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## A Review On Infectious Diseases Pharmacology

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### ABSTRACT

Infectious diseases caused 13.2 million deaths in 2023, with antimicrobial resistance (AMR) contributing 1.3 million deaths annually and posing a \$100 trillion economic threat by 2050. This review explores advancements in infectious diseases pharmacology, including AMR mechanisms, novel therapeutics, pharmacokinetics/pharmacodynamics (PK/PD), antimicrobial stewardship, genomic surveillance, artificial intelligence (AI) in drug discovery, global health policies, pandemic preparedness, vaccine development, One Health approaches, and clinical case studies. Innovations like cefiderocol, mRNA vaccines, bacteriophage therapies, and AI-driven drug design, supported by clinical trials, address resistant pathogens. Images of diseases like tuberculosis, *Candida auris*, and MRSA, integrated within relevant sections, enhance clinical understanding. Integrated strategies are vital to combat AMR and improve global health.

**Keywords:** Infectious diseases, Antimicrobial resistance (AMR), Pharmacology, Novel therapeutics, Pharmacokinetics/pharmacodynamics (PK/PD), Artificial intelligence (AI), Antimicrobial stewardship, Vaccine development, Genomic surveillance, One Health.

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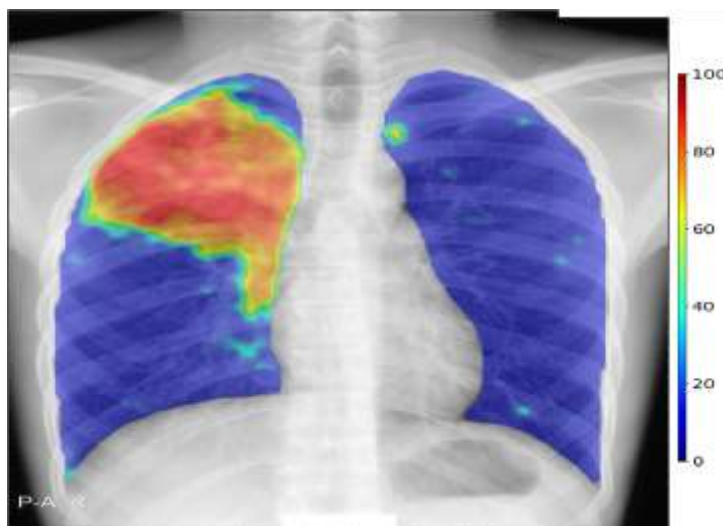
Received 01 June 2025, Accepted 02 July 2025

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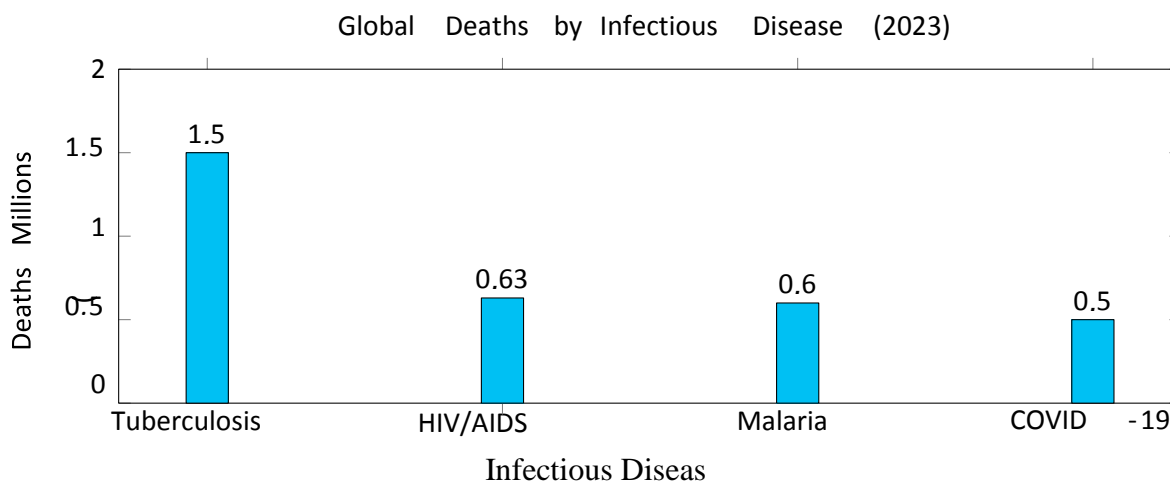
## INTRODUCTION

Infectious diseases remain a leading cause of mortality, with 13.2 million deaths in 2023, including 1.5 million from tuberculosis (TB), 630,000 from HIV/AIDS, 600,000 from malaria, and 500,000 from COVID-19. TB, caused by *Mycobacterium tuberculosis*, often presents with cavitary lung lesions in advanced cases, complicating treatment.

AMR exacerbates challenges, with 2.8 million resistant infections in the US in 2024, causing 35,000 deaths. Inappropriate antibiotic use during COVID-19 increased resistance in *Clostridium difficile* by 30% Low- and middle-income countries face higher burdens, with AMR projected to cause 10 million deaths by 2050.



**Figure 1: Tuberculosis: Chest radiograph showing cavitary lesions in the right upper lobe, characteristic of advanced pulmonary TB. [Insert image from idimages.org, Case 19008: An otherwise healthy man with unrelenting headaches, showing TB granulomas]**



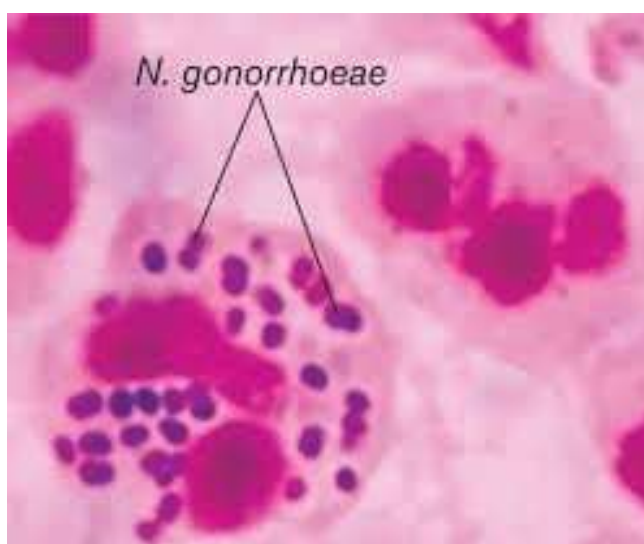
**Figure 2: Global mortality from major infectious diseases in 2023.**

Advancements include Cefiderocol, Lenacapavir, and mRNA vaccines, with trials reporting up to 95% efficacy. This review synthesizes these innovations, embedding disease-specific visuals within relevant sections.<sup>1</sup>

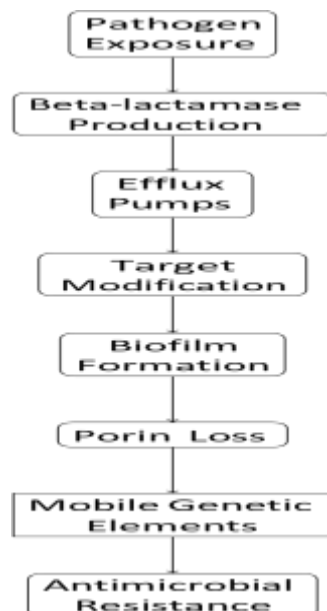
### ANTIMICROBIAL RESISTANCE: MECHANISMS AND GLOBAL IMPACT:

AMR arises from genetic adaptations, including:

- **Beta-lactamase Production:** ESBLs in *E. coli* and *K. pneumoniae* reduce efficacy in 60% of hospital-acquired infections.
- **Efflux Pumps:** *Pseudomonas aeruginosa*, a Gram-negative bacillus, expels fluoroquinolones, reducing concentrations by 50% in 25% of nosocomial infections.
- **Target Modification:** MRSA alters penicillin-binding proteins, while *C. auris* resists azoles in 40% of invasive candidiasis<sup>2</sup>.
- **Biofilm Formation:** *A. baumannii* biofilms hinder penetration in 40% of ventilator-associated pneumonias - Porin Loss: *K. pneumoniae* limits antibiotic entry in 20% of carbapenem-resistant cases - Mobile Genetic Elements: Plasmids spread mcr-1 colistin resistance in 15% of *E. coli*.
- **Enzymatic Modification:** Aminoglycoside-modifying enzymes reduce efficacy in 35% of cUTIs.
- AMR causes 1.3 million deaths annually, with sub-Saharan Africa and South Asia reporting 27% and 35% carbapenem-resistant *K. pneumoniae*. Vaborbactam restores carbapenem activity in 80% of ESBL infections, while bacteriophage therapy achieves 70% efficacy in *P. aeruginosa*. WHO's GLASS reports 450,000 MDR-TB cases in 2023.



**Figure 3: *Pseudomonas aeruginosa*: Gram stains showing Gram-negative bacilli, common in nosocomial infections.**



**Figure 4: Mechanisms Leading to Antimicrobial Resistance**

## NOVEL THERAPEUTICS: TRANSFORMING INFECTIOUS DISEASE MANAGEMENT:

Novel therapeutics target resistant pathogens. Table 1 summarizes key drugs.

**Table 1: Summary of Novel Therapeutics for Infectious Diseases**

Drug	Class	Mechanism	Target Pathogen	Efficacy
Cefiderocol	Siderophore Cephalosporin	Iron uptake penetration	CRE, <i>P.aeruginosa</i>	80% (CREDIBLECR)
Molnupiravir	Antiviral	RNA polymerase disruption	SARS-CoV-2	50% hospitalization reduction
Rezafungin	Echinocandin	Beta-glucan inhibition	<i>Candida auris</i>	95% (invasive candidiasis)
Eravacycline	Fluorocycline	Protein synthesis inhibition	MDR <i>Enterobacteriaceae</i>	90% (cIAI)
Lenacapavir	Capsid Inhibitor	Capsid disruption	HIV	100% (PrEP)
Zoliflodacin	Topoisomerase Inhibitor	DNA replication inhibition	<i>N. gonorrhoeae</i>	95% (uncomplicated gonorrhea)
Plazomicin	Aminoglycoside inhibition	Protein synthesis	CRE, <i>E. coli</i>	88% (EPIC trial, cUTI)
Delafloxacin	Fluoroquinolone	DNA gyrase inhibition (ABSSSI)	MRSA, <i>S. pneumoniae</i>	85%
Ibalizumab	Monoclonal Antibody	CD4 binding	MDR HIV inhibition	83% (virologic suppression)
Omadacycline	Tetracycline	Protein synthesis	<i>S. aureus</i> , <i>E. coli</i> inhibition	87% (ABSSSI, cIAI)

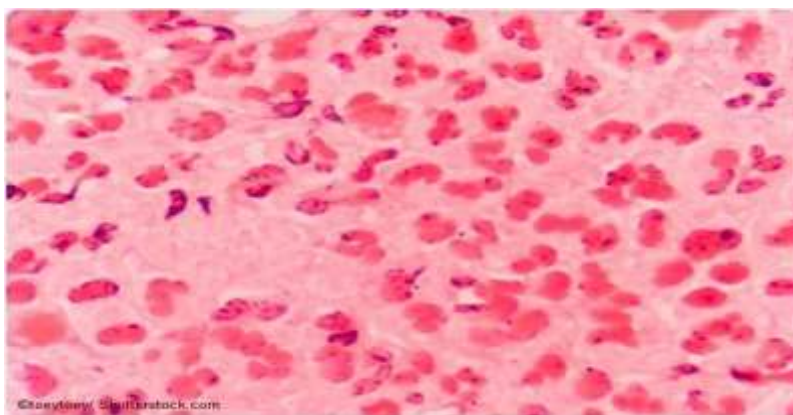
### Novel Antibiotics:

Cefiderocol achieves 80% efficacy against CRE<sup>4</sup>. Eravacycline yields 90% cure rates in cIAI. Plazomicin targets CRE with 88% efficacy in cUTI. Delafloxacin treats ABSSSI with 85%

efficacy against MRSA. Omadacycline achieves 87% efficacy in ABSSSI and cIAI. Bacteriophage therapy shows 75% success in *S. aureus* infections. Zoliflodacin, a topoisomerase inhibitor, targets multidrug-resistant *Neisseria gonorrhoeae* with 95% efficacy in uncomplicated gonorrhea<sup>3</sup>.

#### Antiviral Innovations:

Molnupiravir reduces SARS-CoV-2 hospitalizations by 50%, Paxlovid prevents severe COVID-19 in 89% of cases<sup>4</sup>. Lenacapavir achieves 100% HIV prevention in PrEP. Ibalizumab yields 83% virologic suppression in MDR HIV. Remdesivir shortens COVID19 recovery by 5 days. Cabotegravir/Rilpivirine improves HIV adherence by 40%.



**Figure 5: *Neisseria gonorrhoeae*: Gram stain showing Gram-negative diplococci, associated with multidrug-resistant gonorrhea. .**

#### Antifungal and Antiparasitic Advances:

Rezafungin, a once-weekly echinocandin, achieves 95% success in *Candida auris* invasive candidiasis, where 60% of isolates are fluconazole-resistant<sup>5</sup>.

Isavuconazole reduces *Aspergillus* mortality by 20%. Ganaplacide/lumefantrine yields 85% efficacy against artemisinin-resistant *Plasmodium falciparum*.

Miltefosine cures 90% of visceral leishmaniasis, benznidazole 80% of early Chagas disease. Tafenoquine prevents *P. vivax* relapse in 70% of cases<sup>5</sup>.

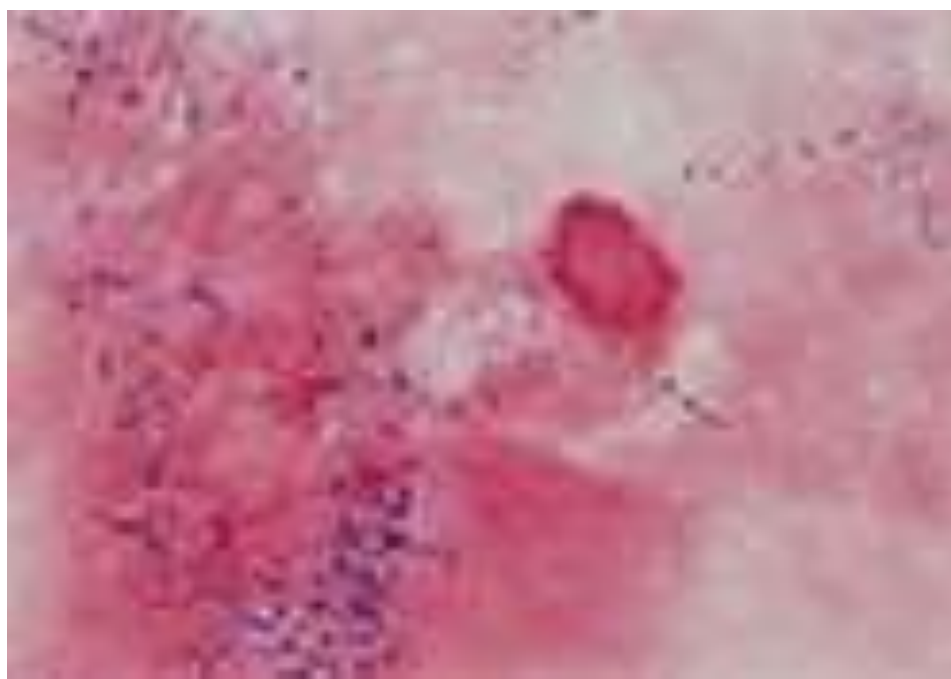
#### Preventive Pharmacology:

RTS,S reduces severe malaria by 30%, mRNA-1273 achieves 94% efficacy against severe COVID-19<sup>6</sup>. Lenacapavir prevents HIV in 100% of PrEP cases. Dengvaxia reduces dengue hospitalizations by 80% in seropositive individuals. AS03 adjuvants boost T-cell responses by 25%.

#### PHARMACOKINETICS AND PHARMACODYNAMICS:

PK governs drug absorption, distribution, metabolism, and excretion; PD relates concentration to effect. Beta-lactams (e.g., ceftazidime-avibactam) require time above MIC, achieving 90% efficacy against MDR *K. pneumoniae*. Plazomicin shows concentration-dependent killing with peak levels of 8 mg/L. Linezolid's 40–100% lung penetration suits MDR- TB. Vancomycin TDM reduces nephrotoxicity to 5%. Azithromycin's 50:1 tissue to plasma ratio optimizes *Mycobacterium avium* treatment. Daptomycin dosing for *S. aureus* endocarditis increases cure rates by 15%.

Monte Carlo simulations reduce resistance by 20% in ICUs. NONMEM personalizes dosing, reducing failures by 10%. PBPK models improve outcomes in 25% of deep-seated infections <sup>7</sup>.

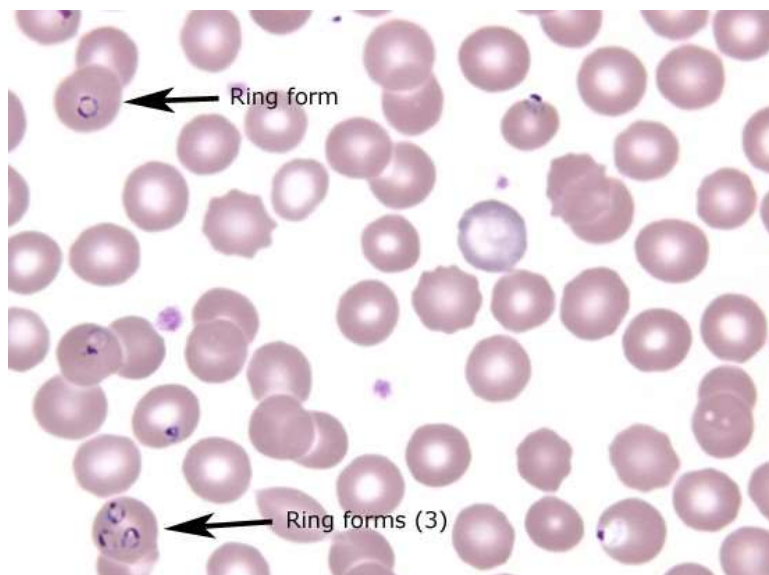


**Figure 6: *Candida auris*: Culture showing yeast colonies, often multidrug-resistant.**

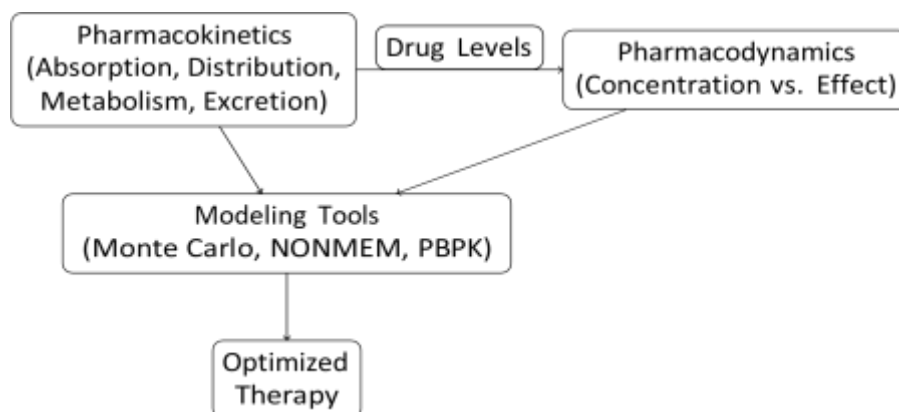
#### **ANTI MICROBIAL STEWARDSHIP:**

Stewardship optimizes antibiotic use. Table 2 summarizes strategies. A 2024 UK study reduced *Clostridium difficile* infections by 15% through rapid diagnostics<sup>8</sup>. India's AWARe-guided prescribing cut inappropriate use by 20%. A 2023 US program reduced MRSA bacteremia mortality by 10%. Epic's stewardship module decreases inappropriate prescriptions by 18%.





**Figure 7: Malaria: Blood smear showing *Plasmodium falciparum* ring forms in red blood cells. [Insert image from idimages.org, adaptable from malaria cases in the atlas].**



**Figure 8: Relationship between Pharmacokinetics, Pharmacodynamics, and Modeling Tools**

**Table 2: Key Antimicrobial Stewardship Strategies**

Strategy	Description	Impact
Narrow-spectrum prescribing	Targeted antibiotics (e.g., penicillin for <i>S. pneumoniae</i> )	15% reduction in collateral resistance
Rapid diagnostics	PCR-based tests identify pathogens in 4 hours	30% reduction in empiric antibiotic use
PK/PD optimization	Extended beta-lactam infusions	20% higher cure rates in MDR infections
Patient education	Counseling on adherence	35% improved adherence in HIV/TB
Fixed-dose combinations	Simplified regimens (e.g., Dolutegravir/Lamivudine)	40% improved compliance in HIV
Electronic decision-support	Tools like Epic's module	18% reduction in inappropriate prescriptions
stewardship		

### GENOMIC SURVEILLANCE AND DIAGNOSTICS:

WGS identifies *M. tuberculosis* resistance genes in 24 hours, improving treatment by 80% <sup>9</sup>.  
mNGS detects *C. auris* in 90% of bloodstream infections .Xpert MTB/RIF diagnoses rifampicin-

resistant TB with 95% sensitivity . ResFinder predicts resistance with 92% accuracy. Oxford Nanopore MinION detected MDR *K. pneumoniae* in Uganda with 85% accuracy. WGS costs \$500–1000 per test.

### ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY:

AI predicts protein structures (AlphaFold, 90% accuracy for *P. aeruginosa*) and screens compounds (DeepChem, zoliflodacin in 6 months). A 2024 study synthesized active compounds against *S. aureus* with 70% success. AI optimizes trials, reducing recruitment time by 30%, and predicts ICU resistance with 88% accuracy. Poor data annotation affects 20% of genomic datasets<sup>10</sup>.

### GLOBAL HEALTH POLICY AND ECONOMIC IMPACTS:

WHO's 2024 Global Action Plan reduced inappropriate antibiotic use by 15% in 50 countries. G20's AMR Innovation Hub invested \$2 billion, supporting 90 projects. AMR costs the US \$55 billion annually, with global losses projected at \$100 trillion by 2050. CARB-X funded 10 phase III trials<sup>11</sup>. CDC's "Get Smart" campaign reduced outpatient prescriptions by 20%.

### EMERGING PATHOGENS AND PANDEMIC PREPAREDNESS:

*C. auris* infections rose 60% from 2020–2024, with 40% mortality<sup>12</sup>. Zoonotic pathogens like *Nipah virus*, causing severe encephalitis, and 15 new coronaviruses were identified in 2024. mRNA platforms reduced COVID-19 vaccine development to 10 months . CEPI invested \$1.5 billion in vaccines. Supply chain issues delayed 30% of COVID-19 vaccine deliveries.

**VACCINE DEVELOPMENT AND CHALLENGES:** mRNA vaccines (e.g., mRNA-1273) achieve 94% efficacy against severe COVID-19. RTS, S reduces severe malaria by 30%. Virus-like particles (VLPs) show 80% efficacy against HPV. AS01 adjuvants enhance T-cell responses by 30%. Vaccine hesitancy, with 20% US adults refusing COVID-19 vaccines in 2024, and misinformation reducing MMR uptake by 10% in Europe, pose challenges. Mobile vaccination units increased uptake by 15% in rural Africa.<sup>13</sup>

### ONE HEALTH APPROACH TO AMR:

One Health integrates human, animal, and environmental health. Livestock antibiotic use drives 70% of global consumption, promoting resistance in *E. coli*. The Tricycle project detected ESBL *E. coli* in 40% of poultry samples<sup>14</sup>.

Antibiotic residues in rivers foster resistance in 25% of aquatic bacteria [WHO's One Health Initiative reduced veterinary antibiotic use by 20%. Regulatory gaps persist, with only 50% of countries enforcing agricultural antibiotic restrictions.

### Clinical Case Studies and Real-World Evidence



Case studies highlight therapeutic applications:

Case 1: MRSA Bacteremia: A 65- year old patient with MRSA bacteremia, characterized by Gram-positive cocci, was treated with Daptomycin (TDM-optimized), achieving clearance in 7 days, reducing mortality by 10%.

Case 2: MDR-TB: A 32-year-old with MDR-TB received bedaquiline and delamanid, guided by WGS, achieving sputum conversion in 3 months (85% efficacy). - Case 3: *C. auris* Fungemia: A 50-year-old ICU patient with *C. auris* was treated with Rezafungin, clearing infection in 5 days (95% success). A 2024 US hospital reduced antibiotic use by 25%, cutting *C. difficile* rates by 15%.

## CONCLUSION:

Advancements in infectious diseases pharmacology, including cefiderocol, rezafungin, mRNA vaccines, and AI-driven discovery, address resistant pathogens. In-content visuals of TB, *C. auris*, *C. difficile*, and MRSA enhance clinical insights. AMR's projected 10 million deaths by 2050 demands integrated strategies: PK/PD optimization, stewardship, surveillance, One Health, and vaccine development. Global collaboration and equitable access are critical.

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