Malaria Microscopy Competence, The Panacea to Malaria Burden and Eradication

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Overview

- The Historical Background of Malaria
- The Nomenclature: Malaria?
- World Malaria Burden
- Malaria Microscopy Incompetence: Drug Trial Problem
- Consequences of Malaria Microscopy Incompetence
- Presumptive Diagnosis
- WHO and National Recommendation
- Malaria Case Management Goal
- Malaria Microscopy Certification (ECAMM and NCAMM)
- Why Malaria Microscopy Competence
- Conclusion and Closing Message

Historical Background of Malaria

- Origin: Evolved from tropical Africa some 2.5million – 3.0 million years ago.
- *Plasmodium falciparum* is believed to have originated as a cross specie transmission from gorillas while *P. vivax* was from ancestral stock of parasite also from gorilla and chimpanzee.
- Spread: It is thought that malaria began to travel out of Africa about 3,000yrs ago hastened by wars and import of human labour during slave trade
- Evidence that malaria is an ancient disease was found in ancient Chinese documents 2,700 BC, Clay tablets from Mesopotamia from 2,000 BC, Egyptian papyri from 1,570 BC, Hindu texts 600 BC
- First evidence of malaria disease in modern world began to surface in the mid-18th century in mediaval Italy.

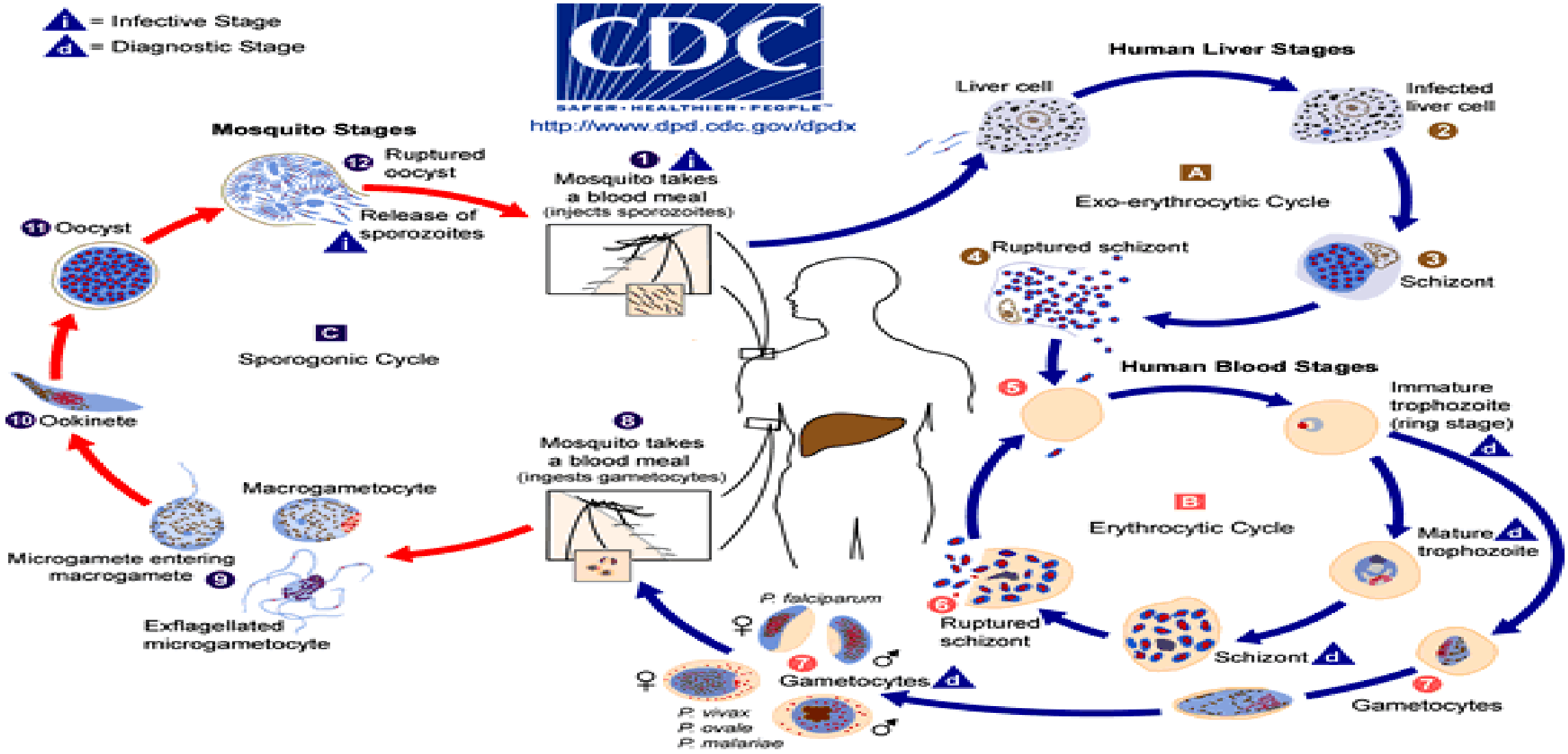
The Nomenclature: malaria

- The name is derived from Italian vocabulary Mal (Bad) aria (Air).
- It was believed in Italy that malaria disease is gotten from foul or bad air from marshy or swamp believed to favor the vector breeding.
- A protozoan infection caused by 5 *Plasmodium specie* that infect man.
- Namely, *P. falciparum, P. vivax, P. malaria, P. ovale and P. Knowlessi*
- Three of these species can be found in Nigeria. Fourth specie of *Pv* has been documented molecularly b
- The emerging last specie is found in South east Asia

How do you get malaria ?

- Vector is female anopheles' mosquitoes.
- About 460 species are recognized but about 100 can transmit human malaria. However, only 30 – 40 species commonly transmit plasmodium of man
- Transmission to man is through the bite of an infected female Anopheles Mosquitoes
- Responsible mosquitoes are *A. funestus, A. gambiense, A. arabisiense, A. melas* and the new *A. stephenson*
- Parasite called sporozoites get into you and begin to multiply
- Becoming sick with symptoms of malaria such as high fever, headache, severe chills or rigor, profuse sweating and general body pain.

Life Cycle of *Plasmodium Specie*



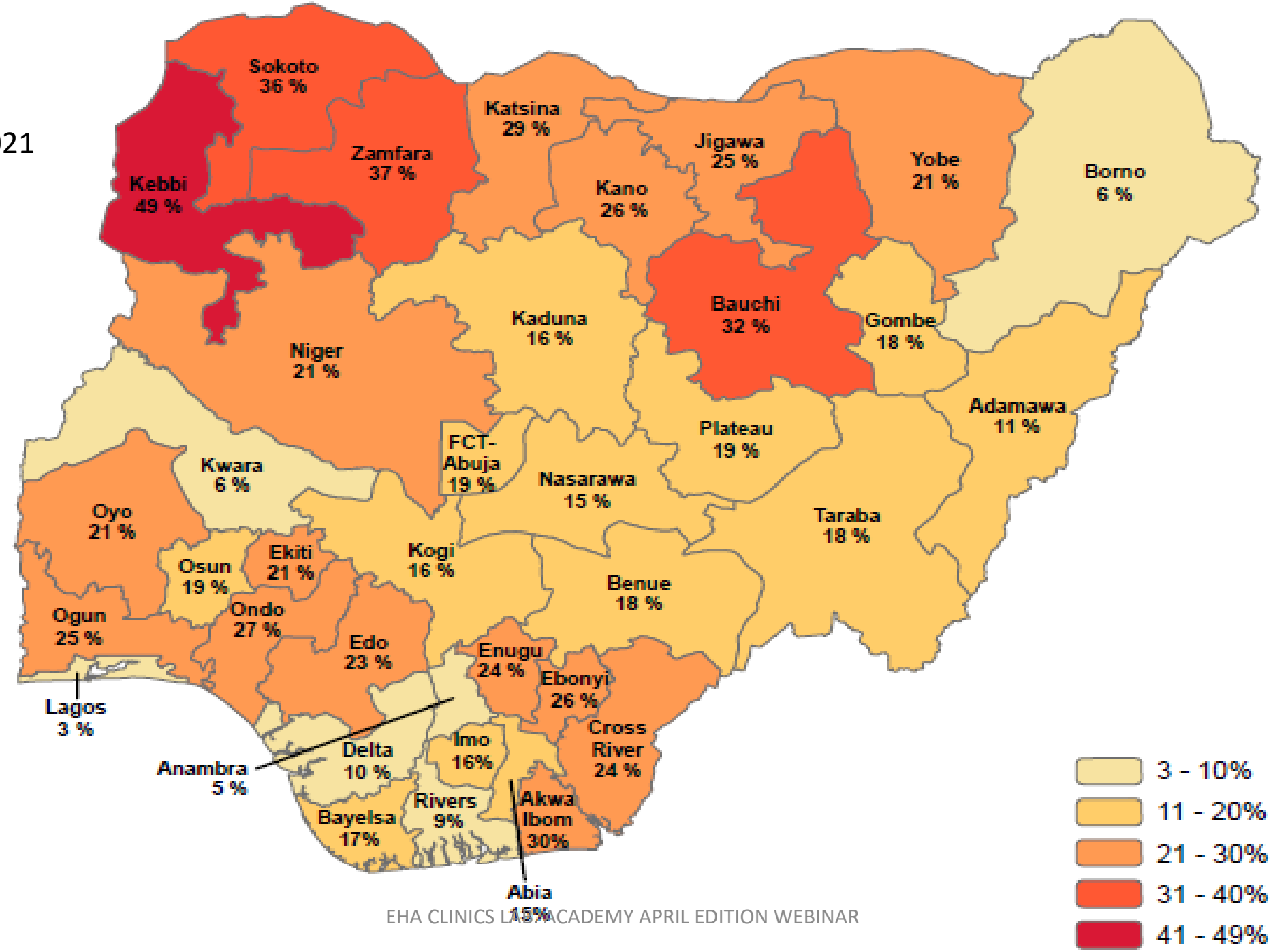
World Malaria Burden

- Half of the world population live in malaria risk region.
- 247 million cases of malaria and 619,000 deaths were reported worldwide in 2021 in 84 countries (2022 WMR).
- Twenty-nine countries accounted for 96% of malaria cases globally, and 4 countries – Nigeria (27%), the Democratic Republic of the Congo (12%), Uganda (5%) and Mozambique (4%) – accounted for almost half of all cases globally.
- The WAR = over 95% (234 million cases) of global malaria cases and over 96% (593,000) of global malaria deaths. 1 child dies per minute
- WAR leads on the number of deaths due to malaria with 4 countries accounting for over half the global malaria deaths (Nigeria–31%, the Democratic Republic of the Congo–13%, Niger–4% and the United Republic of Tanzania–4%).

Nigeria Malaria Burden

- 27% = 66,690,000 = approx. 67million burden
- 31% = 191,890 = Approx. 192,000 death. 60 times more than COVID
- COVID = 3,155 death in 3 years
- Every hour, 22 children die of malaria
- With these figures, detection of malaria parasites by quality assured microscopy followed by prompt and effective case management and preventive interventions are crucial for reducing malaria morbidity and mortality
- Presumptive treatment: Clinical signs and Symptoms failed us.
- Artemisinin resistance in Rwanda, Ghana, Uganda, Angola, DRC and Burkina faso

NMIS, 2021


Sokoto
36 %
Zamfara
37 %
Katsina
29 %
Jigawa
25 %
Yobe
21 %
Borno
6 %
Kebbi
49 %
Kano
26 %
Bauchi
32 %
Gombe
18 %
Kaduna
16 %
Niger
21 %
Adamawa
11 %
Plateau
19 %
FCT-
Abuja
19 %
Kwara
6 %
Nasarawa
15 %
Taraba
18 %
Oyo
21 %
Ekiti
21 %
Kogi
16 %
Osun
19 %
Benue
18 %
Ondo
27 %
Ogun
25 %
Edo
23 %
Enugu
24 %
Ebonyi
26 %
Lagos
3 %
Cross
River
24 %
Imo
16%
Anambra
5 %
Delta
10 %
Rivers
9%
Akwa
Ibom
30%
Bayelsa
17%
Abia
15%
3 - 10%
11 - 20%
21 - 30%
31 - 40%
41 - 49%

The big Question

- With these magnitude of burden
- With these magnitude of death
- With these magnitude of manpower loss to malaria
- With these magnitude of anguish and suffering parents go through in making sure that they rescue their children from malaria
- What other scientific proven strategy do we need to augment other preventing strategies in the case management of malaria
- **Parasitological diagnosis. Malaria Microscopy Competence**

Malaria Microscopy Incompetence: Drug Trial Problems

- 4 drug trial in East Africa in 1993
- Mefloquine Vs. Doxycycline in Indonesia - 1994
- Azithromycin study – 1995
- Challenge study in Washington – 1995
- Drug study in West Africa – 1998
- Drug study in East Africa – 2000
- Dipstick trial in Asia - 2000
- Treatment Trial in Asia - 2004.
- How many more

Protective Efficacy (PE)

- Ability of a drug or vaccine to prevent malaria
- With a good drug (like mefloquine)
  - ✓PE should be >95%
  - ✓Good for positive control arm
- FP impact on the estimate of PE
- Low PE = loss of a good drug

Prophylaxis Trial

- In Africa 2000
- Mefloquine control arm
  - ✓Did not appear to prevent malaria (1% PE)
  - ✓Nearly everyone treated early
  - ✓Many slides could not be traced.
- Re-reading of a sample of those slides traced
  - ✓Mefloquine prevented >95% of malaria
  - ✓Confirmed slide reading problem
  - ✓False positive problem confirmed on testing

Mefloquine Vs. Doxycycline.

- In Indonesia 1993
- The Question:
  - ✓What if FP occur
  - ✓What if FN occur
- Developed re-reading paradigm
- Tested potential new hires
- PCR on microscopy positive samples.

Treatment Trial with SP

- How sort this out?
  - ✓How well does SP work at this location.
  - ✓Re-read some/ all of the slides
    - Slides could not be taken out of the country
    - Some slides were lost/not readable
    - resolution problem.
    - Tried to send pictures from slide –
  - ✓Test the site Microscopists
    - Test set sent from another country
    - All Miscroscopists had the same result
    - Many false positive results
    - Would not send the test back
  - ✓Recommend: send in an expert microscopists.

Consequences of Malaria Microscopy Incompetence

- Accidentally kill a good drug or vaccine
- Less efficacious drug get access to the market
- Need to repeat a trial - $$
- Difficulty understanding published data
- Embarrassment
- Kill our children and Pregnant mothers
- Waste our resources
- Prolong sufferings
- Precipitate Resistance

Magnitude of over-diagnosis /over-treatment

Systematic review: 24 studies

conducted between 1989 and 2005

in 15 different African countries

including 15’331 patients

Proportion of malaria among fevers highly variable: 2% to 81%

MEDIAN PR = 26%

Before 2000	MEDIAN PR = 36%
From 2000-2005	MEDIAN PR = 19%

Courtesy of: V. D’Acremont, C. Lengeler, B. Genton, Philadelphia, November 2007

Country	Proportion of patients diagnosed with malaria having Negative microscopy	Overestimation by clinical diagnosis (%, mean 61%)
Ethiopia	1931/2490	78
The Gambia	248/407	61
The Gambia	122/260	47
Germany	178/231	77 (travelers)
Honduras	106/202	53
India	1806/1945 2536/2885	93 (children) 88 (adults)
India	227/526	43
Indonesia	266/560	48
Malawi	311/983	32
Malawi	211/248	85
Nigeria	788/1384	57
Papua New Guinea	676/2096	32
Sahel countries	137/297 210/220	46 (wet season) 96 (dry season)
Senegal	243/353	69
Tanzania	237/380	62
Tanzania	134/272	49
Tanzania	46/164	28
Thailand	953/1254	76
Thailand	666/913	73
Thailand	106/204	52
Uganda	319/742	43
Uganda	102/180	57
Zimbabwe	189/261	72
Zimbabwe	207/287	73

How, Why, What happened ???

- How did we get to this level of incompetence?
- Why did we allow it to happen ?
- What beclouded us ?
  - Advent of miracle drug chloroquine. So Cheap. Antimalaria. Analgesic. Antiprotozoal
  - Presumptive diagnosis: Treatment base on signs and symptoms
- By late nineties and early 2000, malaria prevail over chloroquine
- Another miracle drug was discovered. Artemisinin
- The damage has been done. Kuala Lumpur meeting to the rescue

Presumptive Diagnosis

Recognizing Malaria may no longer be as easy as *"looking and touching"*

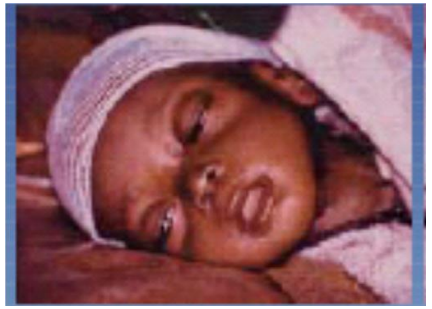
Hot body and Cold

Hot body and irritability

Hot body, weakness and malaise

Cold and rigors

Hot body



Hot body, palor and unconsciousness

COMMON CAUSES OF ACUTE FEVER IN OUTPATIENT CHILDREN UNDER 5 YEARS OF AGE

(in approximate descending order of frequency)[a]

- Upper respiratory tract infections, including otitis media and tonsillitis (viral origin)
- Other viral diseases (influenza, human herpesvirus 6, parvovirus B19, Epstein-Barr virus, cytomegalovirus)
- Pneumonia
- Malaria
- Gastroenteritis
- Urinary tract infection
- Typhoid fever
- Skin infection (abscess, cellulitis)
- Sepsis due to bacteraemia
- Meningitis

[a] From the 'Study to investigate the causes of fever in children living in urban Dar es Salaam and rural Ifakara', Dar es Salaam City Council, Ifakara Health Institute, United Republic of Tanzania and the Swiss Tropical and Public Health Institute (2011).

WHO Recommendation

- *"Prompt parasitologic confirmation by microscopy or alternatively by rapid diagnostic tests (RDTs) is recommended for all patients suspected of malaria before treatment is started*
- *Treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible"*

  WHO Malaria Case Management Guide

Test. Treat. Track

KEY RECOMMENDATIONS

- Every suspected malaria case should be confirmed by microscopy or RDT prior to treatment
- All diagnostic tools must be quality-assured across all levels of the health system
- Scale-up of malaria diagnostic testing should be integrated with efforts to improve the management of other febrile illnesses

KEY RECOMMENDATIONS

- After diagnostic confirmation, every uncomplicated case of *P. falciparum* malaria should be treated with a quality-assured ACT
- Every severe case of *P. falciparum* malaria should be treated with intravenous or intramuscular artesunate, followed by a full course of an ACT
- Antimalarials should be routinely monitored for therapeutic efficacy

KEY RECOMMENDATIONS

- Individual cases should be registered at health facility level. This allows for the recording of suspected cases, diagnostic test results, and treatments administered
- In the malaria control phase, countries should report suspected, presumed and confirmed cases separately, and summarize aggregate data on cases and deaths on a monthly basis
- Countries in elimination phase should undertake a full investigation of each malaria case

National Policy Recommendation

- National Policy on Diagnosis & Treatment of Malaria

- Recommends universal parasite-based confirmation of fevers

Malaria Case Management Goal

❑Overall Public health goal: reduction of the infectious reservoir

Specifically

- Early detection and prompt effective treatment to cure the infection and prevent progression to severe disease
- Proper management of severe disease to prevent death
- Prevention of the onset of drug resistance
- Reduction of malaria transmission

National Malaria Elimination Programme

Implications for Nigeria

Rapid Scaling Up towards "A Malaria Free Nigeria"

SUFI

Scale Up For Impact is a strategy which now focuses on:

- The entire population at risk rather than the vulnerable population.
- All cases of suspected Malaria must be Tested, Treated and Tracked (3Ts)
- **Deploying all available interventions**;
  - Prompt diagnosis and effective case management
  - Chemoprevention: PMC, SMC,
  - Integrated vector management
    - Use of long lasting insecticidal nets (LLINs)
    - Larval source management
    - Indoor residual spraying (IRS)
- Advocacy to policy makers and partners for resource mobilization

How to avoid Microscopy Incompetence

- Microscopist/Laboratory
  - Training and Retraining
  - Education
  - Assessment leading to Certification
    - ECAMM
    - NCAMM
- Malaria microscopy Internal QC
- Malaria microscopy QA

Why Malaria Microscopy Competence

- Parasitological Confirmation of malaria
- Method of choice and reference (Gold) standard for
  - Malaria case management (Test, treat and track)
  - Epidemiological studies (Specie and resistance tracking)
  - Drugs efficacy (Monitor Resistance). Rwanda & Ghana
  - Vaccine trials
  - Quality assurance of RDT (QC panel production and Specimen Banking)
  - Field trial and Evaluation of RDTs
  - Evaluation of other malaria diagnostic tools
  - QA (PT)

Malaria Microscopy Competence: ECAMM

- 2002/3 - Serious issue with Quality Assurance (QA) and accuracy of microscopic diagnosis during drug trials and clinically. Also needed accurate microscopy to compare with RDTs
- WHO regions have collaborated to develop a multi-regional network to support competence assessment & QA for malaria microscopy
- Bi-Regional Workshop for Malaria Microscopy QA, Kuala Lumpur, Apr 05, formally agreed to the plans for the network. Agreed that ACTMalaria coordinate the network in WPRO and SEARO– now coordinated by WHO
- AFRO is supported by AMREF Health Africa now AMREF University and UCAD and the NCG should be deployed to establish NCAMM

ECAMM

- Recommended that courses commence at a national level for senior ‘National Core Group’ (NCG) microscopists in cooperation with national Ministries of Health
- ECAMM has evolved over the years and commenced in WHO AFRO in 2009
- The experience of ECAMM by the NCG should be deployed to establish NCAMM
- WHO recommends that once a country can have 10 – 12 L1 & L2 certified microscopist, such country can go ahead to establish her NCA program which will then be the official country certification programm

Summary of Nigeria Participation in ECAMM

SNo	Course Year	Location	Host	Sponsors	No of Parts.	L 1	L 2	L 3	L 4	Facilitators	Comment
1	July 2010 (4)	Nairobi, Kenya	AMREF	ANDI, CMUL	1	1	0	0	0	Peter Nwatha	First Nigerian & 3rd African x 4
2	Nov 2011 (27&28)	Lagos, Nigeria	ANDI	PMI-MAPs & ANDI	24	0	0	2	22	Emmanuel Yamo & Jide Bamiro	PMI-MAPs Supported state
3	2014	Nairobi, Kenya	AMREF	USDoD/NMOD /WPP-N	6	0	1	1	4	Peter Nwatha & David Isaboke	Mary Adenuga
4	Aug, 2015	Nairobi, Kenya	AMREF	ANDI, CMUL	5	3	1	1	0	Peter Nwatha & Stephen Munene	Jide, Dipo, Ginika, Chinonye and Uche
5	2016	Abuja, Lagos	USDoD/NMOD /WRP-N	PMI	12	2	9	1	0	Felix Adeoye & David Isaboke	Samuel & Theresa
6	2012-2021	Nairobi, Kenya	AMREF	3 self and 2 ANDI, CMUL	6	3	2	0	1	Emmanuel, Peter and Stephen	Adeoye, Ashabi, & Chinonye
7	2018	Nairobi, Kenya	AMREF	WHO / NMEP	3	1	1	1	0	David Isaboke Stephen Munene	Samuel
8	Apr 2019	Nairobi, Kenya	AMREF	2 WHO	2	1	1	0	0	Ken Lilley	Jide & Adeoye
9	Feb, 2020	Owerri Nigeria	FMC, Owerri	10 Self & 2 ANDI	12	0	4	4	4	David Isaboke & Jide Bamiro	
10	Dec, 2020	Lagos, Nigeria	WRP-N & NIMR, Yaba	NMEP / Global Fund	24	9	6	6	3	David Isaboke & Jide Bamiro	Current Certification
11	July & Nov 2022	Nairobi, Kenya	AMREF	WHO	5	2	3	1	0	Bina S David and Stephen	Current Certification
Attempted Participants					100	22	28	17	34		Level 1 22(17)
% participants Performance					100%	22%	28%	17%	34%		Level 2 28 (20)
Recertifying Participants					17	4	6	2	4		Level 3 17 (15)
Total Number					82	17	20 (2)	15	29		Level 4 34 (29)

WHO Facilitator's ECAMM, June 27 – July 1 2022

ECAMM Validates Nigeria MMT

Certification type	Level 1	Level 2	Level 3	Level 4
Pre ECAMM/ NCAMM Certification	5	5	7	7
WHO ECAMM Certification	9	6	6	3

ECAMM Validates Nigeria MMT

SNo	Microscopist	Place of Primary Assignment	PRE ECAMM National Cert. Level	ECAMM Cert. Level
1	MLS 1	[redacted]	1	1
2	MLS 2	[redacted]	3	1
3	MLS 3	[redacted]	3	1
4	MLS 4	[redacted]	2	1
5	MLS 5	[redacted]	2	1
6	MLS 6	[redacted]	2	1
7	MLS 7	[redacted]	1	1
8	MLS 8	[redacted]	1	1
9	MLS 9	[redacted]	3	1
10	MLS 10	[redacted]	1	2
11	MLS 11	[redacted]	3	2
12	MLS 12	[redacted]	3	2

ECAMM Validates MMT

SNo	Microscopist	Place of Primary Assignment	PRE ECAMM National Cert. Level	ECAMM Cert. Level
13	MLS 13	[redacted]	2	2
14	MLS 14	[redacted]	3	2
15	MLS 15	[redacted]	4	2
16	MLS 16	[redacted]	3	3
17	MLS 17	[redacted]	4	3
18	MLS 18	[redacted]	1	3
19	MLS 19	[redacted]	4	3
20	MLS 20	[redacted]	4	3
21	MLS 21	[redacted]	4	3
22	MLS 22	[redacted]	2	4
23	MLS 23	[redacted]	4	4
24	MLS 24	[redacted]	4	4

ECAMM Validates MMT

NCAMM

- April 14, 2022, the NMEP of the FMoH inaugurated the National Core Group of 40 malaria Microscopists
- First 40 malaria Microscopists to be WHO certified
- Establish the National Competence assessment of Malaria Microscopists Program
- Platform for National Competence for both private and public practitioner.
- Nov, 2022, the first NCAMM was held.

1st NCAMM in Nigeria

1st NCAMM Results in Nigeria

Health Facility and State	Microscopist	Parasite Detection (%)	Species ID (%)	Counting (+/- 25%) (%)	Certification Level	Certificate Number
Felade Diagnostic Support Initiative, Abuja, FCT	Felix A. Adeoye	100	98	79	1	NG00001
Diagnostic Laboratory, NIMR, Yaba, Lagos	Samuel Akindele	95	92	79	1	NG00002
Malaria unit, Department of Biochemistry & Nutrition, NIMR, Yaba, Lagos	Adeyinka Adepoju	100	92	57	1	NG00003
NMOD, 68, Army Reference Hospital, Yaba, Lagos	Theresa Obende	95	88	79	2	NG00004
NCAMM Committee, NMEP / MLSCN, Abuja, Lagos	Treasure W. Okoye	95	85	50	2	NG00005
Sacred Heart Catholic Hospital, Obudu, Cross River State	Ndidiamaka Okafor	100	89	43	2	NG00006
General Hospital, Eruwa, HMB, Oyo State	Felix Oladokun	86	85	43	2	NG00007

Malaria Microscopist Certification

ECAMM & NCAMM accreditation levels

Competence Level	Parasite Detection	Species Identification	Parasite Counting (within 25% of the true count)
Level 1	≥ 90%	≥ 90%	≥ 50%
Level 2	≥ 80%	≥ 80%	≥ 40%
Level 3	≥ 70%	≥ 70%	≥ 30%
Level 4	< 70%	< 70%	< 30%

WHO 56 standard slide panel

Slide Set 1 (42 slides): Assessment of presence/absence of parasites, and species identification

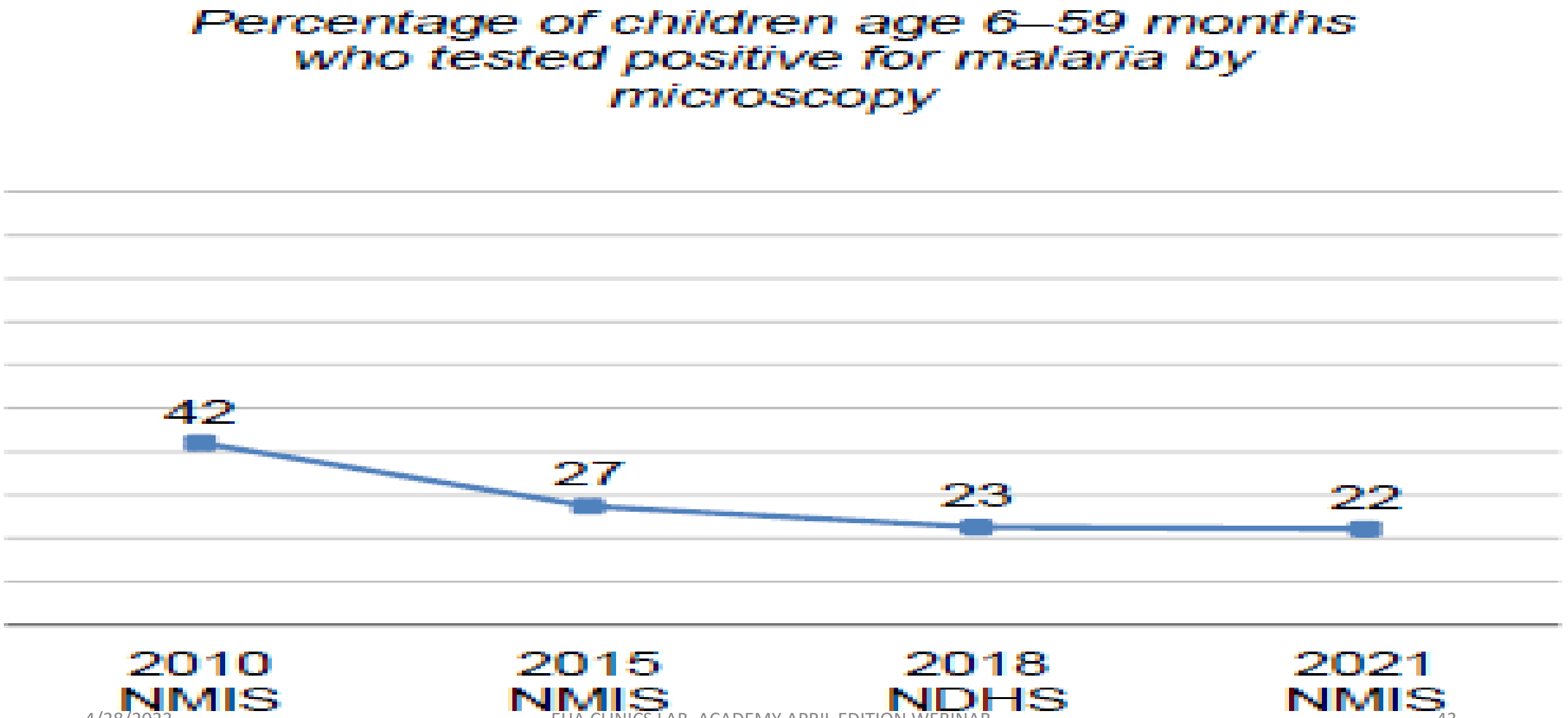
- 20 negative slides ('clean' negatives)
- 22 positive slides of low density (80-200 parasites/µL):
  - 10 *Plasmodium falciparum* slides
  - 4 mixed (2) species slides (include P. *falciparum*. Each species >40 parasites/µL, co-infecting species according to local prevalence)
  - 6 *Plasmodium malariae*, *Plasmodium vivax*, and/or *Plasmodium ovale* slides (include at least 1 of each species, ratio according to local prevalence)

Slide Set 2 (14 positive slides): Assessment of quantitation

- 6 *P. falciparum* (200-500 parasites/µL)
- 6 *P. falciparum* (500-2000 parasites/ µL)
- 2 *P. falciparum* (>100 000 parasites/µL)

Malaria Microscopy Quality Assurance Manual Version 2, 2015

Malaria burden Reduction



Conclusion & Closing Message

- Malaria Microscopy competence has proven to be effective. Only competent malaria microscopist should do malaria microscopy.
- Minimum requirement for malaria microscopy is Level 3 but our target should be a minimum of level
- World malaria burden and death has dropped by almost half since the Kuala lampur workshop in 2005 that adopted malaria competence
- Malaria Microscopy remain the Gold standard only in the hands of an expert or quality assured microscopy – Level 1
- Countries should adopt malaria microscopy competence because it is the most rational way to follow
- Malaria in a year kills 60 times of what COVID 19 kills in three years

Acknowledgements

- WHO AFRO
- WHO, Nigeria
- NMEP, FMoH, Abuja
- ANDI, CMUL, Lagos
- WRP-Kisumu, Kenya
- WRP-Nigeria
- USAID/PMI
- Global Fund
- AMREF University, Nairobi
- NIMR, Yaba, Lagos

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Thank you for Listening. Questions ?