

# VACCINES 2026

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## Biological therapies



## 6 Types of Vaccine Technologies (Pfizer)

### Live-attenuated vaccines (LAVs)

- LAVs: live, weakened bacteria/virus
- IR: strong enough, but the pathogen is incapable of causing disease
- Additional doses, or booster shots, are not always needed
- E.g. MMR, varicella

### Inactivated vaccines

- Pathogen: inactivated or killed
- IR: strong enough, but the pathogen is incapable of causing disease.
- Multiple doses are often needed
- Examples: Polio vaccine, influenza vaccine

### Subunit vaccines

Subunit vaccines are made from a piece of a pathogen, not the whole organism, so they do not contain any live pathogens.

**Polysaccharide vaccines**

**Conjugate vaccines**

**Protein-based vaccines**

### Toxoid vaccines

-> use inactivated toxins to target the toxic activity created by the bacteria, rather than targeting the bacteria itself  
-> **neutralization** of toxins with antibodies through vaccination  
Booster: every 10 years or so...  
E.g. tetanus vaccine, diphtheria vaccine

### Viral vector vaccines

- -> delivering only the genetic code of the antigen
- They trigger a strong IR
- One dose of the shot is needed to develop immunity (Booster may be needed)
- E.g. Ebola vaccine, COVID-19 vaccine

### Messenger RNA (mRNA) vaccines

- Short-lived strands of genetic material
- Fragile molecule!
- A delivery technology had to be developed: lipid nanoparticles, or LNPs.

# How Vaccination Works

- Vaccination introduces a **non-pathogenic form of an antigen** (e.g., inactivated pathogen, protein subunit, mRNA, vector) that mimics infection without causing disease.

## **AFTER ADMINISTRATION:**

- **Antigen-presenting cells (APCs)** (mainly dendritic cells) take up the antigen
- APCs migrate to **secondary lymphoid organs** (lymph nodes, spleen)
- Antigen peptides are presented via **MHC II (→ CD4<sup>+</sup> T cells)** and sometimes **MHC I (→ CD8<sup>+</sup> T cells)**
- Naïve T cells become activated
- Activated CD4<sup>+</sup> T cells provide help to B cells

# How Vaccination Works

Antigen-specific B cells differentiate into:

- **Short-lived plasma cells → early antibody production**
- **Germinal center B cells → affinity maturation**
- **Memory B cells**
- **Long-lived plasma cells**

## **RESULT:**

- ✓ Neutralizing antibodies
- ✓ Memory T cells
- ✓ Memory B cells

# Formation of Immunological Memory

- Clonal expansion of antigen-specific B and T cell
- Somatic hypermutation (SHM) → increases antibody affinity
- Class-switch recombination (CSR) → IgG, IgA, IgE
- Selection of high-affinity clones

## **OUTCOME:**

- **Memory B cells** (rapid recall response)
- **Long-lived plasma cells** (persistent antibody production)
- **Memory CD4<sup>+</sup> and CD8<sup>+</sup> T cells**

# Immunological basis of booster vaccination

## **ON RE-EXPOSURE:**

- Faster response
- Higher antibody affinity
- Stronger magnitude
- Shorter lag phase

# I. LAVs

- LAVs trigger an **immune response that is similar to what would occur during a natural infection,**
- **...but the person is not able to pass on the virus to other people**
- **Lifelong immunity - only one / two doses of the vaccine are needed**

# LAVs - Just weakened, not dead...

...might be unsuitable for people with weakened immune systems...

- Risk of vaccine-related infection: in immunocompromised individuals, the attenuated strain could—very rarely—cause disease similar to the natural infection
- ...or the immune response may be insufficient...
- A weakened immune system may not produce a protective immune response, making the vaccine ineffective.

# Why might LAVs be unsuitable for people with weakened immune systems?

**The vaccine organism can replicate (limited potential)**

*Who may be at risk?*

- People receiving chemotherapy
- Individuals with HIV with low CD4 counts
- Organ transplant recipients on immunosuppressive therapy patients
- Patients on high-dose steroids or biologics (e.g., anti-TNF, Rituximab)
- Individuals with primary immunodeficiencies


# I. LAVs - types of diseases that live-attenuated vaccines are used for :

smallpox combined  
rotavirus vaccine rubella  
chickenpox measles  
mumps  
yellow mmr


- Medical advice should be sought before the vaccine is given
  - It may not be suitable for people with weakened immune systems
- 
- LAVs also need to be kept cool while they are stored
  - They may not be suitable for use in environments where there is little access to refrigeration.

# I. LAVs

## Vaccine advisory committees, representatives



**VACSATC**  
Magyarország



**CLINICAL VACCINATION ADVISERS IN HUNGARY**

Név	Munkahely megnevezése, címe	Telefonszám, rendelési idő
Dr. Mészner Zsófia Dr. Kulcsár Andrea	Szent László Kórház 1097 Budapest, Albert Flórián út 5-7.	Rendelés: H-CS-P: 8-14 h Kedd: 9-14 h Tel.: 06-1-455-8256
Dr. Nyul Zoltán	PTE KK Gyermekgyógyászati Klinika Infektológiai osztály 7624 Pécs, Nyár u. 8.	06-72-507-533 Előzetes telefonrezeztetés ut rendel
Dr. Góg Erzsébet főorvos csecsemő és gyermekgyógyász, klinikai immunológiai és allergológiai szakorvos	Bács-Kiskun Megyei Kórház Szegei Tudományegyetem AOK Gyermek Szakambulancia 6000 Kecskemét, Nyíri út 38.	06-76-516-966 Rendelés: Hétfő: 10-11 h előzetes egyeztetés szükséges
Dr. Zátanyi Adél gyermekgyógyász, neonatólogus főorvos	Pándy Kálmán Kórház Gyermekosztály 5700 Gyula, Kárpát u. 11.	Rendelés: Hétfő: 13-15 h előzetes egyeztetés szükséges 06-66-463-633/3326 m.
	BAZ Megyei Központi Kórház-és Esetemti Oktatókórház	Rendelés:

**Navigation:**

- Nyitólap
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  - Nemzetközi Oltóhelyek Budapesten
  - Nemzetközi Oltóhelyek Vidéken I. (B-K)
  - Nemzetközi Oltóhelyek Vidéken II. (M-Z)
  - **Klinikai védőoltási tanácsadók**
  - Védőoltások bevezetése és főbb változásai Magyarországon
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  - Bakteriális oltóanyagok

Advisory Committee on Immunization Practices (ACIP)

CDC > ACIP Home

**ACIP Committee Members**

[Print](#)

See also: [Archived ACIP Members Roster](#)

[Printer friendly version of ACIP Members list](#) [9 pages]

[ACIP Home](#)

Meeting Information

Committee Information +

**Committee Members -**

ACIP Membership Roster

Apply for ACIP Membership

Work Groups +

Recommendations +

Evidence Based +

The ACIP includes 15 voting members responsible for making vaccine recommendations. The Secretary of the U.S. Department of Health and Human Services (DHHS) selects these members following an application and nomination process.

Fourteen of the members are from the fields of clinical medicine, virology, immunology, epidemiology, and public health that bring related expertise to the committee.

In addition to the members listed below, the ACIP includes 15 voting members responsible for making vaccine recommendations. The Secretary of the U.S. Department of Health and Human Services (DHHS) selects these members following an application and nomination process.

Members	
<p><a href="#">BAHTA, Lynn, RN, MPH, CPH</a> Immunization Program Clinical Consultant Infectious Disease, Epidemiology, Prevention &amp; Control Division Minnesota Department of Health Saint Paul, Minnesota Term: 7/1/2019 – 6/30/2023</p>	<p><a href="#">BELL, Beth P., MD, MPH</a> Clinical Professor Department of Global Health, School of Public Health University of Washington Seattle, WA Term: 7/1/2019 – 6/30/2023</p>
<p><a href="#">BROOKS, Oliver, MD, FAAP</a> Chief Medical Officer Watts HealthCare Corporation Los Angeles, CA Past President, National Medical Association Term: 7/26/2021 – 6/30/2025</p>	<p><a href="#">CHEN, Wilbur H., MD, MS, FACP, FIDSA</a> Professor of Medicine Center for Vaccine Development and Global Health University of Maryland School of Medicine Baltimore, MD Term: 12/23/2020 – 6/30/2024</p>
<p><a href="#">CINEAS, Sybil, MD, FAAP, FACP</a> Associate Professor of Medicine, Pediatrics, and Medical Science (Clinical) The Warren Alpert Medical School of Brown University Associate Program Director Brown Combined Residency in Internal Medicine and Pediatrics Providence, RI</p>	<p><a href="#">DALEY, Matthew F., MD</a> Senior Investigator Institute for Health Research Kaiser Permanente Colorado Aurora, CO Term: 1/4/2021 – 6/30/2024</p>

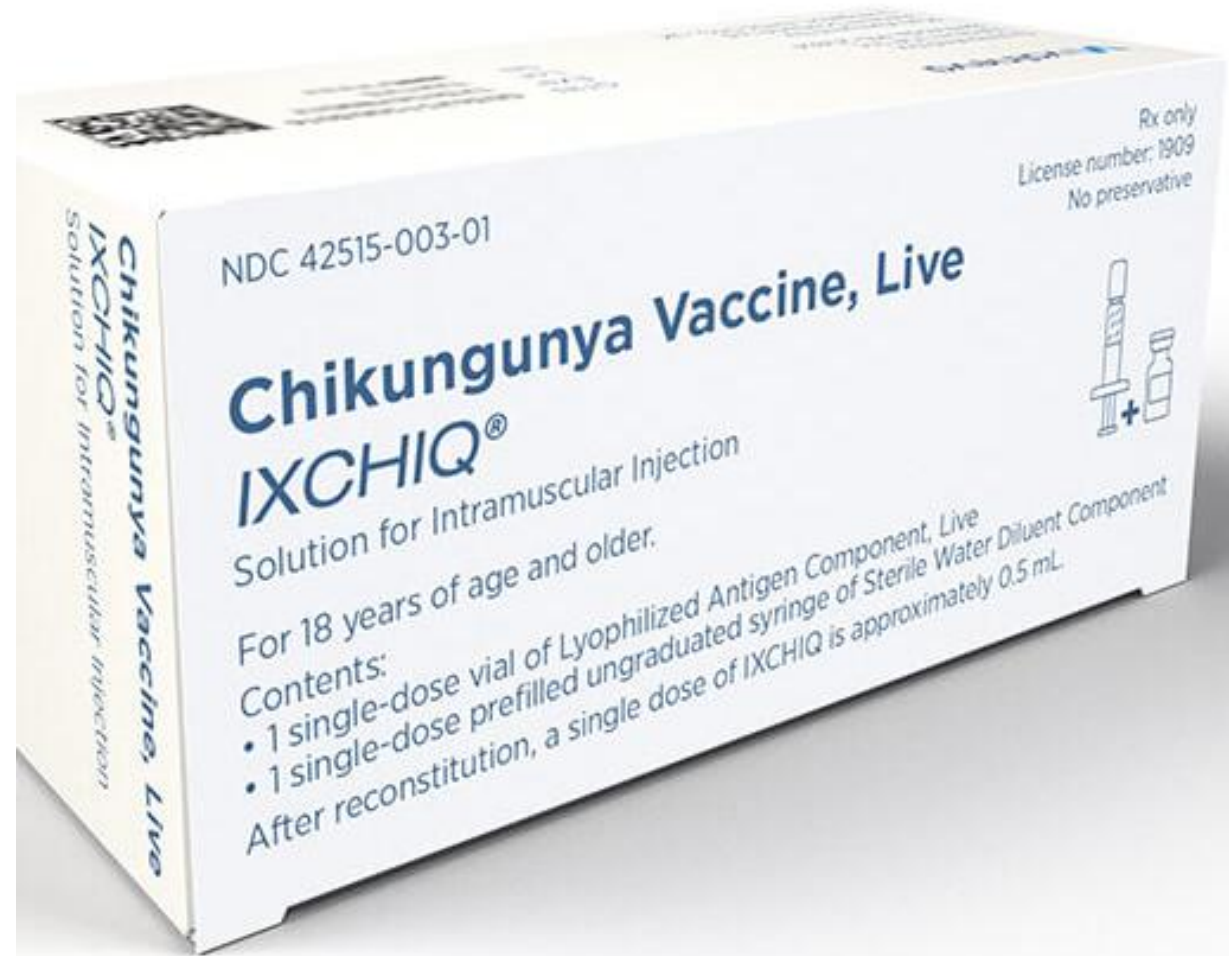
## Country specific!

**LAVs**

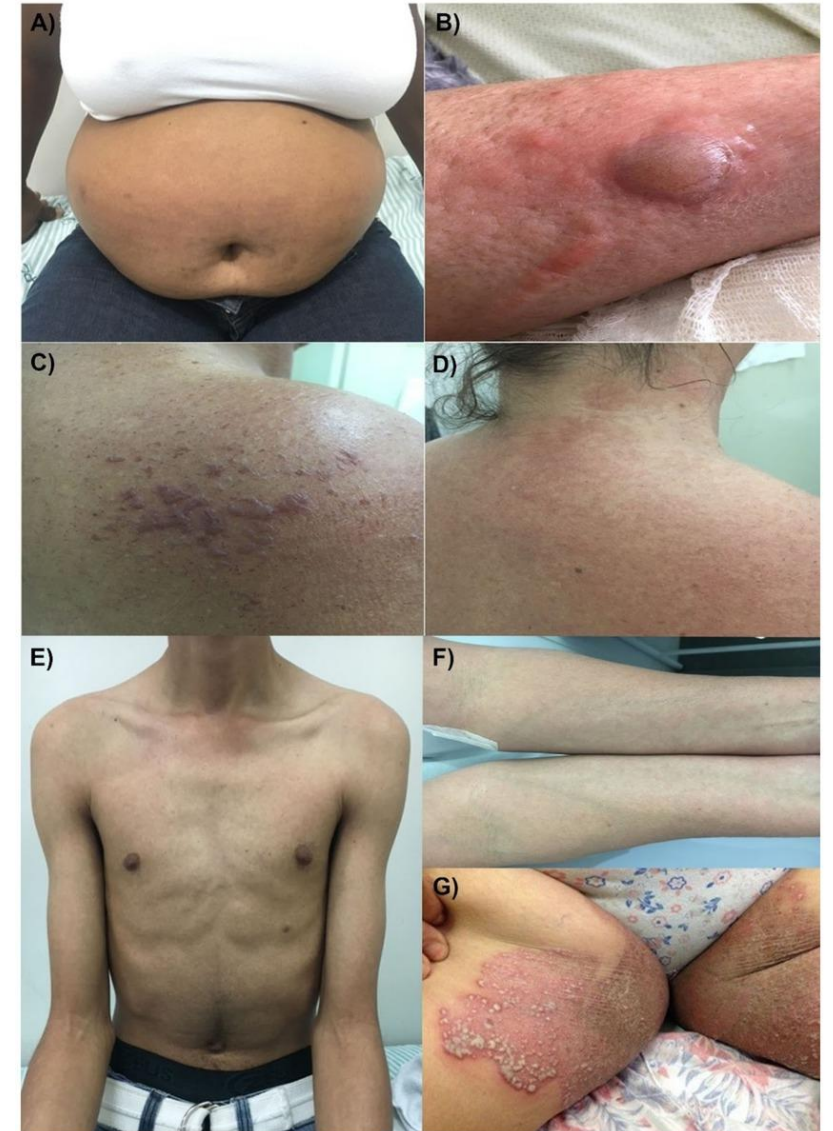
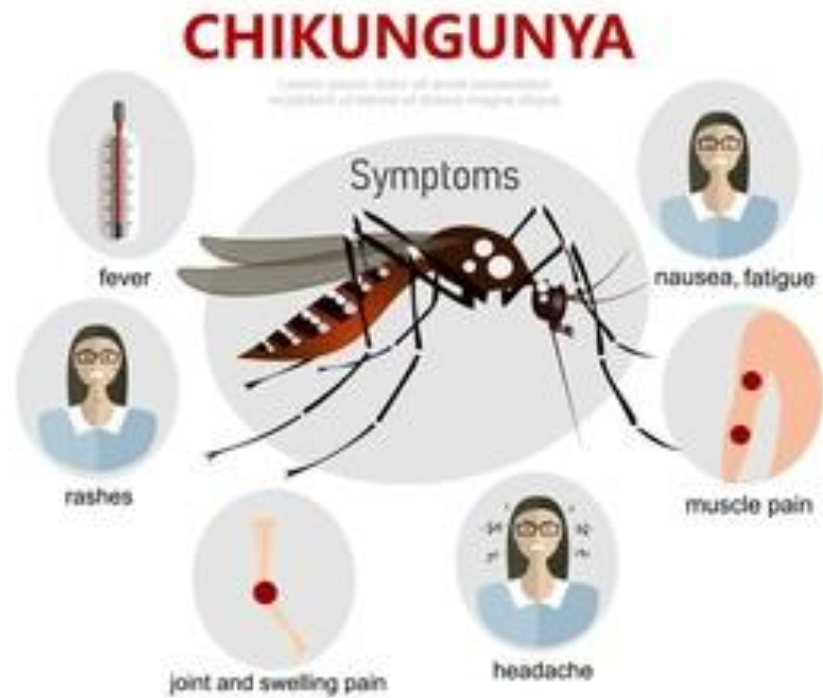
**A more recent example:  
CHIKUNGUNYA**

# IXCHIQ - LAV

- IXCHIQ is the only live-attenuated vaccine (LAV) for CHIKUNGUNYA
- It uses a **weakened strain of the virus** to stimulate an immune response
- It is approved for **people aged 12 to 65 in Europe**



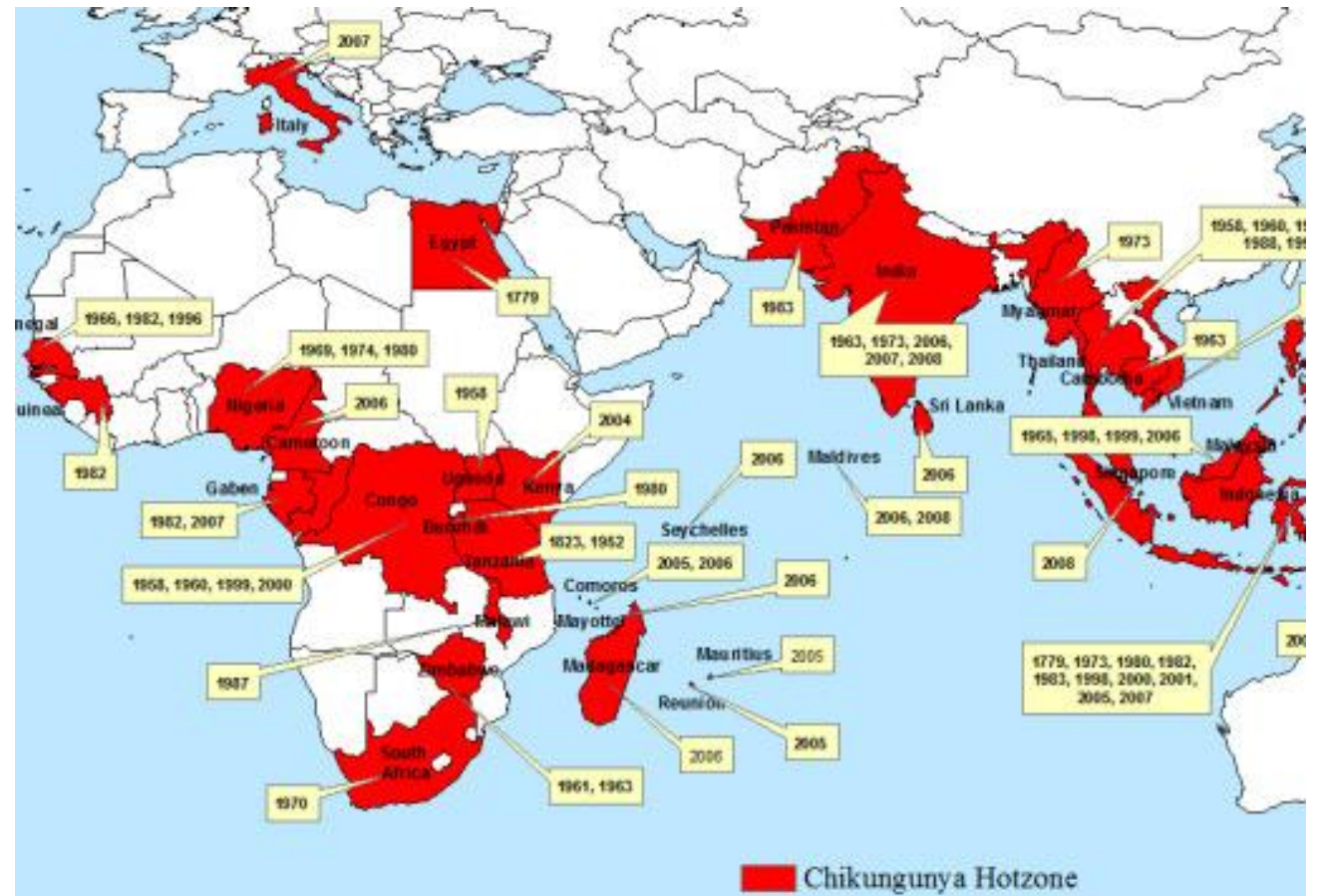
# Chikungunya fever



# Chikungunya active transmission regions - geographic and temporal knowledge of previous outbreaks

The symptoms of chikungunya are similar to those of **Dengue** and **Zika**

→ **easy to misdiagnose!**

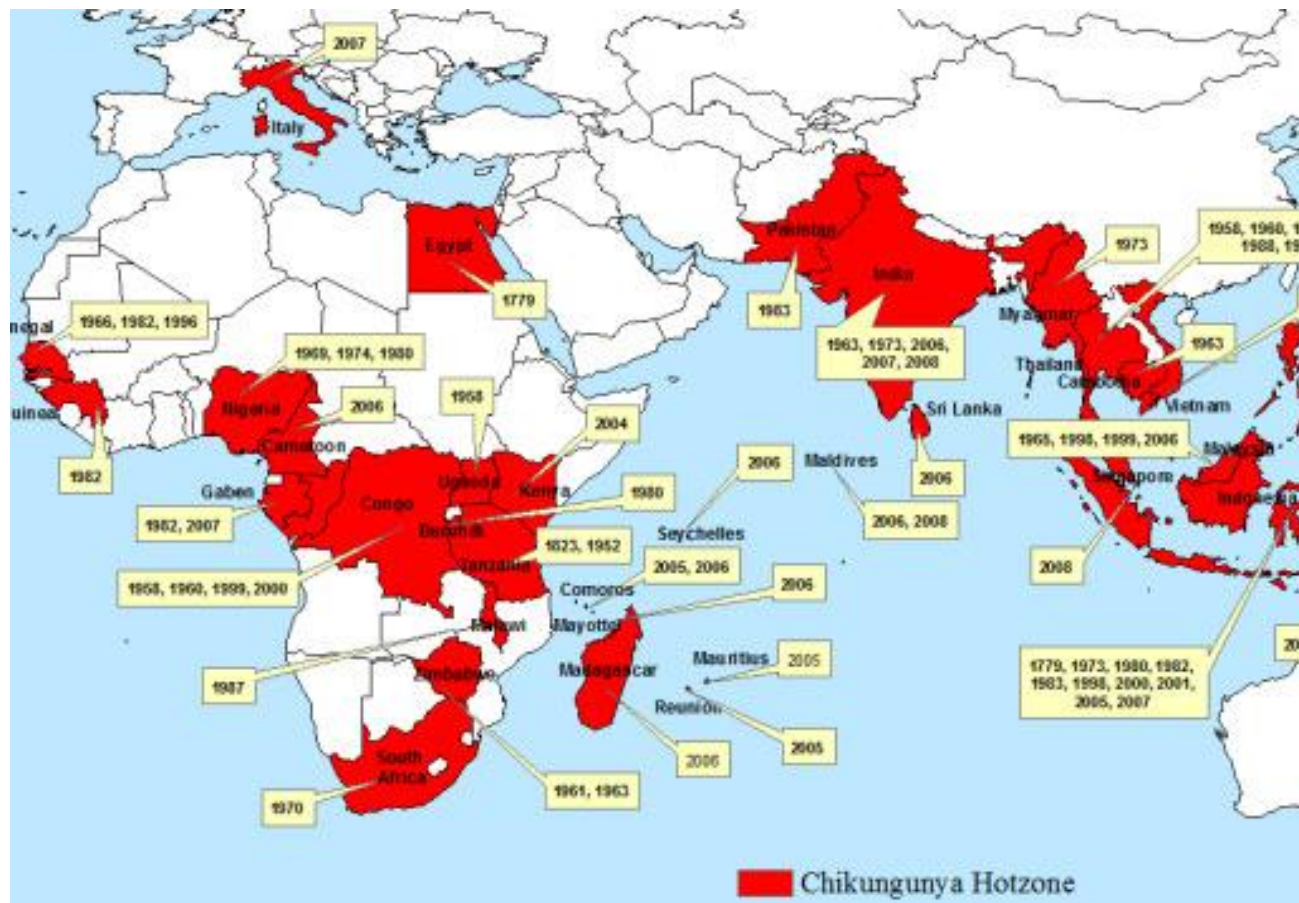


# Chikungunya Fever

Chikungunya fever is originated in East Africa

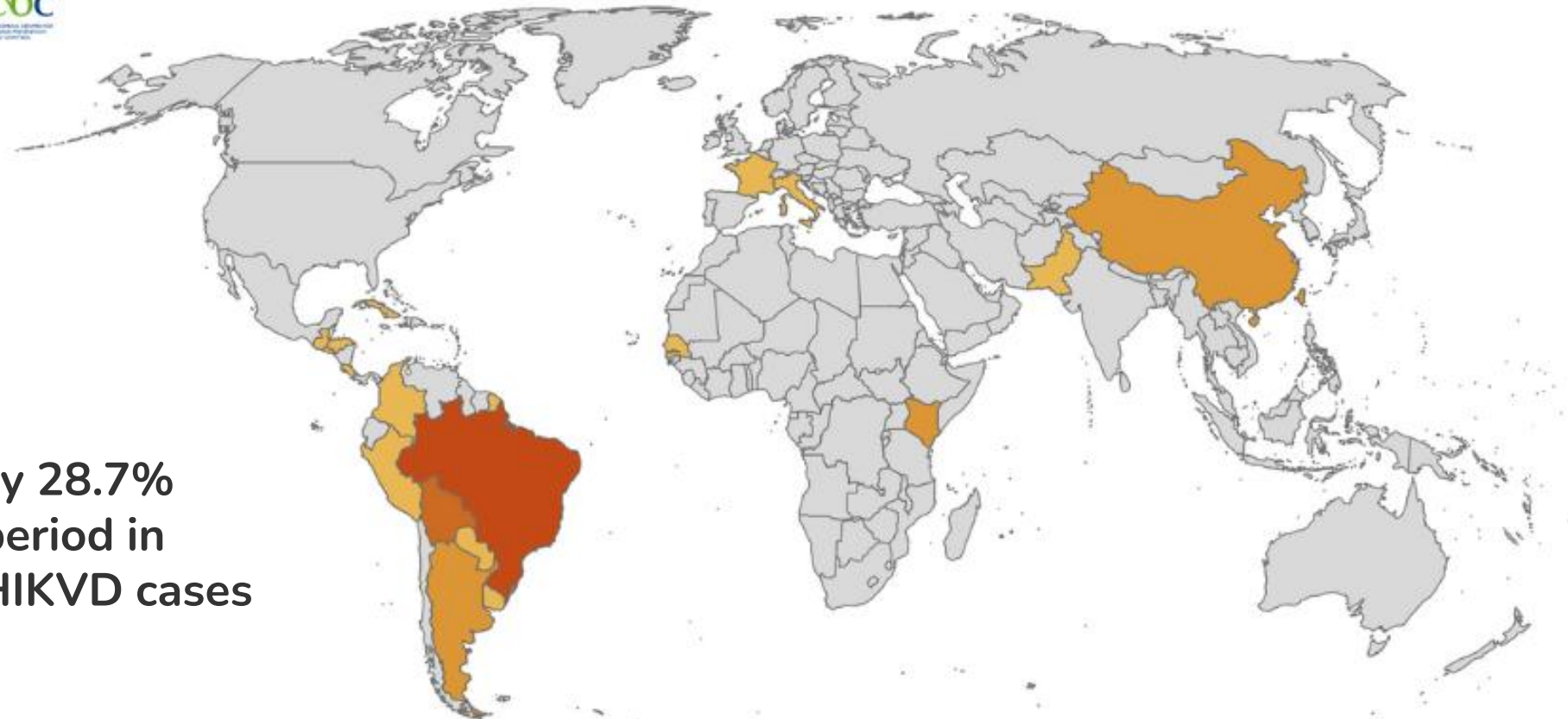
- First identified in Tanzania in **1952**
- Spread to the Indian Ocean islands in **2005**
- In **2013** it reached the Americas, causing epidemics in the **Caribbean** and **Latin America**.

**CHIKUNGUNYA IS NOW CONSIDERED AN EMERGING GLOBAL THREAT IN TROPICAL AREAS!**



# Three-month Chikungunya virus disease case notification rate per 100 000 population, July-September 2025

Notification rate per 100 000 persons



In 2025, there have been 339 822 CHIKVD cases and 145 associated deaths reported worldwide.

Cases have decreased by 28.7% compared to the same period in 2024, when 476 962 CHIKVD cases were reported.

# Chikungunya Fever

The symptoms of chikungunya are similar to those of **Dengue** and **Zika**, making chikungunya easy to misdiagnose

**Chikungunya causes fever and severe joint pain - debilitating and may be prolonged**

Other symptoms include **joint swelling, muscle pain, headache, nausea, fatigue and rash**



FEVER  
WITH CHILL



HEADACHE



JOINT PAIN

CHIKUNGUNYA



SYMPTOMS



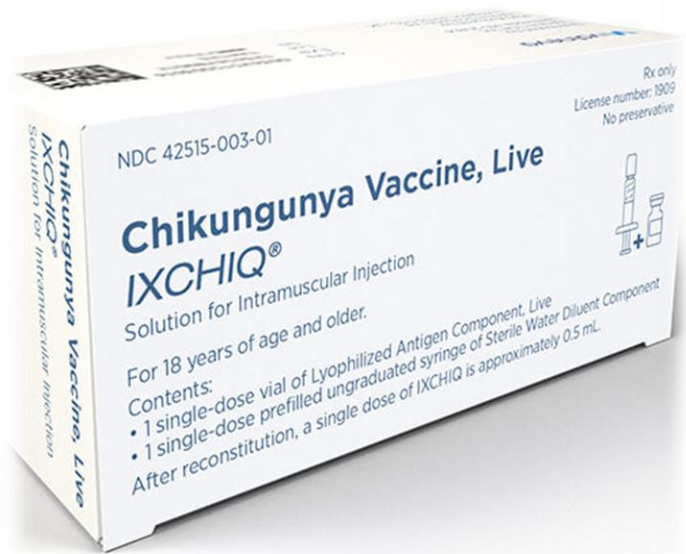
MUSCLE PAIN



SKIN RASHES



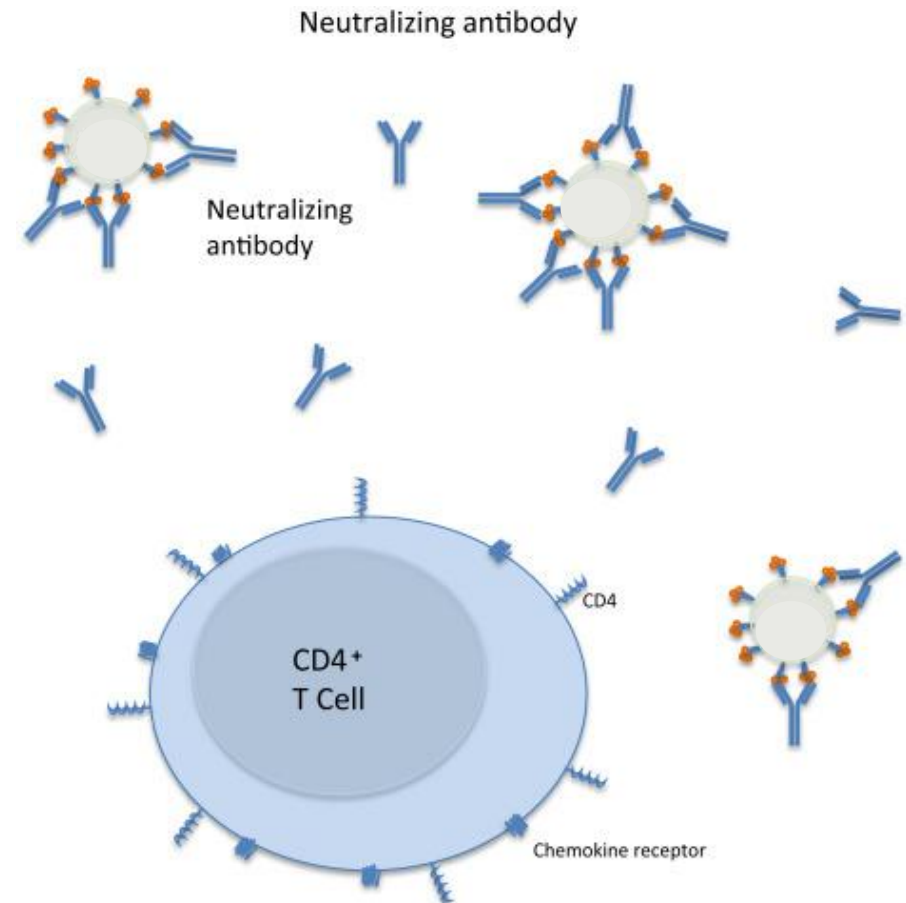
JOINT SWELLING



# The world's first chikungunya vaccine

## Single-dose LAV virus vaccine

- A major advance: LAV chikungunya vaccines
- In 2023, the U.S. FDA approved IXCHIQ® (also known as VLA1553 by Valneva) – the **world's first chikungunya vaccine**
- **INDUCES ROBUST NEUTRALIZING ANTIBODY FORMATION**



# Chikungunya - VLP

In addition to the Valneva vaccine,  
a **virus-like particle (VLP) vaccine**

by Bavarian Nordic

- **Brand name: VIMKUNYA**
- **Licensed in early 2025**
- **Provides a non-live option!**



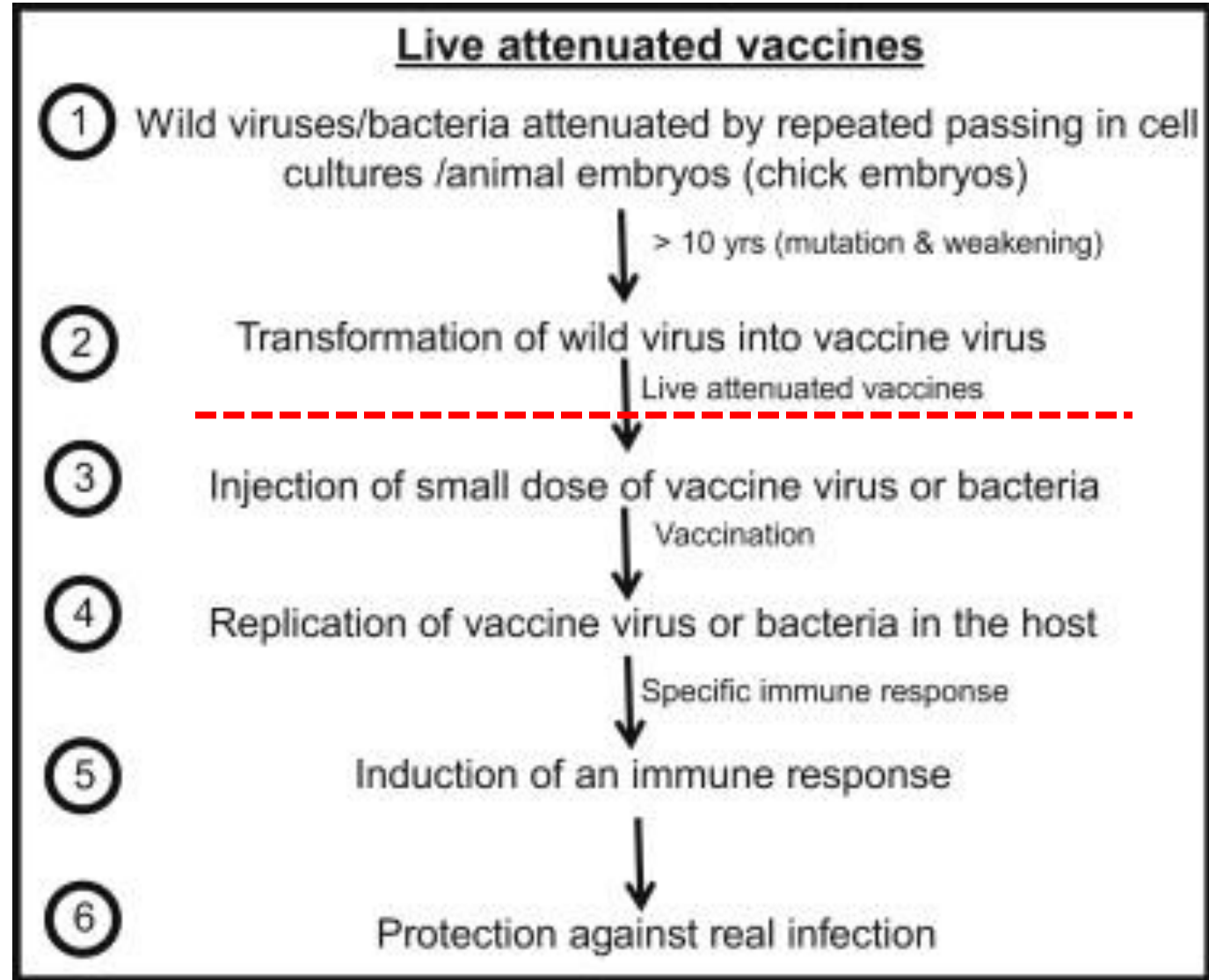
# I. LAVs

## Attenuation

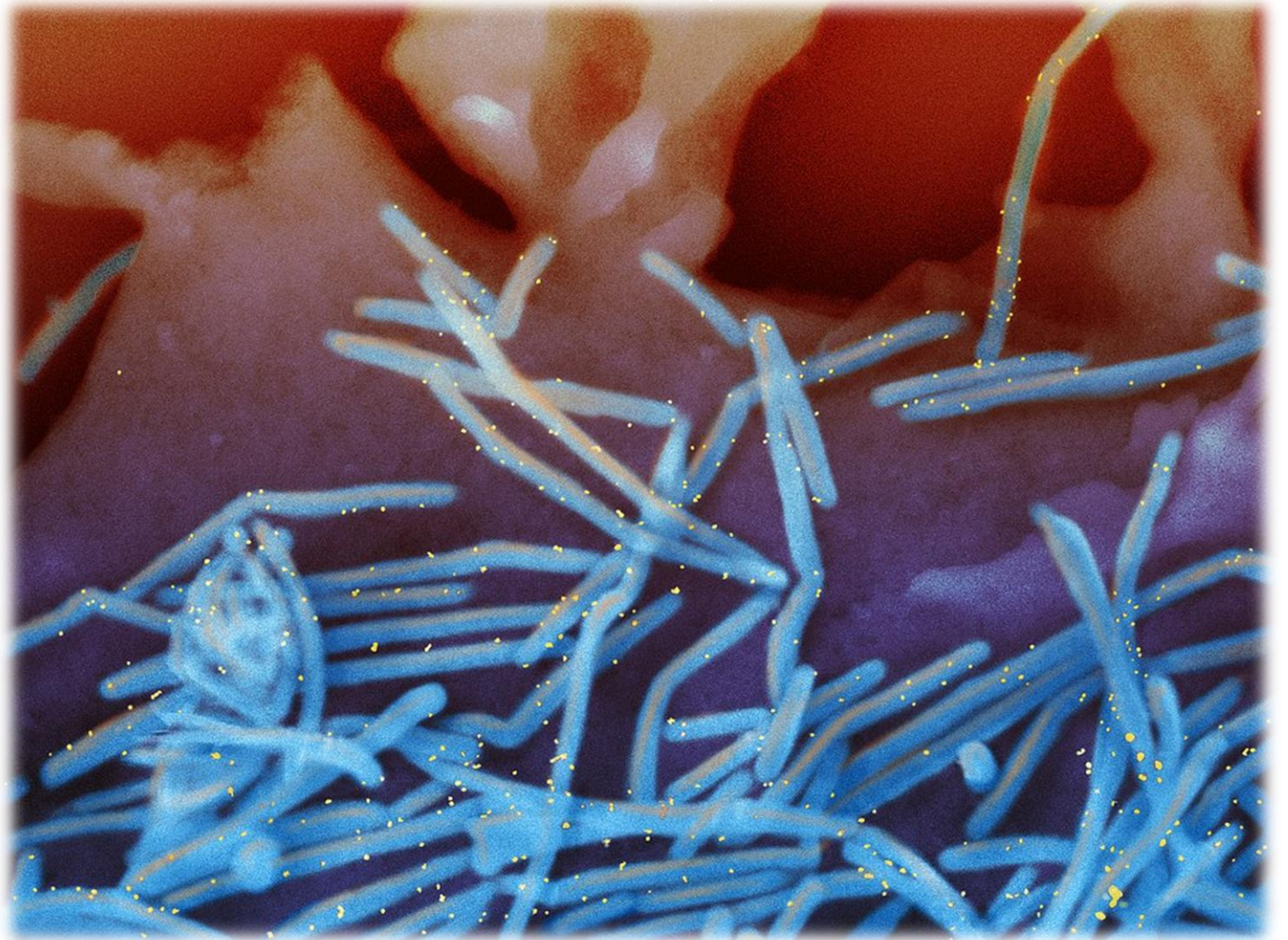
THIS IS NOT THE ONLY OPTION!



GENETIC MODIFICATION OF  
THE VIRAL GENOME  
(reverse genetics)



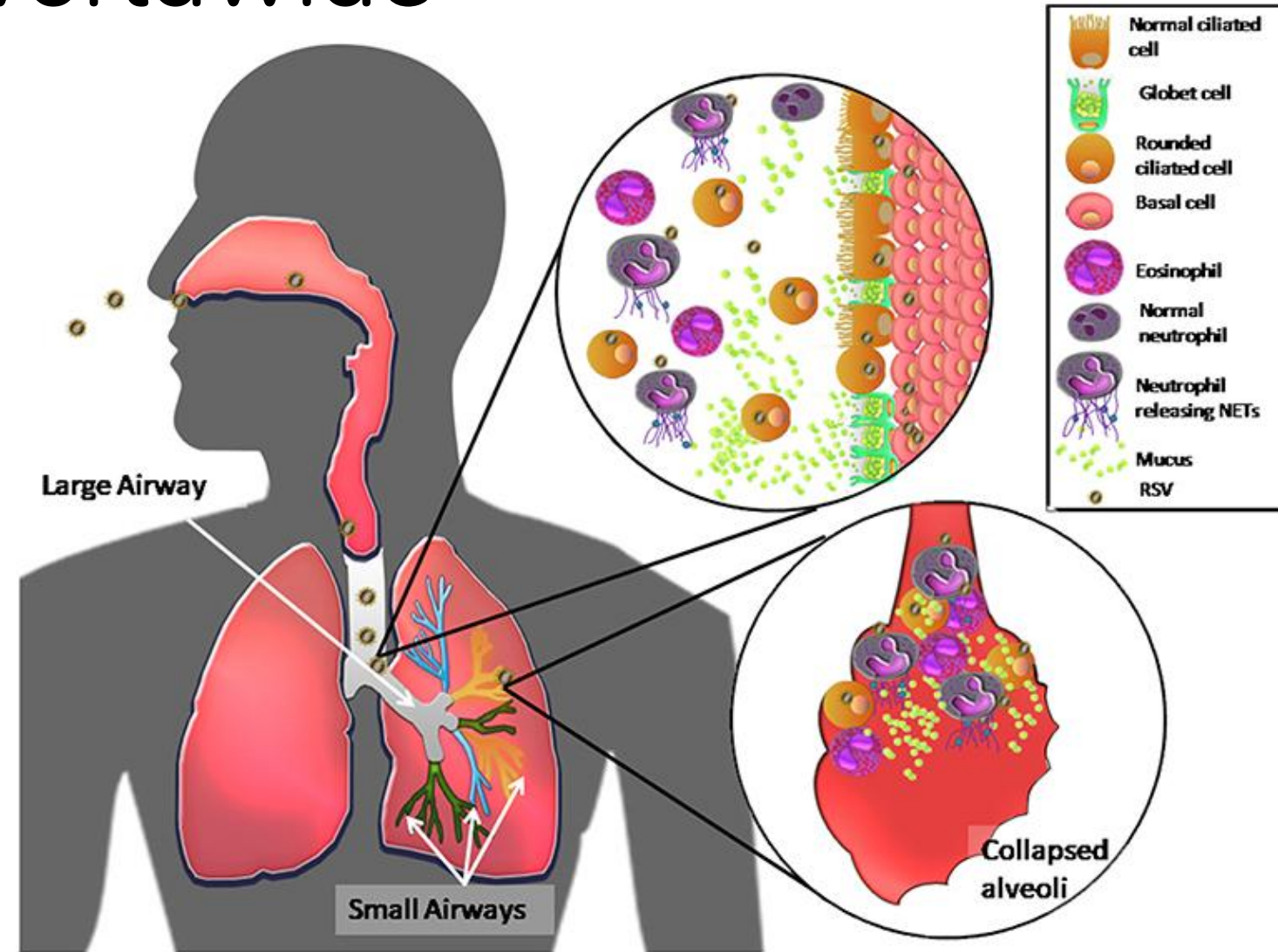
## Respiratory syncytial virus (RSV)



# RSV circulates worldwide

## Respiratory syncytial virus (RSV, hRSV)

- Infections of the respiratory tract
- RSV circulates worldwide and causes seasonal outbreaks every year
- **Virtually all children are infected by age 2 (two) often more than once**
- **Immunity after infection is not long-lasting**
- **Reinfections are common throughout life...**



# RSV can be life-threatening for infants

- RSV can be life-threatening for infants, but the risk is very age- and condition-dependent.

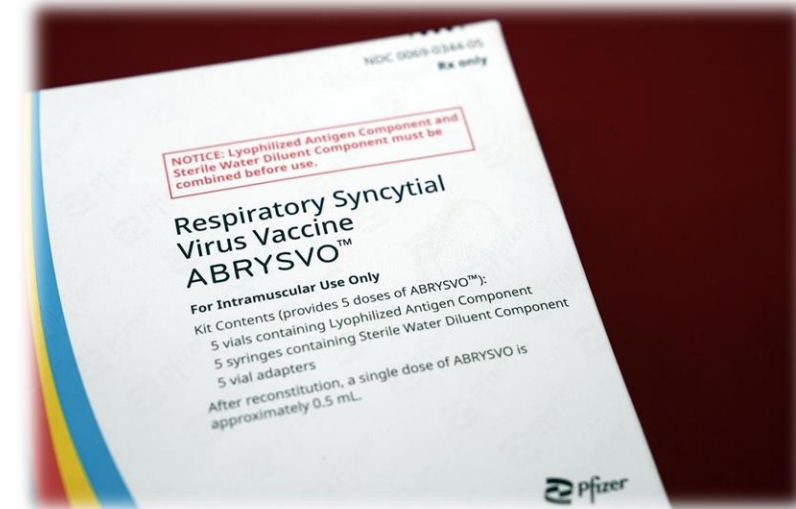
RSV can be lethal in young children, especially in infants under 6 months, premature babies, and those with underlying medical conditions.

- However, with modern medical care, most children recover fully, and fatal cases are rare in high-income countries.

# Good news: prevention is improving

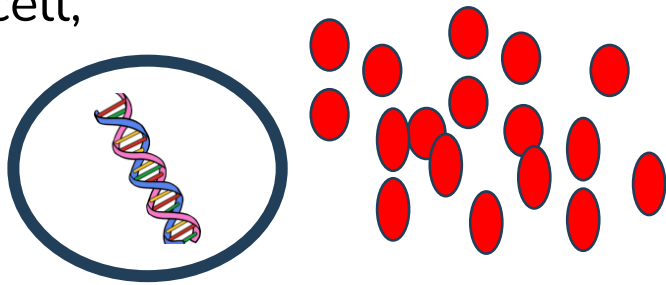
## New preventive options:

- Maternal vaccination (Abrysvo – Recombinant F protein)
- Long-acting mAbs (Nirsevimab)
- + candidate LAVs



# Abrysvo: non-live, bivalent recombinant F protein vaccine

- RSV virus' F protein to trigger an immune response
- **Recombinant** protein: It is created by inserting genetic material from the RSV virus into a cell,



...which then produces the specific protein that is purified and used in the vaccine



→ Abs are produced → to protect against RSV infection



# RSV circulates worldwide

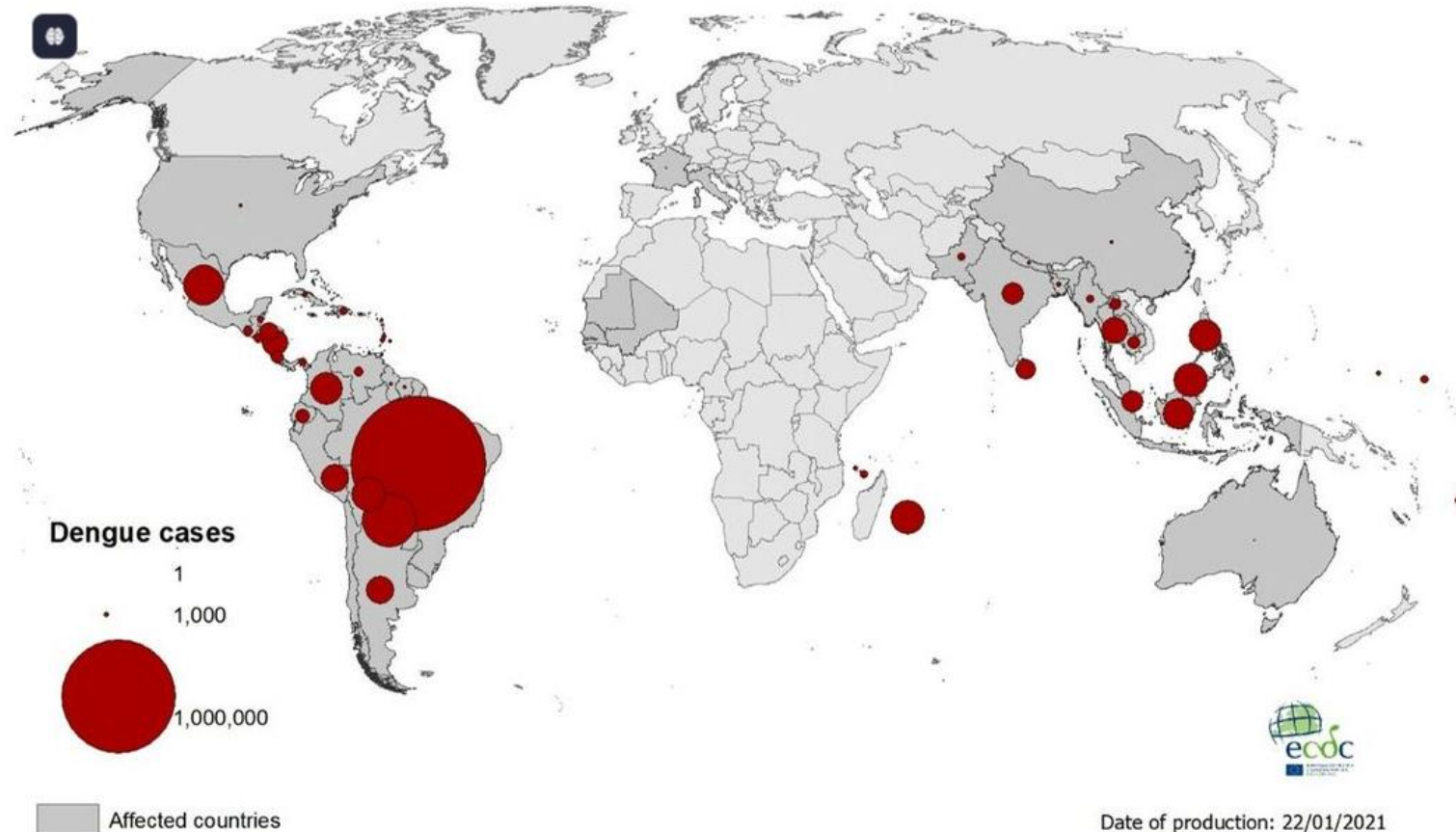
- **NIRSEVIMAB** and **CLESROVIMAB** are **mAbs** that prevent severe RSV disease and are recommended for **infants**.
- **Nirsevimab** is also recommended for some **young children**.
- **mAbs are not vaccines!**
- They do not activate the immune system
- Rather, the antibodies themselves protect against disease

Still LAVs...

Dengue

# Geographical distribution of dengue cases reported worldwide, 2020

Dengue is present in Africa, the Americas, Asia, the Caribbean and the Pacific. In 2020, France and Italy reported autochthonous dengue cases. In 2020, the five countries reporting most cases are Brazil, Paraguay, Mexico, Vietnam and Malaysia.



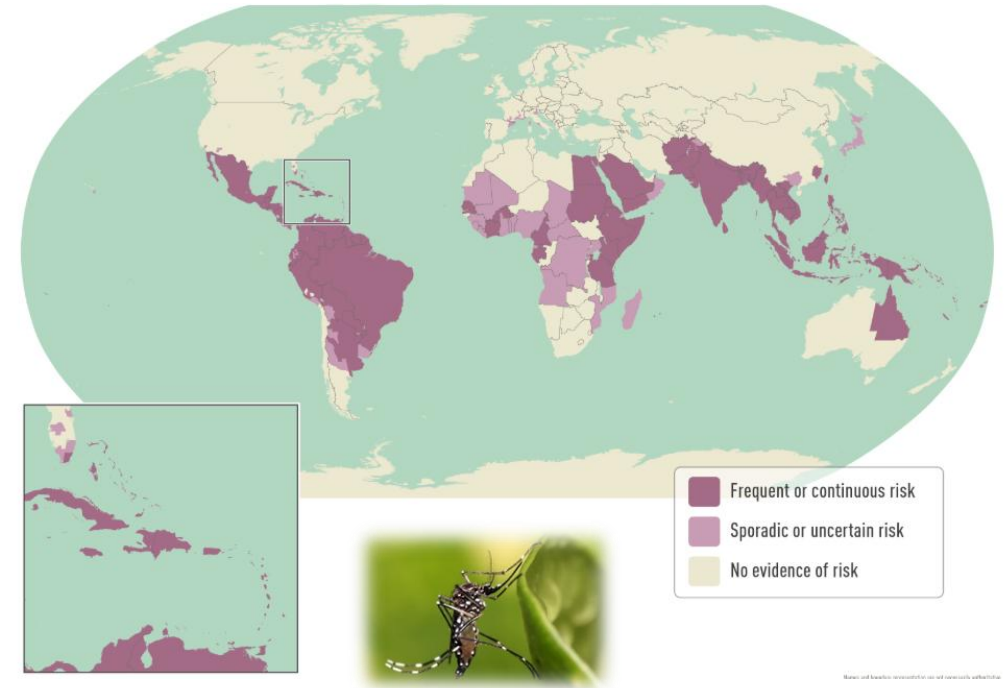
# Development of a live attenuated dengue virus vaccine using reverse genetics

4 serotypes (DEN1-DEN4)

→ endemic in most areas of Southeast Asia, Central and South America, and other subtropical regions.

**THE NUMBER OF CASES IS INCREASING** ↑

→ continued spread of the mosquito vector, *Aedes aegypti*

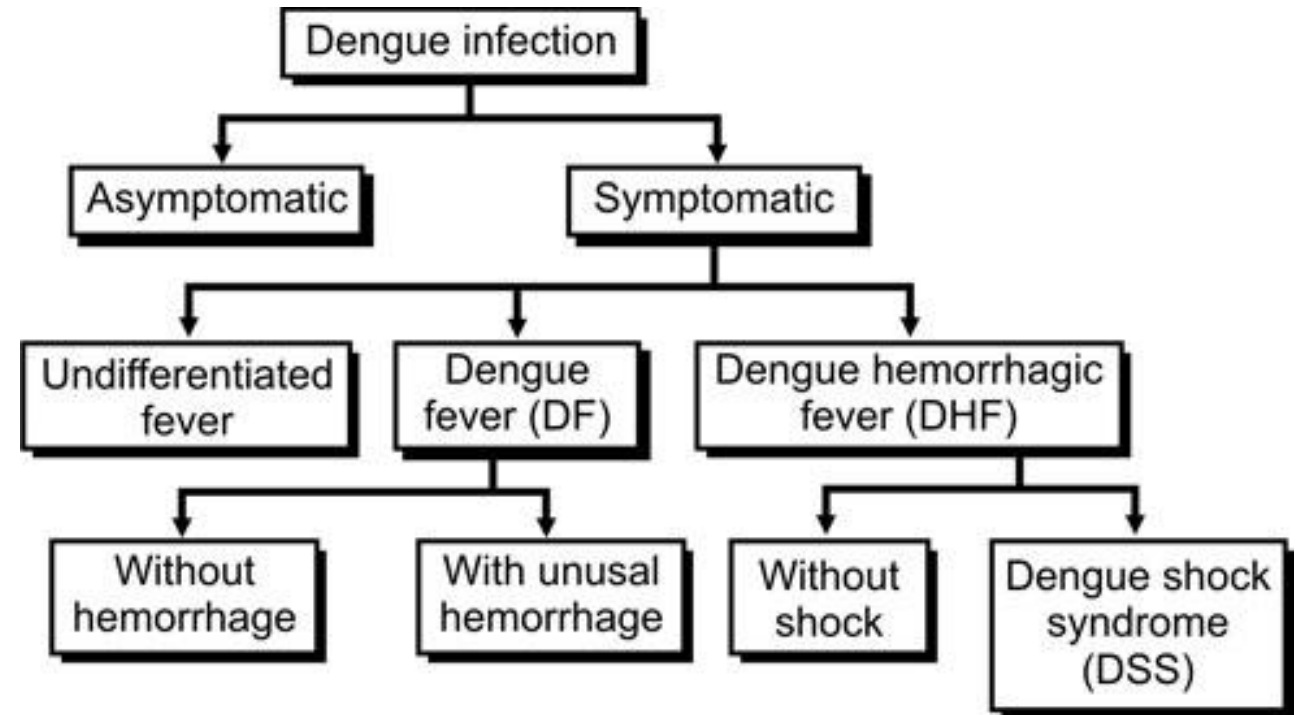


# Development of a live attenuated dengue virus vaccine using reverse genetics



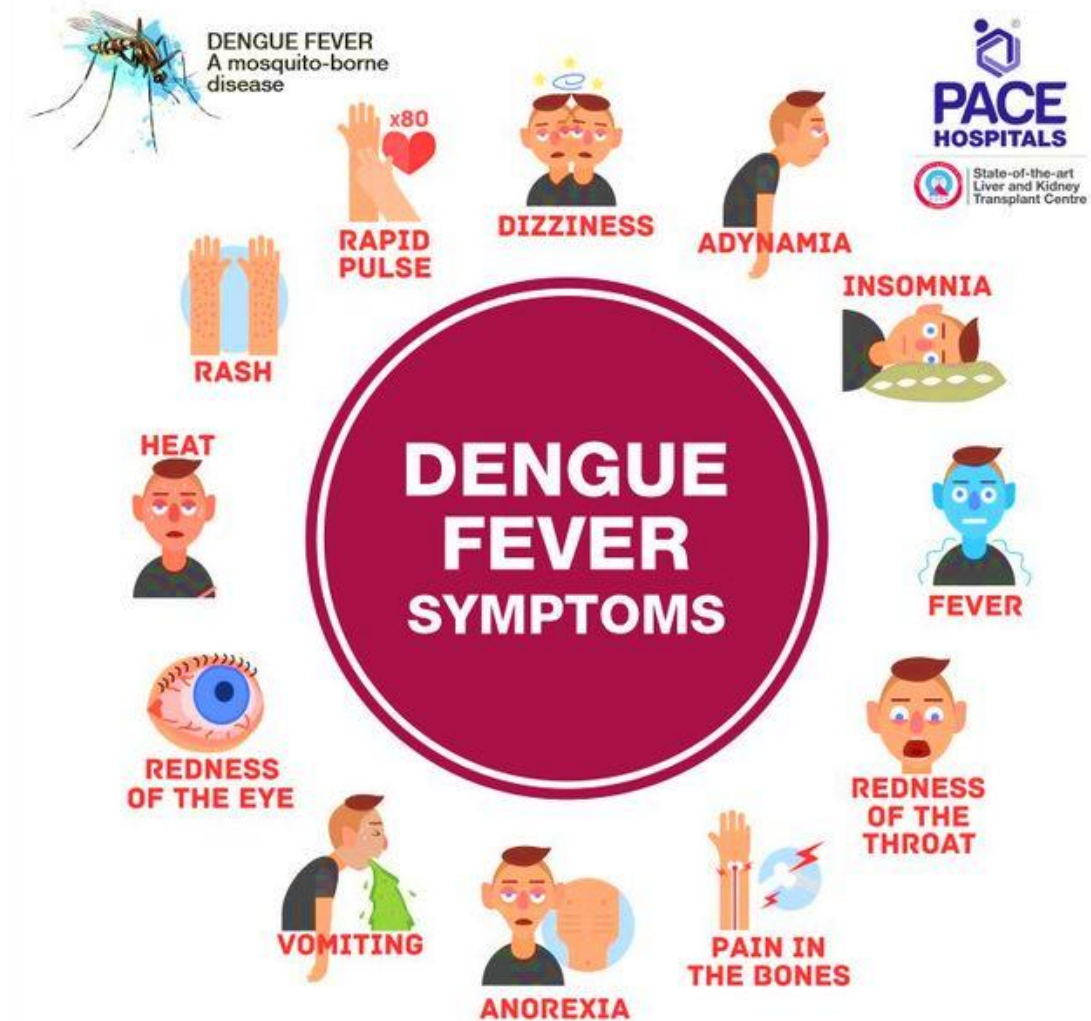
Infection with DEN virus can result in:

- an asymptomatic infection,
- a febrile illness called dengue fever (DF),
- and the very **SEVERE DISEASE CALLED DENGUE HEMORRHAGIC FEVER/DENGUE SHOCK SYNDROME (DHF/DSS)**



# Development of a live attenuated dengue virus vaccine using reverse genetics

**LAV tetravalent DEN virus  
VACCINE CANDIDATE**  
**- using reverse genetics**  
**(2006)**



 Qdenga<sup>®</sup>

*Dengue tetravalent  
vaccine (live, attenuated)*

powder and solvent for solution for injection in pre-filled syringe

**1 dose (0.5 ml)**



0.5 ml

 Qdenga<sup>®</sup>

*Dengue tetravalent  
vaccine (live, attenuated)*

powder and solvent for solution for injection in pre-filled syringe

**1 dose (0.5 ml)**



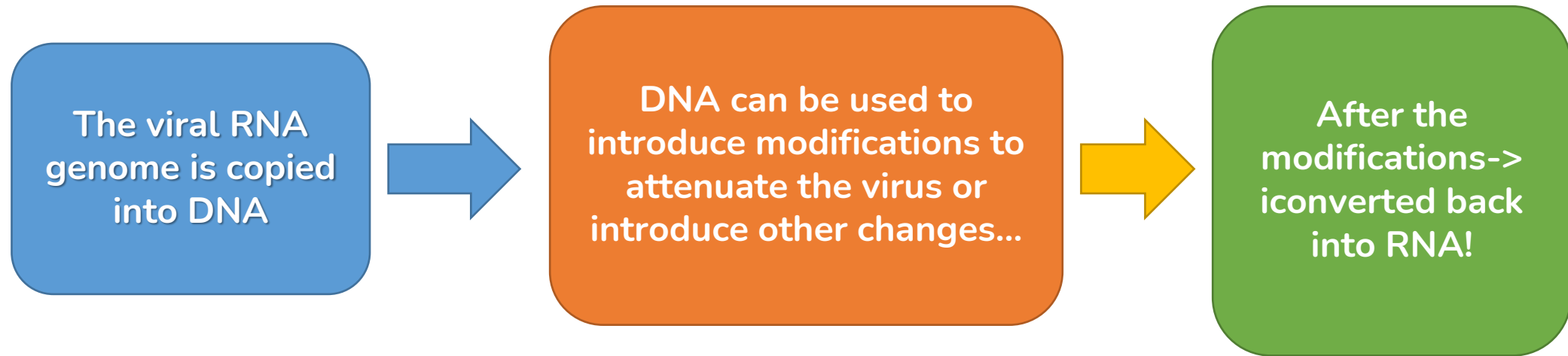
0.5 ml

# LAVs - reverse genetics

## Examples for systems that can be used for precise genetic modification:

- Single-stranded positive-sense RNA viruses
  - Classical swine fever virus (CSFV)
  - Bovine viral diarrhea virus (BVDV)
  - Porcine reproductive and respiratory syndrome virus (PRRSV)
  - Foot-and-mouth disease virus (FMDV)
- Single-stranded negative-sense RNA viruses
  - Newcastle disease virus (NDV)
  - Influenza A virus (IAV)
  - Rift Valley fever virus (RVFV)
  - Double-stranded RNA viruses
- Double-stranded DNA viruses
  - Infectious bursal disease virus (IBDV)
  - Bluetongue virus (BTV)
  - African horse-sickness virus (AHSV)
  - Pseudorabies virus (PRV)
  - Infectious bovine rhinotracheitis virus (IBRV)
  - Modified vaccinia Ankara (MVA)
  - Lumpy skin disease virus (LSDV)
  - African swine fever virus (ASFV)

# For RNA viruses genetic modification is often referred to as "reverse genetics,, ...



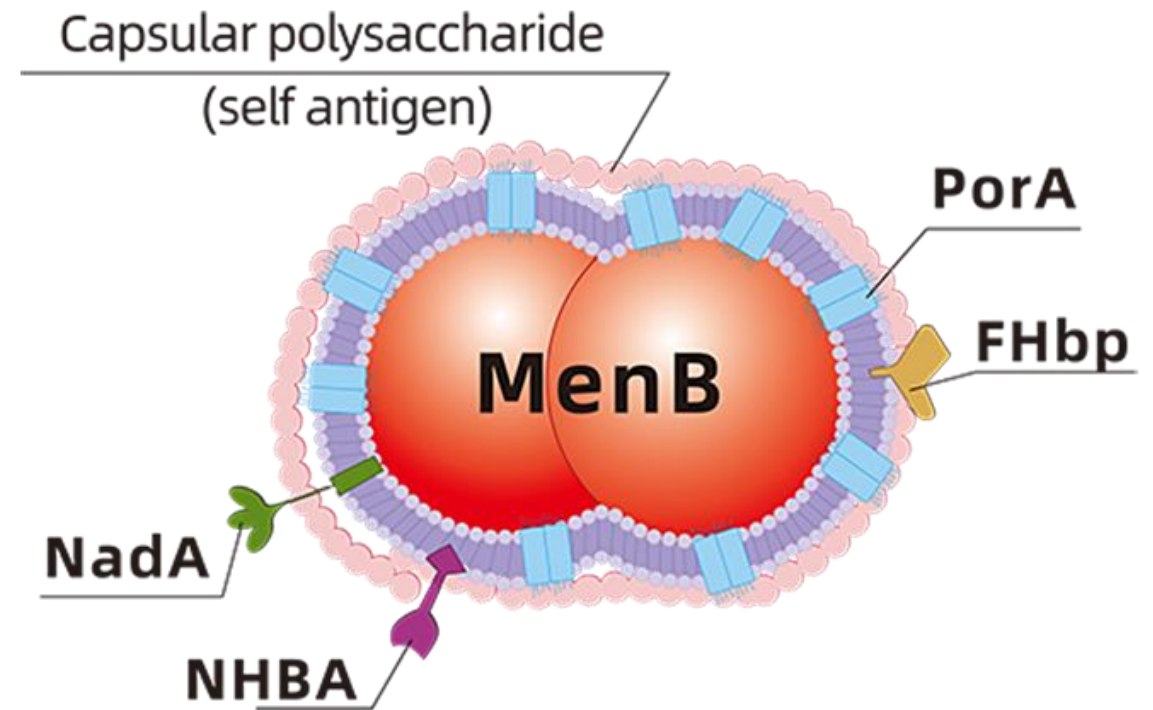
For DNA viruses:

- homologous recombination or CRISPR/Cas-mediated homology-dependent repair (HDR)  
-> for the precise deletion, insertion or replacement of genetic material.

# The Development of a Vaccine Against Meningococcus B Using Reverse Vaccinology

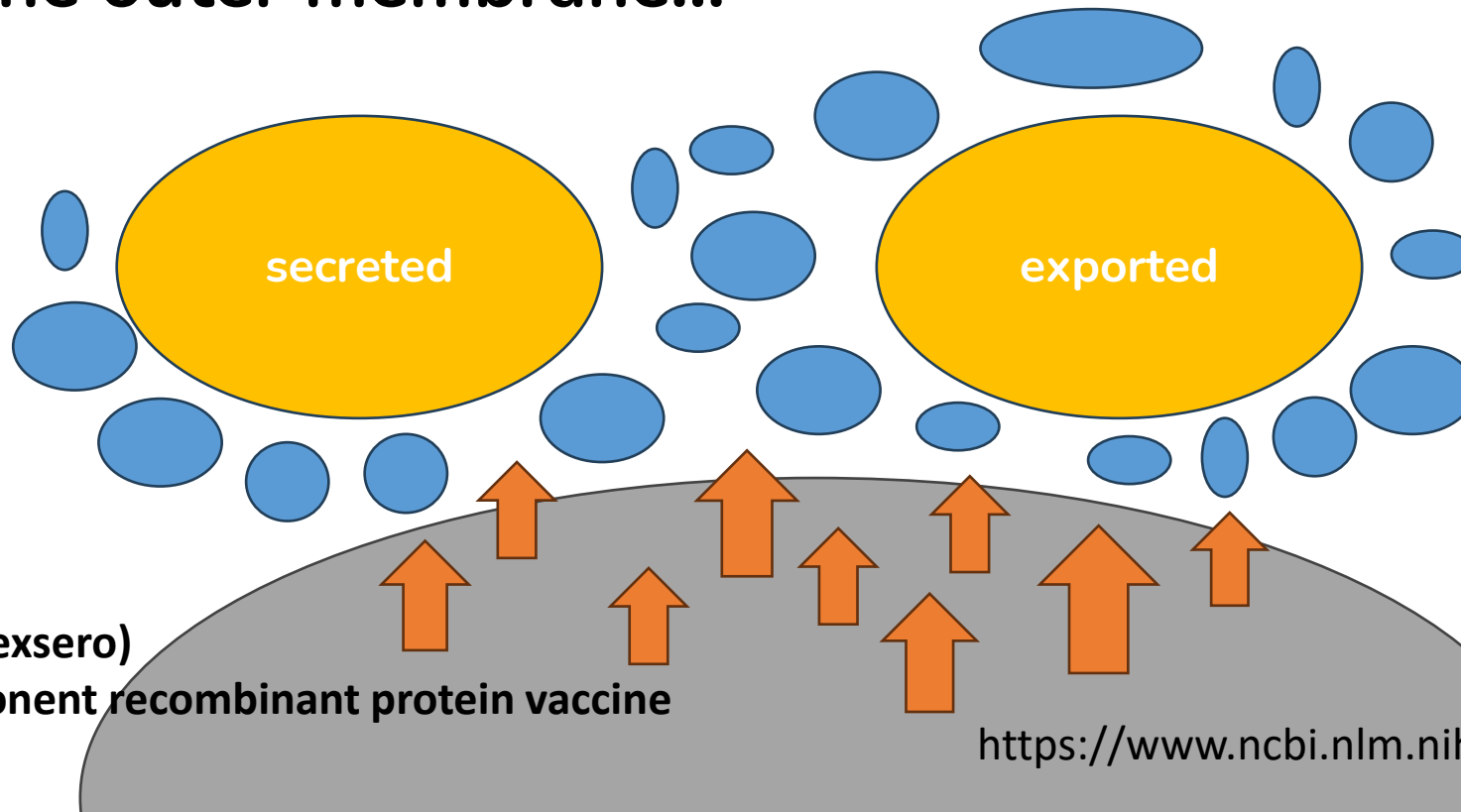
- The discovery of vaccine antigens - whole genome sequencing (WGS) (reverse vaccinology)
- **The complete genome sequence of Neisseria meningitidis serogroup B (MenB) was systematically analyzed**

4CMenB (Bexsero)  
multicomponent recombinant protein vaccine



# The Development of a Vaccine Against Meningococcus B Using Reverse Vaccinology

Identification of proteins predicted to be secreted or exported to the outer membrane...



4CMenB (Bexsero)  
multicomponent recombinant protein vaccine

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6477034/>

# The Development of a Vaccine Against Meningococcus B Using Reverse Vaccinology



This identified **100s of genes** coding for potential **surface-exposed antigens**.



These were amplified, **cloned in expression vectors** and used to **immunize mice**.



**Antisera against 350 recombinant antigens** were obtained and analyzed



... **from which 28 were selected** (SBAs)

**4CMenB (Bexsero)  
multicomponent recombinant protein vaccine**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6477034/>



# The Development of a Vaccine Against Meningococcus B Using Reverse Vaccinology

Testing indicated: no single component is be sufficient

Broad coverage → cross-protective ability is needed!

Multivalent vaccine formulation

To improve immunogenicity - outer membrane vesicle component obtained from the epidemic New Zealand strain (OMVNz) was added

...resulting in 4 component vaccine = 4CMenB

4CMenB (Bexsero)  
multicomponent recombinant protein vaccine



**3 serogroups** cause most meningococcal disease:



**3 vaccines** provide protection:

**MenACWY**

**MenB**

**MenABCWY**

Talk to a healthcare provider about what vaccines are best for you or your child.

[cdc.gov/meningococcal](https://www.cdc.gov/meningococcal)



**4CMenB (Bexsero)**

**multicomponent recombinant protein vaccine**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6477034/>

# 4CMenB

# Meningococcal Type B (4CMenB) Vaccine

Public Health Branch - Factsheet

Immunization is one of the most important accomplishments in public health that has, over the past 50 years, led to the elimination, containment and control of diseases that were once very common in Canada<sup>1</sup>. Vaccines help your immune system to recognize and fight bacteria and viruses that cause disease.

## What is meningococcal disease?

Meningococcal disease is caused by bacteria that can spread from one person to another.

The bacteria spreads by direct contact with respiratory and oral fluid through close face-to-face contact, by kissing or sharing food, drink, musical instruments, water bottles, cigarettes or other things that have been in the mouth of a person with the disease.

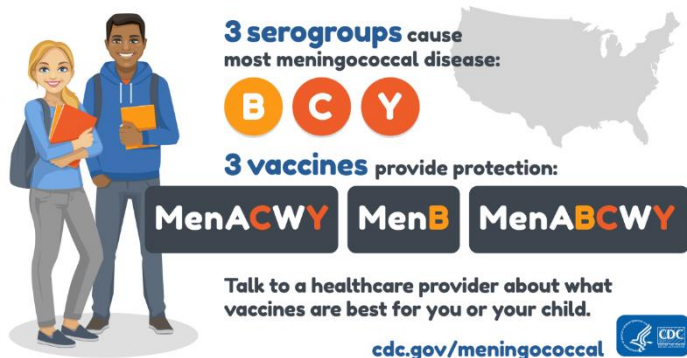
The symptoms of meningococcal disease vary widely, but can include sudden onset of high fever, severe headache, vomiting, stiff neck and rash. Sensitivity to light, sleepiness, confusion, and in severe cases, coma may also occur.

Meningococcal disease can cause serious and sometime life-threatening infections, such as meningitis (infection of the lining of the brain and spinal cord) and sepsis (blood poisoning), even with prompt medical treatment. Those who survive the disease may suffer from permanent brain damage, hearing loss or loss of limbs.

## 4CMenB immunization schedule

Age at series initiation	# of doses	Schedule
2 to 5 months	3	At least 2 months between between first 2 doses. 3 <sup>rd</sup> dose: 6 months after 2 <sup>nd</sup> dose and at age $\geq$ 12 months
6 to 11 months	3	At least 2 months between first 2 doses. 3 <sup>rd</sup> dose: 2 months after 2 <sup>nd</sup> dose and at age $\geq$ 12 months
12 to 23 months	2	At least two months between doses
2 to 25 years	2	At least one month between doses

Why should my child get the meningococcal type B vaccine?



4CMenB (Bexsero)  
multicomponent  
recombinant protein vaccine

## II. INACTIVATED VACCINES

Hepatitis A  
Flu  
Polio  
Rabies

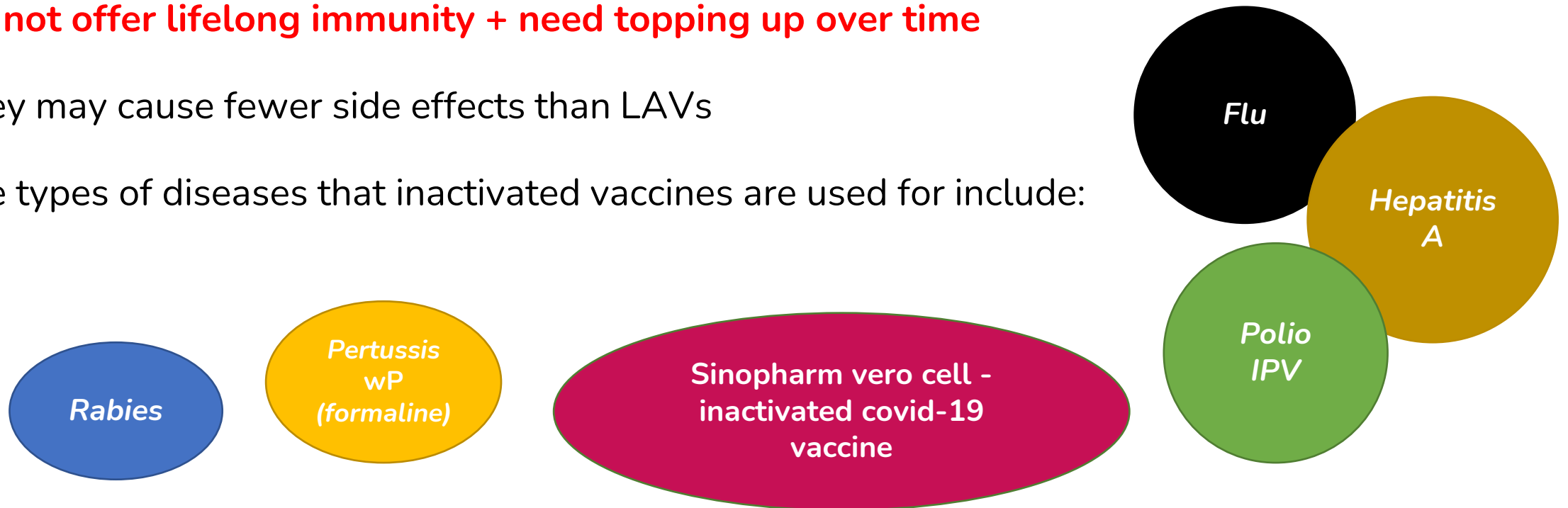
virus  
inactivated  
strain  
killed vaccine

heat

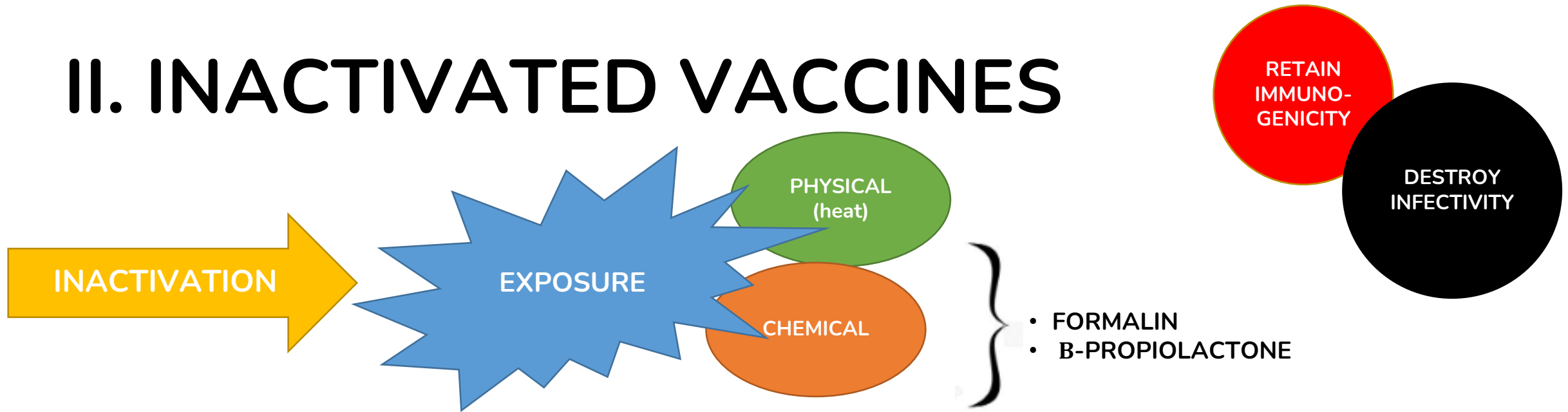
bacteria  
chemicals

# II. INACTIVATED VACCINES

- Dead version of the virus or bacteria is then injected into the body.
- Inactivated vaccines are **the earliest type of vaccine** to be produced
- **They do not trigger an immune response that is as strong as that triggered by LAVs**
- **Do not offer lifelong immunity + need topping up over time**
- They may cause fewer side effects than LAVs
- The types of diseases that inactivated vaccines are used for include:



# II. INACTIVATED VACCINES



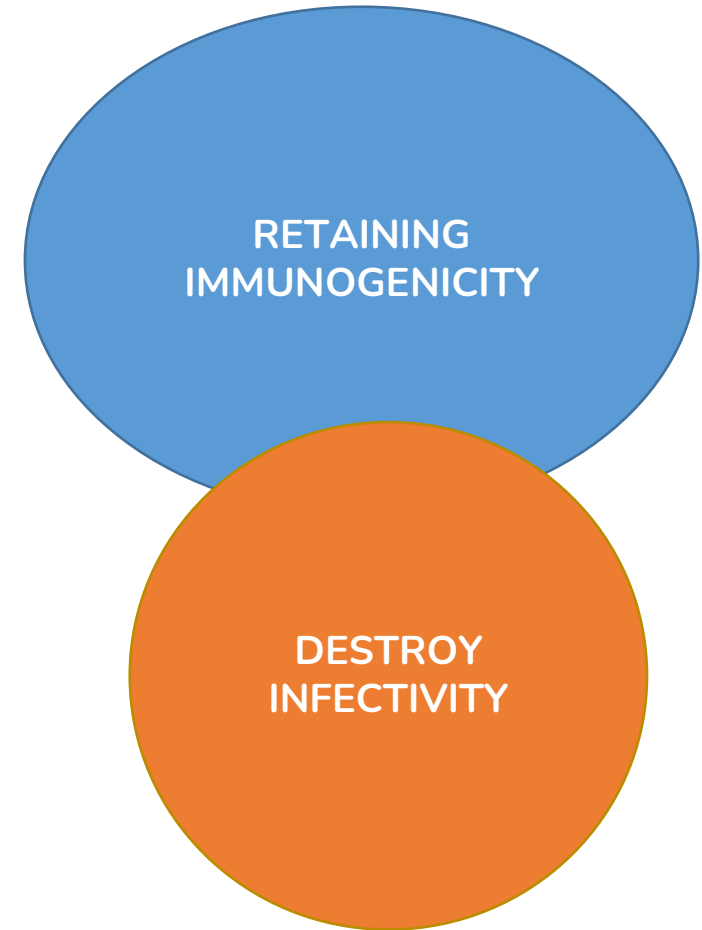
- Initially, virus for this purpose was often obtained from **infected animal sources (mouse brain)**
- Infected **cell cultures** provide cleaner starting material.
- **The need to use large amounts of antigen to elicit an adequate antibody response is a major disadvantage!**

# II. INACTIVATED VACCINES

Primary vaccination course: 2-3 injections + “booster” doses may be required at intervals to maintain protective immunity!

The chemical or physical treatment = INACTIVATION

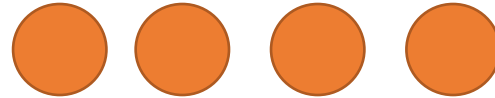
→ may also compromise / modify immunogenicity!



# II. INACTIVATED VACCINES

Inactivated vaccines: up to 4 doses

LAVs: 1-2 doses



**In order to achieve  
the optimal level of  
protection**

*Examples:*

MMR vaccine: only requires **2 doses → lifetime protection**

Inactivated rabies vaccine: **every 6 months – 2 (two) years** for those at increased risk of exposure

Live oral typhoid vaccine: requires repeated doses **every 5 years** for people in endemic regions

Inactivated typhoid vaccine: delivered by injection requires a repeat dose **every 2 years.**

# II. INACTIVATED VACCINES

## STORAGE AND SHIPPING

...the pathogen in the vaccine  
is dead already....

→ easily stored and shipped even to

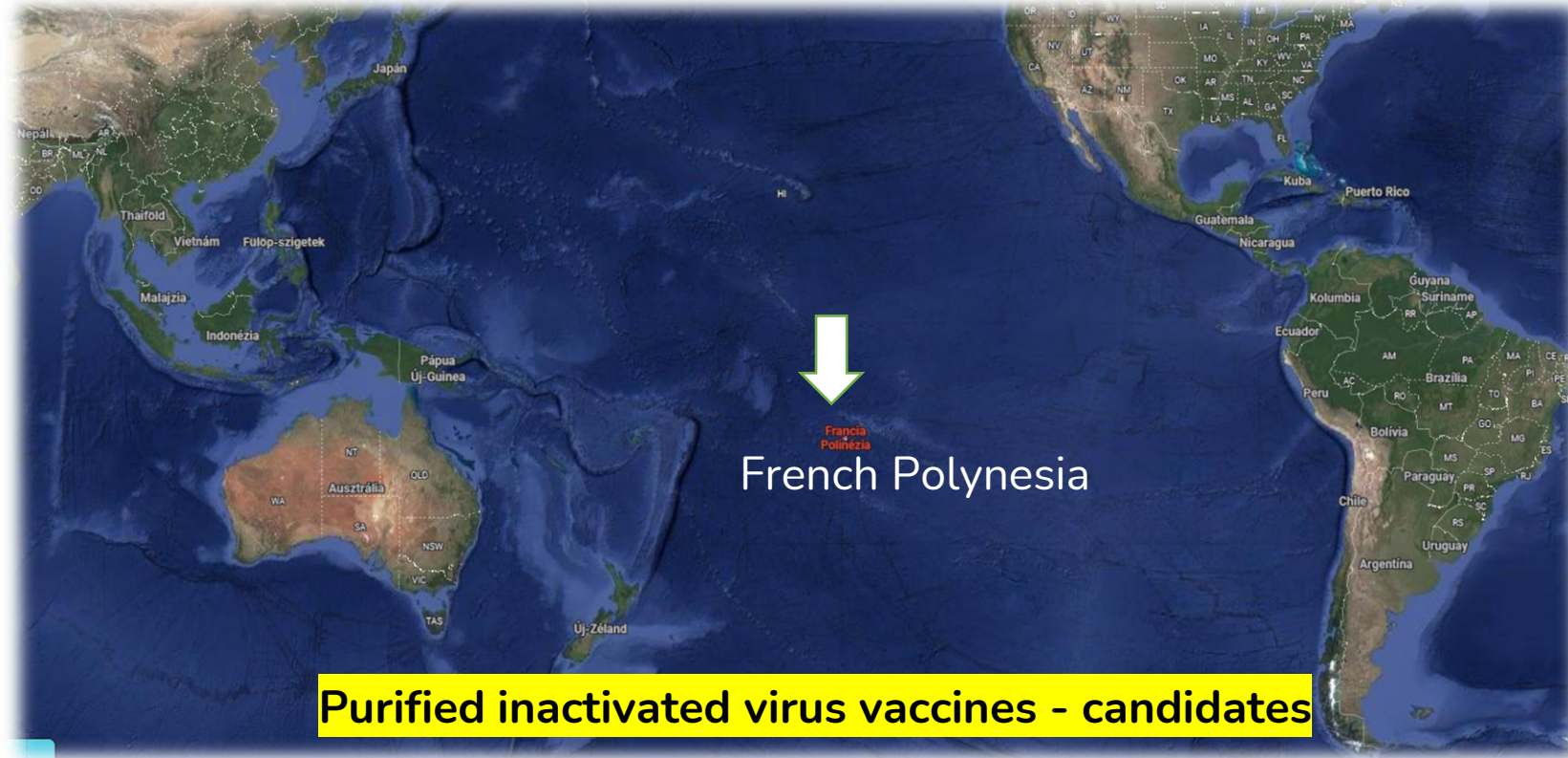
**those parts of the world where resources are limited!**

LAVs, on the other hand, typically require special shipping and storage requirements = limitation in resource-poor areas!



# Zika virus (ZIKV)

- In 2013, Zika virus (ZIKV) emerged in French Polynesia
- **Pacific region 2013 - 2017**
- Vectors: *Aedes* mosquitoes - *Aedes aegypti*, *Aedes polynesiensis*

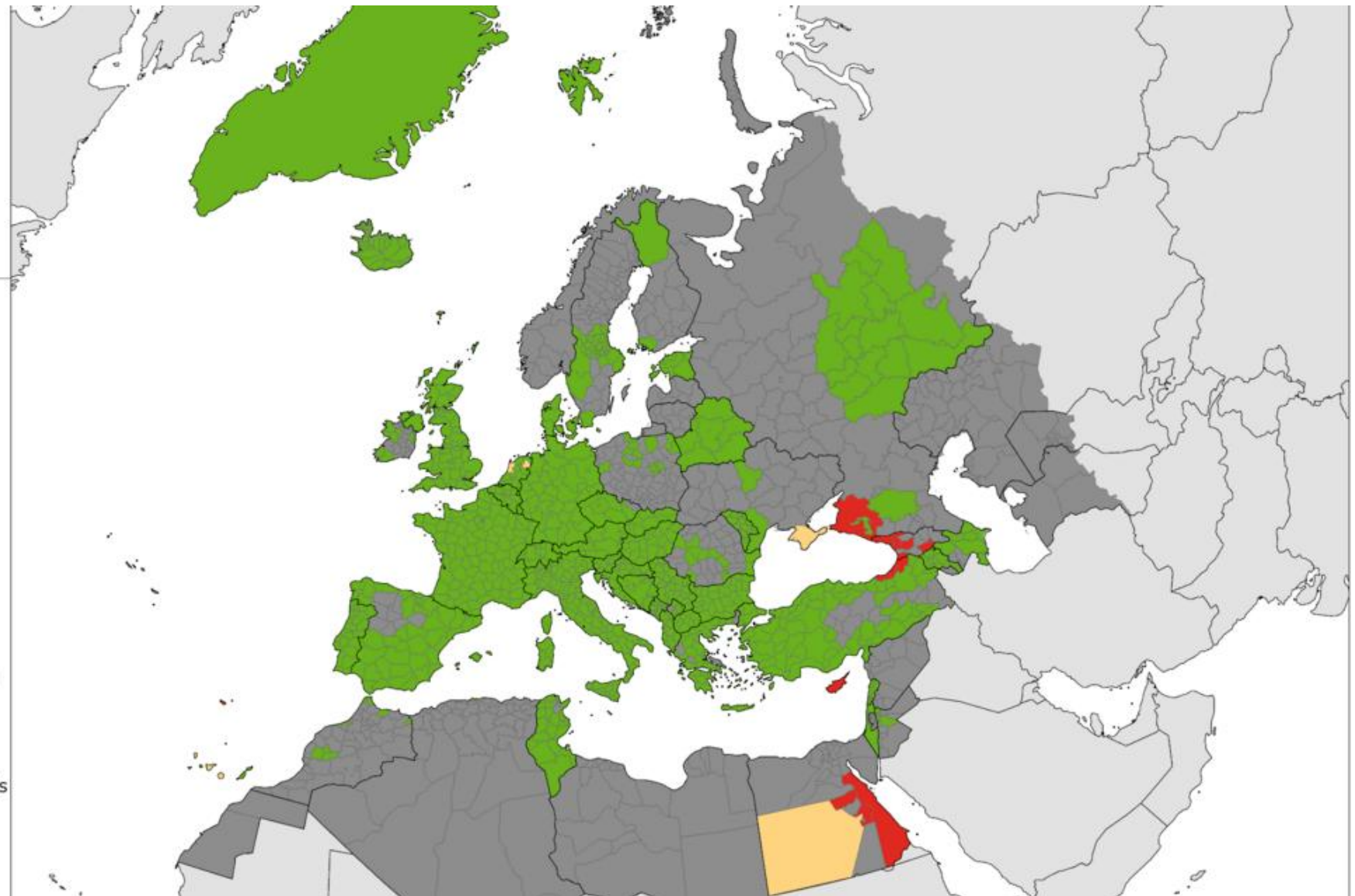


### Legenda

- Established
- Introduced
- Absent
- No data
- Unknown

### Countries/Regions not viewable in the main map extent\*

- Malta
- Monaco
- San Marino
- Gibraltar
- Liechtenstein
- Azores (PT)
- Canary Islands (ES)
- Madeira (PT)

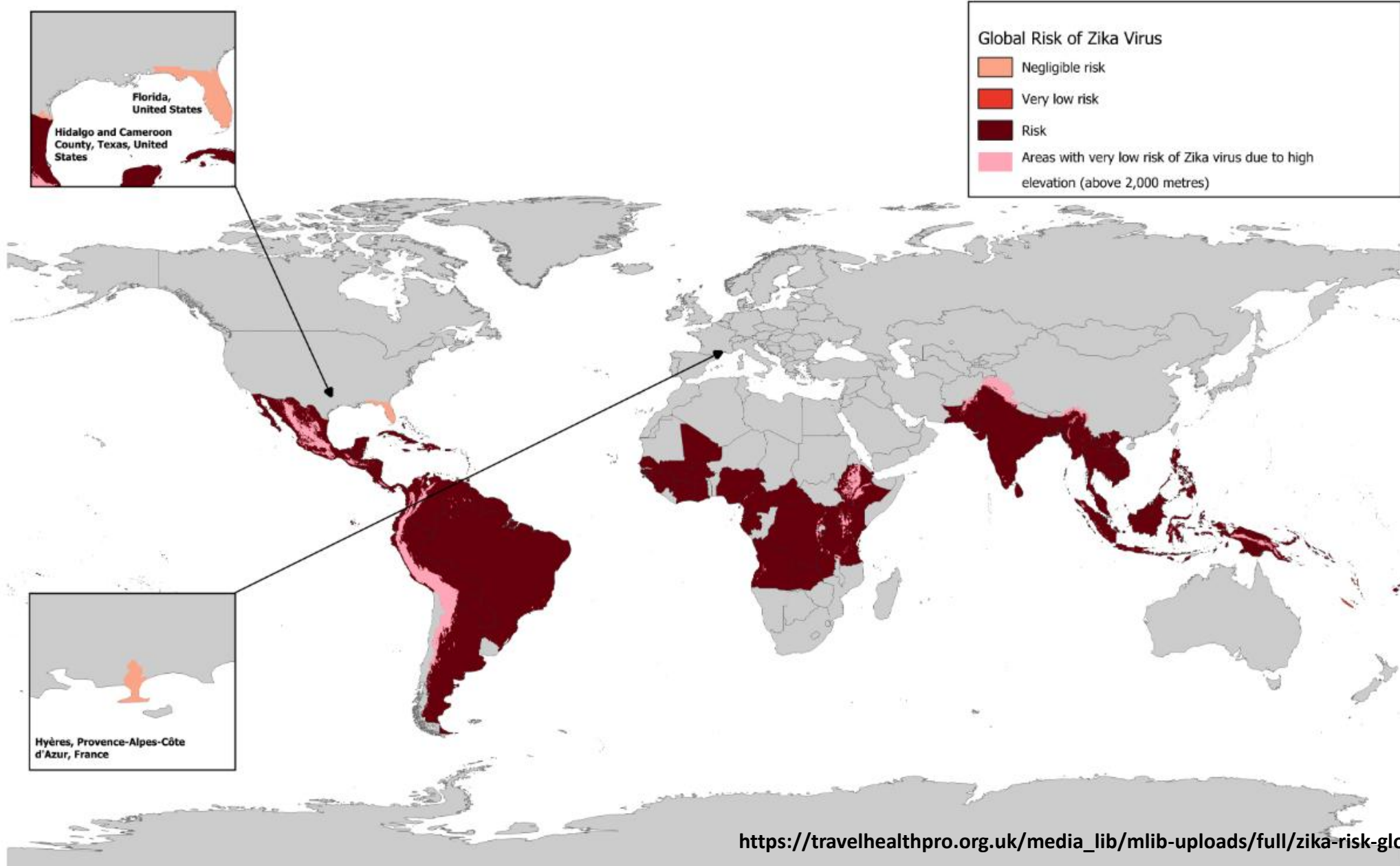


## *Aedes aegypti* - known distribution: May 2024

<https://www.ecdc.europa.eu/en/publications-data/aedes-aegypti-current-known-distribution-may-2024>

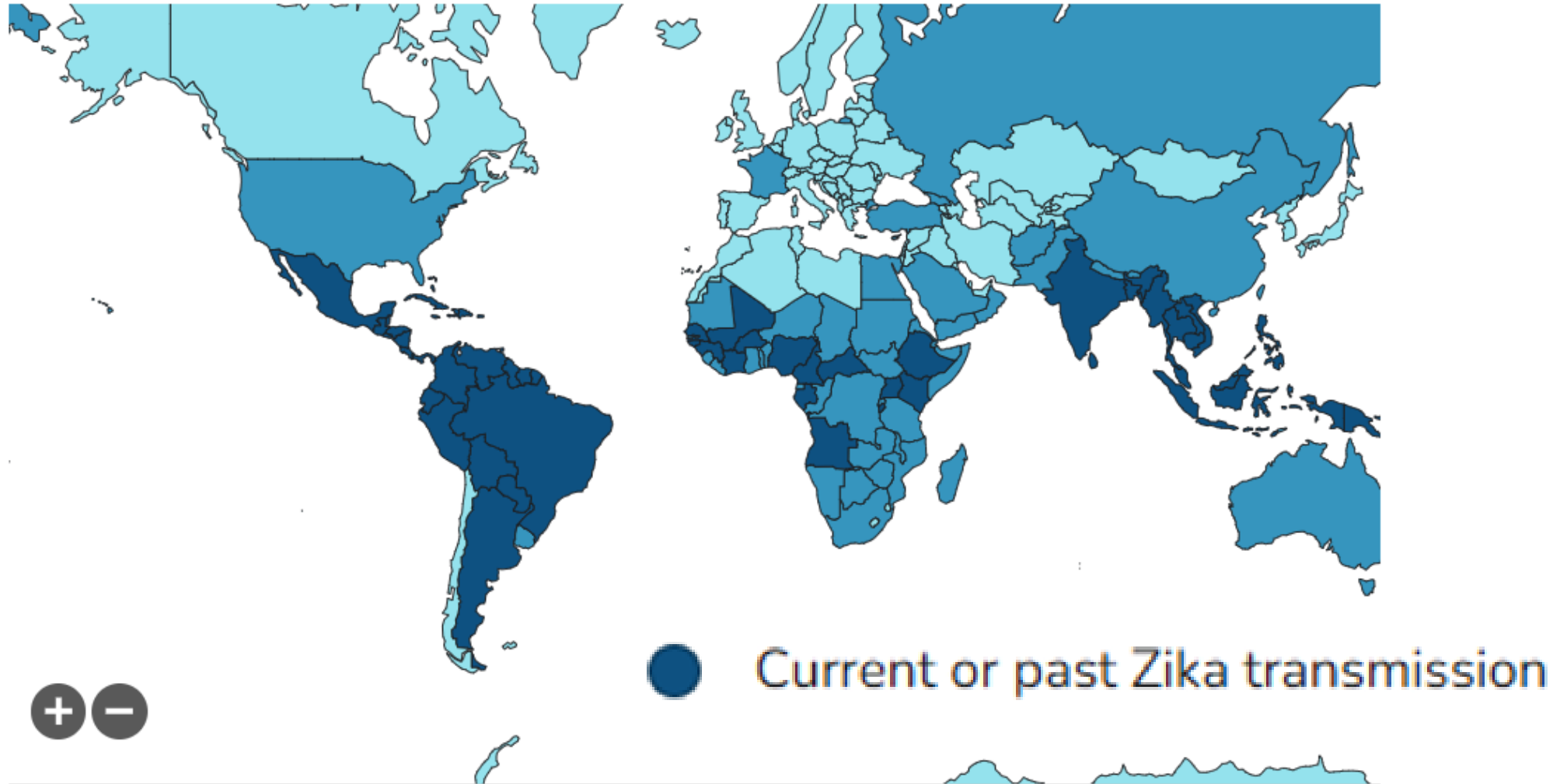


# Global Risk of Zika Virus



# Where has Zika been found?

Zika geographic risk classifications (as of June 20, 2025)<sup>1-4</sup>



## Legend

● Current or past Zika transmission

● Known to have mosquito that transmits Zika, but no reported Zika cases

● Not known to have mosquito that transmits Zika

## Zika epidemics 2014-2017



- Zika virus infections spread primarily in the **Americas** and the **Pacific** region.
- On February 1, 2016, the WHO declared a **Public Health Emergency of International Concern (PHEIC)** due to **clusters of microcephaly and neurological disorders** detected in areas affected by the Zika virus.
- There is now broad consensus regarding the **link between Zika infection and congenital abnormalities**, as well as the development of **Guillain-Barré syndrome (GBS)**.

### Affected areas

The Americas,  
Caribbean, South  
East Asia

### Risk group

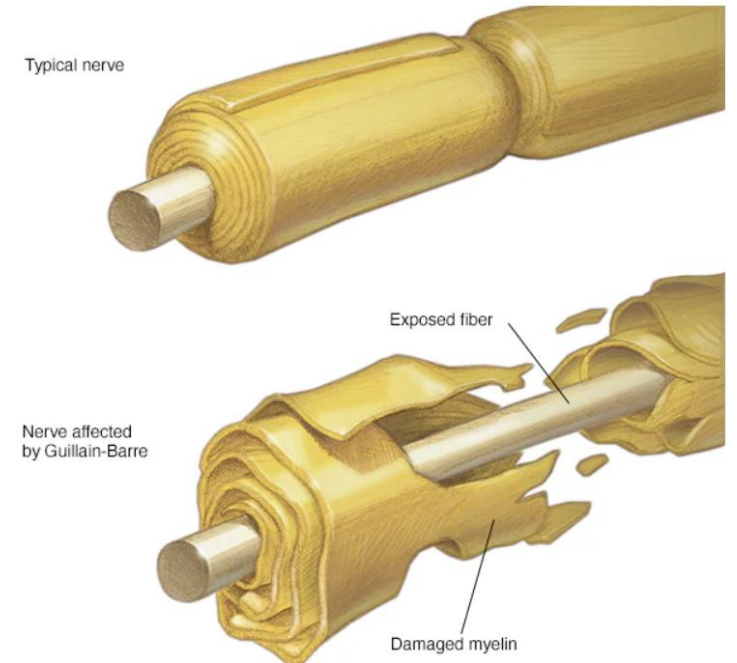
Pregnant woman  
travelling to affected  
areas

### Health risk

Central nervous  
system (CNS)  
malformations and  
microcephaly during  
pregnancy

# Guillain-Barré syndrome – autoimmune condition – post infectious...

- Weakness, numbness or paralysis
- Guillain-Barre syndrome is rare, and the exact cause is not known.
- **But 2/3s of people have symptoms of an infection in the 6 weeks before Guillain-Barre symptoms begin...**
- Infections can include a respiratory or a GI tract infection, including COVID-19...
- **Can be caused by the Zika virus!!!**



„...on February 1, 2016, the WHO declared a Public Health Emergency of International Concern (PHEIC) due to clusters of microcephaly and neurological disorders detected in areas affected by the Zika virus...”

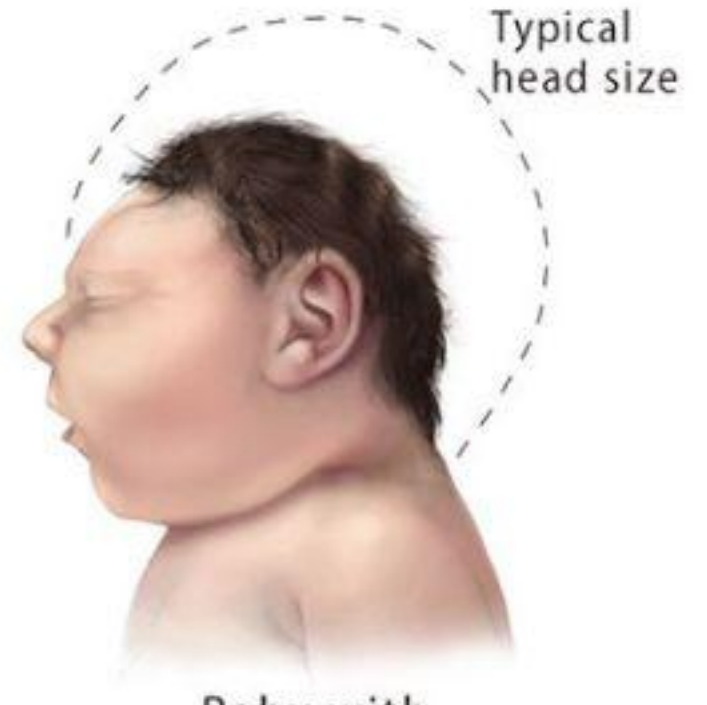
## Microcephaly



Baby with Typical Head Size



Baby with Microcephaly



Baby with Severe Microcephaly

# Zika virus (ZIKV)

**TO DATE, NO ZIKA VACCINE HAS BEEN APPROVED FOR USE!**

**Numerous candidates:**

- ✓ **Purified inactivated virus vaccines** (e.g. a candidate developed by Walter Reed Army Institute – “ZPIV”)
- ✓ **DNA vaccines** (such as a NIAID vaccine that showed immune responses in early trials)
- ✓ **mRNA vaccines** (Moderna tested an mRNA Zika vaccine in a Phase 1 trial), and **viral-vectored vaccines** (for example, a measles virus-vectored Zika vaccine)

Several of these reached Phase 1 or Phase 2 clinical trials during 2016–2018

**However, demonstrating efficacy became challenging because Zika transmission declined sharply after 2016, making large Phase 3 trials infeasible....**

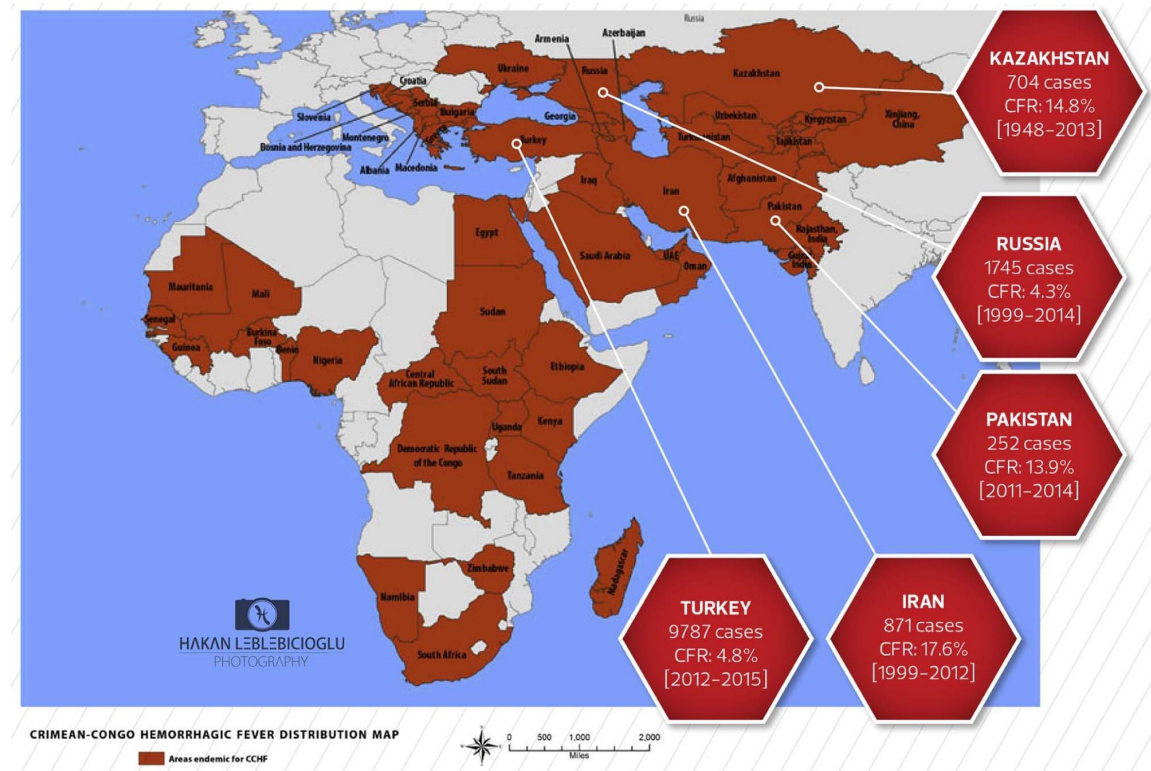
[pubmed.ncbi.nlm.nih.gov](https://pubmed.ncbi.nlm.nih.gov).

<https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006637>

...still inactivated vaccines...

## Crimean-Congo hemorrhagic fever (CCHF)

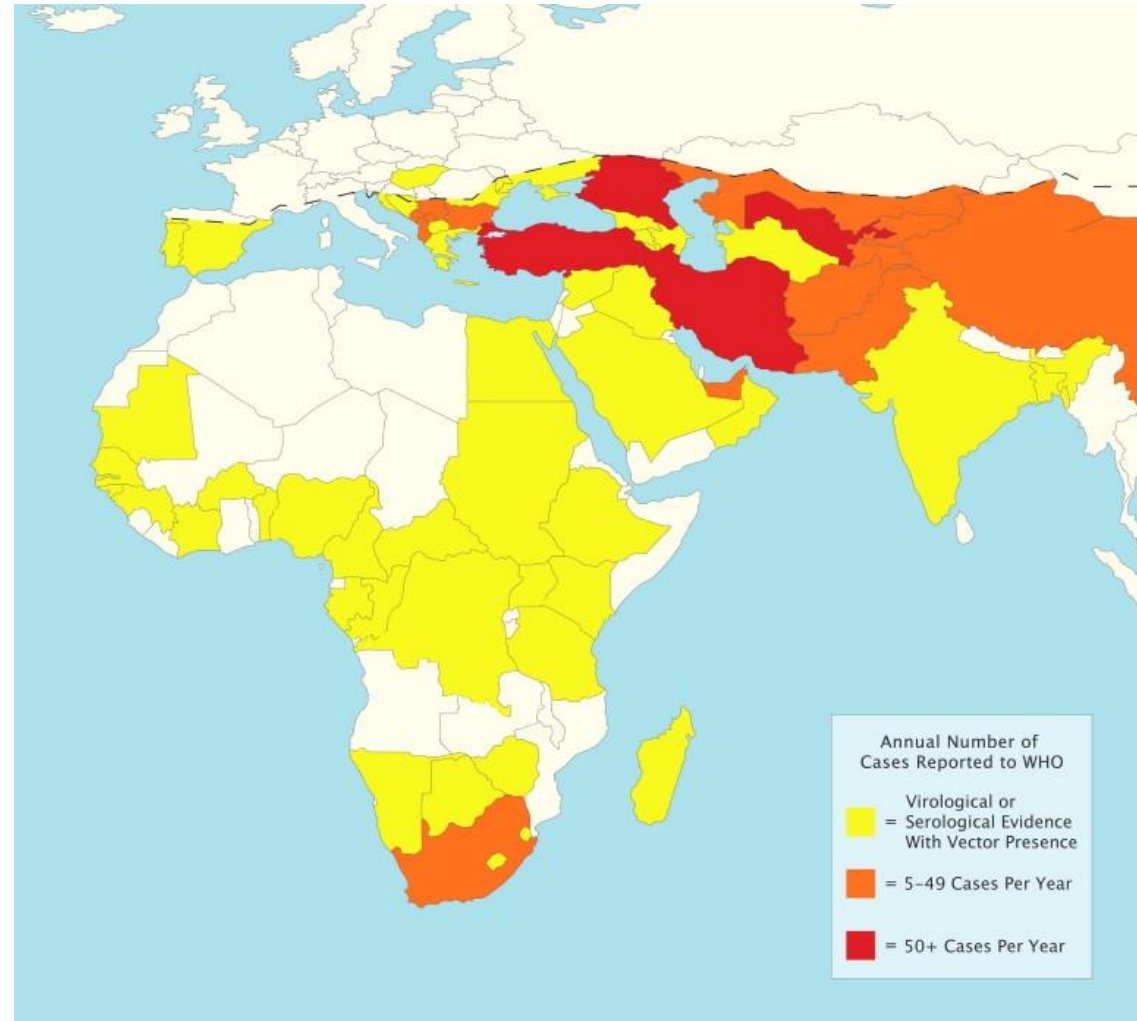
LAV: only to high-risk populations!





# Crimean–Congo Hemorrhagic Fever (CCHF)

- Tick-Borne - **Hyalomma ticks**
- Viral Hemorrhagic Fever
- Caused by: CCHFV (Nairovirus, Bunyavirales)
- **ENDEMIC IN AFRICA, EASTERN EUROPE, THE BALKANS, MIDDLE EAST, CENTRAL ASIA**
- Contact with infected animal blood/tissues
- Nosocomial human-to-human spread
- **CASE FATALITY RATE: 10–40%**



# Crimean–Congo Hemorrhagic Fever (CCHF)

Headache, dizziness, sharp mood swings and confusion, sleepiness, depression, and lassitude  
sore eyes and photophobia (sensitivity to light)

Fever, and sore throat

Neck pain and stiffness, and backache

Myalgia (muscle ache)

Pulmonary failure

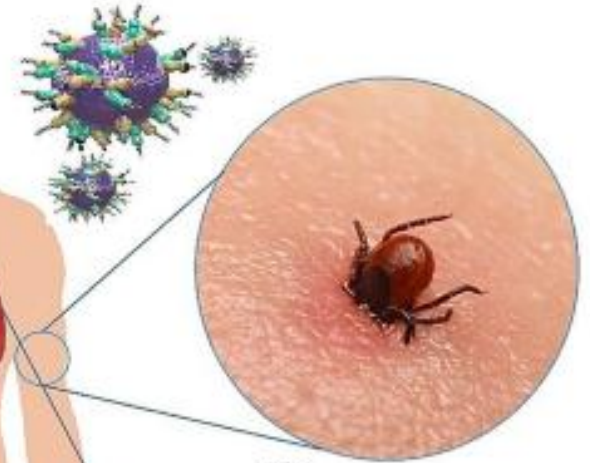
Tachycardia (fast heart rate)

Detectable hepatomegaly (liver enlargement), and sudden liver failure

Severely ill patients may experience rapid kidney deterioration,

Nausea, vomiting, diarrhoea, abdominal pain

Lymphadenopathy (enlarged lymph nodes)



**Hyalomma tick bite**

Petechial rash (a rash caused by bleeding into the skin) on internal mucosal surfaces, such as in the mouth and throat, and on the skin.

The petechiae may give way to larger rashes called ecchymoses, and other haemorrhagic phenomena.



# CCHF- Clinical Features

Sudden fever,  
myalgia, dizziness

GI symptoms →  
vomiting, diarrhea

Rapid progression  
to hemorrhage

Liver failure, shock,  
DIC

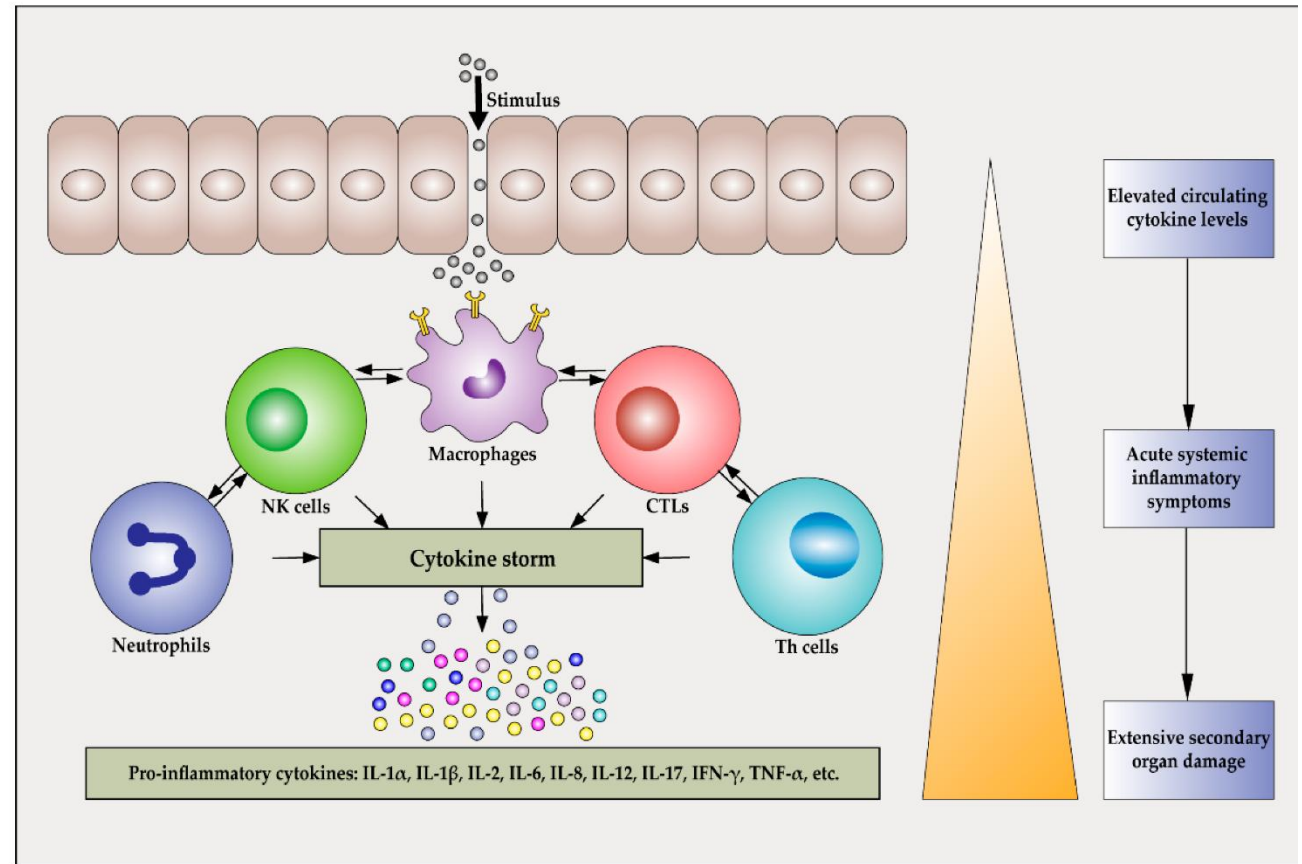
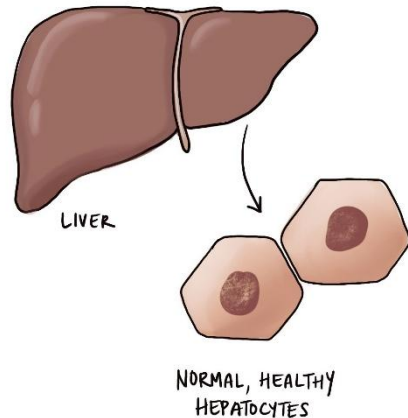
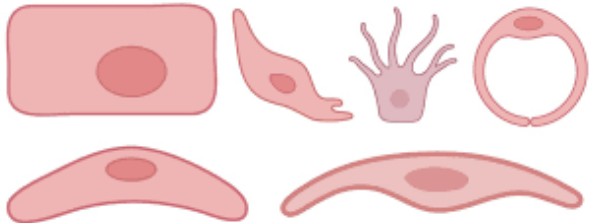
High mortality  
without intensive  
supportive care



# Pathogenesis

- Virus infects **endothelial cells and hepatocytes**
- Leads to: **CYTOKINE STORM**
- Increased vascular permeability
- **COAGULOPATHY AND HEMORRHAGE**
- **Strong correlation: viral load ~ disease severity!**

Endothelial Cells



Inactivated CCHF Vaccine  
(Bulgaria)  
**NOT WHO-APPROVED!**

## Current Treatment / no approved vaccine available

- NO APPROVED ANTIVIRAL FOR CCHF
- RIBAVIRIN: USED IN SOME COUNTRIES - EFFICACY IS CONTROVERSIAL
- SUPPORTIVE THERAPY IS CRITICAL (FLUIDS, BLOOD PRODUCTS)

### **Inactivated CCHF Vaccine (Bulgaria)**

- Used locally since the 1970s
- Formalin-inactivated mouse brain-derived vaccine
- **NOT WHO-APPROVED; LIMITED DATA ON EFFICACY**
- Used for high-risk groups (farm workers, military)

**This is the only vaccine in use, but not globally licensed!**

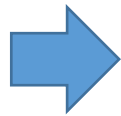
# WHO & CEPI Initiatives – vaccine development

- CCHF is on the WHO Priority Pathogens list
- **CEPI invested in: vector-based vaccines (ChAdOx1)**
- mRNA platforms
- Standardized animal models
- **Goal: bring at least one vaccine to Phase II/III in the coming years!**

# III. SUBUNIT VACCINES

Subunit vaccines are made from a piece of a pathogen, not the whole organism...

SUITABLE FOR:  
PEOPLE WHO  
SHOULD NOT  
RECEIVE "LIVE"  
VACCINES

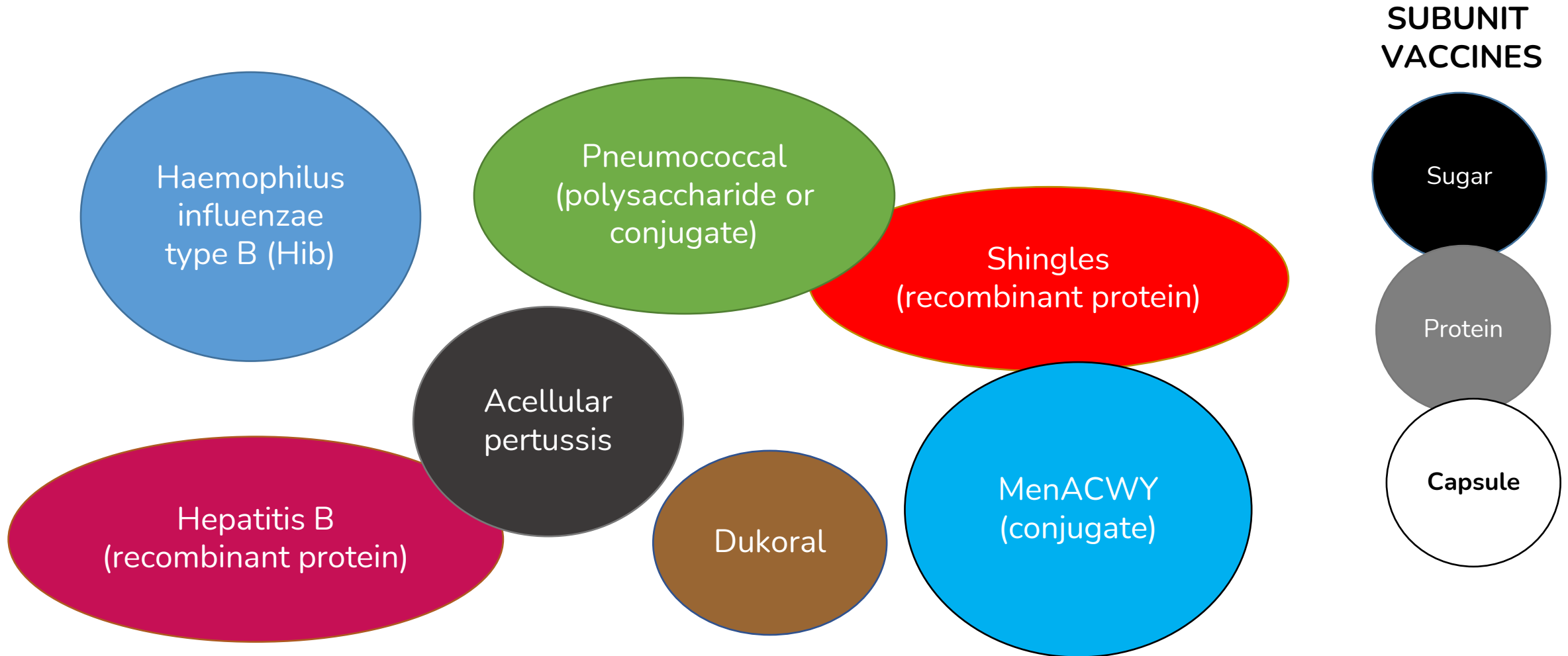


conjugate  
polysaccharide

protein-based



# III. SUBUNIT VACCINES



# III. SUBUNIT VACCINES

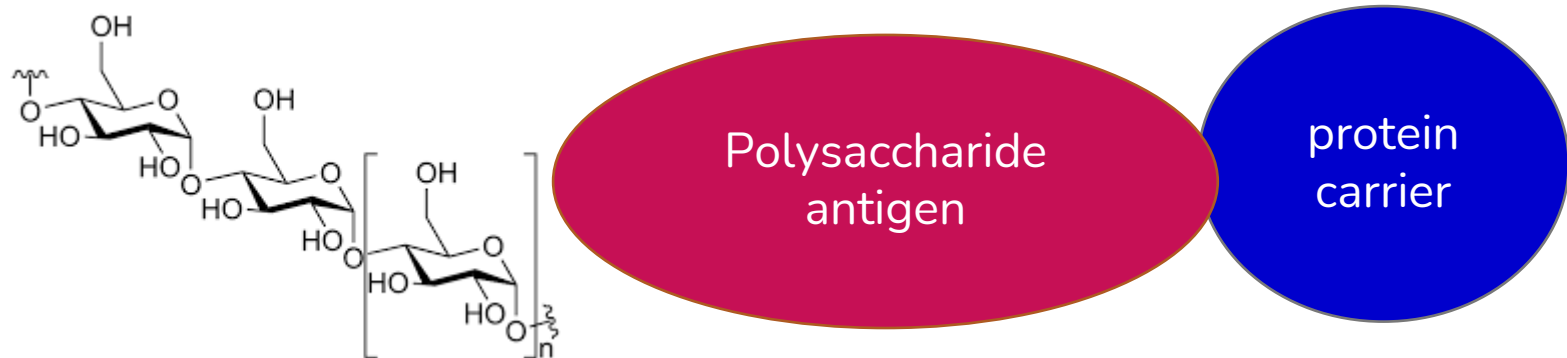
## Conjugate vaccines



The idea of a conjugate vaccine first appeared in experiments involving rabbits in 1927

→ when the immune response to the **Streptococcus pneumoniae type 3 polysaccharide** antigen was **INCREASED...**

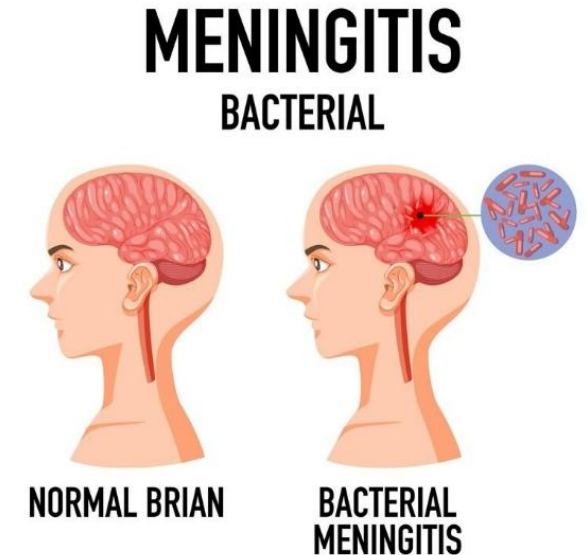
→ by combining the **POLYSACCHARIDE ANTIGEN + PROTEIN CARRIER.**



### III. SUBUNIT VACCINES

## Conjugate vaccines- Haemophilus Influenzae Type b (Hib)

- The first conjugate vaccine - 1987
- Protects against **MENINGITIS**
- Hib can cause severe infections of both the lining of the brain and spinal cord (meningitis) and the bloodstream



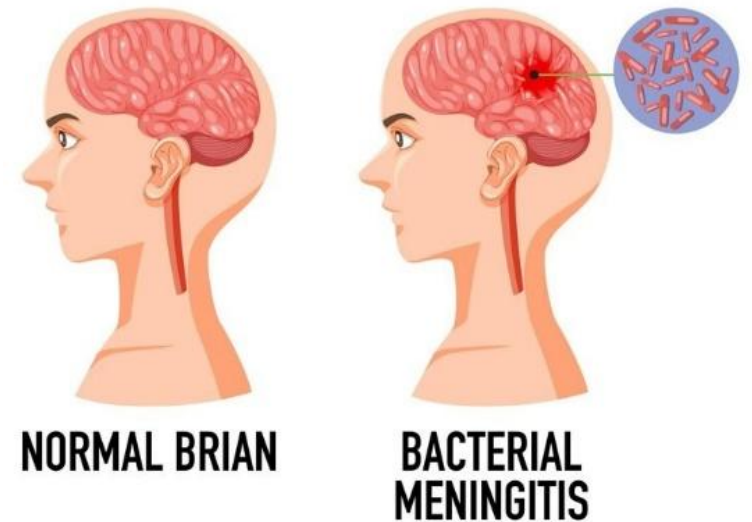
# III. SUBUNIT VACCINES

## Conjugate vaccines- Haemophilus Influenzae Type b (Hib)

**CDC recommends routine Hib vaccination for all children younger than 2 years old!**



### MENINGITIS BACTERIAL



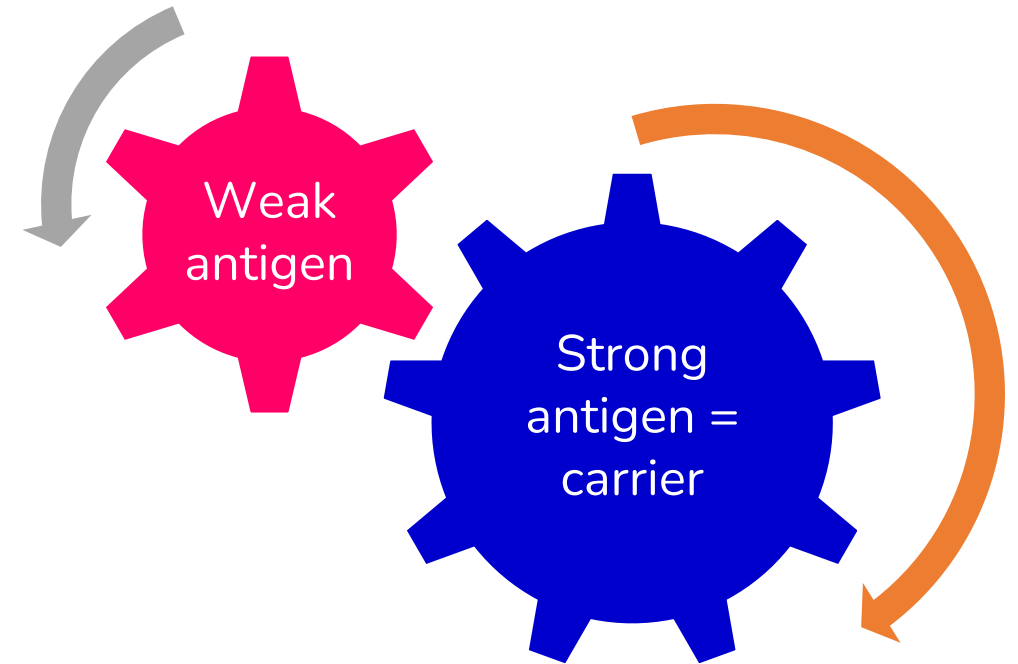
# III. SUBUNIT VACCINES

## Conjugate vaccines

Conjugate vaccines use two different components:

- Outer antigen coat of the bacteria or virus
- ... **not strong enough** to cause illness or generate an immune response in the body ...
- It is linked to a stronger **carrier protein** using chemicals

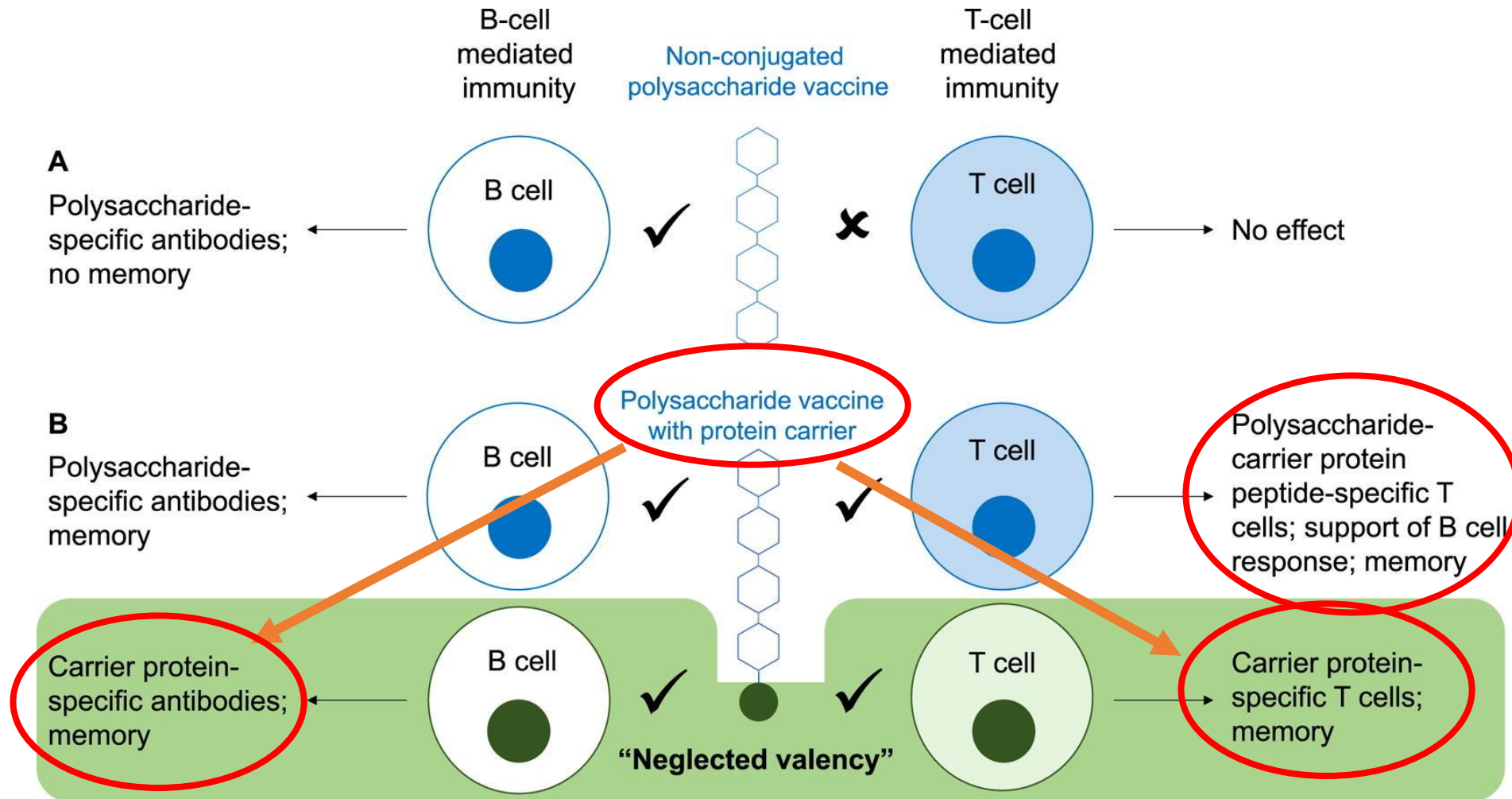
=> **COMBINATION OF WEAK ANTIGEN COAT +  
STRONGER CARRIER PROTEINS = SUFFICIENT IR**



(e.g. weak PS + strong protein)

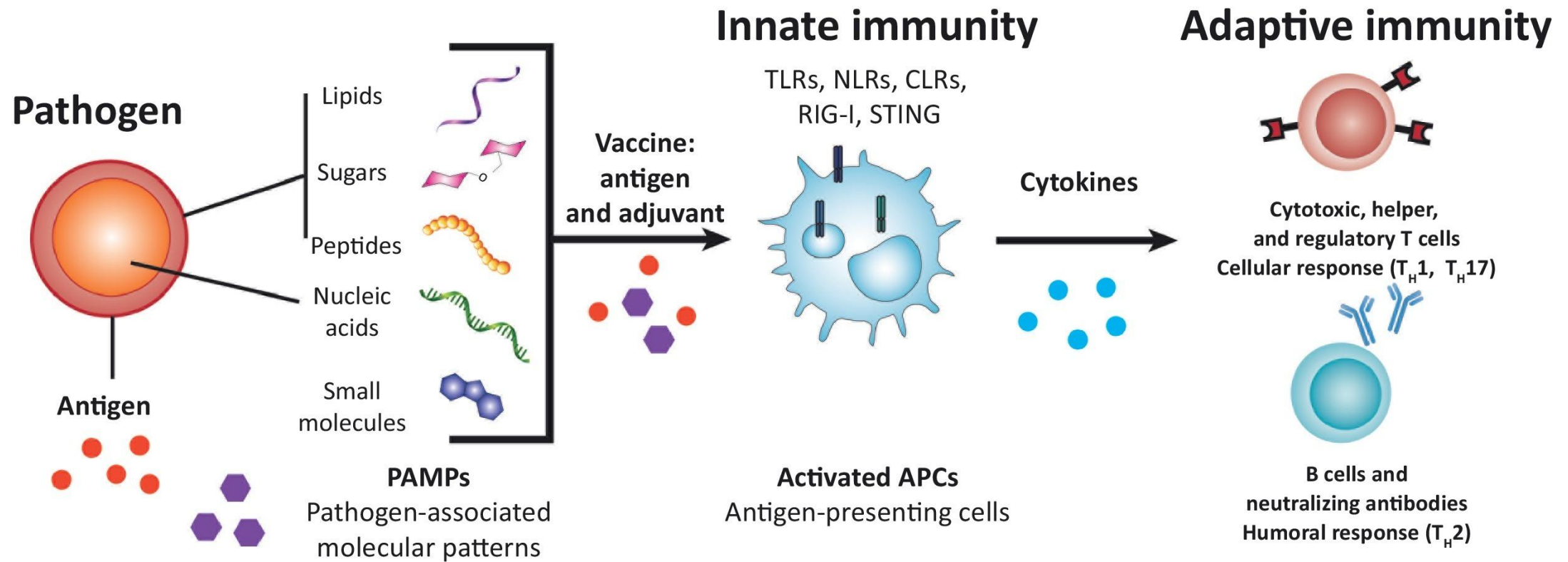
# III. SUBUNIT VACCINES

## Conjugate vaccines



# III. SUBUNIT VACCINES

## Conjugate vaccines



# III. SUBUNIT VACCINES

Influenza vaccines by method of production:

- Whole virion - 3 fluart/fluart
- Split - fluarix tetra/gsk, vaxigrip tetra/sanofi pasteur
- **Subunit - agrippal/seq virus**
- LAVs- Tetra/Astrazeneca

# III. SUBUNIT VACCINES

**Can pregnant women be vaccinated against flu? – Yes!**

... they can and should be vaccinated, especially those who are expected to give birth during the season (January-March in general) (Northern hemisphere)

Optimally in the second to third trimester and with a **split** or **subunit** vaccine.

**It is also essential to vaccinate family members!**

# Vaccine adjuvants

- Intrinsic immunomodulatory properties
- when administered in conjunction with an antigen,
- ...effectively potentiate the host antigen-specific immune responses!
- The most widely used adjuvants in vaccines today are aluminum salts (“alum”), which have been used in injectable vaccines since the turn of the twentieth century (Glenny, 1930).

Adjuvant Name	Composition	Vaccine Type	Main Stimulated Immune Responses
AS01	MPLA + QS-21 in liposomes	<i>Mosquirix</i> : Malaria, <i>Shingrix</i> : Herpes zoster	Ab response, CD8 <sup>+</sup> T-cell response, Th1 type immunity
AS02	MPLA + QS-21 in oil-in-water emulsions	HIV, tuberculosis, HBV	Ab response, Th1 type immunity
AS03	Squalene + $\alpha$ -tocopherol + polysorbate 80	<i>Pandemrix</i> , <i>Arepanrix</i> : Influenza H1N1, <i>Prepandrix</i> : Influenza pre-H5N1	Ab response, Th1/Th2 response
AS04	MPLA + aluminum hydroxide	<i>Fendrix</i> : HBV <i>Cervarix</i> : HPV 16/18	Ab response, Th1 type immunity
MF59	Squalene + polysorbate 80 + sorbitan trioleate	Influenza	Ab response, Th1/Th2 response
AF03	Squalene + polyoxyethylene cetostearyl ether + mannitol + sorbitan oleate	Influenza	Ab response

Ab: Antibody; H1N1: Hemagglutinin type 1 and neuraminidase type 1 (Influenza strain; aka swine flu); H5N1: Hemagglutinin type 5 and neuraminidase type 1 (Avian influenza A); HBV: Hepatitis B virus; HIV: Human immunodeficiency virus; HPV 16/18: Human papillomavirus type 16/18; MPLA: Monophosphoryl lipid A adjuvant; QS-21: A purified *Quillaja saponaria* Molina immunologic adjuvant fraction 21; Th1/Th2: T-helper cell type 1/type 2.

# What alum actually is..

- In vaccines, “alum” usually means:
- Aluminium hydroxide –  $\text{Al}(\text{OH})_3$
- Aluminium phosphate –  $\text{AlPO}_4$
- Occasionally amorphous aluminium hydroxyphosphate sulfate
- These form microparticles that adsorb vaccine Ags on their surface!

What alum does immunologically?

→ Creates a local antigen depot

Alum forms particulate aggregates with the antigen, which:

- retain antigen at the injection site
- allow slow antigen release
- prolong exposure to the immune system

**This increases the probability that APCs will capture the antigen!**

# Neonatal and Infantile Immune Responses to Encapsulated Bacteria and Conjugate Vaccines

ENCAPSULATED BACTERIA ARE RESPONSIBLE FOR THE MAJORITY OF MORTALITY AMONG NEONATES AND INFANTS.

*S. pneumonia* serotypes, *N.meningitidis*, and *H. influenza*

The major components on the surface of these bacteria are:

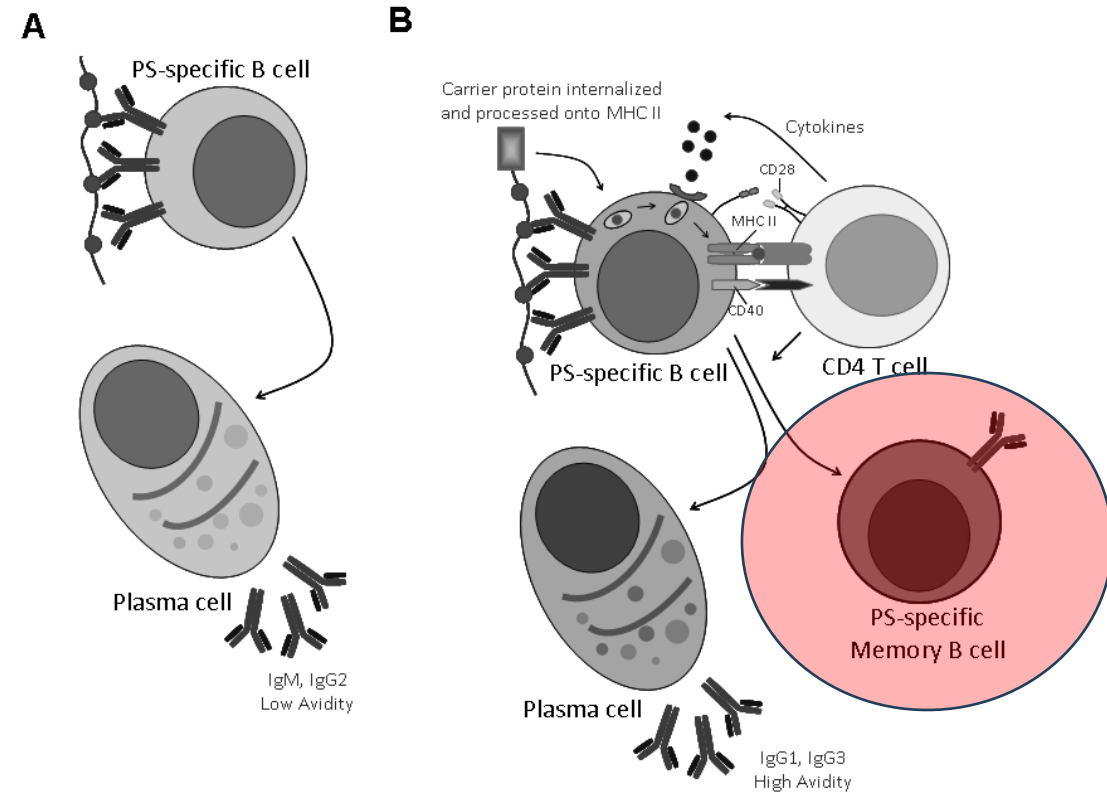
**POLYSACCHARIDES = VIRULENCE FACTORS!**

# Neonatal and Infantile Immune Responses to Encapsulated Bacteria and Conjugate Vaccines

## PROBLEM:

Polysaccharides are thymus-independent (TI)-2 antigens that induce inadequate IR in neonates and infants.

→ lack of immune response may be overcome by conjugating the polysaccharides to a carrier protein!



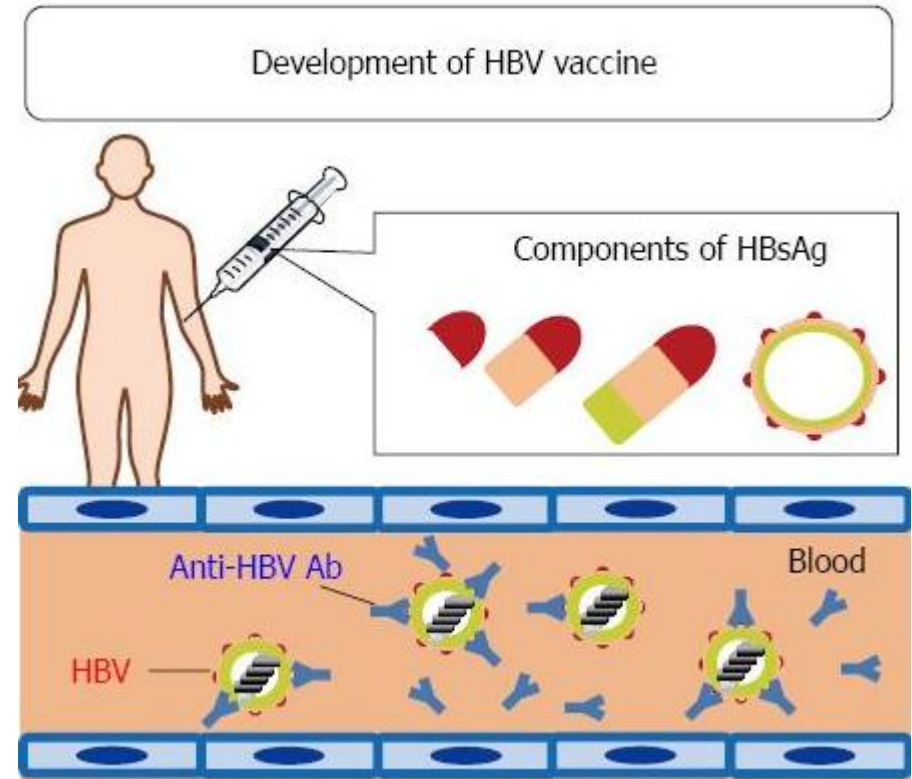
# III. SUBUNIT VACCINES

## Protein-based vaccines

- The first protein-based vaccines relied on

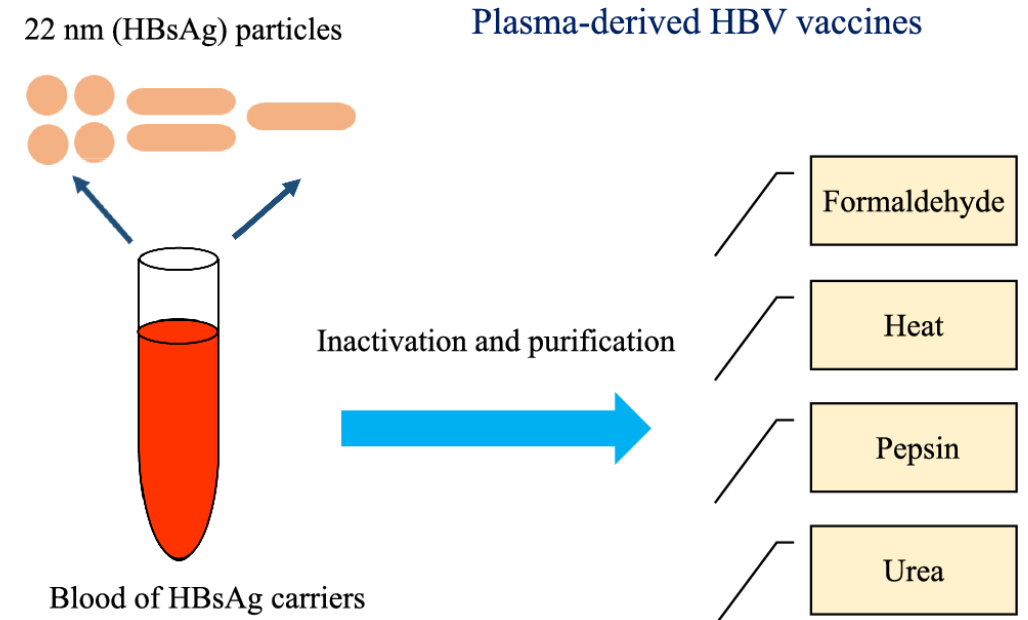
### NATURAL SOURCES OF ANTIGENS →

- Hep B vaccine - human source (plasma) for the vaccine antigen
- **LIVER CELLS** of persons chronically infected with hepatitis B virus:  
-> shed excess viral surface protein, ie., hepatitis B surface antigen (HBsAg)



# III. SUBUNIT VACCINES

## Protein-based vaccines



→ plasma was harvested from long-term chronic hepatitis B carriers

HBsAg was purified

... and the final preparation subjected to inactivation techniques

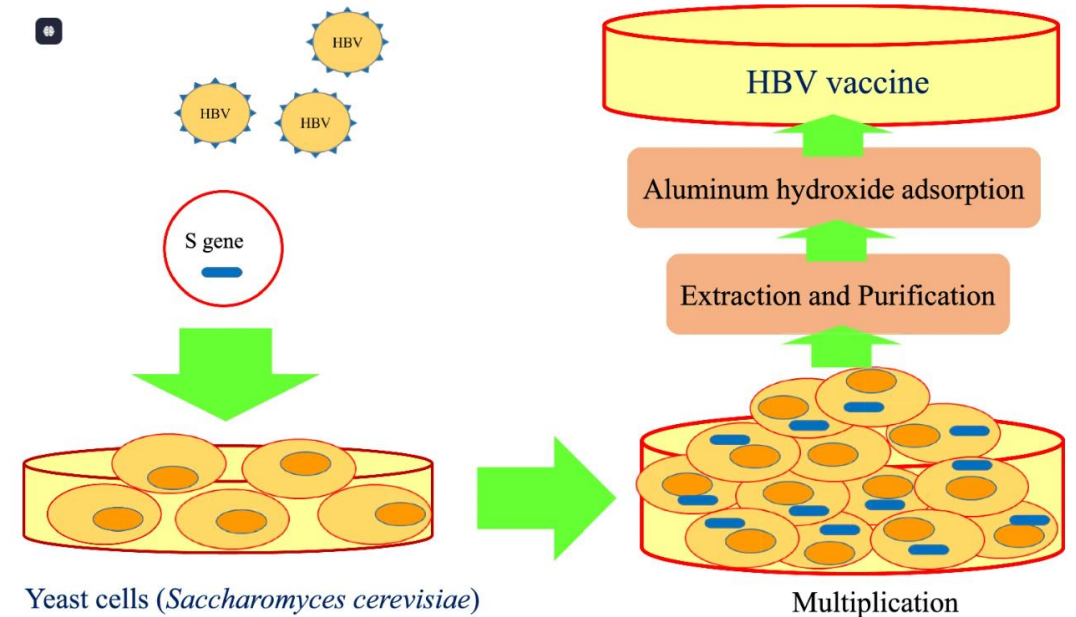
→ **WELL TOLERATED AND HIGHLY EFFICACIOUS VACCINE!**

# III. SUBUNIT VACCINES

## Current Hepatitis B vaccine type (worldwide & Europe)

- Produced by inserting the **HBsAg gene** into yeast (e.g., *Saccharomyces cerevisiae*) or **mammalian cells**
- Resulting in purified HBsAg protein → formulated with aluminum adjuvant
- No live virus, no whole virus, no DNA from HBV.
- **Engerix-B (GSK), HBVAXPRO (Merck/MSD)**
- **Yeast-derived**
- **Sci-B-Vac (VBI) -Mammalian-cell-derived**

From: Hepatitis B virus infection after immunization: How serious it is? An updated review



# Subunit Vaccines & Candidates

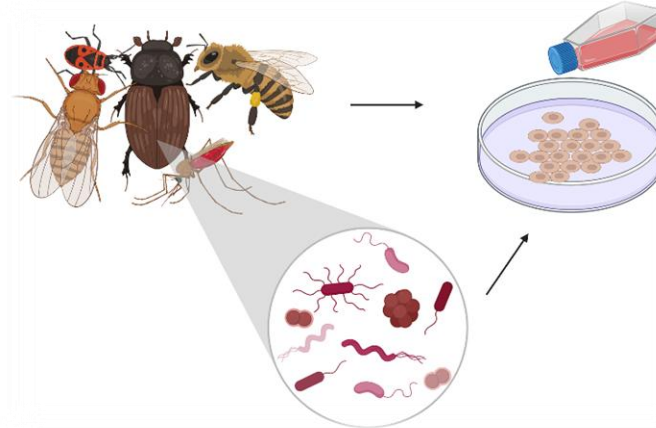
## Short list:

- COVID-19: Novavax NVX-CoV2373 (Spike protein)
- RSV: Arexvy (RSV preF)
- Chikungunya: VIMKUNYA™ (VLP)
- HEV (Hepatitis E Virus) : Hecolin (ORF2 capsid protein)
- Shigella: GMMA subunit vaccines
- MERS-CoV: RBD protein vaccines (candidates)
- Lassa: Recombinant GPC vaccines (candidates)
- Mpox (previously called **monkeypox**) : VLP-based subunit candidates

# III. SUBUNIT VACCINES

## Protein-based vaccines - Novavax

- **Novavax COVID-19 Vaccine, adjuvanted**
- Contains: SARS-CoV-2 spike protein and Matrix-M adjuvant.
- The spike protein in this vaccine is produced in **insect cells**
- The Matrix M-adjuvant contains **saponin extracts** from the bark of the **Soapbark tree** that is native to Chile.



# III. SUBUNIT VACCINES

## Peptide-based vaccines

- Subunit –peptide vaccines are attractive
- Potential to precisely tune the immune response
- **...using antigens from protein fragments or peptides**
- In addition, peptides have potential activities as adjuvants!



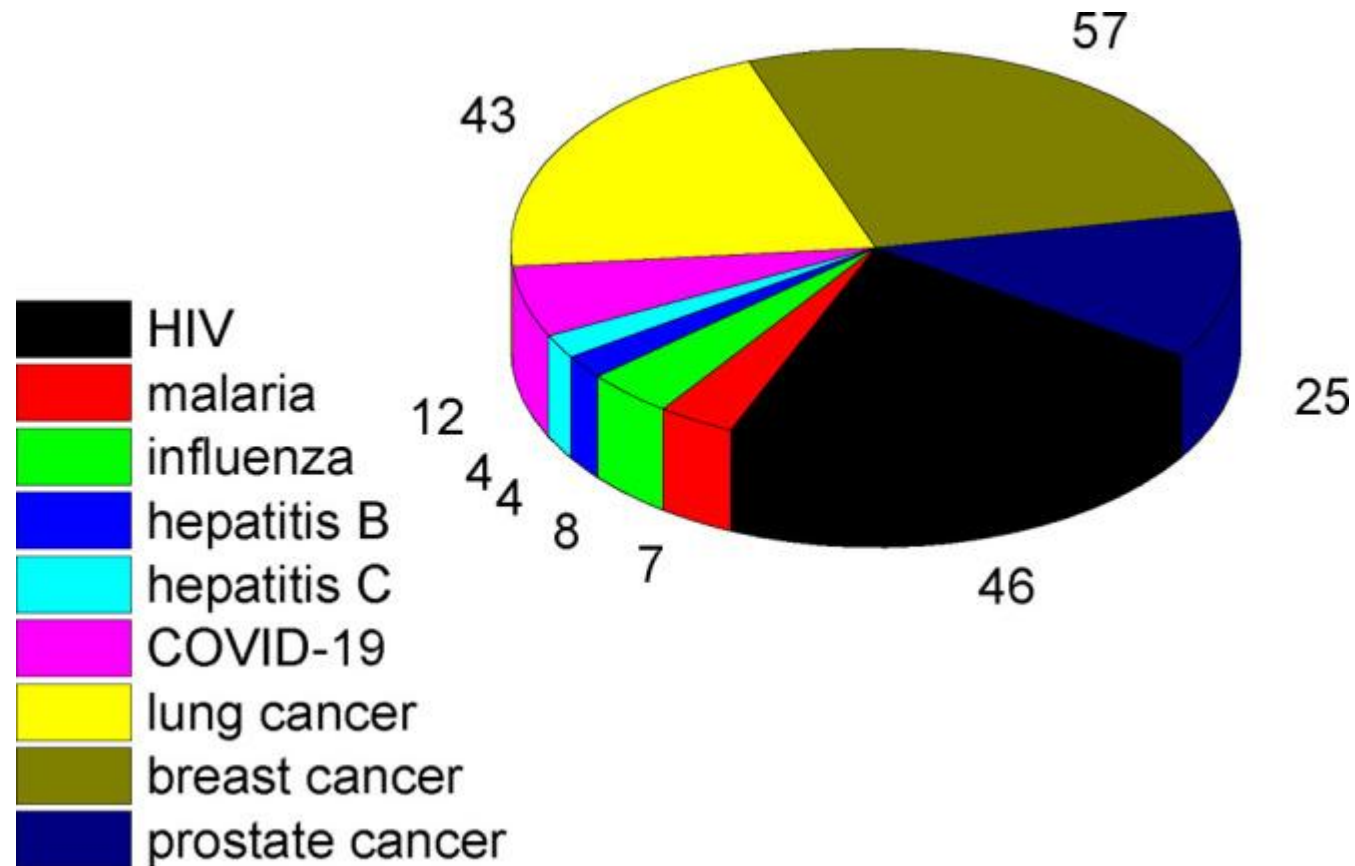
Short  
peptides -  
automated  
synthesis



Longer  
peptides and  
proteins -  
recombinantly

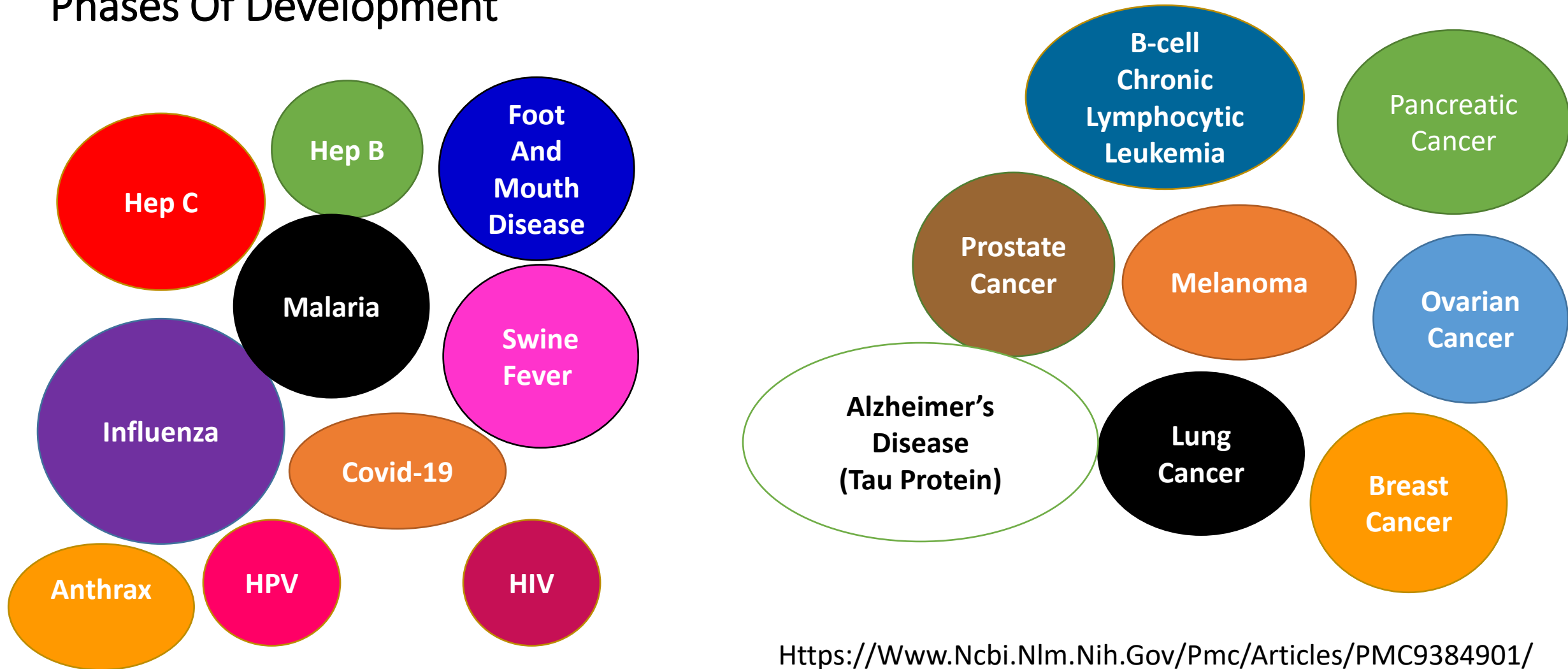
# III. SUBUNIT VACCINES

## Peptide-based vaccines



### III. Subunit Vaccines

Examples Of Peptide-based Candidate Vaccines In Active Or Completed Phases Of Development



# Considerations and Methods for the Design of Peptide Vaccines

- Despite several advantages, peptides are typically poorly immunogenic when used alone, requiring the next generation of adjuvants to overcome this problem. ...
- Delivery: emulsion? Adjuvants? ...are discussed...
- Liposomes?
- Virosomes, ISCOMS and Related Particles?
- Polymeric Particles for delivery?
- Safety Issues related to Delivery Strategies

# Considerations and Methods for the Design of Peptide Vaccines

- Immune Tolerance vs Autoimmunity? TAA –TSA
- **If the peptide is too short**, it can bind to the **MHC of non-professional APCs!**
  - **NO FULL T-CELL ACTIVATION**
  - **leading to a poor T-cell response / IMMUNTOLERANCE!**
- OPTIMAL LENGTH** → amplification of CD4+ and CD8+ response
  - recognition of motifs that lead to enhancement of immunogenicity

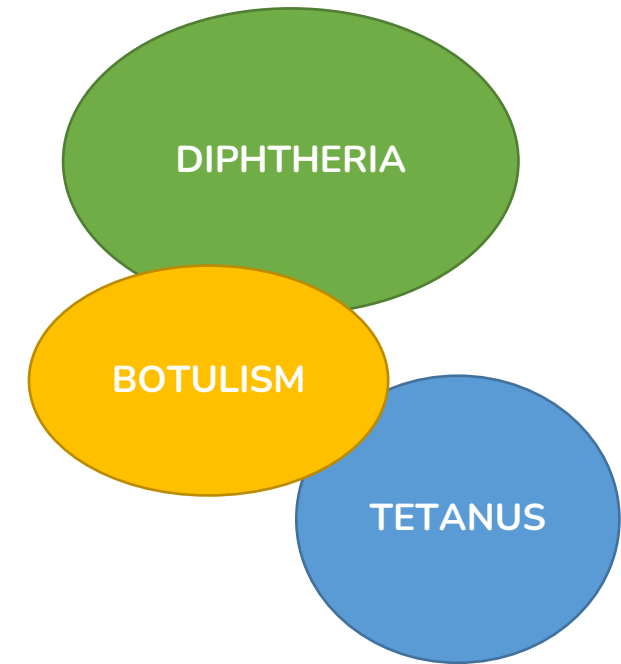
# Considerations and Methods for the Design of Peptide Vaccines

## - Multi-epitope-based strategies are needed!

- Conformational restrictions...
- Identification of the potent and safe immune stimulators -> use of nanotechnology ...
- Potential **TOXICITY OF NANOPARTICLES** (positively charged) the use of biodegradable polymers may result in unexpected complications....
- **YET, a very promising platform!!!**

# IV. TOXOID VACCINES

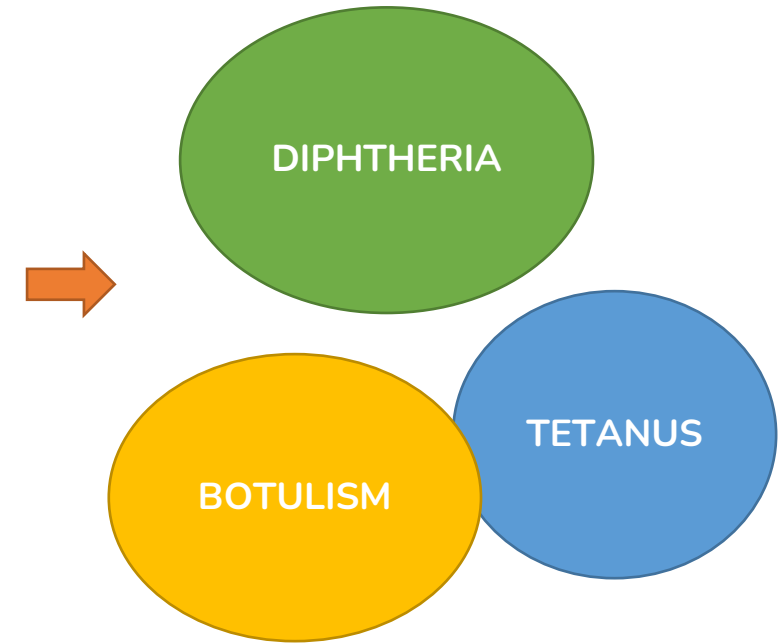
- **USE INACTIVATED TOXINS TO TARGET THE TOXIC ACTIVITY CREATED BY THE BACTERIA**
- **...RATHER THAN TARGETING THE BACTERIA ITSELF!**
- **NEUTRALIZATION OF TOXINS WITH ANTIBODIES THROUGH VACCINATION**
- Boostering: every 5-10 years (+/-) e.g. tetanus vaccine, diphtheria vaccine



# IV. TOXOID VACCINES

Purification of the bacterial exotoxin

- Heat
  - Formaldehyde
- } Toxicity is suppressed / inactivated



VACCINATION WITH TOXOIDS INDUCES ANTI-TOXOID ANTIBODIES THAT ARE ABLE TO BIND WITH THE TOXIN AND NEUTRALIZE IT!

# IV. TOXOID VACCINES

Toxoids are altered forms of toxins (exotoxins secreted by bacteria)



TOXICITY IS WEAKENED

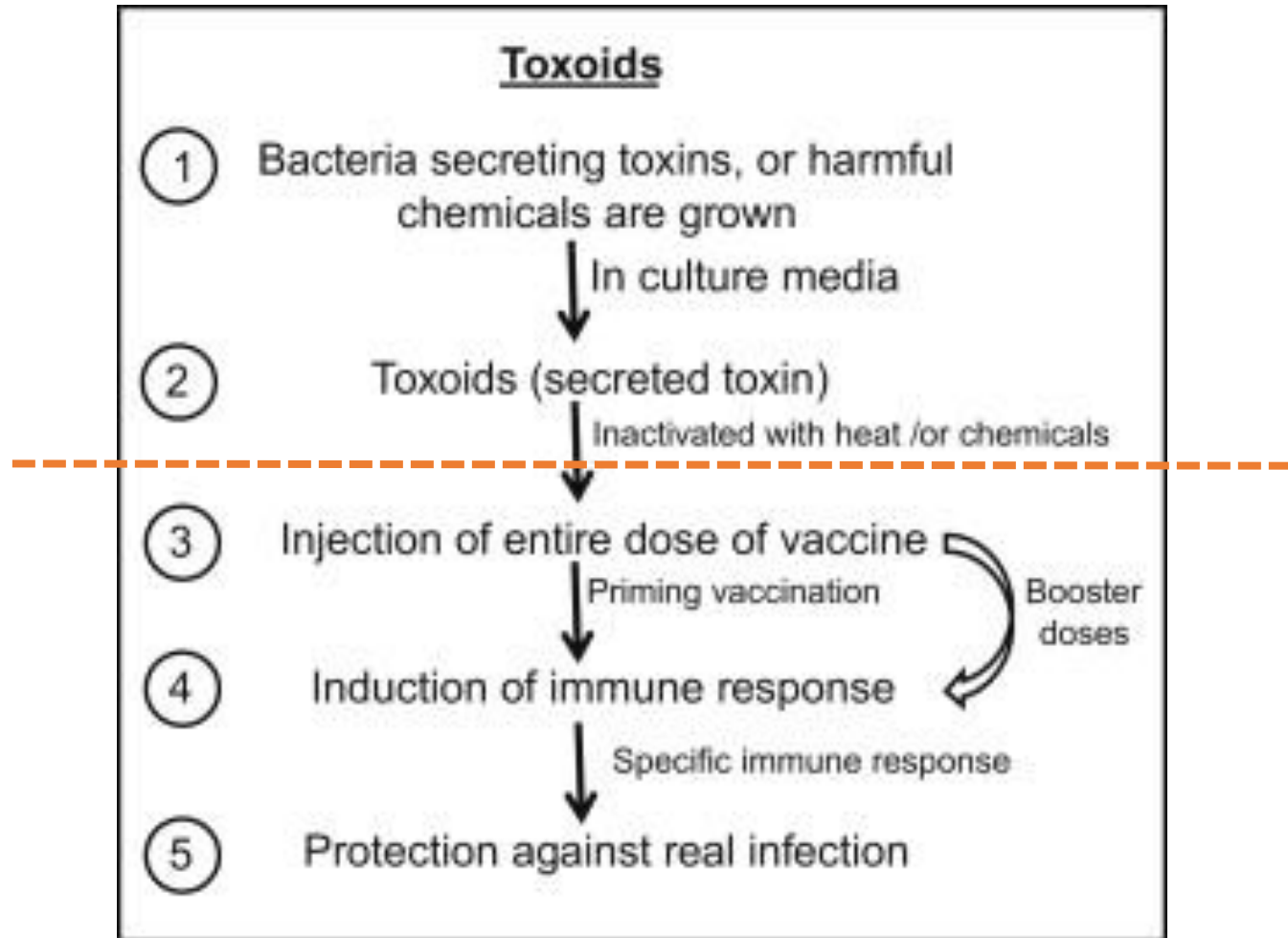
IMMUNOGENICITY IS MAINTAINED



Toxoids are able to cause a protective immune response, but not lead to active toxin-induced disease!

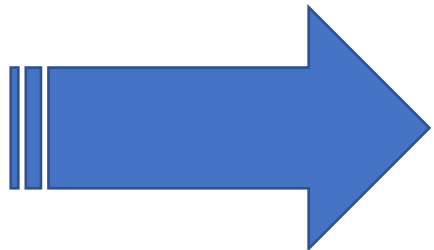
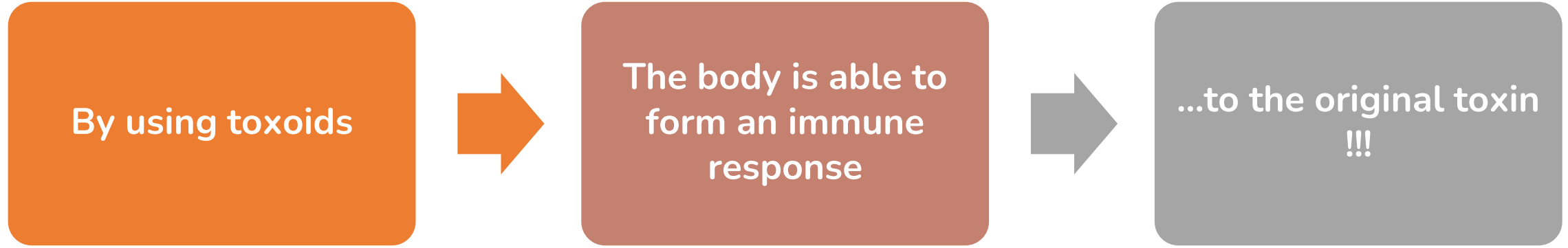
Toxoids are excellent choices to be used in vaccinations against certain bacterial toxins (diphtheria and tetanus)

# IV. TOXOID VACCINES



# IV. TOXOID VACCINES

## What is a toxoid vaccine?



**IMMUNOGENICITY IS MAINTAINED**

# IV. TOXOID VACCINES

## IR, protection

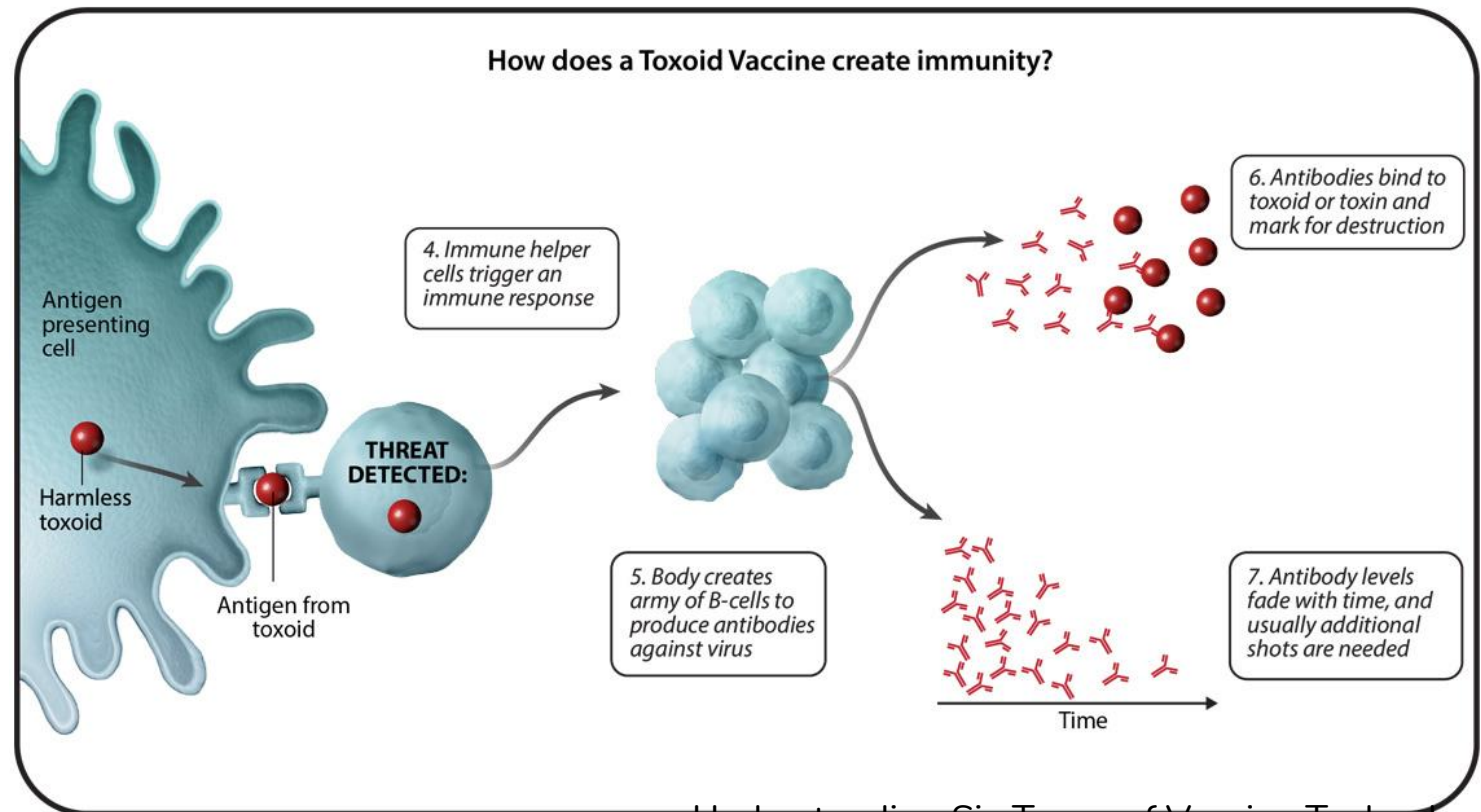
**Multiple doses** throughout childhood and adulthood for **maximum protection**

+ **booster shots** can be given if you are **traveling** to a high-risk country for example...

# IV. TOXOID VACCINES

## Examples of bacterial diseases and toxoid vaccines:

- Tetanus (*Clostridium tetani*),
- Diphtheria (*Corynebacterium diphtheriae*),
- Botulism (*Clostridium botulinum*)
- Whooping cough; pertussis (*Bordetella pertussis* – though this tends to be bacterial components rather than toxoids per se, but components are incorporated alongside toxoids of other bacteria).



Understanding Six Types of Vaccine Technologies | Pfizer

# IV. TOXOID VACCINES



Clostridium Perfringens Type A  
Toxoid Cattle Vaccine



Bravoxin® Suspension for injection  
for cattle and sheep

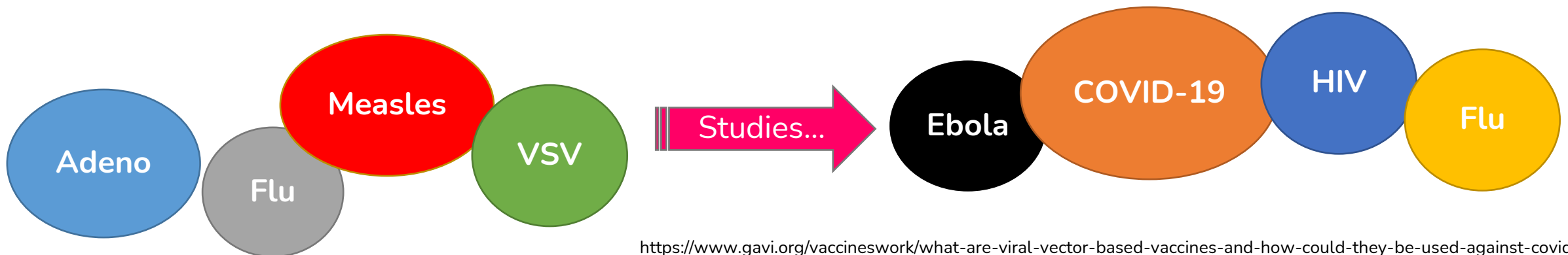
# V. VIRAL VECTOR VACCINES

„ANOTHER VIRUS” is modified + used as a vector,

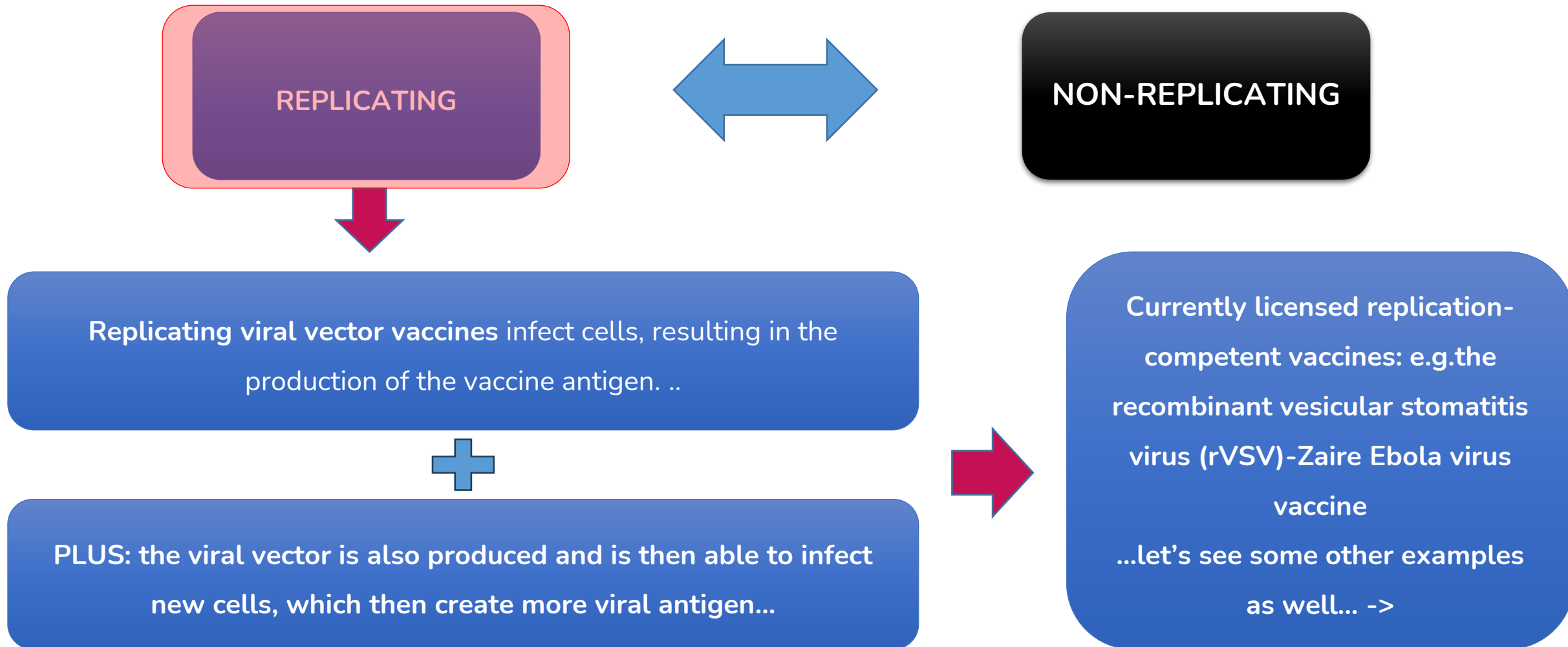
... to deliver protection from the „TARGET VIRUS”

E.g. adenovirus, influenza, measles virus and vesicular stomatitis virus (VSV)

Recent uses of viral vector technology have been in Ebola virus and COVID-19, and studies into its use for Zika, flu and HIV are ongoing...



# V. VIRAL VECTOR VACCINES



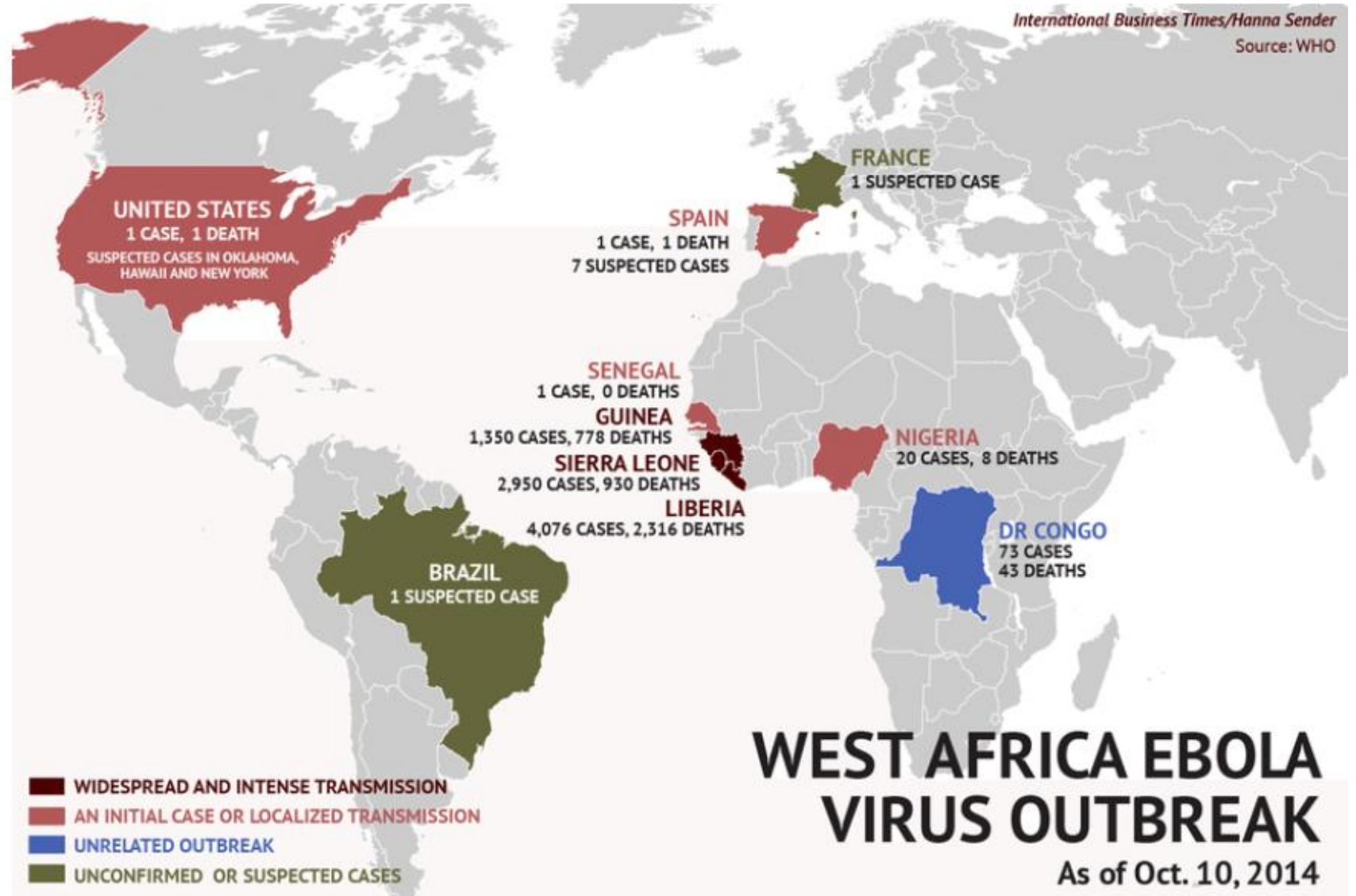
# Filoviruses

The filovirus family includes some of the world's most deadly pathogens, including Zaire ebolavirus – commonly known as Ebola virus. CEPI's filovirus investments focus on expanding access to licensed vaccines against Ebola virus, pioneering the development of broadly protective filovirus vaccines and a filovirus vaccine library, and supporting clinical trials of vaccine candidates for Marburg virus and Sudan ebolavirus during outbreaks.

## Ebola Virus Disease (EVD – Zaire ebolavirus)



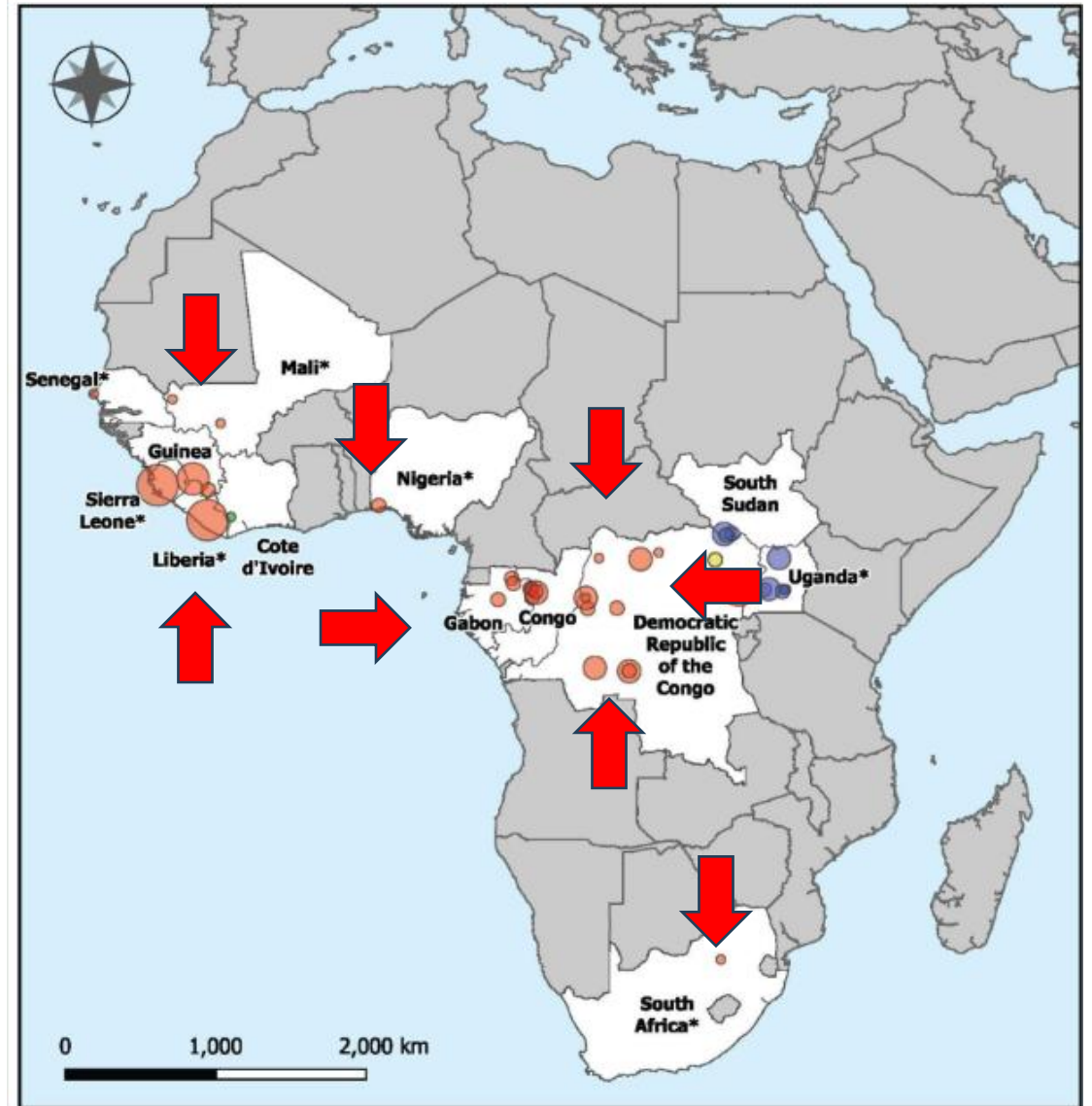
# EBOLA



# Ebola virus

- **WITHOUT TREATMENT, UP TO 90% OF CASES ARE FATAL**
- **2014–2016 outbreak in West Africa, the largest Ebola disease outbreak to date**
- **....MORE THAN 28,600 CASES REPORTED!**
- **2018–2020 outbreak in the DRC + Uganda.**
- Other large outbreaks 100s of cases: **DRC and Gabon.**
- **Smaller outbreaks have also occurred in DRC, Gabon, the Republic of the Congo, and ZA**

<https://www.cdc.gov/ebola/outbreaks/index.html>



**Country reporting past Ebola disease outbreak**

□ Yes  
□ No

**Number of cases**

- 1 - 10
- 11 - 100
- 101 - 1,000
- 1,001 - 10,000
- 10,000+

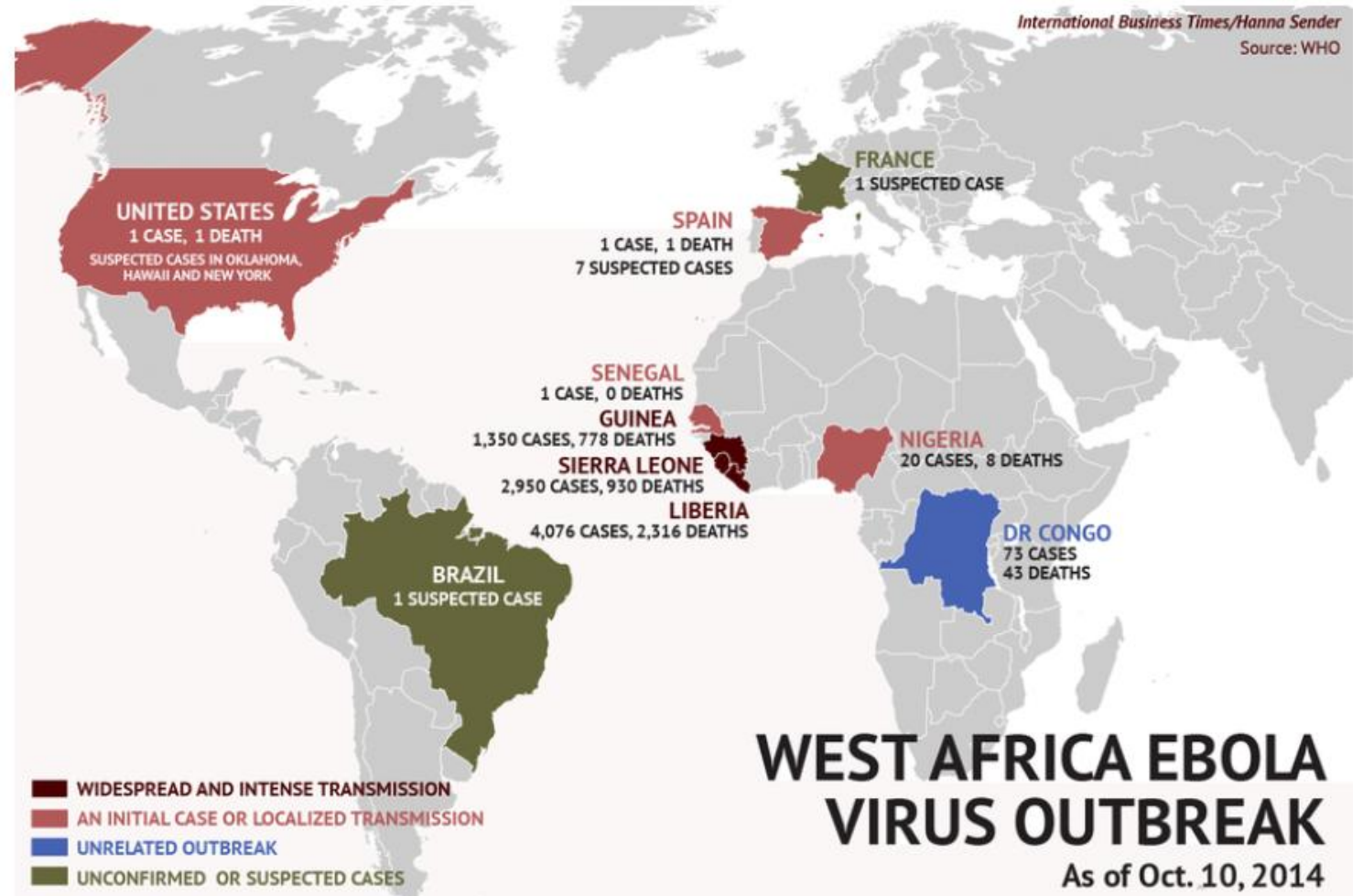
**Orthoebolavirus Species**

- *Orthoebolavirus zairensis* (Ebola virus)
- *Orthoebolavirus sudanense* (Sudan virus)
- *Orthoebolavirus bundibugyoense* (Bundibugyo virus)
- *Orthoebolavirus taiense* (Tai Forest virus)

# Ebola Virus Disease (EVD – Zaire ebolavirus)

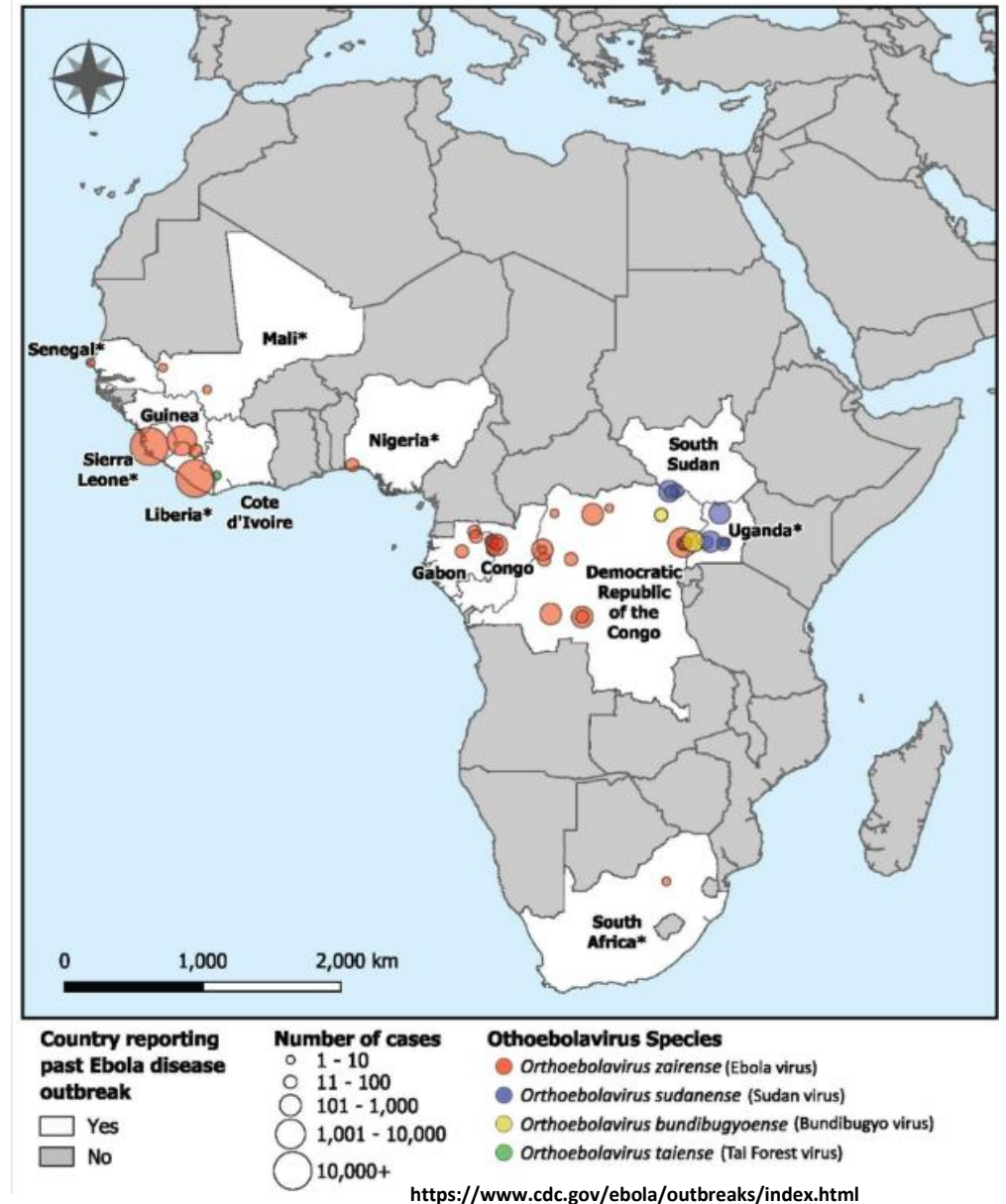
- West African epidemic - more than 28,600 cases reported!
- Ebola was first identified in 1976
- Ervebo (rVSV-ΔG-ZEBOV-GP)  
- first Ebola vaccine 2019

→ Replicating viral vector vaccine



# Ebola virus vaccine - ERVEBO

- ERVEBO (rVSV-ΔG-ZEBOV-GP) became the first Ebola vaccine to be approved- licensed in 2019
- It is a live recombinant VSV (vesicular stomatitis virus) vector (replication comp.) → expressing the Ebola Zaire glycoprotein
- Clinical trials - high efficacy! (during the West African outbreak, including a 2015 ring-vaccination trial in Guinea)
- Single dose!



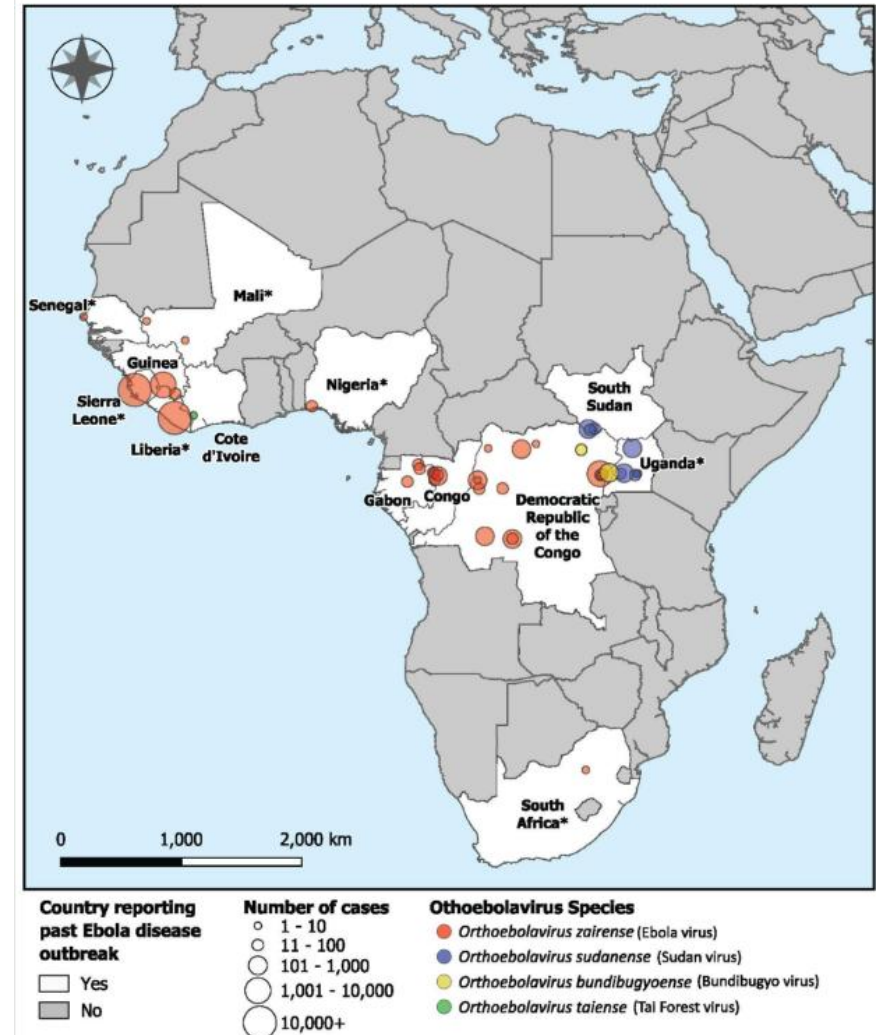
# Ebola virus

- Adenovirus + poxvirus-vectored vaccines

- Another Ebola vaccine regimen by: Johnson & Johnson (a two-dose series of **Ad26.ZEBOV** and MVA-BN-Filo)

## ADENOVIRUS + POXVIRUS-VECTORED VACCINES

- Approval of the European Commission in 2020
- However, the WHO recommendation for outbreak response is to use the **ONE-DOSE ERVEBO** for its rapid protection



<https://www.cdc.gov/ebola/outbreaks/index.html>

cdc.gov

# Lassa hemorrhagic fever

Vaccine candidate: recombinant rVSV-  
vectored Lassa vaccine (rVSVΔG-LASV-GPC)

-> It uses the same vector backbone as  
Merck's Ebola vaccine!

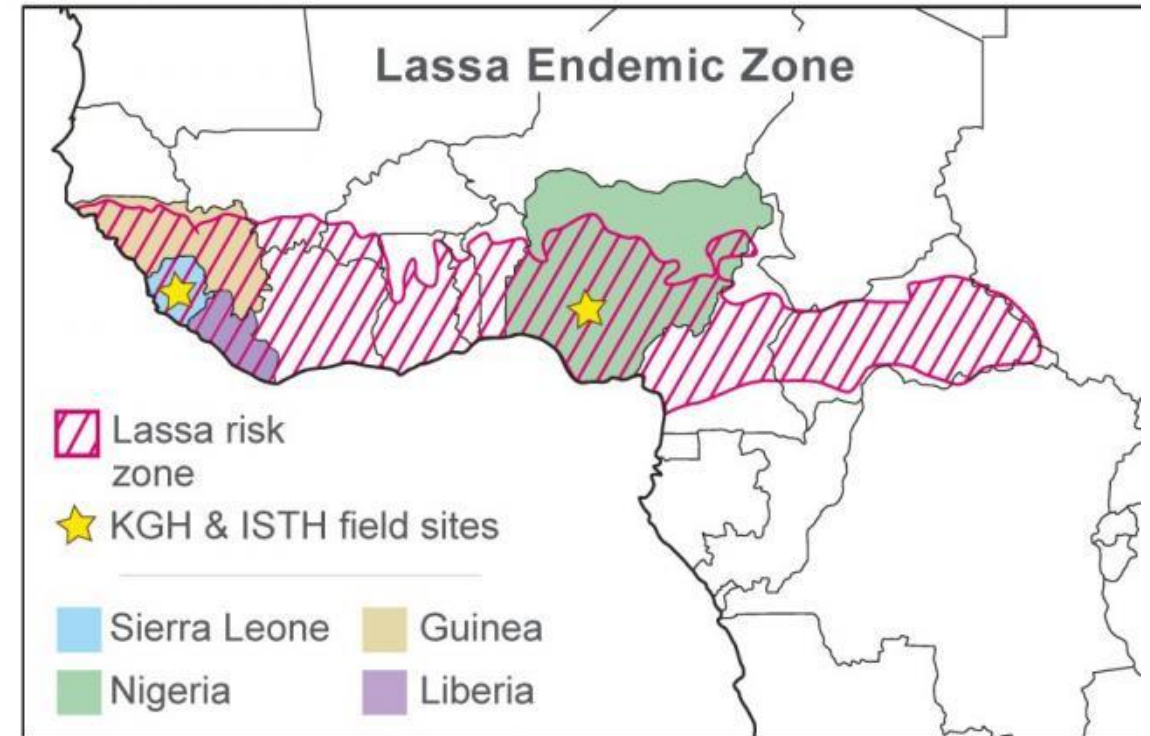


You can get Lassa fever by touching, playing  
with, or cutting up a rat's dead body.

# Lassa Fever

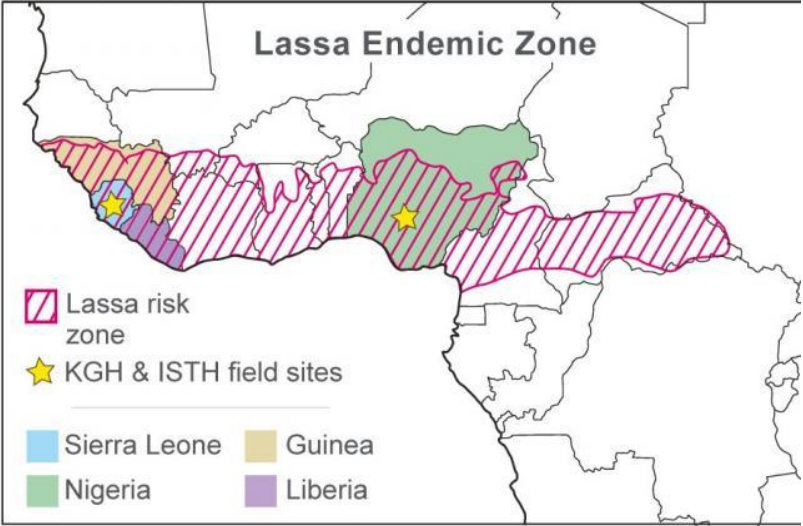
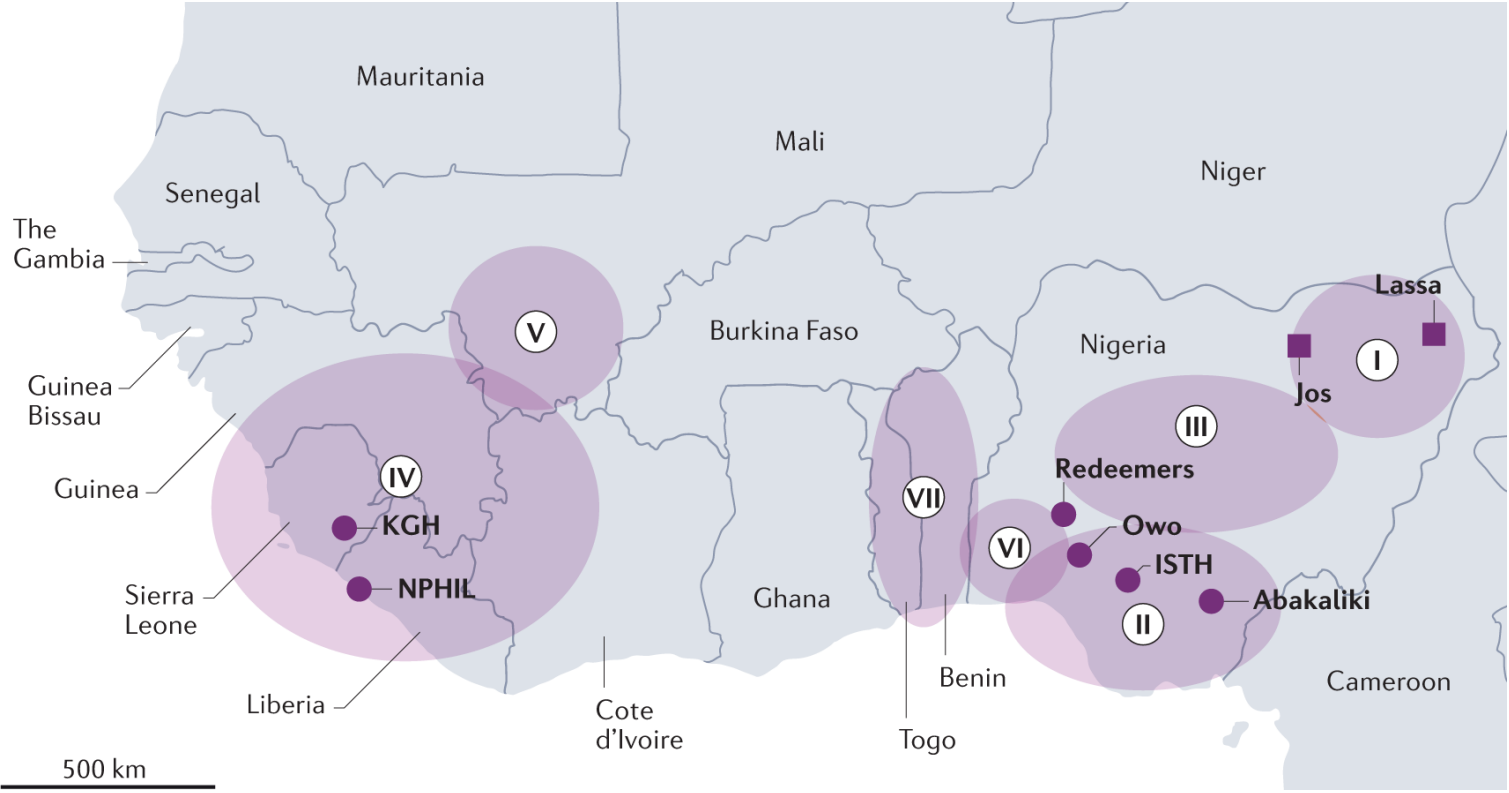
## Endemic to parts of West Africa

- Countries like **Nigeria**, **Sierra Leone**, **Liberia**, and others experience seasonal Lassa outbreaks,
- 100s of thousands of infections annually in **West Africa**
- The disease was first described in the late 1960s- increasing epidemic potential and high mortality in severe cases.
- **AS OF 2025, NO LASSA VACCINE IS YET LICENSED, BUT THERE HAS BEEN SIGNIFICANT PROGRESS ->**



# Lassa fever — the road ahead

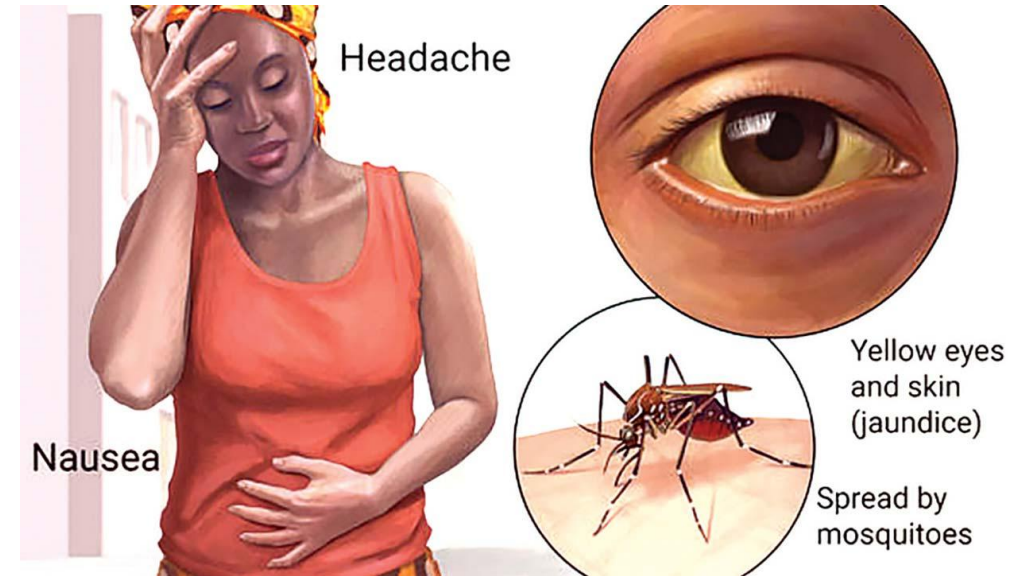
(Nature Reviews Microbiology)



[https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.nature.com%2Farticles%2Fs41579-022-00789-8&psig=AOvVaw2h8ThpAo4ZrZu9NyWVK2UL&ust=1763444302748000&source=images&cd=vfe&opi=89978449&ved=0CBkQ3YkBahcKEwiw9\\_KMvPiQAxUAAAAAHQAAAAAQFw](https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.nature.com%2Farticles%2Fs41579-022-00789-8&psig=AOvVaw2h8ThpAo4ZrZu9NyWVK2UL&ust=1763444302748000&source=images&cd=vfe&opi=89978449&ved=0CBkQ3YkBahcKEwiw9_KMvPiQAxUAAAAAHQAAAAAQFw)

# Lassa hemorrhagic fever -Lassa virus

- Many of those infected by the virus **do not develop symptoms.**
- **Symptoms: fever, weakness, headaches, vomiting, and muscle pains.**
- **Less commonly there may be bleeding from the mouth or GI tract.**
- **The risk of death once infected is about 1% (one percent) and frequently occurs within two weeks of the onset of symptoms**
- Of those who survive, about a **quarter have hearing loss**, which improves within three months in about half of these cases



# Lassa Fever

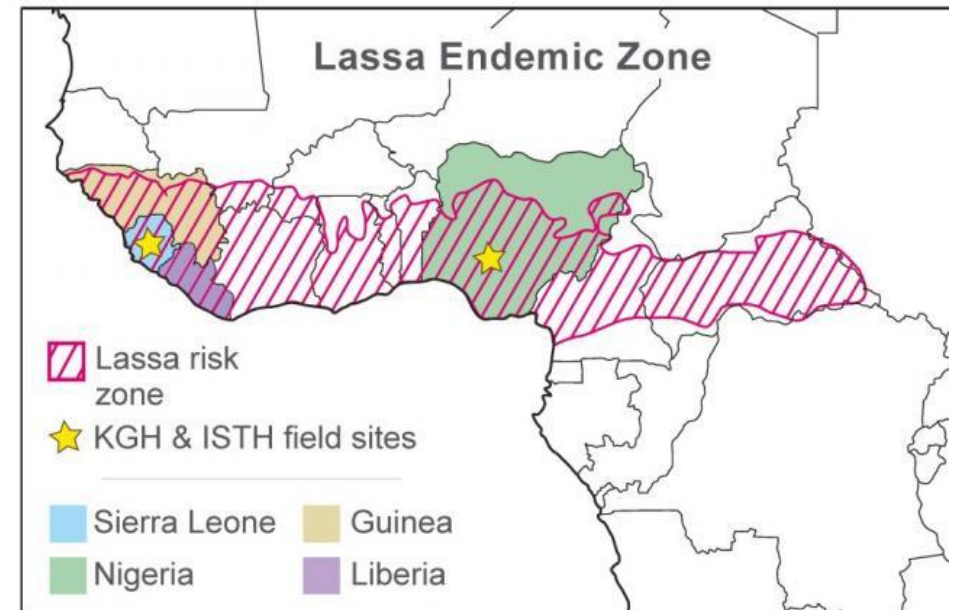
## - recombinant rVSV-vectored Lassa vaccine candidate

- One of the most advanced candidates is a **recombinant rVSV-vectored Lassa vaccine** (rVSVΔG-LASV-GPC) developed by IAVI with support from CEPI
- **THIS VACCINE USES THE SAME VECTOR BACKBONE AS MERCK'S EBOLA VACCINE (VESICULAR STOMATITIS VIRUS)**
- > **EXPRESSES THE GLYCOPROTEIN OF LASSA V.**
- In a Phase 1 trial in 2021–2022, a single dose of rVSV-LASV vaccine was given to over 100 adults in the U.S. and West Africa (cepi.net.)

# Lassa Fever

## - recombinant rVSV-vectored Lassa vaccine candidate

- Phase II trial of a Lassa vaccine began in 2023 across multiple West African countries (Nigeria, Sierra Leone, and Ghana)
- THE VACCINE IS INTENDED TO BE A **SINGLE-DOSE REGIMEN**, WHICH IS IDEAL FOR OUTBREAK CONTROL!



# Marburg virus disease

Disrupts the clotting system – internal bleeding  
- fatal in up to 88% of cases



- rVSV-ZEBOV
- Ad26, ChAdOx1, Ad5
- MVA vektor (Modified Vaccinia Ankara)

Related to Ebola Zaire, Marburg virus disease is fatal in up to 88% of cases, which is why it's an R&D priority for Sabin.

## What is Marburg?

Marburg virus disease is a **hemorrhagic fever** that can disrupt the body's clotting system and lead to **internal bleeding**.



## Did You Know?

Marburg virus disease outbreaks have recently emerged in countries that had never reported cases, including Rwanda and Tanzania.

**There are no approved vaccines and treatments for Marburg virus disease.**



Sabin is one of a few organizations developing a vaccine for Marburg. Phase 2 clinical trials are currently underway in Uganda and Kenya.

Fatality rates can be as high as

**[88%]**

## Symptoms

Early symptoms include:



**HIGH FEVER**



**ACUTE HEADACHE**



**EXTREME FATIGUE**

As the disease progresses, severe symptoms include:



**PANCREATIC INFLAMMATION**



**LIVER & IMMUNE SYSTEM FAILURE**



**SHOCK**



**MASSIVE HEMORRHAGING**

## By the Numbers

There have been **13+ outbreaks** of Marburg virus disease since 1980

Almost all outbreaks occurred in Sub-Saharan Africa:

**2024: Rwanda**  
**2023: Tanzania and Equatorial Guinea**





Sabin is one of a few organizations developing a vaccine for Marburg.

Phase 2 clinical trials are currently underway in Uganda and Kenya.

## Disease Transmission

### INITIAL CONTACT

Transmitted to people from fruit bats.



### SECONDARY SPREAD

Person-to-person transmission occurs through contact with bodily fluids of infected people.



## By the Numbers

There have been **13+ outbreaks** of Marburg virus disease since 1980

Almost all outbreaks occurred in Sub-Saharan Africa:



**2024: Rwanda**

**2023: Tanzania and Equatorial Guinea**



Most recent outbreak:  
**Rwanda (2024)**

Largest and deadliest outbreak:  
**Angola (2004–2005)**

**252 CASES**

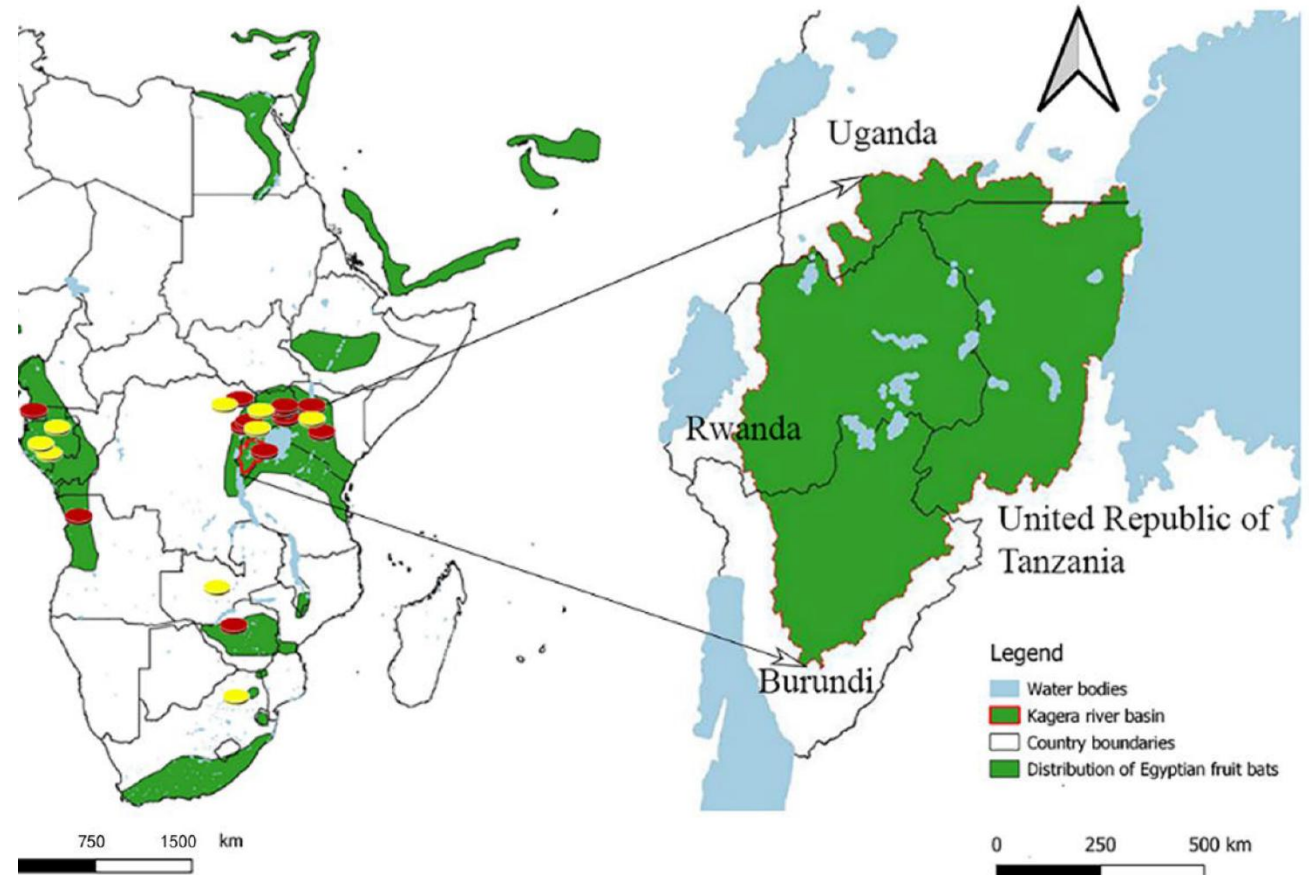
**227 DEATHS**



# Marburg Virus Disease – Key Facts

## Geographic Distribution

- First outbreaks: **1967** (Germany, Serbia)
- Majority of outbreaks since: **Sub-Saharan Africa**
- Occasional isolated cases globally
  
- **Recent Outbreaks**
- **2024 – Rwanda**
- **2023 – Tanzania, Equatorial Guinea**



# Marburg Virus Disease – Key Facts

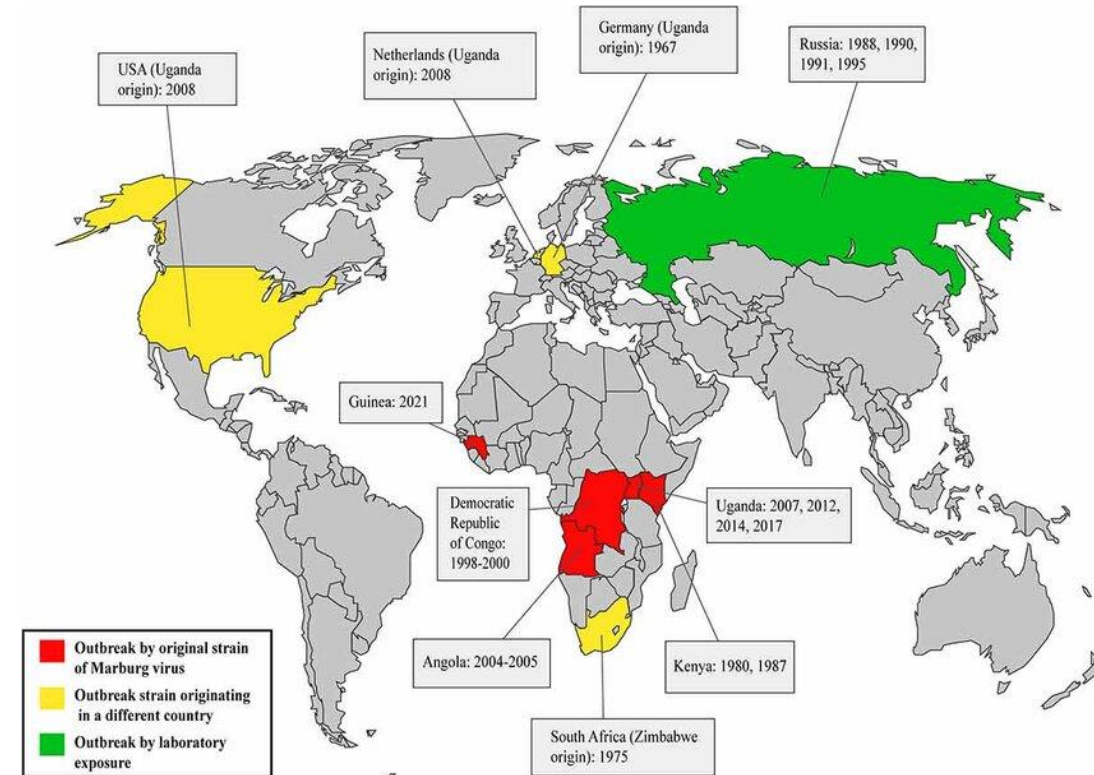
## Transmission

1. Initially: fruit bats

2. Secondary: bodily fluids of infected people

Requires very close contact

- Spread through: Blood, saliva, urine, other bodily fluids
- Contaminated clothing, bedding, medical equipment
- **Usually transmitted from infected or deceased individuals**





# Treatment & Vaccines

- **ONLY SUPPORTIVE TREATMENT**
  - Supportive care + experimental: blood products, immune therapies, antivirals
- **NO APPROVED VACCINE** - Several candidates in development

## Sabin Marburg Vaccine – Status

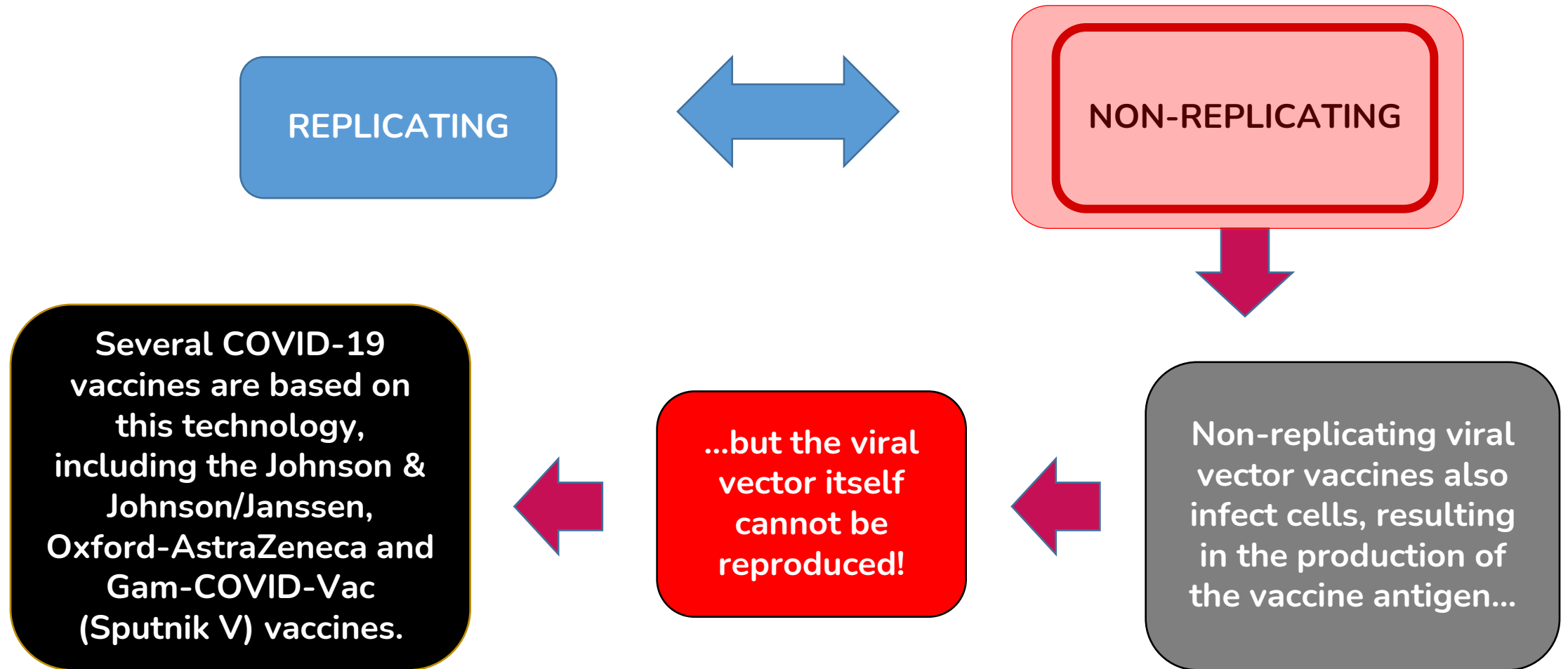
- **Vaccine type:** single-dose candidate
- **Phase:** Phase 2 clinical trial (since Oct 2023)

## Sites:

- **MAKERERE UNIVERSITY WALTER REED PROJECT (KAMPALA, UGANDA)**
- **KENYA MEDICAL RESEARCH INSTITUTE (SIAYA, KENYA)**



# V. VIRAL VECTOR VACCINES



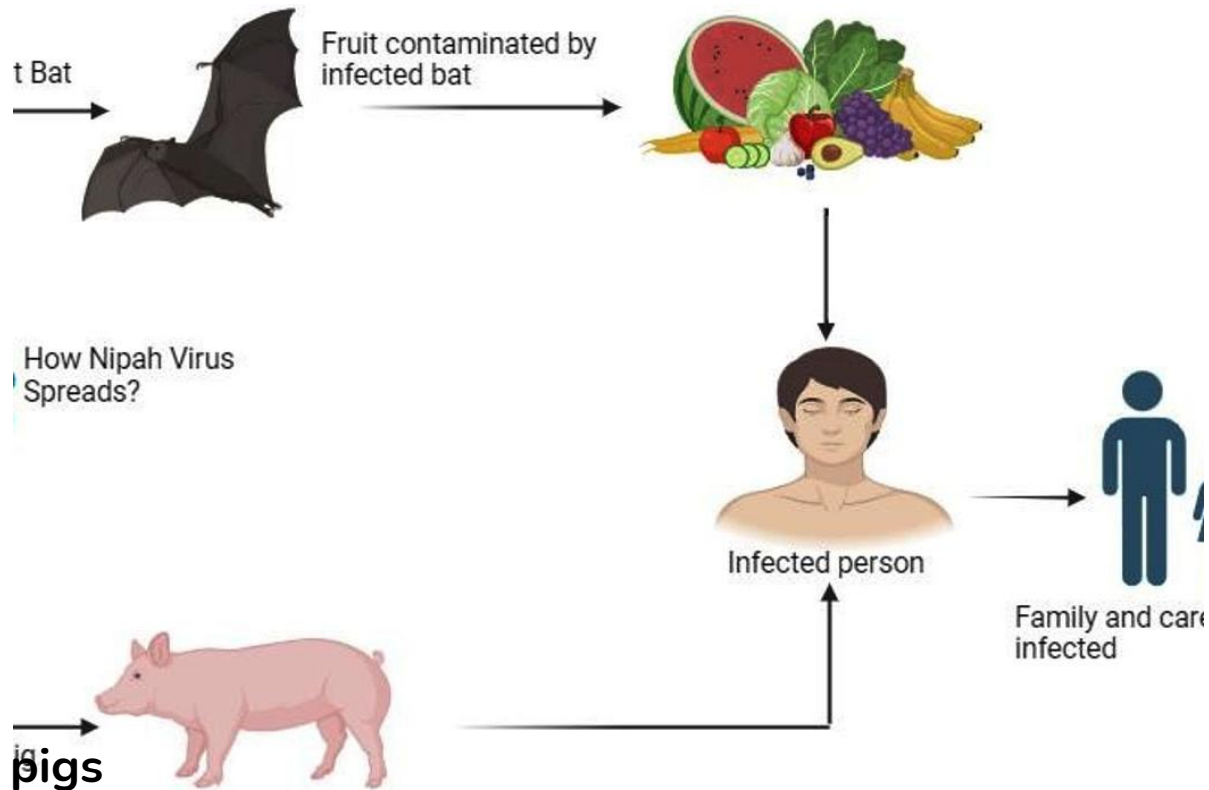


## Nipah virus infection

*ChAdOx1 - chimpanzee-adenovirus Oxford 1 - ChAdOx1  
nCoV-19 (AZD1222)*

[https://www.who.int/health-topics/nipah-virus-infection#tab=tab\\_1](https://www.who.int/health-topics/nipah-virus-infection#tab=tab_1)

# Nipah Virus Infection



- **ZOONOTIC ILLNESS = TRANSMITTED TO PEOPLE FROM ANIMALS**
- **ADDITIONALLY, CAN BE TRANSMITTED THROUGH CONTAMINATED FOOD OR DIRECTLY FROM PERSON-TO-PERSON**
- In infected people, it causes a range of illnesses:  
→ **from subclinical infection to acute respiratory illness...**
- ... and **FATAL ENCEPHALITIS!**
- The virus can also cause **severe disease** in animals such as **pigs**

# Nipah Virus Infection

- During the first recognized outbreak in **MALAYSIA**, which also affected **Singapore**, most human infections resulted from **direct contact with sick pigs or their contaminated tissues.**
- In subsequent outbreaks in **BANGLADESH AND INDIA** - **consumption of fruits or fruit products (such as raw date palm juice) contaminated with urine or saliva from infected fruit bats**
- **HUMAN-TO-HUMAN TRANSMISSION OF NIPAH VIRUS HAS ALSO BEEN REPORTED!**

# Nipah virus- vaccine candidate - October 2025

- **28 October 2025; OSLO; PUNE; OXFORD:** One of the world's deadliest viral pathogens, Nipah virus, could soon have a new line of defense against it ...

**-> WORLD'S LARGEST INVESTIGATIONAL READY RESERVE OF  
A NIPAH VIRUS VACCINE CANDIDATE!**

**100,000 doses!!!**

# Nipah virus- vaccine candidate

- ChAdOx1 NipahB vaccine candidate - Adenovirus vector platform

*ChAdOx1 - chimpanzee-adenovirus Oxford 1 - ChAdOx1 nCoV-19 (AZD1222),*

*Candidate vaccines: MERS, Zika, Chikungunya, Rift Valley Fever*

- The vaccine encodes **NIPAH VIRUS GLYCOPROTEINS** – to elicit **immunity**

# Nipah virus- vaccine candidate

- ChAdOx1 NipahB vaccine candidate - investigational reserve of up to **100,000 doses**

... which could be deployed under **emergency use during a future Nipah virus outbreak**

**Nipah virus vaccines are in mid-stage development (Phase II as of 2025)**

# Rift Valley fever



<https://cepi.net/landmark-african-led-research-map-extent-rift-valley-fever-impact>

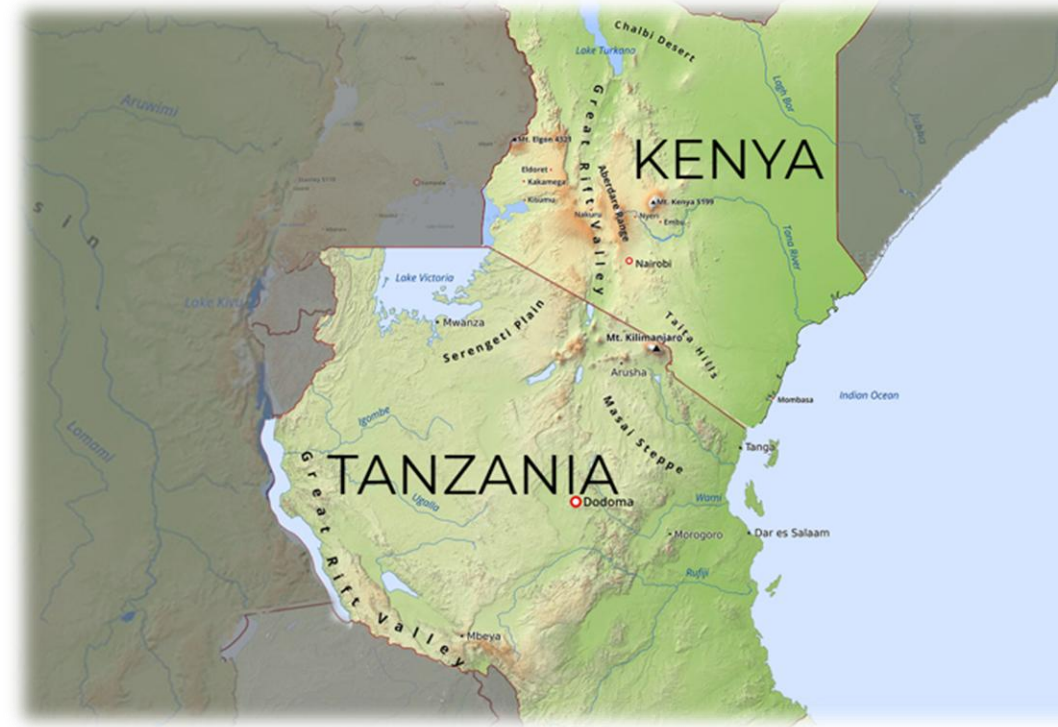


# Rift Valley fever

Two major collaborative projects, led by institutions in **Kenya** and **Tanzania**

Rift Valley fever, first identified in Kenya's Rift Valley in **1930**, is a **mosquito-borne** disease

**-> AFFECTING BOTH HUMANS AND LIVESTOCK, WITH SERIOUS CONSEQUENCES FOR HEALTH, FOOD SECURITY AND LIVELIHOODS.**



# Rift Valley fever (RVF) in humans

- causes mild, flu-like symptoms,
- but in a small percentage of cases, it can lead to:
  - severe complications such as **vision loss,**
  - **brain inflammation (encephalitis),**
  - **severe bleeding disorder (haemorrhagic fever)...**



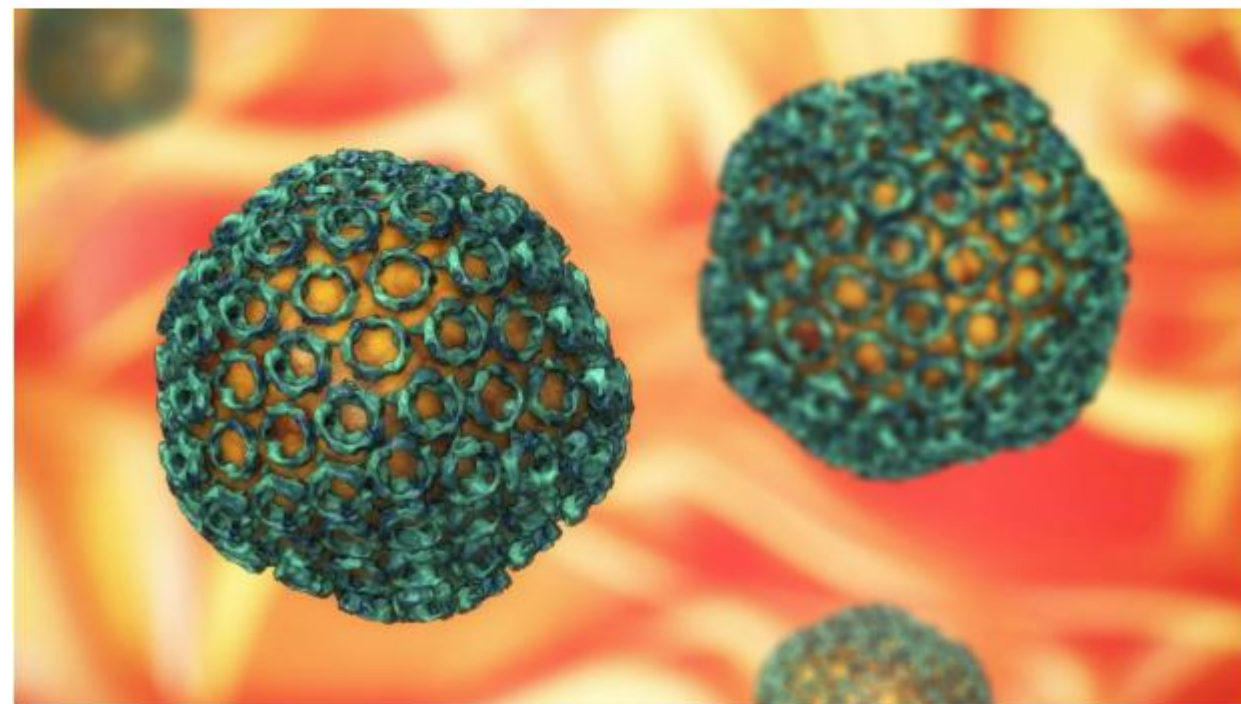
2025

October 13, OSLO, Norway, and NAIROBI, Kenya – A promising human vaccine candidate against the potentially deadly Rift Valley fever

- **Phase II trials in Kenya**
- **ChAdOx1** vaccine platform, the same technology behind the Oxford-AstraZeneca COVID-19 vaccine which has saved millions of lives worldwide.

## Promising human Rift Valley fever vaccine to enter Phase II clinical trials in Kenya

CEPI • 13th oktober 2024



# V. mRNA VACCINES

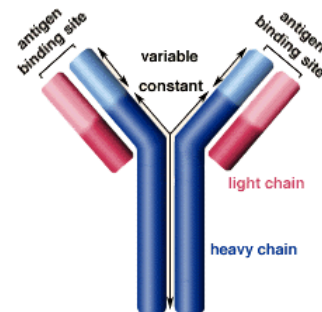
## Messenger RNA (mRNA) vaccines

**mRNA: short-lived strands of genetic material**

**→ prompt our cells to start making SARS-CoV-2 proteins**

**Immune systems develops antibodies (Abs)**

**...which in turn help our immune systems develop antibodies**



**LNPs - delivery technology**

**To protect the fragile molecule as it sneaks into cells:**

**lipid nanoparticles = LNPs**



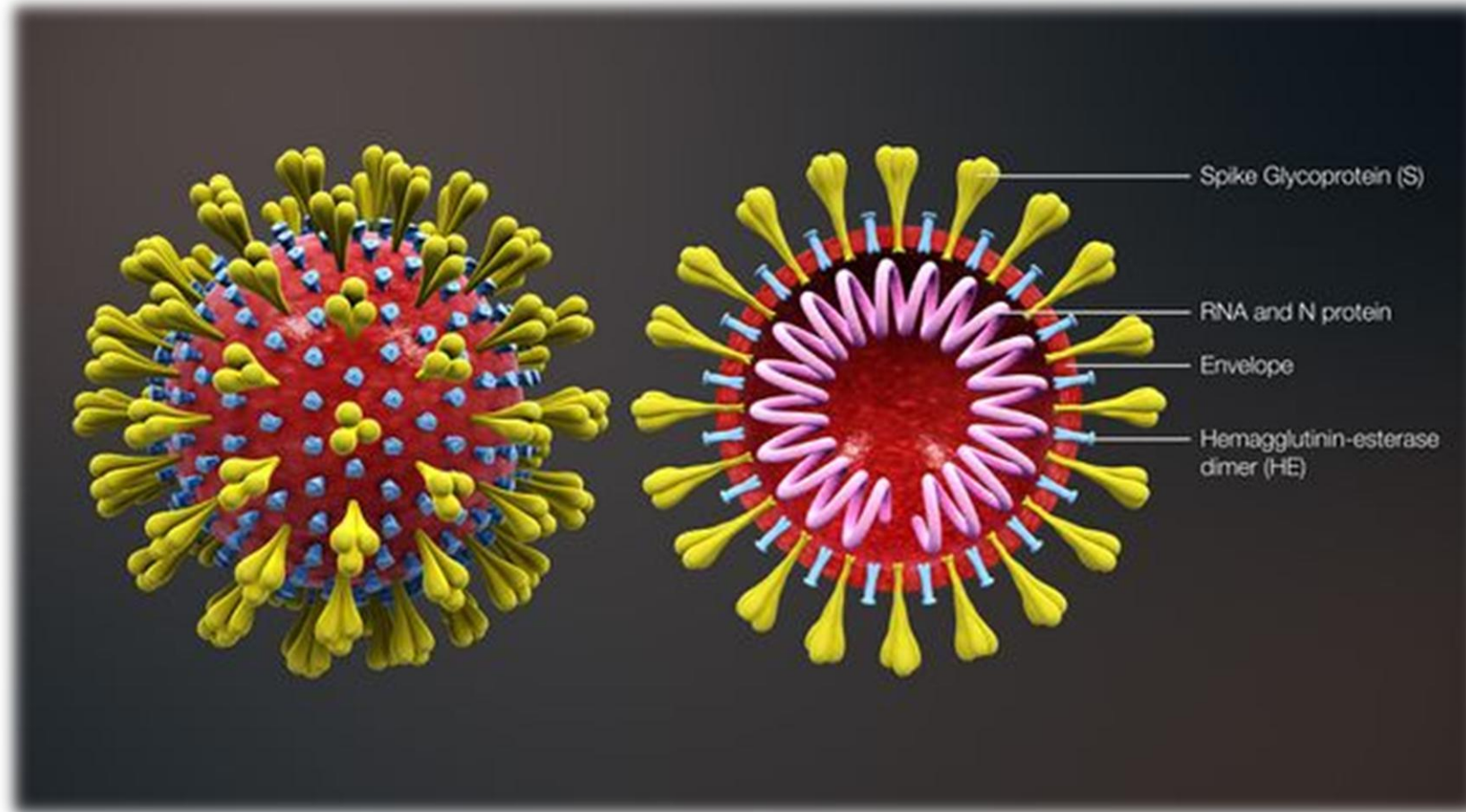
# Preparing for future pandemics

CEPI, the Coalition for Epidemic Preparedness Innovations, is a global partnership working to accelerate the development of vaccines and other biologic countermeasures against epidemic and pandemic threats.

## Global initiatives

- > e.g. WHO's R&D Blueprint and CEPI have prioritized these emerging threats
- > leading to new vaccine platforms (like mRNA and viral vectors) and rapid development timelines

# Coronaviruses



# MERS -Middle East Respiratory Syndrome (MERS-CoV)

- It was a Saturday in September **2012** when an unusual email arrived at
- ...a **British** infectious disease laboratory from a team of virologists in the **Netherlands**...
- The email contained details of a **MYSTERIOUS VIRAL PATHOGEN** that had been found in two patients many miles apart.



# MERS - Middle East Respiratory Syndrome (MERS-CoV)

- One was a **QATARI MAN** who at that time was in an intensive care unit at a British hospital
- The other was an elderly **SAUDI ARABIAN MAN** who had recently died in a hospital in Jeddah after suffering a severe bout of **pneumonia and then renal failure...**



# MERS -Middle East Respiratory Syndrome (MERS-CoV)



- Intrigued, the viral detectives set to work on deciphering the **pathogen's identity...**
- **WITHIN DAYS THE NEW VIRUS WAS CONFIRMED AS ONE NEVER SEEN BEFORE IN HUMANS!**
- **IT WAS A NOVEL CORONAVIRUS** —later to become known as the virus that causes Middle East Respiratory Syndrome, or MERS

# 3 highly pathogenic novel human viruses in the Coronavirus family...

- MERS was the second of 3 (three) highly pathogenic novel human viruses in the Coronavirus family
- The first, SARS-CoV-1, caused a disease known as Severe Acute Respiratory Syndrome, or SARS.
- **And the third, SARS-CoV-2, caused a disease called COVID-19, which swiftly became a global pandemic...**



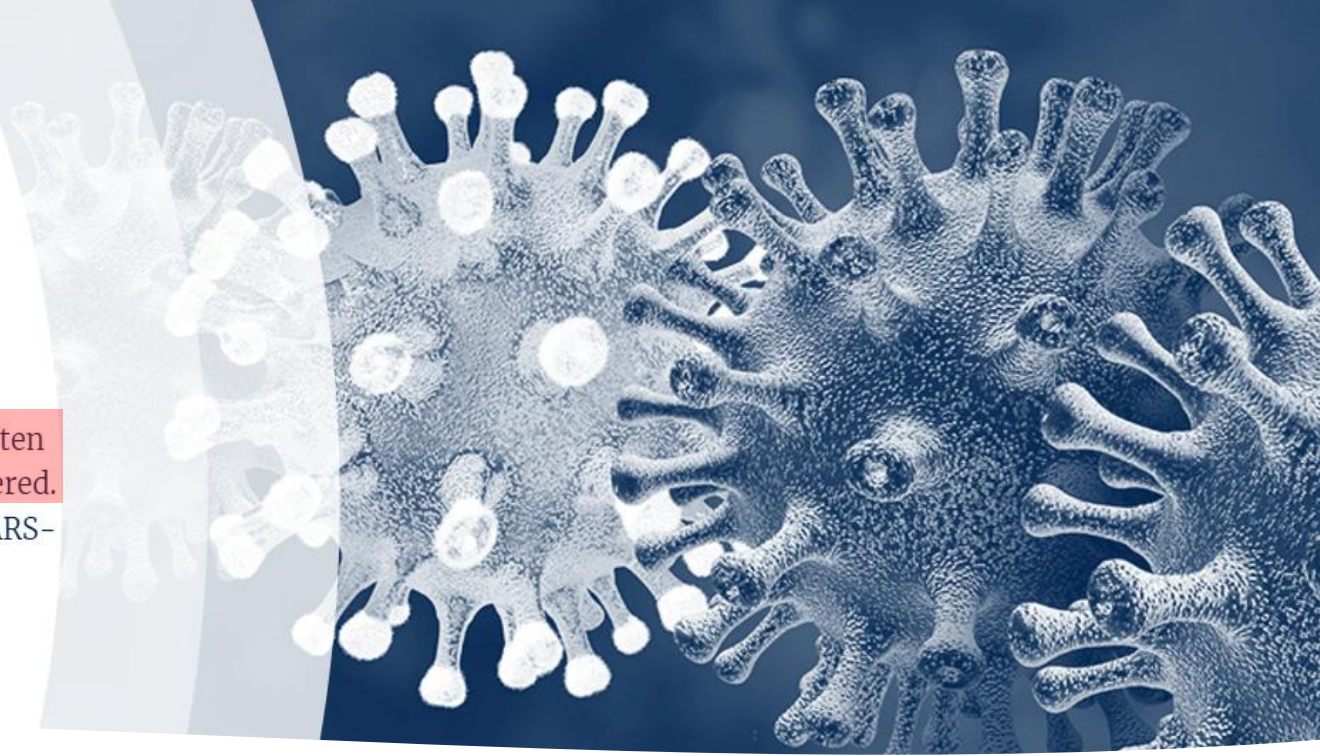
# Coronaviruses

Seven members of the coronavirus family are already known to infect people, often with deadly consequences, and novel coronaviruses are continuing to be discovered.

CEPI's coronavirus R&D investments focus on two of its priority pathogens—SARS-CoV-2 and MERS—as well as broadly protective coronavirus vaccines and the establishment of a coronavirus vaccine library.

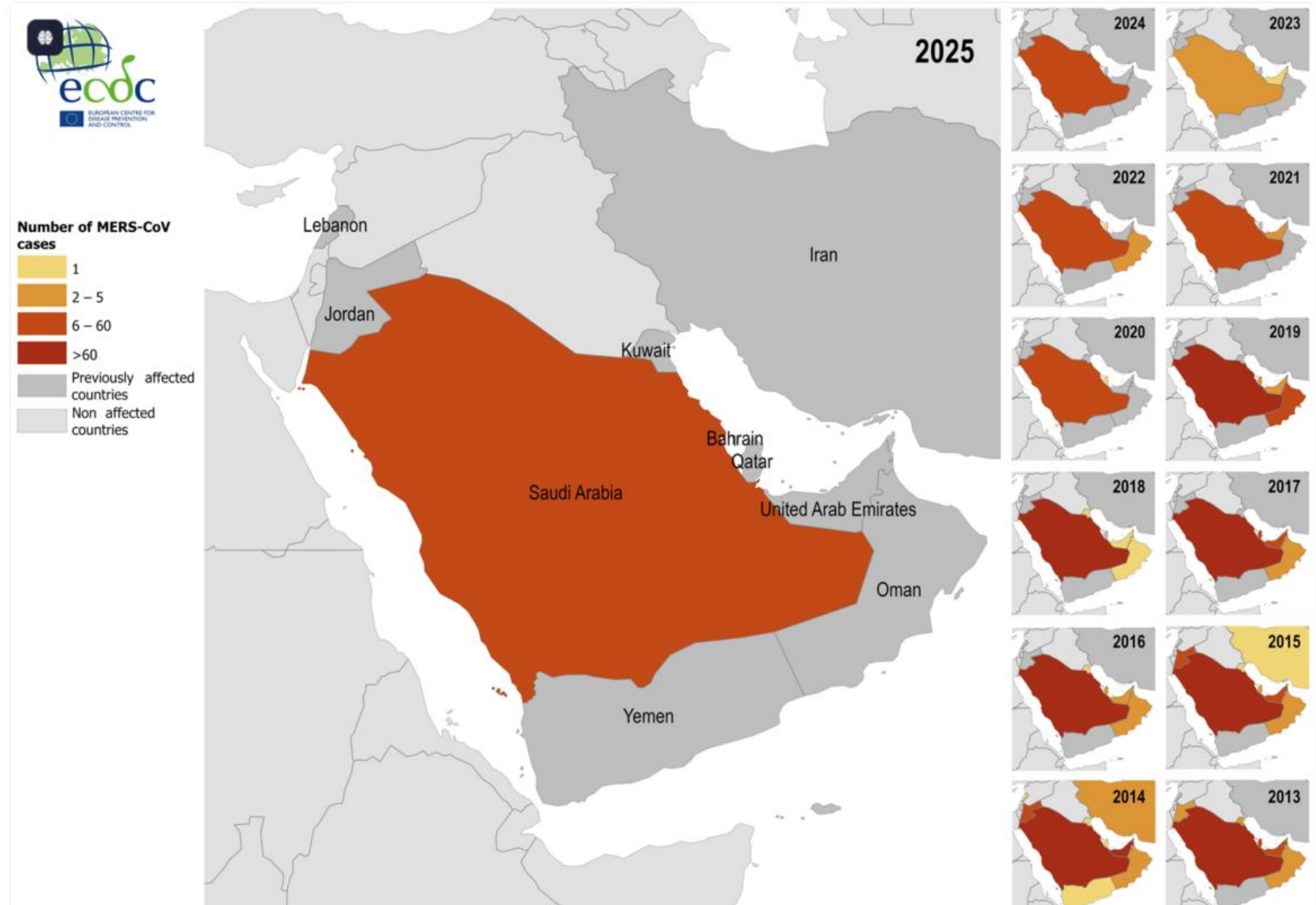
## Middle East Respiratory Syndrome (MERS-CoV)

**...NO VACCINE HAS BEEN APPROVED AGAINST IT SO FAR...**



# MERS

- MERS has caused sporadic outbreaks, mostly on the **Arabian Peninsula**
- A major hospital outbreak in **South Korea** in 2015)
- No vaccine is yet licensed for use...

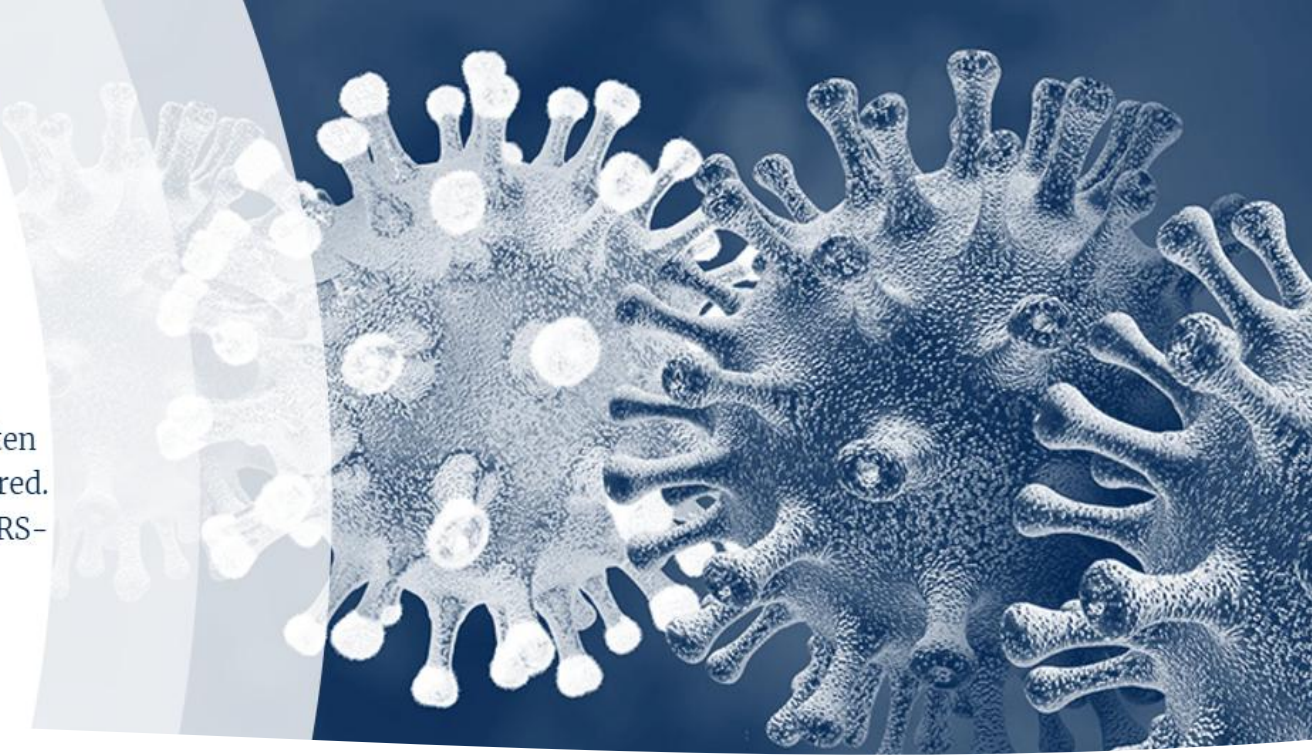


# MERS - no vaccine is yet licensed for use...

- Several vaccine candidates have been developed and tested in early trials over the past decade.
- A leading approach is a **viral-vectored vaccine** using a **chimpanzee adenovirus (ChAdOx1)** encoding the MERS coronavirus spike protein.
- **DNA vaccine** GLS-5300 (Inovio Pharmaceuticals in collaboration with international partners), completed a Phase 1 trial in the U.S. and advanced to Phase 1/2 studies in 2018
- **No MERS vaccine is approved for public use to date**

# Coronaviruses

Seven members of the coronavirus family are already known to infect people, often with deadly consequences, and novel coronaviruses are continuing to be discovered. CEPI's coronavirus R&D investments focus on two of its priority pathogens—SARS-CoV-2 and MERS—as well as broadly protective coronavirus vaccines and the establishment of a coronavirus vaccine library.



## **COVID-19 (SARS-CoV-2)**

-> caused by the novel coronavirus SARS-CoV-2, first identified in Wuhan, China in late 2019...

# COVID-19

Click on a country or territory to see cases, deaths, and recoveries.



[View charts and more data »](#)

TOTAL COUNTS (as of 2 minutes ago)

3,398 / 704 753 890 • DEATHS: 7,010,681 (0.99%) • RECOVERIES: 675,619,811 (95.87%) • VACCINATED: 5,631,263,739 (72.20%)

[MORE INFORMATION](#)

<https://www.covidvisualizer.com/>

# COVID-19 (SARS-CoV-2)

- The first vaccines authorized for emergency use were **mRNA-based vaccines** – notably Pfizer-BioNTech's BNT162b2 and Moderna's mRNA-1273 – in December 2020
- Other vaccine platforms: including **VIRAL VECTOR VACCINES** (e.g., the Oxford/AstraZeneca **ChAdOx1** nCoV-19 and Johnson & Johnson's Ad26.COV2.S, using **adenovirus** vectors
- ...and **inactivated whole-virus vaccines** (Sinopharm, Sinovac vaccines -China)
- A **PROTEIN SUBUNIT VACCINE** (Novavax NVX-CoV2373) was later authorized as well.

# V. mRNA VACCINES

In late 1987, Robert Malone performed a landmark experiment.

He mixed strands of messenger RNA with droplets of fat, to create a kind of molecular stew.

Human cells bathed in this genetic gumbo absorbed the mRNA, and began producing proteins from it

Human cells bathed in this genetic gumbo absorbed the mRNA, and began producing proteins from it



# V. mRNA VACCINES



If cells could create proteins from mRNA delivered into them - he wrote on 11 January 1988- , it might be possible to “treat RNA as a drug”

Later that year, Malone’s experiments showed that frog embryos absorbed such mRNA

It was the first time anyone had used fatty droplets to ease mRNA’s passage into a **LIVING ORGANISM (not just cells)**

Those experiments were a stepping stone towards two of the most important and profitable vaccines in history: the mRNA-based COVID-19 vaccines

# Messenger RNA (mRNA) vaccine

- The vaccine contains **messenger RNA (mRNA)** encoding a viral antigen (e.g., the spike protein of SARS-CoV-2).
- The mRNA is packaged in **lipid nanoparticles (LNPs) that facilitate entry** into host cells after intramuscular injection.
- Once inside the **cytoplasm**, the mRNA is translated by ribosomes into the encoded **viral antigen**.
- The mRNA **does not enter the nucleus and cannot integrate into the genome**.
- **It is rapidly degraded after translation.**

# Messenger RNA (mRNA) vaccine - antigen presentation

- The synthesized antigen is processed and presented via:
- MHC class I → activation of CD8<sup>+</sup> cytotoxic T cells
- MHC class II → activation of CD4<sup>+</sup> helper T cells

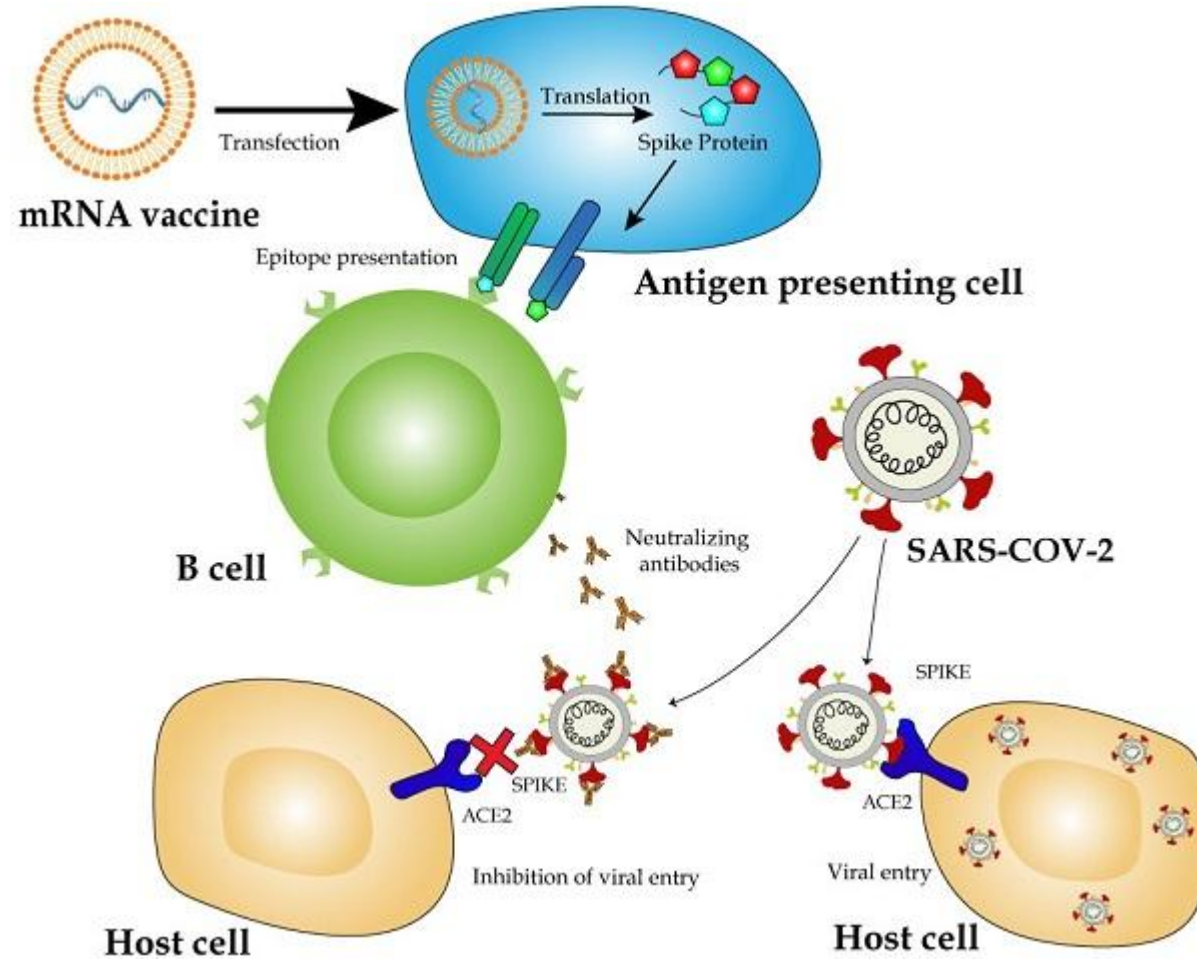
After a **successful vaccination**, the IgG subclasses produced depend on the **type of antigen and the T-helper cytokine environment...**

IgG1 -Most commonly induced IgG subclass after vaccination

IgG3- Also frequently produced during effective antiviral responses

IgG2 (less prominent)  
IgG4 (usually minimal)

# V. mRNA VACCINES



# V. mRNA VACCINES

- Short manufacturing times + low manufacturing costs.
- Have to be kept at low temperatures due to the fragility of the mRNA.
- mRNA vaccines work by triggering an immune response from proteins they synthesize.

# V. mRNA VACCINES

- They induce both cellular and humoral immunity.
- The first mRNA vaccine was approved for COVID-19.
- There is some misinformation that mRNA vaccines can alter a person's DNA, however, they are not able to do that ...

# Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

- Gram-negative bacteria include a number of pathogens that cause disease in humans and animals
  - Although antibiotics are still effective ....
  - **There is alarming increase of antimicrobial resistance (AMR) induced by excessive use of antibiotics**
  - Alternative strategies must be developed
- => OUTER MEMBRANE VESICLES (OMVS)**

## Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

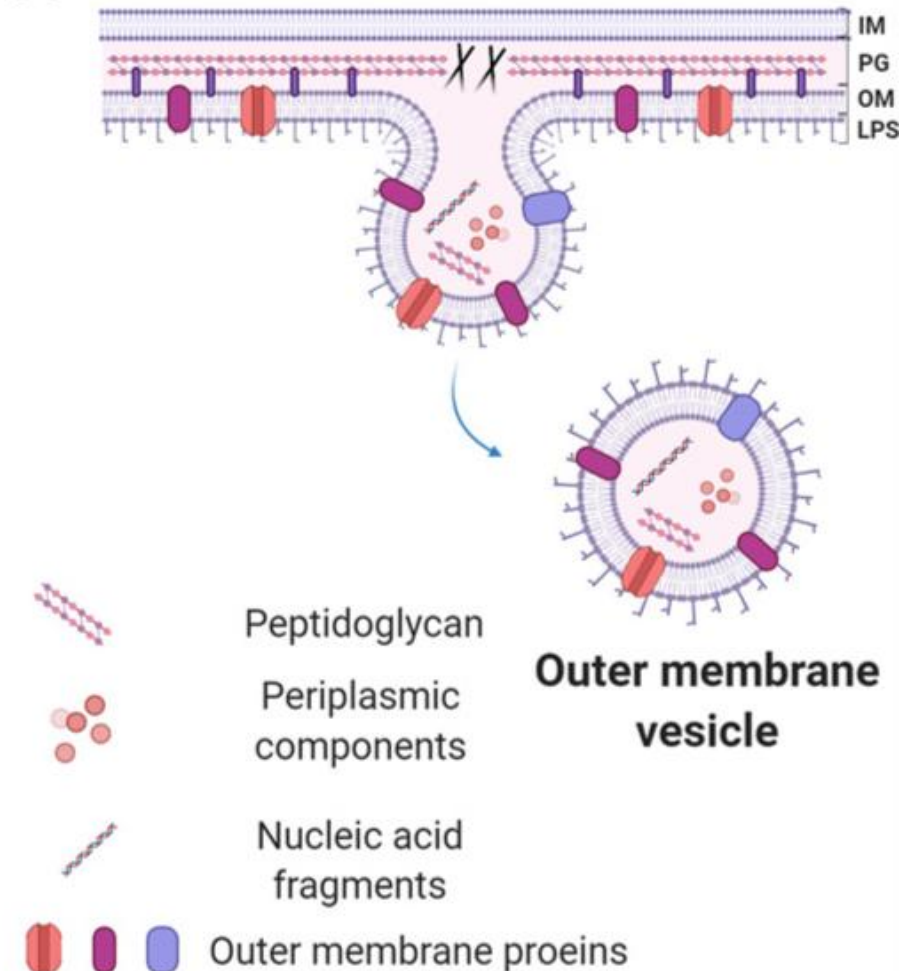
Naturally produced by Gram-negative bacteria,  
-> represent a promising and versatile tool that can be employed as:



**OUTER MEMBRANE VESICLES (OMVS) ARE SPHERICAL PARTICLES SECRETED BY ALL GRAM-NEGATIVE BACTERIA INVESTIGATED TO DATE !**

# Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

- The formation of OMVs starts from:
- ... the breakage of links between the **BACTERIAL OUTER MEMBRANE** and underlying **PEPTIDOGLYCAN (PG) LAYER**.
- The outer membrane then protrude to form **VESICULAR BUDS**,  
**...WHICH CONTINUOUSLY BULGE OUTWARDS UNTIL DETACHING!**
- => it gives rise to OMVs!

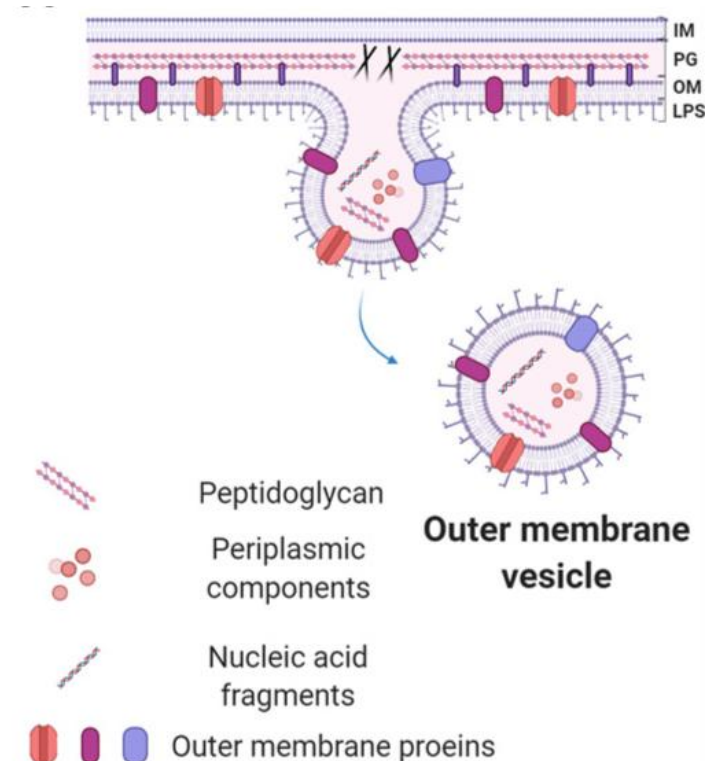


# Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

As protrusions of the parental cell's outer membrane

...OMVs inherit a composition similar to that of the outer membrane, consisting of:

- A. LIPOPOLYSACCARIDE (LPS),
- B. OUTER MEMBRANE PROTEINS (OMPS),
- C. PEPTIDOGLYCAN (PG).

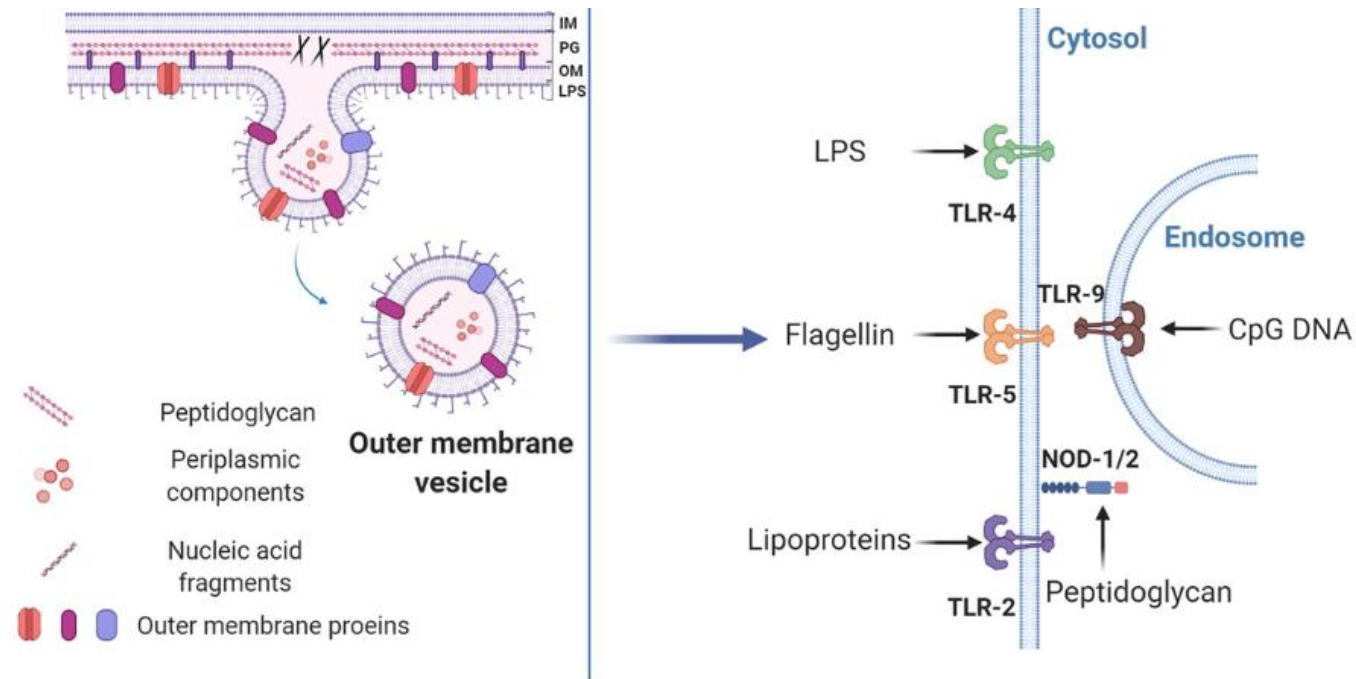


# Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

- It makes them small, non-live antigenic representations of the parent cell,
- including the surface complexity,
- in a way that vaccines made from recombinant proteins cannot!
- **THESE MOLECULES ARE PRESERVED IN NATIVE CONFORMATION!**

# Bacterial Outer Membrane Vesicles as a Versatile Tool in Vaccine Research

The structure of OMVs + ENCLOSED MOLECULES make them accessible to immune cells, endowing OMVs with inherent adjuvanticity and immunogenicity!



# Why OMVs are important - Summary

- Naturally immunogenic (TLR4, TLR2, TLR5 stimulation)
- Intrinsically adjuvanted (contain PAMPs)
- Present antigens in native conformation
- Excellent for mucosal vaccines (intranasal, oral)
- Easy to engineer

# Licensed OMV-based vaccines

## Neisseria meningitidis (MenB) – OMV vaccines

- a. Bexsero (4CMenB, GSK)
- b. MeNZB (New Zealand, epidemic vaccine)
- c. VA-MENGOC-BC (Cuba)

# Current OMV Vaccine Candidates (Preclinical / Clinical)

- 1. OMV-based COVID-19 vaccines
- 2. OMV-based Shigella vaccine
- 3. OMV-based Salmonella Typhi and Paratyphi vaccines
- 4. OMV-based ETEC (Enterotoxigenic E. coli) vaccines
- 5. OMV-based gonorrhea vaccines
- 6. OMV-based pneumococcal vaccine candidates
- 7. OMV-based cancer vaccines

**Major Global High-Security Virus  
Laboratories  
(BSL-4 Facilities)**

# Major Global High-Security Virus Laboratories (BSL-4 Facilities) and Their Focus Areas

A global overview of laboratories safeguarding and researching the world's most dangerous pathogens:

USA, Canada, UK, France, Russia, Switzerland, China, Australia, South Africa

# Major Global High-Security Virus Laboratories (BSL-4 Facilities) and Their Focus Areas

Why High-Security Laboratories:

Operate under WHO and national oversight for biosafety and global health preparedness!

# Major Global High-Security Virus Laboratories (BSL-4 Facilities) and Their Focus Areas

Diagnostics

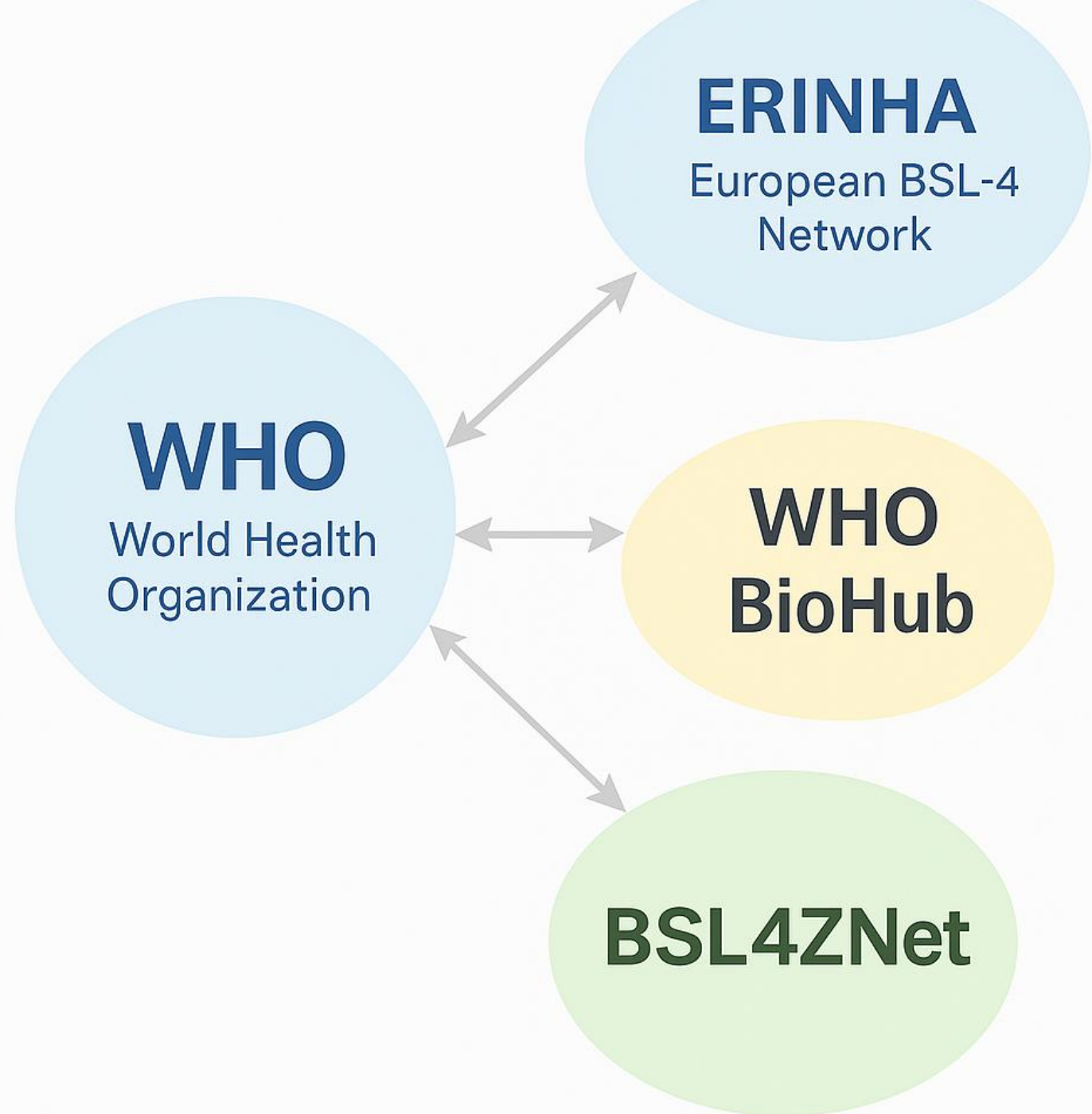
Surveillance

Vaccine + antiviral development

Outbreak response capacity

# International Networks and Oversight

- WHO Collaborating Centres for Variola and Viral Hemorrhagic Fevers (VHFs)
- BSL-4 Zoonotic Laboratory Network (BSL4ZNet)
- European BSL-4 Network (ERINHA)
- WHO BioHub (Spiez Laboratory)



# CDC (Atlanta, USA) - Centers for Disease Control and Prevention

- WHO Collaborating Centre for Smallpox & Poxviruses
- Holds official Variola (smallpox) stocks + Ebola, Marburg, Lassa, mpox

## Focus:

- public health reference lab
- vaccine and antiviral development
- outbreak diagnostics



# VECTOR Institute (Koltsovo, Russia) - State Research Center of Virology and Biotechnology “VECTOR”

- WHO Collaborating Centre for Orthopoxviruses (e.g. smallpox, cowpox, horsepox, camelpox, and mpox)
- Holds Variola virus (2nd official smallpox repository) + Ebola, Marburg, anthrax

## Focus:

- virology research
- vaccine/antiviral development
- high-security storage



# ВЕКТОР



# USAMRIID (Fort Detrick, USA) - U.S. Army Medical Research Institute of Infectious Diseases

- U.S. Department of Defense laboratory
- Holds Ebola, Marburg, Junín, Y. pestis, anthrax, and other Category A biothreats

Focus:

- biodefense,
- medical countermeasures,
- outbreak surge support



# NML (Winnipeg, Canada) - National Microbiology Laboratory (NML)

- Public Health Agency of Canada;
- BSL4ZNet core member
- Holds Ebola, Marburg, Lassa, Nipah, Hendra, CCHF (Crimean-Congo hemorrhagic fever - tick-borne virus that can cause severe illness with a high fatality rate)
- Developed rVSV-ZEBOV Ebola vaccine
- Provides outbreak mobile lab teams and WHO reference diagnostics



# Institut Pasteur / INSERM (Lyon, France)

- Institut Pasteur / INSERM BSL-4 Laboratory
- Member of ERINHA;
- WHO Reference Lab for Variola and Viral Hemorrhagic Fevers (VHFs)
- Holds Ebola, Marburg, Lassa, Nipah, Hendra, CCHF

## **Focus:**

- tropical disease research,
- pathogenesis,
- vaccine candidates,
- outbreak response in francophone Africa



# Porton Down (Wiltshire, UK) - UK Health Security Agency – Porton Down High Containment Labs

- Member of BSL4ZNet
- Historical smallpox work;
- Currently Ebola, Marburg, CCHF, tularemia

## Focus:

- emergency preparedness, diagnostics,
- vaccine testing for high-risk pathogens



# Spiez Laboratory (Switzerland) - WHO BioHub Facility

- Swiss Federal Institute for NBC Protection
- WHO pilot BioHub: neutral global repository for pandemic-threatening pathogens
- Holds SARS-CoV-2 variants, mpox;
- will expand to novel influenza and coronaviruses
- **Focus:**
  - secure storage,
  - global sharing,
  - rapid R&D access



# Wuhan Institute of Virology (China)

- Chinese Academy of Sciences;
- National Virus Resource Center
- Holds extensive bat coronavirus collection, plus clearance for Ebola, Nipah, etc.

## Focus:

- zoonotic virus discovery,
- spillover risk,
- antiviral development



# CSIRO (Geelong, Australia) - Australian Centre for Disease Preparedness (ACDP)

- National veterinary/zoonotic BSL-4 lab;
- BSL4ZNet member
- Holds Hendra, Nipah, lyssaviruses, avian influenzas, Ebola, Zika

## Focus:

- One Health research;
- developed Hendra horse vaccine;
- Asia-Pacific diagnostic hub





 **NATIONAL INSTITUTE FOR  
COMMUNICABLE DISEASES**  
Division of the National Health Laboratory Service

## NICD (Johannesburg, South Africa) National Institute for Communicable Diseases Special Pathogens Unit

- Historic WHO Collaborating Centre for VHF (Africa)
- **Holds Ebola, Marburg, Rift Valley fever and regional outbreak samples**

### Focus:

- outbreak diagnostics,
- hemorrhagic fever monitoring,
- regional capacity-building

Attendance sheet please ...

Thank you for you attention!