

Joop 

Antivaxxers overlijden door hun eigen mening



Asymptomatische mythe



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EMERGING INFECTIOUS DISEASES®

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Volume 27, Number 4—April 2021

Dispatch

Analysis of Asymptomatic and Presymptomatic Transmission in SARS-CoV-2 Outbreak, Germany, 2020

Jennifer K. Bender¹, Michael Brandl¹, Michael Höhle, Udo Buchholz, and Nadine Zeitlmann

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[Suggested citation for this article](#)

Abstract

We determined secondary attack rates (SAR) among close contacts of 59 asymptomatic and symptomatic coronavirus disease case-patients by presymptomatic and symptomatic exposure. We observed no transmission from asymptomatic case-patients and highest SAR through presymptomatic exposure. Rapid quarantine of close contacts with or without symptoms is needed to prevent presymptomatic transmission.

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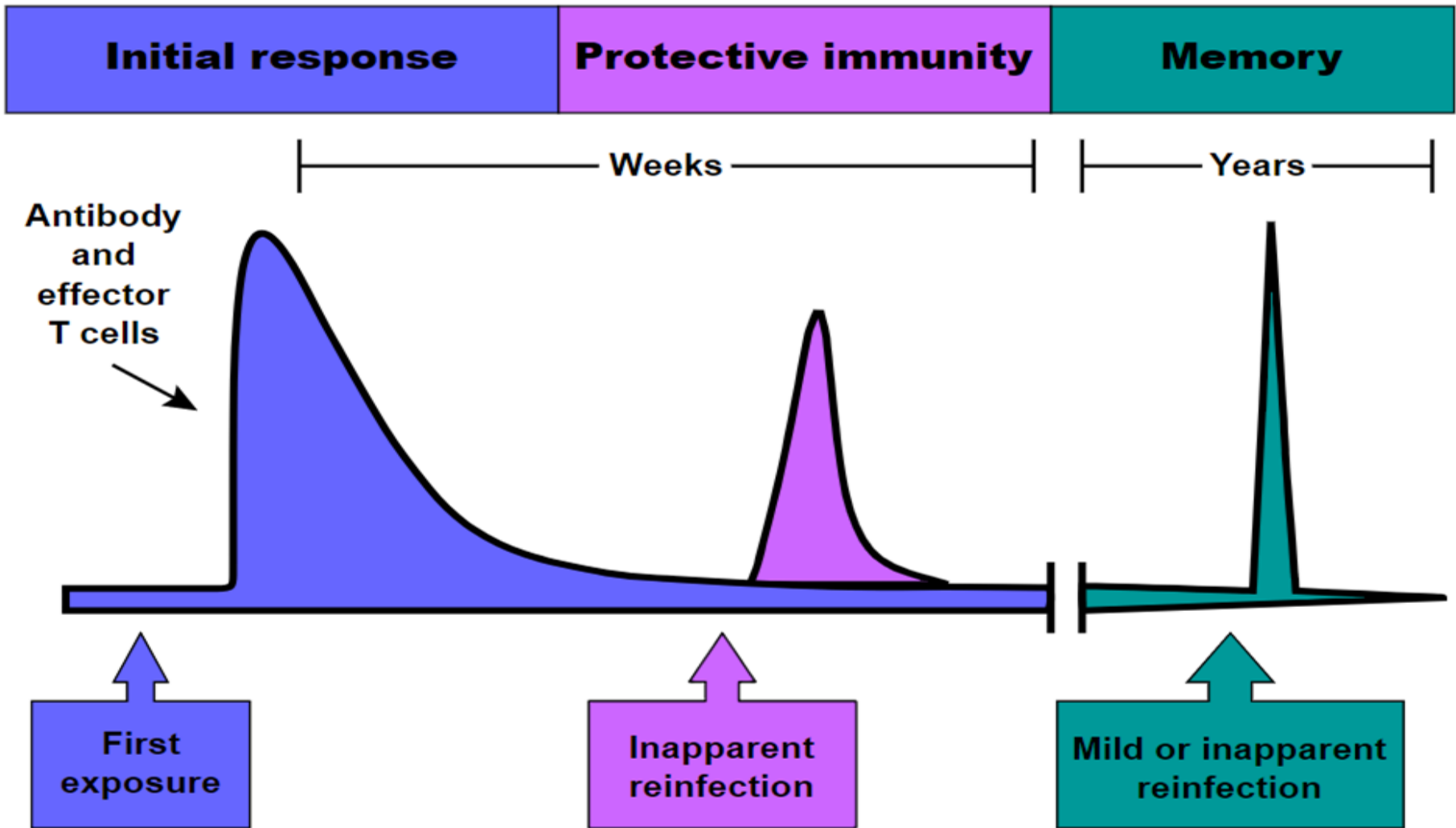
Tables

Conclusions

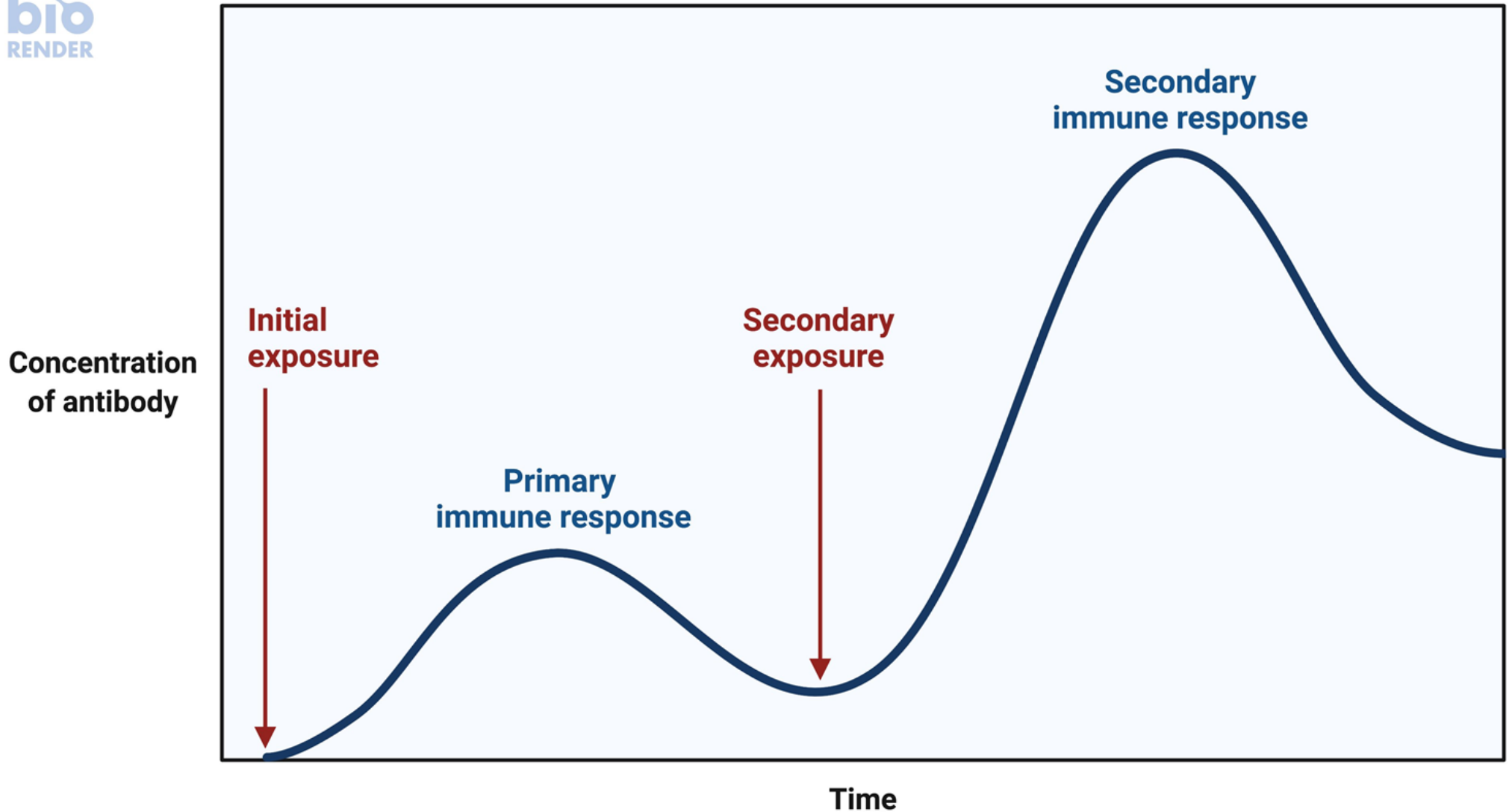
In this cluster of COVID-19 cases, little to no transmission occurred from asymptomatic case-patients. Presymptomatic transmission was more frequent than symptomatic transmission. The serial interval was short; very short intervals occurred.

The fact that we did not detect any laboratory-confirmed SARS-CoV-2 transmission from asymptomatic case-patients is in line with multiple studies (9-11). However, Oran et al. have speculated that asymptomatic cases contribute to the rapid progression of the pandemic (12). Some studies may be prone to misclassify presymptomatic cases as asymptomatic, leading to heterogeneous reporting of SAR of asymptomatic cases, because of different case definitions or differential duration of follow-up. In our study we used a very sensitive case definition for symptomatic cases that did not require specific symptoms (e.g. fever) to be present. Also, timing of our study would have enabled detection of late onset of symptoms, which gives us confidence in our classification of exposure groups.

The 75% of SARS-CoV-2 transmissions in our cohort from case-patients in their presymptomatic phase exceeds reported transmission rates from other investigations (1,13,14). Possible reasons are the prior evidence that infectiousness peaks around the date of symptom onset, declining thereafter (15), and that case-patients probably reduced social contacts themselves once they experienced symptoms or when ordered to self-isolate. A large proportion of cases with presymptomatic transmission in our cluster is further supported by the median serial interval of 3 days.



Idee van booster



Natural infection vs vaccination: Which gives more protection?

Nearly 40% of new COVID patients were vaccinated - compared to just 1% who had been infected previously.

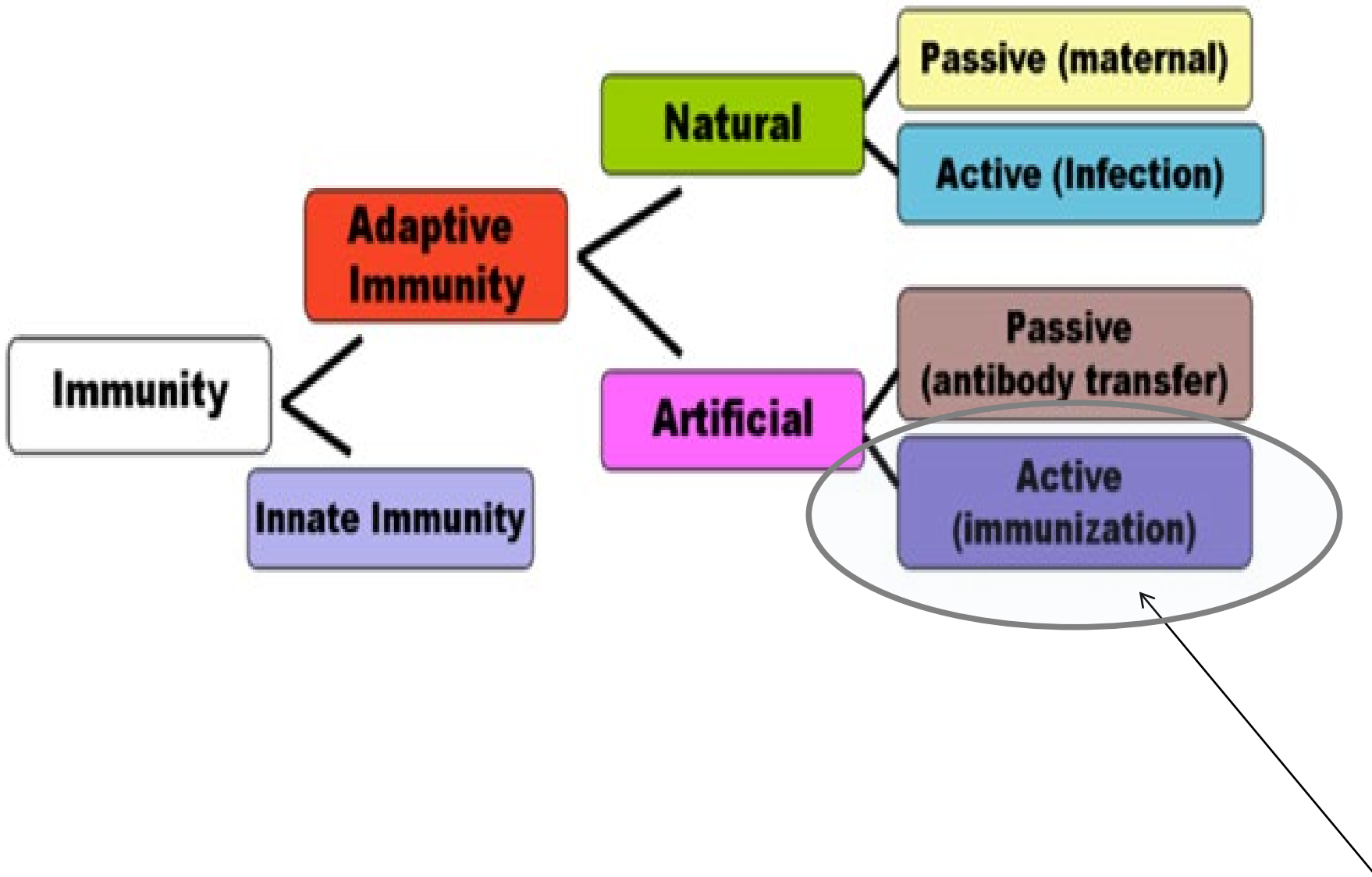
Tags: Vaccine, Coronavirus

Contact Editor David Rosenberg , Jul 13 , 2021 9:24 AM



COVID-19 vaccine

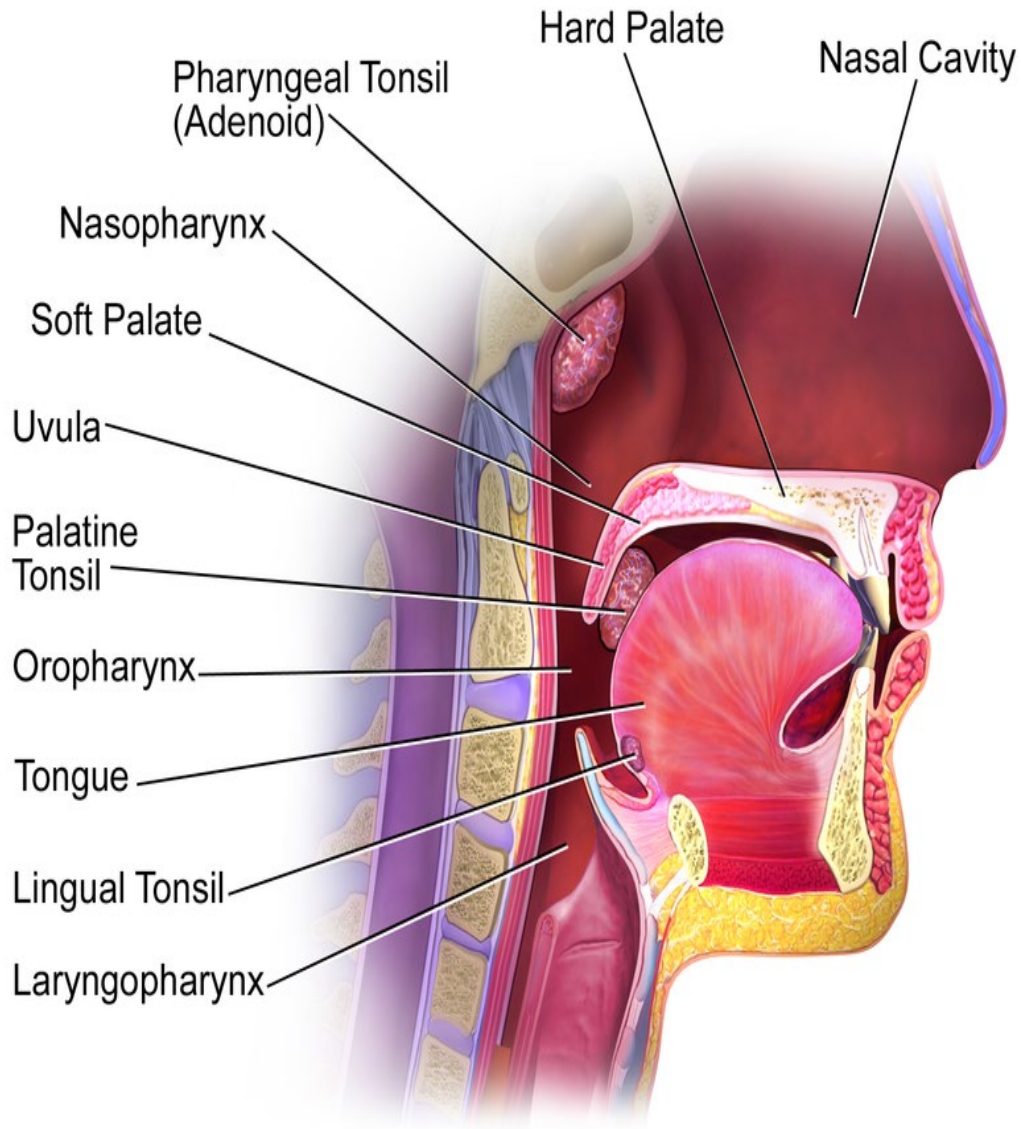
iStock



Anatomical barriers [\[edit \]](#)

Anatomical barrier	Additional defense mechanisms
Skin	Sweat, desquamation, flushing, ^[2] organic acids ^[2]
Gastrointestinal tract	Peristalsis, gastric acid, bile acids, digestive enzyme, flushing, thiocyanate, ^[2] defensins, ^[2] gut flora ^[2]
Respiratory airways and lungs	Mucociliary escalator, ^[3] surfactant, ^[2] defensins ^[2]
Nasopharynx	Mucus, saliva, lysozyme ^[2]
Eyes	Tears ^[2]
Blood-brain barrier	endothelial cells (via passive diffusion/ osmosis & active selection). P-glycoprotein (mechanism by which active transportation is mediated)

Anatomical barriers include physical, chemical and biological barriers. The epithelial surfaces form a physical barrier that is impermeable to most infectious agents, acting as the first line of (shedding) of skin epithelium also helps remove bacteria and other infectious agents that have adhered to the epithelial surfaces. Lack of blood vessels, the inability of the epidermis to rete dermis, produces an environment unsuitable for the survival of microbes.^[2] In the gastrointestinal and [respiratory tract](#), movement due to peristalsis or cilia, respectively, helps remove infection. [Gut flora](#) can prevent the colonization of pathogenic bacteria by secreting toxic substances or by competing with pathogenic bacteria for nutrients or attachment to cell surfaces.^[2] The flush eyes and mouth.^[2]



Tonsils and Throat

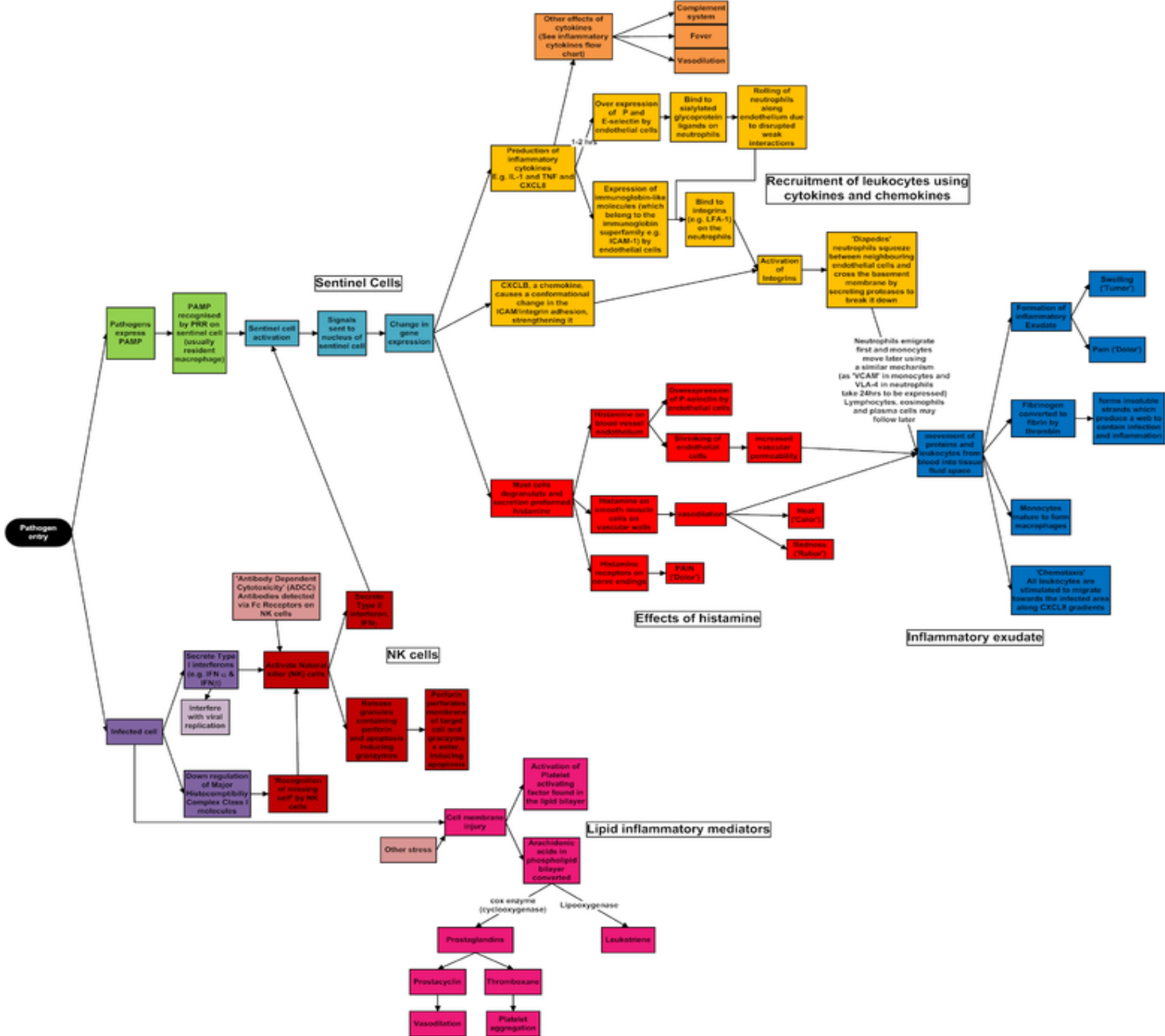
Microbiome

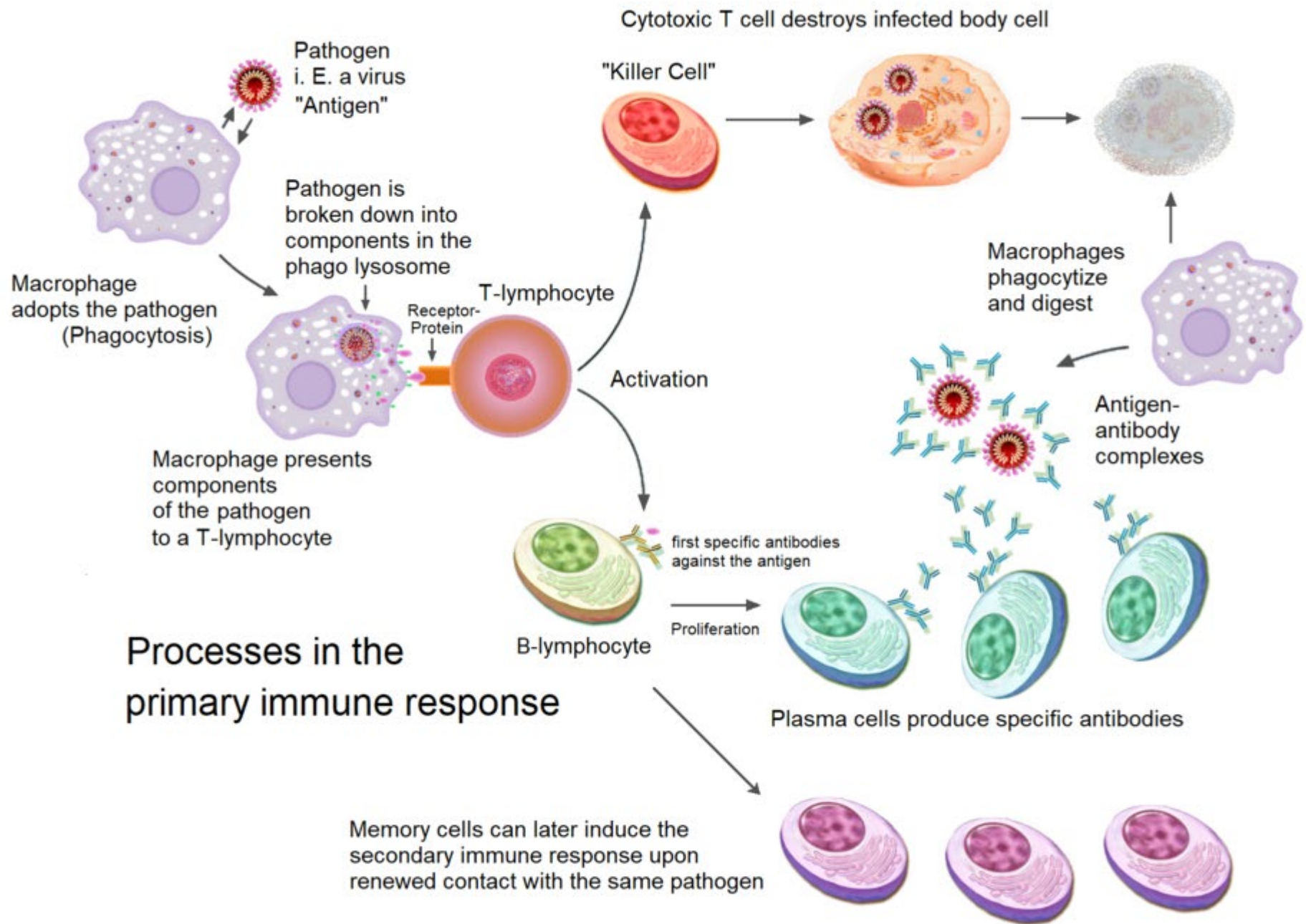
Species of bacteria such as lactobacilli, a

Normal flora found in the adenoid consist

INNATE IMMUNE SYSTEM

By Architha Srinivasan
Cambridge University





antibodies

Antibodies [edit]

Main article: Antibody

Immunoglobulins are [glycoproteins](#) in the immunoglobulin superfamily that function as [antibodies](#). The terms *antibody* and *immunoglobulin* are often used interchangeably. They are found in the blood and tissue fluids, as well as many secretions. In structure, they are large Y-shaped [globular proteins](#). In mammals there are five types of antibody: [IgA](#), [IgD](#), [IgE](#), [IgG](#), and [IgM](#). Each immunoglobulin class differs in its biological properties and has evolved to deal with different antigens.^[5] Antibodies are synthesized and secreted by plasma cells that are derived from the B cells of the immune system.

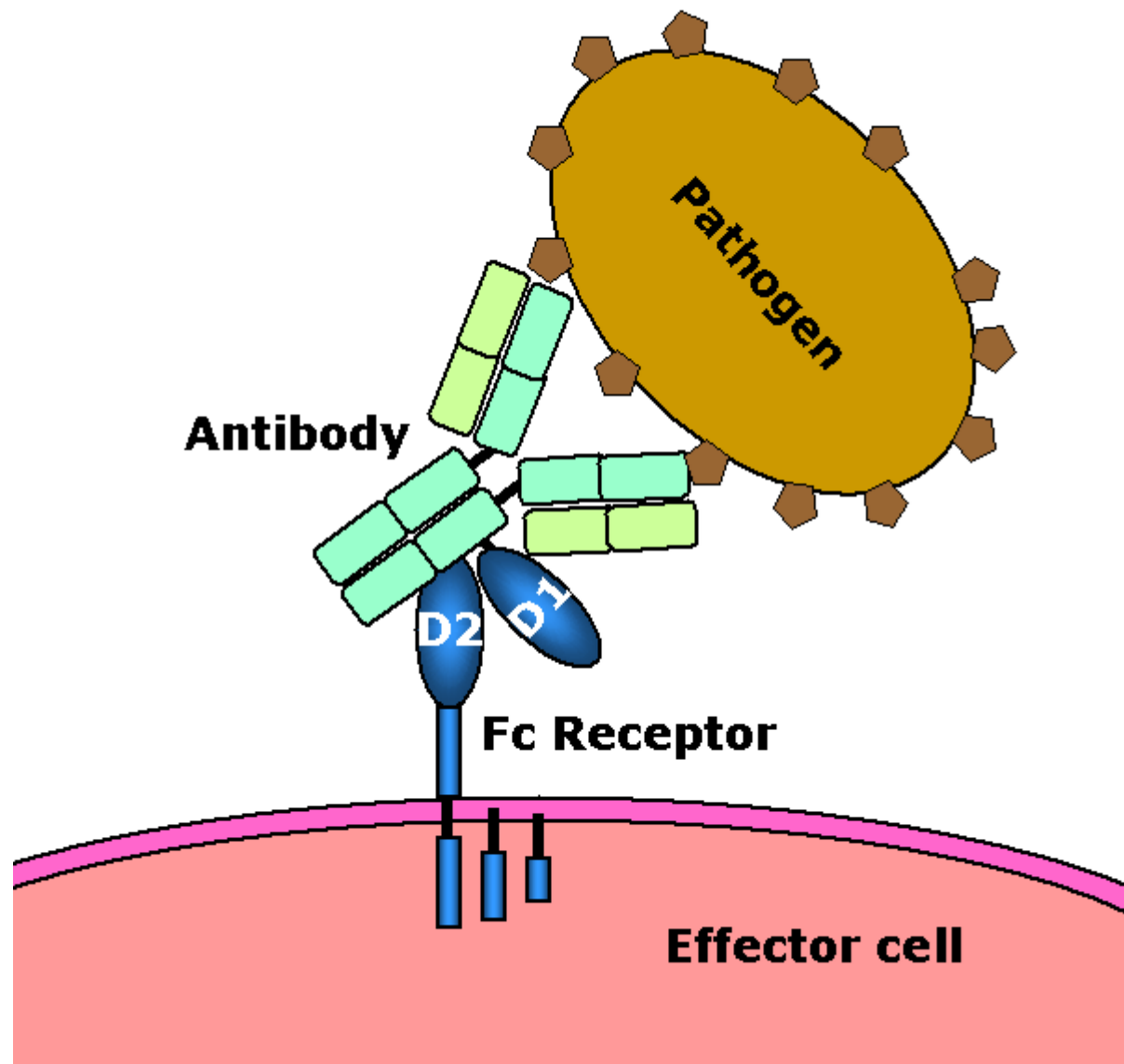
An antibody is used by the acquired immune system to identify and neutralize foreign objects like bacteria and viruses. Each antibody recognizes a specific antigen unique to its target. By binding their specific antigens, antibodies can cause [agglutination](#) and precipitation of antibody-antigen products, prime for [phagocytosis](#) by macrophages and other cells, block [viral](#) receptors, and stimulate other immune responses, such as the complement pathway.

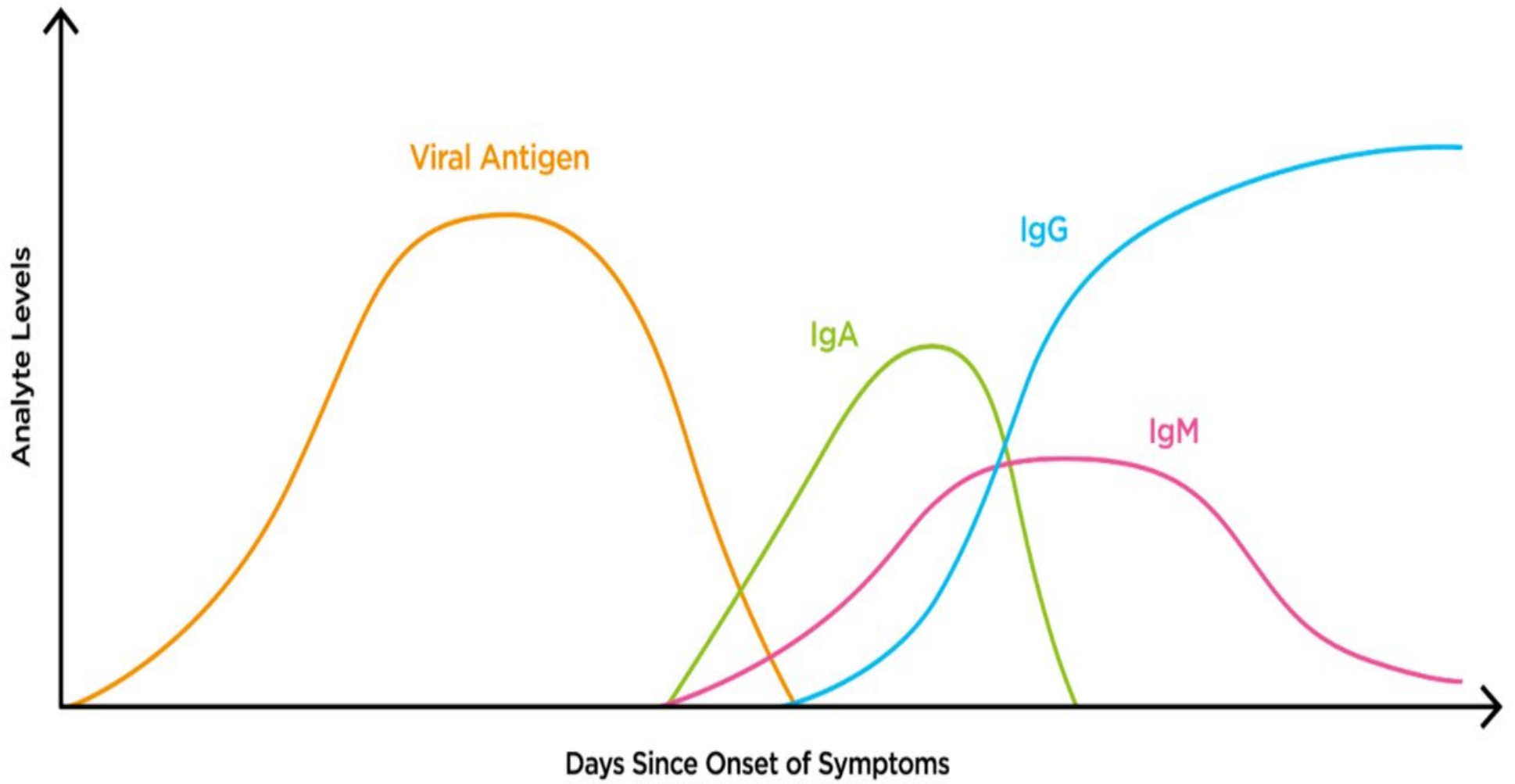
An incompatible [blood transfusion](#) causes a [transfusion reaction](#), which is mediated by the humoral immune response. This type of reaction, called an acute [hemolytic](#) reaction, results in the rapid destruction ([hemolysis](#)) of the donor [red blood cells](#) by host antibodies. The cause is usually a clerical error, such as the wrong unit of blood being given to the wrong patient. The symptoms are fever and chills, sometimes with back pain and pink or red urine ([hemoglobinuria](#)). The major complication is that [hemoglobin](#) released by the destruction of red blood cells can cause [acute kidney failure](#).

Antibody production [edit]

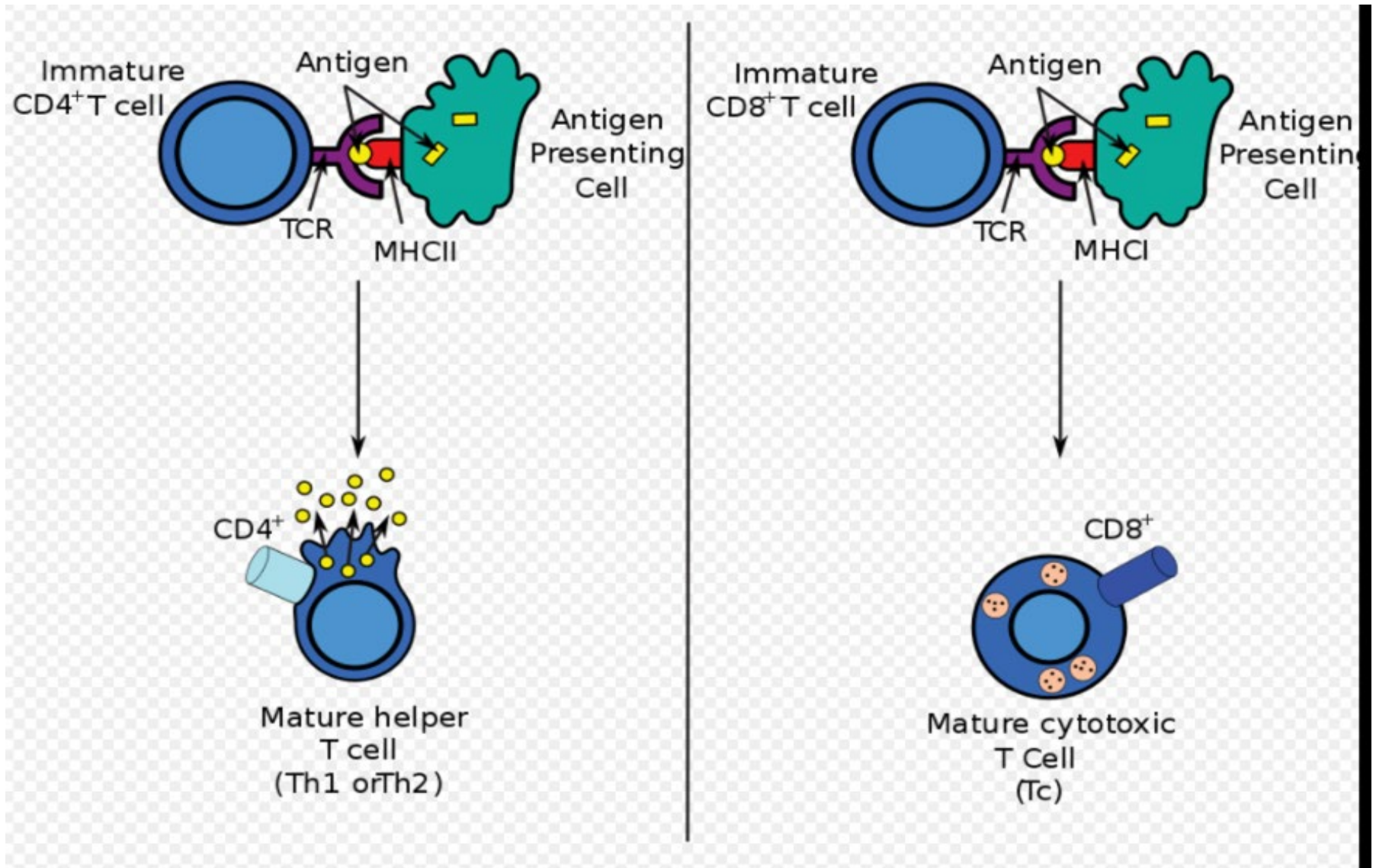
In humoral immune response, the [B cells](#) first mature in the bone marrow and gain [B-cell receptors \(BCR's\)](#) which are displayed in large numbers on the cell surface.^[6]

These membrane-bound protein complexes have antibodies which are specific for antigen detection. Each B cell has a unique [antibody](#) that binds with an [antigen](#). The mature B cells then migrate from the bone marrow to the lymph nodes or other lymphatic organs, where they begin to encounter pathogens.





T cell



development

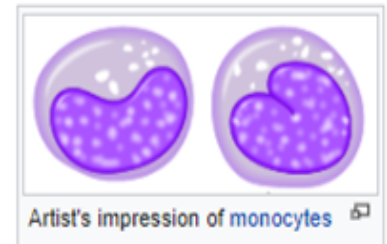
Developmental immunology [\[edit \]](#)

The body's capability to react to antigens depends on a person's age, antigen type, maternal factors and the area where the antigen is presented.^[19] Neonates are said to be in a state of physiological immunodeficiency, because both their innate and adaptive immunological responses are greatly suppressed. Once born, a child's immune system responds favorably to protein antigens while not as well to glycoproteins and polysaccharides. In fact, many of the infections acquired by neonates are caused by low virulence organisms like *Staphylococcus* and *Pseudomonas*. In neonates, opsonic activity and the ability to activate the complement cascade is very limited. For example, the mean level of C3 in a newborn is approximately 65% of that found in the adult. Phagocytic activity is also greatly impaired in newborns. This is due to lower opsonic activity, as well as diminished up-regulation of integrin and selectin receptors, which limit the ability of neutrophils to interact with adhesion molecules in the endothelium. Their monocytes are slow and have a reduced ATP production, which also limits the newborn's phagocytic activity. Although, the number of total lymphocytes is significantly higher than in adults, the cellular and humoral immunity is also impaired. Antigen-presenting cells in newborns have a reduced capability to activate T cells. Also, T cells of a newborn proliferate poorly and produce very small amounts of cytokines like IL-2, IL-4, IL-5, IL-12, and IFN-g which limits their capacity to activate the humoral response as well as the phagocytic activity of macrophage. B cells develop early during gestation but are not fully active.^[20]

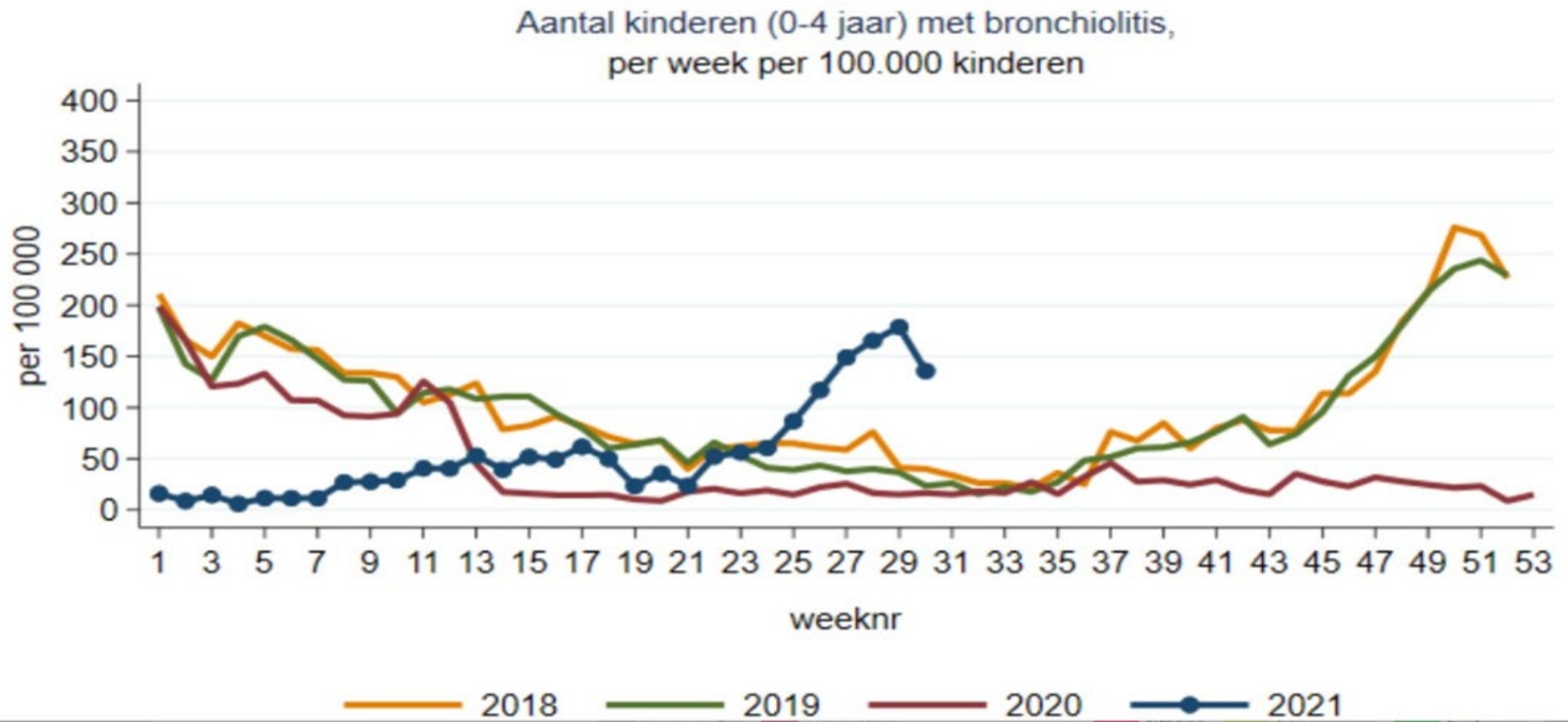
Maternal factors also play a role in the body's immune response. At birth, most of the immunoglobulin present is maternal IgG. These antibodies are transferred from the placenta to the fetus using the FcRn (neonatal Fc receptor).^[21] Because IgM, IgD, IgE and IgA do not cross the placenta, they are almost undetectable at birth. Some IgA is provided by breast milk. These passively-acquired antibodies can protect the newborn for up to 18 months, but their response is usually short-lived and of low affinity.^[20] These antibodies can also produce a negative response. If a child is exposed to the antibody for a particular antigen before being exposed to the antigen itself then the child will produce a dampened response. Passively acquired maternal antibodies can suppress the antibody response to active immunization. Similarly, the response of T-cells to vaccination differs in children compared to adults, and vaccines that induce Th1 responses in adults do not readily elicit these same responses in neonates.^[20] Between six and nine months after birth, a child's immune system begins to respond more strongly to glycoproteins, but there is usually no marked improvement in their response to polysaccharides until they are at least one year old. This can be the reason for distinct time frames found in vaccination schedules.^{[22][23]}

During adolescence, the human body undergoes various physical, physiological and immunological changes triggered and mediated by hormones, of which the most significant in females is 17- β -estradiol (an estrogen) and, in males, is testosterone. Estradiol usually begins to act around the age of 10 and testosterone some months later.^[24] There is evidence that these steroids not only act directly on the primary and secondary sexual characteristics but also have an effect on the development and regulation of the immune system,^[25] including an increased risk in developing pubescent and post-pubescent autoimmunity.^[26] There is also some evidence that cell surface receptors on B cells and macrophages may detect sex hormones in the system.^[27]

The female sex hormone 17- β -estradiol has been shown to regulate the level of immunological response,^[28] while some male androgens such as testosterone seem to suppress the stress response to infection. Other androgens, however, such as DHEA, increase immune response.^[29] As in females, the male sex hormones seem to have more control of the immune system during puberty and post-puberty than during the rest of a male's adult life.



kinderen



MEDICAL TREATMENTS

A Possible Side Effect? Thousands Of People Saw Menstruation Changes Post-Vaccine

August 3, 2021 · 6:39 PM ET

Heard on [All Things Considered](#)



GEOFF BRUMFIEL



4-Minute Listen

+ PLAYLIST



After vaccination, some people have reported heavy periods or breakthrough bleeding. But changes to menstruation are not listed as a possible side-effect since clinical trials haven't investigated it.

Transcript

MARY LOUISE KELLY, HOST:



Besmetting ook immuniteit

Research paper

SARS-CoV-2 elicits robust adaptive immune responses regardless of disease severity

Stine SF Nielsen ^{a, b} , Line K Vibholm ^a, Ida Monrad ^a, Rikke Olesen ^a, Giacomo S Frattari ^a, Marie H Pahuš ^b, Jesper F Højen ^a, Jesper D Gunst ^{a, b}, Christian Erikstrup ^d, Andreas Holleufer ^c, Rune Hartmann ^c, Lars Østergaard ^{a, b}, Ole S Søgaard ^{a, b}, Mariane H Schleimann ^a, Martin Tolstrup ^{a, b}

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<https://doi.org/10.1016/j.ebiom.2021.103410>

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Abstract

Cross immunity



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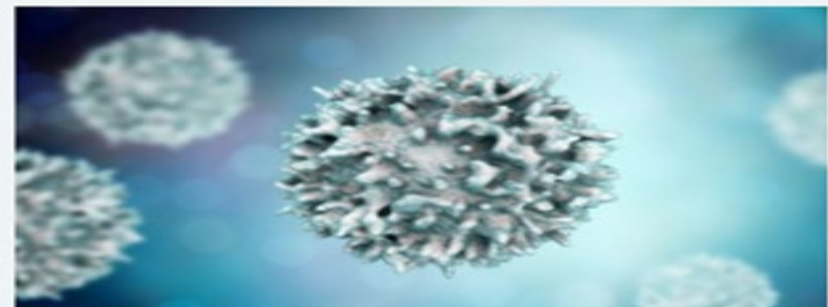
Stanford study ties milder COVID-19 symptoms to prior run-ins with other coronaviruses

In COVID-19 patients whose symptoms were mild, Stanford researchers found that they were more likely than sicker patients to have signs of prior infection by similar, less virulent coronaviruses.

JUL 1
2021

A study by [Stanford University School of Medicine](#) investigators hints that people with COVID-19 may experience milder symptoms if certain cells of their immune systems “remember” previous encounters with seasonal coronaviruses — the ones that cause about a quarter of the common colds kids get.

These immune cells are better equipped to mobilize quickly against SARS-CoV-2, the coronavirus responsible for COVID-19, if they’ve already met its gentler cousins, the scientists concluded.



Killer T cells from patients with mild cases of COVID-19 show indications of recent encounters with other coronaviruses.
Kateryna Kon/Shutterstock

Cross immunity

NATIONAL JOURNAL
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SHORT COMMUNICATION | [VOLUME 105, P304-306, APRIL 01, 2021](#)

Less severe course of COVID-19 is associated with elevated levels of antibodies against seasonal human coronaviruses OC43 and HKU1 (HCoV OC43, HCoV HKU1)

[Martin Dugas](#) ¹  • [Tanja Grote-Westrick](#) ¹ • [Richard Vollenberg](#) • ... [Hartmut Schmidt](#) •

[Phil-Robin Tepas](#) ¹ • [Joachim Kühn](#) ¹ • [Show all authors](#) • [Show footnotes](#)

[Open Access](#) • Published: February 22, 2021 • DOI: <https://doi.org/10.1016/j.ijid.2021.02.085> •






Highlights

- Patients with critical COVID-19 had significantly lower levels of anti-HCoV OC43-NP.
- Anti-HCoV HKU1-NP was also lower in critical COVID-19 patients.

Long lasting

RESEARCH ARTICLE

Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection

 Jennifer M. Dan^{1,2,*},  Jose Mateus^{1,*},  Yu Kato^{1,*},  Kathryn M. Hastie¹,  Esther Dawen Yu¹, Caterina E. Faliti¹,  ...

+ See all authors and affiliations

Science 05 Feb 2021:
Vol. 371, Issue 6529, eabf4063
DOI: 10.1126/science.abf4063

Article

Figures & Data

Info & Metrics

eLetters

 PDF

Variable memory

Immune memory against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) helps to determine protection against reinfection, disease risk, and vaccine efficacy. Using 188 human cases across the range of severity of COVID-19, Dan *et al.* analyzed cross-sectional data describing the dynamics of SARS-CoV-2 memory B cells, CD8⁺ T cells, and CD4⁺ T cells for more than 6 months after infection. The authors found a high degree of heterogeneity in the magnitude of adaptive immune responses that persisted into the immune memory phase.

T-cel 2020

› that inspires

Cell

ARTICLE | [VOLUME 183, ISSUE 1, P158-168.E14, OCTOBER 01, 2020](#)

Robust T Cell Immunity in Convalescent Individuals with Asymptomatic or Mild COVID-19

[Takuya Sekine](#) ¹⁵ • [André Perez-Potti](#) ¹⁵ • [Olga Rivera-Ballesteros](#) ¹⁵ • ... [Hans-Gustaf Ljunggren](#) ¹⁵ • [Soo Aleman](#) ¹⁵ • [Marcus Buggert](#) ^{15, 17}  • [Show all authors](#) • [Show footnotes](#)

[Open Access](#) • Published: August 14, 2020 • DOI: <https://doi.org/10.1016/j.cell.2020.08.017> •



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Highlights



- Acute-phase SARS-CoV-2-specific T cells display an activated cytotoxic phenotype
- Convalescent-phase SARS-CoV-2-specific T cells generate broad responses
- Polyfunctional SARS-CoV-2-specific T cells also occur in seronegative individuals

T-cel 2021

[nature](#) > [scientific reports](#) > [articles](#) > [article](#)

Article | [Open Access](#) | Published: 23 June 2021

Immunodominant T-cell epitopes from the SARS-CoV-2 spike antigen reveal robust pre-existing T-cell immunity in unexposed individuals

Swapnil Mahajan, Vasumathi Kode, Keshav Bhojak, Coral Karunakaran, Kayla Lee, Malini Manoharan, Athulya Ramesh, Sudheendra HV, Ankita Srivastava, Rekha Sathian, Tahira Khan, Prasanna Kumar, Ravi Gupta, Papia Chakraborty  & Amitabha Chaudhuri 

Scientific Reports **11**, Article number: 13164 (2021) | [Cite this article](#)

60k Accesses | **3450** Altmetric | [Metrics](#)

Abstract

The COVID-19 pandemic has revealed a range of disease phenotypes in infected patients with asymptomatic, mild, or severe clinical outcomes, but the mechanisms that determine such variable outcomes remain unresolved. In this study, we identified immunodominant CD8 T-cell epitopes in the spike antigen using a novel TCR-binding algorithm. The predicted epitopes induced robust T-cell activation in unexposed donors demonstrating pre-existing CD4 and

Herd immunity

Indications that Stockholm has reached herd immunity, given limited restrictions, against several variants of SARS-CoV-2

 Marcus Carlsson,  Cecilia Söderberg-Nauclér

doi: <https://doi.org/10.1101/2021.07.07.21260167>

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract

Full Text

Info/History

Metrics

 Preview PDF

Abstract

“When COVID-19 cases go up, public compliance with restrictions is poor, when cases go down, public compliance is good.” In this article, we question this explanation and show that relatively low levels of sero-prevalence helps to keep cases down. In other words, the herd-immunity threshold appears to be much lower than previously thought. We construct a mathematical model taking pre-immunity, antibody waning and more infectious variants of ~~the virus~~ into consideration, thereby providing a theoretical framework in which the cases in

Reprogramming injections

[Comments \(9\)](#)

The BNT162b2 mRNA vaccine against SARS-CoV-2 reprograms both adaptive and innate immune responses

[F. Konstantin Föhse](#), [Büsrhanur Geckin](#), [Gijs J. Overheul](#), [Josephine van de Maat](#), [Gizem Kilic](#), [Ozlem Bulut](#), [Helga Dijkstra](#), [Heidi Lemmers](#), [S. Andrei Sarlea](#), [Maartje Reijnders](#), [Jacobien Hoogerwerf](#), [Jaap ten Oever](#), [Elles Simonetti](#), [Frank L. van de Veerdonk](#), [Leo A.B. Joosten](#), [Bart L. Haagmans](#), [Reinout van Crevel](#), [Yang Li](#), [Ronald P. van Rij](#), [Corine GeurtsvanKessel](#), [Marien I. de Jonge](#), [Jorge Domínguez-Andrés](#), [Mihai G. Netea](#)

doi: <https://doi.org/10.1101/2021.05.03.21256520>

This article is a preprint and has not been peer-reviewed [what does this mean?]. It reports new medical research that has yet to be evaluated and so should *not* be used to guide clinical practice.

Abstract

Full Text

Info/History

Metrics

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Summary

The mRNA-based BNT162b2 vaccine from Pfizer/BioNTech was the first registered COVID-19 vaccine and has been shown to be up to 95% effective in preventing SARS-CoV-2 infections. Little is known about the broad effects of the new class of mRNA vaccines, especially whether

This can also reduce the degree of protection offered by currently available vaccines and those in the pipeline, since the viral spike protein that forms the basis of these first-generation coronavirus disease 2019 (COVID-19) vaccines has undergone several changes under selective pressures.

Despite this, the need to reduce the population risk of severe and fatal illness due to COVID-19 has led to the increasing use of a delayed-second-dose regimen. The intention is to expand the population covered by at least one dose, and therefore the pool of people with some immunity to the virus.

However, following two doses, even though sterile immunity is not induced by the vaccine because mucosal IgA is not induced, the vaccine remains protective against COVID-19, irrespective of falling antibody levels.

The role of memory B cells in immunity

The researchers point out that the decline in the short-term antibody response is not unique to COVID-19. The cooperation of memory B cells and memory plasma cells is more important in long-term immunity, preventing reinfection (or primary infection, in the case of successful vaccination).

Immunititeit door infectie

CONTACT US

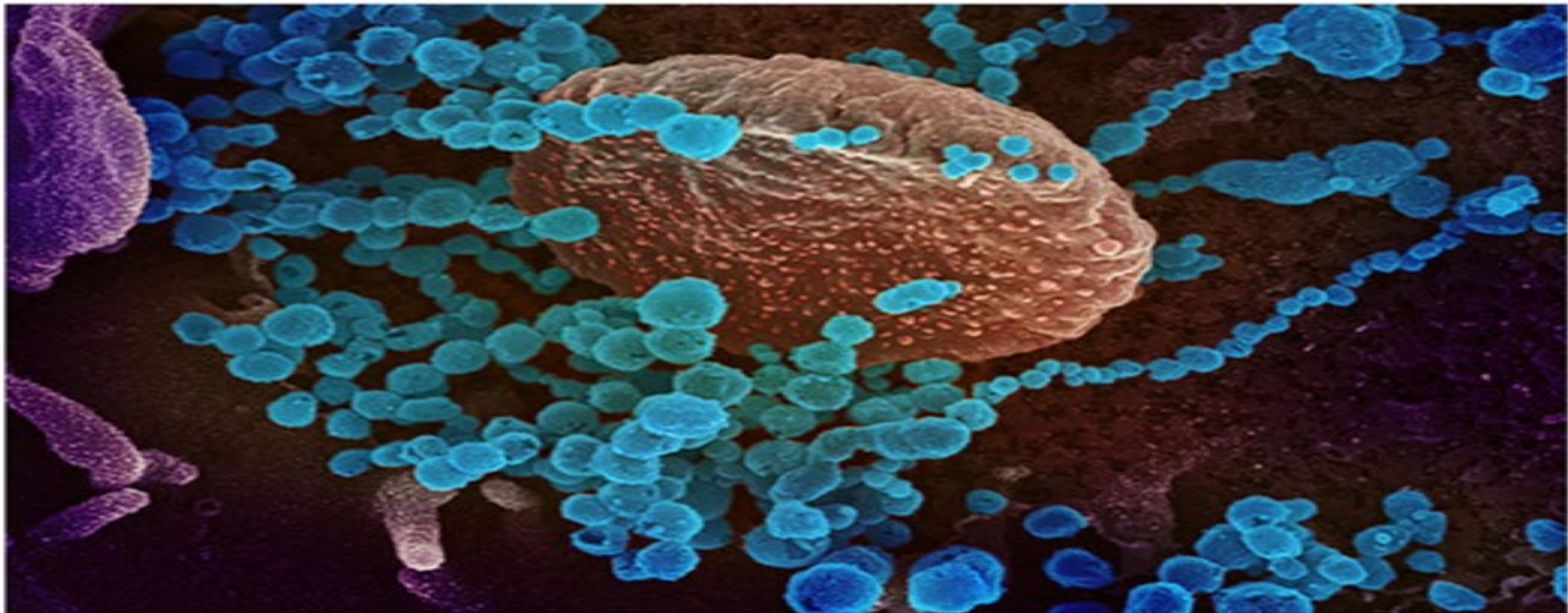
NEWS

COVID-19 survivors may possess wide-ranging resistance to the disease

Conti

Rajee
rajee.

Woodruff Health Sciences Center | July 22, 2021



Recovered COVID-19 patients retain broad and effective longer-term immunity to the disease, suggests a recent Emory University study, which is the most comprehensive of its kind. The findings have implications for expanding understanding about human

SARS-CoV-2-Specific Antibody Detection for Seroepidemiology: A Multiplex Analysis Approach Accounting for Accurate Seroprevalence

Gerco den Hartog , Rutger M Schepp, Marjan Kuijer, Corine GeurtsvanKessel, Josine van Beek, Nynke Rots, Marion P G Koopmans, Fiona R M van der Klis, Robert S van Binnendijk

The Journal of Infectious Diseases, Volume 222, Issue 9, 1 November 2020, Pages 1452–1461, <https://doi.org/10.1093/infdis/jiaa479>

Published: 08 August 2020 **Article history** ▼



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Abstract

Background

The COVID-19 pandemic necessitates better understanding of the kinetics of antibody production induced by infection with SARS-CoV-2. We aimed to develop a high-throughput multiplex assay to detect antibodies to SARS-CoV-2 to assess immunity to the virus in the general population.

pienter

From an immunological point of view, it needs to be established which SARS-CoV-2-specific antibodies correlate with protection. Antibodies to RBD of S1 have been shown to associate with neutralization of the virus in vitro, and preliminary data indicate that the antibodies reported in our assay correlate quantitatively with virus neutralization in vitro as well [6]. The data presented here show detection of total IgG. Another study has shown that IgG subclasses are not equally induced by SARS-CoV-2 infection, with a bias towards the production of IgG3, at least in the first weeks after infection [24]. Infection with SARS-CoV-2 also induces the production of IgA and IgM, which can contribute to protection and in vitro neutralization of the virus, but these isotypes are currently not captured by our assay [7, 8, 25]. Follow-up studies are needed to establish the longevity of the production of antibodies, the degree of protection antibodies confer through various Fc receptor-mediated and

CORRECTED PROOF

Persistence of Antibodies to Severe Acute Respiratory Syndrome Coronavirus 2 in Relation to Symptoms in a Nationwide Prospective Study

Gerco den Hartog , Eric R A Vos, Lotus L van den Hoogen, Michiel van Boven, Rutger M Schepp, Gaby Smits, Jeffrey van Vliet, Linde Woudstra, Alienke J Wijmenga-Monsuur, Cheyenne C E van Hagen ... [Show more](#)

[Author Notes](#)

Clinical Infectious Diseases, ciab172, <https://doi.org/10.1093/cid/ciab172>

Published: 24 February 2021 **Article history** ▼



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Abstract

Background

Assessing the duration of immunity following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a first priority to gauge the degree of protection following infection. Such knowledge is lacking, especially in the general population. Here, we studied changes in immunoglobulin isotype seropositivity and immunoglobulin G (IgG) binding

with SARS-CoV-2 [1–12]. Concurrently, studies report on the decay of antibodies over time, which raises the concern to what degree infected persons may remain protected to reinfection [4, 6, 8, 9, 11]. In addition, rapid decay of these antibodies would make seroprevalence estimates more difficult to interpret later after infection.

Specific antibodies are produced in different isotypes. Following most infections, immunoglobulin M (IgM) production is rapidly upregulated after infection and subsequently declines quickly [13–15]. Specific immunoglobulin A (IgA) and immunoglobulin G (IgG) antibodies typically are initiated later than IgM production. In blood, IgG is the dominant circulating antibody isotype, whereas at mucosal surfaces, including the respiratory tract, IgA antibodies are more dominant [16]. The reported decay of SARS-CoV-2 antibodies will likely differ per isotype, necessitating detailed analyses of the distribution of different antibody isotypes over longer periods of time. The presence of antibodies longer after infection, and rapid upregulation of antibody secretion following reinfection, depends on the presence of B-cell memory. Memory B cells are responsible for the induction of high-quality antibodies that are produced after class switching from IgM to IgG and require editing of the specificity of the antibody to provide an increased fit and binding strength of antibodies, collectively referred to as avidity maturation [17]. Hence, stronger avidity of antibodies is expected to be associated with an underlying cellular response, immune memory, and better ability to confer protection against future infection [18]. In addition to memory B cells, long-lived plasma cells contribute to the secretion of antibodies that can be detected multiple months and even years after an infection [19].

DISCUSSION

In light of the urgent question of the duration of immunity to SARS-CoV-2 following infection in the general population, we systematically studied the dynamics in seropositivity and concentrations of IgM, IgA, and IgG antibodies to the SARS-CoV-2 spike S1 protein among cases with different symptom profiles and investigated IgG maturation over time. Our data confirm that antibodies decline rapidly in the case of IgM and IgA isotypes. **In contrast, 87% of the asymptomatic/mildly symptomatic and 95% of the symptomatic participants remained positive for IgG 7 months after onset of COVID-19 symptoms. Moreover, the estimated 2-fold decrease in concentration of 158 days and the increasing avidity of anti-spike IgG antibodies indicate the presence of memory B cells and/or long-lived plasma cells.**

We showed that IgM and IgA antibodies start to decay within a few months after onset of symptoms, which may help explain the decline in seropositivity in some studies [6, 11, 13–15]. Since IgG antibodies persist much longer than IgM and IgA antibodies, the detection of IgG provides better sensitivity longer after infection, and therefore, IgG should be the isotype of choice in studies aiming to assess seroprevalence >2 months after the infection and in longitudinal studies. IgG may also be the most informative for identifying memory induction, since specific IgG antibody development requires multiple cell divisions and class-switch recombination, processes that are a hallmark of memory formation. The hallmarks of memory formation—IgG antibodies with high avidity and persistence of antibodies—are presented in this study. The 2-fold decrease of IgG estimated in this

Immune surveillance for vaccine-preventable diseases

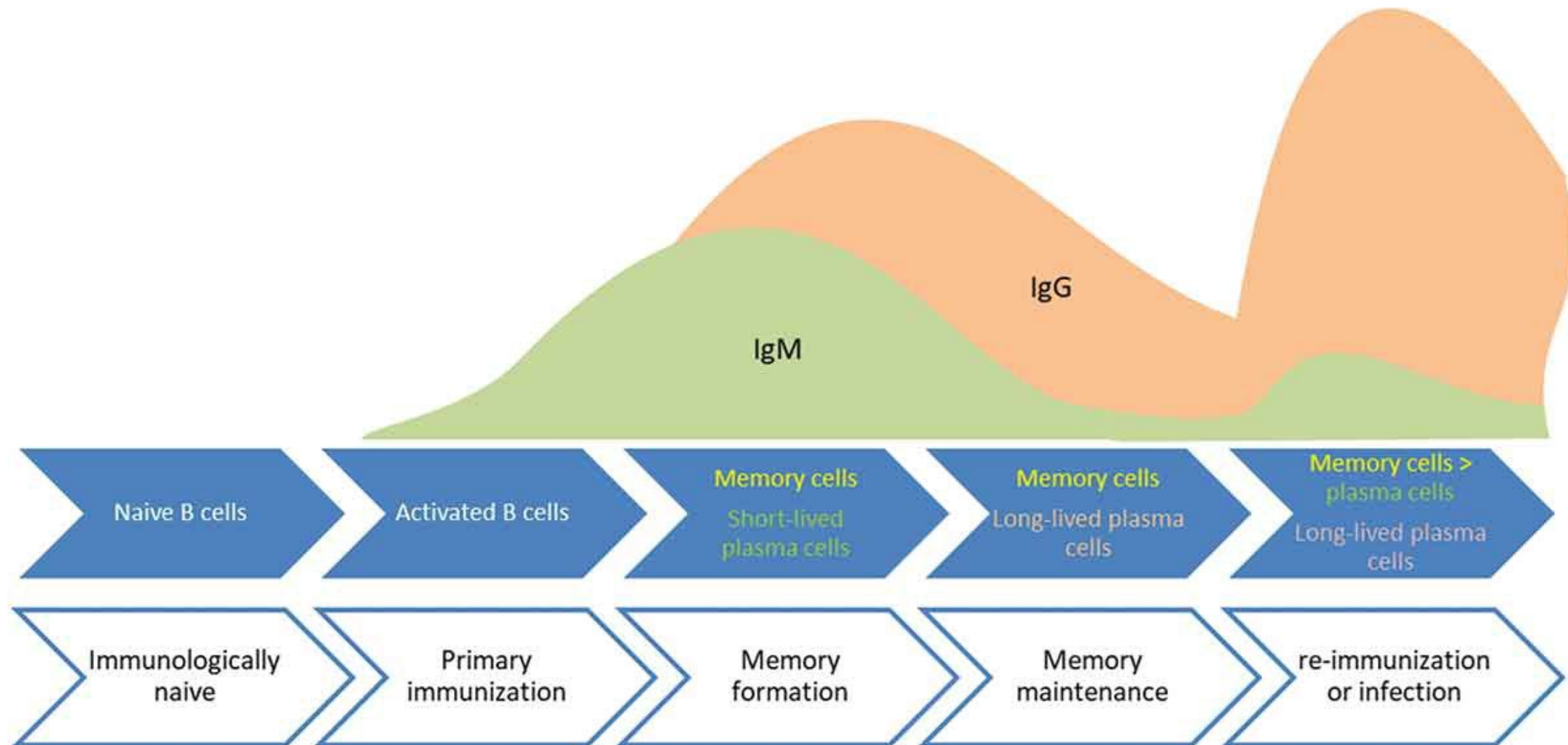


Table 3 of 4

Table 3. Serosurveillance purposes.

Purpose		Antigen in assay	Application
Vaccination response	Vaccine potency	Vaccine-derived	Evaluate the magnitude/strength of the response; estimates can be seroconversion rates, GMCs/serum-titers, significant titer rises, etc.
	Vaccine efficacy	Vaccine-derived	Evaluate immune protection; estimates can be GMCs or seroprevalence, related to an estimated/predetermined cutoff for immune protection
	Vaccine waning	Vaccine-derived	Evaluate the duration of vaccine-acquired immune protection; estimates can be concentration/titer changes in time
Exposure or infection	Infection	Pathogen-derived	Define persons in the population with previous/recent infection
	Breakthrough infection (re-infection)	Pathogen-derived, not part of the vaccine	Discriminate persons with infection history in the background of vaccination
	Emergence	Immunogenic unique, quantitative/qualitative discrimination	(Re-)Emerging pathogens, related to zoonoses and migration cq, international spread
	Evolution	Vaccine and non-vaccine (evolved/adapted trains)	Changes in pathogens related to antigenic drift/shift, or immunity/vaccine escape

Table 4. Type of antibodies related to vaccination and exposure/infection.

Vaccine	composition	Antibodies	Unique infection-induced antibodies	refs
Diphtheria	toxin	IgG		[35]
Tetanus	toxin	IgG		[36]
<i>B. pertussis</i> aP	1-5 proteins	IgG	Non-vaccine proteins, IgA	
<i>B. pertussis</i> wP	Inactivated	IgG, IgA	Unknown?	
<i>S. pneumoniae</i>	polysaccharides	IgG, some IgA	Proteins, IgA	
Hib	polysaccharides	IgG, some IgM and IgA	Proteins	[61,62]
<i>N. meningitidis</i> ACWY				
B	Polysaccharides 3 proteins and 1 OMV	IgG, some IgM, IgA	Proteins Non-vaccine proteins	
Measles	Live attenuated	IgG, some IgM, IgA	IgA	[63,102]
Mumps	Live attenuated	IgG	IgA	[26,64]
Rubella	Live attenuated			[63]
Poliovirus IPV	Inactivated	IgG	IgA	
Poliovirus OPV	live attenuated (oral)	IgG and IgA	-	[65,66]
HPV	L1 Protein VLP	IgG	Much lower levels	
HepB	Surface protein VLP	IgG	Core protein	
Rotavirus	Live attenuated virus			

aP: acellular pertussis; OMV: outer-membrane vesicle; VLP: virus-like particle; wP: whole cellular pertussis.

For many pathogens targeted by vaccines, first entry and infection happen at mucosal surfaces in the respiratory tract (e.g. *B. pertussis*, *N. meningitidis*, *S. pneumoniae*, Hib, measles) or the gastrointestinal tract (e.g. poliovirus, rotavirus). Disease symptoms may even be restricted to the respiratory tract, as is the case for whooping cough (*B. pertussis*) and pneumonia (*S. pneumoniae*). For these reasons in some studies antibody detection is carried out in oropharyngeal specimens such as saliva (also termed oral fluid), as these may be a better proxy for immune protection of the respiratory tract than antibodies in serum [78,85,86]. However, IgG antibody concentrations in saliva specimens are limited, equal, or less than 1% of what can be detected in serum. The relative proportion of IgA antibodies is higher because mucosal surfaces promote the production of protective IgA that can be secreted and neutralize pathogens before infection can occur [87–90]. Moreover, depending on the specific tissue, efficient transport of dimeric IgA can occur through the polymeric Ig receptor resulting in secretory IgA in the lumen of mucosal surfaces such as the respiratory tract [91,92]. Although memory IgA B cells could be detected 1-year post-MenC vaccination, local IgA antibodies induced by vaccination may decline relatively fast [93,94]. Assessing IgA antibodies after vaccination often proves challenging, because well-defined control sera or serum panels with defined concentrations and general knowledge regarding protective

sabotage

Editor's Note: This article was published on April 21, 2021, at NEJM.org.

ORIGINAL ARTICLE

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., [et al.](#), for the CDC v-safe COVID-19 Pregnancy Registry Team*

Article **Figures/Media**

Metrics

32 References 15 Citing Articles

June 17, 2021

N Engl J Med 2021; 384:2273-2282

DOI: 10.1056/NEJMoa2104983

Chinese Translation [中文翻译](#)

Abstract

BACKGROUND

Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.

METHODS

From December 14, 2020, to February 28, 2021, we used data from the “v-safe after vaccination health checker” surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting

Related Articles

EDITORIAL JUN 17, 2021

mRNA Covid-19 Vaccines in Pregnant Women

L.E. Riley

ADVERTISEMENT

OUTCOMES

V-safe outcomes included participant-reported local and systemic reactogenicity to the BNT162b2 (Pfizer–BioNTech) vaccine and the mRNA-1273 (Moderna) vaccine on the day after vaccination among all pregnant persons 16 to 54 years of age and among nonpregnant women 16 to 54 years of age as a comparator. For analysis of pregnancy outcomes in the v-safe pregnancy registry, data were restricted to completed pregnancies (i.e., live-born infant, spontaneous abortion, induced abortion, or stillbirth). Participant-reported pregnancy outcomes included pregnancy loss (spontaneous abortion and

ADVERSE-EVENT FINDINGS ON THE VAERS

During the analysis period, the VAERS received and processed 221 reports involving Covid-19 vaccination among pregnant persons; 155 (70.1%) involved nonpregnancy-specific adverse events, and 66 (29.9%) involved pregnancy- or neonatal-specific adverse events (Table S4). The most frequently reported pregnancy-related adverse events were spontaneous abortion (46 cases; 37 in the first trimester, 2 in the second trimester, and 7 in which the trimester was unknown or not reported), followed by stillbirth, premature rupture of membranes, and vaginal bleeding, with 3 reports for each. No congenital anomalies were reported to the VAERS, a requirement under the EUAs.

pregnant but received vaccination more than 30 days before the last menstrual period, or did not provide enough information to determine eligibility). The registry enrolled 3958 participants with vaccination from December 14, 2020, to February 28, 2021, of whom 3719 (94.0%) identified as health care personnel. Among enrolled participants, most were 25 to 44 years of age (98.8%), non-Hispanic White (79.0%), and, at the time of interview, did not report a Covid-19 diagnosis during pregnancy (97.6%) (Table 3). Receipt of a first dose of vaccine meeting registry-eligibility criteria was reported by 92 participants (2.3%) during the periconception period, by 1132 (28.6%) in the first trimester of

pregnancy, by 1714 (43.3%) in the second trimester, and by 1061 (27.1%) in the third trimester. Adverse outcomes among 724 live-born infants — including 12 sets of multiple gestation — were preterm birth (60 of 636 among those vaccinated before 37 weeks [9.4%]), small size for gestational age (23 of 724 [3.2%]), and major congenital anomalies (16 of 724 [2.2%]): no neonatal deaths were stillbirth in 1 (0.1%), and in other outcomes (induced abortion and ectopic pregnancy) in 10 (1.2%). A total of 96 of 104 spontaneous abortions (92.3%) occurred before 13 weeks of gestation (Table 4), and 700 of 712 pregnancies that resulted in a live birth (98.3%) were among persons who received their first eligible vaccine dose in the third trimester.

Table 4. Pregnancy Loss and Neonatal Outcomes in Published Studies and V-safe Pregnancy Registry Participants.

Participant-Reported Outcome	Published Incidence*	V-safe Pregnancy Registry†
	%	no./total no. (%)
Pregnancy loss among participants with a completed pregnancy		
Spontaneous abortion: <20 wk ¹⁵⁻¹⁷	10–26	104/827 (12.6)‡
Stillbirth: ≥ 20 wk ¹⁸⁻²⁰	<1	1/725 (0.1)§
Neonatal outcome among live-born infants		
Preterm birth: <37 wk ^{21,22}	8–15	60/636 (9.4)¶
Small size for gestational age ^{23,24}	3.5	23/724 (3.2)
Congenital anomalies ^{25**}	3	16/724 (2.2)
Neonatal death ^{26††}	<1	0/724

* The populations from which these rates are derived are not matched to the current study population for age, race and ethnic group, or other demographic and clinical factors.

† Data on pregnancy loss are based on 827 participants in the v-safe pregnancy registry who received an mRNA Covid-19 vaccine (BNT162b2 [Pfizer–BioNTech] or mRNA-1273 [Moderna]) from December 14, 2020, to February 28, 2021, and who reported a completed pregnancy. A total of 700 participants (84.6%) received their first eligible dose in the third trimester. Data on neonatal outcomes are based on 724 live-born infants, including 12 sets of multiples.

‡ A total of 96 of 104 spontaneous abortions (92.3%) occurred before 13 weeks of gestation.

Berekening

827 completed

12% miscarriage (gemiddeld)

~100 verwachte doden

.127 injectie voor 3rd

.16 %

.104 miskr voor 20 w

.700 injectie in 3rd tri

.84%

.1 miskr na 20 weken

.In totaal zijn er voor de groep niet meer miskramen

.In de subgroep 1st en 2nd trimester veel meer.

This is Nuts, Moderna and Pfizer Intentionally Lost The Clinical Trial Control Group Testing Vaccine Efficacy and Safety

August 6, 2021 | [Sundance](#) | [527 Comments](#)

This is not just scientific madness, it appears to be very intentional and purposeful.



The Moderna and Pfizer vaccine tests were conducted, as customary, with a control group; a group within the trial who were given a placebo and not the test vaccine. However, during the trial -and after the untested vaccines were given emergency use authorization- the vaccine companies conducting the trial decided to break protocol and notify the control group they were not vaccinated. Almost all the control group were then given the vaccine.

Purposefully dissolving the placebo group violates the scientific purpose to test whether the vaccine has any efficacy; any actual benefit and/or safety issues. Without a control group there is nothing to compare the vaccinated group against. [According to NPR](#), the doctors lost the control group in the Johnson County Clinical Trial (Lexena, Kansas) **on purpose**:

(Via NPR) [...] “Dr. Carlos Fierro, who runs the study there, says every participant was called back after the Food and Drug Administration authorized the vaccine.

“During that visit we discussed the options, which included staying in the study without the vaccine,”

Meldingen van bijwerkingen na vaccinatie influenza tegenover meldingen van bijwerkingen na vaccinatie Covid
Bron LAREB

influenza	Globaal geschat aantal prikken	meldingen	doden	miskramen	ziekenhuisopnames
2019/2020 ¹	3.000.000	749	3	0	6

corona	Globaal geschat aantal prikken incl. 2 ^{de}	meldingen	doden	miskramen	ziekenhuisopnames
Update t/m 09-05-2021 ²	6.400.000	49.850	320	13 (Pfizer 11x Moderna 1x AstraZ 1x) ³	Nog niet bekend gemaakt

Meldingen over trombose in samengaan met lage bloedplaatjes

AstraZ	15
Pfizer	
Moderna	
Jansen	

Wie meer wilt weten over alle gemelde bijwerkingen kan dat nakijken op de website van Lareb. Even doorscrollen naar beneden, klikken op het soort vaccin en dan klikken op 'alles uitklappen' <https://www.lareb.nl/pages/update-van-bijwerkingen>

¹ https://www.lareb.nl/media/xchdjqpflareb_rapport_griep_2019-2020.pdf#media/xchdjqpflareb_rapport_griep_2019-2020.pdf

² <https://www.lareb.nl/coronameldingen#/>

³ <https://www.rivm.nl/covid-19-vaccinatie/vaccins/zwangerschap> Het RIVM geeft op 28-4-2021 advies aan zwangere vrouwen om zich te laten vaccineren met mRNA vaccin (Pfizer en Moderna) omdat volgens het RIVM na 90.000 injecties in de USA geen ernstige bijwerkingen zijn gemeld. Het is niet duidelijk hoeveel zwangere vrouwen in Nederland tot deze datum zijn gevaccineerd en wat als een niet ernstige bijwerking wordt beschouwd.

Highlights

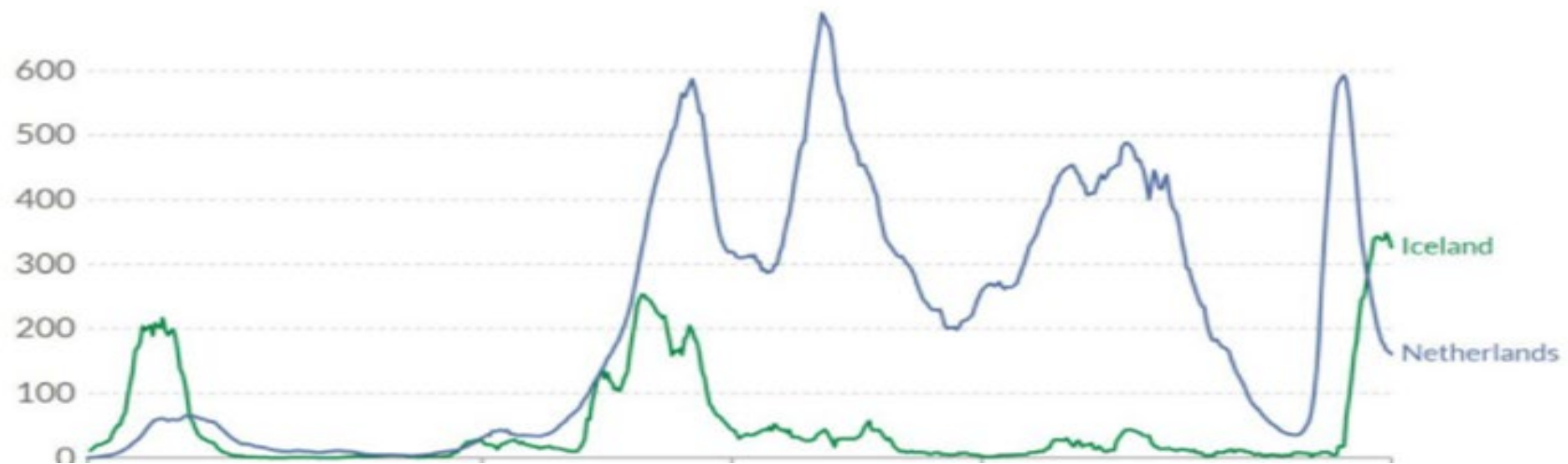
- SARS-CoV-2 vaccine trials did not directly estimate vaccine efficacy against transmission.
- We describe an approach to estimate a lower bound of vaccine efficacy against transmission.

 Lees volledig artikel

Leestijd: 3 minuten

Volledig gevaccineerd IJsland past beleid ingrijpend aan

Enkele dagen geleden hebben we de situatie in IJsland beschreven. Het land kent een heel hoge vaccinatiegraad en beëindigde eind juni vrijwel alle maatregelen. Maar sinds ruim twee weken lopen de cijfers daar weer duidelijk op en [maakt men zich zorgen over de groeiende druk op de zorginfrastructuur](#). [Op deze pagina treft u de kerncijfers aan van IJsland](#). Het land heeft 1/50e van de bevolking van Nederland. In vergelijking met Nederland is dit de ontwikkeling van het aantal positieve testen per miljoen inwoners. [De vaccinatiegraad is hoger dan in Nederland](#). De mix aan type vaccins lijkt enigszins op die van Nederland.



Study from Great Britain

08/07/2021, 2:33 pm

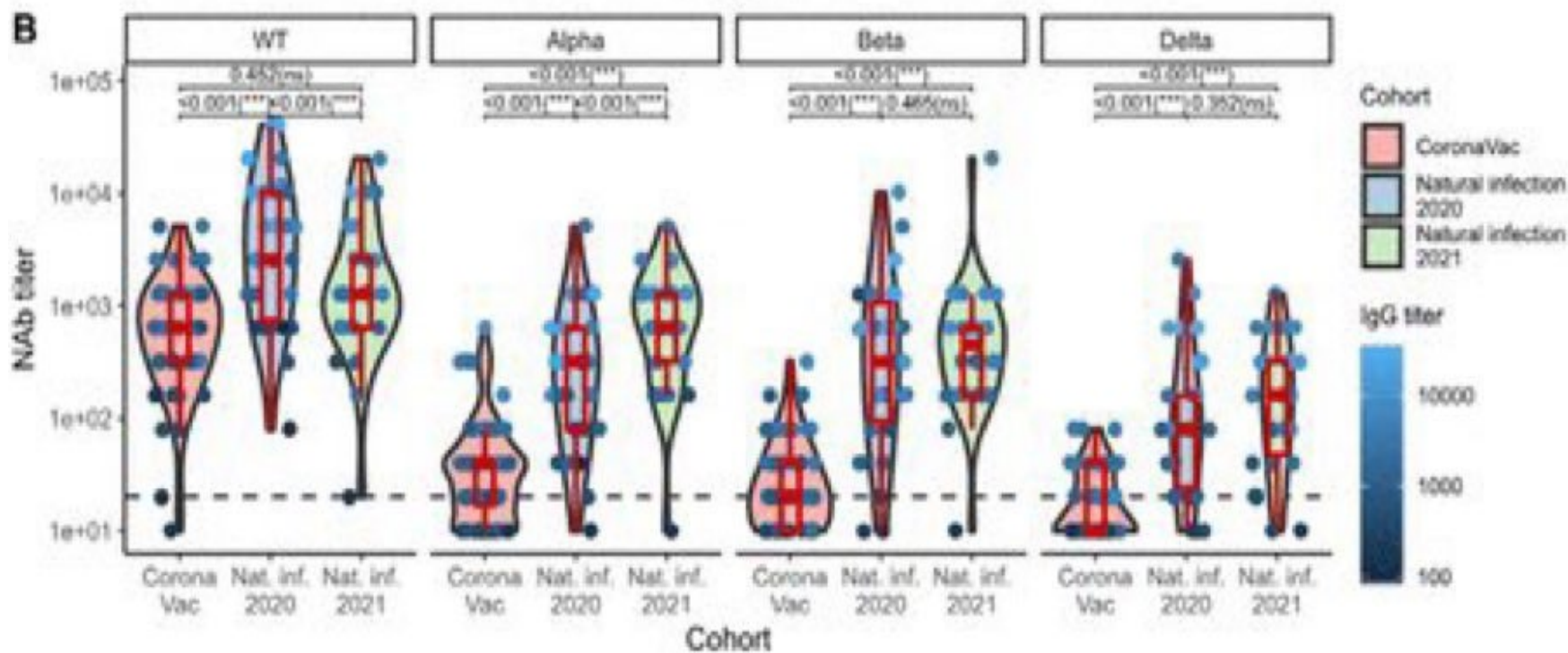
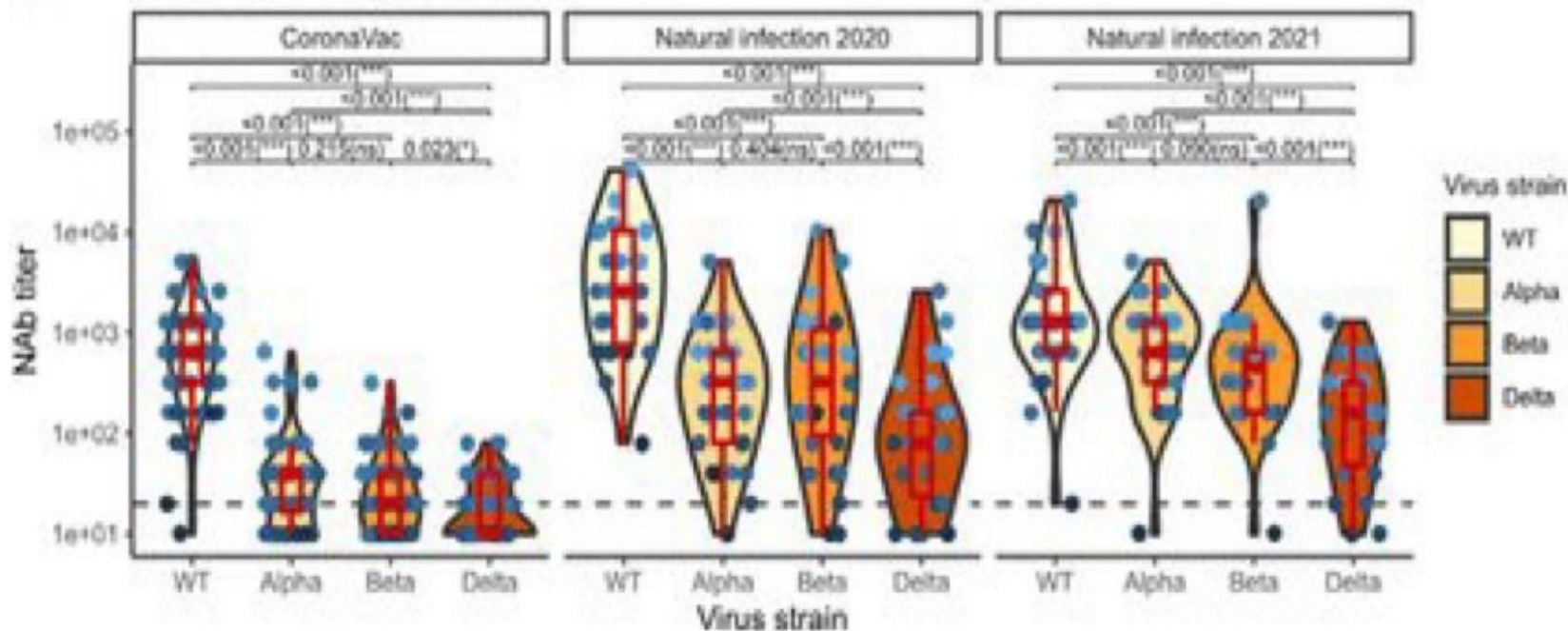
Viral load in vaccinated people as high as unvaccinated Delta infected people

The vaccination against the coronavirus protects against severe courses. However, vaccinated people infected with the Delta variant can be as contagious as unvaccinated people.



Vaccinations do not necessarily protect against infection with the coronavirus. PHOTO: DPA / DANIEL KARMANN

A NAb titre: Tukey contrasts



variants of concern¹. As a result, vaccination of coronavirus disease 2019 (COVID-19) convalescent individuals with currently available mRNA vaccines produces high levels of plasma neutralizing activity against all variants tested^{1, 2}. Here, we examine memory B cell evolution 5 months after vaccination with either Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) mRNA vaccines in a cohort of SARS-CoV-2 naïve individuals. Between prime and boost, memory B cells produce antibodies that evolve increased neutralizing activity, but there is no further increase in potency or breadth thereafter. Instead, memory B cells that emerge 5 months after vaccination of naïve individuals express antibodies that are equivalent to those that dominate the initial response. We conclude that memory antibodies selected over time by natural infection have greater potency and breadth than antibodies elicited by vaccination. These results suggest that boosting vaccinated individuals with currently available mRNA vaccines would produce a quantitative increase in plasma neutralizing activity but not the qualitative advantage against variants obtained by vaccinating convalescent individuals.

Competing Interest Statement

The Rockefeller University has filed a provisional patent application in connection with this work on which M.C.N. is an inventor (US patent 63/021,387). The patent has been licensed by Rockefeller University to Bristol Meyers Squib.

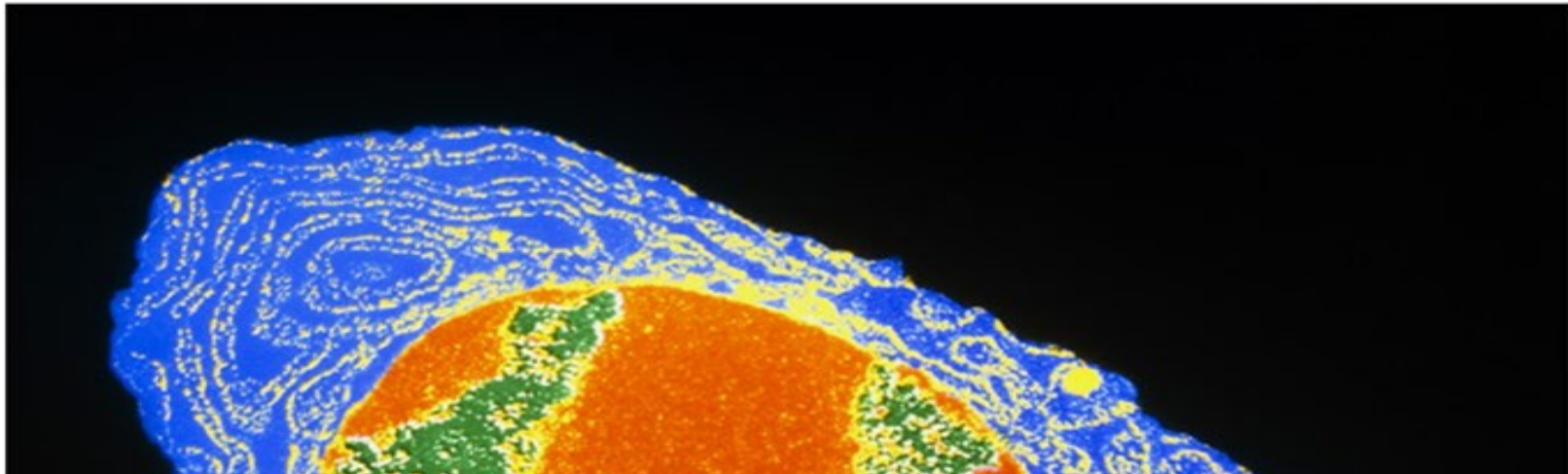
nature > news > article

NEWS | 26 May 2021 | Correction 27 May 2021

Had COVID? You'll probably make antibodies for a lifetime

People who recover from mild COVID-19 have bone-marrow cells that can churn out antibodies for decades, although viral variants could dampen some of the protection they offer.

Ewen Callaway



Janssen

3.2.1 Klinische trials

Momenteel zijn er nog verschillende klinische trials in uitvoering naar het Ad26.COV2.S-vaccin. Eén van de trials onderzoekt de toegevoegde waarde van een tweede dosis vaccin op de immunogeniciteit en werkzaamheid. De immuunrespons die één dosis vaccin opwekt is onderzocht in een fase 1-2-trial bij mensen tussen 18-55 jaar en bij mensen van 65 jaar en ouder.¹² Uit interim-analyses blijkt dat het vaccin 15 dagen na toediening in alle leeftijdsgroepen leidt tot de productie van neutraliserende antistoffen en een T-celrespons (CD4+ Th1-celrespons en CD8+ T-celrespons).

De werkzaamheid van het vaccin is tot nog toe bepaald in ruim 39.000 mensen uit de Verenigde Staten (VS), Zuid-Afrika en verschillende landen in Midden- en Zuid-Amerika (Argentinië, Brazilië, Chili, Colombia, Mexico en Peru).^{10,13} Ongeveer 47% van de deelnemers woont in de VS, ongeveer 13% in Zuid-Afrika, en ongeveer 40% in Midden- en Zuid-Amerika. Het grootste deel was tussen 18 en 64 jaar oud (ongeveer 80%), ongeveer 16% was tussen 65 en 75 jaar oud en ongeveer 4% was 75 jaar of ouder. Ongeveer 40% van de deelnemers had een chronische aandoening (meestal hypertensie, diabetes mellitus type 2, of obesitas). In de totale groep deelnemers werden op basis van een PCR-test bij mensen met klachten 259 gevallen van matige tot ernstige COVID-19 vastgesteld in een periode vanaf 28 dagen na vaccinatie: 193 in de controlegroep (n=19.691) en 66 in de vaccingroep (n=19.630). Dit betekent dat de

werkzaamheid van het vaccin 66% was (95% betrouwbaarheidsinterval (95%BI): 55,0-74,8%). De werkzaamheid was 85% (95%BI: 54,2-96,9%) tegen ernstige COVID-19 – in de vaccingroep kwam ernstige ziekte 14 keer voor, terwijl dat er 60 waren in de controlegroep. Bij mensen van 65 jaar en ouder was de werkzaamheid 74% (95%BI: 34,4-91,4%) – in de vaccingroep werden 6 gevallen van COVID-19 vastgesteld, tegenover 23 in de controlegroep. Een analyse bij mensen met een chronische aandoening liet zien dat de werkzaamheid 59% was (95%BI: 40,6-71,6%) – in de vaccingroep (n=7.684) werden 44 gevallen van COVID-19 vastgesteld, tegenover 105 in de controlegroep (n=7.626).¹³

Per regio bekeken was werkzaamheid 72% (95%BI: 58,2-81,7%) in de VS, 64% (95%BI: 41,2-78,7%) in Zuid-Afrika en 68% (95%BI: 48,8-80,7%) in Brazilië in een periode vanaf 28 dagen na vaccinatie.¹⁰ Deze verschillen worden waarschijnlijk verklaard doordat er in verschillende gebieden verschillende virusvarianten circuleren. In Zuid-Afrika werd bijna 95% van de infecties veroorzaakt door virusvariant B.1.351, waardoor wordt aangenomen dat het vaccin werkzaam is tegen deze virusvariant. Of het vaccin ook voldoende werkzaam is tegen andere virusvarianten, zoals de Engelse (B.1.1.7) en Braziliaanse (P.1) varianten wordt nog onderzocht.

Het is nog niet bekend wat de duur van de werkzaamheid is, omdat het vaccin recent is ontwikkeld en de klinische trials nog in uitvoering zijn.

Ook is nog niet bekend of het vaccin verspreiding kan voorkomen.

Condition or disease ¹	Intervention/treatment ¹	Phase ¹
Healthy	Biological: Ad26.COVS2.S Biological: Placebo	Phase 1

Study Design

Go to

Study Type ¹: Interventional (Clinical Trial)

Actual Enrollment ¹: 250 participants

Allocation: Randomized

Intervention Model: Parallel Assignment

Masking: Double (Participant, Investigator)

Primary Purpose: Prevention

Official Title: A Randomized, Double-blind, Placebo-controlled Phase 1 Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of Ad26.COVS2.S in Adults

Actual Study Start Date ¹: August 11, 2020

Actual Primary Completion Date ¹: February 22, 2021

Estimated Study Completion Date ¹: December 8, 2021

Arms and Interventions

Go to

Arm ¹	Intervention/treatment ¹
<p>Experimental: Ad26.COVS2.S: High Dose</p> <p>Participants (healthy adults aged greater than or equal to (\geq) 20 to less than or equal to (\leq) 55 years [cohort 1] and \geq 65 years [cohort 2]) will receive intramuscular (IM) injection of Ad26.COVS2.S at high dose, as 2-dose schedule on Day 1 and Day 57.</p>	<p>Biological: Ad26.COVS2.S</p> <p>Ad26.COVS2.S will be administered as IM injection at 2-dose (high and low) levels.</p> <p>Other Names:</p> <ul style="list-style-type: none"> JNJ-78436735 Ad26COVS1

Locations

Netherlands

PRA Health Sciences
Groningen, Netherlands, NZ 9728

Sponsors and Collaborators

Janssen Vaccines & Prevention B.V.

Investigators

Study Director: Janssen Vaccines & Prevention B.V. Clinical Trial Janssen Vaccines & Prevention B.V.

More Information

Responsible Party:	Janssen Vaccines & Prevention B.V.
ClinicalTrials.gov Identifier:	NCT04894305 History of Changes
Other Study ID Numbers:	CR109013 2021-001374-30 (EudraCT Number) VAC31518COV1003 (Other Identifier: Janssen Vaccines & Prevention B.V.)
First Posted:	May 20, 2021 Key Record Dates

History of Changes for Study: NCT04894305

A Study of Ad26.COVID.S in Healthy Adults (COVID-19)

[Latest version \(submitted July 6, 2021\) on ClinicalTrials.gov](#)

Study Record Versions

Version	A	B	Submitted Date	Changes
1	<input checked="" type="radio"/>	<input type="radio"/>	May 18, 2021	None (earliest Version on record)
2	<input type="radio"/>	<input type="radio"/>	June 1, 2021	Recruitment Status, Study Status, Oversight, References and Contacts/Locations
3	<input type="radio"/>	<input checked="" type="radio"/>	July 6, 2021	Recruitment Status, Study Status, Contacts/Locations, References and Study Design

Compare

Comparison Format:

- Merged
 Side-by-Side

Maximum Age: 65 Years

Sex: All

Gender Based:

Accepts Healthy Volunteers: Yes

Criteria: Inclusion Criteria:

- Participant must sign an informed consent form (ICF) indicating that he or she understands the purpose, procedures and potential risks and benefits of the study, and is willing to participate in the study
- Participant must be healthy, in the investigator's clinical judgment, as confirmed by medical history, physical examination, and vital signs performed at screening. Participant may have underlying illnesses, as long as the symptoms and signs are medically controlled and not considered to be comorbidities related to an increased risk of severe coronavirus disease-2019 (COVID-19), except for smoking, which is allowed. If on medication for a condition, the medication dose must have been stable for at least 12 weeks preceding vaccination and expected to remain stable for the duration of the study
- All participants of childbearing potential must: a) have a negative highly sensitive urine pregnancy test at screening; b) have a negative highly sensitive urine pregnancy test immediately on the day of and prior to study vaccine administration
- Participant agrees to not donate bone marrow, blood, and blood products from the first study vaccine administration until 3 months after receiving the study vaccine
- Participant must be willing to provide verifiable identification, has means to be contacted and to contact the investigator during the study

Reactogenicity

From Wikipedia, the free encyclopedia

In [clinical trials](#), the term **reactogenicity** refers to the property of a [vaccine](#) of being able to produce common, "expected" adverse reactions, especially excessive immunological responses and associated signs and symptoms, including fever and sore arm at the injection site. Other manifestations of reactogenicity typically identified in such trials include [bruising](#), [redness](#), [induration](#), and [swelling](#).^[1]

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- 4 [References](#)
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Origin [\[edit\]](#)

The term reactogenicity was coined by the US [Food and Drug Administration](#) (FDA). Typically, reactogenicity is observed upon the administration of an [adjuvant](#), which is a chemical additive intended for enhancing the recipient's immune response to the [antigen](#) that is present in a vaccine but can also be observed in non-adjuvanted vaccines. Reactogenicity describes the immediate short-term reactions of a system to vaccines and should not be confused with the long-term consequences [sequelae](#). Assessments of reactogenicity are carried out to evaluate the safety and usability of an experimental vaccine (see [Investigational New Drug](#)). It is unclear whether a higher degree of reactogenicity to a vaccine correlates with more severe [adverse events](#), which would require hospitalization or are life-threatening. Adverse events have been linked to a higher degree of reactogenicity; however, the links might have been coincidental. After assessing large databases relating to these events for



‘Zorgpersoneel en brandweer in Frankrijk leggen werk neer tot vaccinatiepaspoort van tafel is’

◆ 5 AUGUSTUS 2021