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Immune Responses to Viral Capsids and Bacterial Pathogens: Unraveling Molecular Mechanisms of Vaccine-Induced Immunity

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ABSTRACT

Background: Understanding the immune responses to viral capsids and bacterial pathogens is crucial for improving vaccine design and efficacy. This review explores the complex molecular pathways that underlie vaccine-induced immunity, focusing on the interactions between the immune system and different viral and bacterial antigens.

Results: By examining the cellular and humoral immune responses elicited by viral capsids and bacterial pathogens, we highlight key factors that influence vaccine effectiveness, such as antigen presentation, immune memory, and immune evasion mechanisms. Furthermore, we discuss how these molecular interactions can be modulated to enhance vaccine strategies, providing insight into future vaccine development against emerging infectious diseases.

Conclusion: Through a detailed exploration of the molecular dynamics involved, this article aims to deepen our understanding of vaccine-induced immunity and inform the development of more targeted and effective immunotherapies.

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Introduction

Hospital-acquired infections (HAIs), also known as nosocomial infections, are infections that patients acquire during receiving treatment for other conditions in a healthcare setting. These infections can be caused by a wide variety of pathogens, including bacteria, viruses, fungi, and parasites (1). Among these, bacterial and viral pathogens represent the most common causes of HAIs, and their prevalence poses a significant challenge to patient safety, healthcare outcomes, and healthcare systems worldwide. HAIs are a major contributor to increased morbidity, extended hospital stays, higher healthcare costs, and in some cases, mortality. The emergence of multi-drug-resistant (MDR) pathogens has further complicated the situation, making the treatment of these infections increasingly difficult (2).

The importance of the immune system in preventing and controlling infections cannot be overstated. A well-functioning immune response is essential for defending the body against harmful microorganisms, particularly those that cause infections within the hospital setting. The immune system can recognize a wide array of pathogens and mounting an effective response. This recognition is often achieved through the identification of pathogen-associated molecular patterns (PAMPs) that are present on the surface of viral and bacterial particles (3). For viral infections, these PAMPs often come from the virus's outer structure, such as the viral capsid the protein shell that encapsulates and protects the viral genome. Similarly, bacterial pathogens express distinctive molecular patterns, such as lipopolysaccharides (LPS) and peptidoglycans, that are recognized by the immune system to trigger an appropriate defence mechanism (4).

Vaccination has emerged as one of the most powerful tools in preventing infections, including those that occur in hospital settings. Vaccines work by training the immune system to recognize and respond to specific pathogens without causing the disease itself. This is particularly important in the context of HAIs, where vulnerable populations such as the elderly, immunocompromised patients, and those undergoing invasive medical procedures are at greater risk of developing infections (5). Immunization strategies, including vaccines targeting both viral and bacterial pathogens, can dramatically reduce the incidence and severity of HAIs, as well as lower the burden on healthcare resources.

Despite the availability of vaccines for several common pathogens, the growing issue of antibiotic resistance and the complexity of infections in healthcare settings present ongoing challenges. For instance, bacterial infections caused by resistant strains of *Staphylococcus aureus*, *Klebsiella*

pneumoniae, and *Pseudomonas aeruginosa* have become particularly concerning due to the limited treatment options available (6-8). Additionally, viral infections such as Influenza, Hepatitis B, and emerging viruses like SARS-CoV-2 remain significant causes of hospital admissions. In response to these threats, ongoing research efforts aim to better understand the immune system's response to viral capsids and bacterial pathogens, as well as the molecular mechanisms underlying vaccine-induced immunity (9).

This review seeks to investigate the immune responses to various viral capsids and bacterial pathogens, with a focus on elucidating the molecular pathways that drive vaccine-induced immunity. A particular emphasis will be placed on understanding how these immune pathways contribute to the prevention of hospital-acquired infections. By exploring both innate and adaptive immune mechanisms, we aim to uncover insights into how vaccines can be optimized to provide long-term protection against infections in hospital environments. Furthermore, this review will explore the challenges posed by multi-drug-resistant bacteria and the potential of vaccine strategies to combat these pathogens, offering new avenues for improving patient outcomes and reducing the impact of HAIs.

Immune Recognition of Viral Capsids

Viral capsids are complex protein structures that serve multiple vital functions in the viral life cycle. The capsid, composed of protein subunits called capsomers, not only protects the viral genome but also plays a crucial role in the virus's ability to infect host cells (10). It enables the virus to bind to host cell surface receptors, facilitating entry into the host cell, where the viral genome can be replicated and expressed. Beyond this, the capsid itself is often recognized by the host's immune system as a foreign structure, triggering the innate immune response, which is the first line of defence against viral infections (11).

The immune system is adept at recognizing foreign entities like viral capsids through a specialized set of receptors known as pattern recognition receptors (PRRs) (12). These PRRs are expressed on the surface of various immune cells, including dendritic cells, macrophages, B cells, and epithelial cells. PRRs are designed to detect PAMPs conserved, repetitive structures found in pathogens, but not in host cells (13). In the case of viral capsids, PAMPs include unique protein motifs and sugars that are distinct to viruses. These viral components are often highly conserved among virus families, making them ideal targets for immune detection (14).

Among the most prominent PRRs involved in recognizing viral capsids are Toll-like receptors (TLRs), RIG-I-like receptors (RLRs), and C-type lectin receptors (CLRs) (15). TLRs, which are primarily located on the surface of immune cells, are activated upon recognition of viral proteins or glycoproteins on the capsid. TLR3, for example, is known to recognize double-stranded RNA (a common feature of many viruses), while TLR7 and TLR8 recognize single-stranded RNA, a common feature of RNA viruses (16). Similarly, RLRs like RIG-I and MDA5 detect viral RNA, which may be released during the uncoating process or as part of the host's immune response to the infection. CLRs, on the other hand, are carbohydrate-binding receptors that can detect specific sugar molecules present on the surface of viral capsids, particularly in enveloped viruses (17).

Upon the recognition of viral PAMPs, these PRRs trigger complex intracellular signaling pathways. One key pathway activated is the NF-κB pathway, which leads to the production of various pro-inflammatory cytokines, including interleukins and tumor necrosis factor-alpha (TNF-α) (13, 18). Additionally, type I interferons (IFN-α/β) are produced, which play a pivotal role in establishing an antiviral state within infected and surrounding cells. Interferons promote the expression of antiviral proteins, such as PKR (protein kinase R), OAS (2',5'-oligoadenylate synthetase), and Mx proteins, which work collectively to inhibit viral replication. This antiviral state limits the ability of the virus to replicate and spread within the host organism,

thereby controlling the early stages of the infection (19).

Another crucial aspect of the innate immune response to viral capsids involves the activation of natural killer (NK) cells. NK cells are cytotoxic lymphocytes that are particularly effective in eliminating infected cells. In response to viral infection, NK cells are activated through the detection of altered expression of host cell markers, often induced by viral infection (20). These NK cells can release cytotoxic molecules, such as perforin and granzyme, which induce apoptosis (programmed cell death) in infected cells, thus preventing further viral replication and spread (21).

While the innate immune response to viral capsids is essential for limiting viral replication in the early stages of infection, it also plays a key role in activating the adaptive immune system, which provides long-term immunity (22). Dendritic cells, upon encountering and recognizing viral antigens on the capsid, undergo a process known as maturation, during which they increase their expression of co-stimulatory molecules and migrate to lymph nodes (23). There, they present viral antigens to T cells in the context of major histocompatibility complex (MHC) molecules. This antigen presentation activates helper T cells (CD4+), which coordinate the immune response, and cytotoxic T cells (CD8+), which directly kill infected cells (24). Additionally, B cells are activated by antigen presentation and helper T cell signals, leading to the production of antibodies that specifically target viral capsid proteins. These antibodies can neutralize the virus by blocking its ability to enter host cells and mark it for destruction by phagocytic cells (25).

Thus, the immune recognition of viral capsids is an intricate process that involves both innate and adaptive immune responses. The innate immune system provides a rapid response that limits viral spread, while also setting the stage for a more specific and long-lasting adaptive immune response (26). The interplay between these two arms of immunity ensures that the body is equipped to respond effectively to viral infections, including those caused by viruses with complex capsid structures.

Immune Responses to Bacterial Pathogens

Bacterial pathogens, including Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumoniae, are major contributors to HAIs and represent a substantial threat to patient health (27). These bacteria can cause a wide range of infections, including pneumonia, urinary tract infections, surgical site infections, and bloodstream infections, which are particularly concerning in hospitalized individuals who are often immunocompromised or undergoing invasive medical procedures. The immune system's response to bacterial infections is complex and involves both innate and adaptive immune mechanisms that work together to identify and neutralize bacterial threats (28).

The first line of defense against bacterial pathogens is the innate immune system, which rapidly detects and responds to bacterial invaders. The innate immune system is highly effective in recognizing common molecular structures found on bacterial surfaces. These molecular patterns PAMPs, include structures such as lipopolysaccharides (LPS) on the outer membrane of Gram-negative bacteria like *E. coli*, *K. pneumoniae* and *P. aeruginosa*, and peptidoglycans in the cell walls of Gram-positive bacteria like *S. aureus* (29). Other PAMPs include lipoteichoic acids (LTA) and flagellin, components of bacterial cell walls and motility structures, respectively (30, 31).

To detect these PAMPs, the innate immune system relies on pattern recognition receptors (PRRs) expressed on immune cells, such as macrophages, dendritic cells, and neutrophils. Among the most important PRRs in bacterial pathogen recognition are Toll-like receptors (TLRs) and NOD-like receptors (NLRs) (12). TLRs are transmembrane receptors found on the surface of immune cells and intracellular compartments, while NLRs are cytosolic receptors. These receptors detect PAMPs and

initiate signaling cascades that activate various immune responses.

For example, TLR4 is a key receptor involved in the recognition of LPS, which is abundant in the outer membranes of Gram-negative bacteria (32). Upon binding to LPS, TLR4 activates downstream signaling pathways, including the NF-κB pathway, which leads to the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6 (33). These cytokines promote inflammation and recruit additional immune cells to the site of infection.

NLRs, such as NOD1 and NOD2, recognize components of bacterial peptidoglycans and trigger the activation of the inflammasome, a multi-protein complex that plays a critical role in the innate immune response. The inflammasome activates caspase-1, which cleaves and releases pro-inflammatory cytokines such as IL-1β and IL-18. These cytokines further amplify the immune response by increasing vascular permeability, which allows immune cells to move into infected tissues more effectively, and by promoting fever to inhibit bacterial growth (34).

As a result of these immune responses, macrophages and neutrophils are activated and recruited to the site of infection. Macrophages are key players in phagocytosis, the process by which immune cells engulf and digest bacterial pathogens. Neutrophils, the most abundant white blood cells, are also essential in responding to bacterial infections. They are particularly effective at phagocytosis and releasing antimicrobial enzymes and reactive oxygen species (ROS) that help kill bacteria (35, 36).

In addition to phagocytosis, the complement system, a group of plasma proteins, is activated during bacterial infections. Complement activation can occur through various pathways, including the classical pathway (antibody-mediated) and the alternative and lectin pathways (direct pathogen recognition). Once activated, the complement system produces molecules such as C3b, which can bind to bacterial surfaces, tagging them for recognition by phagocytes (a process called opsonization). Complement activation can also lead to the formation of the membrane attack complex (MAC), which directly disrupts bacterial cell membranes, resulting in bacterial lysis and death (37).

While the innate immune system provides an immediate response to bacterial pathogens, the adaptive immune system plays a crucial role in providing long-term immunity and more targeted defense against bacterial infections. The adaptive immune response is slower to activate but is highly specific and capable of remembering the pathogen for future encounters (38).

The first step in the activation of the adaptive immune response is the antigen presentation of bacterial components by antigen-presenting cells (APCs), such as dendritic cells and macrophages. These cells ingest bacterial pathogens, process them, and present bacterial peptides on their surface bound to major histocompatibility complex (MHC) molecules. The MHC class II molecules present bacterial antigens to helper T cells (CD4+), while MHC class I molecules present antigens to cytotoxic T cells (CD8+) (38-40).

Helper T cells (CD4+) are pivotal in orchestrating the adaptive immune response. Once activated by antigen-presenting cells, CD4+ T cells release cytokines that influence the activity of other immune cells. For example, IL-2 promotes the proliferation of T cells, IL-4 and IL-5 help activate B cells, and IFN-γ promotes macrophage activation. Through their action, CD4+ T cells not only enhance the immune response but also help direct the type of response needed to combat a specific pathogen (41-43).

One of the major roles of CD4+ T cells is to assist B cells in producing antibodies. B cells are activated by the cytokines released by CD4+ T cells and, in turn, begin producing antibodies (also known as immunoglobulins). These antibodies are specific to the bacterial antigens presented by the APCs. The antibodies can neutralize bacteria directly by binding to key surface structures, preventing bacterial adhesion to host cells. Additionally, antibodies can tag bacteria for destruction by phagocytic cells (opsonization), activate the complement system to kill bacteria,

and block bacterial toxins from exerting their harmful effects (44).

On the other hand, cytotoxic T cells are responsible for recognizing and killing host cells that are infected with bacteria. CD8+ T cells use their T cell receptor (TCR) to recognize bacterial peptides presented on MHC class I molecules on infected cells. Once activated, cytotoxic T cells release cytotoxic molecules such as perforin, which forms pores in the membrane of infected cells, and granzyme, which enters the infected cells and induces apoptosis (programmed cell death). This targeted killing of infected cells reduces the bacterial load and prevents the spread of infection (45).

In addition to antibody production and T cell-mediated cytotoxicity, the adaptive immune response to bacterial infections also includes the generation of memory B cells and memory T cells. These long-lived cells "remember" the bacterial pathogen and provide a rapid and robust immune response upon re-exposure. This immunological memory is the basis for the effectiveness of vaccines, which prime the immune system to recognize and respond more effectively to future infections by the same pathogen (46).

Vaccine types and Molecular Pathways Involved in Vaccine-Induced Immunity

Vaccination plays a crucial role in public health policy and has proven to be cost-effective in safeguarding both human and animal populations. There are various forms in which vaccines can be produced, including inactivated (killed), toxoid, live attenuated, virus-like particles, synthetic peptides, polysaccharides, polysaccharide conjugates (glycoconjugates), viral vectored (vector-based), as well as nucleic acids (DNA and mRNA), and bacteria-based or synthetic antigen presenting cells (47). The vaccine manufacturing process involves several methodologies, and recent advancements in the fields of medical and biomedical engineering, biology, immunology, and vaccinology have led to the development of innovative nucleic acid vaccines, which represent a new category alongside traditional and subunit vaccines.

Vaccine types

The types of vaccines vary significantly in their formulation and mechanisms of action (table 1), allowing for tailored approaches to immunization based on the pathogenic characteristics and the nature of the immune response desired.

Inactivated vaccines are developed using pathogens that have been killed or inactivated through heat, chemicals, or radiation. This process ensures that the virus or bacteria can no longer cause disease while still retaining the structures that trigger an immune response (46). Upon administration, these vaccines stimulate the immune system to produce specific antibodies and memory cells directed against the inactivated pathogen. However, because the immunity generated is typically weaker compared to live vaccines, inactivated vaccines often require multiple doses or booster shots for sustained protection. Some common examples include the inactivated polio vaccine and the influenza vaccine (48-50).

Live-attenuated vaccines contain a weakened form of the pathogen that retains its ability to replicate but is largely incapacitated regarding virulence. This attenuation allows the vaccine to simulate a natural infection, prompting a robust immune response that involves the production of antibodies, activation of T cells, and generation of memory cells. These responses often last for years, if not a lifetime, reducing the need for booster doses. Live vaccines, however, must be handled carefully as they are sensitive to environmental conditions, and there are specific populations such as immunocompromised individuals for whom these vaccines may pose risks (51). Classic examples include the measles, mumps, and rubella (MMR) vaccine, as well as the yellow fever vaccine (52, 53).

mRNA vaccines employ a novel approach by utilizing messenger RNA encapsulated in lipid nanoparticles. This mRNA carries the genetic

instructions for synthesizing specific viral proteins from the pathogen, which the body's cells then utilize to produce these proteins (54). The immune system recognizes these foreign proteins as threats, leading to the activation of both B cells and T cells, culminating in the production of antibodies and immunological memory. The COVID-19 vaccines, such as those developed by Pfizer-BioNTech and Moderna, are notable examples of this technology, representing a breakthrough in rapid vaccine development due to their relatively swift design and manufacturing processes (55, 56). Subunit, recombinant, polysaccharide, and conjugate vaccines focus on specific pieces of the pathogen, for instance, proteins or sugars (57). Because these vaccines do not contain live components, they are safe for individuals with weakened immune systems. They work by presenting these isolated components to the immune system, provoking an immune response without the risk of disease. This specificity often results in fewer side effects and allows for the inclusion of multiple antigens in a single vaccine for broader protection. Examples of these types include the Hepatitis B vaccine, which uses a recombinant protein, and the pneumococcal vaccine, which utilizes polysaccharide components to enhance immunity (58, 59). Toxoid vaccines specifically target toxins produced by bacteria rather than the bacteria themselves. Toxins are often the primary cause of symptoms in diseases like tetanus and diphtheria, so these vaccines are created by inactivating the toxins (toxoids), allowing the immune system to generate a response without causing the disease. Like inactivated vaccines, toxoids usually require booster doses to ensure ongoing immunity (60, 61).

Lastly, viral vector vaccines incorporate a harmless virus as a delivery system to introduce genetic material coding for pathogenic proteins into host cells. This process triggers an immune response like that of a live vaccine, as the body recognizes and responds to the newly expressed proteins. The Johnson & Johnson COVID-19 vaccine is a prominent example, using a modified adenovirus that cannot replicate in humans, providing protection without the risks associated with live pathogens (62-64).

The diverse types of vaccines available today, each employing distinct molecular mechanisms, ensure comprehensive coverage against a myriad of infectious diseases.

Innate Immune Activation in Vaccine Responses

When a vaccine is administered, whether it contains a viral capsid or bacterial antigen, it is recognized by the innate immune system through the same PRRs that detect pathogens. This recognition is crucial for initiating a proper immune response (65). Vaccines often contain adjuvants substances that enhance the immune response by stimulating PRRs or other immune system components (66). For example, vaccines containing viral capsids often engage TLRs, which initiate the production of cytokines and activation of dendritic cells. These dendritic cells are responsible for processing and presenting antigens to T cells, facilitating the transition from innate to adaptive immunity. The activation of innate immune pathways also helps shape the nature of the adaptive immune response (67). This early recognition primes the immune system, making it more efficient in responding to future infections. Following the activation of the innate immune system, adaptive immune responses are initiated. Helper T cells (CD4+ T cells) recognize processed antigens presented by MHC class II molecules on the surface of antigen-presenting cells. Upon activation, CD4+ T cells release cytokines that help B cells differentiate into plasma cells, which produce antibodies specific to the vaccine antigen (68, 69). In the case of viral capsids, antibodies can neutralize the virus by blocking its ability to bind to host cell receptors. For bacterial vaccines, antibodies can neutralize toxins, opsonize bacteria for phagocytosis, or activate the complement system to promote bacterial killing (70, 71). In addition to antibodies, cytotoxic T lymphocytes (CTLs) play a vital role in eliminating infected cells. These CD8+ T cells recognize antigens presented on MHC class I molecules and directly

kill infected host cells (72). Furthermore, vaccination results in the formation of memory B cells and T cells, which persist long-term in the body. These memory cells enable the immune system to mount a rapid and robust response if the pathogen is encountered again in the future, ensuring long-term immunity (73).

Role of Vaccines in Preventing Hospital-Acquired Infections

The effectiveness of vaccines in preventing hospital-acquired infections is significantly influenced by various host factors, including age, immunocompetence, and pre-existing health conditions. Understanding these factors is essential for optimizing vaccination strategies and improving patient outcomes in healthcare settings.

As individuals age, physiological changes can lead to a decline in immune function, a phenomenon often termed immunosenescence (74). This affects the ability of older adults to mount effective immune responses to vaccines. For instance, studies have shown that the efficacy of the influenza vaccine is notably lower in elderly individuals compared to younger populations. This diminished response is likely due to a reduced capacity of the immune system to produce sufficient levels of antibodies and memory cells after vaccination. Consequently, there is an urgent need for the development of more potent vaccines, or the incorporation of adjuvants specifically designed to enhance immune responses in older adults (75, 76).

Moreover, individuals who are immunocompromised, including cancer patients undergoing chemotherapy, organ transplant recipients, and those with HIV/AIDS, are at increased risk of complications following vaccination. These individuals often exhibit attenuated immune responses, which can significantly diminish the effectiveness of standard vaccination protocols. For example, organ transplant recipients may have their immune systems suppressed to prevent organ rejection, compromising their ability to respond effectively to vaccines (77). Careful consideration of vaccine types and doses, as well as close monitoring of antibody responses in these populations, is crucial for ensuring adequate protection against infections in hospital environments (78).

In addition to age and immunocompromised status, comorbidities such as diabetes, cardiovascular diseases, and chronic obstructive pulmonary disease (COPD) can further impair immune responses to vaccinations. Research indicates that patients with diabetes, for instance, may have an altered immune system that reduces vaccine-induced protective responses, making them more susceptible to infections and complicating their clinical management (79). Similarly, patients with cardiovascular diseases often show a compromised immune response, which can lead to lower vaccine efficacy (80). By considering these comorbidities, healthcare providers can tailor vaccination strategies to optimize protection for at-risk populations.

Given the influence of host factors on vaccine efficacy, healthcare providers should employ a comprehensive approach when determining vaccination strategies for vulnerable populations in hospital settings. This may include the use of higher doses or adjuvanted formulations of vaccines aimed specifically at enhancing immune responses in older adults and those with comorbid conditions (81). Additionally, regular monitoring and follow-up care post-vaccination are critical to assess the development of immune responses, allowing for timely interventions if responses are suboptimal. Furthermore, patient education plays a pivotal role in addressing vaccine hesitancy and ensuring that high-risk individuals understand the benefits of vaccination in preventing hospital-acquired infections (82). By empowering patients with accurate information, healthcare providers can help facilitate informed decisions regarding vaccinations.

Table 1. Various types of vaccines and their effects on immune system.

Vaccine Type	Mechanism of Action	Immune Molecules Involved	Antibodies	Cytokines	T Cells
Live-attenuated Vaccines	Contains weakened forms of pathogens that stimulate a strong immune response without causing disease, leading to long-lasting immunity.	Antibodies, T cells, Cytokines	IgG, IgA, IgM	IL-2, IL-12, IFN-γ	Helper T cells (Th1, Th2), Cytotoxic T cells (CD8+)
Inactivated (Killed) Vaccines	Comprises killed pathogens, which elicits immune responses that can protect against future infections but often requires boosters for sustained immunity.	Antibodies, T cells, Cytokines	IgG, IgA, IgM	IL-2, IL-6, IFN-γ	Helper T cells (Th2), Cytotoxic T cells (CD8+)
Subunit Vaccines	Contains pieces of the virus or bacteria (like proteins), prompting the immune system to recognize and defend against the actual pathogen without using whole pathogens.	Antibodies, T cells, Cytokines	IgG, IgA	IL-4, IL-5, TNF-α	Helper T cells (Th2)
Toxoid Vaccines	Derived from toxins produced by pathogens; these inactivated toxins induce an immune response without the harmful effects of the actual toxins.	Antibodies against toxins, T cells	IgG	IL-6, IL-10	Helper T cells (Th2)
mRNA Vaccines	Use a small piece of genetic material (mRNA) that instructs cells to produce a harmless protein unique to a virus, triggering an immune response once presented.	Antibodies, T cells, Interferons, Cytokines	IgG, IgA	IL-1β, TNF-α, IL-6	Helper T cells (Th1), Cytotoxic T cells (CD8+)
Viral Vector Vaccines	Utilizes a harmless virus to deliver genetic material from the pathogen, prompting an immune response as the body learns to recognize the target pathogen.	Antibodies, T cells, Cytokines	IgG, IgA	IL-2, IL-12, IFN-γ	Helper T cells (Th1), Cytotoxic T cells (CD8+)
DNA Vaccines	Involves injecting genetic material that encodes specific antigens of the pathogen, stimulating the body's immune response to those antigens.	Antibodies, T cells, Interferons, Cytokines	IgG, IgA	IL-12, IFN-γ	Helper T cells (Th1), Cytotoxic T cells (CD8+)

Vaccines Against Hospital-acquired viral Infections and Bacterial Pathogens

Hospital-acquired viral infections are often caused by viruses like influenza, respiratory syncytial virus (RSV), and Hepatitis B virus (HBV) (83). Vaccination programs targeting these viruses are crucial for preventing outbreaks in hospital settings. For example, the seasonal influenza vaccine has been shown to reduce the incidence of influenza in hospitalized patients, especially those who are elderly or immunocompromised. Similarly, vaccines against HBV prevent nosocomial transmission, particularly in healthcare workers and patients undergoing dialysis (84).

The development of vaccines targeting emerging viral pathogens, such as coronaviruses, also has significant implications for preventing hospital-acquired infections. The global vaccination campaigns against COVID-19 provide an example of how vaccines can reduce hospital admissions and severe disease in both healthcare settings and the general population(85).

Vaccines against bacterial pathogens have been essential in reducing the incidence of HAIs. The pneumococcal vaccine, for instance, has significantly reduced the incidence of *Streptococcus pneumoniae* infections, which can lead to pneumonia, bacteremia, and meningitis. Vaccines against *Neisseria meningitidis* and *Haemophilus influenzae* have similarly reduced the burden of invasive bacterial infections in hospital settings (86-88).

One of the challenges in hospital settings is the emergence of multi-drug-resistant (MDR) bacteria, such as Methicillin-resistant *Staphylococcus aureus* (MRSA) and Vancomycin-resistant *Enterococcus* (VRE) (89-91). Although vaccines against these specific MDR pathogens are not yet widely available, the development of broad-spectrum vaccines that can prevent a range of bacterial infections, including those caused by resistant strains, is a promising strategy for controlling HAIs.

Vaccine Efficacy in the Context of Multi-Drug Resistance

The rise of multi-drug-resistant bacteria has created a pressing need for effective vaccines in hospital settings. The increasing prevalence of antibiotic resistance has posed significant challenges to public health, as conventional treatment options are becoming less effective against common bacterial infections. This phenomenon is alarming because some infections previously considered manageable may now lead to severe morbidity and mortality (92).

Vaccines can play a crucial role in combating the spread of multi-drug-resistant pathogens. They offer a proactive measure to prevent infections rather than relying solely on antibiotics, which have been rendered less effective due to resistance mechanisms developed by various bacteria (93). Vaccine-induced immunity could provide an alternative strategy to prevent infections caused by resistant pathogens, thereby reducing the pressure on antibiotics and, in turn, mitigating the emergence of further resistance. For instance, vaccines that bolster the body's immune response can help diminish the incidence of infections that typically require antibiotic treatment, effectively limiting their use (94).

Moreover, the development of vaccines targeting highly conserved bacterial antigens is paramount. Antigens located in the outer membrane proteins (OMPs) of Gram-negative bacteria present an attractive target because they tend to be less variable compared to other bacterial components (95, 96). By creating vaccines that focus on these OMPs, it is conceivable to elicit immunity that could confer protection against a broader spectrum of multi-drug-resistant strains. Such vaccines could prevent colonization by pathogenic bacteria, decrease the overall infection rates, and lower healthcare-associated complications related to multi-drug resistance (97).

In addition to targeting specific bacterial components, vaccines must also enhance the immune system’s ability to recognize and eliminate pathogens efficiently. This can be

achieved through adjuvants that boost immune responses or by employing innovative vaccination strategies that introduce multiple antigens simultaneously. Such approaches hold the promise of training the immune system to respond robustly to infections without relying heavily on antibiotics, thereby reducing the likelihood of resistant infections spreading within hospital environments. There is also a need to explore novel vaccine platforms, such as mRNA vaccines, which have shown great potential in eliciting strong immune responses which can be engineered to encode specific antigens from multi-drug-resistant bacteria, leading to the production of antibodies that target these pathogens, effectively (98, 99).

Conclusion

Hospital-acquired infections is a significant challenge to healthcare systems, particularly with the rise of antibiotic resistance. Understanding the molecular pathways involved in immune responses to viral capsids and bacterial pathogens is essential for developing vaccines that can prevent them. While vaccination is a critical tool in preventing both viral and bacterial HAIs, is a need for vaccines. Continued research focusing on the vaccine efficacy is crucial in mitigating the impact of hospital-acquired infections and improving patient outcomes.

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None.

Conflict of interest

The authors have declared that no competing interests exist.

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