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« Zika virus and blood transfusion »

Conflict of interest

Our research in the prevention of transfusion transmitted infectious diseases is partially funded by Cerus Corporation, Concord, USA

ARBOVIRUSES AND BLOOD TRANSFUSION

- Arboviruses are transmitted by arthropods (ARthropod BOrne VIRUSes), especially mosquitoes

- Non vector-borne transmission
 - Materno –fetal (Zika, chikungunya, dengue, WNV...)
 - Laboratory acquired (dengue, Zika, WNV...)
 - Transfusion:
 - West Nile virus +++
 - Dengue (all serotypes) ++
 - Zika ++: new challenge for blood transfusion safety
 - Ross River, yellow fever vaccine, tick-borne encephalitis viruses

- Prevention of transfusion-transmitted infections (TTIs)
 - Medical questionnaire
 - Laboratory testing of blood donations
 - Pathogen reduction/inactivation (PR) of blood products

MEDICAL QUESTIONNAIRE



➤ Pros

- Screening based on clinical presentation (low cost) +++

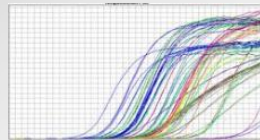
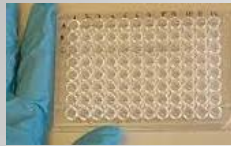
➤ Cons

- Insensitive for asymptomatic infections +++
- Does not detect asymptomatic carriers (HIV, HBV, HCV)
- Most of arbovirus (especially *Flavivirus*) infections (DENV, ZIKV, WNV, YFV...)

LABORATORY TESTING OF BLOOD DONATIONS (SEROLOGY AND MOLECULAR TESTING)



Serology



Nucleic Acid Testing (NAT) +++

- Single plex: 1 pathogen
- Multiplex: several pathogens in the same run

➤ Pros (NAT)

- Sensitivity +++ for a specific pathogen

➤ Cons (NAT)

- Cost
- Require identification of circulating pathogens
- Cannot be implemented for all circulating pathogens (HIV, HBV, HVC, HTLV, malaria, DENV ZIKV CHIKV YFV trypanosomiasis Mayaro Oropouche)
- Require availability of test, licensed tests +++
- Require molecular platform +++

PATHOGEN REDUCTION (PR)

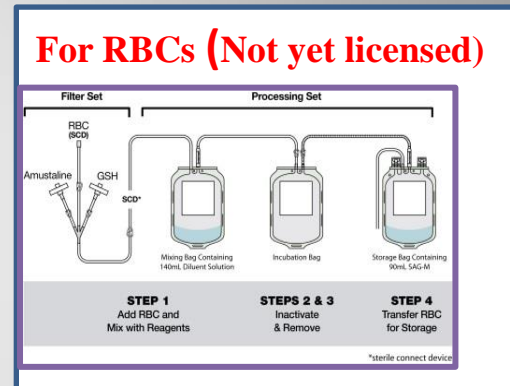
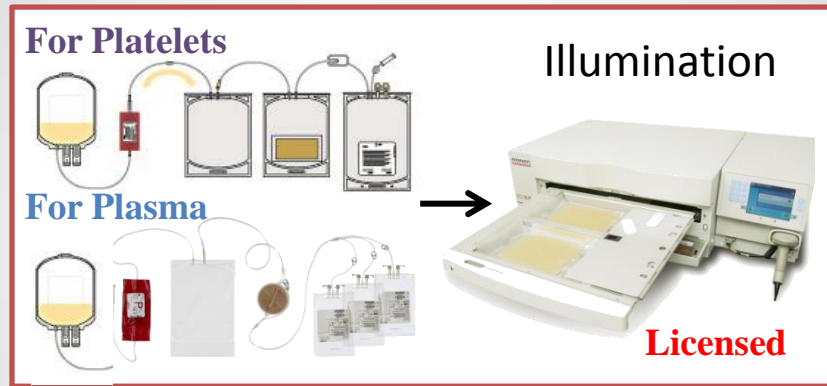
Infected but asymptomatic blood donors (ZIKV?)



Collect contaminated blood products (red blood cells, plasma, platelets)



Pathogen reduction technologies (inhibition of RNA and DNA transcription, replication, translation)



Pathogen reduced blood product **that do not carry infectious pathogens++++**



Can be transfused to recipients



Used in routine practice ++++
Including in French Polynesia

PATHOGEN REDUCTION

➤ Pros

- Proactive strategy +++
- Can be implemented proactively in endemic situation or in the early stages of an “epidemic of unknown origin” (epidemic of “fever and rash” in Brazil)
- Inactivates a broad range of pathogens (bacteria, viruses, parasites) +++
- Does not require identification of circulating pathogens +++

➤ Cons

- Cost
- No approved/licensed system for red blood cells (RBCs)

ZIKA VIRUS AND BLOOD TRANSFUSION

Medical questionnaire

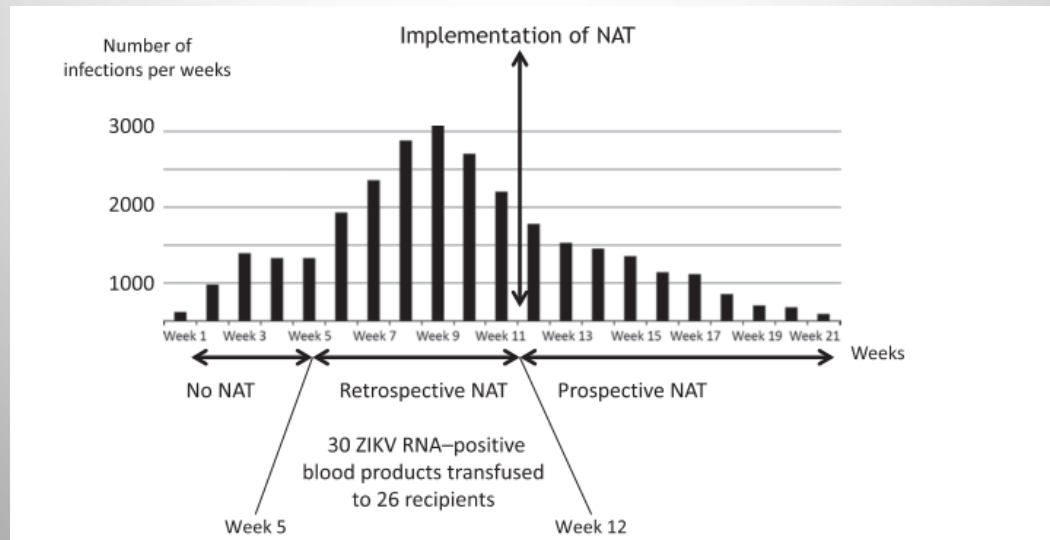
- Lack of sensitivity

NAT

- French Polynesia 2013/2014: 2.8 % of blood donors tested positive for ZIKV RNA
- ZIKV NAT available under investigational new drug (IND) application
- Puerto Rico 2016: 1.1% ZIKV RNA during the peak of the outbreak
- ZIKV NAT implemented in the US → RNA positive blood donations reported in Florida, US

PR

- INTERCEPT Blood System for platelets in routine use in French Polynesia since 2010 to prevent DENV
- Recommended by FDA using approved PR systems for platelets and plasma (INTERCEPT, Octaplas)



FP outbreak

ZIKA VIRUS AND BLOOD TRANSFUSION

ZIKV transfusion transmission infections were confirmed in Brazil in 2016

Incidence of post-transfusion ZIKV infections is underestimated?

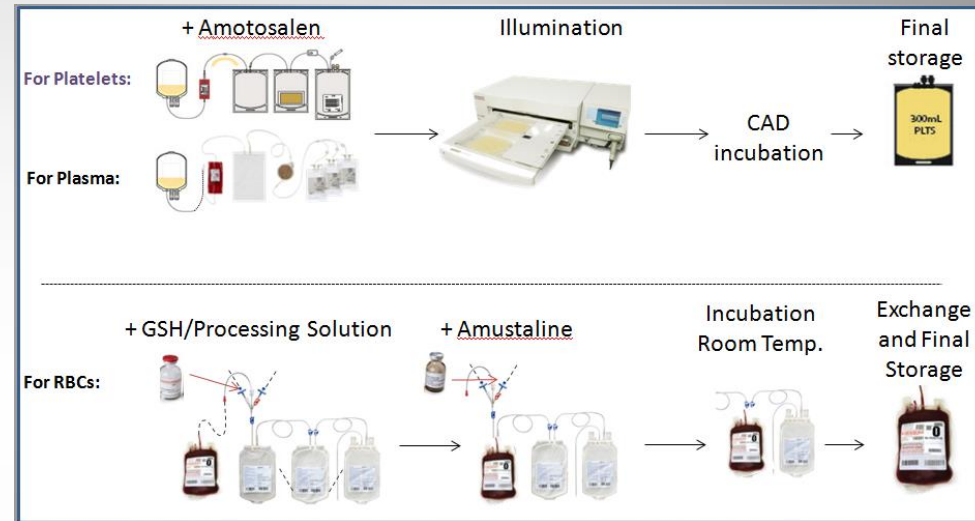
- Most endemic areas lack laboratory capacity to test for ZIKV in pre-donation and to document ZIKV infections
- In endemic areas all the population is also exposed to mosquito bites
- (Same for DENV)

NEW ADVANCES IN THE PREVENTION OF ZIKV (ARBOVIRUSES) TRANSFUSION-TRANSMISSION

Efficacy of pathogen reduction for **ZIKV** was demonstrated **in plasma** using amotosalen/UVA (Aubry *et al.*, Transfusion, 2016)

New data

- Amustaline and glutathione (INTERCEPT Blood Systems for RBCs) inactivates
 - **ZIKV in RBCs** +++ (Laughunn *et al.*, Transfusion, 2017)
 - **DENV and CHIKV in RBCs** (unpublished data)
- Amotosalen/UVA (INTERCEPT Blood System for platelets and plasma) inactivates **ZIKV in platelets** (unpublished data)
- **There are now pathogen reduction systems to inactivate ZIKV (and also DENV and CHIKV) in all blood components +++**



	INTERCEPT Blood Systems (log ₁₀ reduction)		
	Plasma	Platelets	Red blood cells
ZIKV	≥ 6.6 (Aubry, Transfusion 2016)	≥ 4.4 (Unpublished)	≥ 6.0 (Laughunn, Transfusion 2017)
DENV	≥ 5.6 (Musso, Transfusion 2014)	≥ 5.3 (Dupuis, Transfusion 2012)	≥ 6.6 (Unpublished)
CHIKV	≥ 7.6 (Tsetsarkin, Am J Trop Med Hyg 2013)	≥ 6.4 (Tsetsarkin, Am J Trop Med Hyg 2013)	≥ 5.8 (Unpublished) ¹⁰

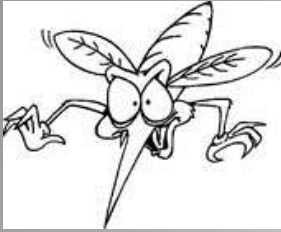
EMERGING PATHOGENS AND BLOOD TRANSFUSION

The risk is unpredictable

- WNV in the US in the 2000's
- ZIKV since 2013
- Which one is the next?

In endemic areas

- Circulating pathogens are not always identified, they are co-circulating
- Reference NAT assay are often lacking
- **Need for a proactive strategy +++++**
- There are now Pathogen Reduction systems to inactivate ZIKV, DENV and CHIKV in plasma, platelets, and RBCs



**WELCOME TO FRENCH POLYNESIA
WE HAVE MORE THAN ZIKV**

