Oral and Systemic Health: Exploring the Connection

OLLI Health Education Series
Friday, October 29, 2021

Timothy E. Gillespie, DMD, MBA

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I Hope I Die Before I Get Old!

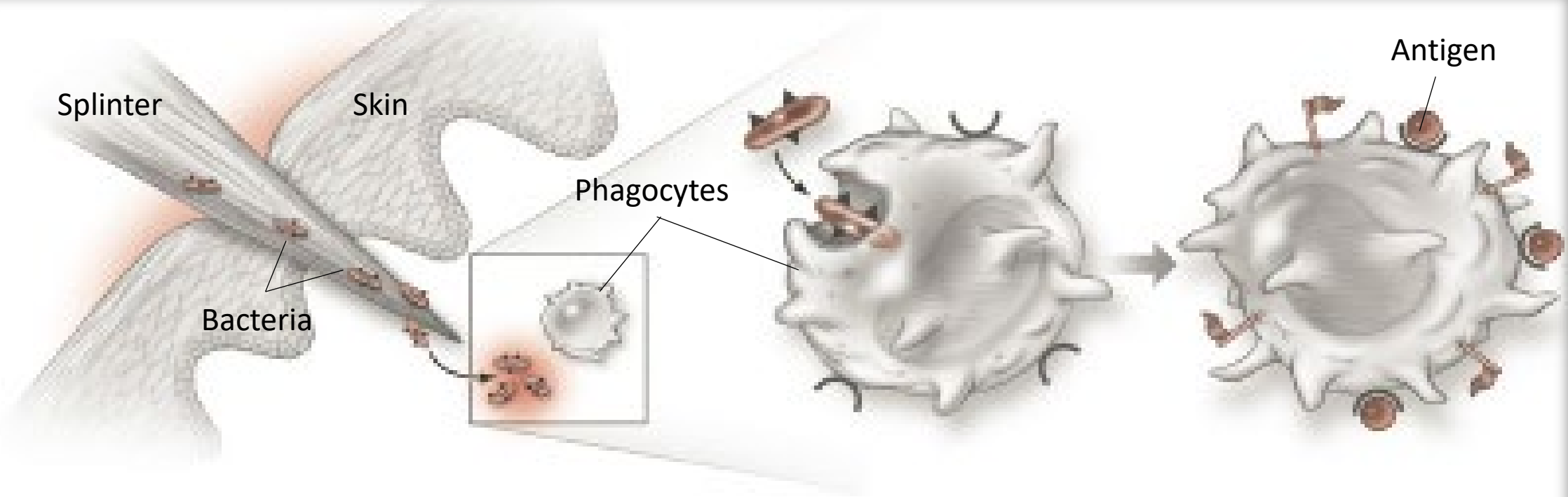
Inflammation: What Is It?

- **The body comes equipped with a built-in defense system—the immune system—a complex army of infection-fighting cells and proteins that warn other cells of invaders, fight them off when they arrive, and heal any damage the resulting conflict produces. Pain, redness, swelling and heat are all associated with this process. Inflammation is an important part of this defensive system and one that is essential for our survival.**

- **The immune response to a breach of the body's defenses occurs in three main stages:**
  1. **Blockage. The Integumentary system—skin—is slightly acidic, mostly dry and covered with "good" bacteria creates an unfriendly environment for microbes. The eyes and oral cavity are exceptions and have their own protective mechanisms. Other bodily systems defend as well.**
  2. **Innate Immunity. We are all born with a rapid-response system that sends Pac Man-like cells after any perceived pathogens, engulfs them and chews them up. It then displays pieces of protein from the invader (antigens) to call in a third line of defense.**
  3. **Adaptive Immunity. This third line of defense learns from experience. It is a more gradual process by which white blood cells (lymphocytes) are primed to distinguish foes from the body's own cells. (Autoimmune diseases result when this process goes awry.)**

Source: Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.

Innate Immune System: Second Line of Defense



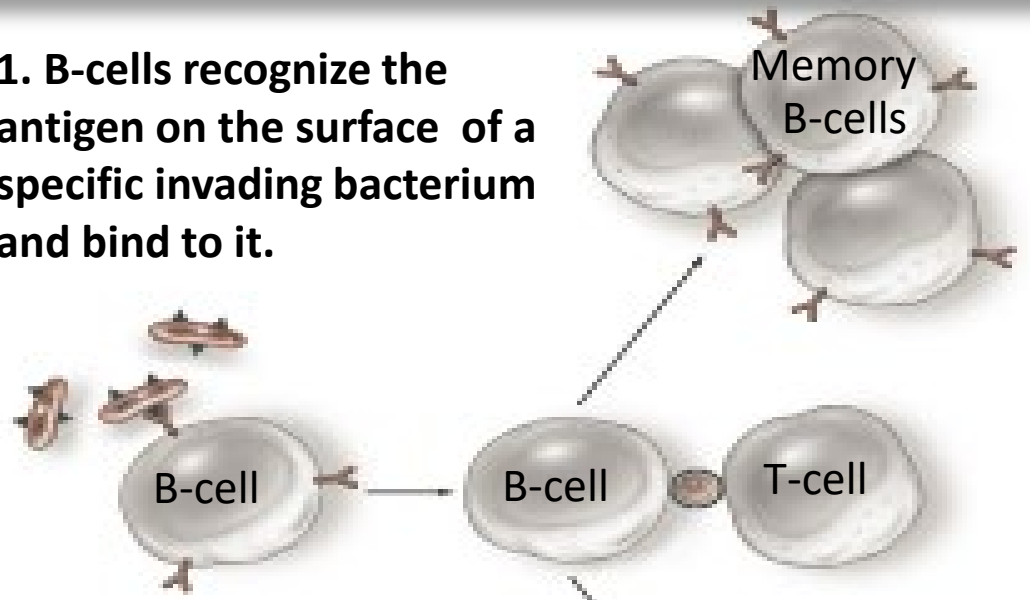
1. Bacteria enter the body on a splinter.

2. Phagocytes engulf the bacteria. Pattern recognition receptors analyze the intruders and raise danger flags on the cell surface.

3. Also on the cell surface, pieces of the bacteria (antigens) are displayed so they can be recognized by cells of the adaptive immune system.

Adaptive Immune System: B-Cell Response

1. B-cells recognize the antigen on the surface of a specific invading bacterium and bind to it.

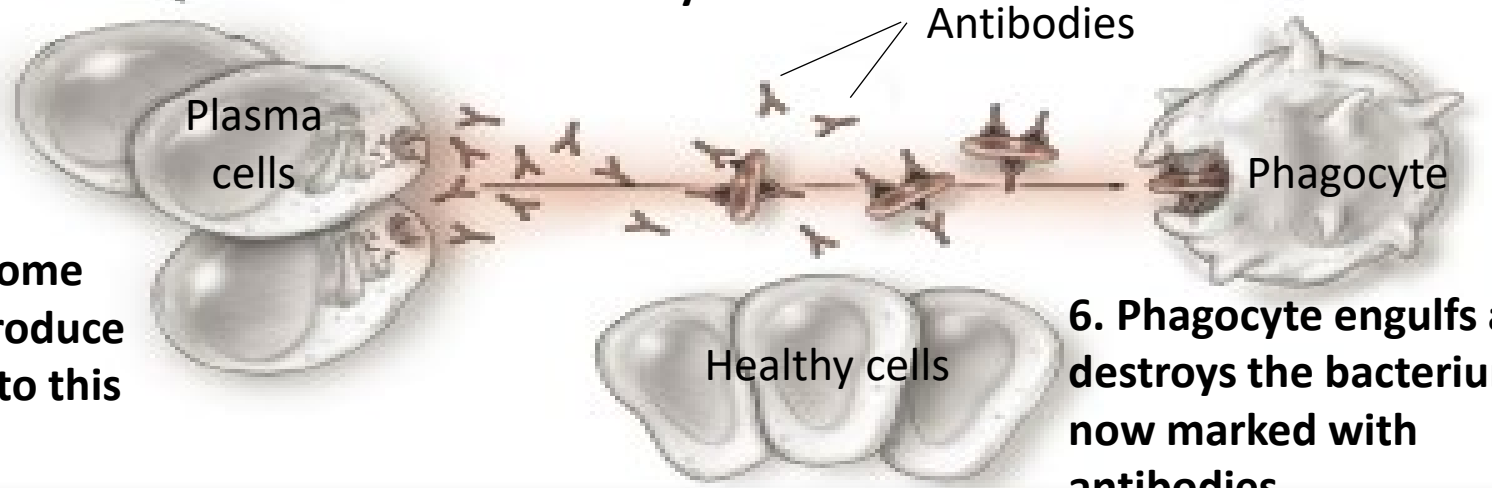


2. B-cell binds with a T-cell and then begins to copy itself.

3. Some copies become plasma cells that produce antibodies specific to this bacterium.

4. Some copies become "memory" B-cells that recognize and destroy the same bacterium the next time it enters the body.

5. Antibodies block receptor sites on the invading bacteria so they can't attach to healthy cells.

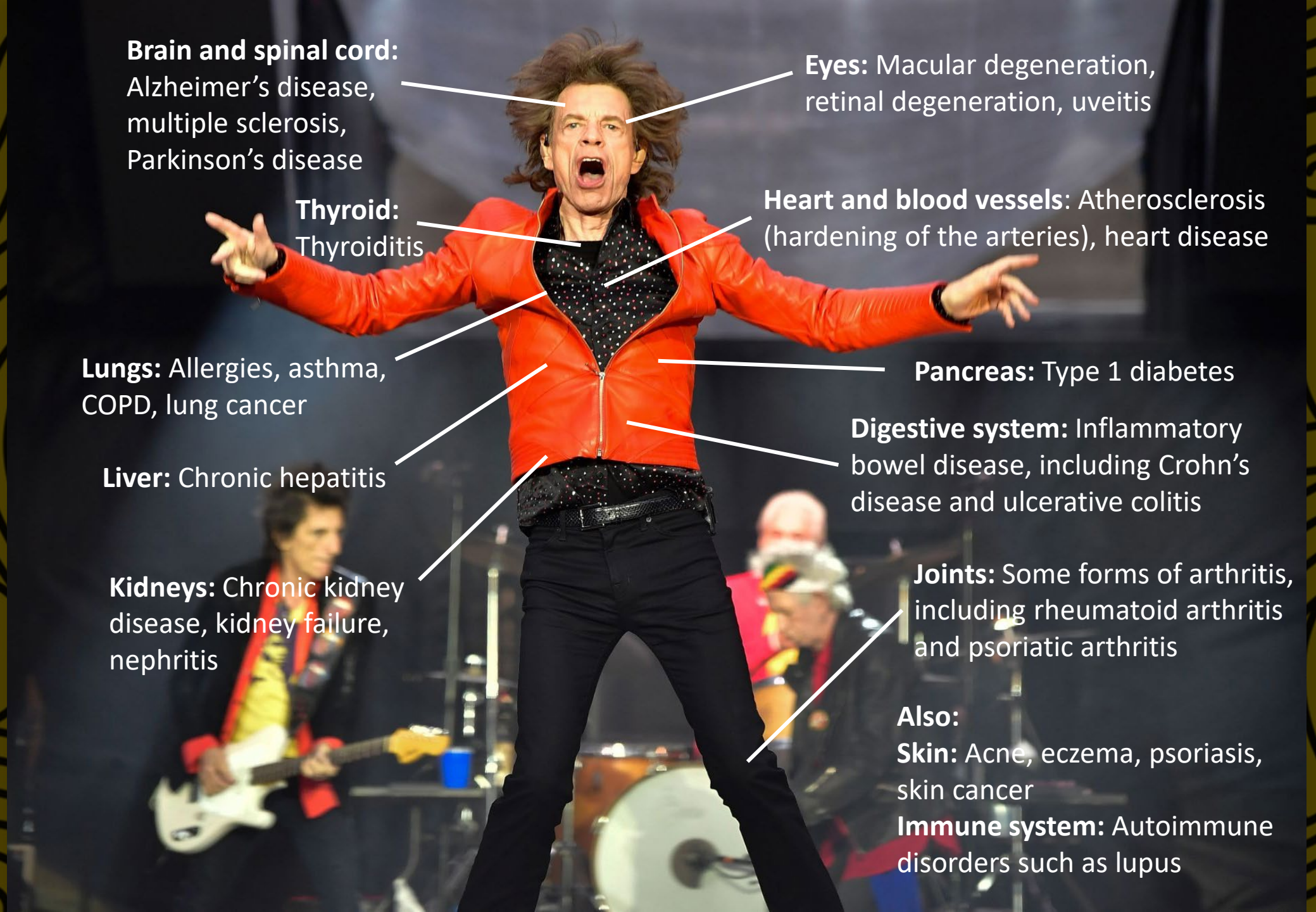


6. Phagocyte engulfs and destroys the bacterium now marked with antibodies.

- **If the body is continuously challenged, the inflammatory response becomes more of a regular—chronic—activity. A growing body of evidence suggests that low-grade, chronic inflammation—the kind that can simmer for decades without your being aware of it—contributes to some of the nation's leading killers, including cardiovascular disease, cancer, and type 2 diabetes, which are together responsible for about two-thirds of all deaths in the United States.**

- **When you have chronic inflammation, your body is in a constant state of high alert. The release of inflammatory chemicals can affect many different systems in your body and be a cause or consequence of multiple diseases.**

Source: Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.


Brain and spinal cord: Alzheimer's disease, multiple sclerosis, Parkinson's disease
Eyes: Macular degeneration, retinal degeneration, uveitis
Thyroid: Thyroiditis
Heart and blood vessels: Atherosclerosis (hardening of the arteries), heart disease
Lungs: Allergies, asthma, COPD, lung cancer
Pancreas: Type 1 diabetes
Liver: Chronic hepatitis
Digestive system: Inflammatory bowel disease, including Crohn's disease and ulcerative colitis
Kidneys: Chronic kidney disease, kidney failure, nephritis
Joints: Some forms of arthritis, including rheumatoid arthritis and psoriatic arthritis
Also:
Skin: Acne, eczema, psoriasis, skin cancer
Immune system: Autoimmune disorders such as lupus

Chronic Inflammation: What Causes It?

- **As mentioned, the immune system, which is supposed to save your life, can end up harming you under various circumstances. If the immune response (with its accompanying inflammation) comes on too strong; if it fails to turn off after an infection goes away; if it misfires, causing either allergies or autoimmune disorders; or if it is continually triggered by lifestyle factors, the body can essentially turn against itself. For the purposes of this lecture, we will focus on lifestyle factors.**

- **So, what are these lifestyle factors?**
    1. **Aging**
    2. **Obesity**
    3. **Diet**
    4. **Sedentary Lifestyle**
    5. **Smoking**
    6. **Stress**
    7. **Oral Health**

Source: Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.

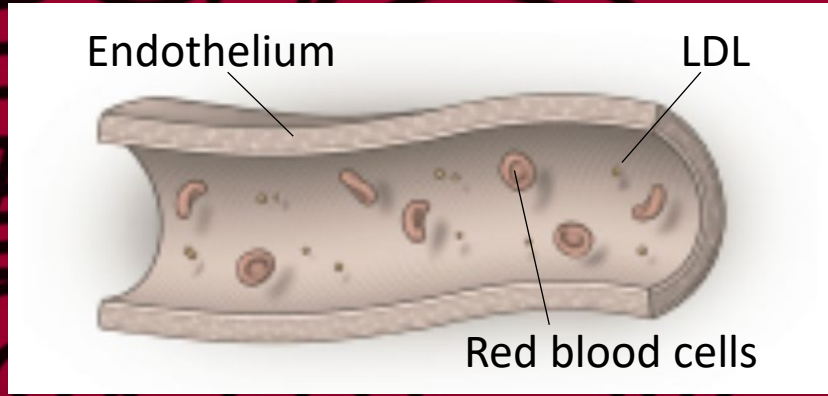
- **Aging—increase in inflammatory cytokines; increased free radicals; declining immune system**
- **Obesity—excess fat-storing (adipose) tissue; larger than normal fat cells which produce inflammatory response**
- **Diet—certain foods (all the good stuff!) directly stimulate the release of inflammatory proteins**
- **Sedentary Lifestyle—hard to say whether inflammation is the direct result of sitting too much, or whether it comes from problems that are often part and parcel of a sedentary lifestyle**
- **Smoking—components of tobacco as well as damaged airway cells send out signals that activate inflammatory response**
- **Stress—the fight-or-flight response works great until the response fires again and again due to stress. The continued release of stress hormones like cortisol eventually makes it less effective in regulating the inflammatory response, so inflammation can spiral out of control**
- **And now, we finally reach our destination for today, the Oral Health connection to Systemic Health!**

Source: Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.

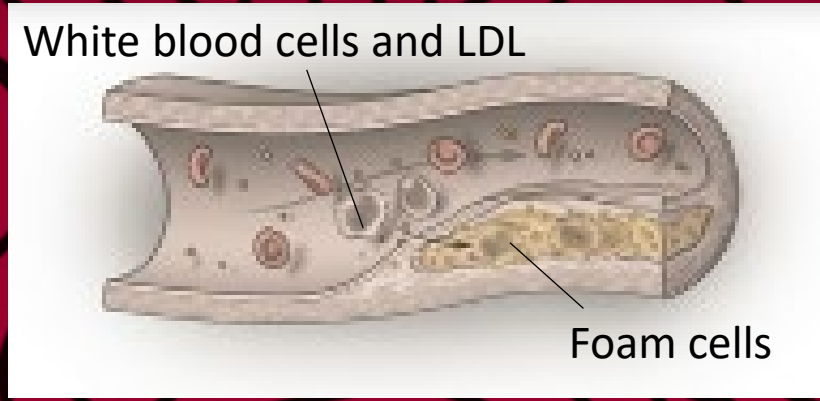
From Healthy Artery To Heart Attack

Heart attacks are not just the result of a buildup of fatty plaque in the arteries. Inflammation, triggered by damage to the inner lining of an artery, sets off the steady growth of atherosclerotic plaque. If a plaque suddenly ruptures, it can lead to a heart attack.

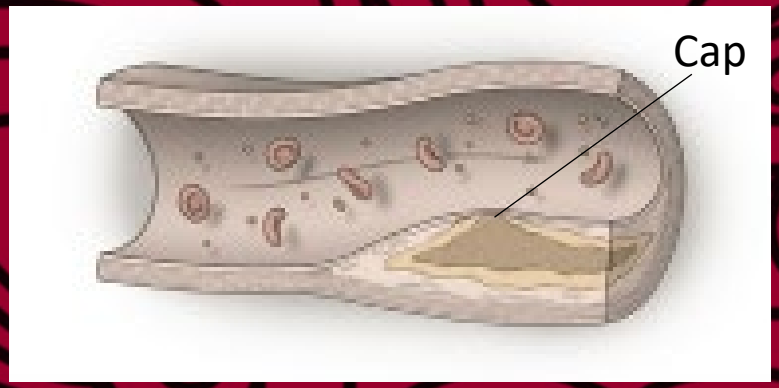
STAGE 1: Excess LDL passes through the artery



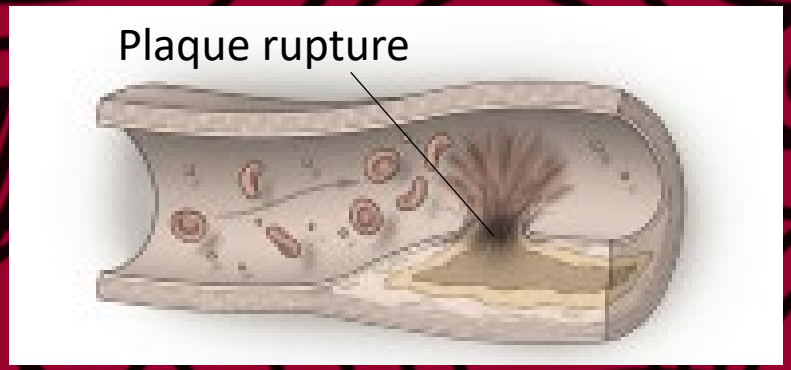
STAGE 2: Plaque builds up and the artery narrows



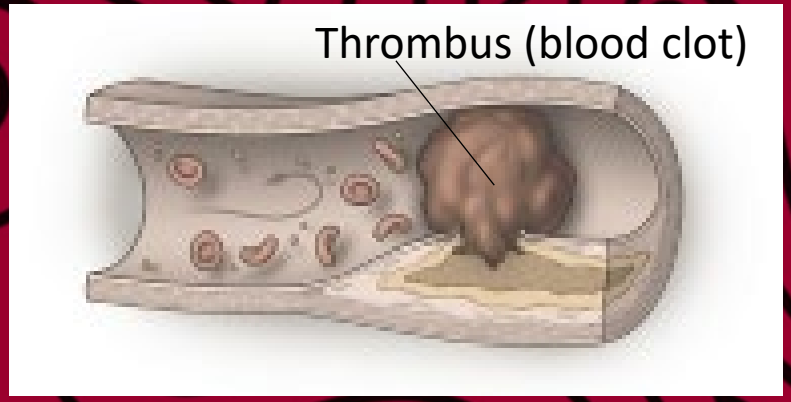
STAGE 3: A fibrous caps tops the plaque



STAGE 4: The plaque ruptures



STAGE 5: A clot blocks the artery



Gum Disease And Cardiovascular Disease

- **Bacterial organisms prevalent in periodontal disease enter the systemic circulation directly, and they produce endotoxins—toxins present within a bacterial cell, which are released when it disintegrates—such as lipopolysaccharides. The endotoxins generate inflammatory cytokines (cell signaling proteins), upregulate endothelial adhesion molecules and induce a pro-thrombotic environment, which, as shown in previous slides, favor the formation of arterial disease and can enhance the risk of an atherothrombotic event.**

- **Inflammation and bacterial burden have been found to be *causal* of vascular destruction. According to the American Heart Association, periodontal disease presents *Level A* evidence that it is independently associated with arterial disease. Half of our adult population has periodontal disease.**

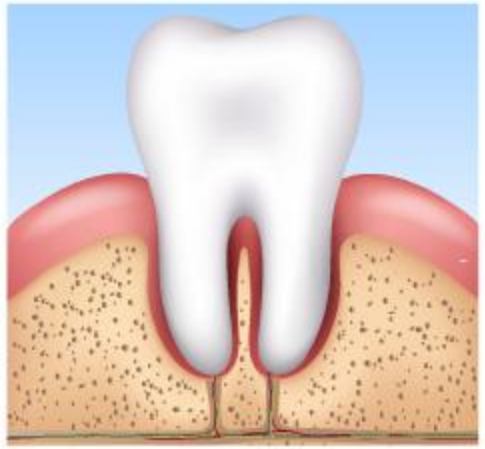
Source: Bale BF, Doneen AL, Vigerust DJ, High-risk periodontal pathogens contribute to the pathogenesis of atherosclerosis. *Postgraduate Medical Journal* 2017;**93:**215-220.

- **Gum disease begins with the sticky mass that builds up around your teeth, known as plaque. This mass is a biofilm formed from the by the action of oral bacteria trying to metabolize sucrose (by the way, dental cavities are caused by the acidic byproducts of this activity). Unless removed, this sticky mass combines with minerals in the saliva and hardens into a harder mass, tartar (calculus), which provides a nice substrate for more plaque accumulation.**

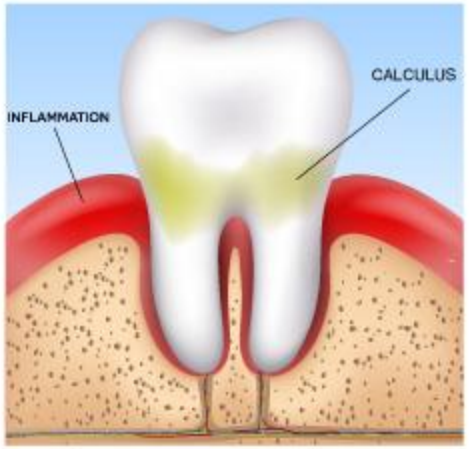
Source: Bale BF, Doneen AL, Vigerust DJ, High-risk periodontal pathogens contribute to the pathogenesis of atherosclerosis. *Postgraduate Medical Journal* 2017;**93:**215-220.

Stages Of Gum Disease

1 HEALTHY GUMS & TOOTH

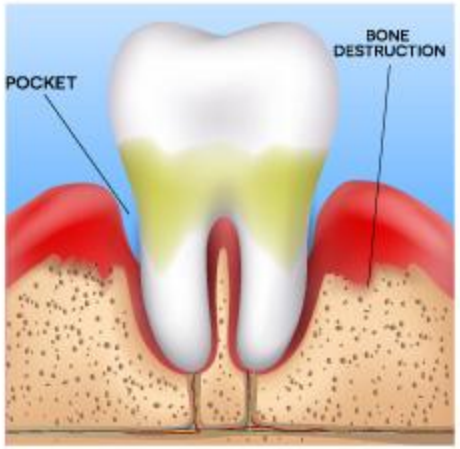


2 GINGIVITIS



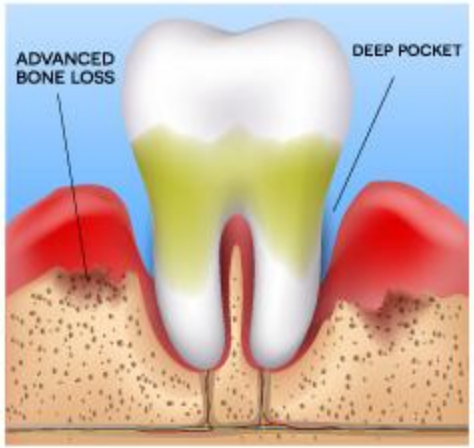
Calculus builds up on teeth and gums are inflamed (red).

3 PERIODONTITIS



Inflammation causes gums to separate from tooth, forming pockets. Early to moderate bone loss.

4 ADVANCED PERIODONTITIS



Severe bone loss, deep pockets. Tooth is in danger of falling out.

The Culprits


Td
Pi
Aa
Ec
Fn
En
Cr
Tf
Cs
Pm
Pg

- **CARDIOVASCULAR DISEASE: Aa, Pg, Tf, Td, Fn and Pi.**

  Persons with untreated periodontal infections have up to a 20% increase in their risk of coronary vascular disease and the risk for stroke and peripheral vascular disease is equal or greater. More specifically, the risk of a first myocardial infarction is associated with periodontal disease even after adjustment for a history of smoking, obesity, diabetes and other socioeconomic factors. The bacteria above are of concern and Fn itself carries a series of virulence factors that can contribute to inflammation of the arterial wall.

- **METABOLIC HEALTH AND DIABETES: Aa, Pg, Tf, Td, Fn.**

  Elevated levels of periodontal bacteria can directly cause hyperglycemia. Long term inflammation associated with increased pathogen burden can affect the health of the pancreas; specifically, there is the risk of the loss of beta cells that produce insulin and respond to elevated blood glucose. Correspondingly, persons with elevated blood glucose are at risk for progressive periodontal infection and inflammation.

Source: OralDNA Labs. (n.d.). *The Consequences of Oral Bacteria and Gum Disease Go Far Beyond the Mouth*.h ttps://www.oraldna.com/ORAL_SYSTEMIC_CONSEQUENCES.pdf

- **HEALTH DURING PREGNANCY: Aa, Pg, Tf, Fn, Ec, Pi.**

  Periodontal inflammation worsens during pregnancy, mostly due to the above bacteria. There is a marked risk of infection of the maternal blood and the placenta, which can lead pre-term labor, lower birth weight and even the chance of fetal loss due specifically to Pg and Fn. Further, the long-term risk for systemic disease in mothers with periodontitis is evident in the progression of atherosclerosis and the increased risk of venous thrombosis due to Fn, Pg, Tf and Aa.

- **DEVELOPMENT OF CANCER & RISK OF PROGRESSION: Aa, Pg, Tf, Td, Fn.**

  Advanced periodontal disease is associated with a 2.5-fold increase in smoking related cancers. In breast cancer, persons with elevated levels of the bacteria Aa and Pg have a greater chance of recurrence or failed response to treatment. A study of persons with high Pg showed a 59% increased risk of pancreatic cancer. There are also reports of oral Aa and Td linked to pancreatic tumors and Pg, Td and Tf are linked to risk of esophageal cancers. Several studies show that Fn can be identified within the primary cancer cells from colonic tumors, and are carried to metastatic sites involving regional lymph nodes.

Source: OralDNA Labs. (n.d.). *The Consequences of Oral Bacteria and Gum Disease Go Far Beyond the Mouth*. https://www.oraldna.com/ORAL_SYSTEMIC_CONSEQUENCES.pdf

- **JOINT AND MUSCULOSKELETAL HEALTH: Pg, Fn, Ec.**

  Rheumatoid arthritis (RA) is a chronic inflammatory condition. In a recent analysis of 21 separate studies, there was a significantly increased risk of periodontitis in people with RA compared to healthy controls. The bacteria are typically found before the onset of symptoms.

- **DEMENTIA AND BRAIN HEALTH: Pg, Cr, Cs.**

  Recent medical studies point to poor oral health and high levels of oral bacteria with an increased risk in developing Alzheimer's and other types of dementia. Specifically, there is now evidence that Pg present in brain tissue and cerebrospinal fluid may be involved in the production of the abnormal proteins that are characteristic of Alzheimer's disease. Additionally, the direct effects of those oral bacteria to cause atherosclerosis in the vessels within the brain impart significant risk for stroke and vascular types of dementia.

Source: OralDNA Labs. (n.d.). *The Consequences of Oral Bacteria and Gum Disease Go Far Beyond the Mouth*. https://www.oraldna.com/ORAL_SYSTEMIC_CONSEQUENCES.pdf

Better Living Through Dentistry

Home Oral Care Recommendations
to Reduce the Risk of Caries and Gum Disease

No two people are the same. Help patients take charge of their oral health at home with these tailored, evidence-based oral care recommendations.

GENERAL RECOMMENDATIONS

Advise all patients to:

- Brush teeth twice a day with fluoride toothpaste
- Clean between teeth daily
- Eat a healthy diet that limits sugary beverages and snacks
- See a dentist regularly for prevention and treatment of oral disease

PERSONALIZED RECOMMENDATIONS

- For patients with **increased risk of gum disease**, consider mouth rinse or toothpaste with proven antimicrobial activity
- For patients with **increased risk of caries**, consider fluoridated mouth rinse
- For patients who **struggle to clean between their teeth**, consider what interdental cleaning tool might be best
- For patients **seeking or needing improved plaque removal**, consider a power toothbrush

LIFESTYLE CONSIDERATIONS

- Discourage practice of do-it-yourself orthodontic treatment
- Recommend that patients drink fluoridated water
- Discuss tobacco cessation (smoking and smokeless tobacco)
- Recommend that patients avoid oral piercings

For more information visit **ADA.org/homecare**.

ADA American Dental Association®
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It's cleaner, brighter Taste means
cleaner, brighter teeth! New Pepsodent,
the only tooth paste containing Irium,
removes the film that makes your teeth look dull—
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Use Pepsodent twice a day—
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MYPERIOPATH®

FINAL REPORT

ORALDNA LABS™
Innovations in Salivary Diagnostics

Sample, Report

Date Of Birth: 09/20/1980 (40 yrs)
Gender: Female
Patient Id: 951750
Patient Location: Test Site A

Ordering Provider

Ronald McGlennen MD
7400 Flying Cloud Drive
Eden Prairie, MN 55344
855-672-5362

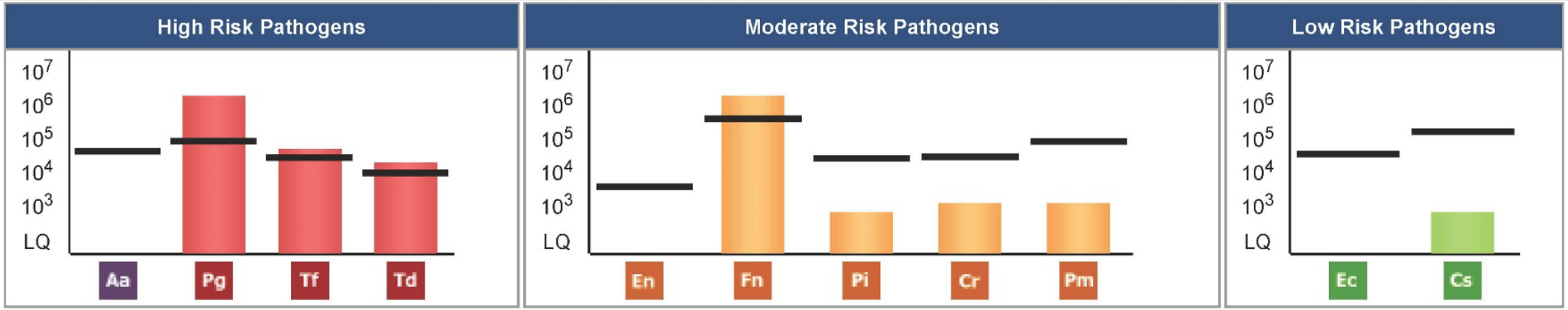
Sample Information

Specimen#: 5033050001
Accession#: 201807-12468
Specimen: Oral Rinse(P)

Collected: 07/08/2018
Received: 07/09/2018 09:57
Reported: 07/10/2018 11:12

MYPERIOPATH MOLECULAR ANALYSIS OF PERIODONTAL AND SYSTEMIC PATHOGENS

Results



Legend: The result graphic displays the bacterial level in genome copies/milliliter in log10 values. The limit of quantification (LQ) is the lowest bacterial level that can be repeatedly measured. The Reference Lines, displayed as black lines through each bar graph, indicate the mean bacterial level observed in patients with ADA III (moderate to severe, and/or with an average pocket depth (PD) of 4-5 mm) chronic periodontitis.

Interpretation of Results

- This result shows 3 high risk (Pg, Tf, Td) and 1 moderate risk (Fn) pathogens above the therapeutic threshold.
- The bacterial species Tf and/or Td are strongly associated with chronic periodontitis, are transmissible and tissue invasive even at low amounts of these organisms. Moreover, Pg is an anaerobic pathogen that often colonizes dental plaque, often along with other red complex bacteria. Note: Fn is a highly prevalent, Gram-negative bacteria that is strongly associated with periodontitis as well as various systemic infections, including those involving the heart.
- The detected pathogens are also risk factors for various systemic diseases, including atherosclerosis, type 2 diabetes, arthritis, dementia and several types of cancer. The American Heart Association supports a causal relationship between periodontal disease and atherosclerosis. Specifically, Td has been shown to accelerate vascular disease of the aorta.

Treatment Considerations: to be determined by the healthcare professional

- **Mechanical/Debridement:** Scaling and root planing (SRP) is a mainstay of therapy to disrupt biofilm, remove plaque and debride compromised tissue. This patient harbors a series of pathogens (Pg, Tf, Pi, Pm) that may be refractory to this treatment.
- **Systemic Antibiotics:** This patient has indicated no allergies.

1 Metronidazole 500 mg bid for 8-10 days
As always, use antibiotics with care

OR

*If patient has intolerance to the first choice consider:

2 Clindamycin 150 or 300 mg tid for 8-10 days

3 Ciprofloxacin 500 mg bid for 8-10 days

- **Local Antibiotics and Chemical Hygiene:** As an adjunct to SRP, sub-antimicrobial doses of doxycycline hyclate lower collagenase activity and reduce periodontal pocket depth. Alternatively, locally delivered antimicrobial agents (LDA) including minocycline microspheres, doxycycline hyclate in an absorbable polymer, or chlorhexidine in a gelatin matrix have been shown to decrease pocket depth modestly.
- **Pocket or Field Decontamination:** Laser decontamination as an adjunct therapy to SRP may be beneficial in reducing probing depth and bacterial loads. The consideration of using lasers as an adjunct to SRP is dependent on type of laser used and the particular protocol.
- **Chemical and Gaseous antiseptics:** Chlorhexidine or Povidine iodine rinses can reduce periodontal pocket depth. Prescription tray application of peroxide gel, as an adjunct to frequent periodontal maintenance appointments for refractory patients, demonstrated significant reductions in bleeding on probing. Ozone is a volatile antiseptic that can disrupt microbial membranes.
- **Probiotics and Prebiotics:** Probiotics are live, beneficial bacteria, typically administered as a food or dietary supplement. Prebiotics are non-digestible ingredients that promote growth of commensal bacteria. Research shows that prebiotics and probiotics control the growth of pathogens and reverse tissue destruction caused by periodontitis.
- **Periodontal Surgery:** When clinical signs & symptoms of a periodontal infection persist, or periodontal anatomy is not conducive to health, periodontal surgical evaluation and/or intervention may be indicated.

Follow up Recommendations

- [x] Good periodontal health depends on compliance of a home care regimen as detailed by your healthcare provider. Daily brushing, flossing, as well as attention to nutrition, proper rest and cessation of smoking are essential.
- [x] Follow-up testing between 6-12 weeks with MyPerioPath is recommended. Persistence of bleeding on probing is often indicative of unresolved infection. Retesting will identify residual or refractory bacteria. Currently there is not a cure for periodontal disease, only periods of remission.
- [x] Assessment of a patient's level of inflammation with Celsus One is valuable in deciding the frequency of patient recall and treatment.

7400 Flying Cloud Drive, Eden Prairie, MN 55344 | Phone: 855-672-5362 | Fax: 952-942-0703 | www.oraldna.com
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Bonus Material: Inflammation And COVID

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- **COVID-19 sickness and fatality appears to be related to an inflammatory process, acute respiratory distress syndrome (ARDS). People develop ARDS after a severe trauma that either directly or indirectly affects their lungs —for example, when they nearly drown, when they breathe in smoke from a fire, or when they develop a severe case of pneumonia. In ARDS, the body's inflammatory response sends immune cells rushing to the lungs. These immune cells cause tiny blood vessels in the area to leak fluid, as is normal during this reaction. But when fluid leaks into the lungs, it builds up in the alveoli, the air sacs through which oxygen normally passes into the bloodstream. The fluid buildup prevents oxygen from getting into the blood, making it hard to breathe. Without good supportive care, ARDS can be fatal.**

- **COVID may also be related to another type of bodily overreaction to inflammation. COVID-19 infection is accompanied by an aggressive inflammatory response with the release of a large amount of pro-inflammatory cytokines in an event known as "cytokine storm." Cytokines are an essential part of the inflammatory process. They are produced by several immune cells including the innate system's macrophages, dendritic cells, natural killer cells and the adaptive T and B lymphocytes. In a cytokine storm, the body's immune response to the virus is hyperactive resulting in an excessive inflammatory reaction. In addition to lung injury, multi-organ failure occurs, leading to death.**

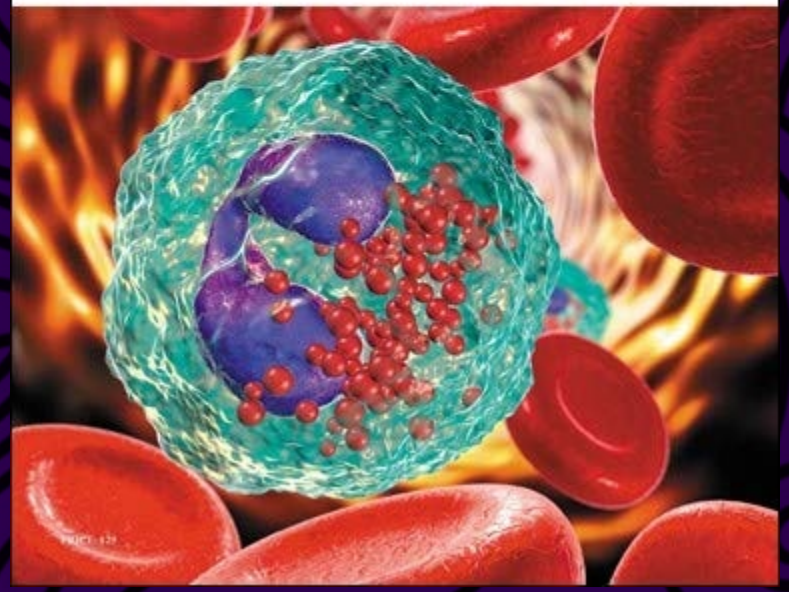
Source: Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.

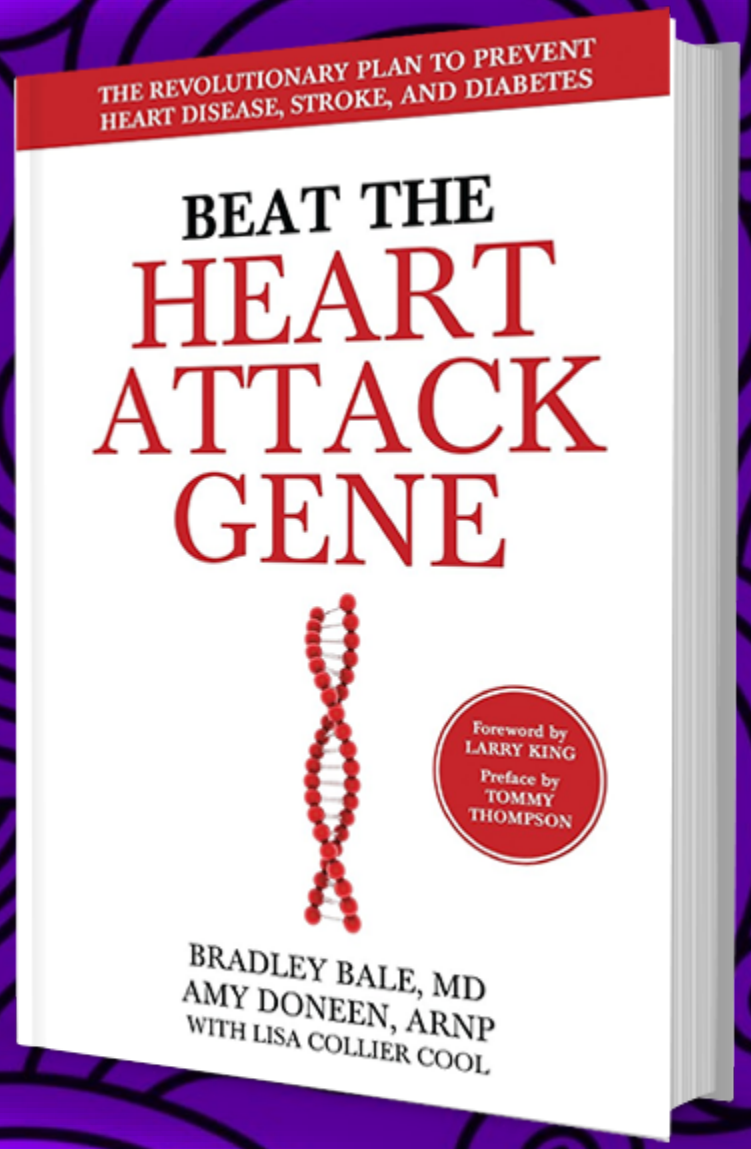
Special Health Report

HARVARD
MEDICAL SCHOOL

Fighting Inflammation

How to stop the damage before it compromises your health




THE REVOLUTIONARY PLAN TO PREVENT HEART DISEASE, STROKE, AND DIABETES
BEAT THE
HEART ATTACK GENE
Foreword by LARRY KING
Preface by TOMMY THOMPSON
BRADLEY BALE, MD
AMY DONEEN, ARNP
WITH LISA COLLIER COOL

References:

Shmerling, R. H., MD, & Underwood, A. (2020). *Fighting Inflammation*. Harvard Health Publishing.

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Cobe, HM
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OralDNA Labs. (n.d.). *The Consequences of Oral Bacteria and Gum Disease Go Far Beyond the Mouth*. https://www.oraldna.com/customerService/ORAL_SYSTEMIC_CONSEQUENCES.pdf?t=1634669330189. Retrieved October 22, 2021, from www.oraldna.com.

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Thank You!

Questions?

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