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Evolutionary History of Periodontitis and the Oral Microbiota—Lessons for the Future

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Abstract

Purpose of Review Currently, periodontal disease is the sixth most prevalent disease in the world. Emerging evidence suggests the possibility of pre-historic humans having relatively low occurrences of oral diseases, particularly periodontitis when compared to modern humans. In this review, we look back into the history of *Homo sapiens* and explore the emerging scientific literature to discuss the evolution of the human oral microbiota and the prevalence of periodontitis from pre-historic to modern times.

Recent Findings Most of the scientific literature points to a more health-associated, eubiotic oral microbiota and a seemingly lower prevalence of periodontitis in pre-historic humans compared to modern times. The oral microbiome has evolved along with humans. Humans of the contemporary era are exposed to a far greater number of risk factors for periodontal disease. Also, major lifestyle changes induced by the agricultural revolution and the industrial revolution have led to the development of a more dysbiotic oral microbiota and a rise in the prevalence of periodontitis in modern humans.

Summary An understanding of the prevalence of periodontitis across human history, the evolution of the oral microbiota, and the factors that influenced its nature and complexity helps identify and modify the disease-associated lifestyle factors acquired through modernization to manage the common worldwide problem of periodontitis.

Keywords Periodontitis · Oral microbiota · Evolution · Pre-historic · Ancient · Paleopathology

Introduction

Modern *Homo sapiens* have been forged over millions of years of evolution with landmark lifestyle adaptations throughout history [1]. Humans (members of the genus *Homo*) diverged from the hominin species named *Australopithecus africanus* several million years ago; according to recent evidence, the origin of the genus *Homo* is dated to 3.36 million years ago [2]. The earliest archaic human species, *Homo habilis* and *Homo erectus*, walked the earth for another two million years before evolving into *Homo heidelbergensis*, *Homo neanderthalensis* (Neanderthals), and us (*H. sapiens*). The rise of our species (*H. sapiens*) is dated to 315,000 years ago [3]. Humans, like all other multicellular species, have co-existed with microorganisms for millions of years.

Microorganisms reside in various ecological niches in the human body; the small and large intestines host the gut microbiota, and the oral cavity hosts the oral microbiota, both of which are the most diverse microbiomes in the human body [4, 5]. The human body and its resident microbiota are considered a single entity called the holobiont [5]. These microbes confer numerous benefits to the human host (metabolic, physiologic, and immunologic benefits). In return, the host provides nutrients and habitat for growth to the microbiota, resulting in a symbiotic relationship between the two [5, 6]. In health, the resident microbial community maintains a state of equilibrium within itself and with the human host (eubiosis) [7•]; disruption of this equilibrium (dysbiosis) can result in disease [5, 6, 8].

The oral microbiota is one of the most complex communities of microbes residing in various niches within the

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oral cavity. We acquire a distinct resident microbiota soon after birth depending upon the mode of childbirth (vaginal or caesarean section) [9]. Various factors influence the oral microbiota throughout life. The oral microorganisms form a soft microbial biofilm on teeth called "dental plaque" (Fig. 1). If allowed to accumulate and remain on the teeth, the soft plaque gradually calcifies into a hard deposit that firmly adheres to the teeth and is termed "dental calculus."

Periodontitis is a chronic inflammation of the tissues surrounding the teeth that gradually reduces tissue attachment and bone levels leading to loss of support for the teeth, eventually leading to tooth loss. In the modern era, severe periodontitis has emerged as the sixth most prevalent disease in the world [10, 11]. Despite the advancements in technology and increasing awareness of oral hygiene practices, modern humans seem to have poorer oral health than pre-historic humans. So, why do modern humans suffer from periodontal disease, despite oral hygiene practices and awareness being at their highest levels in history? Our pre-historic ancestors led a completely different lifestyle compared to us modern humans. Did pre-historic humans also suffer from similar periodontal disease when oral hygiene behavior and awareness were practically non-existent? Was the ancient oral microbiome in equilibrium with its host that lived a vastly different lifestyle?

These questions can only be answered if we understand the changes that occurred along the evolutionary journey of *Homo sapiens*. Next-generation DNA sequencing studies on dental calculus retrieved from archaeological human teeth that serve as microbial fossils suggest that the oral microbiota of pre-historic humans was markedly different

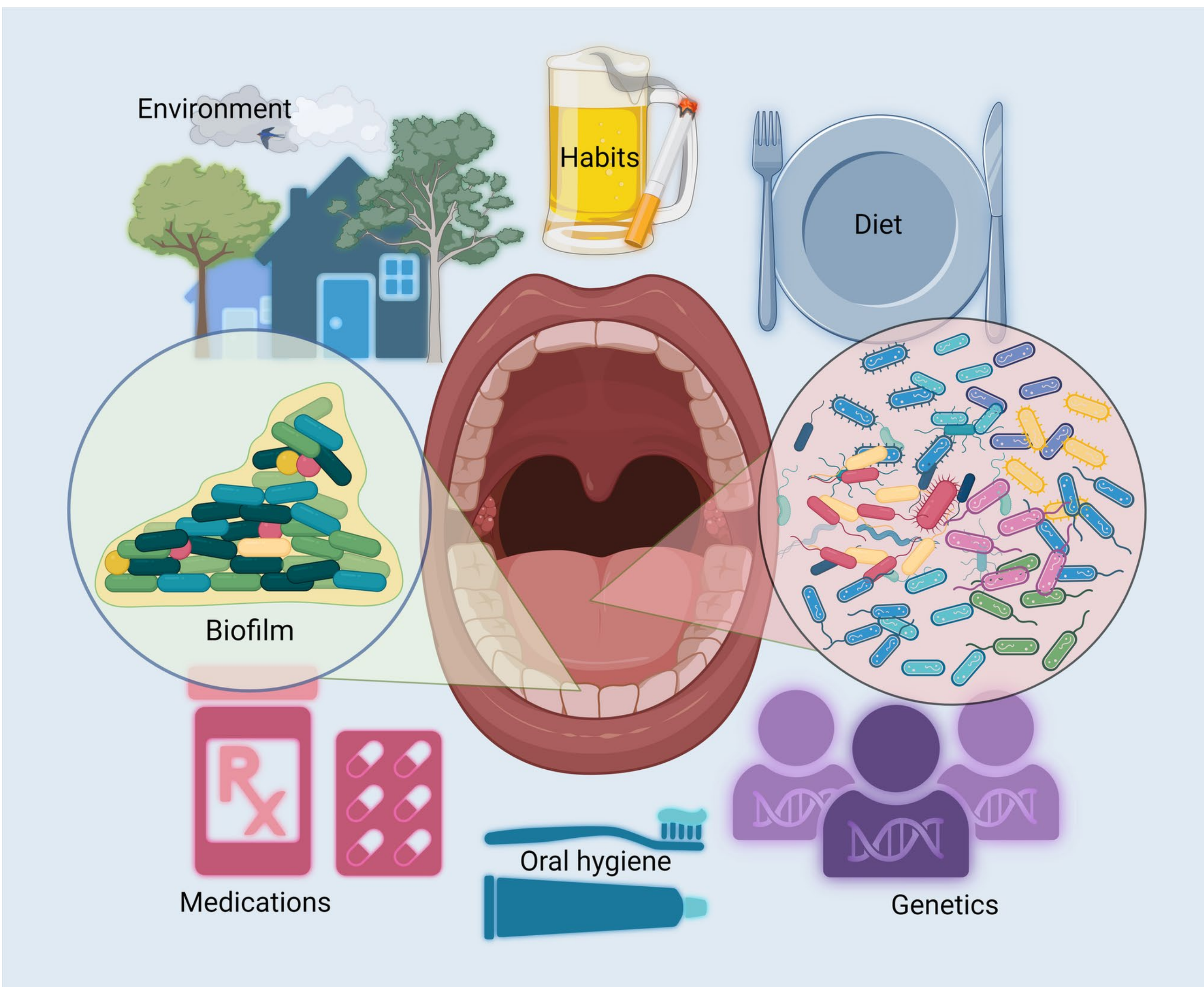

Fig. 1 Factors influencing the oral microbiota: The composition and diversity of oral microbiota are influenced by diet, environment, medications, oral hygiene, oral abusive habits (tobacco smoking, smokeless form of tobacco, alcohol consumption), and genetics (original figure designed in BioRender software)

from modern humans. Like humans, the oral microbiota also has evolved; various factors that shaped this evolution and the comparison of the oral microbiomes of pre-historic and modern times have not been discussed extensively. This review aims to explore and compare the scientific literature to discuss the oral microbiome of pre-historic and ancient humans and track its evolution to the modern era. We also compare the prevalence of periodontitis among pre-historic and modern humans to aid in better future prevention and management of periodontitis.

The Paleolithic and Mesolithic Age

During this period, the planet was home to multiple human species such as *H. sapiens*, Neanderthals, *Homo denisova* (Denisovans), *Homo floresiensis*, and *Homo heidelbergensis* [12]. They all lived as small bands of nomadic hunter-gatherers who foraged plants, nuts, tubers, berries, meat, and other raw materials [13]. The microbiome of these hunter-gatherers, especially the gut microbiome, is found to be highly diverse compared to present-day humans living in industrialized urban societies [14]. The gut microbiota of pre-historic humans consists of higher levels of *Prevotella*, *Proteobacteria*, *Spirochaetes*, *Clostridiales*, and *Ruminobacter*, whereas the modern gut microbiota shows high levels of *Bacteroides*, *Bifidobacterium*, and *Firmicutes* [14]. Similarly, the oral microbiota of Paleolithic and Mesolithic hunter-gatherers was diverse with significantly less periodontitis-associated species such as *Prevotella intermedia*, *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*, *Aggregatibacter actinomycetemcomitans*, and *Eubacterium nodatum* and higher levels of health-associated species [15, 16••]. Also, there seems to be a gradual decrease in the diversity of the human microbiome from pre-historic times to the modern era [14].

Another study found that the Neanderthal oral microbiota was significantly different from the modern human oral microbiota [17]. Despite the presence of organisms like *Porphyromonas gingivalis*, *Tanerella forsythia*, and *Treponema denticola*, the Neanderthal oral microbiota harbored fewer gram-negative species that are associated with periodontal disease than modern humans (77.6% gram-negative species in modern humans versus a mere 18.9% in the Neanderthal samples) [17]. Neanderthals also have less *Fusobacteria*, a species that facilitates the growth and maturation of the dental plaque biofilm [17]. Also, it is noted that despite the presence of periodontitis-associated species, hunter-gatherers show good oral health [18].

The domestication of fire and the adoption of cooking approximately 250,000 years ago [19, 20] brought a significant change in the oral microbiota as diet and nutrition are major lifestyle factors that influence the composition and diversity of the oral microbiota [21, 22••]. The use of fire is an important lifestyle transition that likely affected, not only the oral microbiome but also significant dimensions of human anatomy and physiology. Cooking softened the food and made it easier to digest while improving its nutritional value leading to bigger brains, shorter intestines, and decreased chewing forces leading to smaller jaws and teeth [20]. A study found that consuming cooked food uniquely shapes the gut microbial community compared to raw, uncooked food [23]. Cooking caused certain food items like meat that is difficult to chew and digest, to be more frequently consumed [20, 24]; consuming meat frequently affects the composition of the oral microbiota [22••, 25, 26].

Cooking also improves the digestion of starchy food like tubers and rhizomes while increasing their net available energy, which possibly might have increased the reliance on cooked, starch-rich plant food [27]. Salivary α-amylase is an enzyme in humans that breaks starch into maltose and dextrin, initiating its digestion in the oral cavity [28]. *Streptococcus* species such as *mitis*, *sanguinis*, and *salivarius* express amylase-binding proteins that enable them to use the α-amylase enzyme to break down starch for their nutrient supply. Pre-historic dental calculus from the members of the genus *Homo* reveals an unmistakably dominant and unique presence of these *Streptococcus* species (*mitis*, *sanguinis*, *salivarius*) that express amylase-binding proteins [29]. Thus, the unique presence of these *Streptococcus* species in humans indicates an adaptive shift in the human oral microbiota following a starch-rich diet resulting from the adoption of cooking by humans [27, 29].

Shotgun sequencing of ancient DNA present in the dental calculus of Neanderthal remains from Spy Cave, Belgium, and El Sidrón Cave, Spain, reveals vital information about the Neanderthal diet and oral microbiota [17]. Perhaps, Neanderthals were highly flexible in their diet and depended largely upon their immediate surrounding environment—The dental calculus of Spy Neanderthals showed DNA sequences mapping to sheep and white rhinoceros indicating higher meat consumption. However, El Sidrón Neanderthals did not consume meat; DNA sequences indicated edible mushrooms, pine nuts, forest moss, and poplar consumption. The oral microbiota of Spy Neanderthals and El Sidrón Neanderthals were markedly different from each other, possibly due to the differences in meat consumption [17].

Current evidence indicates that the pre-historic hunter-gatherer populations may have had lower rates of periodontitis and better oral health than Neolithic and modern humans [15, 30••, 31•, 32–34]. One study demonstrated the effect of the "stone-age" diet and lifestyle on gingival and periodontal inflammation in the absence of oral hygiene procedures. Participants who consented to and lived in "stone-age" conditions (environment, clothing, housing, and diet) along the Rhine River consumed a pre-historic diet that was devoid of processed carbohydrates and refined sugar for 4 weeks and did not perform any conventional oral hygiene procedures (except for some participants who used twigs to clean their teeth). At the end of the study, despite the increase in plaque levels due to abstinence from oral hygiene, the participants had a significant decrease in gingival and periodontal inflammation [35]. A recent study also demonstrates the protective effect of an "anti-inflammatory diet" devoid of refined carbohydrates and sugar on gingival inflammation [36].

The Neolithic Revolution

By 10,000 BC, the world was witnessing a revolution in the way of human life. The domestication and cultivation of plants and animals led to the Agricultural Revolution (also known as the Neolithic Revolution), which started in the Middle East's Fertile Crescent [37]. There was a transformation in lifestyle as foragers became farmers. Instead of foraging, humans began cultivating specific crops like wheat, barley, maize, and rice that became dietary staples. The nomadic hunter-gatherers who were physically active, constantly wandering and exploring different geographies in search of food, adopted a relatively sedentary lifestyle and began settling down in strategic locations that were best suited for farming. They started living in large communities and formed and settled in farming villages. And unlike foraging, agriculture produced excess food that could support large populations. However, this lifestyle transformation caused a paradoxical decline in human health and quality of life [38, 39]. The previously diverse diet was replaced by a staple diet of carbohydrate-rich grains; the loss of a diverse diet led to nutritional deficiencies [39]. Also, living in large and dense communities led to a rise in infectious diseases [39]. This change in diet and living conditions brought about by the agricultural revolution holds the potential to alter the microflora of humans.

Through amplicon sequencing, the comparison of the dental calculus microbiomes of pre-Neolithic hunter-gatherers, post-Neolithic farmers, medieval humans, and modern humans reveals that the Neolithic revolution decreased the diversity of the human oral microbiota and significantly increased the abundance of pathogenic species [15]. Dental calculus from post-Neolithic farmers shows high levels of periodontal disease-associated red complex species (belonging to Socransky's microbial complexes [40]) such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* and a less diverse oral microbiota when compared to the hunter-gatherers, possibly due to the introduction of a less diverse, soft, carbohydrate-rich diet from the agricultural revolution [15].

Another study reported that the post-Neolithic farming population showed markedly different oral microbiomes when compared to Paleolithic hunter-gatherers [16••]. This study temporally divided the Neolithic era into the early, middle, final, and late periods and analyzed dental calculus samples only from central-south Italy to eliminate geographical bias. The results revealed that when compared to the Paleolithic hunter-gatherers, the Neolithic farmers had significantly higher levels of red complex species (*Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*), orange complex species (*Campylobacter rectus* and *Prevotella intermedia*), green complex species (*Capnocytophaga endotelialis* and *Eikenella corrodens*), and other periodontitis-associated species like *Parvimonas micra* and *Filifactor alocis*. These species gradually increased in abundance from the early Neolithic period to the Late Neolithic and Copper Age periods (Fig. 2) [16••].

Whereas periodontal health-associated yellow complex species like *Streptococcus gordonii*, *Streptococcus mitis*, *Streptococcus oralis*, and *Streptococcus sanguinis* and purple complex species like *Actinomyces* species are abundant in Paleolithic hunter-gatherers when compared to Neolithic farmers, their abundance gradually decreases from the early Neolithic to the late Neolithic and Copper Age (Fig. 2) [16••]. Also, the Neolithic oral microbiome shows higher virulence factors compared to the Paleolithic oral microbiome [16••].

There is a shift from the health-associated oral microbiota that is seen in the hunter-gatherers to a disease-associated oral microbiota in the Neolithic people, possibly due to the lifestyle changes induced by the agricultural revolution. When compared to the Paleolithic and Mesolithic hunter-gatherers, the farmers of the Neolithic period who consumed an agrarian diet show less diverse and more dysbiotic oral microbiomes with a higher prevalence of periodontal disease-associated organisms. Overall, the social and cultural effects of the Neolithic revolution had a detrimental impact on the human oral microbiota.

After the advent of agriculture and the introduction of a staple agrarian diet that was rich in soft carbohydrates, there was a decline in oral health as dental decay and periodontitis seemingly became more prevalent; Neolithic farmers had poorer oral health than the pre-Neolithic hunter-gatherers [15, 16••, 30••, 31•, 32, 34]. One study evaluating the remains of the Neolithic Jomon population revealed a high prevalence of moderate to severe periodontitis [41]. Women of a present-day foraging population who consume an agrarian diet were shown to have poorer oral health with higher rates of periodontitis and caries than women consuming a wild-type bush diet. However, men who consume a wild-type diet had a higher prevalence of periodontitis, possibly due to the habit of tobacco and marijuana smoking [42]. While this study examined a modern proxy of a pre-historic

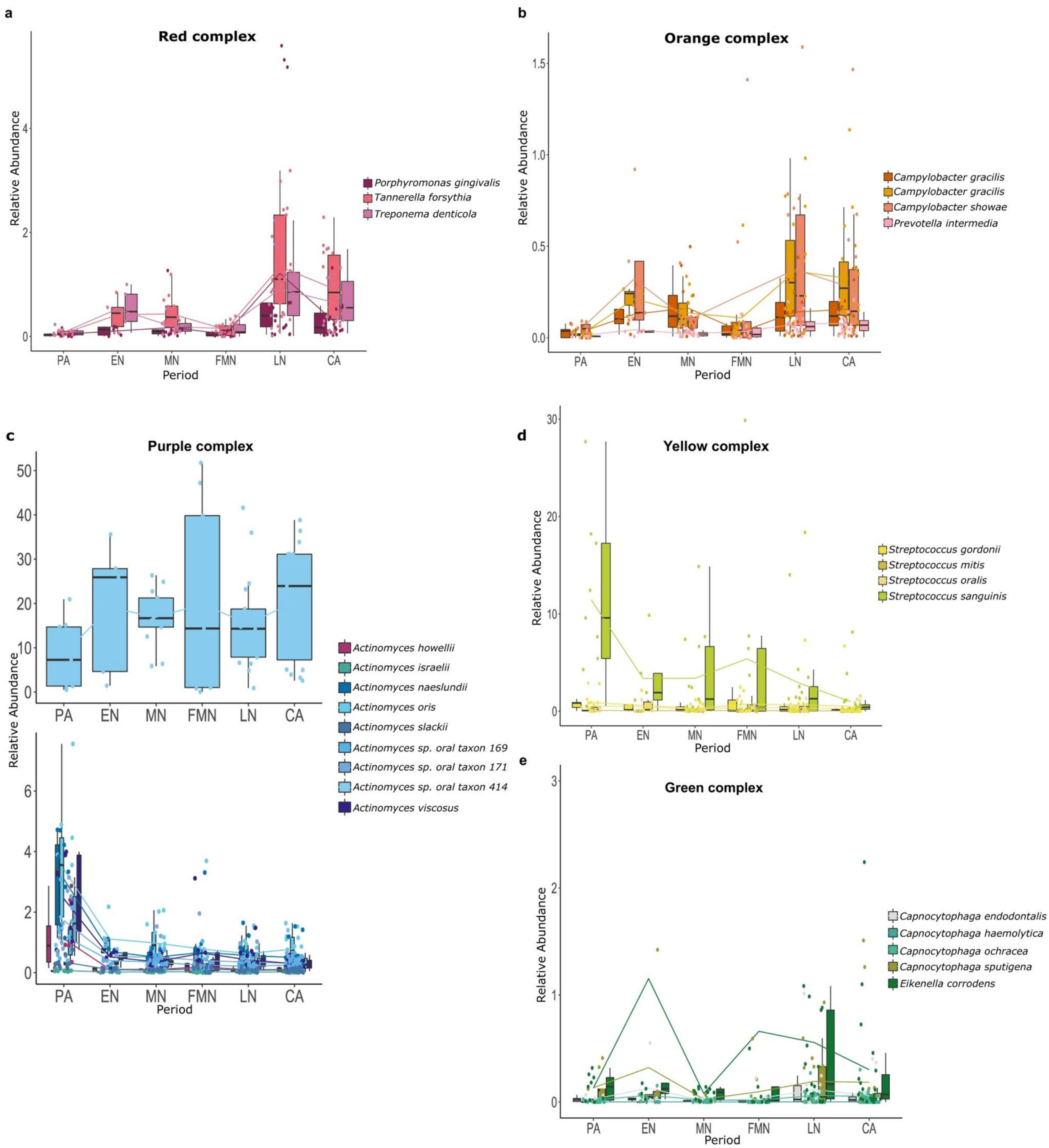

Fig. 2 Socransky's microbial complexes across time: Change in abundance of red, orange, purple, yellow, and green complex species from the Paleolithic and across the Neolithic age. (PA, Paleolithic Age; EN, Early Neolithic; MN, Middle Neolithic; FMN, Final Middle Neolithic; LN, Late Neolithic; CA, Copper Age). Adapted with permission from [16••] http://creativecommons.org/licenses/by/4.0/

foraging population, it goes on to conclude that hunter-gatherers do not always show better oral health than farmers [42]. Another study also presented a contradictory finding that the Natufian hunter-gatherers (10,500–8300 BC) revealed a higher prevalence of periodontitis than Neolithic populations (8300–5500 BC); the study also concludes that both groups might have consumed similar food despite the difference in subsistence strategy [43]. Ancient human remains belonging to 200–400 AD showed a lower prevalence of periodontitis than modern humans [44]. A series of studies evaluating samples from pre-900 AD to 1852 AD concluded that periodontitis was common, but the prevalence of periodontitis was not higher than that of modern populations [45–47].

The Industrial Revolution

The eighteenth and nineteenth centuries saw another important sociocultural and economic transformation in the form of the Industrial Revolution. Food processing became easy and widespread with the advent of steam engines, machine tools, and factories. The Neolithic agrarian diet was modified by the introduction of refined flour, refined sugar, refined seed oils, and other processed dairy products like cheese and butter [48]. The invention of the stone roller mill gave rise to refined wheat flour devoid of the outer bran and germ layer, with reduced nutritional value [48, 49]. Refined and processed sugar with higher purity and a better appearance was introduced leading to a massive worldwide increase in sugar consumption during and after the Industrial Revolution, which continues to rise even in the twenty-first century [48].

The Industrial Revolution popularized the high-sugar, high-fat, ultra-processed diet that had altered and reduced nutritional characteristics, high glycemic load, lower macro- and micro-nutrient proportions, and low fiber content [30••, 48], and is known to induce chronic inflammation and dysbiosis in the body leading to numerous lifestyle diseases of the modern era [30••, 48, 50]. More specifically, consuming excess dietary sugar leads to a chronic state of low-grade systemic inflammation [51] and increases the risk of developing periodontal disease [52, 53]. Consuming this type of diet in the long term causes hyperinsulinemia that leads to metabolic syndrome and insulin resistance. Obesity, type 2 diabetes, and chronic heart diseases are "diseases of civilization" that are tied to hyperinsulinemia and insulin resistance [54].

Microscopic analysis of archaeological dental calculus samples from the industrial period of the UK reveals highly damaged starch granules as signs of extensive food processing techniques such as the milling of flour which was developed during the Industrial Revolution. The specimens also had traces of microcharcoal and burnt debris, possibly indicating air pollution from factory emissions during that period [55]. The oral microbiota of modern post-industrial humans is significantly less diverse when compared to the Neolithic farmers and the Mesolithic hunter-gatherers [15]. Modern humans show high levels of dental decay-associated species *Streptococcus mutans* and *Veillonellaceae* compared to hunter-gatherers and Neolithic farmers, possibly due to the rise of refined sugars during the Industrial Revolution [15]. Modern humans have lower levels of the periodontitis-associated species *P. gingivalis* compared to Neolithic farmers; however, compared to Paleolithic hunter-gatherers, modern humans show higher levels of *P. gingivalis* [15]. Also, modern humans have a higher abundance of immunogenic, disease-associated gram-negative organisms when compared to Paleolithic Neanderthals [17]. A 2021 study revealed that dental calculus microbiomes of pre-industrial humans of the Japanese Edo period (1603–1867) who had a high prevalence of periodontitis lacked the red complex species and *F. nucleatum* which were detected only in modern post-industrial humans [56]. Analysis of calculus samples of a Sardinian rural community from pre-industrial and post-industrial eras revealed that the red complex bacteria that are associated with periodontitis became significantly more prevalent only in post-industrial modern humans [57].

Like the Neolithic revolution, the Industrial Revolution also detrimentally affected the human oral microbiota [15, 22••, 30••, 31•]. With the introduction and increased consumption of highly processed and refined sugars, there was an increase in the prevalence of decay-associated and periodontitis-associated organisms and reduced diversity in the human oral microbiota.

The Contemporary Era

One of the most significant landmarks of the twentieth century is the discovery of penicillin in 1928 which directly led to the development of commercial antibiotics. In the subsequent decades, more and more novel antibiotic drugs were introduced, and many of them were available to the public over the counter leading to self-medication and overuse of antibiotics. This overuse of antibiotics has led to the emergence of bacteria that are resistant to antibiotics and is a severe healthcare crisis looming over humanity [58]. Systemic antibiotics directly alter the human microbiota by simultaneously wiping out multiple pathogenic and commensal species. This collateral damage to commensal species can disrupt the host microbiota and compromise the immunity of the host [59]. Antibiotic exposure during pregnancy alters the mother's gut and vaginal microbiota, influencing the infant's microbiome, including their oral microbiota [59, 60]. Mice exposed to long-term antibiotics developed dysbiosis of the gut and the oral microbiota which aggravated the periodontal disease [61]. Due to the excessive and reckless use of antibiotic drugs, modern humans frequently disrupt their microbiota leading to dysbiosis.

Tobacco smoking is a widespread lifestyle habit of modern humans. Smokers have a less diverse, less resilient, and compositionally different microbiota than non-smokers [62–64]. Smokers have higher levels of *P. gingivalis* and *F. nucleatum* and elevated levels of several other species like *Prevotella*, *Veillonella*, *Treponema*, *Parvimonas*, and *Campylobacter* that are associated with periodontal disease and cardiovascular disease [65, 66]. Smoking affects the immune response by altering neutrophil chemotaxis and neutrophil extracellular trap formation resulting in compromised innate immune response towards oral pathogens [67]. Overall, the modern habit of smoking is an established, major risk factor for periodontal disease [68].

Chronic psychological stress, anxiety, depression, and an increasingly sedentary lifestyle plague our species in the twenty-first century [69]. In the presence of the stress hormone cortisol, there is a community-wide shift in the oral microbiota along with the increased activity of *F. nucleatum* and *Leptotrichia goodfellowii.* There is elevated expression of the genus *Streptococcus* virulence factors as well as a decrease in *Prevotella* [69, 70]. Chronic stress acts as a risk factor for periodontal disease through the behavioral, adrenergic, and hypothalamic–pituitary–adrenal axis [71, 72]. Also, the level of physical activity influences the diversity and composition of the gut microbiota; an active lifestyle was associated with a more diverse microbiota and a higher abundance of health-promoting species [73, 74]. Sedentary children exhibited a less diverse salivary microbiota and increased levels of *Veillonella*, *Prevotella*, and *Streptococcus* [75]. A sedentary lifestyle is a risk factor for periodontitis, whereas a physically active lifestyle decreases the prevalence of periodontitis [76, 77].

Obesity is a modern pandemic that has tripled in prevalence in the past 50 years and is predicted to rise in the coming decades [78]. A sedentary lifestyle and a diet that is high in calories and carbohydrates underlie the obesity pandemic [78, 79]. Obesity induces changes in the composition and diversity of the oral microbiota and pushes the community towards dysbiosis [80–82]. Obesity causes a systemic pro-inflammatory state through various pathways and is identified as an important risk factor for periodontitis [83–86]. Obesity also causes insulin resistance leading to type-2 diabetes mellitus (T2DM) [87]. T2DM is another global healthcare problem of the twenty-first century and is a major cause of mortality and morbidity [88]. T2DM patients show dysbiotic oral microbiota with higher levels of *P. gingivalis*, *T. denticola*, *F. nucleatum*, and *Prevotella melaninogenica* when compared to non-diabetics [89]; T2DM is a well-known risk factor for periodontitis [90].

Apart from the well-known factors, many seemingly innocuous habits of modern humans affect oral microbiota. For example, frequent consumption of takeaway food from plastic containers can induce gut and oral microbiota changes, leading to dysbiosis [91]. Sulfite preservatives added to processed food to increase its shelf life alter oral microbiota composition [92]. Overall, modern humans are at higher risk of dysbiosis of oral microbiota and are exposed to a greater number of risk factors for periodontal disease.

Modern humans seem to have a higher prevalence of periodontitis than pre-historic populations. In the twenty-first century, severe periodontitis has emerged as the sixth most prevalent disease in the world [10, 11]. After industrialization, urbanization, and globalization, humans live a sedentary life with a substandard diet, chronic stress, and a host of other chronic inflammatory lifestyle-related diseases. The high prevalence of periodontitis is possibly due to modern humans being exposed to many risk factors for the disease and a more dysbiotic oral microbiota [15, 17]. This rise in periodontitis occurrence is an important public health problem [93]. The most striking realization is that, despite oral health awareness and the daily habit of following a variety of oral hygiene procedures meant to improve oral health, modern humans suffer from a high prevalence of dental decay and periodontitis.

Interpretation of Evidence

Dental calculus and dental plaque have shown distinct variations in their physical chemical and microbiological properties. Previous research on periodontal microbiota of health and disease in modern humans relies on dental plaque samples. Also, our current knowledge and understanding of microbiological signatures of health and disease are derived from studying plaque samples rather than calculus samples. Hence, comparing dental calculus microbiomes to plaque microbiomes might lead to biased interpretations. Therefore, for an unbiased comparison, the microbiological evidence that is retrieved from pre-historic dental calculus needs to be compared with the data from modern dental calculus, rather than relying on the evidence from modern plaque samples [94].

The clinical case definition for any disease enables us to correctly identify cases which is vital for studying the prevalence of a specific disease. Since the case definition of periodontitis has drastically changed over the years and various studies evaluating the prevalence of pre-historic periodontal disease do not conform to a single standardized case definition of periodontitis, the prevalence of periodontitis reported by these studies needs to be interpreted with prudence [44].

Clinical Relevance and Lessons for the Future

Dysbiosis of the microbial biofilm community that accumulates on the teeth is the primary cause of periodontitis [7•]. This dysbiotic dental plaque biofilm elicits an altered immune response from the body and causes chronic inflammation that results in periodontitis in the long term. However, currently, strategies to prevent periodontitis are unidimensional and merely aim to achieve adequate "plaque control," that is, to remove the accumulated plaque from the teeth and to enforce optimal oral

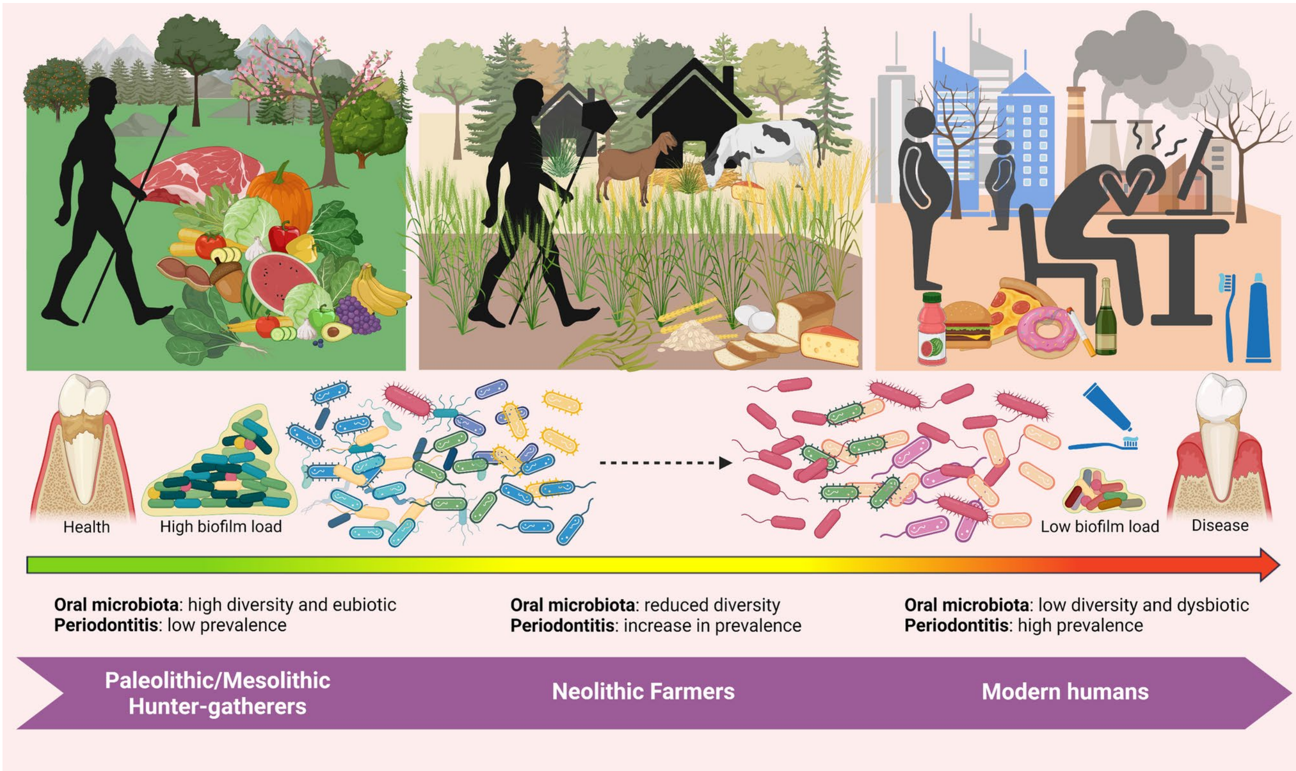

Fig. 3 Temporal transition of oral microbiota and periodontitis prevalence: Along with human evolution and drastic lifestyle changes, the human oral microbiota has become more dysbiotic with a rise in the prevalence of periodontitis (original figure designed in BioRender software)

hygiene habits, with little or no emphasis on identifying and treating the factors responsible for dysbiosis.

Periodontitis must be seen as a complex lifestyle disease resulting from the imbalance between the host and its microbiota. Major lifestyle changes that occurred along our evolution (changes in diet, level of physical activity, stress, and metabolic function) contribute to the host-microbiota imbalance and induce a state of chronic inflammation in the body (Fig. 3). Hence, along with adequate oral hygiene, the prevention and management of periodontitis need to shift focus also towards identifying and modifying the environmental and lifestyle factors to establish eubiosis.

Rather than focusing solely on the oral cavity and its hygiene for the prevention of periodontal disease, the health of the overall host and the eubiosis of its microbiota also need to be considered. There is a quintessential phrase in healthcare—"Oral health for overall health"—that appropriately sums up the impact of oral health on other organ systems and the risk of developing various systemic diseases. Based on emerging evidence about periodontitis, we propose a complementary phrase—"Overall health for good oral health."

Concluding Remarks

The archaeological dental calculus from human fossils that preserve microbial signatures is an important source for studying the human oral microbiota as it enables us to look back in time to study the oral microbiota in pre-historic times. Understanding the evolutionary history of the oral microbiota and the prevalence of periodontitis across human history can be critical for managing periodontal disease in modern times. The nature of the oral microbiota is influenced by the changing lifestyle of humans, the oral microbiota of humans has become more disease-associated, and the prevalence of periodontitis seems to have risen along with human evolution (Fig. 3). Hence, it is necessary to look at our lifestyle habits from a new perspective to recognize the potential factors that contribute to the current rise in the prevalence of periodontitis. Future research needs to study the impact of modern lifestyle factors on oral microbiota and the incidence of periodontitis.

Authors contribution 1. SS conceived the title, the design, and structure of the paper; contributed to the main text; and designed the original figures in the manuscript. 2. NN contributed to the main text and helped in revising the manuscript. 3. SK contributed to the main text and helped in revising the manuscript. 4. AC contributed to the main

text and revised the manuscript. 5. RA contributed to the main text and verified the grammatical correctness of the manuscript. All authors read and approved the manuscript.

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Declarations

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Consent to participate Not applicable.

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- • Of importance
- •• Of major importance

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