Old and new live vaccines in blood donors

Pierre Tiberghien
Etablissement Français du Sang, Paris
Université Marie et Louis Pasteur, Besançon

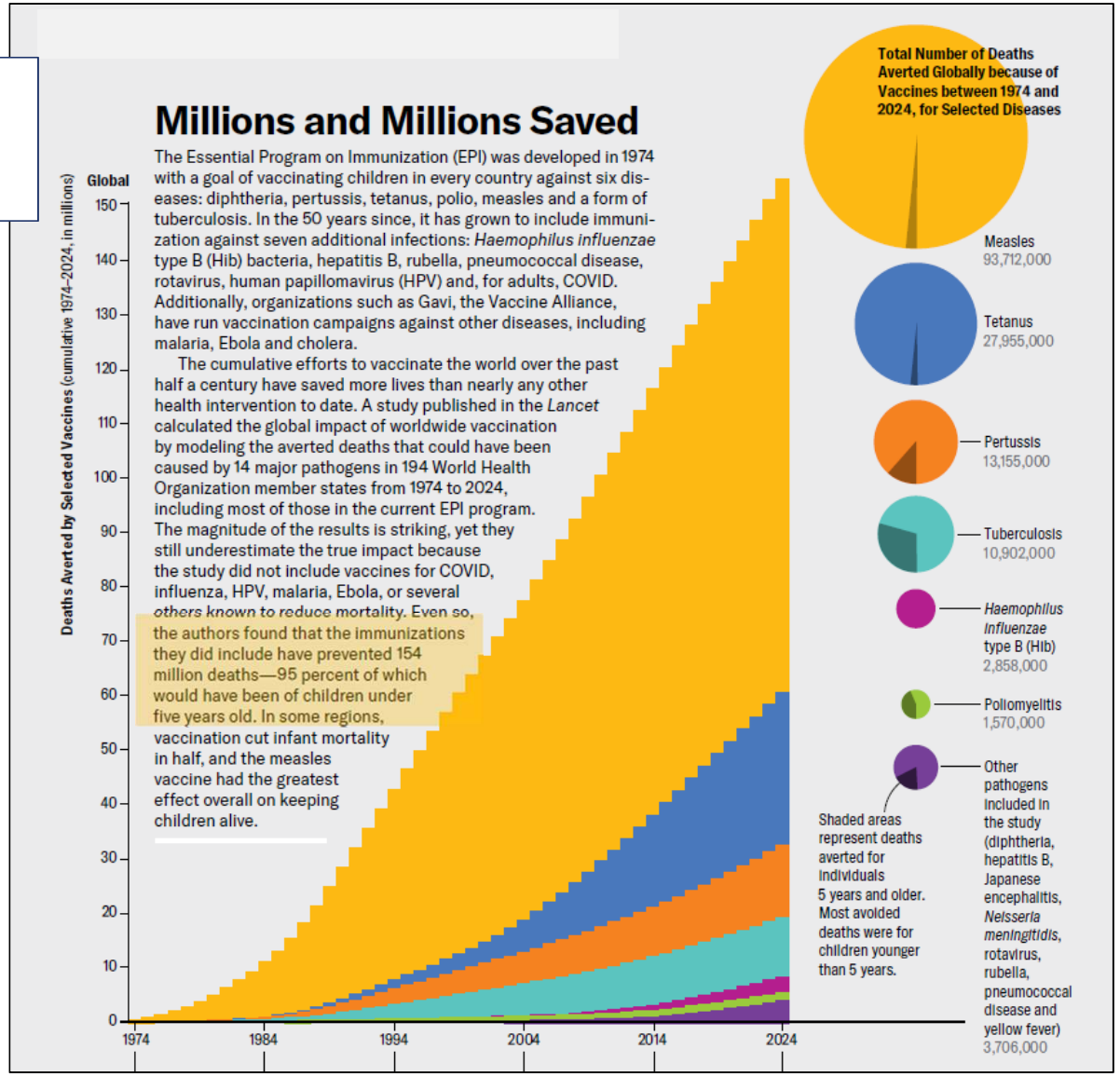


The Staggering Success of Vaccines

Hael et al, Nature, 2024

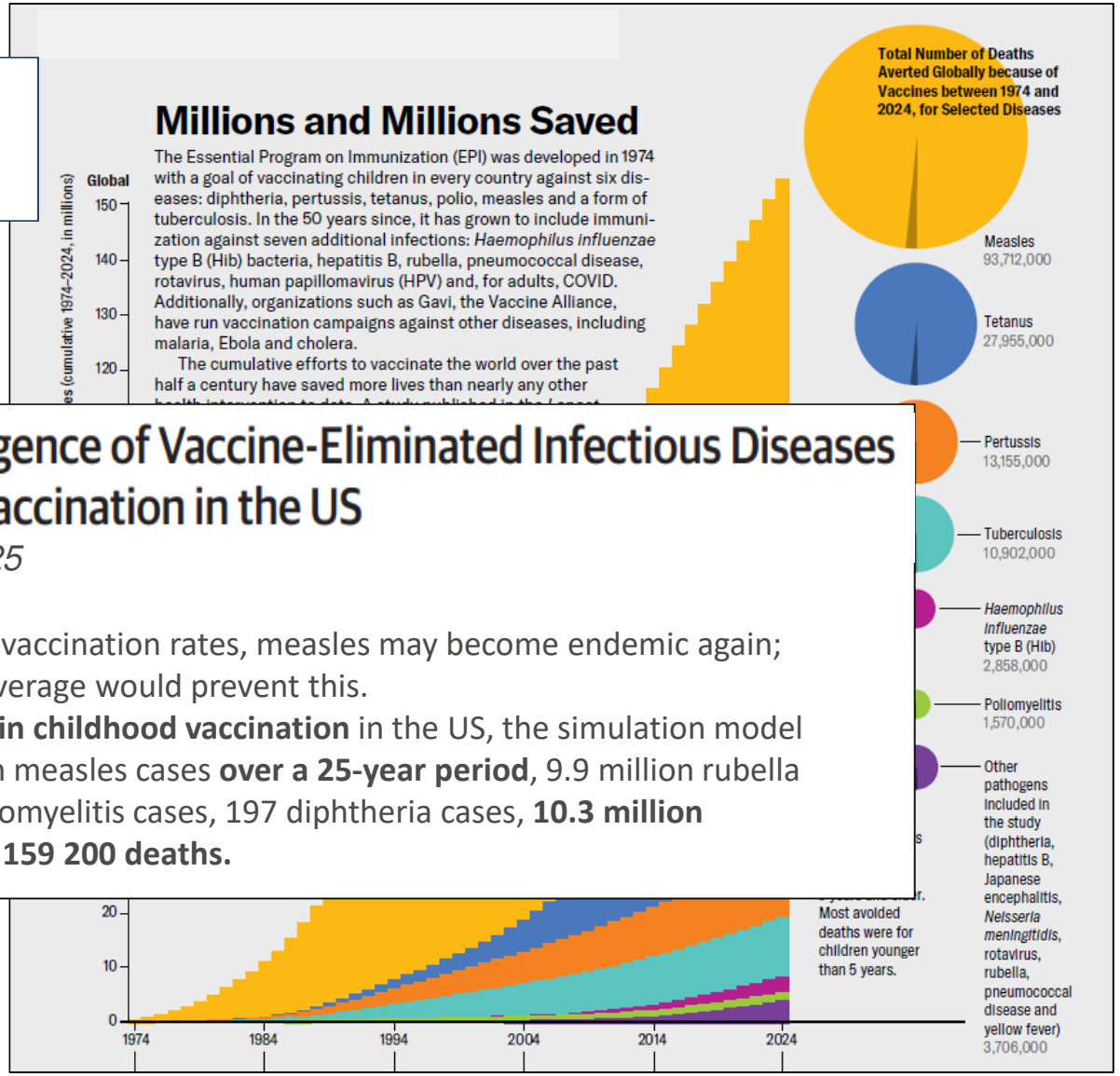
Contribution of Vaccination to Improved Survival and Health: Modelling 50 Years of the Expanded Programme on Immunization.

Shattock et al, Lancet, 2024



The Staggering Success of Vaccines

Hael et al, Nature, 2024



Contribution of Vacci
Survival and Health: I
of the Expanded Prog
Immunization.
Shattock et al, Lancet, 2

Modeling Reemergence of Vaccine-Eliminated Infectious Diseases Under Declining Vaccination in the US

Kiang et al, JAMA, 2025

- At current state-level vaccination rates, measles may become endemic again; increasing vaccine coverage would prevent this.
- Under a **50% decline in childhood vaccination** in the US, the simulation model predicted 51.2 million measles cases **over a 25-year period**, 9.9 million rubella cases, 4.3 million poliomyelitis cases, 197 diphtheria cases, **10.3 million hospitalizations, and 159 200 deaths.**

- May cause **disease in immunocompromised individuals**: may be contraindicated in such individuals
- May **cause transient asymptomatic viremia/bacteremia**: 2 to 4 week deferral for blood donation

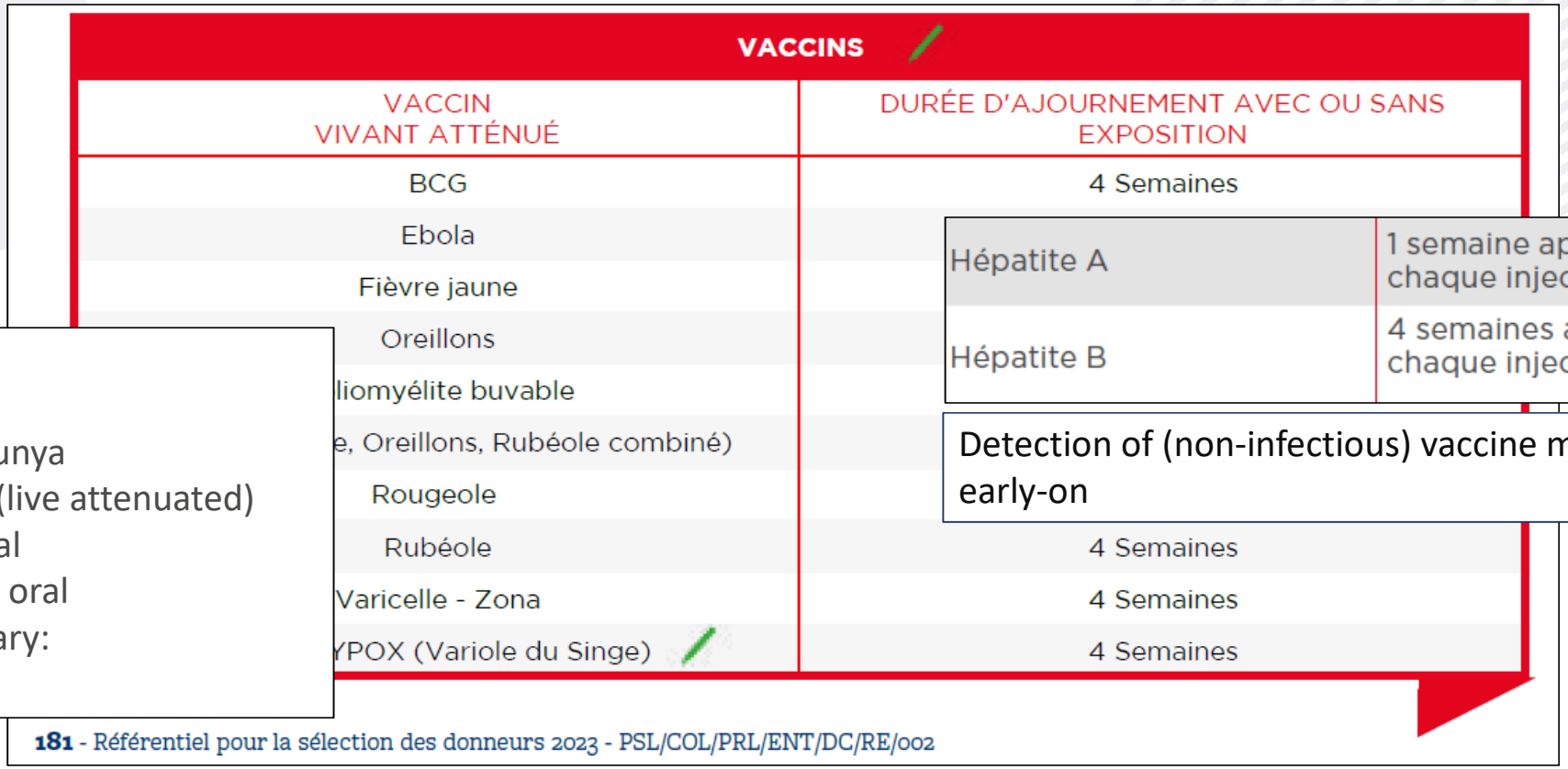
Vaccines	Old vaccines		New vaccines
Live	• Small Pox (Vaccinia virus, Dryvax) (discontinued)		
Live attenuated replicating	• Measles/Mumps/ Rubella (MMR) • Polio (oral) • Shingles (Zostavax®) • Tuberculosis (BCG)	• Small Pox (ACAM2000) • Varicella • Yellow Fever	• Chikungunya • Cholera (Vaxchora®) • Dengue • Ebola (rVSV-ZEBOV) • Typhoid (oral, Vivotif®)
Live attenuated localy replicating			• Influenza (intra-nasal vaccine
Live attenuated non-replicating			• Mpox • Ebola (Ad26.ZEBOV + MVA-BB-Filo)
Non-live (inactivated, recombinant, vectorized or mRNA)	• Cholera (Dukoral®), • Hepatitis A • Hepatitis B • Haemophilus dis. • Papillomavirus dis. • Influenza dis. • Japanese encephalitis	• Meningitis • Pertussis • Pneumoccal dis., • Polio (injected), • Rabies • COVID-19 • Tetanus • Typhoid (injected)	• Respiratory syncytial virus dis. • Shingles (Shingrix®), • Tick-born encephalitis

Blood donor deferral periods for vaccination, France

VACCINS	
VACCIN VIVANT ATTÉNUÉ	DURÉE D'AJOURNEMENT AVEC OU SANS EXPOSITION
BCG	4 Semaines
Ebola	4 Semaines
Fièvre jaune	4 Semaines
Oreillons	4 Semaines
Poliomyélite buvable	4 Semaines
ROR (Rougeole, Oreillons, Rubéole combiné)	4 Semaines
Rougeole	4 Semaines
Rubéole	4 Semaines
Varicelle - Zona	4 Semaines
MONKEYPOX (Variole du Singe)	4 Semaines

181 - Référentiel pour la sélection des donneurs 2023 - PSL/COL/PRL/ENT/DC/RE/002

Blood donor deferral periods for vaccination, France



VACCINS

VACCIN VIVANT ATTÉNUÉ	DURÉE D'AJOURNEMENT AVEC OU SANS EXPOSITION
BCG	4 Semaines
Ebola	
Fièvre jaune	
Oreillons	
liomyélite buvable	
e, Oreillons, Rubéole combiné)	
Rougeole	
Rubéole	4 Semaines
Varicelle - Zona	4 Semaines
YPOX (Variole du Singe)	4 Semaines

Hépatite A	1 semaine après chaque injection
Hépatite B	4 semaines après chaque injection

Detection of (non-infectious) vaccine material early-on

181 - Référentiel pour la sélection des donneurs 2023 - PSL/COL/PRL/ENT/DC/RE/002

Missing:

- Dengue
- Chikungunya
- Cholera (live attenuated)
- Polio, oral
- Typhoid, oral

Not necessary:

- MPox

Blood donor deferral periods for vaccination, elsewhere

Jacobs et al, BJH, 2021

Table 1. Recommended blood donation deferral periods.

Organization	Non-live vaccine	Live vaccine	Indeterminate
WHO[24]	• Up to 7 days for well donors • For symptomatic donors, 7 days after symptom resolution • Clinical trial – 28 days after receipt of the experimental vaccine unless the vaccine subsequently is authorized or licensed by the relevant regulatory authority and an alternative policy regarding donor deferral is established by that authority	• 28 days • Clinical trial – 12 months after receipt of the experimental vaccine unless the vaccine subsequently is authorized or licensed by the relevant regulatory authority	• 28 days
US FDA[25]	• No deferral period	• 14 days	• 14 days
AABB[26]	• No deferral period	• 14 days	• 14 days
Canadian Blood Services[15]	• No deferral period		
Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee[27]	• 7 days	• 28 days	
European Centre for Disease Prevention Control[28]	• No deferral period	• 28 days	• 28 days

WHO, World Health Organization; US FDA, United States Food and Drug Administration; AABB, formerly the American Association of Blood Banks.

Transmission of yellow fever vaccine virus through blood transfusion and organ transplantation in the USA in 2021: report of an investigation

Gould et al, Lancet microbe, 2023

- Four solid organ transplant recipients
- Encephalitis beginning 2–6 weeks after transplantation from a common organ donor
- Yellow fever virus (YFV) identified in cerebrospinal fluid of a recipient
- Confirmation of recent infection with YFV in all four recipients
- Identification of YFV RNA consistent with the 17D vaccine strain in brain tissue from one recipient
- No neurological recovery and death in 2 patients, recovery in the other 2 patients
- Organ donor transfused 3 days before organ procurement
- Yellow fever vaccination of an involved blood donor 6 days before blood donation.

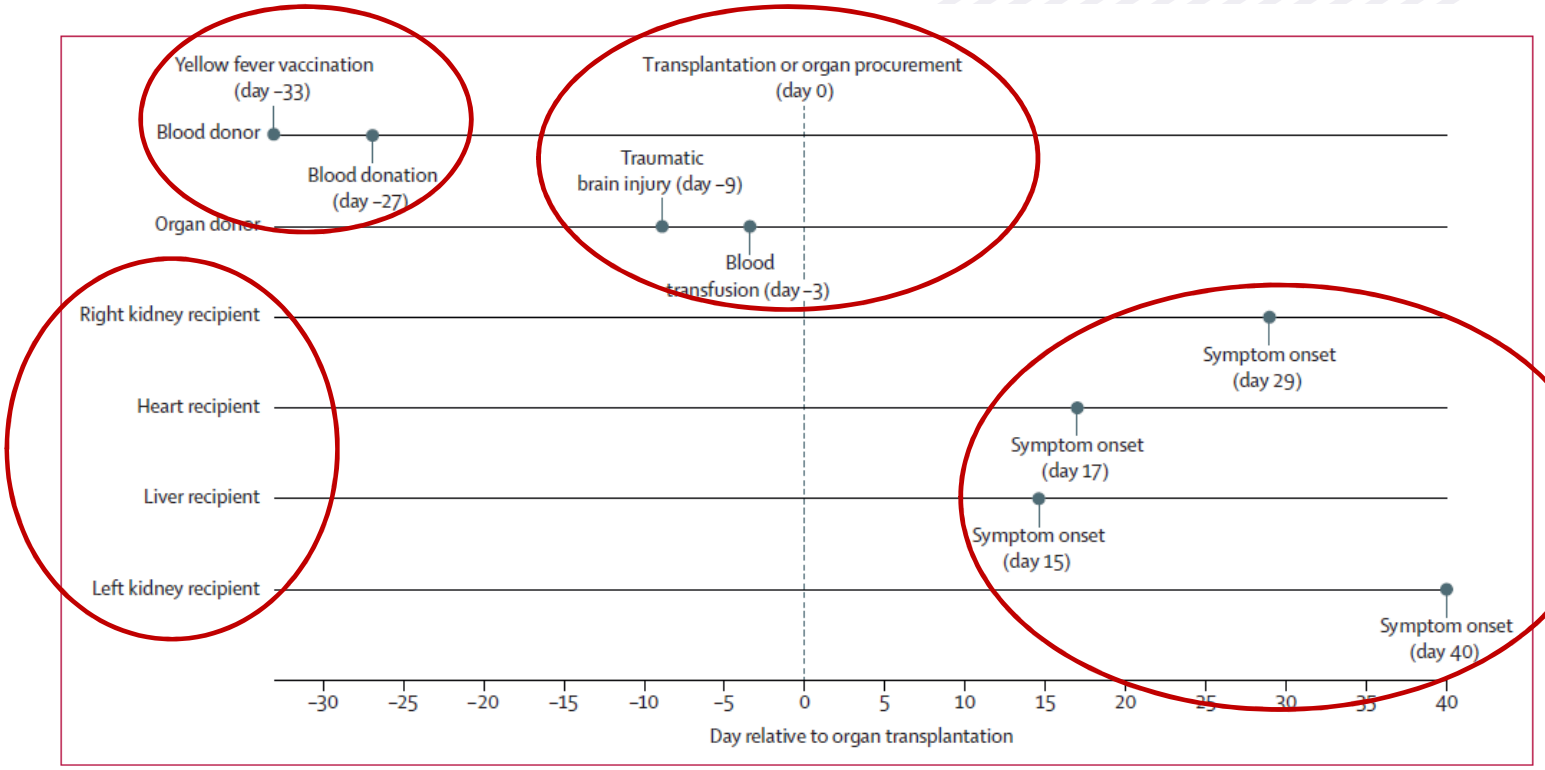


Figure 1: Timeline of events related to the transmission of yellow fever vaccine virus through blood transfusion and solid organ transplantation

Transmission of yellow fever vaccine virus through blood transfusion and organ transplantation in the USA in 2021: report of an in

Gould et al, Lancet r

- Four solid organ tra
- Encephalitis begin after transplantatio organ donor
- Yellow fever virus cerebrospinal fluid
- Confirmation of rec YFV in all four recipi
- Identification of YF with the 17D vacci tissue from one rec
- No neurological re in 2 patients, recov patients
- Organ donor transf organ procurement
- Yellow fever vaccination of an involved blood donor 6 days before blood donation.

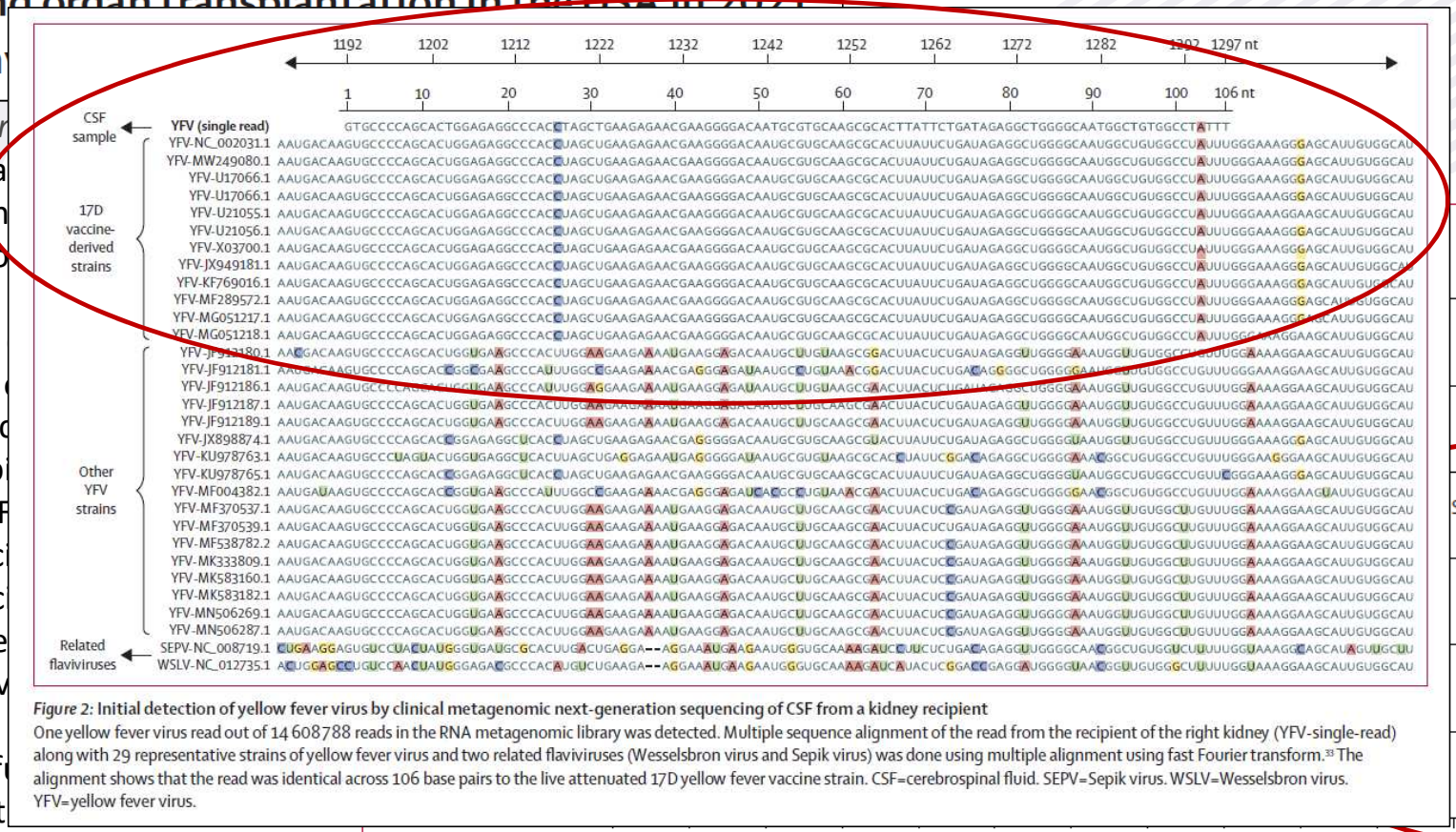


Figure 2: **Initial detection of yellow fever virus by clinical metagenomic next-generation sequencing of CSF from a kidney recipient**
One yellow fever virus read out of 14 608 788 reads in the RNA metagenomic library was detected. Multiple sequence alignment of the read from the recipient of the right kidney (YFV-single-read) along with 29 representative strains of yellow fever virus and two related flaviviruses (Wesselsbron virus and Sepik virus) was done using multiple alignment using fast Fourier transform.[33] The alignment shows that the read was identical across 106 base pairs to the live attenuated 17D yellow fever vaccine strain. CSF=cerebrospinal fluid. SEPV=Sepik virus. WSLV=Wesselsbron virus. YFV=yellow fever virus.

Figure 1: **Timeline of events related to the transmission of yellow fever vaccine virus through blood transfusion and solid organ transplantation**

Transfusion-Related Transmission of Yellow Fever Vaccine Virus — California, 2009

Lederman et al, MMWR, 2010

TABLE. Selected characteristics, clinical outcomes, and laboratory findings of five patients exposed to blood products from donors recently vaccinated with yellow fever vaccine — California, 2009*

Age	Sex	Previous yellow fever vaccine (year)	Blood product received (quantity)	Underlying medical conditions	Symptoms and laboratory abnormalities†	Serologic evaluation: Yellow fever virus IgM ELISA / PRNT§	Serologic evaluation: No. of days post-transfusion
Premature infant (24 wks estimated gestational age)¶	Female	No	Irradiated red blood cells (4 aliquots; 30 cc total)	Prematurity, intraventricular hemorrhage	None	Negative / Not done	37
6 yrs	Male	No	Irradiated platelets (1 unit)	Wilm's tumor (relapsed), recent chemotherapy	None	Positive / 160	36
66 yrs	Male	Yes (1964)	Platelets (1 unit)	Kidney/liver transplant (2005) , diabetes, history of alcohol abuse	None	Positive / 160	33
58 yrs	Male	Yes (1975, 1986)	Fresh frozen plasma (2 units)	Chronic renal insufficiency, peritoneal and pulmonary tuberculosis, psoriasis (received infliximab >2 mos before)	None	Positive / 40,960	26
82 yrs	Male	Yes (1959, 1965)	Irradiated platelets (1 unit)	Diffuse large B cell lymphoma s/p chemotherapy and radiation treatment, prostate carcinoma	Deceased**	Premortem specimen not available for testing	—

* Based on electronic medical record review.
† In the 30 days after blood product transfusion (e.g., fever, rigors, headache, meningismus, paralysis, and mental status changes, and abnormalities in white blood cell count, transaminases, or cerebral spinal fluid [if clinically indicated]).
§ Immunoglobulin M enzyme-linked immunosorbent assay result and plaque reduction neutralization test titer.
¶ Received blood products during days 2, 4, 6, and 9 of life.
** Patient was discharged to inpatient hospice for underlying malignancy and died 20 days after receiving blood products. An autopsy was not performed.

- Blood donation from 89 U.S. active duty trainees who had received Yellow Fever vaccine 4 days before donation
- Six units of blood components transfused into five patients.
- No clinical evidence or laboratory abnormalities consistent with a serious adverse reaction in 4 evaluable patients
- Evidence of serologic response to Yellow Fever vaccine virus in 3 patients.

«Old» live attenuated vaccines on the rise in adults

NEJM, 2017



European Centre for Disease Prevention and Control
An agency of the European Union

Enter your keyword(s)

Infectious disease topics | Publications and data | Training and tools | About ECDC

Home > About ECDC > Media centre > Measles on the rise again in Europe: time to check your vaccination status

Media centre

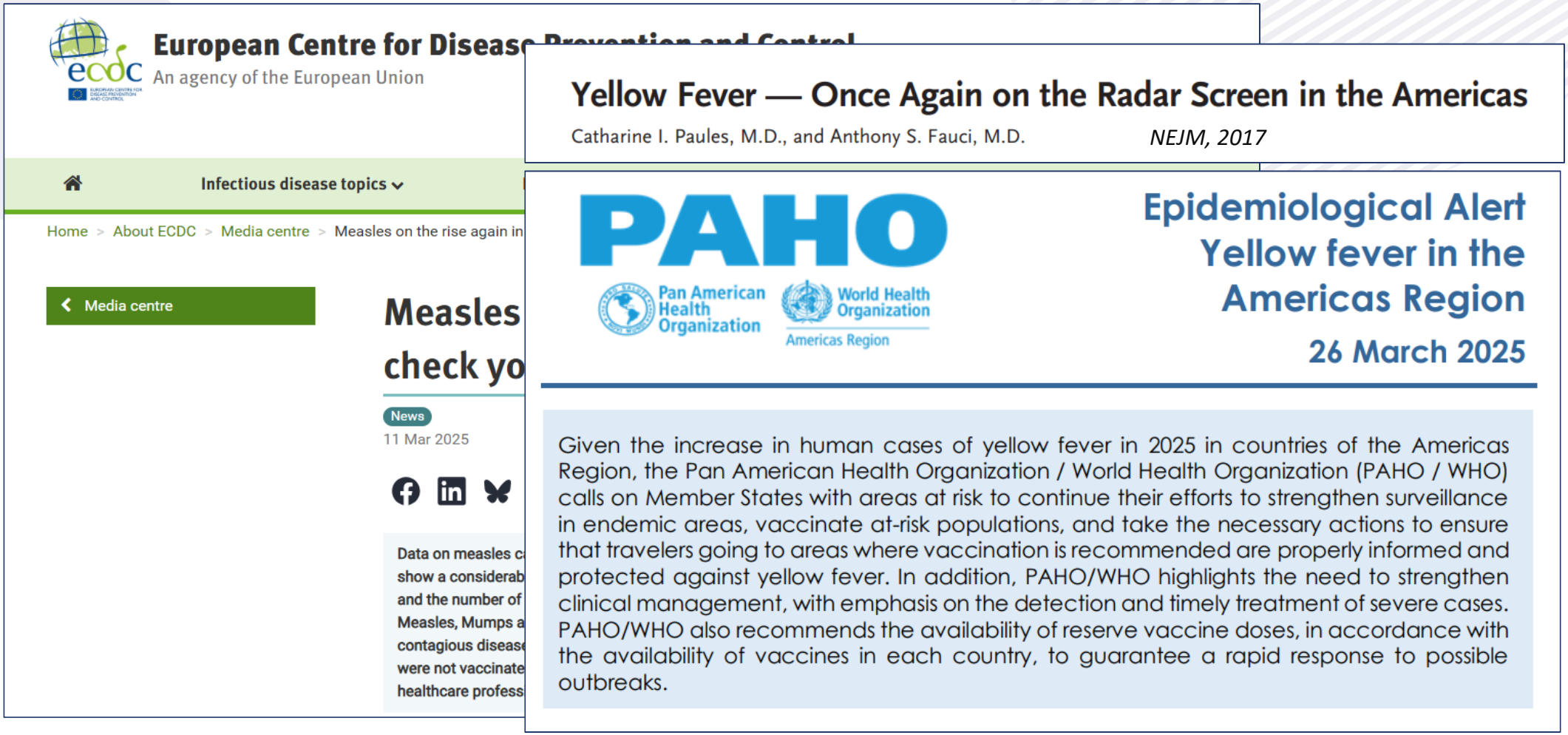
Measles on the rise again in Europe: time to check your vaccination status

News
11 Mar 2025

Translate this page

Data on measles cases in the European Union and European Economic Area (EU/EEA) for the last twelve months show a considerable rise in notifications compared to 2023. This indicates that the virus is circulating in the region and the number of cases will probably increase during the spring of 2025. Immunisation with two doses of the Measles, Mumps and Rubella (MMR) vaccine is the safest and most effective way to protect against this highly contagious disease. However, eight out of ten people who were diagnosed with measles in the EU/EEA in the last year were not vaccinated. Adults and parents are encouraged to check their vaccination history and, if in doubt, consult a healthcare professional.

«Old» live attenuated vaccines on the rise in adults



European Centre for Disease Prevention and Control
An agency of the European Union

Infectious disease topics

Home > About ECDC > Media centre > Measles on the rise again in

Media centre

Measles
check yo

News
11 Mar 2025

Data on measles c
show a considerab
and the number of
Measles, Mumps a
contagious disease
were not vaccinate
healthcare profess

Yellow Fever — Once Again on the Radar Screen in the Americas

Catharine I. Paules, M.D., and Anthony S. Fauci, M.D. *NEJM, 2017*

PAHO
Pan American Health Organization
World Health Organization
Americas Region

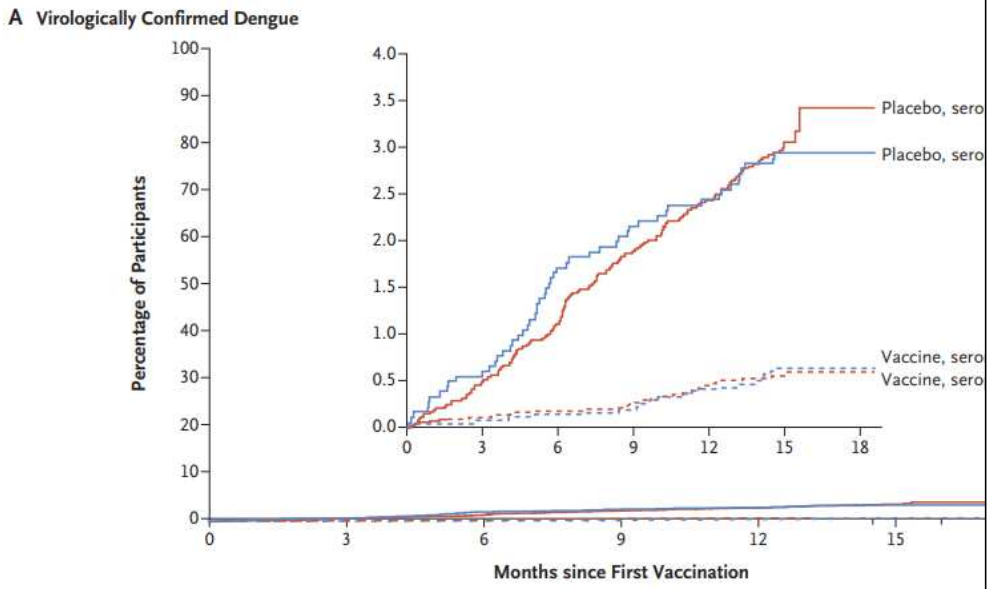
Epidemiological Alert
Yellow fever in the Americas Region
26 March 2025

Given the increase in human cases of yellow fever in 2025 in countries of the Americas Region, the Pan American Health Organization / World Health Organization (PAHO / WHO) calls on Member States with areas at risk to continue their efforts to strengthen surveillance in endemic areas, vaccinate at-risk populations, and take the necessary actions to ensure that travelers going to areas where vaccination is recommended are properly informed and protected against yellow fever. In addition, PAHO/WHO highlights the need to strengthen clinical management, with emphasis on the detection and timely treatment of severe cases. PAHO/WHO also recommends the availability of reserve vaccine doses, in accordance with the availability of vaccines in each country, to guarantee a rapid response to possible outbreaks.

« New » live attenuated vaccines on the rise as well

Efficacy of a Tetravalent Dengue Vaccine in Healthy Children and Adolescents

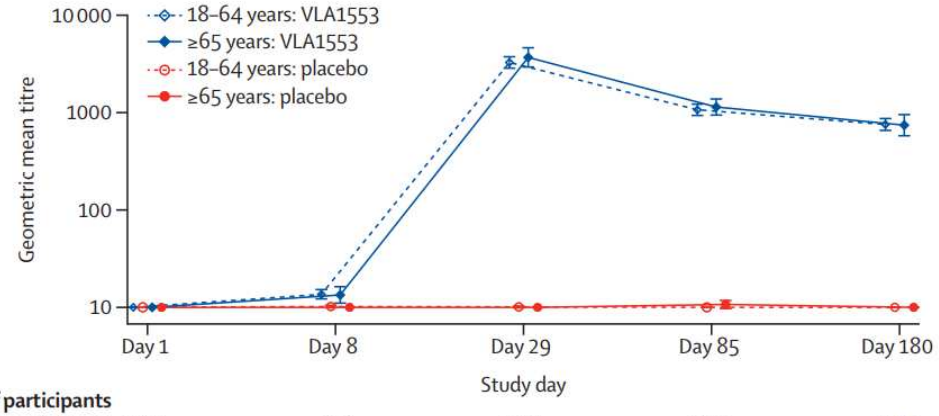
Kallas et al, NEJM, 2019 TAK-003 (Qdenga), Takec



No. of Participants					
Placebo					
Seronegative	1832	1817	1755	1744	94
Seropositive	4852	4805	4637	4607	218
Vaccine					
Seronegative	3714	3690	3625	3615	157
Seropositive	9661	9591	9412	9391	417

Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial

Schneider et al, Lancet, 2023 Ixchiq, Valvena Austria



Number of participants					
18–64 years: VLA1553	207	198	207	194	184
18–64 years: placebo	73	70	73	69	68
≥65 years: VLA1553	59	53	59	52	58
≥65 years: placebo	23	23	23	22	23

Blood donor found positive for Chikungunya virus (ChikV) in a non-endemic region

- Blood donation positive for ChikV by NAT screening (ArboPlex, Griffols)
- Chikungunya vaccination (Ixchiq) in the donor 30 days before donation
- Donor asymptomatic throughout
- Positive PCR with probes specific for the vaccine strain
- Negative PCR with probes specific for the wild-type strain
- Donor apparently seronegative (IgM and IgG) at time of donation
- Blood components from the donation
  - ✓ RBC: destroyed
  - ✓ Platelet (pathogen-reduced buffy coat): transfused
- Platetet recipient: no relevant clinical symptoms, negative PCR and IgM, IgG positive 2,5 months after transfusion

FDA, 2023: Vaccine Ixchiq viremia occurs in the first week following vaccination with resolution of viremia by 14 days after vaccination

Diapositive 14

PT1 Pierre Tiberghien; 11/05/2025

Blood donor found positive for Chikungunya virus (ChikV) in a non-endemic region

- Blood donation positive for ChikV by NAT screening (ArboPlex, Griffols)
- Chikungunya vaccination (Ixchiq) in the d

Dengue and Chikungunya

- Subcutaneous inoculation of a wild type virus + mosquito saliva (mosquito bite): highly infectious
- Subcutaneous inoculation of an attenuated virus (vaccination, no adjuvant): rare reported cases of vaccine-transmitted infection
- Intra-venous (transfusion-mediated) « inoculation » of the wild type virus: no to rare reported occurrence of transfusion-transmitted infection
- Intra-venous (transfusion-mediated) « inoculation » of the vaccine attenuated virus: rare occurrence of as well ?

Nevertheless: a 2 week (USA) or 4 week (Europe, WHO) deferral period for blood donation may be insufficient.

April 25th, 2025

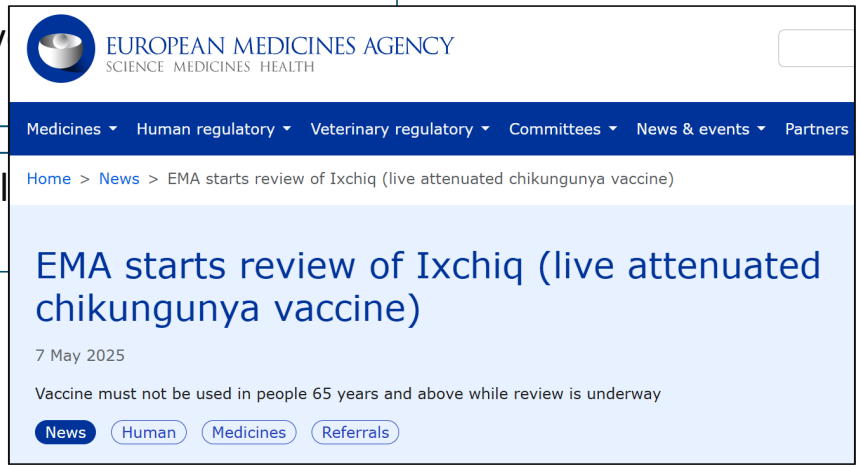
- ANSM, France
- Suspended use of Ixchiq in persons aged 65 years and older
- In response to an ongoing investigation of three cases of serious adverse events (ChikV like disease), including one death, in individuals over 80 years old with pre-existing comorbidities.

coat): transfused

symptoms, negativ

n the first week fol

r vaccination



Diapositive 15

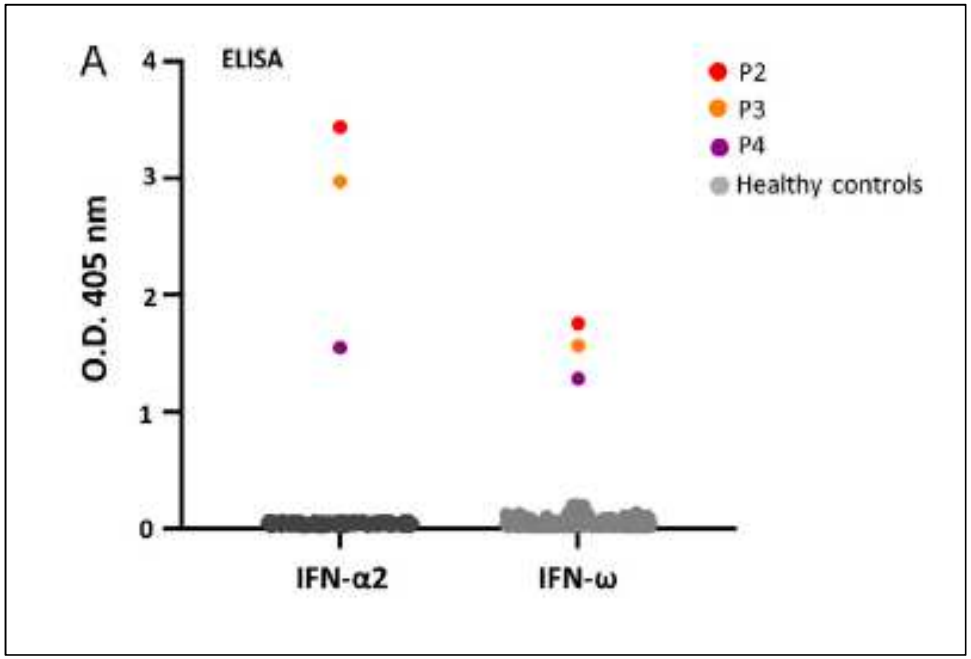
PT1 Pierre Tiberghien; 11/05/2025

Could some vaccinated donors be « riskier » than others?

Auto-antibodies to type I IFNs can underlie adverse reactions to yellow fever live attenuated vaccine

Bastard et al, JEM, 2021

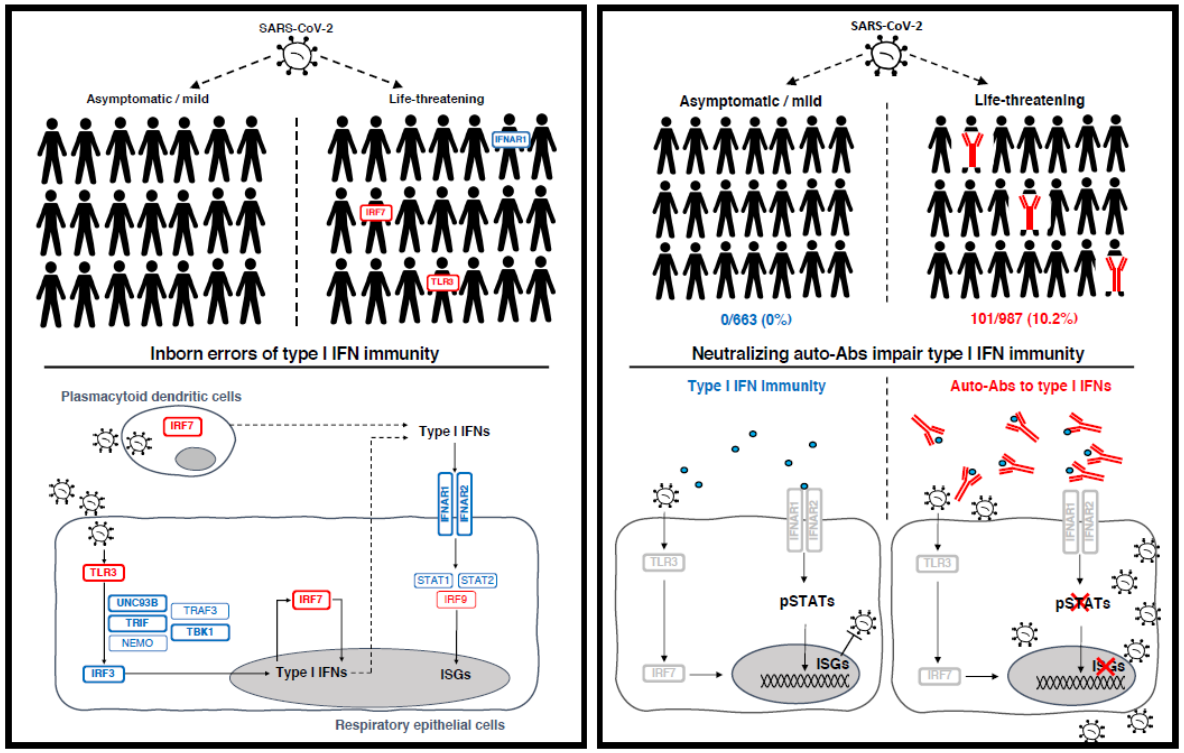
- Yellow fever virus (YFV) live attenuated vaccine can, in rare cases (0.3 to 0.8 / 100 000 vaccines), cause life-threatening disease in individuals with no previous history of severe viral illness.
- In 7 previously healthy individuals with unexplained life-threatening YFV vaccine - associated disease:
  - ✓ One 13-yr-old patient had autosomal recessive complete type 1 IFNs receptor gene deficiency.
  - ✓ Three other patients vaccinated at the ages of 47, 57, and 64 yr had high titers of circulating auto-Abs to type 1 IFNs
- The auto-Abs were neutralizing in vitro, blocking the protective effect of IFN-α2 against YFV vaccine strains.



Could some vaccinated donors be « riskier » than others?

Cite as: P. Bastard *et al.*, *Science* 10.1126/science.abd4585 (2020).

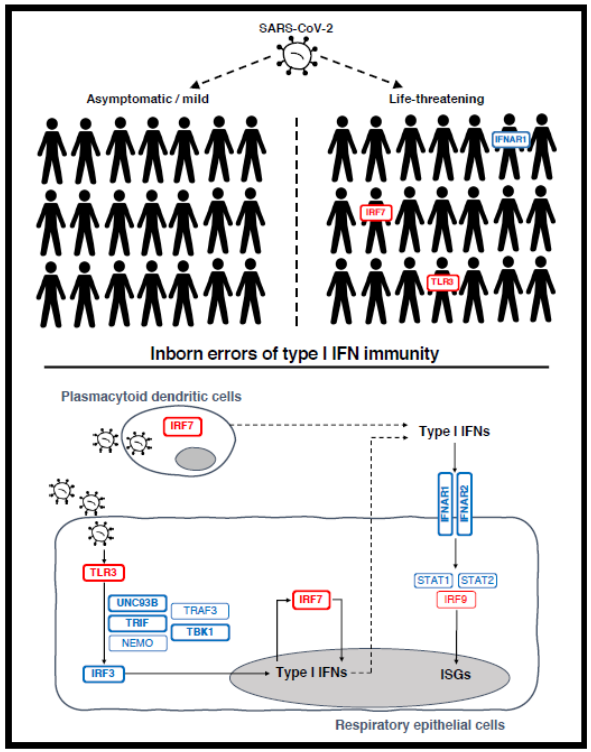
Auto-antibodies against type I IFNs in patients with life-threatening COVID-19

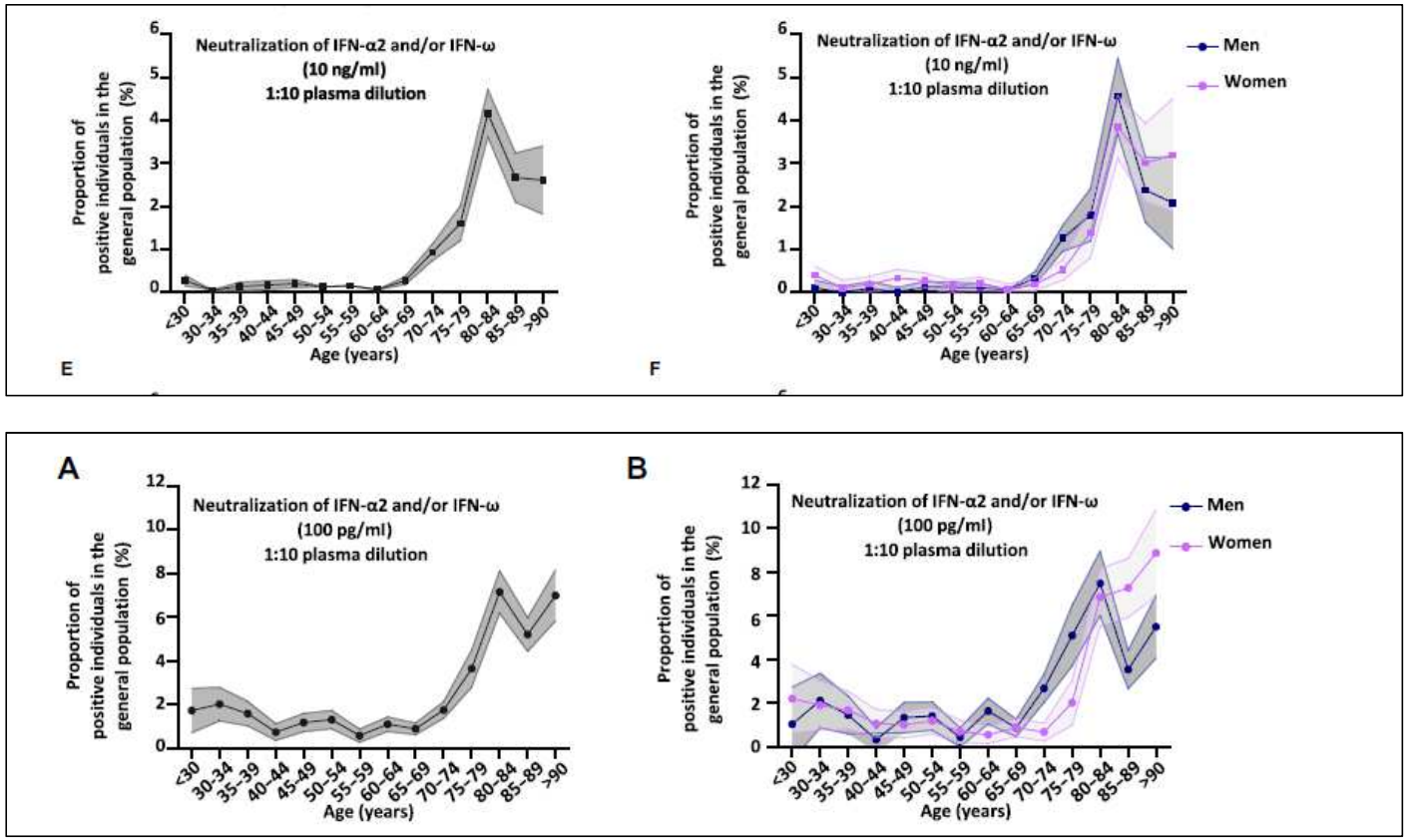


Could some vaccinated donors be « riskier » than others?

Cite as: P. Bastard *et al.*, *Science*
10.1126/science.abd4585 (2020).

Auto-antibodies against type I IFNs in patients with life-threatening COVID-19





Bastard et al, Science Immunol, 2021

Transplant recipients at risk of vaccine-related transfusion-transmitted infection

Transmission of yellow fever vaccine virus through blood transfusion and organ transplantation in the USA in 2021: report of an investigation

Gould et al, Lancet microbe, 2024

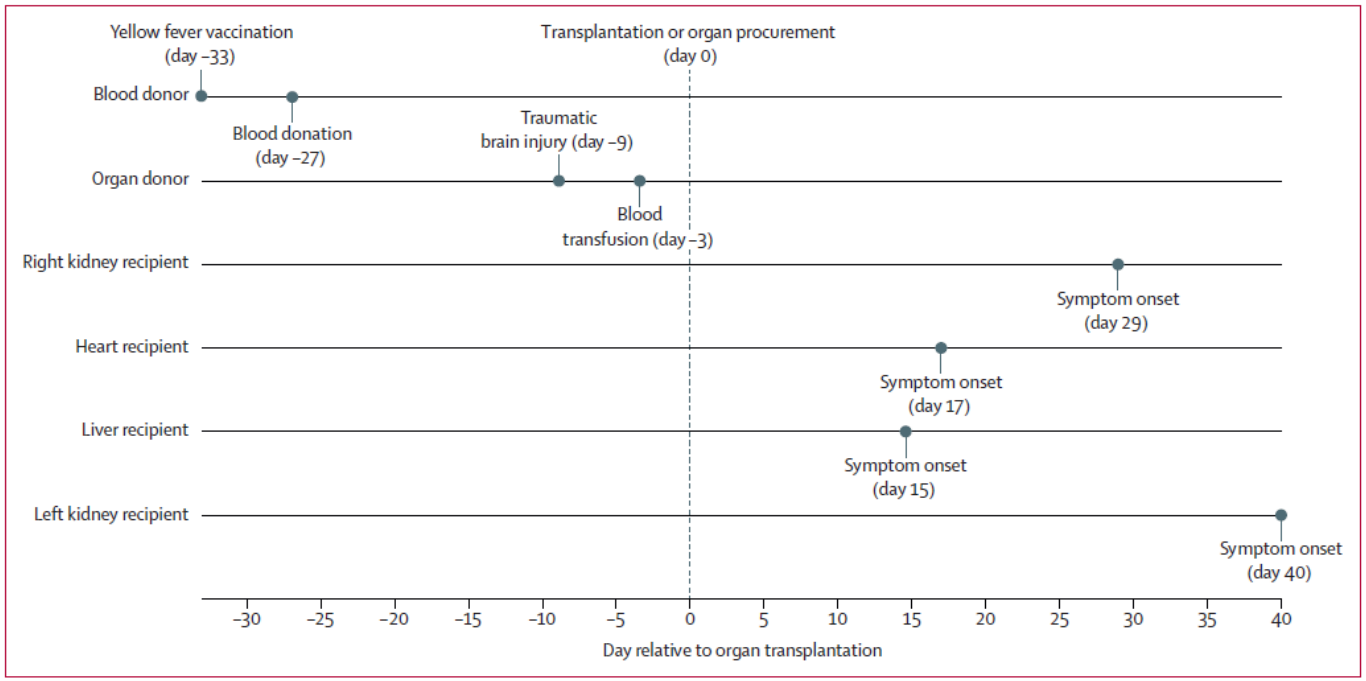


Figure 1: Timeline of events related to the transmission of yellow fever vaccine virus through blood transfusion and solid organ transplantation

Transplant recipients at risk of vaccine-related transfusion-transmitted infection

Transmission of West Nile Virus from an Organ Donor to Four Transplant Recipients

Iwamoto etl al, NEJM, 2013

- West Nile virus infection in an organ donor and in all four organ recipients
- Encephalitis in three recipients, death in one
- No evidence of West Nile virus in the organ donor before blood transfusions
- Positive blood samples in the organ donor at the time of organ recovery
- Transfused organ donor : 53 blood components from 63 blood donors
- One blood donor with West Nile virus viremia at the time of donation

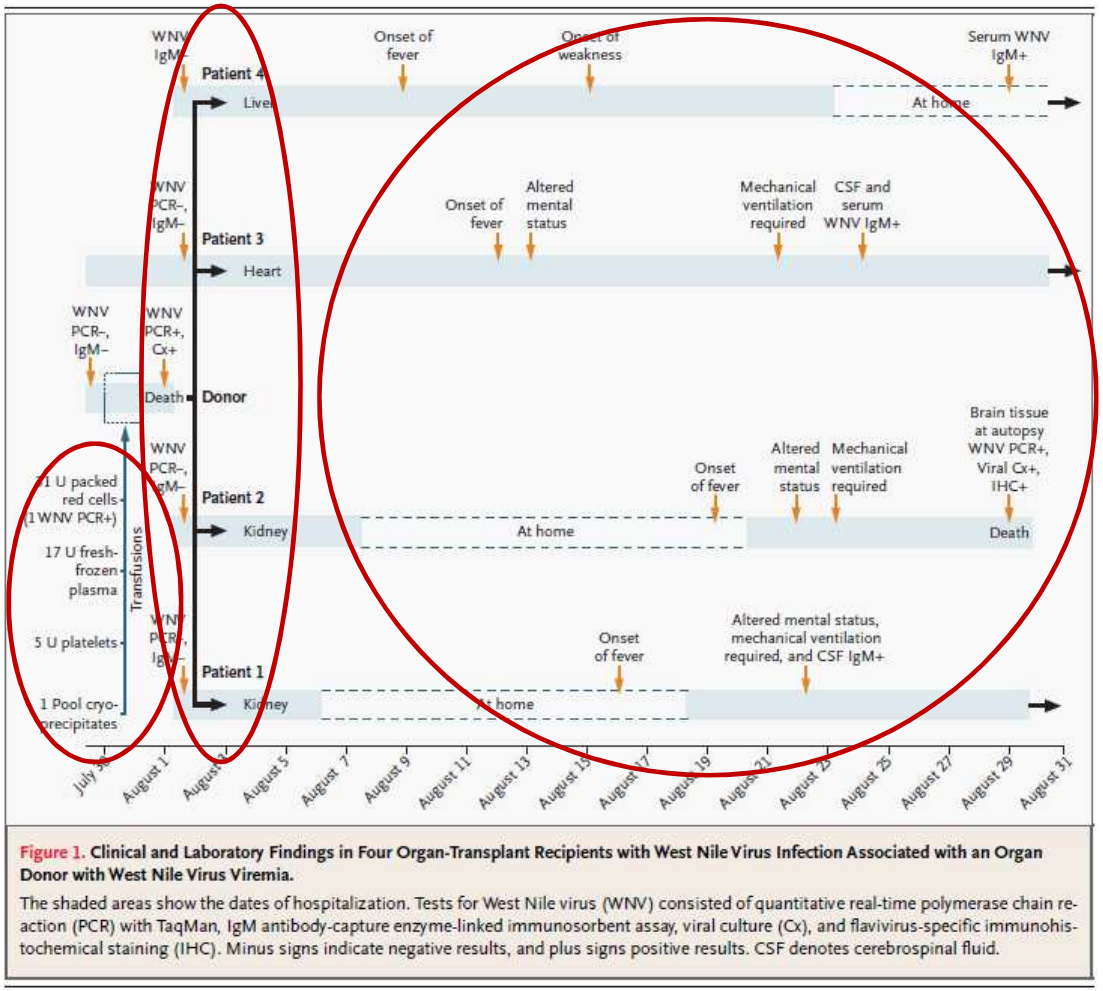


Figure 1. Clinical and Laboratory Findings in Four Organ-Transplant Recipients with West Nile Virus Infection Associated with an Organ Donor with West Nile Virus Viremia.

The shaded areas show the dates of hospitalization. Tests for West Nile virus (WNV) consisted of quantitative real-time polymerase chain reaction (PCR) with TaqMan, IgM antibody-capture enzyme-linked immunosorbent assay, viral culture (Cx), and flavivirus-specific immunohistochemical staining (IHC). Minus signs indicate negative results, and plus signs positive results. CSF denotes cerebrospinal fluid.

Transplant recipients at risk of vaccine-related transfusion-transmitted infection

How frequently is a organ donor transfused?

In addition to :

- Donor transfusion shortly before becoming an organ donor
- Transplant recipient transfusion at time or early after transplantation
  (12 599 kidney transplantation: RBC transfusion in 28%, Gaiffe et al, Frontiers Immunol, 2022)

Ten-year retrospective review of transfusion practices in beating-heart organ donors

Coberly and Booth, Transfusion, 2016

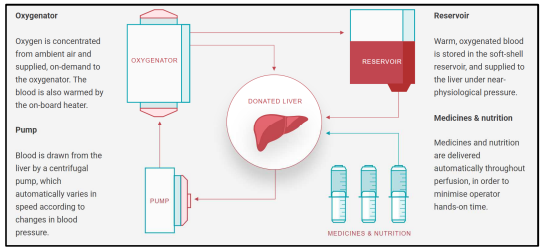
Retrospective review of 439 beating-heart organ donors

- Red blood cell transfusion in 304 donors (69.2%)
- Platelet transfusion in 165 donors (37.6%)
- Plasma transfusion in 217 donors (49.4%)

Normothermic Machine Perfusion of Donor Livers for Transplantation in the United States

A Randomized Controlled Trial

Chapman et al, Ann Surg, 2023





https://www.organox.com/metra-how-it-works

Deferring donors for recent live attenuated vaccination

Are we doing a good job?

VACCINS	
VACCIN VIVANT ATTÉNUÉ	DURÉE D'AJOURNEMENT AVEC OU SANS EXPOSITION
BCG	4 Semaines
Ebola	4 Semaines
Fièvre jaune	4 Semaines
Oreillons	4 Semaines
iomyélite buvable	4 Semaines
e, Oreillons, Rubéole combiné)	4 Semaines
Rougeole	4 Semaines
Rubéole	4 Semaines
Varicelle - Zona	4 Semaines
MONKEYPOX (Variole du Singe)	4 Semaines

181 - Référentiel pour la sélection des donneurs 2023 - PSL/COL/PRL/ENT/DC/RE/002

Missing:

- Dengue
- Chikungunya
- Cholera (live attenuated)
- Polio, oral
- Typhoid, oral

Not necessary:

- MPox

Deferring donors for recent live attenuated vaccination

Are we doing a good job?

In France (EFS):

- Donors properly deferred at time of donor on-site screening (EFS internal reporting)
  - ✓ 2022 : 2 123 occurrences (< 0.1% of all blood donations)
  - ✓ 2023 : 2 364
  - ✓ 2024 : 2 667
- Donors notifying vaccination after donation
  - Early enough to interdict the BCs (EFS internal reporting)
    - ✓ 2022 : 21 occurrences
    - ✓ 2023 : 15
    - ✓ 2024 : 14
  - Too late to prevent BCs / plasma issuing (mandatory reporting to the competent authority)
    - ✓ Since 2017: 6 occurrences
      - MMR vaccine: 3
      - *Mpox vaccine : 1*
      - *HIV experimental vaccine : 1*
      - Chikungunya vaccine: 1

    No reported adverse event in the recipients

Vaccine-mediated transfusion-transmitted infections

- A very rare occurrence, but with potential devastating consequences
- An increasing risk with increasing use of live attenuated vaccines
- Importance of:
  - ✓ Specific information at time of vaccination
  - ✓ Donor education
  - ✓ Donation staff education
  - ✓ Donor deferral for recent live (replicative) attenuated vaccination
  - ✓ Appropriate length of deferral periods

In the future:

- Availability of interconnected electronic health records to ensure donor deferral when appropriate
- Better understanding risk factors for prolonged vaccine viremia to better identify at risk blood donors
- Further development of pathogen reduction technologies to reduce the risk of transmission

Acknowledgments:

Virginie De La Taille, Caroline Bacquet, Pierre Gallian and Syria Laperche, EFS, La Plaine St-Denis

Xavier de Lamballerie, CNR Arbovirus, IHU Méditerranée Infection, Marseille

And all the blood donors

