COVID-19 Vaccines

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Controlling Communicable Diseases

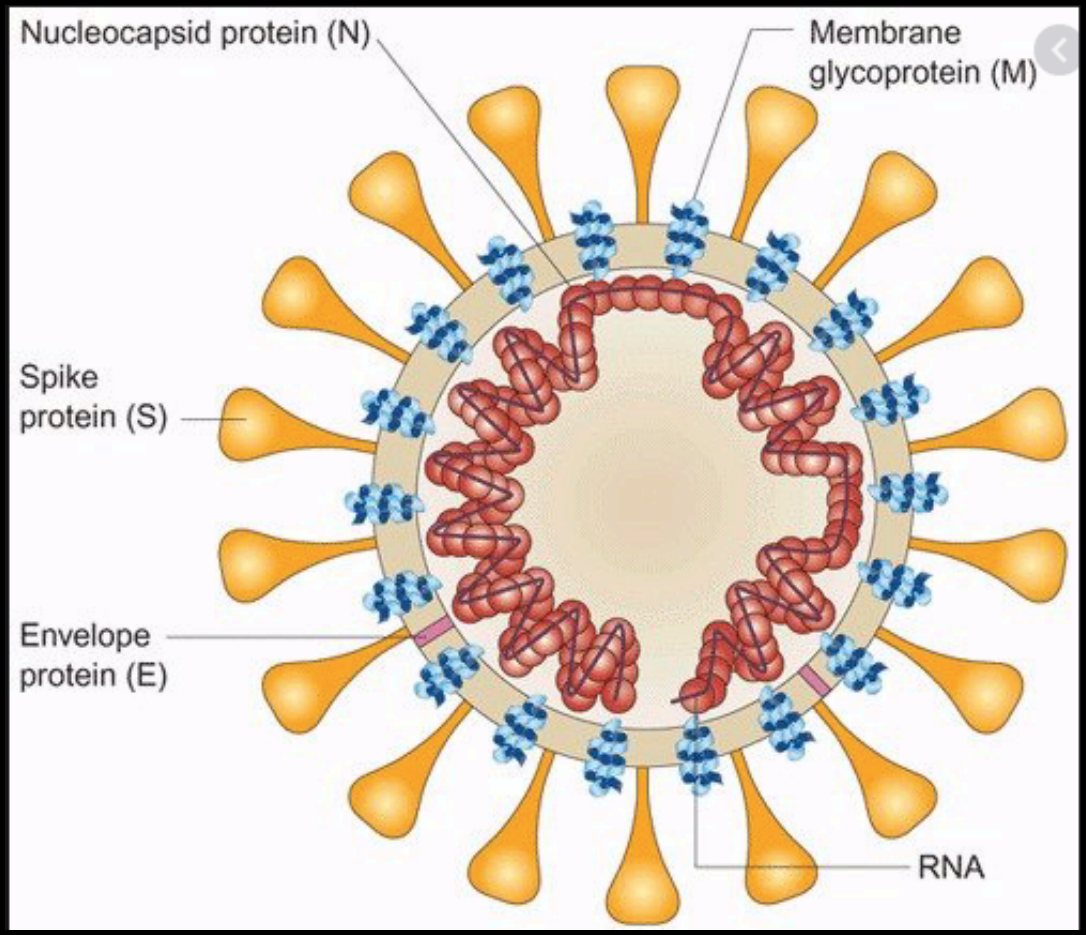
- Change behavior/reduce contact
- If there is contact, lower chances of transmission
- Just treat patients and go on as usual
- Vaccinate!

All viable, depending on the context.
They may/should also be combined

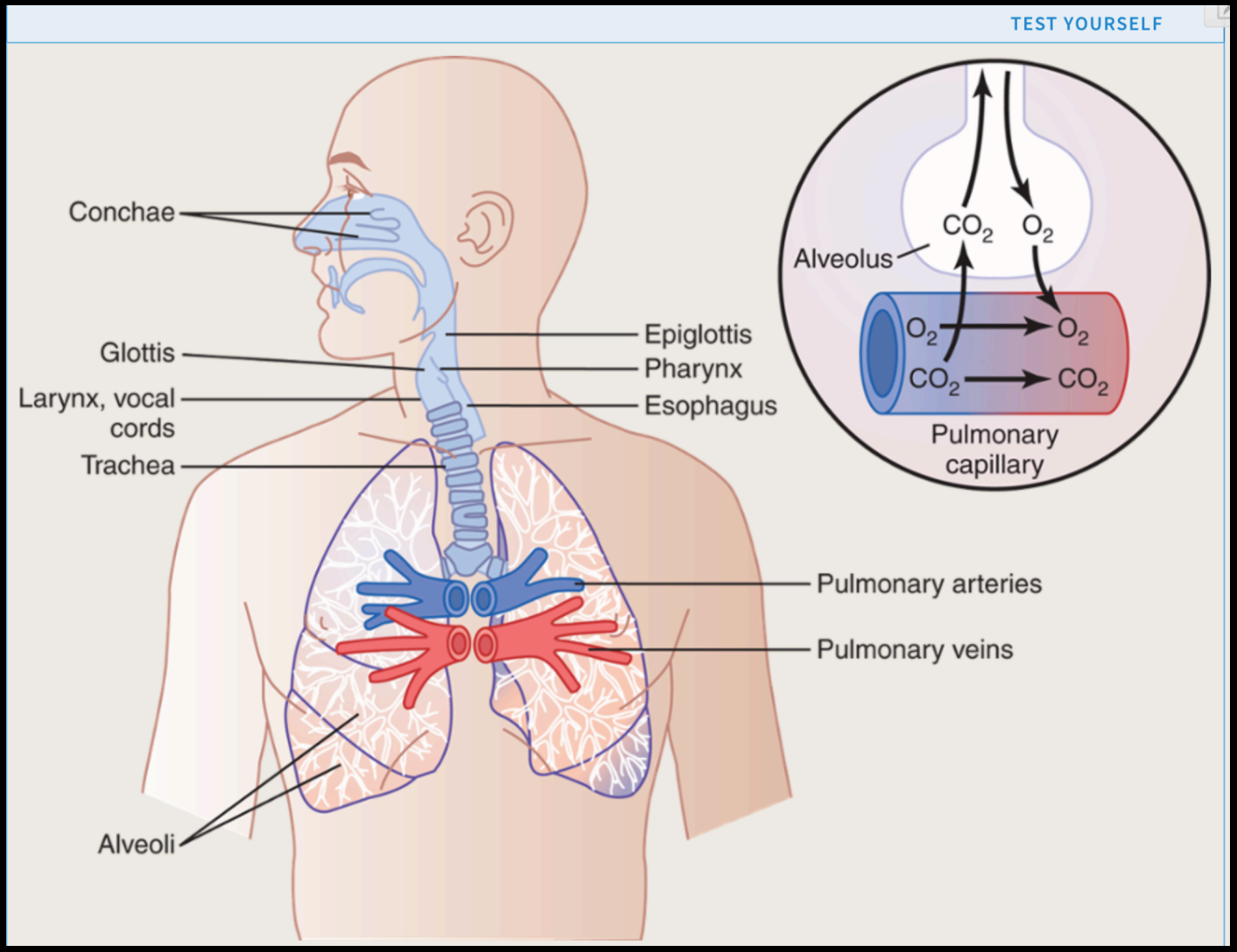
Context of COVID-19: It can be severe, cause death and ?long term impairment, and we all want to be able to resume our lives!

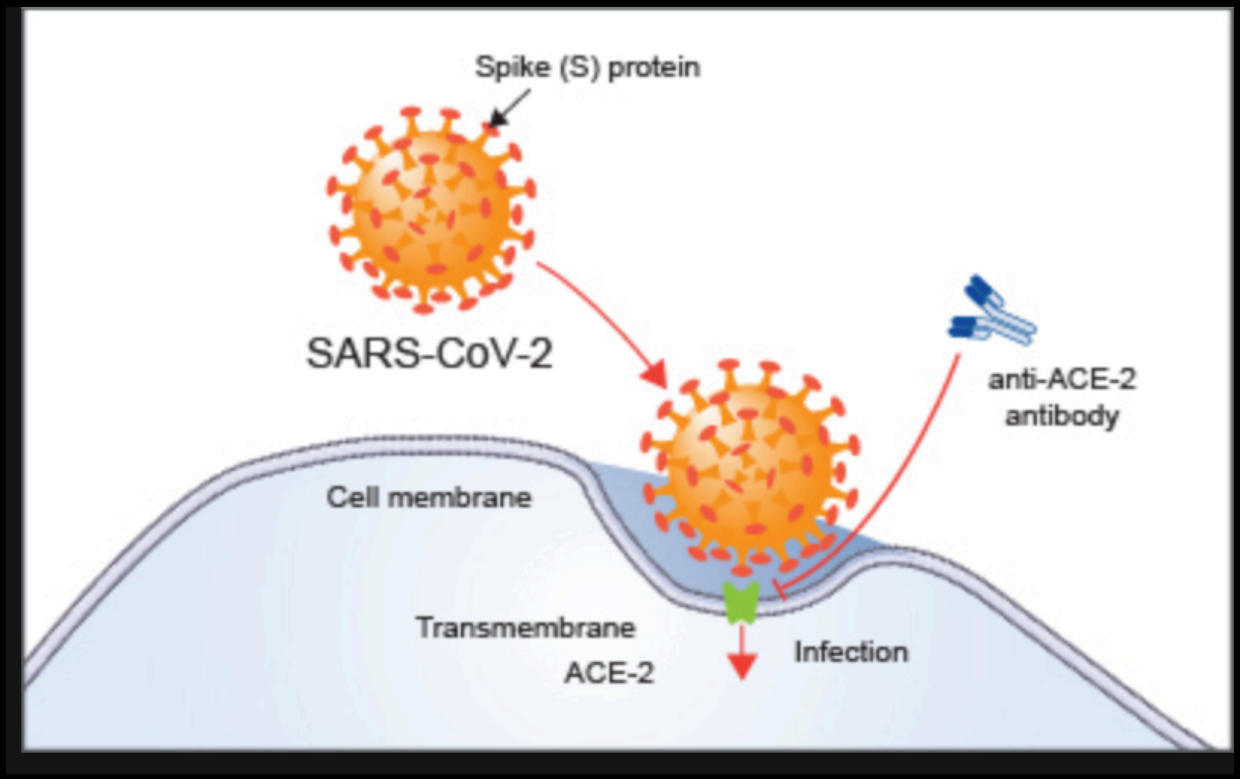
We therefore turn to vaccination to protect ourselves, and protect others

TO REVIEW from last talk…….


Nucleocapsid protein (N)
Membrane glycoprotein (M)
Spike protein (S)
Envelope protein (E)
RNA

Source: Guyton and Hall, Medical Physiology




Spike (S) protein
SARS-CoV-2
anti-ACE-2
antibody
Cell membrane
Transmembrane
ACE-2
Infection

Spike proteins are key

- Allow entry into cells
- Viruses can only reproduce in living cells
- Goal: prevent cell entry and prevent replication

KEY TO ALMOST ALL VACCINES FOR SARS-COV-2:

Produce or emulate spike proteins (but not inject actual virus!!!!)

SO, the search was on, despite obstacles

- Funding—costs $1 billion plus to develop a new vaccine and bring to market
- Disincentive for pharma cos to try
- But sharing the cost between government(s) and companies removes lots of the risk
- Operation “WARP SPEED” did this

Stages in vaccine development include identifying targets, animal testing, and phase 1, 2, and 3 clinical trials

Currently over 30 vaccines for COVID-19 are in clinical trials internationally

Clinical trials

- Test for safety (phase 1)—30-100 people. Also dosage, and looking for immune response
- Continue testing for safety and assess efficacy (usually <1,000 people)
- Randomized control trial (RCT) with thousands
  - (Moderna, Pfizer/BioNtec, Astra Zeneca/Oxford): about 30,000 each
  - Compare risk of developing disease in those vaccinated with those unvaccinated

MODERNA
(posted online Dec)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 4, 2021 VOL. 384 NO. 5

Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

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ABSTRACT

BACKGROUND

Vaccines are needed to prevent coronavirus disease 2019 (Covid-19) and to protect persons who are at high risk for complications. The mRNA-1273 vaccine is a lipid nanoparticle–encapsulated mRNA-based vaccine that encodes the prefusion stabilized full-length spike protein of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes Covid-19.

METHODS

This phase 3 randomized, observer-blinded, placebo-controlled trial was conducted at 99 centers across the United States. Persons at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 μg) or placebo 28 days apart. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2.

RESULTS

The trial enrolled 30,420 volunteers who were randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). More than 96% of participants received both injections, and 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person-

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. El Sahly at the Departments of Molecular Virology and Microbiology and Medicine, 1 Baylor Plaza, BCM-MS280, Houston, TX 77030, or at hana.elsahly@bcm.edu; or to Dr. Baden at the Division of Infectious Diseases, Brigham and Women's Hospital, 15 Francis St., PBB-A4, Boston, MA 02115, or at lbaden@bwh.harvard.edu.

*A complete list of members of the COVE Study Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Baden and El Sahly contributed equally to this article.

This article was published on December 30, 2020, and updated on January 15, 2021, at NEJM.org.

N Engl J Med 2021;384:403-16.
DOI: 10.1056/NEJMoa2035389

Pfizer/BioNTech

(n=45,000)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

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ABSTRACT

BACKGROUND

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the resulting coronavirus disease 2019 (Covid-19) have afflicted tens of millions of people in a worldwide pandemic. Safe and effective vaccines are needed urgently.

METHODS

In an ongoing multinational, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons 16 years of age or older in a 1:1 ratio to receive two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 μg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein. The primary end points were efficacy of the vaccine against laboratory-confirmed Covid-19 and safety.

RESULTS

A total of 43,548 participants underwent randomization, of whom 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of

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*A complete list of investigators in the C4591001 Clinical Trial Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Polack and Thomas contributed equally to this article.

This article was published on December 10, 2020, and updated on December 16, 2020, at NEJM.org.

N Engl J Med 2020;383:2603-15.
DOI: 10.1056/NEJMoa2034577

Both of these use messenger RNA (mRNA) coated in a fatty substance to be taken up by cells in body, and causing these cells to make SARS-CoV-2 spike protein, leading to immune response to this virus

Oxford/AstraZeneca

Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK

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Summary

Background A safe and efficacious vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), if deployed with high coverage, could contribute to the control of the COVID-19 pandemic. We evaluated the safety and efficacy of the ChAdOx1 nCoV-19 vaccine in a pooled interim analysis of four trials.

Methods This analysis includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. Participants aged 18 years and older were randomly assigned (1:1) to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline). Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort). The primary efficacy analysis included symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test-positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to treatment received, with data cutoff on Nov 4, 2020. Vaccine efficacy was calculated as 1–relative risk derived from a robust Poisson regression model adjusted for age. Studies are registered at ISRCTN89951424 and ClinicalTrials.gov, NCT04324606, NCT04400838, and NCT04444674.

Findings Between April 23 and Nov 4, 2020, 23 848 participants were enrolled and 11 636 participants (7548 in the UK, 4088 in Brazil) were included in the interim primary efficacy analysis. In participants who received two standard doses, vaccine efficacy was 62·1% (95% CI 41·0–75·7; 27 [0·6%] of 4440 in the ChAdOx1 nCoV-19 group *vs* 71 [1·6%] of 4455 in the control group) and in participants who received a low dose followed by a standard dose, efficacy was 90·0% (67·4–97·0; three [0·2%] of 1367 *vs* 30 [2·2%] of 1374; $p_{interaction}$=0·010). Overall vaccine efficacy across both groups was 70·4% (95·8% CI 54·8–80·6; 30 [0·5%] of 5807 *vs* 101 [1·7%] of 5829). From 21 days after the first dose,

Lancet 2021; 397: 99–111

Published Online December 8, 2020 https://doi.org/10.1016/S0140-6736(20)32661-1

This online publication has been corrected. The corrected version first appeared at thelancet.com on January 7, 2021

See Comment page 72

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Two terms often confused in media reports

- Vaccine efficacy—this is the relative reduction in disease within a clinical trial or under lab conditions
- Vaccine effectiveness—reduction under everyday, real use conditions
- Most of time, effectiveness less than efficacy
- *WE DO NOT YET KNOW EFFECTIVENESS!!!!!*

AT BEST……..

ABOUT 85% EFFECTIVENESS FOR OUR 2 VACCINES.

AFTER VACCINATION, FOR NEXT 1-2 YEARS, IT WILL BE VERY IMPORTANT TO LIMIT EXPOSURE. MASKS, ONLY SMALL GATHERINGS OF RESPONSIBLE PEOPLE, SOME DISTANCE WILL BE VERY IMPORTANT

IF WE HAVE TIME…OTHER VACCINES, SPREADING DOSES, JOHNSON AND JOHNSON SINGLE INJECTION, SUPPLY CHAIN PROBLEMS, AND HERD IMMUNITY