Detection of Malaria Parasites and Implications for Blood Safety

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Advisory Committee
Blood Safety and Availability
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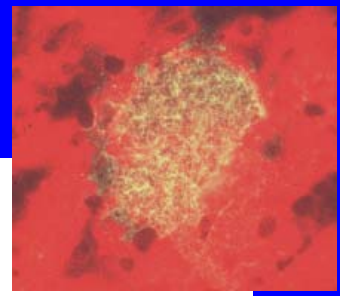

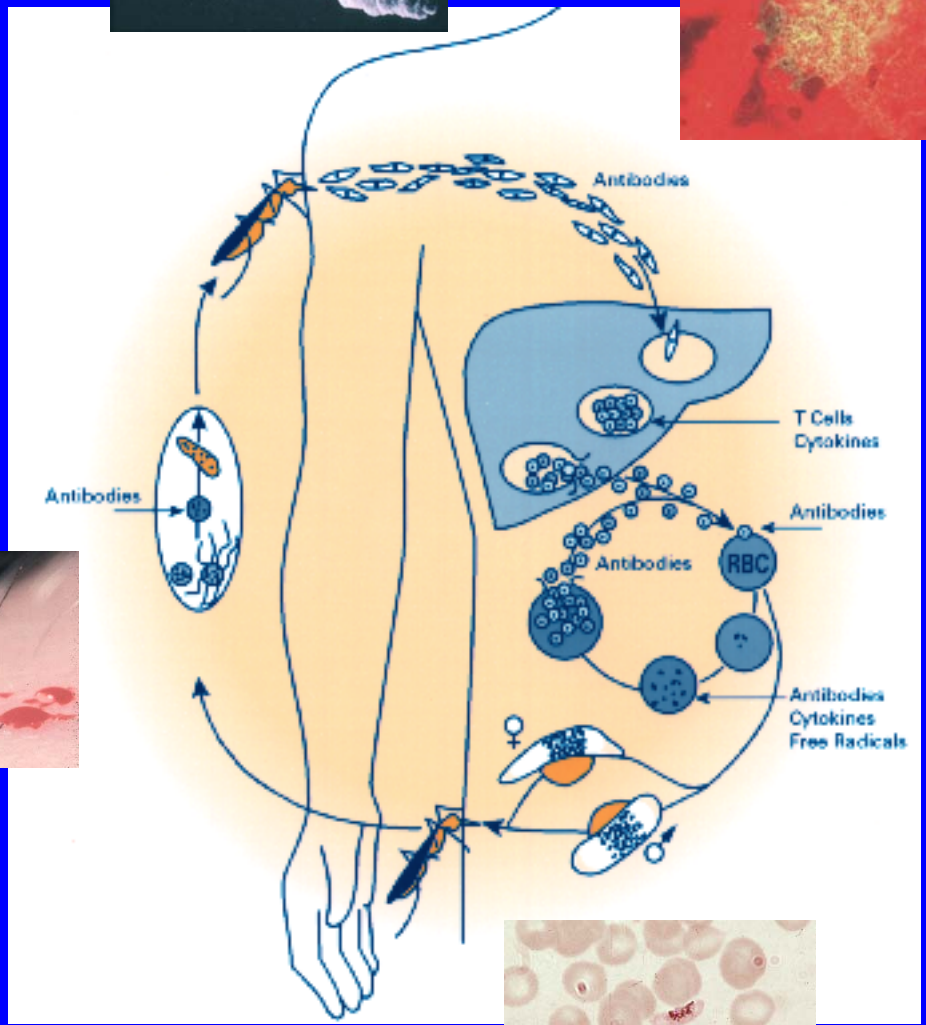
Antibodies
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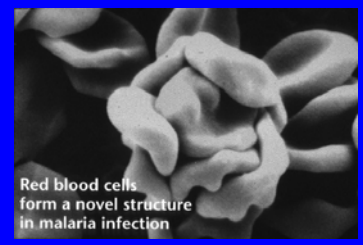
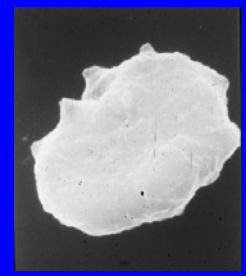
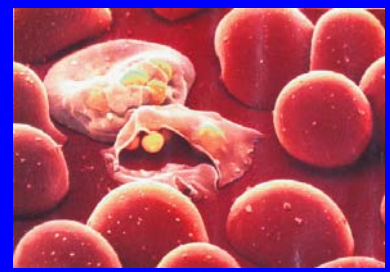
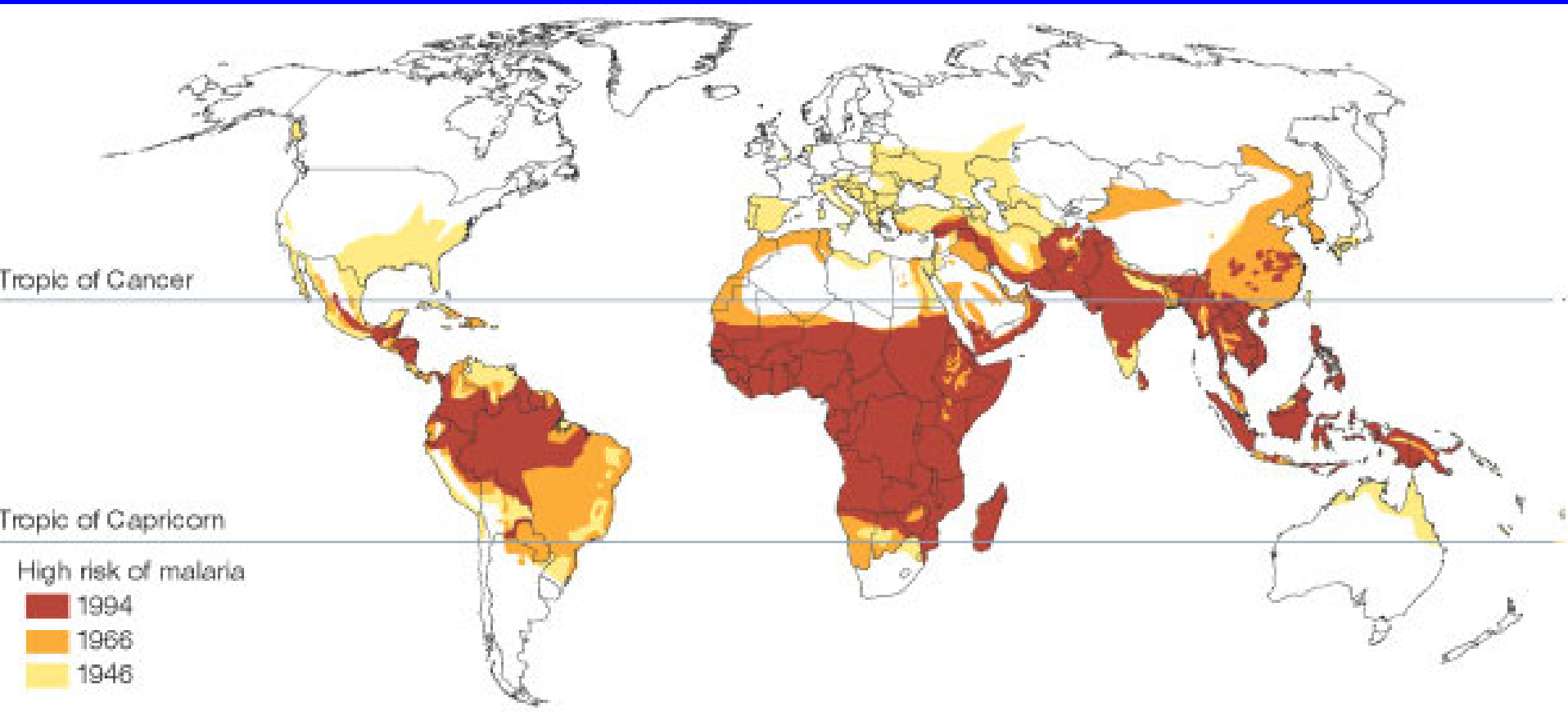

Red blood cells
form a novel structure
in malaria infection





Risk of Malaria 1946, 1966 and 1994



Sacks J Science 2002

FACTS ABOUT MALARIA

- Four species of human malarias
  - More than 90% of deaths from *Plasmodium falciparum*
- There are more individuals with malaria on the planet today then ever before in history
  - 300-500 million new infections/year
  - 1-3 million children die/year from malaria
- In some parts of Africa more than 90% of children are positive for malaria parasite
  - **About 2.4 billion people live in more than 100 countries where malaria is transmitted**

Malaria in the USA

- Each year, more than 27 Million American travelers visit areas of the world with malaria and thousands of US troops are deployed in endemic areas
- In the USA, there are about 1500 annual imported cases of clinical malaria
- There are an average of 3 cases of transfusion malaria per year or 0.25 cases per million units
- 150, 000 donor deferrals due to potential exposure to malaria
- Locally transmitted malaria has been observed

FDA Guidelines for Donor Deferral Based on 1994 Memorandum

- Three-year deferral:
  - History of clinical malaria
  - Prior residents of endemic country
- One-year deferral:
  - Visit to a malaria endemic area by residents of nonendemic countries

Identification of malaria endemic area as provided by CDC:

www.cdc.gov/travel/regionalmalaria/index.htm

Considerations for the modification of the current Guidelines

- Scientific issues
  - Definition of residency
    a) duration of exposure in endemic areas
    b) identifying exposure history in the face of changing global distribution of malaria
  - Reconsideration of donor deferral period based on the nature of malaria exposure

Issues Related to Transfusion Malaria

- In the US, there is no approved test to screen donor blood for the presence of malaria parasites
- Donor deferral is based on history of travel or past residence in endemic areas
- The majority of cases of TTM occur when the deferral policy is not implemented properly
- Some European countries screen for the presence of malarial antibodies to determine a true exposure
  - –The information is used to shorten the deferral period

TTM in the US

- **0.25 cases per million units collected**
- **1963-1998:**
  - **91 cases**
  - **10 deaths**
  - **All 4 *Plasmodium* species**
    - **35% *P. falciparum***
    - **29% *P. vivax***
    - **28% *P. malariae***
    - **4% *P. ovale***
    - **4% mixed or undetermined species**

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

TTM in the US: Changing Pattern of Incidents and Demographics

- 1995 to 2004
  - – 0.04 cases of TTM per million units of blood collected
- 1995 to 2004
  - – 5 of 6 reported incidents of TTM were caused by donors born in a malaria endemic country

Methods to Detect Malaria Parasites

- Direct parasite demonstration
  - Microscopy
    - Thick blood film
    - QBC method
  - Antigen detection
    - HRP, LDH etc. based dip sticks
  - Nucleic acid based methods
    - –PCR test, TaqMan assay, Real-time PCR and Microarray
- Indirect demonstration of parasite exposure
  - Antibody based methods: IFAT, ELISA

THE LANCET.

A Journal of British and Foreign Medicine, Surgery, Obstetrics, Physiology, Chemistry, Pharmacology, Public Health, and News.

IN TWO VOLUMES ANNUALLY.

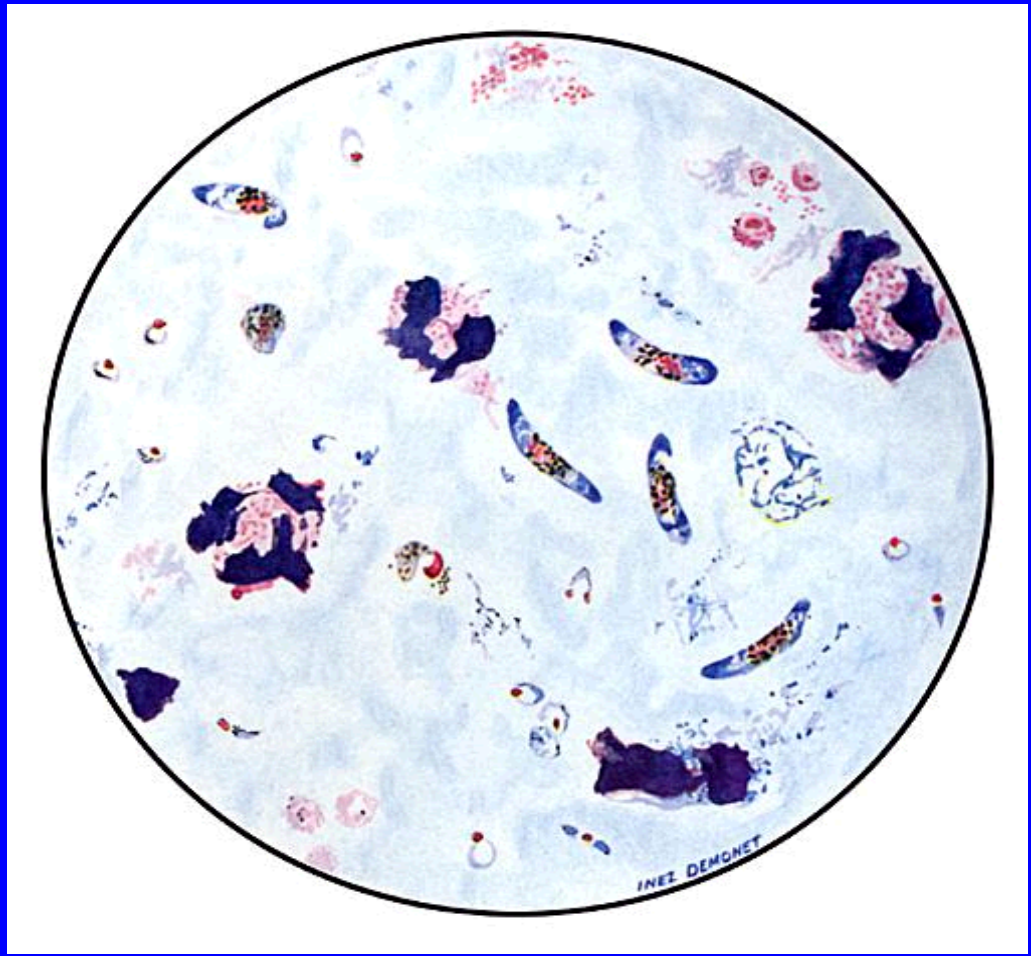
VOL I. FOR 1903.

AN IMPROVED METHOD FOR THE MICROSCOPICAL DIAGNOSIS OF INTERMITTENT FEVER.

BY RONALD ROSS, C.B., F.R.S., F.R.C.S. ENG., D.P.H.,

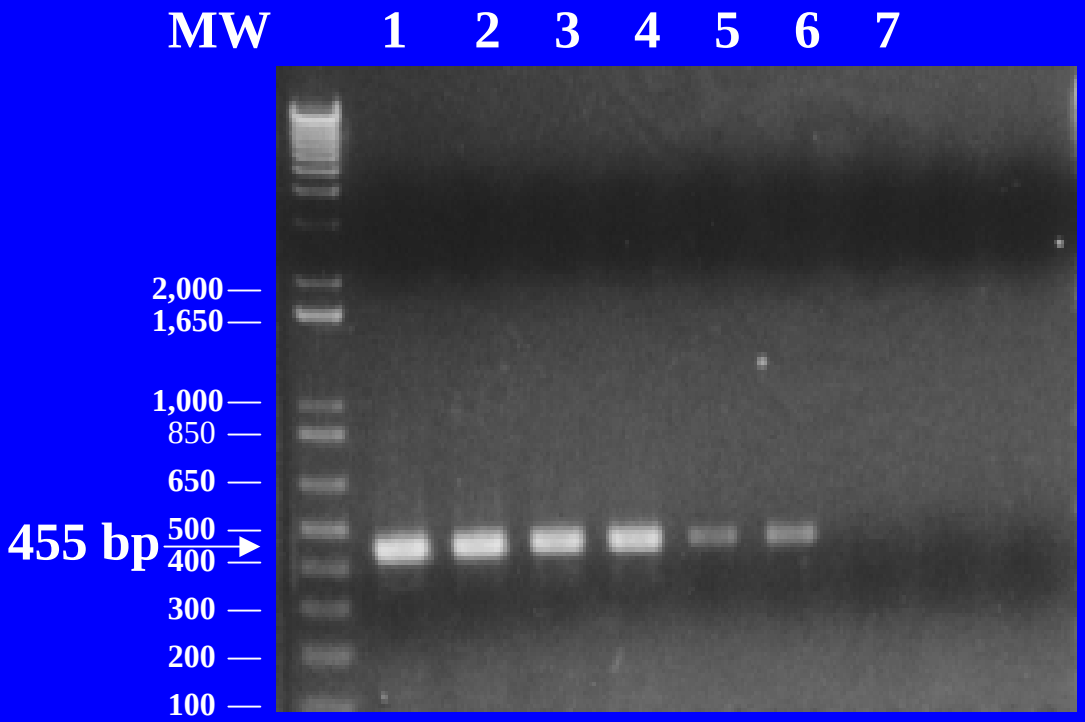
LECTURER ON TROPICAL MEDICINE AT UNIVERSITY COLLEGE, LIVERPOOL; WALTER MYERS LECTURER AT THE LIVERPOOL SCHOOL OF TROPICAL MEDICINE; LATE MAJOR, I.M.S.

Plasmodium falciparum: Blood Stage Parasites Thick Blood Smears



Sensitivity limit: 5 parasites per µL of blood

DNA Based Methods: Nested PCR Amplification of 18 S rRNA Gene Fragment from *P. falciparum* Parasites Spiked in 1 µL of Normal Human Blood

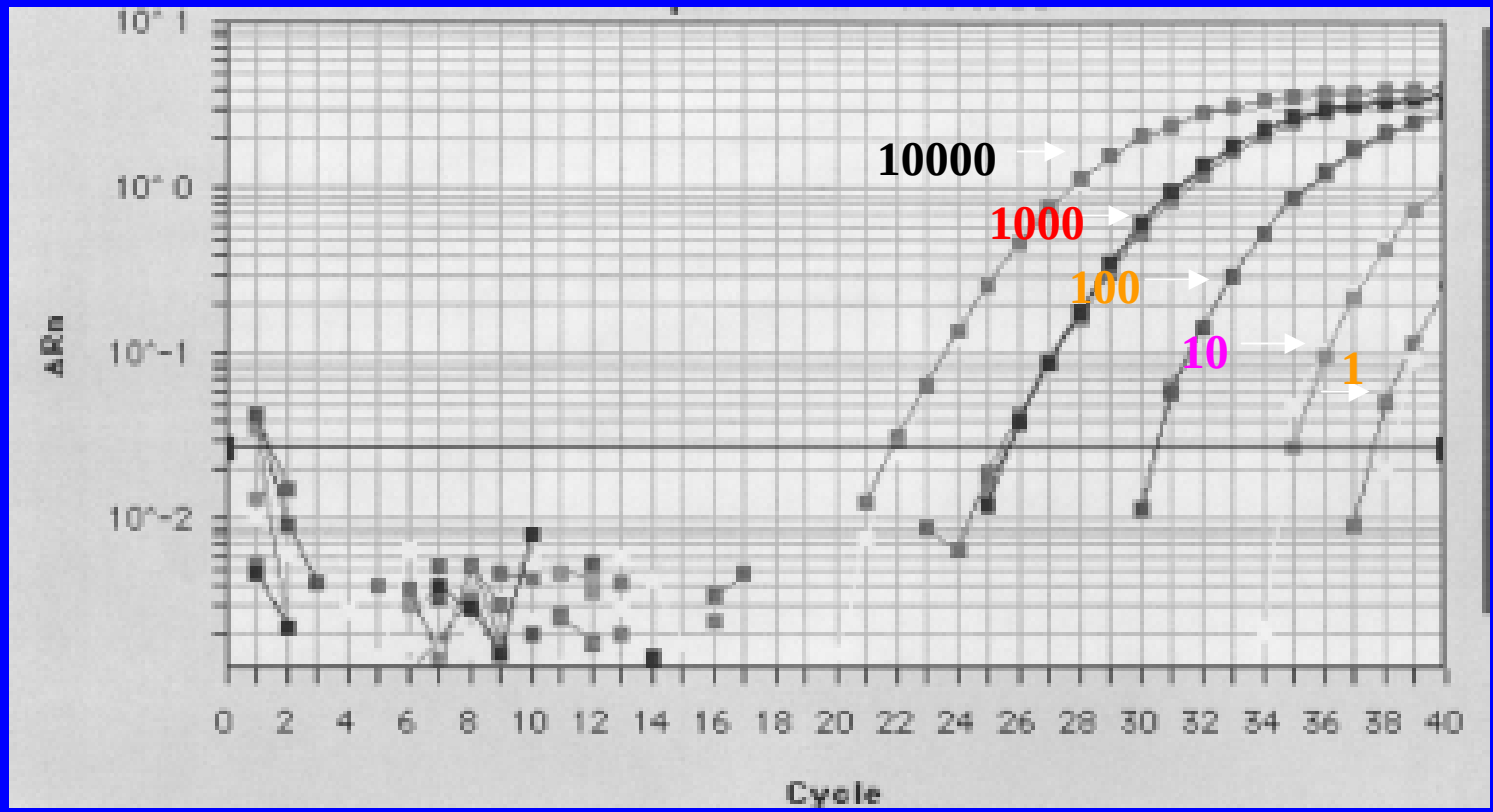


1. 40 parasites
2. 20 parasites
3. 10 parasites
4. 5 parasites
5. 2 parasites
6. 1 parasite
7. Negative control

DNA was prepared by direct boiling of parasite spiked blood. Detection limit – 1 parasite/µL of blood

DNA Based Methods:

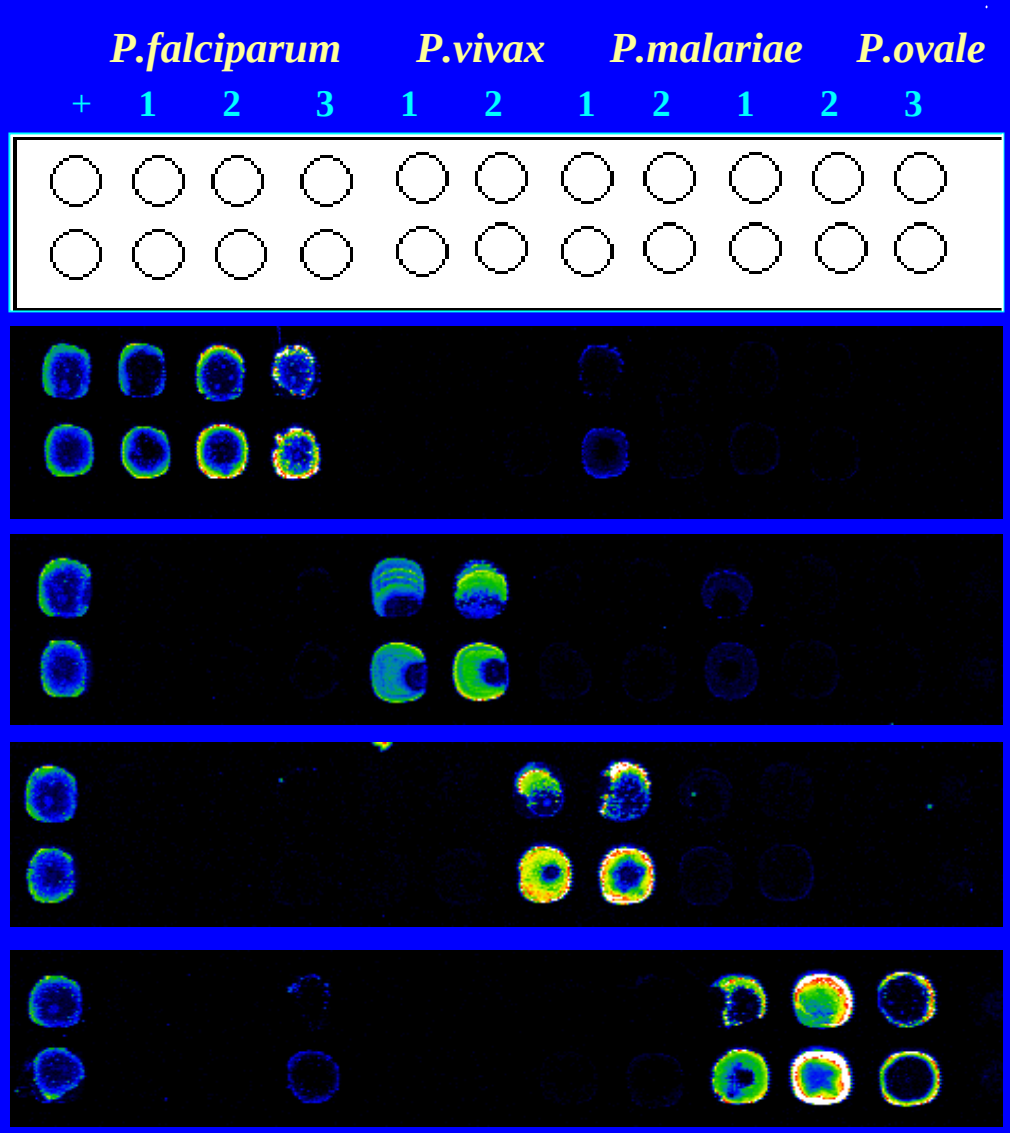
Detection Limit of the TaqMan Assay for *P.falciparum* Parasites Spiked in Normal Blood



Detection limit - 1 parasite/μL of blood

DNA Based Methods:

Microarray Test



Plasmodium DNA oligonucleotide Probes dotting Pattern

Pf ss-DNA

Pv ss-DNA

Pm ss-DNA

Po ss-DNA

Blood Screening Test for Malaria

- A few parasites present in a unit of donor blood can cause TTM
- Both microscopy and DNA based tests are highly sensitive but not suitable for large blood volumes
- Antibody based ELISA is used by European countries
  - Detects antibodies only for *P. falciparum* and *P. vivax* malarias with limited sensitivity
- FDA, in collaboration with CDC, is developing an ELISA based on recombinant proteins from all four species of *Plasmodium*

Acknowledgements

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