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# Species-Specific Antimicrobial Pharmacotherapy – Challenges and Future Directions

RAHMA HAMAYUN[1], SANA JAVED[1*], SANA SHAHZAD[1], AYESHA MUZAMMIL[1], MAIRA RIAZ[1], IQRA FAQEER[1], MUHAMMAD AKMAL FAROOQ[2]

[1]Department of Pharmacy, The University of Faisalabad, Faisalabad, Pakistan
[2]Department of Pharmacy, University of Agriculture, Faisalabad, Pakistan
*Corresponding author: sanajaved.pharm@tuf.edu.pk

**ABSTRACT:** Species-specific pharmacotherapy has revolutionized antimicrobial therapy, placing greater emphasis on pathogen-based approaches to enhance therapeutic effectiveness while simultaneously mitigating the development of resistance and reducing the toxicity associated with antimicrobial agents. In this overview, we consider current strategies for managing the most prevalent categories of pathogens, including bacteria, fungi, viruses, and protozoa, with a specific focus on species-based diagnostics, pharmacokinetic-pharmacodynamics optimization, and precision medicine. Genomic-based drug design, molecular and functional diagnostics, drug repurposing, and biologic supplements have revolutionized the field of antimicrobials, allowing targeted approaches towards multi-drug-resistant MDR pathogens, which provide cures targeting antimicrobial pharmacotherapy, as well as proof demonstrating the importance of species-specific treatment in current medical treatment and forthcoming developments in the era of personalized and precision medicine.
**Keywords:** Species-specific pharmacotherapy, Antimicrobial resistance, Pharmacokinetics, Pharmacodynamics, Pharmacogenomics, Antimicrobial peptides, Bacteriophages, Nanomedicine, Drug repurposing.

## INTRODUCTION

Infectious diseases remain a leading cause of morbidity, mortality, and socio-economic burden to healthcare systems worldwide, with antimicrobial resistance being one of the most significant challenges to public health in the 21st century. Effective antimicrobial pharmacotherapy requires a species-specific approach based on the genetic, metabolic, and pharmacologic nature of the pathogen, with comprehensive antibiosis being toxic and ineffective (Ghazi and El Nekidy, 2023; Raimondi et al., 2022; Tong et al., 2015). Traditional empirical antimicrobial therapy is becoming increasingly unreliable due to false-positive signals and variations in resistance rates worldwide. Additionally, a one-size-fits-all methodology often results in medication failure, negative effects of acute toxicity, and the perpetuation of resistance selection.

Modern therapeutic practice prioritizes the use of species-specific pharmacotherapy that enhances therapeutic efficacy while protecting patients from the danger of resistance and adverse effects, a practice known as pathogen-directed therapy. Developments in whole-genome sequencing, molecular diagnostics, and pharmacokinetics-pharmacodynamics (PK/PD) modeling permit the rapid transition from broad-spectrum empirical regimens to targeted regimens (Raimondi et al., 2022; Weis et al., 2020). Whole-genome and precisely targeted molecular diagnostics identify species and resistance biomarkers, enabling rapid de-escalation. Additionally, bacteriophages, antimicrobial peptides, and drug repurposing offer hope in the battle against multi-resistant pathogens (Glajzner et al., 2024; Górski et al., 2020; Mahlapuu et al., 2016; Singh et al., 2024).

Bacterial pathogens are the most common and best known of all remaining categories of ha pathogens. The following sections review recent advances in pharmacotherapy for the pathogens that cause the most significant morbidity and require the most complex therapeutic interventions, with an emphasis on recent advances and trends continuing to 2025 (Fatima et al., 2023; Ghazi and El Nekidy, 2023; Glajzner et al., 2024; Raimondi et al., 2022; Singh et al., 2024).

## SPECIES-SPECIFIC ANTIBACTERIAL PHARMACOTHERAPY

### Principles of Species-Specific Antibacterial Therapy

The most common indication for prescribing antimicrobial chemotherapy is bacterial infections. But the high diversity of bacterial species, along with their differences in susceptibility to antimicrobials, requires individual species-specific therapy. While the distinction between Gram-positive and Gram-negative bacteria, which are differentiated by the structure of their cell wall, is one of the basics of antibacterial selection, the differences that exist within the species, i.e., in resistance mechanisms, other virulence factors, and metabolic pathways, require a more detailed strategy for treatment (Ventola, 2015).

Currently, antibacterial therapy tends to be directed via species determination and pathogen sensitivity. Although traditional culture-based methods still serve as the main standard for bacterial specimen cultivation and pathogen growth, the developments of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and polymerase chain reaction can identify bacterial pathogens and resistance – a feature that significantly helps determine of the

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treatment which experimental selection turned the balance toward targeted antibacterial chemotherapy to species-specific therapy and overall a much greater cost-effectiveness, which can be associated with a better outcome (Mahlapuu et al., 2016; Raimondi et al., 2022).

**Gram-Positive Bacterial Infections**

Gram-positive bacteria, including staphylococci, streptococci, and enterococci, cause a wide range of infections from skin and soft tissue infections to life-threatening bacteremia and endocarditis. Species-specific considerations are critical for optimal management of these infections (Tong et al., 2015).

***Staphylococcus aureus***

Among gram-positive bacteria, Staphylococcus aureus is the most problematic pathogen. Currently, most isolates are resistant to methicillin and are called MRSA. There are also MRSA strains that harbor the mecA gene but have been isolated from patients in community settings. In contrast, MRSA infections require alternative agents such as vancomycin, daptomycin, linezolid, or newer agents like ceftaroline, with selection based on infection site, severity, and local resistance patterns.

When therapeutic targets cannot be safely reached, the majority of strains displaying intermediate resistance may need alternative agents like daptomycin or linezolid. In order to maximize vancomycin exposure, emerging data also highlight the significance of customized dosing plans directed by therapeutic drug monitoring. Most species of staphylococci remain susceptible to penicillin, which binds to penicillin-binding proteins, so MRSA is treated with vancomycin, with an AUC/MIC% of 400-600 for serious MRSA infections (Liu et al., 2011; Rybak et al., 2020; Turner et al., 2019).

Vancomycin is a glycopeptide antibiotic for treating serious MRSA infection that is associated with toxic effects, i.e., nephrotoxicity. Due to the increasing prevalence of MRSA strains with an increased value of the minimum inhibitory concentration, related to vancomycin, alternatives should be selected, such as daptomycin or a combination therapy. These drugs, like many others, need to be monitored when they are taken specifically. For isolates with elevated vancomycin MICs (≥1.5 μg/mL), alternative agents such as daptomycin or combination therapy may be preferred (Lodise et al., 2020; Rybak et al., 2020).

***Streptococcal* species**

Exhibit remarkable susceptibility to beta-lactam antibiotics, with penicillin remaining the drug of choice for Streptococcus pyogenes (Group A streptococcus) and Streptococcus pneumoniae infections in most cases. he choice for infections caused by, *S. pyogenes* and *S. pneumonia* should be penicillin. Although that form should be guided by the execution of an antibiotic-resistance gene, which can significantly influence the physician's role. Some regional changes in the effectiveness of azithromycin- and clarithromycin-containing medications have been reported with the rise of infections from macrolides. However, macrolide resistance in *S. pneumonia*e has increased in many regions, limiting the utility of azithromycin and clarithromycin for respiratory infections caused by this pathogen. Species identification is particularly important for viridans group streptococci causing endocarditis, as different species exhibit varying susceptibility to penicillin and require tailored treatment regimens (Baddour et al., 2015).

Enterococcal infections, particularly those caused by vancomycin-resistant enterococci (VRE), pose significant therapeutic challenges. Enterococcus faecium is generally more resistant than Enterococcus faecalis, with VRE strains often requiring treatment with linezolid, daptomycin (at high doses for bacteremia), or newer agents such as dalbavancin (Arias and Murray, 2012; O'Driscoll and Crank, 2015).

**Gram-Negative Bacterial Infections**

Gram-negative bacteria remain a continuously growing concern since numerous resistance mechanisms have evolved, including extended-spectrum beta-lactamases, carbapenemases, and multidrug efflux pumps at resistance (Ghazi and El Nekidy, 2023). A species-focused strategy appears to be the only reasonable approach for treating such infections.

Enterobacterales**,** previously known as Enterobacteriaceae, is a large family encompassing various genera, such as *Escherichia coli, Klebsiella pneumoniae*, and Enterobacter species, which exhibit different epidemiology and resistance patterns. An example involving *Escherichia coli, Klebsiella pneumonia* is relevant. Escherichia coli, Klebsiella pneumoniae are two bacterial pathogens that account for a significant number of infections throughout the world. Both species are notable for producing ESBLs, which indicate resistance to all beta-lactam antibiotics except for carbapenems, which are meropenem, imipenem, and tigecycline. However, the quick emergence of the carbapenem-resistant Enterobacterales family has occurred recently. Alternative strategies including polymyxins, tigecycline, and newer beta-lactam/beta-lactamase inhibitor combinations such as ceftazidime-avibactam and meropenem-vaborbactam (Singh et al., 2024).

A specific free-drug area under the steady-state concentration-time curve over 24 hours divided by MIC fAUCss,24h/MIC of ≥22.8 is crucial for eliminating carbapenem-resistant K. pneumoniae infections, according to recent polymyxin B pharmacokinetic studies. However, polymyxins are infamous for quickly accumulating neurotoxicity and nephrotoxicity in a dose-dependent manner. Optimizing and closely monitoring the dosage are essential parts of the strategy because the risk rises with exposure (Singh et al., 2024). *Pseudomonas aeruginosa* should be considered in a species-specific manner mainly because of its intrinsic resistance mechanisms, such as induction of biofilm and loss of permeability, and the potential rapid development of resistance during therapy. Indeed, antipseudomonal beta-lactams piperacillin-tazobactam, cefepime, ceftazidime, and meropenem, plus aminoglycosides or fluoroquinolones, are

traditionally used; agent selection should be based on local susceptibility patterns and sending site of the infection. For multidrug-resistant *P. aeriamonosa*, new combinations or experimental therapies, potentially include bacteriophages, which appear to be promising in terms of targeting the specific resistant species (Górski et al., 2020; Singh et al., 2024).

*Acinetobacter baumannii* has emerged as a prominent nosocomial pathogen, often pan-resistant to standard antibiotics. Carbapenem-resistant *A. baumannii* often requires polymyxin-based regimens, which are usually combined with other agents, such as tigecycline, ampicillin-sulbactam, or, more rarely, minocycline (Singh et al., 2024).

**Anaerobic Bacterial Infections**

The bacteria of other anaerobic genera, particularly Bacteroides species, are critical in intra-abdominal and other polymicrobial infections. Recent genomic studies have demonstrated species-specific resistance mechanisms in the *Bacteroides fragilis* group, with carbapenem resistance mediated by cfiA genes and different upstream insertion sequences in the gene's regulatory region that vary by Bacteroides species. Thus, species-level identification, facilitated by genomics-based resistance prediction, becomes important for therapy optimization in anaerobic infections. Metronidazole remains highly effective for most anaerobes, though resistance has been documented in some Bacteroides species, necessitating consideration of alternatives such as carbapenems or beta-lactam/beta-lactamase inhibitor combinations (Raimondi et al., 2022; Singh et al., 2024).

**Emerging strategies**

In addition to conventional antibiotics, a number of innovative methods offer species-specific bacterial targeting.

**Drug repositioning:** is an example of a fast strategy to introduce new therapy possibilities against multidrug-resistant bacteria. A variety of FDA-approved medications have been evaluated for antibacterial activity on a large scale; many interesting candidates targeting priority pathogens have been identified for potential clinical development. This approach is of high value to deal with such urgent threats to resistance, as traditional drug development is prohibitively lengthy.

**Bacteriophage therapy:** A species-specific biological strategy called "bacteriophage therapy" employs tiny viruses to target and eradicate a particular species or strain of bacteria. Phage therapy is effective in treating multidrug-resistant *P. aeruginosa* and Acinetobacter baumannii infections, as well as other Gram-negative pathogens, although it is still not widely accessible in many nations. There are a number of advantages to phages' high priority for their bacterial pathogens, including a possible decrease in off-target effects on microflora and bacteria's tendency to resist the agent. (Górski et al., 2020).

**Antimicrobial peptides (AMPs):** are being investigated as novel antibacterial agents with broad-spectrum activity and reduced propensity for resistance development. These naturally occurring defense molecules can be designed or selected for species-specific activity, offering a promising complement to traditional antibiotics (Mahlapuu et al., 2016).

**Challenges**

Bacterial pathogens demonstrate significant heterogeneity in resistance mechanisms, virulence, and treatment response. Resistance evolution remains the primary challenge. The global spread of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and carbapenem-resistant Enterobacterales (CRE) exemplifies the failure of generalized therapy (Antimicrobial Resistance Collaborators, 2022). Delayed diagnostics prolong inappropriate empirical treatment, and there are huge variations in species-specific pharmacokinetics (Fatima et al., 2023; Raimondi et al., 2022).

## SPECIES-SPECIFIC ANTIFUNGAL PHARMACOTHERAPY

**Principles of Species-Specific Antifungal Therapy**

Fungal infections can be as mild as superficial mucocutaneous disease or as severe as life-threatening invasive infections in people with weak immune systems. Antifungal therapy relies on species identification, given that various fungal genera and species exhibit distinct susceptibility phenotypes, tissue tropisms, and clinical manifestations. Major classes of antifungal agents including polyenes, azoles, echinocandins, and pyrimidine analogs, exhibit variable spectrums of activity, pharmacokinetics, and species-specific efficacy (Raimondi et al., 2022; Weis et al., 2020).

***Candida* species infections**

Candida species remain the most common fungal pathogens, ranging from mucocutaneous candidiasis to invasive candidemia and deep-seated infections. Candida species must be identified to the species level due to differences in species susceptibility to antifungal agents, as well as distinct clinical and epidemiological properties. *Candida albicans* remains the most common species, but it is universally lacking, responsible for harsh infections, and susceptible to antifungals in all major classes. Fluconazole is generally acceptable for C. albicans infections, although echinocandins are the most frequently used antifungal due to their fungicidal ability and favorable safety history. For critically ill or critically ill patients who have received prior azoles, echinocandins are recommended as the first-line anti-infective for candidemia (Romanyuk et al., 2022).

Non-albicans Candida species infections have become more common, with species-specific antifungal treatment for serious infections. Candida glabrata is naturally azole-resistant, with many strains being fluconazole-resistant. Therefore, echinocandins are the first spontaneous choice of antifungal for clinical infection. *Candida parapsilosis* may be azole-sensitive but is a species azole-susceptible, with elevated echinocandin MICs compared to other species. Candida auris has established itself as a global threat, with multiple isolates harboring multidrug resistance, including fluconazole and

amphotericin B resistance, necessitating echinocandin therapy and arduous infection control measures (Romanyuk et al., 2022).

### *Aspergillus* species infections

*Aspergillus* species, notably *Aspergillus fumigatus*, generate invasive pulmonary infection in immunocompromised patients. Voriconazole is the ordinary first-line agent for invasive aspergillosis. Due to its improved efficacy, compared with amphotericin B, it is used. Resistance to *A. fumigatus* is increasingly common globally, which has grown due to both environmental exposure and patient treatment. Susceptibility testing is urgent for severe infection (Patricio et al., 2022).

Isavuconazole provides an alternative triazole with a comparable efficacy to voriconazole sulfate but with fewer drug interactions and improved tolerability. Furthermore, liposomal amphotericin B remains a vital drug for azole-resistant strains or azole intolerance. Furthermore, combination therapy of voriconazole sulfate and echinocandin sulfate may improve the antimycotic response in critically immunocompromised patients, but this approach is currently limited to clinical trials. Inhaled and nano amphotericin B are novel delivery agents for Pulmonary Aspergillosis to enhance lung concentrations and reduce systemic levels. These approaches show promise in animal models and formulation studies for improving outcomes in pulmonary fungal infections (Patricio et al., 2022).

### *Cryptococcus* species infections

*Cryptococcus* (*C.*) *neoformans* and *C. gattii* are pathogens that cause meningoencephalitis and systemic disseminated infections linked to immunosuppression and occur more frequently in healthy patients and likely need longer treatment times. The standard treatment protocol comprises 2-week induction therapy with amphotericin B plus flucytosine or fluorocytosine, sequentially accompanied by fluconazole follow-up. These species-specific regimen procedures have been further refined by clinical testing and are one of the most reliable antifungal therapeutic strategies. cause meningoencephalitis and disseminated disease, primarily in immunocompromised individuals. Species identification influences epidemiology and potentially treatment, as *C. gattii* infections occur more frequently in immunocompetent hosts and may require longer treatment durations (Fatima et al., 2023). Therapeutic drug monitoring of 5-fluorocytosine is an essential effort to assure better antifungal efficacy without exacerbating bone marrow toxicity (Fatima et al., 2023).

### Challenges

Fungal infections create unique problems because of the large number of fungal strains, few drug kinds, and significant host toxicity, making them considerably more difficult to treat. Candida auris resistance and azole-resistant Aspergillus fumigatus resistance evolution complicate treatment. Furthermore, difficulties in diagnosis and dangerous adverse events have made antifungal therapy more challenging to give.

### Advances

The safe use of echinocandins, caspofungin, and micafungin has revolutionized the treatment of Candida. Amphotericin B distribution using nanotechnology improves treatment, and isavuconazole protects against infection without damaging the liver (Weis et al., 2020).

## SPECIES-SPECIFIC ANTIVIRAL PHARMACOTHERAPY

### Principles of Species-Specific Antiviral Therapy

Antiviral pharmacotherapy has bright prospects for recent decades, as highly effective agents can be efficiently formulated to act on the target viral species and even genotype. Unlike antibacterial and antifungal treatments, which facilitate the attack of more conservative microbial entities, antiviral agents must target virus replication as they cannot damage the host's own living cells. This calls for precise action of antiviral agents to be selective of viral enzymes and processes. Species-specific antiviral therapy is required not only because DNA and RNA can be found in viruses, but the vast differences between them must be negated by the said drugs. The COVID-19 crisis has accelerated and increased the output of antiviral medication, prompting manufacturers to capitalize on the speed with which broad-spectrum antiviral and host-directed therapies can be developed and distributed during an outbreak (Dechtman et al., 2023).

### DNA Virus Infections

**Herpes viruses:** (including herpes simplex virus types 1 and 2, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, and human herpesvirus 6) are among the most common viral pathogens requiring species-specific therapy. Acyclovir and its prodrug valacyclovir are highly effective for herpes simplex and varicella-zoster infections, acting as nucleoside analogs that selectively inhibit viral DNA polymerase. On the other hand, ganciclovir is recommended for severe cytomegalovirus infections in immunosuppressed patients. It is used extensively in most patients, though foscarnet and cidofovir are recommended when resistance has developed. Likewise, Hepatitis B infection is suppressed with entecavir and tenofovir in all infected patients (Dechtman et al., 2023). Ganciclovir (or its prodrug valganciclovir) is the first-line treatment for cytomegalovirus (CMV) infections in immunocompromised patients, who need more effective antiviral therapy. Ganciclovir resistance may arise, especially during extended treatment, requiring the use of other medications like foscarnet or cidofovir. Compared to ganciclovir, letermovir, a novel CMV terminase complex inhibitor, has a different mechanism of action and less myelotoxicity. It is approved for prophylaxis in transplant recipients.

**Hepatitis B virus (HBV):** Nucleotide analogs that block viral reverse transcriptase, like entecavir or tenofovir, are necessary for long-term suppressive treatment of the hepatitis B virus (HBV). Although current first-line agents show efficacy across genotypes, species-specific factors include HBV genotype, which may affect treatment response and disease

progression. Although nucleotide analog monotherapy is typically preferred due to better tolerability, combination therapy with pegylated interferon may be considered in certain patients (Fatima et al., 2023).

**RNA Virus Infections**

Early treatment of influenza viruses necessitates the use of both the novel polymerase inhibitor baloxavir marboxil and neuraminidase inhibitors like oseltamivir and zanamivir. Since natural or acquired resistance varies between influenza A and B viruses and among influenza A subtypes, respectively, pathogen species and strain have an impact on the risk of resistance as well as the ideal length and timing of treatment. The tracking of acquired resistance to baloxavir and marboxil in certain influenza strains highlights the significance of ongoing surveillance and species-specific resistance monitoring (Dechtman et al., 2023; Fatima et al., 2023).

**Hepatitis C virus (HCV):** treatment has been revolutionized by direct-acting antivirals (DAAs) that target specific viral proteins, including NS3/4A protease, NS5A, and NS5B polymerase [8]. Modern HCV therapy utilizes genotype-specific or pan-genotypic DAA combinations that achieve cure rates exceeding 95% across all major HCV genotypes. Species-specific considerations include HCV genotype and subtype, presence of resistance-associated substitutions, and extent of liver fibrosis, all of which influence regimen selection and duration (Mahlapuu et al., 2016).

**Human immunodeficiency virus (HIV):** needs antiretroviral treatment for the rest of one's life, using combinations of drugs that target different stages of the viral life cycle. Integrase strand transfer inhibitors, non-nucleoside reverse transcriptase inhibitors, nucleotide reverse transcriptase inhibitors, and protease inhibitors are used in different combinations in modern HIV therapy (Mahlapuu et al., 2016).

**Respiratory syncytial virus (RSV):** a major cause of severe respiratory disease in infants and adults, now has treatment options. Incidence is limited with the recombinant monoclonal antibody nirsevimab, providing passive immunization for newborns. Presatovir is a fusion inhibitor that is being researched for use in patients with infected infections.

**SARS-CoV-2 and Emerging Viral Threats**

The COVID-19 pandemic has driven unprecedented antiviral drug development, resulting in several species-specific therapies for SARS-CoV-2. Nirmatrelvir-ritonavir (Paxlovid) inhibits the SARS-CoV-2 main protease and reduces progression to severe disease when administered early in infection. Molnupiravir, a nucleoside analog that induces viral mutagenesis, offers an alternative oral antiviral option. Remdesivir, an intravenous nucleotide analog, is indicated for hospitalized patients and demonstrates broad-spectrum activity against coronaviruses (Liu et al., 2011).

**Challenges**

Viruses exhibit extraordinary genetic diversity and mutation rates, leading to the rapid emergence of resistance. Limited broad-spectrum antivirals and resistance evolution during chronic therapy (e.g., HIV, HBV) remain key obstacles (Fatima et al., 2023).

**Advances**

Direct-acting antivirals (DAAs) have achieved over 95% cure rates for hepatitis C. Novel CMV agents such as letermovir offer safer prophylaxis, while COVID-19 therapeutics like remdesivir and nirmatrelvir–ritonavir highlight rapid species-specific drug development (Liu et al., 2011).

**SPECIES-SPECIFIC ANTIPROTOZOAL PHARMACOTHERAPY**

Protozoal parasites cause significant global morbidity and mortality, particularly in resource-limited settings. Species-specific diagnosis and treatment are essential as different protozoa exhibit distinct life cycles, tissue tropisms, and drug susceptibilities. Antiprotozoal agents target parasite-specific metabolic pathways and structures, though many exhibit significant host toxicity (Ventola, 2015).

**Malaria**

*Plasmodium* (*P.*) spp. that cause malaria require species-specific treatment approaches since their drug susceptibility, relapse potential, and clinical severity vary (*P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi*). Artemisinin-based combination treatments (ACTs) are the first line of treatment for uncomplicated P. falciparum malaria, with WHO-recommended regimens including artemether-lumefantrine, artesunate-amodiaquine, and dihydroartemisinin-piperaquine (van der Pluijm et al., 2021).

Species identification is crucial because *P. vivax* and *P. ovale* necessitate further therapy with primaquine or tafenoquin to eradicate dormant liver stages (hypnozoites) and avoid relapse. Glucose-6-phosphate dehydrogenase (G6PD) testing is required before primaquine treatment due to the danger of hemolysis in G6PD-deficient people. Severe malaria requires intravenous artesunate regardless of species, and this regimen demonstrates greater efficacy compared to quinine (van der Pluijm et al., 2021).

Antimalarial resistance poses ongoing challenges, particularly artemisinin resistance in *P. falciparum* in Southeast Asia, necessitating surveillance and adaptation of treatment policies. Species-specific resistance patterns influence regimen selection in endemic regions.

**Toxoplasmosis**

*Toxoplasma gondii* causes severe disease in immunocompromised patients and congenital infections. The standard treatment combines pyrimethamine and sulfadiazine with leucovorin (folinic acid) to prevent bone marrow toxicity. Alternative regimens for sulfa-allergic patients include pyrimethamine plus clindamycin or atovaquone. Species-specific diagnosis is important to distinguish toxoplasmosis

from other causes of cerebral lesions in AIDS patients (van der Pluijm et al., 2021).

### Other Protozoal Infections

*Entamoeba histolytica*, causing invasive amebiasis, requires treatment with tissue-active agents (metronidazole or tinidazole) followed by luminal agents (paromomycin or iodoquinol) to eliminate intestinal colonization. Giardia lamblia and Trichomonas vaginalis are effectively treated with metronidazole or tinidazole, though resistance has been reported. Trypanosoma species causing African and American trypanosomiasis require species-specific and stage-specific therapy, with treatment options including pentamidine, suramin, melarsoprol, nifurtimox, and benznidazole depending on species and disease stage (van der Pluijm et al., 2021).

### Novel Antiprotozoal Strategies

Antimicrobial peptides and venom-derived compounds demonstrate in vitro and preclinical antiparasitic activity against various protozoa, representing potential leads for future drug development. While these agents remain experimental, they illustrate the ongoing search for novel antiprotozoal mechanisms that may overcome resistance to existing drugs. Authoritative clinical resources provide detailed species-specific diagnostic and therapeutic approaches for protozoal diseases, supporting evidence-based treatment decisions (van der Pluijm et al., 2021).

### Challenges

Protozoa exhibit complex life cycles and variable susceptibility. Resistance in malaria parasites threatens control, particularly with artemisinin-resistant *P. falciparum* (Antimicrobial Prescribing Guidelines, 2021). Toxicity and limited drug innovation remain persistent issues.

### Advances

Artemisinin-based combination therapies (ACTs) remain the cornerstone for malaria. G6PD testing before primaquine administration enhances safety, while nanocarrier systems improve targeted delivery (Fatima et al., 2023; Glajzner et al., 2024).

## PHARMACOKINETIC AND PHARMACODYNAMIC CONSIDERATIONS

### PK/PD Principles In Antimicrobial Therapy

Optimal antimicrobial therapy takes into account both pharmacokinetic (PK) factors (drug absorption, distribution, metabolism, and elimination) and pharmacodynamic (PD) factors (the link between drug concentration and antimicrobial effect). Species-specific PK/PD optimization takes into consideration pathogen susceptibility (MIC), infection location, and patient-specific variables to improve efficacy while reducing harm and resistance selection. Three main PK/PD factors predict antibacterial efficacy: Time above MIC (T>MIC) for time-dependent medicines like beta-lactams, peak concentration to MIC ratio (Cmax /MIC) for concentration-dependent agents like aminoglycosides, and area under the curve to MIC ratio (AUC/MIC) for mixed-pharmacodynamic agents like fluoroquinolones and vancomycin (Weis et al., 2020).

### Species-specific PK/PD Optimization

Recent therapeutic trials have identified species-specific PK/PD targets, which improve therapy outcomes. Polymyxin B is effective against carbapenem-resistant K. pneumoniae with fAUCss,24h/MIC ≥22.8, although larger exposures raise the risk of nephrotoxicity and neurotoxicity. Because of the limited therapeutic window, careful dose selection and therapeutic medication monitoring are required whenever possible. Current guidelines for vancomycin against MRSA recommend AUC/MIC objectives of 400-600, which can be accomplished using dosing algorithms and therapeutic drug monitoring. However, these aims must be evaluated against the potential of nephrotoxicity, particularly in critically sick patients and those receiving concomitant nephrotoxic medications (Wierzbowski AK et al., 2007).

Beta-lactam antibiotics demonstrate time-dependent killing, with bacterial eradication correlating with the time that free drug concentrations remain above the MIC. For serious infections caused by less-susceptible organisms, prolonged or continuous infusion strategies can optimize T>MIC and improve outcomes compared to intermittent dosing (Weis et al., 2020; Rybak et al., 2020).

### Site-Specific Considerations

The infection site profoundly influences antimicrobial selection and dosing due to variable drug penetration. Central nervous system infections require agents with excellent CSF penetration (e.g., ceftriaxone, meropenem, linezolid) and often higher doses to achieve adequate concentrations. Bone and joint infections necessitate prolonged therapy with agents demonstrating good bone penetration, such as fluoroquinolones, rifampin, and linezolid (Raimondi et al., 2022).

Pulmonary infections benefit from agents achieving high lung concentrations, with novel delivery strategies including inhaled antibiotics and antifungals showing promise for optimizing local drug exposure while reducing systemic toxicity. Intra-abdominal infections require agents with activity against anaerobes and adequate peritoneal fluid penetration (Rybak et al., 2020; Weis et al., 2020).

## ANTIMICROBIAL RESISTANCE AND MANAGEMENT

### Species-Specific Resistance Mechanisms

Antimicrobial resistance pathways differ among microbial species, demanding species-specific expertise for effective medication selection. Bacterial pathogen genomic investigations have revealed that resistance determinants are frequently species-specific, with mobile genetic elements and

chromosomal alterations contributing to resistance in species-specific patterns.

Carbapenem resistance in *Bacteroides fragilis* is mediated by cfiA genes and upstream insertion sequences that differ between species, highlighting the importance of species-level genomics in resistance prediction. Similarly, different Candida species have varied resistance mechanisms, with C. glabrata exhibiting intrinsic reduced azole susceptibility through activation of efflux pumps, whereas C. auris commonly harbors azole-resistant ERG11 mutations.

### Antimicrobial Management

Antimicrobial management programs aim to optimize antimicrobial use, improve patient outcomes, reduce resistance, and decrease costs. Species-specific approaches are fundamental to effective management, enabling transition from broad-spectrum empirical therapy to targeted, narrow-spectrum agents once pathogen identification and susceptibility data are available.

Key strategies include implementing restriction policies for broad-spectrum and last-resort agents, utilizing rapid diagnostics for early species identification and resistance detection, and applying PK/PD principles to optimize dosing. Audit and feedback, prospective review with intervention, and formulary restriction represent proven interventions that reduce inappropriate antimicrobial use while maintaining or improving patient outcomes (Raimondi et al., 2022).

### Novel Therapeutic Strategies

Emerging antimicrobial strategies offer potential solutions to the resistance crisis. Drug repositioning rapidly expands therapeutic options by identifying antibacterial activity in approved non-antibiotic drugs, accelerating development timelines compared to novel drug discovery. Bacteriophage therapy provides species-specific bacterial targeting with minimal disruption of commensal microbiota, though regulatory and technical challenges remain (Raimondi et al., 2022).

Antimicrobial peptides, anti-biofilm agents, and immunotherapies represent next-generation approaches that may complement or replace traditional antimicrobials. Non-digestible oligosaccharides and other microbiome-protective strategies aim to preserve beneficial microbiota while eliminating pathogens. Nanoparticle-based drug delivery systems offer improved pharmacokinetics and targeted drug release at infection sites (Ghazi and El Nekidy, 2023; Weis et al., 2020).

## FUTURE DIRECTIONS

The next generation of antimicrobial pharmacotherapy will integrate genomics, AI, and precision dosing. Rapid point-of-care diagnostics, bacteriophage-based therapeutics, and AI-driven stewardship programs will personalize antimicrobial use. Global surveillance networks are essential to track emerging resistance trends (Antimicrobial Resistance Collaborators, 2022).

## CONCLUSION

Species-specific antimicrobial pharmacotherapy reflects the present and future of infectious illness management, taking advantage of breakthroughs in diagnostics, genetics, and pharmacology to improve treatment outcomes. The combination of quick species identification, resistance gene detection, and PK/PD-guided dose will limit antimicrobial therapy to what works best and causes the least harm. However, specific priorities must be followed to achieve these aspects. First, there should be continued focus on implementing rapid diagnostic technologies to allow a timely transition to targeted therapy and reduce broad-spectrum antimicrobial exposure. Second, TDM and PK/PD considerations should be expanded to address individual patients' and pathogens' needs. Third, consideration must be given to novel antimicrobials, immunotherapies, and other methods, such as phages and peptides. Fourth, Antimicrobial stewardship must be strengthened globally to ensure effective new agents and rational use of older ones. Finally, there should be a focus on surveillance to provide experts with data for guidelines (Arias et al., 2012). The COVID-19 pandemic has shown that the current reserve mobilization drawdown is an issue in combating just one pathogen, but it at least provides the funding necessary for a rapid response. With costs distributed among many common costly conditions, there should be enough money in the system to cover all bases in normal years. The COVID-19 pandemic has highlighted the challenges posed by emerging infections and shown how quickly progress can be made when people come together.

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