

Literature Review:
Mucosal Immunity/Intranasal Vaccine Administration for SARS-CoV-2

CONTENT:

SARS-CoV-2

1. Key studies on mucosal immunity post intramuscular SARS-CoV-2 vaccination
2. Key studies on natural mucosal immunity to SARS-CoV-2
3. Ongoing studies for intranasal SARS-CoV-2 vaccines
 - a. Preclinical studies
 - b. Clinical trials
4. Approved SARS-CoV-2 intramuscular vaccines under consideration for intranasal administration

Other Diseases

5. Existing mucosal-immunisation strategies for other diseases
6. Pre-clinical studies for mucosal-immunisation strategies for other diseases

SARS-CoV-2

1. Key studies on mucosal immunity post intramuscular SARS-CoV-2 vaccination

i. Study: Preprint on mucosal antibody response to mRNA SARS-CoV-2 vaccination induced in previously infected individuals

<https://www.medrxiv.org/content/10.1101/2021.12.06.21267352v1>

Findings: Vaccination induced only a weak mucosal SIgA response in individuals without pre-existing mucosal antibody responses to SARS-CoV-2 while SIgA induction after vaccination was efficient in COVID-19 survivors.

ii. Study: Paper on mucosal immunity response in Pfizer COVID-19 vaccine recipients

[https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964\(21\)00582-X/fulltext](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00582-X/fulltext)

Findings: The Pfizer vaccination elicits a strong systemic immune response by drastically boosting neutralizing antibodies development in serum, but not in saliva. This suggests that at least oral mucosal immunity is poorly activated by this vaccination protocol, therefore failing in limiting virus acquisition upon entry through the respiratory tract.

iii. Study: Paper on immune responses in fully vaccinated individuals following breakthrough infection with the SARS-CoV-2 delta variant

<https://www.science.org/doi/full/10.1126/scitranslmed.abn6150>

Findings: Individuals vaccinated with either Pfizer, Moderna or J&J lacked IgA/IgG mucosal immunity. Mucosal immunity is substantially gained only after a jabbed person has a natural infection.

iv. Study: Personal view on the prevention of host-to-host transmission by SARS-CoV-2 vaccines

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00472-2/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00472-2/fulltext)

Findings: Since SARS-CoV-2 can infect the oral epithelial cells, generating antibody and cellular immunity within the oral mucosa could effectively block viral transmission at the source.

2. Key studies on natural mucosal immunity to SARS-CoV-2

i. Study: Review of mucosal immunity to SARS-CoV-2

<https://pubmed.ncbi.nlm.nih.gov/33899752/>

Findings: Mucosal immune responses in the respiratory tract play a key role in the early restriction of viral replication and the clearance of SARS-CoV-2.

ii. Study: Paper on IgA dominating the early neutralizing antibody response to SARS-CoV-2

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7857408/>

Findings: These findings suggest that IgA-mediated mucosal immunity may be a critical defence mechanism against SARS-CoV-2 at the individual level that may reduce infectivity of human secretions and consequently viral transmission as well. This finding may also inform the development of vaccines that induce specific respiratory IgA responses to SARS-CoV-2.

iii. Study: Paper on longitudinal systemic and mucosal immune responses to SARS-CoV-2 Infection

<https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiac065/6533756?login=false>

Findings: SARS-CoV-2 proved highly effective at inducing mucosal IgA in the respiratory tract. The induction of mucosal IgA, which is locally produced and can uniquely transcytose across the epithelial cell barrier, can be postulated to be critical in the inactivation of viruses like SARS-CoV-2 that replicate primarily in the respiratory tract and must be a target for vaccine-induced immunity

iv. Study: Paper on persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients

<https://www.science.org/doi/10.1126/sciimmunol.abe5511>

Findings: The data shows that a durable IgG response against SARS-CoV-2 antigens is generated in both the saliva and serum in most patients with COVID-19. Of the three isotypes measured, the IgA response correlates the least between serum and saliva, particularly for the RBD antigen. This may suggest some compartmentalization of the IgA response in the oral cavity versus the periphery.

v. Study: Paper on how systemic and mucosal immune profiling in asymptomatic and symptomatic SARS-CoV-2-infected individuals reveal unlinked immune signatures

<https://www.science.org/doi/10.1126/sciadv.abi6533>

Findings: The data suggest independent evolution of antibody responses in the mucosal sites as reflected in differential IgM/IgG/IgA epitope repertoire compared with serum. Antibody affinity against SARS-CoV-2 prefusion spike for both serum and nasal washes was significantly higher in asymptomatic adults compared with symptomatic COVID-19 patients. Last, the cytokine/chemokine responses in the nasal washes were more robust than in serum. These data underscore the importance of evaluating mucosal immune responses for better therapeutics and vaccines against SARS-CoV-2.

vi. Study: Preprint on mucosal antibody response to SARS-CoV-2 vaccination in previously infected individuals (*Florian Krammer*)

<https://www.medrxiv.org/content/10.1101/2021.12.06.21267352v1>

https://cdn.who.int/media/docs/default-source/blue-print/platforms_florian-krammer_whoconsultation_covid19framework_23feb2022.pdf?sfvrsn=f5a1e435_7 (explanatory slides)

Findings: The results showed that vaccination induced only a weak mucosal SIgA response in individuals without pre-existing mucosal antibody responses to SARS-CoV-2 while SIgA induction after vaccination was efficient in COVID-19 survivors.

vii. Study: Preprint on SARS-CoV-2 Omicron being specifically restricted in its replication in human lung tissue, compared to other variants of concern

<https://www.biorxiv.org/content/10.1101/2022.03.31.486531v1>

Findings: The susceptibility of the nasal viral entry site to Omicron may support person-to-person transmission, whereas its restricted replication in the lungs could contribute to the milder clinical course of Omicron. An augmented mucosal innate immune response to Omicron could capture the virus at the upper respiratory tract and limit viral infection and pathology in the lungs.

Viii. Study: Paper on a longitudinal study of Mucosal Antibody Response to SARS-CoV-2 in Paediatric and Adult Patients: A Longitudinal Study

<https://www.mdpi.com/2076-0817/11/4/397>

Findings: Early and intense nasal S1-specific IgA levels link to a rapid decrease in viral load. These results provide insights into the role of mucosal immunity in SARS-CoV-2 exposure and protection.

3. Intranasal Vaccine Administration for SARS-CoV-2

This paper in The Lancet provides a review of the current status of Intranasal COVID-19 vaccines: [https://www.thelancet.com/pdfs/journals/ebiom/PIIS2352-3964\(22\)00025-1.pdf](https://www.thelancet.com/pdfs/journals/ebiom/PIIS2352-3964(22)00025-1.pdf)

a. Pre-clinical studies

i. Study: Paper on protective mucosal immunity against SARS-CoV-2 after nasal booster

<https://www.nature.com/articles/s41467-021-27063-4>

Findings: In contrast to two intramuscular applications of an mRNA vaccine, intranasal boosts with adenoviral vectors induce high levels of mucosal IgA and lung-resident memory T cells (TRM); mucosal neutralization of virus variants of concern is also enhanced.

ii. Study: Paper on ChAdOx1 nCoV-19 (IM & IN) vaccine candidate significantly reducing SARS-CoV-2 shedding in ferrets

<https://www.nature.com/articles/s41541-021-00315-6>

Findings: All ChAdOx1 nCoV-19 administration combinations resulted in significant reductions in viral loads in nasal-wash and oral swab samples. This study indicates the potential for intranasal administration as a way to further improve the efficacy of this vaccine candidate.

iii. Study: Paper on a single-dose intranasal ChAd-SARS-CoV-2-S vaccine protecting upper and lower respiratory tracts against SARS-CoV-2

[https://www.cell.com/cell/fulltext/S0092-8674\(20\)31068-0?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420310680%3Fshowall%3Dtrue#sectitle0010](https://www.cell.com/cell/fulltext/S0092-8674(20)31068-0?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420310680%3Fshowall%3Dtrue#sectitle0010)

Findings: A single intranasal dose of ChAd-SARS-CoV-2-S induces high levels of neutralizing antibodies, promotes systemic and mucosal immunoglobulin A (IgA) and T cell responses, and almost entirely prevents SARS-CoV-2 infection in both the upper and lower respiratory tracts.

iv. Study: Paper on SARS-CoV-2 nucleocapsid protein intranasal inoculation induces local and systemic T cell responses in mice

<https://pubmed.ncbi.nlm.nih.gov/33386773/>

Findings: This paper suggests that SARS-CoV-2 N vaccination might have certain unique advantage(s) over previously described coronavirus N proteins, especially through intranasal inoculation.

v. Study: Paper on intranasal ChAdOx1 nCoV-19 vaccination reducing viral shedding after SARS-CoV-2 Delta variant

<https://pubmed.ncbi.nlm.nih.gov/34315826/>

Findings: Intranasal vaccination with ChAdOx1 nCoV-19/AZD1222 reduced virus concentrations in nasal swabs in two different SARS-CoV-2 animal models, warranting further investigation as a potential vaccination route for COVID-19 vaccines.

vi. Study: Paper on intranasal ChAd-SARS-CoV-2-S vaccine durably protects against SARS-CoV-2 variants in mice

<https://pubmed.ncbi.nlm.nih.gov/34289385/>

Findings: In mice, intranasal immunization with ChAd-SARS-CoV-2-S provides durable protection against historical and emerging SARS-CoV-2 strains.

vii. Study: Paper on a single intranasal dose of chimpanzee adenovirus-vectored vaccine protecting against SARS-CoV-2 infection in rhesus macaques

<https://pubmed.ncbi.nlm.nih.gov/33754147/>

Findings: A single intranasal dose of ChAd-SARS-CoV-2-S induces neutralizing antibodies and T cell responses and limits or prevents infection in the upper and lower respiratory tracts after SARS-CoV-2 challenge.

viii. Study: Preprint on unadjuvanted intranasal spike vaccine booster elicits robust protective mucosal immunity against sarbecovirus (*Yale University - led by Akiko Iwasaki*)

<https://www.biorxiv.org/content/10.1101/2022.01.24.477597v1>

<https://medicine.yale.edu/news-article/nasal-approach-to-covid-vaccination-gains-traction-at-yale/> (Press-release)

https://cdn.who.int/media/docs/default-source/blue-print/composition_akiko-iwasaki_whoconsultation_covid19framework_23feb2022.pdf?sfvrsn=e928d86b_7 (explanatory slides)

Findings: The study demonstrated that Prime and Spike significantly reduced the viral load in the nasal cavity and the lung compared to injected vaccine alone, indicating the promise of Prime and Spike in reducing infection and transmission.

ix. Press-release: eTherNA Launches an International Consortium and Starts Development of Cross-strain Protective CoV-2 mRNA Vaccine for High Risk Populations (24/03/2020)
<https://www.etherna.be/news-archive2020/#24march2020>

x. Study: Preprint on inhalable polymer nanoparticles for versatile mRNA delivery and mucosal vaccination
<https://pubmed.ncbi.nlm.nih.gov/35350207/>

Findings: Mucosal vaccination with PACE-mRNA induced systemic and lung resident adaptive immunity and protected mice from a lethal viral challenge.

xi. Study: Paper on respiratory mucosal delivery of next-generation COVID-19 vaccine providing robust protection against both ancestral and variant strains of SARS-CoV-2 (McMaster University, Canada)
[https://www.cell.com/cell/fulltext/S0092-8674\(22\)00145-3](https://www.cell.com/cell/fulltext/S0092-8674(22)00145-3)

Findings: The findings indicate that respiratory mucosal delivery of Ad-vectored multivalent vaccine represents an effective next-generation COVID-19 vaccine strategy to induce all-around mucosal immunity against current and future VOC.

xii. Study: Preprint on an intranasal spray using a new found molecule (N-0385) with potential to both prevent and treat SARS-CoV-2 (Cornell University & University of Sherbrooke)
https://www.nature.com/articles/s41586-022-04661-w_reference.pdf (preprint)
<https://news.cornell.edu/stories/2022/03/promising-nose-spray-could-prevent-and-treat-covid-19> (press-release, with an explanatory video)

Findings: N-0385 was shown to protect mice from infection prior to exposure, while also providing effective treatment when administered up to 12 hours after exposure.

Xiii. Study: Preprint on Prime-pull immunization of mice with a BcfA-adjuvanted vaccine eliciting mucosal immunity and prevents SARS CoV-2 infection and pathology
<https://www.biorxiv.org/content/10.1101/2022.04.06.487394v1>

Findings: This research shows that systemic priming followed by a mucosal booster with a BcfA adjuvanted subunit vaccine provides sterilizing immunity against wildtype SARS CoV 2, and a variant of concern. Importantly, in contrast to alum alone, the addition of BcfA prevents respiratory pathology. These results suggest that a BcfA-adjuvanted mucosal booster may elicit mucosal immunity in individuals previously immunized systemically with approved vaccines.

Xiv. Study: (1) Paper on protection against SARS-CoV-2 infection by a mucosal vaccine in rhesus monkeys

(2) Preprint on an intranasally administered SARS-CoV-2 beta variant subunit booster vaccine

(1) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8262352/>

(2) <https://www.biorxiv.org/content/10.1101/2021.10.19.464990v1.full>

Findings: (1) This study compared the protective efficacy of 2 adjuvanted subunit vaccines with spike protein S1: an intramuscularly primed/booster vaccine and an intramuscularly primed/intranasally boost mucosal vaccine in rhesus macaques. Following SARS-CoV-2 challenge, neither group showed detectable subgenomic RNA in upper or lower respiratory tracts versus naive controls, indicating full protection against viral replication. Furthermore,

the mucosal vaccine seems more efficient at rapidly clearing the input virus (gRNA) in the upper respiratory tract than the systemic counterpart, providing a potent strategy to prevent viral transmission. **(2)** This study assessed the protective efficacy of an intranasal booster composed of beta variant-spike protein S1 with IL-15 and TLR agonists in previously immunized macaques. The macaques were first vaccinated with Wuhan strain S1 with the same adjuvant. One year later, negligibly detectable SARS-CoV-2-specific antibody remained. Nevertheless, the booster induced vigorous humoral immunity including serum- and bronchoalveolar lavage (BAL)-IgG, secretory nasal- and BAL-IgA, and neutralizing antibody against the original strain and/or beta variant. Following SARS-CoV-2 beta variant challenge, the vaccinated group demonstrated significant protection against viral replication in the upper and lower respiratory tracts, with almost full protection in the nasal cavity.

b. Clinical trials

A list of 12 registered clinical trials (as of January 2022) for IN SARS-CoV-2 vaccines can be found here:

<https://clinicaltrials.gov/ct2/results?cond=COVID-19&term=vaccine%2C+intranasal+vaccine&cntry=&state=&city=&dist=&Search=Search>

This is a helpful SARS-CoV-2 vaccine tracker: <https://covid19.trackvaccines.org/vaccines/>

The following clinical trial results have been published:

COVI-LIV [*Previously called COVI-VAC*] (Codagenix)

[Codagenix Intranasal COVID-19 Vaccine Shows Potent Cellular Immune Response Against Conserved Viral Proteins, Indicating Potential for Immunogenicity Against Omicron and Future Variants in Phase 1 Data^{\[PDF\]} | Codagenix](#) (Phase 1 press release)

- A live attenuated vaccine
- CoviLiv induced strong cellular immune response in healthy adults against many conserved proteins in known variants of SARS-CoV-2, in particular, a peptide pool >99% Omicron BA.2. Spike protein focused vaccines have shown lower protection against viral mutants.
- Unlike other spike-only vaccine approaches that may need to re-formulate as COVID evolves, this interim Phase 1 CoviLiv data demonstrates the classic benefits of a live-attenuated vaccine: broad immunity without the need for re-formulation.
- CoviLiv also induced a mucosal antibody response and blocked nasal replication, suggesting it may be the only vaccine candidate with the potential to reduce viral transmission.

NDV-HXP-S (Laboratorio Avi-Mex) [Florian Krammer]

<https://pubmed.ncbi.nlm.nih.gov/35169806/> (Phase 1 preprint)

- In the interim analysis reported here, the vaccine was found to be safe and the higher doses tested were found to be immunogenic when given intramuscularly or intranasally followed by intramuscular administration, providing the basis for further clinical development of the vaccine candidate.

<https://www.medrxiv.org/content/10.1101/2022.01.25.22269808v1> (Phase 1 preprint-intramuscular)

- This vaccine uses an engineered version of the harmless Newcastle disease virus studded with coronavirus spike proteins to teach the immune system to recognize and attack the virus that causes SARS-CoV-2.
- Researchers found that NDV-HXP-S induces proportionally more antibodies that can neutralize the virus and fewer non-neutralizing antibodies than the current mRNA vaccines from Moderna or Pfizer.

Razi Cov Pars (Razi Vaccine and Serum Research Institute) [granted Emergency Use Authorisation in Iran on 31/10/21]

- Undergoing Phase 3 trials
- The vaccine contains fragments of coronavirus spike proteins and is delivered in three doses: two injections and one nasal spray.
- The Tehran Times reported on 12 October 2021 that a nasal dose of the vaccine reduces the transmission of the virus by as much as 90 percent.
<https://www.tehrantimes.com/news/465937/Nasal-dose-of-COV-Pars-reduces-virus-transmission-by-90>

Ad5-nCoV (CanSino/Beijing Institute of Biotechnology)

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00396-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00396-0/fulltext) (Phase 1 paper)

- A nasal dose equal to a fifth of the usual injected dose induced antibody and cellular immune responses.
- Although RBD-binding IgG and IgA concentrations at day 28 after two nasal doses were lower than those at day 28 after one injected dose, SARS-CoV-2 neutralising antibody titres in the aerosol vaccination groups were similar to those in patients who received an intramuscular injection.
- This finding suggests that the different vaccination routes produce different antibody compositions, and that nasal vaccination could trigger a higher ratio of neutralising antibodies to total antibodies than intramuscular vaccination.
- A paper on Ad5-nCoV preclinical study can be found here:
<https://www.nature.com/articles/s41467-020-17972-1>

BBV154 (Bharat Biotech) - [This is ChAd-SARS-CoV-2-S developed by Washington University School of Medicine]

<https://www.bharatbiotech.com/intranasal-vaccine.html> (Study website)

- Due to undertake two different Phase III trials - one to study an intranasal booster dose following 2 IM doses of either Covishield or Covaxin, and another to study the nasal as a heterologous second dose with Covishield/Covaxin.
<https://www.clinicaltrialsarena.com/news/bharat-biotech-to-start-phase-iii-intranasal-covid-19-booster-trial/> (news article)
- <https://www.youtube.com/watch?v=6rX8YCjA1GE> (interview with Chairperson of Bharat Biotech)

pHOXWELL (pHOXBIO Ltd., London)

<https://www.qmul.ac.uk/media/news/2021/smd/queen-mary-researchers-help-develop-nasal-spray-that-prevents-covid-19.html>

- A novel prophylactic nasal spray

- Phase II/III results showed 13.1 per cent of those receiving the spray tested positive for SARS-CoV-2, significantly less than the 34.5 per cent who received the placebo treatment.
- pHOXBIO said that its self-administered prophylactic nasal spray is designed to offer a robust, variant-agnostic mechanism of action and that it provides six to eight hours of protection with two sprays per nostril.

AdCOVID (Altimune) [Discontinued]

Phase 1 announcement (29/06/2021)

<https://ir.altimmune.com/news-releases/news-release-details/altimmune-announces-update-adcovidtm-phase-1-clinical-trial>

- AdCOVID was well tolerated but did not stimulate an adequate immune response in healthy volunteers
- Altimune discontinued further development of AdCOVID

[In the pipeline] IN mRNA vaccine

eTheRNA announced in 2020 that a consortium had been formed with North American and European partners to develop a novel mRNA vaccine against CoV-2 to be administered intranasally and preclinical development had started. No updates shared since then.

<https://epivax.com/news/press-release-etherna-consortium-cov-2-mrna-vaccine-for-high-risk-populations>

4. Approved SARS-CoV-2 intramuscular vaccines under consideration for intranasal administration

a. AstraZeneca (ChAdOx1 nCoV-19)

IN Preclinical study: Intranasal format of the ChAdOx1 nCoV-19/AZD1222 (AstraZeneca vaccine currently in clinical use) administered in hamsters and rhesus macaques.

<https://www.science.org/doi/10.1126/scitranslmed.abh0755> (Preclinical paper)

IN Preclinical findings: Intranasal vaccination reduced viral shedding after SARS-CoV-2 challenge relative to control animals. In hamsters, intranasal vaccination generated increased neutralizing antibody titers as compared to intramuscular vaccination, although both routes were effective at reducing viral loads.

IN Phase 1 clinical trials: Phase 1 clinical trials are currently ongoing and expected to conclude in May 2022.

<https://www.ox.ac.uk/news/2021-03-25-university-oxford-study-nasal-administration-covid-19-vaccine> (Press release for Phase 1 clinical trials)

<https://www.jenner.ac.uk/volunteer/recruiting-trials/covid-19-vaccine-intranasal-study-cov008> (Study website)

b. Convidecia (AD5-nCOV)

Convidecia is a single-dose IM viral vector vaccine and is currently under evaluation for WHO Emergency Use Listing (currently approved in some countries in Asia, Europe and Latin America) https://en.wikipedia.org/wiki/Convidecia#cite_note-19-12

IN Phase 1 clinical trial findings: Results showed that aerosolised Ad5-nCoV is well tolerated, and two doses of aerosolised Ad5-nCoV elicited neutralising antibody responses, similar to one dose of intramuscular injection. An aerosolised booster vaccination at 28 days after first

intramuscular injection induced strong IgG and neutralising antibody responses.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8313090/> (Paper on Phase 1 findings)

IN Phase II/III: Authors of the Phase I trial recommended that the efficacy and cost-effectiveness of aerosol vaccination should be evaluated in future studies.

c. Gam-COVID-Vac (Sputnik V) [IN variation now registered in Russia]

- Russia has registered a nasal version of the Sputnik V vaccine.
<https://tass.com/world/1431285>
- In January, the Russian news agency TASS reported that the nasal vaccine against Covid-19 will be in civil circulation and available for Russians in three to four months. [A. Gintsburg](#), Gamaleya Center head: "Sputnik nasal vaccine, world's 1st registered COVID vaccine in nasal form, is especially effective vs highly transmissible Omicron & other emerging variants not only in terms of protection from infection but also at preventing transmission"
- There are no published results from clinical trials. No recruitment has been posted yet on their registered trials:
<https://clinicaltrials.gov/ct2/show/NCT05248373?term=sputnik+nasal&draw=2&rank=1>

Other Diseases

5. Existing mucosal-immunisation strategies for other diseases

Eight oral vaccines are currently licensed for use against cholera, salmonella, poliovirus and rotavirus. Live attenuated influenza vaccines remain the sole licenced intranasal vaccines. To date, live attenuated and inactivated vaccines have proved the most successful platforms for mucosal vaccine design. However, live attenuated vaccines are not usable in [immunocompromised](#) groups or pregnant individuals.

Adjuvanted inactivated vaccines have had safety concerns. After an inactivated intranasal influenza vaccine was introduced in Switzerland during the 2000–2001 influenza season, 46 cases of Bell's palsy were reported. A study was published in 2004 suggesting a strong association between the inactivated intranasal influenza vaccine used in Switzerland and Bell's palsy. This vaccine is no longer in clinical use:
https://www.nejm.org/doi/10.1056/NEJMoa030595?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200www.ncbi.nlm.nih.gov

(for overview of mucosal vaccines: <https://www.nature.com/articles/s41577-021-00583-2>)

Approved Nasal Vaccines against Seasonal Influenza

- **FluMist/Fluenz Tetra** (MedImmune//Astra Zeneca) authorised for use in the US and Europe, respectively. <https://www.flumistquadrivalent.com/>

- **Nasovac** (Serum Institute of India Ltd.) authorised for use in India.
https://www.seruminstitute.com/product_influenza_vaccines.php

Both vaccines make use of a live attenuated influenza virus. The vaccines have been administered to several million patients so far without any reports of severe adverse events or [vaccine failure](#) and are shown to produce a long-lasting, humoral and cellular immune response which closely resembles natural immunity. Further, nasal vaccination against influenza provides increased protection against virus drift variants and, especially, infants and children are better protected than with the inactivated, injectable [influenza vaccine](#). However The US CDC (Centre for Disease Control) Advisory Committee on Immunization Practices (ACIP) voted that the Flumist nasal spray live attenuated influenza vaccine (LAIV) (sic), should not be used during the 2016–2017 flu season, based on “data showing poor or relatively lower effectiveness of LAIV from 2013 through 2016.”

6. Pre-clinical studies for mucosal-immunisation strategies for other diseases

i. Study: Paper on prime and pull strategy for a therapeutic HSV vaccine

<https://www.nature.com/articles/s41541-019-0129-1>

Findings: using glycoprotein vaccines to boost HSV immunity and intravaginal/topical imiquimod to pull these immune cells into the vaginal tract significantly reduced recurrent genital HSV lesions and the shedding of HSV-2 into the vaginal tract.

ii. Study: Paper on intranasal priming inducing local lung-resident B cell populations that secrete protective mucosal antiviral IgA

<https://www.science.org/doi/10.1126/sciimmunol.abj5129>

Findings: These findings add to the growing evidence that mucosal vaccination strategies show enhanced efficacy in establishing frontline mucosal immunity against respiratory pathogens.

iii. Study: Paper on mucosal immunity against neuraminidase preventing influenza B virus transmission in guinea pigs

<https://pubmed.ncbi.nlm.nih.gov/31113896/>

Findings: The data suggest that supplementing vaccine formulations with neuraminidase and vaccinating via the intranasal route may broadly prevent transmission of influenza B viruses.

