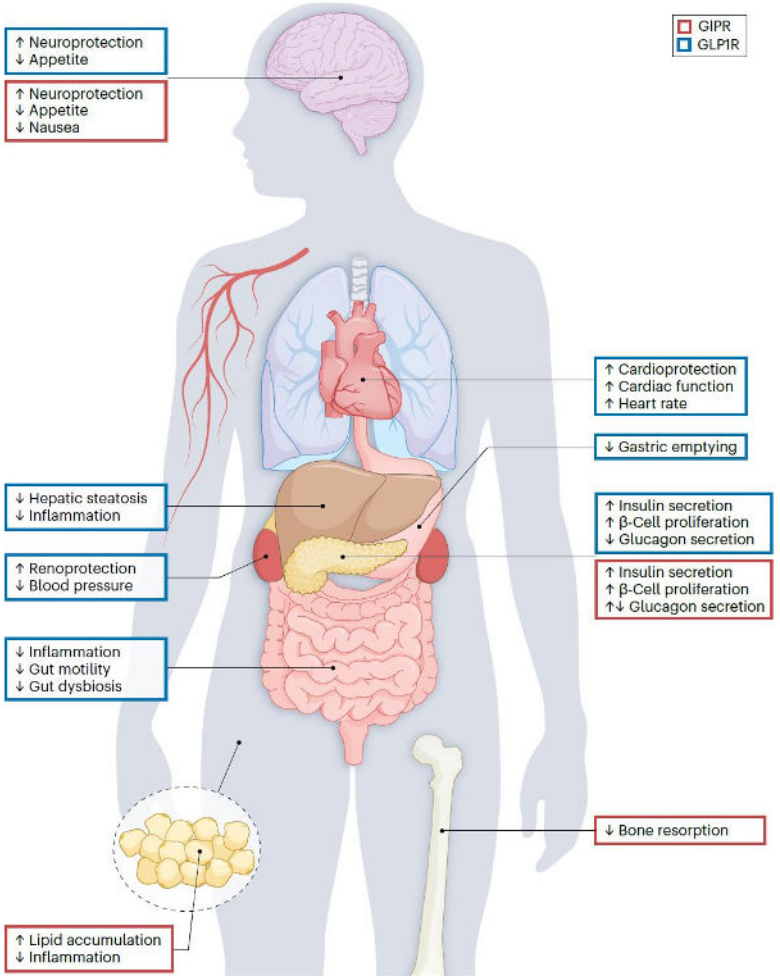
https://www.ncbi.nlm.nih.gov/pmc/articles/instance/9903633/bin/13293_2023_490_Fig1_HTML.jpg



https://pubmed.ncbi.nlm.nih.gov/24789701/

GUT MICROBIOTA AND GLP-1

BIOLOGICAL ACTIONS OF GLP-1



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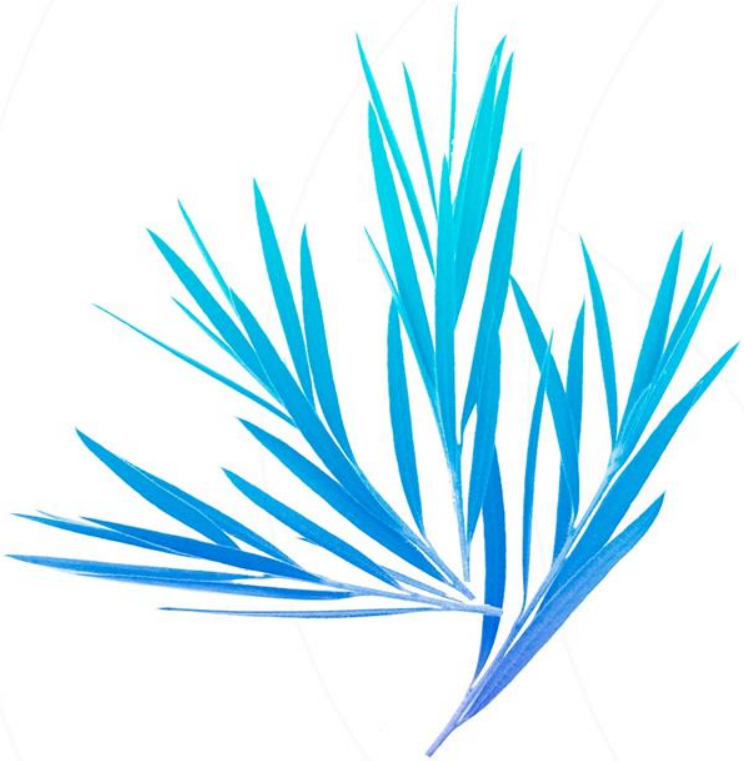
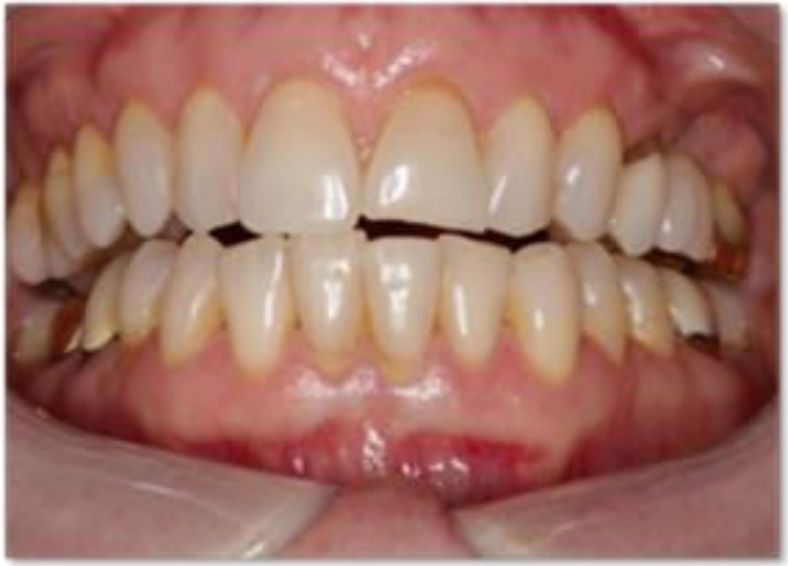


METABOLIC HEALTH AND THE ORAL MICROBIOME

THE ORAL MICROBIOME

- 700+ species of bacteria in the mouth, with a mean of 296
- 1 milliliter of saliva = 10^8 microorganisms (100,000,000)
- We swallow one liter or more of saliva each day!



https://www.drkarafitzgerald.com/tag/oral-microbiome/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6057715/
https://www.nature.com/articles/sj.bdj.2016.865
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5274568/
https://pubmed.ncbi.nlm.nih.gov/9673163/

Photo provided by Barbara Tritz, Queen of Dental Hygiene

THE IMPACT OF ORAL HEALTH

- Periodontal disease (gingivitis and periodontitis) – the most common inflammatory disease globally
- Affects 50% of adults over 30, and 70% of those over 65 years old
- This is an easy area to make a big impact without adding to supplement burden

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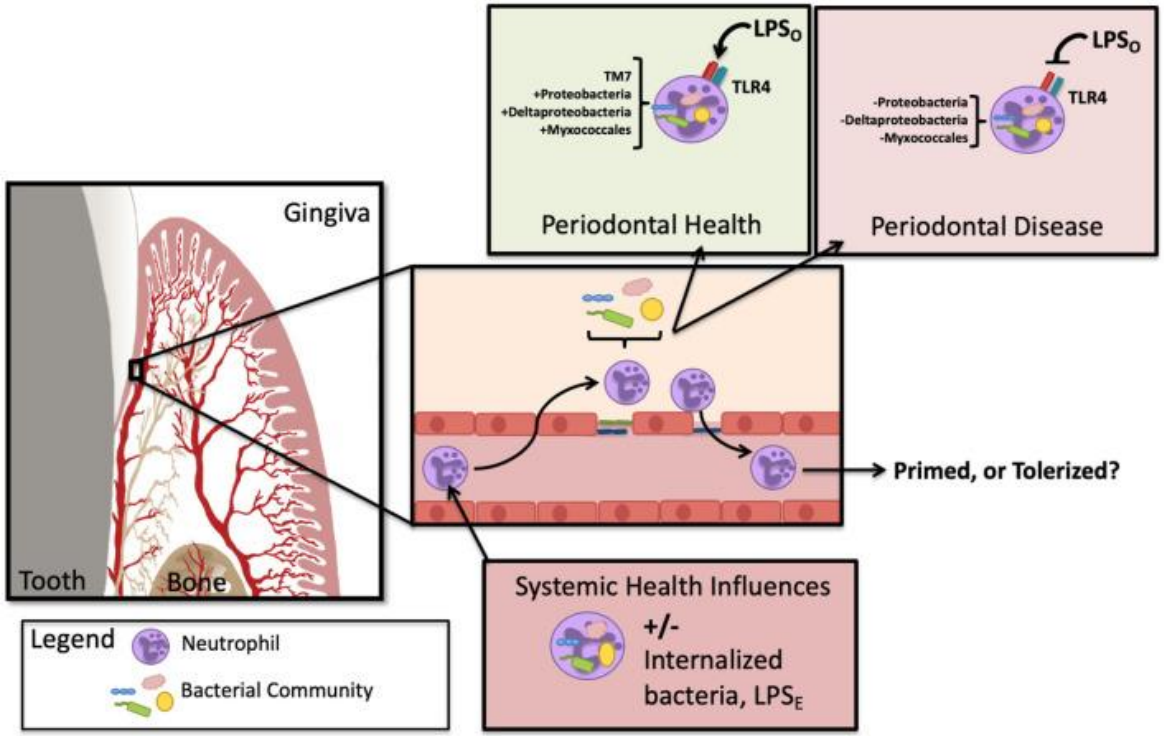
ORAL CONTRIBUTIONS TO ENDOTOXEMIA

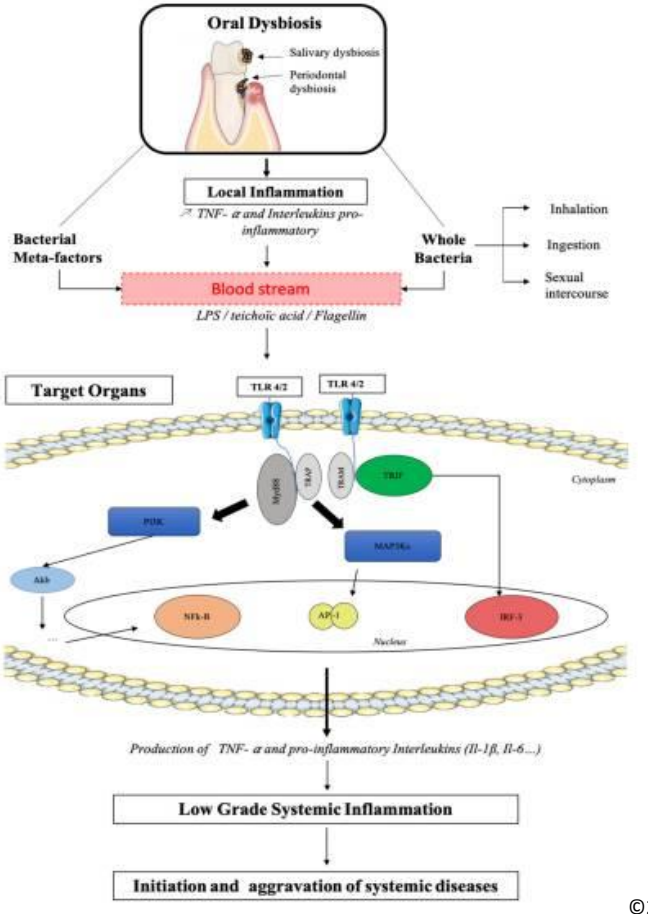
"Induction of metabolic endotoxemia in clinical and animal models has been primarily through a high fat, low fiber diet, or direct injection of E. coli LPS but subsequent study of metabolic endotoxemia and periodontitis has shown that ingestion of perio-pathogens can induce similar pathology."



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9169450/

ORAL-SYSTEMIC INFLAMMATION

“In fact, oral microbiota and its balance play a major role in an individual’s general homeostasis. Any disruption leads to an increase in certain bacterial species, especially Gram-negative ones, associated with the massive production of pro-inflammatory cytokines, which causes or maintains chronic low-grade inflammation.
“



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ORAL-SYSTEMIC INFLAMMATION

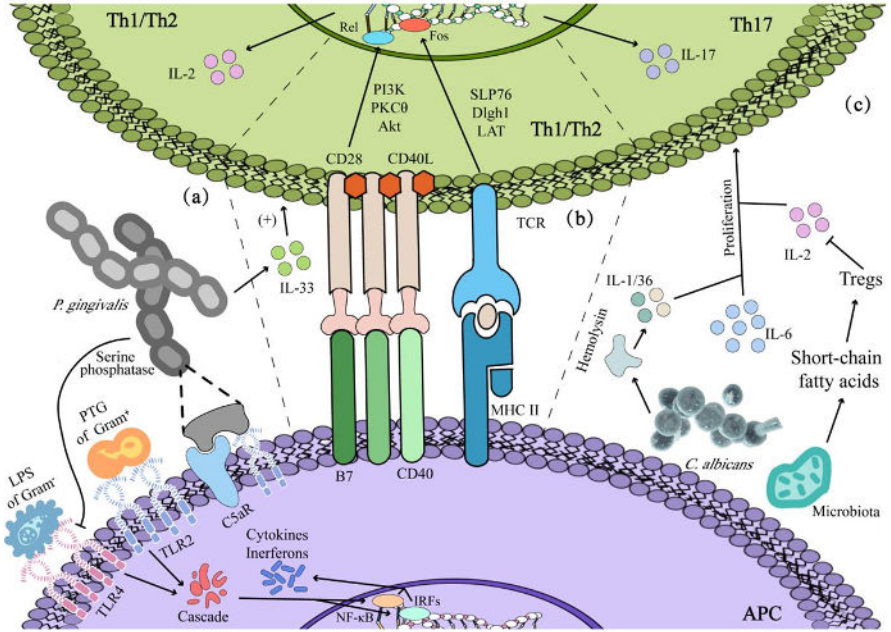


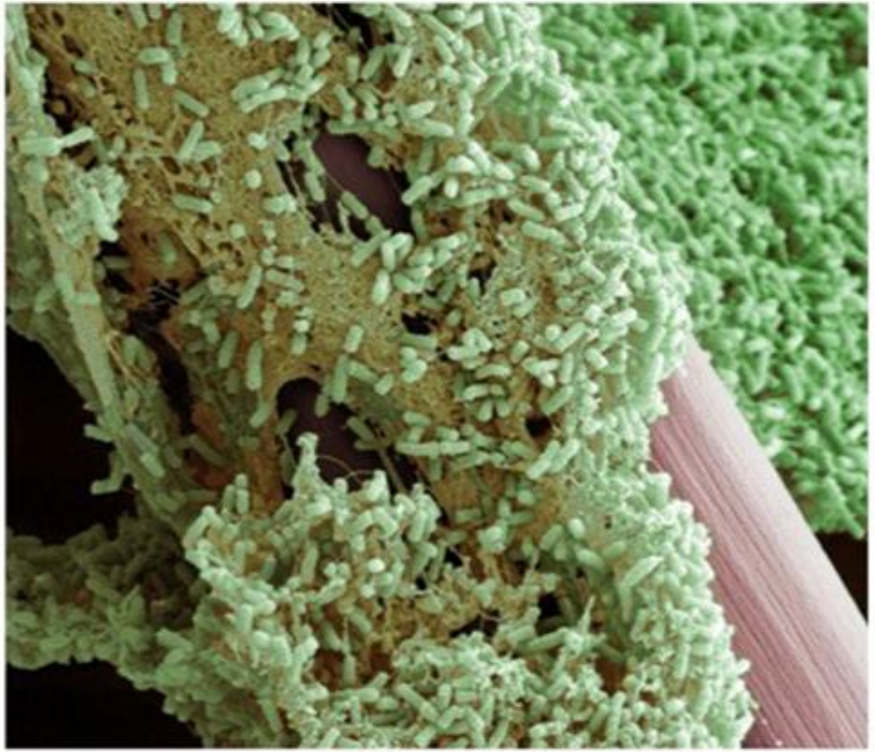
FIGURE 3

Dysbiosis-induced immunoreaction: **(a)** innate immunity: lipopolysaccharide (LPS) and Peptidoglycan (PTG) contribute to the activation of immune and inflammatory responses in Th1/2. **(b)** Adaptive immunity: *Porphyromonas gingivalis* enhanced Th2 cytokine-mediated inflammatory immune response by prompting the secretion of IL-33 of epithelium, and antigen presentation by antigen–presenting cells (APCs) could activate Th1/2 by signal 1 and signal 2. **(c)** *Candida albicans* producing cytokines such as IL-1/IL-36 mediates the expression of IL-17 and the proliferation of Th17 cells, and short-chain fatty acids produced by microbiota facilitate the viability of Th17 with regulating the Tregs.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9948764/pdf/fmicb-14-1061032.pdf

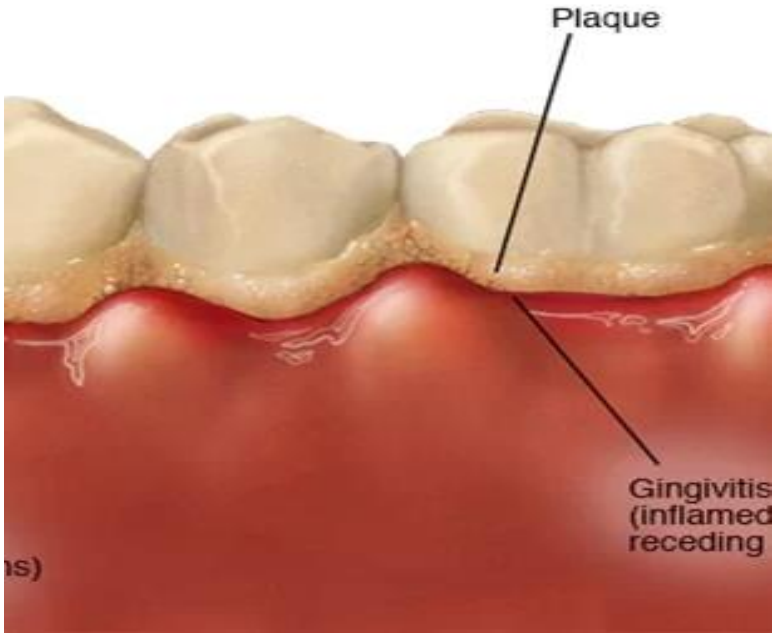
ORAL BIOFILMS

Biofilm on a toothbrush bristle



Biofilm on a toothbrush bristle (higher magnification)

PLAQUE: THE VISIBLE BIOFILM



The distinct structure of teeth (smooth surfaces, pits and fissures, proximal sites, and exposed roots) enables large masses of microbes to accumulate as dental plaque biofilm.

The plaque biofilm does not naturally shed as it accumulates, which is **a key driver to dysbiosis** if not removed with proper oral hygiene.

As plaque accumulates, potentially pathogenic bacteria may dominate and an incipient oral dysbiosis develops.

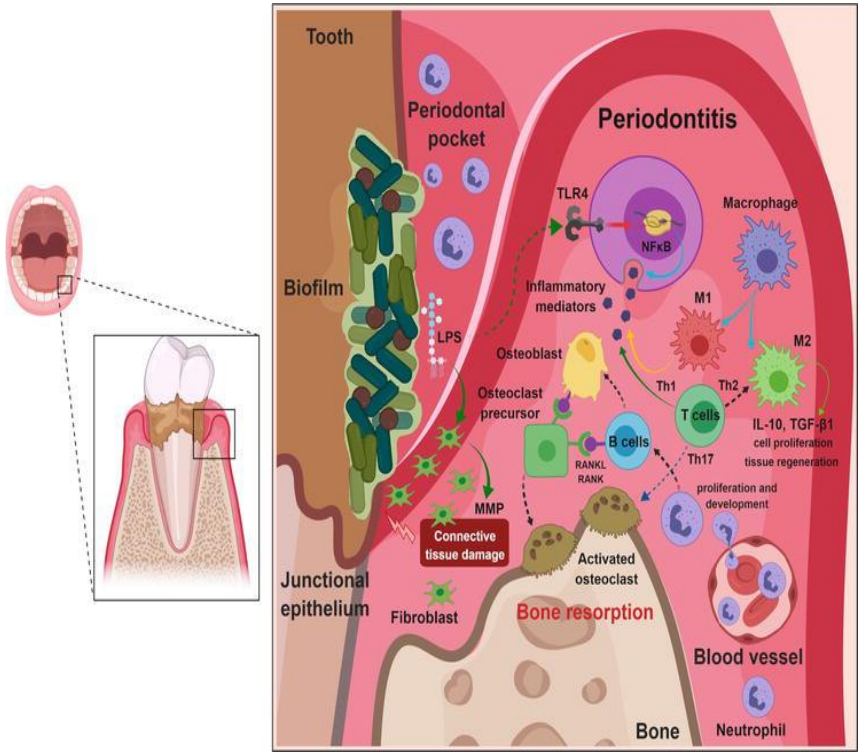
MICROBIAL MOVEMENT

THE PROBLEM SPREADS

The bloodstream adjacent to the periodontal pocket is a mere single cell layer thick. This creates the potential for:

- Transfer of bacterial products and inflammatory mediators from host defense.[2]
- Translocation of the microbes themselves into the bloodstream, where they
  travel to distant sites such as the heart, lungs, brain, and joint space.

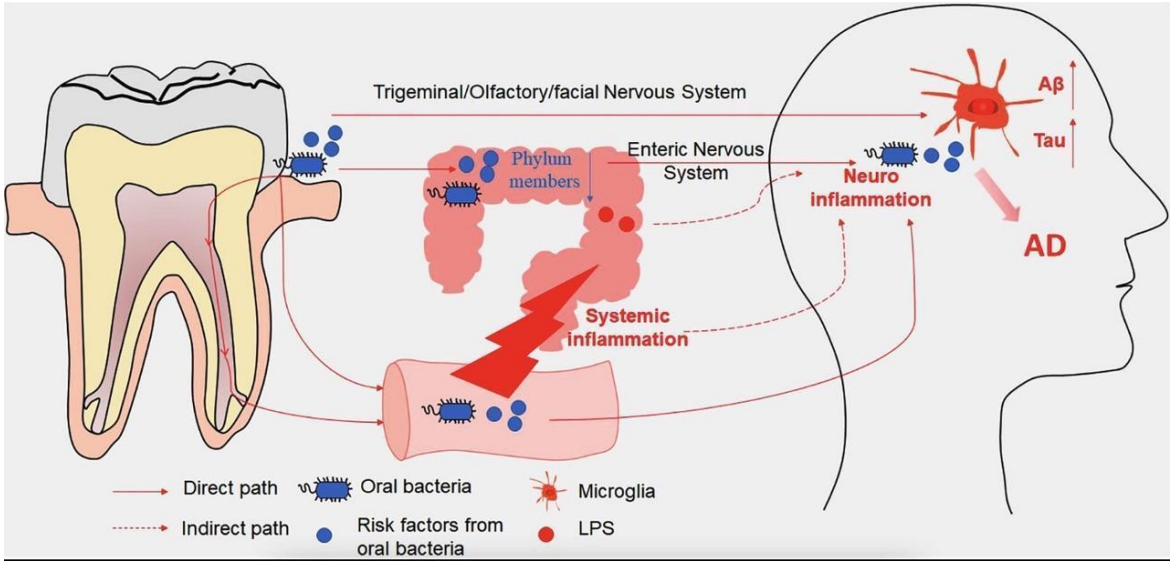
"Less than 1 minute after an oral procedure, organisms from the infected site may have reached the heart, lungs, and peripheral blood capillary system".



SYSTEMIC IMPLICATIONS OF ORAL IMBALANCE

Possible mechanisms of effect:

- Translocation of pathogens
- Toxins produced by microbes
- Inflammation
- Traveling via nerves

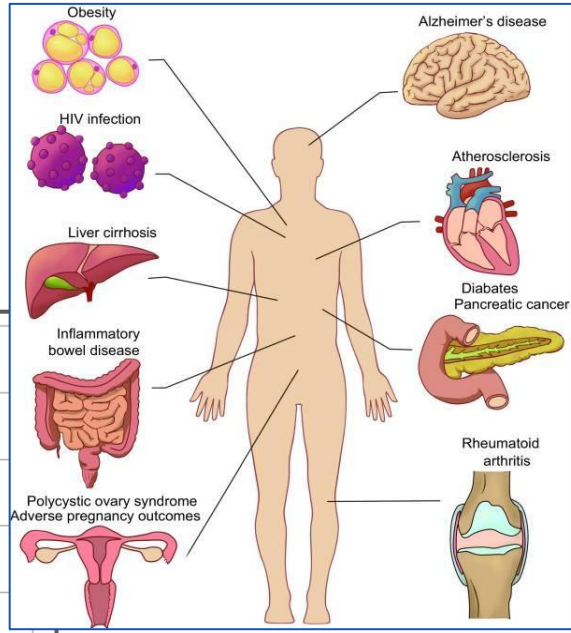


https://www.frontiersin.org/files/Articles/633735/fncel-15-633735-HTML/image_m/fncel-15-633735-g001.jpg [23]

ORAL DYSBIOSIS AND CARDIOVASCULAR DISEASE

"People with untreated tooth infections are 2.7 times more likely to have cardiovascular problems, such as coronary artery disease, than patients who have had treatment of dental infections."

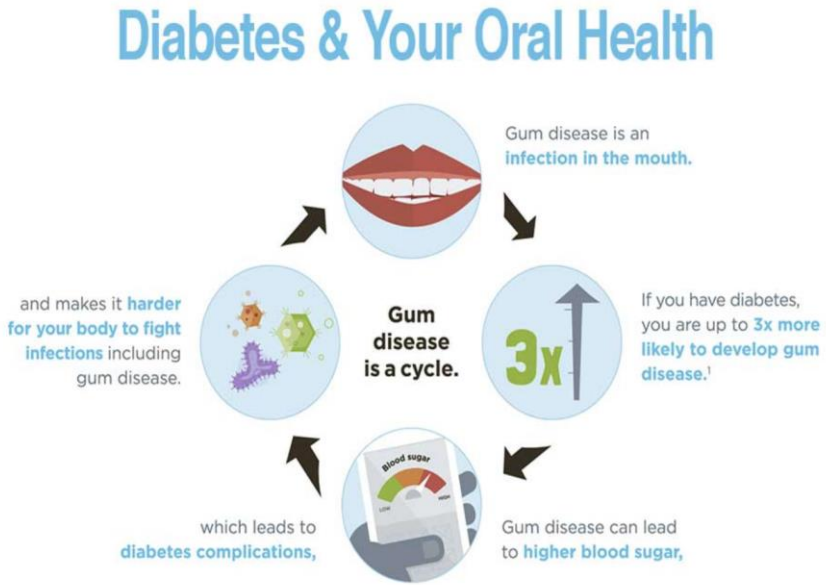
Neuroinflammation (Alzheimer's, mental health)	**Cancer** (oropharyngeal, esophageal, colorectal)
Cardiovascular Disease	Appendicitis
Inflammatory Bowel Disease	Obesity
Autoimmunity	Diabetes Mellitus
Respiratory Tract Infection	Abscess (brain, lung, liver, spleen)
Meningitis	Adverse Pregnancy Outcomes



Liljestrand JM, Mäntylä P, Paju S, et al. Association of Endodontic Lesions with Coronary Artery Disease. *J Dent Res*. 2016;95(12):1358-1365. doi:10.1177/0022034516660509

ORAL DYSBIOSIS & DIABETES

- Diabetes is a major risk factor for periodontal disease, with an increased risk factor of 2-3 times above people without diabetes.
- The control of periodontitis has a pivotal effect on the control of blood sugar.
- The presence of lipopolysaccharide (LPS – found in the outer membrane of gram-negative bacteria) leads to metabolic endotoxemia, which worsens glycemic control.
- Inflammation affects insulin signaling pathways – reducing insulin sensitivity.
- Increased systemic inflammation affects blood glucose metabolism via enhanced glucocorticoid stimulation.



PORPHYROMONAS GINGIVALIS

Cardiovascular
- Atherosclerotic plaque
- Myocardial infarction
- Abdominal aortic aneurysm
- Hypertension

Metabolic
- Diabetes
- Non-alcoholic fatty liver disease

Pulmonary
- Pneumonia
- COPD

Neurological
- Alzheimer's
- Depression

Rheumatological
- Arthritis

Obstetrics
- Poor pregnancy outcomes

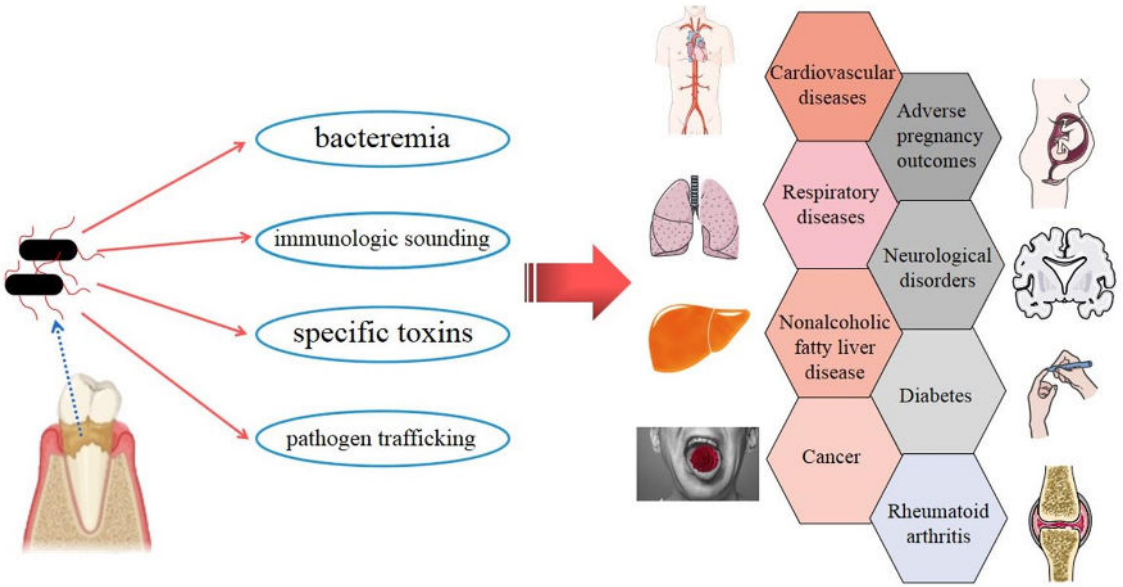
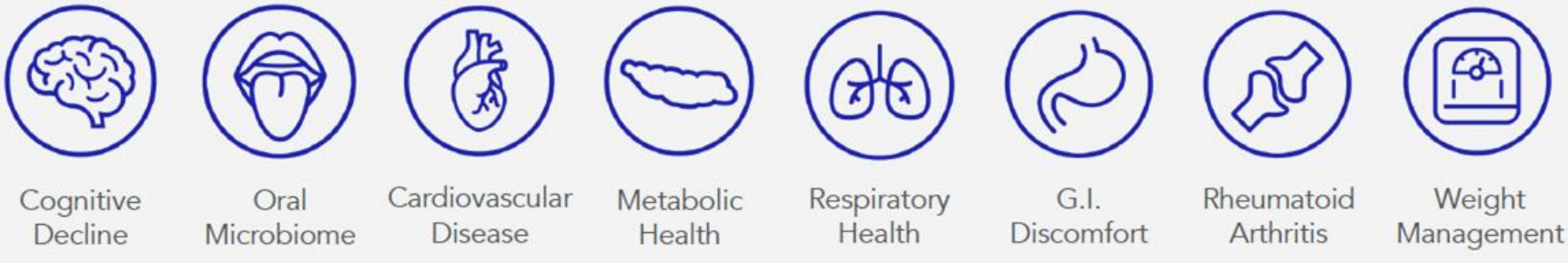


Figure 4. Strategies by which *Porphyromonas gingivalis* can invade the whole body, along with simple a schematic representation of *Porphyromonas Gingivalis*-associated systemic diseases

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7696708/pdf/pathogens-09-00944.pdf

WHOLE-BODY HEALTH BEGINS IN THE MOUTH

When oral dysbiosis occurs, pathogenic bacteria reach levels that may lead to infections, such as tooth decay and gum disease,[4] and ultimately a predisposition to many systemic diseases and conditions. Research has shown that more than 120 diseases originate in the mouth.[5]



[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346134/
[5] https://www.google.com/url?q=https://www.deltadentalnj.com/blog/entry/2019/Den-tists-Can-Identify-up-to-120-Diseases-in-Your-Mouth&sa=D&source=docs&ust=1659726865432277&usg=AOvVaw39kvwjtvqbgAxnx_vX2MUf
[6] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6468093/
[7] https://www.frontiersin.org/articles/10.3389/fpsyt.2021.814177/full
[8] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7375741/5
[9] https://www.frontiersin.org/articles/10.3389/fimmu.2020.591255/full
[10] https://www.hopkinsrheumatology.org/2017/01/gum-disease-linked-to-rheumatoid-arthritis/ 11 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5813989/

Cognitive Decline
Poor oral health and periodontitis are associated with increased risk of dementia and Alzheimer's disease.[6]

Neurological Health
Oral dysbiosis is associated with neuroglial activation, anxiety, depression, insomnia, brain fog and poor concentration.[6]

G.I. Discomfort
Dysbiosis (imbalance of microorganisms) in the mouth may translocate to the G.I. tract and contribute to discomfort such as gas, bloating, belching, reflux, abdominal pain, and/or altered stool function. Remember: What grows in the mouth will grow in the gut![8]

Blood Sugar Dysregulation
People with gum disease have more difficulty controlling their blood sugar levels, while gum disease appears more frequent and severe among people with diabetes.[6]

Cardiovascular Disease (CVD)
Oral bacteria have been found in arterial plaques and the inner lining of the heart chambers and valves. People with periodontal disease are 25% more likely to develop cardiovascular disease.[6]

Autoimmunity
The translocation of oral microorganisms, their components, or their metabolites from periodontal tissues could be involved in the occurrence of autoimmune responses at a systemic level.[9]

Rheumatoid Arthritis (RA)
Aggregatibacter actinomycetemcomitans (Aa) is associated with gum disease and a process known as hypercitrullination (the formation of immune complexes that can initiate autoimmune activity). RA patients have elevated citrullinated proteins in the joint space, and half of RA patients have evidence of Aa infection. Treating periodontal disease has been shown to reduce pain caused by RA.[10]

Respiratory Health
Bacteria in your mouth can be respired into your lungs, causing pulmonary dysbiosis, pneumonia, and predisposition to other respiratory diseases.[6]

Weight Management
Research shows that people with higher body weight have subpar oral health, including oral inflammation, cavities, and periodontitis. Conversely, poor oral health can affect blood glucose control and may contribute to weight gain.[11]

ORAL DYSBIOSIS & GUT HEALTH

The Oral-Gut Microbiome Connection

Brushing after meals resulted in a dramatic reduction in stool levels of *C. albicans* …

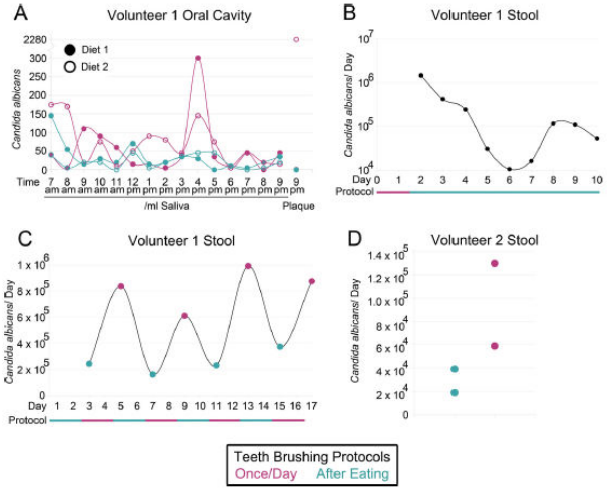


FIG 5 *Candida albicans* levels were decreased in the mouth and stool of healthy human volunteer(s) when teeth were brushed more often. (A) Concentrations of *C. albicans* in saliva throughout days when an adult volunteer either did or did not perform tooth brushing after eating. The volunteer consumed the same diet on both tooth-brushing protocols, the experiment was performed for two different diets, and levels of *C. albicans* were measured in a sample of plaque at the end of each day. (B) The total number of *C. albicans* cells in the stool of a volunteer over time (plotted on a log axis). Following a period of brushing teeth just once per day, the volunteer performed tooth brushing after every meal for 8 consecutive days. The diet was not the same from day to day but contained similar levels of sugars throughout the time period. (C and D) Lastly, the total number of *C. albicans* cells was measured in the stool of (C) a volunteer who alternately followed different tooth-brushing protocols for 2 days over the course of 16 days or of (D) a second volunteer who twice conducted each tooth-brushing protocol on nonconsecutive days. For all experiments, saliva, plaque, or stool was plated on Sabouraud plates containing antibiotics. Possible *C. albicans* colonies were later spotted on chromogenic media to distinguish the *C. albicans* colonies from closely related species and to adjust *C. albicans* numbers.

Biocidin Botanicals™

THE POWER OF BOTANICALS

POWER OF BOTANICALS

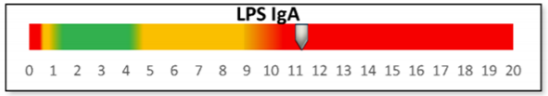
- Plants have developed tools to grow and flourish under the same environmental stressors that we face. They have an innate capacity to protect themselves – producing antimicrobial compounds, antioxidants, biofilm disruptors, and immune modulators. (Yes, plants have immune systems, too!)

- Far-reaching effects include support for:
  - Immunomodulation
  - Adaptogenic activity
  - Anti-Inflammatory
  - Nervous system support

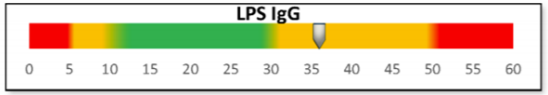
BOTANICAL ANTIMICROBIAL & LPS

Pre-test 5/11/21

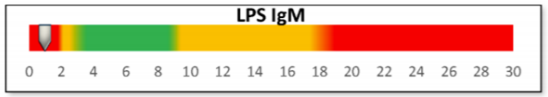
11.25
Normal RANGE: 0.83-4.47 µg/mL
HIGH



35.94
Normal RANGE: 9.09-31.5 µg/mL
BORDERLINE HIGH

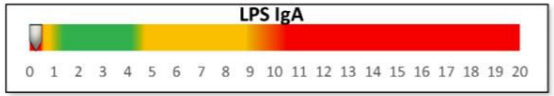


0.96
Normal RANGE: 2.5-9.4 µg/mL
LOW



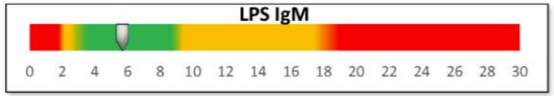
Post-test 06/23/21

0.10
Normal RANGE: 0.83-4.47 µg/mL
LOW



16.16
Normal RANGE: 9.09-31.5 µg/mL
NORMAL

5.67
Normal RANGE: 2.5-9.4 µg/mL
NORMAL



BOTANICAL ANTIMICROBIAL & LPS

12/10/21

ADVANCED INTESTINAL BARRIER ASSESSMENT (PLASMA) | 2/2

5.71 Normal RANGE: 0.83-4.47 µg/mL BORDERLINE HIGH	LPS IgA	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
74.58 Normal RANGE: 9.09-31.5 µg/mL HIGH	LPS IgG	0 5 10 15 20 25 30 35 40 45 50 55 60
19.27 Normal RANGE: 2.5-9.4 µg/mL HIGH	LPS IgM	0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30

03/08/22

ADVANCED INTESTINAL BARRIER ASSESSMENT (PLASMA) | 2/2

1.55 Normal RANGE: 0.83-4.47 µg/mL NORMAL	LPS IgA	0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
3.27 Normal RANGE: 9.09-31.5 µg/mL LOW	LPS IgG	0 5 10 15 20 25 30 35 40 45 50 55 60
7.93 Normal RANGE: 2.5-9.4 µg/mL NORMAL	LPS IgM	0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30

DYSBIOSIS AND MAFLD – A CASE STUDY

	09/02/21	10/22/21	BCP	01/11/22	02/01/22	02/24/22	04/20/22	05/26/22	06/09/22	07/22/22	11/02/22	03/03/23
Alk Phos (40-150)		67		56			51			55	58	64
ALT (6-40)	51	66		40			40	44	46	44	37	48
AST (10-40)	43	50		31			32	36	37	36	43	30
Hgb A1C (<5.7)	5.7				5.5	5.3						
Glucose (70-99)	117				111	105		105	111			116 (NF)
Total Cholesterol (114-200)	233					148					164	121
HDL (40-60)	28					29					27	22
LDL (<100)	133					93					85	65
Triglycerides (10-200)	358					130					130	170

MAFLD

Pre Botanical Antimicrobial 3/15/21	Post Botanical Antimicrobial 2/2/23
CAP (Steatosis) Score: 387 dB/m **(severe)**	CAP (Steatosis) Score: 293 dB/m **(mild)**
Fibrosis Score: 9.5 kPa **(significant)**	Fibrosis Score: 6.3 kPa **(insignificant)**

METABOLIC HEALTH AND THE MICROBIOME

Vibrant Testing	March 1, 2023	July 21, 2023	November 28, 2023
sdLDL (mg/dL)	31.3	18.5	20.6
Lp(a) (mg/dL)	8	7	<7
Glucose (mg/dL)	99	87	68
HbA1c	5.5	5.6	5.5
Insulin	46.2	14.7	19.9
ALT	28	81 H	35 H
AST	24	34 H	28
Alkaline Phosphatase	116 H	131 H	130 H

METABOLIC HEALTH AND THE MICROBIOME

Vibrant Testing	March 1, 2023	July 21, 2023	November 28, 2023
Cholesterol, Total (mg/dL)	180	205	216
LDL Calculation (mg/dL)	99	125	130
HDL Direct (mg/dL)	46	58	56
Cholesterol/HDL Ratio	3.9	3.5	3.9
Triglyceride (mg/dL)	175	108	148
Homocysteine	13	9	11
Hs-CRP (mg/L)	4.2	4.2	7.3
Ox-LDL (U/L)	43.1	28.6	50.1

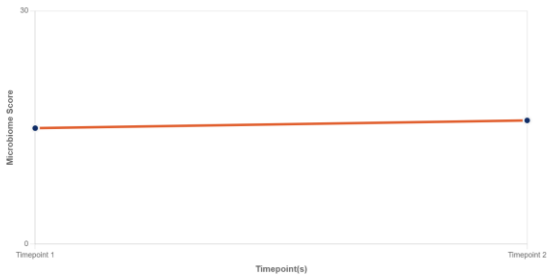
BOTANICALS AND SCFAs

Short-Chain Fatty Acids			
	Before	After	Normal Range
Acetate	68.7%	63.8%	60.2 - 72.7%
Butyrate	11.8%	12.5%	5.1 - 12.4%
Propionate	16.6%	21.2%	15.4 - 30.3%
Valerate	.2%	.9%	.8 - 3.5%
Total SCFAs	39.7 micromol/gram	46.4 micromol/gram	45.4 - 210.1 micromol/gram

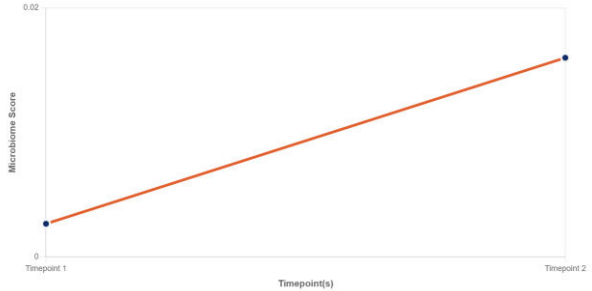
BOTANICALS & THE MICROBIOME

- Pilot study was completed in 2020 with 13 participants using a botanical antimicrobial liquid and a binder for 8 weeks at maximum dosing.
- 69% (9/13) of the participants had an increase in probiotic abundance.
- 73% (8/11) of the participants had an increase in *Akkermansia muciniphila*.

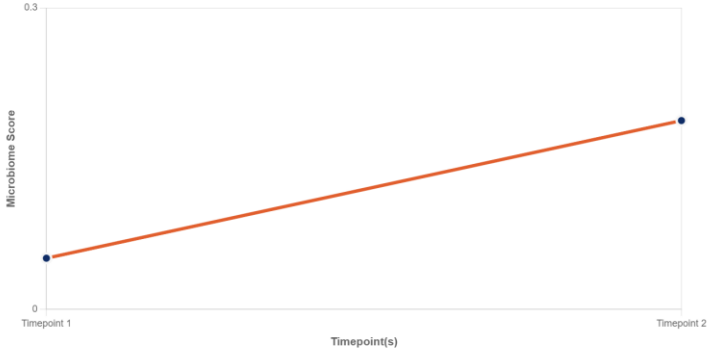
Faecalibacterium prausnitzii



Lactobacillus plantarum



Akkermansia muciniphila



BIOFILM RESEARCH STUDY

- Remarkable effectiveness in addressing biofilms of all yeast and bacteria species tested
- Planktonic and biofilm communities were tested
- Within 24 hours, both were eradicated
- Graph shows results on *E. Coli* and *Pseudomonas*
- Additional microorganisms studies were *Klebsiella pneumonia*, *Candida albicans, Staphylococcus aureus.*

Subsequently, biofilms were exposed to a fixed concentration of Biocidin® for a period 24 hours and cell viability was monitored.

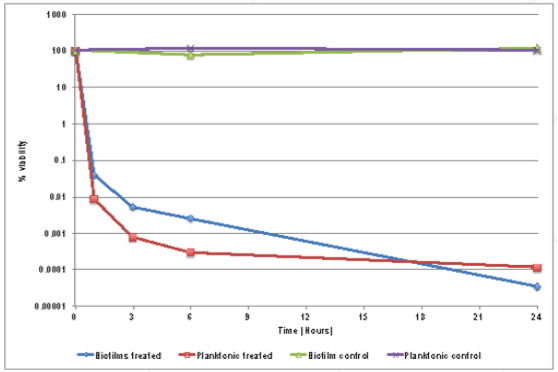


Figure 1. *P. aeruginosa* biofilms exposed to 50% Biocidin® for a period of 24 hours. At 24 hrs, most of the biofilm and planktonic populations were eradicated.

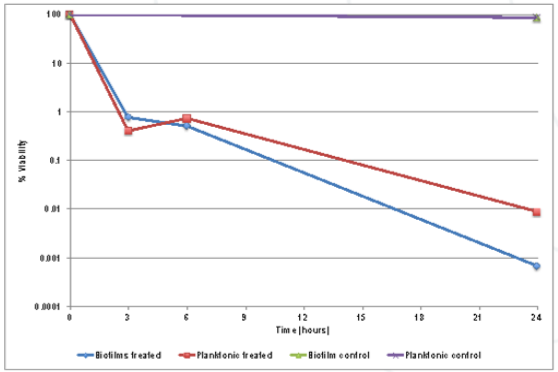


Figure 2. *E. coli* biofilms exposed to 50% Biocidin® for a period of 24 hours. At 24 hrs, most of the biofilm and planktonic populations were eradicated.

BIOCIDIN® LIQUID & CAPSULES

POTENT BROAD-SPECTRUM BOTANICAL COMBINATION

SUPPORTS MICROBIAL BALANCE* | DISRUPTS BIOFILMS*

- ***Supports gut health by addressing unwanted organisms****
- ***Dismantles biofilms****
- *Selectively enhances beneficial organisms**
- Immunomodulatory activity*
- May improve regularity and reduce bloating and gas*
- Helps improve vitality and mental clarity*
- Supports healthy mobility and body comfort*

Biocidin Botanicals

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease.

G.I. DETOX®+

ZEOLITE, CHARCOAL, & HERBAL FORMULA

- Assists in “mop up” of microbial and biofilm components*
- Supports healthy detoxification and full-body cleansing*
- Supports clearance of mold metabolites*
- Helps in the neutralization of histamine*
- Supports a more comfortable cleansing experience*
- May reduce bloating and gas*
- Supports microbiome balance*
- Recommended for use with Biocidin®

Biocidin Botanicals

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ROOTED IN SCIENCE *Bacillus subtilis* DE111®

dE 111® PROBIOTIC

DIGESTION

- 41 subjects, 30 days
- 5 billion CFU daily
- Controls microbial populations
- Aids in digestion
- Maintains general health
  - Cholesterol, Glucose, Triglycerides

REGULARITY

- 50 subjects, 90 days
- 1 billion CFU daily
- Reduction of alternating constipation and diarrhea
- Increase in proportion of normal stools

SPORTS NUTRITION

- 23 female athletes, 10 weeks
- 5 billion CFU daily w/protein drink
- Improvements in body composition, decreased body fat
- Improved lower body strength/exercise performance

SPORTS NUTRITION

- 25 male athletes, 12 weeks
- 1 billion CFU daily w/protein drink
- Decreased levels of TNF-alpha (indicator of inflammation)
- Trend towards decreased cortisol

CHILDREN - MICROBIOME

- 91 subjects (ages 2-6), 8 weeks
- 1 billion CFU daily
- Positive modulation of gut microbiome
- Increase in alpha-diversity
- Pro-immune support microbiome shift

CHILDREN – IMMUNE

- 81 subjects (ages 2-6), 8 weeks
- 1 billion CFU daily
- Reduced duration of vomiting, hard stools and GI discomfort
  - Trend towards reduced incidence and duration of GI infections

CARDIO-VASCULAR

- 43 subjects, 4 weeks
- 1 billion CFU daily
- Improved Reactive Hyperemia Index (RHI)
- Reduction in total and non-HDL cholesterol
- Trend towards reduction in LDL cholesterol

IMMUNITY

- 44 subjects, 4 weeks
- 1 billion CFU daily
- Decrease in basal levels of immune cell populations
- Increase in response ratio to stimulated inflammation (LPS)

BIOCLEAR® MICROBIOME DETOX PROGRAM

CONVENIENTLY PACKAGED 30-DAY DETOX PROGRAM

- Supports healthy detoxification and full-body cleansing*
- Supports microbial balance in the GI tract*
- Selectively enhances beneficial organisms*
- Supports a more comfortable cleansing experience*
- Supports vitality and mental clarity*
- May reduce bloating and gas*

Biocidin Botanicals

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RESTORE

BRING BALANCE AND HEALING

G.I. InnerCalm™

- Supports healthy gut mucosa and gut barrier integrity
- Helps manage occasional heartburn, gas, and bloating
- Supports digestive health and GI motility
- Contributes to a healthy nervous system, mood, and sleep
- Supports a healthy stress response
- Contains glycine to support digestion, protein synthesis, and connective tissue
- Glutamine-free to avoid neurological irritation experienced by some patients
- Includes herbal ingredients that support the benefits of zinc carnosine, quercetin and deglycyrrhizinated licorice (DGL)
    - Botanicals - Chamomile, Lemon Balm, Aloe, and Ginger

Biocidin Botanicals

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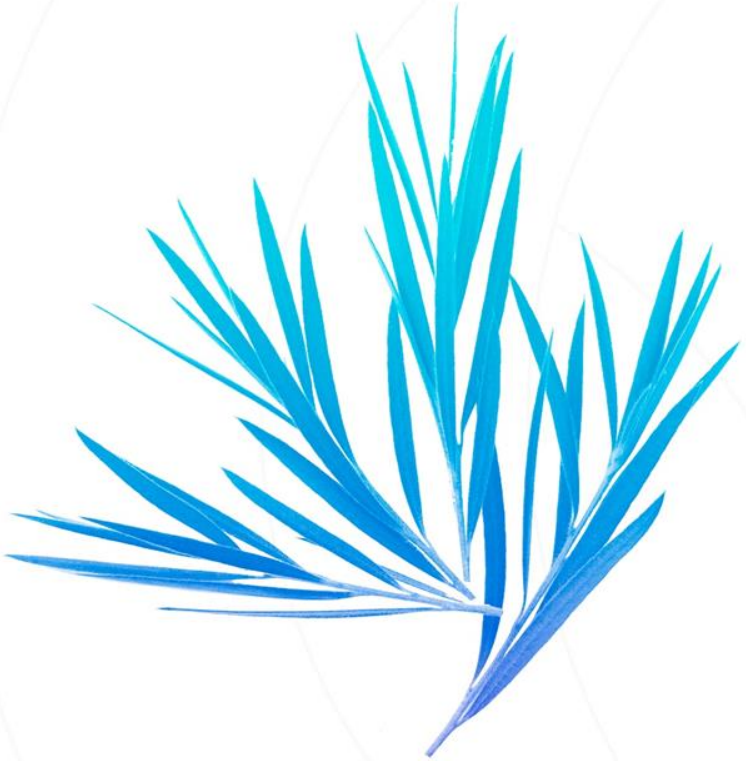


HEALING ORAL DYSBIOSIS

HEALING ORAL DYSBIOSIS

Effective treatment requires **restoration of a healthy microbiome**. That must include:

- Antimicrobial activity against pathogenic species
- Support for probiotic abundance, and
- Management of biofilms.

Botanicals provide activity in all of these areas.

While biofilms are resistant to host immune responses and difficult to eradicate with antibiotics, botanical and essential oils have proven the most effective in treatment.[10] **Garlic, oregano, bilberry, bladderwrack, goldenseal, thyme, lavender, tea tree, grapeseed, bilberry, black walnut, echinacea, gentian, shiitake mushroom, olive leaf,** and **raspberry** are all helpful in controlling biofilms. In vitro pilot research shows that not only is this combination of botanicals effective against organisms in their free-floating form, but also against biofilm communities.

WHAT WORKS?

Disrupting oral biofilms is the first step in healing oral dysbiosis. Other considerations include **seeding with oral probiotics** to shift the host terrain, ruling out **mouth breathing** as a contributing factor, and **dialing in diet**.

Achieving this **delicate balance in the oral microbiome** is essential to achieving optimal systemic health. You can make a difference for your patients by including:

- an oral examination
- oral microbiome testing
- providing the simple nutritional recommendations
- offering “dentalceutical” solutions.

EAT RIGHT FOR YOUR MOUTH

In addition to working at the surface, what you put in your mouth will also help maintain healthy microbial balance in your mouth. Consider these nutritional tips:

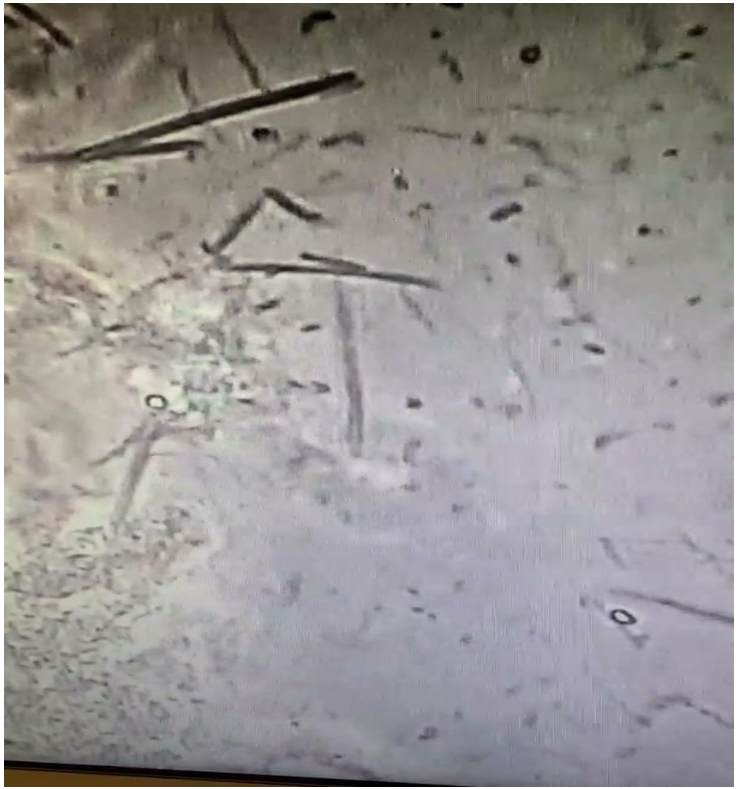
- A healthy diet high in proper minerals (think calcium, magnesium, zinc) can inhibit tooth plaque build-up and help keep your mouth feeling fresh and clean.
    - Mineral rich foods: Nuts. Seeds. Cruciferous vegetables. Eggs. Avocados. Berries. Tropical fruits. Leafy greens.
- The presence of fat-soluble vitamins A, D, E, and K can help maintain tooth structure and prevent decay.
    - Food sources of vitamin A: Eggs. Oily fish. Carrots. Sweet potatoes. Red peppers. Mangos. Apricots.
    - Sources of vitamin D: Oily fish. Egg yolks. Dairy products. Adequate sun exposure.
    - Food sources of vitamin E: Nuts. Seeds. Green leafy vegetables. Eggs. Avocados.
    - Food sources of vitamin K: Green leafy vegetables. Cruciferous vegetables. Prunes. Kiwi. Avocado.
- The antioxidants in fresh produce can help keep gums healthy and protect them from mouth bacterial infection.

BOTANICALS AND THE ORAL MICROBIOME

Dental Pilot Study by
John Rothchild, DDS

- 9 Participants
- Used Phase-Contrast Microscopy to identify elevated pathogenic microorganisms (gram-negative rods and spirochetes) in gingival crevicular fluid from periodontal tissues
- 7 out of 9 participants had a significant reduction or elimination of pathogens when using Biocidin® LSF for one month

BARBARA TRITZ, RDH, BS, MSB | DENTALCIDIN® LS



SERIOUS SCIENCE BEHIND EVERY SMILE™

COMMITMENT TO RESEARCH

Collaboration between Bio-Botanical Research, Inc. and Binghamton University

Problem to be studied: Development of dental plaque

In this work we propose to study whether the liposomal Biocidin® (Dentalcidin® LS) treatment can prevent and/or kill microbial single and multiple species biofilms of *Porphyromonas gingivalis, Streptococcus mutans,* and *Candida albicans.*

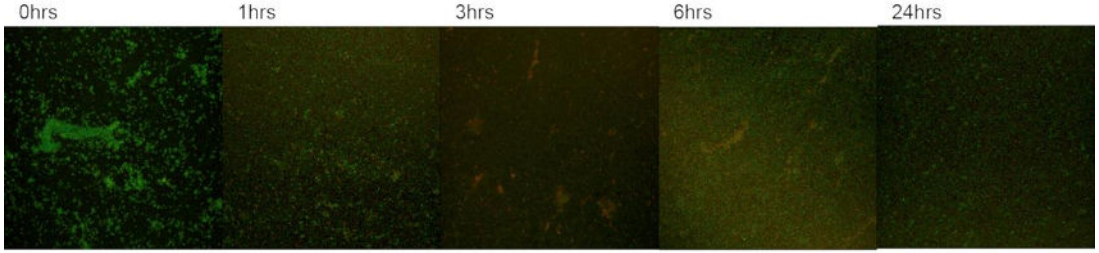


Figure 4. *C. albicans* biofilms exposed to 25% Biocidin® for a period of 24 hours

Marques, C. (2013). Preliminary Report on Activity of Biocidin against Multiple Species of Biofilms (Rep.). Binghamton University Biological Sciences Dept.

PROBIOTICS TO SUPPORT THE ORAL MICROBIOME

- Prebiotics feed the good bacteria – fiber from a variety of food sources. Eat the rainbow!
- A strong presence of healthy bacteria keeps the opportunistic bacteria in check.
- Oral probiotic lozenges, chewable tablets, mouth rinses, and drinks allow for the bacteria to stay within the mouth longer than if immediately swallowed.
- Some good bacteria to consider:
    - *Lactobacillus reuteri*
    - *Lactobacillus salivarius*
    - *Streptococcus salivarius K12*
    - *Streptococcus salivarius M18*
    - *Lactobacillus paracasei*
    - *Lactobacillus sakei*

DENTALFLORA™

- Promotes healthy teeth and gums*
- Supports periodontal health*
- Xylitol may help reduce the risk of tooth decay*
- Helps populate the oral cavity with beneficial bacteria*
- Proprietary blend of 4 targeted, research-backed probiotics
- Clinically proven BLIS M18® included at researched levels
- Dentist-formulated
- Exceptionally shelf-stable with guaranteed 5 billion CFU at manufacture and 3 billion CFU at 18-month expiration
- No refrigeration required

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DENTALCIDIN® ORAL CARE SYSTEM

TWO-STEP DENTACEUTICAL™ SOLUTION

- Supports oral microbiome balance for whole-body health*
- Utilizes liposomal technology for deeper penetration in the periodontal area*

DENTALFLORA®

DAILY ORAL PROBIOTICS

- Helps populate the oral cavity with beneficial bacteria*
- Promotes fresh breath*

Biocidin Botanicals

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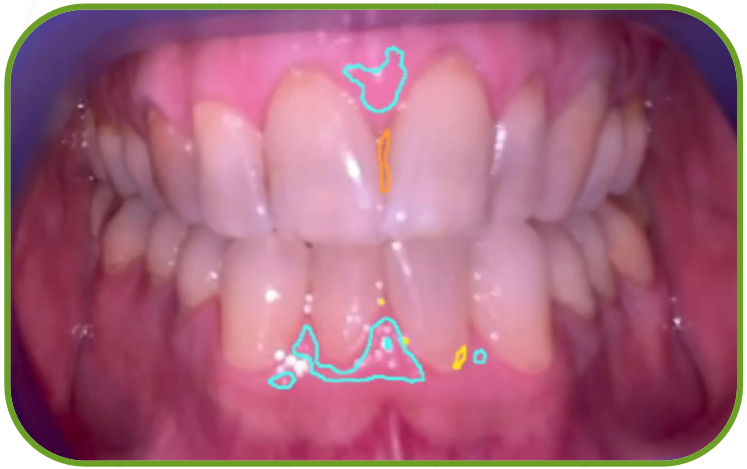
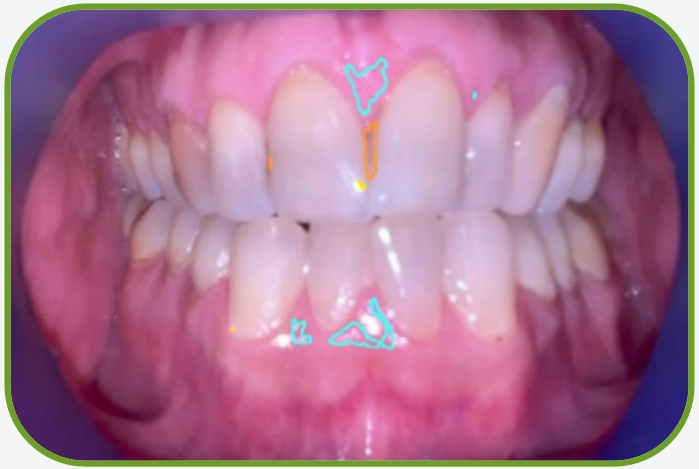
PARTICIPANT #1

WEEK 1

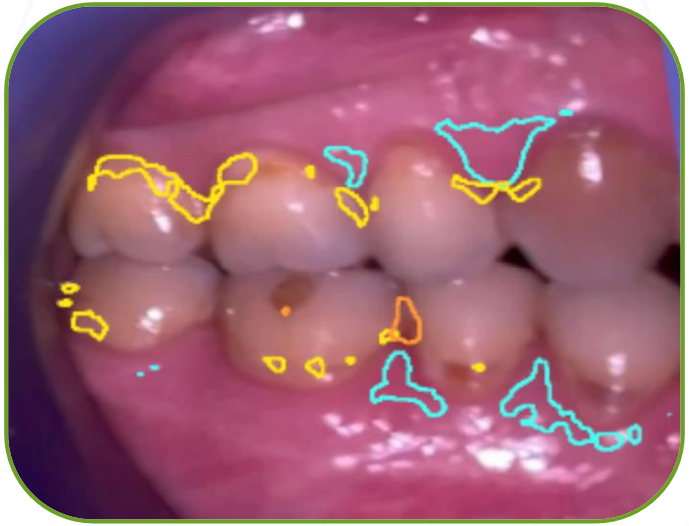


WEEK 5

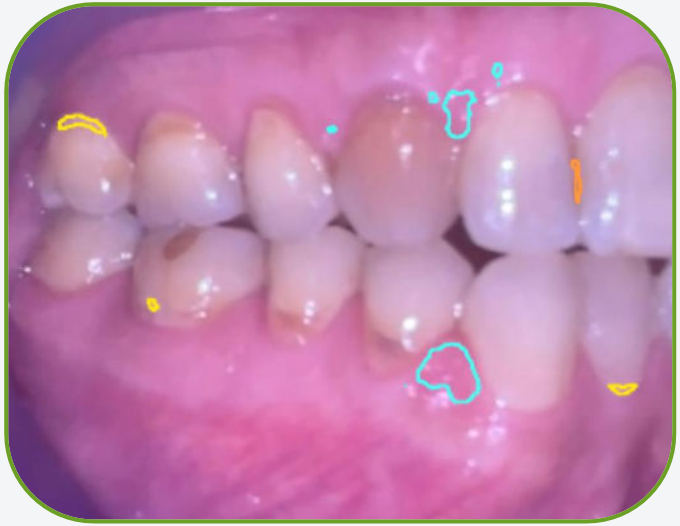


PARTICIPANT #1

WEEK 1

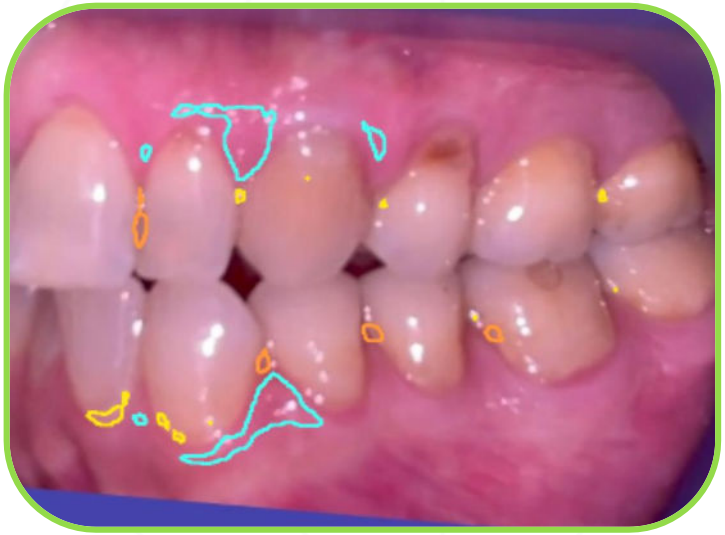


WEEK 5

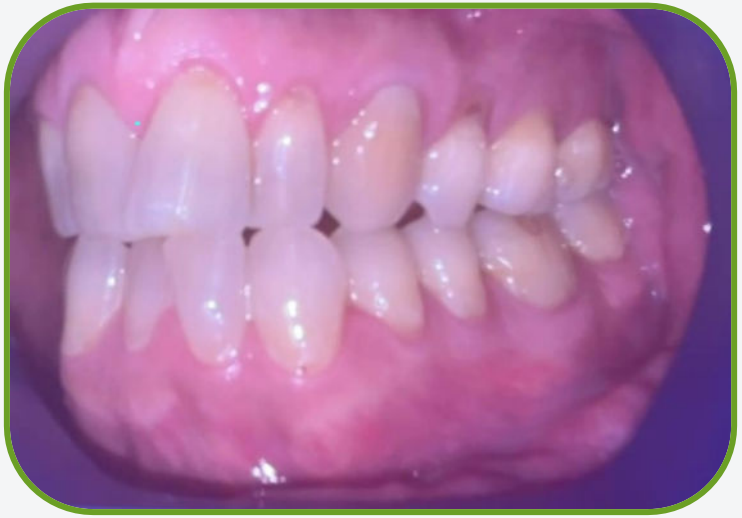


PARTICIPANT #1

WEEK 1

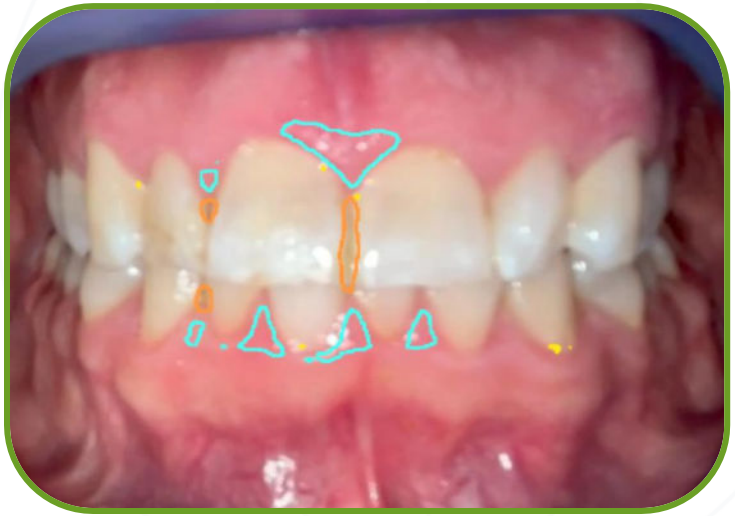


WEEK 5

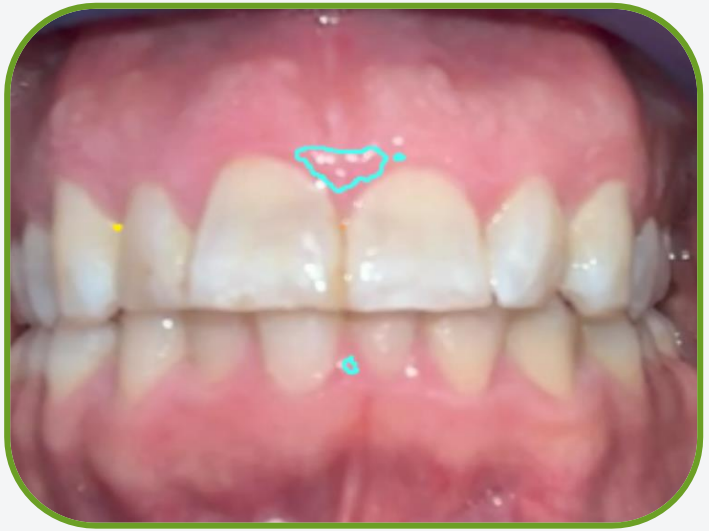


PARTICIPANT #2

WEEK 1

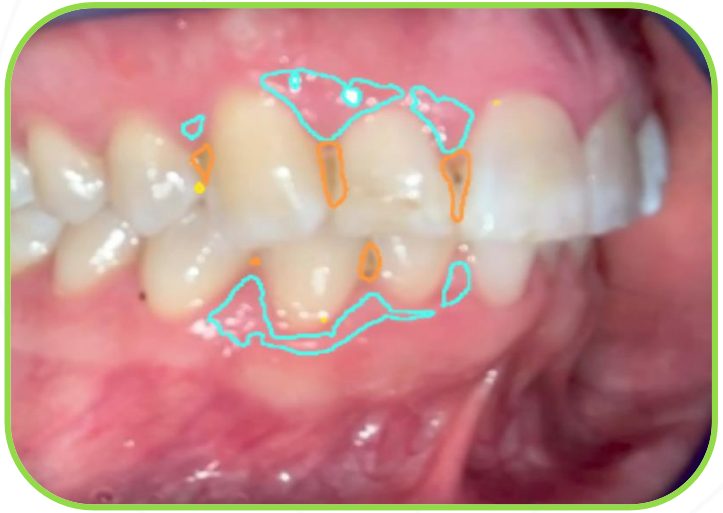


WEEK 6

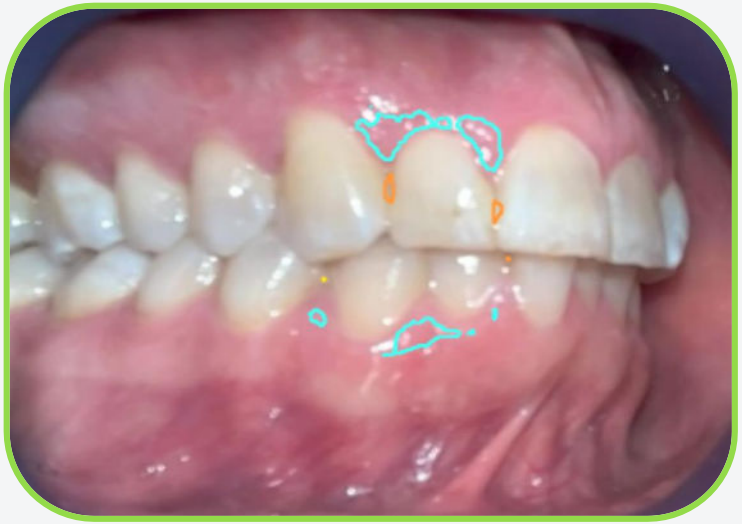


PARTICIPANT #2

WEEK 1

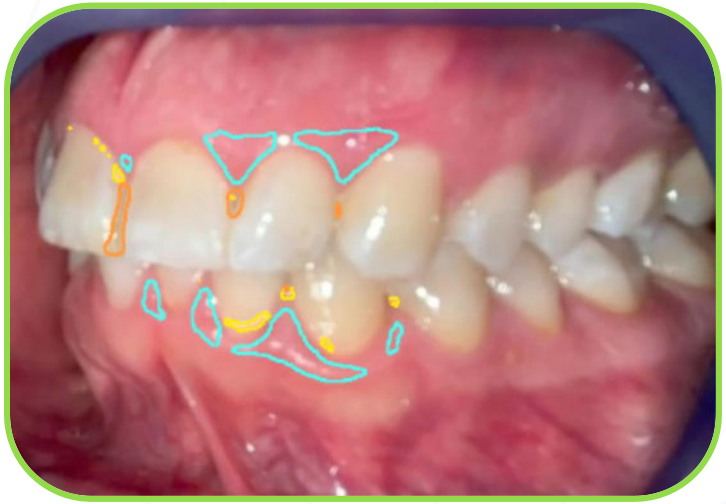


WEEK 6

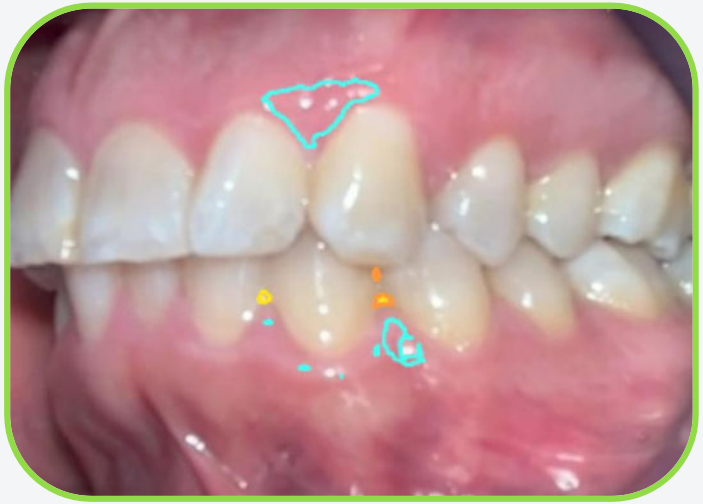


PARTICIPANT #2

WEEK 1



WEEK 6



THANK YOU FOR ATTENDING

Please activate one-time offer for 15% off all products with promo code during the show

24NANP15

Offer expires May 09, 2024, exclusions apply