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Next-Generation Vaccinology Against Antimicrobial-Resistant Pathogens: Advances, Challenges, and Future One Health Perspectives

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Abstract

Background: Antimicrobial Resistance (AMR) has emerged as a defining global health challenge, threatening the effectiveness of existing therapeutics and reversing gains in infectious disease control. Vaccination offers a preventive strategy that reduces infection incidence, limits antimicrobial use, and slows the emergence of resistant strains.

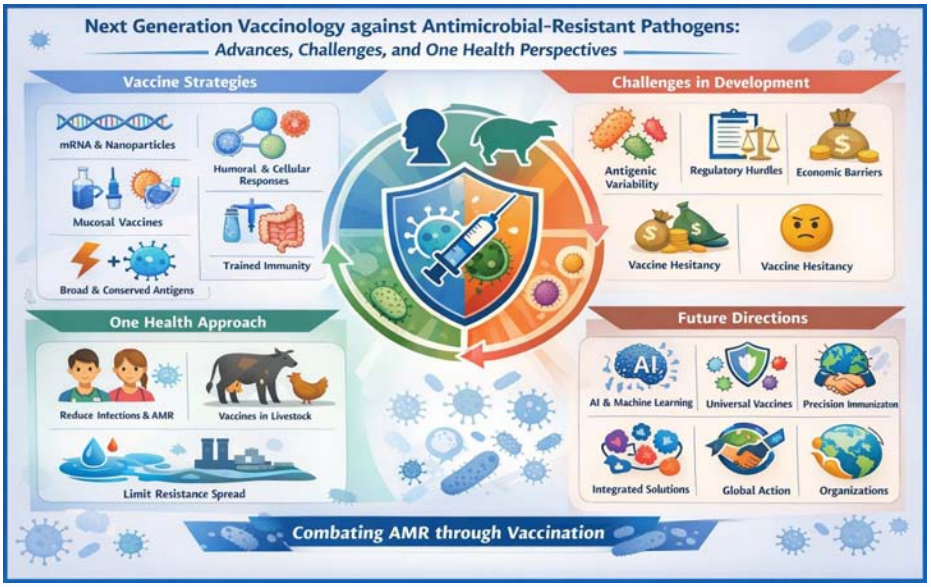
Objective: This review examines recent advances in next-generation vaccinology targeting antimicrobial-resistant pathogens, highlighting technological innovations, translational barriers, and future directions within a One Health framework.

Methods: A narrative synthesis of recent literature (2021-2026) was undertaken, focusing on emerging vaccine platforms, immunological strategies, and policy-oriented approaches relevant to AMR mitigation.

Results: Novel vaccine technologies, including mRNA, DNA, viral vector, and nanoparticle-based systems, have expanded the scope of vaccinology beyond traditional paradigms. Epitope-based design, reverse vaccinology, and systems immunology approaches are improving antigen selection and immunogenicity. These advances are complemented by increasing recognition of vaccines as tools to reduce antibiotic consumption and interrupt transmission of resistant pathogens. Despite progress, several challenges persist, including antigenic variability, limited correlates of protection, high development costs, and regulatory complexities. In addition, disparities in vaccine access and implementation, particularly in low- and middle-income settings, constrain global impact.

Conclusion: Next-generation vaccines represent a critical yet underutilized strategy in combating AMR. Their integration into broader One Health initiatives, alongside strengthened surveillance, policy alignment, and equitable distribution, will be essential for sustainable impact. Continued investment in interdisciplinary research and innovative development pathways is required to translate scientific advances into effective public health interventions.

Keywords: Vaccinology; Antimicrobial-Resistant; Pathogens; Advances; Challenges; One Health



Graphical Abstract:

Introduction

Antimicrobial Resistance (AMR) has become one of the most serious threats to global health, food security, and economic stability. The continued emergence and spread of resistant bacterial, viral, fungal, and parasitic pathogens undermine the effectiveness of existing antimicrobial therapies and complicate the management of both community-acquired and nosocomial infections. Recent estimates indicate that AMR was directly responsible for approximately 1.27 million deaths globally in 2019, with projections suggesting a steady rise if no effective interventions are implemented [1]. The burden is disproportionately higher in low- and middle-income countries, where weak health systems, limited diagnostic capacity, and unregulated antimicrobial use contribute to the acceleration of resistance [2].

Traditional approaches to combating infectious diseases have relied heavily on antimicrobial agents. However, the pace of new antibiotic development has slowed significantly, creating a widening gap between the emergence of resistant strains and the availability of effective treatments [3]. This has prompted a shift toward preventive strategies, with vaccination emerging as a critical component in the fight against AMR. Unlike antibiotics, which exert selective pressure on microbial populations, vaccines reduce infection incidence, thereby decreasing the need for antimicrobial use and limiting opportunities for resistance development [4].

Vaccination has historically demonstrated profound public health benefits. Established vaccines against pathogens such as Streptococcus pneumoniae and Haemophilus influenzae have not only reduced disease burden but also led to a measurable decline in antibiotic-resistant infections [5]. More recently, the global deployment of vaccines during the COVID-19 pandemic has illustrated the potential of rapid vaccine development platforms, particularly messenger RNA (mRNA) technologies, to address emerging infectious threats [6]. These advances have reinvigorated interest in applying next-generation vaccinology tools to AMR-associated pathogens.

Next-generation vaccinology represents a paradigm shift from conventional empirical vaccine design to a more rational, data-driven approach. Techniques such as reverse vaccinology, structural vaccinology, and systems immunology enable the identification of novel antigenic targets and the optimization of immune responses [7]. Advances in genomics, proteomics, and bioinformatics have facilitated the discovery of conserved epitopes across diverse pathogen strains, thereby addressing the challenge of antigenic variability [8]. In parallel, innovative delivery platforms, including viral vectors, nucleic acid-based vaccines, and nanoparticle systems, are improving vaccine stability, immunogenicity, and scalability [9].

Despite these promising developments, several scientific and operational challenges remain. Many AMR pathogens, such as Acinetobacter baumannii and Pseudomonas aeruginosa, exhibit complex immune evasion mechanisms and lack well-defined correlates of protection, complicating vaccine design [10]. Furthermore, the economic model for vaccine development against AMR pathogens is less attractive compared to chronic disease therapeutics, resulting in limited private sector investment [11]. Regulatory pathways for novel vaccine platforms also require further harmonization to ensure timely approval without compromising safety [12].

The complexity of AMR extends beyond human health, encompassing animal health and environmental reservoirs. The One Health concept recognizes the interconnectedness of these domains and emphasizes coordinated action across sectors. Vaccination strategies targeting livestock and zoonotic pathogens can reduce antimicrobial use in agriculture, thereby limiting the transmission of resistant organisms through the food chain and environment [13]. Environmental interventions, including improved sanitation and waste management, further complement these efforts by reducing the dissemination of resistant genes [14].

In recent years, global policy frameworks have increasingly acknowledged the role of vaccines in AMR mitigation. Organizations such as the World Health Organization and the Global Action Plan on AMR advocate for expanded vaccine coverage and the development of new vaccines targeting priority resistant pathogens [15]. However, achieving meaningful impact will require not only scientific innovation but also equitable access, robust surveillance

systems, and sustained political commitment.

This review explores the evolving landscape of next-generation vaccinology in the context of AMR. It examines technological advances, immunological strategies, and translational challenges, while highlighting the importance of integrating vaccine development within a broader One Health framework. By addressing both scientific and systemic barriers, next-generation vaccines have the potential to become a cornerstone in the global response to antimicrobial resistance.

Methodology

This review adopts a structured narrative approach to synthesize current evidence on next-generation vaccinology strategies targeting Antimicrobial-Resistant (AMR) pathogens. The methodology was designed to ensure comprehensive coverage of recent advances, while maintaining a clear focus on translational relevance within a One Health framework.

Literature search strategy

A systematic search of peer-reviewed literature published between January 2021 and March 2026 was conducted using major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar. Search terms were developed to capture key thematic areas and included combinations of the following keywords: "antimicrobial resistance," "vaccines," "next-generation vaccines," "mRNA vaccines," "reverse vaccinology," "nanoparticle vaccines," "One Health," and "emerging pathogens." Boolean operators (AND, OR) were used to refine search outputs and improve specificity.

In addition to database searches, relevant reports and policy documents from international organizations such as the World Health Organization and the Food and Agriculture Organization were included to provide context on global AMR strategies and vaccine implementation efforts [16, 17]. Reference lists of selected articles were also screened to identify additional relevant studies.

Inclusion and exclusion criteria

Studies were included if they met the following criteria:

(i) Published in English between 2021 and 2026;

(ii) Focused on vaccine development, immunological mechanisms, or implementation strategies relevant to AMR;

(iii) Reported on emerging vaccine platforms or innovative antigen discovery approaches;

(iv) Addressed human, animal, or environmental dimensions of AMR within a One Health context.

Exclusion criteria included:

(i) Studies published before 2021 unless they provided essential foundational insights;

(ii) Articles lacking sufficient methodological detail;

(iii) Opinion pieces without supporting empirical or experimental evidence;

(iv) Studies unrelated to vaccinology or AMR.

Data extraction and synthesis

Relevant data were extracted systematically from selected studies, including information on vaccine platforms, target pathogens, antigen design strategies, immunogenicity outcomes, and translational challenges. Additional variables such as study design, population characteristics, and geographic context were also considered where applicable.

A thematic synthesis approach was employed to organize findings into key domains: (i) emerging vaccine technologies, (ii) immunological innovations, (iii) challenges in vaccine development, and (iv) One Health integration. This approach enabled the identification of recurring patterns, knowledge gaps, and areas of consensus across studies [18].

Quality assessment

The methodological quality of included studies was evaluated using established criteria appropriate to study design. Experimental and preclinical studies were assessed based on reproducibility, sample size, and validation techniques, while clinical studies were evaluated for study design robustness, statistical rigor, and reporting transparency. Review articles were assessed for comprehensiveness, clarity of methodology, and relevance to the research objectives [19].

Priority was given to high-impact journals and studies with clear methodological frameworks. Where conflicting findings were identified, emphasis was placed on studies with stronger experimental validation or broader consensus within the scientific community.

Limitations of the methodology

Despite efforts to ensure comprehensive coverage, this review has inherent limitations. The restriction to English-language publications may have excluded relevant studies from non-English-speaking regions, particularly in areas heavily affected by AMR. In addition, the rapidly evolving nature of vaccine technologies means that some recent developments may not yet be fully captured in published literature.

Furthermore, variability in study designs, pathogen focus, and vaccine platforms presents challenges for direct comparison across studies. The reliance on publicly available data also limits the inclusion of proprietary or industry-based research that may be relevant to vaccine development pipelines [20].

Advances in Next-Generation Vaccinology

The landscape of vaccinology has undergone a profound transformation in recent years, driven by advances in molecular biology, immunology, and computational sciences. These developments have enabled the transition from traditional whole-pathogen vaccines to more precise, scalable, and adaptable platforms. In the context of Antimicrobial Resistance (AMR), next-generation vaccines are increasingly recognized as strategic tools capable of preventing infections caused by resistant pathogens, thereby reducing reliance on antimicrobial therapies.

Nucleic acid-based vaccines

Nucleic acid vaccines, particularly messenger RNA (mRNA) and DNA vaccines, represent one of the most significant breakthroughs in modern vaccinology. mRNA vaccines function by delivering genetic instructions encoding antigenic proteins into host cells, leading to in situ antigen production and subsequent immune activation. Their rapid design, scalability, and capacity for inducing both humoral and cellular immune responses make them highly suitable for addressing emerging AMR threats [6, 21].

The success of mRNA vaccines during the COVID-19 pandemic

has demonstrated their potential for rapid deployment against novel pathogens. This platform is now being explored for bacterial pathogens associated with resistance, including Mycobacterium tuberculosis and Staphylococcus aureus [22]. DNA vaccines, while historically limited by lower immunogenicity, have benefited from advances in delivery systems such as electroporation and nanoparticle carriers, improving their clinical applicability [23].

Viral vector-based vaccines

Viral vectors, including adenoviruses and Modified Vaccinia Ankara (MVA), serve as effective delivery systems for antigenic genes. These platforms elicit strong cellular immune responses, which are particularly important for intracellular pathogens. Viral vector vaccines have shown promise in targeting resistant pathogens by enhancing T-cell mediated immunity, a critical component in controlling persistent infections [24].

Recent innovations have focused on improving vector safety and minimizing pre-existing immunity that may reduce vaccine efficacy. Heterologous prime-boost strategies, combining different vectors or platforms, are also being explored to enhance immunogenicity and durability of protection [25].

Protein subunit and conjugate vaccines

Protein subunit vaccines remain an important component of next-generation vaccinology, particularly when combined with advanced adjuvants. These vaccines utilize purified antigenic proteins or peptides, reducing the risk of adverse reactions associated with whole-pathogen formulations. Conjugate vaccines, which link polysaccharide antigens to protein carriers, have been especially effective against encapsulated bacteria and have contributed to reductions in resistant infections [5].

Recent advances include the identification of conserved protein targets through reverse vaccinology, enabling the design of broadly protective vaccines against genetically diverse pathogens [7]. Improved adjuvant systems, such as Toll-Like Receptor (TLR) agonists, are further enhancing immune responses and vaccine efficacy [26].

Nanoparticle-based vaccine platforms

Nanoparticle-based vaccines have emerged as versatile tools for antigen delivery and immune modulation. These platforms can encapsulate antigens and adjuvants, protecting them from degradation while facilitating targeted delivery to antigen-presenting cells. Lipid nanoparticles, in particular, have played a central role in the success of mRNA vaccines [27].

Beyond delivery, nanoparticles can be engineered to mimic pathogen structures, enhancing immune recognition and response. This approach has shown promise in developing vaccines against multidrug-resistant organisms, where traditional strategies have been less effective [28].

Reverse vaccinology and immunoinformatics

Reverse vaccinology has revolutionized antigen discovery by leveraging genomic data to identify potential vaccine targets without the need for pathogen cultivation. This approach enables the identification of conserved antigens across multiple strains, addressing the challenge of antigenic variability in AMR pathogens [7].

Advances in immunoinformatics and machine learning have further refined this process, allowing for the prediction of B-cell and T-cell epitopes with high accuracy. These tools facilitate the design of multi-epitope vaccines capable of eliciting broad and robust immune responses [29]. Structural vaccinology complements these approaches by providing detailed insights into antigen-antibody interactions, guiding the optimization of antigen design [30].

Systems vaccinology and personalized approaches

Systems vaccinology integrates high-throughput omics technologies with computational modeling to provide a comprehensive understanding of immune responses to vaccination. By analyzing transcriptomic, proteomic, and metabolomics data, researchers can identify biomarkers of vaccine efficacy and predict individual responses [31].

This approach holds promise for the development of personalized vaccines, particularly for populations with variable immune profiles, such as the elderly or immunocompromised individuals. In the context of AMR, systems vaccinology may help identify optimal strategies for inducing protective immunity against complex and highly adaptable pathogens [32].

Immunological Strategies in Vaccine Design against AMR Pathogens

Effective vaccine development against Antimicrobial-Resistant (AMR) pathogens depends not only on technological platforms but also on a clear understanding of host immune mechanisms. Unlike many viral infections where neutralizing antibodies are sufficient for protection, several AMR-associated pathogens require a coordinated interplay between humoral and cellular immunity. The complexity of these immune interactions has driven the adoption of targeted immunological strategies aimed at achieving durable and broad-spectrum protection.

Humoral immunity and antibody-mediated protection

Antibody-mediated immunity remains a central pillar in vaccine-induced protection. Neutralizing antibodies can prevent pathogen adhesion, invasion, and toxin activity, thereby reducing disease severity and transmission. In bacterial infections, opsonizing antibodies enhance phagocytosis and clearance by immune cells, an important mechanism for controlling extracellular pathogens such as Streptococcus pneumoniae and *Klebsiella pneumoniae* [33].

Recent advances in monoclonal antibody research have provided valuable insights into protective epitopes and mechanisms of immune evasion. These findings are increasingly being translated into vaccine design, with emphasis on inducing broadly neutralizing antibodies that target conserved antigenic regions across resistant strains [34]. However, antigenic variability and capsule diversity in certain bacteria remain significant obstacles to achieving consistent antibody-mediated protection [35].

Cellular immunity and t-cell responses

Cell-mediated immunity, particularly T-cell responses, plays a crucial role in combating intracellular pathogens and chronic infections. $CD4^+$ T-helper cells coordinate immune responses by activating macrophages and supporting antibody production, while $CD8^+$ cytotoxic T lymphocytes directly eliminate infected cells [36].

For pathogens such as Mycobacterium tuberculosis, robust T-cell responses are essential for containment and clearance. Vaccine strategies targeting AMR pathogens increasingly aim to elicit strong

Th1-type immune responses characterized by interferon-gamma production and macrophage activation [37]. The induction of tissue-resident memory T cells has also gained attention, as these cells provide rapid localized protection at sites of infection [38].

Mucosal immunity

Many AMR pathogens enter the host through mucosal surfaces, including the respiratory, gastrointestinal, and urogenital tracts. As such, mucosal immunity represents a critical but often underutilized component of vaccine design. Secretory Immunoglobulin A (IgA) antibodies play a key role in neutralizing pathogens at mucosal surfaces, preventing colonization and subsequent infection [39].

Advances in mucosal vaccine delivery systems, including intranasal and oral formulations, have shown promise in eliciting localized immune responses. These approaches may be particularly valuable in reducing asymptomatic carriage and transmission of resistant organisms, thereby complementing systemic immunity [40].

Innate immunity and trained immunity

The innate immune system provides the first line of defense against infections and also shapes adaptive immune responses. Recent evidence suggests that certain vaccines can induce "trained immunity," a phenomenon in which innate immune cells exhibit enhanced responsiveness upon subsequent exposure to pathogens [41].

This concept has important implications for AMR, as trained immunity may provide broad, non-specific protection against multiple pathogens, including resistant strains. Adjuvants that stimulate pattern recognition receptors, such as toll-like receptors, are being explored to enhance both innate and adaptive immune responses in next-generation vaccines [42].

Correlates of protection and immune profiling

A major challenge in vaccine development against AMR pathogens is the lack of well-defined correlates of protection. Unlike established vaccines where antibody titers serve as reliable indicators of immunity, protection against many resistant pathogens involves complex and multifactorial immune responses [12].

Advances in systems immunology and high-throughput immune profiling are helping to identify biomarkers associated with vaccine efficacy. These include specific cytokine signatures, T-cell phenotypes, and gene expression profiles that correlate with protective immunity [31]. Such insights are essential for guiding vaccine design, optimizing dosing regimens, and evaluating clinical trial outcomes.

Immune evasion and antigenic diversity

AMR pathogens often possess sophisticated mechanisms for evading host immune responses. These include antigenic variation, biofilm formation, and the secretion of immune-modulatory factors. For example, Pseudomonas aeruginosa and Acinetobacter baumannii can form biofilms that protect them from both immune attack and antimicrobial agents [43].

To address these challenges, vaccine strategies are increasingly focusing on conserved antigens and multi-component formulations that target multiple virulence factors simultaneously. This approach reduces the likelihood of immune escape and enhances the breadth of protection across diverse strains [44].

Challenges in the Development of Vaccines Against AMR Pathogens

Despite substantial progress in next-generation vaccinology, the development and deployment of vaccines targeting Antimicrobial-Resistant (AMR) pathogens remain constrained by a range of scientific, economic, and operational challenges. These barriers are often interconnected and require coordinated efforts across disciplines to overcome.

Antigenic variability and pathogen diversity

One of the most persistent scientific challenges in vaccine development is the high degree of antigenic variability exhibited by many AMR pathogens. Bacteria such as *Klebsiella pneumoniae* and Pseudomonas aeruginosa possess diverse surface structures and virulence factors that vary across strains, limiting the effectiveness of single-antigen vaccines [45]. This diversity complicates antigen selection and reduces the likelihood of achieving broad protective coverage.

In addition, horizontal gene transfer contributes to rapid genetic evolution, allowing pathogens to acquire resistance determinants and alter antigenic profiles. This dynamic adaptability necessitates the development of multi-component or conserved antigen-based vaccines capable of targeting a wide spectrum of strains [46].

Limited correlates of protection

The absence of well-defined correlates of protection remains a major obstacle in the evaluation of vaccine efficacy against AMR pathogens. While antibody titers serve as reliable markers for several viral vaccines, protection against many bacterial infections involves complex interactions between humoral, cellular, and innate immune responses [12].

This lack of clear immunological benchmarks complicates clinical trial design and regulatory approval processes. It also increases the cost and duration of vaccine development, as large-scale efficacy trials are often required to demonstrate protective outcomes [47].

Biological complexity of target pathogens

Many AMR pathogens exhibit sophisticated mechanisms of immune evasion that hinder vaccine effectiveness. These include biofilm formation, intracellular survival, and secretion of virulence factors that modulate host immune responses. For example, Acinetobacter baumannii can persist in hostile environments and evade immune detection through alterations in its outer membrane structure [48].

Furthermore, polymicrobial infections and interactions within microbial communities can influence disease progression and immune responses, adding another layer of complexity to vaccine design [49].

Economic and market barriers

The economic landscape for vaccines targeting AMR pathogens is less favorable compared to other therapeutic areas. Unlike vaccines for widespread viral diseases, those targeting specific resistant bacteria often address smaller or less predictable markets. This reduces the potential return on investment and discourages private sector involvement [11].

In addition, the high cost of research and development, coupled with uncertain demand, creates significant financial risk. Public-

private partnerships and incentive mechanisms, such as advanced market commitments and push-pull funding models, have been proposed to address these challenges [50].

Regulatory and clinical trial challenges

Regulatory pathways for next-generation vaccines, particularly those based on novel platforms such as mRNA and nanoparticle systems, are still evolving. Ensuring safety and efficacy while maintaining accelerated approval timelines presents a delicate balance for regulatory agencies [12].

Clinical trials for AMR vaccines also face unique challenges, including difficulties in identifying appropriate target populations and endpoints. The relatively low incidence of certain infections in specific regions may necessitate large, multicenter trials, increasing logistical complexity and cost [51].

Manufacturing and distribution constraints

Scaling up vaccine production remains a critical challenge, particularly for advanced platforms that require specialized infrastructure. Manufacturing processes must ensure consistency, stability, and quality across large batches, which can be technically demanding for complex formulations such as lipid nanoparticle-based vaccines [27].

Distribution challenges are especially pronounced in low- and middle-income countries, where cold chain requirements, limited healthcare infrastructure, and logistical barriers can hinder vaccine accessibility. These disparities contribute to unequal global protection against AMR threats [52].

Vaccine hesitancy and public perception

Public acceptance of vaccines plays a crucial role in their success. Vaccine hesitancy, driven by misinformation, cultural beliefs, and concerns about safety, can significantly reduce uptake and limit population-level benefits [53]. In the context of AMR, where the benefits of vaccination may be less immediately visible compared to acute outbreaks, promoting awareness and trust becomes even more important.

Effective communication strategies, community engagement, and transparent reporting of vaccine safety and efficacy are essential for addressing these concerns and improving acceptance [54].

One Health Perspectives in Vaccinology Against AMR

The growing complexity of Antimicrobial Resistance (AMR) has reinforced the need for integrated strategies that extend beyond human health. The One Health concept recognizes the interconnected nature of human, animal, and environmental systems, emphasizing that the emergence and spread of resistant pathogens are driven by interactions across these domains. Vaccinology, when applied within this framework, offers a preventive approach capable of reducing antimicrobial use and limiting resistance transmission at multiple levels.

Vaccination in human health

In human populations, vaccines serve as a primary preventive measure against infectious diseases, thereby reducing the need for antimicrobial therapy. This indirect effect is particularly important in limiting the selective pressure that drives resistance development. Vaccines targeting bacterial pathogens such as Streptococcus pneumoniae and Salmonella enterica have demonstrated reductions in both disease burden and antibiotic use [4].

Expanding vaccine coverage, especially in regions with high infectious disease prevalence, can significantly reduce the incidence of resistant infections. In low- and middle-income countries, improved access to vaccines has the potential to address both AMR and broader public health challenges, including childhood mortality and healthcare-associated infections [55].

Vaccination in animal health and agriculture

The use of antimicrobials in livestock production is a major contributor to the development and spread of resistant pathogens. Vaccination in animals offers a viable alternative by preventing infections and reducing the need for routine antibiotic use. For example, vaccines against bacterial infections in poultry and aquaculture have been shown to lower antimicrobial consumption and improve productivity [56].

In addition, vaccination of livestock can reduce the transmission of zoonotic pathogens to humans. Pathogens such as Campylobacter and Salmonella can be transmitted through the food chain, and controlling these infections at the animal level is critical for reducing human exposure [57]. The development of effective veterinary vaccines is therefore an essential component of AMR mitigation strategies.

Environmental dimensions of vaccinology

The environment serves as a reservoir and transmission pathway for antimicrobial-resistant organisms and resistance genes. Contamination of water, soil, and food systems with resistant bacteria is often linked to improper waste management, agricultural runoff, and pharmaceutical discharge [14].

While vaccines do not directly target environmental reservoirs, their role in reducing infection incidence and antimicrobial use has downstream effects on environmental contamination. By decreasing the volume of antimicrobials entering ecosystems, vaccination indirectly limits the selection and spread of resistance in environmental microbial communities [58].

Integrated surveillance and data sharing

Effective implementation of One Health vaccinology requires robust surveillance systems that integrate data from human, animal, and environmental sources. Such systems enable the identification of emerging resistance patterns and inform vaccine development priorities. Advances in genomic surveillance and data analytics have improved the ability to track pathogen evolution and transmission across sectors [59].

Collaborative platforms that facilitate data sharing among researchers, policymakers, and healthcare providers are essential for coordinated action. These efforts support evidence-based decision-making and enhance the global response to AMR.

Policy frameworks and global initiatives

International policy frameworks increasingly emphasize the role of vaccines within broader AMR strategies. Organizations such as the World Health Organization, the Food and Agriculture Organization, and the World Organisation for Animal Health advocate for integrated approaches that include vaccination, antimicrobial stewardship, and infection prevention measures [15, 17].

The success of these initiatives depends on sustained political commitment, adequate funding, and cross-sector collaboration.

National action plans that align with global strategies are essential for translating policy into practice, particularly in regions with high AMR burden.

Equity and access considerations

A critical challenge in implementing One Health vaccinology is ensuring equitable access to vaccines across different regions and populations. Disparities in healthcare infrastructure, financing, and supply chains often limit vaccine availability in low-resource settings. These gaps not only affect human health but also extend to veterinary services and environmental management [52].

Addressing these inequities requires targeted investments, technology transfer, and capacity building. Strengthening local manufacturing capabilities and improving distribution networks can enhance vaccine accessibility and sustainability. Equitable access is not only a matter of social justice but also a practical necessity for effective global AMR control.

Future Perspectives and Emerging Directions

The continued evolution of Antimicrobial Resistance (AMR) demands forward-looking strategies that extend beyond current vaccine technologies and implementation models. While recent advances in vaccinology have laid a strong foundation, future progress will depend on the integration of emerging scientific innovations, adaptive development frameworks, and coordinated global action. This section outlines key directions likely to shape the next phase of vaccine development against AMR pathogens.

Artificial intelligence and machine learning in vaccine design

Artificial Intelligence (AI) and machine learning are increasingly being applied to accelerate vaccine discovery and optimization. These tools enable the rapid analysis of large genomic and proteomic datasets, facilitating the identification of novel antigenic targets and immune epitopes. Predictive modeling can also improve the selection of vaccine candidates with higher probabilities of success in preclinical and clinical stages [60].

AI-driven approaches are particularly valuable in addressing antigenic variability among AMR pathogens, as they allow for the identification of conserved regions that may not be readily apparent through conventional methods. In addition, machine learning algorithms can assist in predicting host immune responses, thereby refining vaccine design and reducing development timelines [61].

Pan-pathogen and universal vaccine strategies

The concept of universal or pan-pathogen vaccines is gaining attention as a means of overcoming the limitations of strain-specific approaches. These vaccines aim to provide broad protection against multiple strains or even different species of pathogens by targeting conserved antigens or shared virulence mechanisms [62].

In the context of AMR, such strategies could significantly reduce the burden of resistant infections by offering cross-protection against diverse bacterial populations. Advances in structural biology and epitope mapping are supporting the development of these broad-spectrum vaccines, although achieving consistent efficacy across heterogeneous pathogens remains a challenge [30].

Combination approaches and adjunct therapies

Future vaccine strategies are likely to incorporate combination approaches that integrate vaccines with other therapeutic modalities. These may include monoclonal antibodies, immunomodulators, and microbiome-based interventions. Such combinations can enhance immune responses, improve pathogen clearance, and reduce the likelihood of resistance development [34].

In addition, vaccines may be used alongside antimicrobial stewardship programs to optimize treatment outcomes. By reducing infection incidence, vaccines can decrease the need for antibiotics, thereby preserving their effectiveness for cases where they are truly needed [4].

Advances in adjuvant and delivery systems

The development of next-generation adjuvants and delivery systems will continue to play a central role in improving vaccine efficacy. Novel adjuvants designed to target specific immune pathways can enhance both the magnitude and durability of immune responses. For example, adjuvants that activate pattern recognition receptors can stimulate robust innate and adaptive immunity [42].

Emerging delivery technologies, including microneedle patches and thermostable formulations, offer practical advantages in terms of ease of administration and reduced dependence on cold chain infrastructure. These innovations are particularly relevant for improving vaccine accessibility in resource-limited settings [63].

Personalized and precision vaccinology

Personalized vaccinology represents a shift toward tailoring vaccine strategies based on individual or population-specific factors, including genetic background, age, and immune status. Advances in systems biology and immune profiling are enabling the identification of biomarkers that predict vaccine responsiveness [31].

This approach is especially important for vulnerable populations, such as the elderly and immunocompromised individuals, who may exhibit reduced responses to conventional vaccines. Precision strategies can help optimize dosing regimens and antigen selection, thereby improving overall vaccine effectiveness [32].

Strengthening global collaboration and policy integration

Addressing AMR through vaccinology requires sustained global collaboration across scientific, regulatory, and policy domains. International partnerships are essential for sharing data, coordinating research efforts, and ensuring equitable access to vaccines. Initiatives that align vaccine development with global AMR action plans can enhance the efficiency and impact of interventions [15].

In addition, strengthening regulatory harmonization can facilitate the timely approval and distribution of new vaccines. Adaptive regulatory frameworks that accommodate innovative technologies while maintaining rigorous safety standards will be critical for accelerating progress in this field [12].

Expanding the one health approach

Future efforts must deepen the integration of One Health principles into vaccine research and implementation. This includes expanding vaccination programs in animal health, improving environmental management practices, and enhancing surveillance systems that capture data across sectors [13].

The incorporation of environmental microbiology, climate science, and socio-economic factors into vaccinology research will provide a more comprehensive understanding of AMR dynamics. Such interdisciplinary approaches are essential for developing

sustainable and effective solutions.

Conclusion

Antimicrobial resistance continues to challenge the foundations of modern medicine, demanding innovative and sustainable solutions. Vaccination offers a preventive approach that addresses the root of the problem by reducing infection rates, limiting antimicrobial use, and slowing the emergence of resistant strains. The advent of next-generation vaccine technologies, including nucleic acid platforms, nanoparticle systems, and computationally guided antigen design, has expanded the possibilities for targeting complex and adaptable pathogens.

Despite these advances, significant challenges remain. Scientific uncertainties, such as antigenic variability and the lack of clear correlates of protection, continue to complicate vaccine development. Economic constraints, regulatory complexities, and disparities in global access further limit the impact of these innovations. Addressing these barriers requires coordinated efforts that integrate scientific research with policy, funding, and infrastructure development.

The One Health framework provides a comprehensive approach to tackling AMR by recognizing the interconnected roles of human, animal, and environmental health. Vaccination strategies that extend across these domains can reduce antimicrobial use and interrupt transmission pathways, contributing to a more sustainable response to resistance.

Looking ahead, the integration of emerging technologies such as artificial intelligence, systems biology, and precision medicine will further refine vaccine design and implementation. At the same time, strengthening global collaboration and ensuring equitable access will be essential for translating scientific progress into public health impact.

In sum, next-generation vaccinology holds considerable promise as a cornerstone in the fight against antimicrobial resistance. Its success will depend on sustained investment, interdisciplinary collaboration, and a commitment to addressing both scientific and societal challenges in a unified manner.

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