

DOI: 10.11766/trxb202111100608

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SHENG Hongjie, WANG Fang, XIANG Leilei, FU Yuhao, WANG Ziquan, XU Min, MEI Zhi, LIU Yu, DOU Qingyuan, JIANG Xin, JAMES M. Tiedje. Environmental Behavior and Control of Antibiotic Resistance Genes in Soil – A Review[J]. Acta Pedologica Sinica, 2023, 60 (1): 39–49.

土壤中抗生素抗性基因的环境行为与阻控研究进展*

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摘要: 抗生素抗性基因 (Antibiotic resistance genes, ARGs) 的传播威胁着生态环境安全和人体健康, 已成为一个全球性的问题。土壤中抗生素抗性基因的分布、来源、扩散传播以及消减技术已成为一个研究热点。本文在简要介绍自然环境和受人类活动干扰土壤中抗生素抗性基因分布水平的基础上, 分析了土壤中抗生素抗性基因的主要来源, 剖析了抗生素抗性基因由土壤向其他环境介质 (水、植物) 传播的规律及其影响因素, 如土壤理化性质、农艺调控和环境中的污染物等。进而探讨了环境中各种生物和非生物因素对土壤中抗生素抗性基因持久性的影响和环境中抗生素抗性基因的消减技术, 包括好氧堆肥、厌氧发酵、水处理工艺等。最后, 提出遵循“大健康 (One Health)”准则, 以跨学科的方法控制抗生素抗性基因在环境中的传播, 以更全面地将抗生素抗性基因对人类的健康风险降低至最低水平。

关键词: 抗生素抗性基因; 抗生素抗性细菌; 土壤; 水平基因转移; 大健康

中图分类号: X53 **文献标志码:** A

Environmental Behavior and Control of Antibiotic Resistance Genes in Soil — A Review

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* 国家自然科学基金项目 (41977137、42007133、41991333)、中国科学院前沿科学重点研究项目 (QYZDJ-SSW-DQC035)、江苏省自然科学基金项目 (BK20191107) 资助 Supported by the National Natural Science Foundation of China (Nos. 41977137, 42007133, 41991333), the Key Program of Frontier Sciences, Chinese Academy of Sciences (No. QYZDJ-SSW-DQC035), and the Natural Science Foundation of Jiangsu Province, China (No. BK20191107)

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收稿日期: 2021–11–10; 收到修改稿日期: 2022–01–04; 网络首发日期 (www.cnki.net): 2022–03–21

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Abstract: Over the past several decades, the long-term misuse and abuse of antibiotics in human health and livestock production have significantly contributed to the widespread dissemination of antibiotic resistance. Antibiotic resistance has been regarded as the top of the six emerging environmental issues and global challenges humans face in this century. Antibiotic-resistant bacteria (ARB) and antibiotic resistance genes (ARGs) in natural and agricultural environments such as soil may have a substantial impact on the spread of resistance determinants to the human microbiome. Research on the distribution, source, diffusion and elimination techniques of ARGs in soil has become a hot topic.

ARGs have been widely identified in diverse environments affected or unaffected by human activities, including soil, water sources, and atmosphere. Soil undoubtedly contains a complex natural resistome and also acts as a key reservoir for ARB and ARGs in the environment. The ARGs in soil primarily originate from internal resistance and external input. The internal resistance in microorganisms mainly indicates the presence of ARGs in the genomes of microbes. However, the antibiotic resistance in microbial can also be ascribed to the random mutation of genes under special conditions. In addition, with the widespread use of antibiotics in clinical care, livestock and agricultural production, more ARB and ARGs are introduced into the soil, resulting in an increased enrichment of ARGs.

The transfer of ARGs often occurs via environmental media. However, recent studies have shown that they may also be transmitted between parents and offspring or among different species of bacteria by vertical and horizontal gene transfer (HGT), respectively. ARGs in the soil can be transferred to surface/groundwater, atmosphere and the phytosphere. Both natural factors and human activities play vital roles in ARGs transmission in soils. For example, soil physicochemical properties (pH, organic matter, water content, etc.), agronomic regulations (cropping patterns, reclaimed water irrigation, organic fertilization, etc.), and environmental contaminants (heavy metals, nanoparticles, microplastics, etc.) can significantly affect the structural diversity and function of soil microbial communities. They have been identified as important environmental pressures that induce the evolution and spread of antibiotic resistance.

ARGs are also identified in human clinical pathogens conveyed by soil microbes. When comparing the multidrug-resistant resistome of soil bacteria with those in clinical human pathogens, the functional metagenomic analysis indicated a high nucleotide identity (>99%). This inferred possible HGT among bacteria from various environments. To reduce the threat posed by ARGs, treatment measures (aerobic composting, anaerobic digestion, and wastewater treatment technologies) have been examined to alleviate the selective pressure and reduce the import of ARGs into the soil. Generally, the reduction of ARGs in the environment is mainly related to extracellular DNA and cell transport, death of the host, and attenuation of extracellular ARGs.

Although the threat of ARB and ARGs to humans is generally recognized, it is difficult to determine threshold values for the maximum admissible levels of ARB and ARGs in diverse environments highly related to human activities. Furthermore, there is insufficient information to quantitatively evaluate the associated human health risks. Considering the urgency of the problem, it is necessary to establish a global systematic and publicly available monitoring network, for consecutively measuring antibiotic usage and the diversity of antibiotic resistance from clinical and agricultural practices. Continuous surveillance of antibiotic resistance can contribute to disease therapy, effective antimicrobial management and policy formulating. Thus, the “One Health” theory was proposed to manage the development and spread of ARGs in an interdisciplinary manner, and holistically reduce human risk to the lowest level. More attention should be paid to ARGs pollution with investment in both fundamental and applied research, to provide a strong scientific basis for formulating effective alleviation actions and a standardized assessment system. This will serve as a baseline for preventing, reducing, and removing these environmental contaminants.

Key words: Antibiotic resistance genes; Antibiotic-resistance bacteria; Soil; Horizontal gene transfer; One Health

抗生素为保证人类健康、动物生长和提高农业生产做出了巨大贡献。然而，随着人类活动和畜禽

养殖过程中长期过度使用和滥用抗生素，抗生素抗性基因（Antibiotic resistance genes, ARGs）在全世界范围内广泛传播，抗生素抗性基因已被认为是人类在本世纪面临的六大新环境问题和全球性挑战问题之首^[1-3]。即使低浓度下的抗生素残留也会对细菌产生选择性压力，伴随着人类活动的加剧，抗生素抗性细菌（Antibiotic-resistant bacteria, ARB）和抗生素抗性基因在环境中广泛共存（包括畜禽养殖排泄物、废水、污泥、大气和土壤等），前者具有普遍性和多样性，后者具有可转移性^[4]。ARGs 可以通过垂直转移和水平基因转移（Horizontal gene transfer, HGT）在亲本和子代之间或不同种类的细菌之间传播，导致其在环境介质中进行转移，其中水平基因转移被认为是 ARGs 传播的主要途径^[5]。

抗生素抗性在环境中的传播与 ARB 和 ARGs 极为相关，其中，土壤中 DNA 序列丰度最高、微生物种类最多，微生物在交流和竞争过程中，通过代谢活动不断产生抗生素、毒素等代谢产物，当前临床医疗和畜禽养殖过程中使用的大部分抗生素均来源于土壤中的微生物，其对抗生素抗性的产生和传播具有重要的影响。此外，土壤中的重金属等污染物对 ARGs 的协同选择作用以及移动基因元件

（Mobile genetic elements, MGEs）均能够促进土壤中 ARGs 的传播。携带 ARGs 的微生物死亡后，体内的 DNA 释放到环境中，在土壤矿物和有机胶体的保护下，能够长期存在于土壤环境中，容易被其他微生物吸收而获得抗生素抗性^[6]。

环境中抗生素抗性研究需要遵循“大健康（One Health）”准则，包括跨学科的认知和三个主要领域的综合研究，即人类健康、动物健康和环境健康^[3-7]。其中，土壤是“大健康”准则中的重要组成部分，其自身具有多种天然抗性，同时由于人类的农业生产和临床医疗等活动，造成大量抗性基因汇入土壤，土壤已然成为环境中 ARB 和 ARGs 的储存库。此外，ARB 和 ARGs 还可以通过多种途径转移到人类和动、植物体内^[8]（图 1），从而引发一系列土壤生态风险和人体健康问题。

1 土壤中抗性基因的分布和来源

1.1 内部来源

微生物的“内在抗性”是指存在于微生物基因组上的抗性基因或尚未表达抗性的抗性基因^[9]，微生物在一定环境中还可通过随机突变而获得抗生素抗性，微生物“内在抗性”是环境中 ARGs 的重要组成

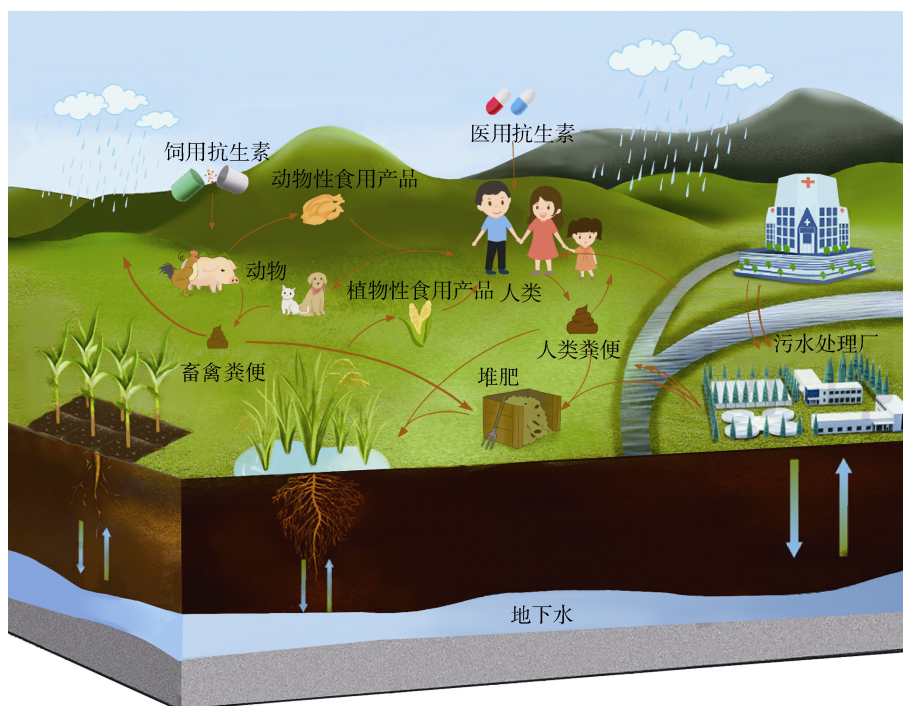


图 1 抗生素抗性细菌和抗生素抗性基因在环境中的传播

Fig. 1 The spread of antibiotic-resistant bacteria and antibiotic resistance genes in the environment

部分^[10]。土壤环境中存在大量由微生物合成的天然抗生素,形成一定的环境压力,使微生物种群获得内在抗性,其中微生物的内在抗性是未受人类活动影响土壤环境中 ARGs 的主要来源。

20 世纪初,在抗生素时代被提出之前,ARGs 就已经在环境中存在和传播^[11]。在远离人类活动影响的阿拉斯加冻结土壤中,多种新 β -内酰胺酶和氯霉素类抗性基因被发现,并首次检测到双功能 β -内酰胺酶抗性基因,表明该抗性基因能够自然存在于环境中^[12]。在 3 万年前的白令永久冻土中,晚更新世生物体内 DNA 中存在着高度多样性的 ARGs,对 β -内酰胺类、四环素类和糖肽类抗生素具有抗药性^[11]。在南极洲的冈瓦纳大陆研究站和新建 Jang Bogo 研究站共检测到 8 个主要 ARGs 类别,包括 73 个 ARGs 和 MGEs (整合子、转座子、质粒和基因盒)^[13]。以上研究均证实,在抗生素被人类广泛使用之前,ARGs 就已经存在于土壤环境中。随着第二代高通量测序技术和第三代单分子实时测序和纳米孔测序等测序技术的发展,人们能够更加全面且准确地揭示不同环境中 ARGs 以及与 ARGs 水平转移相关的基因元件的分布水平。

1.2 外部来源

由于人类活动的加剧,来自人类和动物的新型致病菌和抗生素进入土壤环境,成为重要的环境污染物质^[14]。从而促使 ARGs 在环境中广泛传播,其中与人类活动相关的 ARGs 在土壤环境中逐渐富集^[15-16]。

随着畜牧业一体化的发展,规模化畜禽养殖场是动物粪便的主要来源。畜禽养殖场动物肠道和粪便中含有丰富的 ARB 和 ARGs,粪便堆肥施用可能是动物体内 ARGs 进入土壤环境的主要途径^[17-18]。粪肥及其堆肥中 ARGs 的种类呈现多样性,对四环素类、 β -内酰胺类、氨基糖苷类、氯霉素、磺胺类抗生素等多种药物具有抗性^[19-20]。堆肥施用过程中,粪肥中许多 ARGs 均由质粒或整合子携带,ARGs 与 MGEs 共存能够促进 ARGs 的转移和传播^[21]。粪肥中携带 ARGs 的外来微生物进入土壤往往难以与土著微生物竞争存活,其释放到环境中的 ARGs 有可能通过水平基因转移进入土著微生物体内而使其获得抗生素抗性。粪肥中的有机质和养分能够促进微生物生长,导致 ARGs 在土壤环境中持续富集^[22]。此外,粪肥携带的抗生素残留对土壤微生物造成了

持续性的选择压力,导致微生物体内 ARGs 被诱导表达,同时固有基因也有可能发生基因突变产生新的 ARGs,促使共生微生物和病原微生物之间的基因交换,从而增加 ARGs 和 MGEs 从粪肥向土壤环境传播的风险^[19-23]。

废水的再利用,是解决水资源短缺问题的一种实用的解决方案,可显著缓解水资源压力。尤其是在农业生产中,污水经污水处理厂处理后直接排入河流或用于农业灌溉。然而,医疗废水和动物养殖场污水中的 ARGs 进入污水处理系统后,现有水处理技术不能彻底去除抗生素及 ARGs,污水处理厂的出水中仍然富含抗生素、病原微生物和营养物质,被视作 ARGs 选择和转移的高风险“热点”区域^[24],同时也是其他水体环境中 ARGs 最重要的来源之一。在我国南部珠江三角洲地区,采用鱼塘水灌溉土壤中残留的四环素和磺胺甲噁唑及其相应的 ARGs 显著高于生活污水。灌溉水中抗生素及其 ARGs 的浓度显著高于灌溉土壤,这表明废水是土壤环境中抗生素及 ARGs 的主要来源^[25]。使用未经处理的污水作为灌溉水源,土壤中 ARGs 的绝对丰度普遍提高两个数量级(除 *tetQ*、*aadA*、*int11*、*qacE+qacE Δ I* 和 *IncP-1* 质粒)^[26]。在澳大利亚维多利亚州地区,经处理后废水灌溉的城市公园土壤中共鉴定出 40 个特有的 ARGs,其中 β -内酰胺类抗性基因最为普遍^[27]。

在污水处理过程中,污泥能够大量富集抗生素和 ARGs。活性污泥中 ARGs 的含量相较于进水样品增加了 947 倍,这可能是由于微生物量的增加导致的结果^[28]。因此,污泥是微生物 ARGs 和 MGEs 富集的“热点”区域。堆肥还田是污泥处置和再生产品使用的重要方式,在此过程中携带移动基因元件的外来微生物与土著微生物通过水平基因转移共享遗传信息,也是 ARGs 向农田土壤中扩散的关键途径^[29]。相比于未改良土壤,经污泥改良后的土壤中,尽管 ARGs 的相对丰度无明显变化,但绝对丰度在 20 d 内有短期增加^[30]。

2 土壤中抗性基因的传播和影响因素

2.1 土壤中抗性基因的传播

土壤中富集的 ARGs 能够通过多途径传播到水、大气等介质,厘清 ARGs 在不同介质中的传播

规律及其影响因素对于有效评估环境中 ARGs 的生态风险尤为重要。

在淋溶和渗滤作用下，土壤中的 ARB 和 ARGs 能够转移至地表水、地下水和饮用水^[31]，导致水环境中存在多种与畜禽养殖等人类活动密切相关的 ARGs，严重威胁人体健康。目前，水体环境及水生生物体内的 ARGs 污染已经十分普遍。不仅在饮用水中检测到四环素类和磺胺类抗性基因，在饮用水源中分离的 Enterobacteriaceae 菌株中也有 4 种 ARGs 被检测出^[32-33]。Koike 等^[34]发现，养猪场附近的池塘和地下水中同时存在 7 种四环素抗性基因 (*tetM*、*tetO*、*tetQ*、*tetW*、*tetC*、*tetH* 和 *tetZ*)，其中地下水中的基因序列与池塘中的基因序列高度一致，甚至在地下水中还发现了新的序列簇和独特的抗性基因库。

土壤中的 ARGs 能够以生物气溶胶的形式进入到大氣中，在风力、气流等作用下，空气中的 ARGs 在不同的地区远距离传播，之后通过干/湿沉降传播至受人类影响较小的偏远地区土壤，从而导致 ARGs 在全球范围传播^[35]。污染严重的空气中颗粒物浓度较高，为 ARB 和 ARGs 提供了更多的附着点^[36]。例如，在畜禽养殖及其粪便处理过程中，土壤中大量的污染物和 ARB 极易发生雾化，导致地球表层成为 ARGs 重要的载体和储存库，从而促使 ARGs 在土壤与大气之间发生传播^[37]。

土壤微生物组是植物获得 ARGs 的重要来源，在根际环境中，水通量增加和养分输入可以刺激微生物代谢以及体内质粒的转移接合，促进抗性细菌从土壤微生物组向植物微生物组迁移，根际和叶际环境成为植物界微生物基因转移的“热点”区域^[38-39]。众多研究发现，植物内生菌（根际内生菌和叶际内生菌）能够通过多种途径从施加粪肥的土壤中获得抗生素抗性，是抗性基因组和移动基因元件的主要载体和传播者^[40]。经堆肥处理后，土壤中的 ARGs 具有转移到蔬菜体内的风险，尤其需要注意的是生食或轻加工的蔬菜^[41]。例如，猪粪堆肥施用增加了胡萝卜组织尤其是外表皮中 ARGs 的累积，食用前去皮是降低人体健康风险的有效策略^[42]。此外，植物界中潜在的可转移基因库与宿主密切相关，具有高度的流通性^[39]。由于这些“热点”区域处于非均质的动态环境，如根际微生物及其分泌物（糖、有机酸和氨基酸等）可能会对 ARGs 从土壤向植物体内

的迁移产生影响^[43]，在不同条件下难以评估这些因素对 ARGs 水平基因转移的影响。

2.2 土壤中抗性基因传播的影响因素

临床医疗和畜禽养殖活动中抗生素的大量使用，以及农业生产中动物粪便和污泥的处理再利用，对 ARGs 传播产生了关键性的选择压力。此外，其他环境自然因素也影响微生物的抗生素抗性，如营养匮乏、极端温度胁迫和氧化还原条件等^[44-45]。其中，土壤理化性质、农艺调控及环境污染物等对土壤中 ARGs 的传播起到至关重要的作用。

土壤理化性质（pH、温度、有机质、含水率等）可以显著影响土壤中微生物群落的结构多样性和功能，已被确定为诱导抗生素抗性进化和传播的重要环境因素^[46]。在长期施有机肥土壤中，ARGs 的丰度与抗生素浓度和土壤理化性质（pH 和有机质）紧密相关，且随着土壤深度的增加，四环素类药物浓度和 ARGs 丰度普遍降低^[47]。Wu 等^[48]报道，在猪饲养场附近的土壤中，*tet* 基因绝对拷贝数不仅与土壤中四环素残留浓度显著相关，还受土壤有机质等环境因子的影响。土壤 pH 通过影响养分有效性或微生物生理活性对其产生了较大的选择性压力，并对微生物的丰度和多样性产生影响，进而影响了 ARGs 在土壤环境中的传播^[49]。土壤含水率也能够通过影响微生物活性来干扰抗生素和 ARGs 的去除，同时含水率改变也会影响土壤孔隙度、吸附系数和离子电位，从而影响土壤中 ARGs 的持久性^[50]。

常见的农艺调控措施，如施肥、种植模式、灌溉水源和农药喷施等会影响土壤固有的抗生素抗性。不同的施肥和种植体系（如旱地和水稻中）能够影响土壤中 ARGs 和 MGEs 的丰度水平。有机粪肥中含有适应细菌生长的丰富碳源，并且含有抗生素、重金属、有机污染物等共选择物质，能够促进抗生素抗性在土壤环境中的传播^[51]。尤其是农业土壤在长期施用堆肥的过程中，土壤中的 ARGs 水平在初始阶段呈上升趋势，显著增加了粪肥中 ARGs 向土壤环境中传播的风险^[52]。Wang 等^[53]报道，在水稻和旱地两种种植体系中，水稻土中的 ARGs 积累量和相应的微生物量高于旱地土壤，其中堆肥施用对两种种植体系土壤中的 ARGs 累积效果均不显著，而化肥施用增加了旱地土壤中 ARGs 的相对丰度，降低了水稻土中 ARGs 的相对丰度。此外，草

甘磷、草铵磷和草甘菊等除草剂的喷施同样能够改变土壤微生物群落的遗传组成,促使 ARGs 和 MGEs 土壤中累积。除草剂暴露还提高了多药抗性质粒的细胞膜通透性和偶联频率,促进了 ARGs 在微生物间的交换^[54]。与此同时,生物炭作为土壤改良剂已被广泛应用于农业生产过程,其中抗生素能够和生物炭上的芳香环之间通过 π - π 键发挥相互作用,从而驱动土壤微生物间 ARGs 的选择或共选择^[55]。生物炭改良剂普遍被认为可显著降低非种植土壤中 ARGs 的丰度,其潜在机制可归因于生物炭的吸附作用降低抗生素和重金属的流动性,同时生物炭的添加还能够影响细菌群落结构的变化和抗体的产生^[56-58]。

土壤中的污染物(重金属、微塑料、纳米颗粒等)能够显著影响 ARGs 的类型、丰度和迁移过程,导致 ARGs 在污染土壤中传播风险的不可预测性。重金属可通过共抗性、交叉抗性、共调控作用对环境中 ARGs 产生选择性压力,从而使土壤中 ARGs 丰度维持较高水平^[59]。与抗生素不同,重金属在环境中长期存在,了解重金属对抗生素抗性和对环境中细菌群落结构变化的驱动至关重要^[60]。微塑料比表面积大、吸附性强,可吸附环境中的重金属、抗生素、抗性基因和抗性细菌等污染物,微塑料逐渐成为微生物抗生素抗性的新“热点”区域^[61-62]。例如,在设施蔬菜土壤中,微塑料的粒径越大、风化作用越强或蔬菜种植期越长,其能够从周围环境中吸附更多的抗生素、重金属和移动基因元件,从而提高微塑料表面 ARGs 的种类和数量^[63]。研究表明微塑料对 ARGs 的富集量与微塑料的浓度成反比,能够大量富集环境中的 ARGs,特别是胞外 ARGs,从而显著提高 ARGs 的迁移能力^[64]。尽管纳米颗粒广泛存在于土壤、废水和污泥等多种环境中,但其对 ARB 和 ARGs 的影响还缺乏全面了解。Zhu 等^[65]发现 AgNPs 暴露能够干扰跳虫肠道细菌群落的组成,降低弹尾虫肠道微生物群中 ARGs 的发生率。然而, Qiu 等^[66]报道纳米 Al_2O_3 的使用显著促进了质粒 RP4、RK2 和 pCF10 携带的耐药基因的水平基因转移,这可能是由于纳米 Al_2O_3 能够通过诱导氧化应激损伤细菌细胞膜,从而增强接合基因表达。该结果表明纳米材料可能会促进敏感细菌获得抗生素抗性,从而带来一定的环境和人体健康风险。

3 土壤中抗性基因的消减技术

为了减少土壤、水、大气等环境介质中 ARGs 的传播,降低环境中抗生素抗性的风险,科研人员重点研发各种 ARGs 消减技术,如好氧堆肥、厌氧发酵和水处理工艺,其目的是减少有机肥、污泥还田、污水灌溉等农业生产过程造成的土壤中抗生素和外源性 ARGs 的输入和富集。其中,环境中 ARGs 的削减主要与细胞的运输、宿主的死亡以及胞外 ARGs 的衰减有关^[46-67]。

好氧堆肥技术常被用于畜禽粪便和污泥的无害化处理以及肥料的资源化利用,同时也能够有效削减畜禽粪便中的 ARGs,其中,温度等处理工艺影响着有机废弃物中 ARGs 的丰度。连续高温堆肥过程中,温度的变化能够显著降低动物粪便中 ARGs 和整合子的多样性和丰度^[68]。此外,沸石、过磷酸钙和硫酸亚铁的添加能够有效去除畜禽粪便中的 ARGs,去除率分别达到 86.5%、68.6%和 72.2%^[69],此外,生物炭和鼠李糖脂、吐温 80 等表面活性剂的添加也能够对 ARGs 的去除起到一定作用^[70-71]。然而,好氧堆肥技术难以去除所有类型的 ARGs,好氧堆肥产品仍然是 ARGs 的重要储存库^[22]。

厌氧发酵技术也常被用于处理畜禽粪便和污泥等有机固体废弃物。畜禽粪便经厌氧发酵后,可以减少动物粪便和有机污泥中 ARB 和 ARGs 的数量和丰度,并且其残渣可作为有机肥施用,是农业废弃物中 ARGs 去除和实现可持续性利用的有效方法^[72]。Sun 等^[73]通过采用预处理、高温消化、两段消化、添加剂和固态消化等处理手段,研究厌氧发酵对 ARGs 的去除效果。其中,操作参数对 ARGs 的去除效率起着至关重要的作用,例如在污泥厌氧消化过程中,温度越高、水力停留时间越长,ARGs 去除率越高^[74]。

水处理工艺技术亦能够有效削减污水、污泥以及饮用水中的 ARGs。在废水处理过程中,紫外线杀菌、氯气和臭氧消毒等技术被用来诱导细菌损伤,从而有效去除水体环境中的 ARGs^[75]。抗性细菌的杀菌过程与消毒剂的相对活性和重要细胞成分(包括氨基酸、糖类、脂类和核酸)的消耗量密切相关^[76]。在不同的紫外线或氯离子浓度下测定废水中 ARGs 的转移频率,结果表明紫外线和氯化消毒能

够影响 ARGs 的接合转移，其中紫外线强度和氯气剂量是去除 ARGs 的重要因素^[77]。已有研究发现，污水处理厂各处理环节对 ARGs 去除的影响不同，例如，生物处理和化学处理能够造成 ARGs 丰度发生不同变化^[78]。在废水处理过程中，尽管抗性细菌因细胞结构遭到破坏而失活，但 ARGs 仍可能存在于细胞碎片中，对人体健康构成潜在的风险。因此，需要严格评估现有的水处理工艺，以发挥它们在缓解环境中 ARGs 风险的潜力。

4 土壤中抗性基因与人体健康

大部分与临床相关的 ARGs 来自于环境中的微生物^[79]，同时土壤微生物携带的 ARGs 也存在于人类临床病原体，以及对磺胺类、氨基糖苷类和 β -内酰胺类等药物具有高水平抗性的新型细菌体内^[80]。采用宏基因组技术对土壤微生物进行功能分析，研究发现土壤微生物和人类临床病原体的耐药组核苷酸同源性较高 (>99%)，由此推断不同环境中微生物之间的 ARGs 可能存在水平基因转移。在自然和受人类影响的环境中，整合子被证实是多种 ARGs 的主要载体^[14]。例如，*intI1* 属于 I 类整合子，与同一基因位点上多个 ARGs 的整合密切相关，促进了 ARGs 的水平基因转移过程^[21]。

目前，关于 ARGs 从环境微生物向人类病原体转移的认识仍存在一定局限性。土壤中施加有机肥后，在叶菜（芝麻菜、香菜）表面检测到多种 ARGs，该 ARGs 极易通过摄食过程进入人类体内，表明土壤环境、植物和人类之间存在直接的食物链联系^[81-82]。将生菜或香菜叶富集培养，经检测在人体大肠杆菌中发现多个抗性质粒^[81]。当细菌基因组中的多个 ARGs 同时出现在质粒上时，“超级细菌”可能会在全球范围内爆发。例如，黏菌素曾用作应对多重耐药细菌爆发威胁的最后一道防线，但如今，我国上海首次报道在动物和人类肠道内发现携带黏菌素抗性基因 *mcr-1* 的质粒，随后该抗性基因出现在世界各地人类病原体、家禽、猪肉等样本中，导致其在全球范围内广泛传播^[83]。

5 结论与展望

目前，由于人类活动和畜禽养殖过程中长期过

度使用和滥用抗生素，土壤中 ARB 和 ARGs 污染已经广泛存在，但其生态风险缺乏严格管控，难以确定土壤环境中 ARB 和 ARGs 的最大允许阈值，更难以客观地评估与其相关的人类健康风险。同时，关于土壤中 ARGs 的传播阻控和削减技术研究仍然不足。因此，在“大健康”准则下，亟需建立一个公开的全球网络监测预警系统，能够持续掌握抗生素生产使用情况以及评估农业生产和临床医疗活动中抗生素抗性的潜在风险；进一步厘清 ARGs 在土壤环境中的传播和扩散机制；在此基础上研发新型高效的 ARGs 传播阻断和消减技术，从而控制土壤中抗生素抗性的产生和传播。

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