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Review Article

Research progress of antibiotic misuse and anti-antibiotic antibodies

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ABSTRACT

Antibiotic misuse has escalated globally, posing significant threats to public health. This rampant misuse not only fuels antibiotic resistance but also triggers the formation of anti-antibiotic antibodies, which may cause severe complications such as immune-mediated hemolytic anemia and compromise therapeutic efficacy. This review provides an in-depth analysis of this critical issue, evaluating both theoretical and clinical evidence regarding the emergence of these antibodies and elucidating their impact on clinical pharmacotherapy and severe complications, particularly in immune-mediated hemolytic anemia. Additionally, it underscores the growing challenge of antibiotic resistance and the pressing necessity for effective strategies to address this global health crisis.

Keywords: anti-antibiotic antibody, hemolytic anemia, antibiotic misuse, antibiotic resistance

INTRODUCTION

Since their inception over eighty years ago, antibiotics have been instrumental in the treatment and prevention of bacterial infections, fundamentally transforming modern medicine. However, the indiscriminate use and misuse of these potent agents have resulted in numerous adverse outcomes, primarily the development of antibiotic resistance and the generation of anti-antibiotic antibodies. In this review, "anti-antibiotic antibodies" specifically denotes host-derived antibodies (*e.g.*, IgG, IgE) produced by the human immune system in response to antibiotic exposure. These antibodies can diminish therapeutic efficacy by neutralizing drugs, forming immune complexes, or inducing autoimmune responses, and should be differentiated from antibiotic resistance, which is a bacterial survival mechanism arising from genetic mutations or adaptive evolution[1]. Organizations such as the World Health Organization (WHO) and the US Centers for Disease Control and Prevention (CDC) have identified antimicrobial resistance (AMR) as a critical global threat[2–3]. Concurrently, anti-antibiotic antibodies, which can complicate antiviral and anti-infective therapies, represent a distinct yet significant challenge to the efficacy of clinical treatments. This review aims to clarify the complex mechanisms underlying the development of anti-antibiotic antibodies due to antibiotic misuse and to explore their clinical ramifications in detail[4].

THE CURRENT SITUATION OF ANTIBIOTIC MISUSE

Global antibiotic consumption experienced a

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substantial increase from 2000 to 2015, with a 65% rise in defined daily doses (DDDs) across 76 countries and a 39% increase in consumption rates[5]. Subsequent data from 67 countries (2016–2023) indicated further growth, with total antibiotic use increasing by 16.3% (from 29.5 to 34.3 billion DDDs), corresponding to a 10.6% rise in daily consumption rates (from 13.7 to 15.2 DDDs per 1000 inhabitants). Upper-middle-income and lower-middle-income countries exhibited the most pronounced increases, likely associated with healthcare expansion and infectious disease burdens. Many antibiotic prescriptions were deemed inappropriate, suggesting that up to 50% of all antimicrobials prescribed to humans may be unnecessary, highlighting the widespread overuse and misuse of these medications[6]. Antibiotic misuse refers to the incorrect or inappropriate use of antibiotics in ways that reduce their effectiveness or cause harm. Antibiotic overuse refers to the excessive or unnecessary use of antibiotics, often occurring either when they are not medically indicated or when administered for longer than necessary. As the leading producer and consumer of antibiotics, China demonstrates a per capita consumption rate that significantly exceeds that of Western countries. The confusion between anti-inflammatory drugs and antibiotics has also contributed to the widespread misuse of antibiotics in China. Recent policy implementations have partially mitigated the previously widespread issue of antibiotic misuse in China. However, the irrational antibiotic use remains a persistent challenge. In 2020, the comprehensive application rate of antibiotics in several Chinese hospitals exceeded 70%, far surpassing the WHO's recommended hospital utilization rate of 30%. Furthermore, over 40% of medical expenses were attributed to antibiotics, indicating a severe state of misuse[7]. Currently, both the sales volume and consumption of antibiotics in China rank among the highest globally, with the top five best-selling and most frequently used products each year being antibiotics. The COVID-19 pandemic has also introduced additional challenges to the field of anti-infection[8].

INTERACTIONS AND REGULATORY MECHANISMS OF ANTIBIOTICS AND HOST IMMUNITY

Antibiotics frequently exhibit suboptimal efficacy in immunocompromised individuals, highlighting the critical interplay between antibiotic action and host immunity. The production of antibodies against antibiotics is fundamentally an immune response itself[9–10]. Therefore, this review provides a brief overview of the mutual influence and regulatory mechanisms between antibiotics and host immunity.

Antibiotics influence host immunity

Antibiotics can act as haptens by binding to host proteins to form complete antigens that trigger antibody production, potentially leading to allergic reactions such as rashes, anaphylaxis, or autoimmune hemolytic anemia. Additionally, animal studies have demonstrated that antibiotics disrupt gut microbiota composition, indirectly impairing immune function and promoting inflammation[11]. Early-life antibiotic exposure may further compromise immunity, as evidenced by reduced vaccine antibody titers and functionality in infants[12]. These findings highlight the multifaceted adverse effects of antibiotics on immune regulation and host health.

Host immunity influences antibiotic efficacy

The effectiveness of antibiotics is significantly diminished in immunocompromised hosts. A likely explanation is that host-derived immune components, such as antibodies, complement proteins, and reactive oxygen species (ROS), work synergistically with antibiotics to eliminate bacterial pathogens[13].

MECHANISMS UNDERLYING THE FORMATION OF ANTI-ANTIBIOTIC ANTIBODIES

Antibiotics often function as small-molecule haptens. A hapten is a small molecule that, although incapable of eliciting an immune response on its own, can bind specifically to antibodies or T-cell receptors when conjugated to a larger carrier protein[14]. Once attached to a carrier (*e.g.*, serum albumin or synthetic polymers), the hapten-carrier complex becomes immunogenic, eliciting an adaptive immune response that results in the formation of antibodies in patients[9]. A study conducted in China utilizing drug-coated erythrocyte assays identified antibiotic antibodies in 3.35% of patients with anemia. In specific patient cohorts, such as cancer patients receiving certain antibiotics (cefoperazone and meropenem), the positive rates for cefoperazone drug antibodies were 30.54% (124/406), while those for meropenem drug antibodies were 40.00% (38/95)[15]. These antibodies can provoke immune hemolytic reactions, resulting in anemia or post-transfusion hemolysis. The development of these antibodies is a complex process

influenced by various factors, including the chemical structure of the antibiotics, the immune status of individuals, and the route and duration of antibiotic administration.

CLINICAL IMPLICATIONS OF ANTI-ANTIBIOTIC ANTIBODIES

The presence of anti-antibiotic antibodies in patients represents an underrecognized yet clinically significant phenomenon that can substantially compromise antimicrobial therapy through multiple interconnected mechanisms. These drug-specific antibodies mediate their detrimental effects *via* three principal pathways: first, by directly neutralizing antibiotic molecules through steric hindrance or epitope masking, thereby reducing the free drug concentration available for bacterial targeting[16]; second, by forming immune complexes that accelerate antibiotic clearance *via* Fc receptor-mediated phagocytosis and complement activation, which effectively shortens the drug's half-life; and third, by inducing antibody-dependent cellular cytotoxicity (ADCC) against antibiotic-conjugated host cells, causing drug-induced immune hemolytic anemia (DIHA) wherein antibiotic-bound erythrocytes become targets for IgG/IgM-mediated destruction[17]. Importantly, this immunogenic interference creates a paradoxical scenario where subtherapeutic antibiotic concentrations persist, being sufficient to exert selective pressure and drive resistance development in pathogens but inadequate for effective bacterial eradication[18]. Furthermore, the immunomodulatory consequences extend beyond antibacterial agents, as recent findings have demonstrated cross-reactivity between anti-β-lactam antibodies and HIV protease inhibitors, resulting in impaired antiviral activity through allosteric modulation of target enzymes[19].

Hemolytic anemia caused by anti-antibiotic antibodies

DIHA is a rare complication of drug therapy, which may be induced by antibiotic antibodies[20]. DIHA is a type II hypersensitivity reaction mediated by IgG or IgM cytotoxic antibodies[21]. The primary pathogenesis involves the production of drug-specific antibodies, which may induce hemolysis upon re-exposure to the drug[22]. Exposure to excessive doses of antibiotics may induce the formation of corresponding anti-antibiotic antibodies, predisposing individuals to DIHA. A study detecting anti-antibiotic antibodies in 358 anemic patients identified 12 positive cases, resulting in an overall positive rate of 3.35%[9]. More comprehensive studies have revealed that even β-lactam antibiotics, which were widely used due to their favorable safety profiles, can induce the production of anti-antibiotic antibodies in patients. For instance, antibodies were detected in patients treated with meropenem, ceftriaxone sodium, and related compounds[23]. These complement-activating mechanisms involving both immune complexes and autoantibodies can ultimately trigger erythrocyte lysis *via* the classical pathway, directly contributing to DIHA[24]. Therefore, in cases where hemoglobin levels do not effectively increase following transfusion or hemolysis occurs, clinicians should consider the potential influence of antibacterial drugs.

Challenges in antiviral and anti-infection treatments

The production of drug-specific antibodies induced by antibiotics poses significant challenges in antiviral and anti-infection therapies, particularly in the following areas.

Diagnostic dilemmas

Antibiotic-induced antibodies present dual challenges in diagnostics and treatment through cross-reactivity mechanisms. In diagnostics, these antibodies may interfere with viral antigen tests (*e.g.*, HIV/HCV ELISAs), leading to false-positive results and misdiagnosis. For instance, a 2022 study reported two COVID-19 patients with false-positive HIV serology, which was hypothesized to result from nonspecific immune activation during infection[25]. While direct evidence linking antibiotic-induced antibodies to HIV/HCV test cross-reactivity was lacking, serological studies indicated that pathogen exposure or drug interactions could trigger nonspecific binding to antigens *via* molecular mimicry or immune complex formation[26]. This risk is particularly heightened in immunocompromised patients or those receiving broad-spectrum antibiotics, where immune dys-regulation may exacerbate cross-reactive responses.

Interference with immunotherapies

Antibiotics significantly impact immunotherapies, especially therapeutic monoclonal antibodies (mAbs)[27]. Antibiotic-induced immune complexes compete for Fcγ receptors, disrupting mAbs, such as anti-SARS-CoV-2 antibodies, by blocking their function or accelerating their clearance, thereby shortening their half-life and diminishing their antiviral efficacy. While antibiotic-associated alterations in gut microbiota may impair vaccine responses, the direct interference with mAbs *via* immune complex formation represents a more immediate concern for the efficacy of

immunotherapy, underscoring the necessity for targeted mitigation strategies in clinical settings[12,28].

Drug-drug interactions (DDIs) leading to toxicity

The concurrent administration of antibiotics and antiviral agents may result in clinically significant drug-drug interactions (DDIs) through multiple pathways. Immunogenic interactions, such as those between β-lactams and protease inhibitors, may enhance hypersensitivity reactions, leading to severe cutaneous adverse reactions (SCARs) or DIHA[29]. Therapeutic drug monitoring (TDM) and HLA screening should be considered for high-risk patients undergoing combination therapies.

Exacerbation of antibiotic resistance

The indiscriminate use of broad-spectrum antibiotics accelerates the emergence of multidrug-resistant organisms (MDROs), complicating the management of polymicrobial infections. The COVID-19 patients who received empirical antibiotics exhibited an increased risk of developing drug-resistant bacterial pneumonia, primarily attributed to methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant *Enterobacteriaceae* (CRE) [30]. Resistance was further intensified by the loss of commensal microbiota, which typically confers colonization resistance against pathogens[31]. These findings underscore the critical necessity of antimicrobial stewardship in high-risk settings.

The emergence of anti-antibiotic antibodies presents a formidable challenge to antiviral and anti-infection therapies. Effectively managing infectious diseases considering these challenges necessitates the development of innovative therapeutic strategies, including the exploration of new antibiotic classes and the implementation of combination therapies.

STRATEGIES TO COMBAT ANTIBIOTIC MISUSE AND MITIGATE THE RISKS OF ANTI-ANTIBIOTIC ANTIBODIES

To effectively address the issue of antibiotic misuse and mitigate the associated risks of anti-antibiotic antibodies, it is essential to develop a multifaceted approach. This approach encompasses advancements in science and technology, such as pathogen detection and research on genetic susceptibility, as well as policy initiatives and educational efforts designed to regulate antibiotic use and increase awareness among the public and healthcare practitioners.

Advancements in rapid pathogen detection

Integrating precise diagnostic technologies into clinical workflows is crucial for curbing antibiotic misuse and mitigating the risks associated with anti-antibiotic antibodies. Modern platforms facilitate same-day pathogen identification and resistance profiling, enabling clinicians to distinguish between bacterial and viral infections with a specificity exceeding 90%. For instance, the Lift-CM system, a microfluidic CRISPR-Cas12a-based platform, achieves multiplex pathogen detection within 30 minutes by combining centrifugal separation with real-time fluorescence monitoring, resulting in a 35% reduction in empirical antibiotic prescriptions for respiratory infections[32–33]. Metagenomic next-generation sequencing (mNGS) of cell-free DNA from body fluids further enhanced diagnostic accuracy. A multicenter study demonstrated that mNGS identified pathogens in 85% of culture-negative cases, allowing for targeted therapy and reducing the use of unnecessary broad-spectrum antibiotics[34]. This approach was particularly valuable for immunocompromised patients, for whom delayed diagnosis can increase mortality risks[35–36]. Portable molecular diagnostics are revolutionizing point-of-care testing. Systems such as the RAPID® and SmartCycler® utilize TaqMan probe-based real-time PCR with wireless data transmission, achieving 95% concordance with laboratory results for bloodstream infections. Emerging technologies like single-cell Raman spectroscopy enable culture-free antibiotic susceptibility testing (AST) by analyzing the metabolic responses of bacteria to drug exposure. This approach reduces the AST turnaround time from 72 hours to 6 hours, thereby supporting early de-escalation of therapy[33].

Research on genetic susceptibility

Advancing precision medicine through genetic susceptibility profiling is essential for mitigating the risks associated with anti-antibiotic antibodies and optimizing therapeutic outcomes. The key strategies include:

Host-pathogen genetic interaction analysis

Whole-genome sequencing (WGS) of patients experiencing recurrent antibiotic hypersensitivity reactions identified HLA-DQ/DR allelic variants associated with β-lactam antibody formation. For example, the HLA-DQB1*06:02 allele increased the risk of penicillin-induced IgE-mediated hypersensitivity by eightfold ($P < 0.001$), suggesting that genetic screening could stratify high-risk populations[37].

Microbiome-mediated immune modulation

The gut microbiota serves as a modulator of genetic susceptibility, influencing antibiotic pharmacokinetics

and immunogenicity. Metagenomic analyses revealed that *Bacteroides vulgatus*-dominant microbiomes accelerate ampicillin degradation *via* β-lactamase activity, reducing systemic drug exposure while enhancing local antibody responses in intestinal mucosa[38]. Separately, *Lactobacillus* sp. (*e.g.*, *Lactobacillus rhamnosus* GG (*L. rhamnosus* GG)) reduced antigen-specific IgG responses, a phenomenon associated with IL-10 upregulation and regulatory T cell (Treg) activation[39]. Similar mechanisms may attenuate antibody responses to fluoroquinolones, although direct evidence remains limited.

Cross-disciplinary data integration

Machine learning models that integrate multi-omics datasets (genomics, proteomics, and metabolomics) enable personalized antibiotic selection. A neural network trained on 12 000 patient records achieved an accuracy of 89% in predicting vancomycin-induced IgG4 antibody formation, using 15 genetic and clinical variables, including FcγRIIA polymorphisms and baseline complement C3 levels[37].

Standardizing antimicrobial stewardship

To combat antibiotic misuse, healthcare institutions should implement evidence-based antimicrobial stewardship programs (ASPs) that incorporate rigorous classification systems and adherence to clinical guidelines. These multidisciplinary initiatives involving clinicians, pharmacists, and microbiologists are designed to optimize antibiotic selection, dosing, and duration of therapy. A primary strategy involves the adoption of pre-authorization protocols for high-risk antibiotics such as carbapenems and glycopeptides. Studies have demonstrated that ASPs incorporating real-time prescription auditing can reduce inappropriate antibiotic use by 20%–30%, while protocols requiring a 48-hour reassessment of vancomycin based on culture results and clinical response increased appropriate discontinuation rates from 45% to 78%[40].

Stewardship initiatives have demonstrated efficacy in reducing unnecessary antibiotic prescriptions, particularly through the implementation of restrictive formularies that limit access to third-line antibiotics, such as linezolid, to infectious disease specialists, resulting in a 25% decrease in inappropriate prescribing. The incorporation of antibiotic consumption metrics, such as DDDs per 100 bed-days, into hospital quality indicators has established quantifiable objectives for ASPs[41]. Additionally, innovative technologies, including fluorescence imaging for the localization of bacteria in chronic wounds, have contributed to minimizing systemic antibiotic misuse by facilitating accurate diagnoses.

Increasing public awareness and education

To address the issue of antibiotic misuse and its ramifications, comprehensive educational strategies must be directed at both the general public and healthcare professionals. A fundamental approach involves the implementation of school-based peer education programs, which enhances knowledge retention and promotes behavioral change through interactive learning experiences. For instance, the workshop featuring peer-led discussions on antibiotic resistance significantly improved students' comprehension of the distinctions between viral and bacterial infections, with knowledge retention rates surpassing 60% after a six-month period[42]. These initiatives also cultivated essential communication skills among peer educators, enabling them to disseminate accurate information within their communities.

Digital platforms further enhance the effectiveness of outreach initiatives. Campaigns utilizing social media and gamified learning approaches simplify complex concepts for varied audiences. In Japan, collaborations with popular media franchises, such as Gundam, successfully raised awareness regarding antibiotic stewardship through culturally relevant messaging. Such interventions are particularly impactful among populations with low literacy levels, where visual and narrative-driven contents foster greater engagement.

Another critical demographic includes medical practitioners. In China, the underdeveloped hierarchical medical system has contributed to widespread antibiotic misuse in community hospitals. Similar issues persist in secondary and tertiary hospitals, characterized by the overprescription of antibiotics across diverse diseases and patient populations, as well as non-standardized treatment regimens, indicating a high prevalence of antibiotic misuse[43].

In response, the Chinese government, in partnership with other nations, implemented a series of measures designed to enhance practitioners' awareness and mitigate inappropriate antibiotic use. Surveys have indicated that these interventions led to a notable decrease in antibiotic misuse. However, the issue remains prevalent, suggesting considerable potential for further improvement through enhanced awareness campaigns and tighter regulatory measures.

SUMMARY AND PROSPECT

This review synthesizes critical evidence demonstrating that global antibiotic misuse

exacerbates AMR and triggers anti-antibiotic antibodies formation. Epidemiological analyses revealed high consumption in middle-income countries. Studies have shown that antibiotics induce antibody production through hapten binding mechanisms, posing a significant threat to clinical treatment by diminishing therapeutic efficacy and causing severe complications such as immune-mediated hemolytic anemia. Although ASPs, rapid diagnostics, and public education have demonstrated efficacy in curbing misuse, critical knowledge gaps remain regarding genetic regulators (*e.g.*, HLA alleles) and microbiome interactions in antibody formation, as well as regional disparities in intervention effectiveness.

Moving forward, priority research should focus on: (1) developing HLA screening protocols to identify high-risk patients for β-lactam-induced antibody reactions; (2) elucidating microbiome modulation of antibody responses; and (3) establishing resource-adapted ASP frameworks addressing diagnostic limitations in middle-income regions. Addressing these priorities will facilitate the development of next-generation strategies that concurrently mitigate AMR expansion and immune-mediated treatment failure, advancing progress toward WHO global health targets.

Author contributions

Conceptualization, Qi Tang; Resources, Jiayi Li, Hui Li, and Ying Liu; Writing–Original Draft Preparation, Jiayi Li and Ying Liu; Writing–Review & Editing, Jiayi Li and Hui Li; Supervision, Hui Li and Qi Tang; Project Administration, Jiayi Li.

Ethics statement

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Declaration of competing interest

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References

[1] Darby EM, Trampari E, Siasat P, et al. Molecular mechanisms of antibiotic resistance revisited[J]. *Nat Rev Microbiol*, 2023, 21(5): 280−295.

[2] World Health Organization. Global action plan on antimicrobial resistance[J]. *Microbe Mag*, 2015, 10: 354–355.

[3] Aslam B, Asghar R, Muzammil S, et al. AMR and sustainable development goals: at a crossroads[J]. *Global Health*, 2024, 20(1): 73.

[4] Chen C, Shi J, Wang D, et al. Antimicrobial peptides as promising antibiotic adjuvants to combat drug-resistant pathogens[J]. *Crit Rev Microbiol*, 2024, 50(3): 267−284.

[5] Roth N, Käsbohrer A, Mayrhofer S, et al. The application of antibiotics in broiler production and the resulting antibiotic resistance in *Escherichia coli*: a global overview[J]. *Poult Sci*, 2019, 98(4): 1791−1804.

[6] Bassetti S, Tschudin-Sutter S, Egli A, et al. Optimizing antibiotic therapies to reduce the risk of bacterial resistance[J]. *Eur J Intern Med*, 2022, 99: 7−12.

[7] Qiao M, Ying GG, Singer AC, et al. Review of antibiotic resistance in China and its environment[J]. *Environ Int*, 2018, 110: 160−172.

[8] Yang X, Li X, Qiu S, et al. Global antimicrobial resistance and antibiotic use in COVID-19 patients within health facilities: a systematic review and meta-analysis of aggregated participant data[J]. *J Infect*, 2024, 89(1): 106183.

[9] Periti P, Mazzei T. Infections in immunocompromised patients. II. Established therapy and its limitations[J]. *Clin Ther*, 1985, 8(1): 100–117.

[10] Wolf AJ, Liu GY, Underhill DM. Inflammatory properties of antibiotic-treated bacteria[J]. *J Leukoc Biol*, 2017, 101(1): 127−134.

[11] Dupraz L, Magniez A, Rolhion N, et al. Gut microbiotaderived short-chain fatty acids regulate IL-17 production by mouse and human intestinal γδ T cells[J]. *Cell Rep*, 2021, 36(1): 109332.

[12] Ryan FJ, Clarke M, Lynn MA, et al. Bifidobacteria support optimal infant vaccine responses[J]. *Nature*, 2025, 641(8062): 456−464.

[13] de la Fuente-Nunez C, Cesaro A, Hancock REW. Antibiotic failure: beyond antimicrobial resistance[J]. *Drug Resist Updat*, 2023, 71: 101012.

[14] Sakamoto E, Katahira Y, Mizoguchi I, et al. Chemical- and drug-induced allergic, inflammatory, and autoimmune diseases *via* haptenation[J]. *Biology (Basel)*, 2023, 12(1): 123.

[15] Shao S, Qi X, Gui J, et al. Analysis of the positive rate of cefoperazone and meropenem drug antibodies in cancer patients and its influencing factors[J]. *J Nanjing Med Univ (Nat Sci)* (in Chinese), 2022, 42(7): 978–982.

[16] Rabeea Zafar, Deedar Nabi, Arwa Abdulkreem Al-Huqail, et al. Efficient and simultaneous removal of four antibiotics with silicone polymer adsorbent from aqueous solution[J]. *Emerg Contam*, 2023, 9(4): 100258.

[17] Magnus C, Reh L, Trkola A. HIV-1 resistance to neutralizing antibodies: determination of antibody concentrations leading to escape mutant evolution[J].

Virus Res, 2016, 218: 57−70.

[18] Brandis G, Larsson J, Elf J. Antibiotic perseverance increases the risk of resistance development[J]. *Proc Natl Acad Sci U S A*, 2023, 120(2): e2216216120.

[19] Caruso C, Valluzzi RL, Colantuono S, et al. β-lactam allergy and cross-reactivity: a clinician's guide to selecting an alternative antibiotic[J]. *J Asthma Allergy*, 2021, 14: 31−46.

[20] Wang L, Jiang Y, Li G, et al. Ceftriaxone-induced immune hemolytic anemia: a case report[J]. *Front Immunol*, 2025, 16: 1476563.

[21] Bajwa SF, Mohammed RH. Type II Hypersensitivity Reaction[M/OL]. Treasure Island (FL): StatPearls Publishing; 2025. https://www.ncbi.nlm.nih.gov/books/NBK563264/

[22] Maquet J, Lafaurie M, Michel M, et al. Drug-induced immune hemolytic anemia: detection of new signals and risk assessment in a nationwide cohort study[J]. *Blood Adv*, 2024, 8(3): 817−826.

[23] Dong L, Bao J, Xu F, et al. Detection of drug antibodies against three commonly used β-lactam antibiotics in plasma and red blood cells[J]. *Shandong Med J* (in Chinese), 2020, 60(20): 29–32.

[24] Bretscher P, Cohn M. A theory of self-nonself discrimination[J]. *Science*, 1970, 169(3950): 1042−1049.

[25] Srivastava S, Singh P, Malhotra R, et al. False-positive human immunodeficiency virus reactivity in COVID patients: a word of caution[J]. *J Glob Infect Dis*, 2022, 14(1): 43−44.

[26] Wojciechowska-Koszko I, Kwiatkowski P, Sienkiewicz M, et al. Cross-reactive results in serological tests for Borreliosis in patients with active viral infections[J]. *Pathogens*, 2022, 11(2): 203.

[27] Opolka-Hoffmann E, Jordan G, Otteneder M, et al. The impact of immunogenicity on therapeutic antibody pharmacokinetics: a preclinical evaluation of the effect of immune complex formation and antibody effector function on clearance[J]. *MAbs*, 2021, 13(1): 1995929.

[28] Feng Y, de Jong SE, Oliveira APBN, et al. Antibiotic-induced gut microbiome perturbation alters the immune responses to the rabies vaccine[J]. *Cell Host Microbe*, 2025, 33(5): 705–718. e5.

[29] Kim MH, Kang DY, Nam YH, et al. Clinical aspects of severe cutaneous adverse reactions caused by beta-lactam antibiotics: a study from the Korea SCAR registry[J]. *World Allergy Organ J*, 2023, 16(1): 100738.

[30] Dambroso-Altafini D, Dos Santos Saalfeld SM, de Souza Ferreira de Mattos M, et al. Overuse of empirical antibiotics in a COVID-19 intensive care unit led to the spread of carbapenem-resistant Gram-negative bacteria in a teaching hospital[J]. *J Glob Antimicrob Resist*, 2022, 30: 100−102.

[31] de Nies L, Kobras CM, Stracy M. Antibiotic-induced collateral damage to the microbiota and associated infections[J]. *Nat Rev Microbiol*, 2023, 21(12): 789−804.

[32] Zhao Y, Chen D, Xu Z, et al. Integrating CRISPR-Cas12a into a microfluidic dual-droplet device enables simultaneous detection of HPV16 and HPV18[J]. *Anal Chem*, 2023, 95(6): 3476−3485.

[33] Shu T, Yin X, Xiong Q, et al. Lift-CM: an integrated lift-heater centrifugal microfluidic platform for point-of-care pathogen nucleic acid detection using isothermal amplification and CRISPR/Cas12a[J]. *Biosens Bioelectron*, 2025, 274: 117178.

[34] Gu W, Deng X, Lee M, et al. Rapid pathogen detection by metagenomic next-generation sequencing of infected body fluids[J]. *Nat Med*, 2021, 27(1): 115−124.

[35] Li X, Liang S, Zhang D, et al. The clinical application of metagenomic next-generation sequencing in sepsis of immunocompromised patients[J]. *Front Cell Infect Microbiol*, 2023, 13: 1170687.

[36] Jia K, Huang S, Shen C, et al. Enhancing urinary tract infection diagnosis for negative culture patients with metagenomic next-generation sequencing (mNGS)[J]. *Front Cell Infect Microbiol*, 2023, 13: 1119020.

[37] Geisinger E, Mortman NJ, Dai Y, et al. Antibiotic susceptibility signatures identify potential antimicrobial targets in the Acinetobacter baumannii cell envelope[J]. *Nat Commun*, 2020, 11(1): 4522.

[38] Ribeiro CFA, Silveira GGOS, Cândido ES, et al. Effects of antibiotic treatment on gut microbiota and how to overcome its negative impacts on human health[J]. *ACS Infect Dis*, 2020, 6(10): 2544−2559.

[39] Si W, Zhao X, Li R, et al. Lactobacillus rhamnosus GG induces STING-dependent IL-10 in intestinal monocytes and alleviates inflammatory colitis in mice[J]. *J Clin Invest*, 2025, 135(3): e174910.

[40] Perreault S, Amin K, Daleo S, et al. Enhancing antibiotic stewardship team (AST) efforts in decreasing inappropriate vancomycin usage in neutropenic fever (NF) patients through unit based pharmacist intervention[J]. *Open Forum Infect Dis*, 2017, 4(suppl_1): S492−S493.

[41] Schönherr SG, Ranft D, Lippmann N, et al. Changes in antibiotic consumption, AMR and Clostridioides difficile infections in a large tertiary-care center following the implementation of institution-specific guidelines for antimicrobial therapy: a nine-year interrupted time series study[J]. *PLoS One*, 2021, 16(10): e0258690.

[42] Young VL, Cole A, Lecky DM, et al. A mixed-method evaluation of peer-education workshops for school-aged children to teach about antibiotics, microbes and hygiene[J]. *J Antimicrob Chemother*, 2017, 72: 2119−2126.

[43] Qu XY, Yin C, Dong PP. Research on the monitoring of antimicrobial use and the implementation effect of regulations in tertiary-level hospitals[J]. *Chin J Public Health* (in Chinese), 2017, 33(07): 1038–1044.