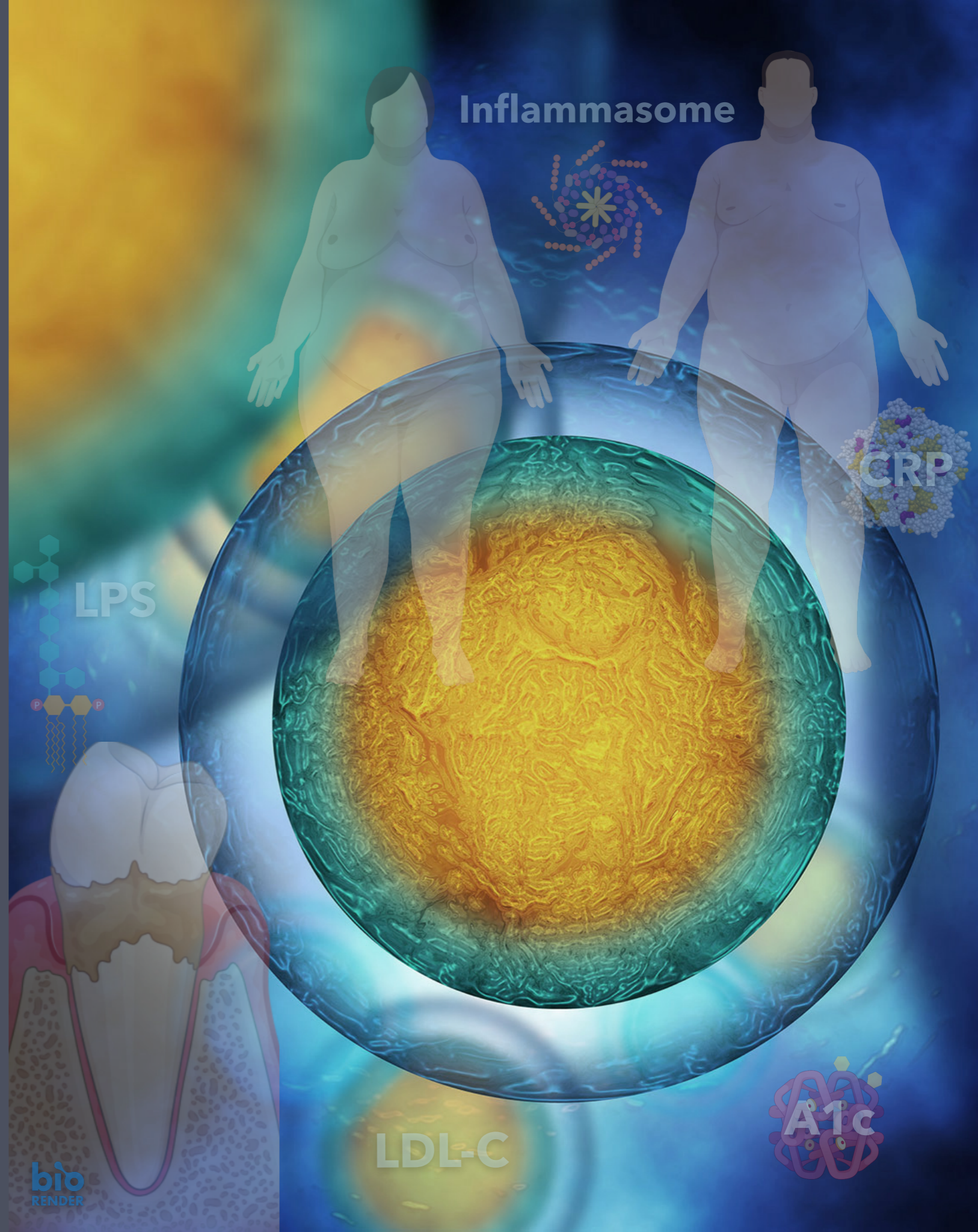




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# THE PERIODONTAL-SYSTEMIC CONNECTIONS

An Inflammatory Tale

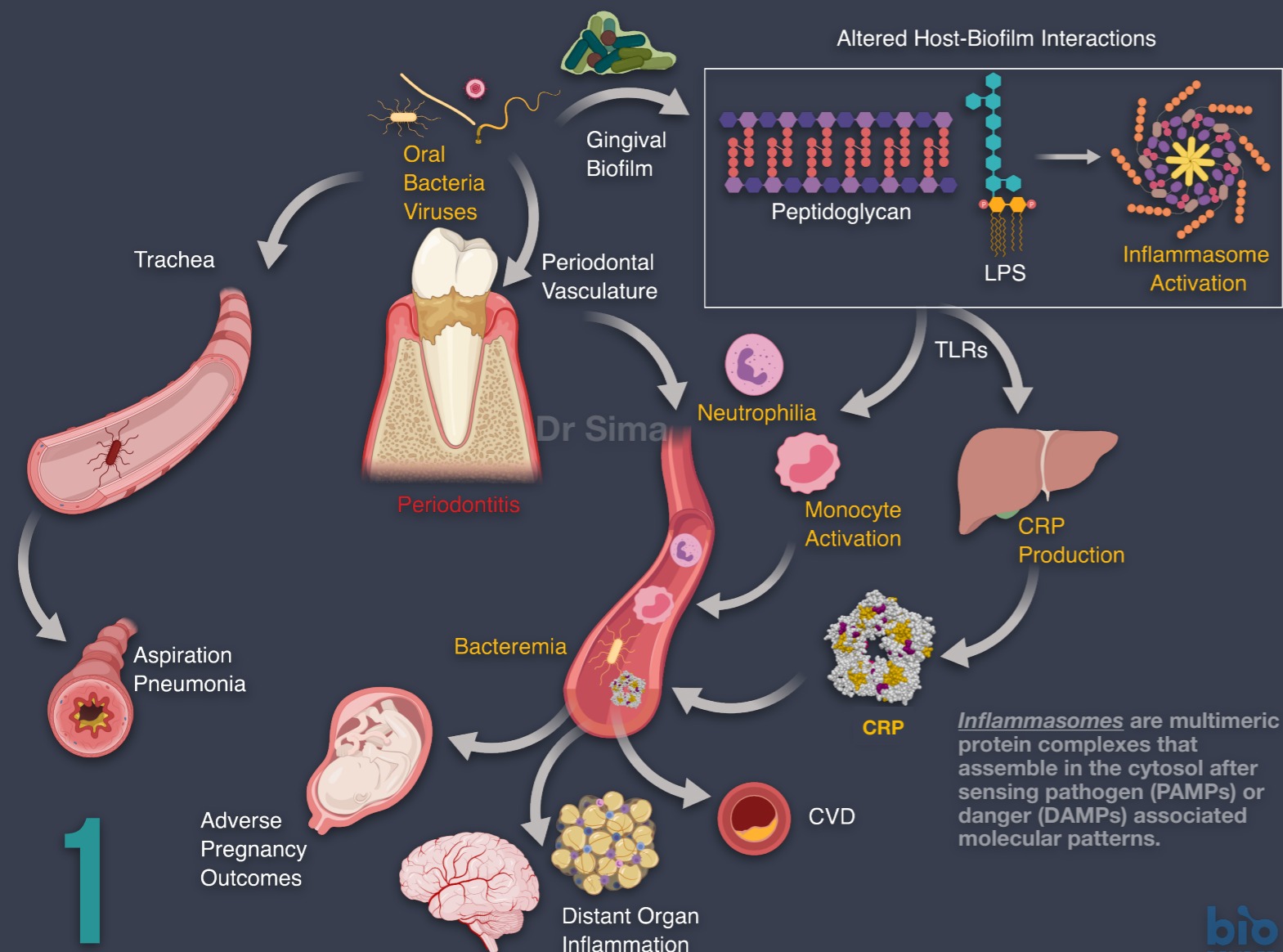


# PERIODONTITIS

USA: 65M ADULTS - 47% OF 30+ YEARS OLD  
- 70% OF 65+ YEARS OLD

Perio-Systemic

# MECHANISMS



Periodontitis (PD) is a highly prevalent chronic non-communicable systemic inflammatory disease, ranking **the 6th most common human disease**. Severe PD affects 11.2% of the world's population. Several studies have shown links between PD and other systemic diseases. While causal relationships have not been conclusively established, data suggest that **PD may contribute to the onset and progression of other diseases**.<sup>1</sup>

Multiple lines of evidence link **untreated PD** to systemic adverse outcomes through **aspiration or vascular dissemination of microbes** or their derivatives (LPS - lipopolysaccharide; TLRs - toll-like receptors etc.) and through sustained **low-grade inflammation** measured systemically as priming of the immune system (markers of innate immune activation e.g. CRP - C reactive protein).<sup>2</sup>

Evidence suggests a higher risk of **bacteremia** associated with gingival inflammation following daily activities (toothbrushing, flossing, chewing or biting an apple) and subgingival instrumentation, and a higher frequency and magnitude in PD compared to gingivitis.<sup>3</sup>

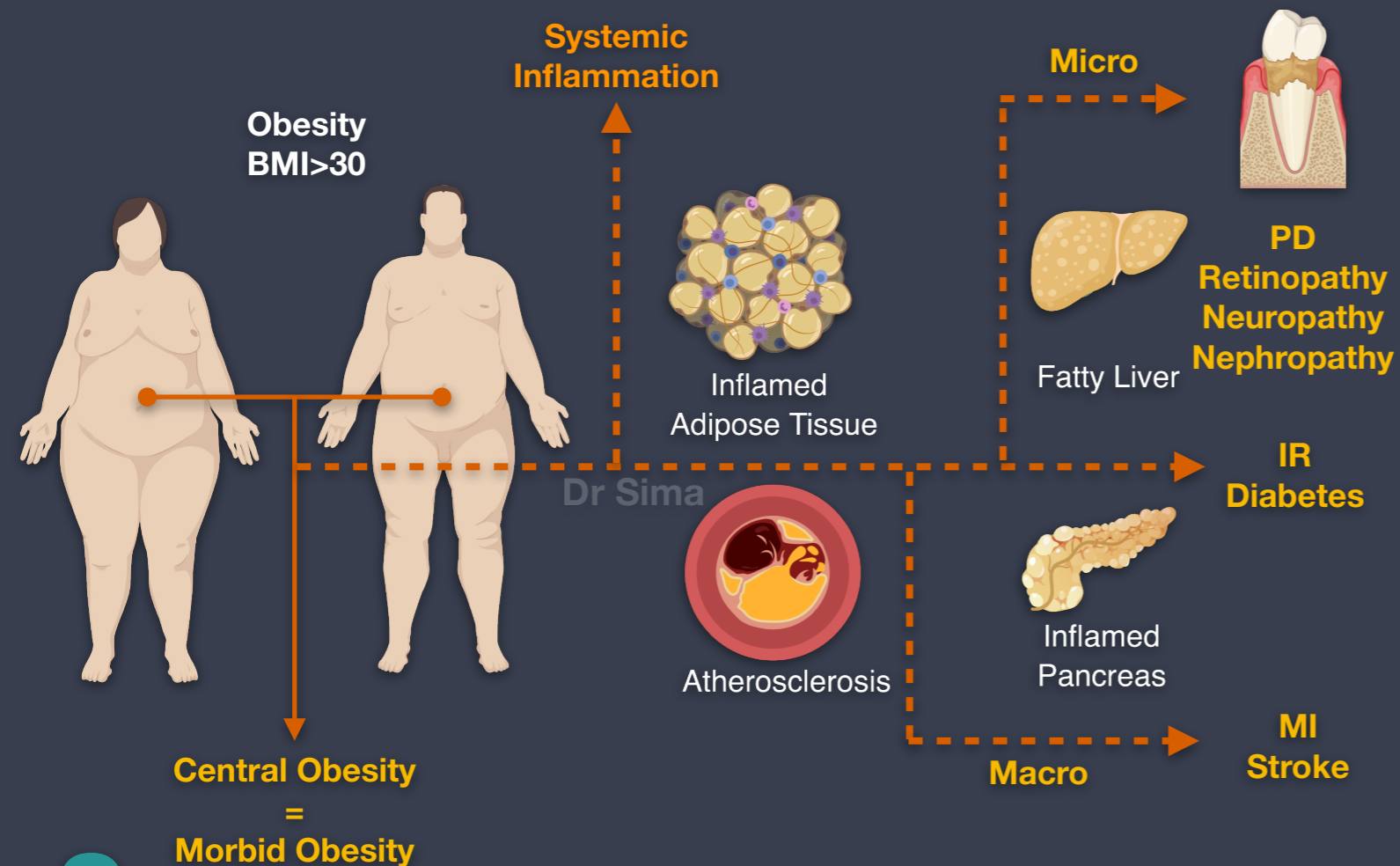
1. Villoria, GEM. et al. 2024. Periodontal disease: A systemic condition. Perio 2000
2. Hajishengallis, G & Chavakis, T, 2021. Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities. Nat Rev Immunol.
3. Tomás, I. et al. 2012. Periodontal health status and bacteraemia from daily oral activities: systematic review/meta-analysis. J Clin Periodontol

## Perio-Systemic

# OBESITY - DIABETES

USA: 34M ADULTS - DIABETES

88M ADULTS - PREDIABETES



In normal individuals ~ 4% of hemoglobin A undergoes glycation at the amino-terminal valines of the  $\beta$ -chain forming the HbA1c subfraction.

**Morbid obesity** (central obesity) is associated with **systemic inflammation** that leads to insulin resistance (IR) and **diabetes mellitus** in susceptible individuals, ultimately resulting in *macrovascular* (atherosclerotic cardiovascular disease - CVD, myocardial infarction - MI, stroke) and *microvascular* (neuropathy, nephropathy, retinopathy, PD) complications when **uncontrolled (HbA1c >7%)**.

**Glycated hemoglobin (HbA1c)** is an advanced glycation end-product and serves as measure of blood glucose level control over 2-3 months (the average red blood cell lifespan is 120 days).

People with diabetes are **2 times more likely to have PD** than people without diabetes. Diabetes impacts healing and the ability to fight infections, including those against pathogenic oral bacteria associated with PD.

**Treatment of diabetes improves periodontal health and treatment of periodontitis improves diabetes control**, as reflected in lower HbA1c.<sup>4</sup> Uncontrolled diabetes can make PD more severe and PD may make it harder to control diabetes.<sup>5</sup>

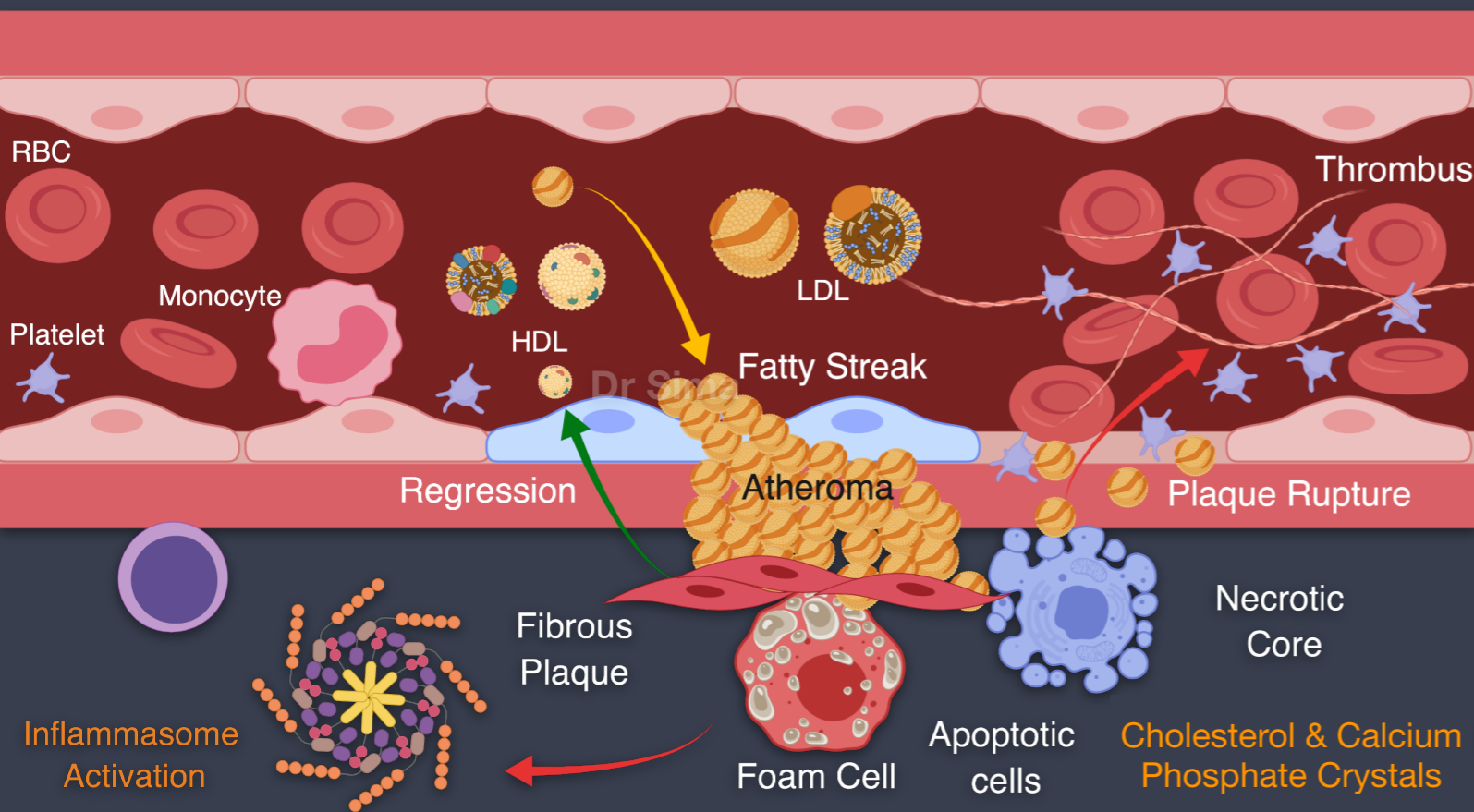
4. Teeuw, WJ et al. 2010. Effect of periodontal treatment on glycemic control of diabetic patients: a systematic review and meta-analysis. *Diabetes Care*.

5. Preshaw, PM. et al. 2012. Periodontitis and diabetes: a two-way relationship. *Diabetologia*

Perio-Systemic

# CARDIOVASCULAR DISEASE

USA: 127M ADULTS



**Heart disease** (including Coronary Heart Disease, Hypertension, and Stroke) remains the **number 1 cause of death** in the USA. CVD, listed as the underlying cause of death, accounts for nearly 850,000 deaths in the US, or 1 of every 3 deaths. Cardiovascular outcome measures include health-related quality of life, endothelial function, intima-media thickness, CRP, BP, angina, MI, death.

PD and atherosclerotic CVD are associated independent of known confounders. The two disorders **share inflammatory pathogenesis and several common risk factors**, including smoking, age, and diabetes mellitus. There is robust epidemiological evidence for positive associations between PD and heart disease, and its complications.<sup>6</sup>

Available research data indicate a general trend toward a **periodontal treatment-induced suppression of systemic inflammation** and improvement of markers of atherosclerotic CVD and endothelial function, suggesting improved vascular health.<sup>7,8</sup>

6. Sanz, M et al. 2020. Periodontitis and cardiovascular diseases: Consensus report. *J Clin Periodontol.*

7. Tran, AH et al. 2026. Periodontal Disease and Atherosclerotic Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*

8. Higashi, Y & Taguchi, A. 2025. Vascular Endothelial Function in Periodontal Disease: Role of Inflammation. *J Am Heart Assoc.*

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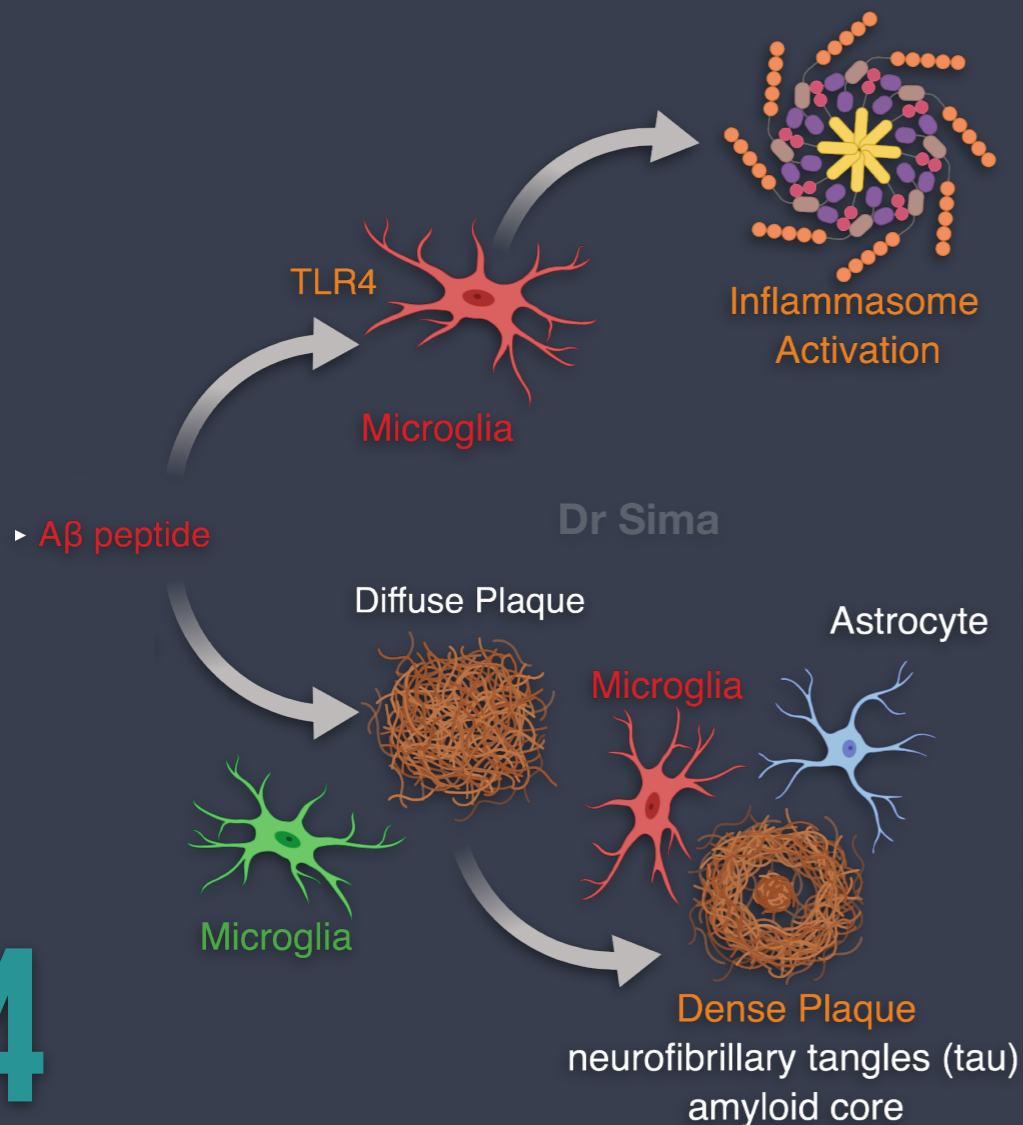
Periodontal bacteria *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia* have been identified in blood and lesion tissues of patients with myocardial infarction, peripheral artery disease, and abdominal aortic aneurysm.<sup>8</sup>

## Perio-Systemic

# ALZHEIMER'S

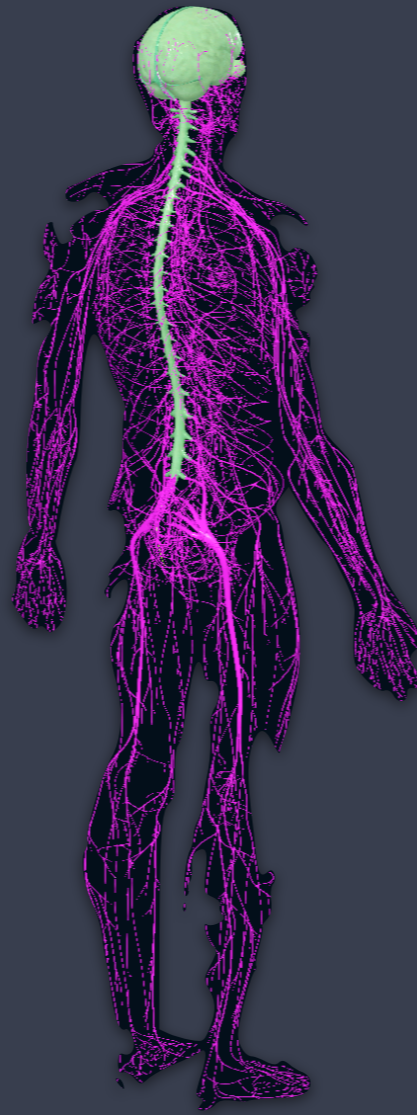
The most common cause of dementia. Progressive loss of cognitive function independent of the state of attention.

## USA: 6M ADULTS



The largest NHANES survey to date provided evidence for an association between periodontal pathogens and AD, which was stronger for older adults.<sup>11</sup>

Effectiveness of periodontal pathogen treatment on reducing sequelae of neurodegeneration should be tested in randomized controlled trials.



The fundamental abnormality in AD is the deposition of Aβ peptides and **pro-inflammatory activation of microglia** is thought to play an important role in its pathogenesis.

AD outcome measures include Cornell Scale for Depression in Dementia (CSDD), quality of life for AD and dementia (QOL- AD, QUALIDEM), Symbol Digit Substitution Test (SDST), the Serial Digit Learning Test (SDLT), reflexes, muscle tone, coordination, balance, sense of sight and hearing.

Worse scores on three measures of oral health status (BOP, CAL, tooth loss) were significantly associated with poorer performance on measures of cognitive function SDST and SDLT after adjustment for age and other covariates.<sup>9</sup>

A fixed effects meta-analysis of PD-AD showed that the presence of PD is associated with the presence of AD (OR 1.69). When only severe forms of PD were evaluated, a significant association was also observed (OR 2.98).<sup>10</sup>

9. Stewart et al. 2008 Oral Health and Cognitive Function in the Third National Health and Nutrition Examination Survey (NHANES III); *Psychosomatic Med.*

10. Leira et al. 2017 Is Periodontal Disease Associated with Alzheimer's Disease? A Systematic Review with Meta-Analysis. *Neuroepidemiol.*

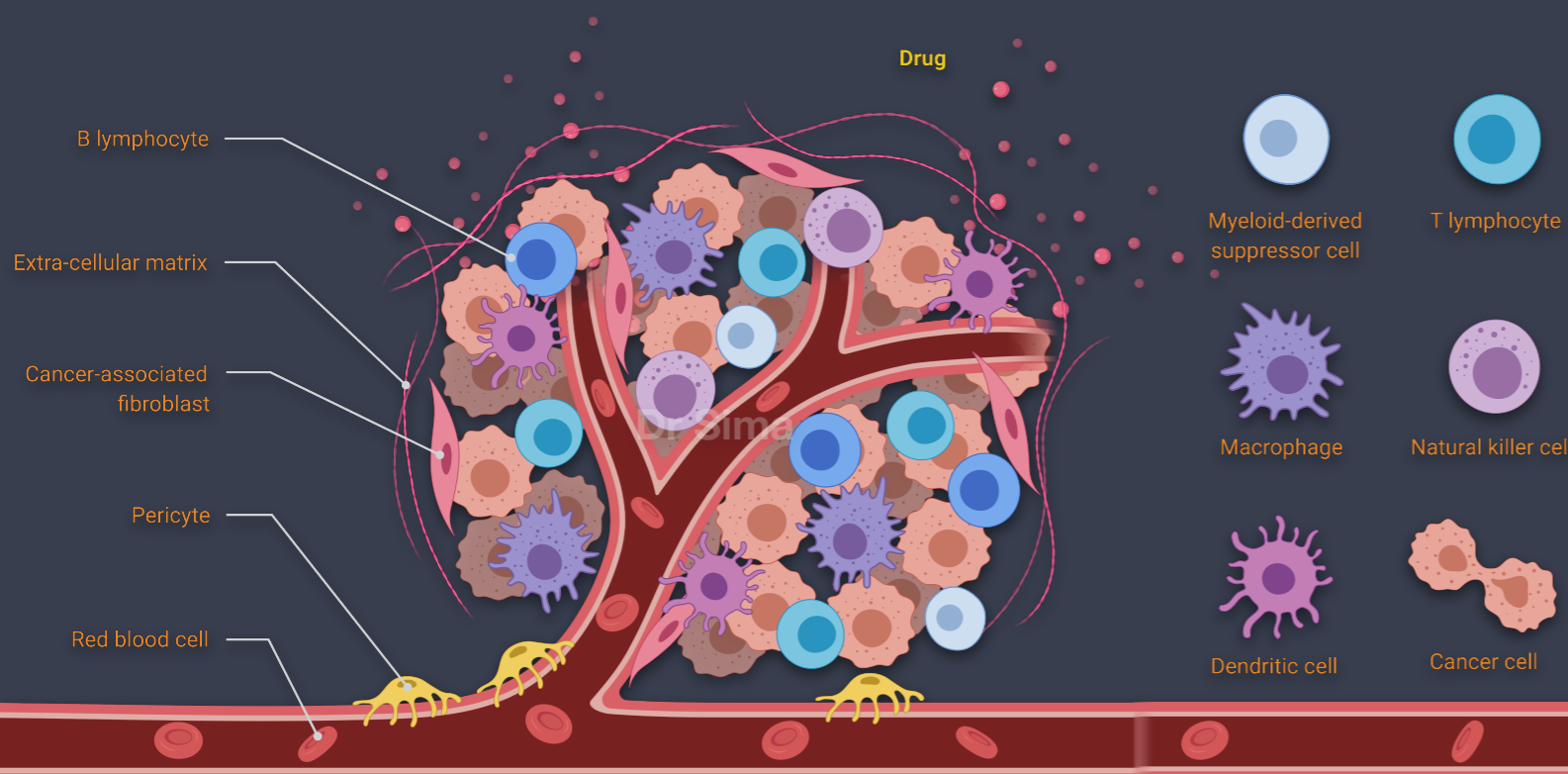
11. Beydoun, MA et al. 2020. Clinical and Bacterial Markers of Periodontitis and Their Association with Incident All-Cause and Alzheimer's Disease Dementia in a Large National Survey. *J Alzheimers Dis*

## Perio-Systemic

# CANCER

## USA: 18.6M SURVIVORS (2025)

PD may induce a chronic systemic low-grade inflammatory state and the spreading of oral pathobionts with carcinogenic potential.<sup>14</sup>



Since **chronic inflammation facilitates tumor progression** and treatment resistance, potential links between PD and cancers were investigated.

The largest cohort study assessing PD as potential risk factor for cancer mortality indicated an increased risk of overall (RR 1.27) and pancreatic cancer (RR 1.69) mortality. After adjustment, the results showed even stronger associations of PD with overall (RR 1.33) and pancreatic cancer (RR 2.32) mortality.<sup>12</sup>

In another large cohort study Michaud et al found a 13% increase in total cancer among men reporting PD at baseline, and a 45% increase in risk among men with advanced PD.<sup>13</sup> PD was not associated with prostate cancer, colorectal cancer or melanoma, the three most common cancers in this cohort of never smokers, but a 33% increase in risk was observed for smoking-related cancers (lung, bladder, oropharyngeal, esophageal, kidney, stomach and liver cancers; HR = 1.33). Men with advanced PD had an HR of 2.57 for smoking-related cancers, compared with men who did not have PD.

12. Heikkilä, P et al. 2018. Periodontitis and cancer mortality: Register-based cohort study of 68,273 adults in 10-year follow-up. [International journal of cancer](#)

13. Michaud, DS et al. 2016. Periodontal disease and risk of all cancers among male never smokers: an updated analysis of the Health Professionals Follow-up Study. [Ann Oncol](#)

14. Baima, G et al. 2024. Periodontitis and risk of cancer: Mechanistic evidence. [Periodontol 2000](#)

## Perio-Systemic

# SYSTEMIC OUTCOMES OF PERIODONTAL THERAPY

Treatment of PD moderately but significantly ***reduces systemic inflammatory markers*** such as high sensitivity CRP (hs-CRP) and IL-1 and 6 for up to 6 months.<sup>15, 16</sup>

## Role of periodontal therapy in management of common complex systemic diseases and conditions: An update<sup>17</sup>

15. Demmer, RT et al. 2013. The influence of anti-infective periodontal treatment on C-reactive protein: a systematic review and meta-analysis of randomized controlled trials. PLoS One

16. Orlandi, M et al. 2022. Impact of the treatment of periodontitis on systemic health and quality of life: A systematic review. J Clin Periodontol

17. Sabharwal, A. et al., 2018. Role of periodontal therapy in management of common complex systemic diseases and conditions: An update. Periodontol 2000.

A 2018 review<sup>17</sup> summarized the results of ***randomized trials reported since 2010*** that assessed the effect of periodontal interventions on at least one systemic outcome in human subjects of any age, gender or ethnicity. Oral outcome measures included gingivitis, pocket depth, CAL and/or radiographic bone loss and oral hygiene indices.

Results suggested that:

- ***Nonsurgical periodontal intervention provided to pregnant women is safe and improves periodontal status without preventing adverse pregnancy outcomes.***
- Nonsurgical periodontal intervention provides ***modest improvement in glycemic control in individuals with type 2 diabetes mellitus and PD.***
- Improving oral care through mechanical or chemical control of dental-plaque biofilm formation can contribute to the ***prevention of respiratory infections*** in differing clinical settings, including hospitals and nursing homes, and in patients with chronic obstructive pulmonary disease.
- ***No clinical trials*** were reported that tested the effect of periodontal interventions on medical outcomes of atherosclerosis, CVD, stroke, rheumatoid arthritis, Alzheimer's disease, chronic kidney disease or malignant neoplasia.