



口腔微生态在衰老相关稳态失衡及系统性疾病中的作用研究进展*

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【摘要】 微生态在衰老过程中的调控作用日益受到关注。口腔微生态作为人体重要的微生物生态系统,在维持机体健康和参与疾病发生发展中具有独特地位。本文综述了健康和疾病状态下口腔微生态中特定菌属的动态变化,分析了衰老过程中口腔生理性改变对微生态的影响,并详细阐述了衰老相关口腔微生态失衡参与口腔疾病及系统性疾病的作用机制。鉴于口腔微生态与衰老之间的密切互作关系,其在促进健康老龄化中的作用愈发凸显。深入探究口腔微生态的演替规律,不仅有助于解析老年系统性疾病高发的内在机制,也为开发基于微生态重塑的老年健康干预策略及发现新型早期预警标志物提供了重要的理论依据。

【关键词】 衰老 口腔 生态失调 疾病 健康老龄化 综述

Research Advances on the Role of the Oral Microbiota in Age-Related Homeostatic Dysregulation and Systemic Diseases

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[Abstract] The regulatory role of the microbiota in the aging process has increasingly attracted attention. As a crucial microbial ecosystem of the human body, the oral microbiota plays a unique role in maintaining host health and contributing to disease development. This review summarizes the dynamic changes in specific oral microbial genera under both healthy and diseased conditions, analyzes the impact of age-related physiological alterations of the oral cavity on the microbiota, and comprehensively elucidates the mechanisms by which age-associated oral microbial dysbiosis participates in oral and systemic diseases. Given the close interplay between the oral microbiota and aging, its significance in promoting healthy aging has become increasingly prominent. Investigating the succession patterns of the oral microbiota not only helps to unravel the mechanisms underlying the high incidence of systemic diseases in the elderly, but also provides a theoretical basis for developing microbiota-based intervention strategies and identifying novel early-biomarkers for healthy aging.

[Key words] Aging Oral cavity Dysbiosis Disease Healthy aging Review

口腔稳态是指人类口腔这一复杂开放生态系统中,细菌、真菌、病毒等多种微生物与宿主共同构成的动态平衡状态^[1]。作为人体重要屏障,口腔微生态在维持局部健康中发挥着关键作用^[2]。同时,微生物及其代谢产物可通过吞咽、血液循环等途径向全身迁移,参与系统性炎症反应及远端器官功能调控,形成“口腔-肠道轴”及“口腔-全身轴”等多维度的微生态调控网络^[3-5]。随着全球人口老龄化进程加速,衰老导致的宿主生理性退变深刻影响着这一稳

态平衡。衰老过程常伴随免疫监视功能下降、口腔黏膜屏障减弱、唾液腺分泌衰退以及口腔自洁能力降低^[6-8]。这些组织与免疫层面的生理退化显著改变了口腔微生态的定植环境,驱动微生物群落结构发生重塑,突出表现为核心有益共生菌的丰度下降与潜在致病菌群的富集^[9]。

在此背景下,老年个体的口腔微生态失衡不仅直接参与龋病、牙周炎及口腔黏膜病等局部疾病的发生发展^[10],还可通过细菌移位、炎症介质释放等途径影响远端器官,促进神经退行性疾病、心血管疾病、糖尿病等多种衰老相关系统性疾病的发展^[11-12]。研究表明,牙周炎是最常见的年龄相关性炎症性疾病之一^[13],与炎症性肠病、糖尿病

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等多种炎症性疾病并存^[14]。鉴于口腔微生物失调在老年局部病变与全身生理衰退中的重要作用,探究衰老对口腔微生态的影响,对于揭示老年系统性疾病的高发机制具有重要的学术价值。基于此,本文以衰老驱动的口腔生理微环境改变为切入点,梳理健康与非健康老龄化人群中口腔微生态的群落演替特征,重点阐述其在老年局部疾病及全身系统性疾病中的作用机制,以期延缓衰老相关疾病的发生、发现早期预警生物标志物及开发基于“微生态重塑”的老年健康干预策略提供理论依据。

1 老年人群口腔微生态群落结构特征

衰老通常伴随机体微生物群落多样性的波动与生态恢复力的下降,而口腔微生态的演替特征在健康老龄化与病理性老龄化人群中呈现出截然不同的轨迹^[14]。通过高通量测序解析不同健康状态下老年个体的口腔菌群结构,是揭示衰老与口腔稳态失衡内在联系的关键环节。

1.1 健康老龄化人群的口腔微生态变化特征

衰老往往伴随着微生物多样性与生态恢复力的降低,其中口腔微生态的失衡被认为是影响老年健康的重要因素之一^[15]。健康老年人的口腔微生态变化主要表现为菌群多样性和组成的动态调整,但研究结果尚不一致。部分研究表明,老年人唾液或口咽部菌群的 α 多样性较年轻人增加,提示微生物丰富度和均匀度提高;而另一些研究则发现多样性下降,认为衰老伴随生态稳定性减弱^[16]。此外,还有研究指出口腔微生态多样性可能呈U型变化趋势,即中年最低而老年再次升高^[17]。这种差异可能与研究人群、取样部位、饮食结构及牙齿数量等多种混杂因素有关。尽管如此,健康老年人的口腔微生态菌群多样性虽较青年人有所变化,但整体仍保持一定的生态平衡。研究表明,长寿组和老年组的口腔核心细菌属丰度均随年龄增长而降低,但在长寿群体中下降幅度相对缓和,核心菌群结构较为稳定,且部分与健康相关的共生菌仍保持一定丰度,提示其口腔微生态可能具有更强的稳态维持能力^[18]。

在属水平上,健康老年人群口腔中阿洛普雷沃菌属(*Alloprevotella*)和韦荣球菌属(*Veillonella*)随年龄增加而减少,而噬二氧化碳纤维菌属(*Capnocytophaga*)、营养缺陷菌属(*Abiotrophia*)、聚集杆菌属(*Aggregatibacter*)、奈瑟菌属(*Neisseria*)、卟啉单胞菌属(*Porphyromonas*)和坦纳菌属(*Tannerella*)则随年龄增加而升高^[19]。此外,健康老年人口腔内某些特定菌属的富集具有双重生态学意义。例如,乳酸杆菌(*Lactobacillus*)在健康老年人口腔中的丰度显著高于年轻人群^[20]。在生态平衡状态下,其代谢产物可通过竞争性抑制变异链球菌(*Streptococcus*

mutans, *S. mutans*)等高致龋菌的过度定植;但当局部微环境发生剧烈波动时,该菌亦可能加速老年根面龋的发生与发展^[21]。综上,健康长寿人群的口腔微生态呈现出致病菌轻度增加与共生菌适应性调节相协同的复杂特征,这种相对平稳的微生态过渡,为实现健康老龄化提供了重要的局部微生态基础。

1.2 病理性衰老状态下的口腔微生态特征

与健康老龄化人群相比,疾病老年人群表现出更为显著的口腔微生态紊乱。研究证实,在属水平上,除阿洛普雷沃菌属(*Alloprevotella*)外,疾病老年人群的消化球菌属(*Peptococcus*)随年龄增加而显著降低,而链球菌属(*Streptococcus*)和韦荣球菌属(*Veillonella*)则随年龄增加而显著升高。值得注意的是,韦荣球菌属(*Veillonella*)在健康老龄化人群与疾病老年人群中随年龄增长所呈现的丰度变化趋势截然相反,提示其可能成为疾病老年人群口腔微生态失衡的重要研究靶点^[19]。

至少存在一种重大疾病(如肿瘤、神经系统疾病、心血管疾病、慢性肺部疾病、糖尿病/糖尿病并发症)的老年人,其口腔菌群 α 多样性通常降低,微生态稳定性下降,某些关键共生菌如嗜血杆菌属(*Haemophilus*)、梭杆菌属(*Fusobacterium*)和噬二氧化碳纤维菌属(*Capnocytophaga*)等也显著减少^[14],从而削弱了对致病菌的竞争能力。这些变化提示疾病状态可能加速口腔微生态的失衡。同时,疾病老年人常伴随牙齿缺失、咀嚼功能下降及唾液分泌减少,这些因素可改变口腔生态位,进而影响菌群组成;口腔功能下降还可通过改变营养摄入和代谢状态,间接影响微生态平衡,进一步加重全身衰弱状态。更为关键的是,非健康老龄化人群口腔中特定致病菌的富集与其全身疾病的进展呈高度正相关。例如,在伴有衰弱综合征或患有吸入性肺炎的老年患者中,口腔内链球菌属(*Streptococcus*)及韦荣球菌属(*Veillonella*)等可能移位至下呼吸道的病原体比例异常升高^[22];而在阿尔茨海默病、肌少症等退行性疾病患者中,牙龈卟啉单胞菌(*Porphyromonas gingivalis*, *P. gingivalis*)等牙周核心致病菌的检出频率及丰度显著增加^[10]。这些富集的致病菌不仅加剧了局部组织破坏,其分泌的毒力因子与促炎介质更成为驱动全身系统性疾病恶化的重要外源性刺激。因此,病理性衰老中的口腔微生态失衡已超越单纯的局部病理现象,成为加速全身功能衰竭的关键风险因素。

2 衰老对口腔微生态定植环境的生理性影响

口腔微生态是由多种微生物与宿主共同构成的复杂

生态系统,其中定植的微生物包括细菌、病毒、真菌、古细菌和原生动物,其中以细菌为优势群体^[1,23-24]。现有研究表明,口腔内可定植的微生物种类超过700种,不同微生物在长期进化过程中形成了相对稳定的共生关系^[25]。

根据解剖结构及微环境差异,口腔内可被划分为多个相互独立但又彼此联系的生态位,如龈上与龈下、舌背、颊黏膜及唾液等,这些生态位具有各自特异性的菌群组成与结构特征。

2.1 唾液腺功能退变改变微生物定植生态位

唾液在维持口腔微环境的理化稳态,如pH缓冲、抗菌物质输送及机械清洗等方面发挥着不可替代的作用。随着年龄增长,老年人群常出现唾液分泌量减少及自洁能力降低^[6-8];此外,老年个体常因共患多种系统性疾病而长期服药,药物的副作用进一步加剧了唾液流量的降低^[26]。唾液流速与缓冲能力的下降直接打破了局部的酸碱稳态,不仅削弱了对致病微生物的抑制作用,还促使菌群结构向更厌氧或耐酸的病理群落演替^[27]。

牙齿为微生物定植提供了独特的硬组织表面,而衰老伴随的牙齿缺失显著降低了口腔生态位的多样性,直接导致局部微生物群落结构的转变^[28]。对于佩戴义齿的老年人,义齿基托的覆盖不仅物理性阻断了唾液对局部黏膜的冲刷与缓冲,还为微生物提供了新的附着界面^[29]。此外,老年人因手部灵活性下降导致日常口腔卫生维护能力受限,这一行为学因素进一步加剧了衰老过程中的微生物演替与失调。

2.2 口腔黏膜免疫衰老影响口腔屏障功能

宿主免疫系统及黏膜屏障是监控和限制致病菌过度增殖的核心机制。在老龄化背景下,口腔黏膜的物理屏障功能发生退行性减弱,宿主局部免疫力显著下降。这种增龄性的免疫功能衰退使得宿主对口腔微生态的监视与调控效能大打折扣,原本能够被健康免疫系统有效识别并控制的条件致病菌,在老年免疫监视减弱的微环境中获得了逃逸和扩张的机会。例如,老年个体T细胞表现出典型的细胞衰老特征,包括程序性死亡受体1(programmed cell death protein 1, PD-1)和细胞毒性T淋巴细胞相关蛋白4(cytotoxic T-lymphocyte-associated protein 4, CTLA-4)等免疫检查点分子表达升高、增殖能力下降,以及衰老标志物p16和p21表达增加,从而形成免疫抑制性微环境,削弱机体对病原体和肿瘤细胞的免疫监视能力^[30]。

同时,衰老状态下组织修复能力的降低以及宿主环境因素(如遗传、代谢状态和整体健康状况的改变)的综合作用,使得宿主与微生物之间的动态平衡被打破^[7]。例如,牙

龈卟啉单胞菌(*Porphyromonas gingivalis*, *P. gingivalis*)可感染树突状细胞并诱导细胞衰老,通过衰老相关分泌表型(senescence-associated secretory phenotype, SASP)的传播导致局部免疫功能紊乱^[31]。宿主防御机制的削弱与病原微生物的富集形成恶性循环,不仅直接改变了口腔微生态的组成,也为后续局部炎症的暴发及向全身靶器官的侵袭创造了条件。

3 口腔微生态失调与老年口腔疾病

衰老过程中口腔微生态的显著改变——包括群落多样性的波动、功能代谢的重塑及致病菌比例的升高——并非仅停留在分子与生态学层面,而是直接转化为局部组织的破坏^[32-33]。老年人群中高发的口腔疾病,如重度牙周炎、根面龋及口腔黏膜感染等,本质上均为特定类型微生态失调的临床表现。

3.1 牙周病

牙周炎是老年人群中最普遍的慢性炎症性口腔疾病,也是导致老年人牙齿松动和最终脱落的首要原因。随年龄增长,中性粒细胞免疫功能下降,削弱了宿主对牙周菌群的免疫监视和清除能力,使得牙龈沟及牙周袋等低氧微环境中的致病共生菌,如牙龈卟啉单胞菌(*Porphyromonas gingivalis*, *P. gingivalis*)、具核梭杆菌(*Fusobacterium nucleatum*, *F. nucleatum*)等逐渐占据主导地位,形成高度致病性的炎性微生态^[34]。失衡的菌群持续激活宿主炎症反应,促进白细胞介素-1 β (interleukin-1 β , IL-1 β)、白细胞介素-6(interleukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)等炎症因子释放,增强核因子 κ B受体活化因子配体(receptor activator of nuclear factor- κ B ligand, RANKL)介导的牙槽骨吸收;而持续炎症又进一步加剧中性粒细胞功能障碍,形成菌群失衡与慢性炎症相互促进的正反馈循环,最终推动牙周炎持续进展^[35]。这些富集的病原体及其分泌的毒力因子(如脂多糖、牙龈蛋白酶等)持续突破老化的牙周上皮屏障,过度激活宿主的破坏性免疫应答^[36]。此外,严重的牙周感染如同一个炎症储库,显著增加老年人罹患动脉粥样硬化及其他系统性疾病的风险^[37]。

3.2 根面龋

根面龋是老年群体的特征性牙体硬组织疾病,其发病与牙周炎及微生态失调密切相关^[38]。首先,老年人普遍存在的牙周炎或牙龈生理性退缩,导致缺乏牙釉质保护的牙根面广泛暴露。其次,在唾液流量及缓冲能力双重下降的微环境中,口腔菌群逐渐向“产酸-耐酸”型演替,大量产酸菌如变异链球菌(*Streptococcus mutans*, *S.*

mutans)通过持续发酵碳水化合物产生有机酸,降低局部 pH 值,促进牙骨质和牙本质脱矿,从而驱动根面龋的发生与发展;同时,这些细菌在粗糙的暴露牙根表面定植并形成致病性生物膜^[27]。由于牙根面的临界脱矿 pH 值远高于牙釉质,其对酸性环境的抵抗力极为脆弱^[39],导致老年根面龋不仅发病率高,且进展迅速。

3.3 真菌性口炎

除细菌群落的失衡外,衰老引发的口腔微生态紊乱同样波及真菌群落。健康口腔生态系统中,细菌与真菌存在相互拮抗的制约关系,但在老年宿主的口腔中,这种生态制约被打破^[5]。白色念珠菌(*Candida albicans*, *C. albicans*)作为最常见的机会致病真菌,可趁机过度增殖,该现象在佩戴可摘义齿的老年人群中尤为突出。义齿基托阻隔唾液冲刷与机械自洁,营造局部微缺氧及酸性环境,为 *C. albicans* 的附着与定植提供理想条件,从而导致口腔念珠菌病的发生^[40]。

4 老年口腔微生态失调对全身系统性影响

老年个体的口腔微生态失调不仅局限于局部病变,失衡的微生物群落及其代谢产物可通过受损的口腔黏膜屏障进入血液循环,或通过吞咽沿消化道及呼吸道向下迁移,进而对远端靶器官产生深远影响。这种以口腔致病菌播散为特征的机制,深度参与了老年人多种系统性疾病的发生与发展

4.1 老年口腔微生态失调与神经系统疾病

阿尔茨海默病是一种神经系统退行性疾病^[41]。研究报告,慢性牙周炎病史超过 10 年者患阿尔茨海默病的风险增加,同时高血脂、抑郁和创伤性脑损伤的患病率也升高^[42]。一方面,老年人口腔微生态失衡后易致厌氧微生物增殖,促使 IL-1 β 、IL-6、TNF- α 等促炎细胞因子水平升高,引发炎症反应并削弱血脑屏障完整性^[43]。另一方面,丰度持续增加的致病菌(如 *P. gingivalis*)可经受损的血脑屏障进入大脑,影响小胶质细胞活化,促进 β -淀粉样蛋白(amyloid β -protein, A β)沉积及微管相关蛋白(Tau)磷酸化,这些因素可能共同促进阿尔茨海默病的病理进展^[44-45]。

4.2 老年口腔微生态失调与心血管疾病

牙周炎是心血管疾病的重要危险因素^[46-47],老年口腔微生态失调后易患慢性牙周炎。牙周致病菌可进入全身循环系统,导致菌血症或异位定植于其他器官。牙周炎患者发生动脉粥样硬化的风险显著高于非牙周炎者^[48]。牙周相关细菌可破坏机体免疫稳态,刺激 TNF- α 、IL-1 β 、IL-6 等炎症因子产生,通过 Toll 样受体/核因子 κ B(Toll-like receptor/nuclear factor- κ B, TLR/NF- κ B)等炎症信号通路

放大免疫反应,引起血管内皮损伤,促进动脉粥样硬化斑块形成^[49]。研究显示,心肌梗死患者(平均年龄 59 岁)口腔微生物组中厚壁菌门和嗜血杆菌属丰度较低,且血栓形成与口腔菌群丰度降低相关^[50]。

4.3 老年口腔微生态失调与消化系统疾病

口腔微生态与消化道疾病密切相关^[51],具核梭杆菌(*Fusobacterium nucleatum*, *F. nucleatum*)被认为是炎症性肠病的关键致病菌之一。研究发现, *F. nucleatum* 在老年人胃肠道中的丰度高于年轻人,其在肠道中的移位或过度增殖可能加剧肠道菌群失调与炎症^[52]。这种微生态失衡可增加胃肠道黏膜通透性,促进口腔致病菌向血液移位^[53]。此外,老年人口腔中富集的 *P. gingivalis* 等牙周致病菌可调控免疫应答并诱导肠道炎症,在牙周炎与肠道炎症性疾病之间建立潜在联系^[54]。*P. gingivalis* 还可通过诱导肝脏氧化应激和脂质过氧化,抑制谷胱甘肽过氧化物酶 4/溶质载体家族 7 成员 11(glutathione peroxidase 4/solute carrier family 7 member 11, GPX4/SLC7A11)抗铁死亡系统,促进肝细胞铁死亡(ferroptosis),加速非酒精性脂肪性肝病的发生与进展^[55]。综上,老年口腔微生态失调可通过菌群迁移、炎症调控、免疫失衡及代谢改变等多种机制,参与炎症性肠病及消化道肿瘤等疾病的发生发展。

4.4 老年口腔微生态失调与类风湿关节炎

类风湿关节炎是一种以全身关节炎症为特征的自身免疫性疾病,在老年人中的发病率逐渐升高^[56]。大量研究表明,牙周炎与类风湿关节炎在发病机制、遗传易感性、治疗策略及病理表现(如软组织损伤、骨侵蚀和炎症细胞因子分泌)等方面具有诸多相似性,提示两者密切相关^[57]。老年口腔微生态失调后易患慢性牙周炎,实验证实 *P. gingivalis* 入侵可破坏免疫细胞发育,促进破骨细胞生成,导致骨丢失^[58]。此外,类风湿关节炎患者血清和关节液中可检测到 *P. gingivalis* DNA 及高滴度抗牙龈卟啉单胞菌抗体^[42]。

5 总结与展望

全球人口老龄化持续加剧,衰老相关疾病的防控已成为重要的公共卫生议题。口腔微生态作为人体微生态的重要组成部分,在衰老及相关疾病的发生发展中发挥重要作用。本文梳理了衰老过程中健康和疾病状态下的口腔微生态动态变化特征,其中韦荣球菌属(*Veillonella*)在两类人群中的显著差异值得深入探究;论述了衰老对口腔微生态定植环境的生理性影响;阐述了老年口腔微生态失衡在口腔及全身系统性疾病中的重要作用, *P.*

*gingivalis*和*F. nucleatum*等已被证实参与多种全身系统性疾病的发生发展。同时,口腔微生态在疾病预防、治疗及预后评估中的潜在价值正逐步应用于临床,高通量测序可于龋病发生前客观评估老年人牙体龋坏风险^[59];在消化道肿瘤防治中,清除口腔幽门螺杆菌有助于老年人胃部肿瘤的早期预防^[60]。

然而,现有研究仍存在一定局限,如因果关系证据不足、机制研究尚不深入及个体差异较大等问题,尤以健康长寿人群的研究最为匮乏。未来应结合多组学技术与纵向队列研究,深入解析口腔微生态在衰老及疾病中的动态变化及其分子机制,推动其在促进健康老龄化方面的深入研究与临床应用。

* * *

作者贡献声明 何卓家负责调查研究、初稿写作和审读与编辑写作,李栋梁负责初稿写作和审读与编辑写作,彭显负责论文构思、经费获取、提供资源、监督指导和审读与编辑写作。所有作者已经同意将文章提交给本刊,且对将要发表版本进行最终定稿,并同意对工作的所有方面负责。

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参 考 文 献

- [1] Baker J L, Mark Welch J L, Kauffman K M, *et al.* The oral microbiome: diversity, biogeography and human health[J]. *Nat Rev Microbiol*, 2024, 22(2): 89-104. DOI: [10.1038/s41579-023-00963-6](https://doi.org/10.1038/s41579-023-00963-6).
- [2] Guo Z L, Cui M W, Dong Y L, *et al.* The oral microbiome as a regulatory hub for systemic health: a systematic review of mechanistic links and clinical implications[J/OL]. *J Oral Microbiol*, 2026, 18(1): 2635233. <https://doi.org/10.1080/20002297.2026.2635233>.
- [3] Schmidt T S, Hayward M R, Coelho L P, *et al.* Extensive transmission of microbes along the gastrointestinal tract[J/OL]. *eLife*, 2019, 8: e42693. <https://doi.org/10.7554/eLife.42693>.
- [4] Kitamoto S, Nagao-Kitamoto H, Jiao Y, *et al.* The intermucosal connection between the mouth and gut in commensal pathobiont-driven colitis[J]. *Cell*, 2020, 182(2): 447-462, e14. DOI: [10.1016/j.cell.2020.05.048](https://doi.org/10.1016/j.cell.2020.05.048).
- [5] Deng L, Guan G, Cannon R D, *et al.* Age-related oral microbiota dysbiosis and systemic diseases[J]. *Microb Pathog*, 2025, 205: 107717. DOI: [10.1016/j.micpath.2025.107717](https://doi.org/10.1016/j.micpath.2025.107717).
- [6] Kroemer G, Maier A B, Cuervo A M, *et al.* From geroscience to precision geromedicine: understanding and managing aging[J]. *Cell*, 2025, 188(8): 2043-2062. DOI: [10.1016/j.cell.2025.03.011](https://doi.org/10.1016/j.cell.2025.03.011).
- [7] López-Otín C, Blasco M A, Partridge L, *et al.* Hallmarks of aging: an expanding universe[J]. *Cell*, 2023, 186(2): 243-278. DOI: [10.1016/j.cell.2022.11.001](https://doi.org/10.1016/j.cell.2022.11.001).
- [8] Toan N K, Ahn S G. Aging-related metabolic dysfunction in the salivary gland: a review of the literature[J]. *Int J Mol Sci*, 2021, 22(11): 5835. DOI: [10.3390/ijms22115835](https://doi.org/10.3390/ijms22115835).
- [9] Lamont R J, Koo H, Hajishengallis G. The oral microbiota: dynamic communities and host interactions[J]. *Nat Rev Microbiol*, 2018, 16(12): 745-759. DOI: [10.1038/s41579-018-0089-x](https://doi.org/10.1038/s41579-018-0089-x).
- [10] Dominy S S, Lynch C, Ermini F, *et al.* *Porphyromonas gingivalis* in Alzheimer's disease brains: evidence for disease causation and treatment with small-molecule inhibitors[J/OL]. *Sci Adv*, 2019, 5(1): eaau3333. <https://doi.org/10.1126/sciadv.aau3333>.
- [11] Schenkein H A, Loos B G. Inflammatory mechanisms linking periodontal diseases to cardiovascular diseases[J]. *J Clin Periodontol*, 2013, 40(Suppl 14): S51-S69. DOI: [10.1111/jcpe.12060](https://doi.org/10.1111/jcpe.12060).
- [12] Zhang P, Wang Q, Nie L, *et al.* Hyperglycemia-induced inflamm-aging accelerates gingival senescence via NLRC4 phosphorylation[J]. *J Biol Chem*, 2019, 294(49): 18807-18819. DOI: [10.1074/jbc.RA119.010648](https://doi.org/10.1074/jbc.RA119.010648).
- [13] Hajishengallis G, Chavakis T. Local and systemic mechanisms linking periodontal disease and inflammatory comorbidities[J]. *Nat Rev Immunol*, 2021, 21(7): 426-440. DOI: [10.1038/s41577-020-00488-6](https://doi.org/10.1038/s41577-020-00488-6).
- [14] Singh H, Torralba M G, Moncera K J, *et al.* Gastro-intestinal and oral microbiome signatures associated with healthy aging[J]. *GeroScience*, 2019, 41(6): 907-921. DOI: [10.1007/s11357-019-00098-8](https://doi.org/10.1007/s11357-019-00098-8).
- [15] Carbone E, Fabrizi E, Rivabene R, *et al.* Human oral microbiome in aging: a systematic review[J]. *Mech Ageing Dev*, 2025, 226: 112080. DOI: [10.1016/j.mad.2025.112080](https://doi.org/10.1016/j.mad.2025.112080).
- [16] Liu S, Wang Y, Zhao L, *et al.* Microbiome succession with increasing age in three oral sites[J]. *Aging (Albany NY)*, 2020, 12(9): 7874-7907. DOI: [10.18632/aging.103108](https://doi.org/10.18632/aging.103108).
- [17] Xu X, He J, Xue J, *et al.* Oral cavity contains distinct niches with dynamic microbial communities[J]. *Environ Microbiol*, 2015, 17(3): 699-710. DOI: [10.1111/1462-2920.12502](https://doi.org/10.1111/1462-2920.12502).
- [18] Ji Y, Sun H, Wang Y, *et al.* Characterizing the oral and gastrointestinal microbiome associated with healthy aging: insights from long-lived populations in northeastern China[J]. *GeroScience*, 2024, 47(2): 2275-2292. DOI: [10.1007/s11357-024-01419-2](https://doi.org/10.1007/s11357-024-01419-2).
- [19] Declercq V, Wright R J, Nearing J T, *et al.* Oral microbial signatures associated with age and frailty in Canadian adults[J/OL]. *Sci Rep*, 2024, 14: 9685. <https://doi.org/10.1038/s41598-024-60409-8>.
- [20] Percival R S, Challacombe S J, Marsh P D. Age-related microbiological changes in the salivary and plaque microflora of healthy adults[J]. *J Med Microbiol*, 1991, 35(1): 5-11. DOI: [10.1099/00222615-35-1-5](https://doi.org/10.1099/00222615-35-1-5).
- [21] Spatafora G, Li Y, He X, *et al.* The evolving microbiome of dental caries[J/OL]. *Microorganisms*, 2024, 12(1): 121. <https://doi.org/10.3390/microorganisms12010121>.
- [22] Akata K, Noguchi S, Kawanami T, *et al.* Microbiology of aspiration pneumonia[J]. *J UOEH*, 2019, 41(2): 185-195. DOI: [10.7888/juoeh.41.185](https://doi.org/10.7888/juoeh.41.185).
- [23] Santacrose L, Passarelli P C, Azzolino D, *et al.* Oral microbiota in human health and disease: a perspective[J]. *Exp Biol Med*, 2023, 248(15): 1288-1301. DOI: [10.1177/15353702231187645](https://doi.org/10.1177/15353702231187645).
- [24] Silva D N de A, Casarin M, Monajemzadeh S, *et al.* The microbiome in periodontitis and diabetes[J/OL]. *Front Oral Health*, 2022, 3: 859209. <https://doi.org/10.3389/froh.2022.859209>.
- [25] Deo P N, Deshmukh R. Oral microbiome: unveiling the fundamentals[J]. *J Oral Maxillofac Pathol*, 2019, 23(1): 122-128. DOI: [10.4103/jomfp.JOMFP_304_18](https://doi.org/10.4103/jomfp.JOMFP_304_18).
- [26] Li X, Liu Y, Yang X, *et al.* The oral microbiota: community composition, influencing factors, pathogenesis, and interventions[J/OL]. *Front Microbiol*, 2022, 13: 895537. <https://doi.org/10.3389/fmicb.2022.895537>.
- [27] Prodan A, Brand H S, Lichtenberg A J M, *et al.* Interindividual variation, correlations, and sex-related differences in the salivary biochemistry of young healthy adults[J]. *Eur J Oral Sci*, 2015, 123(3): 149-157. DOI: [10.1111/eos.12182](https://doi.org/10.1111/eos.12182).
- [28] Kazarina A, Kuzmicka J, Bortkevica S, *et al.* Oral microbiome variations related to ageing: possible implications beyond oral health[J]. *Arch Microbiol*, 2023, 205(4): 116. DOI: [10.1007/s00203-023-03464-5](https://doi.org/10.1007/s00203-023-03464-5).
- [29] Sarafidou K, Alexakou E, Talioti E, *et al.* The oral microbiome in older adults: a state-of-the-art review[J/OL]. *Arch Gerontol Geriatr Plus*, 2024, 1(4): 100061. <https://doi.org/10.1016/j.aggp.2024.100061>.
- [30] Elsayed R, Elashiry M, Liu Y, *et al.* Microbially-induced exosomes from

- dendritic cells promote paracrine immune senescence: novel mechanism of bone degenerative disease in mice[J]. *Aging Dis*, 2023, 14(1): 136-151. DOI: [10.14336/AD.2022.0623](https://doi.org/10.14336/AD.2022.0623).
- [31] Elsayed R, Elashiry M, Liu Y, *et al.* *Porphyromonas gingivalis* provokes exosome secretion and paracrine immune senescence in bystander dendritic cells[J/OL]. *Front Cell Infect Microbiol*, 2021, 11: 669989. <https://doi.org/10.3389/fcimb.2021.669989>.
- [32] 徐欣, 何金枝, 周学东. 口腔微生物群落在口腔与全身疾病预警中的作用[J]. *华西口腔医学杂志*, 2015, 33(6): 555-560. DOI: [10.7518/hxkq.2015.06.001](https://doi.org/10.7518/hxkq.2015.06.001).
- Xu X, He J Z, Zhou X D. Oral microbiota: a promising predictor of human oral and systemic diseases[J]. *West China J Stomatol*, 2015, 33(6): 555-560. DOI: [10.7518/hxkq.2015.06.001](https://doi.org/10.7518/hxkq.2015.06.001).
- [33] 李雅卓, 陈雨晴, 陈帅, 等. 衰老背景下口腔微生态失调与功能减退在阿尔茨海默病进程中的作用[J]. *四川大学学报(医学版)*, 2026, 57(1): 56-64. DOI: [10.12182/20260160510](https://doi.org/10.12182/20260160510).
- Li Y Z, Chen Y Q, Chen S, *et al.* Aging-Associated Oral Microbiota Dysbiosis and Hypofunction: Their Role in Alzheimer's Disease Pathogenesis[J]. *J Sichuan Univ (Med Sci)*, 2026, 57(1): 56-64. DOI: [10.12182/20260160510](https://doi.org/10.12182/20260160510).
- [34] Yue Z, Li C, Yan F, *et al.* The oral microbiome in aging: a window into health and longevity[J/OL]. *J Oral Microbiol*, 2025, 17(1): 2589648. <https://doi.org/10.1080/20002297.2025.2589648>.
- [35] Wang Z, Saxena A, Yan W, *et al.* The impact of aging on neutrophil functions and the contribution to periodontitis[J]. *Int J Oral Sci*, 2025, 17: 10. DOI: [10.1038/s41368-024-00332-w](https://doi.org/10.1038/s41368-024-00332-w).
- [36] Takeuchi H, Nakamura E, Yamaga S, *et al.* *Porphyromonas gingivalis* infection induces lipopolysaccharide and peptidoglycan penetration through gingival epithelium[J/OL]. *Front Oral Health*, 2022, 3: 845002. <https://doi.org/10.3389/froh.2022.845002>.
- [37] Ren Y, Chen M, Wang Z, *et al.* Oral microbiota in aging and diseases[J]. *Life Med*, 2024, 3(3): lnae024. DOI: [10.1093/lifemedi/lnae024](https://doi.org/10.1093/lifemedi/lnae024).
- [38] Yu L X, Wang X, Feng X P, *et al.* The relationship between different types of caries and periodontal disease severity in middle-aged and elderly people: findings from the 4th national oral health survey of China[J/OL]. *BMC Oral Health*, 2021, 21(1): 229. <https://doi.org/10.1186/s12903-021-01585-1>.
- [39] Okuyama K, Yanamoto S. Saliva in balancing oral and systemic health, oral cancer, and beyond: a narrative review[J/OL]. *Cancers*, 2024, 16(24): 4276. <https://doi.org/10.3390/cancers16244276>.
- [40] Altarawneh S, Bencharit S, Mendoza L, *et al.* Clinical and histological findings of denture stomatitis as related to intraoral colonization patterns of *C. albicans*, salivary flow, and dry mouth[J/OL]. *J Prosthodont*, 2013, 22(1): 13-22. <https://doi.org/10.1111/j.1532-849X.2012.00906.x>.
- [41] Visentin D, Gobin I, Maglica Ž. Periodontal pathogens and their links to neuroinflammation and neurodegeneration[J/OL]. *Microorganisms*, 2023, 11(7): 1832. <https://doi.org/10.3390/microorganisms11071832>.
- [42] Li Y, Guo R, Oduro P K, *et al.* The relationship between *Porphyromonas gingivalis* and rheumatoid arthritis: a meta-analysis[J/OL]. *Front Cell Infect Microbiol*, 2022, 12: 956417. <https://doi.org/10.3389/fcimb.2022.956417>.
- [43] Shoemark D K, Allen S J. The microbiome and disease: reviewing the links between the oral microbiome, aging, and Alzheimer's disease[J]. *J Alzheimers Dis*, 2014, 43(3): 725-738. DOI: [10.3233/JAD-141170](https://doi.org/10.3233/JAD-141170).
- [44] Zeng F, Liu Y, Huang W, *et al.* Receptor for advanced glycation end products up-regulation in cerebral endothelial cells mediates cerebrovascular-related amyloid β accumulation after *Porphyromonas gingivalis* infection[J/OL]. *J Neurochem*, 2021, 158(3): 724-736. <https://doi.org/10.1111/jnc.15096>.
- [45] Li R, Wang J, Xiong W, *et al.* The oral-brain axis: can periodontal pathogens trigger the onset and progression of Alzheimer's disease?[J/OL]. *Front Microbiol*, 2024, 15: 1358179. <https://doi.org/10.3389/fmicb.2024.1358179>.
- [46] Habashneh R A, Khader Y S, Alhumouz M K, *et al.* The association between inflammatory bowel disease and periodontitis among Jordanians: a case-control study[J]. *J Periodontol Res*, 2012, 47(3): 293-298. DOI: [10.1111/j.1600-0765.2011.01431.x](https://doi.org/10.1111/j.1600-0765.2011.01431.x).
- [47] Gualtero D F, Lafaurie G I, Buitrago D M, *et al.* Oral microbiome mediated inflammation, a potential inductor of vascular diseases: a comprehensive review[J/OL]. *Front Cardiovasc Med*, 2023, 10: 1250263. <https://doi.org/10.3389/fcvm.2023.1250263>.
- [48] Sreedevi M, Ramesh A, Dwarakanath C. Periodontal status in smokers and nonsmokers: a clinical, microbiological, and histopathological study[J/OL]. *Int J Dent*, 2012, 2012: 571590. <https://doi.org/10.1155/2012/571590>.
- [49] Huang X, Xie M, Lu X, *et al.* The roles of periodontal bacteria in atherosclerosis[J/OL]. *Int J Mol Sci*, 2023, 24(16): 12861. <https://doi.org/10.3390/ijms241612861>.
- [50] Kwun J S, Kang S H, Lee H J, *et al.* Comparison of thrombus, gut, and oral microbiomes in Korean patients with ST-elevation myocardial infarction: a case-control study[J/OL]. *Exp Mol Med*, 2020, 52(12): 2069-2079. <https://doi.org/10.1038/s12276-020-00543-1>.
- [51] Adil N A, Omo-Erigbe C, Yadav H, *et al.* The oral-gut microbiome-brain axis in cognition[J/OL]. *Microorganisms*, 2025, 13(4): 814. <https://doi.org/10.3390/microorganisms13040814>.
- [52] Iwachi M, Horigome A, Ishikawa K, *et al.* Relationship between oral and gut microbiota in elderly people[J/OL]. *Immun Inflamm Dis*, 2019, 7(3): 229-236. <https://doi.org/10.1002/iid3.266>.
- [53] Tan X, Wang Y, Gong T. The interplay between oral microbiota, gut microbiota and systematic diseases[J/OL]. *J Oral Microbiol*, 2023, 15(1): 2213112. <https://doi.org/10.1080/20002297.2023.2213112>.
- [54] Tanwar H, Gnanasekaran J M, Allison D, *et al.* Unraveling the link between periodontitis and inflammatory bowel disease: challenges and outlook[J/OL]. *ArXiv*, 2023, 2308.10907v1. <https://doi.org/10.48550/arXiv.2308.10907>.
- [55] Yao C, Lan D, Li X, *et al.* *Porphyromonas gingivalis* is a risk factor for the development of nonalcoholic fatty liver disease via ferroptosis[J]. *Microbes Infect*, 2023, 25(1/2): 105040. DOI: [10.1016/j.micinf.2022.105040](https://doi.org/10.1016/j.micinf.2022.105040).
- [56] Serhal L, Lwin M N, Holroyd C, *et al.* Rheumatoid arthritis in the elderly: characteristics and treatment considerations[J]. *Autoimmun Rev*, 2020, 19(6): 102528. DOI: [10.1016/j.autrev.2020.102528](https://doi.org/10.1016/j.autrev.2020.102528).
- [57] Hitchon C A, Chandad F, Ferucci E D, *et al.* Antibodies to *Porphyromonas gingivalis* are associated with anticitrullinated protein antibodies in patients with rheumatoid arthritis and their relatives[J]. *J Rheumatol*, 2010, 37(6): 1105-1112. DOI: [10.3899/jrheum.091323](https://doi.org/10.3899/jrheum.091323).
- [58] Zhao Y, Li Z, Su L, *et al.* Characterization and regulation of osteoclast precursors following chronic *Porphyromonas gingivalis* infection[J]. *J Leukoc Biol*, 2020, 108(4): 1037-1050. DOI: [10.1002/jlb.1hi0620-230r](https://doi.org/10.1002/jlb.1hi0620-230r).
- [59] Teng F, Yang F, Huang S, *et al.* Prediction of early childhood caries via spatial-temporal variations of oral microbiota[J]. *Cell Host Microbe*, 2015, 18(3): 296-306. DOI: [10.1016/j.chom.2015.08.005](https://doi.org/10.1016/j.chom.2015.08.005).
- [60] Song H Y, Li Y. Can eradication rate of gastric *Helicobacter pylori* be improved by killing oral *Helicobacter pylori*?[J/OL]. *World J Gastroenterol*, 2013, 19(39): 6645-6650. <https://doi.org/10.3748/wjg.v19.i39.6645>.

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