Evaluation of the performances of two rapid diagnostic tests (Cyscope®mini and Paracheck-*Pf*®) in the diagnosis of malaria among febrile children in Southwest Nigeria.

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Background

- Malaria is a major cause of morbidity and mortality in endemic areas of which Nigeria is one.
- Young children and pregnant women are most at risk.
- Malaria diagnosis was presumptive most of the time with attendant problems of over-diagnosis.
- WHO now advocates universal parasite-based diagnosis before treatment (WHO, 2010).

Background contd.

- Microscopy is the current gold standard has a lot of challenges
  - Tedious and time consuming
  - Needs functional microscope and electricity supply
  - Expertise to read the slides
- Rapid Diagnostic Test (RDTs) a viable option.
  - Fast (15 -20 minutes)
  - No equipment or electricity required
  - Minimal training required
- Antigens targeted by malaria RDTs
  - HRP2, pLDH, Aldolase, MSP and CSP antigens

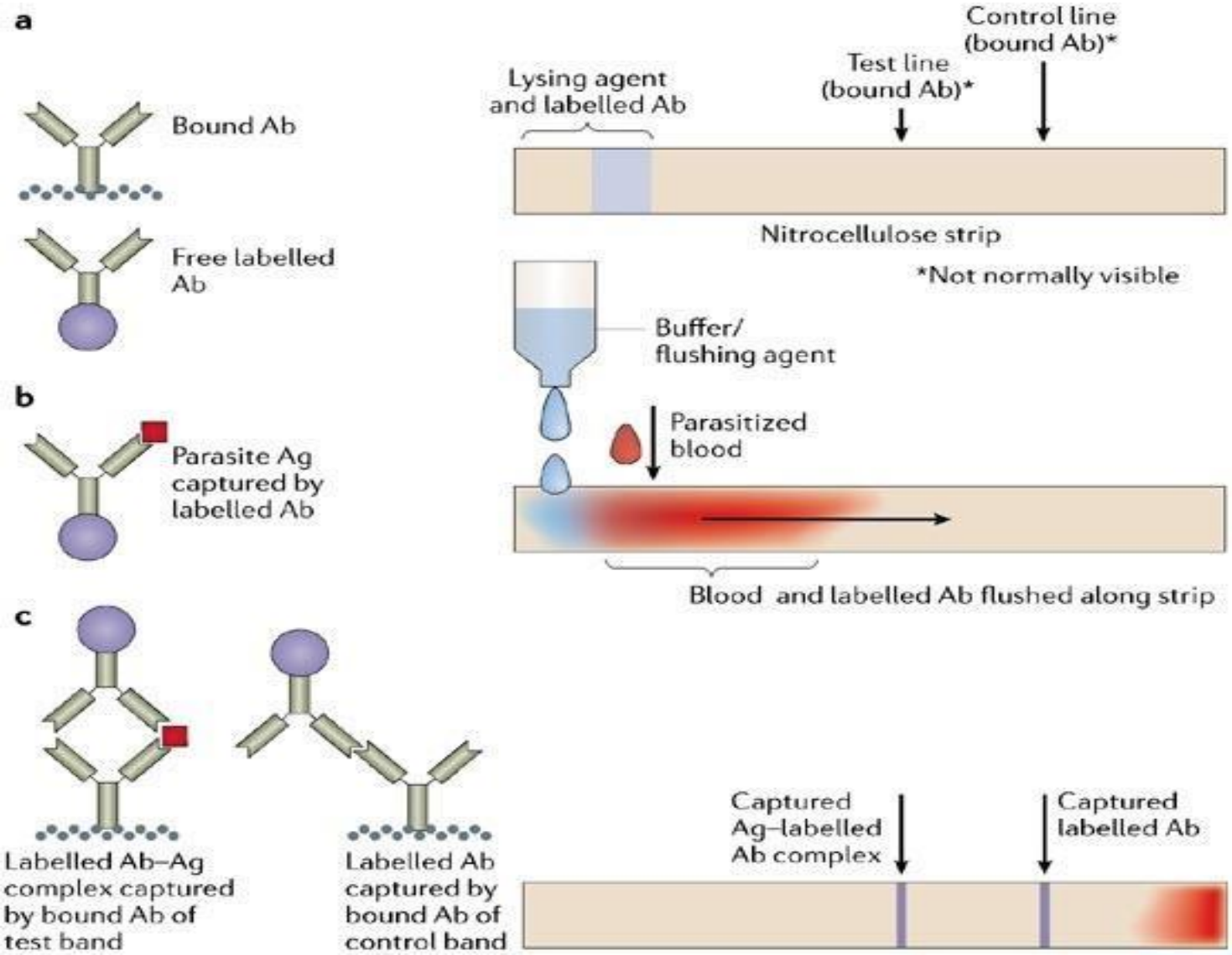


Fig. 1: *Mechanism of action of common malaria RDTs (Bell et al. 2006).*

Objective

- To test the diagnostic performances of Cyscope®mini (Partec, Germany) and Paracheck-Pf® (Orchid Biomedical Systems, Goa, India) among febrile children using light microscopy as gold standard.

Patients and methods

- **Ethical approval -** from the University of Ibadan/University College Hospital Ethical Review Committee, Ibadan.
- **Study site -** GOP, UCH, Ibadan.
- **Target population** – Febrile children of both sexes aged 6mths – 12 years presenting with fever.
- Informed consent from parents/guardians of study volunteers.
- **Study duration** – 6 mths starting Sept. 2010

Patients and methods contd.

- Questionnaires administered for age, sex, height, weight, temperature, presenting features & treatment history.
- Capillary blood from finger prick for
  - haematocrit determination (PCV)
  - thick and thin films
  - Cyscope®mini slide and
  - Paracheck-Pf® cassette test.
- Data analysis using SPSS version 16.0 statistical software (Chicago, IL).
- The overall diagnostic performances were calculated using OpenEpi version 2.3

Formulae for calculation of diagnostic performance.

- Sensitivity =TP/(TP+FN)
- Specificity=TN/(TN+FP)
- Positive predictive values PPV=TP/(TP+FP)
- Negative predictive values NPV=TN/(TN+FN)
- Test accuracy =(TP+TN)/(total number of tests)

- Overall reliability= $\frac{[(TPxTN) - (FPxFN)]}{[(TP+FN) \times (TN+FP)]}$

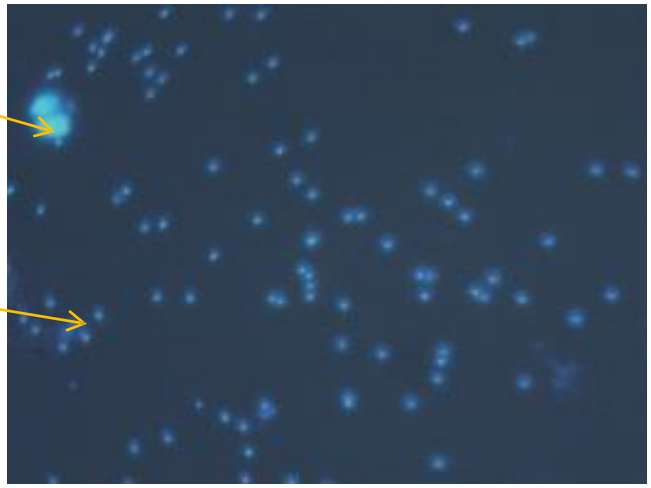
- TP - number of true positives
- TN - number of true negatives
- FP - number of false positives
- FN - number of false negatives

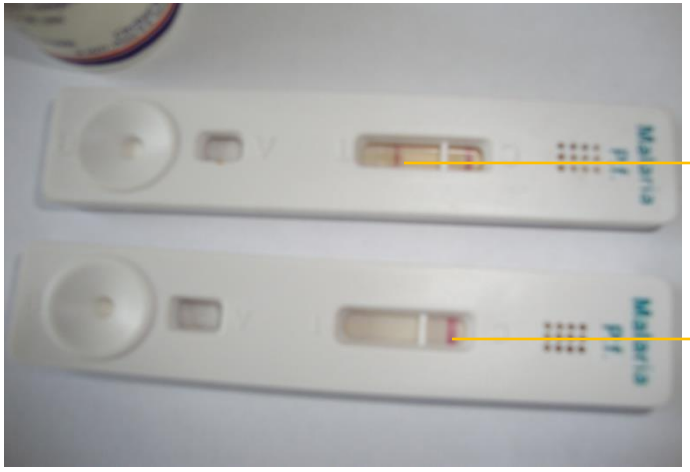
(Wanji *et al.* 2008)

Cyscope®mini

WBC

Parasites





Test band

Control band

Paracheck-Pf®

Fig. 2: Images of the two RDTs

Results - *Patients' parameters*

- Total no of enrollees - 209 children
  - 209 – Microscopy & Cyscope®mini
  - 142 – Microscopy & Paracheck-*Pf*®
- 50.7% (106/209) males and 49.3% (103/209) females.
- The average age - 40±30.38months (3 years 4 months)
- Mean weight - 13.7 ± 6.1kg.
- Mean temperature - 37.4 ±1.1°C
- Mean haematocrit was 32 ± 5.5%.

Results - *Presenting symptoms*

- A history of fever or fever at presentation - 90.4% (above 37.4°C – 45.5%).
- Cough - 51.2%
- Loss of appetite - 49.3%
- Catarrh - 37.8%
- Headache - 37.8%

Results - *Detection of malaria parasite by microscopy*

- Malaria parasite prevalence of 22.0% (46/209).
- Parasite density ranged from 40/µL to 203,883/ µL.
- Parasite density was ≤1000/µL in 21.7% (10/46) of the enrollees.
- Majority (67.4%) of the children positive for malaria had parasite densities within the range of 1,001- 100,000/µL .

Results - *Malaria parasite detection by Cyscope®mini relative to microscopy*

- Prevalence rate of 85.2% (178/209).
- 86.4% (19/22) parasite detection at densities ≤10,000/µL.
- At parasite densities >10,000/µL, the detection rate was 95.8% (23/24).
- Sensitivity - 91.3%
- Specificity - 16.56%

Results - *Malaria parasite detection by Paracheck-Pf® relative to microscopy*

- Prevalence rate of 32.1% (45/140).
- 90.9% (10/11) parasite detection at parasite density ≤10,000/µL.
- At parasite densities >10,000/µL, the detection rate was 83.3% (15/18).
- Sensitivity – 86.21%
- Specificity - 81.98%

Table 1: Analysis of results obtained from RDTs compared to microscopy

RDT	TP grouped by parasite densities				FP	TN	FN	Total
	<1000 µL	(1001-10,000) µL	(10,001-100,000) µL	>100,000 µL				
Cyscope®mini	9	10	18	5	136	27	4	209
Paracheck-Pf®	4	6	10	5	20	91	4	140

Key: TP – True positives, FP – False positives, TN – True negatives, FN – False negatives

Table 2: Summary of comparative diagnostic performances of Cyscope®mini and Paracheck-Pf® in patients screened with both RDTs ($p<0.05$).

	Cyscope®mini	Paracheck-Pf®
Sensitivity	100%	86.21%
Specificity	13.51%	81.98%
Positive Predictive Value (PPV)	23.2%	55.56%
Negative Predictive Value (NPV)	100%	95.79%
Diagnostic Accuracy	31.43%	82.86%
Likelihood ratio of a Positive Test	1.156	4.784
Likelihood ratio of a Negative Test	0.0	0.1682
Cohen's kappa (unweighted)	0.0608	0.5665

Summary of Results

- The sensitivities of the two RDTs were quite impressive relative to microscopy.
- The sensitivities of Paracheck-Pf® and Cyscope®mini were lower than the WHO standards for RDTs.
- Cyscope®mini recorded a high number of false positives.
- The diagnostic performance of Paracheck-Pf® was significantly higher than that of Cyscope®mini.

Conclusions and Recommendation

- RDTs will be good complements for microscopy
  - Requires no expertise
  - Suitable in places with poor electricity supply.
- High rate of false positives reported in the use of Cyscope®mini should be carefully examined.
- More research to improve on Paracheck-Pf® and Cyscope®mini sensitivities and specificities.

Acknowledgements

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Thank you for Listening