



口腔微生物组: 稳态维持、疾病关联及致病机制*

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【摘要】 口腔微生物组是一个复杂且高度结构化的生态系统,由细菌、真菌、病毒等多种微生物构成,与宿主形成密切的共生关系。其在牙齿、黏膜等不同生态位点的组成受年龄、遗传、生活方式等多因素调控,稳定的微生物群落是维持口腔及全身健康的重要屏障。本综述系统探讨了口腔微生物组在健康与疾病状态下的结构与功能,重点分析了菌斑生物膜的形成机制及其在龋病、牙周炎发生发展中的关键作用。龋病主要由产酸、耐酸菌如变形链球菌、乳酸杆菌等主导,伴随微环境酸化与釉质脱矿;牙周炎则与龈下菌斑中“红色复合体”等病原微生物的富集及宿主免疫失调密切相关。此外,口腔微生物的生态失调,特别是核梭杆菌、牙龈卟啉单胞菌等病原体的异常增殖,不仅参与口腔鳞癌的发生发展,亦可通过炎症诱导、免疫抑制及菌群移位等机制,与心血管疾病、糖尿病、类风湿关节炎及胰腺癌等多种全身系统性疾病密切相关。系统揭示口腔微生物组的生态学及致病机制,将为维护口腔微生态稳态、防治口腔及全身相关性疾病提供重要的理论依据。

【关键词】 口腔微生物组 菌群失调 牙周炎 龋病 综述

The Oral Microbiome: Maintenance of Homeostasis, Disease Associations, and Mechanisms of Pathogenesis

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This work was supported by the National Key Research and Development Program of China (No. 2022YFC2405900, No. 2022YFC2405902).

[Abstract] The oral microbiome is a complex and highly structured ecosystem composed of diverse microorganisms, including bacteria, fungi, viruses, and other microbes, which establish an intimate symbiotic relationship with the host. Its composition across distinct ecological niches, such as teeth and mucosa, is modulated by multiple factors, including age, genetics, and lifestyle. A stable microbial community acts as an essential barrier for sustaining oral and systemic health. This review systematically examines the structure and function of the oral microbiome under healthy and diseased conditions, with an emphasis on the formation mechanisms of plaque biofilms and their pivotal roles in the initiation and progression of dental caries and periodontitis. Dental caries is predominantly driven by acidogenic and aciduric bacteria, such as *Streptococcus mutans* and *Lactobacillus spp.*, accompanied by microenvironmental acidification and enamel demineralization. Periodontitis is closely associated with the enrichment of pathogenic microorganisms, including the "red complex" in subgingival plaque, and host immune dysregulation. Furthermore, ecological dysbiosis of the oral microbiome, particularly the abnormal proliferation of pathogens such as *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, not only contributes to the development and progression of oral squamous cell carcinoma but also closely correlates with numerous systemic disorders, including cardiovascular diseases, diabetes mellitus, rheumatoid arthritis, and pancreatic cancer, via mechanisms such as inflammatory induction, immunosuppression, and microbial translocation. Systematic elucidation of the ecological characteristics and pathogenic mechanisms of the oral microbiome will provide a critical theoretical foundation for maintaining oral microecological homeostasis and for preventing and treating oral and systemic comorbidities.

[Key words] Oral microbiome Dysbiosis Periodontitis Dental caries Review

口腔微生物组是由细菌、真菌、病毒等构成的复杂生态系统,其组成受年龄、生活方式和遗传背景等多种因

素影响,并在不同个体及不同口腔生态位中表现出明显差异。在健康状态下,口腔微生物群与宿主维持动态平衡,共同参与口腔内环境稳态的维持^[1-2]。一旦这种平衡被打破,菌群失调可通过慢性炎症、免疫调节异常及菌群移位等机制,参与龋病、牙周炎以及多种全身系统性疾病的发生

* 国家重点研发计划(No. 2022YFC2405900, No. 2022YFC2405902)资助

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出版日期: 2026-05-20

生发展^[3-4]。因此,深入认识口腔微生物组在健康与疾病中的组成和功能变化,对相关疾病的防治具有重要意义。

1 菌斑生物膜的形成

1.1 获得性膜形成

依据“先锋物种扩展生态斑块”假说,口腔健康状态下的动态稳定阶段表现为微生物群落能够通过代谢调节维持局部微环境稳态^[5]。牙齿清洁后数分钟内,唾液中的糖蛋白等生物聚合物即可吸附于釉质表面,逐渐形成获得性膜,并在约120 min内成熟,为微生物定植提供基础^[6]。随后,非变形链球菌和放线菌等先锋菌通过氢键、疏水作用、钙桥及范德华力等初始物理化学作用,以及后续黏附素—受体的特异性识别,稳定附着于牙面^[7-8]。在无龋且牙龈健康的区域,奈斯兰氏放线菌、口腔放线菌、戈登链球菌、血链球菌和口腔链球菌等是主要早期定植菌,它们与获得性膜蛋白结合并通过共聚作用构建初始生物膜框架,为后续菌群定植提供位点^[9]。其中,链球菌属因较强的环境适应性在龈上早期生物膜形成中占主导地位,戈登链球菌尤为关键^[10]。

1.2 初期黏附菌

在牙菌斑生物膜形成早期,链球菌属在数量和种类上迅速增加,是驱动初始组装的关键类群。血链球菌、口腔链球菌等早期定植菌不仅可通过配体—受体识别黏附于获得性膜,还可通过跨物种共聚促进生物膜的初步构建^[11]。作为兼性厌氧菌,它们能够优先定植于暴露的牙釉质表面,并适应生物膜成熟过程中逐渐形成的低氧环境。链球菌表达多种黏附素结合蛋白,从而增强其对牙面的稳定附着;同时,其可通过 comCDE 操纵子介导的群体感应系统调控细胞增殖、环境应答及局部 pH 稳态^[12]。在此基础上,血链球菌的精氨酸脱氨酶途径与奈斯氏放线菌的尿素酶系统可通过产氨缓冲酸性微环境,而韦永氏菌属则利用链球菌产生的乳酸建立代谢互惠关系,促进其在酸性条件下的定植^[13]。因此,群体感应、代谢协作和酸碱缓冲共同塑造了早期生物膜的生态演替方向,并在口腔健康维持与疾病发生之间发挥重要调控作用。

1.3 早期定植菌

随着早期定植菌在牙面持续积累,生物膜的空间结构与局部微环境发生协同变化。先锋菌的增殖可通过消耗氧气、改变营养供给及促进酸性代谢产物积累,推动微生态由稳态向失衡转变;同时,糖摄入增加和口腔干燥等因素可进一步加剧这一过程。细菌最初沿牙面扩展,随后向垂直方向聚集,逐步形成具有三维结构的生物膜,该结构有利于耐酸性更强、代谢适应性更高的菌群获得竞

争优势。早期定植菌之间通过特异性共黏附构建结构化生物膜框架,戈登链球菌、血链球菌和口腔链球菌等虽多被视为共生菌,但因其菌斑结构建立中的核心作用,也被认为具有促进致病菌后续定植的“辅助性病原体”特征。随着酸性环境持续存在,酸敏感菌受到抑制,而变形链球菌、乳酸杆菌等耐酸菌逐渐富集,促使牙釉质脱矿并为致龋菌进一步定植创造条件^[14]。相反,若局部酸度得到有效缓冲,菌群代谢可恢复平衡,并有利于牙釉质再矿化及早期龋损逆转^[15]。

1.4 菌斑生物膜的演变

在微生物群落的演替过程中,继发定植菌群逐渐取代以链球菌、放线菌和韦永氏菌为主要成分的早期群落,促使牙菌斑进入生态牙菌斑假说所定义的酸性阶段。在此阶段,变形链球菌、乳酸杆菌、双歧杆菌及斯卡多维亚菌等作为生物膜的顶极群落,凭借其更为广泛的代谢能力以及更强的产酸耐酸特性,显著改变生物膜微环境的特征,并可能协同增强其他菌种的致病潜能。随着酸性代谢产物的持续累积,牙釉质发生脱矿及结构崩解,最终形成龋损。若病变未能得到有效控制,可进一步向深层牙本质组织蔓延,标志着龋病进程的实质性推进^[16-17]。

1.5 菌斑生物膜成熟

在生物膜成熟阶段,胞外多糖基质持续沉积,逐步形成复杂的三维结构,从而显著增强菌群的黏附稳定性及对外界干扰的耐受性。该结构不仅为微生物提供物理保护,还可通过限制抗菌物质渗透和免疫细胞侵袭,维持群落在宿主免疫和外源干预下的持续存活。与此同时,微生物通过群体感应协调代谢活动,进一步稳定酸性微环境,促进耐酸菌的优势定植,使成熟生物膜成为龋病持续进展的重要载体^[18]。成熟生物膜中,各菌种依赖胞外多糖介导的黏附、聚集及种间互作,形成具有空间分区和功能互补特征的结构化群落,从而维持局部低pH状态并促进牙体硬组织脱矿^[19]。其中,胞外多糖与蛋白质、糖脂及细胞外DNA等共同构成具有水凝胶特性的聚集性基质,为微生物提供稳定附着和营养交换的微环境;因此,靶向EPS结构的干预被认为是削弱生物膜完整性的重要策略^[20-21]。当跨物种凝集达到一定程度后,生物膜进入成熟并发生结构重组及程序性脱落,完成其生命周期,而这一高度组织化的生态过程也是持续产酸和釉质脱矿的重要基础^[22]。

2 龋病发展的微生物组动态变化

2.1 龋白斑

龋白斑是早期龋损的典型临床表现,其形成符合生

态斑块假说,即生物膜中产酸菌和耐酸菌比例较健康状态显著升高。尽管变形链球菌长期被视为主要致龋菌,但研究表明其在不同个体和病变中的丰度差异较大,且并非所有进展性龋损中均占优势^[23]。除变形链球菌外,龋相关微生物群还包括血链球菌、唾液链球菌、放线菌、韦永氏菌、乳杆菌及普雷沃菌等,其中韦永氏菌在白垩斑形成中的预测价值已受到关注。这些证据提示,初发龋并非由单一致病菌驱动,而是多种产酸和耐酸微生物共

同参与的生态失调过程。

从生态演替角度看,初发龋菌群处于由动态稳态向酸性失衡转变的过渡阶段,部分兼具产酸和耐酸特征的菌群可能与病变的可逆性相关。近期研究发现,变形链球菌可在白斑表面形成聚集结构,提示其可能在局部釉质脱矿中发挥重要作用^[24]。见图1。但由于微生物群落组成复杂且现有取样方法存在局限,不同菌种在早期龋形成中的具体贡献仍有待进一步阐明。

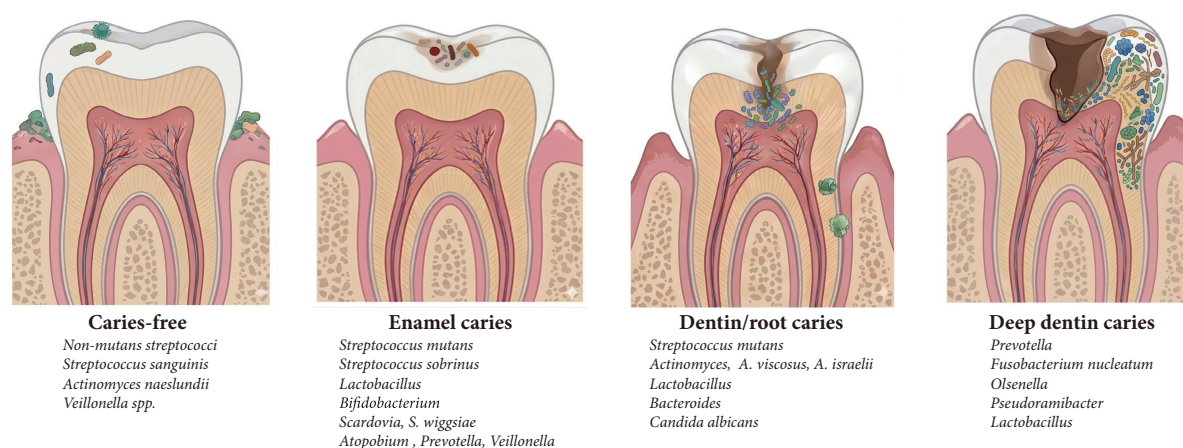


图1 无龋病、釉质龋、牙本质及牙根龋中鉴定的主要菌种

Fig 1 Main bacterial species identified in caries-free, enamel caries, dentin caries, and root caries

2.2 根面龋

根面龋的微生物群落较釉质龋更为复杂,主要由变形链球菌、血链球菌、放线菌、乳酸杆菌及韦永氏菌等产酸、耐酸微生物构成^[25]。随着培养技术和分子生物学方法的发展,研究者进一步发现,根面龋相关菌群还包括双歧杆菌、丙酸杆菌、酵母菌、粪肠球菌、阿托波菌及多种普雷沃菌等^[26]。见图1。这些结果表明,根面龋并不存在固定的“核心致龋菌群”,而是表现出较强的个体异质性。值得注意的是,部分早期被认为具有致病作用的放线菌,在健康与龋坏牙根生物膜中表现出相似的转录特征,提示其在牙根表面可能更多参与局部微生态调控,而非直接充当致病菌^[27]。因此,根面龋的发生更可能是多种微生物共同驱动的生态失衡过程,其具体致病机制仍有待进一步阐明。

2.3 牙本质龋

牙本质龋可由表层釉质龋向深部进展形成,也可直接发生于暴露的根面^[28]。由于牙根部牙骨质和牙本质矿化程度低于釉质、抗酸能力较弱,在牙龈退缩及根面暴露后更易发生菌斑堆积和酸蚀,因此病变进展往往更快,且易累及深层牙本质。唾液分泌减少是牙本质龋的重要宿主危险因素,其可削弱机械清除、酸缓冲和再矿化能力,从而在根面等薄弱部位形成更有利于致龋菌定植的微环境^[29]。

现有研究表明,牙本质龋的微生物组成具有较高复杂性和异质性,其是否随病变深度发生明确分层变化尚无一致结论。不同检测方法识别出的优势菌群存在一定差异,但总体上,变形链球菌、乳酸杆菌、韦永氏菌、普雷沃菌及梭杆菌等均与牙本质龋相关,其中变形链球菌虽是重要致龋菌,却未必在深层病变中占据优势^[30]。进一步研究提示,牙本质龋可表现为乳酸杆菌主导型、普雷沃菌主导型或混合型等不同微生态模式,并常伴随较高的菌群多样性(图1)。局部pH是影响菌群组成的重要因素:低pH条件下,乳酸杆菌等耐酸菌富集,而在pH相对较高的区域,普雷沃菌等蛋白水解菌更为常见^[31]。与冠部龋相比,深层牙本质病变中的微生物对可发酵碳水化合物的依赖相对较低(图1),更易受唾液成分、氧张力及宿主免疫因子的影响;其中产酸菌主要参与脱矿过程,而蛋白水解菌则通过降解有机基质促进病变向深部扩展^[32]。总体而言,牙本质龋并非由单一病原体驱动,而是多种微生物与局部微环境共同作用的结果。

3 主要龋相关细菌

3.1 变形链球菌

变形链球菌被广泛认为是与龋病发生最密切相关

的关键致龋菌之一,其生物学特征基本符合经典致龋菌判定标准。该菌以蔗糖等可发酵碳水化合物为主要底物,具有较强的产酸、耐酸及糖代谢能力,因此能够在酸化微环境中获得竞争优势并持续定植于牙面^[33]。此外,变形链球菌可将蔗糖导入胞外多糖合成途径,促进细菌黏附、生物膜积累及局部酸性代谢产物滞留,从而增强生物膜的结构稳定性和致龋潜能^[34-35]。不过,现有基因组研究提示,龋活跃个体与无龋个体来源菌株之间尚未发现稳定的特异性遗传位点,说明其致龋作用可能更多依赖于菌株表型差异及所处微生态环境,而非单一遗传标志。

3.2 乳杆菌属

乳杆菌属为革兰氏阳性菌,具有较强的产酸和耐酸

能力,其生长依赖可发酵碳水化合物。尽管该属在人体多个部位广泛定植,且多数成员在健康状态下属于共生或有益菌,但口腔中的部分乳杆菌与龋病发生密切相关。研究表明,乳杆菌可在婴幼儿早期定植于口腔,其定植过程受母婴传播及喂养方式等因素影响,并与龋病风险增加相关;其丰度通常与龋病发生率及严重程度呈正相关,而在无龋个体中检出率相对较低。现有研究还显示,乳杆菌属与龋病的关联具有明显异质性,不同检测方法所得结果并不完全一致:在早期龋损中,乳杆菌通常并非优势菌群,但其丰度和分布已发生改变;而在晚期牙本质龋损中,乳杆菌则更常被检出^[36-37]。因此,乳杆菌更可能在龋病进展,尤其是深部病变阶段发挥重要作用,而非作为早期龋发生的唯一主导菌(图2)。

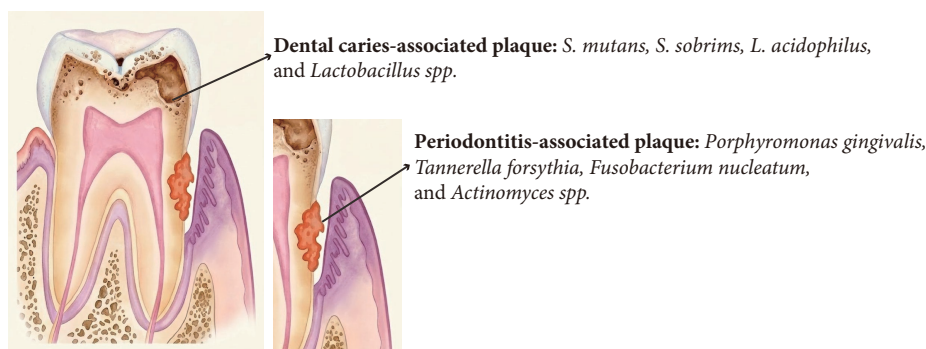


图 2 细菌主要定植于特定部位

Fig 2 Main colonization sites of oral bacteria

4 牙周炎过程中菌群的变化

牙周病本质上是一类由多微生物群落失衡驱动的慢性感染性疾病,其发生发展并非由单一致病菌引起,而是宿主—微生物互作失衡及群落结构整体改变的结果。动物研究表明,结扎可在常规啮齿类模型中诱导牙周炎症和骨破坏,而无菌动物在相同刺激下不发生类似损伤,提示微生物群落是牙周病发生的必要条件^[38]。基于此,菌群失调假说认为,牙周健康向疾病转化的核心在于牙周袋内微生物相对丰度、功能互作及宿主应答的系统性重塑,而非单一病原体的简单入侵^[39]。

健康龈下菌群具有较高多样性,以链球菌、放线菌等革兰阳性兼性厌氧菌为主,并伴有韦永氏菌、具核梭杆菌等菌群共同构成稳定的共生网络^[40-41]。这些微生物通过共聚作用、代谢协同、资源竞争及抗菌物质分泌维持局部生态稳态,其中链球菌、放线菌、罗氏菌、棒杆菌和奈瑟菌等在生物膜构建、氧化还原调节及硝酸盐代谢中发挥重要作用^[42-43]。梭杆菌则作为“桥梁菌”连接早期和晚期

定植菌群,普雷沃菌通过代谢底物供给参与群落稳定^[44-45]。整体而言,健康龈下生物膜表现为空间有序、功能互补的结构化生态系统(图2)。

在牙周炎进展过程中,龈下菌群发生显著重塑,原本以革兰阳性共生菌为主的群落逐渐转变为以革兰阴性厌氧菌富集为特征的致病型群落,其中牙龈卟啉单胞菌、齿垢密螺旋体、福赛斯坦纳菌等“红色复合体”以及梭杆菌、普雷沃菌等显著增加^[46]。与龋病等疾病中菌群多样性下降不同,牙周炎常伴随更高的微生物多样性,这可能与炎症环境下营养来源增加、复杂生态位形成及宿主免疫防御受损有关^[47-48]。值得注意的是,牙周炎中的生态失调主要表现为群落组成比例和功能状态的改变,而非健康相关菌种的完全消失;在炎症微环境中,部分原有共生菌亦可能获得更强的致病潜能,并与优势病原体协同促进炎症持续和牙槽骨吸收^[49-50]。随着牙周袋加深,梭杆菌、卟啉单胞菌等菌属进一步富集,推动群落结构演替和功能失调,最终导致牙周组织进行性破坏^[51-52]。因此,从群落生态失衡角度理解牙周炎的发生机制,对于发展基于

微生态调控的防治策略具有重要意义。

5 主要牙周相关细菌

5.1 牙龈卟啉单胞菌

牙龈卟啉单胞菌虽在牙周微生物群中通常处于低丰度状态,但被广泛认为是驱动菌群失调的关键病原体,其存在与牙周病的发生、进展及治疗反应不佳密切相关^[53-54]。该菌可通过重塑群落结构和功能,促进福赛斯坦纳菌、密螺旋体等病原体协同增殖,从而推动牙周炎的发展。其致病作用主要体现在对宿主免疫和炎症反应的双重调控:一方面,脂多糖可通过TLR2/TLR4激活炎症信号;另一方面,荚膜、菌毛和外膜囊泡有助于其逃避免疫清除,而牙龈蛋白酶则可诱导IL-1 β 、IL-6和TNF- α 等促炎因子释放,并降解免疫球蛋白和补体,削弱宿主防御^[55-57]。此外,牙龈卟啉单胞菌与福赛斯坦纳菌、齿垢密螺旋体共同构成“红色复合体”,在牙周袋厌氧环境中形成高度组织化的多菌种生物膜,增强病原体的定植能力和对治疗的耐受性。值得注意的是,该菌还可经血流播散并诱导系统性炎症与异常免疫激活,提示其在局部牙周破坏及全身相关疾病中均具有重要致病意义^[58-59]。

5.2 伴放线放线杆菌

伴放线放线杆菌是一种与晚期牙周炎及局限性侵袭性牙周炎密切相关的革兰阴性兼性厌氧菌,其定植可能受宿主遗传背景影响,并被视为牙周附着丧失进展的重要生物学标志物。该菌可通过多种黏附素在不同口腔生态位中定植和扩增,其致病性主要与白细胞毒素LtxA有关。LtxA能损伤中性粒细胞等免疫细胞,削弱宿主防御,并可激活巨噬细胞的炎症小体相关通路,诱导IL-1 β 异常释放,从而放大局部炎症反应^[60-62]。其中,JP2基因型因启动子缺失而具有更强的毒力,高毒力菌株的携带与青少年牙周附着丧失风险增加显著相关。此外,LtxA表达差异与侵袭性牙周炎严重程度密切相关,进一步提示该毒素在疾病发生发展中具有核心作用^[63-64]。

6 外部因素对牙周稳态的影响

牙龈沟稳态易受宿主因素、微生物群落及噬菌体调控变化的共同影响而被破坏^[65]。其中,牙龈卟啉单胞菌虽通常为低丰度成员,却可通过抑制宿主防御、重塑局部营养环境和推动群落结构重组,促进潜在致病菌定植,因此被视为典型的关键病原体^[66]。动物研究进一步表明,该菌单独定植不足以诱导牙周骨破坏,但在共生菌群存在时可触发炎症放大和骨吸收,提示其致病作用本质上依赖于对宿主—微生物互作网络的调控。

吸烟是牙周炎发生与进展的重要外部危险因素,可同时损害中性粒细胞功能、扰乱体液免疫,并通过改变局部氧分压、唾液成分及菌群竞争格局诱导菌群失调,而且这种变化可早于临床症状出现^[67]。此外,修复体表面粗糙化、完整性受损及材料离子释放均可促进细菌黏附和成熟生物膜形成,增加继发龋、牙周炎及种植体周围炎风险^[68-69]。不同材料的化学特性亦会影响微生物定植,例如玻璃离子水门汀释放的氟离子可抑制产酸和胞外多糖合成,而复合树脂未充分聚合时残留单体可能反而促进致龋菌附着^[70-71]。因此,外部环境因素可通过持续改变宿主免疫状态与微生态结构,共同推动致病菌在牙周微生态中占据优势。

7 口腔鳞癌

口腔是人体重要的微生物储存库之一,栖息着细菌、真菌、病毒及噬菌体等复杂微生物群落。口腔微生态失衡可通过诱导慢性炎症、免疫抑制及宿主防御受损等机制参与肿瘤发生,而吸烟、饮酒等外部因素既可扰乱菌群结构,本身也是肿瘤发生的重要危险因素,因此可能通过驱动菌群失调进一步促进肿瘤进展^[72]。在口腔鳞状细胞癌中,特定菌群丰度改变已逐渐被揭示,表现为消化链球菌、消化球菌、丝状杆菌和卡托菌等在肿瘤组织中富集,而放线菌在癌旁正常组织中相对更丰富^[73-74]。此外,唾液中链球菌属、韦永氏菌等菌群的变化也显示出潜在的非侵入性生物标志物价值^[75]。除局部作用外,口腔机会致病菌还可参与远端肿瘤发生,例如具核梭杆菌已被证实是结直肠癌的重要促进因子,而牙周健康不良亦与食管癌、胰腺癌等风险升高相关^[76]。总体而言,口腔微生物群失调不仅参与口腔局部肿瘤发生,也可能通过多种机制影响全身肿瘤进展与治疗反应。

8 与口腔鳞癌密切相关的细菌

8.1 具核梭杆菌

梭杆菌属为革兰氏阴性厌氧菌,是口腔常驻菌群中的重要成员,同时也是典型的机会性致病菌。近年来,多项研究表明,具核梭杆菌在多种肿瘤组织中呈异常富集。在口腔鳞状细胞癌中,其特定亚种丰度升高;在结直肠癌中,16S rRNA测序、宏基因组测序及qPCR等研究一致显示,具核梭杆菌在肿瘤组织及粪便样本中的相对丰度显著增加,且与口腔来源菌株具有较高同源性,提示其可能由口腔迁移而来^[77-79]。进一步研究发现,该菌不仅在结直肠肿瘤组织中富集,还与较差的临床预后相关,提示其具有潜在的诊断和预后评估价

值。除结直肠癌外,具核梭杆菌在食管鳞状细胞癌和胃癌中亦有检出增加,并与不良生存结局及较差化疗反应相关,提示其可能参与肿瘤进展及治疗耐受^[80-81]。机制上,具核梭杆菌携带多种膜和表面相关蛋白,可介导其与宿主细胞及其他微生物的黏附和相互作用,从而增强侵袭、免疫逃逸及促肿瘤效应;但其作用在不同癌种中可能存在异质性^[82-83]。

8.2 牙龈卟啉单胞菌

牙龈卟啉单胞菌是一种重要的牙周致病菌,近年来也被认为与口腔癌及上消化道肿瘤的发生发展密切相关^[84]。研究显示,该菌可在口腔鳞状细胞癌组织中检出,提示其可能参与局部肿瘤形成;同时,其较强的侵袭和迁移能力使其有可能沿口腔-消化道轴扩散,并与化疗耐药相关,从而增加肿瘤治疗的复杂性^[85-86]。除局部作用外,牙龈卟啉单胞菌在食管鳞癌组织中的检出率及相关抗体水平亦明显升高,提示其具有潜在的诊断价值。在胰腺癌中,口腔样本测序和血清学研究均表明,该菌富集及其抗体升高与胰腺癌风险增加相关;牙周炎及牙齿脱落与胰腺癌风险的流行病学关联也进一步支

持其可能通过血行播散或消化道相关途径参与远端肿瘤进程^[87]。

9 口腔微生物组与全身系统性疾病

口腔是消化道的起始部位,栖息着仅次于肠道的复杂微生物生态系统。近年来研究表明,口腔微生物组失衡不仅参与龋病、牙周炎等局部疾病的发生发展,还可通过菌群移位、慢性炎症、免疫调节异常、分子模拟及口腔-肠道轴等多种机制影响远隔器官,与多类全身系统性疾病密切相关。牙周炎等状态下,牙龈屏障受损为口腔病原体进入血液循环提供了条件,牙龈卟啉单胞菌、具核梭杆菌等可播散至远隔组织并诱发局部病变^[88]。见图3。同时,口腔病原菌及其毒力因子可持续激活宿主免疫反应,诱导IL-1 β 、IL-6和TNF- α 等促炎因子释放,形成低度全身性炎症状态,进而促进多种慢性疾病进展。此外,部分口腔微生物抗原与宿主组织具有结构相似性,可诱发交叉免疫反应;而每日吞咽的大量口腔微生物还可进入肠道,改变肠道菌群组成和黏膜屏障功能,进一步放大全身炎症反应^[89]。

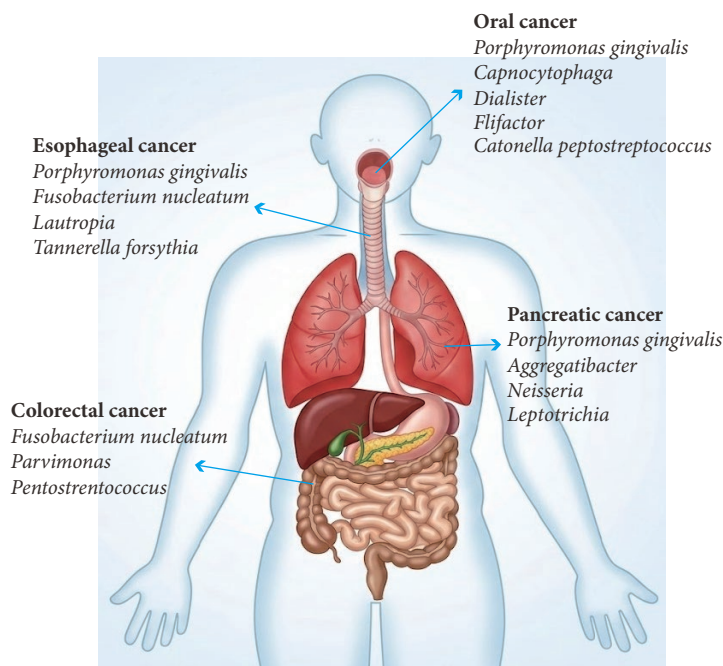


图3 口腔微生物群与相关癌症的分布

Fig 3 Distribution of oral microbiota and associated cancers

目前,口腔微生物与心血管疾病、糖尿病、类风湿关节炎、消化系统疾病、神经系统疾病及呼吸系统疾病之间的关联已受到广泛关注。流行病学和机制研究均提示,牙周炎是动脉粥样硬化、心肌梗死及脑卒中的重要危险因素,牙周病原体可通过血行播散促进血管壁炎症、泡沫细胞形成及血栓相关损伤^[90]。糖尿病与口腔菌群失调

之间存在双向关系:牙周炎可加重胰岛素抵抗,而高血糖环境又可促进牙周病原菌增殖,牙周治疗对改善代谢控制具有一定价值。在自身免疫性疾病中,牙龈卟啉单胞菌可通过诱导蛋白瓜氨酸化参与类风湿关节炎的免疫病理过程。在消化系统疾病中,具核梭杆菌已被证实是结直肠癌的重要促进因子,并可能通过黏附、促增殖和免疫

逃逸等机制推动肿瘤进展^[91]。此外,牙周病原体还与阿尔茨海默病、帕金森病、吸入性肺炎、慢性阻塞性肺疾病急性加重及移植后并发症等有关^[92]。总体而言,口腔微生物组失衡是连接口腔健康与全身健康的重要生物学纽带,深入阐明其作用机制,将为相关疾病的早期干预和微生态治疗提供新的理论基础。

10 小结与展望

口腔微生物组是维持口腔微生态稳态的关键组成,其结构与功能失衡贯穿龋病、牙周炎及口腔癌等多种疾病的发生发展过程。现有研究表明,尽管上述疾病均与菌群失调有关,但其主导菌群、代谢特征及宿主应答模式并不相同:龋病主要表现为产酸、耐酸菌富集及牙体硬组织脱矿,牙周炎则以龈下致病菌扩增和炎症失控为主要特征,而口腔癌更多涉及特定病原体定植、慢性炎症持续激活及免疫微环境重塑。由此可见,口腔微生物相关疾病并非单一病原体驱动的结果,而是多物种协同作用及宿主—微生物互作失衡的综合体现。

随着宏基因组、宏转录组及多组学技术的发展,口腔微生物研究正由菌群组成描述逐步转向功能解析和机制阐释。未来仍需结合空间组学、代谢组学及宿主免疫学证据,进一步揭示不同疾病状态下微生物群落的动态演替规律及其关键调控节点。在此基础上,围绕微生态重塑开展的干预策略,如靶向抑菌、益生菌调控和生态位干预等,或将为口腔疾病及其相关全身性病变的精准防治提供新的思路。

* * *

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Author Contribution CHEN Zeyuan is responsible for conceptualization and writing--original draft. ZHANG Xu is responsible for conceptualization, funding acquisition, and writing--review and editing. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

利益冲突 所有作者均声明不存在利益冲突

Declaration of Conflicting Interests All authors declare no competing interests.

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(2025 - 12 - 05收稿, 2026 - 04 - 16修回)

编辑 吕 熙



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