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在线全文

中医“治未病”指导口腔-全身抗衰老机制与干预策略*

艾黄萍[1]，李春财[2]，金 钊[3]，左渝陵[1△]

1. 成都中医药大学附属医院 口腔科（成都 610075）；2. 成都中医药大学临床医学院（成都 611137）；
3. 成都中医药大学基础医学院（成都 611137）

【摘要】 在全球人口老龄化背景下，衰老相关性疾病已成为重大公共卫生挑战，其核心病理基础炎性衰老与口腔健康状态密切相关。当前该领域存在口腔与全身防治割裂、缺乏阻断口腔-全身恶性循环的系统性策略等瓶颈问题。本文从口腔-全身双向调控抗衰老的机制与干预策略两个方面着手进行综述，提出口腔是全身衰老的前驱预警窗口，深入剖析了口腔-全身通过免疫-炎症网络形成双向恶性循环的深层机制，并从分子层面揭示了脂多糖（lipopolysaccharide, LPS）/Toll样受体4（Toll-like receptor 4, TLR-4）/核因子-κB（nuclear factor kappa-B, NF-κB）、晚期糖基化终末产物（advanced glycation end products, AGEs）/晚期糖基化终末产物受体（receptor for advanced glycation end products, RAGE）及口-脑神经反馈三条关键途径。在此基础上，构建了以中医治未病思想为指导、覆盖全生命周期的三级协同干预体系，并以多学科协作为横向支撑，实现“预警-干预-康复”一体化新模式，为应对老龄化挑战提供融合中医整体观与现代生命科学的解决方案。

【关键词】 治未病 抗衰老 口腔-全身 慢性炎症 中西医协同干预 综述

Oral-Systemic Antiaging Mechanisms and Intervention Strategies Guided by Traditional Chinese Medicine Principle of Preventive Treatment of Disease

Ai Huangping[1], *Li Chuncai*[2], *Jin Zhao*[3], *Zuo Yuling*[1△]. 1. *Department of Stomatology, Hospital of Chengdu University of Traditional Chinese Medicine, Chengdu 610075, China*; 2. *School of Clinical Medicine, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China*; 3. *School of Basic Medicine, Chengdu University of Traditional Chinese Medicine, Chengdu 611137, China*

△ Corresponding author

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[Abstract] Population aging has become a global issue, and aging-related diseases have emerged as a major public health challenge. Inflammatory aging—the fundamental pathological basis of aging-related diseases—is closely associated with oral health status. However, current research and clinical practice remain limited by bottleneck issues, such as the separation of oral and systemic prevention and treatment strategies and the lack of systematic approaches to break the oral-systemic vicious cycle. This review addresses both the mechanisms and intervention strategies of the bidirectional oral-systemic regulation in anti-aging. We propose that the oral cavity serves as a precursory warning window for systemic aging and provide an in-depth analysis of the underlying mechanisms by which the oral cavity and the whole body form a bidirectional vicious pathogenic cycle through the immune-inflammatory network. At the molecular level, 3 key pathways are highlighted, including the lipopolysaccharide (LPS)/Toll-like receptor 4 (TLR4)/nuclear factor kappa-B (NF-κB) axis, the advanced glycation end products (AGEs)/receptor for advanced glycation end products (RAGE) axis, and the oral-brain neural feedback pathway. On this basis and under the guidance of the traditional Chinese medicine (TCM) principle of preventive treatment of disease, a three-tier collaborative intervention system covering the entire life course is proposed. Supported by multidisciplinary collaboration, a new integrated model incorporating early warning, intervention, and rehabilitation is established, thereby providing a comprehensive solution that integrates the holistic approach of TCM with modern life sciences to address the challenges of population aging.

[Key words] Preventive treatment of disease Antiaging Oral-systemic Chronic inflammation Integrated traditional Chinese and Western medicine intervention Review

全球人口结构正经历不可逆转的老龄化趋势。据联合国《世界人口展望2022》报告，到2050年，全球65岁及以上人口比例将从2022年的10%上升至16%[1]。中国老龄化进程尤为迅速，预计在2035年左右进入重度老龄化阶段[1]。心脑血管疾病、糖尿病、神经退行性病变、骨质疏松、恶性肿瘤等慢性疾病已成为威胁人类健康的核心挑战[1]。近年来，现代医学对口腔健康与全身疾病关联的认识取

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△ 通信作者

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得了突破性进展[2]。口腔局部慢性感染引发的系统性低度炎症与氧化应激,成为多种衰老性疾病的独立危险因素[3-4]。然而,现有防治模式仍存在重心滞后、防治割裂、个体化不足等局限,难以实现抗衰老关口前移的目标[2,5]。

中医治未病思想与整体观为此提供了独特的理论视角与实践智慧。《黄帝内经》确立的“未病先防、既病防变、瘥后防复”三级预防体系,其“整体观念”与“辨证论治”的核心思想与现代抗衰老研究的系统调控理念高度契合[6-7]。近年来,基于治未病理论的抗衰老干预手段已得到广泛研究,其在调节机体整体平衡、改善衰老等方面的有效性已被证实[8]。中医理论将口腔视为脏腑之窗,构建口腔与全身在生理相连、病理互传的完整理论依据[9-10]。其对衰老本质“五脏衰、阴阳虚”的认识,更为理解口腔与全身衰老的同步性提供了内因解释[11-12]。然而,目前关于治未病理论与抗衰老的研究多聚焦于全身层面,对口腔局部与全身衰老的协同调控机制探讨不足。因此,本文立足治未病思想核心,系统整合全身抗衰老与口腔疾病防治的相关研究,深入剖析二者的内在关联,明确口腔-全身协同的核心机制与干预策略,为推动中医治未病理论在抗衰老领域的深度应用提供理论支撑[11]。

1 中医治未病思想与抗衰老理论的核心关联

1.1 治未病思想的核心要义

治未病理论贯穿中医诊疗体系,“未病先防”即在疾病发生之前,通过养护正气、规避邪气,维持机体阴阳平衡,从源头阻断疾病的发生。《素问·上古天真论》提出“恬淡虚无,真气从之,精神内守,病安从来”,强调情志调畅、正气充足是抵御疾病与衰老的关键;“既病防变”指疾病发生后及时干预,防止病情发展与传变,避免疾病进一步损耗机体正气,加速衰老进程。如《金匮要略》所言“见肝之病,知肝传脾,当先实脾”,体现了中医对疾病传变规律的把握与早期干预的重要性;“瘥后防复”即疾病痊愈后通过调理机体功能、巩固疗效,防止疾病复发,促进机体恢复至最佳状态,避免因疾病反复导致正气耗伤,延缓衰老[13-14]。

治未病理论本质上是“整体观”与“平衡观”的体现,认为机体是一个有机整体,并与自然、社会环境相统一。衰老与疾病的发生均源于机体阴阳失衡、正气亏虚、邪气侵袭[8]。这一理论不仅关注疾病防治,更注重机体生理功能的养护与生命质量的提升。治未病思想与抗衰老延缓功能衰退、预防衰老相关疾病的核心目标高度契合。

1.2 治未病思想与抗衰老理论的内在关联

中医对衰老与疾病的认知始终以整体观为核心。衰老的本质是机体正气渐亏、阴阳失衡、气血失调、脏腑功能衰退的渐进过程。因此衰老与疾病发生的病机高度同源。《素问·评热病论》言“邪之所凑,其气必虚”,明确邪气侵袭的前提是正气亏虚。而衰老正是正气持续耗损、机体防御能力逐步下降的过程。中年以后肾精渐耗、脾胃功能减弱,气血生化不足,不仅出现须发早白、腰膝酸软等衰老表现,也成为高血压、糖尿病、骨质疏松等衰老相关疾病的高发阶段[12]。这种衰老——正气亏虚——疾病易感性增加的递进关系,揭示了治未病与抗衰老在病机层面的内在统一性。

治未病与抗衰老均以维系机体正常生理功能、提升生命质量为核心。抗衰老的核心目标是延缓生理功能衰退,减少衰老相关疾病。治未病理论的目标则是“未病先防、既病防变、瘥后防复”。本质上均是通过维持机体的整体平衡,避免正气耗损,减少疾病对机体功能的破坏,最终实现“形与神俱,而尽终其天年”。二者均遵循“整体调控、辨证施护”的核心逻辑。治未病理论强调从饮食、情志、运动、方药等多维度调理机体整体状态,与现代抗衰老研究倡导的系统调控理念不谋而合[15]。治未病理论注重顺时养生、辨证施养,根据不同体质制定个性化方案,这与抗衰老中个体衰老异质性的干预需求高度一致,可实现精准抗衰老。

2 口腔-全身协同抗衰老的核心机制

2.1 基于正邪互作的口腔-全身双向恶性循环机制

口腔-全身的双向调控并非简单的线性因果关系,而是互为因果、相互加重的恶性循环。随着年龄的增长,机体出现“肾精亏虚”与“脾胃虚弱”。肾精亏虚,骨枯髓减,可导致牙龈萎缩、牙槽骨吸收;脾胃为“后天之本,气血生化之源”,脾胃功能减弱会导致气血不足,口腔黏膜失于濡养而功能障碍;全身内分泌与神经功能衰老,特别是糖尿病神经末梢损伤会影响唾液腺分泌[16-17]。唾液分泌异常则会破坏口腔微生态平衡,增加口腔疾病易感性[16-17]。全身衰老性疾病可通过系统性病理改变的影响、共病交互形成的恶性循环,以及药物治疗相关副作用影响口腔局部微环境的改变,在临床上形成一系列衰老相关的口腔表现[18]。衰老导致的免疫紊乱,使得口腔菌群失调,机会致病菌优势定植[19-20]。此时,口腔局部微环境失衡,为后续病理产物入血提供条件。

衰老相关性口腔疾病通过全身-口腔的双向循环、免疫网络等,反向加剧全身衰老进程。口腔作为机体黏膜-免疫屏障的重要组成部分,其微生态失衡与局部炎症可通过血液循环扩散至全身,引发或加重全身慢性炎症[19]。

而慢性炎症是加速衰老的核心机制之一。牙周炎患者的牙周袋内存在大量致病菌,其产生的脂多糖、酶类及炎症因子可进入血液循环,损伤血管内皮功能,促进动脉粥样硬化的发生发展,增加心血管疾病风险[21-22];同时,这些炎症因子还会激活全身免疫系统的过度反应,加剧氧化应激,损伤肝细胞、心肌细胞等,加速全身脏腑功能衰退[2,23]。此外,口腔微生物成分还可经血液传播进而引发全身免疫刺激、通过三叉神经和迷走神经通路进行的神经信号传导,以及通过口-肠-脑轴改变肠脑交流环境[24-25]。口腔致病菌进入肠道后会破坏肠道菌群平衡,影响营养物质吸收与代谢废物排泄,进一步加剧全身衰老[19,26]。口腔卫生状况差、牙周炎严重的人群,其认知障碍、糖尿病等衰老相关疾病的发病率显著升高,印证了口腔对全身衰老的加剧作用。

2.2　口腔作为全身性衰老疾病的前驱预警窗口

口腔临床表现具有易观察、早出现的特点,是全身性衰老疾病的重要前驱预警窗口[23]。其预警价值的发挥,源于口腔与全身衰老疾病的发生在病机上的同源性及病理通路中的关联性[23]。与内脏器官衰老表现的隐匿性不同,口腔临床表现可通过常规口腔检查早期识别和评估。不同口腔表现对应不同衰老疾病的预警,唾液分泌功能障碍可作为神经退行性疾病[27]、通过整合现代分子生物学机制,作者揭示了口腔微生态与免疫代谢在抗衰老过程中的关联内分泌代谢系统[28]等衰老相关疾病的前驱预警性表现;口腔微生态失衡引发的唾液分泌减少也可提前预警心血管疾病的发生[21,29]。牙周病变的炎症因子水平与冠心病[30]、认知障碍[31]、糖尿病[18]等衰老性疾病的发病风险呈正相关;不明原因的反复牙龈出血,可能是血管内皮功能衰退的前驱预警信号[22]。口腔黏膜功能障碍不仅与口腔局部病理改变相关,还可与心血管疾病、神经退行性疾病[22]和代谢性疾病[23]等相关;口腔黏膜变薄是全身皮肤黏膜衰老的局部直观表现[32];味觉减退则与神经退行性疾病相关[33],有可能是阿尔茨海默病等认知障碍疾病的早期信号[34]。口腔表现的前驱预警价值,为抗衰老早期干预提供了可观察的窗口。可通过识别并干预口腔早期异常表现,阻延全身性衰老相关疾病的发生发展。见图1。

3　“治未病”思想指导全身-口腔双向调控抗衰老的分子机制与干预靶点

口腔微环境与全身系统之间并非孤立存在,而是通过各种信号通路与免疫微环境形成复杂的双向调控网络。这也是治未病思想在现代分子生物学层面的精准物质基础映射(图2)。

牙周致病菌可视为外邪,当机体正气不足、免疫防御下降时,牙周及口腔致病菌通过牙周袋直接侵入流注全身。这一过程的生物学实质是牙龈卟啉单胞菌(*P. gingivalis*, *P.g*)等革兰氏阴性菌释放的LPS介导的炎性级联反应[35]。牙周炎患者受损的牙周微环境允许细菌LPS易位进入血液循环[22]。而LPS作为炎症因子的配体,特

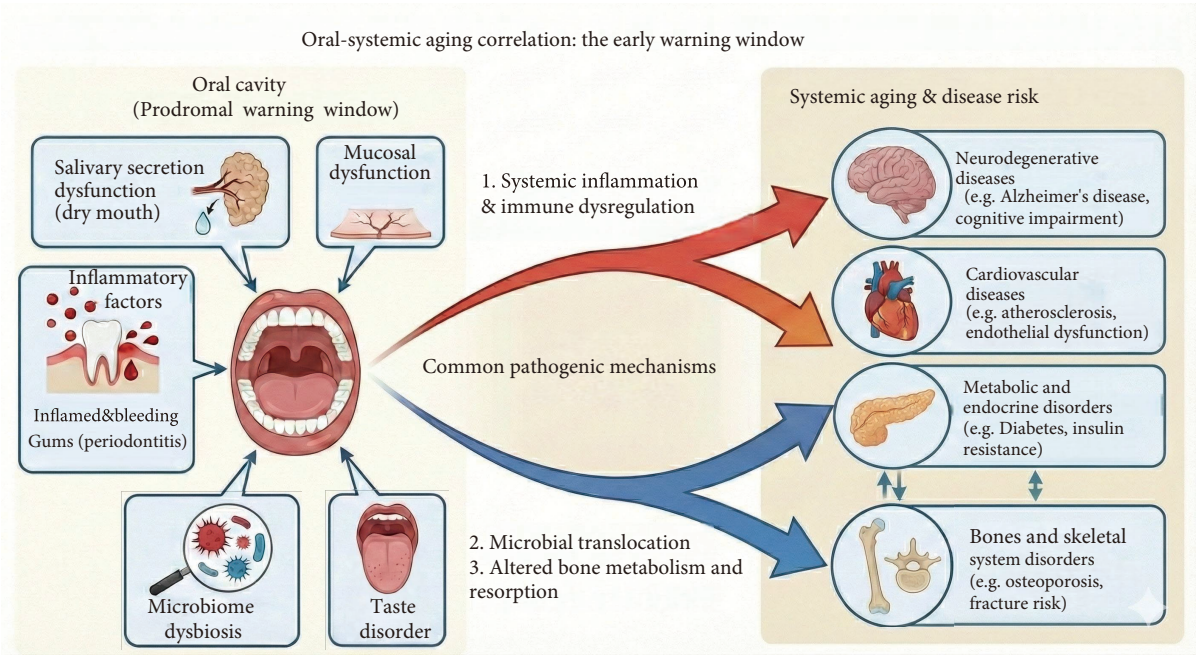


图 1　口腔作为全身性衰老疾病的前驱预警窗口图

Fig 1　Oral cavity as a precursory warning window for systemic aging diseases

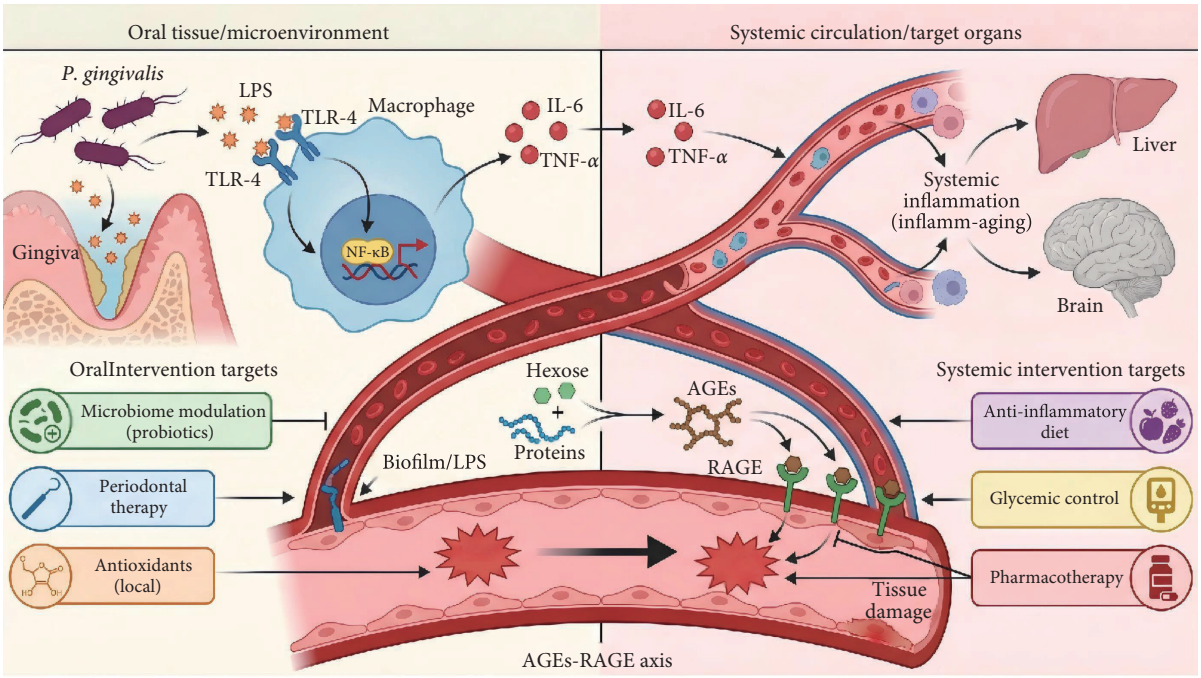


图 2 全身-口腔双向调控抗衰老的分子机制图

Fig 2 Molecular mechanisms of systemic-oral bidirectional regulation in anti-aging

LPS: lipopolysaccharide; TLR-4:Toll-like receptor 4; NF-κB: nuclear factor kappa-B; ROS: reactive oxygen species; AGEs: advanced glycation end products; RAGE: receptor for advanced glycation end products; IL-6: interleukin-6; TNF-α: tumor necrosis factor-α.

异性结合全身免疫细胞表面的TLR-4[36]。这一结合激活了下游的NF-κB信号通路,促使细胞核转录并释放促炎细胞因子[37]。持续升高的循环炎症因子诱导肝脏合成C反应蛋白,导致全身处于低度慢性炎症状态,加速了血管内皮损伤、胰岛素抵抗及骨代谢失衡[38]。因此,基于中医治未病思想未病先防/既病防变,在抗衰老的过程中应在早期就注重全身微生态的重塑及修复口腔局部物理屏障。

衰老的不断发展与晚期糖基化终末产物(advanced glycation end products, AGEs)的堆积及氧化应激密切相关[39]。高血糖或代谢紊乱导致口腔与全身的AGEs水平升高,形成一个恶性循环[40]。AGEs可激活NF-κB、丝裂原活化蛋白激酶(mitogen-activated protein kinase, MAPK)等促炎信号通路[41-42],从而导致氧化应激、促炎细胞因子释放及基质金属蛋白酶(matrix metalloproteinase, MMP)活化[43-45]。这一过程可通过抑制胶原合成,进而破坏细胞外基质的稳态[44]。而特定的AGEs可直接诱导成骨细胞凋亡[46],从而导致牙槽骨病理性骨吸收[47]。同时,AGEs还可通过激活免疫细胞和感觉神经元[48-49],调控神经-免疫交互作用[50]。这会形成一个复杂的炎症网络加剧组织损伤,引发疼痛和慢性疾病的发生[51]。此外,AGEs还可与牙周组织细胞表面的特异性受体结合,激活还原型辅酶Ⅱ氧化酶(NADPH oxidase, NOX),导致活性氧(reactive oxygen species, ROS)大量生成[52]。ROS不仅直接破坏牙周结缔组织,诱导成纤维细胞凋亡,还加剧了唾液腺功能的退化[53]。ROS还可氧化修饰低密度脂蛋白,进一步激活全身血管壁的RAGE,促进泡沫细胞形成,加重动脉粥样硬化[54]。因此,基于中医治未病思想既病防变,在抗衰老的过程中应阻断慢性炎症的发展及多疾病共同管理。

“齿为骨之余,肾主骨生髓,脑为髓海”牙齿功能的丧失被视为肾精亏虚、脑髓失养的信号。因此全身衰老的发生也与口-脑神经反馈回路的重建有密切的关系[55]。牙周膜含有丰富的本体感受器,咀嚼运动通过三叉神经中脑核向海马体和前额叶皮层投射信号,调节脑源性神经营养因子的表达[56]。缺牙导致的咀嚼刺激丧失会导致海马体突触可塑性下降,加速认知功能衰退[55]。慢性牙周炎症因子可破坏血脑屏障,使*P. g*及其分泌的牙龈蛋白酶侵入脑实质,促进β-淀粉样蛋白沉积,形成阿尔茨海默病的病理基础[57-58]。因此,基于中医治未病思想瘥后防复,在抗衰老的过程中应支持咬合重建及神经保护。义齿修复不仅是形态恢复,更是为了重启神经反馈回路,通过咀嚼增加脑血流量[59]。通过控制口腔炎症维护血脑屏障的完整性,阻断神经毒素入脑。

4 治未病思想指导下的全身-口腔协同抗衰老防治体系的构建

基于上述分子机制,构建了覆盖全生命周期的全身-

口腔三级协同干预体系(图3)。该体系打破了传统单病种、单科室的诊疗局限,以时间轴为纵向指引,以多学科协作(multidisciplinary team, MDT)为横向支撑,旨在实现抗衰老效益的最大化。

4.1　未病先防:微生态稳态与代谢免疫的双向调控

作为体系的前置防控环节,“未病先防”聚焦于衰老启动前的生理稳态维持。核心在于实现口腔-肠道微生态平衡与全身代谢免疫功能的双向调控。口腔微生态作为全身微生态系统的重要前置门户,其菌群结构失衡可通过黏膜屏障损伤、代谢产物异位定植等途径,诱发全身低度炎症,加速代谢紊乱与免疫衰老进程[60]。而全身代谢免疫状态的异常,亦会反向影响口腔菌群定植抗力,打破微生物稳态[61]。本环节通过靶向调控口腔益生菌群丰度、优化黏膜屏障功能,同步结合营养干预[62]、运动指导[63]等全身方案调节代谢水平、增强免疫监视能力[64]。构建“口腔微生态-代谢-免疫”的良性循环,从源头阻断衰老相关病理进程的启动,实现“防患于未然”的防控目标。

4.2　既病防变:炎症阻断与慢病共管机制

针对已出现牙周炎、全身代谢综合征等早期衰老相关病理信号的人群,以炎症精准阻断为核心,建立全身-口腔慢病协同共管机制。口腔局部炎症作为全身低度炎症的重要诱因,可通过炎症因子级联反应扩散至全身,加重心脑血管疾病[5]、糖尿病[65]等慢性疾病的进展。而此类慢病亦会反向加剧口腔组织损伤与衰老,二者形成“局部炎症-全身慢病”的恶性循环[66]。将依托口腔科、内分泌科、心血管内科、风湿免疫科等MDT团队,实现口腔局部炎症的精准干预与全身慢病的规范化管理,通过靶向抑制炎症通路关键分子、调节炎症微环境,打破二者的恶性循环。延缓病理损伤向更深层次、更广范围进展,降低严重并发症的发生风险。

4.3　瘥后防复:功能代偿与神经-脏器保护网络构建

“瘥后防复”作为体系的收尾巩固环节,针对经干预

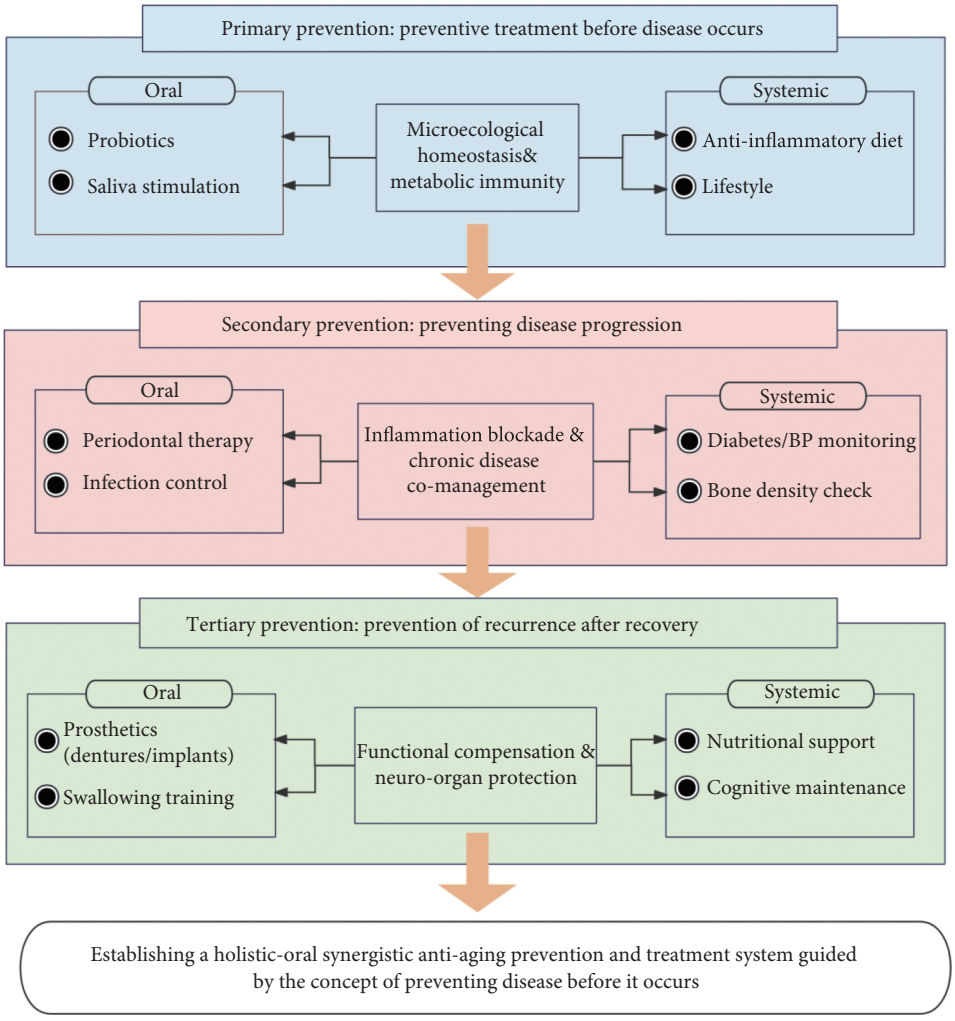


图 3　治未病思想指导下的全身-口腔协同抗衰老防治体系的构建图

Fig 3　Diagram of the construction of a systemic-oral synergistic anti-aging prevention and treatment system guided by the concept of preventative treatment of disease

后病情缓解或功能改善的人群，重点构建功能代偿体系与神经-脏器保护网络，预防衰老相关病理状态的复发与反弹。口腔与全身功能会出现进行性衰退，且神经-体液调节网络的失衡会进一步加剧功能损伤的反复。本环节通过口腔咀嚼功能训练[67]、营养支持优化[68]等个体化功能康复训练方式促进受损组织的功能代偿。同时聚焦神经-脏器调控通路[1]，通过保护神经递质平衡、改善脏器微循环、增强组织抗氧化能力，构建多维度保护网络，维持全身与口腔的长期生理功能稳态，实现“愈后不复发、功能稳维持”的目标。

5 小结

在中医治未病思想指导下，口腔健康是全身性抗衰老战略中一个不可忽视且极具干预潜力的关键环节。通过构建并实施“三级防控”与中西医协同的实践框架，能够有效打破口腔-全身之间的恶性链条。这不仅是中医整体观在现代健康管理中的生动实践，也为实现从“以疾病治疗为中心”向“以健康促进和衰老延缓为中心”的医学模式转变，提供了重要的理论依据和实践路径。本文通过系统论证，揭示了抗衰老过程中全身与口腔并非孤立进程，而是通过复杂的生物学通路构成紧密的双向恶性循环[15, 40, 44, 64]。中医治未病思想的整体观与三级预防架构，为理解和干预这一循环提供了成熟的理论框架与实践智慧。

在理论上，明确了治未病思想与抗衰老在维系机体平衡、预防功能衰退目标上的一致性。从现代分子机制层面揭示了口腔作为全身衰老疾病的前驱预警窗口。

明确了口腔微生态失衡与局部炎症是驱动全身慢性炎性衰老的关键因素。基于此，构建了中医治未病思想指导下，以MDT作为横向支撑的全生命周期防治体系，实现从理论到实践路径的跨越。通过践行“全身-口腔”一体化协同防治新范式，有望延缓衰老进程，提升全民健康衰老，为应对老龄化社会挑战提供可行性方案。

* * *

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利益冲突 所有作者均声明不存在利益冲突

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