



Emerging Pathogens: Safety of Plasma Protein Products From and Protection by Immunoglobulins Against, with an Increasingly Global Plasma Supply



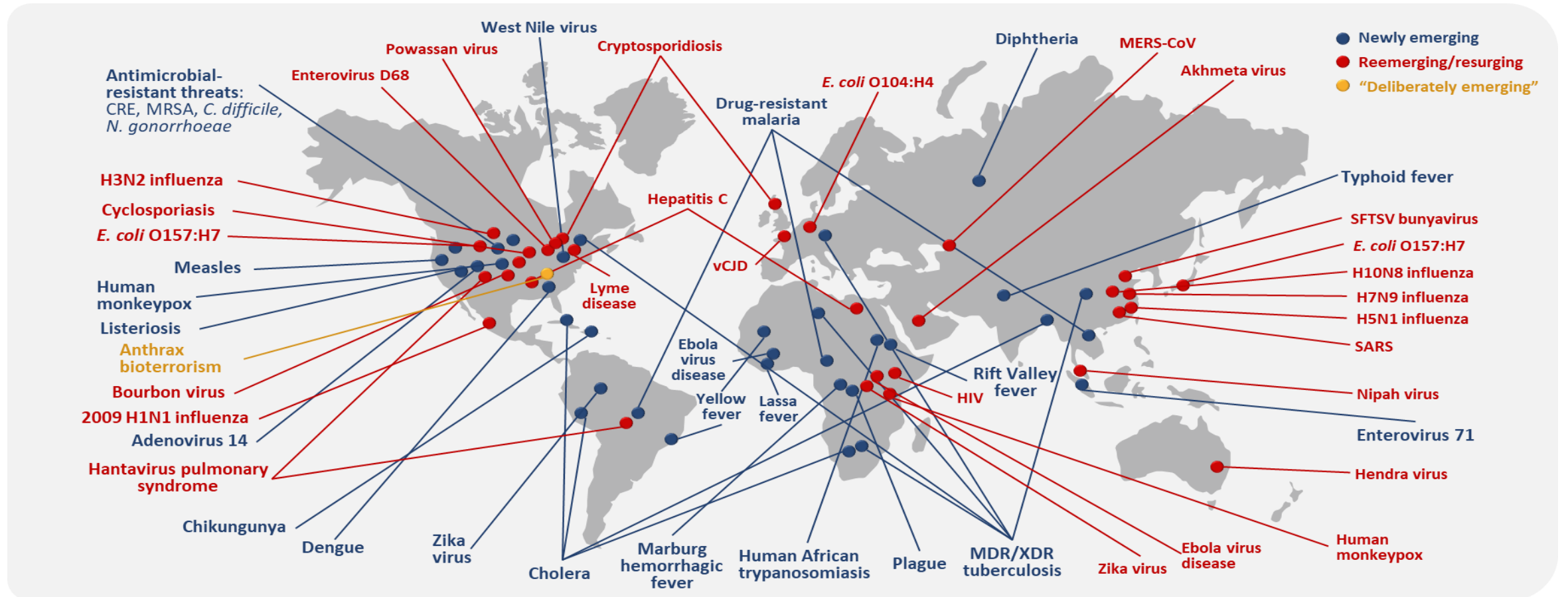
Thomas R. Kreil, Global Pathogen Safety

IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens
May 10, 2023 – Bologna, Italy

PDMPs & Emerging Pathogens: *Safety ... From*



A volatile microbiological environment

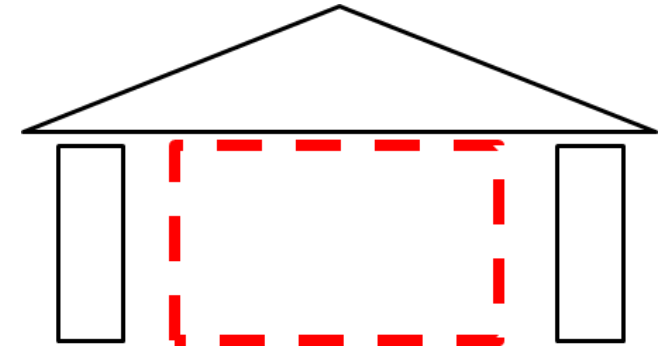


Safety from Virus Transmissions

Blood Components for Transfusion, and Plasma-Derivatives: Collected from the Same Vein, yet very Different Safety Margins

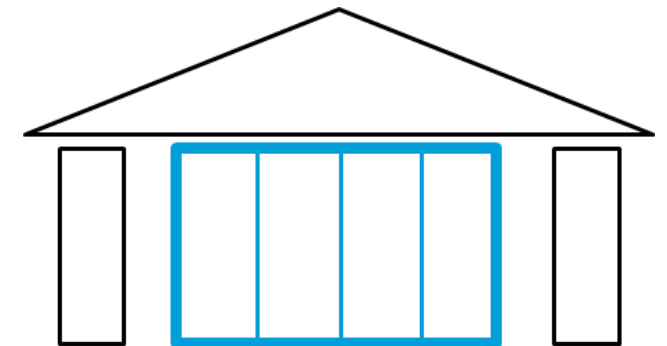
Blood

- Selection, testing:
limited by what is known, and LoD



Plasma

- Selection, Testing
- Manufacturing with dedicated virus reduction:
robust, generic, effective, also unknown viruses

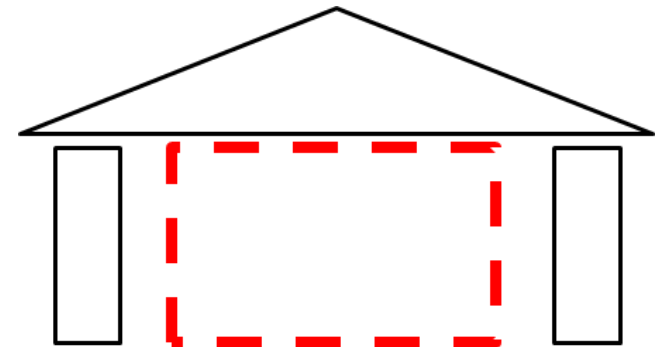


Safety from Virus Transmissions

Emergence of West Nile Virus in the US

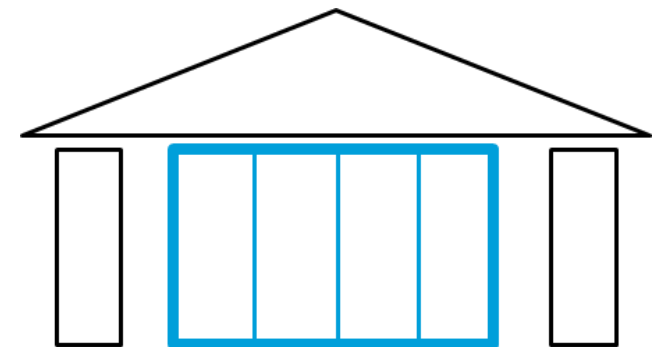
Blood

- Selection, Testing: **NAT**
→ 2003–15: 12 transfusion-associated transmissions¹



Plasma

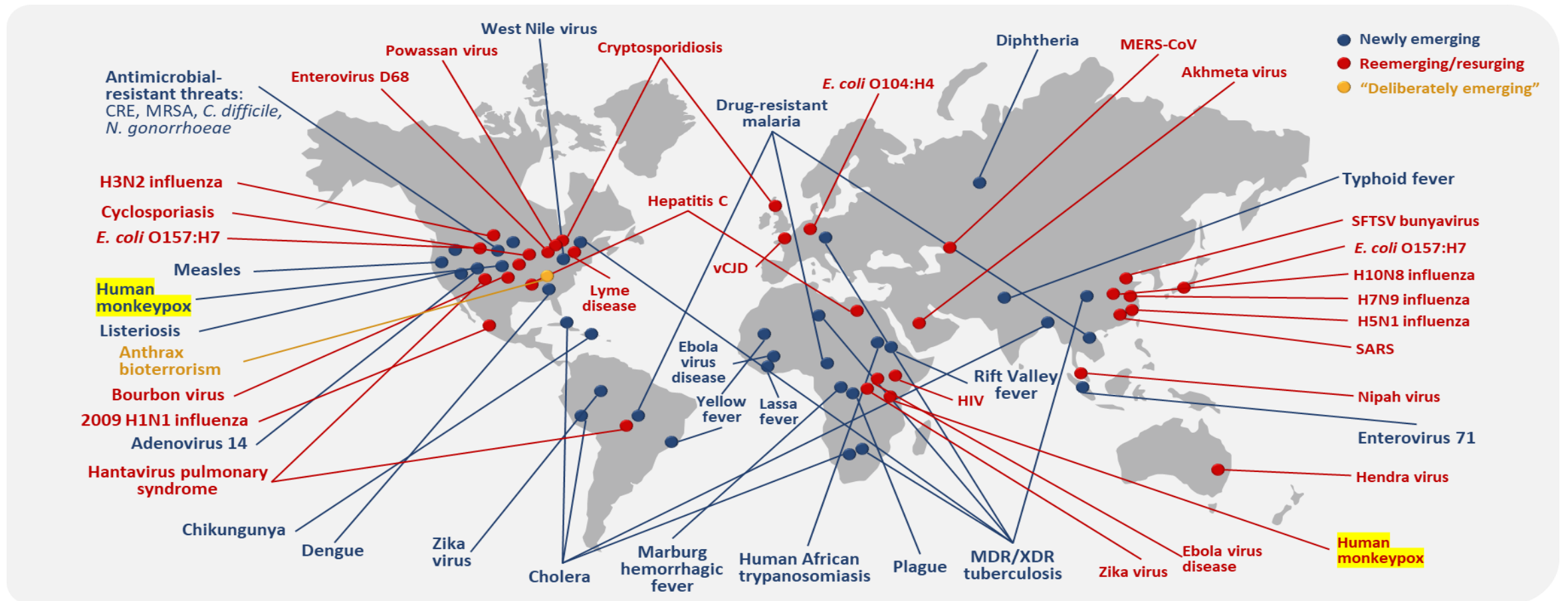
- Selection, Testing: NAT not required
- Manufacturing with virus reduction²
→ no virus transmissions



³ | 1) Groves JA, et al. Transfusion. 2017;57(3pt2):850-856
| 2) Kreil TR, et al. Transfusion. 2003;43(8):1023-1028

PDMPs & Emerging Pathogens: *Safety ... From ?!*

2022/23: 90.000 MPOX cases reported in >100 non-endemic countries



Safety from Virus Transmissions

Emerging Viruses of Concern: Reduction → Verification

Blood

- NAT required for WNV (US), HEV (EU)
→ transmissions have (do) still occur(ed)

Plasma

- NAT not required (!)
→ no transmissions

MPOX-model

West Nile virus and the safety of plasma derivatives: verification of high safety margins, and the validity of predictions based on model virus data

Thomas R. Kreil, Andreas Berting, Otfried Kistner, and Johanna Kindermann

H5N1 influenza virus and the safety of plasma products

T.R. Kreil, U. Unger, S.M. Orth, G. Petutschnig, O. Kistner, G. Poelsler, and A. Berting

Chikungunya virus and the safety of plasma products

Sandra M. Leydold, Maria R. Farcet,* Johanna Kindermann, Jens Modrof, Gerhard Pölsler, Andreas Berting, M. Keith Howard, P. Noel Barrett, and Thomas R. Kreil*

Hepatitis E virus and the safety of plasma products: investigations into the reduction capacity of manufacturing processes

Maria R. Farcet, Cornelia Lackner, Gerhard Antoine, Philip O. Rabel, Andreas Wieser, Andreas Flicker, Ulrike Unger, Jens Modrof, and Thomas R. Kreil

Zika virus is not thermostable: very effective virus inactivation during heat treatment (pasteurization) of human serum albumin

Maria R. Farcet and Thomas R. Kreil

Orthopox viruses and the safety margins of solvent-detergent treated plasma-derived medicinal products

Johanna Kindermann | Michael Karbiener | Thomas R. Kreil

PDMPs & Emerging Pathogens: *Safety ... From → AND NEXT ?*



Recent Study from China

- *Potential cross-species transmission of ...*
 - *RNA viruses: paramyxovirus, astrovirus (NLE, 28-35 nm)*
 - *DNA viruses: PRV, porcine circovirus (NLE, 17 nm), parvovirus (NLE, 18-26 nm)*
- ... nuanced view of the frequency of host-jumping events ... zoonotic risk.*

→ Virus Reduction, Worst Case: **Small, non-lipid Enveloped (NLE)**

Need

- *... surveillance of pathogens at the wildlife-domestic animal-human interface ...*

PDMPs & Emerging Pathogens: *Safety ... From → CHINA ?*



Global Village

- Austria
 - 715.000 Arrivals from China
 - Hallstadt →
SARS-COV-2 variant monitoring
in wast water implemented
- Chinese Plasma Products
 - *11 products ... registered in nearly
20 countries ... able to export*



Pathogens & Immunoglobulins (IG), *Protection ... Against*



Exposure

- Immunization
- Infection



Geography

- EU
- US



Manufacturing Process

- Plasma flavor (S vs R)
- Enzymes (?)



Pathogens & IG, *Protection ... Against*

Stakeholder Perspective

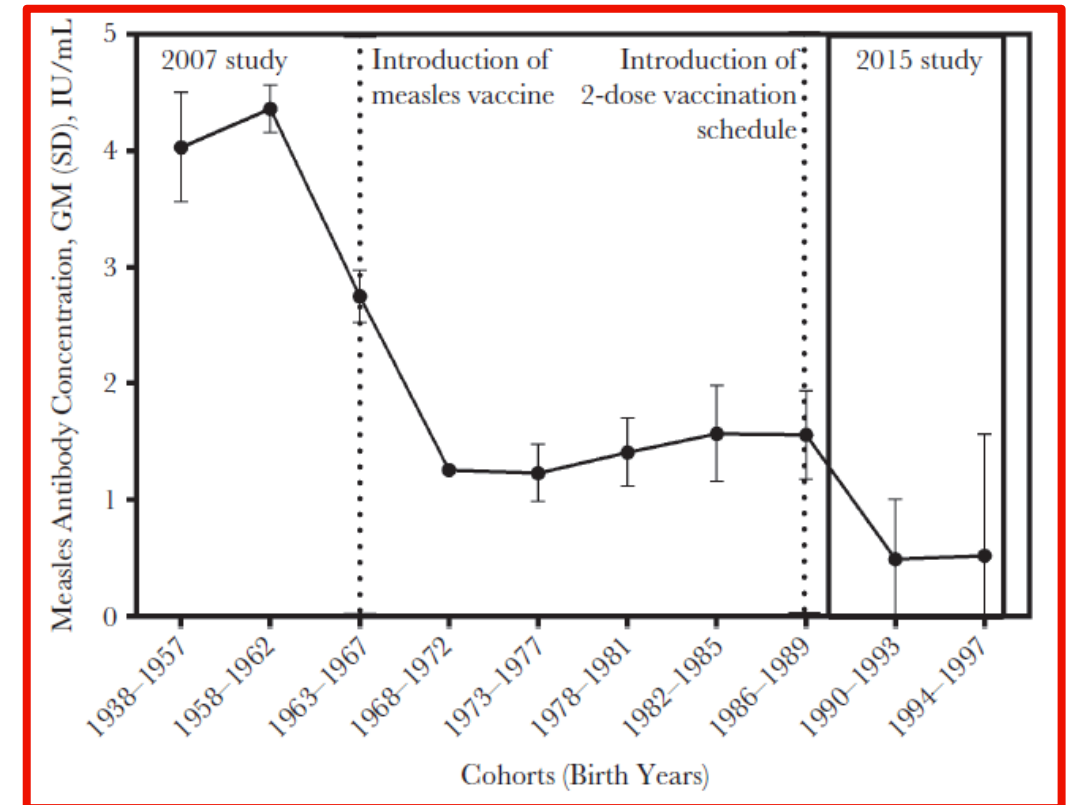
- **Advances and Challenges of the Decade** ¹
The COVID-19 pandemic has highlighted the need for immunoglobulin products to be assessed for antibodies targeting specific pathogens.
- **FDA CFR:**
measles, polio, diphtheria → anachronistic
- **FDA – PPTA workshop:**
hAdV5, RSV, hPIV3 → the future ? ²

Virus Neutralization by IGs, and Eliminating Pathogens



Measles Virus, and Vaccination against → Decrease

- Antibody titers are lower after vaccination than after natural infection
- Vaccination since 1963:
→ lower antibody titers in population
- IG preparations:
FDA release specification met,
passive protection expected

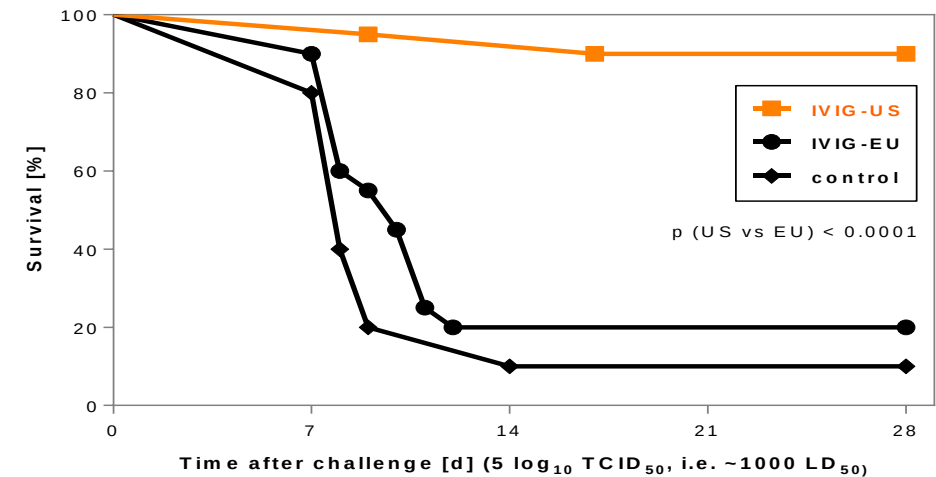
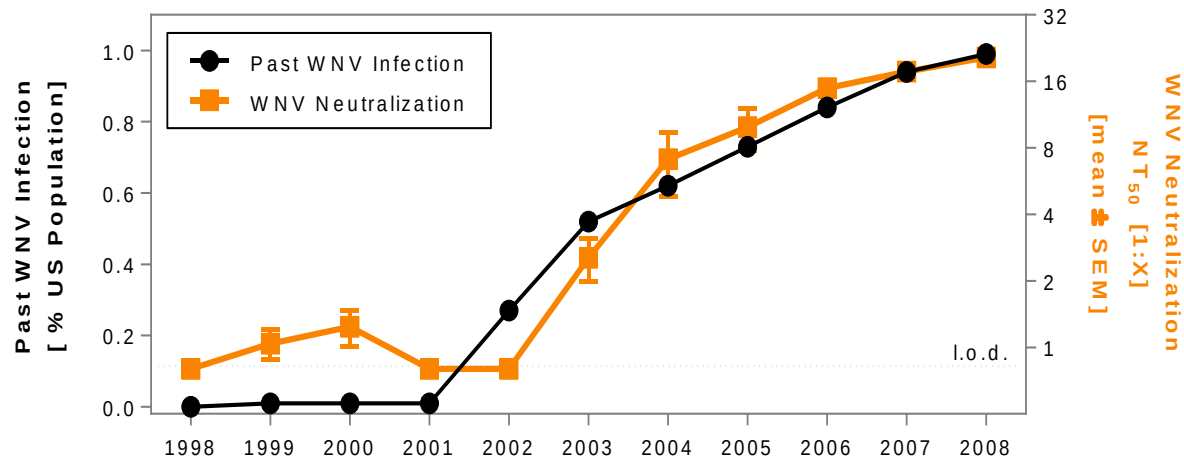
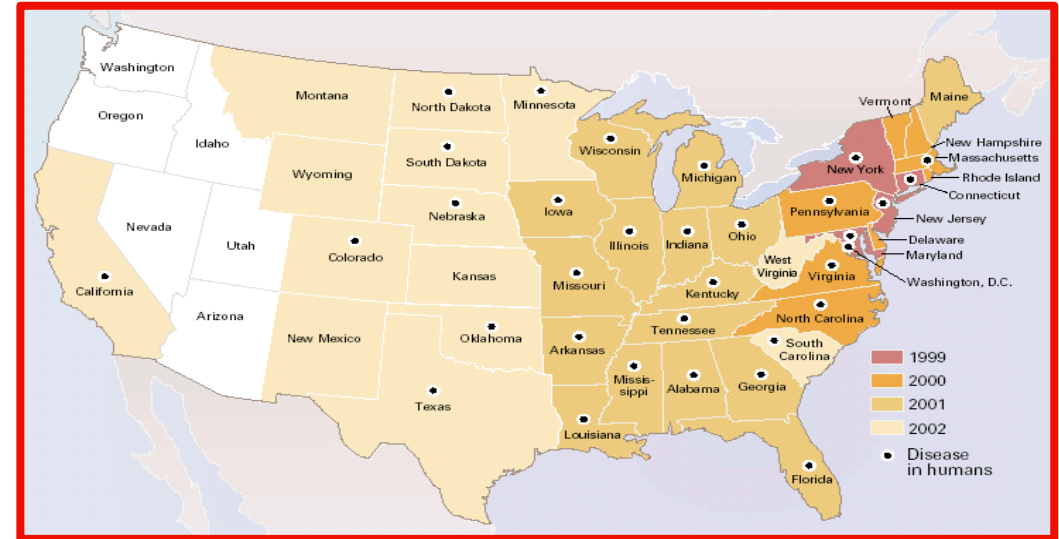


Virus Neutralization by IGs, and Emerging Pathogens



West Nile Virus in the US → Increase

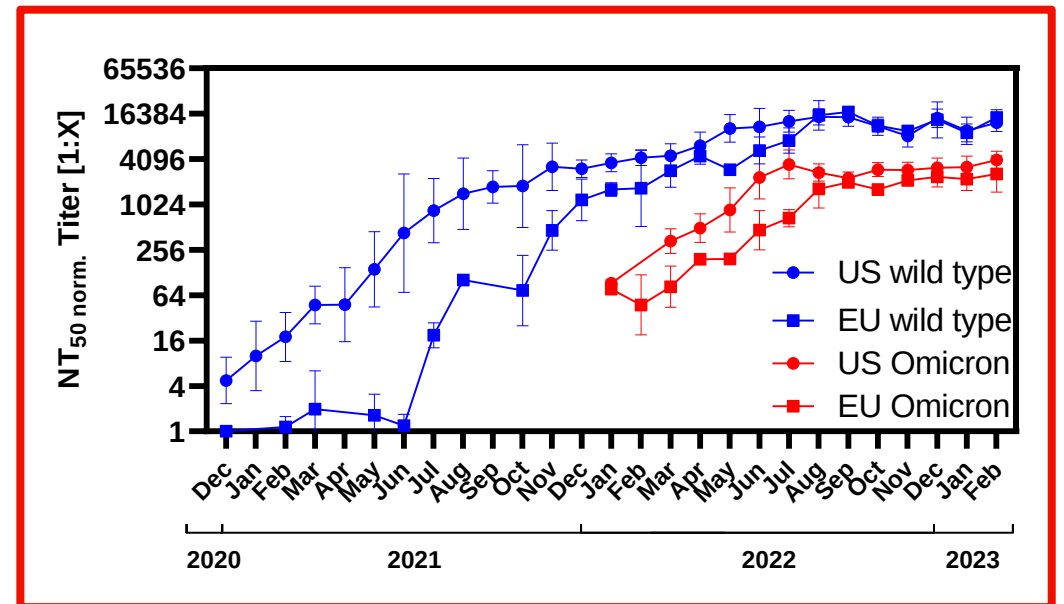
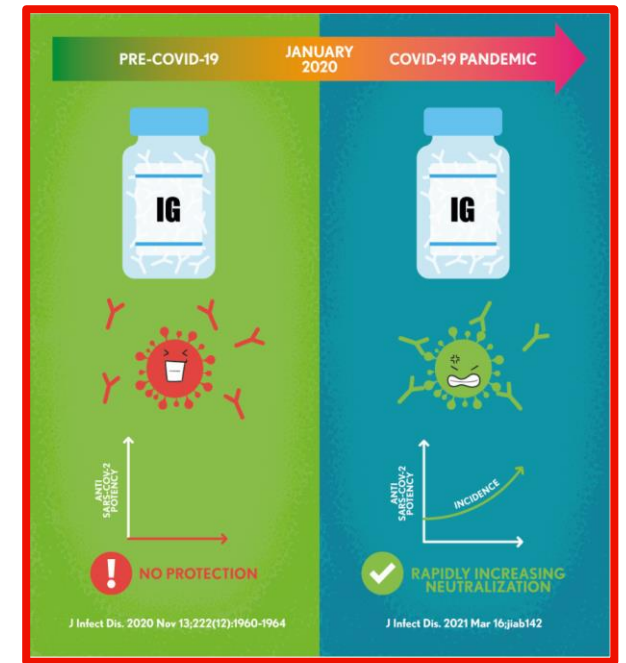
- 1999: 62 human cases; NOW: endemic
- Cumulative incidence → seroprevalence
- Neutralizing antibodies → protection



Virus Neutralization by IGs, and a Pandemic Pathogen

Pandemic of **SARS-CoV-2** → Increase (!)

- *No SARS-CoV-2 Neutralization Before ...* ¹
- *Rapidly Increasing... During ...* ²
- *Highly Potent ... Vaccinated ...* ³
- *Omicron ... US and Europe* ⁴
- IGs “Auto-Adjust” to Virus Variants
- Monoclonals: NOT (!)

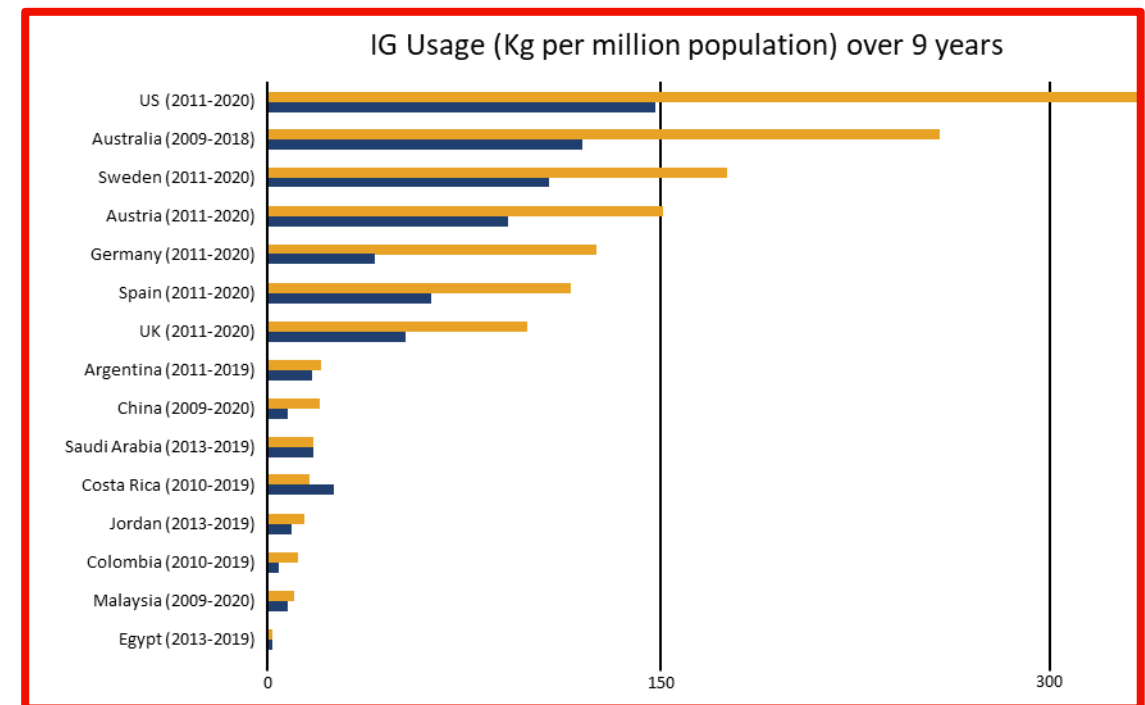


Virus Neutralization by IGs

A Changing Landscape ...

- **Target: VIRUSES**
 - Primary IG endpoint efficacy endpoint: severe bacterial infections ¹
→ antibiotics (!)
- Primary immune deficiency
 - Immunodeficient
- Secondary immune deficiency
 - Immune compromised (oncology)

→ IG replacement therapy: **GROWTH** ²



Plasma-Derived Medicinal Products (PDMPs)

A Global Need, and Growing

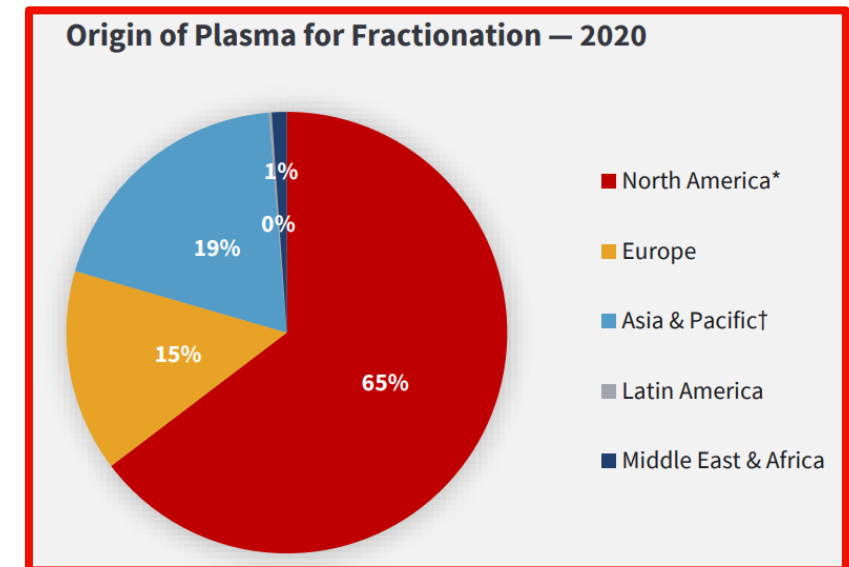
- **WHO Model List of Essential Medicines**
 - ... *minimum medicine needs for a basic health-care system, listing the most efficacious, safe and cost-effective medicines ...*
 - Plasma-derived medicines
 - Immunoglobulins → CAGR 6+%, 2023-2031¹, CAGR 6.8%, 2023-2031²
 - Factor VIII
 - Factor IX

Plasma-Derived Medicinal Products (PDMPs)



Supply

- Currently, US-centric
- Europe
 - 60% public & NGO
 - 40% private, few countries
- Asia & Pacific: 75% China



Plasma-Derived Medicinal Products (PDMPs)



Supply → Changes

- UK Plasma, *HHS Giving=Living campaign*
 - BSE, vCJD „risk“ managed → regulatory framework adjusted
- European SoHO Regulation (excerpt)*
 - ... provision of SoHO therapies, ... high safety and quality standards ...
 - ... harmonisation across Member States, facilitating cross-border exchange of SoHO ...
 - improves crisis preparedness and resilience to safeguard access to therapies

Plasma-Derived Medicinal Products (PDMPs)

Decentralization, Resilience: Gaining Traction

- United Nations Institute for Training and Research (UNITAR)
 - Argentina & Malaysia pilots
- International Coalition for Safe Plasma Proteins (ICSPP)
 - Dakar, Senegal – first project
- SUPPLY project, EC EU4Health program-funded*
 - ... availability, quality, safety and cost-effectiveness of the blood ... supply

SUMMARY

- Plasma Protein Products ***Safety From*** Viruses: Safety Tripod
 - Emerging Pathogens → Inevitable, When not IF
- IG Protection Against Viruses: Changing, Needs Research
 - Plasma Protein Products → Demand needs Supply
- Increasingly Global Plasma Supply → Facets to Consider ...

THANK YOU !

Global Pathogen Safety

- Our Values „Up-Front“
 - Patient
 - Trust
 - Reputation
 - Business
- Living Our Values Every Day

