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2006;100(10):917-925. Of the three sibling species tested, species A was found to be the most susceptible to infection, as measured by oocyst abundance and sporozoite maturation; species B was the least susceptible to infection, bordering on being a non-vector (Adak et al., 1999). An important initiative recently introduced by the National Rural Health Mission (NRHM) is the provision of village-based Accredited Social and Health Activist (ASHAs), personnel that have been trained in malaria diagnosis by rapid diagnostic tests (RDTs), and antimalarial drug administration. The NVBDCP has introduced the use of RDTs to help facilitate early detection and also the deployment of insecticide-treated bed nets in high-risk regions for prevention. Furthermore, due to this incomplete scope of detection, malaria parasite diversity and the distribution of malaria drug resistance on the Indian subcontinent may not be optimally characterized. A major component of the CSCMI is to survey the circulating Plasmodium parasite populations in three different eco-epidemiological regions in India. Current scenario of malaria in India. However, surveillance for artemunate resistance is a challenge. By pooling the substantial expertise in entomology and intervention trials in India with the expertise in vector and parasite ecology and evolution in the United States, this work will contribute substantially to malaria control in India and generate novel insights into basic biological processes applicable to disease processes globally. First, research will be conducted to quantify the role of environmental conditions in determining malaria transmission intensity (risk) in different eco-epidemiological contexts, including the future effects of climate change. vivax in India which prevents resistance evolution, in very sharp contrast to the experience with CQ against P. The difficulty in making these estimations is further exacerbated by (i) highly variable malaria eco-epidemiological profiles, (ii) the transmission and overlap of multiple Plasmodium species and Anopheles vectors, (iii) increasing antimalarial drug resistance and insecticide resistance, and (iv) the impact of climate change on each of these variables. vivax co-circulate, fluctuating proportions of the two species complicate diagnosis and treatment. 2007;13:199-206. A first step to resistance management is resistance surveillance. vivax cases have decreased; the ratio of P. 2009;25(10):452-457. Identification of all members of the Anopheles culicifacies complex using allele-specific polymerase chain reaction assays. Currently only a single reference genome sequence of an isolate of P. Molecular evidence of misidentification of Anopheles minimus as Anopheles fluviatilis in Assam (India) Acta Tropica. Proc Natl Acad Sci. Dash and Dr. V. [PubMed] [Google Scholar] [Trigg PJ, Kondrachine AV. [PMC free article] [PubMed] [Google Scholar] Singh N, Kataria O, Singh MP. The approach we propose to investigate uses deep sequencing to identify the presence of 'tolerant' or 'resistant' parasite clones present in low levels in a patient - clones which are rare because resistance is newly arisen and associated with fitness costs. Treatment is based upon the primary species identified in an infection by standard microscopy diagnosis, subjecting all species in a single host to the same drug treatment, likely contributing to this surge in drug-resistant parasite strains. Approximately 65% of those at risk for becoming infected with malaria in Southeast Asia are individuals residing in India (WHO 2010). vivax, next generation compounds or formulations for P. The CSCMI is a close partnership between Indian and United States scientists, and aims to address major gaps in our understanding of the complexity of malaria in India, including changing patterns of epidemiology, vector biology and control, drug resistance, and parasite genomics. [Google Scholar] Wakabi W. [PMC free article] [PubMed] [Google Scholar] Sharp BL, Riddi FC, Govender D, Kulinski J, Kleinschmidt I. malariae has been reported in the eastern Indian state of Orissa (Sharma et al., 2006), while P. Similar complexity exists for the other principle malaria vectors in India. [PMC free article] [PubMed] [Google Scholar] Dash AP, Adak T, Raghavendra K, Singh OP. 2002;15:278-293. [PubMed] [Google Scholar] Joy DA, Feng X, Mu J, Furuya T, Chotivanich K, Kretzli AU, Ho M, Wang A, White NJ, Suh E, Beery P, Su XZ. Once evolution has generated enough treatment failures to arouse suspicions of resistance, the spread of resistance is probably well advanced in an area. The approaches we propose here are designed to develop tools necessary for improved surveillance for resistance against drugs in use in India now, and not least for P. Nature. 1998;76:11-16. The NIMR has a network of 10 field units spread across India that serve as units for testing these new technologies (Figure 2). [PubMed] [Google Scholar] Singh V, Mishra N, Awasthi G, Dash AP, Das A. vivax in different geographical regions is necessary in order to understand the diversity and population structure of the species in different areas. vivax, and the Nadiad field station (Gujarat State) in the western plains has both P. [PubMed] [Google Scholar] Goswami G, Raghavendra K, Nanda N, Gakhar SK, Subbarao SK. The billion-dollar malaria moment. The rationale behind this work is that most of the key components of R0 (basic reproduction number) for vector borne diseases are temperature dependent, including the rate of development of mosquitoes (and hence under many conditions, mosquito densities) and the rate of development of malaria parasites inside mosquitoes. The total number of reported malaria cases has decreased since 1995, primarily through a reduction in the number of reported P. Moreover, diverse genetic mechanisms can be responsible for resistance in different regions, against different drugs and indeed in different malaria parasite species. The Center for the Study of Complex Malaria in India (CSCMI) is a partnership between Indian and U.S.-based investigators to develop the knowledge, tools and evidence-based strategies needed to support the intervention and control programs of Indian government organizations, and to build research capacity in India and help train the next generation of malaria and mosquito vector biologists. Emerg Infect Dis. vivax may exhibit a greater degree of genetic polymorphism within populations and greater divergence among populations in disparate geographic locations (Gupta et al., 2011). The CSCMI is a collaborative scientific research center working towards the goal of enhancing malaria intervention and control programs in India. We thank the previous NIMR Directors Professor A. Commentary: Malaria control in the 1990s. [PMC free article] [PubMed] [Google Scholar] Feachem R, Sabaol O. The three NIMR field stations incorporated as part of the CSCMI are: Nadiad (Gujarat), Rourkela (Orissa) and Chennai (Tamil Nadu), each with different eco-epidemiological profiles as shown. The monsoon strikes the Indian southwestern coast in June every year, marking the beginning of the rainy season. In addition, statistics from the treatment of malaria cases in the private sector are hard to come by. This future-proofing is an important aspect of our aims. First, we plan to use new generation sequencing technologies to detect evidence of the early signs of failure of ACT in P. [PubMed] [Google Scholar] Subbarao SK, Nanda N, Vasantha K, Dua VK, Malhotra MS, Yadav RS, Sharma VP. falciparum in India, and has been replaced with the more expensive artemisinin-based combination therapy (ACT). vivax appears not to be a serious concern in India, despite over 50 years of chloroquine use (Shah et al., 2011). 2007;92:1571-1578. [PubMed] [Google Scholar] Anonymous. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain. Adak T, Kaur S, Singh OP. Currently, there is a 1:1 ratio of P. In fact, close to 60 morphologically distinct species have been described in India; six of these have been found to vector malaria (Table 1), although An. culicifacies is responsible for 60-65% of the malaria burden (Goswami et al., 2006; Dash et al., 2008; Singh et al., 2009). vivax; P. However, the development of insecticide resistance threatens to halt these once effective methods of control and prevention. 2005;95(2):92-99. Antimalarial drug resistance of Plasmodium falciparum in India: changes over time and space. [PubMed] [Google Scholar] Goswami G, Singh OP, Nanda N, Raghavendra K, Gakhar SK, Subbarao SK. 2004;4(3):239-248. falciparum, which is thought to have undergone one or more bottlenecks in recent history (Joy et al., 2002), P. [PubMed] [Google Scholar] Mu J, Joy DA, Duan J, Huang Y, Carlton J, Walker J, Barnwell J, Beerli P, Charleston MA, Pybus OG, Su XZ. vivax is thought to have had a more stable demographic past (Mu et al., 2003), which could mean that P. [Google Scholar] Dash AP, Valecha N, Anvikar AR, Kumar A. 2007;370:1895-1896. 2007;6:52. In so doing they address a need recently identified by the World Health Organization to evaluate the effectiveness of approaches such as IVM to simultaneously control disease, respond to ecological change and reduce pesticide use and insecticide resistance, in different settings (WHO 2009). Malaria imposes a major global health burden in large part because the Plasmodium parasite readily evolves drug resistance. The NVBDCP achieves evaluation of its programs in collaboration with the National Institute of Malaria Research (NIMR), one of the permanent institutes of the Indian Council of Medical Research (ICMR; under the Department of Health Research, Ministry of Health and Family Welfare, Government of India). [PubMed] [Google Scholar] Sallum MA, Peyton EL, Wilkerson RC. The NVBDCP goals are to develop a well-informed and self-sustained health care system in India with equitable access to quality health care and to ensure that the program activities are in accord with the Millennium Development Goal of halting and reversing the incidence of malaria and other vector-borne diseases by the year 2015. The major strategies being pursued by the NVBDCP to help achieve its objectives are: (i) disease management through early case detection and complete treatment, (ii) integrated vector management (IVM) to reduce the risk of vector-borne transmission; and (iii) supportive interventions which include communicating behavior change, capacity building and monitoring and evaluation of programs. This work was supported by National Institute of Allergy and Infectious Diseases, National Institutes of Health (NIH) grant U19AI089676. 2008;372:1193. Battling the malaria iceberg with chloroquine in India. Lessons from the past: managing insecticide resistance in malaria control and eradication programmes. 2008;24(5):228-235. The institute has also established quality assurance of malaria RDTs for NVBDCP. The National Institute of Malaria Research (NIMR) was established in 1977 and is the only research institute in India completely devoted to malaria research. Such climatic variation is due to a sharp temperature gradient caused by atmospheric changes in wind circulation and precipitation, leading to seasonally-dependent asymmetric heating patterns of India's peripheral bodies of water and land. The changing dynamics of Plasmodium vivax and P. While strategies and capacity for resistance surveillance exist through the NIMR and the NVBDCP, insecticide resistance is increasing in India. [PubMed] [Google Scholar] World Health Organization. Thus, CQ resistant P. This has important implications as it suggests that widespread sampling of P. vivax has been the major infecting species; however, over the past several years P. [PubMed] [Google Scholar] Carlton JM, Adams JH, Silva JC, Bidwell SL, Lorenzi H, Caler E, Crabtree J, Anguilo SV, Merino EF, Amodeo P, Cheng Q, Coulson RM, Crabb BS, Del Portillo HA, Essien K, Felkblum TV, Fernandez-Becerra C, Gilson PR, Gueye AH, Guo X, Kang'a S, Kooji TW, Korsinczyk M, Meyer EV, Nene V, Paulsen I, White O, Ralph SA, Ren Q, Sargeant TJ, Salzberg SL, Stoeckert CJ, Sullivan SA, Yamamoto MM, Hoffman SL, Wortman JR, Gardner MJ, Galinski MR, Barnwell JW, Fraser-Liggett CM. falciparum. [PMC free article] [PubMed] [Google Scholar] Dhingra N, Jha P, Sharma VP, Cohen AA, Jotkar RM, Rodriguez PS, Bassani DC, Suraweera W, Laxminarayan R, Peto R. The central and eastern regions of India report the most malaria (Figure 2), particularly the eastern states of Orissa, West Bengal, and Jharkhand, the central states of Chhattisgarh and Madhya Pradesh, and the western states of Gujarat, Karnataka and Rajasthan, with the largest number of deaths reported in Orissa (Joshi et al., 2008). This paradox is most likely due to the refractoriness of P. State boundaries are color-coded according to total malaria endemicity (see key). Malaria cases in India are reported throughout the year, since a perfect combination of average temperature (15-30°C), rainfall and precipitation-inducing conditions persist across the different parts of the country over all the seasons. [PubMed] [Google Scholar] N'Guessan R, Corbel V, Akogbeto M, Rowland M. 2008;371:1633-1635. vivax and P. vivax whole genome sequencing described above. falciparum to P. Such claims reinforce the need for robust and comprehensive epidemiological surveillance studies across the country (Singh et al., 2009) to determine the actual burden. Malaria cases and changing species pattern in India during the years 1995-2010. Estimating the Global Clinical Burden of Plasmodium falciparum Malaria in 2007. We are also indebted to Dr. Hema Joshi who was central to the project before her untimely death in March 2010. Despite its near elimination in the mid-1960's, malaria resurged to ~6.45 million cases in 1976. 2011;377:252-269. falciparum transmission Disease surveillance for malaria in India is generally facilitated by passive case detection (PCD) and active case detection (ACD) of fever cases forthrightly. Several commentaries and research reports have emerged in the last several years highlighting the ongoing struggle of adequate infectious disease surveillance and control across India, including malaria surveillance (Sharma 2007; Hay et al., 2007; Dhingra et al., 2010; John et al., 2011). Chemical insecticides against adult mosquitoes are among the most effective malaria control tools yet developed. For new drugs like artemunate, little can be known in advance about the underlying resistance mechanisms. Pest Manag Sci. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Fogarty International Center or the National Institutes of Health. Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. vivax cases. Curr Sci. Vivax malaria is a critical part of the Indian malaria picture, but globally, the genetic analysis of resistance in the species lags far behind that of P. Increasing insecticide resistance surveillance, especially in India's rural regions, is a necessity to prevent the dissemination of double and triple resistant strains. 2009;361:455-467. 2004;9(3):364-371. For example, An. fluviatilis s.l. exists as a complex of four sibling species (S, T, U, and V) (Subbarao et al., 1994). An. minimus s.l. a complex of three sibling species (Singh et al., 2010 ) (An. minimus, An. harrisoni and E) and An. dirus a complex of at least seven sibling species two of which, An. baimaii and An. elegans, occur in India (Dash et al., 2008). The National Vector Borne Disease Control Programme (NVBDCP) is the agency responsible for the prevention and control of all vector-borne diseases in India, including malaria. falciparum is the dominant parasite in Orissa, and mixed-species infections are prevalent in the west (e.g., Gujarat state). Lancet Infect Dis. PCR-RFLP of mitochondrial cytochrome oxidase subunit II and ITS2 of ribosomal DNA: markers for the identification of members of the Anopheles culicifacies complex (Diptera: Culicidae) Acta Trop. This will provide preliminary data for a haplotype map that can be used for association studies of drug resistance. Malaria vector control by indoor residual insecticide spraying on the tropical island of Bioko, Equatorial Guinea. Continuing challenge of infectious diseases in India. [PubMed] [Google Scholar] Singh OP, Nanda N, Dev V, Bali P, Saha M, Mehrunisa A, Adak T, Dash AP. Lancet. Katoch, for project permissions and encouragement. vivax cases. India's expansive geography and diverse climate supports ideal environments for sustaining malaria parasites and their vectors. 2004;9:846-856. vivax from El Salvador is available for the malaria research community (Carlton et al., 2008). Understanding how this will impact malaria transmission across different eco-epidemiological contexts is imperative for malaria control. Data taken from the National Vector Borne Disease Control Programme ( for year 2010. EIR: entomological inoculation rate; API: annual parasite incidence. The diverse malaria epidemiology in India is mirrored by high diversity of malaria vector species, most of which exist as complexes comprising several cryptic species that vary in vectorial capacity (Dash et al., 2007; Singh et al., 2009). Inferring the evolutionary history of Indian Plasmodium vivax from population genetic analyses of multilocus DNA fragments. However, the standard relationships used to describe the influence of temperature on key mosquito and parasite life history traits derive from research done in the early part of last century with a mishmash of species. Thus NIMR, through its ten field stations (see below), evaluates new insecticides and diagnostic kits, conducts clinical trials, and monitors resistance to insecticides among vectors and drug therapy among parasites. As a service to our customers we are providing this early version of the manuscript. Molecular Ecology. 2010;376:1716-1717. Science. In 2004, artesunate plus SP replaced SP alone as the second-line drug for use in CQ-treatment failure. Without this knowledge there is only partial insight into the sustainability of current control programs and the utility of prospective resistance management strategies. Malaria imposes a major Indian global health burden in large part because the Plasmodium parasite readily evolves drug resistance. Malaria J. In contrast to P. falciparum in forest/riparian ecology, while the urban Chennai field station (Tamil Nadu) in the south of the country has predominantly P. falciparum versus P. Since then, confirmed cases have gradually decreased to 1.6 million cases and ~1,100 deaths in 2009 (Figure 1). However, these methods do not account for individuals who are asymptomatic, or present symptomatically but are missed by active surveillance. 2005;22(8):1686-1693. Host Switch Leads to Emergence of Plasmodium vivax Malaria in Humans. Precisely which NGS platform we intend to install at NIMR remains to be decided, although several have obvious advantages for implementing in a field location (Table 2). Next generation sequencing platforms and their suitability for endemic country field settings. Deep sequencing of a polymorphic marker will enable detection of rare clones (Juliano et al., 2010) even if the less-susceptible clone is at a frequency of 5 in 2000 parasites, whereas conventional PCR methods cannot, since they struggle to find alleles at frequencies

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