Working Party on Transfusion Transmitted Infectious Diseases

Annual Meeting Cairo (Egypt)

21-22 March, 2009

Different Approaches to Prevent TT of Malaria in Non Endemic Countries

A. ASSAL

French Blood Services

EFS / France

BACKGROUND

- **Four species of malaria parasites can infect humans:**

- ***Plasmodium falciparum*, *P. vivax*, *P. ovale* and *P. malariae*.**

- ***P. falciparum* and *P. vivax* cause the most infections worldwide.**

- ***Plasmodium falciparum* causes the most severe and potentially fatal form of malaria.**

BACKGROUND

- ***Plasmodium vivax*** **and** ***P. ovale*** **have dormant liver stage parasites ("hypnozoites") which can reactivate ("relapse") and cause malaria several months or years after the infecting mosquito bite.**
- ***Plasmodium malariae*** **produces long-lasting infections and can persist asymptomatically for years, even a lifetime.**

Donor population at risk of transmitting malaria

- People with history of clinical malaria
- Travelers
- Residents

Donor population at risk of transmitting malaria

• Travelers

• Travelers from malaria-free regions going to areas where there is malaria transmission are highly vulnerable.

• No, or almost no immunity to malaria

• Almost always symptomatic if parasites present; thus excluded from donation.

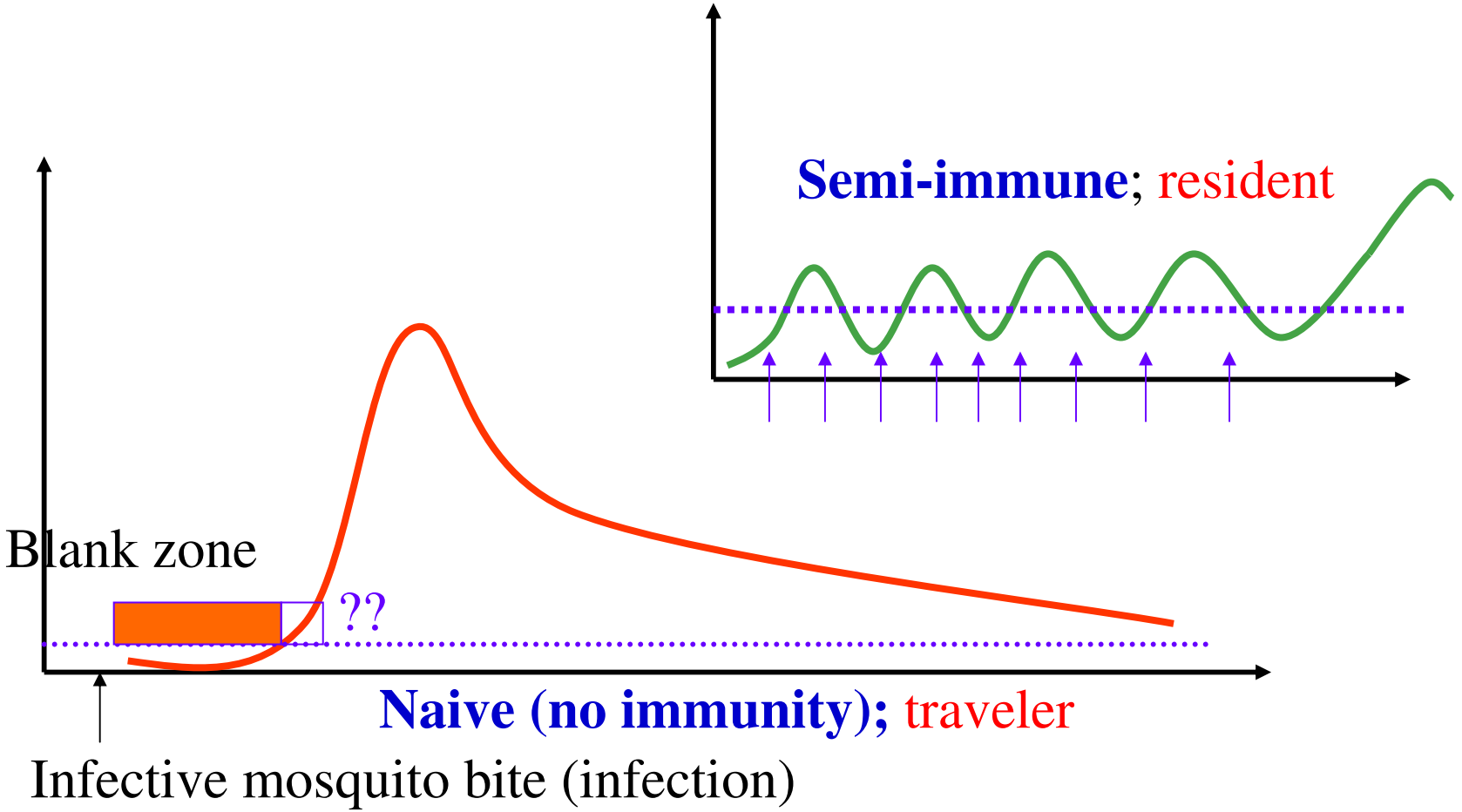
• Almost all *P. falciparum* in this group occurs in the first 2 months; virtually none after 6 months.

Donor population at risk of transmitting malaria

- **Residents**

- **Persons born or who have lived during a given length of time in an endemic area.**
- **Partially immune to malaria disease (semi-immune)**
- **May be asymptomatic but parasitaemic**
- **May harbour *P. falciparum* for years.**
- **In France, almost all brought up in sub-saharan Africa.**

Antibody response to malaria



Transfusion-Transmitted Malaria Cases

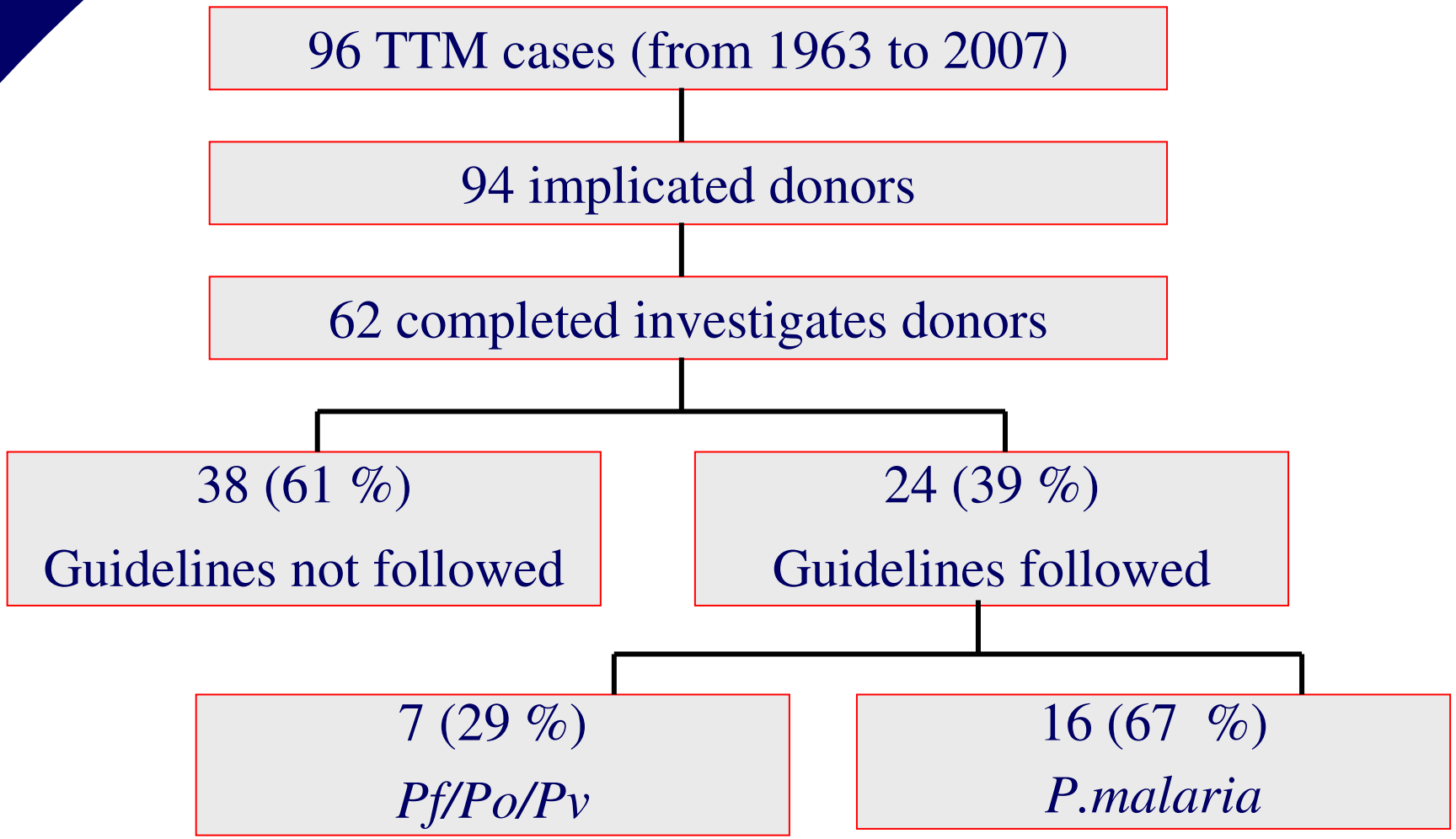
- **Transfusion-transmitted malaria (TTM) is rare in non endemic countries.**
- **But it is a potential severe complication in blood recipients.**

	Number of TTM cases last 10 years [a]
France	2[b]
Italy	7
Tunisia	1
Japan	1
Canada	3
USA	10

[a] **Reesink** H.W. **European strategies against the parasite transfusion risk.** Transf Clin Biol 2005;12:1-4.

[b] **Updated**

Implicated donors in US TTM



After Monica Parise, FDA Worksho. Testing for Malarial Infections in Blood Donors. July 12, 2006

Approaches to reduce Transfusion Transmitted Malaria (TTM) in non endemic areas

- Vary worldwide depending upon at-risk populations and donor-selection criteria.
- Blood safety from TTM is based on:
  - Deferral policies based on donor questioning for :
    - History of malarial infection;
    - Travel and residence in malaria endemic countries.
  - In some countries, testing for malarial antibodies (IFAT or ELISAs)

European guidelines

European directive: 2004/33/EC

Donor situation	Duration of deferral period
• Individuals with a history of malaria	• 3 years following cessation of treatment AND absence of symptoms, accept thereafter only if an immunologic or molecular genomic test is negative
• Individuals who have lived in a malarial area within the first 5 years of their life	• 3 years following return from last visit to any endemic area, provided person remains symptom free; may be reduced to 4 months if an immunologic or molecular genomic tests is negative at each donation

European guidelines

Donor situation	Duration of deferral period
• Asymptomatic visitors to endemic areas	• 6 months after leaving the endemic area unless an immunologic or molecular genomic test is negative
• Individuals with history of undiagnosed febrile illness during or within 6 months of a visit to an endemic area	• 3 years following absence of symptoms. May be reduced to 4 months if an immunologic or molecular genomic tests is negative

French Policy

- **History of malaria or known positive serology: Deferral 3 years, accepted thereafter if serologic test negative at the first donation**

- **Return from endemic areas since less than 4 months: Deferral 4 months after return**

French Policy (2)

	4 months < Return < 3 years	> 3 years
Born or have lived in a malarial area within the first 5 years of their life	Donation accepted If No SYM and a serologic test is negative at each donation during the period	Donation accepted If absence of symptoms AND an serologic test is negative at first donation
Individuals who have stayed > 6 consecutive months in a malarial area	Donation accepted If No SYM and serologic test negative at each donation during the period	Donation accepted If absence of symptoms AND an serologic test is negative at first donation
Others	Donation accepted If No SYM and serologic test negative at first donation	Donation accepted in absence of symptoms

UK Donor Selection Guidelines

Implemented November 2005

Donors who have had malaria diagnosed:

- If more than 3 years have passed since anti-malarial therapy has been completed and symptoms caused by malaria have resolved, perform a validated test for malaria antibody. If this is negative, **accept**.

For others donors

- If at least 6 months has passed since the date of the last potential exposure to malaria, or the date of recovery from symptoms that may be caused by malaria, a validated test for malaria antibody is negative, **accept**.

Spanish Policy

After Maria Piron. Blood and Tissue bank. Barcelona. Spain.

At risk donors	Test not available in the blood center	Test available
have lived in a malarial area within the first 5 years of their life	Deferral for 3 years after last visit to endemic area	Deferral reduced to 4 months if serologic test or PCR negative
History of malaria	Permanent deferral	Deferral 3 years, after TTT. Accept thereafter if No SYM and serologic test or PCR negative
Individuals with history of fever of unknown origin during stay in EA or 6 months after return	Deferral for 3 years after end of symptoms	Deferral reduced to 4 months if serologic test or PCR negative
Asymptomatic visitors to E.A.	Deferral for 6 months	No deferral if test negative

Deferral policy in the USA

July 26, 1994 Guidance. Recommendations for deferral of donors for malaria risk

Current policy: questions and deferral

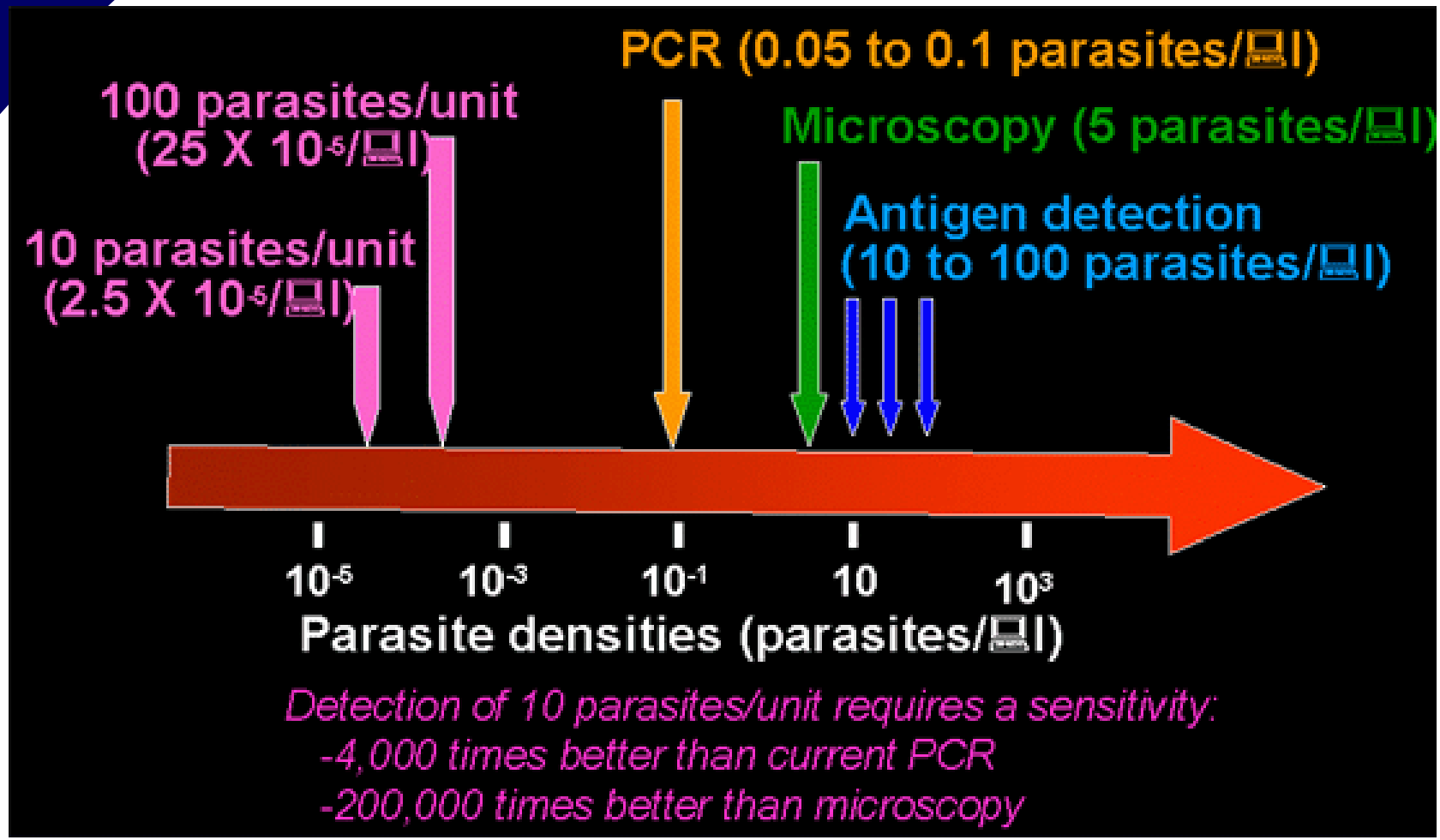
- **Deferral for 1 year:**
  - Residents from non-endemic area who travel to endemic areas
- **Deferral for 3 years:**
  - If donor had malaria: defer for 3 years after becoming asymptomatic.
  - Immigrants, refugees, citizens or residents of malaria endemic countries: defer for 3 years after departure [1].

[1] the guidance does not define residence. It may be 3 to 5 years depending upon interpretation of current FDA guidance issued in 1994 as opposed to a draft guidance released in 2000.

Diagnostic tools for malaria detection

- Blood film examination.
- Antibody detection: IFA, ELISA.
- Ag detection.
- DNA detection: PCR.

Marianna Wilson. FDA Workshop. Testing for Malarial Infections in Blood Donors. July 12, 2006



The infectious parasite burden is very low: 10 parasites in infected RBC in case of human *P.vivax* malaria

Malaria antibody testing
In France and UK

- **Antibody testing seems to be the most suitable screening tool. It has proven its efficiency in safeguarding the blood supply (France, UK)**
- **In 2005, shift to an ELISA format : DiaMed Malaria Antibody Test (Switzerland)**
- **Combination of a soluble *P. falciparum* antigen and recombinant antigens of *P. vivax* (MSP1 and CSP1).**
- **UK: IFA ?**

ELISA testing outcomes in 2007

- Number of blood donations collected: 2 497 614
- Number of blood donations tested for malaria antibodies with ELISA: 132 940 (5.32%)
- Repeat reactive donations: 1496 (1.12 % of screened blood donations)
- Only 1256 could be tested by IFA:
  - 454 were ELISA positive / IFA positive (0.34 % of tested donations)
  - 802 were ELISA positive / IFA negative (Indeterminate: 0.60 % of tested donations)

Discussion

- **In Europe, despite common directive some differences still exist in the application of the guidelines:**
  - ✓ **No consensus about the definition of residence.**
  - ✓ **Variation of the deferral period for visitors to endemic areas.**
  - ✓ **Testing is not generalized.**

Discussion (2)

- **TTM cases are due to history taking and testing bypass.**
- **Since malaria testing implementation in 1986, serologic testing (first IFA, then ELISA) never failed as we never recorded a TTM related to a tested donor.**

Discussion (3)

- TTM prevention strategy based only on questions and donor deferral would result in an unacceptable loss of donors.

- Antibody testing provides a safeguard which is additional and complementary to history taking and time exclusion and should not be seen as a replacement for those measures.

- Serologic screening results in the exclusion of some uninfected donors but overall increases the amount of blood available.