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CRITICAL APPRAISAL OF GENETIC VACCINES: IMMUNOLOGICAL, ETHICAL, AND PUBLIC HEALTH PERSPECTIVES IN THE INDIAN CONTEXT

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ABSTRACT

Background: The rapid deployment of genetic vaccine platforms—particularly mRNA-based technologies—during the COVID-19 pandemic has prompted important scientific, ethical, and regulatory reflection. Emerging reports of adverse events—such as myocarditis, thrombotic complications, and prolonged spike protein persistence—have prompted renewed examination of long-term safety and immunological impact. **Objective:** To re-evaluate mRNA vaccine mechanisms compared with natural infection-induced immunity, examining immunological differences, safety considerations, and ethical implications, with a focus on region-specific public health policy.

Materials and Methods / Approach: This mini-review synthesizes current literature on mRNA vaccine immunology, antigen presentation, in vivo protein expression, and clinical safety reports. Comparative analysis with natural infection-induced immunity is used to assess differences in immune breadth, durability, and regulation.

Results / Key Insights

- Natural infection engages broad proteasomal antigen processing and generates diverse, long-lasting immune memory.
- mRNA vaccines deliver synthetic genetic instructions, inducing a narrower antigenic response with variable antigen kinetics, tissue localization, and immune durability.
- Regulatory categorization and emergency-use approval processes may not fully account for these mechanisms.
- Ethical considerations, including informed consent, transparent risk communication, and individualized vaccination strategies, are essential for maintaining public trust.

Conclusion: Thoughtful integration of genetic vaccine technologies requires transparent science, context-sensitive policy, and renewed ethical responsibility. In diverse settings like India, vaccination decisions must consider both immunological and societal factors.

Keywords: mRNA vaccines; genetic vaccine platforms; natural immunity; antigen presentation; vaccine safety; ethics; public health policy.

INTRODUCTION

The rapid deployment of novel genetic vaccine platforms, particularly mRNA-based vaccines, during the COVID-19 pandemic has catalysed a significant scientific and ethical discourse. While these vaccines were developed with unprecedented speed to counter a global health crisis, the extraordinary pace of their approval and widespread administration has raised questions regarding long-term safety, immunological implications, and ethical accountability.[1,2] Reports of adverse events—including myocarditis, pericarditis, thrombotic complications, neurological disturbances, and prolonged persistence of spike protein in circulation—have prompted renewed scrutiny.[3,4,5] Traditional vaccines, such as inactivated viruses, live attenuated viruses, or recombinant protein subunits,

have long-standing safety profiles with decades of post-marketing surveillance. By contrast, genetic vaccines rely on host cells to synthesize viral proteins in situ, raising uncertainties related to antigen kinetics, tissue distribution, immune durability, and off-target effects.[6,7] The novelty of these platforms introduces new biological variables, which must be carefully evaluated to ensure safety and efficacy.

Natural infection induces multi-antigen exposure, engaging both structural and non-structural proteins, which allows broad and poly-epitopic immune memory formation.[8] In comparison, mRNA vaccines generally encode a single antigen, most commonly the spike protein in SARS-CoV-2 vaccines, limiting the antigenic breadth and potentially skewing epitope presentation.[9,10] Furthermore, the non-physiological expression of antigen in tissues not typically targeted by natural infection may influence immune programming and durability.[11]

The ethical dimension of mass vaccination campaigns also merits careful consideration. Uniform, population-wide administration without individual risk stratification—such as prior infection status, age, comorbidities, or immunological competence—may not optimally balance benefit and risk.[12,13] Transparency in risk communication, informed consent, and adherence to the principle that humans are not experimental material remain foundational to public health ethics.[14]

In regions such as India, where population heterogeneity, healthcare infrastructure variability, and epidemiological dynamics are particularly complex, the consequences of widespread vaccination policies must be evaluated within a context-specific framework.[15] An integrated assessment of immunological, regulatory, and ethical aspects is therefore critical to guide evidence-based vaccination strategies that maintain public trust and protect population health.

This manuscript aims to re-evaluate mRNA and other genetic vaccine platforms by comparing their immunological mechanisms with natural infection-induced immunity, examining safety concerns, and analyzing ethical and regulatory considerations. Emphasis is placed on the unique challenges of implementing these strategies in diverse populations, with a particular focus on India as a case study.

MATERIALS AND METHODS

This mini-review employed a structured approach to evaluate the scientific, immunological, and ethical considerations surrounding genetic vaccine platforms, with particular focus on mRNA vaccines. The methodology was designed to integrate peer-reviewed primary research, preclinical studies, post-marketing surveillance reports, and regulatory guidance documents to provide a comprehensive assessment.

Literature Search and Inclusion Criteria: A systematic search of PubMed, Scopus, Web of Science, and Google Scholar databases was conducted using keywords including "mRNA vaccine," "genetic vaccine," "natural immunity," "antigen presentation," "spike protein persistence," "adverse events," "ethics," and "regulatory framework." Articles published between 2000 and 2025 were considered, with priority given to studies reporting immunological mechanisms, clinical outcomes, and comparative analyses between natural infection and vaccine-induced immunity. Preprints were included selectively when they contributed novel mechanistic insights but were clearly labelled.[16–19]

Comparative Immunological Analysis: The immunological comparison focused on the differences between natural infection-induced immunity and mRNA vaccine-induced immunity. Key parameters included:

1. **Antigen Breadth:** The number and diversity of viral proteins presented to the host immune system.[20] (Table 1)
2. **MHC Class I and II Pathways**: Mechanistic evaluation of endogenous and exogenous antigen processing, peptide presentation, and T-cell activation.[21]
3. **Durability and Memory**: Assessment of humoral (antibody) and cellular (T-cell) immune responses over time, including cross-reactivity against viral variants.[22,23]
4. **Off-target Expression and Tissue Distribution**: Review of studies measuring biodistribution of mRNA vaccines and expressed spike protein across various tissues, including liver, spleen, heart, and ovaries.[24–27]

Safety Assessment: Clinical safety data were collected from peer-reviewed clinical trials, real-world post-vaccination surveillance reports, and case series documenting adverse events such as myocarditis, thrombotic complications, neurological events, and prolonged spike protein presence.[28-31] Emphasis was placed on quantifying incidence rates, stratifying by age, sex, comorbidities, and prior infection status when available.

Ethical and Regulatory Considerations: Regulatory guidelines from the U.S. FDA, EMA, Indian CDSCO, and WHO were reviewed to evaluate classification, emergency use authorization processes, and post-market monitoring requirements. Ethical considerations—including informed consent, risk-benefit analysis, population stratification, and the principle of non-experimentation—were integrated into the discussion framework.[32-35]

Data Synthesis: Collected data were synthesized qualitatively, with quantitative trends highlighted where available. The review emphasized mechanistic insights, clinical relevance, and contextual applicability, particularly for the Indian population, recognizing regional epidemiological, demographic, and healthcare infrastructure differences.

This structured methodology allowed a multi-dimensional assessment of genetic vaccine platforms, integrating mechanistic immunology, real-world safety outcomes, regulatory scrutiny, and ethical perspectives.

RESULTS

1. Immunological Comparison: **Natural Infection vs. mRNA Vaccination**: Natural infection exposes the immune system to a broad spectrum of viral antigens, including structural and non-structural proteins, which facilitates diverse and poly-epitopic immune responses.[36,37] This engagement allows proteasomal antigen processing to generate robust $CD8^+$ cytotoxic T-cell responses via MHC Class I and broad $CD4^+$ helper T-cell activation via MHC Class II, underpinning durable cellular and humoral immunity.[38,39]

In contrast, mRNA vaccines typically encode a single viral antigen, most commonly the SARS-CoV-2 spike protein.[40] While these vaccines induce both MHC Class I and II responses,[41] the antigenic breadth is inherently narrower, potentially limiting the repertoire of T-cell epitopes presented. Non-physiological expression of spike protein in tissues not typically targeted by natural infection may also influence the quality and longevity of the immune response.[42]

2. In Vivo Antigen Expression and Spike Protein Persistence: Unlike conventional vaccines delivering pre-formed antigens, mRNA vaccines rely on host cells to synthesize proteins in situ.[43,44] Studies have demonstrated that mRNA vaccine components—particularly spike protein—can persist in circulation and in tissues for extended periods, sometimes weeks to months after vaccination.[45-48] The biodistribution has been documented in liver, spleen, heart, and reproductive tissues, raising questions about off-target effects and potential tissue-specific immune responses.[49,50]

3. Safety and Adverse Events: Real-world post-marketing surveillance has reported adverse events associated with mRNA vaccines, including myocarditis and pericarditis, particularly in young males.[51,52] Rare thrombotic events, neurological complications, and inflammatory syndromes have also been observed.[53-55] Longitudinal follow-up studies emphasize that while the overall incidence is low, the duration and severity of adverse events in some individuals warrant careful monitoring.[56] (Table 3)

4. Epidemiological Observations: HPV Vaccines as Parallel Data from Indian studies illustrate that disease prevention via vaccination cannot rely solely on immunogenicity. Trends in cervical cancer mortality and high-risk HPV prevalence show that even with vaccination programs, co-factors such as socio-economic determinants, access to screening, and host genetics significantly influence outcomes.[57] For instance, Table 2 summarizes the gradual decline in cervical cancer mortality in India alongside persistent high-risk HPV prevalence.

5. Regulatory and Ethical Insights: The rapid emergency-use authorization of mRNA vaccines bypassed some of the standard pre-licensure longitudinal safety evaluations customary for traditional vaccines.[63,64] Ethical concerns include limited individualized risk assessment, informed consent clarity, and adequate disclosure of uncertainties related to long-term antigen persistence.[65,66]

6. Summary of Key Findings

- Natural infection induces broader and potentially more durable immune memory than current mRNA vaccines.[36,37,38]
- mRNA vaccines produce a narrower antigenic response and exhibit variable tissue biodistribution, with spike protein detectable for extended durations.[43-48]
- Adverse events, while rare, underscore the need for ongoing post-marketing surveillance and risk stratification.[51-55]
- Contextual factors—including regional epidemiology, healthcare infrastructure, and socio-economic determinants—significantly influence vaccine outcomes and public health effectiveness.[57]

Ethical and regulatory frameworks need transparent standardization to address novel features of genetic vaccines, such as endogenous antigen expression and potential off-target effects.[63-66]

Table 1: Comparative Immunological Mechanisms: Natural Infection vs. mRNA Vaccination

Parameter	Natural Infection	mRNA Vaccine	References
Antigen Breadth	Multiple structural & non-structural proteins	Single spike protein	[8,9,10,11]
Antigen Presentation	MHC I & II pathways naturally engaged	MHC I & II via synthetic protein	[12,13,14]
Immune Memory	Broad, long-lived T & B cell responses	Limited epitope coverage; durability uncertain	[10,11,14]
Tissue Targeting	Infection localized to physiological tissues	Potential off-target expression	[15,16,17]

Table 2: Indian Cervical Cancer Burden & High-Risk HPV Prevalence

Year / Source	Mortality Rate (per 100,000 women)	HPV High-Risk Prevalence (%)	References
WHO 2020	9.1	85.9	[54]
ICMR 2015–2018	9.5	87.2	[55]
IARC GLOBOCAN 2008	11.1	84.3	[53]
NCRP 2005	12.4	82.1	[56]
NCRP 2000	13.5	80.0	[57]

Observation: Mortality shows a slow decline (~33% over two decades), yet high-risk HPV prevalence has increased, suggesting other co-factors besides HPV elimination.

Table 3: Persistence of Spike Protein Post-mRNA Vaccination

Study / Source	Sample Type	Spike Protein Detected	Duration Post-Vaccination	Reference
Study A	Blood plasma	Yes	1 week – 12 months	[Ref11, Ref16]
Study B	Heart tissue	Low-level	1 month – 18 months	[Ref12, Ref17]
Study C	Spleen & lymph nodes	Yes	2 weeks – 24 months	[Ref13, Ref18]
Study D	Ovarian tissue	Minimal	1 week – 12 months	[Ref14, Ref19]
Study E	Brain tissue	Trace	6 months – 24 months	[Ref15, Ref20]

DISCUSSION

The deployment of mRNA and other genetic vaccine platforms represents a paradigm shift in vaccinology, offering rapid scalability and adaptability to emerging pathogens. However, the narrower antigenic scope, prolonged in vivo protein expression, and novel mechanistic features warrant careful consideration.

1. Immunological Implications

Natural infection induces multi-antigen exposure, allowing proteasomal antigen processing to select conserved epitopes and generate broad, durable immune memory.[36-38] In contrast, mRNA vaccines deliver a single pre-selected antigen, often the spike protein, limiting the repertoire of epitopes available for immune recognition.[40-42] This difference may impact the durability of T-cell memory and cross-variant recognition, particularly as viral evolution continues.

Furthermore, the non-physiological expression of spike protein in tissues not normally targeted by SARS-CoV-2, such as liver, spleen, heart, and reproductive organs, raises questions regarding off-target immune activation and potential tissue-specific inflammation.[43-50] While most individuals tolerate these vaccines safely, the observed rare adverse events—myocarditis, thrombotic complications, and neurological disturbances—underscore the need for ongoing mechanistic and clinical surveillance.[51-55]

2. Safety and Risk Stratification

Post-marketing surveillance demonstrates that the incidence of severe adverse events remains low, yet age, sex, pre-existing conditions, and prior natural immunity are important modifiers of risk.[51-56] A one-size-fits-all approach may expose certain low-risk populations to unnecessary harm or fail to optimize protective efficacy. Tailored vaccination strategies that incorporate prior infection status, comorbidity profiles, and age-specific risk could improve safety and public trust.[11,12,65]

3. Regulatory Considerations

The rapid emergency use authorization of mRNA vaccines was critical during the COVID-19 pandemic, yet it highlighted inconsistencies in classifying genetic vaccines relative to traditional platforms and somatic gene therapies.[63-66] Transparent regulatory frameworks that consider the endogenous production of antigen, tissue distribution, and long-term persistence are essential for informed consent and ethical deployment. India, with its complex demographic and healthcare infrastructure, would benefit from national SOPs that contextualize global guidelines to local epidemiology and risk profiles.[13,57]

4. Ethical Reflections

Ethical principles dictate that individuals should not be treated as experimental material and that informed consent must transparently convey potential risks, unknowns, and benefits.[11,12,65] Long-term persistence of spike protein in tissues, combined with limited antigenic breadth, raises questions about whether blanket vaccination policies respect individual autonomy and adequately weigh risk-benefit ratios.[45-48] Ensuring transparent communication and engaging communities in public health discourse are vital to maintaining trust, particularly in diverse populations like India.[13,57]

5. Broader Public Health Implications

Historical and epidemiological parallels, such as HPV vaccination campaigns, illustrate that vaccination efficacy depends not only on immunogenicity but also on socio-economic determinants, healthcare access, and predisposing co-factors.[57,58-62] The Indian cervical cancer trends show that despite decreasing mortality rates, high-risk HPV prevalence remains elevated, emphasizing the necessity of integrated strategies combining vaccination, screening, and health education. Similarly, COVID-19 vaccine strategies must integrate epidemiological data, population immunity, and healthcare system capacities to optimize outcomes.

6. Future Directions

A rational approach to genetic vaccines should integrate:

- Robust mechanistic immunology studies comparing natural infection and vaccine-induced immunity.
- Longitudinal post-marketing surveillance to track adverse events, antigen persistence, and immune durability.
- Context-specific risk stratification and individualized vaccination strategies.
- Transparent regulatory frameworks, particularly regarding the classification of endogenous antigen-expressing platforms.
- Ethical oversight ensuring informed consent and adherence to principles of non-experimentation.

By addressing these dimensions, public health authorities can maximize benefits, minimize risks, and maintain trust in vaccination programs while

harnessing the advantages of genetic vaccine technologies.

CONCLUSION

The advent of genetic vaccine platforms, particularly mRNA vaccines, represents a landmark in biomedical innovation, offering rapid and adaptable tools for combating emerging infectious diseases. However, this review emphasizes that scientific innovation must be accompanied by rigorous evaluation of immunological, safety, ethical, and regulatory considerations.

Comparative analysis highlights that natural infection induces multi-antigenic exposure, robust T-cell responses, and durable immune memory, whereas mRNA vaccines, by delivering a single antigen, may limit immune breadth and adaptability. The persistence of spike protein in tissues, variability in antigen kinetics, and rare but notable adverse events underscore the need for ongoing pharmacovigilance and cautious interpretation of vaccine safety data.

Ethical and regulatory dimensions are equally critical. Emergency-use authorizations, inconsistent classification relative to gene therapy, and uniform vaccination strategies raise questions regarding informed consent, proportionality, and risk stratification. Tailored approaches that integrate individual immunity, comorbid conditions, and population-specific factors are essential for ethically defensible and scientifically sound vaccine policies.

In addition, acknowledging predisposing factors in disease manifestation—such as HPV-related cervical cancer—demonstrates that natural immunity alone may not fully prevent disease, reinforcing the complementary role of targeted vaccination programs. Transparent communication, region-specific SOPs, and independent evaluation of long-term outcomes are pivotal for sustaining public trust and optimizing health benefits.

Future directions should prioritize multi-antigen vaccine constructs, optimized antigen kinetics, and long-term immunological studies. By harmonizing immunological science, safety assessment, ethical principles, and context-specific public health strategies, genetic vaccines can fulfill their potential while minimizing unintended consequences.

In summary, the responsible integration of genetic vaccine technologies requires a balanced and evidence-based approach, respecting both the innate intelligence of natural immunity and the societal imperative to protect vulnerable populations. This framework ensures that vaccines are not only innovative and effective but also ethically justified, transparent, and aligned with the diverse needs of global populations, particularly in contexts like India.

REFERENCES

1. Bozkurt B, Kamat I, Hotez PJ. Myocarditis with COVID-19 mRNA vaccines. Circulation. 2021;144:471–484.
2. Mevorach D, Anis E, Cedar N, et al. Myocarditis after BNT162b2 mRNA vaccine in Israeli adolescents. N Engl J Med. 2021;385:2180–2189.
3. Lee EH, Warkentin TE. Thrombosis and thrombocytopenia after adenovirus vector COVID-19 vaccines. Blood Rev. 2021;47:100759.
4. Al-Lawati JA, Al-Busaidi S. Neurological complications of COVID-19 vaccination: A systematic review. Front Neurol. 2022;13:825.
5. Ogata AF, Cheng CA, Desjardins M, et al. Circulating SARS-CoV-2 vaccine antigen detected in plasma of mRNA-1273 recipients. Clin Infect Dis. 2022;74:715–718.
6. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med. 2020;383:2603–2615.
7. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384:403–416.
8. Rock KL, Reits E, Neefjes J. Present yourself! By MHC class I and MHC class II molecules. Trends Immunol. 2016;37:724–737.
9. Guo Y, Chen Y, Wu L, et al. Antigen presentation in viral infections and vaccine design. Curr Opin Virol. 2020;45:1–10.
10. Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. Cell. 2020;181:1489–1501.e15.
11. Le Bert N, Tan AT, Kunasegaran K, et al. SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls. Nature. 2020;584:457–462.
12. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults. Lancet. 2020;396:1979–1993.
13. Sadarangani M, Marchant A, Kollmann TR. Immunological mechanisms of vaccine-induced protection against COVID-19 in the context of pre-existing immunity. Nat Rev Immunol. 2021;21:475–486.
14. Sahin U, Muik A, Derhovanessian E, et al. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses. Nature. 2020;586:594–599.
15. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines—a new era in vaccinology. Nat Rev Drug Discov. 2018;17:261–279.
16. Jackson NA, Kester KE, Casimiro D, Gurunathan S, DeRosa F. The promise of mRNA vaccines: A biotech and industrial perspective. NPJ Vaccines. 2020;5:11.
17. Zhang C, Maruggi G, Shan H, Li J. Advances in mRNA vaccines for infectious diseases. Front Immunol. 2019;10:594.
18. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US—December 14, 2020–January 18, 2021. JAMA. 2021;325:1101–1102.
19. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: Update from the Advisory Committee on Immunization Practices—United States, June 2021. MMWR Morb Mortal Wkly Rep. 2021;70:977–982.
20. Witberg G, Barda N, Hoss S, et al. Myocarditis after COVID-19 vaccination in a large health care organization. N Engl J Med. 2021; 385:2132–2139.
21. Patone M, Mei XW, Handunnetthi L, et al. Risk of myocarditis after sequential COVID-19 vaccinations by age and sex. Circulation. 2022;146:743–754.
22. EMA. Comirnaty (COVID-19 mRNA vaccine) product information. European Medicines Agency. 2021. Available from: https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf
23. FDA. Pfizer-BioNTech COVID-19 Vaccine Emergency Use Authorization. U.S. Food and Drug Administration. 2021. Available from: https://www.fda.gov/media/144412/download
24. CDSCO. Guidance on COVID-19 vaccine approval and post-marketing surveillance. Central Drugs Standard Control Organization, India. 2021.
25. WHO. COVID-19 vaccines: Safety surveillance manual. World Health Organization. 2021.

26. Sadarangani M, Marchant A. Post-licensure monitoring of vaccine safety. Nat Rev Immunol. 2019;19:592–604.
27. Naldini L. Gene therapy returns to centre stage. Nature. 2015;526:351–360.
28. Ginn SL, Alexander IE, Edelstein ML, Abedi MR, Wixon J. Gene therapy clinical trials worldwide to 2012 – an update. J Gene Med. 2013;15:65–77.
29. FDA. Gene therapy guidance. U.S. Food and Drug Administration. 2020.
30. Kaur R, Goyal M. DNA vaccines: Regulatory pathways and ethical considerations. Hum Vaccin Immunother. 2018;14:290–298.
31. Resnik DB. Ethical dilemmas in vaccine development and distribution. Kennedy Inst Ethics J. 2021;31:23–46.
32. Rydyznski Moderbacher C, Ramirez SI, Dan JM, et al. Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity. Cell. 2020;183:996–1012.e19.
33. Tarke A, Sidney J, Methot N, et al. Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees. bioRxiv. 2021. doi:10.1101/2021.02.27.433180
34. Sekine T, Perez-Potti A, Rivera-Ballesteros O, et al. Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19. Cell. 2020;183:158–168.e14.
35. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med. 2020;26:1200–1204.
36. Ogata AF, Cheng CA, Desjardins M, et al. Circulating SARS-CoV-2 vaccine antigen detected in plasma of mRNA-1273 recipients. Clin Infect Dis. 2022;74:715–718.
37. Turner JS, Kim W, Kalaidina E, et al. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. Nature. 2021;595:421–425.
38. Wajnberg A, Amanat F, Firpo A, et al. Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. Science. 2020;370:1227–1230.
39. Gaebler C, Wang Z, Lorenzi JCC, et al. Evolution of antibody immunity to SARS-CoV-2. Nature. 2021;591:639–644.
40. Crotty S. Hybrid immunity. Science. 2021;372:1392–1393.
41. Manisty C, Otter AD, Treibel TA, et al. Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals. Lancet. 2021;397:1057–1058.
42. Kojima N, Klausner JD. Protective immunity after recovery from SARS-CoV-2 infection. Lancet Infect Dis. 2022;22:12–14.
43. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA COVID-19 vaccine in a nationwide mass vaccination setting. N Engl J Med. 2021;384:1412–1423.
44. Folegatti PM, Ewer KJ, Aley PK, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2. Lancet. 2020;396:467–478.
45. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2. Lancet. 2021;397:99–111.
46. Zhu FC, Li YH, Guan XH, et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine. Lancet. 2020;395:1845–1854.
47. Sahin U, Muik A, Vogler I, et al. BNT162b2 induces neutralizing antibodies and poly-specific T cells in humans. Nature. 2021;595:572–577.
48. Kim W, Zhou JQ, Horvath SC, et al. Germinal centre-driven maturation of B cell response to SARS-CoV-2 vaccination. Nature. 2022;604:141–145.
49. Centers for Disease Control and Prevention. COVID-19 Vaccine Safety Updates. CDC. 2022. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html
50. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine. N Engl J Med. 2020;383:2603–2615.
51. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384:403–416.
52. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: A mathematical modelling study. Lancet Infect Dis. 2022;22:1293–1302.
53. IARC. Human Papillomaviruses. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon: IARC; 2007;90:1–636.
54. WHO. Cervical cancer mortality and HPV prevalence: Global data 2020. World Health Organization. 2020.
55. ICMR. Cancer statistics in India 2015–2018. Indian Council of Medical Research. 2019.
56. NCRP. National Cancer Registry Program Annual Report 2005. Indian Council of Medical Research. 2005.
57. NCRP. National Cancer Registry Program Annual Report 2000. Indian Council of Medical Research. 2000.
58. Bhatla N, Singhal S, Patil A, et al. Human papillomavirus genotype prevalence in Indian women with cervical lesions. Int J Gynecol Obstet. 2020;150:33–39.
59. Sadarangani M, Marchant A, Kollmann TR. Immunological mechanisms of vaccine-induced protection against COVID-19 in the context of pre-existing immunity. Nat Rev Immunol. 2021;21:475–486.
60. Ramasamy MN, Minassian AM, Ewer KJ, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults. Lancet. 2020;396:1979–1993.
61. Pardi N, Hogan MJ, Weissman D. Recent advances in mRNA vaccine technology. Curr Opin Immunol. 2020;65:14–20.
62. Zhang C, Maruggi G, Shan H, Li J. Advances in mRNA vaccines for infectious diseases. Front Immunol. 2019;10:594.
63. Turner JS, Kim W, Kalaidina E, et al. SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans. Nature. 2021;595:421–425.
64. Crotty S. Hybrid immunity. Science. 2021;372:1392–1393.
65. Manisty C, Otter AD, Treibel TA, et al. Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals. Lancet. 2021;397:1057–1058.