RESOURCE HUB *Correspondents*

7th International Conference on *Plasmodium vivax* Research (ICPvR)2019

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MESA Correspondents bring you cutting-edge coverage from the 7th International Conference on Plasmodium vivax Research (ICPvR).

26-28 June 2019

Institut Pasteur, Paris, France

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Day 1: 26th June 2019

Setting the stage for the 7th International Conference on *Plasmodium vivax* research were a series of experienced speakers. **Chetan Chitnis** (Institut Pasteur, France), the panel chair, reminded the group of the current global status of *Pv*, including the impressive reductions in burden at the beginning of the 21st century, as well as the limits that have been reached through use of standard control measures. He recognized the research contributions of **Dr Louis Miller** (NIAID, NIH, United States), who then reminded the group of the major breakthroughs and remaining challenges of *P. vivax* research. The crucial challenges he identified were the need to develop drugs for the hypnozoite stage of *P. vivax* and the ability to culture *P. vivax,* which could lead to significant developments in the understanding of the parasite.

George Snounou (French National Center for Scientific Research, CNRS, France), took us on a journey through malaria history, exploring many key discoveries since the 1800s. A particularly fascinating look at experimental malariology revealed the richness of this data source, including 13000 reports between 1917 and 1945 of malaria therapy inoculations with *P. vivax* around the world. He presented a philosophy to "be ignorant and be imaginative" in scientific inquiry, giving examples of dogmas that remained long unchallenged before being ultimately disproved. He identified some examples of current "wobbly dogmas", including that *P. vivax* is the 'benign' malaria, that *P. vivax* cannot infect Duffy negative individuals and the possibility of sequestration and cryptic cycles.

We were treated to a comprehensive overview of the biology of *P. vivax* by **Wai-Hong Tham** (Walter and Eliza Hall Institute, Australia). She highlighted research and tools that have or will greatly contribute to our understanding of *P. vivax* biology, such as the use of drug screens to investigate new treatments for hypnozoites that utilise tiny technologies and 3D cultures. She also talked about molecular insights into parasite invasion of reticulocytes and the use of biomarkers for hypnozoites being key to the future of surveillance methods. Finally, she spoke about the need for a *vivax* model due to its inability to culture, current available options include using a similar *Plasmodium* species with orthologues, chimeric humanized mouse models or carrying out controlled human infection trials.

In the session on the Epidemiology of *Plasmodium vivax* malaria burden, a wide range of topics were covered, however, there were a few recurring topics that were emphasised. One was the use of primaquine at high dose as a universal cure. **Ric Price** (Menzies School of Health Research and Charles Darwin University, Australia, and University of Oxford, United Kingdom) highlighted evidence that indicated that higher dose primaquine dramatically reduces the risk of recurrent infections. Moreover, Ric highlighted that the majority of *P. vivax* is in children and in remote areas and emphasised the importance of targeting these vulnerable populations and ensuring treatment reaches them. Ric also discussed the importance of ensuring that interventions and policy are context-specific, which made it especially valuable to hear specific studies carried out in the Pacific and South America. **Dionicia Gamboa** (Universidad Peruana Cayetano Heredia, Peru) discussed the strides that are being made in malaria burden reduction in South America. In particular, they found that there are many socio-demographic and ecological factors that determine spatial heterogeneity and lead to localised regions of malaria across Peru. She presented an overview of the Malaria Plan Zero, a more realistic long-term malaria elimination plan that is being supported by the government in Peru. **Leanne Robinson** (Walter and Eliza Hall Institute, Australia) offered insight on the *P. vivax* situation in Papua New Guinea. She emphasised that in their study they found a different rate of vivax reinfection to a previous study, illustrating the heterogeneity throughout the country and region. Moreover, she spoke about how after intervention implementation the reduction in vivax was much slower than that of falciparum.

Katherine Battle (Malaria Atlas Project, University of Oxford, United Kingdom) presented her novel maps on global *P. vivax* burden. She spoke about the shift from using prevalence surveys to routine case surveillance and how this is a particular challenge in Africa because of limited data. The importance of these changing trends was emphasised, this may be particularly important given the frequently reported rise in proportion of vivax cases as transmission declines.

Aimee Taylor (Harvard T.H. Chan School of Public Health, United States) examined the cause of *Pv* recurrence by examining 3-9 highly polymorphic microsatellites, which were fed into a novel population statistical model to estimate the time to recurrence and genetic relatedness. She found that her model could reliably distinguish relapse from reinfection. Overall, she found that population supervised high dose primaquine could avert 99% of relapses.

John Henry (Institute for Health Metrics and Evaluation, United States) described an analysis of malaria therapy records, which observed a relationship in logged mean and variance of asexual parasite densities consistent with Taylor's law and showed correlation between increased parasite density higher fraction of fevers. Both *Pf* and *Pv* displayed these general characteristics, however, the periodicity of the parasite densities differed between species.

The Turbo Talks highlighted unique epidemiological characteristics of *P. vivax* in diverse geographic settings. In the Mancio Lima area of Brazil, haplotype analysis presented by **Thais De Oliveira** (University of Sao Paulo, Brazil) showed that infections were mainly due to local transmission, rather than introduced cases. **Mirco Sandfort** (Institut Pasteur and Sorbonne University, France) showed two cross-sectional surveys that examined the burden of malaria near forest regions of Cambodia. **Inge Sutanto** (University of Indonesia, Indonesia) presented a multi-center study bringing worrying news that close to 40% recurrence of *P. vivax* was not prevented by high dose primaquine treatment. Finally, a novel finding was brought to the forefront by **Kate Twohig** (Malaria Atlas Project, United Kingdom) as she discussed evidence for the presence of *P. vivax* in 29 African countries, with 9 of these countries showing evidence of infection in Duffy negative individuals.

The results presented by **Ingrid Felger** (Swiss Tropical and Public Health Institute, Switzerland) demonstrated the power of ultra-sensitive qPCR methods using multiple copies of mitochondrial 18S region over standard low copy qPCR. She found that the ultra-sensitive qPCR was far more sensitive than the standard practice for asymptomatic infections. Moreover, she found that using finger prick blood samples instead of venous blood samples for the ultra-sensitive qPCR captured the majority of sub-microscopic infections, including 91% gametocyte carriage. Importantly, this meant that all infections with high enough parasitemia to be transmissible were identified.

Matthias Marti (University of Glasgow, United Kingdom) explored the conundrum of severe *Pv* infection with low observed peripheral blood parasitemia and the hypothesis of an additional parasite reservoir contributing to this clinical presentation. Through amplification of markers of different stages of parasite development, he found evidence to support extravascular sequestering and parasite maturation in the bone marrow.

Amelie Vanteaux's (Institut Pasteur, Cambodia) presentation examined malaria epidemiology with a vector focus in Cambodia. Following a large mosquito collection, 20% of the mosquitoes were captured from 6am to 6pm, suggesting that vector control tools that protect only at night (such as insecticide-treated nets) may be less effective. Another interesting finding was that more infectious mosquitoes were collected in the forest compared to other sites (3.2% and 1.9% respectively).

Transmission-blocking vaccines remain a high priority research item on the malaria control agenda. **Arianna Marini** (University of Oxford, United Kingdom) presented an investigation to improve the

immunogenicity of a key vaccine candidate, Pvs25, with the Plug-and-Display technology using virus-like particles. This platform was further improved through the Matrix-M adjuvant and similar candidate products are being prepared for Phase 1 clinical trials.

One of the highlights of the talks on day one was undoubtedly the presentation by **Steven Kho** (Menzies School of Health Research, Australia), who examined the evidence for a hidden *P. vivax* biomass in the spleen. He convincingly described evidence from splenectomies that showed that 95% of the individuals tested (n = 21) had asymptomatic *Plasmodium* infection, seven infections were vivax, 13 were falciparum and 1 was a mixed infection. They found more asexual stages in the spleen than in the peripheral blood, predominantly in the *P. vivax* cases, and that there were increased immature reticulocytes in these spleens which could evidence that it may be a site for parasite development. This presentation thus seems to break the dogma that the unique function of the spleen in malaria is the destruction of infected red blood cells.

The first Turbo Talks from the second session transported the audience from Brazil to Myanmar: **Ana Paula Duarte** (State University of Amazonas-UEA and Tropical Medicine Foundation Dr Heitor Vieira Dourado, Brazil) described the inhibition of *P. vivax* infection in *Anopheles aquasalis* through silencing of JNK and Toll immune pathways, providing improved understanding of this dominant vector in the Brazilian Amazon area. She was followed by **Victor Chameau** (Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Thailand and University of Oxford, United Kingdom), who presented on the impact of mass drug administration on the entomological inoculation rate and showed that the entomological inoculation rate was reduced by 12.5 fold. However, the reservoir of *vivax* was reconstituted within 3 months, presumably due to relapses.

Finally, **Henry Surenda** (London School of Hygiene & Tropical Medicine, United Kingdom and Gadjah Mada University, Indonesia) and **Liz Musset** (Institut Pasteur in French Guiana, France) (on behalf of **Emilie Mosnier** (Andrée Rosemon Hospital and University of French Guiana, France) spoke on topics that intersected malaria control and operational research. **Henry** demonstrated the predictive power of serological analysis, commenting on the capacity to improve targeting of interventions in low endemic settings and **Liz** showed a retrospective analysis of a *P. vivax* outbreak on the French Guiana/Brazil border.

We have had a great first day at the 7th International Conference on *Plasmodium vivax* Research. Looking forward to hearing more tomorrow!

*This daily report has been written by **Emma Collins** and **Kate Twohig** (University of Oxford) as part of the MESA Correspondents program. Senior editorial support and expertise have been provided by **Prof Hernando del Portillo** (ISGlobal & Institut d'Investigació Germans Trias i Pujol (IGTP)).*

Day 2: 27th June 2019

The main focus of the presentations on day two of the 7th International Conference on *Plasmodium vivax* Research was on laboratory exploration of *P. vivax* biological characteristics, parasite development stages and host-parasite interaction. There was a lively poster session during the lunch period and a conference dinner at the magnificent Musée d'Orsay.

Poster session

***Plasmodium vivax* sporozoites and liver stages (hypnozoites, invasion, vaccines, immunity)**

We started the day with an excellent talk from **John Adams** (University of South Florida, United States) presenting his investigation to find the essential genes involved in activation and infectivity of *P. vivax* sporozoites in order to find a target for inhibition. He spoke about using phylogenetic genomics information from *P. falciparum*, *P. berghei* and *Toxoplasma* as a proxy to study essential genes in *P. vivax*. He emphasised that the ideal targets would have the following characteristics: present in blood stage parasites, expressed in multiple life stages and not transcriptionally repressed. He also described implementation of semi-automated HTP methods for quantitative analysis of live sporozoite motility, traversal cell assays and inhibition of liver stage development for drug and vaccine development.

Erika Flannery (Novartis Institute of Tropical Diseases, United States) spoke about the continued uncertainty in the mechanisms underlying *P. vivax* relapse and radical cure within the liver. She demonstrated the importance of using schizonticidal drugs before adding hypnozoicidal drugs to remove confounding factors in the studies of hypnozoite biology and demonstrated that hypnozoites are transcriptionally silent and can be reactivated. She described techniques for drug discovery using the in vitro culture of *P. cynomolgi*, which permits the use of reverse genetics to create transgenic lines, the use of iPS cell lines capable of differentiating to hepatocytes as an unlimited source for in vitro culture of hypnozoites, and of liver chimeric humanised mouse models to assess if drug exposure at different infection stages could prevent or halt hypnozoite formation and activation.

Arturo Reyes-Sandoval (Jenner Institute, University of Oxford, United Kingdom) described challenges for vaccine development for *P. vivax*, including the life cycle complexity and genetic diversity across parasite populations. The consequences of these challenges are that a new vaccine would ideally target multiple components and stages. He demonstrated the use of transgenic *P. berghei* parasites expressing *P. vivax* vaccine candidates as surrogate markers in vaccine antigen screening and prioritization. Trials of three main vaccine candidates, Pv CelTOS, PvTRAP and PvCSP (PvR21) demonstrated that the PvCSP utilising HepB S VLP was the most promising, leading to 100% protection in two mice models; thus, paving the road for near future clinical trials. Further improvements using a combination of proteins (e.g. PvR21 with TRAP) are being pursued.

Steven Maher (University of Georgia, United States) emphasized the value of collaboration in the optimization and innovation of drug screening processes. They have harvested more than a billion sporozoites to use in hepatocyte challenge experiments and emphasized the importance of implementing semi-automated HTP methodologies for drug screening which have allowed them to test over 18,000 compounds.

Alison Roth's (Walter Reed Army Institute of Research) research screened large numbers of compounds for novel anti-relapse hypnozoicidal drugs in a *P. cynomolgi* liver model, balancing toxicity with reactivity and efficacy. **Josue da Costa Lima Junior (**FIOCRUZ, Brazil) discussed his characterisation of the humoral response to PvTRAP protein, finding that IgG1 was the main immune response elicited. For drug and vaccine development, generation of large numbers of sporozoites is required. **Rosa Santana** (Tropical Medicine Foundation Dr Heitor Vieira Dourado, Brazil) presented work demonstrating higher sporozoite production in *An. darlingi*, compared with *An. aquasalis*. **Dennis Shanks** (Australian Defence Force Malaria, Infectious Disease Institute, and University of Queensland, Australia) completed the morning session with a presentation of the correlation between blood transfusion with *P. vivax* hypnozoite initiation for infection relapses from an analysis of historical data from US Army records. From this, he hypothesised that apoptosis of hepatocytes could be the trigger for hypnozoite activation.

Ex vivo and in vivo models to study *Plasmodium vivax*

Dennis Kyle (University of Georgia, United States) discussed the importance of understanding the characteristics of hypnozoites in order to discover a radical cure for *P. vivax.* They found that the PI4K activity varies between hypnozoites, generally arising between three and six days post infection, and that PI4K insensitivity may be a marker for hypnozoites. Their drug screening found that Monensin is an effective drug against schizonts and hypnozoites and mentioned screening several different libraries such as MMV libraries and ReFRAME, from which they have identified 14 new compounds.

For decades **Bruce Russell** (University of Otago, New Zealand) has been trying to culture *P. vivax*, finally attempting to replicate a 1981 study to culture *P. cynomogi* as a proxy. He failed to culture with common *P. cynomolgi* strains B and M but had great success with the Berok strain. This technology has been transferred to many different laboratories worldwide and is available upon request. The ability to culture one strain and not others led him to investigate the differences in reticulocyte invasion between the strains. He recalled the audience´s attention about misconceptions of reviewers on *P. vivax* research and the importance of pursuing efforts to continue emphasizing the fundamental biological differences between *P. falciparum* vs *P. vivax*.

A comprehensive talk on how a model of *P. cynomolgi* infection in rhesus macaques can be used to further elucidate insights into relapse infection biology was given by **Chet Joyner** (Emory University,

United States). He reiterated that although this model provides a similar context in which to investigate *P. vivax*, noting the similarity in observed clinically silent infections, we don't know the full extent to which these parasites differ. He provided evidence using changes in the host transcriptome that infections are modulating B cell related immune responses.

In the absence of *P. vivax* cultures or *in vivo* models, **Rob Moon** (London School of Hygiene and Tropical Medicine, United Kingdom) described how transgenic *P. knowlesi* can be used as an effective model for *P. vivax* vaccine candidates. He has refined the mutagenesis of *P. knowlesi* using CRISPR cas9 to substitute the *P. knowlesi* Duffy binding protein (DBP) for the vivax DBP and also knocked out the beta and gamma DBPs. This swap provided insight for the parasite host preference, as the transgenic parasite had more affinity for human cells than macaque cells.

Anne-Marie Voorber-van der Wall (BPRC, The Netherlands) successfully described her development of a double reporter line of *P. cynomolgi.* She inserted a green fluorescent protein (GFP) at a constitutive promoter so it was expressed in all parasites while inserting mCherry to be regulated by Lisp2, which has recently shown to mark early liver stages in *P. cynomolgi.* The transgenic parasite exhibited no loss of fitness, and after 6 days hypnozoite development could occur. This transgenic model is an exciting new tool that can be used to study compounds that trigger hypnozoite development and allowed the first unequivocal evidence of true hypnozoite reactivation.

Catlin Cooper (University of Georgia, United States) spoke about her efforts to create a proxy for *P. vivax* continuous culture. She achieved long-term culture of the *P. cynomolgi* Berok RLV9 strain, while improving sustainability using human serum. **Florian Bach** (University of Edinburgh, United Kingdom) reported the results of the first blood-stage infection trial from which he hypothesised that *P. vivax* malaria reprograms the immune system to reduce inflammation and minimise pathology. He hopes to investigate this idea further by monitoring the immune responses of volunteers with repeated infections. **Letusa Albrecht** (FIOCRUZ and UNICAMP, Brazil) compared RNA of parasites with weak and strong levels of rosetting and demonstrated that there are over 150 genes involved in the process, with around 16% of them associated with membrane proteins. Moreover, she observed increased rosetting capacity observed in sexual parasite stages. **Gabriel Rangel** (Harvard T.H. Chan School of Public Health, United States) investigated whether there was further discrimination in reticulocytes choice for parasite invasion and discovered that *P. vivax* had a high preference for and survived better in SLC12A6+ cells.

Plasmodium vivax blood stages (invasion, immunity, pathogenesis and vaccines)

In 1976, the first study that described the protection of Duffy blood group negativity against *P. vivax* was published, and today **Peter Zimmerman** (Case Western Reserve University, United States) presented contradictory evidence of *P. vivax* infections in Duffy negative individuals from Madagascar. A study carried out in Ampasimpotsy district illustrated a decrease in prevalence of *P. vivax* infections in Duffy negative individuals and lower levels in Duffy heterozygotes, suggesting that it still has a protective effect. However, the mechanism of entry into Duffy negative cells remains unknown. Given the finding of Duffy positive red blood cells in the bone marrow of Duffy negative individuals, he is using bone marrow cells to try developing the in vitro culture system of P. vivax and showed data of sustaining cultures for 500 days.

Innovation in *P. vivax* preventative interventions is limited by challenges in acquiring sufficient parasite for inoculation. **Angela Minassian** (Jenner Institute, University of Oxford, United Kingdom) demonstrated the implementation of the first European controlled human malaria infection (CHMI)

facilities to carry out clinical trials of *P. vivax*. A meticulous approach following European regulations allowed the production of 190 vials of *P. vivax* infected blood, which she encouraged other groups to use in vaccine trials. Undoubtedly, this kind of collaboration will enable the malaria research community to accelerate the rate of breakthroughs and hopefully hasten the production of an effective *P. vivax* vaccine. Two different candidates of the Duffy Binding Protein are now entering in these CHMI clinical trials.

The evolutionary history of *P. vivax* was examined through research presented by **Virginie Rougeron** (French National Center for Scientific Research, CNRS, France) on the relatedness to the *P. vivax*-like parasite that infects African great apes. Through genomic characterization from whole genome amplification and short read illumina sequencing, two distinct clades for *P. vivax* and the vivax-like parasite are determined, including further discovery of two vivax-like sub-lineages.

With a panel of monoclonal antibodies from the first in-human trials of leading *P. vivax* vaccine candidate, the Duffy-binding protein (PvDBP), **Tom Rawlinson** (Jenner Institute, University of Oxford, United Kingdom) used growth inhibition assays to characterise the invasion inhibitory properties in a transgenic *P. knowlesi* parasite line.

Current research has identified only two red blood cell host receptors that mediate *P. vivax* parasite invasion: the Duffy Antigen Receptor for Chemokines (DARC) and the reticulocyte restricted transferrin receptor (TfR/CD71). The presentation by **Usheer Kanjee** (Harvard T.H. Chan School of Public Health, United States) provided insight into the functional impact of these proteins, showing that DARC knockout and TfR mutants individually reduced *P. vivax* parasite invasion. Promising reductions in *P. vivax* invasion from a SLC4A1 knockout study also called attention to a possible species-transcendent host factor.

We heard three turbo talks this afternoon, the first was from **Camille Roesch** (Institut Pasteur, Cambodia) who demonstrated the functional impact of increased PvDBP gene copies associated with higher PvDBP gene expression, aiding the understanding of why this protein gene is amplified even in areas of low Duffy-negativity. Following on from yesterday's presentation revealing high spleen parasite biomass, **Haruka Toda** (Barcelona Institute for Global Health (ISGlobal)), showed research supporting cytoadherence of uninfected spleen fibroblasts as a result of stimulation due to extracellular vesicles from infected cells.

Martha Clark (Harvard T.H. Chan School of Public Health, United States) and her flow cytometry lysis assay demonstrated that there was increased osmotic fragility associated with reticulocyte development and decreased osmotic stability during parasite maturation.

Finally, **Herbert Opi** (Burnet Institute for Medical Research and Public Health, Australia) spoke about how we often rely on increased antibody production to identify potential target molecules, however, we should focus more on the functional antibody response.

Dinner at the magnificent Musée d'Orsay

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Day 3: 28th June 2019

Wrapping up the 7th International Conference on *Plasmodium vivax* Research, day three focused on the topics of *P. vivax* drugs and approaches for *P. vivax* elimination.

Kevin Baird (Eijkman Oxford Clinical Research Unit, Indonesia) started with the history of 8-aminoquinolines, and the link between their treatment development and the needs of soldiers at or returning from war. Thus, the primary purpose of these drugs was to address this need, without sufficient investigation of the observed haemolytic toxicity, nor adequate prioritization of the needs of the majority rural populations that would be the end users. The most recently developed hypnozoicide, tafenoquine, was selected during drug discovery trials due to the extended half-life of the drug (16 days). It was subsequently discovered that tafenoquine is just as haemolytically toxic as primaquine. Kevin emphasised that the history of 8-aminoquinine development demonstrates a rush towards implementation, without sufficient investigation into optimization of drug efficacy and reduced toxicity in combination with partner blood schizonticides.

Marcus Lacerda (FIOCRUZ, Brazil) also talked about the extensive list of current issues with primaquine; course length, lack of paediatric formula, issues with CYP2D6, limited drug production, temperature and humidity instability and that testing for G6PD deficiency increases costs for control programmes. The Roll-oUT study in Brazil is trying to supplement primaquine use by introducing tafenoquine to treat *P. vivax* in patients with at least 70% glucose-dehydrogenase enzyme activity. Over a year they hope to treat 10,000 patients and gain more understanding of how tafenoquine could improve malaria treatment standards.

The assessment of drug treatment in G6PD-deficient individuals was investigated retrospectively by **J De Brito Sousa** (Tropical Medicine Foundation Dr Heitor Vieira Dourado and Amazonas State University, Brazil)**,** who used historical clinical data of hospitalised *P.vivax*-infected patients to assess the adverse reactions of primaquine treatment. He found that most individuals were admitted on the 3rd or 4th primaquine dose and 58.5% had severe anaemia. Almost half of the patients required transfusions, reiterating the need for quantitative G6PD deficiency diagnosis to improve the safety of 8-aminoquinoline administration.

The presentation by **Kamala Thriemer** (Menzies School of Health Research, Australia), on behalf of the hard work of the IMPROV Study Group, showed their findings on the non-inferiority analysis of short-course, high-dose primaquine, compared with the 14-day treatment protocol. For primary and secondary endpoints including one-year recurrence rates, 42-day cure rates and both asymptomatic and symptomatic risk, the 7-day schedule demonstrated comparable effectiveness, and this study confirmed the major reduction of infection recurrence with primaquine treatment compared to the placebo arm. There remained some challenges in gastrointestinal tolerability, which would need to be addressed to truly ameliorate patient adherence.

Robert Commons (Menzies School of Health Research, Australia) discussed a trial comparing the efficacy of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) with and without primaquine (PQ). At day 42 there was a 12-fold increase in risk with the use of AL over DP alone. The use of primaquine additionally reduced the risk by 37%. **Robert James** (Walter and Eliza Hall Institute of Medical Research, Australia) presented his work in the Solomon Islands investigating efficacy of *P. vivax* treatment policies in this specific context. It was determined that the current AL+PQ combination is sub-optimal for preventing recurrence and that even in a controlled setting there was risk for haemolytic toxicity.

Bob Taylor (MORU, Thailand) examined haemoglobin dynamics following weekly primaquine administration in G6PD-deficient and G6PD-normal individuals in a Cambodian study, noting that G6PD deficiency, high initial parasitaemia, and thalassaemia were associated with the most rapid declines in haemoglobin concentration. Expanding hypnozoicides for paediatric treatment would target a considerable infected population and **Hema Sharma** (GlaxoSmithKline) shared a population pharmacokinetic model that was used to calibrate an ongoing paediatric clinical study. **Ghyslaine Bruna Djeunang Dongho** (University of Cameroon, Cameroon and Sapienza University of Rome, Italy) evaluated the considerations for appropriate *P. vivax* treatment in Duffy positive and negative individuals in Cameroon. The study found that 99% of patients were CYP2D6 normal metabolisers and there was a low G6PD deficiency proportion. **Narimane Nekkab** (Institut Pasteur, France) described the utility of a robust mathematical model to approximate the impact of tafenoquine in Brazil, showing the complex variety of treatment pathway options and estimating a 60% decrease in incidence rate associated with change in treatment policy.

Pedro Alonso (World Health Organization) provided a perspective on national and international policy and guidelines for elimination. He described the apparent division of countries into two groups; those that are nearing elimination and high burden countries. He mentioned that *P. vivax* is often the residual parasite, with recent examples of Sri Lanka and China. Pedro underlined these examples, and more, to show that elimination of *P. vivax* is possible, but that robust health systems and political willpower are major determinants of success. He insisted that elimination is based on three pillars, universal access, acceleration towards elimination, and surveillance tools that will help the global technical strategy against malaria. The need to accelerate the malaria elimination effort and new tools and technologies such as diagnostics, novel drugs and vaccines is the best way to do this.

Francois Nosten (Shoklo Malaria Research Unit, Thailand) examined the necessity of *P. vivax*-specific control measures to achieve malaria elimination; asking if, when and how these should these be implemented. Examples of increasing *P. vivax* under intense falciparum-focused intervention at the Thai-Myanmar border, alongside Sri Lanka's achievement of elimination of both parasites at approximately the same time, showed that it is imperative to know how *P. vivax* behaves in different contexts. He emphasized that the sub-microscopic reservoir of *P. vivax* can sustain transmission and that this reservoir may require targeted efforts such as mass drug administration.

Insights into the evolution of *P. vivax* was the overarching objective of the work presented by **Sarah Auburn** (Menzies School of Health Research and Charles Darwin University, Australia) from the vivax Genomic Epidemiology Network (vivaxGEN). This group aims to provide increased access to and utility of vivax-specific genomic tools, with a variety of potential use-cases. She gave an example of the general action plan relating to two priority applications: detection of antimalarial resistance and identifying imported infections. The plan includes; creating a collaborative network with high geographic scope, developing tools for high-throughput genotyping, producing online tools for data sharing and partnering with countries for pilot studies.

Nicanor Obaldia (Instituto Conmemorativo Gorgas de Estudios de la Salud, Panama and Harvard T.H. Chan School of Public Health, United States) provided an example of the insights to be gained from *P. vivax* genetic analysis in the pre-elimination context of Panama. Using selective whole genome amplification from samples gathered between 2009 and 2012, it was determined that there was low local diversity, and evidence of clusters that were genetically related to parasites from South America. Due to changes in population movement through Panama, future analysis with samples from 2014-2019 may reveal interesting spatial patterns.

Jason Rosado (Institut Pasteur and Sorbonne University, France) discussed the difference in sensitivity between light microscopy and PCR and suggested that the measurement of antibody responses to previous infections could aid with the detection of latent hypnozoite carriage. He proposed a modification to standard MDA called SeroTAT, which would treat only those who have antibodies present. This could reduce the number of people that would have to take an unpleasant primaquine course by 80%.

Two turbo talks concluded the scientific sessions. **Sadudee Chotiriat** (Mahidol University, Thailand) confirmed that RBP2b could be used as a proxy for recent exposure in Thailand and that serological exposure markers could be used to improve detection of asymptomatic infection burden. Finally, a completely different, but vitally important, subject was covered by **Angela Devine** (Menzies School of Health Research and University of Melbourne, Australia)**.** She estimated the global economic cost of *P. vivax* to healthcare providers and patients was US$533 million per year, but that the introduction of G6PD deficiency testing could reduce this by US$234 million.

The day concluded with a round table discussion. **Ivo Mueller** (Institut Pasteur, France) chaired the panel which included: **Pedro Alonso** (World Health Organization)**, Kevin Baird** (Eijkman Oxford Clinical Research Unit, Indonesia)**, Neena Valecha (**WHO –SEARO, India**), Alejandro Llanos Cuentas** (Universidad Peruana Cayetano Heredia, Perú), **Fitsum Tadesse** (Armauer Hansen Research Institute, Ethiopia), **Scott Miller (**Bill and Melinda Gates Foundation, United States), and **Alexandra Cameroon** (UNITAID, Switzerland).

The session began with a series of individual questions/answers posed to the panellists. **Alejandro** explained that Peru has a credible road-map for elimination as the government has recently fully endorsed it through a permanent law approved by Congress. **Scott** recognized the enormous progress that the vivax research community has achieved in the past years, particularly in developing and implementing technologies in areas such as diagnostics and drug discovery. However, he made an appeal to reinforce the study of vector biology in the next ICPvR as novel and promising technologies have been developed. **Pedro** was asked how WHO acquires and maintains government's commitment to malaria elimination. He provided insight that governments need to feel they have ownership and leadership in order to commit to complete malaria elimination programmes**. Fitsum** reinforced the importance of developing local individual strategies for elimination and drilled into this concept by explaining the different areas of transmission of *P. vivax* (above 1000m in the mountains) and *P. falciparum* (below 1000m in lowlands) in Ethiopia. **Neena** emphasised that India is responsible for nearly 50% of the burden associated with *P. vivax* infections and that surveillance needs to be tailored for each area. Her wish is for increased collaboration to help overcome the current challenges in *P. vivax* research. **Alexandra** reinforced the importance of accurately determining the burden of vivax infections in children to elaborate a precise investment plan for this vulnerable population. **Kevin** expressed his belief that an operational and cost-effective G6PD test would revolutionise progress towards elimination. On the other hand, **Pedro** encouraged researchers not to abandon vaccination development efforts as they represent a cost-effective public health tool that could accelerate us towards elimination. Moreover, he appealed to hear more from researchers, particularly those working on the ground, to report any areas they would like additional guidance from WHO to support control efforts.

Chetan Chitnis (Institut Pasteur, France) ended by acknowledging the funders who made possible the 7th edition of ICPvR, in particular, the generous gift by the Bill and Melinda Gates Foundation, the invaluable help of the local and international Scientific Committees and the essential and effective help of the Secretariat at Pasteur. Last, it was announced that the 2021 ICPvR will be held in India!

*This daily report has been written by **Emma Collins** and **Kate Twohig** (University of Oxford) as part of the MESA Correspondents program. Senior editorial support and expertise have been provided by **Prof Hernando del Portillo** (ISGlobal & Institut d'Investigació Germans Trias i Pujol (IGTP)).*

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