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Essential guidance on malaria elimination in its history

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One Giant Leap...

This specially themed issue of the *Journal of Vector Borne Diseases* highlights the obstacles and opportunities before us in striving to achieve what would be a historic elimination of endemic malaria transmission. Perhaps most readers of this august *Journal* would not have been born before the 20th of July 1969 when American astronaut Neil Armstrong became the first human to set foot on another celestial body, the Moon. That technological achievement elicited perhaps the single greatest global outpouring in our time of public faith in and enthusiasm for monumental scientific endeavours. And yet, just 4 days later, the 22nd World Health Assembly quietly but firmly surrendered its 14-year global campaign to eradicate malaria. While the resolution politely refers to "…this revised strategy of malaria eradication.", it also expressed "…in the regions where eradication does not yet seem feasible, control of malaria with means available should be encouraged and may be regarded as a necessary and valid step…"[1]. The resolution, with less than two seemingly unremarkable pages, was a historic white flag of strategic defeat for humanity. It effectively acknowledged that we lacked the resources, tools, know-how, or will need to annihilate the plasmodia. We had to mitigate the harm done by malaria with practical measures of control rather than chase what seemed the unattainable vision of eradication.

The historic and technical context of that surrender and its aftermath merits examination today. Even as late as 1969 the accomplishments of the Global Malaria Eradication Campaign remained largely intact and, in retrospect, formidable. Among the 1.8 billion people who had been living with malaria in 1955, endemic transmission had been eliminated where 0.7 billion lived[2]. Estimated global malaria mortality had been reduced by 80%[3], and in India, specifically an estimated 75 million cases in 1947 had been reduced to just under 50,000 by 1961 and fewer than 350,000 in 1969[4]. India and most other nations beyond sub-Saharan Africa had achieved what today appear to have been astonishing successes putting them on the near verge of elimination success[5–6]. What stopped them?

Programmatic, scientific, and strategic poverty

There is no simple explanation for World Health Organization (WHO) surrendering its eradication aspiration in the wake of such success. Over-reliance on DDT spraying for vector control and chloroquine for therapy in the light of emergent resistance to both by 1969 and a lack of options to them due to deep neglect of basic, applied, and operational research on malaria—surely discouraged strategists, implementers, and sponsors. One analysis showed, however, that only 24 of 75 studied resurgences of malaria in this era occurred as a direct result of resistance to insecticides or drugs; whereas 68 of 75 occurred with weakened control programmes, mostly due to funding constraints[6].Also, discouraging must have been the campaign having had almost no impact whatsoever in most of sub-Saharan Africa: among the 220 million Africans living where "originally malarious", in 1969 only slightly more than 4 million lived where elimination had been achieved[2]. Perhaps more than any other reasons, disillusionment and demoralization beset the campaign as a consequence of the unrealistic expectation of quickly achieving complete eradication—the victories of tremendous progress as in India and elsewhere instead seemed to be defeats.

Science and Technology put humans on the moon in 1969 but had provided almost no options to the failing tools of malaria control, practical tools of any kind for holo-endemic Africa, and a mindset of failure for anything less than complete eradication of the plasmodia. Moreover, what had been highly effective methods of malaria control like vector species sanitation or other locally tailored environmental interventions[7] had been almost completely abandoned by 1950 after the advent of the "one-size-fits-all" ease of DDT and modern synthetic antimalarial commodities[8]. A monolithic non-adaptive strategy had offered only complete success or utter failure. When the latter occurred, there was no

technical or strategic back-up or fallback, and the calamity of a global resurgence in malaria morbidity and mortality followed for people all across the endemic globe[6].

Resignation and resurgence

The great malaria epidemic of the early 1970s in India foreshadowed what would ultimately occur far more broadly: the nadir of tens of thousands of cases annually during the 1960s expanded to millions of cases annually during the 1970s, peaking at 6.5 million in 1976[4]. Similarly, steep and broad epidemics later occurred in virtually every still-malarious nation that had neared elimination success[6]. The Fig. 1 illustrates Asian national examples of that very near proximity to success and the awful rapidity of its deterioration. Throughout this period of resurgence, humanity had almost no vector control will or capacities, and implemented a control strategy wholly reliant on diagnosis and treatment using microscopes and failing antimalarial drugs in use since the 1940s and 1950s[9]. Uncounted millions perished before humanity finally responded in the early 2000s.

Americans have an apt saying for the inadequacy of the near-accomplishment of a targeted goal: "Close only counts in horseshoes and hand grenades." One may win a contest of horseshoes without actually hitting the targeted stake, and the efficacy of explosives at near distance is self-evident. As the history above suggests, malaria eradication requires striking the bulls eye of complete extinction of the plasmodia from the natural world. Getting very close, as we did during the 1960s (outside of Africa), seemed futile and even quite dangerous in the long run. But that may be an over simplification-programmes running into the problems of dwindling resources, less effective commodities, and demoralized workers and supporters, also seemed to run out of ideas to sustain continuing efforts. The loss of a single precious commodity, DDT, by dwindling efficacy or funds killed momentum and derailed progress just short of victory in

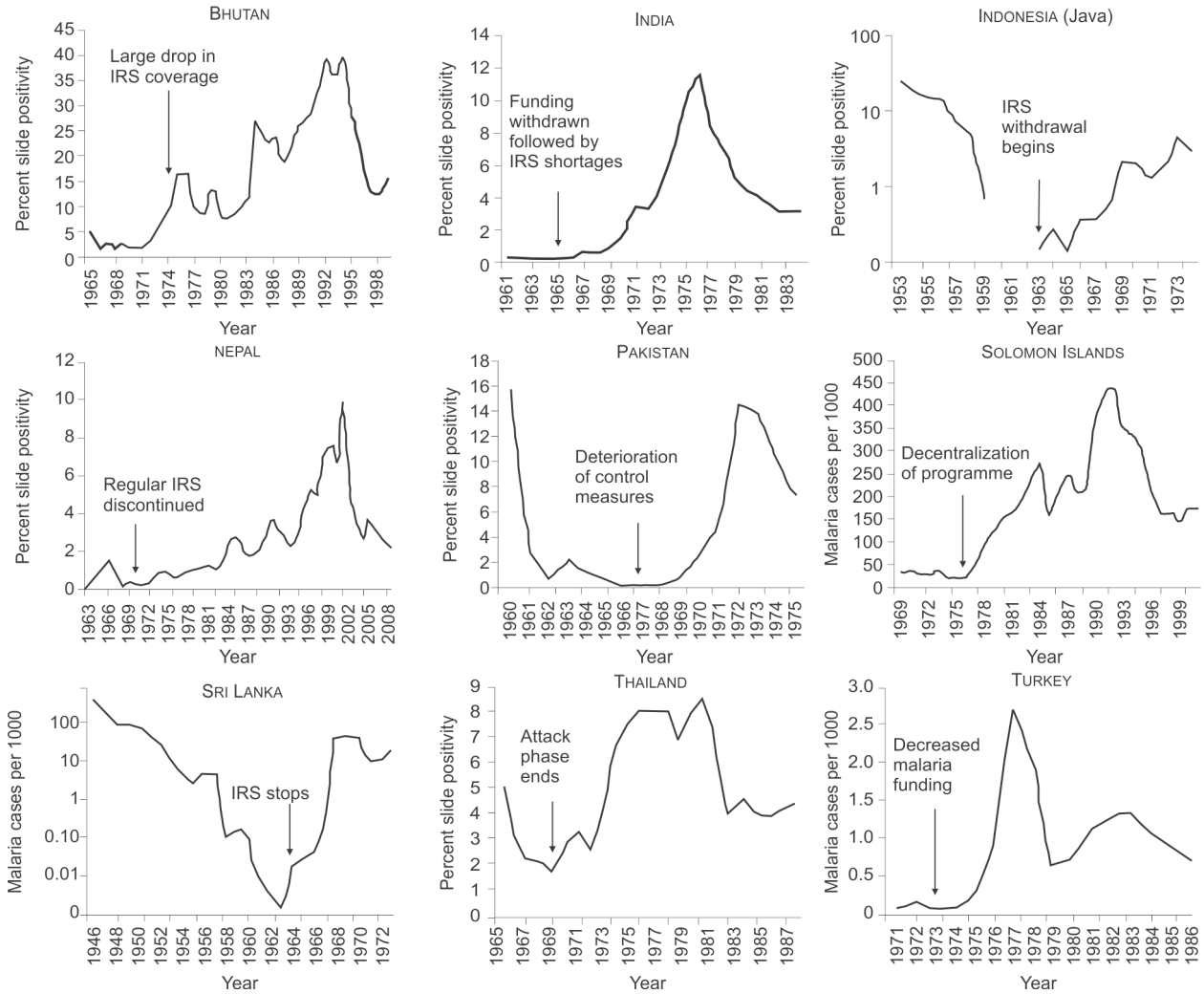

Fig. 1: Examples of the proximity to malaria elimination success and the rapidity of its erosion during the latter 20th century. Reproduced from Cohen *et al*[6] with permission.

many nations. The eradication programme indeed struck close to target, but it lacked the strategic agility needed to then switch tactics and press on to the nearby target. Everything simply stopped just shy of it. Close did not count because without a strategy to allow it as an advantage to capitalize, resignation and resurgence ensued.

Strategic agility

As this special issue of the *Journal* expresses, humanity again takes aim at the target of malaria elimination and ultimately, eradication. Like our predecessors over a half-century ago, we possess precious few commodities to realize this ambition: effective artemisinin combined therapies (ACT), point-of-care rapid diagnostic tests (RDT), long-lasting insecticide-treated nets (LLIN), and indoor residual spraying of insecticides (IRS). The loss of any one or set of these commodities to adequate availability or effectiveness, respectively by economics or biology — as indeed appears to be a real risk – would perhaps prove as threatening to our collective will to press on to successful elimination as it did in 1969. The deep dependency on these commodities for that success may impose the greatest risk to it. What technical strategy for protecting gains and mitigating harm have we developed for dealing with the possibility of unavailable or failed commodities?

In 1970, in response to the surrender of eradication ambition months earlier, the WHO published a synopsis of post-malaria eradication thinking and actions[2]. The document expresses no clear strategy to at least sustain the great gains accomplished in the prior decades, but it offered detailed attention to strikingly modest and scattered advances in research on malaria in that era. Real strategy and action applying definitive tools seems to have yielded to mere hope for better of both – there appears to have been no proverbial "Plan B". The possibility of the ultimately realized failure does not seem to have been considered or anticipated – it was a tragic error of hubris and it allowed the great global resurgence of malaria through the latter 20th century.

History instructs and warns us to anticipate the failure of our commodities with a strategy more substantial than hope or faith in research delivering better commodities. Research is important and necessary and it did eventually deliver the commodities that arrested and reversed the global resurgence[10]. Malaria research scope and activity in the prior two decades vastly exceeds that which occurred in the same period before 1969, and hope in new and better tools is certainly better placed today than it was before the global resurgence. Nonetheless, technical strategies for controlling malaria without complete reliance on these commodities may be the wiser Plan B. The wisdom in doing so may lie more in approach– reliance on local rather than distant know-how – than mitigation of risk of lost commodities.

Environmental vector control

During the period between the discovery of mosquitoes as vectors of malaria by Ross at Secunderabad, India in 1897 and the availability of DDT and chloroquine by 1945, malariologists controlled malaria by altering environments in ways that disfavoured anopheline breeding. Today we tend to view malaria control before 1945 as unscientific and ineffective, but both characterizations are demonstrably untrue modern conceits. Gachelin *et al*[11] provide a useful historic summary of those methods and evidence, and Keiser *et al*[7] conducted a systematic review estimating an average of 88% reductions in measures of malaria burden where these methods were implemented. The "problem" with these approaches is their highly site-specific strategic character, *i.e.* effective control strategy cannot be guided from afar with commodities that work in any environment, but strategy must be locally derived after detailed study of a particular environment and the specific vector anopheline species and behaviours occurring in it. Once that ecology is understood, locally practical and effective interventions may be developed and implemented. Technical guidance or devices from afar do not play in this approach—it is a local control solution managed locally.

A good example of this approach may be the control of malaria that occurred on the island of Java in the East Indies (modern Indonesia) before 1945. Most endemic malaria in the interior of Java arose by man modifying the environment for rice cultivation, involving the vector *Anopheles aconitus* (Diptera: Culicidae). The Indonesian malariologist Raden Soesilo studied its breeding behaviours, discovering discreet periods where larval numbers of them peaked in flooded rice paddies. Flushing of paddies during those periods was prescribed and spleen indices in areas of implementation fell from about 90% to less than 5% within a decade[12]. Soesilo's solution required only the entomological know-how he brought to it. His prescription remains in practice today, protecting many tens of millions of residents of rice cultivating areas of Java from an otherwise onerous malaria burden. Numerous similar examples of approach, efficacy, practicality, and durability occurred in Panama, Cuba, Italy, Greece, Palestine, India, Malaya, Singapore, and many others[12–15].

During the pre-war 1930s, the Malaria Commission

of the League of Nations and the influential Rockefeller Foundation in New York had urged the global adoption and expansion of species sanitation in malaria control[15]. Refinement and advancement of the technology had thus been poised for strategic dominance in malaria control, but the Second World War and the advent of DDT and chloroquine immediately following it saw environmental approaches to malaria control abruptly halted and then almost wholly abandoned. The post-war rise of modern technological commodities in malaria control achieved an overwhelming strategic dominance that persists up to the present day – despite the conspicuously dangerous shortcomings of commodities dependency demonstrated by events of global resurgence during the latter third of the 20th century[8].

Local control

The tools that could ultimately lead us to successful malaria elimination may not spring from the advanced biotechnological laboratories of Europe and North America, or from the advice of experts residing in Geneva, London, Washington, or Seattle, but from local malariologists across the endemic globe defining as many different practical solutions to malaria transmission as there are environments supporting it. We should certainly be creating and then exploiting the technological tools and commodities being made available, but we need not – indeed explicitly should not – wholly depend upon them for progress and success. Practical local malariology had been conceived, optimized, and validated before 1945 but had already been lost when so badly needed in 1969 when it could have enabled the final push to achieve elimination where it had been so very close at hand – a strategic pivot instead of paralysis and resignation.

This article speaks directly to malariologists working today in malaria endemic nations – your path to malaria elimination success may necessarily be uniquely your own, mapped and hewn by your own hands and local tools precisely aimed at your problem anophelines. Technologically marvelous drugs, vaccines, diagnostics, and insecticides may be available to your efforts, but what will you then do if they are not? That question does not appear to have been raised before 1969 and we have lived with the terrible consequences since. Practical malariology applied where malaria transmission occurs using technological approaches validated a century ago may be the surest means available to us to achieve, consolidate, and protect the gains being made in our march to malaria elimination success. Commitment to that expertise, method, and assurance may only be found and developed locally.

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