National Health Research Policy was put on the web to initiate public debate with the intention to outline priorities and formulate steps in the right direction. It contains a proposal for a Bill on Research on Human Subjects and establishment of National Biomedical Research Authority, along with strategies to harmonize the various guidelines developed for health research. To support these initiatives, the Indian government could formulate legal measures similar to the US Department of Justice that had already started investigating cases of corrupt practices like payments, etc. offered to doctors conducting clinical trials (http://www.timesofindia.indiatimes.com/.../US-probes-pharmacos...bribing-doctors/.../6334175, 19 August 2010). The investigations were triggered by a report that 40–65% of clinical trials for FDA-regulated products were conducted outside the US, which brought concern about the reliability of the data (http://oig.hhs.gov/oei/reports/oei-01-08-00510.pdf, 2010).

Conclusion

India is certainly prepared to undertake clinical trials both on domestic products and sponsored clinical trials from abroad. The clinical research industry in India touched US$ 320 million in 2009, starting from US$ 140 million in 2006. An estimate shows that clinical research in India is expected to be US$ 630 million by 2012 (http://www.researchandmarkets.com/reports/1212074/, 2010). Currently there are more than 150 CROs operating in the country, but only 20 of them are ICH–GCP compliant; more are coming up in view of the business potential. However, in order to avoid exploitation, the emphasis should be on linking science to benefit the society and educating the professionals on finer aspects of clinical research. There is a need to understand the significance of an ethical review by researchers in view of outsourcing of clinical trials to developing countries. The proposed National Health Research Policy by the Indian government may bring in the desired changes and encourage health research by giving well-defined directions. Finally, it can be concluded that educational efforts with a focus on ethical and regulatory requirements would definitely improve not only the quality of clinical trials, but clinical research in our country.

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Malaria recession and the way forward

Vas Dev

Malarial threat is receding with reported decline in malaria cases not only locally, but also globally. Worldwide map of the distribution of cases is shrinking and subject experts are now contemplating malaria eradication in many parts of the globe that were earlier intractable. In the next decade there will be a huge challenge that would present an unprecedented opportunity for research and investment on new potent antimalarials, scaling up interventions, and developing stronger health systems ensuring equitable healthcare access and all-round economic development.

India shares the success stories related to malaria research, including the Nobel Prize-winning discovery that malaria is transmitted by mosquitoes by Ronald Ross in Secunderabad on 20 August 1897 and control operations during 1960s under the National Malaria Eradication Programme (NMEP)[1]. With the advent of DDT post-independence, the malaria eradication programme in India became popular the world over for its well-organized action towards freedom from the disease.

But the euphoria of success did not last long, when focal disease outbreaks with 6.47 million cases were reported in 1976, the highest ever resurgence. Among several constraints that led to resurgence, drug-resistance in malaria parasite and insecticide resistance in mosquito vectors continued to hinder the equitable development in many parts of the country. To

arrest the development and spread of drug-resistant malaria the national antimalarial drug policy, first drafted in 1982 by the programme officials (http://www.nvbdcp.gov.in/), was subject to periodic reviews by a panel of experts to ensure rational deployment and proper use of these drugs for effective treatment. Despite the policy being in place there were focal disease outbreaks in different eco-epidemiological zones of the country. Of the two common parasite species that are prevalent in India, *Plasmodium vivax* and *Plasmodium falciparum*, the proportions of the latter continued to rise despite additional inputs under the *Plasmodium falciparum* Containment Programme during (1978–1988), presently contributing >45% of the reported cases[2]. Apparently, the chloroquine-resistant *P. falciparum* first documented in Assam in 1973 became widespread, and increase in resistant foci mirrored the escalation in proportions of *P. falciparum* cases. The scenario was no better for the second line drug, sulfadoxine-pyrimethamine; the resistance precipitated much faster, within 5–6 years of usage. In the 1990s, the situation deteriorated further with disease outbreaks and death, largely ascribed to multi-drug resistant *P. falciparum* malaria (the killer parasite)[3].

Continued research for alternative therapy led to the development of artemisinin (extracted from the Chinese herb, *Artemisia annua*) derivatives which are not only fast-acting schizontocidal, but also convenient to administer. Anticipating the problem of drug resistance using artemisinin monotherapy in line with the recommendation from WHO for using artemisinin-based combination therapy, in 2007 India decided to roll out artesunate plus sulfadoxine-pyrimethamine in high-risk pockets to check the spread of multi-drug resistant strains[4]. Implementation of this drug policy now three years in practice has resulted in dramatic decrease in transmission reduction in pockets formerly intractable such that research projects had to be abandoned due to lack of cases.

Malarial threat is now receding with decline in malaria cases locally as well as globally (http://www.who.int/malaria/world_malaria_report-2009/). Worldwide map of distribution of cases is shrinking and subject experts are now contemplating malaria eradication in many parts of the globe[5,6]. The credit goes to the Roll Back Malaria Initiative, established in 1998 (even though initially the subject experts expressed their dissatisfaction for not making any substantial headway) lending to increased allocation of resources, newer interventions, public–private partnership for scaling up intervention tools that are community-driven, and strong political commitment. Additional inputs and research efforts are now yielding dividends. These efforts were bolstered by the UN Millennium Developmental Goals Malaria Summit held in New York on 25 September 2008, with increased allocation of resources to the tune of US$ 3 billion for scaling up the existing technologies to near universal coverage, increased awareness and political will in reducing mortality to half from 2000 levels by 2010 and eliminating deaths by 2015, eliminating malaria transmission in feasible countries and moving towards eradication with newer tools and evidence-based approaches[7].

Drug discovery for effective chemotherapy is the key element for control of malaria. What is worrisome is the resistance to artemisinin-based combination therapy that has surfaced in neighbouring South East Asian countries along Thai–Cambodian border (hotbed for multi-drug resistance) which could reverse the gains in malaria control[8,9]. It calls for continued research efforts for newer antimalarials that are effective and affordable[10]. It is in this perspective that Gamo *et al.*[11] and Guiguemde *et al.*[12] reported their research findings that enhance our understanding of the 'chemical space' in search for new molecules with potential to be developed as antimalarial drugs of tomorrow. Both groups assayed thousands of compounds active against blood-stage asexual parasites and short-listed a number of novel compounds making them non-proprietary, available freely to the global community for further research and development. It is projected that among probable hits, protein kinase inhibitors (still unexploited for antimalarials) and disruptors of host–pathogen interaction-related targets can be a rich source of drug leads that could help develop new antimalarial therapeutic strategies. There is an imperative need for the development of potent drugs against sexual stages of malaria parasite and for dormant liver stages of *P. vivax*, for which there are few alternatives.

The next decade presents an unprecedented opportunity for research and investment on new efforts in controlling malaria. With climate change, the disease epidemiology is rapidly changing in the face of population explosion, rapid urbanization, deforestation, population migration, and developmental projects. It would be necessary to estimate true disease burden and tailor situation-specific interventions to avert impending disease holocausts. Subject experts estimate the disease burden manifold on account of inadequate surveillance, asymptomatic carriers that remained undiagnosed, malaria in pregnant women, and private sector for which there is no existing mechanism for data retrieval[13]. To reduce the hidden malaria parasite burden, it would be necessary to delimit these population groups and formulate appropriate antimalarial dosing regimens for administering radical treatment enabling transmission disruption[14].

Situational analyses of many high-risk districts unequivocally established that tools in practice were not only inapt, but also poorly applied to the changing disease epidemiology, and more so in understanding human behaviour or awareness for disease prevention. To avoid the reverses, it is important to maintain intensive disease surveillance and case management by monitoring therapeutic efficacy and upgrading drug policy. Equally important is to keep a vigil against emerging zoonotic malaria that is making inroads in human populations in South East Asia, which may result in human-to-human transmission, particularly in forest fringe communities[15]. These measures combined with political commitment for large-scale introduction of insecticide-treated nets/long-lasting insecticidal nets for strengthening interventions for vector control would yield rich dividends in achieving the millennium developmental goals. What is tantamount to these measures is the build up of local human capacity and strengthening health systems for delivery of services to the outreach population group that carries the brunt of disease burden. A good beginning has been made under the National Rural Health Mission (http://mohfw.nic.in/NRHM.htm) presently in force, which has brought sea change in community outreach programmes for healthcare access. There is increased sense of confidence, and awareness on disease prevention and control. Sound investment that would invigorate further

research and development for new potent antimalarials that are safe, practicable and affordable, scaling up interventions, and developing stronger health systems in alleviating malaria and poverty is the need of the hour.

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Smile with Science

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