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ANTIMICROBIAL RESISTANCE IN BACTERIAL PATHOGENS: MECHANISMS, TRANSMISSION AND ONE HEALTH CONTROL STRATEGIES

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ABSTRACT

Antimicrobial resistance (AMR) is the capacity of microorganisms to survive exposure to medicines that previously inhibited or killed them. Among bacteria, resistance now compromises the treatment of urinary tract, bloodstream, respiratory, gastrointestinal and wound infections. This review examines the molecular basis, ecological transmission and control of bacterial AMR. Resistance may arise through mutation or horizontal gene transfer and is expressed through enzymatic drug inactivation, target alteration, reduced permeability, active efflux, metabolic bypass and biofilm-associated tolerance. Selection is intensified by inappropriate antimicrobial use in human medicine, livestock and agriculture, while resistant bacteria and genes move through hospitals, communities, food systems, animals, wastewater and natural environments. The paper argues that AMR cannot be controlled by drug discovery alone. Effective containment requires microbiological diagnosis, antimicrobial stewardship, infection prevention, vaccination, safe water and sanitation, standardized surveillance, responsible animal use and environmental management. A One Health framework is essential because humans, animals and ecosystems share microbial populations and mobile resistance determinants. Strengthening laboratory capacity and linking local antibiograms to clinical policy are particularly important in resource-constrained settings.

KEYWORDS: ***antimicrobial resistance; bacteria; resistance genes; horizontal gene transfer; biofilm; surveillance; stewardship; One Health***

1. INTRODUCTION

Antibiotics transformed medicine by making many bacterial infections treatable and enabling surgery, transplantation, cancer chemotherapy and intensive care. Their effectiveness, however, creates selection pressure. Susceptible organisms are removed while resistant variants survive and multiply. Antimicrobial resistance is therefore an evolutionary phenomenon accelerated by the intensity, duration and distribution of antimicrobial exposure. The World Health Organization (WHO) reported that approximately one in six laboratory-confirmed

bacterial infections worldwide in 2023 was resistant to antibiotics, illustrating the scale of the problem (WHO, 2025).

AMR is often described as a clinical problem, but its origins and routes of spread are ecological. Bacteria exchange genetic material across species and habitats; antimicrobial residues and resistant organisms move through sewage, manure, soil, surface water and food chains. This paper reviews bacterial resistance mechanisms, major drivers, transmission pathways, laboratory detection and coordinated control. It is a narrative review and does not present invented experimental results.

2. OBJECTIVES AND REVIEW APPROACH

The objectives are: (i) to explain the principal cellular and genetic mechanisms of bacterial resistance; (ii) to analyse how antimicrobial use and environmental conditions select resistant populations; (iii) to describe transmission among hospitals, communities, animals, food and the environment; and (iv) to assess microbiological and public-health interventions within a One Health framework. The review synthesizes established microbiology literature, WHO surveillance guidance and major burden studies. Emphasis is placed on mechanisms that have direct implications for diagnosis and control.

3. GENETIC BASIS OF RESISTANCE

Intrinsic resistance is a natural property of a bacterial species. For example, absence of a drug target, low outer-membrane permeability or constitutive efflux may make an organism inherently insusceptible. Acquired resistance develops when a previously susceptible population obtains a mutation or new genetic element. Mutations may alter drug targets, regulatory systems or membrane proteins. Their frequency is low, but antibiotic exposure strongly selects the rare cells carrying advantageous changes.

Horizontal gene transfer rapidly disseminates acquired resistance. Conjugation transfers plasmids through cell-to-cell contact; transformation incorporates extracellular DNA; and transduction is mediated by bacteriophages. Plasmids often carry multiple resistance genes along with integrons and transposons that capture and mobilize gene cassettes. Co-selection occurs when exposure to one antibiotic, biocide or metal maintains a mobile element containing several unrelated resistance determinants. Consequently, reducing a single drug may not immediately remove multidrug resistance.

4. MAJOR BIOCHEMICAL MECHANISMS

Enzymatic inactivation is among the most important mechanisms. Beta-lactamases hydrolyse the beta-lactam ring of penicillins, cephalosporins or carbapenems. Extended-spectrum beta-lactamases, AmpC enzymes and carbapenemases differ in substrate range and inhibitor susceptibility. Other enzymes modify aminoglycosides through acetylation, phosphorylation or adenylation, lowering their affinity for ribosomal targets.

Target modification prevents effective drug binding. Altered penicillin-binding proteins contribute to methicillin resistance in Staphylococcus aureus, while changes in DNA gyrase and topoisomerase IV can produce fluoroquinolone resistance. Ribosomal methylation or mutation affects macrolides, lincosamides, tetracyclines and

related agents. Acquisition of alternative targets, such as resistant dihydrofolate reductase, allows essential metabolic pathways to continue despite antimicrobial exposure.

Reduced intracellular concentration results from decreased permeability and active efflux. Loss or modification of porins restricts entry into Gram-negative bacteria. Efflux pumps export structurally diverse compounds and may generate multidrug phenotypes. These mechanisms often interact: a modestly active beta-lactamase can produce clinically important resistance when combined with porin loss and efflux.

Biofilms add a physiological layer of protection. Cells embedded in an extracellular matrix display restricted penetration, slow growth, altered gene expression and persister formation. Biofilm-associated tolerance is not identical to inherited resistance, but it allows survival during therapy and creates opportunities for mutation and gene exchange. Catheters, implants, chronic wounds and respiratory secretions provide important biofilm habitats.

5. PRIORITY BACTERIAL PATHOGENS

Clinically important resistant bacteria include methicillin-resistant Staphylococcus aureus, vancomycin-resistant enterococci, drug-resistant Mycobacterium tuberculosis, and multidrug-resistant Gram-negative organisms. Escherichia coli and Klebsiella pneumoniae commonly acquire extended-spectrum beta-lactamases and carbapenemases. Acinetobacter baumannii and Pseudomonas aeruginosa combine low permeability, efflux, enzymes and biofilm formation. Resistant Salmonella, Shigella, Neisseria gonorrhoeae and Campylobacter connect AMR with foodborne, sexually transmitted and community infections.

The clinical significance of resistance depends on the infection site, bacterial burden, host immunity, pharmacokinetics and available alternatives. A laboratory result should therefore be interpreted with clinical information rather than treated as an isolated label. Colonization must also be distinguished from infection to avoid unnecessary treatment and additional selection pressure.

6. DRIVERS OF EMERGENCE AND SELECTION

In human health care, major drivers include antibiotics prescribed for viral illness, unnecessarily broad-spectrum empirical therapy, incorrect dose or duration, self-medication, non-prescription access and poor adherence. Inadequate diagnostics encourage treatment based on uncertainty. At the opposite extreme, lack of access to quality-assured antibiotics, delayed care and substandard medicines can expose bacteria to ineffective concentrations and also worsen outcomes.

Antimicrobials used in food animals can select resistant intestinal bacteria that reach people through direct contact, food products or the environment. Manure and aquaculture discharge may contain antimicrobial residues, resistant organisms and resistance genes. Pharmaceutical and hospital effluent can create environmental hotspots when treatment is inadequate. The relevant unit of analysis is therefore not only the patient but the connected microbial ecosystem.

Crowding, poor hand hygiene, unsafe water, inadequate sanitation and weak infection-control systems amplify transmission. Global travel and trade then move successful clones and plasmids across borders. AMR reflects the

combination of selection and transmission: improved prescribing reduces selection, while infection prevention reduces the number of organisms that must be treated.

7. TRANSMISSION ACROSS ONE HEALTH INTERFACES

The One Health concept recognizes that human, animal, plant and environmental health are interdependent. Resistant bacteria circulate between household members, patients, health-care workers, animals and environmental reservoirs. Food processing and preparation can introduce or amplify exposure, while wastewater connects hospitals and communities to rivers, agriculture and coastal ecosystems.

Direction of transmission is often difficult to prove because identical genes may occur in different bacterial hosts and mobile elements. Whole-genome sequencing, plasmid analysis and epidemiological metadata help distinguish clonal spread from independent acquisition. Surveillance should therefore integrate microbiological data with antimicrobial use, patient movement, animal production and environmental sampling where feasible.

8. LABORATORY DETECTION AND SURVEILLANCE

Reliable antimicrobial susceptibility testing is the foundation of treatment and surveillance. Phenotypic methods include disk diffusion, broth microdilution, gradient diffusion and automated systems. Results are interpreted with standardized breakpoints and quality-control strains. Minimum inhibitory concentration data can provide greater resolution, but clinical categorization also depends on dosing and infection site. Laboratories must follow recognized standards, maintain internal quality control and participate in external quality assessment.

Molecular methods detect specific resistance genes or mutations rapidly, but the presence of a gene does not always predict expression, and a negative targeted test cannot exclude an unknown mechanism. Culture-based testing remains essential. Whole-genome sequencing is increasingly valuable for outbreak investigation and resistance prediction, although cost, bioinformatics and representative sampling remain challenges.

Hospital and regional antibiograms summarize susceptibility patterns and guide empirical therapy. Data should be stratified by specimen, location and patient group and should remove duplicate isolates where appropriate. WHO's Global Antimicrobial Resistance and Use Surveillance System (GLASS) promotes standardized national reporting for common bacterial infections. Surveillance quality depends on sampling coverage; data from tertiary hospitals alone may overrepresent severe and resistant infections.

9. ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship seeks the best clinical outcome with the least avoidable harm and selection pressure. Core measures include evidence-based guidelines, diagnostic sampling before therapy when safe, review of empirical treatment after 48-72 hours, de-escalation, dose optimization, intravenous-to-oral switch and appropriate duration. Reserve agents should be protected without denying timely treatment to patients who need them.

Stewardship is most effective when microbiologists, clinicians, pharmacists, nurses and infection-control teams collaborate. Audit and feedback, formulary restriction and clinical decision support should be adapted to local

resources. Success should not be measured only by reduced consumption; mortality, treatment failure, Clostridioides difficile infection and equitable access must also be monitored.

10. INFECTION PREVENTION AND ONE HEALTH CONTROL

Preventing infection reduces antibiotic demand. Hand hygiene, environmental cleaning, sterilization, safe injection, screening during outbreaks and isolation precautions interrupt health-care transmission. Vaccination prevents susceptible infections and can reduce antimicrobial use. Safe water, sanitation, food hygiene and waste management have comparable importance in communities.

Animal-sector measures include veterinary oversight, vaccination, biosecurity, husbandry improvements and elimination of medically important antimicrobials for routine growth promotion. Environmental action requires better treatment of hospital, municipal, farm and manufacturing waste, together with enforceable discharge standards. Public communication should discourage self-medication while avoiding messages that cause patients to stop prescribed therapy prematurely.

Research priorities include rapid affordable diagnostics, vaccines, bacteriophages, anti-virulence approaches, microbiome-based interventions and genuinely innovative antimicrobials. New products must be paired with access and stewardship models; otherwise either under-access or rapid overuse will undermine public benefit.

11. CHALLENGES AND FUTURE DIRECTIONS

Many surveillance systems lack representative community sampling, standardized denominator data and links between laboratory results and clinical outcomes. Resource-limited laboratories face shortages of trained personnel, quality reagents, equipment maintenance and information systems. Strengthening routine bacteriology may provide greater immediate value than adopting advanced sequencing without sustainable foundations.

Future policy should connect local action with national networks. Colleges and microbiology departments can contribute through teaching, public awareness, small-scale surveillance partnerships and research on wastewater, food, animal and clinical isolates. Ethical sample handling, biosafety, validated methods and transparent reporting are essential. AMR control must be viewed as long-term microbial risk management rather than a temporary campaign.

12. CONCLUSION

Bacterial antimicrobial resistance emerges through evolution but becomes a public-health crisis through human patterns of antimicrobial use and microbial transmission. Mutation, mobile genetic elements, enzymatic inactivation, target modification, permeability changes, efflux and biofilms produce complex phenotypes that can defeat multiple drug classes. These mechanisms circulate across hospitals, communities, animals, food and environmental systems.

No single intervention is sufficient. Accurate diagnosis, standardized susceptibility testing, stewardship, infection prevention, vaccination, sanitation, responsible animal practices, environmental protection and coordinated surveillance must operate together. A One Health approach provides the necessary framework because

resistance genes do not respect institutional or ecological boundaries. Sustained laboratory capacity and locally relevant data will determine whether global policy becomes effective practice.

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