CDC Experience with Laboratory Tests Used to Investigate Incidents of Transfusion-Transmitted Malaria

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DIAGNOSTIC TOOLS AVAILABLE AT CDC

- Blood film examination
- Antibody detection - IFA
- DNA detection - PCR

MALARIA IFA TEST

Antigen: washed cell thick smears of RBCs infected with one species

- *P. falciparum*
- *P. malariae*
- *P. ovale*
- *P. vivax*

MALARIA IFA TEST

- **Sensitivity 89/92 = 98%**
  - Based on Pv and Pf infections
- **Specificity 1/184 = 99.5%**
  - *Babesia* may cross-react

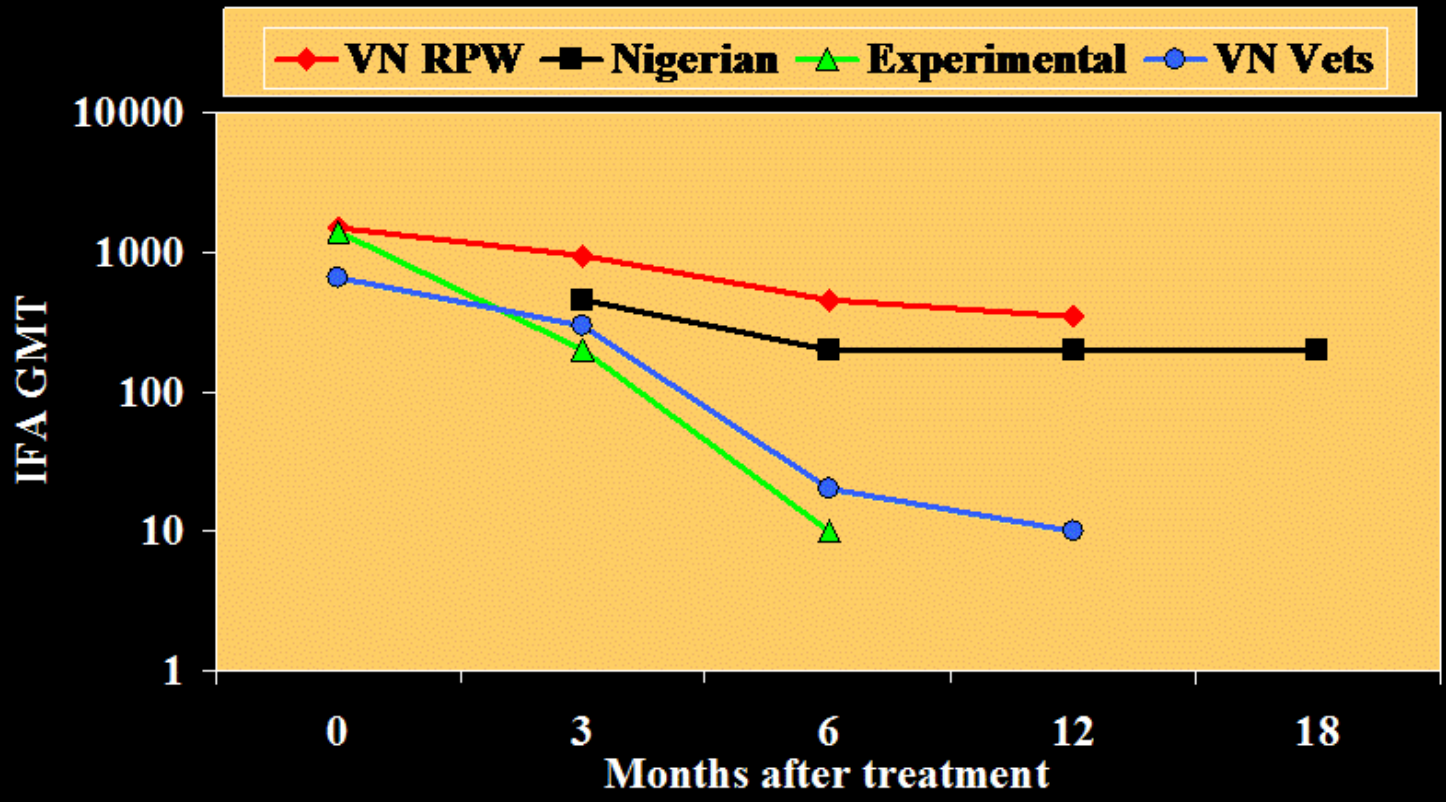
MALARIA IFA TEST

Human Experimental Infections

- Parasitemia preceeds antibody
  - P. falciparum 4-6 days
  - P. vivax 2-6 days
  - P. malariae 4-6 days
- If parasitemia is suppressed, may still develop detectable antibody

MALARIA IFA TEST

Antibody Persistence Post-Rx



Typical Malaria IFA Results

Slide Diagnosis	IFA			
	P. falcip	*P. malariae*	*P. ovale*	*P. vivax*
P. falciparum	1:16384	1:4096	1:1024	1:64
P. falciparum	1:1024	Neg	Neg	Neg
P. ovale	Neg	Neg	1:256	Neg
P. vivax	Neg	Neg	1:64	1:1024
P. malariae	1:1024	1:1024	1:64	1:64

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CDC PCR FOR MALARIA

Two-step nested PCR

- Genus-specific primers followed by
- Species-specific primers
  (Snounou et al, 1993)

CDC PCR FOR MALARIA

Sensitivity & Specificity
100%+

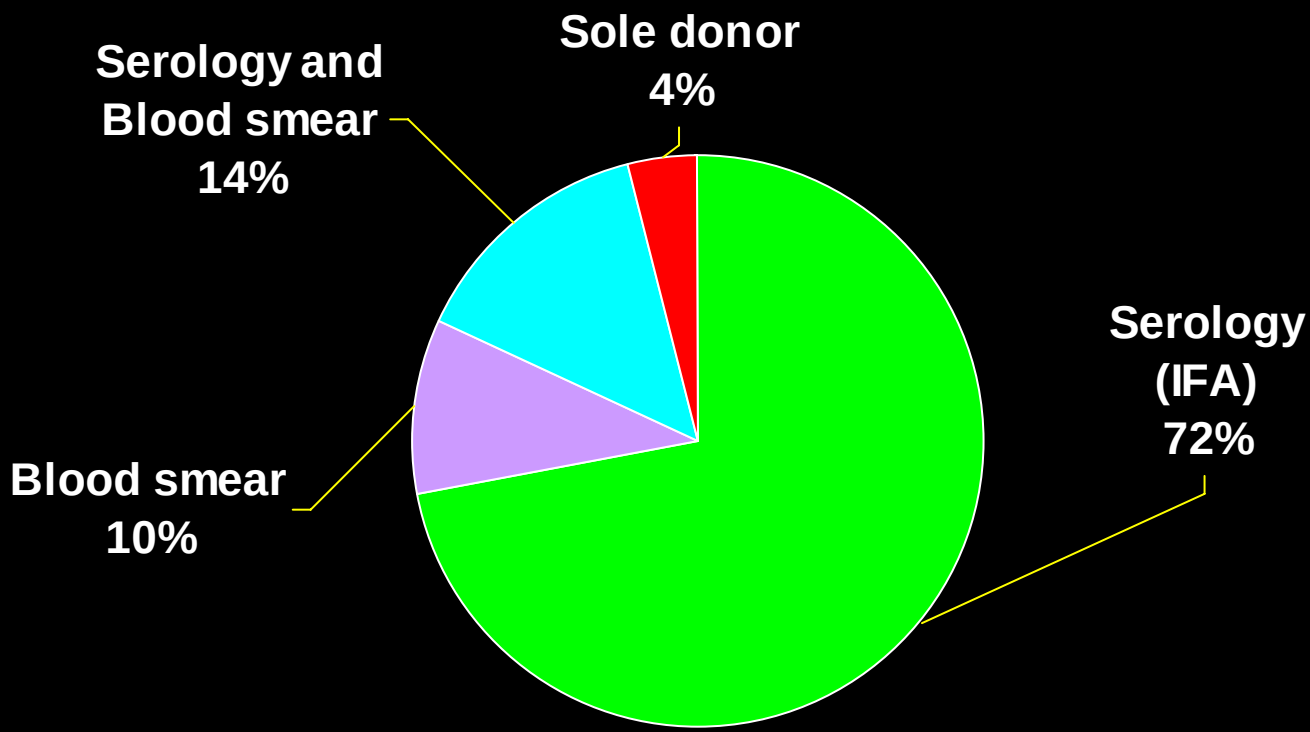
based on smear results

ALGORITHM FOR LABORATORY TESTING OF SUSPECT DONORS

- Screen with serology
- PCR on IFA positives
- Blood film examination on IFA positives

TRANSFUSION TRANSMITTED MALARIA, 1963-1998

How 65 implicated donors were identified



TRANSFUSION TRANSMITTED MALARIA, 1963-1998

In implicated donors, where information was available:

- 98% had positive serology
- 33% had positive blood smear

Laboratory investigation of blood donors, 1996-2005

Year	*Species*	*Donors*	*IFA +*	*PCR +*
1996	Falcip	7	1	1
1998	Falcip	4	1	1
2002	Malariae	10	1	0
2003	Falcip	2	1	0
2005	Falcip	150	1/100	0

Laboratory investigation of blood donors, 1996-2005

Year	*Tx date*	*Spec date*	*Slide result*	*PCR result*
1996	11/12/96	3/1997	Pos	Pos
1998	1/15/98	?1/15/98	Neg	Pos
2002	5/1/02	7/11/02	Neg	Neg
2003	3/1/03	4/03	Neg	Neg
2005	6/30/05	8/29/05	Neg	Neg

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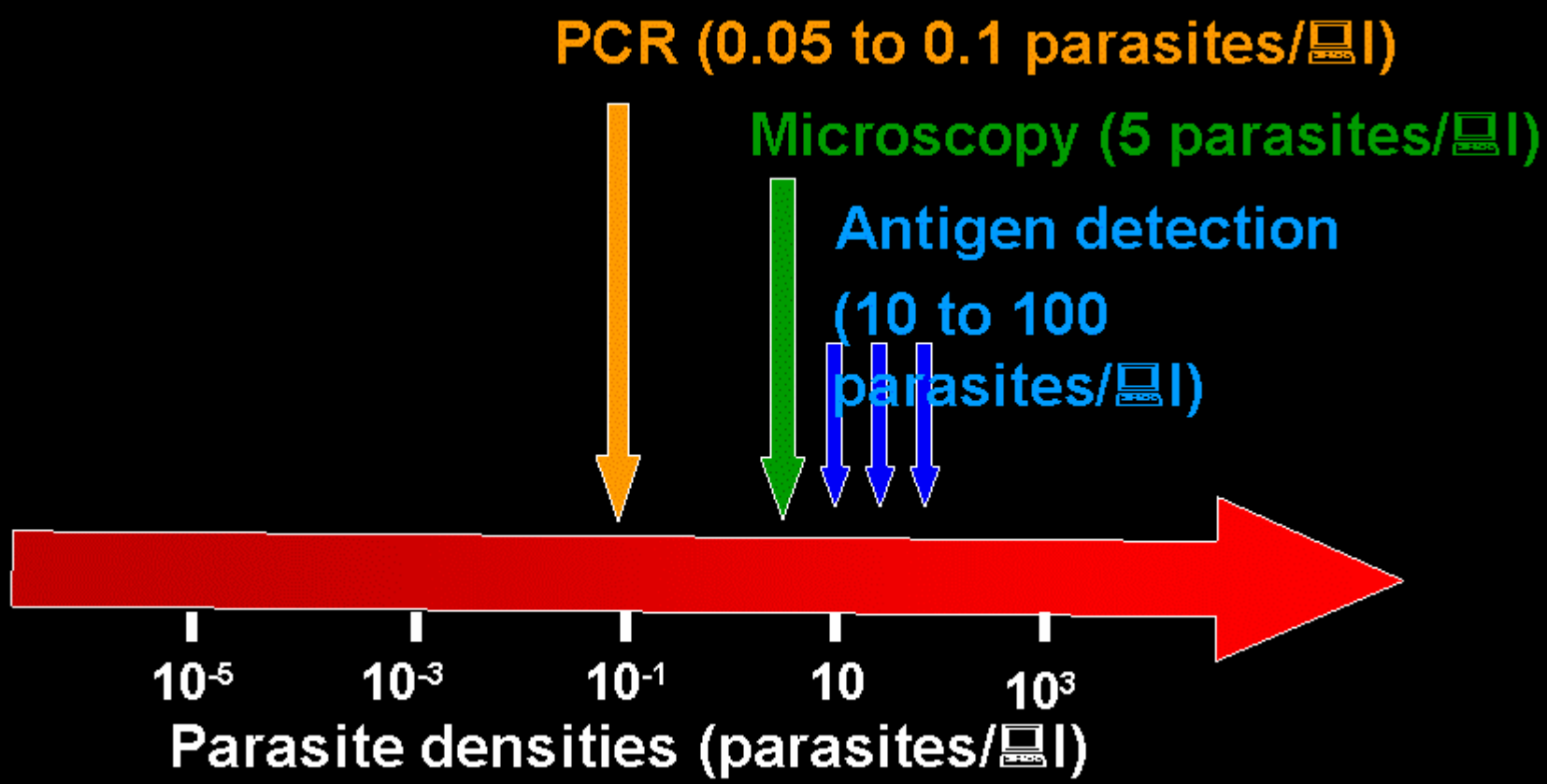
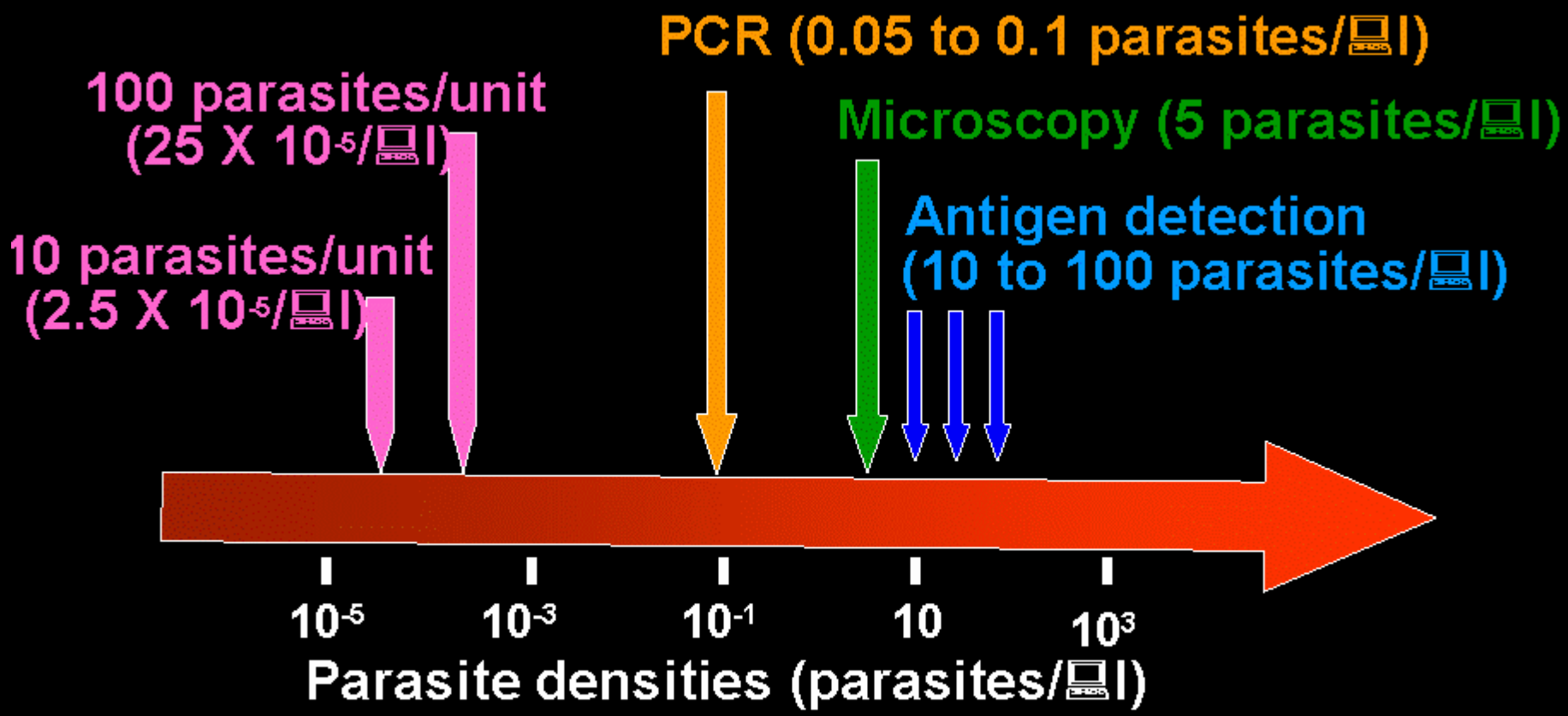
Detection of Parasites/Parasite Products



Detection of Parasites/Parasite Products



Detection of 10 parasites/unit requires a sensitivity:

-4,000 times better than current PCR

-200,000 times better than microscopy

Selected References

IFA

- Collins et al, Amer J Trop Med Hyg 1964;13:256
- Collins et al, Amer J Trop Med Hyg 1964;13:777
- Sulzer et al, Amer J Trop Med Hyg 1969;18:199
- Wilson et al, Amer J Trop Med Hyg 1970;19:401
- Gleason et al, Amer J Trop Med Hyg 1971;20:10

PCR

- Snounou et al, Mol Biochem Parasitol 1993;61:315
- Johnston et al, J Clin Microbiol 2006;44:1087