Article @ Virology

Exploration of the Mechanisms of Human Rabies Vaccine Immunization Failure and Strategies to Enhance Vaccine Efficacy

*Jia Li, Xiaohong Wu**

National Institutes for Food and Drug Control , Beijing 102629 , P. R. China

ABSTRACT

Rabies, as a highly lethal viral disease, vaccination is a key means of prevention and control. Despite the widespread use of modern cell-cultured vaccines globally, cases of vaccine failure have been reported, particularly among immunocompromised populations. This article reviews typical cases of vaccine failure in human rabies vaccination, the potential mechanisms of vaccine failure, and discusses future strategies to enhance vaccine efficacy in conjunction with the latest research progress in vaccine design and immune responses related to current vaccine research hot spots such as COVID-19 and influenza. By analyzing the latest clinical and basic research data, the importance of immune monitoring and the necessity of personalized immunization strategies are emphasized, providing theoretical support and practical guidance for clinical practice and vaccine development.

Article History: Submitted: 30/01/2024; Revised: 29/02/2024; Accepted: 06/03/2024

DOI:10.21092/jav.v13i1.113

Key Words: Rabies Vaccine, Immune Failure, Immunosuppression, Immune Monitoring, Vaccine Design, Immune Evasion Mechanisms.

Abbreviations: PEP, Post-Exposure Prophylaxis; WGS,Whole-genome Sequencing; MHC, Major Histocompatibility Complex; MPLA, Monophosphoryl Lipid A; ELISA, Enzyme-linked Immunosorbent Assay; RFFIT, Rapid Fluorescent Focus Inhibition Test.

* Corresponding author, Prof. XH Wu, Major in Quality Control on Vaccines
E-mail:wuxiaohong@nifdc.org.cn Tel.: +86-10-53851787

Introduction

Rabies is a severe viral infectious disease that poses a significant global health threat, primarily transmitted to humans by infected animals, especially dogs. Despite a decline in rabies incidence in recent years due to vaccination and public health awareness efforts, it remains a major public health issue in many countries, particularly in developing nations [1,2]. According to data from the Chinese Center for Disease Control and Prevention, 26,315 cases of rabies were reported in China between 2004 and 2018. Although the mortality rate has shown a downward trend, there is still a significant risk of infection in specific regions and populations[2]. Notably,middle-aged and elderly populations (particularly those aged 50-60) exhibit a higher risk of infection, indicating the need to consider regional and age-related differences in the formulation of public health strategies[1].

Vaccination against rabies is considered the most effective method for preventing the disease. The history of rabies vaccination dates back to the 19th century, originally developed using attenuated viruses[3]. Modern vaccines are primarily based on cell culture technology, aimed at improving the safety and efficacy of the vaccine. Research shows that cell culture vaccines perform well in inducing immune responses and can effectively prevent the occurrence of rabies. However, cases of vaccine immunological failure do arise, which may be related to various factors such as individual immune function, timing of vaccination, and method of vaccine administration[4,5]. For instance, in certain individuals with impaired immune function, the efficacy of the vaccine may be significantly affected, necessitating special adjustments and optimizations in vaccination strategies for these patients [6].

Immunological failure is typically defined as the inability of an individual to produce a sufficient immune response to provide protection after vaccination, which is also true for rabies vaccination. Although cases of immunological failure are relatively rare, their study holds significant value as it can provide important insights into vaccine immunological mechanisms and improve--ments in vaccination strategies[7,8]. Particularly in individuals with impaired immune function, the immune effectiveness and protection rates of vaccines may significantly decline, thus healthcare professionals need to closely monitor and assess these patients in clinical practice to ensure timely implementation of appropriate preventive measures.

This review aims to summarize the current research progress on immunological failure of rabies vaccines, explore its significance in public health, and provide references for future research directions. Through a comprehensive analysis of existing literature, we hope to offer new perspectives and ideas for improving rabies prevention and control strategies, thereby contributing to the goal of eliminating rabies deaths by 2030 [4].

Clinical Case Analysis of Immune Failure in Human Rabies Vaccination

1. Review of Typical Immune Failure Cases

In 2021, a notable case of rabies vaccine immune failure occurred in Minnesota, USA, involving an 84-year-old male patient. The patient received timely post-exposure prophylaxis (PEP) after being bitten by a bat infected with rabies; however, unfortunately, he died of rabies six months later. This was the first reported case of rabies PEP failure since the introduction of modern cell-cultured vaccines in the United States, highlighting the limitations of vaccination [5].

Researchers conducted an in-depth analysis of the case, first reviewing the patient's medical history, laboratory results, and autopsy findings, and performing whole-genome sequencing (WGS) to compare the patient's viral sequence with that of the bat. The results showed that despite appropriate vaccination, the rabies virus antibodies in the serum and cerebrospinal fluid were non-neutralizing. More importantly, laboratory tests revealed that the patient had unrecognized monoclonal gammopathy, which may have led to immune dysfunction, preventing him from effectively combating the virus after infection [5].

Additionally, the autopsy results indicated that the patient also had metastatic prostate adenocarcinoma, suggesting that his immune system may have been suppressed due to the presence of the tumor, further increasing the risk of immune failure. When assessing 332 individuals who may have been exposed to the patient, only 3 (0.9%) required PEP, demonstrating the uniqueness and complexity of this case. The study emphasizes the importance of recognizing immunosuppressive states in clinical practice, particularly in elderly patients, and recommends measuring rabies neutralizing antibody titers if there is suspicion of immune dysfunction after completing PEP, to timely adjust and optimize subsequent treatment strategies [5].

In conclusion, this case not only provides profound insights into the efficacy of rabies vaccines but also highlights the complexity of considering multiple potential factors when dealing with elderly and immunosuppressed patients. For clinicians, this case calls for more detailed monitoring and assessment after vaccination to ensure that high-risk populations receive optimal preventive outcomes.

2.Epidemiological Characteristics of Immune Failure Cases

Immune failure refers to the inability of an individual to generate a sufficient immune response to fend off infections from corresponding pathogens after vaccination. The increasing number of immune failure cases worldwide, particularly following rabies vaccinations, has garnered attention from the medical community. According to a study, Hunan Province reported 59 cases of rabies in 2020, most of which were due to animal bites, with approximately 72.88% classified as severe injuries. This indicates that immune failure may be closely related to the severity of injuries and subsequent immune management [9].

Globally, the reported frequency and distribution of immune failures vary significantly across different regions. Studies have shown that even in areas with high vaccination rates, cases of breakthrough infections due to immune failure still occur; for example, vaccinated individuals have experienced breakthrough infections during measles outbreaks in certain countries. These phenomena suggest that the effectiveness of vaccines may be insufficient in specific populations, especially among the elderly and those with underlying health conditions.

Analysis of high-risk populations reveals that children and young adults are often the most affected groups for immune failure. Due to physiological and immunological characteristics, these individuals may be more susceptible to infections. For instance, in a study on measles vaccine failures, it was found that young adults had a higher incidence of secondary vaccine failures, which may be related to their underdeveloped immune systems during their growth period. Other high-risk factors include age at vaccination, underlying diseases, nutritional status, and socioeconomic factors, all of which may influence vaccine effectiveness and individual immune responses.

In summary, the epidemiological characteristics of immune failure cases indicate that the phenomenon of immune failure on a global scale is a complex issue involving the interaction of multiple factors. Analyzing the characteristics of high-risk populations can aid public health policymakers in formulating more effective vaccination strategies to reduce the incidence of immune failure and enhance the effectiveness of public health prevention and control. Effective vaccination and subsequent immune monitoring measures are crucial for reducing the risk of immune failure, especially against the backdrop of the COVID-19 pandemic and other vaccine-preventable diseases.

3.Clinical Diagnosis and Differential Diagnosis of Immune Failure

The clinical diagnosis and differential diagnosis of immune failure are essential for understanding and managing immune-related diseases, particularly in cases of immune failure following rabies vaccination, where accurate diagnostic processes and laboratory testing methods are critical.

In terms of clinical manifestations and diagnostic processes, immune failure typically presents as an inability to generate the expected immune response post--vaccination, such as antibody levels below the protective threshold or ineffective control of clinical symptoms. Patients may exhibit local reactions at the vaccination site, systemic symptoms, and neurological symptoms related to rabies. Clinicians must consider the patient's medical history, vaccination status, and clinical manifestations to develop an appropriate diagnostic strategy. For rabies vaccine immune failure, regular monitoring of antibody levels is necessary to assess the effectiveness of the immune response. Furthermore, during the diagnosis, other conditions that could lead to similar symptoms, such as bacterial infections or viral encephalitis, must be ruled out through detailed clinical assessments and historical records [10].

Laboratory testing methods and their limitations are another key factor in diagnosing immune failure. Current laboratory methods used to assess immune status include ELISA, RT-qPCR, etc., which can help determine the presence and levels of antibodies. However, these methods may have limitations in certain situations. For example, ELISA requires an appropriate time window for antibody detection; testing too early or late may yield false-negative results. Additionally, certain laboratory testing methods (such as cerebrospinal fluid analysis) may affect result accuracy due to improper sample collection techniques or handling. Moreover, specific detection methods for rabies virus may exhibit technical differences across different laboratories, impacting the reproducibility and reliability of results. Therefore, close collaboration between clinical and laboratory settings, along with the combined use of multiple testing methods, is an effective strategy to improve the accuracy of immune failure diagnosis.

In summary, the clinical diagnosis and differential diagnosis of immune failure require a comprehensive consideration of clinical manifestations, medical history, and laboratory test results. By establishing a systematic diagnostic process and enhancing the accuracy of laboratory testing, it is possible to effectively identify and manage cases of rabies vaccine immune failure, thereby providing more precise medical services to patients.

Discussion on the Immunological Mechanisms of Immune Failure

1.The Role of Immunosuppression and Immune Dysfunction

In the context of immunosuppression and immune dysfunction, the functionality of the immune system is significantly affected, leading to a decrease in the immunogenic efficacy of vaccines. Immunosuppression may arise from various factors, such as pharmacological treatment, underlying diseases, or genetic factors. Among these, monoclonal immunoglobulin disease, as a specific immune abnormality, cannot be overlooked regarding its impact on vaccine response.

Firstly, monoclonal immunoglobulin disease is a condition caused by the abnormal proliferation of a single clone of B cells. Research indicates that this disease suppresses the function of specific immune cells within the patient's body, resulting in defects in immune response, particularly in the ability to respond to vaccine antigens. Patients may have inadequate antibody responses to vaccines, which significantly diminishes the protective effect of the vaccine. This is particularly evident in the case of rabies vaccination, where the patient's immune system fails to effectively recognize and respond to the pathogen antigens provided by the vaccine, leading to immune failure [11].

Secondly, the defect in the immune system's response to vaccine antigens may also be closely related to the state of immunosuppression. Studies have shown that in patients undergoing immuno-suppressive therapy, the immune response following vaccination is often significantly diminished. For example, patients receiving chemotherapy or immunosuppressants exhibit reduced responses to vaccines, increasing the risk of infection. This phenomenon is particularly pronounced in patients with chronic diseases, whose immune functions are already compromised, and they may still experience immune failure after vaccination, being unable to produce sufficient antibodies to fend off pathogen invasion [12,13].

Additionally, research indicates that in patients undergoing organ transplantation, immunosuppressive therapy is essential, but it may also lead to immune dysfunction post-vaccination. In such cases, the patient's immune system is suppressed and cannot effectively mount an immune response against vaccine antigens, thereby increasing the risk of immune failure after rabies vaccination [14].

In summary, the roles of immunosuppression and immune dysfunc-tion in rabies vaccination are complex and multifaceted. Immune abnormalities such as monoclonal immunoglobulin disease significantly affect the immune response to vaccines, while defects in the immune system's response to vaccine antigens exacerbate this issue. Therefore, in clinical practice, particular attention should be paid to the immune status of these patients, and individualized vaccination plans should be developed to enhance the protective effectiveness of vaccines.

2.The Relationship Between Antibody Neutralization Capacity and Immune Protection

Post-vaccination, the neutralization capacity of antibodies is considered an important indicator of immune protection. Studies have shown a positive correlation between the titers of neutralizing antibodies and immune protection. However, this correlation may vary for different pathogens and individuals' immune backgrounds. For instance, research on SARS-CoV-2 found that antibody titers in plasma are negatively correlated with the risk of infection, especially after vaccination, where the titer of neutralizing antibodies can serve as a crucial parameter for evaluating vaccine efficacy. Nevertheless, there is currently a lack of quantifiable data regarding effective antibody titers, complicating the determination of a minimum threshold for protective neutralizing antibody levels. Different studies indicate that the neutralization titer thresholds for various viral variants also differ, necessitating consideration of these disparities in formulating vaccination strategies.

In addition to the presence of neutralizing antibodies, the impact of non-neutralizing antibodies should not be overlooked. Although non-neutralizing antibodies do not directly prevent viral infection, they can participate in protection through other immune mechanisms. For example, some studies show that non-neutralizing antibodies enhance antiviral immune responses by mobilizing immune cells such as natural killer cells and macrophages [15]. These non-neutralizing antibodies may, in certain situations, promote the coordination of immune responses and enhance cell-mediated immune protection.

Cellular immune responses also play a critical role in immune protection. Research indicates that the activation and function of T cells are related not only to antibody production but also to the clearance of infections. Taking SARS-CoV-2 as an example, although the levels of neutralizing antibodies may decline over time following vaccination, memory T cells can be rapidly activated upon re-exposure to the virus, providing swift immune protection [16]. The existence of this cellular immunity can maintain a certain level of protective effect even when antibody levels drop, which is particularly important in the elderly or individuals with compromised immune function.

In conclusion, the relationship between the levels of neutralizing antibodies and immune protection is complex and influenced by various factors, including individual immune backgrounds, types of vaccines administered, and characteristics of the pathogens. Future research needs to delve deeper into how to optimize antibody and cellular immune responses to improve vaccine efficacy while providing a basis for developing more effective vaccination strategies.

3.Viral Escape Mechanisms and Their Impact on Vaccine Efficacy

Viral escape mechanisms refer to the strategies employed by viruses to evade recognition and attack by the host immune system, allowing them to continue infecting and replicating. This mechanism has direct and profound implications for the efficacy of vaccines. Taking the rabies virus as an example, its escape mechanisms primarily include mutations in the viral genome and antigenic changes, along with molecular mechanisms of immune evasion.

Firstly, mutations in the viral genome are a crucial means of viral escape. Due to a high mutation rate, especially in RNA viruses, viruses can rapidly accumulate mutations during replication. These mutations may affect the structure of surface antigens, altering their interactions with the host immune system. For instance, the spike protein of SARS-CoV-2 has undergone multiple mutations in different variants, enabling the virus to evade immune responses triggered by previous infections or vaccinations [17]. Particularly, the Omicron variant has multiple mutations that significantly enhance its ability to escape existing vaccines, leading to a decrease in vaccine efficacy [18,19].

Secondly, the molecular mechanisms of immune evasion are continually being studied. The expression of ligands for the NKG2D receptor, downregulation of major histocompatibility complex (MHC) molecules, and regulation of cytokines are all important strategies used by viruses to evade host immune surveillance. For example, SARS-CoV-2 reduces the expression of MHC-I molecules, decreasing the chances of host cells being recognized by CD8+ T cells, thereby escaping cellular immune attacks. Additionally, some viruses induce the release of inhibitory cytokines such as TGF-β, further suppressing immune responses [20].

These viral escape mechanisms directly affect vaccine efficacy. Vaccines are typically designed based on specific antigens of the virus, and mutations in the virus may render these antigens ineffective, preventing vaccinated individuals from generating effective immune responses. For example, in vaccines targeting the rabies virus, if viral mutations lead to changes in antigenicity, vaccinated individuals may not achieve the expected protective effects, thereby increasing the risk of infection [21].

In summary, there exists a complex interaction between viral escape mechanisms and vaccine efficacy. To improve vaccine effectiveness, future vaccine development needs to consider the mutational potential and escape mechanisms of viruses, possibly requiring the development of broad--spectrum vaccines targeting multiple variants, along with ongoing monitoring and updates to address the continuously evolving viral strains.

Latest Research Progress in Vaccine Design and Immune Response

1.Advantages and Limitations of Cell Culture Vaccines

Cell culture vaccines, as an emerging vaccine production technology, have gradually replaced traditional chicken embryo vaccines in global vaccine production in recent years. The manufacturing process of modern vaccines mainly relies on cell culture technology, which can quickly and flexibly respond to potential epidemic threats. The advantages of cell culture vaccines lie in their production process, which does not rely on embryonated chicken eggs. This change not only improves production efficiency but also reduces the risks associated with chicken embryo vaccines. Studies have shown that cell culture vaccines perform better in terms of safety, tolerance, efficacy, and immunogenicity. For example, cell culture--derived quadrivalent influenza vaccines can generate higher levels of protective antibodies after vaccination, which is significant for addressing the disease burden associated with influenza B virus[22]. Additionally, the production process of cell culture vaccines is relatively straightforward, allowing for large-scale production to meet the needs of public health emergencies.

However, cell culture vaccines also face some limitations. First, the risk of contamination during the cell culture process still exists, especially during large-scale production, where the selection of cell lines and culture conditions must be strictly controlled to ensure the purity and safety of the vaccine. Second, the production cost of cell culture vaccines is relatively high, which may become an obstacle to vaccine promotion in some developing countries [23]. Furthermore, although cell culture technology has shown good performance in enhancing vaccine immunogenicity, some studies suggest that under certain specific conditions, the immunogenicity of cell culture vaccines may not meet expectations compared to chicken embryo vaccines, which needs to be validated through further clinical trials.

Moreover, the relationship between vaccine purity, dosage, and immunogenicity cannot be overlooked. The purity of the vaccine directly affects its immunogenicity; vaccines with higher purity typically can more effectively stimulate the immune response, generating stronger antibody levels [24]. Research indicates that the performance of cell culture vaccines in terms of immunogenicity is closely related to the cell lines and culture conditions used during production, which means that optimizing production processes will have a significant impact on the final efficacy of the vaccine. Therefore, in the development and production of cell culture vaccines, it is essential to strictly adhere to standard operating procedures to ensure the safety and efficacy of the vaccine.

In summary, cell culture vaccines, as an emerging vaccine production method, demonstrate significant advantages, especially in terms of flexibility and efficiency in responding to public health emergencies. However, the challenges and limitations in the production process also warrant attention, and future research should focus on optimizing production processes to improve vaccine quality and accessibility. At the same time, continued exploration of the application of cell culture technology in vaccine development is necessary to promote advancements in vaccine technology.

2. Application of Novel Vaccine Carriers and Adjuvants

With the continuous progress in vaccine development, the research on novel vaccine carriers and adjuvants has gradually become an important direction for enhancing vaccine immune efficacy. In recent years, significant progress has been made in the research of phage and viral vector vaccines. For example, modified adenoviral vectors (Ad4) have been developed for the delivery of respiratory vaccines, which demonstrate lower innate immune responses and higher immuno--genicity compared to traditional Ad5 vectors, showing promising prospects in vaccine development. Additionally, in the development of avian influenza vaccines, research utilizing avian influenza virus and turkey herpesvirus as recombinant vaccine carriers has also shown good safety and efficacy, indicating the potential of viral vectors in vaccine development [25].

In terms of vaccine adjuvants, the application of novel adjuvants such as MPLA-AddaVax has also attracted widespread attention. MPLA (monophosphoryl lipid A), as a potent TLR4 agonist, can significantly enhance the immune response to vaccines. Studies have shown that this adjuvant promotes the activation and proliferation of lymphocytes by activating dendritic cells and macrophages, thereby improving the immune response to vaccine antigens [26]. Furthermore, the use of MPLA-AddaVax can improve antibody tolerance and enhance vaccine safety, making it an extremely promising adjuvant choice.

The combination of research on novel vaccine carriers and adjuvants not only helps to improve the immune efficacy of vaccines but also addresses challenges faced by traditional vaccines, such as inadequate immune responses and resistance issues. These advancements lay a foundation for the development of the next generation of vaccines, while also providing new ideas and directions for future vaccine research.

3.Immune Enhancement Strategies and Their Clinical Potential

Immune enhancement strategies play an important role in vaccine development, especially in addressing immune failure situations for human rabies vaccines. The development of multivalent vaccines and immune modulators is currently a hot topic. Multivalent vaccines can enhance the overall response of the immune system by simultaneously providing protection against multiple viral strains. For example, multivalent vaccines targeting influenza have shown enhanced immune responses, and this strategy has also been applied in the development of rabies vaccines to improve their immune efficacy. Additionally, heterologous immunization strategies, combining different types of vaccines (such as DNA vaccines and protein subunit vaccines), have been shown to significantly enhance the strength and duration of immune responses, particularly in the research of tumor vaccines and infectious disease vaccines, yielding positive results.

In establishing immune memory and long-lasting protection, research indicates that enhancing the memory cell response of vaccines is key to improving the long-term protective effects of vaccines. By modulating the immune system to better remember disease antigens, the intensity of subsequent immune responses can be significantly enhanced. For instance, vaccine strategies using adenoviral vectors have been proven to effectively enhance the memory characteristics of T cells, allowing for rapid immune responses when facing the same pathogens. Furthermore, by using specific immune modulators, the immune memory and durability of vaccines can be further enhanced, which is critical for preventing viral infections such as rabies.

In terms of clinical application, the implementation of immune enhancement strategies can not only boost the immune response of vaccines but also play an important role in the prevention and treatment of diseases. For example, strategies combining traditional vaccines with novel biological agents can significantly improve resistance to infections and the clinical efficacy of vaccines. In clinical trials of rabies vaccines, optimizing vaccination protocols and using new immune modulators have shown significant safety and efficacy, further validating the clinical potential of immune enhancement strategies.

In conclusion, immune enhancement strategies show great promise in the research and clinical application of rabies vaccines. Through multivalent vaccines, immune modulators, and innovative immune memory establishment strategies, the immune efficacy and durability of vaccines can be significantly improved, providing direction for the future development of vaccines.

Immune Monitoring and Risk Assessment of Immune Failure

1.Monitoring Indicators of Immune Response to Rabies Vaccine

Monitoring the immune response to the rabies vaccine is an important aspect of assessing vaccine efficacy and individual immune status. To ensure that individuals can generate sufficient immune responses after vaccination, neutralizing antibody titer testing and auxiliary assessments of cellular immune indicators are typically employed.

Firstly, neutralizing antibody titer testing is one of the standard methods for monitoring the immune response to the rabies vaccine. Neutralizing antibodies are specific antibodies against the rabies virus; they can neutralize the virus and prevent it from infecting host cells. Generally, enzyme-linked immunosorbent assay (ELISA) and rapid fluorescent focus inhibition test (RFFIT) are used to detect the titer of neutralizing antibodies. Studies have shown that individuals vaccinated against rabies will generate a certain level of neutralizing antibodies after vaccination, and a neutralizing antibody titer greater than 0.5 IU/mL is generally considered a marker of effective protection. For high-risk populations, regular monitoring of antibody titers is a necessary measure to ensure sustained immunity. For example, one study indicated that individuals with occupational exposure who received the rabies vaccine needed to undergo booster immunization if their antibody titer fell below the standard value [27].

Secondly, the auxiliary assessment of cellular immune indicators is also crucial for a comprehensive understanding of the immune response. Cellular immune responses primarily rely on the activation and proliferation of T cells, which play a key role in the early stages of viral infection. Through techniques such as flow cytometry (FACS), the composition, activation status, and cytokine production of T cell subsets can be detected, including interferon-γ (IFN-γ) and tumor necrosis factor-α (TNF-α). The levels of these cytokines can reflect the intensity and nature of the immune response to the rabies vaccine. Research has found a certain correlation between cellular immune response and antibody production; an enhancement in cellular immune response often indicates effective antibody generation. Furthermore, the expression levels of certain cytokines are positively correlated with the protective effect of the vaccine, thus monitoring cellular immune indicators can provide important supplementary data for evaluating the immune efficacy of the rabies vaccine [28,29].

In summary, the monitoring indicators for the immune response to the rabies vaccine include the detection of neutralizing antibody titers and the auxiliary assessment of cellular immunity, both of which complement each other and together form a scientific basis for assessing vaccine immune efficacy. Monitoring these indicators not only helps to understand individuals' immune status but also provides important references for the management and development of subsequent immunization strategies post-vaccination.

2.Special Monitoring Needs for Immunocompromised Populations

In immunocompromised populations, the monitoring needs after vaccination are particularly important because these groups are more susceptible to infections, and the immune effects of the vaccine may be significantly reduced. Immunosuppressed patients (such as those undergoing chemotherapy, organ transplantation, or long-term use of immunosuppressive agents) require special monitoring programs after vaccination to ensure they receive adequate protection.

The vaccination monitoring program for immunosuppressed patients should include regular testing of antibody levels to assess the immune response to the vaccine. For example, studies have shown that immunosuppressed patients receiving the COVID-19 vaccine produce antibodies at a lower rate than healthy individuals, indicating a need for more frequent antibody testing after vaccination to timely detect immune failure. Additionally, physicians should adjust the timing and type of vaccination based on the patient's health status and potential infection risk.

Identifying and managing high-risk individuals for immune failure is also crucial. Research indicates that patients with specific immunodeficiencies (such as common variable immunodeficiency) may experience higher rates of infection and mortality after vaccination [30]. Therefore, monitoring for these patients should not only include antibody levels but also focus on their clinical symptoms and the occurrence of complications. Furthermore, adopting a multidisciplinary team management model can facilitate coordination among different medical specialties to provide comprehensive care and monitoring programs, ensuring the health and safety of immunocompromised patients [31].

Thus, addressing the special monitoring needs of immunocompromised populations requires developing suitable vaccination monitoring programs and emphasizing the identification and management of high-risk individuals. By enhancing the efficacy and safety of vaccinations, the infection risk for these patients can be effectively reduced, improving their quality of life.

3. The Application of Immune Monitoring in Clinical Decision-Making

After rabies vaccination, immune monitoring is an important tool for assessing vaccine efficacy and making clinical decisions. By monitoring individual immune status, healthcare providers can better determine the timing and rationale for booster vaccinations, thereby optimizing immunization strategies and reducing the risk of immune failure.

Firstly, the timing and rationale for booster vaccinations depend on the individual's immune response. Studies have shown that responses to vaccines vary among individuals, which is related to multiple factors, including age, underlying diseases, and immune status. For instance, certain high-risk groups, such as immunocompromised patients, may require more frequent monitoring and booster vaccinations to ensure their immune systems can produce sufficient protective antibodies. Therefore, clinicians need to develop personalized vaccination plans based on the specific circumstances of the patients to enhance the efficacy of vaccinations.

Secondly, immune monitoring can help identify cases of immune failure after vaccination. In some instances, despite vaccination, patients may still become infected with the rabies virus due to insufficient immune response. According to relevant literature, vaccine failure can be categorized into primary and secondary failures; primary failure typically occurs when individuals do not generate an immune response after vaccination, while secondary failure results from waning immunity over time [32]. Regular immune monitoring can promptly identify these failure cases and take appropriate measures, such as adjusting vaccination schedules or providing additional immunotherapy.

Furthermore, the development of individualized immune strategies depends not only on the results of immune monitoring but also on a comprehensive consideration of the patient's clinical background and epidemiological data. Understanding the protective efficacy of the vaccine and its performance in specific populations can help formulate more targeted vaccination plans. For example, adjustments may be necessary in the timing and frequency of vaccinations to ensure adequate herd immunity and reduce the risk of rabies transmission based on the epidemiological characteristics of specific regions or populations [33].

In summary, immune monitoring plays a crucial role in clinical decision-making for rabies vaccination. By evaluating the immune response to the vaccine and identifying cases of immune failure, healthcare providers can formulate more scientific and personalized immune strategies, thereby enhancing the efficacy and safety of vaccinations, ultimately achieving effective control and prevention of rabies.

The Relationship between Immune Evasion and Virus Structural Characteristics

1.Virus Capsid Structure and Immune Recognition

The outer structure of the rabies virus significantly impacts its immune recognition, particularly in immune responses following vaccination. Rabies virus belongs to the Rhabdoviridae family, and its capsid is composed of membrane proteins and nucleoproteins, forming a complex viral particle structure. Research indicates that the stability of the rabies virus capsid is closely related to its antigenicity. The binding ability of antibodies and their capacity to neutralize the virus largely depend on the conformation and amino acid sequence characteristics of the capsid proteins. For instance, the G protein of the rabies virus is the primary immunogen, and its surface structure can effectively activate the host's immune system, especially in generating neutralizing antibodies from B cells [34]. Furthermore, there are significant differences between the capsid structures of rabies virus and other highly variable viruses, such as HIV. The capsid of HIV exhibits a high degree of intrinsic disorder, which complicates the effective binding of antibodies and leads to immune evasion [35]. In contrast, the capsid structure of the rabies virus is relatively stable, making it more easily recognized and targeted by the host's immune system. This structural difference directly influences vaccine design and immune efficacy.

In comparison to highly variable viruses like HIV, the rabies virus capsid demonstrates superior antigenicity and immune recognition capability. The high variability and instability of the HIV capsid proteins pose significant challenges for vaccine development, while the relative stability of the rabies virus provides favorable conditions for vaccine development. For example, rabies virus vaccines can effectively prevent rabies by inducing a strong neutralizing antibody response, whereas the rapid mutation of HIV hampers successful vaccine development. Therefore, studying the relationship between the structure of the rabies virus capsid and immune recognition mechanisms not only aids in understanding its pathogenic mechanisms but also provides important references for developing vaccines against highly variable viruses.

In summary, there is a close relationship between the structure of the rabies virus capsid and immune recognition, with higher antigenicity and structural stability giving it advantages in vaccine development. Comparisons with highly variable viruses like HIV further highlight this point, emphasizing the importance of in-depth research on viral capsid structure. Further exploration in this field will provide new ideas and methods for improving vaccine efficacy and developing novel vaccines.

2. Intrinsic Disorder of Capsid Proteins and Immune Evasion Mechanisms

2.1 Theoretical Models and Their Implications for Vaccine Design

The intrinsic disorder of capsid proteins plays a crucial role in the immune evasion mechanisms of viruses. Studies have shown that many viral capsid proteins exhibit high levels of intrinsic disorder, a characteristic that makes it difficult for antibodies to bind to the viral surface antigens, leading to immune evasion. Specifically, the high disorder of the viral capsid allows for rapid spatial structural changes, forming multiple conformations, which increases the difficulty of antibody recognition [35]. This theoretical model provides important insights for vaccine design, especially for viruses that are challenging to vaccinate against (such as HIV and HCV), as understanding the intrinsic disorder of their capsid proteins can help scientists devise more targeted vaccine strategies.

For instance, research indicates that classic viruses, such as rabies virus, have relatively stable capsid protein structures, while difficult-to-vaccinate viruses like HIV exhibit a high degree of intrinsic disorder. This structural difference may explain why effective vaccines can be developed for the former, but not for the latter [36]. Therefore, identifying and targeting the intrinsic disorder characteristics of viral capsid proteins may be key to designing effective vaccines during the vaccine development process.

2.2 Structural Differences Between Classic Viruses and Difficult-to-Vaccinate Viruses

There are significant structural differences between classic viruses and difficult-to--vaccinate viruses concerning capsid proteins, and these differences directly affect their immune evasion capabilities. Classic viruses like rabies virus typically have relatively stable capsid proteins with defined three-dimensional conformations, which can effectively induce targeted immune responses in the host [35]. In contrast, viruses that are challenging to develop vaccines for (such as HIV and certain coronaviruses) show higher intrinsic disorder in their capsid proteins, allowing them to rapidly change shape within the host immune system to evade immune detection.

Specifically, the gp120 protein of HIV contains numerous intrinsically disordered regions, and the high variability of these regions is closely linked to the virus's immune evasion capability. Studies have found that HIV's immune evasion is achieved through sequence variations and structural changes in its capsid proteins, making it difficult for antibodies to bind effectively and neutralize the virus. In contrast, the rabies virus capsid can effectively activate the host's immune response after infection, leading to protective immunity.

These structural differences not only impact the virus's infectivity and pathogenicity but also provide direction for vaccine development. Understanding the biological mechanisms behind these differences will facilitate the development of more targeted vaccines, particularly in the face of currently uncontrolled viruses, emphasizing the relationship between intrinsic disorder and immune evasion for vaccine design and optimization.

3. Assessment of the Impact of Immune Evasion on Vaccine Efficacy

In the study of immune evasion, monitoring and early warning of escape variants are crucial. Taking the novel coronavirus (SARS-CoV-2) as an example, research has shown that the virus's mechanism of escaping host immune responses through mutations has become increasingly complex, especially in its spike protein, where multiple key mutations (such as Arg346Lys, Lys417Asp, etc.) have been found to significantly affect antibody recognition and binding capability, thereby reducing vaccine efficacy. In the context of ongoing global vaccination efforts, timely monitoring of the emergence of these variants and their effects on immune responses has become particularly important. Studies indicate that certain variants (such as Omicron) exhibit a strong capacity for immune evasion, leading to a significant decline in the protective efficacy of vaccines produced against them [37].

Future vaccine design strategies to combat immune evasion should incorporate various technical approaches. First, vaccine developers might consider designing vaccines targeting broadly circulating variants, such as employing multivalent vaccines that combine antigens from different variants to enhance the breadth and durability of immune responses[38]. Additionally, vaccines targeting specific variants (such as those based on the Omicron variant) should also be prioritized to address the challenges posed by emerging variants [39]. The integration of new vaccine delivery technologies, such as mRNA vaccines and adenoviral vector vaccines, may offer new avenues for improving vaccine tolerance against variants [40].

In summary, effective monitoring and early warning mechanisms for immune evasion can assist in timely adjustments in strategies during vaccine development and optimization to address the continuously changing viral variants, thereby protecting public health. Research on immune evasion will provide important theoretical foundations and practical guidance for the design and implementation of future vaccines.

Advances in Molecular Biology Research on Immune Failure

1.Application of Whole Genome Sequencing in Immune Failure Research

Whole genome sequencing (WGS) plays a crucial role in studying the mechanisms of immune escape and vaccine immune failure. By comparing the sequences of viruses and host genomes, researchers are able to identify genetic variations in viruses and how they affect immune evasion. Recent studies have shown that after vaccination, certain viral strains may change their antigenicity through mutations, allowing them to evade the host immune response. For instance, research on the novel coronavirus (SARS-CoV-2) revealed genetic differences among various variants that may be related to the virus's ability to exhibit immune escape after vaccination [41].

In cases of immune failure with rabies vaccines, whole genome sequencing has helped researchers identify critical mutation sites associated with immune evasion. For example, by performing whole genome sequencing on viral samples from infected patients, certain mutations that may affect the virus's ability to invade host cells and escape immune surveillance have been identified. These mutations may occur in the virus's surface glycoproteins or other key functional genes, resulting in antibodies produced by vaccines being unable to effectively neutralize the virus, thereby leading to infection [5].

Identifying key mutation sites not only aids in understanding the evolution and adaptation mechanisms of viruses but also provides important information for the design of future vaccines. By comparing genomic sequences among different viral strains, scientists can identify which mutations are associated with immune escape. This genome-based research approach provides a theoretical foundation for the improvement of vaccines and the development of new vaccines, assisting public health authorities in formulating more effective immunization strategies to address emerging viral variants and prevent vaccine immune failure [42].

In summary, the application of whole genome sequencing in immune failure research provides profound insights into the mechanisms by which viruses escape host immunity, while also guiding the development and improvement of future vaccines. Through in-depth analysis of viral genomes, researchers can better address public health challenges, enhance vaccine efficacy, and ultimately improve population health.

2. Polymorphisms in Immune-Related Genes and Vaccine Reactivity

The immune response to vaccines is significantly influenced by the host's genetic background, particularly polymorphisms in immune-related genes. After vaccination, individuals exhibit significant variations in their responses to vaccines, closely related to their genetic backgrounds. For example, polymorphisms in HLA genes are associated with antibody responses generated by vaccines. Studies have shown that certain HLA genotypes are negatively correlated with neutralizing antibody levels for the measles vaccine, suggesting that these genotypes may lead to lower vaccine reactivity. Additionally, polymorphisms in immune regulatory genes such as IL-10 and TNF-α are also believed to impact vaccine reactivity. Research has found significant correlations between specific IL-10 genotypes and the effectiveness of immunotherapy, indicating a crucial role for this gene in regulating immune responses [43]. Therefore, the role of host gene polymorphisms in vaccine reactivity cannot be overlooked.

In light of these polymorphisms in immune-related genes, researchers have conducted several studies to explore their relationship with vaccine immune failure. For instance, studies have found that individuals with specific genotypes exhibit lower antibody responses after receiving the influenza vaccine, which may be related to immune response mechanisms influenced by their genotypes[44]. Moreover, the reactivity to measles, mumps, and rubella vaccines also shows significant genetic correlations, emphasizing the central role of genetic factors in vaccine immunity [45]. These findings suggest that understanding the polymorphisms of immune-related genes not only helps explain individual variations in vaccine responses but also aids in providing a basis for personalized vaccination strategies.

Current research has also found that certain gene polymorphisms may influence antibody production after COVID-19 vaccination. Specifically, studies have shown that polymorphisms in genes like NLRP3 and OAS1 are associated with antibody levels following COVID-19 vaccination, indicating that variations in these genes may play a key role in individual differences in vaccine responses [46]. Furthermore, with advancements in genomics and bioinformatics, researchers are beginning to explore how to utilize individuals' genetic information to optimize vaccination protocols, thereby enhancing vaccine efficacy and safety.

In summary, polymorphisms in immune--related genes play an important role in vaccine reactivity. Variations in these genes not only affect individual immune responses but also influence the overall effectiveness of vaccines. Therefore, future research should continue to explore the relationship between these genes and vaccine responses to provide more precise guidance for vaccination.

3.Potential of Molecular Biomarkers in Predicting Immune Failure

The screening and validation of biomarkers are crucial steps in studying immune failure. In recent years, significant progress has been made in identifying potential biomarkers, thanks to advancements in molecular biology and bioinformatics technologies. Regarding clinical applications, the role of biomarkers in predicting immune failure has become increasingly significant. By comprehensively analyzing the molecular characteristics of patients, more timely and accurate prognostic assessments can be achieved. For instance, studies have shown that specific cytokines, such as S100B protein, MMP-9, and IL-10, are associated with the risk of malignant brain edema in patients with acute ischemic stroke, providing new biomarkers for clinical intervention [47]. Additionally, changes in IL-17 levels in urine show potential for predicting treatment responses in patients with lupus nephritis, further illustrating the importance of biomarkers in personalized medicine.

In conclusion, the application of molecular biomarkers in predicting immune failure not only helps improve the accuracy of clinical diagnoses but also provides a basis for personalized treatment. Moving forward, as technology continues to advance, research on biomarkers may reveal more mechanisms of immune response, thereby improving patient treatment outcomes and prognoses. Continuing to explore and validate the potential of these biomarkers will be an important direction for future research.

Clinical Management and Prevention Strategies for Immune Failure

1.Immune Function Assessment and Pre-Vaccination Screening

Before rabies vaccination, assessing immune function and screening high-risk individuals are crucial steps to ensure vaccine effectiveness. First, the criteria and methods for identifying high-risk individuals are vital. High-risk individuals typically include those who have had contact with rabid animals, such as animal handlers, veterinarians, and those dealing with wildlife or stray animals. The vaccination strategy for these individuals needs to be tailored based on their immune status to ensure maximum protection. By utilizing modern immune assessment technologies, such as ELISA, flow cytometry, and quantitative PCR, an individual's immune function can be effectively evaluated. These methods can not only detect antibody levels post-vaccination but also assess the intensity and durability of cellular immune responses [48].

The pre-vaccination immune status assessment process typically includes the following steps: first, collecting patient history and exposure history through questionnaires and clinical examinations. Next, blood samples are collected to detect specific antibody levels. For instance, antibody testing for rabies virus can be performed using techniques like ELISA to help determine if an individual has sufficient immune protection. Furthermore, combining biomarker detection results provides a more accurate immune function assessment, serving as a basis for developing personalized vaccination plans. Research indicates that a comprehensive evaluation of clinical presentations and biomarkers will become an effective method for future immune function assessments [49].

During the pre-vaccination screening process, in addition to assessing individual immune status, considerations must include the patient's age, health condition, and potential immunosuppressive factors, as these could affect the vaccine response. Vaccination for the elderly or those with compromised immune function should be approached with caution, considering the use of higher doses or multiple vaccinations to ensure adequate immune protection. Additionally, employing emerging immune scoring models, which combine lymphocyte numbers, functions, and phenotypes, can more effectively assess an individual's immune status, optimizing vaccination strategies [50].

In summary, immune function assessment and pre-vaccination screening are key components to ensure the success of rabies vaccination. By accurately evaluating individual immune status and identifying high-risk individuals, more scientific vaccination strategies can be developed, thus enhancing vaccine effectiveness and reducing rabies incidence.

2. Clinical Management Measures

Immune failure is a rare event that may occur after rabies vaccination, particularly in high-risk populations such as immuno--compromised patients. Therefore, clinical management measures for special populations must focus on enhancing immunity, developing alternative immune therapy options, and effectively applying immunomodulators.

First, enhancing immune therapy is one of the key measures. Clinical recommendations suggest conducting additional vaccinations to boost immune responses on top of the original vaccination regimen. Specifically, high-titer vaccines or vaccines of different serotypes can be administered for revaccination. Studies have shown that timely booster immunization for patients who do not generate sufficient antibody responses can not only elevate antibody levels but also significantly reduce the risk of viral infection [4].

Secondly, exploring alternative immune therapy options is particularly important; using immunoglobulins as adjunctive treatment helps provide temporary passive immunity. Research has found that administering an appropriate dose of rabies immunoglobulin can effectively raise antibody levels in patients in the short term, thereby enhancing their defense against the rabies virus[5]. When combined with traditional vaccination strategies, the use of immunoglobulin not only compensates for immune deficiencies following vaccination but also effectively prevents the occurrence of rabies.

At the same time, research on the application of immunomodulators is continually evolving. In recent years, immunomodulators such as interferons and interleukins have shown promising prospects in enhancing immune responses. These medications help regulate the immune system, promote antibody production, and improve the body's resistance to viruses. For special patients, exploring combined therapies using immunomodulators may provide new treatment ideas for clinicians. Moreover, with a deeper understanding of immune mechanisms, more specific treatment strategies for certain immune deficiencies may be proposed in the future.

In conclusion, clinical management measures for rabies vaccine immunity in special populations should include the implementation of enhanced immune and alternative immune therapy plans, as well as the effective application of immuno--modulators. Through these comprehensive measures, the immune protection of vaccinated patients can be significantly improved, reducing the risk of rabies infection and providing safer and more effective treatment options for patients.

3.Public Health Response and Risk Communication

In public health responses to cases of immune failure following rabies vaccination, epidemiological tracking and risk communication are two indispensable components. The epidemiological tracking of immune failure cases not only helps identify the effectiveness of vaccination and its potential flaws but also provides data support for subsequent public health decisions. By conducting detailed case analyses and epidemiological investigations on immune failure cases, public health agencies can collect information regarding the clinical characteristics of vaccine failure, patient backgrounds, and vaccination history, thereby better understanding the mechanisms behind immune failure. For example, some studies have found that certain populations (e.g., immunosuppressed patients) are more likely to exhibit insufficient immune responses after receiving rabies vaccination [51]. Therefore, it is particularly important to develop personalized vaccination plans for these high-risk groups.

At the same time, public education and vaccine confidence-building play important roles in risk communication. Vaccination is not only a personal health choice but also a crucial means of achieving herd immunity. Public trust in vaccines directly affects vaccination rates. To enhance public trust, public health agencies need to communicate transparently about vaccine effectiveness, safety, and potential side effects. For instance, regarding cases of immune failure with rabies vaccines, public health departments should promptly release relevant information to explain the factors that may lead to immune failure and alleviate public concerns. Additionally, conducting vaccination promotion and education through various channels, such as social media and community activities, can raise public awareness and enhance willingness to get vaccinated [52].

The effectiveness of risk communication also depends on how information is conveyed. During periods of outbreaks or vaccination peaks, using simple and understandable language, visual data presentations, and engaging with the audience are all important strategies to enhance information delivery. For example, during the COVID-19 pandemic, public health organizations interacted with the public through social media, promptly addressing public concerns and questions; this approach significantly improved public acceptance and compliance with health recommendations. Therefore, in promoting rabies vaccines, public health departments should draw on these successful experiences and employ diverse communication methods to ensure effective information dissemination.

In summary, public health response and risk communication are crucial in addressing cases of immune failure following rabies vaccination. By identifying high-risk cases through epidemiological tracking and combining effective public education with transparent communication, public trust in vaccines can be enhanced, thereby increasing vaccination rates and ultimately achieving the goal of herd immunity.

Future Research Directions and Challenges

1.In-depth Analysis of Vaccine Immune Mechanisms

The study of vaccine immune mechanisms is key to understanding vaccine efficacy and optimizing vaccine design. Current research indicates that there is a close relationship between the functions of immune cell subsets and vaccine responses. Different types of cells in the immune system, such as B cells, T cells, and dendritic cells, play various roles after vaccination. For example, B cells neutralize pathogens by producing specific antibodies, while T cells regulate the immune response by directly killing infected cells or secreting cytokines. Studies have shown that specific immune cell subsets are activated and expanded after vaccination, thereby enhancing the body's response and memory capabilities to the vaccine.

In terms of discovering new immune modulation targets, researchers are increasingly recognizing the important roles of different cytokines and receptors in vaccine immunity. For instance, IL-25, as a pro-immune cytokine, can significantly enhance the antibody response induced by vaccines, which is crucial for improving the immune efficacy of vaccines[53]. Furthermore, the use of novel vaccine carriers, such as mRNA vaccines, has demonstrated strong activation of immune cells and durable immune memory, providing new ideas and directions for vaccine development.

Additionally, research has found that nanomaterials have great potential as immune enhancers. Gold nanoparticles (AuNPs) and other nanomaterials can effectively enhance the immune response to vaccines by boosting antibody production and cytokine secretion, thereby improving vaccine efficacy[54]. The study of these novel immune modulators not only provides possible solutions for improving vaccine immune efficacy but also offers important scientific foundations for future vaccine design.

Overall, an in-depth analysis of vaccine immune mechanisms helps us better understand the differences in immune responses among different populations and promotes the development of personalized vaccination strategies targeting specific groups. Continuous progress in this field will provide a stronger immune defense for humanity against infectious diseases.

2. Development of Personalized Vaccine Strategies

In the development of personalized vaccine strategies, the integrated application of genomics and immunology is gradually becoming an important research direction. With the rise of vaccinomics and system vaccinology, the concept of personalized vaccines is becoming widely accepted. The core of this concept is to tailor vaccines according to individuals' genetic and immune characteristics to improve vaccine efficacy and safety. By integrating insights from genomics, transcriptomics, proteomics, and immunology, personalized vaccines are expected to achieve revolutionary breakthroughs in the effectiveness and safety of vaccination. This personalized strategy not only enhances the immune response to specific pathogens but also reduces unnecessary side effects. However, the process of developing personalized vaccines faces multiple challenges, including technical, ethical, economic, and regulatory issues. These challenges need to be addressed through interdisciplinary cooperation and ongoing research to ensure the fairness and safety of personalized vaccine strategies, thereby supporting the optimization of immune responses and alleviating disease burden.

The design and evaluation of adaptive immune schemes is also a key aspect of developing personalized vaccine strategies. In this process, researchers need to fully consider individuals' immune backgrounds and pathogen characteristics to formulate the optimal immune scheme. Adaptive immune schemes not only include immune responses to specific antigens but also require real-time assessment and adjustment based on individuals' immune status and response rates. By employing modern technologies, such as single-cell sequencing and high-throughput screening, researchers can better understand the complexity of individual immune responses, providing more precise bases for vaccine design. Additionally, clinical trial results also show that personalized vaccination strategies can effectively improve vaccination rates and immune efficacy. Therefore, ongoing research and clinical trials are essential for advancing personalized vaccine strategies, offering new ideas and methods for future vaccination. Through these efforts, personalized vaccine strategies have the potential to play a greater role in public health, helping to achieve higher levels of immune protection.

3.Innovation in New Vaccine Technologies and Platforms

With the continuous advancement of vaccine technologies, innovation in new vaccine technologies and platforms has become an important research direction in the field of public health. In recent years, viral vector vaccines and mRNA vaccines have demonstrated immense potential, particularly in responding to emerging infectious diseases. Viral vector vaccines use harmless viruses as carriers to introduce target antigens into host cells, thus eliciting a strong immune response. The advantage of this technology lies in its ability to effectively induce cellular and humoral immunity while providing flexibility for the rapid development of various vaccine candidates. For instance, vaccines utilizing adenoviral vectors were rapidly approved during the COVID-19 pandemic, highlighting their significance in swiftly addressing epidemics [55].

On the other hand, the rise of mRNA vaccine technology, especially in the development of COVID-19 vaccines, has showcased its capacity for rapid design and production. The advantages of mRNA vaccines include an efficient immune response and flexibility in the manufacturing process. By simple modifications, scientists can quickly design vaccines against different variants, which is particularly important in addressing the challenges posed by viral mutations. Moreover, mRNA vaccines are relatively low-cost to produce and can be rapidly manufactured on a large scale without the need for live viruses, providing new ideas for future vaccine development [56].

In the application of nanotechnology and delivery systems, recent studies have shown that nanoparticles can serve as effective delivery systems for vaccines. These nanoparticles can protect vaccine components from degradation, enhance the stability of antigens, and improve targeted delivery to specific immune cells, thereby boosting the intensity and duration of immune responses. The use of nanotechnology opens up new possibilities for the production and application of vaccines, particularly in the development of vaccines for chronic diseases and cancers that require strong immune responses.

In summary, innovation in new vaccine technologies and platforms provides robust support for vaccine research and development. The successful development of viral vector and mRNA vaccines not only offers effective means to address current public health crises but also lays the groundwork for future vaccine technology advancements. As technology continues to progress, the integration of nanotechnology and other cutting-edge technologies will further propel the vaccine development process, enhancing vaccine safety and efficacy to better tackle emerging and re-emerging infectious disease challenges.

4.Improvement of Immune Failure Monitoring Systems

During the vaccination process, the monitoring system for immune failure is crucial, especially in the use of rabies vaccines. To enhance vaccine efficacy and its monitoring, we need to improve the immune failure monitoring system from multiple aspects.

First, the promotion of high-throughput testing technologies is an important means to improve immune failure monitoring. High-throughput testing can process a large number of samples in a short time, providing accurate immune response data that quickly identifies cases of immune failure post-vaccination. Research indicates that employing high-throughput technology significantly enhances immune response monitoring capabilities, helping to identify potential immune-deficient patients so that vaccination strategies can be promptly adjusted and personalized immune interventions can be implemented. The application of this technology not only improves monitoring efficiency but also provides scientific evidence for public health decisions, ensuring the effectiveness and safety of vaccinations [57].

Secondly, data sharing and multi-center collaborative research are also important components of improving the immune failure monitoring system. By establishing national or regional immune monitoring databases, systematic analysis and research of immune failure cases can be achieved. Multi-center collaborative research can gather vaccination and immune failure data from different regions, forming a more comprehensive epidemic monitoring network. In this way, various research institutions can share information, resources, and experiences, enhancing the understanding of immune failure phenomena while promoting research progress in related fields. For example, studies from certain countries have shown that cross-regional data sharing and joint analysis can better identify potential risk factors for immune failure, thereby enabling targeted interventions to reduce the incidence of immune failure following vaccination [58].

Additionally, establishing standardized monitoring processes and standardized operating procedures is also a necessary step to enhance the effectiveness of the immune failure monitoring system. By formulating unified monitoring indicators and assessment standards, consistency among participating units in the immune monitoring process can be ensured, thereby improving the comparability and scientific nature of the data. Coupled with modern information technology, developing intelligent vaccination record and monitoring systems can enable real-time tracking and recording of immune responses post-vaccination, allowing for timely identification of abnormalities and interventions.

In summary, improving the immune failure monitoring system requires the promotion of high-throughput testing technologies, strengthening data sharing and multi-center collaborative research, and establishing standardized monitoring processes. These measures will provide a solid foundation for increasing vaccination success rates and controlling the spread of vaccine-related diseases.

Conclusion

The research progress of rabies vaccines indicates that although the incidence of vaccine immune failure is low, its potential clinical impact cannot be ignored, especially in patients with impaired immune function, where this issue is particularly severe. The causes of immune failure are complex, involving both abnormal host immune states and viral escape mechanisms. To effectively prevent such immune failures, monitoring vaccine immune responses is particularly important.

The development of modern cell culture vaccines provides new options for rabies prevention; however, relying solely on this technology still makes it difficult to comprehensively ensure immune efficacy across all populations. The combination of personalized immune strategies and new vaccine technologies can enhance protective effects while minimizing the risk of immune failure. Assessing the immune status of different individuals aids in formulating more precise vaccination plans, thus achieving higher rates of immune protection.

Future research should further delve into the analysis of immune mechanisms and explore the molecular basis of immune escape to provide theoretical foundations for vaccine improvement and the development of new vaccine platforms. With advancements in science and technology, innovations in vaccine design will offer more possibilities to address the issue of rabies vaccine immune failure and enhance our ability to control this disease.

In clinical practice, especially for high-risk populations, regular assessments of immune function and immune monitoring are recommended. This not only ensures the effectiveness and safety of vaccination but also provides data support for personalized health management. Through this approach, we can better balance different research perspectives and findings, forming a more comprehensive and systematic rabies vaccine immune management strategy.

In conclusion, although rabies vaccine immune failure is relatively rare, its potential impact should not be underestimated. Future research and clinical practice should work together to effectively prevent and manage the issue of rabies vaccine immune failure by deepening understanding of immune mechanisms, innovating vaccine technologies, and implementing personalized immune strategies, thus providing a more solid guarantee for public health.

Competing interests

The authors declare all financial and non-financial competing interests.

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