Malaria eradication or malaria control: what is possible?

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Past Context

The previous malaria eradication campaign:

Positive aspects

• Elimination of the problem from large areas of the world
  – Focalisation in the tropics & areas of anarchic economic development
  – Regretably, contributed to deterioration of the problem in many areas

• From the first time acted throughout the affected areas
  – This concern with total coverage stimulated the general use of maps and the collection of epidemiological information from the periphery
  – In the absence of health services created networks of treatment posts which in some countries served as a basis for extending PHC

• Nevertheless, its failures taught more than its successes
  – E.g. Smallpox « active epidemiological approach » was inspired by the failure of the consolidation phase of the campaign
Past Context

Errors in the planning of the campaign

• Global nature but inadequate knowledge of what to do in Africa
• The economic argument that a ‘one-time’ investment is always preferable to the indefinite repetition of expenditure, without considering resource availability and the discount rate for future expenditure
• The belief that consolidation and maintenance would be cheaper than the attack
• The expectation that elimination would be easy in areas of unstable transmission
Some lessons learned ... and to be avoided in future

1.- Tendency to extrapolate elsewhere a success from a specific region

In the study of malaria problems and in the formulation of control programmes, action based on generalizations is likely to be followed by the most disastrous consequences. It has been well said that the most hazardous of human tendencies is the drawing of general conclusions from limited experience, and in no instance it is more applicable than in the planning of malaria control measures.

Some lessons … *continued*

2.- Irresistible fascination with a ‘cheap, effective and safe intervention’, even if success was in part due to its application on a declining problem

*The simplicity in theory of prophylaxis against malaria is only equalled by its difficulty in practice.*

*Sir Leonard Rogers*
Some lessons ... continued

3.- Ignoring the social and political realities of malaria

- Future success was assumed to depend only on technical feasibility, economic benefits and political support
- People were seen as passive recipients, only expected to comply
- Very often it failed to overcome cultural barriers and local aspirations
Dr Togba (Liberia)... Large-scale malaria control might present no great difficulties in a relatively well-developed country like Venezuela or an island like Ceylon, but the magnitude of the task of spraying residual insecticides in every village of Liberia, in the face of bad communications and adverse weather conditions, could hardly be imagined unless it had been experienced... He thought that it would be ill advised to arouse the hopes of governments and run the risk of censure when results failed to come up to expectations”  

WHO official Records, 8th World Assembly
4.- Insistence on operational management

- « a task to be performed » not a « problem to be solved »
- New recruits were trained in eradication, displacing existing professionals

5.- Inability to connect to normal public health work

- Problems of territoriality, lack of flexibility, program fragmentation
Malaria control should not be a campaign, it should be a policy, a long term program. It cannot be accomplished or maintained by spasmodic effort. It requires the adoption of a practicable program, the reasonable continuity of which will be sustained for a long term of years.

Key Limitations ... continued

6. - Assumption that all the information needed was available

- Neglect of research and history: inability to connect with past policies
- Eradication became a belief system, not needing empirical observation

“Throughout the world support for further research into malaria, even that concerned with insecticides and chemotherapeutics, contracted swiftly. Worse still, the apparent imminent demise of a once important disease removed the necessity for training scientists in malariology. It took 10 years and a war to halt this tragic trend”.

Disconnect of Research from Control & Eradication Activities

The “In-depth Evaluation of the Malaria Control Programme” in India, described

“a curious rivalry between the malaria programme and outside research bodies”

Comments that the majority of research projects had no relation to the needs of the control programme and the latter lacks

“the capacity either to carry out research, to guide it, to generate issues for research based on analysis of incoming information, or to translate into operational use research carried out by other institutions”

(Evaluation Committee, 1985)
Renewed vision and activities over the last several years to improve and intensify efforts against malaria

- October 2007 *Global Malaria Forum* led by Bill & Melinda Gates Foundation and other agencies re-establish the goal of malaria eradication.

- September 2008 RBM launches ¨Global Malaria Action Plan¨

…but a number of countries had been moving towards elimination over the last decade
The targets of the Global Malaria Action Plan are ambitious

- **Achieve** universal coverage by 2010 and **sustain** universal coverage indefinitely;
- **Reduce** global malaria cases from 2000 levels by 50% in 2010 & by 75% in 2015;
- **Reduce** global malaria deaths from 2000 levels by 50% in 2010 & to near zero in 2015;
- **Eliminate** malaria in 8-10 countries by 2015 and afterwards in all countries in the pre-elimination stage today; and
- In the long term, **eradicate** malaria world-wide through progressive elimination in countries

By meeting these targets, the malaria MDG will be achieved and there will be progress towards the other MDGs
Today, there are 109 malarious countries in 4 regions

Africa: 50 countries, most with significant malaria deaths

50 malarious countries
• 46 in control and 4 in elimination

Malaria targets in Africa
• Reduce cases from 365 M -> 158 M -> 79 M in 2015
• Reduce deaths from 963 K -> 480 K -> near 0 in 2015

Priority support for
• Human resource and managerial capacity building
• Better monitoring and evaluation systems
• Regionally-tailored R&D and operational research
• Stronger procurement and supply chain systems
• Streamlining donor financing and reporting processes
• More effective emergency response mechanisms
• Treating people infected with HIV / AIDS and malaria

Funds needed to support all countries
• US$ 2.2 billion in 2009
• US$ 2.7 billion in 2010

1) Includes prevention of reintroduction countries
WHO defines multiple steps for elimination

Unstable low transmission

- SPR < 5% in fever cases
- < 1 case/1000 population at risk

Stable high transmission

Control

Consolidation phase

Pre-elimination

1st programme reorientation

Elimination

2nd programme reorientation

Prevention of reintroduction

WHO certification

3 years

Source: “Malaria Elimination: A Field Manual for Low and Moderate Endemic Countries” WHO 2007
GMAP proposes 3-part global strategy to achieve targets

1. CONTROL
   - Scale-up for impact (SUFI)
   - Sustained Control

2. ELIMINATION

3. RESEARCH
Global malaria research and development costs

Peak costs ~US$ 886 million

Source: GMAP costing model
check point

• Can malaria be eliminated from all endemic countries?
  – with currently available tools?
  – current political context?
  – current health systems?
• Can we aim for global malaria eradication in the foreseeable future?
Clarifying the goals and definitions

- **Control** – reduction of disease incidence and burden to the point where it is no longer a public health priority

- **Elimination** – interruption of transmission of the pathogen and a fall in disease incidence to zero in a defined geographical area

- **Eradication** – interruption of pathogen transmission worldwide & fall in disease incidence to zero as a result of deliberate efforts, obviating the need for further control measures

- **Extinction** – disappearance of the pathogen from the planet (naturally from control efforts or by active destruction of all sources and stocks)
Clarifying the goals and definitions

- Disease and infection by *Plasmodium falciparum*?
- Disease and infection by *P. falciparum* and *P. vivax*?
- Disease and infection by all *Plasmodium* species that affect humans?
What adjustments are needed in our research strategy?

from control, i.e. reducing morbidity and mortality
to elimination / eradication, i.e. interruption of transmission

P. falciparum & P. vivax (the neglected human malaria parasite and the more difficult one to eliminate)

Elimination / eradication and the concept of $R_0$

Less than one new case per existing case
What are the adjustments required to our current research strategy?

- What are the critical knowledge gaps in malaria parasite biology, immunology, epidemiology, vector biology and interactions with the human host that are an impediment to development of malaria eradication tools?
- Does the current pipeline of drugs, vaccines, vector control tools and diagnostics include the development of tools for elimination in the hardest endemic areas?
- What novel technological approaches can we consider to facilitate development of efficacious tools?
Some questions for Vaccines

- Biology of the malaria parasite and its interaction with the host
- Targets and mechanisms of naturally acquired protective immunity
- Develop a predictive animal model and immunological assays
- Develop human challenge models, including both sporozoite and blood-stage challenge
- Development of a global malaria vaccine portfolio and agreement on desired target product profiles for the eradication goal
- Develop effective adjuvants
- Comparative evaluation of vaccine candidates using harmonized protocols and assays
Some Questions for Vector Control

- Systematic review of current strategies to help guide programs
- Gain better understanding of secondary vectors
- Develop age grading techniques
- Genomic/serologic lab techniques in the field to determine species structure, monitor population dynamics and link to interventions, and genomic studies and vector sub species
- Methodological issues for vector control trials and assessment of interventions: sampling methods, performance criteria, etc
- Understand the biological basis for resistance
- Develop TPPs for: Sampling and traps (entomological monitoring), tools for determining longevity/age grading, novel insecticides. application equipment, information management (surveillance) standard operating procedures, quality assurance of the chemical application.
Some Questions for Drugs

- Biology of the stages tailored by drugs that could hit transmission (hypnozoites and gametocytes of P. vivax and P. falciparum)
- Early sporogony biology
- Fundamental interactions of parasites and vector hosts in terms of transmission
- Relapses
- Asexual stage of P. vivax
- Determination of parameters that serve as indicators of gametocyte carriage
- Animal model with true human gametocytes
- Models to know the impact of what it would mean to have a determined percentage of transmission blocking
- Re visiting chemoprophylaxis
Some Questions for Health Systems/OR/Diagnostics

• Malaria elimination and eradication require an integrated and systemic approach, which are the key determinants of different health systems that need to be addressed when moving towards elimination and eradication?

• Which comparative analyses are required to understand health systems performance; specifically:
  – the key basic research questions that will enhance our understanding of how to achieve effective and equitable health systems?
  – the key operational research questions that emerge from ongoing efforts of malaria control and elimination that will enhance health systems performance?
  – the basic research needs for the individual and community diagnostic tools and strategies that will enhance health systems performance?

• Role of improved diagnostics
Questions for M&E

- What research is needed to improve existing or develop and standardize new M&E indicators?
- What research is needed to improve existing or develop new technologies and tools for: Diagnostics?, Communications? (e.g. cell phones), Information systems/data management? (e.g. PDAs/GIS)
- Surveillance: What research is needed to enhance existing or develop new detection, reporting, and response paradigms for case surveillance?
- Special studies: What research is needed to improve existing or develop new surveillance approaches for assessing resistance?
- How can these special studies be most efficiently done in the setting of near zero transmission?
- Transmission: What research is needed to identify best methods to monitor measure transmission as we approach elimination/eradication In people? In vectors?
- For all the above considerations, also consider what additional tools and strategies are needed for *P. viva* elimination/eradication
Issues for Modeling

- Providing a quantitative framework to the biology of the parasite and its transmission
- Informing when to shift public health strategies from control to elimination.
- Prediction of sustainability of existing tools in terms of both efficacy and effectiveness.
- Prediction of the best intervention mix/package(s) for specific settings and of the likely impact of different, sub-optimal packages/combinations.
- Inform the design of simple M&E tools to accompany control and eradication.
- Assist the strategic planning for control and elimination at national level.
- Assistance in selection of tools and investments in R&D; particularly assist in establishing TPPs.
Proposed Response

The creation of the Malaria Eradication Research Agenda (malERA) initiative with the

**Overall Goal**: to develop a multi-disciplinary, global R&D agenda that can be actionable by research and public health agencies and sponsors.
The aim is not to prescribe the research agenda for any given institution, but to engage in a rigorous process that builds consensus among institutions on current and future directions of malaria R&D.
MalERA structure

- **3 tiered governance**
  - **Steering Committee:** 15 independent scientists representing malaria research areas
  - **International Advisory Committee:** 28 experts in malaria and other research areas and policy makers, to provide technical advice
  - **Leadership Council:** Members from leading international and governmental organizations engaged in malaria research
    - Margaret Chan (WHO)
    - Awa Coll-Seck (RBM)
    - Anthony S. Fauci (NIAID)
    - Mark Walport (Wellcome Trust)
    - Tadataka Yamada (BMGF)
Structure ... continued

Additional structures include:

- Consultative Groups
- IT Platform
  - Hosted by TropIKA [www.tropika.net](http://www.tropika.net)
  - Created to incorporate a broader base of knowledge and experience
  - A space dedicated to sharing information and gaining feedback
- Support Secretariat based at CRESIB / Univ. Barcelona
Consultative Groups

1. Drugs
2. Vaccines
3. Vector control
4. Modeling
5. Monitoring and evaluation, and surveillance
6. Integration strategies
7. Health systems/operational research/diagnostics

8. Young Investigators / Basic Biology
9. Diagnostics
MalERA Outputs

- Journal articles for specific topics
- Definition of next steps for the agenda setting process
- White paper(s) outlining the R&D agenda
“The history of special antimalarial campaigns is chiefly a record of exaggerated expectations followed sooner or later by disappointment and abandonment of the work. This record of failure and disappointed hopes makes it clear that the only prospect of real progress lies in renewed activity in the continuous study of the disease in all its aspects”.