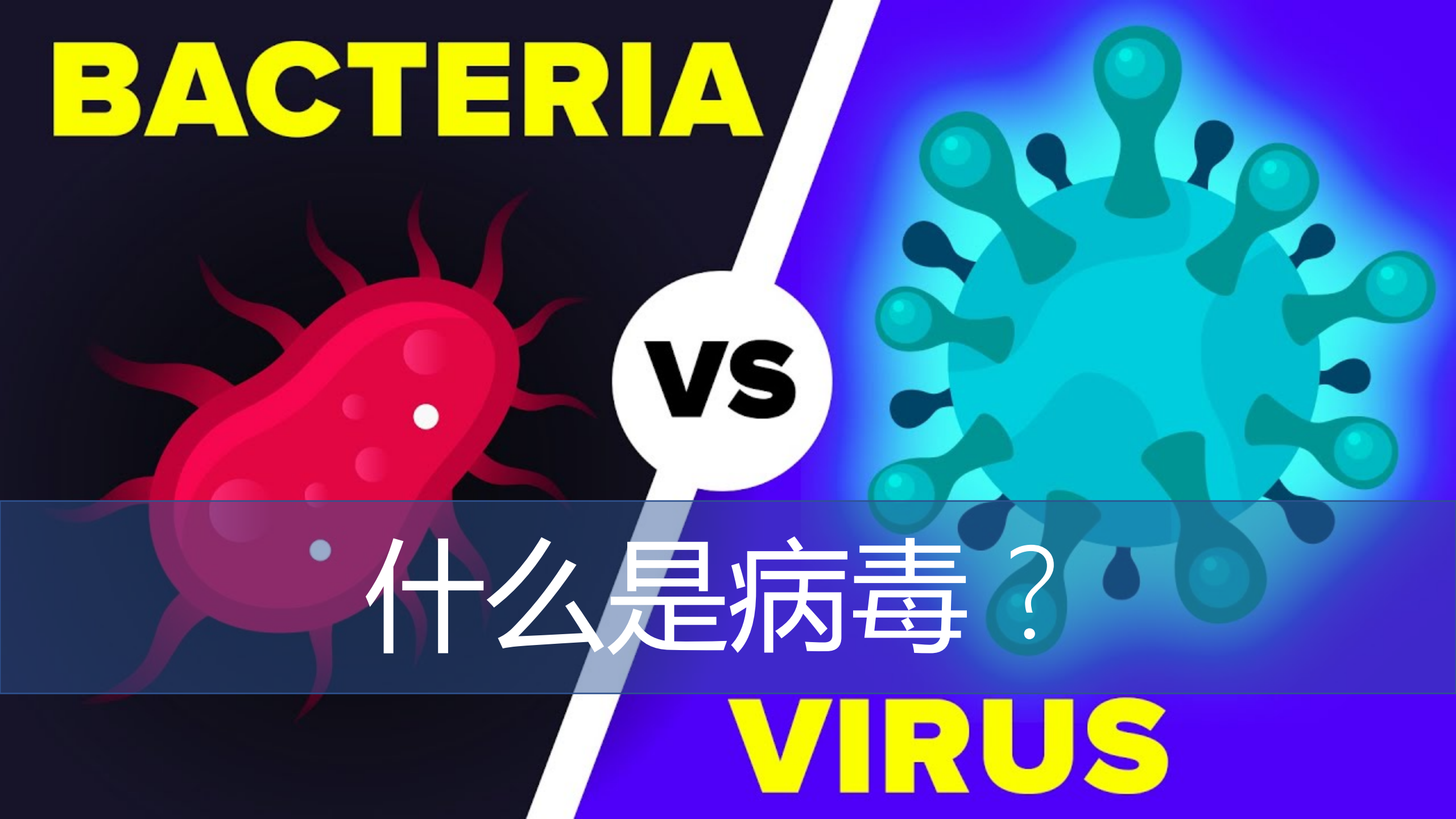
Brief introduction to

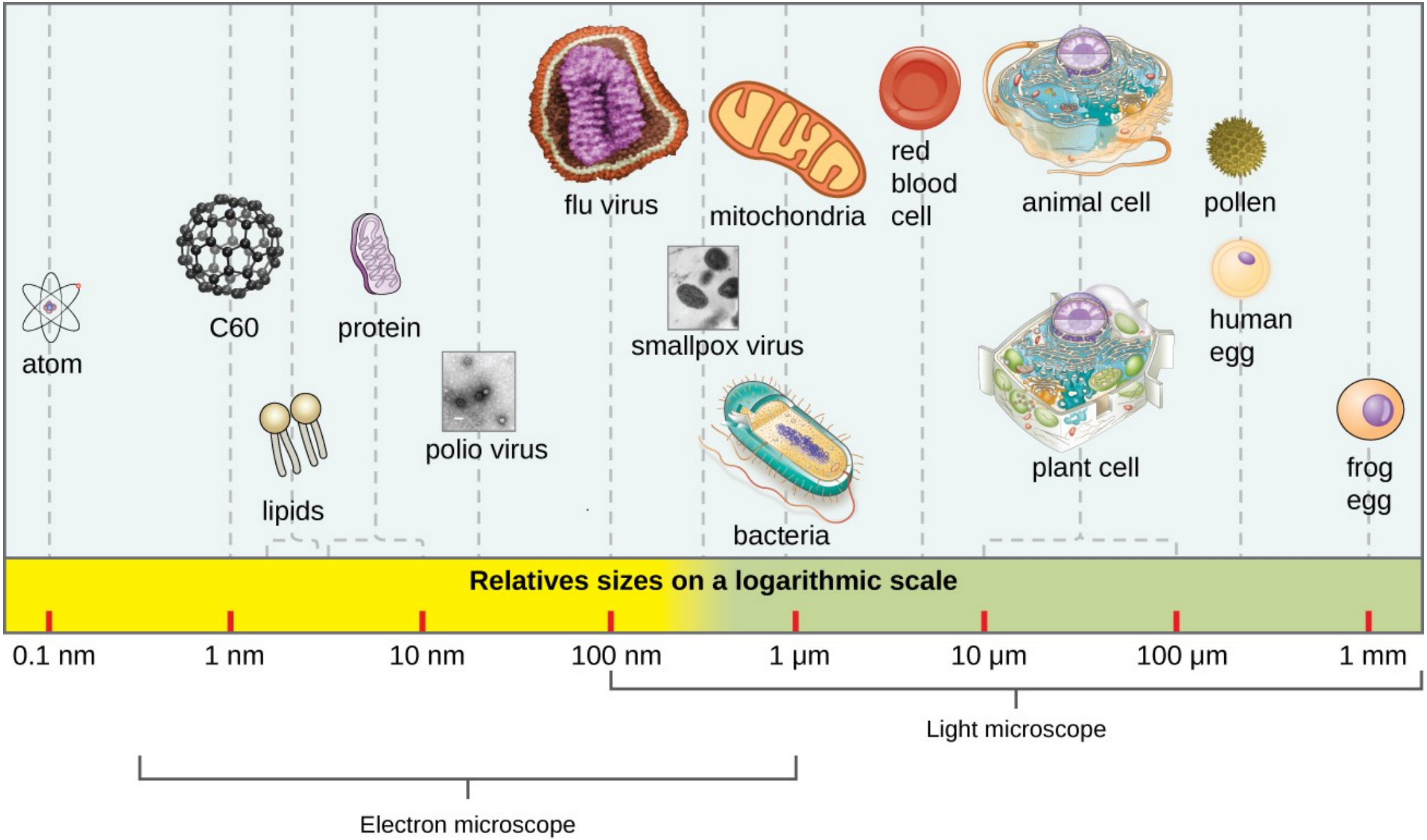
COVID-19 Prevention

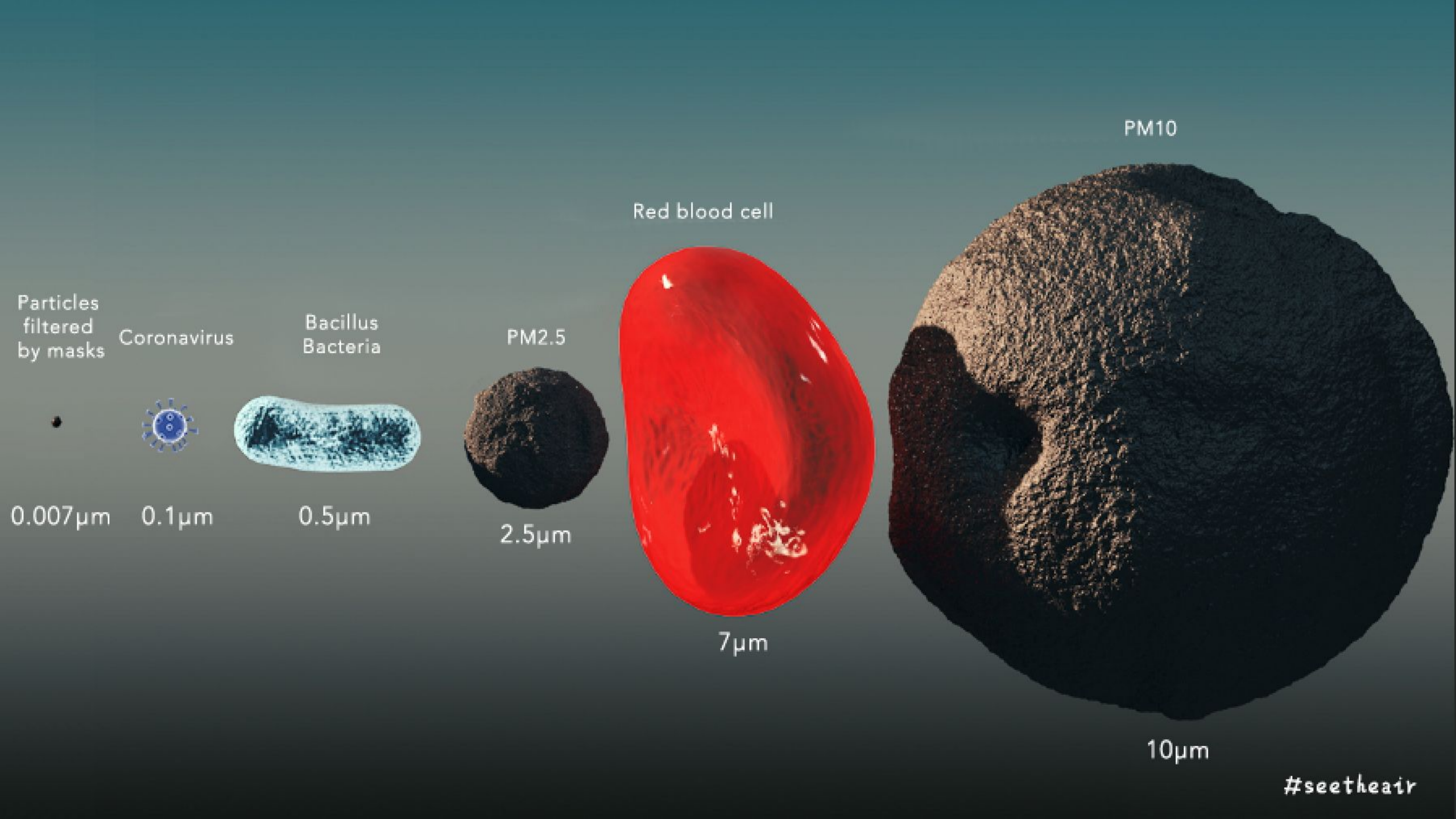
浅谈新冠病毒预防

Henry Huang



什么是病毒？


atom
C60
protein
lipids
polio virus
flu virus
smallpox virus
mitochondria
bacteria
red blood cell
animal cell
plant cell
pollen
human egg
frog egg
Relatives sizes on a logarithmic scale
0.1 nm
1 nm
10 nm
100 nm
1 µm
10 µm
100 µm
1 mm
Light microscope
Electron microscope


Particles filtered by masks
0.007μm
Coronavirus
0.1μm
Bacillus Bacteria
0.5μm
PM2.5
2.5μm
Red blood cell
7μm
PM10
10μm
#seetheair

細菌

細菌是顯微鏡下才看得見的微生物，通常是無害的，但有時也可能引發如肺結核、肺炎這一類的全球性重大疾病。

沙門氏菌
（食物中毒）

弧菌
（霍亂）

梅毒螺旋
（雅司病、梅毒）

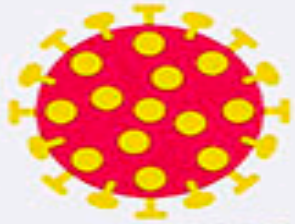
鏈球菌
（肺炎、支氣管炎）

病毒

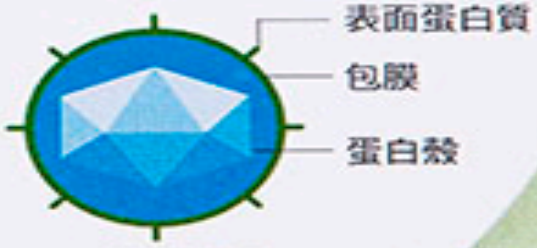
病毒是所有生物中最小且最簡單的，僅由它們包覆在蛋白質外殼中的遺傳物質（DNA或RNA）構成。病毒與其他病原體不同，需要宿主的細胞才能生存和繁殖。

腺病毒
（扁桃腺炎、結膜炎）

狂犬病毒
（狂犬病）



慢病毒
（人類免疫缺損病毒/愛滋病）



皰疹病毒
（B型肝炎、唇皰疹）

抗生素

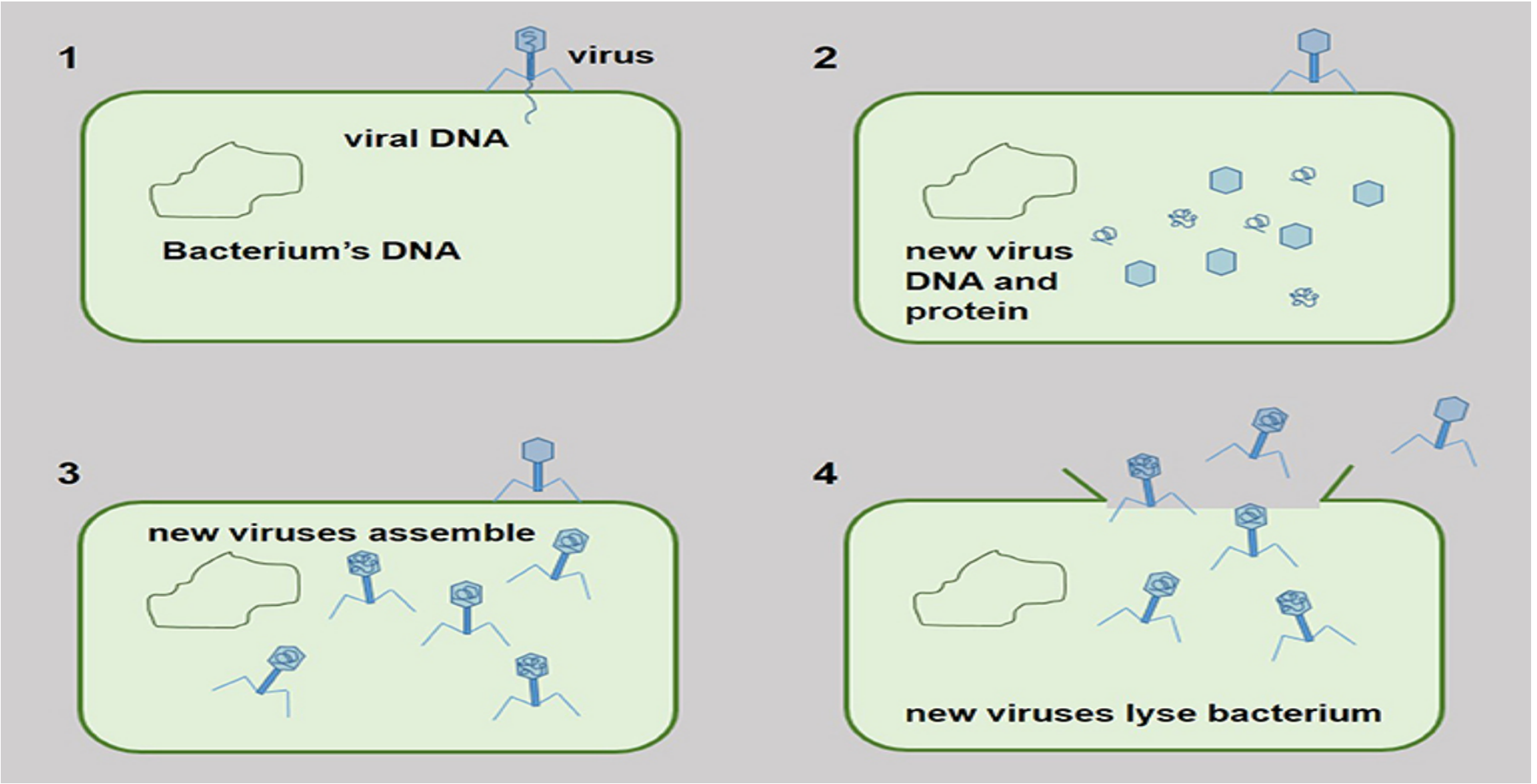
抗生素普遍用於細菌感染，它們會分解細菌的細胞壁，或中斷它們的生長。然而抗生素無法分辨好細菌和壞細菌。

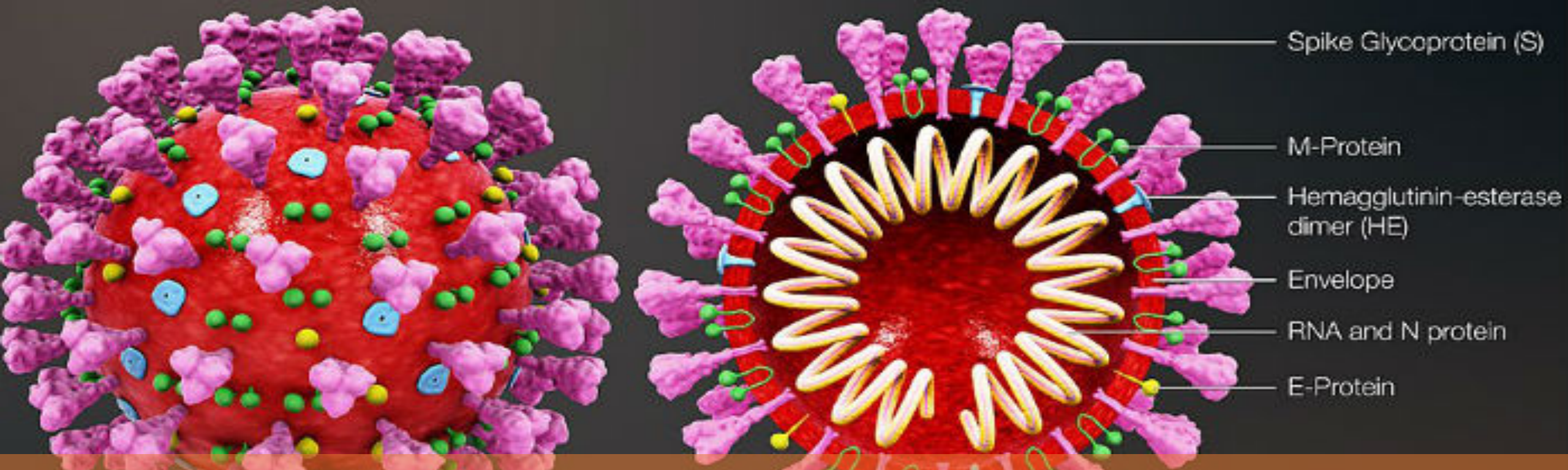
疫苗

防止病毒感染擴散的最佳方法是使用疫苗。疫苗能幫助免疫系統辨識病毒，並立刻發動攻擊（參照第184-185頁）。

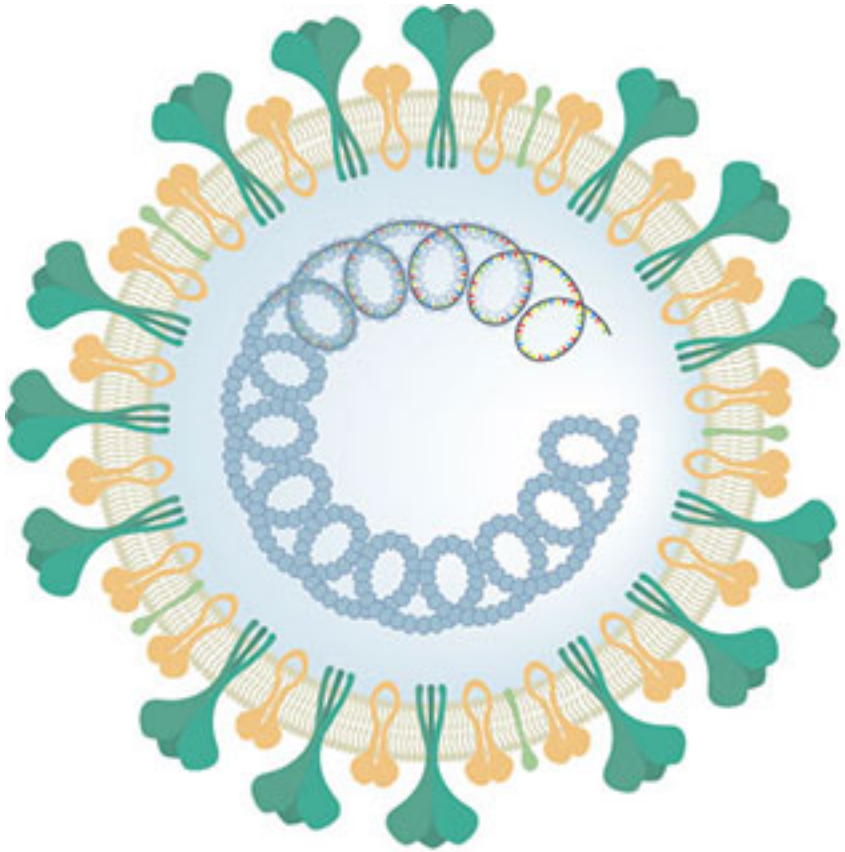
《我的人體實用手冊：看圖就能懂的生命奧祕》

病毒的形成机制


1
virus
viral DNA
Bacterium's DNA
2
new virus
DNA and
protein
3
new viruses assemble
4
new viruses lyse bacterium


Spike Glycoprotein (S)
M-Protein
Hemagglutinin-esterase dimer (HE)
Envelope
RNA and N protein
E-Protein

什么是新型冠状病毒

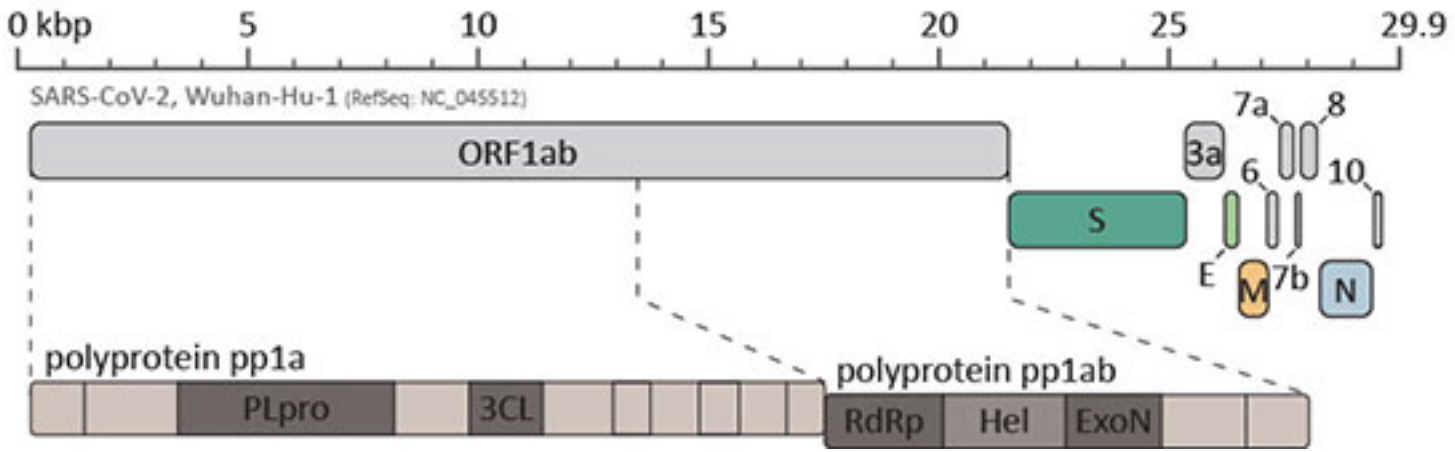


Spike Protein (S) 刺突蛋白
glycosylated, trimeric protein
binds to ACE2 on host cells
proteolytic activation by TMPRSS2
10nm size, ~100 trimers/virion#

Membrane Protein (M) 基质蛋白
interferon antagonist§
~2000 copies#

Envelope Protein (E) 包膜蛋白
viroporin (host cell lysis)#
~20 copies‡

Nucleocapsid (N) 核蛋白
interferon antagonist#
~1000 copies#

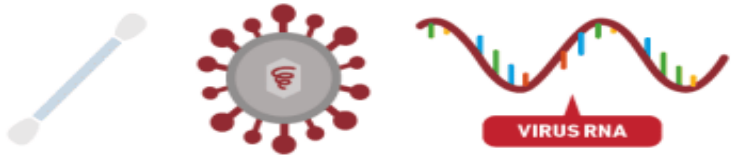


COVID-19核酸抗体检测

HOW DO THE TESTS FOR CORONAVIRUS WORK?

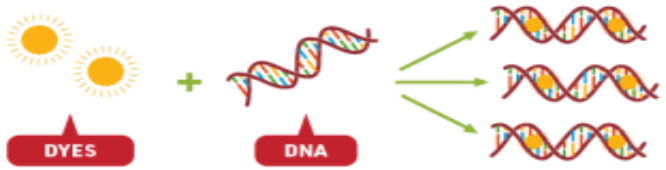
HOW CURRENT TESTS WORK

1. A swab is taken of the inside of a patient's nose or the back of their throat. This sample is then sent to a lab to test.

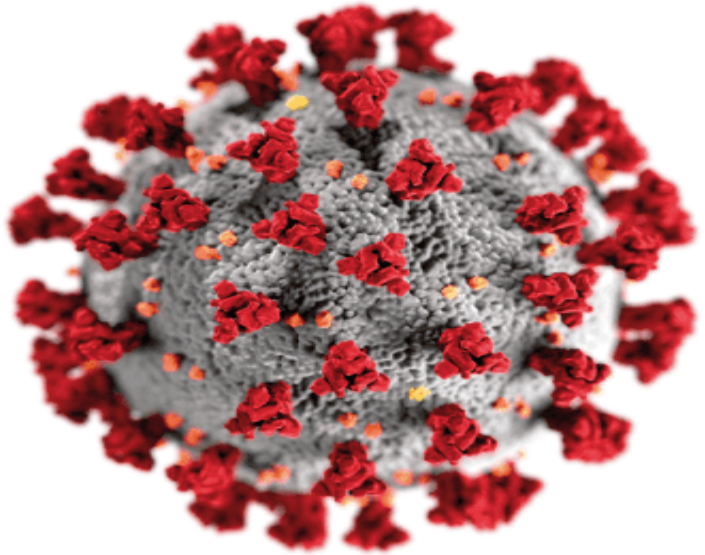


2. The RNA of the virus is extracted and purified. An enzyme, reverse transcriptase, converts the RNA to DNA.

3. The DNA is mixed with primers, sections of DNA designed to bind to characteristic parts of the virus DNA. Repeatedly heating then cooling DNA with these primers and a DNA-building enzyme makes millions of copies of virus DNA.



4. Fluorescent dye molecules bind to the virus DNA as it is copied. Binding makes them give off more light, which is used to confirm the presence of the virus in the sample.



ISSUES WITH TESTING

REAGENT ISSUES

High demand and issues with reagents have delayed testing in some countries.

TIME-CONSUMING

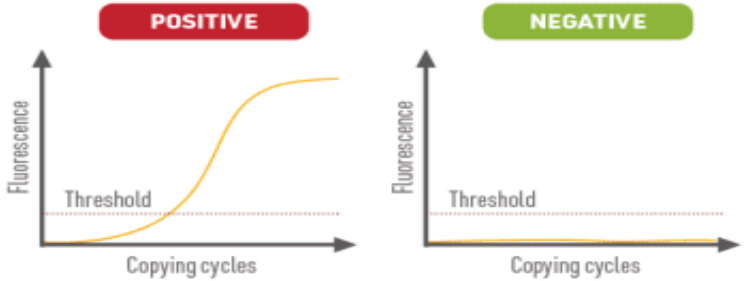
It takes a few hours to get results from the test, limiting how many tests can be done.

FALSE POSITIVES AND NEGATIVES

In some cases sample degradation or contamination can affect the results.

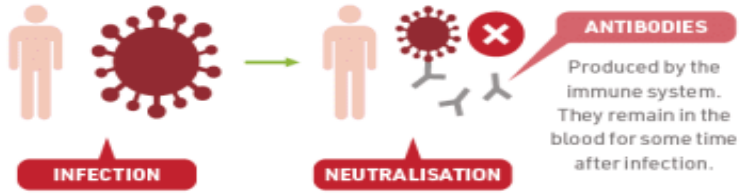
POSITIVE AND NEGATIVE TESTS

The fluorescence increases as more copies of the virus DNA are produced. If it crosses a certain threshold, the test is positive. If the virus isn't present, no DNA copies are made and the threshold isn't reached. In this case, the test is negative.

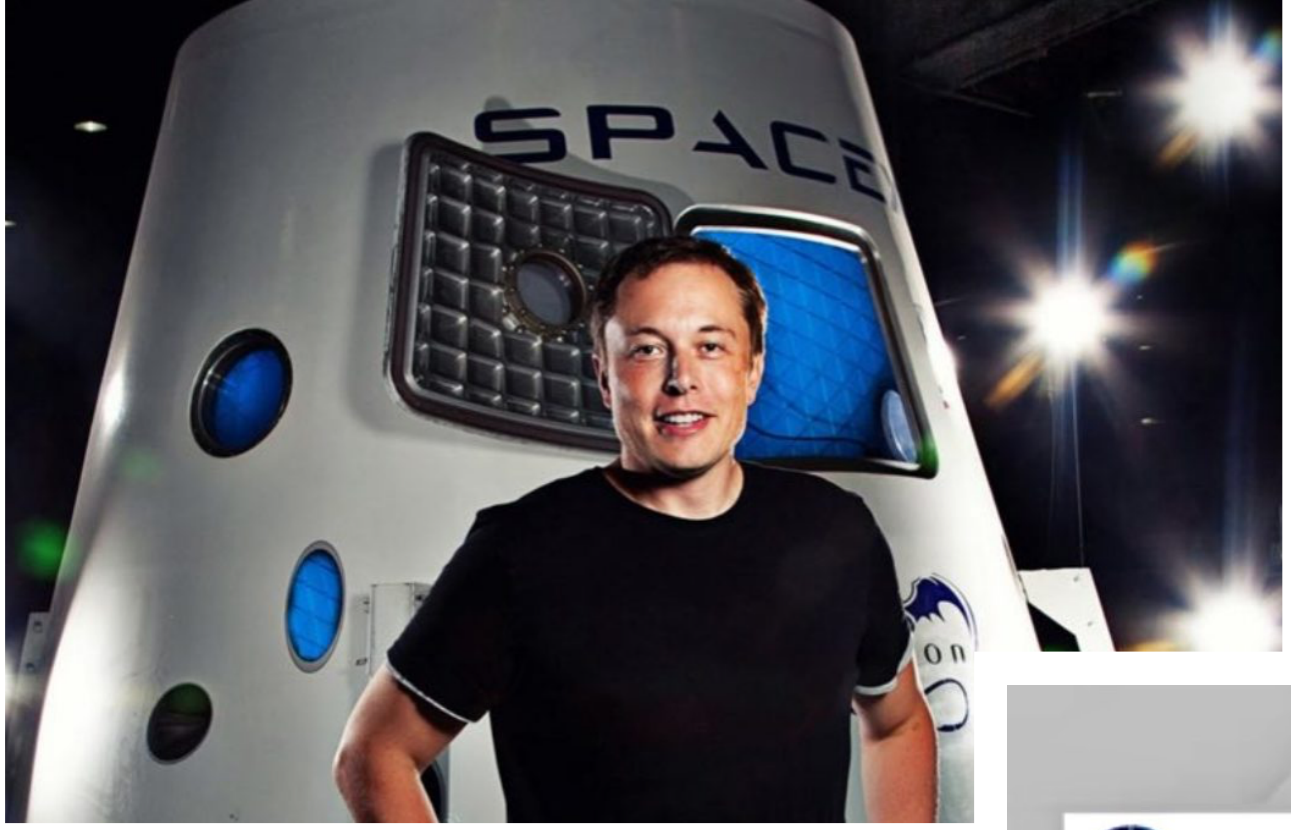


FUTURE TESTS

The current tests are good for diagnosing an infection – but they can't tell us if someone has had it and then recovered. Tests that look for antibodies against the virus can do this.



Tests that look for proteins on the surface of the virus are also in development. These tests are faster, but less accurate.


SPACE


Elon Musk
@elonmusk
Something extremely bogus is going on. Was tested for covid four times today. Two tests came back negative, two came back positive. Same machine, same test, same nurse. Rapid antigen test from BD.
12:47 AM · Nov 13, 2020 · Twitter for iPhone

什么是COVID-19 疫苗？

Why we use vaccines 为什么要使用疫苗

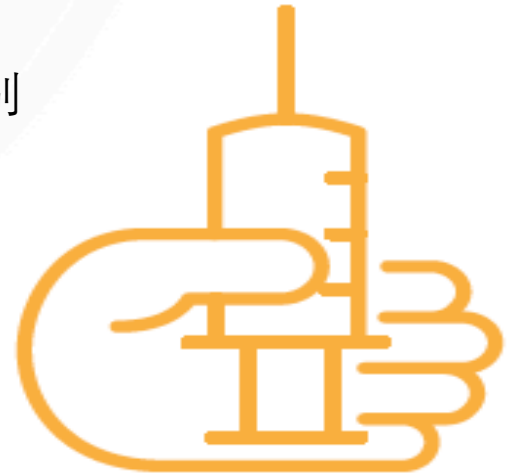
- **Vaccines can prevent infectious diseases.** Examples of vaccine-preventable diseases are: measles, polio, hepatitis B, influenza and many others. 疫苗能够预防感染性疾病
- When most people in a community are vaccinated against a disease, the ability of the pathogen to spread is limited. This is called 'herd' or 'indirect' or 'population' immunity. 当社区中大多数接受免疫，病毒传播能力就下降
- When many people have immunity, this also indirectly protects people who cannot be vaccinated, such as very young babies and those who have compromised immune systems.

  当社区中大多数人有免疫后，会间接保护无法接受疫苗的人群，比如小孩和无法接种的人群

How vaccines work 疫苗的作用机制是什么呢？

- Vaccines greatly reduce the risk of infection by training the immune system to recognize and fight pathogens such as viruses or bacteria 疫苗能够训练免疫系统去识别并消灭病原体，比如细菌获病毒
- Vaccines safely deliver an **immunogen** which is a *specific type of antigen that elicits an immune response*, to train the immune system to recognize the pathogen when it is encountered naturally.

  疫苗安全的提供肌体一个能够引起特意型免疫反应免疫抗原，从而训练免疫系统识别病原体。

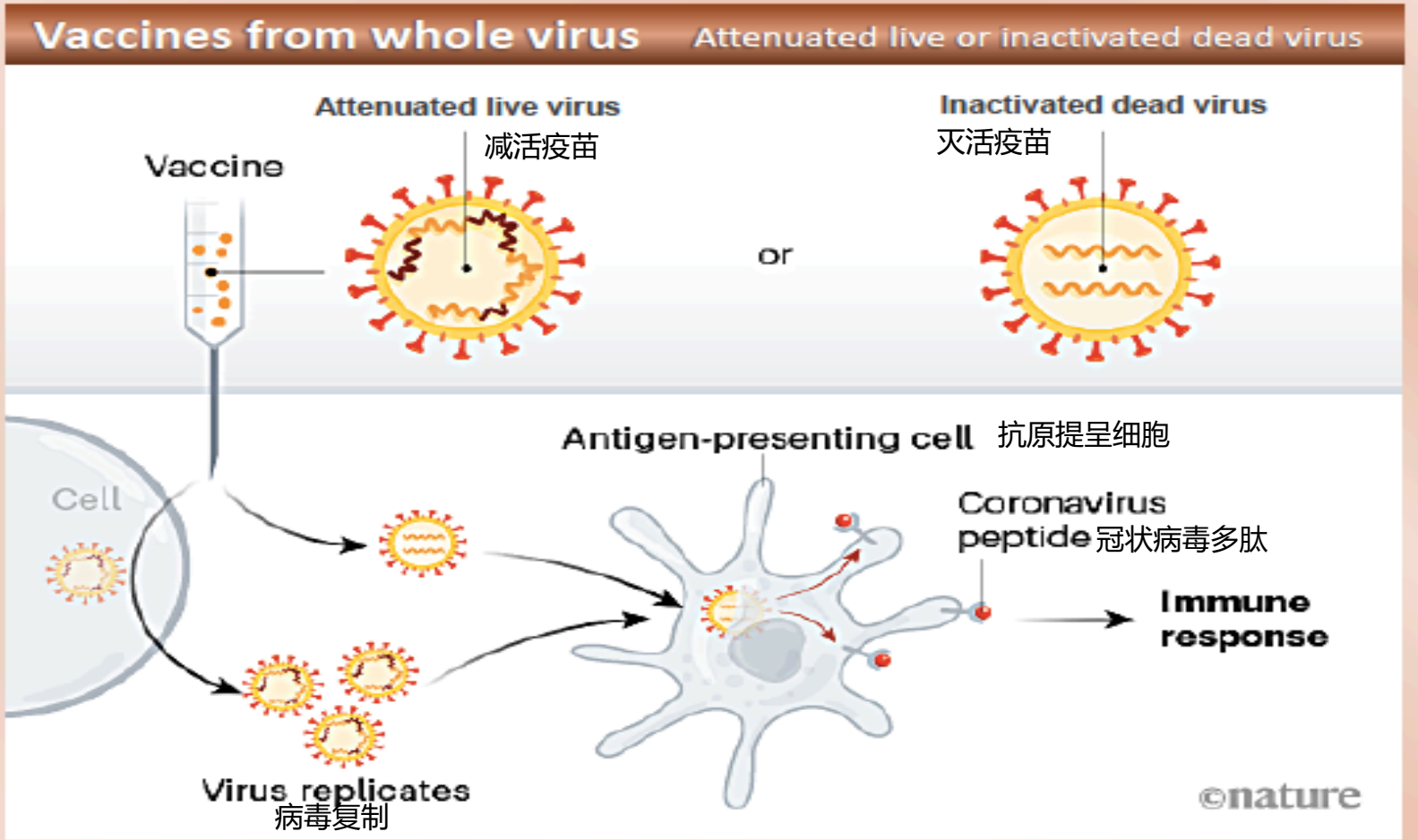


Virus vaccines 病毒型疫苗（减活或灭活型疫苗）

- **Virus is selected, modified (weakened) or completely inactivated** so that it will not cause disease

病毒型疫苗是通过选择和优化（弱化）或者完全无活性。因此它不会导致疾病

Note:
This illustration shows injectable vaccines. Some vaccines in this category are administered orally

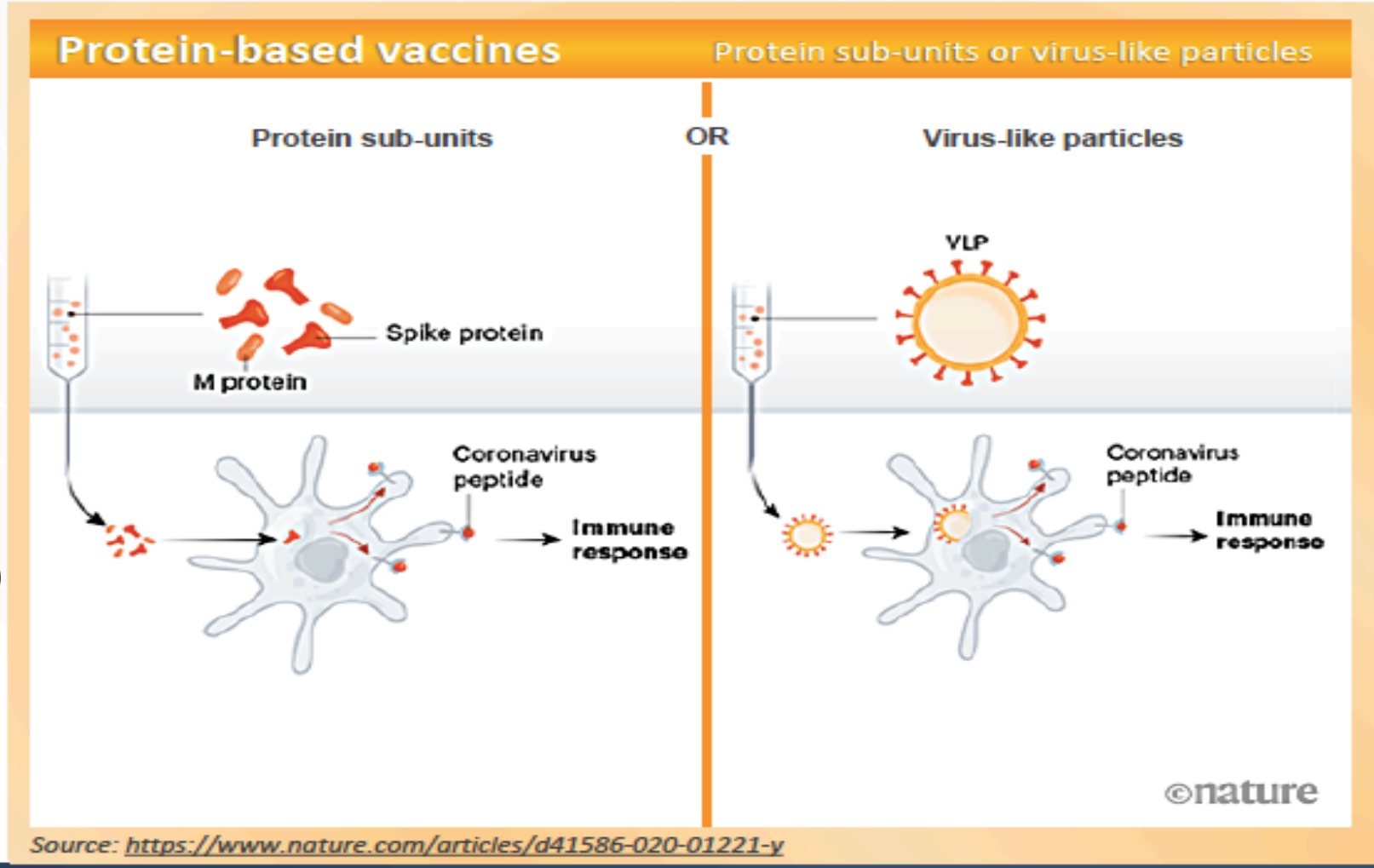


Source: https://www.nature.com/articles/d41586-020-01221-y

Protein-based vaccines 蛋白质型疫苗 （亚单位型疫苗）

- **A protein is extracted from the virus** (alive or inactivated), purified, and injected as a vaccine
- For coronavirus, this is most commonly the spike protein
- Virus-like particles work in the same way

- 从病毒中提取的蛋白（活性或非活性）纯化后注入人体的疫苗
- 对于冠状病毒，最常见的是**刺突蛋白**
- 病毒类似体

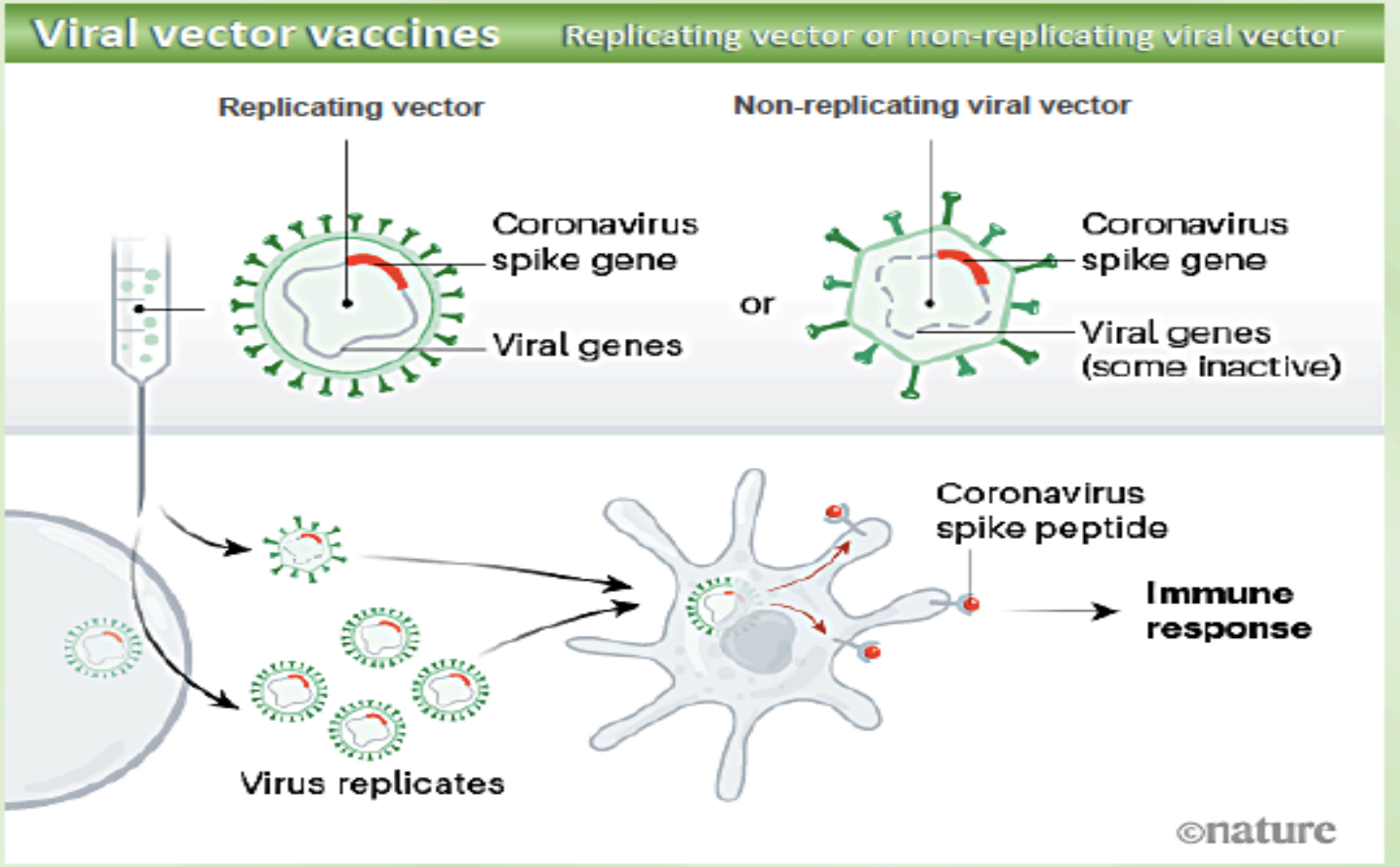


Source: https://www.nature.com/articles/d41586-020-01221-y

Viral vector vaccines 病毒载体型疫苗（重组疫苗）

- **The gene for a pathogen protein is inserted into a different virus** that can infect someone without causing disease
- The safe virus serves as a 'platform' or 'vector' to deliver the protein that triggers an immune response
- The safe virus is then injected as a vaccine
- Some replicate (reproduce) in the body and some do not

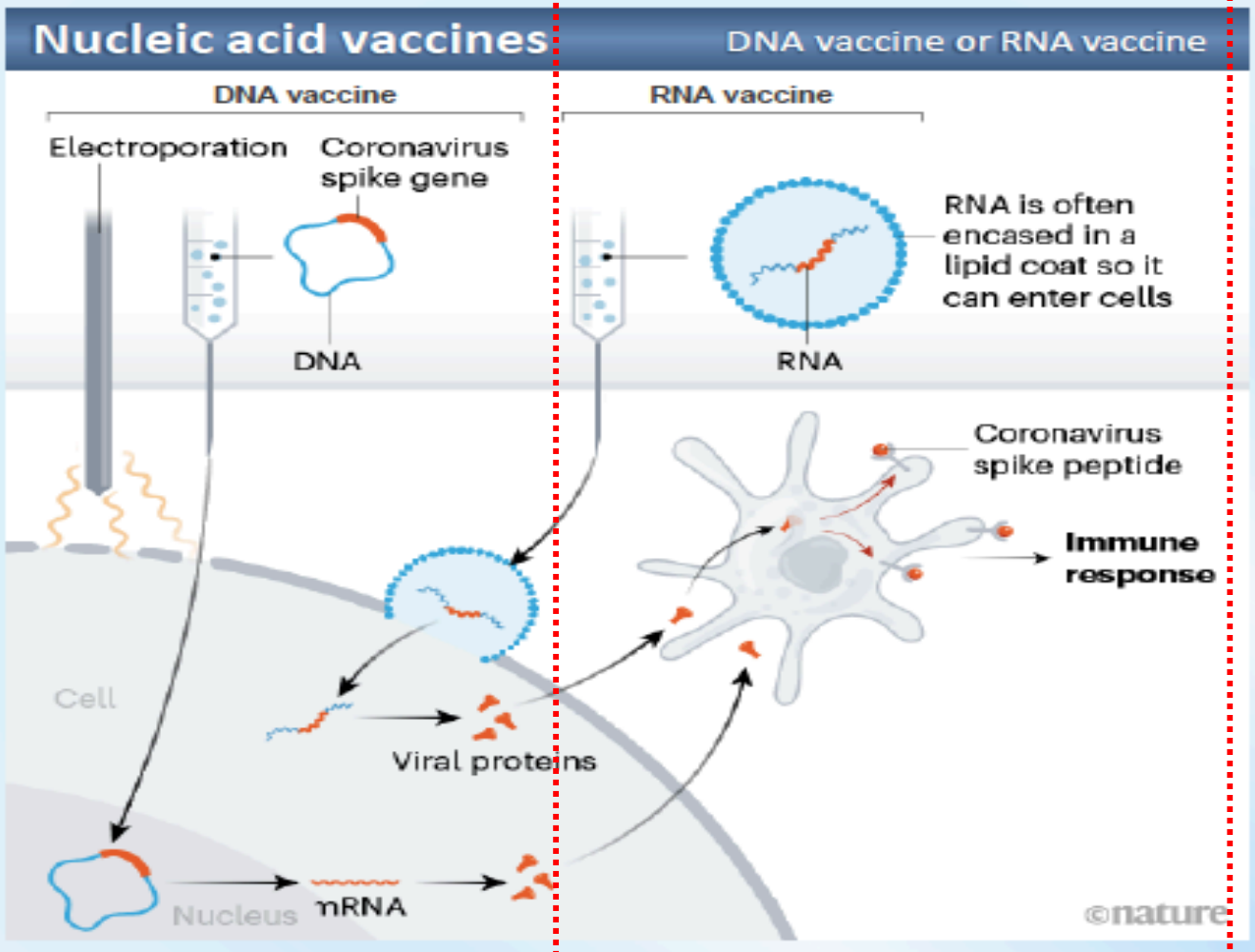
含病原体蛋白的基因插入不致病的病毒中



Source: https://www.nature.com/articles/d41586-020-01221-y

Nucleic acid vaccines 核酸型疫苗 （亚单位疫苗）

- Instead of a virus, a protein antigen, or a virus expressing the protein, **nucleic acid coding for the antigen is injected** 核酸片段信息
- DNA plasmid: enters nucleus, translated to mRNA for expression of protein DNA 质体
- Or mRNA can be injected. More direct (no translation required) but less stable than DNA mRNA
- This is new technology – no other vaccines for human use have used this 全新技术，未用于人类



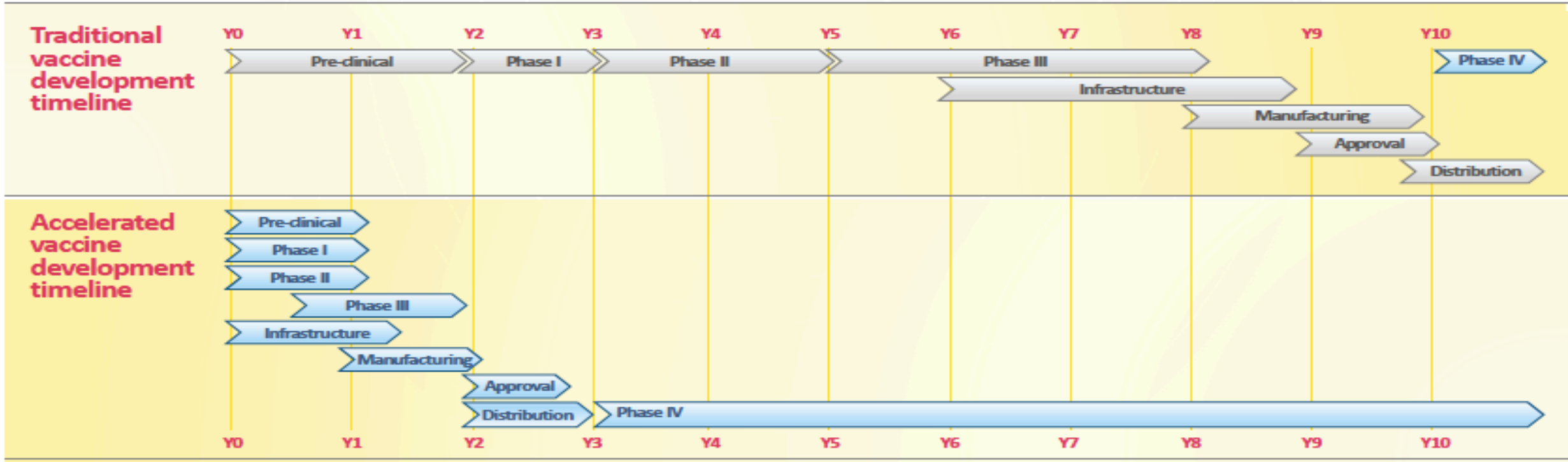
Source: https://www.nature.com/articles/d41586-020-01221-y

Steps in vaccine development 疫苗的研发过程

Actions taken to ensure a new vaccine is safe and works well

- **Pre-clinical studies**
  Vaccine is tested in animal studies for efficacy and safety, including challenge studies
- **Phase I clinical trial**
  Small groups of healthy adult volunteers receive the vaccine to test for safety
- **Phase II clinical trial**
  Vaccine is given to people who have characteristics (such as age and physical health) similar to those for whom the new vaccine is intended
- **Phase III clinical trial**
  Vaccine is given to thousands of people and tested for efficacy and safety
- **Phase IV post marketing surveillance**
  Ongoing studies after the vaccine is approved and licensed, to monitor adverse events and to study long-term effects of the vaccine in the population
- **Human challenge studies**
  Studies in which a vaccine is given followed by the pathogen against which the vaccine is designed to protect. Such trials are uncommon in people as they present considerable ethical challenges

COVID-19 vaccine accelerated development 新冠加速研发



- Normal vaccine development performs each step in sequence
- To accelerate COVID-19 vaccine development, **steps are done in parallel**
- All usual safety and efficacy monitoring mechanisms remain in place; such as adverse event surveillance, safety data monitoring & long-term follow-up
- **Phase IV post-marketing surveillance** for side effects is critical and essential

COVID-19 vaccine candidates in Phase III trials

进入三期临床的新冠疫苗公司

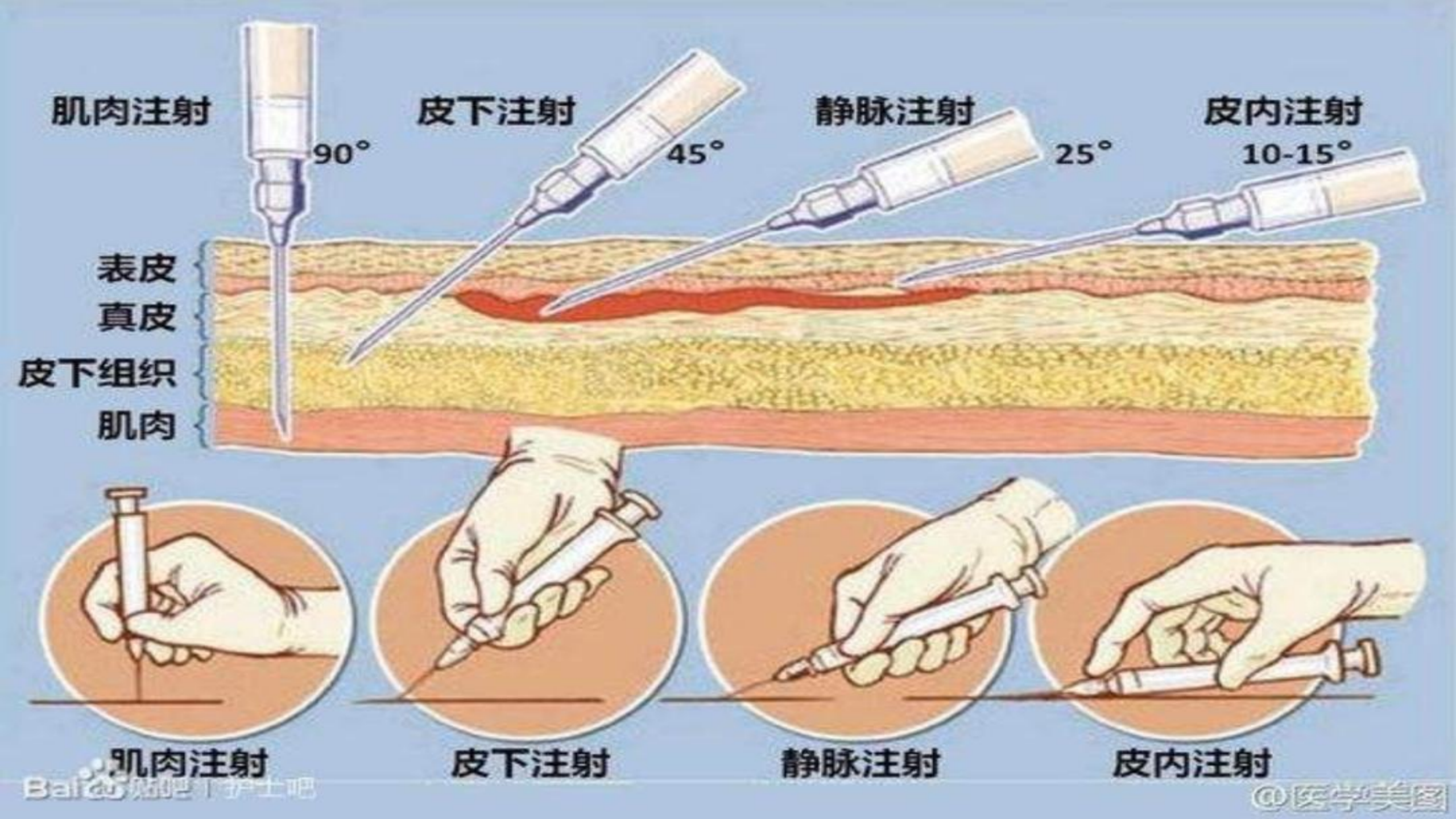
- As of 02 October 2020 there are **42 COVID-19 candidate vaccines** in clinical evaluation of which **10 in Phase III trials**
- There are another **151 candidate vaccines in preclinical** evaluation
- Phase III trials usually require **30,000 or more participants**
- All top candidate vaccines are for **intra-muscular** injection
- Most are designed for a **two-dose** schedule (exceptions with a * in table are single dose)

10 CANIDATE VACCINES IN PHASE III CLINICAL EVALUATION	VACCINE PLATFORM	LOCATION OF PHASE III STUDIES
Sinovac	Inactivated virus	Brazil
Wuhan Institute of Biological Products / Sinopharm	Inactivated virus	United Arab Emirates
Beijing Institute of Biological Products / Sinopharm	Inactivated virus	China
University of Oxford / AstraZeneca	Viral vector *	United States of America
CanSino Biological Inc. / Beijing Institute of Biotechnology	Viral vector *	Pakistan
Gamaleya Research Institute	Viral vector	Russia
Janssen Pharmaceutical Companies	Viral vector	USA, Brazil, Colombia, Peru, Mexico, Philippines, South Africa
Novavax	Protein subunit	The United Kingdom
Moderna / NIAID	RNA	USA
BioNTech / Fosun Pharma / Pfizer	RNA	USA, Argentina, Brazil

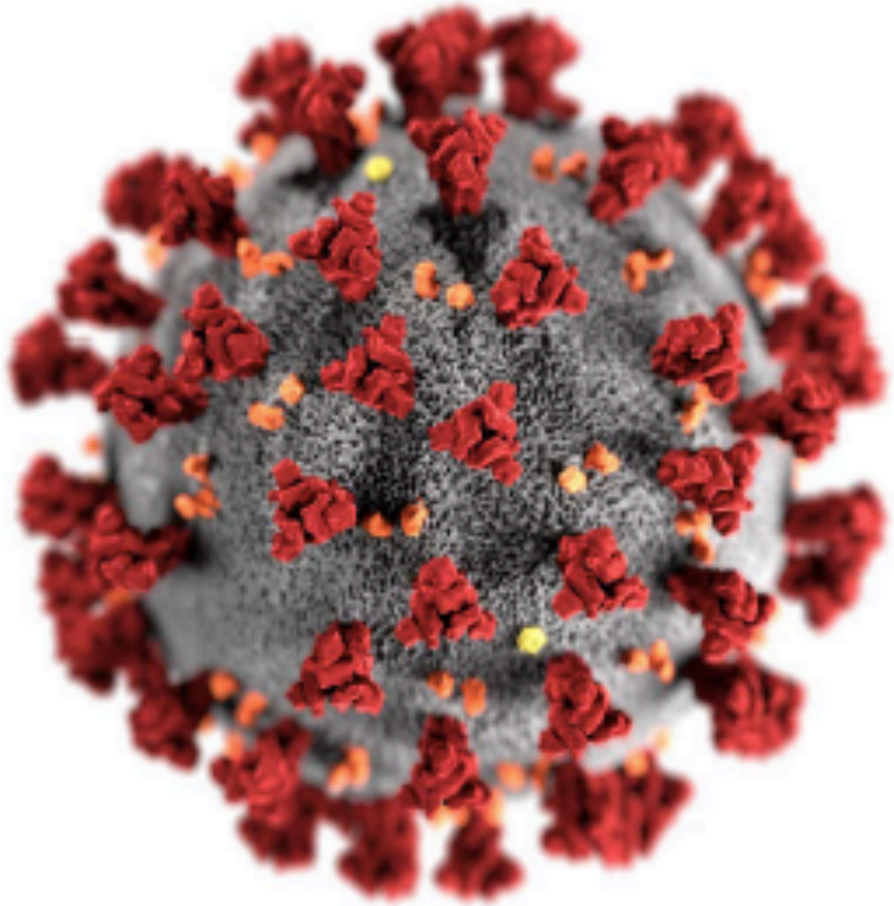
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

* Single dose schedule

Prizer 的疫苗安全有效吗？


肌肉注射
皮下注射
静脉注射
皮内注射
90°
45°
25°
10-15°
表皮
真皮
皮下组织
肌肉
肌肉注射
皮下注射
静脉注射
皮内注射

ACIP COVID-19 Vaccines



EtR Framework:

Pfizer-BioNTech COVID-19 vaccine

Sara Oliver MD, MSPH

ACIP Meeting

December 12, 2020

Advisory Committee on Immunization Practices (ACIP)

Evidence to Recommendations Framework

Evidence to Recommendations (EtR) Framework

- Structure to describe information considered in moving from **evidence** to ACIP vaccine **recommendations**

- Provide **transparency** around the impact of additional factors on deliberations when considering a recommendation

EtR Domain: Public Health Problem

Public Health Problem

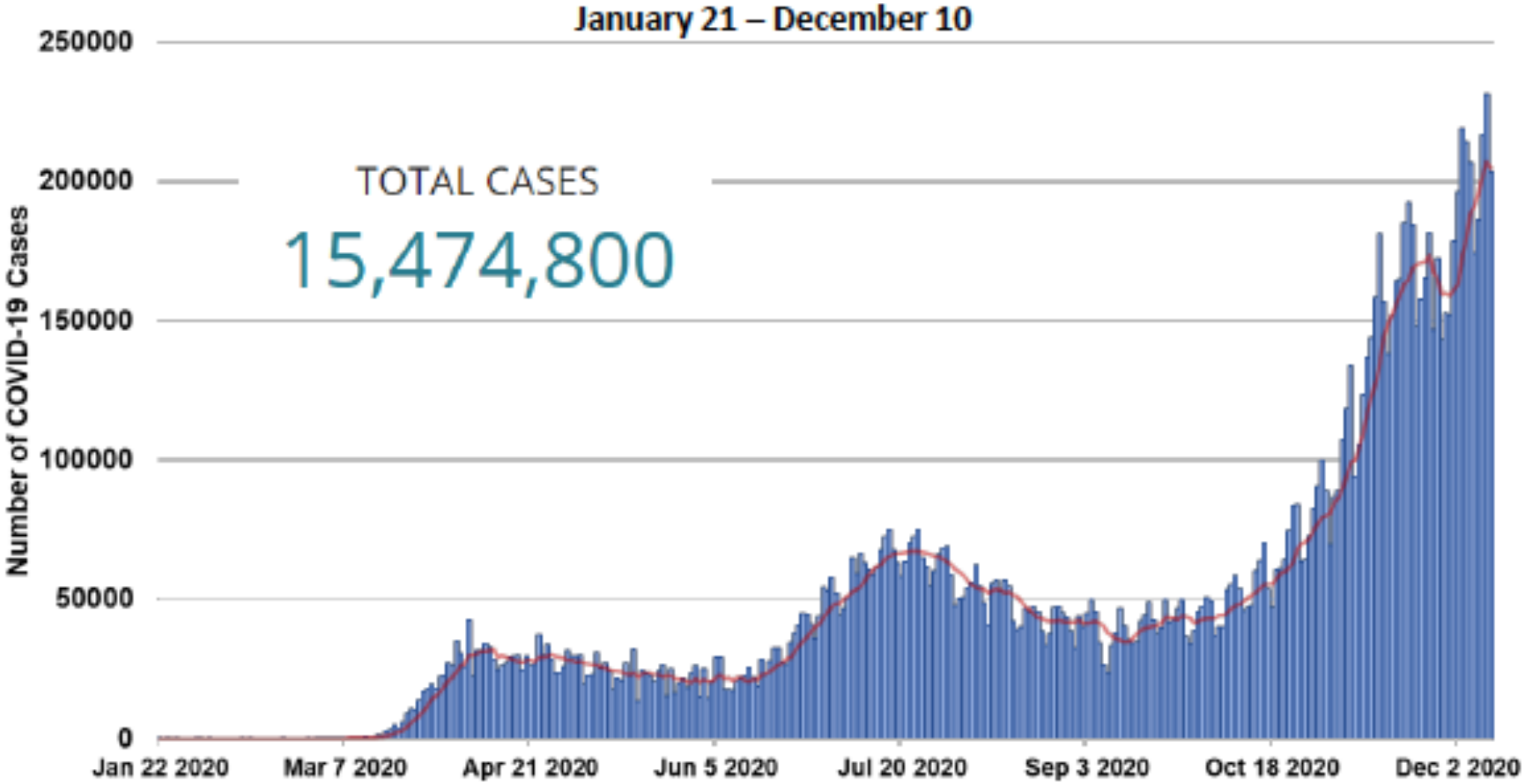
Is COVID-19 disease of public health importance?

- Are the consequences of COVID-19 serious?
- Is COVID-19 urgent?
- Are a large number of people affected by COVID-19?
- Are there populations disproportionately affected by COVID-19?

○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know

Public Health Problem:

Review of the available evidence



https://covid.cdc.gov/covid-data-tracker/#trends_dailytrendscases

Public Health Problem:
Summary of the available evidence

- **Hospitalization**
  - Cumulative hospitalization rate between March 1 and December 5, 2020 was **278.7** per 100,000 population
  - Among those hospitalized, **32**% required care in an intensive care unit and **15**% died

- **Mortality**
  - As of December 10, 2020, there were **291,522** COVID-19-associated deaths reported in the United States
  - Estimates of the SARS-CoV-2 infection fatality ratio range from 0.5% to 1.4%

https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html .
https://gis.cdc.gov/grasp/COVIDNet/COVID19_5.html .
Hauser, A. et al. Estimation of SARS-CoV-2 mortality during the early stages of an epidemic: a modeling study in Hubei, China, and six regions in Europe. PLoS medicine, 17(7), p.e1003189
Yang, W. et al. Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: a model-based analysis. Lancet Infect Dis. 2020
DOI:https://doi.org/10.1016/S1473-3099(20)30769-6

Public Health Problem:

Work Group Interpretation

Is COVID-19 disease of public health importance?

○ No	○ Probably no	○ Probably yes	○ Yes	○ Varies	○ Don't know

EtR Domain: Benefits and Harms

Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is a desirable effect?

○ Minimal ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know

Benefits and Harms:

Summary of the Available Evidence: Benefits

- The clinical trial for the Pfizer-BioNTech COVID-19 vaccine demonstrated very high efficacy of the 2-dose regimen against symptomatic, laboratory-confirmed COVID-19. The overall efficacy was 95% (95% CI: 90.3%, 97.6%).

High certainty of evidence

- For hospitalization due to COVID-19, 5 events occurred, all in the placebo group. Vaccine effectiveness against hospitalization was 100% (95% CI: -9.9%, 100%).

Low certainty of evidence

- Deaths were uncommon, 2 in the vaccine group and 4 in the placebo group.

Very low certainty of evidence

Benefits and Harms:

Summary of the Available Evidence: Harms

- Serious adverse events were reported in a similar proportion among recipients of vaccine and placebo (0.6% vs 0.5%).

Moderate certainty of evidence

- Severe reactions were more common in vaccinated; any grade ≥3 reaction was reported by 8.8% of vaccinated vs. 2.1% of placebo group.

High certainty of evidence

Summary of GRADE

Outcome	Importance	Design (# of studies)	Findings	Evidence type
Benefits				
Symptomatic lab-confirmed COVID-19	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine is effective in preventing symptomatic COVID-19	1
Hospitalization due to COVID-19	Critical	RCT (1)	Pfizer-BioNTech COVID-19 vaccine may prevent COVID-19-resulting in hospitalization, but the uncertainty is high because this is a rare outcome	3
All-cause Death	Important	RCT (1)	Pfizer-BioNTech COVID-19 vaccine may prevent death, but the uncertainty is high because this is a rare outcome	4
SARS-CoV-2 seroconversion	Important	No studies	Data not yet available from any studies	ND
Asymptomatic SARS-CoV-2 infection	Important	No studies	Data not available from any studies	ND
Harms				
Serious adverse events	Critical	RCT (2)	SAEs were balanced between vaccine and placebo arms. Two SAEs were judged to be related to vaccination.	2
Reactogenicity	Important	RCT (2)	Severe reactions were more common in vaccinated; any grade ≥3 reaction was reported by 8.8% of vaccinated vs. 2.1% of placebo group	1

Evidence type: 1=high; 2=moderate; 3=low; 4=very low; ND, no data.

Benefits and Harms

How substantial are the desirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is a desirable effect?

○ Minimal	○ Small	○ Moderate	○ Large	○ Varies	○ Don't know

Benefits and Harms

How substantial are the undesirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is an undesirable effect?

○ Minimal	○ Small	○ Moderate	○ Large	○ Varies	○ Don't know

Benefits and Harms

How substantial are the undesirable anticipated effects?

- How substantial is the anticipated effect for each main outcome for which there is an undesirable effect?

○ Minimal	○ Small	○ Moderate	○ Large	○ Varies	○ Don't know

RESEARCH SUMMARY

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

F.P. Polack, et al. DOI: 10.1056/NEJMoa2034577

CLINICAL PROBLEM

Safe and effective vaccines to prevent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and Covid-19 are urgently needed. No vaccines that protect against betacoronaviruses are currently available, and mRNA-based vaccines have not been widely tested.

CLINICAL TRIAL

A randomized, double-blind study of an mRNA vaccine encoding the SARS-CoV-2 spike protein.

43,548 participants ≥16 years old were assigned to receive the vaccine or placebo by intramuscular injection on day 0 and day 21. Participants were followed for safety and for the development of symptomatic Covid-19 for a median of 2 months.

RESULTS

Safety:
Vaccine recipients had local reactions (pain, erythema, swelling) and systemic reactions (e.g., fever, headache, myalgias) at higher rates than placebo recipients, with more reactions following the second dose. Most were mild to moderate and resolved rapidly.

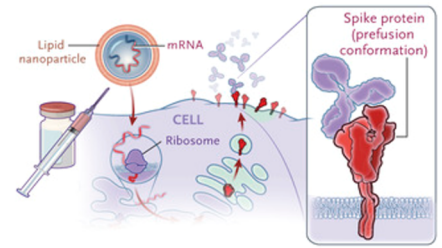
Efficacy:
The vaccine showed some early protection 12 days after the first dose; 7 days after the second dose, 95% efficacy was observed.

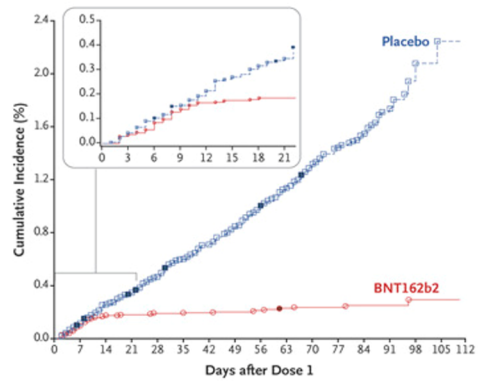
LIMITATIONS AND REMAINING QUESTIONS

Further study is required to understand the following:

- Safety and efficacy beyond 2 months and in groups not included in this trial (e.g., children, pregnant women, and immunocompromised persons).
- Whether the vaccine protects against asymptomatic infection and transmission to unvaccinated persons.
- How to deal with those who miss the second vaccine dose.

Links: Full article | NEJM QuickTake | Editorial





	BNT162b2 Vaccine	Placebo
Symptomatic Covid-19	8	162
	N=18198	N=18325
Severe Covid-19	1	9
	N=21669	N=21686

Vaccine efficacy of 95% (95% credible interval, 90.3–97.6%)

CONCLUSIONS

Two doses of an mRNA-based vaccine were safe over a median of two months and provided 95% protection against symptomatic Covid-19 in persons 16 years of age or older.

summary

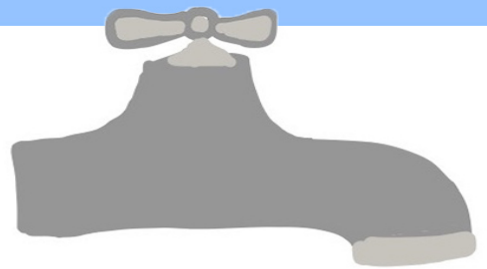
Product: Pfizer-BioNTech COVID-19 vaccine

Issue: Two individuals in the U.K. reported severe allergic reactions to Pfizer BioNTech's COVID-19 vaccine on December 8, 2020. As vaccine roll-out begins in Canada, Canadians may be wondering about the risks of allergic reactions and if they should receive this vaccine if they have allergies to foods or other medications.

What to do: People with allergies to any of the ingredients in the Pfizer-BioNTech COVID 19 vaccine should not receive it. Speak with your health professional about any serious allergies or other health conditions you may have before you receive this vaccine.

Trudeau offers sombre Christmas message but says 500,000 vaccine doses are coming early in the new year

CBC news



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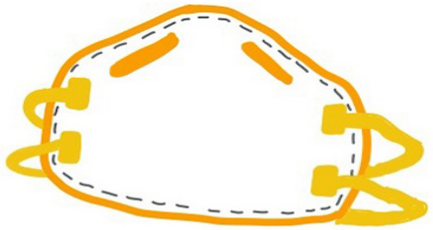
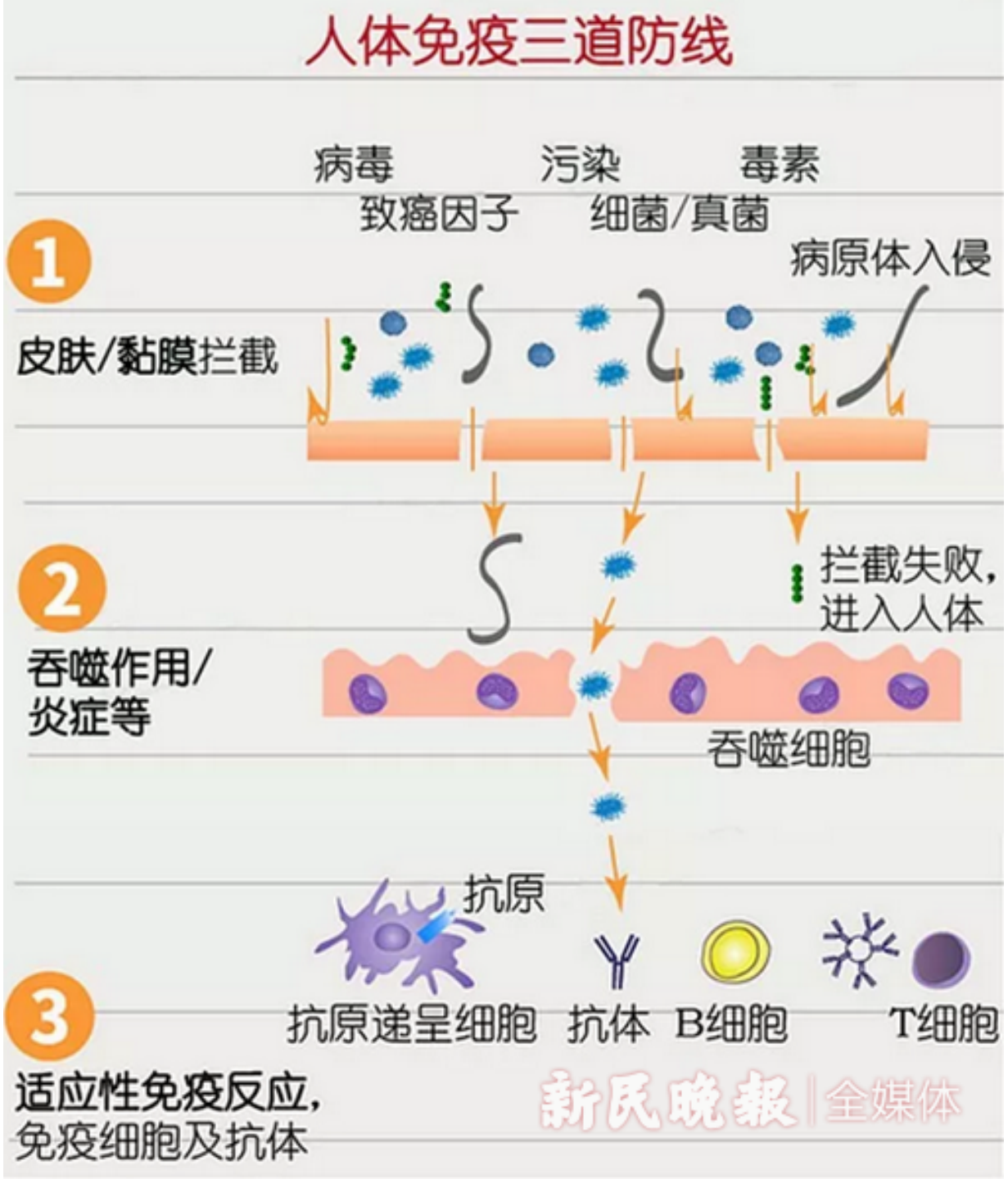
INFECTION PREVENTION



COVID-19

By Clara Liao

非特异性免疫



特异性免疫

六步洗手法

◆ 掌心相对，手指并拢，相互揉搓；

◆ 手心对手背沿指缝相互揉搓，交换进行；

◆ 掌心相对，双手交叉指缝相互揉搓；

◆ 弯曲手指使关节在另一手掌心旋转揉搓交换进行；

◆ 左手握住右手大拇指旋转揉搓，交换进行；

◆ 将五个手指尖并拢，放在另一手掌心旋转揉搓，交换进行。

How to protect ourselves & others

9 important COVID-19 prevention measures

01 **Stay home and self-isolate** if you feel unwell, even with mild symptoms

02 **Clean hands frequently** with soap & water for 40 seconds or with alcohol-based hand rub

03 **Cover your nose and mouth** with a disposable tissue or flexed elbow when you cough or sneeze

04 **Avoid touching** your eyes, nose and mouth

05 Maintain a minimum physical **distance of at least 1 metre** from others

06 **Stay away from crowds** and avoid poorly ventilated indoor spaces

07 **Use a fabric mask** where physical distancing of at least 1 metre is not possible

08 **Use a medical / surgical mask** if you may be at higher risk (age, medical conditions)

09 **Regularly clean & disinfect** frequently touched surfaces

Thank You