

M A L A R I A



40 Years of Research in PNG



Madang 24-26 August 2016

40
years of research

Papua New Guinea Institute of Medical Research

MALARIA

Colloquium Magazine



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Papua New Guinea Institute of Medical Research

Malaria Colloquium

40 years of malaria research in PNG

‘Continuing innovative research for effective malaria
control and elimination’

Madang

24-26 August 2016

The 40th Malaria Colloquium magazine was compiled and edited by Geraldine Vilakiva and Cynthea Leahy,
Communications Unit, PNGIMR

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Message from the Colloquium Patron



It is my great pleasure to welcome you all to the first PNG Institute of Medical Research Malaria Colloquium as we commemorate 40 years of malaria research in PNG. We have a rich history of research work done on malaria in our country that has put PNG on the world map for malaria research, particularly over the past four decades through the work of PNG Institute of Medical Research.

We commemorate years of truly commendable work undertaken by PNGIMR through its Vector Borne Disease Unit and the international collaborating partners in the field of malaria research and its efforts to control malaria. At the heart of PNGIMR's impressive list of achievements in the fight against malaria, guidelines and strategies have greatly been improved that are now been used to control and treat malaria both domestically and globally. Malaria research in the country has contributed significantly to the health sector that has resulted in employment opportunities for hundreds of Papua New Guineans. Funding from research grants worth millions of kina has been brought into the country over the years and has contributed greatly in capacity building for Papua New Guinea scientists, many of whom have gone to obtain Honours, Master's and Doctorate degrees.

In this modern era, we have great advancement in technology, giving rise to scientific breakthrough in malaria research, and with the increased global partnership in the fight against malaria, I would like to embrace the goal of eradicating malaria. Eliminating malaria will make our country a better, safer place for future generations and enable our people to reach their full potential. Ending malaria transmission improves human health, it will increase the quality of life of our people and free up the resources that are currently been used to fight the disease.

As a country we need to prioritize resources for more efforts and tools guided by our scientific community to stop mosquito-borne diseases and deaths in our provinces. Advances in research and tools to fight malaria will help transform how we combat other diseases like the Zika virus or dengue fever. Research institutions such as PNGIMR will provide the research work and the intelligence for early and timely response towards ending not only malaria but other known and emerging health threats.

As Patron for the malaria colloquium and as Minister for Higher Education Research Science and Technology, may I emphasize that we have the science and tools to eradicate malaria and the malaria deaths are thus, unacceptable. But this cannot happen in isolation, I urge the global health community and partners, national leaders, political leaders in endemic countries to maintain the commitment to provide universal access to interventions and end needless suffering from this preventable and treatable disease. As we work together, with more effort, commitment and funding, we can do what we thought was impossible.

It is with great honour that I deliver the Patron's welcome message for the first malaria colloquium after 40 years of research in malaria by the PNG Institute of Medical Research.

Thank you all.

Honourable Malakai Tabar

Malaria Colloquium Patron

Welcome remarks from the PNGIMR Director



Greetings and a warm welcome to delegates attending the colloquium to celebrate the 40th Anniversary of Malaria Research in PNG, in Madang, Papua New Guinea (PNG). I would like to acknowledge the presence of former PNG Institute of Medical Research (PNGIMR) staff members from within PNG and abroad who have dedicated many years to malaria research in performing various responsibilities as investigators, field, clinical and laboratory staff, and data management and administrative staff. Your contributions were very vital in successfully implementing many malaria research programs, and without your commitment and perseverance much of the research activities would not have been completed. It also gives me great pleasure to extend a very special welcome to our past and present collaborators within PNG and abroad for their financial and technical support over many years in assisting the PNGIMR undertake malaria research.

Malaria research has been high on the agenda at PNGIMR since it was established, and we are proud of our achievements in this field of research. Research conducted at the Maprik and Madang research sites has been internationally recognised, and our current work continues to meet international bench-marks in excellence and is relevant to the needs of PNG. It is also important to acknowledge the participation and contribution of the communities where malaria research is conducted, because their direct involvement has determined the viability and successful completion of the research programs. The PNGIMR remains committed to malaria research, and our current research activities on the biology and epidemiology of the disease will contribute towards national malaria control policies, and also contribute towards global knowledge in our bid to eradicate malaria.

As we gather during this week to celebrate 40 years of malaria research and acknowledge the achievements that have been made, we must not forgo the opportunity to plan for the next 40 years of malaria research. PNG has performed very low in our struggle to meet Millennium Development Goal four: to reduce childhood mortality by two-thirds between 1990 and 2015. This goal cannot be met without combating malaria, one of the greatest causes of childhood death in PNG (and globally). We, as health researchers, must do all we can to establish research activities that will pave the way for the much needed decrease in child and maternal mortality. I hope that delegates can continue to foster strong collaborations between the IMR and national/international institutions that will help us meet our goals of decreasing the burden of malaria in PNG, and increase the capacity of malaria scientists to lead the way in future research.

Finally, I know that an informative, interesting and entertaining scientific and social program is planned for this gathering. I wish to thank the Organising Committee, led by Dr Moses Laman and Dr Leanne Robinson in bringing this colloquium into fruition. I hope you enjoy catching up with old friends, establish new friendships, reminisce about the past and plan for the future.

Professor Peter Siba

Director

Papua New Guinea Institute of Medical Research

Foreword from the Colloquium Chairman



As Chairman of the PNGIMR 40th Malaria Colloquium organized by the Vector Borne Diseases Unit, I am delighted that you are able to come to Madang to celebrate this special moment with us. We know how busy you are and we are truly grateful that you are still able to find time and resources to attend.

In Melanesian society, my community and my relationship with others within and outside of my community are invaluable elements that maintain peace and govern the way most people live. This means my community, the PNGIMR, must do everything we can to protect and improve the value of our collaborative relationships. You are very important to us and we are truly grateful that you are able to join us to celebrate and reflect on the past 40 years of malaria research in PNG as we continue to stride forward. Your presence and support as a collaborator, colleague, mentor and friend that enabled this colloquium to eventuate will always be remembered.

I'm sure you will agree with me that the malaria research programs at PNGIMR that have kept the Vector Borne Diseases Unit going over the past 40 years have made outstanding contributions in guiding policy and generating knowledge, both locally and globally. This exceptional achievement is special, considering the fact that the research is often conducted to very high standards by hundreds of different people over the past four decades, despite many limitations in a logistically challenging environment. As you will learn from the stories in this magazine, the successes of PNGIMR's research programs are often grounded on a strong community-based approach, staff that has a heart to serve this Institute, and strong collaborative relationships. As you read through, I hope you enjoy the historical and scientific perspectives put together by some of our outstanding past and present pioneers who significantly contributed to making PNGIMR Vector Borne Diseases Unit what it is today.

For us, the younger generation, we know that this is only the beginning of a lot of work that we still need to do, but we look forward to these challenges. Our aim is to sustain the momentum that has been gained in malaria research in PNG and collaboratively advance PNGIMR to higher standards in the coming years. To do this, we will no doubt need your support. But rest assured, we are ready to work hard, learn as much as we can, ensure our collaborative relationships are beneficial to all institutions involved and most importantly, for us, we want to improve the poor health status of our country.

Finally but not the least, I would like to take this opportunity to thank our sponsors and the staff of PNGIMR for your outstanding and tireless efforts in raising funds that has enabled us to host this colloquium. This colloquium would not be possible without your commitment. I am confident that we all will appreciate what has happened over the past 40 years of malaria research in PNG and learn something new over the next couple of days.

Thank you and I hope you enjoy this special moment with us.

Dr Moses Laman

Chairman of the Malaria Colloquium

40 years of malaria studies at PNGIMR: local action that changed the world

John Reeder

Director of TDR and former director of PNGIMR



Congratulations to PNGIMR on 40 years of malaria research. Forty years in which the research has not only advanced our understanding of the disease and the parasites that cause it, but helped forge the tools necessary to combat malaria, not only in PNG but throughout the world. Forty years in which the Institute has not just done research, but profoundly influenced the way that research is done.

My own engagement with the PNGIMR malaria program goes back well over 25 years, to the early 1990's when I was a VSO volunteer teaching laboratory skills at the Highlands Regional Disease Control Unit in Goroka. This was where I picked up a fascination for this disease that took me into a research career at the Walter and Eliza Hall Institute, where I continued to collaborate closely with the IMR in Madang and the Sepik, before later returning to PNG as Director of the Institute. It was then that I had the privilege of seeing the malaria program in all its exceptional parts and could appreciate the richness of the work that was being done and capacity that had been built. Capacity that I continued to benefit from once more as a collaborator when I returned to Melbourne, at the Burnet Institute.

I am sure that there will be much said at the celebratory symposium on the scientific achievements of the program; spanning a dazzling range of topics including vector biology, epidemiology, parasite and host genetics, diagnostics, interventions and treatments, drug resistance, parasite biology, malaria mapping, vaccines, immunology and many other areas. No corner of our understanding of malaria today is untouched by research findings from Papua New Guinea. This is an incredible record for the PNGIMR and its committed international collaborators. However, I think there is something here even greater than the sum of these very impressive parts, and this is a pioneering approach to how research is done in disease affected countries.

If one considers the even earlier history of research at the PNGIMR, in kuru and pneumonia, and the deep principles of community involvement and social and anthropological analysis, it was hardly surprising that the PNGIMR brought these values to malaria research. While some other parts of the world were subjected to 'commando research', the IMR program was built on the solid foundation of community participation. This of course took time and painstaking patience, but it is undoubtedly the reason for the longevity and productivity of this research program. One of the great demonstrations of the value of this approach was the Combination B malaria vaccine trial in the mid 1990's. Building on years of hard work in establishing the study site in the Sepik, a malaria vaccine trial of remarkable quality was carried out, involving broad community mobilisation and participation. Importantly, because of the participatory way the trial was conducted, while many sites across the world close down after a single study, the Sepik site is still today an important centre for biological and social studies on malaria. These are lessons that some investigators world-wide are only learning today, yet were in the heart of the PNG malaria program 40 years ago.

So what of the relevance of the PNGIMR malaria program in a world where fortunately the burden of malaria disease and death has fallen dramatically and people again dare speak of malaria elimination? Of course, the best thing a health research program can do is put itself out of business by eliminating the disease it studies, but we are not there yet. Important questions remain to be answered, such as the impact on parasite dynamics brought about by tools such as ITNs and ACT, the rising importance of latent vivax infections and the challenges of surveillance in low prevalence, to name but a few. The recent trend of the research program to engage even more closely with the malaria control program is commendable in the assistance it brings to PNG's malaria control ambitions, but again there will also be a global resonance to this work. The PNGIMR and its collaborators are well placed to capitalise upon its unique mix of excellent science and community grounding, to provide the research necessary to enter into the malaria endgame well-armed with solid research evidence.

It might seem strange to finish a birthday greeting by saying I sincerely hope the malaria program doesn't go for another 40 years! I hope malaria is long gone from PNG by then. Indeed, I hope it is on its last legs worldwide. When this time comes though, PNGIMR can hold itself up with immense pride that it fought in this war against a terrible disease with distinction and really made a global difference. What is more, the Institute can take the well proven model it has created and turn it towards the important new priorities of the day.

Stories about malaria from 40 years of research at the PNG Institute of Medical Research

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Research into malaria has been carried out on the island of New Guinea and associated islands since the 19th Century, including significant early work by Robert Koch, and has embraced many aspects of malaria, in particular major studies on the mosquito vectors throughout the 20th Century. During the Second World War research was an important component of the Australian Army's campaign against malaria in New Guinea. After the war research was conducted to strengthen the systematic campaigns using indoor residual spraying of houses with insecticide as part of the Global Eradication Campaign against Malaria, a military-style operation driven by the World Health Organization (WHO) in the 1950s and 1960s. Reading old accounts of malaria is an activity that I can recommend, since it is not only enjoyable but also leads to unexpected insights into the disease. Much has been written about malaria in the Pacific region and ways into this extensive literature include historical accounts of malaria in Papua New Guinea (PNG) (1,2), the Bibliography of Medicine and Human Biology of Papua New Guinea (3) and the focus issues of the Papua New Guinea Medical Journal devoted to malaria -- Vol 16 No 4-Vol 17 No 1, Dec 1973-Mar 1974; Vol 29 No 1, Mar 1986; Vol 35 No 4, Dec 1992; and Vol 57 No 1-4, Mar-Dec 2014.

The Papua New Guinea Institute of Medical Research (PNGIMR) was founded (as the Institute of Human Biology) in 1968. Greg Crane, a haematologist working for the Department of Public Health in the Territory of Papua and New Guinea, carried out research on malaria, with a special interest in hyperreactive malarious splenomegaly, and brought this research with him when he became the inaugural Deputy Director of the Institute. However, the formal beginning of a comprehensive Malaria Research Program at the Institute did not occur until 1977, when I became the second Director of the Institute. In reality this research program had begun in the previous year, 1976, during a conversation between Graham Mitchell and myself on a plane travelling from Melbourne to Canberra. This was the starting point of our collaboration on malaria, the point from which new concepts took off and we were fired into action: thus 1976 becomes the benchmark year.

What Graham and I agreed on was that the time was ripe for a concerted effort to develop a vaccine against malaria. It was possible to grow the falciparum malaria parasite in vitro. Malarial antigens could be studied and immunity to them tested. Through recent advances in recombinant genetic technology it would be possible to make large quantities of relevant malarial antigens and create a subunit malarial vaccine. We knew that adults in a malaria-endemic area established their own protective immunity and a vaccine might protect children from dying of malaria. That is about as far as the conversation went, but we became excited and enthusiastic about these ideas. The concepts needed to be refined, and there were massive unknowns – but that was part of the challenge. Research operates at the edge of the unknown: we thought we could identify this interface and ask the right questions to move forward. Also, critically, research is the art of the soluble: we thought that by then we had the tools to enable us to solve the problems that these questions would raise.

At that time I was in the process of becoming the new Director of the PNGIMR and was planning my strategic research programs, which would be designed to investigate the principal diseases that affected Papua New Guineans. Malaria was one of these. Graham was in charge of filariasis research at the Walter and Eliza Hall Institute of Medical Research (WEHI) in Melbourne. I started developing a comprehensive research program on malaria and gathering all the collaborative support that I could in Australia. The support that I received was remarkable. Much of it came from colleagues who were not working on malaria but agreed to apply their skills and the human resources of their institution to study malaria in PNG. They included Chev Kidson, Director of the Queensland Institute of Medical Research, who recruited Allan Saul and others in his Institute to work on malaria, Robert Clancy and his team in the University of Newcastle Medical School, and Sue Serjeantson and Ian Clark at the Australian National University in Canberra. Greg Crane, then

back in Sydney at Concord Hospital, was happy to join the program and revive his work in PNG. Meanwhile Graham Mitchell spoke to Gustav Nossal, the Director of WEHI, who was instantly supportive. Graham added malaria to his portfolio and Gus recruited Graham Brown to the program as a clinical scientist and Robin Anders to do the laboratory work developing appropriate malaria antigens. This provided a big boost to the incipient program and showed a firm commitment to our collaborative research effort on the part of WEHI. When, later, Graham Mitchell left WEHI, Dave Kemp joined the team and, when Dave left, support for the work of the team continued unabated.

On my way to Goroka at the beginning of 1977 to take up my appointment I stopped in Sydney to see Professor Robert Black in the School of Public Health and Tropical Medicine. He was the most renowned malariologist in Australia: indeed, perhaps the only one at that time who had an international standing in the field. He was a consultant to WHO and one of the architects of the Global Eradication Campaign against Malaria. Although by then WHO had formally renounced the Campaign and was promoting enhanced national malaria control programs Professor Black still believed that properly conducted insecticidal campaigns could reduce vector numbers sufficiently to eradicate malaria. He was bitter that the great goal had been prematurely abandoned. He poured scorn on all my ideas for investigating malaria and especially for working towards a malaria vaccine, which was in his opinion 'pure obfuscation'. I did not get much help from that quarter. A few years later, when our malaria research program was well established, Professor Black retired from the University of Sydney. Our collaborative group joined with colleagues in Sydney to organize a Festschrift in his honour, which he attended. It was a great meeting (4), but sadly he did not enjoy it: he complained to the bitter end about the futility of studying the immunology of malaria. It is interesting that malariologists had always paid attention to immunity in malaria infection – it was conceptually an important part of Robert Koch's work in Madang, for example – but they used their own terminology and it was hard, even in the 1980s, to persuade the old guard that modern concepts of immunology applied equally to malaria as to other infections. In fact, malaria was regarded by malariologists as a special case in every way and they kept it to themselves for a long time: even now, as a relic of the past, we attend international conferences of tropical medicine and malaria, following the amalgamation of the malaria society with the one representing tropical medicine more broadly.

I was sad that not long after our collaborative program had become fully established and was going strong Graham Mitchell left it and moved on to other things. Nevertheless, research on malaria expanded at WEHI and several outstanding people were brought into the program. When the Walter and Eliza Hall Institute was seeking to get a new building the malaria program was used as a key

lever for government funding, based on the claim that the scientists at WEHI were on track to develop a malaria vaccine within 2 years. Gus Nossal got his new building – and a lot of media coverage. This was at the time when we were building our malaria program in the field in the Wosera, with a base in Maprik, in the expectation of testing a prototype malaria vaccine there. We had explained to the people that we were engaged in the development of a malaria vaccine that was designed to protect children from getting severe malaria and dying from it. Though it might be 10 years before the vaccine became available we had to prepare the ground well so that we could test it in a population where the characteristics of malaria were well known. The people accepted this argument and, because they recognized malaria as a serious disease, and one that was often fatal in children, they were happy to participate in our long-term malaria research program. At that time every village had at least one radio and the national news was listened to every day; in fact we regularly used the local network to send out a 'tok save' to particular villages. This news item from Australia about the new malaria vaccine being developed at WEHI was picked up by the media in PNG and broadcast as relevant and exciting news. The next day we were confronted by our friends in Wosera villages saying, "What's going on here? We want this new malaria vaccine from Australia that will be ready in 2 years. What's the point in taking part in your study of a vaccine that we may not get for another 10 years!" That took a little explaining. Sometime later I was in Melbourne and told this story to Gus Nossal, complaining that he had made life difficult for us working in the field. He thought for a minute and acknowledged that, scientifically, my assessment of the time frame for the vaccine was correct; however, looking around at his Institute's grand new building, he added that, politically, he thought that his estimate was correct. We both smiled. Political correctness comes in several guises.

Though Graham Mitchell was no longer involved in the malaria vaccine research program his initiating role was not forgotten. Despite many setbacks and delays a malaria vaccine with three antigens (Combination B) was eventually produced by our commercial partner Biotechnology Australia and formulated with an adjuvant



Michael speaks to Kunjingini villagers about the malaria survey.



Henry Dagoro dissects mosquitos in the entomology laboratory at Yagaum, Madang.

for use in children in a malaria-endemic area. For ethical reasons it first had to be tested for safety and immunogenicity in adults. We took adult volunteers from the Wosera to Goroka, located in a non-endemic area, for the preliminary safety trial. On a day in 1996, 20 years after our high-flying conversation, I injected the first participant with the long-awaited malaria vaccine and called Graham from Goroka to tell him the news. For him the call was as much from the past as the present, but he was pleased and suitably gratified.

To go back to the early days of the PNGIMR's Malaria Research Program, during 1977 the collaborations that I had established were strengthened and specific research projects formulated. I made as many new contacts as I could, in the health services, in government departments, national and provincial, in international agencies and in the community. I found that there was a project underway in Madang looking at chemoprophylaxis with amodiaquine in young children being conducted by John Stace, the paediatrician at Madang Hospital. Funding for this had been provided by the IMR and so I incorporated it into our overall program. One of the early appointments made to the Institute staff was George Nurse as Research Fellow in Genetics and he was encouraged to study human genetics in relation to malaria. To study malaria we obviously needed a site on the coast and Madang was chosen. I started negotiations with the Lutheran Church to use unoccupied buildings at Yagaum Hospital after its post-Independence conversion to a health centre. We reached an agreement that the IMR could take over the buildings in return for any necessary repairs and restoration and their ongoing permanent maintenance. As a first move I needed to secure funding for our proposed work, and two things helped. Firstly, WHO had funds for applied field research through the Special Programme for Research and Training in Tropical Diseases (TDR – Tropical Diseases Research). Secondly, the PNG Government had committed budgetary funds for expanded departmental activities to the National Public Expenditure Plan (NPEP) and these funds, which were open to all government departments and statutory bodies, had to be applied for competitively through the National Planning Office. With support from the WHO Regional Office in Manila we were successful in getting an integrated package of proposals funded through TDR, which certainly would not be possible today. These proposed projects are set out in the Seventh Annual Report 1976-78 of the PNGIMR (5) and include as co-investigators John Stace, George Nurse, Graham

Mitchell, Robert Clancy, Chev Kidson and Greg Crane. The NPEP was advantageous to the IMR, since I had good relations with the National Planning Office and we were experienced in writing proposals. After a successful first round that provided funding for a new building to replace our temporary accommodation in Goroka and a Pneumonia Research Program, we applied for a Malaria Research Program and a Nutrition Research Program, and got everything we asked for. This included funds for refurbishing the buildings in Yagaum and the establishment of parasitological and entomological laboratories, including facilities for in vitro culture, and offices and accommodation for staff, as well as the necessary staff positions.

We set up our research program in Yagaum and neighbouring communities and in the Madang General Hospital. Peter Heywood, who had initially been appointed as Research Fellow in Nutrition, became the Deputy Director of the Institute in his second contract period and was installed as the officer in charge of the Madang branch of the Institute based in Yagaum. We employed new staff and welcomed some extraordinary people to PNG, as well as gaining a cadre of skilled and enthusiastic Papua New Guineans who have continued for decades to contribute loyally to malaria research at the IMR. Establishing rigorous microscopic diagnosis of malaria was fundamental to all our research projects; this was achieved by David Gibson and Arthur Narara, who then supervised the ongoing, endless support that has been provided to all our projects by the microscopists. David had worked with the great names in malaria from the British Colonial Service in Africa. He joined our team somewhat reluctantly because he came from the school that believed that we already knew all the essential things about malaria and therefore he could see little point in further research. As our program developed David contributed to the conceptual as well as the technical aspects of our work and gradually came to realize that there was an enormous amount that we still had to learn about malaria. When he retired he gave me his collection of old malaria classics, books that he had acquired during his time in Africa; they remain treasured possessions in my library. Derek Charlwood was recruited to be our first entomologist and Jackie Cattani to lead our epidemiological studies. Karen Day came first as an immunologist in our lymphatic filariasis research program, but later returned to work on malaria. Helena Vrbova, among other things, established our first longitudinal study of malaria in Gonoa village. Her pioneering work and tragic death shortly before she was about to leave to undertake a course in London are acknowledged in a set of tributes published in the Papua New Guinea Medical Journal (6).

One of the studies that Helena undertook was a rigorous expansion of John Stace's trial of chemoprophylaxis. We were planning to use weekly doses in young children of amodiaquine or Maloprim (a combination of pyrimethamine and dapsone), antimalarials that were taken for prophylaxis by expatriates living in PNG. When I took this idea to Geneva, the old guard were horrified since it was part of established malaria dogma that European children needed weekly protection from malaria in the tropics but on no account should this be given to 'native' children since it would prevent them from establishing their own protective immunity. Of course in a malaria-endemic area children did establish protective immunity but in the process many of them died of malaria. This dogma had arisen in the colonial world but there was no evidence for it. Nor did anybody want to look for evidence since if there was shown to be value in giving all these children weekly drugs for a few years to protect them from death while they were slowly developing their own immunity, then no doubt it should be done – but who would pay

for it? This was not unreasonable but the question had been avoided by reference to a convenient but specious piece of dogma. Brian Greenwood was my only supporter, and he managed to do a study in The Gambia which showed that immunity was not impaired once children had completed a period of chemoprophylaxis. Helena carried out a placebo-controlled trial of chemoprophylaxis with amodiaquine or Maloprim in semi-immune school children as a preliminary to more definitive studies in young children. The results showed an effect on parasitaemia and spleen size but neither regimen was completely successful in preventing parasitaemia. The publication of this study did not occur until 10 years after Helena's death, when her draft paper was revised and completed by Katharine Trenholme (7). However, the study in young children was not undertaken. Firstly, we discovered to our dismay that we were facing not only increasing resistance of the malaria parasites to chloroquine and amodiaquine but also to the pyrimethamine-based drugs (Fansidar and Maloprim) used respectively for treatment and prevention (8): it would not be a good time to start using Maloprim for a widespread prophylaxis program. Secondly, this was an intervention which, if successful, would have to be considered for implementation by the Health Department, and they were cautious about the idea. In keeping with the philosophy that underpinned all of the research carried out at the PNGIMR, the malaria research program engaged in studies that were designed ultimately to lead to an intervention. If such an intervention could not, or would not, be implemented then clearly there was little point in carrying out the research. It is true that we need art as well as science to interpret this rule and doing so is not always straightforward, but in this case we already had another good reason to support our decision. As it turned out, the idea of chemoprophylaxis in the community was at least released from dogma and did not die entirely, since years later successful studies of IPTi and IPTp – intermittent preventive treatment of malaria in infancy and pregnancy, respectively – were carried out in PNG by Ivo Mueller and his colleagues.

We chased all kinds of ideas to understand and control malaria: treating children in village communities through volunteer health workers, longitudinal parasitological and immunological studies, the use of insecticide-treated bed nets, analysing the behaviour of the mosquito vectors, investigating human genetic polymorphisms conveying resistance to malaria, identifying small-area variation in the epidemiology of malaria and the importance of local ecologies, developing a blood-stage malaria vaccine, monitoring drug resistance, and so on. We supported the use of indoor residual spraying in certain circumstances, such as in the highlands, but we did not subscribe to its use in highly endemic areas to eradicate malaria. Though the WHO global malaria program had switched from eradication to control in 1969, the dogma of eradication through spraying persisted, even among advisers to the malaria control program in PNG. I had a jubilant message from one such colleague who had gone off to work in the Solomons: "I tell you: spraying works. We have shown it here." For the agnostic, spraying works – for sure, sometimes, in some circumstances. For the religious believer, however, it always works – and if it doesn't, this means that it was not applied properly. We had a meeting in Port Moresby in August 1980 on malaria in the region organized by the WHO Manila Office, with all the interested parties invited, which was attended by the Chief Malaria Adviser from WHO Geneva. All the senior malaria staff from the PNGIMR were there and were each given a place on the program. I was to give the overview of our collaborative research program. Before the meeting the

organizer took me aside and said, "We are very interested in the research that you and your team are doing and are proposing to do. Present your ideas as freely as you wish. But please do not make any disparaging remarks about spraying. Though eradication has now been formally dropped, spraying is still sacrosanct among the senior staff in Geneva, and we do not want to cause offence." Dogma was firmly entrenched in malaria, as we have seen, but this was a pillar of their religion. There is both a science and an art in malaria control – for example, choosing the right drugs and the right time in making a change to standard treatment. We do not also need dogmatic religion to guide our decisions. This fascinating but idiosyncratic and inward-looking aspect to malaria in the past may seem unbelievably remote from the multidisciplinary sweep of the molecular science of today. However, we should still be careful not to overreach the bounds of our scientific knowledge; we can learn a lot from the mistaken grand schemes, entrenched dogmas and false hopes of the past to inform our current global approaches to controlling malaria.

One of our ideas was to provide insecticidal mosquito nets to people living in malaria-endemic areas as a way of controlling the disease. This also did not go down well initially in Geneva. The idea was considered a bit of a joke. It was fine for Europeans to sleep under large nets in their houses to stop getting bitten at night, but it was considered somewhat ludicrous to expect this to work for 'natives' in their village huts. Just providing a net would, indeed, probably not have worked but the added insecticide was likely to have a major effect. The feasibility of doing this was brought to our attention by colleagues at Simon Fraser University in Canada, from where Bruce Millen joined us and conducted research for his Masters on insecticide-treated mosquito nets; the results were encouraging. Our team was then augmented by two outstanding entomologists, Tom Burkot and Patricia Graves. Tricia conducted a trial of the impact of permethrin-impregnated nets on falciparum malaria in young children and the positive outcome (9) had a significant influence on WHO policy. Insecticide-treated bed nets became not only respectable but a key component of the global effort to control malaria.



Dr James Moir and Frank Dockery briefing north coast villagers on the approaching meeting of big men to outline the malaria intervention program.



The first participants in the Malaria Vaccine Trials in PNG. From left to right, Timothy Yalenge, Jim Wingu, Felix Maim and Edward Yangia of the Wosera, East Sepik Province.

It might be thought that I have exaggerated the entrenched attitudes and dogmatic beliefs of the malaria establishment in the past. I do not think so: it was another world, of its own kind (*sui generis* is the term they would probably have used), now consigned to the past. Nor were the colonial connections far-fetched: they were part of the same wide world of tropical medicine, which in the early days was necessarily a colonial enterprise. The colonial attitudes were not explicit but deeply embedded, as they usually are. Indeed they have not entirely gone away in some quarters – about which there are a few good stories, which I am not going to relate here. The attitudes emerge in many contexts, often simple ones. For example, the terms ‘active’ and ‘passive’ case detection have a long history and are based on the ‘active effort’ required by the investigators to go out and detect cases of a disease, in contrast to those cases that are detected because they ‘passively’ turn up. However, if you think of it from the point of view of the patients who constitute the cases the effort goes the other way. If in a community-based study we are to regard the people and patients in the community as participants in the study and not the subjects of it, there is good reason to choose more neutral and objective terms to describe what we are doing (10).

Our malaria research program began with the idea of a malaria vaccine and work towards developing and then testing our vaccine continued for more than 20 years. As development proceeded to the point where the eventual production of a vaccine did look feasible in the future (at a time estimated by a choice of scientific or political criteria!), it became essential to establish an appropriate field site for its evaluation. Our program was well set up in Madang, but we began to realize that the population was too urbanized, with good roads, a convenient, well-equipped hospital and ready availability of antimalarial drugs in local stores, and too influenced by our ongoing research activities to be a suitable site for a major field trial of a vaccine in children. So we needed to find somewhere else. We sent Paul Garner and Peter Heywood to investigate the Wosera area near Maprik in East Sepik Province and do some studies there. From what we learned it seemed to be ideal for the purpose. However, how were we going to fund a new branch of the Institute? Then we had a serendipitous offer from the United States Agency for International Development (USAID). There was a sporozoite vaccine under development at New York University and USAID had agreed to support the evaluation of the vaccine. For this they needed a field site in the tropical, malaria-endemic world, and we were encouraged to apply. I wrote the grant proposal in a sleepless week and our application

was successful. It was agreed between both parties that we would test a US vaccine as a priority but that the site could also be used to test any other malaria vaccine that became available. USAID agreed, after review, that the study site in Madang was not sufficient for the purpose of the evaluation project and that they would fund a completely new field site in the Wosera, with a base in Maprik consisting of new buildings for laboratory facilities, offices and staff accommodation and a transit house for the project in Wewak. We bought a house in Wewak, which worked well even though we were not allowed to use project funds to support the upkeep of the swimming pool – in the end we filled it in. We secured land in Maprik and had our architect design the buildings that we wanted. We had a lot of support from senior USAID staff and from the US Ambassador in Port Moresby. Getting building contractors to construct the buildings to our requirements in Maprik was a major problem, and the first builder went bankrupt. That is absolutely the worst thing that can happen in a construction project, since you have no redress and are at the mercy of a second contractor, if you can get one. Our second contractor failed and we finished the construction by buying all the materials ourselves and carting them from Wewak to Maprik for a builder who was working on-site. Finally, it was done, and the US Ambassador came from Port Moresby to officially open the building. We had established the Maprik branch of the PNGIMR.

As a sequel to this, we did finally evaluate our vaccine in the Wosera and the US vaccine never came to anything – at least nothing was produced for us to test. However, after its good start the project did not go entirely to plan. Indeed, in 1993 the whole enterprise nearly fell apart, with nothing achieved at all. After the Berlin Wall came down in 1989 and the subsequent unification of Germany, a new market for US aid opened up, and USAID decided to delete its Pacific aid program entirely and put all these resources into Eastern Europe. All contracts were cancelled and we were given 3 months of funding to close down the project. End of story. Well, it could easily have been. I had an emergency meeting with the National Planning Office, who were very supportive. Jointly we approached the Australian Agency for International Development (AusAID). In what I felt was a remarkably generous act, AusAID agreed to take over where USAID had dropped out. They gave us equivalent funding for 18 months to cover a transition period while we were developing a formal proposal to AusAID to continue the project. They wanted the proposal written ‘in the AusAID way’ and would send advisers from Australia to help me do that. In the end a good outcome was achieved and our malaria vaccine epidemiology and evaluation project was able to continue uninterrupted and fully funded. The extra things that AusAID required were funded separately and since they were not feasible in the context of our work did not actually happen! So it came about that when we eventually tested the Australian malaria vaccine we did so within a project that was supported by Australian aid funding.

To return to the heady days of moving into Maprik, we set up our field studies as planned, which were much more comprehensive than just a vaccine trial (11). We also had support from USAID for the more sophisticated molecular parasitology and immunology investigations being conducted in our Yagaum laboratories, and for entomology, which I had to fight for in a big way against the expert advice being given to USAID. Blaise Genton as clinician and epidemiologist, Inoni Betuela and Lawrence Rare were in charge of the field studies, which were conducted in the villages of the South Wosera and Kunjingini Health Centre. In order to strengthen our presence in the Wosera, a project house was later built in Kunjingini. Fadwa Al-

Yaman as immunologist and Hans-Peter Beck and Ingrid Felger as molecular parasitologists, with supporting technical staff, carried out their essential studies as part of the overall program. We all spent a lot of time travelling between Wewak and Maprik. We got used to delays in fording the rivers and to making decisions about whether we were brave enough to attempt the first crossing from a long line of waiting cars. However, it was only Blaise who had the experience of facing a plane making an emergency landing on the road he was driving along. The necessary baseline studies were conducted (12,13). Meanwhile the combination vaccine with 3 antigens (MSP-1, MSP-2 and RESA) was being produced by Biotechnology Australia in Sydney. After safety and immunogenicity studies in adults and children the vaccine trial with natural challenge (phase 2b) in children was finally achieved (14). The vaccine had been designed from the beginning to prevent severe malaria and death in young children. In the trial we used parasite density as a surrogate for severe malaria, and the principle of this vaccine was proved in the trial through a significant reduction in density. The vaccine was never intended to prevent malaria infection. It was designed to be given to children in malaria-endemic areas and was not aimed at tourists or the military to prevent them from getting malaria. Even some of our research team failed to get that point. The trial also showed that MSP-2 was the important component, but only one of its two world-wide families was represented in the vaccine, so that the first breakthrough infections following vaccination were from the other family. Clearly the next thing to do was to formulate a vaccine that contained both families of MSP-2. Sadly, there was not to be a 'next thing' since our manufacturer ceased operating and we had nowhere to go to find a way forward.

That is a sad note to end on. However, that is certainly not the last story from the PNGIMR's malaria research program: not by far – but I have to draw a line at some point. Nor is it even the last story from the vaccine trial – I could describe the amazing level of compliance that we had from the children in the trial. But that is Inoni's story, and I hope that he will tell it at the Colloquium.

ACKNOWLEDGEMENTS

There are so many people that I have to acknowledge – and I should also honour the memory of those who have died. I can get pleasure thinking about them all but it would not be sensible to try and make a long list of their names here. For those who are not named be assured that you are not forgotten. Some of you I have mentioned in the text. An additional small number appear in the references, which I have been assiduous in restricting to the very minimum. It would be a good idea for everyone to consult the list of malaria papers from the PL (the PNGIMR Publication List). You might be somewhat staggered by what has been achieved over the years – and from the names of authors you will find the people that I have to thank. Outcomes and achievements are undeniably important but what I remember most is the spirit of good humour and collegiality that imbued all our hard work. As well as those who became authors I have to thank our support staff of many kinds and members of the Health Department, National Planning Office, World Health Organization and funding agencies who have provided needed assistance to the staff, especially me, and the scientific work of the Institute over many years. In malaria we also had support from the Medical Faculty and I take this opportunity to pay tribute to my friend Sirius Naraqi, who was Professor of Medicine at

the University of Papua New Guinea and studied malaria in Port Moresby. I acknowledge the Institute Council, and particularly during my time the influence of Adolf Saweri, and the Buttressing Coalition, whose current chair is Brendan Crabb. I thank Raymond Paru, Manasseh Baea and others who had the unenviable task of being in charge of a branch of the Institute, Dawn Parsons, who mothered us all, and our architect John Proctor. We have enjoyed valuable input from clinical scientists, such as Steve Allen, David Mokela and Laurens Manning in Madang and Jim Kazura and Tim Davis as senior collaborators. Of course the malaria research program goes way beyond me, and was continued by John Reeder, Ivo Mueller, Manuel Hetzel and many others until we reached our 40-year mark, held high by Leanne Robinson, Livingstone Tavul and Moses Laman. They can do so because of their own stature but also because they represent, respectively, the continuous, ongoing commitment from the Walter and Eliza Hall Institute to our collaborative malaria research program, the decades of competent and loyal service contributed by our long-serving technical and scientific staff, and the bright future for sustained programs of research being created by the growing Papua New Guinean college of qualified, innovative medical scientists.

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Going from strength to strength: reflection on the malaria research at the Papua New Guinea Institute of Medical Research in the new millennium

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After having had the chance to visit PNG and the PNG Institute of Medical Research in 1998 during my PhD, I arrived in Goroka in June 2000 as a young, enthusiastic and maybe even a little 'pushy' postdoc at a moment when the Institute and the malaria program was entering a new period. Just before I arrived, John Reeder had taken over the IMR directorship after Michael Alpers had stepped down after 23 enormously successful years as IMR Director. As John was starting to implement his vision for the IMR in general, the IMR malaria program was visibly 'catching its breath' after the malaria vaccine research program had its major first goal with the successful Combination B phase IIb trial conducted in the Wosera (1) and the key people that had led that program, Blaise Genton and Fadwa Al-Yaman, had returned home to Switzerland and Australia, respectively.

While working through the results of that Combination B trial and awaiting the next round of studies with an improved version of the vaccine, a smaller program of more basic research studies was continuing, led by Moses Bockarie together with Chris King. Pete Zimmerman and Jim Kazura from Case Western Reserve University in Cleveland, USA, the IMR teams in Madang and Sepik (with Charles Mgone from IMR Goroka) conducted studies into immune responses to *P. vivax* and *P. falciparum* malaria, investigated the effect of different red cell polymorphisms and conducted the studies into the evolution of antimalarial drug resistance. Among the key findings of these collaborative IMR-Case Western studies was i) the discovery that some people in the Wosera carried a Duffy FY*A(null) allele (2), which in its heterozygote provided protection against *P. vivax* malaria (3); ii) strong indications of an independent evolution of *P. falciparum* chloroquine resistance in PNG (4); iii) the description of genetics and ovalocytic phenotype of the Gerbich blood group (5), and iv) the first in-depth studies of immune responses to the *P. vivax* Duffy-binding protein and the *P. falciparum* liver stage antigen 1. All this excellent work would not have been possible without the great contribution of many different IMR staff including (among many others), Lawrence Rare, Moses Baisor, Moses Lagog, Kerry Lorry, Benson Kinoboro and also Will Kastens.

A few months before I arrived, Alfred and Ariadna Cortés joined the IMR from Barcelona, Spain. Alfred took over the leadership of the molecular parasitology section and with his team (including among others Marta Mellombo who started as a cleaner at IMR and went on to become an excellent research assistant) immediately started to look into vaccine antigen diversity (6) and to study invasion and adhesion phenotypes of *P. falciparum* in SAO cells. Ariadna joined the Entomology Unit where she helped Moses Bockarie and the entomology team to establish the molecular assays that allow the identification of the different species in the *An. punctulatus* complex. Alfred and Ariadna returned to Spain in 2003.

In this 'in-between period' the clinical malaria research program was kept going almost single handed by Inoni Betuela and Meza Ginny, who conducted a small drug trial in Madang.

While the program in Madang and particularly Maprik was waiting for the next round of vaccine studies to commence, I had great fortune to receive support from WHO and TDR to set up a program to map the extent of malaria transmission in the PNG highlands (7). Between December 2000 and July 2005 we conducted 153 surveys with >22,000 participants in 112 villages throughout the central PNG highlands. This involved going to very remote areas, fantastic walks to and between villages and catching small planes landing on sometime rather scary landing strips. Walking through the highlands regions with John Taime, Albert Sie, Rex Ivivi and our friends from the Malaria Surveillance and Control Unit, meeting many, many wonderful local villager that offered us incredible hospitality and with whom we swapped both stories and supplies, are some my most treasured memories of my 15 years of working in PNG.

When it became clear that there would not be any further vaccine trials for the foreseeable future, the malaria program needed to re-orient and find a new focus. A first opportunity to re-shape the malaria program presented itself by a joint NHMRC-Wellcome Trust tropical health research program. Together with our colleagues from WEHI, University of Melbourne and Case Western as well as colleagues from the UK and Kenya, an ambitious proposal to study both the natural acquisition of immunity and host genetic adaptations to malaria and investigate methods to prevent malaria and anaemia was put together. While our proposal was eventually unsuccessful, the ideas and collaborations contained in it provided the basis for much of the program that was jointly developed by IMR and its international collaborators in the coming year.

A first, crucial step that seemed small when we undertook it was the small cohort study that we conducted in the Mugil area on the Madang North Coast in 2004. There, Pascal Michon, who joined IMR just before, and Livingstone Tavul followed 206 local Mugil elementary school children for 6 months to determine how often they are infected and with which *Plasmodium* species. This study not only showed that children acquire immunity to *P. vivax* malaria much faster than that to *P. falciparum* (8) but also provided the samples for over 20 different in-depth studies on immune responses (9,10), as well as parasite and host genetics (11). This combination of combining excellent field studies with state-of-the-art laboratory investigations set the stage for many of our future studies in both Madang and the Sepik.

The next key success was that the then IMR director John Reeder was able to convince the Bill and Melinda Gates Foundation to consider making an investment into malaria research in PNG. This led to two major randomized controlled trials of the intermittent preventative treatment with antimalarial for the prevention of malaria and anaemia in infants (IPTi), (12) and pregnant mothers (IPTp) (13). These two very large clinical trials (IPTi: 1100 children in Madang and 500 in Maprik) were the first studies to prove that these interventions were able to prevent both *P. falciparum* and *P. vivax* malaria in children and prevent placental malaria and improve birth weights outside Africa and in areas with *P. vivax* malaria. These results have important public health implications and IPTp is now part of the PNG National Standard treatment guidelines. Equally important, these studies assisted in re-establish capacity for conducting large interventions trials at PNGIMR and brought a new generation of talented, young PNG clinicians into the IMR malaria research program. These studies were so successful because they were carried by great collaborative teams: from an excellent clinical field team, lead by Nicolas Senn, Patricia Rarau, Maria Ome, late Regina Wangnapi and Holger Unger; the laboratory teams headed by Danielle Stanisic, Leanne Robinson and Alex Umbers; and, to the different overseas PIs and collaborators (in particular Stephen Rogerson, James Beeson and Louis Schofield).

At the same time the IMR was able to start a very successful collaboration with a group led by Tim Davis from the University of Western Australia. Together we established excellent capacity for clinical malaria research at the Alexishafen Health Centre, that started with Harin Karunajeewa and then followed by the team of John Benjamin, Moses Laman and Brioni Moore. A long series of drug studies ranging from pharmacokinetic studies in children and pregnant women to drug efficacy studies of existing (14) and novel antimalarial treatments (15) has now been conducted. Besides providing important research results and training opportunities, these studies

have also contributed significantly to formulating the current PNG national treatment guidelines.

With support from the Global Malaria Genetic Epidemiology Network (MalGEN, coordinated by Oxford University and the Sanger Centre), an opportunity arose in 2006 to re-start studies on severe malaria at Modilon Hospital. Building on the great work done by IMR in the 1990s, Irwin Law and Moses Laman (with support from Tim and Harin) set up a new clinical research unit at Modilon and started enrolments into a case-control study. Soon after, this initially small team, was greatly strengthened by the arrival of Laurens Manning and further funding from a joint NHMRC grant led by Tim Davis. After establishing excellent relationships with the hospital and setting-up a bacteriology, clinical biochemistry and haematology lab at Modilon, Laurens, Moses and their team screened almost 5,000 children admitted to the Modilon Paediatric Ward and conducted not only an in-depth assessment of clinical patterns and prognosis of severe malaria in PNG children (16) but (among other things) also investigated bacterial meningitis, viral encephalitis and evaluated the diagnostic utility of lumbar puncture in the PNG setting (17). Together with results on association of red-cell polymorphism in the IPTi trials and the Mugil cohort studies, we were also able to conclusively show that that South-East Asian Ovalocytosis provide strong protection against *P. vivax* malaria (11), only the second red cell polymorphism to show such a vivax-specific protection. With still ongoing analyses of human genetic markers, investigations into host immune responses and parasite characteristic, this study is going to continue making great contribution to our understanding of both severe malaria and human genetic adaptations to malaria.

After the discontinuation of the Combination B vaccine development program, the IMR Maprik faced particularly difficult challenges to maintain both the world-class field site (with demography and continuous health centre surveillance) in the Wosera and the highly qualified field staff. A series of (ongoing) population-based studies with Peter Zimmerman and Jim Kazura provided some immediate relief. The IPTi study was also originally designed as a two-site study but after 15 years of continuous malaria research and recent bednet distribution by an NGO, malaria incidence in Wosera communities had dropped significantly. While fantastic news for the local population, this low level made it impossible to continue the IPTi study in the Wosera and with heavy heart we had to shut it down. After consultation with community and Wosera demography leaders, it became apparent that



Yule Ele, Entomology Technician, working in the Entomology Lab in Madang, 2001.



Staff, supervisors and reporters of the Wosera Health and Demographic Surveillance System at Kunjigini in 2009.

after 15 years of intensive malaria research in the Wosera, the Wosera communities were looking for 'a bit of a break'. With heavy hearts the decision was therefore made to 'pause' the malaria research program in the Wosera and only continue with a basic demography and morbidity surveillance.

In response to this decision, the IMR evaluated several other communities in the Maprik and Middle Sepik area and identified the Ilaia and Albinama areas as alternative malaria research sites. Getting through this difficult times and managing this sometimes challenging transition would not have been possible without the great local IMR Maprik leadership of both Lawrence Rare and Benson Kiniboro. They and the entire IMR Maprik team are exemplary in their commitment and hard work and have always been most welcoming and supportive to myself and other visiting scientists. They have not only helped conduct great research but made us all feel like we had a 'home away from home' at IMR Maprik.

At the new Ilaia and Albinama sites, we conducted several in-depth paediatric cohort studies that have helped us shed great light into the difference in the molecular epidemiology of *P. vivax* and *P. falciparum*. In the first study conducted by Benson and Enmoore Lin in Ilaia in 2006-2007, we showed that PNG children acquired clinical immunity to *P. vivax* starting in their second year of life while *P. vivax* burden increases into the fourth year of life (18). With Ingrid Felger and her students, we develop a novel epidemiological parameter, the molecular force of blood-stage infections (molFOB) and showed the children acquired many more *P. vivax* than *P. falciparum* infections (19,20). In two further studies, one conducted in 2007-2008 in Ilaia by Inoni Betuela and Anna Rosanas (21) and another by Leanne Robinson and Inoni in Albinama in 2009 (22), that randomized children to either only blood-stage or blood and liver stage treatment, we proved that 4 of every 5 *P. vivax* blood-stage infections were due to relapses. These studies thus clearly highlight the challenge of eliminating *P. vivax* malaria without directly attacking its long-lasting liver stages.

Another important line of operational malaria research opened itself up in 2008 when the IMR and its malaria program were asked by the PNG National Malaria Control (PNG NMCP) Program to assist with evaluation of the impact of the Global Funds for AIDS, TB and Malaria (GFATM) support malaria control program. These studies, coordinated by Manuel Hetzel and Justin Pulford with a large team based at IMR Goroka, conducted several

national indicator surveys and established a national network of sentinel sites and provided both essential data to the NMCP and assured an in-depth scientific evaluation of the program's impact. Very sadly, five talented young IMR scientists, Gibson Gideon, Leonard Vavana, George Dogoya, Tania Oakiva and Lydia Petrus, went missing when on patrol in a boat off West New Britain. While we are still waiting to know all the facts of what happened, all 5 remain forever in our hearts and our memories.

The free distribution and the change to a parasitologically confirmed treatment of malaria cases with artemisinin combination treatment has resulted in reduction of up to 80% in both prevalence of infections and incidence of malaria cases. Malaria is thus truly in retreat across almost all of PNG. While the MALCON project continues to monitor and highlight the tremendous impact of the PNG program, in order to sustain these gains and lay the ground for a further acceleration of control towards a potential future elimination, it is essential to better understand how the control program is impacting on the interaction between parasites, hosts and vectors and how transmission is maintained in the face of control pressure. These questions are the main focus of the two large malaria research programs that I had the pleasure to help initiate before I left the IMR at the end of 2010.

The International Centres of Excellence in Malaria Research (ICEMR) is a global program initiated by National Institutes of Health that aims to provide an up-to-date picture of the epidemiology and transmission of malaria in all endemic areas of the world. Under the leadership of Jim Kazura, the PNGIMR together with colleagues from Australia (WEHI, James Cook University, and Burnet Institute), Switzerland (Swiss TPH) and the Solomon Islands (SI National Health Training and Research Institute) were successful in securing 1 of 10 such ICEMR centres. During its 7 years (2010-2017) the Southwest Pacific ICEMR program will conduct a coordinated series of epidemiological, entomological and host immunity studies in Madang and Maprik and in the Central Province of the Solomon Islands.

The Transmission Epidemiology (TransEPI) project was a Gates Foundation supported multi-country project that aimed at gaining an in-depth understanding into how transmission is maintained at different levels of transmission by identifying who in a given populations has *P. falciparum* and *P. vivax* gametocytes and is thus potentially infective and by investigating the relationships between gametocyte carriage and density and infectivity to mosquitoes. Together these studies will help to determine (among other things) the relative contributions of symptomatic and asymptomatic infections to transmission in PNG, Thailand and Brazil.

After 10 years of work at the PNGIMR, I finally left at the end of 2010, I did it with a heavy heart but knowing the program was in very good condition and was being left in the very capable hands of Leanne Robinson, Moses Laman, Maria Ome, John Benjamin, Brioni Moore, Manuel Hetzel, Justin Pulford and Inoni Betuela. In the 5 years since I left, they have not only continued the excellent work that we started together but have started several excellent new studies.

While the last 15 years have produced a lot of excellent sciences that built on and extended on the world-class IMR malaria research program of the 1980s and 1990s, the greatest success is the cadre of excellent young PNG scientists that have risen through the program and are now step-by-step starting to take the leadership of the

IMR malaria program. Moses Laman and Inoni Betuela have completed their PhDs in Australia and Spain, while Livingstone Tavul is in the process of completing a PhD through UPNG. Similarly, Patricia Rarau, Maria Ome and John Bosco have started their own PhDs in Australia and the US, respectively, and are making great progress. Many other IMR scientists have completed their MSc and Hons degrees both in PNG and overseas (Australia, Switzerland and USA) in the last 10 years and are now getting ready to take the next step in their careers. Seeing this group of very talented, young scientists working collaboratively with the next generation of expatriate colleagues not only gives me a lot of pride but also gives me certainty that the IMR malaria research will continue to go from strength-to-strength in the next 40 years.

Thanks

When looking back at my almost 20 years of malaria research in PNG, I have accumulated uncountable, wonderful memories, made lots of friends for life and learned a lot more from my colleagues, collaborators but also from all the wonderful people of PNG that I will never be able to adequately give back. I would like to give my most heartfelt thanks in particular to John Reeder for giving a young post-doc with no experience a chance, to Peter Siba for believing in me and for pulling me back when my enthusiasm was getting me into hot water, to Inoni Betuela for looking after me as a brother, to John Taime (and family) for making me part of the 'Kina Beach clan' and Por village, to Lawrence Rare for always being there for me when I came to Maprik, to Leanne Robinson for all her support, friendship and cool head in times of chaos, and most of all the great IMR researchers, the field and support staff, to the entire wonderful IMR family in Goroka, Madang and Maprik that made every day of working in PNG not a toil but an immense pleasure. Thank you all so much for all that you have given me!

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Dr Patricia Rarau (second from right) with the Maprik IPTi clinical field team in 2008.

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Nathan Yalapus and PNGIMR Maprik field team providing community with feed back from recent malaria studies.



Curious village kids - during a research clinic in Transgogol, Madang Province.



Sr Noline Pitus performing follow-up assessment in the field.



Dr Inoni Betuela and children enrolled in the Albinama Reinfection Study.

Supporting the National Malaria Control Program with the ‘MalCon’ Project

Manuel Hetzel



As we are celebrating 40 years of malaria research by PNGIMR, it is worthwhile to also briefly look at the history of malaria control in PNG. First focal attempts to control malaria started in the early 20th century using a variety of methods including environmental modification (eg, Samarai Island and Wahgi Valley), larviciding (Rabaul), larvivorous fish (Kavieng), or house spraying with dichloro-diphenyl-trichloroethane (DDT). A pilot project with DDT in 1957 at Maprik laid the foundation for a country-wide elimination campaign reaching about 70% of the population by the early 1970s and showing significant initial impact. Unfortunately, a number of obstacles (reviewed in more detail in two recent editorials, *PNG Med J* 2009;52(1-2) and 2014;54(1-4)) led to the cessation of the program in the early 1980s and a transfer of the responsibility for all control operations to the provinces. Yet funding, infrastructure and human resources for malaria control were inadequate and as a direct result there was only limited action and increasing burden. And while PNGIMR was publishing numerous important research findings, including one of the first trials demonstrating the impact of insecticide-treated mosquito nets in 1985, coverage with malaria control interventions remained minimal across most parts of the country.

The year 2004 then again marked the beginning of a new era of malaria control in PNG. The Government secured a first grant of 16 million USD from the Global Fund to Fight AIDS, Tuberculosis and Malaria to support its malaria control program. Together with partners in the provinces and districts, and in collaboration with Rotarians Against Malaria (RAM), the National Department of Health (NDoH) re-established its vector control efforts with a free country-wide distribution of 2.4 million long-lasting insecticidal nets (LLINs).

In 2008, PNGIMR was engaged by the Health Department to provide evidence of the outcomes and impact of this nationwide roll-out of LLINs. The Institute conducted the first national malaria survey reaching out to 83 villages across the country and establishing LLIN coverage (33% use) and malaria prevalence (12% *Plasmodium* spp.) in the general population. This engagement set in motion an important process of strengthening the link and regular interaction of the PNGIMR with the National Malaria Control Program (NMCP). When PNG started negotiating a further malaria grant from the Global Fund (120 million USD which the country obtained in 2009), the Institute was involved as a key partner from the very start. In the new multi-stakeholder NMCP, with the slogan ‘Yumi Rausim Malaria’, the PNGIMR became a sub-recipient charged with evaluating the outcomes and impact of the LLIN distribution by RAM, the introduction of rapid diagnostic tests, artemisinin-based combination therapy and health worker training by NDoH, Oil Search Health Foundation and Divine Word University, and the behaviour change campaigns by PSI.

PNGIMR’s National Malaria Control Program Evaluation or ‘MalCon Project’ as it was simply referred to, was accommodated in the newly created Population Health and Demography Unit (PHDU) in Goroka and employed, once in full operation, 3 post-doctoral researchers, 15 scientific officers, 4 research assistants, 3 microscopists, 19 nurses, 5 data management staff, 5 project management staff and 3 drivers. From 2009 onwards, the MalCon field teams ventured around the country surveying households and health facilities in an effort to evaluate the intense malaria control activities implemented by the other NMCP partners. The teams reached many remote and exciting places, but travel logistics were difficult and the teams frequently encountered adverse conditions which required a high degree of flexibility from them and from our MalCon logistics team. Between 2009 and today, the household survey and health facility survey teams reached almost every corner of the country.

In addition to the surveys in random villages and facilities, the project established seven sentinel surveillance sites to closely monitor malaria trends. In each site, a PNGIMR nurse screened and tested suspected malaria patients while at the same time supporting the local health staff and establishing good relationships with the communities. Thanks also to the support of the organizations operating the sentinel facilities, the sites quickly became well established PNGIMR field sites which could be used as platforms for additional studies, such as entomological surveys carried out by the IMR team from Madang or for investigations of G6PD prevalence or

durable insecticidal wall lining. More extensive preparatory work was required for establishing a study site in Milne Bay Province for monitoring antimalarial drug efficacy, another task of MalCon. As no such previous work had been carried out in Milne Bay, a completely new team had to be recruited and the setting up of the necessary lab infrastructure and procedures required a lot of ground work – particularly compared to Maprik, the second site in which the efficacy of first- and second-line antimalarials was tested but where the institute is well established.

As in all research projects, careful planning is paramount. In the MalCon project this became even more important considering the diversity of the activities and the uncertainties faced when venturing to distant and unknown destinations. The project management team did a tremendous job arranging the complex logistics (which often required quite some degree of creativity) and finances for the many field trips. The very tight financial rules put in place by the donor did not make this job any easier and the financial reporting to the donor was an immense effort requiring the project to establish its own accounting team (led by Joyce Obed whom we were devastated to lose during the birth of her child). In spite of meticulously planning and local health officials accompanying the team on every survey, surprises when travelling to or arriving at a village were often guaranteed. Sadly, the MalCon project was not spared the most horrible experience. On the 1st of August 2011, one of our teams of five young staff members disappeared without a trace while conducting a household survey in West New Britain Province. Gibson Gideon, Tania Oakiva, Leonard Vavana, Lydia Petrus and George Dogoya, together with their boat crew, became the victims of criminals in a remote and difficult-to-access part of the province. A coronial inquest concluded in April 2014 that our team had most likely perished in foul play, but that official investigations into the matter had been poor and insufficient. Until today, no traces of the PNGIMR team members' remains have been found, making it incredibly hard for the families, friends and colleagues to find closure and consolation without knowing that those responsible have been brought to justice. Credit goes to all those who supported us during this difficult period and to all team members who still found the motivation to continue with

the important work of MalCon.

In the end, the MalCon project was able to demonstrate a substantial reduction in malaria burden (prevalence from 12% in 2008-2009 to 2% in 2013-2014) and transmission after the roll-out of LLINs and provide additional evidence supporting the NMCP in its negotiations for continued funding from the Global Fund. Challenges to the malaria program were also revealed such as the question of how health workers should deal with non-malaria fevers, the substantial amount of outdoor biting, or the resurgence in malaria incidence in some of our sentinel sites. These issues were also taken up in a recent workshop held in PNG that aimed to model the chances of malaria elimination in the country using almost exclusively the data generated by PNGIMR. It concluded that maintaining high coverage with LLIN was the least the country should do to prevent a resurgence in malaria cases. The NMCP therefore needs to make sure it can convince the PNG Government of spending sufficient money for malaria control to complement the decreasing investment from the Global Fund and at least maintain the current level of malaria control activities across the country. In the meantime, PNGIMR remains a key partner supporting the NMCP and the Health Department with evidence of what works and what doesn't. The capacity of PNGIMR to undertake scientifically sound malaria research in PNG is therefore paramount considering the challenges posed by the complex local malaria epidemiology and the weak health system in the context of international pressure and commitments to accelerate the move towards malaria elimination. With the successes of the past years and the challenges ahead, there is no doubt that PNGIMR will (and has to) play a key role in the continued fight against malaria in PNG building on the experiences and partnerships established over the past 40 years.

The MalCon project has provided numerous opportunities for young PNG scientists to build their research and project management capacity, on the job as well as in national and international diploma and degree programs (BSc Hons, MA, MPH, PhD). To date, 21 peer reviewed scientific publications, all co-authored by PNG scientists, have resulted from the MalCon project.



Gibson Gideon and carriers conducting their household survey in 2011.



Many hands make light work of installing plastic sheeting in a home in Masumave, Eastern Highlands Province.

Responding to change – current perspectives on malaria research at the Papua New Guinea Institute of Medical Research

Leanne J. Robinson

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Burnet Institute; Walter and Eliza Hall Institute



Any perspectives on the history of the malaria and vector borne diseases (VBD) research program at the PNGIMR over the last 40 years are perhaps best observed through the experiences of the inspirational individuals that have preceded my own time at PNGIMR. There is a truly fascinating mix of chance encounters between like-minded individuals as well as strategically planned studies. As I have reflected on this, it seems to me that the capacity – indeed, the necessity – to grab hold of opportunities and respond to changing circumstances not only in funding and resource priorities but also scientifically, has underpinned much of the historical VBD research strategy. And so it continues to be today.

A visit to the mainstay of malaria research at the sites in Yagaum and Maprik would have you think that perhaps not too much has changed over the past decade. We are certainly lucky enough to have quite a few long-term staff from the early days still working as part of the IMR family. I won't list all their names here, but many of their stories appear in this colloquium magazine. We owe a great deal to their dedicated service and the consistency and commitment they have maintained in the face of real change and occasional great challenge.

Sadly, the tired old office and laboratory buildings at Yagaum still sit relatively unchanged and the highly anticipated move of these labs to the proposed new site in Madang town should, ideally, have occurred prior to this celebration. Alas that was not to be, but there has, however, also been great change and great achievement. In the past seven years there has been a radical shift in the malaria situation both in Papua New Guinea as well as globally. The priority focus has shifted from one of sustained malaria control to that of global malaria eradication, through a country by country, region by region strategy of malaria elimination. This has necessitated an overall shift in the way malaria research questions are prioritized, funded and implemented.

In Papua New Guinea, with support from the Global Fund to fight AIDS, TB and Malaria, and evidence generated from the PNGIMR's own research program, the country embarked upon an intensified program of malaria control in 2008 with the nationwide distribution of long-lasting insecticide treated nets (LLINs), alongside changes to diagnosis and treatment protocols. Since then, the prevalence of malaria has declined by more than 80% across the country.

The PNGIMR has been a key partner in this National Malaria Control Program, monitoring its effectiveness via the establishment of a highly multi-disciplinary 'MalCon' operational research team; based within the Population Health and Demography Unit at Goroka IMR under the guidance of Dr Manuel Hetzel and Dr Justin Pulford, but effectively working in every corner of Papua New Guinea. Through serial malaria indicator surveys, sentinel site surveillance and health facility surveys, as well as vector and insecticide resistance surveys, this program continues to deliver evidence to inform the broader national program. This program has also provided many opportunities for PNG researchers, to take leading roles and gain valuable experience as independent researchers. Dr Livingstone Tavul, completed his PhD on one such study, monitoring the therapeutic efficacy of artemether-lumefantrine in Milne Bay Province and East Sepik Province and, in doing so, providing key evidence to the National Department of Health, Malaria Program and WHO that our first-line anti-malarials remain highly efficacious in PNG. Tragically, five highly skilled members of the MalCon team went missing whilst they were conducting surveys in West New Britain Province in 2011 – an immeasurable loss for their families, the MalCon team, PNGIMR and their country. They will always be remembered.

One of the first field trials that I took a leading role on after joining the IMR in a full-time capacity in early 2009 was with Prof. Ivo Mueller and Dr Inoni Betuela on the Albinama treatment to re-infection study. I'm not sure any of us expected it to be quite as tedious, all-consuming or, indeed, as satisfying as it was. It was



Benson Kiniboro enrolling children into the Albinama Cohort Study.

certainly worthwhile in the end – not only providing clear evidence that hypnozoites are responsible for 80% of *P. vivax* infections in PNG children, but laying the groundwork for an extremely solid, ongoing working relationship that continues today. I remain highly indebted to both Ivo and Inoni for their professional support, encouragement and guidance, not to mention some culinary insights and life lessons during shared times in Sepik. Inoni was Head of VBDU from 2010 to 2012, whilst simultaneously completing his PhD at the University of Barcelona, and continues to provide guidance and support to many of us. Despite officially moving on from PNGIMR in 2010, Ivo has remained closely involved in the programs he had set up, providing enormous support and opportunity to many of us – something that I will certainly always be grateful for. Both the form and function of the current VBDU owes a great deal to Ivo's personal and professional input.

A major program of the VBDU over the past seven years has been to develop a more detailed understanding of the impact that reduced transmission is having on the epidemiology of malaria – in particular interaction between hosts, parasites and vectors, the acquisition of natural immunity, parasite diversity and the abundance and behaviour of major *Anopheles* vectors. These coordinated epidemiological, entomological and host immunity studies have been conducted as part of two large international programs: the National Institutes of Health (NIH) International Centre of Excellence in Malaria Research (ICEMR) program, led by Prof. James Kazura and the Bill and Melinda Gates Foundation Epidemiology of Malaria Transmission (TransEPI) consortium, led by Prof. Ivo Mueller. On the ground, I have shared all the joy and pain of executing these large and intensive epidemiological field studies with a really experienced and tremendously enthusiastic team, without whom the work would truly not have been possible. Most especially, the contribution of Dr Maria Ome-Kaius has been immense, but so many people (Mary Salib, Daisy Mantila, Dulcie Lautu-Ninda, Bethuel Kotty, Henson Dima, Benson Kiniboro, Matthew Philip – just to name a few) have poured so much of themselves into this work.

These highly collaborative programs are not only yielding extremely valuable insights into the impact of intensified malaria control on the epidemiology of malaria in PNG, but have also allowed us to develop considerable capacity

here in PNG that, in turn, is allowing us to do the kind of research that reduced transmission demands. In particular, the infrastructure and capacity to perform high-throughput DNA extraction, RNA extraction and real-time quantitative PCR diagnosis of malaria infections (asexual and sexual stage) is now well established within the VBDU. The past efforts of Dr Anna Rosanas-Urgell and Dr Eline Kattenberg (with steady support and encouragement from Prof. Ingrid Felger) to implement systems of quality control and to up-skill and cross-skill everyone in the group, has ensured that molecular epidemiology will remain a strength of the program into the future. There has also been continued support and capacity development under these programs for the strong program of immuno-epidemiological studies that Dr Danielle Stanic initiated during her years in Madang. In particular we have had strong collaborations with Prof. Chris King (CWRU) – investigating i) the impact of in-utero exposure to malaria on the development of infant immune responses and the risk of all cause morbidity in the first year of life and, ii) immunoregulatory networks elicited by an episode of clinical malaria, both in the acute and convalescent phase; and Prof. James Beeson (Burnet) – investigating antibody responses to *P. falciparum* and *P. vivax* merozoite surface proteins and developing the capacity to conduct functional assays (eg, complement fixation). In addition to developing considerable 'on-the-job' capacity, the NIH ICEMR program is also providing direct research support to Dr Moses Laman – to conduct surveillance for severe malaria and paediatric illness at Modilon General Hospital; to John Bosco Keven – in his PhD studies investigating the non-random feeding preferences of *Anopheles* vectors in PNG and, finally, a key component of the PhD of Dr Maria Ome-Kaius is a child cohort study from the ICEMR program.

With continued ICEMR funding (until mid-2017) and new TDR funding (PI Dr Moses Laman), we have commenced a multi-disciplinary but highly integrated project on the north coast of Madang, investigating the magnitude and drivers of residual malaria transmission after the roll-out of standard interventions – which human, vector and/or parasite behavior/characteristics are the most important obstacles to elimination? A first of its kind trilateral partnership, the China-Papua New Guinea-Australia Pilot Cooperation on Strengthening Malaria Diagnosis in PNG is also providing support for operational malaria research at the Sentinel sites, and offering up the potential for new relationships with National Institute of Parasitic Diseases and unique training opportunities. Dr Moses Laman and I are also hopeful that a new NIHICEMR proposal with Prof. Ivo Mueller – "Understanding, tracking and eliminating malaria transmission in the Asia-Pacific region" – that was submitted for funding earlier this year will allow us to secure solid funding for continued malaria epidemiological fieldwork in PNG from 2017-2024.

In recent years, several highly challenging areas of laboratory research, membrane feeding transmission studies and *Plasmodium vivax* invasion assays have all been re-established in the VBDU. Investigating human to mosquito transmission of malaria and vector competence was an important component of work conducted by Prof. Patricia Graves and Prof. Tom Burkot during their years at IMR and Dr Lisa Reimer and the team re-established a colony of *Anopheles farauti* 1 and membrane feeding assays in 2009-2013, allowing this work to proceed once again. Under the TransEPI project and in collaboration with Prof. Jetsumon Sattabongkot Prachumsri and her team at Mahidol University Thailand we have been able to strengthen our capacity to conduct this work and within a continued collaboration led by with Prof. Ingrid Felger, we

will soon commence a study investigating the molecular epidemiology of ultra-low density malaria infections and their relevance for transmission. We are also working to establish short-term *P. vivax* culture in the molecular lab in the context of an on-going SAO and *P. vivax* invasion collaboration with Dr Anna Rosanas-Urgell and her team at Institute of Tropical Medicine in Antwerp. Together with the aforementioned membrane feeding assays, this line of research is extremely challenging but represents a great opportunity for the VBDU going forward, as the demand to assess the efficacy of potential transmission blocking antibodies continues to escalate.

Clinical trials have once again been a major feature of our program, as well as an area of substantial capacity development and a clear strength for the future. The implementation of two large and complex individually randomised trials of intermittent preventative treatment infants (IPTi) and intermittent preventative treatment in pregnancy (IPTp) were a highlight for the Unit. These trials not only facilitated on-the-ground input from international clinicians and scientists such as Prof. Stephen Rogerson, Prof. Ivo Mueller, Prof. James Beeson, Dr Nicolas Senn, Dr Danielle Stanisic, Dr Sarah Hanieh, Dr Alex Umbers and Dr Holger Unger but provided the necessary scope for PNG clinicians such Dr Patricia Rarau, Dr Maria-Ome-Kaius and Dr Regina Wangnapi to complete their Masters degrees and develop into experienced and independent clinical researchers. I had the privilege of directly working alongside Dr Patricia Rarau to complete the IPTi trial during my first two years at the IMR. She not only introduced me to IMR Madang, the trial team and all the intricacies of the trial itself, but has been a good friend ever since.

Earlier this year, we mourned the tragic loss of our colleague and sister, the late Dr Regina Wangnapi – a woman who had achieved so much in her 35 years – a medical doctor, a Masters level clinical researcher forging her career, a wife and mother – her legacy will continue to shine brightly, enlightening and inspiring us to be a better version of ourselves, every day.

This period has also seen the continuation of a highly productive collaboration on drug efficacy and pharmacokinetic studies with Prof. Tim Davis and Dr Brioni Moore at the University of Western Australia, producing high quality data that are continuing to inform policy decisions in PNG. Dr Moses Laman completed a highly successful PhD as part of this collaboration in 2014, demonstrating that Artemisinin-naphthoquine is non-inferior to artemether-lumefantrine in PNG children with falciparum malaria and has greater efficacy against vivax malaria.

Beyond the scope of only malaria, we have also expanded into large public health intervention trials, investigating alternative mass drug administration regimens for the elimination of lymphatic filariasis (LF). This work has been led by the Maprik team, in particular James Suamani and Nelly Sanuku, with long-term collaborators Prof. Jim Kazura, Prof. Chris King and Dr Daniel Tisch, developing considerable capacity in this area and highlighting the great potential that the triple drug therapy (ivermectin, DEC and albendazole) has for eliminating LF in settings such as PNG. With additional Bill and Melinda Gates Foundation support, we are about to embark upon an expanded community safety, efficacy and acceptability trial of this triple drug regimen in Bogia next month. This new treatment could make a very significant difference in the global effort to eliminate LF by accelerating elimination and reducing the number of rounds of MDA required for elimination. The greatest impact of this new treatment

may be in areas with high infection rates where MDA has not yet been introduced, but it also could be very useful for areas where LF infection persists despite several years of annual MDA with current 2-drug regimens. In PNG, both areas exist and continue to present a challenge to LF elimination efforts.

It is important to note that with declining prevalence of malaria and an increasing proportion of infections exhibiting no clinical symptoms, our malaria studies have become increasingly challenging – requiring larger sample sizes, innovative methods, increased funding and even stronger relationships with communities than ever before. This causes me to reflect on my first experiences in PNG during my PhD studies back in 2006-2007. I was in awe of the way the PNGIMR teams worked with communities and the genuine enthusiasm that communities had for being involved in the study we were doing. By effectively involving communities in the research, not only through participation but also as community reporters, village health volunteers or mosquito collectors, we were not only making the research possible and successful, but also allowing communities access to health promotion information and a greater understanding of the infections most commonly affecting them and their children. This was the kind of research I wanted to be involved with and I am grateful and proud of being able to do so. Equally, everyone involved with the PNGIMR should be really proud of having established such a community-based participatory health research model so early on and ensuring that we continue to uphold these high standards decades later, despite new challenges.

Personally I've had the pleasure and privilege of working alongside these teams for the past 7 years and I feel like we are constantly teaching each other new things as we progress our research. In addition, I have derived a great deal of pleasure from being part of the IMR family during a time that we have prioritised – perhaps above all else – the development of technical, scientific and research capacity, in particular, through the formal Honours, Masters and PhD training of Papua New Guinean researchers. For the VBDU, this previously culminated in 2014-2015 with Dr Inoni Betuela and Dr Moses Laman being conferred their PhDs and during this event we will celebrate Dr Livingstone Tavul having been awarded his PhD. In addition, Mr John Bosco Keven and Dr Maria Ome-Kaius continue to undertake their own PhD research. Very recently, the IMR congratulated Dr Janet Gare from our Goroka headquarters, for obtaining her PhD in HIV



Dr Maria Ome-Kaius, Anastasia Kali, Dr Leanne Robinson and Mary Salib discussing participant enrolment at Mugil Health Centre on the north coast of Madang.

research, the first Papua New Guinean woman at the IMR to be awarded a PhD; hopefully the first of many more to come. Last year, we celebrated the vast achievements of Dr Moses Laman, when he was awarded the inaugural Prime Minister's Excellence Award – Papua New Guinean of the Year, on Independence Day – such a deserved award for a colleague whom is greatly admired by many, including myself, and who provides me with immense support in leading the VBDU.

It is this group of highly dedicated, self-sacrificing individuals, who often need to leave their families behind

in order to pursue their post-graduate studies abroad, that truly take the work of the PNGIMR to new levels: rising to the challenge of changing circumstances, embracing new tools and technologies, forging tight relationships with health centres, hospitals, provincial and national departments of health, to ensure the research being done is directly relevant to the health problems of PNG and can be translated into new tools and new policies for implementation. It's for this reason I'm not only most hopeful, but also confident, that another 40 years of malaria research will not be needed!



Gussy Koimbu, Lisa Reimer, John Keven and Ned Walker enjoying kulau during an entomology field trip.



Dr Moses Laman in the paediatric ward, Modilon General Hospital.



Lincoln Timinao, Dr Cyrille Czeher and the team providing study awareness to children and parents.



Scientific officers at the VBDU with Jessica Atwell after a six-week epidemiology workshop.

Andrew Raiko, Site Manager, Madang



I started my employment with the PNG Institute of Medical Research in June 1984 as a young Medical Laboratory Technician with the immunology parasitology section of PNGIMR Madang. At that time our section was headed by Dr Karen Forsyth now Prof Karen Day. In those early days, 90% of the employees were expatriates and only 10% were Papua New Guineans. The few national staff, were tasked to do various jobs like being drivers, field officers, clinical staff – to screen and recruit study participants, perform laboratory procedures and laboratory management. I would say many of us were multi-skilled. During the years, I have contributed and worked on many malaria studies, while working under 3 different section heads: Dr Karen Day, Dr Kathrine Threnholm, and Dr Fadwa Al-Yaman.

Back then, people didn't really know what PNGIMR was doing as many thought the IMR was another hospital set up to see and treat patients. Research was a new thing in our communities. After some time people slowly came to understand the work of IMR. We had to inform our study population about our work, as in Madang we were mainly studying malaria.

While working with the Immunology Laboratory the first malaria study I worked on was the Malaria Demography Surveillance Program conducted in both the north and south coast of Madang District. For this study we had to drive to the villages, set up and recruit participants by filling in an enrolment form, conduct clinical examination for spleen size, record weight and height, and bleed and make blood films for all participants. Blood samples were collected into EDTA tubes and were brought back to the laboratory for processing.

For another project, I worked on a severe malaria study which aimed to recruit children with cerebral malaria at the Paediatrics Ward of Modilon Hospital. I also worked on the Wosera Census and Demography Surveillance, the Alpha Thalassemia Project in Madang, and the dynamics of malaria parasite associated with febrile illness in children from rural areas of Madang. Apart from malaria, I have worked on the filariasis study in the Drekkir area of East Sepik and a hookworm study in Kevasob village on Karkar Island.

However, in 1997 I was tasked by the IMR management to assist Dr Moses Bockarie as head of site, with the administration of the Madang branch. After working with the administrative team in Madang for about five years, I was transferred to Maprik in 2002 as a site manager for five years. In May of 2008, I was recalled back to Madang, and became the site manager in the following year. While in the administrative team, my main role was to support the work of science by ensuring that logistics, funds, supplies, and human resources were made available to all science projects in order for them to conduct their operations.

Malaria remains endemic in PNG and one of my greatest challenges while working on malaria studies is that the parasite is very clever and it is always changing its way of survival despite the intervention programs that we have been studying and conducting. Despite these challenges, I am still hopeful that one day a malaria intervention program or a combination of intervention programs will put an end to malaria. I will be proud to see that if it happens.

My main understanding and aim for working with malaria at PNGIMR is that malaria is one of the killer diseases in PNG that mostly kills children under 5 years of age and pregnant women with low levels of immunity. However, I have seen a lot of work been done in the past on malaria research and seen tests and experiments being done manually in the laboratories. This trend has now been changed to high tech molecular level machines running these tests with results being produced to scientists to further elaborate their work. I am proud that some of these tests can be done here at the IMR rather than sending samples overseas, as in the past.

In my personal opinion, people at all levels have contributed to researching malaria either scientifically, socially or economically and I know a lot of information has been published on this particular disease. However, more is yet to be discovered on malaria and its vector behaviour. Despite the challenges, malaria research at PNGIMR has had some positive achievements over the years. For example, a malaria vaccine was developed and tested out in the Wosera area of East Sepik; there have been changes in the standard treatment of malaria in PNG; and, very recently the distribution of treated bed nets throughout the country has reduced the rate of malaria transmission to its lowest level. I really hope that one day all the hard work of malaria researchers, both in PNG and overseas, will result in the elimination of malaria.

Thomas Adiguma, IT Manager, Madang



I started work with PNGIMR in 1993 as a data manager. My probation period was spent at the head office in Goroka. I was transferred to Tari for a year and a half to manage the pneumonia and the Tari demography data. Towards the end of 1994, I was transferred to the Madang site to take over from Steven Mellor, an Australian volunteer worker.

The job was a big challenge for me as my background was in Physics/Earth Science and I only had a little experience in databases from my previous employments.

My first challenge with the PNGIMR was fixing corrupted FoxPro, DOS databases in Goroka. My Supervisor was out of the province and I had no support to fix the databases. I called him and he directed me on how to fix the databases. In those early days internet access was very hard and I couldn't access the internet to get help from other forums.

My next major challenge was fixing the brand new CRT monitors that didn't work. Although the machines were under warranty, my supervisor wanted to see if I could fix them. I had theoretical background in electronics, but had no practical experience. Following the circuit diagrams I was given I managed to fix the three monitors. These two major challenges were faced during my probation period.

I passed my probation after 3 months and was sent to Tari to work on the Tari demography database as well as pneumonia and other health centre databases. Tari was challenging both from the work perspective (databases) as well as the social aspects of life there. Many times we couldn't do our work in the field because of tribal fights, but we had good reporter supervisors and community relations officers that helped the IMR to do the research.

When I was transferred to Madang to manage the databases both in Madang and the Sepik it was a big challenge for me as I had only 3 weeks to take over from an Australian volunteer. I had to multi-task in my work, from computer hardware, programming and managing databases, field census and GPS mapping and production of maps for the Wosera demography project. The main research work that I was involved in were the Vitamin A and Zinc Study headed by Dr Anuraj Shankar from John Hopkins, the malaria vaccine trial headed by Dr Blaise Genton and Dr Betuela, the ICIDR project in Dreikirir, the Usino filariasis study and various other drug studies conducted in the Alexishafen area of Madang.

After all these years of work, I feel that it is now time to let the younger people carry on with PNGIMR's efforts to find solutions to the health problems facing our people. There are new challenges now, but the availability of the internet and partnership collaborations will help our young scientists and support staff lead the PNGIMR into the future.



Lina Lorry, Senior Microscopist, Madang



I started working with PNGIMR at Yagaum as a malaria trainee microscopist on a Case Western Reserve University funded project beginning on 4 December 2001 – this was the Malaria Vaccine Trial Project in the Wosera area of East Sepik Province. As part of this study, I did staining and reading of malaria parasites from the stained thick and thin blood films of blood slides. Over the years, I worked for many projects. A few papers were successfully published where I was a co-author, and these included the following: i) Risk factors for *Plasmodium falciparum* and *Plasmodium vivax* gametocyte carriage in Papua New Guinean children with uncomplicated malaria; ii) Strategies for understanding and reducing the *Plasmodium vivax* and *Plasmodium ovale* hypnozoite reservoir in Papua New Guinean children: a randomised placebo-controlled trial and mathematical model; iii) Population pharmacokinetics, tolerability, and safety of dihydroartemisinin-piperaquine and sulfadoxine-pyrimethamine-piperaquine in pregnant and non pregnant Papua New Guinean women; and, iv) Artemisinin-naphthoquine versus artemether-lumefantrine for uncomplicated malaria in Papua New Guinean children: an open-label randomized trial.

Over the years, I also worked on other projects apart from malaria studies such as the micro-filarial worm study by collaborators of the Case Western Reserve University, doing filtration, staining and quantifying worms from glass slides. I also assisted collaborators from James Cook University in hookworm studies by filtering human faecal matters and quantifying worms. I took lead in experimenting with a new malaria diagnostic tool called 'cyscope' out in the field and in the laboratory to detect the parasite's presences in fresh human blood. In my current role, I also mentor junior microscopists and assist to train new microscopists in the Microscopy Unit.

My greatest challenge working for malaria projects has been as a women working amongst a male dominant field – it is challenging when it comes to decision making. Given directives and working closely with other colleagues who may lack the skills and knowledge in malaria microscopy is often a challenge. But one thing I enjoy about malaria research is that there is no ending. Every time there is always new ideas and techniques developed for research which increases the knowledge and learning capacity with new result findings which makes research interesting. At the end of the day the results are achieved regardless of the setbacks through the sheer endless effort of many people. This will only come through if everyone involved does their part.

Regardless of what we all do, understanding the core business of PNGIMR in our research activities is important. We should be innovative, proactive and work smart in our respective fields of expertise. I personally believe in collective ideas and effort. With more training of researchers and adequate funding allocated for research activities specifically, one day there may be a breakthrough in malaria research with regards to malaria control and elimination.

Locally, we still have a lot to achieve. I challenge the younger generation of PNG scientists to do more malaria research and to especially convince the government of PNG to invest in vector borne research. Currently, most malaria research activities are funded externally, which is good because this creates employment, but at the end of the day we maybe disadvantaged because funding and ideas are not originally ours. The Vector Borne Diseases Unit also needs its own research facility in Madang town and there is still a lot of work to do in terms of building relationships with other stakeholders and the general public about the work of malaria research in the country. Nevertheless, I can say that the Institute has achieved a lot in malaria research over the past 40 years and I'm proud to be part of the team that has contributed to these outstanding achievements.



Walter+Eliza Hall
Institute of Medical Research

Lawrence Rare, Site Manager, Maprik



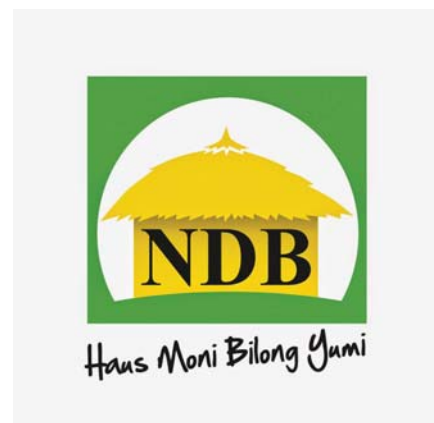
I first joined the malaria research program at Yagaum 34 years ago when I worked as a research field assistant with the Malaria Research Intervention Studies in late 1982. As part of this study we worked around the Ambenob and North Coast areas of Madang Province. I was involved mainly in giving out 'tok saves' and helping out with the field team doing finger pricks and filling out case report forms. Later, I was tasked to look after the mortality component of the study, interviewing relatives of those who had died, to find out their likely cause of death.

Since then, I worked on several other malaria research projects both in Madang and East Sepik. I spent the last 24 years of my career in Maprik, East Sepik. I was involved as the supervisor for the Wosera Demographic Surveillance field team for many years, and later become the assistant site manager, assisting Manase Baea and later Andrew Raiko. I become the site administrator in Maprik in 2008. Currently I am involved in the administration as the Maprik site administrator, overseeing various malaria research projects and providing logistics support to enable malaria researchers to have easy access to carry out their work effectively.

I have experienced a lot of challenges while working for the PNGIMR. Some of these include working on various malaria projects for long hours, and on the logistic challenges of the field, especially in Maprik. But my time spent working for various malaria projects is not in vain because I hope to help find possible ways to help the entire population from the attacks of malaria since malaria is a killer disease that has killed so many people in PNG and around the world. My main hope is to find possible ways to prevent people from getting malarial attacks, probably by use of a vaccine.

So far the malaria research program is running well but the PNG National Government with other collaborating agencies need to put more effort into giving adequate support in order to keep this Institute going so that it can conduct more research and be able to recommend more long-term sustainable solutions. My personal opinion, as a member of the Vector Borne Diseases Unit, is that I strongly believe this Institute with its malaria research programs has done a fabulous job in controlling and preventing people from getting malarial attacks, although a lot is yet to be done. From a community perspective, and even from some of the allied health workers' perspectives, it has been seen that the incidence of malaria has been going down and a lot of credit has been given to PNGIMR, although it may have been the result of hard work by many other institutions as well.

In conclusion, I would like to request that the National Government and other collaborating agencies continue to assist the malaria research programs we conduct. Malaria research still has a lot to achieve and is able to do more, but lack of funding will cripple these good achievements gained so far.



Livingstone Tavul, Senior Scientific Officer, Madang



On the 40th year of malaria research in PNG – the very reason for the 2016 celebrations – I am very grateful for the opportunity to reflect on the past 25 years, the present, and a promising future. I pay tribute to our colleagues who have passed on but left behind stepping stones for the research that we do today. I also acknowledge and I am proud to mention that many of our friends and colleagues providing quality leadership in malaria research projects around the globe had their humble beginnings doing malaria research in PNG.

When I joined the Institute in 1990, treating malaria was a big challenge. Parasites were becoming more resistant against the common antimalarials, there were no rapid diagnostic tests (RDTs), and long-lasting treated bed nets were unavailable. This is not the case anymore as RDTs are now widely available, research into antimalarial drug resistance is ongoing at a fast pace, and many more new treatment options including artemisinin combination therapies are available.

As I look back over the last two decades, a great deal of progress has been made in the fight against malaria. This has been possible through the implementation of control policies backed up by evidence from research. It seems the dream to see a malaria-free world is almost within reach and I hope it will become a reality by 2050 or earlier. Another milestone in malaria research is seeing a lot more Papua New Guineans being trained in higher degrees and mentored to take lead in carrying out research in the country. Thank you to our research partners who have taken the lead and responsibility in seeing our young scientists being trained through their affiliated institutions.

The future looks brighter for malaria research in PNG, hence better malaria control measures, prevention, and eradication. However, the international-donor-dependent tradition is a concern. Our health care systems should be much more active in finding and treating malaria patients and advocating preventive measures against further transmission. Apart from accumulating shared knowledge on the advances in malaria, research must continue to generate data to guide policy makers to focus on malaria prevention and eradication priority areas. Total ownership must be emphasized and more research funding and commitment should come from within rather than from overseas donors. Nevertheless, we have a thousand more reasons to celebrate today for the achievements we have attained from carrying out malaria research over the last 40 years. Congratulations PNGIMR and happy 40 years in malaria research celebrations!



Margie Marem, Data Management Unit, Madang



I commenced employment with the Papua New Guinea Institute of Medical Research in 2001 as a data entry clerk. I initially worked with the ICIDR filariasis project and Duffy vivax research that was conducted in Maprik. My task involved ensuring that data was backed up at the end of the day; this was successfully completed in 2006.

As well as the work I did for the Duffy vivax project, I also became involved in data entry work for filariasis and other projects like ICEMR, PIH, IPTP and microscopy related data.

I did not only do data entry for the projects mentioned above. One of the tasks I most enjoyed was the translating of Tok Pisin to English for the cost effectiveness study which I helped Carol Davis with; similarly, the translation of interviews in Tok Pisin into English for the TB project headed by Erin.

I also worked as administration assistant – transport officer, pay mistress, procurement officer and assisted in the general running of the office for the Case Western University project from 2000 to 2006.

Being with PNGIMR has both its memorable and challenging moments. I must say the greatest challenge I have experienced as a data entry clerk is entering case report forms that have not been properly cross checked out in the fields.

Nevertheless, knowing that malaria is a burden in my country and that the research work done at PNGIMR is helping to reduce and improve this health problem, as a long time data entry person, I know that the data collected is very important to achieve this. Thus my aim is to ensure that data is carefully and correctly entered, and safely filed away so that it can contribute to improving the malaria burden in PNG.

As a long time serving staff with the Institute, I can say that the future of malarial research in PNG looks promising in that there has been a reduction in malaria over the past few years. However, that does also mean that more challenges lie ahead in terms of controlling malaria completely. But with the right attitude and continued commitment of staff, the Institute and PNG will continue to see more high quality research outputs and achievements being made.



Absalom Mai, Safety Officer and Entomology Technician, Madang

I started working for PNGIMR on the 9th of January 1991. I was working with Dr Jeffery Hii and was with him until 1997. I did field mosquito collections in Wosera, Buksak and around the Madang District. I also did data entry using entomology field forms and got trained to do circumsporozoite ELISA. I also had the opportunity to do on-the-job training at James Cook University in Townsville, Australia. I was involved in the malaria vaccine trial that occurred between 1996 and 1997. I mainly conducted immunological assays. In 1998 I worked with Dr Steven and did a lot of laboratory work within immunology and haematology.

Dr Moses Bockarie came in 2000 and I worked with him. I learnt to do filarial filtration. During that time I became involved with the hookworm project in Naru. While carrying out my normal lab duties, I was appointed as the transport officer managing the PNGIMR Madang fleet of vehicles. I also did an on-the-job training at Queensland University. Dr Bockarie left in 2010 and Dr Lisa Reimer and Eddie Thomson took over. I continued with the lab work and became the entomology lab manager and was responsible for ordering reagents and lab consumables. I received training in occupation health and safety and biosafety (OHS), and currently oversee OHS at PNGIMR Madang.

Dr Anne Boissarie came in 2013 after Dr Lisa and Eddie left. I continued to assist with lab work, managing the lab and was more involved in setting up the OHS committee in PNGIMR Madang. Dr Boissarie was not with us for too long and left at the end of that year and Dr Cyrille took over.

I am quite happy to be working for PNGIMR. I have noticed a lot of changes but the main ones are that there are more scientific officers now than in the past. Between 1991 and 2000, we as technicians, literally did everything from field collection, lab processing to data entry ourselves. I can also see some improvement in the OHS policies that we have nowadays. Also there is more government funding as compared to the past.

When looking back, I can say that I started from 'scratch' and PNGIMR helped and supported me with many training opportunities, locally and internationally, both in the field of laboratory science, biosafety, and OHS and including some in-house trainings as well. I really love my work with PNGIMR and this motivates me to work hard and to produce good results, some of which have been published in many journals.



Absalom working in the Entomology lab, 2001.



Two village families in Nanda village, Wosera awaiting testing by the malaria epidemiology survey team.

Short profiles of long serving staff of the Vector Borne Disease Unit



Yule Ele, Entomology Technician, Madang

I started work with PNGIMR in 1982. This year marks my 34th year of service to PNGIMR. I started as a village recorder with the demography team and worked there until 27th of October 1985 when the unit ceased work. At that time, my role was to record births, deaths, migrations and changes in location. I later moved on to work with the entomology section in 1987 and I have been with that section since then. I really enjoy working in the field and also in the lab. This work has allowed me to travel to different parts of PNG and to meet many other people whom I would not have been able to meet if I had not been working for PNGIMR. In the past, there were only expat staff, who did all the work while we collected data for them but now I am happy to see a lot of PNG scientists taking the lead, especially the young scientific officers, nurses and medical doctors. During my earlier times there were no national scientific officers. I would like to see more nationals rise up and take leading roles in research and become principle investigators. This has been in my heart to tell our young scientists but it is difficult for me because they are more educated than me. But with this opportunity to say something, I hope my message can be heard.



Siub Yabu, Entomology Technician, Madang

I have been working in the field of malaria for over 42 years, beginning with the Malarial Control Program from 1974 to 1980 – before I joined the PNGIMR under the supervision of Dr Derek Charlwood in 1981. I have been working with PNGIMR for a total of 35 years, mainly as an entomology technician, collecting mosquitoes and larvae. We did a lot of field work and travelled within Madang Province and out of the province. I mainly did work for malaria projects but with Dr Moses Bokari we also did filariasis work. We did field collection of mosquitoes and then stained them and examined them for the filarial worm under the microscope. We did similar work with Dr Jeffry Hii as well.

Now we have stronger vehicles compared to the past and also we have more vehicles to assist us with our work. I see that we have more nationals doing the work that was usually done by our expat scientists in the past. This makes me really happy to see that we can have Papua New Guineans working at that level. We have worked through big changes – from not receiving travelling allowances to receiving only K3 to now where we are paid well. I have enjoyed my time working for PNGIMR and through this I have been able to travel to many different places.



Penina Kusunan, Administration Assistant/Procurement Officer, Madang

I began working with the PNGIMR 12 years ago, beginning on January 5th 2004. I have been in procurement and administration since my commencement of work, facilitating the ordering and purchase of supplies and equipment for all projects on site. The greatest challenge I have had is in relation to logistics – getting orders and supplies, especially large pieces of equipment and cold shipments, delivered to IMR Yagaum, directly from overseas. But we have managed to improve on this process over the years and I am happy to have contributed. Although my line of duty has been mainly in the administration, I enjoy learning new things, and I am happy to have contributed to the malaria research program at the Vector Borne Diseases Unit.



Lemen Kilapak, Entomology Technician, Madang

I started in 1981 and this will be my 35th year working for the PNGIMR. My first supervisor was Dr Derek Chalwood. We did field work which included mosquito collection, pupae collection, larvae collection and human baits. I also did similar work with Dr Tom Burkot. During this time, I learnt how to dissect the *Anopheles* thorax for filarial worms. When Dr Moses Bockarie came, we started doing morphological identification of mosquitoes that were collected in the field. I also learnt how to dissect the *Anopheles* mosquito midgut for oocysts and their salivary glands for sporozoites. When Eddie and Dr Lisa Reimer came we continued with the same work but also helped out with doing insectary work where we reared *Anopheles farauti* mosquitoes. We did field work that was more focused on malaria and not filariasis. Dr Cyrille came after Eddie and Lisa left. Under Dr Cyrille, we also did field work with the collection of larvae which we reared back in the lab or at the field and tested them against repellents. We are still continuing with this work with Dr Stephan Karl at the moment. I have really enjoyed my years of working for PNGIMR. Through the work that I have done, I have been able to see places in PNG that I never thought I would go to. I know that what we are doing is for the country and sometimes we will not be able to see the results of our work quickly but that is fine with me because over time, our future generations will benefit from our hard work.



Nandao Tarongka, Senior Microscopist, Madang

I commenced employment with PNGIMR 21 years ago, on June 26th 1995. The first malaria project that I was part of was the vaccine study in Wosera where I began work as a malaria microscopist. Over the years I have read slides for many other studies such as the cohort studies, drug efficacy trials, vivax studies, filariasis studies, the MalCon project, IPTi, IPTp, the ICEMR study, and many more. I am still employed as a microscopist and I carry out all duties under the Microscopy Unit. In the past I have also assisted in field work which included collecting blood samples, examinations, enrolment of study participants, administering treatments, following-up on adverse events after treatments, collecting stool specimens and supervising field projects. In recent years I have been doing mainly my main duty as a microscopist, supervising the Microscopy Unit, as well as assisting in the training of younger microscopists for various field projects. One of my greatest challenges relates to understanding the technical side of microscopy. Another challenge is in relation to meeting deadlines for each study. But I know that malaria is a deadly disease and I am happy to work for PNGIMR to reduce malaria and hopefully one day we can eliminate the disease. I think if support and funding for malaria projects continues in the future, elimination of malaria will be possible.



Lemen Kilapak, Derek Chalwood and Raymond Paru collect mosquito larvae in a Madang sago swamp.



IMR audio visual officer, Travis Jenkins and police wait at the gate for the VIPs arrival to the new IMR Maprik laboratory facilities.



Mary Salib, Clinical Research Nursing Officer, Madang

I have been working with the PNGIMR for the past 12 years as a clinical research nursing officer, beginning on 15 March 2004. In 2004 I worked for an efficacy study of camoquine and fansidar, and also assisted in a safety and efficacy study of artesunate suppositories. In 2005 I worked for the Mugil cohort study, before joining the IPTi team in 2006, under the supervision of Dr Senn and Dr Rarau. The IPTi trial ended in late 2009/early 2010, and I joined the drug study team under the supervision of Dr Laman in 2011. After we completed that study, I was employed under the Mugil cohort reinfection study in 2013 under the supervision of Dr Ome and Dr Robinson. Then, from 2014 to 2016, I worked with the acute malaria B cell study which is a sub-study of the ICEMR project. I enjoy working for IMR, knowing that my contribution as a clinical research nurse in assisting scientific and clinical research to combat malaria and other health issues is appreciated in PNG and abroad. I strongly hope that the scientific and clinical researchers, through their endless efforts, will one day find a way to eradicate malaria.



Moses Baisor, Community Health Worker, Madang

I was employed by the IMR from 1991 to 2009, serving the Institute for a total of 17 years. On January 7th 1991, I joined the IMR, and was attached with the epidemiology section at Yagaum. My first task was to do a malaria morbidity study in children, under the supervision of Dr Karen Day. In 1992, I was posted to Kunjingini Health Centre where I worked with Dr Blaise Genton, conducting active malaria surveillance case detection. From 1994 to 1995 I was heavily involved in the vaccine safety and efficacy study, under the supervision of Dr Genton, Dr Fadwa Al-Yaman and Dr Inoni Betuela. In 1996, I worked as a senior field supervisor on a study investigating vitamin A and zinc supplements under the direction of Dr Anuraj Shankar. Then in 1997, I was posted back to Madang where I worked with Drs Moses Bockarie, Pete Zimmerman and Chris King on the ICIDR project. From 1998 to 1999 I went to work on Bagbag Island with a study on impregnated bednets used against malaria and filariasis. As part of this study, we also monitored adverse events following treatment. This study was under the direction of Drs Jim Kazura, Moses Bockarie and Chris King. From 2000 to 2002, I worked as a field coordinator, conducting baseline survey, census and demographic surveys at Usino, as part of the filariasis ICIDR project. In 2003, we began conducting mass drug administration at Usino as part of the filariasis study. From 2006 to 2008, I worked as the field team leader for the ICIDR filariasis study at Dreikir in East Sepik. My last project was in 2009 when I worked for the Preg Vax study at Alexishafen health centre and Modilon Hospital to study the cytoadhesive properties of *P. vivax*. I am no longer employed by the IMR but I have a lot of friends who are still employed there. Currently, I work as a community health worker at Josephstaal Health Centre. I am happy to have contributed to the many scientific studies and publications that have been produced by the PNGIMR in the fight against malaria and filariasis.



Andrew Nasi, Gardener and Cleaner, Madang

Andrew Nasi, 35 years old, is currently the only gardener and cleaner at PNGIMR Yagaum. He is a second generation employee of PNGIMR, his father Nasi Sinop was the cleaner who kept PNGIMR Madang in order for over 30 years before he retired in 2009, handing over his responsibilities to his son Andrew. Andrew's father is now 69 years old and has returned to their village in Begasin, leaving his son to take care of his previous responsibilities. Andrew joined as a casual in 2007, and after the retirement of his father, became a contracted staff of PNGIMR, replacing his father. When interviewed, Andrew said, "Mi bikpela long han bilong IMR an mi hamamas long work long dispela Institute." (I grew up under the care of IMR and I'm happy to serve this Institute.)

Collaboration between the School of Medicine and Pharmacology, University of Western Australia and the PNGIMR

Timothy M.E. Davis, Group Leader, 2002-2015



A meeting between Tim Davis, Ken Ilett and Michael Alpers in 2001, and the recruitment of Harin Karunajeewa, to the team soon afterwards started a fruitful collaboration between the University of Western Australia's School of Medicine and Pharmacology and the PNGIMR. The research started with relatively small pharmacokinetic studies of artemisinin derivatives and partner drugs in PNG children admitted to Modilon Hospital in Madang Town, with initial funding provided by the Rotary Club of Scarborough Beach in Perth. The group had ambitions for bigger things and, together with Ivo Mueller from the IMR's Vector Borne Diseases Unit, submitted an application for an intervention trial to the Wellcome Trust in 2002. Although this was unsuccessful, it was used as a template to leverage Rotary Against Malaria and WHO Western Pacific Region support and then a larger grant from the Australian National Health and Medical Research Council. Harin Karunajeewa spearheaded the group's attempts to find a suitable field site and the trial started at the Alexishafen Health Centre just north of Madang Town as well as at the Kunjingini Health Centre in East Sepik Province. The results of the trial were published in the *New England Journal of Medicine* at the end of 2008 and formed the basis of Harin's PhD thesis.

After the trial closed out, the group continued to carry out pharmacokinetic studies at Alexishafen but had expanded recruitment to pregnant women. With the retirement of Ken Ilett, Kevin Batty took over as lead of the antimalarial drug assay facility and moved the laboratory and its senior scientist, Madhu Page-Sharp, to Curtin University in Perth. Laurens Manning and Moses Laman joined the team in Madang and they started a suite of NHMRC-funded observational studies of severe infections in children at Modilon Hospital in 2007. This dovetailed well with the MalariaGen studies that Irwin Law helped to establish. These studies underpinned Lauren Manning's PhD thesis and he has since stayed with the group through an appointment as an Associate Professor in the School of Medicine and Pharmacology. He assumed leadership of the group last year. Moses Laman then enrolled in a PhD himself in 2011, taking responsibility for a second intervention trial in young children at Alexishafen and Mugil Health Centres, the results of which were published in *PLoS Medicine* at the end of 2014. Moses' PhD thesis received the University of Western Australia's Faculty of Medicine Dean's commendation because of its quality. Moses continues as a member of the group in his current role with IMR and with Modilon Hospital as a paediatrician.

Additional research activities have been co-ordinated by Brioni Moore who joined the group as a post-doctoral Fellow in 2009 and who continues to oversee studies of young children and pregnant women at Alexishafen. There have been a number of other people who have worked with the group as researchers completing post-graduate degrees or as co-investigators on specific projects. These include Rina Wong, Tamara Koleala, Sam Salman, Dulcie Lautu, Stephan Karl, John Benjamin and Leanne Robinson. They have contributed to the >60 clinical and laboratory papers published by the group since 2003.

In a brief review such as this, there is insufficient space to record and acknowledge the invaluable contributions made by a range of other people including nurses, laboratory technicians, microscopists, data entry personnel and administrative staff working mainly at the IMR but also in Perth. The group is most grateful for all their support, and especially for the help and guidance provided by Peter Siba as Director of IMR. We are also indebted to the NHMRC which has funded most of the studies carried out by the group since 2005. We have every expectation that the collaboration between the School of Medicine and Pharmacology and IMR will go well beyond its first 15 productive years.

Contribution of Alexishafen Health Centre 1985-1988 to malaria pregnancy research

Bernard Brabin

Emeritus Professor of Tropical Paediatrics, University of Liverpool

We arrived at the IMR in Madang in April 1985 eager to establish a systematic study on malaria in pregnancy. In the early 1980s clinical trials in pregnancy were few, including in PNG. Our study aimed to obtain detailed epidemiological data, especially on the effectiveness of chloroquine prophylaxis, which was still the mainstay of malaria prevention in pregnancy. This research received unequivocal support from Michael Alpers and the staff at the IMR but would also not have succeeded without operational assistance from the health centre staff at Alexishafen, a Christian missionary hospital on the north coast. Sister Valentildes, an outstanding midwife, who ran the service, was legendary as she always made herself available for deliveries at any time of the day or night. I attributed the high pregnancy antenatal coverage, compliance with malaria prophylaxis, tetanus vaccination, and attendance for health centre delivery to the goodwill of staff running the maternity services. Sister Valentildes allowed us to set up our research laboratory next to the delivery unit enabling rapid and overnight sample processing, kindly provided a freezer for sample storage, provided free office space and supported clinical

data collection including participant follow-up. Equivalent academic laboratory support was available from staff at the IMR, with David Gibson efficiently running the malaria laboratory. This commitment helped establish a platform for malaria research in pregnancy at IMR. The importance of the problem has eventually led to pregnancy becoming a global priority for malaria control, catalysing studies also on placental pathophysiology, molecular biology and drug pharmacokinetics in pregnancy.

We are indebted to Michael Alpers, IMR and Alexishafen Health Centre staff for their support and collaboration during three years of productive research. This greatly influenced our careers. Loretta, my wife, delivered our son in Madang General Hospital and went on to complete her PhD at the University of Leiden based on field studies investigating cultural factors associated with infectious disease transmission in Madang coastal villages. My work on malaria in pregnancy continued and hopefully has contributed to improving antenatal care for women and better pregnancy outcomes with malaria control.



Sister Valentildes, senior Midwife, Alexishafen 1980s.



Sister Valentildes, Julie Sapau and mobile clinic staff at Alexishafen.



**HOPE SPECIALIST
HEALTH CARE**

Message from Graham Mitchell formerly from the Walter and Eliza Hall Institute of Medical Research (WEHI), Melbourne



Dear PNGIMR friends,

Heartiest congratulations to the Institute on the occasion of the 40th Anniversary Malaria Colloquium celebrations from someone who was fortunate enough to be reasonably close to the very beginning of the 40 year adventure.

Although The Walter and Eliza Hall Institute of Medical Research (WEHI) in Melbourne has been involved in health and medical research in PNG for many decades (eg, Macfarlane Burnet et al.) it was 40 years ago almost to the day that the current research collaboration on malaria between WEHI and PNGIMR was initiated. The precise starting point was a conversation between myself and Michael Alpers on a plane – I think travelling between Melbourne and either Sydney or Brisbane. [Michael will remember which it was being a mere youngster relative to myself!].

The WEHI Parasitology Program commenced in 1975 with initial focus on the immunology of host-parasite relationships in mouse models but extending to veterinary parasites of economic importance in Australia. It was always the intent to move to human parasitic diseases – WEHI was an institute of medical research after all – but Melbourne wasn't exactly a hotbed of such diseases or expertise in them. The abovementioned conversation with Michael as the new Director of PNGIMR was quickly followed by award of a major Rockefeller Foundation grant (Ken Warren's Great Neglected Diseases (GND) Program) and rapid evolution of the program to human parasitic diseases and, as a condition of the GND grant in fact, strengthened our new linkages with disease-endemic countries in the region, specifically PNG (malaria and filariasis) and the Philippines (schistosomiasis and filariasis).

Key personnel involved in building the GND (and WHO-TDR) – funded WEHI-PNGIMR malaria relationship were Graham Brown and Robin Anders and I was delighted to learn that my former WEHI colleagues will both be joining you for the August celebrations (but only believe some of their anecdotes about our time together in PNG!). Other WEHI folk involved included Russell Howard, Karen Day and Ross Coppel working on both malaria and filariasis. A boost to the relationship was a linkage to the Queensland Institute of Medical Research (QIMR) in Brisbane under the Directorship of Chev Kidson and this collaboration evolved into an Australian Government-funded Malaria Vaccine Joint Venture involving WEHI, QIMR, two commercial parties, CSL Limited (in Melbourne) and Biotechnology Australia (in Sydney) with, of course, the link with PNGIMR a key element of the basic and translation research aimed at developing a blood-stage malaria vaccine.

As we all know, a highly-protective malaria vaccine has proven elusive and I am sure that much of the discussion at your colloquium will focus on this particular quest [that is certainly not for the faint-hearted or the dilettante!] and prospects for further achievements through a deeper understanding of the adversary and host-protective immunity as well as the assembly of a multiplicity of tools, expertise and structures to translate the technology and knowledge into products of enormous public health value such as malaria vaccines.

Best wishes for future success over the next 40 years and beyond and that the WEHI-PNGIMR relationship continues to prosper now in different hands than was so all those 40 years ago!

With kindest regards,

Yours, Graham Mitchell

We remember:

Greg Crane
Henry Dagoro
Robert Desowitz
George Dogoya
David Gibson
Nicky Gibson
Gibson Gideon
Willie Gribai
Carol Jenkins
Damien Jolley
Lubus Kaukesa
David Kemp
Chev Kidson
Tania Oakiva
Joyce Obed
Samuel Pariva
Lydia Petrus
Albert Sie
Ray Spark
Patricia Toliman
Leonard Vavana
Helena Vrbova
Mathew Wan
Regina Wangnapi-Taput
Titus Wangunara
Medir Yahimau

Malaria Colloquium

40 years of malaria research in PNG

‘Continuing innovative research for effective malaria control and elimination’

24-26 August 2016

Tentative Program Outline

24 August	
2.00-6.30 pm	(Andrew, Penina, Leah, MSOA members) Arrivals and Registrations - Madang Resort Haus Win
6.30-9.30 pm	(Colloquium Committee) Welcome Dinner – Madang Resort
25 August	Day 1 Sessions
8:30-9.00 am	(Siar Singing Group, Madang Resort) Colloquium Opening Procession for Guest Speakers and Leaders
9.00-9:30 am	(Chair: Prof. Peter Siba, Madang Resort Sana Room) Welcome Address – Hon Jim Kas MP, Governor, Madang Province
9:30-10:00 am	(Hon Malakai Tabar MP, Higher Education Research Science and Technology - Colloquium Patron) Launching and Opening of Colloquium
10.00-10:30 am	Tea Break
	Keynote Addresses – 40 years of malaria research in PNG (Sana Room, Chair: Dr Moses Laman)
10:30-11:00 am	Keynote Speaker: Prof. Michael Alpers
11:00-11:20 am	Speaker: Prof. Paul Garner
11:20-11:40 am	Speaker: Prof. Patricia Graves
11:40-12:00 pm	Speaker: Prof. Ivo Mueller
12:00-12.20 am	Speaker: Prof. Sir Isi Kevau
12.30-1:30 pm	Lunch Break

	Malaria Control and the changing epidemiology of malaria (Sana Room, Chair: Dr Leanne Robinson)
1:30-1:45 pm	Speaker: Prof. Jim Kazura
1:45-2:00 pm	Speaker: Mr Leo Makita
2:00-2:15 pm	Speaker: Ms Diana Timbi
2:15-2:30 pm	Speaker: Mr Tim Freeman
2:30-2:45 pm	Speaker: Mr John Keven
2:45-3:00 pm	Speaker: Mr Raymond Paru
3:00-3:30 pm	Tea Break
	Clinical studies and trials (Sana Room, Chair: Prof. Francis Hombhanje)
3:30-3:45 pm	Speaker: Prof. Graham Brown
3:45-4:00 pm	Speaker: Dr Moses Laman
4:00-4:15 pm	Speaker: Prof. Stephen Rogerson
4:15-4:30 pm	Speaker: Dr Maria Ome-Kaius
4:30-4:45 pm	Speaker: Dr Livingstone Tavul
4:45-5:00 pm	Speaker: Dr Brioni Moore
7.00-10.00 pm	Governor's Dinner, Madang Resort Hotel Keynote address: Prof. Marcel Tanner
26 August	Day 2 Sessions
	Molecular tools for understanding malaria (Sana Room, Chair: Dr Livingstone Tavul)
8:00-8:30 am	Speaker: Prof. Ingrid Felger
8:30-8:45 am	Speaker: Prof. Alan Cowman
8:45-9:00 am	Speaker: Ms Lilah Tol
9:00-9:15 am	Speaker: Dr Alyssa Barry
9:15-9:30 am	Speaker: Mr Lincoln Timinao
9:30-9:45 am	Speaker: Ms Michelle Katusele
9:45-10:15 am	Tea Break

	Vaccines, antigenic diversity and host immunity (Sana Room, Chair: Dr Clement Malau)
10:15-10:30 am	Speaker: Prof. Robin Anders
10:30-10:45 am	Speaker: Prof. Karen Day
10:45-11:00 am	Speaker: Prof. Hans Peter Beck
11:00-11:15 am	Speaker: Ms Benishar Kombut
11:15-11:30 am	Speaker: Prof. Louis Schofield
11:30-11:45 am	Speaker: Prof. Christopher King
11:45-12:00 am	Speaker: Prof. Denise Doolan
12:00-1:00 pm	Lunch Break
	Strengthening research and research partnerships – the next 40 years (Sana Room, Chair: Ms Dulcie Lautu)
1:00-1:15 pm	Speaker: Dr Kulala Mulung
1:15-1:30 pm	Speaker: Dr Sibauk Bieb
1:30-1:45 pm	Speaker: Dr Leanne Robinson
1:45-2:00 pm	Speaker: Dr Evelyn Lavu
2:00-2:15 pm	Speaker: Ms Olga Saweri
2:15-2:30 pm	Questions and Discussions
2:30-3:00 pm	Closing remarks: Prof. Peter Siba/Dr Leanne Robinson/Dr Moses Laman
3.00-3.15 pm	Tea Break
3:30-5:00 pm	Activities and tours
6:30-9:30 pm	Colloquium Patron's Farewell Dinner





