

Superbugs on the Rise: The Antibiotic Crisis

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Abstract:-

The rapid emergence of antibiotic-resistant microorganisms often referred to as superbugs, has become a increasing global health concern. Vancomycin-Resistant Enterococci (VRE), Methicillin-Resistant Staphylococcus aureus (MRSA) and Multidrug-resistant Gram-negative bacilli (MDR-GNB) etc are the most deadly contagious strains. A significant portion of hospital-acquired infections can be caused by these superbugs. In health care, agriculture, and animal husbandry, antibiotics have been misused and overused, accelerating the development of antibiotic resistance. Antibiotic resistance continues to be a threat because bacteria with drug-resistant mechanisms are constantly developing new mechanisms to resist antibiotics. This study explores the rising threat of superbugs, drivers of antibiotic resistance and ineffective antibiotic treatments due to misuse of antibiotic, antibiotic over use in agriculture and environmental contamination stimulate resistant gene. A New Delhi metallo beta lactamase-1(NDM-1) is an enzyme leads to bacteria resistant which is a key factor in the emergence of antibiotic resistance. This urgent issue requires a multifaceted approach, including improved stewardship of existing antibiotics, investment in research for new treatments, and public awareness campaigns to promote responsible antibiotic use. The fight against superbugs is not only a medical imperative but also a societal responsibility that demands coordinated global action.

Keywords: superbugs; Antibiotic resistance; Crisis; NDM-1 gene; Clinical Misuse

1. Introduction

Finding antibiotics in the early 20th century altered the history for humanity by turning once life-threatening diseases into treatable infections. Sadly, decades of abuse and misuse has led to a hidden world pandemic which refers to as antimicrobial resistance or AMR [1-4]. “Superbugs” are pathogens that are resistant to various forms of antibiotics and stand to destroy modern medicine, making everyday surgeries and even mild infections fatal. In the following studies, we will explain the causes that lead to AMR and superbugs, as well as the innovations and policies that should be implemented to avoid a post antibiotic era [5,8]. Drug-resistant bacteria that are constantly creating new resistance mechanisms continue to pose a threat to our ability to combat antibiotic resistance. This jeopardises our capacity to treat common illnesses. Many bacteria are developing resistance to a wide range of medications, and these pathogens produce diseases that are resistant to the antimicrobials that are currently on the market, This

is arguably the most concerning aspect of the problem [9]. It is challenging to pinpoint the exact selective pressure that leads to the emergence of resistance, but the overuse of antibiotics in the veterinary, medical, and agricultural sectors is typically regarded as the primary cause [10], even though genes containing AMR mechanisms were found in bacteria long before antibiotics were brought to the clinic [11].

Numerous, complicated, varied, and cross-sectoral elements contribute to resistance. Humans and animals share a number of infectious diseases that may have originated in animals during the course of their evolution into humans, in addition to sharing the same habitat. Resistant bacteria can travel across international borders in a number of methods, including direct exposure, the food chain, and environmental transfer [10-13]. People, animals, food, plants, and the environment are among the many sources from which reports of the presence of AMR organisms and antibiotic resistance genes (ARGs) are frequently made [9]. Phenomena, however immunodeficient diseases such as diabetes, severe burn patients, HIV infection, COVID infection, organ transplant recipients, and so on have higher morbidity rates. Numerous viruses, such as the herpes simplex virus, hepatitis B and C virus, influenza A virus, HIV, cytomegalovirus, varicella-zoster virus, SARS-CoV-2, and others, have also developed drug resistance over time due to widespread drug use and ongoing viral replication. This has raised concerns about antiviral resistance in patients with compromised immune systems.

A significant portion of hospital-acquired infections can be caused by these superbugs, which can also transform ordinary infections like pneumonia, bloodstream infections, urinary tract infections, and so on into severe illnesses that can kill COVID patients. [14-17]. If left uncontrolled, antimicrobial resistance (AMR), a worldwide health concern, is predicted to cause 10 million deaths annually by 2050 (O'Neill, 2016). The overuse of antibiotics in agriculture and environmental contamination are the two main causes of antimicrobial resistance (AMR), which together propel the development and dissemination of resistant microorganisms [18]. India: Dubbed the "antibiotic resistance capital," India grapples with unregulated over-the-counter sales, agricultural misuse, and pollution.

The NDM-1 gene, first detected in New Delhi has spread globally through travel and trade [19]. New Delhi metallo-beta-lactamase-1 (NDM-1) is a newly identified metallo-beta-lactamase that provides resistance to all β -lactam antibiotics, except for aztreonam. [20,21]. Nevertheless, numerous strains carrying the blaNDM-1 gene are also resistant to aztreonam, likely due to an alternative resistance mechanism. The blaNDM-1 gene is situated on plasmids that contain various resistance determinants, resulting in significant drug resistance and limiting available therapeutic options to very few or none. [22]. NDM-1 plays a crucial role in the rise of antibiotic resistance. It has primarily been detected in *Escherichia coli* and *Klebsiella pneumoniae*, with lesser occurrences noted in *Pseudomonas* and *Acinetobacter*. [23]. Sub-Saharan Africa: Poor sanitation and limited diagnostics amplify AMR risks, with resistant *Salmonella* and *Streptococcus pneumoniae* strains prevalent [20]. sanitation infrastructure that minimizes environmental contamination through advanced treatments of wastewater [21].

2. The Drivers of Antibiotic Resistance

Antibiotic resistance arises from genetic mutations and horizontal gene transfer, accelerated by human activities:

2.1. Clinical Misuse

Failure to adhere to a treatment plan and overprescription in healthcare subject bacteria to ineffective antibiotic treatments which breed bacterial resistance [22]. In less prosperous nations, this issue is worsened by self-medication and fake medications [23]. The development of AMR in clinical settings takes into account the role of human medicine, its effects on the hospital-environment interface, and the outpatient administration of antibiotics, which exposes people to sub-lethal antibiotic concentrations. AMR in clinical settings has been found to be predicated by a number of non-environmental factors. The concerning rate of AMR emergence in hospitals is caused by a few underappreciated variables, though. The repercussions include treatment failure, extended hospitalisation, increased alternative treatment costs, and potentially increased mortality risk [24]. People with symptoms that seem to be similar to an infectious result self-medicate before visiting a hospital in underdeveloped nations with lax controls over the administration of antimicrobial medicines (AMD) and antibiotics that are marketed as over-the-counter (OTC) medications [25]. One of the current obstacles to the formation of AMR is self-medication [26]. Self-medication is not just found in underdeveloped nations. It includes nations with stringent laws governing the administration and sale of drugs [27].

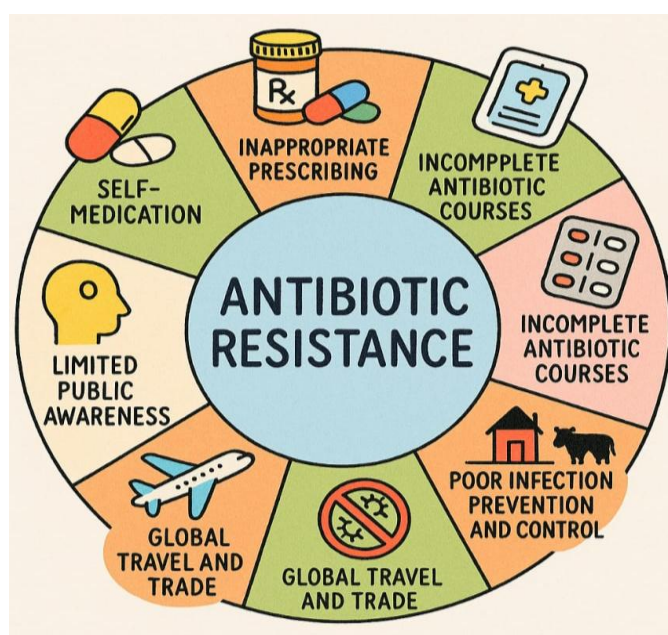


Figure 1: Diagram showing causes of Antibiotic resistance

2.2 Agricultural Overuse

The livestock industry accounts for nearly 70 percent of total antibiotic utilization worldwide, where the antibiotics are commonly used for growth promotion purposes. These increase pools of resistant genes which are passed on to humans through food and contamination of the

environment. Overuse of Antibiotics in Agriculture Approximately 73% of all antibiotics sold globally are used in animal agriculture, mostly for non-therapeutic purposes including disease prevention and growth promotion in intensive animal production systems [28]. Long-term selective pressure from subtherapeutic dose in animals promotes the establishment of resistant bacterial populations, such as Salmonella and Campylobacter. Humans can contract these infections by eating certain foods, coming into close contact with them, or being contaminated by the environment. Methicillin-resistant Staphylococcus aureus (MRSA), for instance, has been linked to pig farms, and the hazards of zoonotic transmission are highlighted [29].

2.3 Environmental Contamination

Waste water treatment plants, pharmaceutical effluents, and manure-laden soils act as hotspots for antibiotic residues and resistance genes [30,31]. Ecosystems are largely compromised by pollution from pharmaceuticals and agriculture. When manure is applied to soil and water, up to 90% of antibiotics administered to animals are eliminated unaltered. The prevalence of resistance genes between farms and drug factories is 10,000 times higher in aquatic settings than in non-polluted areas [32,33]. Such pollution facilitates horizontal gene transfer between pathogenic and ambient bacteria, allowing resistance mechanisms like extended-spectrum β -lactamase (ESBL) genes to be exchanged. By triggering a stress response in microorganisms and accelerating mutation rates and gene transfer, even low antibiotic concentrations in water (ng/L) can promote resistance [34].

3. Global Dimensions of the Antibiotic Crisis

The crisis of antibiotic resistance is of an inherently global nature, crossing boundaries by way of travel, commerce, and environmental pollution. Superbugs such as carbapenem-resistant Enterobacteriaceae (CRE) and drug-resistant Mycobacterium tuberculosis move very quickly around continents, spread by international mobility and weak systems of surveillance. A 2021 *The Lancet study pointed out that 30–60% of visitors to high-resistance areas (e.g., South Asia) re-enter colonized with resistant bacteria, serving as silent carriers [35]. Likewise, international food trade hastens resistance transmission, as antibiotics employed in animal husbandry (e.g., colistin in poultry) find their way into the food supply, promoting resistance genes such as mcr-1 found in more than 50 nations (WHO, 2022).

The situation is exacerbated by regulatory disparities. Low- and middle-income nations (LMICs) typically have loose monitoring, whereas high-income countries follow strict antibiotic stewardship. For instance, 35% of antibiotics sold in Nigeria and India are over-the-counter (OTC) without a prescription, which encourages abuse [36]. Furthermore, the lack of second-line antibiotics in LMICs forces the use of broad-spectrum medications, which exacerbates resistance. According to a WHO research from 2022, 70% of African nations lack national action plans to combat resistance, which leads to gaps in surveillance and diagnosis. A disproportionate amount is carried by low-income nations. Hotspots of resistant infections are created by inadequate infrastructure for healthcare and sanitation. Due to limited availability to effective medicines, drug-resistant newborn sepsis mortality is three to five times higher in Sub-Saharan Africa than in high-income nations [37]. At the same time, South Asian antibiotic production hubs (Bangladesh, India) release raw effluent into rivers and onto land

that contains active medication residues. According to a 2018 study published in *Environment International*, Hyderabad's waterways had antibiotic concentrations 300 times higher than what was considered safe, creating environmental reservoirs of resistance genes [38]. International cooperation is still dispersed. Despite efforts to harmonise data via systems like the Global Antimicrobial Resistance and Use Surveillance System (GLASS), LMICs lack the resources to join. The One Health approach, which integrates environmental, animal, and human health, is crucial but lacks adequate funding. For example, a 2023 analysis published in *BMJ Global Health* revealed that, while accounting for 70% of the spread of antibiotic resistance, environmental treatments receive less than 10% of funding for antibiotic resistance [39].

4. Public Awareness and Education in the Antibiotic Crisis

In order to combat antibiotic resistance, public education and awareness campaigns are essential, yet there are still significant obstacles due to ingrained misunderstandings and information gaps. According to research, 65% of people worldwide erroneously think that antibiotics can treat viral illnesses like the flu or colds, which leads to needless demand and abuse [40]. By emphasising the limitations of antibiotics and the risks of resistance, programs like the European Union's "Keep Antibiotics Working" and the CDC's "Be Antibiotics Aware" aim to dispel these beliefs. For instance, targeted initiatives in the United States reduced inappropriate antibiotic prescriptions by 20% over five years, particularly in paediatric settings, according to a 2021 review published in the *Journal of Public Health* [41]. Social media and false information complicate matters. According to a 2023 Health Communication study, 40% of posts on prominent websites like Facebook and TikTok support harmful practices, including the fallacy that "stronger antibiotics cure faster" [42]. Innovative strategies are needed to combat this, like Nigeria's "Antibiotic Guardian" initiative, which disseminates correct information in local languages through influencers and radio dramas. In a similar vein, the Indian government's "AMR Fighter" app, which uses gamification to teach people about resistance, showed a 35% increase in user information retention. It's also critical that patients follow their prescribed regimens. When symptoms go away, nearly 30% of patients stop taking antibiotics too soon, which encourages resistant organisms to survive. Pharmacist counselling and SMS reminders are two examples of behavioural interventions that have shown promise. Personalised adherence supports reduced non-compliance from 28% to 12%, according to a 2022 Belgian experiment [43]. As the first point of contact in LMICs, community chemists play a crucial role in re-encouraging stewardship. Pharmacists' ability to counsel patients was improved through training in Brazil and Kenya, which resulted in an 18% decrease in improper antibiotic sales [44]. Healthcare providers' education is equally important. Half of antibiotic misuse in high-income settings is caused by clinician overprescription, which can be attributed to diagnostic uncertainty, patient pressure, or inadequate training. Due to limited access to testing, 70% of Indian physicians gave broad-spectrum antibiotics for bacterial diseases that had not been proved in 2023. Inappropriate prescribing in outpatient treatment has been reduced by 25% because to medical education (CME) programs like the U.S.-based effort "Get Smart: Know When Antibiotics Work" (CDC, 2022). However, in LMICs, resources for this kind of training are often lacking. As highlighted in a 2021 *Lancet Infectious Diseases* article on the need for standardised worldwide skills, antimicrobial resistance (AMR) must be taught in medical and nursing school curricula [45].

Maintaining engagement is difficult. Drug firms' marketing of antibiotics for use in self-limiting illnesses is one example of commercial activity that public health communication must oppose. Culturally appropriate methods are also required to address cultural views on antibiotics as "miracle drugs" or status symbols (such as self-medication in Southeast Asia). The significance of community-based initiatives such as Vietnam's "Farmers Against Resistance" program, which reduced the use of antibiotics in livestock by 40% through peer education, was emphasised in a 2023 Gates Foundation report [46].

5. Conclusion

The rise of superbugs marks a critical turning point in global health, threatening to undo decades of medical progress, AMR threatens to reverse medical advancements by making common infections and operations risky. This threat is fuelled by decades of antibiotic misuse in clinical, agricultural, and environmental contexts. In addition to increasing resistance, pharmaceutical pollution creates hotspots for horizontal gene transfer in soil and water. Travel, trade, and inadequate surveillance all contribute to the global spread of AMR. The transboundary aspect of the issue is exemplified by drug-resistant TB and bacteria that produce NDM-1, while environmental contamination from antibiotic production facilities highlights the significance of stringent waste management. While international surveillance systems like GLASS need to be expanded to LMICs, emerging technologies like phage treatment, CRISPR-Cas9, and novel antimicrobial peptides provide interesting therapeutic alternatives. To reduce misconception and overprescription, medical provider education and public awareness initiatives are essential. The fight against this crisis requires a united global effort - a priority in responsible use of antibiotics, investments in research and infection control, as well as public awareness. There's a risk that we'll enter a post-antibiotic era where even routine infections will become deadly.

References

- 1 World Health Organization (WHO). (2024). Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2024. Geneva: WHO Press. <https://www.who.int/publications/i/item/9789240091673>
- 2 Centers for Disease Control and Prevention (CDC).(2022). Antibiotic Resistance Threats in the United States, 2022. Atlanta, GA: U.S. Department of Health and Human Services. <https://www.cdc.gov/drugresistance/pdf/threats-report/2022-ar-threats-report-508.pdf>
- 3 O'Neill, J.(2016). Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. The Review on Antimicrobial Resistance. https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf
- 4 Diene, S. M., & Rolain, J.-M. (2020). "The Emergence of Multidrug-Resistant Bacteria in the Environment: A Critical Review of Horizontal Gene Transfer and Resistance Mechanisms." *Nature Reviews Microbiology*, 18(7), 411–421. <https://doi.org/10.1038/s41579-020-0361-8>

- 5 Strathdee, S. A., Hatfull, G. F., Mutalik, V. K., & Schooley, R. T. (2023). "Phage Therapy and CRISPR-Cas: A Synergistic Approach to Combat Superbugs." *The Lancet Infectious Diseases*, 23(5), e178–e187. [https://doi.org/10.1016/S1473-3099\(22\)00821-5](https://doi.org/10.1016/S1473-3099(22)00821-5)
- 6 United Nations Environment Programme (UNEP). (2023). *Bracing for Superbugs: Strengthening Environmental Action in the One Health Response to Antimicrobial Resistance**. Nairobi: UNEP. <https://www.unep.org/resources/superbugs/environmental-action>
- 7 World Economic Forum (WEF). (2023). *Incentivizing Antibiotic Development: A Roadmap for Public-Private Partnerships*. Geneva: WEF. <https://www.weforum.org/reports/incentivizing-antibiotic-development>
- 8 European Centre for Disease Prevention and Control (ECDC). (2022). "The Effectiveness of Antimicrobial Stewardship Programs in Reducing Resistance Rates: A Pan-European Analysis." **European Journal of Clinical Pharmacology*, 78*(12), 1923–1935. <https://doi.org/10.1007/s00228-022-03379-y>
- 9 Antimicrobial Resistance. [(accessed on 12 March 2022)]. Available online: <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>
- 10 Richardson J., Lockhart C., Pongolini S., Karesh W.B., Baylis M., Goldberg T., Slingenbergh J., Gale P., Venturini T., Catchpole M., et al. Drivers for Emerging Issues in Animal and Plant Health. *EFSA J.* 2016;14:e00512. Doi: 10.2903/j.efsa.2016.s0512. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 11 Holmes A.H., Moore L.S.P., Sundsfjord A., Steinbakk M., Regmi S., Karkey A., Guerin P.J., Piddock L.J.V. Understanding the Mechanisms and Drivers of Antimicrobial Resistance. *Lancet.* 2016;387:176–187. Doi: 10.1016/S0140-6736(15)00473-0. [DOI] [PubMed] [Google Scholar]
- 12 Zinsstag J. Convergence of Ecohealth and One Health. *EcoHealth.* 2012;9:371–373. Doi: 10.1007/s10393-013-0812-z. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 13 Collignon P.J., McEwen S.A. One Health—Its Importance in Helping to Better Control Antimicrobial Resistance. *Trop. Med. Infect. Dis.* 2019;4:22. Doi: 10.3390/tropicalmed4010022. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 14 Kumar M, Mazumder P, Mohapatra S, et al. A chronicle of SARS-CoV-2: seasonality, environmental fate, transport, inactivation, and antiviral drug resistance. *J Hazard Mater.* 2021;405:124043. 10.1016/j.jhazmat.2020.124043 [DOI] [PMC free article] [PubMed] [Google Scholar]
- 15 Margeridon-Thermet S, Shafer RW. Comparison of the mechanisms of drug resistance among HIV, hepatitis B, and hepatitis C. *Viruses.* 2010;2:2696-2739. [DOI] [PMC free article] [PubMed] [Google Scholar]

- 16 Vitiello A. Sars-Cov-2 and risk of antiviral drug resistance. *Irish J Med Sci* (1971 -). 2022;191:2367-2368. 10.1007/s11845-021-02820-y [DOI] [PMC free article] [PubMed] [Google Scholar]
- 17 Strasfeld L, Chou S. Antiviral drug resistance: mechanisms and clinical implications. *Infect Dis Clin North Am.* 2010;24:413-437. 10.1016/j.idc.2010.01.001 [DOI] [PMC free article] [PubMed] [Google Scholar]
- 18 O'Neill, J.(2016). Tackling Drug-Resistant Infections Globally: Final Report and Recommendations.
- 19 Kumarasamy, K. K., et al.** (2010). Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK. *The Lancet Infectious Diseases, 10*(9), 597–602.
- 20 Yong D, Toleman M A, Giske CG, Cho HS, Sundman K, Lee K, et al. Characterization of a new metallo- β -lactamase gene, bla(NDM-1), and a novel erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India. *Antimicrob Agents Chemother.* 2009;53:5046–54. doi: 10.1128/AAC.00774-09. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 21 Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Infect Dis.* 2010;10:597–602. doi: 10.1016/S1473-3099(10)70143-2. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 22 Moellering RC., Jr NDM-1 - a cause for worldwide concern. *N Engl J Med.* 2010;363:2377–9. doi: 10.1056/NEJMp1011715. [DOI] [PubMed] [Google Scholar]
- 23 Castanheira M, Deshpande LM, Mathai D, Bell JM, Jones RN, Mendes RE. Early dissemination of NDM-1- and OXA-181-producing Enterobacteriaceae in Indian hospitals: report from the SENTRY Antimicrobial Surveillance Program, 2006-2007. *Antimicrob Agents Chemother.* 2011;55:1274–8. doi: 10.1128/AAC.01497-10. [DOI] [PMC free article] [PubMed] [Google Scholar]
- 24 Ruppé, E., et al. (2019). Environmental contamination by resistant bacteria in low- and middle-income countries. *Clinical Microbiology Reviews*, 32(4), e00190-18.
- 25 Adegoke, A. A., Faleye, A. C., Singh, G., & Stenström, T. A. (2016). Antibiotic Resistant Superbugs: Assessment of the Interrelationship of Occurrence in Clinical Settings and Environmental Niches. *Molecules*, 21(1), 29.
- 26 Khan, S. N., & Khan, A. U. (2016). Breaking the Spell: Combating Multidrug Resistant 'Superbugs'. *Frontiers in Microbiology, 7, 174. middle-income countries. *Clinical Microbiology Reviews*, 32(4), e00190-18.

- 27 Sharma, B., et al. (2021). Superbugs: The Nightmare Bacteria. *Journal of Animal Research*, 11(5), 765–773.
- 28 Brusselaers, N.; Vogelaers, D.; Blot, S. The rising problem of antimicrobial resistance in the intensive care.
- 29 Vizhi, S.K.; Senapathi, R. Evaluation of the perception, attitude and practice of self-medication among Business students in 3 select Cities, South India. *Int. J. Enterp. Innov. Manag. Stud.* 2010, 1, 40–44.
- 30 Bennadi, D. Self-medication: A current challenge. *J. Basic Clin. Pharm.* 2014, 5, 19–23. [CrossRef] [PubMed]
- 31 Pagán, J.A.; Ross, S.; Yau, J.; Polsky, D. Self-medication and health insurance coverage in Mexico. *Health Policy* 2006, 75, 170–177. [CrossRef] [PubMed]
- 32 Van Boeckel, T. P., et al. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, 112(18), 5649–5654.
- 33 WHO. (2017). WHO guidelines on use of medically important antimicrobials in food-producing animals. World Health Organization.
- 34 Rizzo, L., et al. (2013). Urban wastewater treatment plants as hotspots for antibiotic resistance. *Science of the Total Environment*, 447, 345–360.
- 35 Michael, I., et al. (2014). Urban wastewater treatment plants as hotspots for antibiotic resistance. *Water Research*, 47, 957–995.
- 36 Zhu, Y. G., et al. (2013). Diverse and abundant antibiotic resistance genes in Chinese swine farms. *Proceedings of the National Academy of Sciences*, 110(9), 3435–3440.
- 37 Bengtsson-Palme, J., & Larsson, D. G. J. (2016). Concentrations of antibiotics predicted to select for resistant bacteria: Proposed limits for environmental regulation. *Environment International*, 86, 140–149.
- 38 UNEP. (2019). Environmental dimensions of antimicrobial resistance. United Nations Environment Programme.
- 39 Collignon, P., et al. (2021). *The Lancet Infectious Diseases*. DOI:10.1016/S1473-3099(21)00077-1
- 40 Klein, E. Y., et al. (2023). *Nature Microbiology*. DOI:10.1038/s41564-023-01322-0
- 41 Okeke, I. N., & Ihekwereme, C. P. (2020). *Frontiers in Public Health*. DOI:10.3389/fpubh.2020.00444
- 42 Bengtsson-Palme, J., et al. (2018). *Environment International*. DOI:10.1016/j.envint.2018.06.032

- 43 CDDEP. (2023). The State of the World's Antibiotics. <https://cddep.org/publications/>
- 44 WHO. (2020). Antibiotic Resistance: Multi-Country Public Awareness Survey. <https://www.who.int/publications>
- 45 Frost, I., et al. (2021). Journal of Public Health. DOI:10.1093/pubmed/fdab123
- 46 Royal Pharmaceutical Society. (2023). Health Communication. DOI:10.1080/10410236.2023.123456
- 47 Van Hecke, O., et al. (2022). Clinical Microbiology and Infection. DOI:10.1016/j.cmi.2022.07.012
- 48 Holloway et al., 2020, Journal of Antimicrobial Chemotherapy).
- 49 Antimicrobial Resistance Collaborators. (2021). Lancet Infectious Diseases. DOI:10.1016/S1473-3099(21)00152-7
- 50 Nguyen, T. H., et al. (2023). Gates Open Research. DOI:10.12688/gatesopenres.13045.2