Single shot vaccine

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Abstract

Single-shot vaccines represent a pivotal advancement in immunobiotechnology, designed to elicit robust and durable protective immunity following a solitary administration. Unlike traditional multi-dose regimens, which require booster vaccinations to achieve adequate seroconversion, single-dose formulations are engineered to induce rapid, high-magnitude humoral and cellular responses. The development of these vaccines addresses critical logistical challenges associated with cold-chain storage, distribution costs, and patient compliance, particularly in low-resource settings and during rapidly evolving epidemics. This abstract reviews current platforms utilizing live-attenuated viruses, viral vectors, and novel lipid nanoparticle-encapsulated mRNA constructs. Furthermore, it explores immunological strategies such as the incorporation of molecular adjuvants and particulate antigen delivery systems designed to prolong antigen presentation. The efficacy of single-shot vaccines is examined through the lens of recent clinical successes against pathogens such as Ebola, COVID-19, and Measles. Despite the promise of this technology, challenges remain in ensuring long-term memory retention and managing reactogenicity. Ultimately, the widespread adoption of single-dose vaccines is essential for achieving global vaccine equity and improving pandemic preparedness.

Key Words : Single-shot vaccine, , Immunogenicity ,Prime-boost strategy , Adenovirus, Long- term immunity, COVID-19, Single-dose vaccine, Single-administration vaccine (SAV), single- injection

Introduction

Vaccination stands as one of the most monumental achievements in modern medicine, having saved billions of lives and eradicated or controlled numerous devastating infectious diseases. However, the efficacy of many of our most critical vaccines is intrinsically linked to complex, multi-dose administration schedules. From the diphtheria-tetanus-pertussis (DTP) vaccine given in infancy to the human papillomavirus (HPV) vaccine administered to adolescents, the requirement for multiple injections over weeks, months, or even years presents a formidable array of logistical, financial, and behavioral challenges that undermine global immunization efforts [0, 12]. These multi-dose regimens create significant burdens on healthcare systems, necessitate robust cold-chain infrastructure, and, most critically, lead to suboptimal patient compliance. The consequence is a well-documented decline in vaccination coverage between the first and final doses, leaving individuals and communities vulnerable to preventable diseases. For instance, global coverage for the third dose of the DTP vaccine is consistently 5-10% lower than for the first dose, a gap that translates into millions of unprotected children and a persistent risk of outbreaks [0]. In 2018 alone, an estimated 19.4 million children worldwide did not complete the recommended three-dose DTP series, highlighting a critical failure in achieving universal immunization [14]. These challenges are profoundly amplified in low- and middle-income countries (LMICs) with limited healthcare access, during public health emergencies like pandemics or natural disasters, and in mobile or hard-to-reach populations. The urgent need to overcome these barriers has catalyzed a paradigm shift in vaccinology, driving an intense global research and development effort focused on single-shot vaccines (SSVs), also known as single- administration vaccines (SAVs). Single-shot vaccines are designed to elicit complete, durable, and protective immunity after just one administration. Their development is not merely an incremental improvement but a transformative strategy aimed at fundamentally reshaping immunization programs worldwide. By condensing a prime-boost regimen into a single intervention, SSVs promise to dramatically simplify vaccination logistics, enhance patient compliance, reduce overall healthcare costs, and, most importantly, maximize vaccine coverage rates [0, 7, 14]. The potential impact is vast: a single-dose vaccine could ensure that a child in a

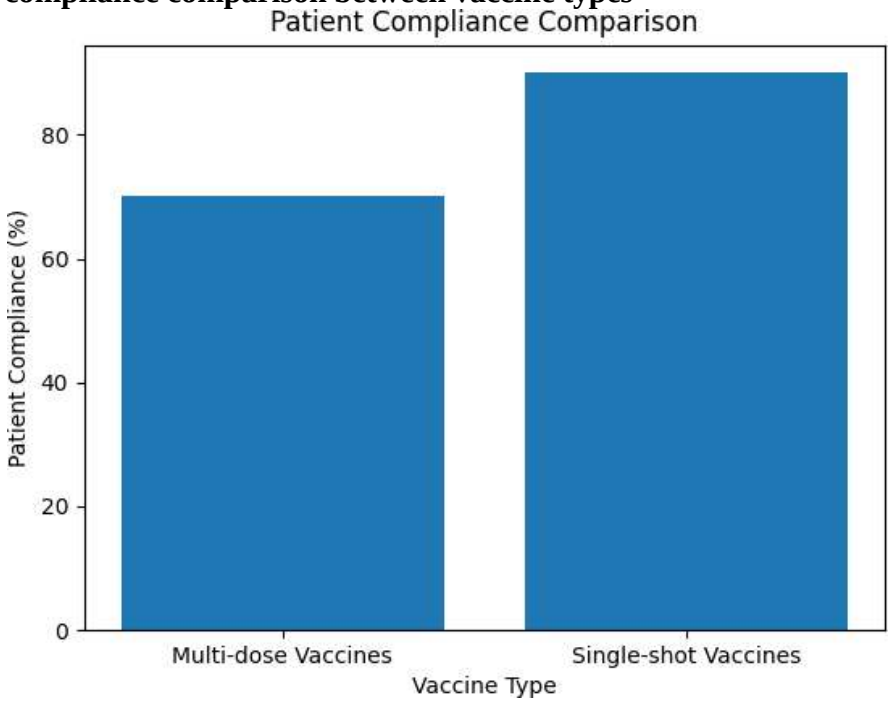
remote village is fully protected with one visit, that a traveler can be rapidly immunized before departure, and that a population can be swiftly and comprehensively covered during an emerging outbreak. The 2015 cholera outbreak in Juba, South Sudan, serves as a powerful real-world example. Faced with insufficient vaccine supply for a two-dose regimen, health authorities opted for a single-dose strategy, which ultimately demonstrated 80.2% effectiveness and had a remarkable positive public health impact [14]. This experience underscores the profound value of maximizing coverage rapidly, even with a potentially suboptimal single dose, and provides a compelling case for the dedicated development of SSVs. The World Health Organization (WHO) recognized this imperative decades ago, identifying single-dose vaccine formulation as a goal for its Special Programme for Vaccine Development in the 1980s [0]. More recently, the COVID-19 pandemic has further illuminated the critical need for vaccines that can be deployed rapidly and widely with minimal logistical complexity, injecting new urgency and resources into the SSV field [0].

The scientific pursuit of effective single-shot vaccines hinges on the ability to replicate the immunological dynamics of a multi-dose schedule. A typical prime-boost regimen works by first "priming" the adaptive immune system and then providing one or more "boosts" to amplify and mature the response, leading to the generation of long-lived plasma cells and memory B and T cells. Achieving this robust and sustained immunity from a single administration requires sophisticated delivery platforms capable of controlling the spatio- temporal presentation of antigens to the immune system [0, 14]. This has led to extensive research into controlled-release technologies, primarily involving biodegradable polymers like poly(lactic-co-glycolic acid) (PLGA), lipid- and polymer-based nanoparticles, liposomes, in situ gelling systems, and microneedle patches [0, 12]. These platforms aim to either provide a sustained, low-level release of antigen over an extended period (mimicking multiple small boosts) or to deliver discrete, pulsatile antigen releases at predetermined intervals that align with the timing of a conventional multi-dose schedule [12]. The goal is to ensure that antigen-presenting cells (APCs) are exposed to the antigen in a manner that optimally stimulates both humoral (antibody-mediated) and cellular immunity. The integration of advanced technologies, particularly artificial intelligence (AI) and computational modeling, is now revolutionizing this field. AI-driven tools are being used for precise epitope identification, prediction of immunogenicity, optimization of antigen stability, and the design of controlled-release mechanisms, thereby accelerating and refining the entire vaccine development process [7]. This review will delve into the cutting-edge advancements in single-shot vaccine development, exploring the innovative delivery platforms, the transformative role of computational design, the promising preclinical and clinical candidates emerging for various diseases, and the critical translational challenges that must be navigated to bring these next-generation immunization tools from concept to global reality.

Mechanism

Single-shot vaccines utilize advanced delivery systems such as biodegradable polymers, microneedle patches, and viral vectors. These systems release antigens in a controlled manner, mimicking booster doses and stimulating long-lasting immune memory.

Figure 1: Patient compliance comparison between vaccine types



Examples of single shot vaccine

1. COVID-19 Vaccines

The Ad26.COV2.S vaccine (Johnson & Johnson/Janssen) was created as a single-dose COVID- 19 vaccine during the pandemic. Clinical trial data revealed around 66-67% efficacy against mild to severe COVID-19, as well as increased protection against hospitalization and death 28 days following immunization.

- Strong protection: Later studies reveal long-lasting humoral and cellular immunity, including neutralizing antibodies and T-cell responses, even against SARS-CoV-2 variations of concern.
- Real-world effectiveness: Large cohort studies conducted in the U.S. showed steady effectiveness of ~79% against infection and ~81% against hospitalization.

Despite these findings, booster doses provide even greater protection, prompting health- care providers to recommend more shots in a variety of situations.

2. Human Papillomavirus (HPV) Vaccine

Recent research reveals that a single dosage of HPV vaccine can provide equivalent protection (~97%) against cancer-linked HPV strains for at least five years, compared to the traditional two or three doses used to prevent HPV infection and cervical cancer.

Implementation of single-dose HPV vaccine could have a significant influence on world health, particularly in low-resource areas where several visits are difficult.

3 Chikungunya Vaccine Candidates

Phase 3 trials of a single-shot chikungunya virus vaccine (VLA1553) demonstrated safety and strong immunogenicity, triggering protective antibody responses in nearly all participants.

While definitive efficacy against disease remains under study due to low virus circulation in trial areas, the data indicate strong potential for single-shot protection.

Advantages of single shot vaccine

1. Rapid Population Coverage and Outbreak Control

The most significant mathematical advantage of a single-shot regimen is speed. In the context of a pandemic or a rapidly spreading outbreak, vaccinating two people with one dose each is epidemiologically more effective than vaccinating one person with two doses. It creates a wall of immunity twice as fast, reducing the transmission rate (R0) more quickly.

2. Improved Adherence and Completion Rates

Multi-dose regimens suffer from "attrition" or "drop-off." Patients often fail to return for the second dose due to forgetfulness, logistical hurdles, or a perceived lack of need after the first dose. A single-shot

vaccine guarantees that 100% of recipients complete the full vaccination schedule at the moment of administration.

3. Reduced Logistical and Economic Burden

Administering a vaccine twice doubles the operational costs. A single-shot regimen reduces the need for additional storage space, transportation (cold chain), medical supplies (syringes, needles), and healthcare worker hours. This is particularly critical in low- and middle-income countries (LMICs) where healthcare infrastructure is limited.

4. Simplified Implementation in Hard-to-Reach Populations

For marginalized populations—such as the homeless, migrant workers, or those living in remote rural areas—accessing a healthcare provider twice is difficult. A single-shot vaccine is ideal for "catch-up" campaigns and mobile vaccination units, allowing providers to administer a vaccine during a brief encounter without needing to track the patient for a follow-up.

Disadvantages

1. Lower Peak Immunogenicity (Antibody Titers)

The most significant disadvantage of a single-shot vaccine is that it generally elicits a lower peak immune response than a two-dose regimen.

The Mechanism: The "prime-boost" strategy uses the first dose (prime) to introduce the antigen to the immune system and the second dose (boost) to activate memory B-cells, driving them to produce high-affinity antibodies. A single shot relies on the persistence of the antigen (e.g., via a viral vector replicating) to mimic this effect, which often results in lower total antibody levels.

Real-World Example: Comparative studies found that neutralizing antibody levels in recipients of the single-dose Johnson & Johnson (Ad26.COV2.S) vaccine were significantly lower than those observed in recipients of two-dose mRNA vaccines.

2. Faster Waning Immunity (Durability Issues)

Single-shot vaccines tend to offer protection that wanes more rapidly over time compared to multi-dose vaccines.

The Mechanism: Without a booster shot to reinforce the memory cell pool, the concentration of circulating antibodies declines more steeply. This leaves individuals vulnerable to infection sooner after vaccination.

Real-World Example: Studies during the Delta and Omicron waves showed that the effectiveness of the single-dose Ad26.COV2.S vaccine against severe disease declined faster than that of two-dose vaccines, eventually necessitating a booster shot (effectively turning it into a multi-dose regimen).

3. Reduced Efficacy Against Variants

Single-shot regimens may provide a narrower breadth of immunity, making them less effective against mutated variants of a virus.

The Mechanism: The "affinity maturation" process—which allows antibodies to evolve and better recognize slightly different viral structures—is maximized by repeated exposure (boosting). A single exposure may lock the immune system into a response that is specific only to the original (wild-type) strain of the virus.

Real-World Example: During the prevalence of the Delta and Omicron variants, single-shot vaccine platforms showed a steeper drop in efficacy compared to platforms that utilized a boost, particularly regarding mild-to-moderate infection.

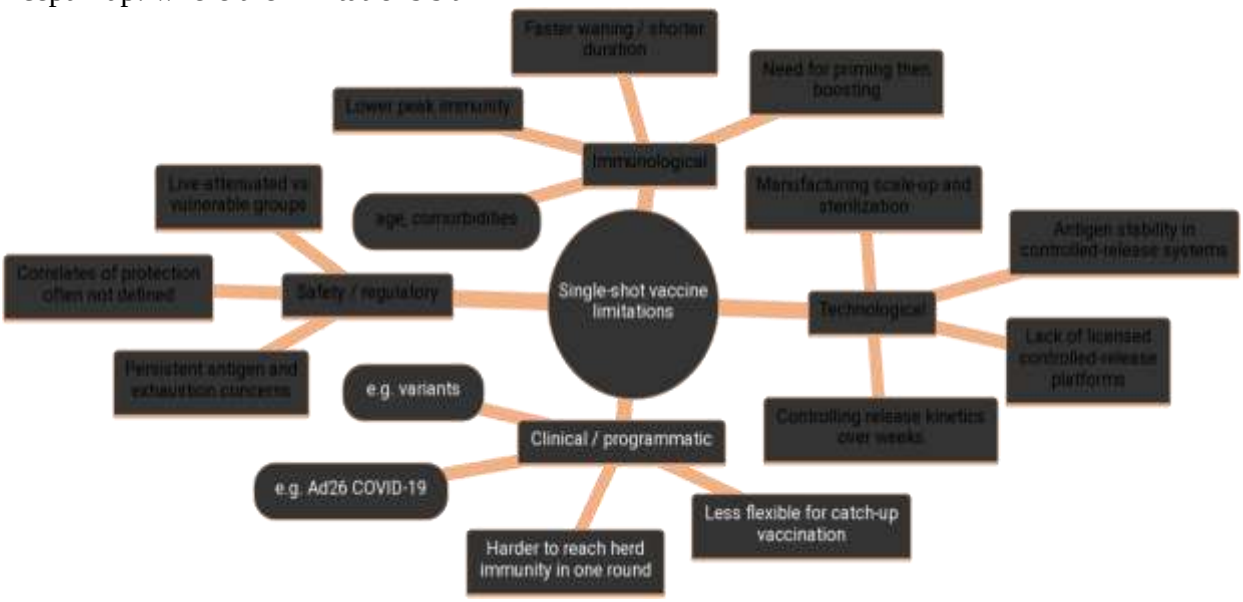
4. Limited Dose-Sparing Flexibility

In a pandemic, "dose-sparing" (using half-doses to vaccinate more people) is easier to implement in multi-dose regimens because the booster can be adjusted.

The Disadvantage: If a single-shot vaccine requires a full volume to be effective, it is less flexible. If the formula does not produce a strong enough immune response in a specific population (e.g., the immunocompromised), there is no scheduled follow-up to "fix" it, requiring clinicians to deviate from the standard protocol ad-hoc.

challenges and limitations of single-shot vaccines

1. Concept map: where the limitations sit



2. mmunological challenges and limitations

- Lower peak immune response and slower protection 1)multi-dose schedules are explicitly designed to:

-prime the immune system,
-then expand B- and T-cell memory through germinal-center reactions, maturation of antibody affinity, and generation of long-lived plasma cells and memory cells.
2)A single bolus often gives:
-lower antibody titers,
-lower T-cell responses and slower achievement of protective titers. Examples:

- Janssen Ad26.COV2.S (Johnson & Johnson) COVID-19 vaccine:

WHO reports that two doses (given 2 months apart) had about 94% efficacy in the US, while a single dose was about 72%.
Moreover, in the single-dose trial, efficacy against symptomatic disease had fallen to ~50% by two months after vaccination.
This clearly shows that a single shot provided only modest and rapidly waning protection compared with two doses.

- Inactivated influenza vaccine in children:

A randomized trial in children 3–8 years old compared:
one dose vs two doses of quadrivalent inactivated influenza vaccine (IIV4) in vaccine-unprimed children, vs one dose in vaccine-primed children.
Two doses in vaccine-unprimed children gave significantly higher seroprotection rates (SPR) than one dose:
approximately +4% SPR for H1N1, +6% for H3N2, +12% for BY (B/Victoria), and +11% for BV (B/Yamagata).
The authors concluded that two doses were needed for adequate protection, especially for influenza B strains.

3. Technological and formulation challenges (for “single-administration vaccines”)

Much of the modern work on single-dose vaccines focuses on converting multi-dose regimens into “single-administration vaccines” (SAVs) that control how antigen and adjuvant are released over time. This area faces major technical hurdles.

- Antigen stability during manufacturing and after injection

The Expert Review of Vaccines article on “Single administration vaccines” emphasizes:
Current vaccines often require multiple doses; missed doses lead to incomplete coverage and program failures.
There is growing interest in converting multi-dose vaccines into single-dose formats using pulsatile or

controlled-release formulations, but this is technically difficult.
Specific issues:
For poly(lactide-co-glycolide) (PLG/PLGA) microspheres, a leading controlled-release approach:
The encapsulation process can damage protein antigens:
Organic solvents, agitation, interfaces, and the acidic micro-environment during polymer degradation can cause unfolding, aggregation, and loss of conformational epitopes.
This impairs antigenicity and immunogenicity.
These problems have repeatedly limited translational success, even though animal data often looked promising.

4. Clinical and programmatic limitations

- Lower real-world effectiveness and need for boosters

Even when a single-shot vaccine is authorized, experience has often shown: Lower effectiveness in the field compared with two-dose regimens.
Need for boosters due to waning immunity and variants. Ad26.COV2.S COVID-19 again:
1 dose ≈ 72% initial efficacy vs ≈ 94% with two doses in US data; single-dose efficacy fell to ≈ 50% by two months.
This led to recommendations for a second dose and subsequent boosters, similar to other COVID-19 vaccines.
A review of COVID-19 vaccine effectiveness notes:
Single-shot Ad26-based vaccines could provide more durable immunity than some mRNA regimens, but they demonstrated lower protection and reduced antibody levels at peak compared with two-dose mRNA vaccines.
Emerging variants and waning immunity have driven authorities to recommend additional doses across multiple platforms.

5. Biological and Safety Limitations

- Risk of Immune Exhaustion: Platforms designed for prolonged antigen release (like viral vectors or controlled-release systems) may overstimulate the immune system, leading to T-cell exhaustion.
- Safety of Live Attenuated Vectors: Many effective single-dose platforms rely on live attenuated viruses, which pose safety risks to immunocompromised individuals (e.g., pregnant women, HIV patients).

Conclusion

Single-shot vaccines represent a promising evolution in vaccine technology. With continued research and development, they have the potential to significantly improve global vaccination strategies. The pandemic has unleashed imagination about the wonders and future possibilities of single-shot vaccines. Concepts like “one-and-done” capture the hope for time-efficient urgencies and contradictory connotations of haste. Amidst sociocultural complexities, a creative inquiry offers a fresh perspective on singular qualities.
History inspires scientists and healthcare communicators to articulate a single-shot strategy beyond “one.” Visual metaphors unite diverse ideas and complex scientific concepts into a seed. The captivating spark motivates vaccine exploration beyond efficacy, warranty, or safety. Instead, urgency compels attention to the single dose’s role in triggering cascade reactions within the immune system. (McGuire, 2021)

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