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## Type of COVID-19 antibodies after vaccination compared with after COVID-19 infection

**ID of request:** 27024  
**Date of request:** 12th January, 2021  
**Date of completion:** 14th January, 2021

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**Sources searched**  
EMBASE (9)  
MEDLINE (8)

**Date range used** (5 years, 10 years): 2020 -   
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**Search terms and notes** (full search strategy for database searches below):

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Searched Medline, EMBASE, Google Scholar

Google Scholar search strategy: (coronavirus OR "corona virus" OR covid\* OR "2019-nCoV" OR "SARS-Cov\*") AND mrna OR mRNA-1273 OR BNT162b2 OR CoronaVac OR AZD1222 OR "Sputnik V" OR BBIBP-CorV OR EpiVacCorona OR ChAdOx1) AND (antibod\* OR immunoglobin\*)

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## A. Original Research

1. **Antibody responses to SARS-CoV-2 in healthy individuals returning to Shenzhen**  
   Zhang C. Journal of Medical Virology 2021;93(2):1154-1157.

To verify reliability of antibody detection and investigate population immunity to severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) in the local Chinese population. A cross-sectional study was conducted in Shenzhen to detect anti-coronavirus antibodies including, immunoglobulin G (IgG), immunoglobulin M (IgM), and immunoglobulin A (IgA). In the COVID-19 group, nine patients were enrolled after diagnosis. In the control group, 1589 individuals without clinical symptoms (cough, fever, and fatigue) and returning from outside Shenzhen were enrolled. The first study enrollment occurred at the end of February 2020; the final study visit was 18 March 2020. In the COVID-19 group, the seven of nine patients were positive for IgM, IgG, and IgA. Meanwhile, six of the 1589 healthy individuals were found to be weakly positive for IgG. According to SARS-CoV-2 nucleic acid tests, the six individuals were all negative. Strong supplemental support for clinical information can be provided by antibody detection, especially for IgA. According to comparison with overseas reports, the infection rate of the Chinese population outside Shenzhen, China, is significantly low, so most of the population in China is still susceptible. Hence, social distancing measures are still inevitable until a vaccine is developed successfully.<br/>Copyright &#xa9; 2020 Wiley Periodicals LLC

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1. **Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial.**  
   Xia Shengli The Lancet. Infectious diseases 2021;21(1):39-51.

BACKGROUNDThe ongoing COVID-19 pandemic warrants accelerated efforts to test vaccine candidates. We aimed to assess the safety and immunogenicity of an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine candidate, BBIBP-CorV, in humans.METHODSWe did a randomised, double-blind, placebo-controlled, phase 1/2 trial at Shangqiu City Liangyuan District Center for Disease Control and Prevention in Henan Province, China. In phase 1, healthy people aged 18-80 years, who were negative for serum-specific IgM/IgG antibodies against SARS-CoV-2 at the time of screening, were separated into two age groups (18-59 years and ≥60 years) and randomly assigned to receive vaccine or placebo in a two-dose schedule of 2 μg, 4 μg, or 8 μg on days 0 and 28. In phase 2, healthy adults (aged 18-59 years) were randomly assigned (1:1:1:1) to receive vaccine or placebo on a single-dose schedule of 8 μg on day 0 or on a two-dose schedule of 4 μg on days 0 and 14, 0 and 21, or 0 and 28. Participants within each cohort were randomly assigned by stratified block randomisation (block size eight) and allocated (3:1) to receive vaccine or placebo. Group allocation was concealed from participants, investigators, and outcome assessors. The primary outcomes were safety and tolerability. The secondary outcome was immunogenicity, assessed as the neutralising antibody responses against infectious SARS-CoV-2. This study is registered with www.chictr.org.cn, ChiCTR2000032459.FINDINGSIn phase 1, 192 participants were enrolled (mean age 53·7 years [SD 15·6]) and were randomly assigned to receive vaccine (2 μg [n=24], 4 μg [n=24], or 8 μg [n=24] for both age groups [18-59 years and ≥60 years]) or placebo (n=24). At least one adverse reaction was reported within the first 7 days of inoculation in 42 (29%) of 144 vaccine recipients. The most common systematic adverse reaction was fever (18-59 years, one [4%] in the 2 μg group, one [4%] in the 4 μg group, and two [8%] in the 8 μg group; ≥60 years, one [4%] in the 8 μg group). All adverse reactions were mild or moderate in severity. No serious adverse event was reported within 28 days post vaccination. Neutralising antibody geometric mean titres were higher at day 42 in the group aged 18-59 years (87·7 [95% CI 64·9-118·6], 2 μg group; 211·2 [158·9-280·6], 4 μg group; and 228·7 [186·1-281·1], 8 μg group) and the group aged 60 years and older (80·7 [65·4-99·6], 2 μg group; 131·5 [108·2-159·7], 4 μg group; and 170·87 [133·0-219·5], 8 μg group) compared with the placebo group (2·0 [2·0-2·0]). In phase 2, 448 participants were enrolled (mean age 41·7 years [SD 9·9]) and were randomly assigned to receive the vaccine (8 μg on day 0 [n=84] or 4 μg on days 0 and 14 [n=84], days 0 and 21 [n=84], or days 0 and 28 [n=84]) or placebo on the same schedules (n=112). At least one adverse reaction within the first 7 days was reported in 76 (23%) of 336 vaccine recipients (33 [39%], 8 μg day 0; 18 [21%], 4 μg days 0 and 14; 15 [18%], 4 μg days 0 and 21; and ten [12%], 4 μg days 0 and 28). One placebo recipient in the 4 μg days 0 and 21 group reported grade 3 fever, but was self-limited and recovered. All other adverse reactions were mild or moderate in severity. The most common systematic adverse reaction was fever (one [1%], 8 μg day 0; one [1%], 4 μg days 0 and 14; three [4%], 4 μg days 0 and 21; two [2%], 4 μg days 0 and 28). The vaccine-elicited neutralising antibody titres on day 28 were significantly greater in the 4 μg days 0 and 14 (169·5, 95% CI 132·2-217·1), days 0 and 21 (282·7, 221·2-361·4), and days 0 and 28 (218·0, 181·8-261·3) schedules than the 8 μg day 0 schedule (14·7, 11·6-18·8; all p<0·001).INTERPRETATIONThe inactivated SARS-CoV-2 vaccine, BBIBP-CorV, is safe and well tolerated at all tested doses in two age groups. Humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 μg dose or 4 μg dose on days 0 and 14.FUNDINGNational Program on Key Research Project of China, National Mega projects of China for Major Infectious Diseases, National Mega Projects of China for New Drug Creation, and Beijing Science and Technology Plan.

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1. **Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial.**  
   Ramasamy Maheshi N. Lancet (London, England) 2021;396(10267):1979-1993.

BACKGROUNDOlder adults (aged ≥70 years) are at increased risk of severe disease and death if they develop COVID-19 and are therefore a priority for immunisation should an efficacious vaccine be developed. Immunogenicity of vaccines is often worse in older adults as a result of immunosenescence. We have reported the immunogenicity of a novel chimpanzee adenovirus-vectored vaccine, ChAdOx1 nCoV-19 (AZD1222), in young adults, and now describe the safety and immunogenicity of this vaccine in a wider range of participants, including adults aged 70 years and older.METHODSIn this report of the phase 2 component of a single-blind, randomised, controlled, phase 2/3 trial (COV002), healthy adults aged 18 years and older were enrolled at two UK clinical research facilities, in an age-escalation manner, into 18-55 years, 56-69 years, and 70 years and older immunogenicity subgroups. Participants were eligible if they did not have severe or uncontrolled medical comorbidities or a high frailty score (if aged ≥65 years). First, participants were recruited to a low-dose cohort, and within each age group, participants were randomly assigned to receive either intramuscular ChAdOx1 nCoV-19 (2·2 × 1010 virus particles) or a control vaccine, MenACWY, using block randomisation and stratified by age and dose group and study site, using the following ratios: in the 18-55 years group, 1:1 to either two doses of ChAdOx1 nCoV-19 or two doses of MenACWY; in the 56-69 years group, 3:1:3:1 to one dose of ChAdOx1 nCoV-19, one dose of MenACWY, two doses of ChAdOx1 nCoV-19, or two doses of MenACWY; and in the 70 years and older, 5:1:5:1 to one dose of ChAdOx1 nCoV-19, one dose of MenACWY, two doses of ChAdOx1 nCoV-19, or two doses of MenACWY. Prime-booster regimens were given 28 days apart. Participants were then recruited to the standard-dose cohort (3·5-6·5 × 1010 virus particles of ChAdOx1 nCoV-19) and the same randomisation procedures were followed, except the 18-55 years group was assigned in a 5:1 ratio to two doses of ChAdOx1 nCoV-19 or two doses of MenACWY. Participants and investigators, but not staff administering the vaccine, were masked to vaccine allocation. The specific objectives of this report were to assess the safety and humoral and cellular immunogenicity of a single-dose and two-dose schedule in adults older than 55 years. Humoral responses at baseline and after each vaccination until 1 year after the booster were assessed using an in-house standardised ELISA, a multiplex immunoassay, and a live severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) microneutralisation assay (MNA80). Cellular responses were assessed using an ex-vivo IFN-γ enzyme-linked immunospot assay. The coprimary outcomes of the trial were efficacy, as measured by the number of cases of symptomatic, virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were by group allocation in participants who received the vaccine. Here, we report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses. This study is ongoing and is registered with ClinicalTrials.gov, NCT04400838, and ISRCTN, 15281137.FINDINGSBetween May 30 and Aug 8, 2020, 560 participants were enrolled: 160 aged 18-55 years (100 assigned to ChAdOx1 nCoV-19, 60 assigned to MenACWY), 160 aged 56-69 years (120 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY), and 240 aged 70 years and older (200 assigned to ChAdOx1 nCoV-19: 40 assigned to MenACWY). Seven participants did not receive the boost dose of their assigned two-dose regimen, one participant received the incorrect vaccine, and three were excluded from immunogenicity analyses due to incorrectly labelled samples. 280 (50%) of 552 analysable participants were female. Local and systemic reactions were more common in participants given ChAdOx1 nCoV-19 than in those given the control vaccine, and similar in nature to those previously reported (injection-site pain, feeling feverish, muscle ache, headache), but were less common in older adults (aged ≥56 years) than younger adults. In those receiving two standard doses of ChAdOx1 nCoV-19, after the prime vaccination local reactions were reported in 43 (88%) of 49 participants in the 18-55 years group, 22 (73%) of 30 in the 56-69 years group, and 30 (61%) of 49 in the 70 years and older group, and systemic reactions in 42 (86%) participants in the 18-55 years group, 23 (77%) in the 56-69 years group, and 32 (65%) in the 70 years and older group. As of Oct 26, 2020, 13 serious adverse events occurred during the study period, none of which were considered to be related to either study vaccine. In participants who received two doses of vaccine, median anti-spike SARS-CoV-2 IgG responses 28 days after the boost dose were similar across the three age cohorts (standard-dose groups: 18-55 years, 20 713 arbitrary units [AU]/mL [IQR 13 898-33 550], n=39; 56-69 years, 16 170 AU/mL [10 233-40 353], n=26; and ≥70 years 17 561 AU/mL [9705-37 796], n=47; p=0·68). Neutralising antibody titres after a boost dose were similar across all age groups (median MNA80 at day 42 in the standard-dose groups: 18-55 years, 193 [IQR 113-238], n=39; 56-69 years, 144 [119-347], n=20; and ≥70 years, 161 [73-323], n=47; p=0·40). By 14 days after the boost dose, 208 (>99%) of 209 boosted participants had neutralising antibody responses. T-cell responses peaked at day 14 after a single standard dose of ChAdOx1 nCoV-19 (18-55 years: median 1187 spot-forming cells [SFCs] per million peripheral blood mononuclear cells [IQR 841-2428], n=24; 56-69 years: 797 SFCs [383-1817], n=29; and ≥70 years: 977 SFCs [458-1914], n=48).INTERPRETATIONChAdOx1 nCoV-19 appears to be better tolerated in older adults than in younger adults and has similar immunogenicity across all age groups after a boost dose. Further assessment of the efficacy of this vaccine is warranted in all age groups and individuals with comorbidities.FUNDINGUK Research and Innovation, National Institutes for Health Research (NIHR), Coalition for Epidemic Preparedness Innovations, NIHR Oxford Biomedical Research Centre, Thames Valley and South Midlands NIHR Clinical Research Network, and AstraZeneca.

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1. **The dynamic changes of serum IgM and IgG against SARS-CoV-2 in patients with COVID-19**  
   Zhou W. Journal of Medical Virology 2021;93(2):924-933.

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a worldwide pandemic since it emerged in December 2019. Previous studies have reported rapid antibody response to SARS-CoV-2 in the first 2 to 3 weeks after symptom onset. Here, we retrospectively described the dynamic changes of serum immunoglobulin M (IgM) and IgG specifically against SARS-CoV-2 in later weeks (mainly 4-10 weeks) in 97 hospitalized patients with COVID-19. We observed that serum IgM and IgG, especially in patients with moderate-to-high levels, declined significantly between week 4 to 10 after illness onset. Notably, IgG levels in high percentage of patients (77.5%, 31 of 40) rapidly declined by half, from 212.5 (range, 163.7-420.3) to 96.3 (range, 75.0-133.4) AU/mL, within 1 to 2 weeks in the second month and then sustained at around 100 AU/mL until discharge from hospital. Significant reduction of IgM was also observed as SARS-CoV-2 nucleic acid turned negative (P =.002). In the recovery stage, serum IgG declined significantly (early vs late recovery stage, n = 16, P =.003) with a median reduction of 50.0% (range, 3.7%-77.0%). Our results suggested that the decline of IgM may be an indicator of virus clearance and recovered patients may have a robust immunity against reinfection within at least 3 months after illness onset. Yet, the rapid reduction of IgG by half rises serious concerns on the robustness and sustainability of the humoral immune response in the period after discharge, which is crucial for immunity strategy and developing a vaccine.<br/>Copyright &#xa9; 2020 Wiley Periodicals LLC

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1. **Analysis of humoral immune responses in SARS-CoV-2 infected patients**  
   Henss L. The Journal of infectious diseases 2020;:No page numbers.

BACKGROUND: The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection has caused a pandemic with tens of millions of cases and hundreds of thousands of deaths. The infection causes COVID-19, a disease of the respiratory system of divergent severity. Here, the humoral immune response of a cohort of 143 COVID-19 patients from the University Hospital Frankfurt/Main, Germany was characterized. <br/>METHOD(S): SARS-CoV-2-specific antibodies were detected by enzyme-linked immunosorbent assay (ELISA). SARS-CoV-2 and hCoV NL63 neutralization activity was analyzed with pseudotyped lentiviral vectors. <br/>RESULT(S): COVID-19 severity increased with age and male patients encountered more serious symptoms than females. Disease severity correlated with the amount of SARS-CoV-2 specific IgG and IgA and the neutralization activity of the antibodies. The amount of SARS-CoV-2 specific IgG antibodies decreased with time after PCR conformation of the infection and antibodies directed against the nucleoprotein waned faster than spike directed antibodies. In contrast, for the common flu coronavirus NL63, COVID19 disease severity seemed to correlate with low NL63-neutralizing activities, suggesting the possibility of cross-reactive protection. <br/>CONCLUSION(S): The results describe the humoral immune responses against SARS-CoV-2 and might aid the identification of correlates of protection needed for vaccine development.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

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1. **Antibody response to SARS-CoV-2 infection in humans: A systematic review**  
   Post N. PLoS ONE 2020;15(12):No page numbers.

Background Progress in characterising the humoral immune response to Severe Acute Respiratory Syndrome 2 (SARS-CoV-2) has been rapid but areas of uncertainty persist. Assessment of the full range of evidence generated to date to understand the characteristics of the antibody response, its dynamics over time, its determinants and the immunity it confers will have a range of clinical and policy implications for this novel pathogen. This review comprehensively evaluated evidence describing the antibody response to SARS-CoV-2 published from 01/01/2020-26/06/2020. Methods Systematic review. Keyword-structured searches were carried out in MEDLINE, Embase and COVID-19 Primer. Articles were independently screened on title, abstract and full text by two researchers, with arbitration of disagreements. Data were double-extracted into a pre-designed template, and studies critically appraised using a modified version of the Public Health Ontario Meta-tool for Quality Appraisal of Public Health Evidence (MetaQAT) tool, with resolution of disagreements by consensus. Findings were narratively synthesised. Results 150 papers were included. Most studies (113 or 75%) were observational in design, were based wholly or primarily on data from hospitalised patients (108, 72%) and had important methodological limitations. Few considered mild or asymptomatic infection. Antibody dynamics were well described in the acute phase, up to around three months from disease onset, but the picture regarding correlates of the antibody response was inconsistent. IgM was consistently detected before IgG in included studies, peaking at weeks two to five and declining over a further three to five weeks post-symptom onset depending on the patient group; IgG peaked around weeks three to seven post-symptom onset then plateaued, generally persisting for at least eight weeks. Neutralising antibodies were detectable within seven to 15 days following disease onset, with levels increasing until days 14-22 before levelling and then decreasing, but titres were lower in those with asymptomatic or clinically mild disease. Specific and potent neutralising antibodies have been isolated from convalescent plasma. Cross-reactivity but limited cross-neutralisation with other human coronaviridae was reported. Evidence for protective immunity in vivo was limited to small, short-term animal studies, showing promising initial results in the immediate recovery phase. Conclusions Literature on antibody responses to SARS-CoV-2 is of variable quality with considerable heterogeneity of methods, study participants, outcomes measured and assays used. Although acute phase antibody dynamics are well described, longer-term patterns are much less well evidenced. Comprehensive assessment of the role of demographic characteristics and disease severity on antibody responses is needed. Initial findings of low neutralising antibody titres and possible waning of titres over time may have implications for sero-surveillance and disease control policy, although further evidence is needed. The detection of potent neutralising antibodies in convalescent plasma is important in the context of development of therapeutics and vaccines. Due to limitations with the existing evidence base, large, cross-national cohort studies using appropriate statistical analysis and standardised serological assays and clinical classifications should be prioritised.<br/>Copyright: &#xa9; 2020 Post et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

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1. **Comparative analyses of SARS-CoV-2 binding (IgG, IgM, IgA) and neutralizing antibodies from human serum samples**  
   Mazzini L. Journal of Immunological Methods 2020;:No page numbers.

A newly identified coronavirus, named SARS-CoV-2, emerged in December 2019 in Hubei Province, China, and quickly spread throughout the world; so far, it has caused more than 49.7 million cases of disease and 1,2 million deaths. The diagnosis of SARS-CoV-2 infection is currently based on the detection of viral RNA in nasopharyngeal swabs by means of molecular-based assays, such as real-time RT-PCR. Furthermore, serological assays detecting different classes of antibodies constitute an excellent surveillance strategy for gathering information on the humoral immune response to infection and the spread of the virus through the population. In addition, it can contribute to evaluate the immunogenicity of novel future vaccines and medicines for the treatment and prevention of COVID-19 disease. The aim of this study was to determine SARS-CoV-2-specific antibodies in human serum samples by means of different commercial and in-house ELISA kits, in order to evaluate and compare their results first with one another and then with those yielded by functional assays using wild-type virus. It is important to identify the level of SARS-CoV-2-specific IgM, IgG and IgA antibodies in order to predict human population immunity, possible cross-reactivity with other coronaviruses and to identify potentially infectious subjects. In addition, in a small sub-group of samples, a subtyping IgG ELISA has been performed. Our findings showed a notable statistical correlation between the neutralization titers and the IgG, IgM and IgA ELISA responses against the receptor-binding domain of the spike protein. Thus confirming that antibodies against this portion of the virus spike protein are highly neutralizing and that the ELISA Receptor-Binding Domain-based assay can be used as a valid surrogate for the neutralization assay in laboratories that do not have biosecurity level-3 facilities.<br/>Copyright &#xa9; 2020 The Authors

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1. **CoVaccine HT™ Adjuvant Potentiates Robust Immune Responses to Recombinant SARS-CoV-2 Spike S1 Immunization.**  
   Haun Brien K. Frontiers in immunology 2020;11:599587.

The current COVID-19 pandemic has claimed hundreds of thousands of lives and its causative agent, SARS-CoV-2, has infected millions, globally. The highly contagious nature of this respiratory virus has spurred massive global efforts to develop vaccines at record speeds. In addition to enhanced immunogen delivery, adjuvants may greatly impact protective efficacy of a SARS-CoV-2 vaccine. To investigate adjuvant suitability, we formulated protein subunit vaccines consisting of the recombinant S1 domain of SARS-CoV-2 Spike protein alone or in combination with either CoVaccine HT™ or Alhydrogel. CoVaccine HT™ induced high titres of antigen-binding IgG after a single dose, facilitated affinity maturation and class switching to a greater extent than Alhydrogel and elicited potent cell-mediated immunity as well as virus neutralizing antibody titres. Data presented here suggests that adjuvantation with CoVaccine HT™ can rapidly induce a comprehensive and protective immune response to SARS-CoV-2.

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1. **COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses.**  
   Sahin Ugur Nature 2020;586(7830):594-599.

An effective vaccine is needed to halt the spread of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic. Recently, we reported safety, tolerability and antibody response data from an ongoing placebo-controlled, observer-blinded phase I/II coronavirus disease 2019 (COVID-19) vaccine trial with BNT162b1, a lipid nanoparticle-formulated nucleoside-modified mRNA that encodes the receptor binding domain (RBD) of the SARS-CoV-2 spike protein1. Here we present antibody and T cell responses after vaccination with BNT162b1 from a second, non-randomized open-label phase I/II trial in healthy adults, 18-55 years of age. Two doses of 1-50 μg of BNT162b1 elicited robust CD4+ and CD8+ T cell responses and strong antibody responses, with RBD-binding IgG concentrations clearly above those seen in serum from a cohort of individuals who had recovered from COVID-19. Geometric mean titres of SARS-CoV-2 serum-neutralizing antibodies on day 43 were 0.7-fold (1-μg dose) to 3.5-fold (50-μg dose) those of the recovered individuals. Immune sera broadly neutralized pseudoviruses with diverse SARS-CoV-2 spike variants. Most participants had T helper type 1 (TH1)-skewed T cell immune responses with RBD-specific CD8+ and CD4+ T cell expansion. Interferon-γ was produced by a large fraction of RBD-specific CD8+ and CD4+ T cells. The robust RBD-specific antibody, T cell and favourable cytokine responses induced by the BNT162b1 mRNA vaccine suggest that it has the potential to protect against COVID-19 through multiple beneficial mechanisms.

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1. **Enhanced SARS-CoV-2 neutralization by dimeric IgA**  
   Wang Z. Science translational medicine 2020;:No page numbers.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), primarily infects cells at mucosal surfaces. Serum neutralizing antibody responses are variable and generally low in individuals that suffer mild forms of COVID-19. Although potent IgG antibodies can neutralize the virus, less is known about secretory antibodies such as IgA that might impact the initial viral spread and transmissibility from the mucosa. Here we characterize the IgA response to SARS-CoV-2 in a cohort of 149 convalescent individuals following diagnosis with COVID-19. IgA responses in plasma generally correlated with IgG responses. Further, clones of IgM-, IgG-, and IgA-producing B cells were derived from common progenitor cells. Plasma IgA monomers specific to SARS-CoV-2 proteins were demonstrated to be two-fold less potent than IgG equivalents. However, IgA dimers, the primary form of antibody in the nasopharynx, were on average fifteen times more potent than IgA monomers against the same target. Thus, dimeric IgA responses may be particularly valuable for protection against SARS-CoV-2 and for vaccine efficacy.<br/>Copyright &#xa9; 2020, American Association for the Advancement of Science.

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1. **IgA dominates the early neutralizing antibody response to SARS-CoV-2**  
   Sterlin D. Science translational medicine 2020;:No page numbers.

Humoral immune responses are typically characterized by primary IgM antibody responses followed by secondary antibody responses associated with immune memory and comprised of of IgG, IgA and IgE. Here we measured acute humoral responses to SARS-CoV-2, including the frequency of antibody-secreting cells and the presence of SARS-CoV-2-specific neutralizing antibodies in the serum, saliva and broncho-alveolar fluid of 159 patients with COVID-19. Early SARS-CoV-2-specific humoral responses were dominated by IgA antibodies. Peripheral expansion of IgA plasmablasts with mucosal-homing potential was detected shortly after the onset of symptoms and peaked during the third week of the disease. The virus-specific antibody responses included IgG, IgM and IgA, but IgA contributed to virus neutralization to a greater extent compared with IgG. Specific IgA serum concentrations decreased notably one month after the onset of symptoms, but neutralizing IgA remained detectable in saliva for a longer time (days 49 to 73 post symptoms). These results represent a critical observation given the emerging information as to the types of antibodies associated with optimal protection against re-infection, and whether vaccine regimens should consider targeting a potent but potentially short-lived IgA response.<br/>Copyright &#xa9; 2020, American Association for the Advancement of Science.

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1. **Magnitude and kinetics of anti-SARS-CoV-2 antibody responses and their relationship to disease severity**  
   Lynch K.L. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020;:No page numbers.

BACKGROUND: SARS-CoV-2 infection can be detected indirectly by measuring the host immune response. For some viruses, antibody concentrations correlate with host protection and viral neutralization, but in rare cases, anti-viral antibodies can promote disease progression. Elucidation of the kinetics and magnitude of the SARS-CoV-2 antibody response is essential to understand the pathogenesis of COVID-19 and identify potential therapeutic targets. <br/>METHOD(S): Sera (n=533) from patients with RT-PCR confirmed COVID-19 (n=94 with acute infections and n=59 convalescent patients) were tested using a high-throughput quantitative IgM and IgG assay that detects antibodies to the spike protein receptor binding domain and nucleocapsid protein. Individual and serial samples covered the time of initial diagnosis, during the disease course, and following recovery. We evaluated antibody kinetics and correlation between magnitude of the response and disease severity. <br/>RESULT(S): Patterns of SARS-CoV-2 antibody production varied considerably. Among 52 patients with 3 or more serial specimens, 44 (84.6%) and 42 (80.8%) had observed IgM and IgG seroconversion at a median of 8 and 10 days, respectively. Compared to those with milder disease, peak measurements were significantly higher for patients admitted to the intensive care unit for all time intervals between 6 and 20 days for IgM, and all intervals after 5 days for IgG. <br/>CONCLUSION(S): High sensitivity assays with a robust dynamic range provide a comprehensive picture of host antibody response to SARS-CoV-2. IgM and IgG responses were significantly higher in patients with severe than mild disease. These differences may affect strategies for seroprevalence studies, therapeutics and vaccine development.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

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1. **Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine.**  
   Keech Cheryl The New England journal of medicine 2020;383(24):2320-2332.

BACKGROUNDNVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 (rSARS-CoV-2) nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant.METHODSWe initiated a randomized, placebo-controlled, phase 1-2 trial to evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5-μg and 25-μg doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. In phase 1, vaccination comprised two intramuscular injections, 21 days apart. The primary outcomes were reactogenicity; laboratory values (serum chemistry and hematology), according to Food and Drug Administration toxicity scoring, to assess safety; and IgG anti-spike protein response (in enzyme-linked immunosorbent assay [ELISA] units). Secondary outcomes included unsolicited adverse events, wild-type virus neutralization (microneutralization assay), and T-cell responses (cytokine staining). IgG and microneutralization assay results were compared with 32 (IgG) and 29 (neutralization) convalescent serum samples from patients with Covid-19, most of whom were symptomatic. We performed a primary analysis at day 35.RESULTSAfter randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤2 days). One participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose-sparing, and induced a T helper 1 (Th1) response. The two-dose 5-μg adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively).CONCLUSIONSAt 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype. (Funded by the Coalition for Epidemic Preparedness Innovations; ClinicalTrials.gov number, NCT04368988).

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1. **Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults.**  
   Mulligan Mark J. Nature 2020;586(7830):589-593.

In March 2020, the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)1, a pandemic. With rapidly accumulating numbers of cases and deaths reported globally2, a vaccine is urgently needed. Here we report the available safety, tolerability and immunogenicity data from an ongoing placebo-controlled, observer-blinded dose-escalation study (ClinicalTrials.gov identifier NCT04368728) among 45 healthy adults (18-55 years of age), who were randomized to receive 2 doses-separated by 21 days-of 10 μg, 30 μg or 100 μg of BNT162b1. BNT162b1 is a lipid-nanoparticle-formulated, nucleoside-modified mRNA vaccine that encodes the trimerized receptor-binding domain (RBD) of the spike glycoprotein of SARS-CoV-2. Local reactions and systemic events were dose-dependent, generally mild to moderate, and transient. A second vaccination with 100 μg was not administered because of the increased reactogenicity and a lack of meaningfully increased immunogenicity after a single dose compared with the 30-μg dose. RBD-binding IgG concentrations and SARS-CoV-2 neutralizing titres in sera increased with dose level and after a second dose. Geometric mean neutralizing titres reached 1.9-4.6-fold that of a panel of COVID-19 convalescent human sera, which were obtained at least 14 days after a positive SARS-CoV-2 PCR. These results support further evaluation of this mRNA vaccine candidate.

1. **Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia.**  
   Logunov Denis Y. Lancet (London, England) 2020;396(10255):887-897.

BACKGROUNDWe developed a heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein (rAd26-S and rAd5-S). We aimed to assess the safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.METHODSWe did two open, non-randomised phase 1/2 studies at two hospitals in Russia. We enrolled healthy adult volunteers (men and women) aged 18-60 years to both studies. In phase 1 of each study, we administered intramuscularly on day 0 either one dose of rAd26-S or one dose of rAd5-S and assessed the safety of the two components for 28 days. In phase 2 of the study, which began no earlier than 5 days after phase 1 vaccination, we administered intramuscularly a prime-boost vaccination, with rAd26-S given on day 0 and rAd5-S on day 21. Primary outcome measures were antigen-specific humoral immunity (SARS-CoV-2-specific antibodies measured by ELISA on days 0, 14, 21, 28, and 42) and safety (number of participants with adverse events monitored throughout the study). Secondary outcome measures were antigen-specific cellular immunity (T-cell responses and interferon-γ concentration) and change in neutralising antibodies (detected with a SARS-CoV-2 neutralisation assay). These trials are registered with ClinicalTrials.gov, NCT04436471 and NCT04437875.FINDINGSBetween June 18 and Aug 3, 2020, we enrolled 76 participants to the two studies (38 in each study). In each study, nine volunteers received rAd26-S in phase 1, nine received rAd5-S in phase 1, and 20 received rAd26-S and rAd5-S in phase 2. Both vaccine formulations were safe and well tolerated. The most common adverse events were pain at injection site (44 [58%]), hyperthermia (38 [50%]), headache (32 [42%]), asthenia (21 [28%]), and muscle and joint pain (18 [24%]). Most adverse events were mild and no serious adverse events were detected. All participants produced antibodies to SARS-CoV-2 glycoprotein. At day 42, receptor binding domain-specific IgG titres were 14 703 with the frozen formulation and 11 143 with the lyophilised formulation, and neutralising antibodies were 49·25 with the frozen formulation and 45·95 with the lyophilised formulation, with a seroconversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2·5% CD4+ and 1·3% CD8+ with the frozen formulation, and a median cell proliferation of 1·3% CD4+ and 1·1% CD8+ with the lyophilised formulation.INTERPRETATIONThe heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular immune responses in participants. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19.FUNDINGMinistry of Health of the Russian Federation.

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1. **Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial.**  
   Folegatti Pedro M. Lancet (London, England) 2020;396(10249):467-478.

BACKGROUNDThe pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) might be curtailed by vaccination. We assessed the safety, reactogenicity, and immunogenicity of a viral vectored coronavirus vaccine that expresses the spike protein of SARS-CoV-2.METHODSWe did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18-55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 at a dose of 5 × 1010 viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. Humoral responses at baseline and following vaccination were assessed using a standardised total IgG ELISA against trimeric SARS-CoV-2 spike protein, a muliplexed immunoassay, three live SARS-CoV-2 neutralisation assays (a 50% plaque reduction neutralisation assay [PRNT50]; a microneutralisation assay [MNA50, MNA80, and MNA90]; and Marburg VN), and a pseudovirus neutralisation assay. Cellular responses were assessed using an ex-vivo interferon-γ enzyme-linked immunospot assay. The co-primary outcomes are to assess efficacy, as measured by cases of symptomatic virologically confirmed COVID-19, and safety, as measured by the occurrence of serious adverse events. Analyses were done by group allocation in participants who received the vaccine. Safety was assessed over 28 days after vaccination. Here, we report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses. The study is ongoing, and was registered at ISRCTN, 15281137, and ClinicalTrials.gov, NCT04324606.FINDINGSBetween April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and many were reduced by use of prophylactic paracetamol, including pain, feeling feverish, chills, muscle ache, headache, and malaise (all p<0·05). There were no serious adverse events related to ChAdOx1 nCoV-19. In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493-1802; n=43). Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96-317; n=127), and were boosted following a second dose (639 EU, 360-792; n=10). Neutralising antibody responses against SARS-CoV-2 were detected in 32 (91%) of 35 participants after a single dose when measured in MNA80 and in 35 (100%) participants when measured in PRNT50. After a booster dose, all participants had neutralising activity (nine of nine in MNA80 at day 42 and ten of ten in Marburg VN on day 56). Neutralising antibody responses correlated strongly with antibody levels measured by ELISA (R2=0·67 by Marburg VN; p<0·001).INTERPRETATIONChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.FUNDINGUK Research and Innovation, Coalition for Epidemic Preparedness Innovations, National Institute for Health Research (NIHR), NIHR Oxford Biomedical Research Centre, Thames Valley and South Midland's NIHR Clinical Research Network, and the German Center for Infection Research (DZIF), Partner site Gießen-Marburg-Langen.

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1. **What are protective antibody responses to pandemic SARS-cov-2?**  
   Henderson J.P. Journal of Clinical Investigation 2020;130(12):6232-6234.

Human antibody responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) hold intense interest, with research efforts directed at optimizing antibody-based interventions and monitoring immune status. By relating individual variations in antibody response to coronavirus disease 2019 (COVID-19) severity, beneficial antiviral immune responses may be identified in detail. In this issue of the JCI, Secchi and collaborators describe antibody response profiles in 509 patients with COVID-19 from Italy during the 2020 pandemic. The research team found that multiple antibody types to multiple SARS-CoV-2 antigens developed over four weeks. Notably, IgG against the spike receptor binding domain (RBD) was predictive of survival and IgA against the viral spike protein (S protein) associated with rapid virologic clearance. These results may help guide selection of convalescent plasma, hyperimmune products, monoclonal antibodies, and vaccine strategies for COVID-19.<br/>Copyright &#xa9; 2020, American Society for Clinical Investigation.

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| 9. | Medline | (pfizer OR Comirnaty OR biontech OR moderna OR astrazeneca OR oxford OR sinopharm OR mrna OR mRNA-1273 OR BNT162b2 OR CoronaVac OR AZD1222 OR "Sputnik V" OR BBIBP-CorV OR EpiVacCorona OR ChAdOx1).ti,ab | 515410 |
| 10. | Medline | (8 OR 9) | 745761 |
| 11. | Medline | (4 AND 7 AND 10) | 1106 |
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| 17. | Medline | (11 AND 16) | 193 |
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