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Executive Summary by Professor Jeremy Farrar

“The world becomes more interdependent every day; and we now know that the fate of all of us depends on the fate of each of us. Nowhere is this more true than in the field of global health, where diseases spread at least as fast as the knowledge to contain them. It is in such global collaboration that our future lies.”

Sir Ka-shing Li

The University of Oxford–Li Ka Shing Foundation Global Health Programme was created in 2007 with a vision to build a model of international collaboration that would harness global expertise and experience to tackle contemporary challenges in global health. This report reviews the remarkable educational and research achievements of the University of Oxford–Li Ka Shing Foundation Global Health Programme since its inception.

We hope you will agree that it has been an outstandingly productive partnership which has addressed some of the greatest health challenges of the 21st century with impressive speed and efficiency. The research programme has completed groundbreaking work on the major public health threats of pandemic influenza, emerging infections, malaria, and HIV/AIDS, yet has also tackled the broader threats of environmental and social change. The diversity yet relevance and impact of the research programme to both global health and to the health of disadvantaged people across Asia has been a great achievement. The investment in young people, our Li Ka Shing Fellows, who will we hope become the leaders of tomorrow, has been a part of the University of Oxford–Li Ka Shing Foundation Global Health Programme of which we are particularly proud.

This educational programme has supported young students from across Asia and beyond to study at the University of Oxford, strengthening knowledge and understanding, and creating a resource, of both people and relationships, to carry forward the global health research agenda. As a result of this we have built new partnerships, including establishing the Shantou Oxford Clinical Research Unit (SOCRU) at the Shantou University Medical School. The SOCRU links very closely with the University of Oxford Asia Research Programme and with Hong Kong University and the Chinese University of Hong Kong and will be a major focus of the University of Oxford–Li Ka Shing Foundation Global Health Programme in the coming years. Li Ka Shing Fellows such as Mr Laiwen Lu, Dr Binglin Cui and Miss Xueqiong Gan, all from Shantou, are now back in China building their own research careers and helping link Shantou and Oxford Universities. They represent the future leaders of the Shantou Oxford Clinical Research Unit and the University of Oxford Asia Research Programme.

We have been delighted and honoured to develop with the Li Ka Shing Foundation the University of Oxford–Li Ka Shing Foundation Global Health Programme. We are very proud of the Programme, its global impact on public health, and the genuine spirit of international collaboration in which its diverse research endeavours have been undertaken. To many of those involved this has been the most enjoyable, most productive and most collaborative partnership we have been associated with. With the setting up of the Shantou Oxford Clinical Research Unit at the Shantou University Medical School we believe the coming years will be even more productive as we work together to address the challenges of public health in the 21st century.
The Li Ka Shing Global Health MSc Scholarship Programme

The Li Ka Shing MSc Scholarship Programme began in 2007 and has subsequently funded 11 Masters students. The Scholarships enable the students to attend a one-year Master of Science course at the University of Oxford. Since the beginning of the Li Ka Shing Scholarship Programme, 10 students have successfully obtained an MSc in Global Health Science and one student has achieved an MSc in Integrated Immunology.

The Li Ka Shing Scholarship Programme is overseen by Professor Ray Fitzpatrick, Dr Emma Plugge and Miss Christelle Kervella from the Department of Public Health and Primary Care. The programme has one year left and there remain places for four more students.

Class of 2010/11

For the academic year 2010/11, the Department of Public Health and Primary Care awarded two Li Ka Shing MSc Scholarships to Miss Ying Chen from China and Dr Rahul Pradhan from Nepal.

MISS YING CHEN
CHINA

Miss Chen obtained her undergraduate degree in Bio-Medical English at Peking University Health Science Centre in China in 2008. During her undergraduate study, she engaged in public health research projects, where her interest in the field began. After graduation, Ying worked for one year at The George Institute for International Health, China as a research and administrative assistant. Through this experience, she identified her interests by becoming involved in several large-scale international collaborative epidemiology projects. She began considering public health issues from a global perspective, and yearned to know more about Global Health Science.

“The MSc programme will help me to further identify my research interests for my future career, because we were able to cover large areas of public health through the different course modules. The programme’s emphasis is on training students to identify problems and to think in a creative yet scientific way. It also encourages students to resolve problems independently. This will benefit me enormously in the future. Moreover, students are encouraged to initiate small-scale public health projects with the aim of providing us with practical experience for future research. Students on the course come from around 16 different countries, and it is exciting to study global health science in such an ‘international community’. In addition, this global network of friends will facilitate our research in the future where global collaboration is needed.” Ying Chen.

After the MSc, Ying plans to apply for a PhD in a specialised area of public health.
Dr Rahul Pradhan  
Nepal

Before starting the MSc Dr Pradhan worked as a senior research fellow at Patan Hospital, Kathmandu, Nepal. His research was in paediatric infectious and vaccine preventable diseases. He undertook surveillance of infectious diseases for three years and researched the nasopharyngeal colonisation, burden and pattern of diseases caused mostly by H. influenzae and S. pneumoniae. Currently, Rahul is involved in a randomised controlled trial of 10-valent Pneumococcal Conjugate Vaccine in Nepalese children.

“I am interested in research and improving the health of people. Coming from a low-income country, this course is a great opportunity for me because it is concerned with global health issues including those of developing countries. The various compulsory and optional modules, as well as the research placement, will provide me with the knowledge and wisdom regarding global health science which I can use to make a significant difference in my pursuit of better health for society.” Rahul Pradhan

After the MSc, Rahul plans to either undertake a DPhil at the University of Oxford or return to Nepal and find a research position in Global Health.

Class of 2009/10

Mr Laiwen Lu (Clark)  
Shantou University Medical College, China

Before starting his Masters degree, Mr Lu trained as an epidemiologist at Shantou University Medical College. Following this he worked as a Research Scientist at the Mahidol–Oxford Research Unit (MORU) in Bangkok, Thailand where he conducted research on the history of the antimalarial drug Artemisinin (Qinghasu).

Clark’s most memorable experience of the MSc in Oxford was participating in a leadership course with classmates from all around the world; he says he learned the basic principles of working efficiently in a team.

During the third term of the MSc, he started his research placement at the Unit of Health-Care Epidemiology, Oxford University, during which he undertook database analysis of a fractured neck of the femur. As a result the title of his thesis was: ‘Hospital admission rate, mortality and underlying cause of death after a fractured neck of femur in England 1999-2004: Linkage database study’.

“The MSc in Global Health course gave me the chance to communicate with really talented scientists. Not only did I learn the latest developments in public health research, but I also had a great social life. I feel more confident about my career after graduation.” Laiwen Lu

Since completing the MSc, Clark was awarded an Oxford–Li Ka Shing DPhil Scholarship (part of the new LKS Donation to Oxford 2010) to study Clinical Medicine at the University of Oxford.

In addition to his academic progress, Clark is enjoying married life and fatherhood. Clark married Miss Yongru Chen in August 2010 and they recently announced the birth of their first daughter.
Mr Jiming Zhu
China

In 2010 Mr Zhu took a short break from the MSc course in Oxford to complete two internships at the International Poverty Reduction Centre in China (IPRCC) and at the United Nations Children’s Fund (UNICEF). After completing these internships, Jiming rejoined the MSc course in March 2011 for the third and final term.

During the last term Jiming will undertake a research placement at the Health Economics Research Centre in Oxford; his duties are to assist with the communication between Oxford and Ningxia Province, help channel their project in the evaluation of the health system there, and arrange research materials for data analysis. In addition to this, Jiming will also write a thesis, the title of which is: ‘Monitoring, Evaluation and Incentive Scheme of the Health System in China: Based on the Case Study in Ningxia Province’.

Jiming is due to complete the MSc in September 2011.

“The MSc has helped me to become familiar with the structure of the global health arena and broaden my understanding of international issues.”
Jiming Zhu

Class of 2008/09

Miss Xueqiong Gan (Rosa)
Shantou University Medical College
China

Miss Gan, from Shantou University Medical College, was awarded a Li Ka Shing Fellowship in 2008 to join the MSc in Global Health Science course. She graduated in 2009.

At present, Rosa works in Beijing as an Assistant Researcher in the Centre for Human and Economic Development Studies, School of Economics at Peking University; she is working on a public health project related to health in rural China. The project aims to assess the health and risk factor profile of the rural population of China as well as the health-seeking behaviour of sick people who may, or may not, chose to seek medical help. The aim is to determine the level, use and pattern of need for health services in rural China. On the provider side of the health services, the project studies the rural health system with a focus on human resources for hospitals and public health institutions. The objective is to forecast the need for human resources for the health of the rural population of China.

Rosa plans to continue with her work, gain experience and increase her understanding of public health issues in rural China. Rosa has undertaken some field trips, which have given her a visual impression of where the problems lie in China.

“It’s always fascinating to see so many changes happening in China and I’m lucky if I’m able to contribute to the changes in health in rural China.” Rosa Gan
Dr Kremlin Wickramasinghe
Sri Lanka

Following completion of the Global Health MSc in 2009, Dr Kremlin Wickramasinghe began working as a researcher for the British Heart Foundation Health Promotion Research Group, in the Department of Public Health at the University of Oxford. Kremlin works on the coronary heart disease statistics project and is currently developing a rating score for Cardiovascular Disease databases. In addition, Kremlin is studying for a DPhil in Public Health, which he is due to complete in 2014.

Special achievements
In October 2010, Kremlin was invited to attend the World Health Organization consultation on prioritisation of a research agenda for non-communicable diseases held in Geneva.

He was appointed as Chair for the Early Career Network of the Asia Pacific Academic Consortium for Public Health (APACPH).

He won a fellowship to visit the World Health Organization Collaborative Centre for Obesity Prevention, at Deakin University, Australia; he was invited to stay for 10 weeks in 2011 as an academic visitor.

Kremlin has also been invited to speak at several symposia on urbanisation and non-communicable disease prevention (his MSc Global Health thesis topic) at the International Union for Health Promotion and Education Conference (June 2010 in Geneva) and at the Asia Pacific Academic Consortium for Public Health Conference (November 2010 in Bali).

In addition to these achievements, a paper arising from Kremlin’s research on his MSc thesis was accepted for publication by the Journal of Urban Health.

Kremlin’s future plans are to continue his career in non-communicable disease prevention.

Dr Binglin Cui (Jane)
Shantou University Medical College,
China

After completing the MSc in Oxford, Dr Cui returned to Shantou and married Dr Hui Pan.

Jane is currently working as a research fellow at the Shantou Oxford Clinical Research Unit at Shantou University Medical College. She is responsible for a study on the causes of respiratory infections in the first affiliated hospital of Shantou University. This research study started in January 2011, and so far over 800 nose and throat samples have been collected from the outpatient children with respiratory infections. She is also preparing for a new study of the bacterial carriage among healthy kindergarten children.

Jane plans to take the IELTs (International English Language System) exam with the aim of studying for her DPhil.
**Class of 2007/08**

**Dr Suchismita Roy**  
**Bangladesh**

“The Li Ka Shing Scholarship Award was vital in my being able to take up the position offered to me by Oxford University, and because of it I was later able to obtain the Aga Khan Foundation International Scholarship Award, enabling me to pursue a PhD in my chosen area at the London School of Hygiene and Tropical Medicine. I am very grateful to have been one of the first 2007-2008 recipients at Oxford University.”  
Suchismita Roy

In early October 2007, during her time on the MSc course in Oxford, Dr Roy met her husband, Mani Shankar Narayanan. They were married in December 2009.

Suchismita is currently studying a full-time PhD in Epidemiology and Population Health at the London School of Hygiene and Tropical Medicine. She is due to complete her PhD in September 2013.

Suchismita’s immediate aims are to write up her PhD research paper on the ‘Assessment of the impact of maternal complications and level of care received during labour and delivery in increasing the risk of preventable stillbirths and 1st week of life death (perinatal deaths) in rural Bangladeshi infants with little or no access to care’. Suchismita’s other research includes a ‘South Asia systematic review on the relation of complications and care with perinatal deaths’.

In the future, Suchismita hopes to work in the area of reproductive and newborn health in developing countries, in a research and academic/teaching capacity.

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**Dr Samir Koirala**  
**Nepal**

After completing the MSc course in 2009, Dr Koirala returned to Nepal to work at the Oxford University Clinical Research Unit, Patan Hospital, as one of the leading clinical researchers. He is currently conducting clinical research in typhoid fever and other infectious diseases, for example: Hepatitis E and infections related to the nervous system. Samir is also working on a typhoid vaccination project in collaboration with the International Vaccine Institute, Seoul, Korea.

Special achievements:
Samir was appointed as a lecturer in the Department of Community Health Sciences at Patan Academy of Health Sciences. Recently a publication of which he is a co-author was accepted by the *Lancet Infectious Disease Journal*; the publication is on clinical drug trials in typhoid fever.

In the future Samir plans to study for a DPhil in infectious diseases at the University of Oxford.
The highlights and activities of the Teaching Programme in the final year of the 2007-2010 Li Ka Shing donation were as follows.

- The Mandarin version of the Infectious Diseases Section of the *Oxford Textbook of Medicine* (fourth edition) was published.
- Medical Students (Miss Haiting Guo and Miss Xiaodan Huang) from Shantou University Medical College travelled to Oxford to take part in the eight-week Medical Elective Programme at the John Radcliffe Hospital.
- Student: Mr Thomas Pouplin was awarded an Oxford–Li Ka Shing MSc top-up grant to enable him to complete his MSc in Experimental Therapeutics at the University of Oxford.

**Published: Oxford Textbook of Medicine (fourth edition) Infectious Diseases section in Mandarin**

One of the aims of the postgraduate training programme in infectious diseases in Beijing, headed up by Professor David Warrell, was to translate the Infectious Diseases section of the *Oxford Textbook of Medicine* (fourth edition) into Mandarin to use as course teaching material.

The Chinese version of the textbook was produced under the supervision of Associate Professor Jun Lu (YouAn Hospital, Capital Medical University) and the translation was checked by Dr Hongyi Zhang, Consultant Medical Virologist, Cambridge, UK. It was published in 2010 by the Beijing Peoples’ Printing House and Oxford University Press.

**The Oxford Medical Elective Programme**

**March 2010: Miss Xiao Yang and Mr Siqi Qiu, Shantou University Medical College**

In March 2010, Oxford University Medical School hosted two students from Shantou University Medical College to learn alongside Oxford medical students. Miss Xiao Yang and Mr Qiu Siqi joined the Medical Elective Programme for eight weeks in the Nuffield Department of Clinical Medicine at the John Radcliffe Hospital, Oxford. During the elective the students were required to participate in ward rounds, surgical rounds, outpatient clinics and routine ward work. They took part in case presentations to members of their clinical team and were involved in bedside teaching, seminars and tutorials with other students.

**February 2011: Miss Haiting Guo and Miss Xiaodan Huang, Shantou University Medical College**

In February 2011 two more students from Shantou University Medical College arrived in Oxford to start the medical elective: Miss Haiting Guo (Jophy) and Miss Xiaodan Huang (Bernice).
Below are evaluation reports by Mr Qui Siqi and Miss Xiao Yang on their time spent on the medical elective programme in Oxford in March 2010.

**Medicine has no borders**

**Miss Xiao Yang**

**Shantou University Medical College**

Thanks to the University of Oxford I travelled to this world-class academic institution at the beginning of spring 2010. I enjoyed eight weeks of clinical study in the general medicine department of the John Radcliffe Hospital and it was an unforgettable experience!

During the elective programme I learned how the UK’s National Health System (NHS) operates. The NHS is run by the UK government and provides free medical services to every citizen in the UK. It is the spirit of equality because health care is guaranteed for everyone, whether rich or poor. The hospitals have to be well-equipped and the doctors who work for the NHS are all very kindhearted and hard-working people.

During ward rounds with the doctors, we would communicate with the patients. The most important thing I learned is that, as future doctors, we should treat every patient with full respect and that every patient is a good teacher to us. We should also care about the human beings, and not just the disease they have; the meaning of ‘health’ not only includes physiological health but also mental health and social adaption. Armed with this attitude, when facing future patients I will be respectful because I care about their lives, dignity and struggles.

The atmosphere for studying here is fantastic. We have had the chance to put into practice our clinical skills which we have learned from our textbooks. We have also had access to the Oxford University library and were able to refer to the large medical database. In addition we felt free to ask questions – both to our patients during ward rounds and to all the doctors we were in contact with. Our clinical tutor, Dr Angus, was an excellent teacher and would always attend the students’ case presentations and join group discussions like a friend. What’s more, we were invited to various lectures to study. Participating in this delightful studying environment encouraged me to think more, to ask more, to learn more.

Outside my studies, I made good friends with students from Oxford and other countries; it was interesting socialising with people from a variety of cultures and backgrounds. Communicating with each other in a mostly English environment improved my English a lot. I enjoyed living in Oxford; it is a beautiful city which is full of history and impressive architecture.

The eight week elective programme was a spectacular experience; it widened my horizons, taught me the right attitude with which to treat patients and inspired me to study harder to become a good doctor. I would like to give my sincere thanks to the Oxford University Medical School, the Li Ka Shing Foundation, Dr Angus, Dr Law and everyone who helped me during the elective programme – with your selfless help I had a smooth eight week study. I learned that the caring spirit of medicine has no borders, and this is what I want to bring back to my college to inspire the others and to encourage myself in the future days!

“I learned that the caring spirit of medicine has no border, and this is what I want to bring back to my college to inspire the others and to encourage myself in the future days!”
How time flies! Two months has passed and it has been a really great opportunity to spend time on a clinical attachment at the John Radcliffe Hospital, Oxford – one of the biggest clinical training bases in Europe. The two months I spent studying in Oxford will always stay with me and for that I would like to thank the University of Oxford and the Li Ka Shing Foundation for giving me the opportunity. I would also like to thank everyone who made the experience possible, in particular Dr Law, Dr Angus, Dr Tan, Dr Khalid, Mr Chen, Mr Thompson, Mr Zhang, Miss Alexander, and Mrs Li.

I learned a lot during the two months and I would like to divide this into two parts; firstly the clinical knowledge and secondly the medical morality. I was impressed by how patiently Dr Khalid taught us from the very basic medical terms to the complicated diseases. In addition I sincerely appreciated how all the students helped each other learn during the course. The doctors’ discussion of patients left me with a deep impression that we should not just treat the disease, but we should treat the social problems and the psychological problems of patients as well. After everything we had learned we were happy to be able to clerk patients by ourselves.

Sir Ka-shing Li encourages medical students to be excellent at both medical morality and medical skills. He put morality at the forefront, which I think shows how important medical morality is and that it is the basis of being a good doctor. During my attachment at the John Radcliffe Hospital, I was affected deeply by the doctors’ hard-working and gentle attitude towards the patients, their respect of patients’ privacy and their way of treating patients as syntheses of society, biology and psychology. I thought that the combination of these skills demonstrated medical morality.

My medical skills and knowledge of medical morality has improved greatly. I have also learned many life skills. I learned to cook, manage money and time, to respect others’ habits and not to waste things. I had the opportunity to experience the wonderful culture and architecture of England. I was intoxicated with the archaic churches and cultural relics when I visited London, Cambridge and the city centre of Oxford.

I made many good friends in Oxford who really helped me in both study and daily life. Some of them taught me how to cook, others shared the culture of their country and some invited me into their homes. I appreciate everything they have done for me and I truly hope that we can reunite one day.

Two months’ study in Oxford is a short time, but the memory is everlasting and I know this experience will benefit me in my career as a doctor. I would like to thank you very much again for making this possible.
The Shantou University Medical Elective Programme

Mr Haseeb Rahman, a medical student at the University of Oxford, travelled to China to spend time at Shantou University Medical College on a medical elective programme organized by Shantou. Below is Mr Rahman’s report on his time in China.

MR HASEEB RAHMAN
UNIVERSITY OF OXFORD

I intended to observe how medicine was practiced in a rapidly developing country. This would enable me to see with relative ease both advanced medical practices and very basic levels of care within a small area. Shantou was unique in that being a medium sized town by China’s standard, one would expect rudimentary healthcare facilities. However, due to the Li Ka Shing Foundation setting up a Cleft Lip programme, cataract surgery in local villages, hospice work and more, a much higher level of healthcare than anticipated was provided. Yet as most of China’s population still resides within rural areas, one doesn’t have to travel far to see very basic levels of care. The hospitals, on the other hand, boasted MRI and CT machines with expert levels of care. There was also much practice of traditional Chinese medicine, which may have uses in areas where Western medicine falls short, such as chronic diseases and particularly chronic pain. Though initially skeptical of its efficacy, after spending three days learning and observing it, I’m certainly more open-minded about it.

Much of my hospital work involved shadowing the senior physician / surgeon in various departments, with each having their own individual teaching style. Some would prefer to go through patient case studies, discussing differential diagnoses and then going over investigations and finally management, providing memorable segments of sometimes quite rare diseases. Others would conduct a ward round, simply explaining what was wrong with each patient, which still proved valuable due to the unique nature of some of the diseases. The aspect of advanced medical equipment and facilities with diseases found in a developing country setting was an interesting juxtaposition. I also observed the provision of primary care in surrounding townships, a rewarding if somewhat overwhelming experience. It would be interesting to see how Shantou will have moved on in five or 10 years’ time, and I fully intend to return to find out.
Thomas Pouplin was awarded an Oxford–Li Ka Shing grant to cover part of his fees for a two-year MSc course in Experimental Therapeutics in the Department for Continuing Education at the University of Oxford.

During the MSc course, Thomas splits his time between Oxford and Vietnam. He is currently leading the clinical pharmacology department at the Oxford University Clinical Research Unit (OUCRU) based at the Hospital for Tropical Diseases in Ho Chi Minh City, Vietnam. His main focus is the pharmacokinetics of anti-infective drugs in Tuberculosis and CNS infections.

The title of his thesis is: ‘Childhood Tuberculosis. A review of the pharmacokinetics of the first line drugs in children, risk factors and outlooks.’

“The Experimental Therapeutics MSc course, going through a broad spectrum of clinical pharmacology aspects, provides me additional important skills and updates that are highly beneficial as I immediately implement them in my daily work.”

Thomas is due to complete his Masters in September 2011.
Collaborative Research Programme 2007-2010

The collaborative research programme funded 12 research projects in 2007. Eleven of the research projects were funded for three years.

The first 11 final reports below were funded from 2007-2010, and in 2009 were each awarded additional seed funding which allowed the research to continue after the end of the programme in 2010. The twelfth report was funded from 2007-2008.

These final reports will describe the aim(s) of the research, progress and breakthroughs, new partnerships and collaborations formed, the impact on other research and if extra funding and support was secured in addition to the Oxford Li Ka Shing Global Health Award. The projects will also list the publications, presentations and patents that have arisen from the research.

1. Mapping Malaria in the Asia-Pacific Region through the Malaria Atlas Project

Investigators
Dr Nguyen Van Kinh, National Hospital for Tropical Diseases (NHTD), Vietnam
Dr Nguyen Manh Hung, National Institute for Malariology, Parasitology and Entomology (NIMPE), Vietnam
Dr Din Syafruddin, Eijkman Institute for Molecular Biology, Indonesia
Professor Bob Snow, University of Oxford and KEMRI Wellcome Programme, Kenya
Dr Kevin Baird, University of Oxford and Eijkman Institute, Indonesia
Dr Peter Horby, University of Oxford and NHTD, Vietnam
Dr Simon Hay, Department of Zoology, University of Oxford

Aims of the project
This project aims to build and foster a regional network of malaria mapping expertise in the Asia-Pacific region. Through this process we will provide information and tools of increased local value to assist Ministries of Health, disease control agencies and their funding bodies to monitor the burden of malaria in order to prioritise cost-effective intervention packages and define spatial targets of control or elimination. Special emphasis has been placed on mapping the risks of Plasmodium vivax, a particular challenge for the sub-region, and much neglected by the research community.
Malaria is the ninth most important cause of death and disability globally, and the bulk of this is caused by two parasites: *Plasmodium falciparum* and *P. vivax*. Understanding the geographical distribution of malaria risk is central to the effective planning, implementation, monitoring and evaluation of malaria control or elimination. The Malaria Atlas Project (MAP), with the support of the Li Ka Shing Foundation (LKSF), has compiled the most extensive dataset and applied the most advanced spatial statistical tools to achieve significant advances in describing the epidemiology of malaria.

MAP has utilized two main sources of data on malaria occurrence: the annual reported number of confirmed malaria infections (the annual parasite incidence - API), and community surveys of the prevalence of malaria parasites in blood smears (the parasite rate - PR). The 2007 iteration of the *P. falciparum* global spatial limits used API data to define the limits of *P. falciparum* malaria transmission [Guerra CA et al., 2008]. In 2009 this exercise was repeated, and the spatial resolution in the Southeast Asia region was substantially improved through the establishment of the MAP nodes in Vietnam and Indonesia, and the regional linkages these nodes have fostered. As a result, the API data used in the 2007 versus the 2009 iterations increased from 281 to 351 administrative units in Indonesia and from 61 to 670 administrative units in Vietnam. Advanced spatial analysis of API data has been used to assist the national malaria control programs of Vietnam and Yunnan Province, China to identify high-risk areas where control and surveillance resources can be targeted [Bui HM et al., 2011; Clements ACA et al., 2009] (Figure 1. Legend: Number of cases of malaria caused by *Plasmodium vivax* reported by district in Vietnam in: (a) 2007; and (b) 2008). In 2010 MAP used API data to develop and publish the first ever global map of the limits and population at risk of *P. vivax* malaria [Guerra CA et al., 2010] (Figure 2. Legend: The global spatial limits of *Plasmodium vivax* malaria transmission in 2009.) Transmission was defined as stable (red areas, where PVAPI≥0.1 per 1,000 people p.a.), unstable (pink areas, where PVAPI<0.1 per 1,000 p.a.) or no risk (grey areas). The medical intelligence and predicted Duffy negativity layers are overlaid on the *P. vivax* limits of transmission as defined by the PvAPI data and biological mask layers. Areas where Duffy negativity prevalence was estimated as ≥90% are hatched, indicating where PAR estimates were modulated most significantly by the presence of this genetic trait). The results show that 2.85 billion people were exposed to risk of *P. vivax* transmission in 2009: with the vast majority (91%) living in Central and Southeast Asia. This map provides desperately needed information on the range, extent and potential for elimination of *P. vivax*.

In 2009, MAP published the global limits of stable and unstable *P. falciparum* transmission using PR survey data, incorporating data for 15 Southeast Asian countries that had increased by 160% as a result of the LKSF supported regional activities [Hay SI et al., 2009]. The publication was translated into Vietnamese and Bahasa Indonesian by the MAP team and circulated widely with a press release in both countries in 2009. This work showed that over 70% of the 2.4 billion people at some risk of infection with *P. falciparum* live in areas of unstable or low endemic risk, where the technical obstacles to malaria control are relatively small. The MAP database now includes information on the prevalence of *P. vivax* from 4,998 cross-sectional community surveys. This *P. vivax* PR dataset will...
be used to map the endemicity of *P. vivax* transmission within the spatial limits defined in the 2010 map developed from API data [Guerra CA et al., 2010].

These MAP products provide the evidence-based benchmark against which future control and elimination priorities will be set and evaluated in pursuit of key targets defined by the Millennium Development Goals and the recently launched Roll Back Malaria Global Malaria Business Plan.

**Additional support and funding secured**

The Li Ka Shing award has stimulated MAP to overcome the technical challenges of *P. vivax* cartography, to better define the distribution and intensity of *P. vivax* transmission, and to provide better estimates of the population at risk of the disease and its clinical burden. This culminated in the award to Dr Simon Hay of a Wellcome Trust Senior Research Fellowship in Basic Biomedical Science, titled ‘Defining the population at risk and burden of disease of *Plasmodium vivax* malaria’. Budget: £982,243. Duration: 2011-2016.

MAP activities in Indonesia indirectly but substantially helped the Eijkman Institute/Eijkman-Oxford Clinical Research Unit/ALERTAsia Foundation secure a $2 million award from the Bill and Melinda Gates Foundation for the assessment of spatial repellents in malaria control on Sumba Island. The activities under this award also led directly to modest awards supporting a variety of activities. These include a Wellcome Trust supported collaboration with Liaquat University Medical Centre in south-eastern Pakistan, and support from the World Health Organization to examine G6PD deficiency and primaquine sensitivity in Cambodia.

The LKSF award has also stimulated an interest in applying similar approaches to mapping the distribution and endemicity of dengue globally. This led to a successful application to the European Union that will start in 2011: 2011-2016. European Union Collaborative Project (#281803) FP7-HEALTH-2011-single-stage. ‘IDAMS - International Research Consortium on Dengue Risk Assessment Management and Surveillance’. Total budget: €5,999,213. Jeremy Farrar is the overall chair of the IDAMS consortium and Simon Hay is the leader of Work Package Four dedicated to the epidemiology and mapping of dengue globally. Environmental change and urbanisation are thought to be key drivers of the emergence and spread of dengue, and the disease is increasingly being seen in southern China. It is hoped that this work will link with colleagues in Guangdong Province and in Shantou in particular.

**New partnerships and collaborations formed**

The LKSF support has enabled MAP-Asia to build strategic linkages with research groups and ministries of health in the region. The MAP node in Hanoi, Vietnam has developed links with the National Institute for Malariaology, Parasitology and Entomology (NIMPE), and two Vietnamese researchers (Bui Huu Manh and Le Viet Thanh) have travelled to the University of Queensland to learn Bayesian geo-statistics. This has resulted in one publication, with a further publication in preparation [Bui HM et al., 2011]. The award has also resulted in a link between the Vietnam group and the Research Institute of Tropical Medicine in the Philippines. Iqbal Elyazar, from the Indonesia MAP node at the Eijkman Institute, matriculated as a DPhil. student at the University of Oxford in October 2009 and has now begun his doctoral research on the spatial epidemiology of malaria in Indonesia.

The Indonesia MAP node has developed strong links with the Indonesian Malaria Control Programme, supporting the design of training materials on the use of global positioning system tools and geographic information system for malaria mapping and data analysis. The materials will be used for training 51 district malaria programme managers in Kalimantan and Sulawesi in 2011. A similar relationship has been developed with the Malaysian malaria control authorities.

**Impact on other research**

Despite advances in mapping the distribution and intensity of malaria transmission, the ability to provide strategic advice for malaria control programmes remains constrained by the lack of evidence-based maps of the distribution of the dominant vectors of human malaria, the Anopheline mosquitoes. This is because appropriate vector control interventions vary according to the characteristics and behaviours of different Anophelus species. MAP has therefore begun to map the contemporary geographic distributions of the dominant mosquito vectors of human malaria [Hay SI et al., 2010]. This activity is building upon the links built through the LKSF award and the Asia MAP nodes are contributing data on Anopheles species distribution in the Asia-Pacific region.

Inherited blood disorders (IBDs) are important medical problems in their own right, but are also important for malaria control since they influence the distribution of malaria risk and the safety of certain anti-malarial drugs. A presentation in 2009 on MAP’s work on IBD mapping to Dr Alida Harahap of the Eijkman Institute for Molecular
Biology in Jakarta now forms the basis of a collaboration on mapping the important inherited blood disorders of Southeast Asia with future possibilities of PhD and post-doc support from Oxford. Mentorship on the mapping of one important IBD, glucose-6-phosphate dehydrogenase (G6PD) deficiency, is currently being developed at the Eijkman Institute in Jakarta through support to Ms Dewi by Dr Fred Piel from Oxford.

The work on malaria has stimulated the partners to begin work on establishing cartographic techniques for dengue, the most common vector borne viral disease of humans with an estimated 50 million infections every year and around 2.5 billion people living in areas at risk. The Asia Pacific region is most heavily affected by dengue, reporting ~75% of global morbidity and mortality.

MAP publications and presentations


2. A new Global Health Research Facility in Hanoi

Investigators
Dr Nguyen Van Kinh, National Hospital for Tropical Diseases
Dr Peter Horby, Oxford University Clinical Research Unit, Hanoi, Nuffield Department of Clinical Medicine

Aims of the project
The aim of this project was to develop a new research facility dedicated to basic, clinical and population based infectious disease research conducted by the Oxford University Clinical Research Unit (OUCRU) and the National Hospital for Tropical Diseases (NHTD) in partnership with other national and regional collaborators.

Project progress and breakthroughs
All stages of the new facility were completed in September 2010 and His Royal Highness Prince Andrew, Duke of York, His Excellency the Minister of Health, Mr Nguyen Quoc Trieu, and the Director of NHTD, Dr Nguyen Van Kinh, officially opened the facilities on 11 October 2010.

The laboratory component now comprises a suite of modern diagnostic and research laboratories (500m²), with substantially enlarged and improved facilities for microbiology, mycobacteriology, parasitology, and biochemistry, plus extended capabilities for molecular diagnostics, sequencing, and immunology. A generator has been installed that ensures continuity and stability of electricity to the laboratory suite, avoiding disruption of diagnostic and research activities and the waste of expensive reagents and vital clinical specimens. In 2008, two of the three research freezers containing irreplaceable research specimens were broken as a result of power surges; there have been no power surges or loss of electricity since the new facilities were inaugurated. The laboratories have a restricted card-entry system and controlled airflow with a pressure cascade to ensure staff safety and to reduce the risk of contamination of sensitive molecular techniques. The laboratories are home to both the diagnostic team of the National Hospital for Tropical Diseases and the joint Oxford-NHTD research team. This close working relationship means that the facility directly benefits patients through both immediate access to improved diagnostic services and through establishing the NHTD laboratories as a national benchmark for infectious diseases laboratory services. The new laboratories have allowed the research group to flourish, with research ongoing into Vibrio cholerae;
Streptococcus suis; Klebsiella pneumoniae; Acinetobacter baumanii; measles; seasonal, pandemic and avian influenza; dengue; the causes of community acquired pneumonia; and antibiotic resistance.

The laboratory staffs are close to completing a revision of all workflows and standard operating procedures for laboratory tests, data management, quality assurance and quality control practices, and bio-safety. The result is an international-standard clinical laboratory service that is enhancing patient care, acting as a national resource and training centre for the laboratory diagnosis of infectious diseases, and supporting research into infectious diseases of importance in Vietnam and regionally.

New research offices and a seminar room (65m²) were completed in February 2010, finally rehousing the research team and providing space to expand the research group, which was recently joined by a Senior Clinical Research Fellow and a Clinical Research Coordinator.

Additional support and funding secured
The total cost of the new facility was approximately $350,000, with $180,000 provided through the University of Oxford–Li Ka Shing Foundation Global Health Programme. Co-financing for the remaining costs and for the upgrade of laboratory equipment was obtained from the Wellcome Trust and the South East Asia Infectious Diseases Clinical Research Unit. The new facilities have contributed to the success of the Oxford University Clinical Research Unit–NHTD collaboration in securing substantial funding that ensures the growth and development of the Unit over the next five years. Research funding bodies supporting the work of OUCRU-Hanoi now include the Wellcome Trust UK, the US National Institutes of Health, the World Health Organization, Resources for the Future, the UK Medical Research Council, and the European Union.

The Ministry of Health of Vietnam has provided $800,000 for an extension to the hospital that will integrate with the Li Ka Shing Foundation’s work and provide additional expansion of the laboratory space. Construction of this government-funded enhancement began in January 2010 and was completed in April 2011. This provided an extra 200 square metres of space into which the laboratories will expand.

New partnerships and collaborations formed
The OUCRU-NHTD research group now has collaborations with over 15 different national and International Institutions in Asia, Europe and the Americas.

Vietnam collaborators
National Hospital for Pediatrics
National Hospital for Tuberculosis and Respiratory Diseases
National Institute of Hygiene and Epidemiology
National Institute of Malaria, Parasitology and Entomology
Hanoi Medical University

International collaborators
Chinese Centre for Disease Control and Prevention, Beijing China
Shantou Oxford Clinical Research Unit, Shantou University Medical College
Genome Institute of Singapore
Research Institute of Tropical Medicine, Philippines
Resources for the Future
Oxford University
London School of Hygiene and Tropical Medicine
Cambridge University
Amsterdam Medical Centre
Food and Drug Administration, U.S.

This project has provided the infrastructure that is the foundation for the research program of OUCRU-Hanoi.
Publications and presentations


Hay SI, Guerra CA, Gething PW, Patil AP, Tatem AJ, Noor AM, Kabaria CW, Manh BH, Elyazar IRF, Brooker S, Smith DL,


3. Serological surveillance for asymptomatic H5N1 influenza human infection in southern China and Vietnam

Investigators
Professor Yi Guan, Shantou University Medical College, University of Hong Kong
Dr Menno D. de Jong, Oxford University Clinical Research Unit, Vietnam, Nuffield Department of Clinical Medicine, University of Oxford
Professor Jeremy Farrar, Oxford University Clinical Research Unit, Vietnam, Nuffield Department of Clinical Medicine, University of Oxford
Dr Honglin Chen, Shantou University Medical College, University of Hong Kong

Aims of the Project
The main objective of this proposal was to investigate the asymptomatic human infection of H5N1 influenza virus in southern China and southern Vietnam. There are three lineages of avian influenza A virus, including two H9N2 viruses (Qa/HK/G1/97-like and Dk/HK/Y280/97-like) and one H5N1 virus (Gs/GD/1/96-like) which have been circulating in poultry in southern China since the mid-1990s. As each of the viruses from those three lineages were reported having been detected in sporadic human infection cases, all of the viruses are considered to have pandemic potential. So we screened the antibodies against both H5N1 and H9N2 viruses by hemagglutinating inhibition test (HAI) and neutralising test (NT), respectively.

Project progress and breakthroughs
Antibodies to H9N2 viruses screened by HAI test showed that, of 6,763 sera, about 185 sera were positive for H9N2 viruses (HAI titre ≥1:40). Guangxi had a higher seroconversion rate than that of Jiangsu (146, 3.59% to 39, 1.45%). The findings also showed the cross reaction between those two different virus lineages. However, some sera could be distinguished as being infected by G1-like virus through the further NT assay. Based on the criteria of World Health Organisation (WHO), to confirm the diagnosis of avian influenza infection via single serum the NT titre must be higher than 1:80. In this regard, Jiangsu only had one positive serum detected, while Guangxi had eight sera converted. It was noted that some sera even had low HAI titre (1:20) but gave higher NT titre (1:80). These findings suggest that detection of the H9N2 avian influenza infection in southern China is not rare. Our results also suggest that the confirmation of such infection should combine both HAI and NT assays.

Antibodies to H5N1 virus: amongst the 6,762 sera tested, only 13 sera had minor HAI activity with titres ranging from 1:10 to 20. Only a single serum collected from Guangxi had 1:20 HAI titre that gave rise to 1:40 titre in NT assay, while the remaining sera were all negative in NT assay.

New partnerships and collaborations formed
This project led to new partnerships between the University of Oxford Guangxi Center for Disease Control and Prevention and between
Professors Guan Yi, Menno de Jong and the Shantou University Medical College, Shantou Oxford Clinical Research Unit and the University of Hong Kong.

Impact on other research
While the project was ongoing, a novel H1N1 swine-origin influenza virus caused the first human pandemic influenza in the 21st century. We used those human sera collected in 2008 to conduct a ‘Serologic Survey of Pandemic (H1N1) 2009 Virus’ to understand how many people were seroconverted before the pandemic strain circulation.

Publications and presentations

4. Evaluating health interventions for children in rural China

Investigators
Professor Sian Griffiths, School of Public Health and Primary Care, the Chinese University of Hong Kong
Professor Nathan Congdon, Department of Ophthalmology, the Chinese University of Hong Kong
Professor Harold Jaffe, Department of Public Health, Oxford University
Professor Dennis, Lam Department of Ophthalmology, the Chinese University of Hong Kong
Professor Song Yue, Joint Shantou International Eye Center, Shantou
Professor Frieda Law, Department of Pediatrics, Shantou University
Professor Li-ping Li, Center for Injury Prevention, Shantou University
Mr Abhishek Sharma, DPhil student, Oxford University

Aims of the Project
This project consists of two parts: the myopia study and the healthy lifestyle study. The aims of the myopia study are to identify and develop a sustainable intervention model that provides low cost spectacles and promotes good behaviour and health education to rural Chinese students. It also aims to evaluate the effectiveness and efficiency of a school-based myopia correction intervention programme based on student services uptake and health outcomes.

The aims of the healthy lifestyle study are to identify the problems of nutritional health and health risk behaviour and to pilot a theme-based intervention programme for antismoking among rural Chinese students.

In the short and medium term this project has assessed the vision status and health related behaviour among rural Chinese students and has identified ‘left-behind’ children (those whose parent(s) migrated out for work for more than six months at a time) who were more likely to engage in high risk health behaviour. Through interventions, the project has also improved the knowledge and attitudes toward, and practice of, spectacle wearing and antismoking.

Project progress and breakthroughs
With regards to the myopia study, 15,404 children were screened for myopia, 8551 randomised to intervention and 6853 randomised to no intervention. 75% of children were examined as planned, 36% required glasses, and 75% of these children were followed up (over 3000 children).
For the healthy lifestyle study, a two-day field investigation was conducted in September 2007 to explore the potential major health challenges among the study population. Based on the observation, a self-administered questionnaire was then developed to collect information about eating behaviour, physical activity, sedentary behaviour, smoking, drinking, internet use, emotional problems, bicycle injury, as well as parental migration and other demographic characteristics. Height and weight were also measured in order to estimate stunting and obesity prevalence rates among the students.

The survey was conducted among 17 middle schools in Fuyang and Liangying townships, covering more than 10,000 students starting from December 2007. We found that unhealthy eating, smoking, drinking, emotional problems and bicycle injury were prevalent among the rural Chinese students. Around 18.1% of students were ‘left-behind’ and parental migration was recognised as an encouraging factor for students to practice risk behaviour, especially for ‘left-behind’ boys. Based on those findings, a theme-based intervention programme for antismoking was developed and conducted in two schools in Liangying Township during November 2009 to April 2010. The intervention lasted for one month and consisted of two educational seminars for students, one workshop for teachers, a letter and leaflet sent to parents, a blackboard-creating competition and short video-creating competition. Information on smoking, intention to smoke, self-efficacy, attitude toward smoking and subjective norm were collected by self-administered questionnaires before, immediately after and three months after the intervention. We found that students whose parents migrated had lower self-efficacy and were more vulnerable to smoking. Multiple regression among boys revealed that the influence of parental migration on smoking was at least partly mediated by self-efficacy. The intervention was effective in discouraging girls from smoking, but had no effect for boys.

**Additional support and funding secured**

This project, funded by the Li Ka Shing Foundation, assisted Professor Nathan Congdon’s grant application to the Chinese government; he received $2 million through the Thousand Man Programme to further study techniques to reduce the myopia burden in rural China.

**New partnerships and collaborations formed**

Through this project a new partnership developed with Zhongshan Ophthalmic Centre in Guangzhou, China.

**Impact on other research**

The project has influenced further studies of children’s myopia in Guangzhou, and aided in securing funding to support these.
Publications and presentations


Ye YR, Li LP, Lu YG, Gao Y, Griffiths SM. 潮汕地区农村留守儿童自行车伤害发生的现况研究. Prize for excellent paper of young investigators, presented in the 3rd Chinese Preventive Medicine Association Annual Conference in Beijing, China, 25-29 October 2009

Ye YR, Li LP, Lu YG, Gao Y, Griffiths SM. ‘Bicycle injury among Left-behind Children in the Southern Rural Areas of China’. Young Investigator Award, presented in the 41st APACPH conference in Taipei, Taiwan, 3-6 December 2009
5. Health Impact of Heat Wave

Investigators
Professor Emily Chan, School of Public Health and Primary Care, the Chinese University of Hong Kong
Professor Sian Griffiths, School of Public Health and Primary Care, the Chinese University of Hong Kong
Professor Li-ping Li, Professor and Director, Injury Prevention Research Center, Deputy Director of MPH Education Center, Medical College of Shantou University
Professor Harold Jaffe Department of Public Health and Primary Care, University of Oxford

Aims of the Project
The ‘Health Impact of Heat Wave’ project aimed to explore the effect of heat waves on human mortality and morbidity in urban settings of China and to identify risk factors associated with these adverse consequences towards human lives.

Project progress and breakthroughs
The Oxford–Li Ka Shing Global Health Programme funding (2007-2010) provided the resources to conduct various foundation studies which included but were not limited to literature reviews of 1) a retrospective analysis of health and climate related data in Hong Kong and China and 2) a study based on interviews with stakeholders. These pilot projects have established the technical capacity of our research team to conduct temperature, climate change and health related research in Asia. Statistical analyses using both time-series and case-crossover approaches have been carried out to determine mortality patterns, and a model has been developed to identify risk factors and vulnerable populations in Hong Kong and Shantou. Retrospective analyses of the Hong Kong community’s response to extreme temperatures were also conducted.

Additional support and funding secured
This project is the first target funded academic-based climate change health research in Hong Kong and China. In 2010, a major research grant was obtained from HKSAR government health and health service research grant (2010-2011) to continue with the investigation of the health impacts of heat waves in morbidity patterns in urban cities. Whilst the project officially ended in September 2010, during the three years funding period 15 international academic conferences and presentations were conducted, three academic research papers were published and two high profile press conferences related to temperature and health outcomes were carried out.

New partnerships and collaborations formed
In Hong Kong, the project has facilitated a research collaboration with CUHK and the Senior Citizen Home Safety Association (‘SCHSA’) in order to identify high risk population groups and to determine the specific morbidity profile and the community expressed needs during extreme temperatures from 1998 to 2008.

In addition, working partnerships were also formed between major environmentally concerned non-government organisations (WWF and Greenpeace). The research team was able to support community climate change and health related advocacy efforts through providing technical findings with its research results.

Illustrations
This graph below compares the percentage increase in natural mortality for a 10°C drop below the threshold. Overall we estimate a 10°C drop below 24°C for the period from 1998-2008 in mean temperatures, including delayed effects associated with a 3% increase in natural deaths.

% increase in natural mortality for 1°C drop below threshold

<table>
<thead>
<tr>
<th>City</th>
<th>Value % Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stockholm</td>
<td>1.00</td>
</tr>
<tr>
<td>London</td>
<td>1.50</td>
</tr>
<tr>
<td>15 cities</td>
<td>2.00</td>
</tr>
<tr>
<td>Athens</td>
<td>2.50</td>
</tr>
<tr>
<td>Sao Paulo</td>
<td>3.00</td>
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<tr>
<td>Hong Kong</td>
<td>3.50</td>
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<tr>
<td>Bangkok</td>
<td>4.00</td>
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<tr>
<td>Monterey</td>
<td>4.50</td>
</tr>
<tr>
<td>Stockholm</td>
<td>5.00</td>
</tr>
</tbody>
</table>
This graph shows the relationship between socio-demographic factors and the percentage increase in natural deaths associated with a 1°C lower daily mean temperature. Stronger effects are found among those who are older, deaths from causes other than cancer, and those living in low-income areas.

Publications and presentations


Chan EYY, Kim JH, Ng YLN. ‘A study of socio-demographic predictors of public perception and awareness of


Chan EYY, Kim J, Griffiths SM. ‘Climate Change and Health Risk Perception in Hong Kong’. Paper presented in the 2009 Annual Scientific Meeting Hong Kong College of Community Medicine, organized by Hong Kong College of Community Medicine, Free 10 pgs. Hong Kong, Hong Kong, 2009.06.14.

Chan EYY, Goggins III WB, Kim JJ, Timothy MA KW, Griffiths SM. ‘An analysis of community emergency help-seeking behaviors during elevated temperatures in a Chinese population using the general additive (poisson) temperature outcome model’. Paper presented in the 2009 Annual Scientific Meeting Hong Kong College of Community Medicine, organized by Hong Kong College of Community Medicine, Free Paper 12 pgs. Hong Kong, Hong Kong, 2009.06.14.


Chan EYY, Goggins WB, Kim JH, Griffiths S, ‘Climate Change and health: Preliminary Evidence of the impact of socioeconomic factors on temperature related mortality in Hong Kong’. Presented and awarded as the Best Poster Presentation at the 1st SPH Annual research day, 23 February 2008.
6. The frequency and spectrum of clinical disease caused by Plasmodium vivax mono-infection among patients in north eastern Papua admitted with a diagnosis of malaria

Investigators
Dr Din Syafruddin, Eijkman Institute for Molecular Biology, Jakarta, Indonesia
Dr Yohana Sorontou, Faculty of Medicine, University of Cendrawasih, Papua, Indonesia
Dr Kevin Baird, Eijkman Oxford Clinical Research Unit Jakarta, Indonesia
Dr Bob Taylor, Mahidol Oxford Research Unit, Bangkok, Thailand
Dr Stuart Blacksell, Mahidol Oxford Research Unit, Bangkok, Thailand

Aims of the Project
The hypothesis which formed the basis of this study was that exposure to natural infection by Plasmodium vivax can develop into severe clinical disease similar to that of P. falciparum. Concomitant infections with other species of human plasmodia or other pathogens may alter the clinical manifestation. We believe that a prospective study which employs more precise and reliable diagnostic procedures in patients admitted to hospital with a diagnosis of malaria, in an area where chronic heavy exposure occurs to both P. falciparum and P. vivax, may allow an accurate diagnosis of severe and complicated vivax, and assess the risk of severe vivax malaria in patients admitted to hospital with malaria. This exploratory prospective study will collect data that may later justify further investment of resources leading to a deeper understanding of the pathophysiology.

The broad aims of this study are to gain more knowledge of the P. vivax infection in patients admitted to hospital with a diagnosis of malaria and to strengthen the research capacity at the RSUP and Cendrawasih University.

This study has four principal objectives:
1) To measure and characterise the burden of disease caused by P. vivax among hospitalised patients in a hyper endemic region.
2) To define the incidence, clinical characteristics, and risk of death of severe and complicated P. vivax malaria (having excluded other causes of fever).
3) To conduct exploratory analyses to compare and contrast the features of severe vivax malaria with severe P. falciparum and non-severe malaria.
4) To support the rational development of a longer-term prospective study to evaluate the demographic, nutritional, pharmacological, host genetic, parasite genetic and immunological risk factors for, and the treatment of, severe and complicated vivax malaria in north eastern Papua, Indonesia.

Project Progress and breakthroughs
Implementation of this project enabled us to prove that malaria vivax could in fact progress to forms as severe as those of falciparum malaria. Following rigorous diagnostic procedures and laboratory tests we proved that certain subjects that were infected with Plasmodium vivax developed a severe form of malaria without any concomitant infection with other species of parasite or a wide variety of other pathogens that could have possibly explained clinical illness (e.g., dengue fever, scrub typhus, leptospirosis, and others). These findings represent the first series of prospective cases reported of clearly defined severe vivax malaria. This work breaks the long-held conviction that vivax malaria is a rare and fastidious potential killer. We also found that the majority of the P. vivax causing severe malaria carried drug-resistant alleles. Several other new findings are in the process of verification through further laboratory examinations.

With regard to capacity building, this study successfully created a critical mass for clinical research activity in the University of Cenderawasih, particularly within the staff of the medical programme and the hospital. During the implementation of this study, we conducted a short course for Good Clinical and Laboratory Practice to all medical doctors, nurse and clinical laboratory technicians and microscopists in the hospital. Several results of this study have been disseminated to the local health community and medical practitioners.

Additional support and funding secured
The Li Ka Shing award had a profound impact on our competitiveness to apply for other international funding. The confidence of Oxford–Li Ka Shing Global Health Programme in our laboratories inspired the same in some other major donors. Thus far we have won the following research grants in the wake of the initial LKS funding:
The Bill and Melinda Gates Foundation (BMGF) for malaria control project in Sumba, Indonesia,
The Bill and Melinda Gates Foundation (BMGF) for Malaria Transmission Consortium (MTC), Indonesia
UNICEF: Malaria Elimination in Sabang Municipality, Indonesia (Contractor of the Mass blood Survey project)
UNICEF: Establishment of Quality assurance in Malaria Microscopy, in Aceh, Indonesia (Contractor of the project)
The Medicines for Malaria Venture for clinical trials of antimalarials.

New partnerships and collaborations formed
We have formed a partnership with colleagues in the A-Star Group in Singapore to investigate P. vivax phenotypes possibly linked to disease severity. We have also partnered with colleagues at Oxford University and at Karitas Hospital in Sumba, Indonesia to study the impact of human genetic factors on vivax malaria severe disease. This project enabled us to collaborate with the Paediatrics Department at Liaquat University (Hyderabad, Sindh Province, Pakistan) to help examine their high burden of severe disease caused by vivax malaria. Much of this work will also be a featured piece of the application for a Senior Investigator award to the Wellcome Trust by Dr Baird in 2011.

Publications and presentations


Asih PBS, Syafruddin D, Taylor RW, Blacksell S, Baso SM, Arunggear Y, Rohim A, Nurlela S, Nababan R, Baird JK. ‘Severe malaria vivax in Papua associated with multiple drug-resistant parasite.’ (Part of this study has been presented at the annual meeting of the American Society of Tropical Medicine and Hygiene in Washington, USA, November-December, 2009. Dr Puji BS Asih, one of the associated researchers in this project, won a Travel Award to attend the ASMTH meeting at New Orleans, USA to present this work).

It should be expressed that the research team has only very recently completed the complex battery of laboratory assays aimed at eliminating potential confounding by co-infections. The team fully anticipates the publication of at least four peer-reviewed papers in high calibre journals describing our findings.
7. Efficacy and safety of Dihydroartemisinin-Piperaquine (DHA-PQ, ARTEKIN™) for the treatment of malaria in Afghanistan in comparison with current standard treatment

Investigators
Dr Ghulam Rahim Awab, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand; Ministry of Public Health, Islamic Republic of Afghanistan, Kabul, Afghanistan
Dr Faizullah Kaker, Ministry of Public Health, Islamic Republic of Afghanistan, Kabul, Afghanistan
Professor Sasithon Pukrttayakamee, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Dr Mallika Imwong, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Professor Pratap Singhasivanon, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Dr Arjen Dondorp, Mahidol Oxford Clinical Research Unit, University of Oxford
Dr Charles Woodrow, Mahidol Oxford Clinical Research Unit, University of Oxford
Dr Sue Jean Lee, Mahidol Oxford Clinical Research Unit, University of Oxford
Professor Nicholas Day, Mahidol Oxford Clinical Research Unit, University of Oxford
Professor Nicholas White, Mahidol Oxford Clinical Research Unit, University of Oxford

Aims of the project
Malaria is a major public health problem in Afghanistan and continues to place an unacceptable burden on health and economic development. Currently the policy for malaria treatment in Afghanistan is artesunate plus sulfadoxine/primaquine (AS-SP) as the first-line treatment of slide confirmed *P. falciparum* malaria. For slide proven vivax malaria, chloroquine (CQ) is the treatment of choice. CQ-SP is the recommended treatment for presumptive malaria, and as diagnostic tests for malaria are usually unavailable most patients receive this. If dihydroartemisinin-piperaquine (DP) could be shown to be as good or better than CQ-SP for the treatment of vivax malaria, and as good as or better than AS-SP for falciparum malaria, then it would represent an excellent option for the treatment (including presumptive) of all malaria in the country. We aimed to conduct studies to assess the efficacy of DP in both vivax and falciparum malaria.

Project progress and breakthroughs
Two studies were started in 2007, one comparing DP with CQ in vivax malaria, the second comparing DP with AS-SP in falciparum malaria. Both were initiated in three geographically distinct sites (see map).

The first of these studies enrolled 536 patients with acute malaria caused by *P. vivax* randomising them to either CQ or DP. Patients were followed up weekly for 56 days. After 28 days the cure rate was 100% in both groups, but after that recurrent vivax infections began to occur. At 56 days, 8.9% of patients treated with CQ had developed a recurrent infection, compared with only 2.8% in the DHA-PQ group – a statistically significant difference. Both treatment regimens were well tolerated and no serious adverse events were reported. We concluded that both CQ and DP are efficacious treatments for vivax malaria in Afghanistan, but that in situations where ‘radical cure’ with primaquine...
cannot be given DP increases the period before relapses start to occur – so called ‘post-treatment prophylaxis’. Results from this study also provide the only efficacy data currently available from the Northwestern region of Afghanistan. Recruitment was completed in 2009, and the results were analysed, written up and published in 2010 in the Malaria Journal.

Because of a lower and reducing incidence of disease, it was not possible to obtain sufficient numbers of participants to complete the \textit{P. falciparum} study as originally planned. However the evidence we have so far is that both DP and AS-SP have very high efficacy against \textit{P. falciparum} in Afghanistan, and we are currently completing a single arm trial of AS-SP across Afghanistan (for which we have obtained WHO support).

Currently primaquine is still not routinely given to vivax malaria patients because of concerns that it may cause haemolysis and acute severe anaemia in individuals with a common genetic variant leading to deficiency of the enzyme G6PD. Having completed our study of acute \textit{P. vivax} treatment, in 2009 we began a third randomised controlled trial looking at the action of primaquine in preventing relapse in \textit{P. vivax} in Afghanistan. This is a very large trial involving long-term, longitudinal follow-up over 1-2 years of more than 500 subjects. This promises to determine the benefits of primaquine in preventing relapse in this population under typical field conditions.

During all these studies we collected samples for later analysis in Bangkok, including molecular studies of parasite and host, drug measurement and parasitological analysis that complement the trials themselves. We have also collected a large body of control blood samples from a wide range of ethnic groups within Afghanistan in order to look at the incidence of G6PD deficiency in these groups.

Additional support and funding secured
The Li Ka Shing funds enabled Dr Awab and his team to show that they could conduct high quality clinical malaria research in often difficult circumstances. This has leveraged support from the World Health Organization (WHO) for further trials in the treatment of falciparum malaria, and also from the Wellcome Trust for the ongoing studies on primaquine safety and efficacy in the treatment of vivax malaria.

New partnerships and collaborations
A new partnership has developed between the study team and WHO in Afghanistan.

### Publications and presentations


### 8. IMMUNOGENICITY OF INACTIVATED H5N1 VACCINE IN HUMANS

**Investigators**

Dr Xiaoning Xu, University of Oxford  
Professor Andrew McMichael, University of Oxford  
Dr Chris Li, University of Oxford  
Dr Hai Hong, University of Oxford  
Professor Yuelong Shu, Chinese Centre for Disease Control and Prevention, China  
Professor Xiaoping Dong, Chinese Centre for Disease Control and Prevention, China  
Dr Weidong Yin, Sinovac Ltd

**Aims of the project**

The aim of this project was to study the immunogenicity of adjuvanted H5N1 vaccine in healthy volunteers. About 300 healthy adults were immunised twice with alum adjuvanted H5N1 vaccine and their blood samples were assayed for neutralising antibodies and antigen-specific T cell responses. The findings of the project have had a significant impact on the immunogenicity of novel H5N1 antigens. Data showed that two immunisations with adjuvant were required to induce the immunogenicity required for licencing. Moreover, the projects mapped numerous T cell epitopes in human samples vaccinated with H5N1 and following natural H5N1 infection. These are invaluable in
vaccine validation and to facilitate novel vaccine development.

The project has led to enhanced training and communications between scientists in the UK and China. This has strengthened the relationships to include technical and management skills and establishes a framework to study other new infections such as the outbreak of pandemic H1N1 in 2009.

Project progress and breakthroughs
The H5N1 vaccine projects were completed and led to three peer-reviewed articles in PLOS Pathogens, PLOS One, Journal of Infectious Diseases. The project also laid down a framework to respond rapidly to new infections such as pandemic H1N1 when it emerged in 2009. The established relationship between the MRC Human Immunology Unit, Oxford University and China CDC led to a rapid response on pandemic vaccine study at the time of outbreak. Another three peer-reviewed articles in Vaccine, Clinical Infectious Disease, Journal of Medical Virology were published in 2010 with the generous support of the Li Ka Shing Foundation.

Scientifically, the project has mapped numerous T cell epitopes in human samples vaccinated with H5N1 and natural H5N1 infection. These are useful in the vaccine validation and novel vaccine development.

Additional support and funding secured
This project has led to funding from the MRC UK and Natural Science Foundation, China to cover the cost of clinical trials. A project entitled ‘Immunity correlates to an inactivated H5N1 vaccine in humans (number G0700647)’ was awarded to Xiaoning Xu by MRC UK. A similar grant was awarded to Professor Xiaoping Dong, China CDC by the Natural Science Foundation, China.

New partnerships and collaborations formed
The project has led to new partnerships with Professor Hualan Chen, Harbin Veterinary Institute and Professor Wuchun Cao, Institute of Microbiology, Beijing.
9. The clinical epidemiology of febrile illness (fever) in children in North Western Cambodia

Investigators
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Dr Chheng Kheng, Angkor Hospital for Children, Seam Reap, Cambodia
Dr Yos Pagnarith, Angkor Hospital for Children, Seam Reap, Cambodia
Ms Lina Sin, Angkor Hospital for Children, Seam Reap, Cambodia
Mr Hor Putchat, Angkor Hospital for Children, Seam Reap, Cambodia
Mr Bun Sen, Angkor Hospital for Children, Seam Reap, Cambodia
Ms Soeng Son, Angkor Hospital for Children, Seam Reap, Cambodia
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Mrs Vanaporn Wuthiekanun, MORU, Tropical Medicine Faculty, Mahidol University, Bangkok, Thailand
Mrs Premjit Amornchai, MORU, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
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Dr Catrin Moore, Mahidol Oxford Research Unit, Bangkok, Thailand, University of Oxford
Dr Emma Nickerson, MORU, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Dr Chris Parry, MORU, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Professor Sharon Peacock, MORU, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Professor Nicholas Day, Mahidol Oxford Research Unit, Bangkok, Thailand, University of Oxford
Aims of the project

Child mortality is unacceptably high in Cambodia, with 9% of all children dying before their fifth birthday. Most of these deaths are thought to be due to infectious causes, but there is little information from Cambodia on exactly which infectious diseases are responsible and what anti-infective drugs should be used to treat them.

The aim of this project is to provide this information for Siem Reap Province in Northwestern Cambodia, so that the treatment of children with serious infections can be improved. Specific aims of the project are to: A) build and support a clinical microbiology laboratory at the Angkor Hospital for Children (AHC), the provincial paediatric hospital; B) conduct clinical studies on the causes of serious infections in children attending AHC and in the communities from which they come; and C) through training and long-term support build capacity at AHC for the diagnosis and appropriate treatment of infections (a clinical microbiology service), and for the conduct of clinical research into clinical problems that are important in this clinical setting.

Project progress and breakthroughs

Capacity building and training

A successful collaboration has been established with Angkor Hospital for Children with a number of epidemiological and clinical studies completed or underway. A new microbiology lab has been built, equipped and staffed under a joint initiative between Oxford (funded by the Li Ka Shing Foundation) and AHC. The staffs of AHC have worked closely with collaborators from Thailand and Oxford to develop and expand the research agenda to address the most pressing clinical questions faced by this extremely resource-poor community.

There are now three full time microbiologists, trained in Thailand and Laos as part of the collaboration. The collaboration has also attracted funding from the Oxford Tropical Network Fund and from the North London Postgraduate Deanery to place a research physician and UK-trained microbiologist full-time in AHC, to help build sustainable research and microbiological capacity. In addition a promising young Cambodian doctor has been identified for training as a clinical microbiologist. A training course has been developed for him, with the help of one of the senior MORU clinical microbiologists.

Clinical studies and breakthroughs

Melioidosis is a devastating often fatal bacterial infection common in rice farming communities in Southeast Asia, though it has not previously been described in Cambodia. We showed that children seen at AHC often had antibodies in their blood to Burkholderia pseudomallei, the cause of melioidosis, suggesting that the bacterium is present in the soil in Cambodia and that children are often exposed to it. Once established, the microbiology laboratory was able to isolate the bacterium itself on multiple occasions from the blood of septic patients with suspected melioidosis, confirming for the first time that melioidosis is indeed a major clinical problem in Cambodia. These findings were presented in 2010 at a national conference held in Phnom Penh to raise awareness of melioidosis, and have since been written up and published.
Methicillin resistant *Staphylococcus aureus* (MRSA), the superbug which is the scourge of health systems in rich countries, was isolated from several patients, and typing suggested that these organisms may be derived from carriage of this resistant organism. An epidemiological study of the prevalence of MRSA in the community around Siem Reap has been completed, analysed and published. The results show that community-acquired MRSA is in fact a major public health problem.

A comprehensive clinical and laboratory study of the causes of fever in children attending AHC was carried out for one year from September 2009. The clinical data is currently being collated and patient samples are undergoing diagnostic reference testing. We hope to have provisional analysis completed by June 2011. This study, funded by the Li Ka Shing Foundation, will provide robust information on the causes of febrile illness in Cambodian children and, in the case of bacteria, their susceptibility to antibiotics. These results will inform decisions on the best empirical therapy for the treatment of these children in AHC and elsewhere in Northwestern Cambodia.

**Additional support and funding secured**

Support for new academic medical staff from the Oxford Tropical Network Fund and the North London Deanery has been established, and the development of the microbiology laboratory at AHC has enabled the hospital to leverage charitable donations from individuals and organisations to support both the lab and the associated programs.

**New partnerships and collaborations**

This project has strengthened the collaboration between AHC and Oxford, leading to a number of important research projects and capacity-building initiatives. We are also in active collaboration with the Cambodia-based and US-funded ‘Diagnostic Laboratory Development Program’ (DMDP).

**Impact on other research**

The development of the microbiology laboratory and associated research projects has catalysed the development of an active research agenda and a whole range of new projects at AHC.

**Publications and presentations**


10. HIV-SPECIFIC IMMUNITY IN A RURAL VILLAGE COHORT OF INFECTED AND EXPOSED UNINFECTED CHINESE PLASMA DONORS

Investigators
Professor Sarah Rowland-Jones, Weatherall Institute of Molecular Medicine, University of Oxford
Dr Tao Dong, Weatherall Institute of Molecular Medicine, University of Oxford
Dr Yong Hong Zhang, Weatherall Institute of Molecular Medicine, University of Oxford and Beijing YouAn Hospital
Professor KeYi Xu, Beijing DiTan Hospital
Professor HuiPing Yang, Beijing YouAn Hospital

Aims of the project
The aim of this project is to characterise the virology and immunology, looking at host-virus interactions, in a cohort of HIV-1-infected former plasma donors. Our work has identified that this is a highly unusual cohort, in which many of the confounding factors in most cohort studies (ethnicity, timing and route of infection and the infecting virus strain) are controlled. We have trained an excellent DPhil student, a Chinese physician Dr Yonghong Zhang, who has now returned to a senior position in one of the collaborating hospitals in Beijing, and we are currently training a second physician (from the other collaborating hospital).

Project progress and breakthroughs
We have made good progress to characterise the host-virus interactions in a village cohort of HIV-1-infected plasma donors, with the aim of defining correlates of protective immunity in HIV-1 infection. Studies of the pro-viral sequence (pol, nef and gag genes) in over 200 members of the cohort strongly suggest that donors in the (SM) village cohort were infected with same clade B HIV-1 viral strain. This has been confirmed by our collaborators in Perth, using criteria that meet forensic standards of proof. We have analysed the evolution of the virus under immune selection pressure by looking at whether or not viral mutations are associated with HLA type and we have identified many strong associations, which implies that T cell responses are playing an important role in shaping the virus. This area of research has been controversial and we expect our data to make a major contribution in the field. We have now written up these data and submitted our paper to a high profile journal for publication (Blood, under review).

We have also mapped T cell responses to HIV-1 in cohort members who have not yet started anti-retroviral therapy and have determined the immunodominance hierarchy in the cohort. We have focused particularly on studies of T-cell responses restricted through HLA alleles that are strongly associated with delayed disease progression and lower viral load in this cohort, such as HLA-B51 and B57. HLA-B51 is a very common class I HLA allele in Asian populations and therefore these data could be particularly useful for HIV-1 vaccine design and evaluation in the Chinese population. Our colleagues in Japan (Professor M. Takiguchi, Kumamoto) have shown that the prevailing
clade B virus has adapted to the high prevalence of B51 in that population by mutation of a B51-driven escape mutant to fixation (Journal of Immunology, under review). We are planning to extend these studies to other common HLA alleles in China, such as HLA-B40, B13 and A30.

We have recently recruited 279 healthy controls from a village near the SM village, who are deemed to be at low risk of HIV infection. These samples will be particularly valuable (as a controlled cohort) for determining potential genetic associations with HIV-1 infection and clinical outcome, since so many of the other sources of variability in outcome (such as viral strain, route and timing of infection) are controlled in our cohort.

Additional support and funding secured
As a result of the Oxford–Li Ka Shing Foundation’s support, Sarah Rowland-Jones has secured a strategic grant from the MRC (2009-2012), which specifically requested funding for a Chinese PhD student to work on this project from Ditan hospital. An application for further funding has been submitted to the MRC as a programme grant proposal.

New partnerships and collaborations formed
This project has allowed our Oxford–China collaborations to strengthen, and new collaborations have formed with investigators in the UK (Wellcome Trust, Sanger Institute, Cambridge UK) who are interested in host genetics and exome sequencing for ‘extreme phenotypes’.

Impact on other research
We are expanding our collaboration with China Beijing YouAn and Ditan infectious diseases hospitals in the area of HIV infection (with which most of the plasma donor cohort is infected).

Publications and presentations
We have presented our data in the form of posters and talks at several major international HIV meetings (Keystone symposium on HIV pathogenesis 2009, 2010, HIV Vaccine conference Paris 2009), with very positive feedback. Professor Sarah Rowland-Jones and Dr Tao Dong have been invited to give presentations at international conferences and seminars (Plenary talk (TD) at AIDS Global COE International Young Investigator Symposium; (Sarah Rowland-Jones): Keynote speaker, An integrated approach to research in infectious diseases, Ditan Hospital Beijing 2008, Keynote speaker Australian national HIV conference, Perth 2008).

Submitted papers:

Central Nervous System Infections and Tuberculosis in Cambodia

Investigators
Dr. Duong Veasna, Institut Pasteur, Cambodia
Professor Yit Sunnara, Kantha Bopha Hospital, Cambodia
Dr. Philippe Buchy, Institut Pasteur, Cambodia

Aims of the project
Meningoencephalitis (ME) is a major cause of mortality and long term neurological sequelae. It is among the most frequent and severe causes of paediatric hospitalisation across Asia (Wills et al., 2000). There are several causes of infections of the central nervous system (CNS), but the most common causes are infections by either bacteria or viruses. Despite the accessibility to molecular biology, the etiologies of CNS infections remain unknown in more than 70% of patients.

The aim of this project is to determine the viral and bacterial etiologies of meningoencephalitis in Cambodia, to define the clinical and epidemiological patterns of patients with meningoencephalitis, to determine the risk factors for mortality and severe sequelae, to describe the long term clinical and developmental outcome of patients (to be developed in the second phase since additional funds are necessary for this activity), to design diagnostic and therapeutic algorithms and to form a specimen bank which could serve for the identification of new or unusual pathogens. This project will provide the opportunity to train neurologists (a rare medical specialty in Cambodia) through the international programme for post-graduate physicians coordinated by the French Ministry of Foreign Affairs. Workshops and on-the-job training will be organized in participating sites by the Project Team. It would also be possible for individuals from this project to register for a PhD through the programme in Vietnam. The project will be an opportunity for Institut Pasteur in Cambodia (IPC) to provide training to staff from the National Institute of Public Health (NIPH) in virology and bacteriology. These personnel would subsequently be able to implement cascade training for lab technicians in peripheral hospitals (a potential site of the surveillance system).

Project progress and breakthroughs
For this preliminary pilot study, we aimed to recruit 150 children clinically diagnosed with encephalitis and admitted to Jayavarman VII hospital in Siem Reap, Cambodia. Between 19 July 2010 and 18 January 2011, 110 children were enrolled. The age average was 7.2 years old (ranging from 3.6 months to 14 years). The molecular detection techniques were used to detect major viruses (flaviviruses, enteroviruses, herpes simplex virus, cytomegalovirus, Epstein-Barr virus, influenza virus, and other viruses according to specific clinical symptoms) and bacteriae (Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis and streptococcus suis) responsible for encephalitis in our region (Le VT et al., 2010). Molecular methods (PCR/RT-PCR) were used to test the 110 patients and a pathogen was detected in 14 cases (13%) in the cerebrospinal fluid (CSF) and/or in plasma samples. The detection of anti-dengue (DENV) and anti-Japanese encephalitis (JEV) virus IgM antibodies in plasma and CSF was done using in-house serologies. In total, and by using both approaches, the identification of the cause of the disease was clearly established in 27% of cases and a ‘probable’ diagnostic was recognised in 18% of patients. The most common pathogen was JEV (n=23) followed by DENV (n=4), Enterovirus (n=1), Haemophilus influenzae (n=1) and...
Streptococcus pneumoniae (n=1). The most frequent ‘probable’ causative agents (cases where virus, bacteria or the IgM against the pathogen were found in plasma only) was JEV (n=5), DENV (n=5), undifferentiated flaviviruses (n=5) and Orientia tsutsugamushi (agent of the scrub typhus) (n=5).

This is the first study of the central nervous system infection in Cambodia and our preliminary results show that JEV is the major viral cause of encephalitis (similar to the study in Vietnam), (Le VN et al., 2010) followed by dengue and rarely enterovirus. Surprisingly, there was no other virus (herpes, etc) detected in these children, while they are common pathogens reported elsewhere in the literature. The bacteria detected in this study are common in meningoencephalitis except for O. tsutsugamushi. This has to be confirmed by other tests as this bacteria was not found in CSF. However, the etiology remains unknown in more than 50% encephalitis. The remaining unknown etiology was probably due to the non-exhaustive research for all potential infectious causes of encephalitis and in addition, undiagnosed encephalitis may be caused by unknown human or zoonotic pathogens. Therefore, efforts to identify novel or previously unrecognized pathogens in these undiagnosed patients are essential for future prevention and treatment strategies.

New partnerships and collaborations formed
This project has led to the establishment of a strong research partnership between Institut Pasteur in Cambodia (IPC) and the Oxford University Clinical Research Unit in Vietnam. The project has allowed us to strengthen the diagnostic capacities in order to address a major public health problem in Cambodia. The success of this project has brought a better collaboration between IPC and the biggest paediatric hospital in Cambodia (Kantha Bopha foundation). This close collaboration will undoubtedly facilitate future projects with this paediatric hospital. The regional workshop on encephalitis (held in May 2011) will provide additional opportunities to improve capacities and to seek new funds. This workshop could significantly improve the collaboration between IPC and the National Institute for Public Health Cambodia for the establishment of a national surveillance system for encephalitis in Cambodia.

Impact on other research
This project allowed us to obtain funds for a collaborative project between IPC, Institut Pasteur Paris and Institut Pasteur in Shanghai for a project entitled: ‘ACIP Pathogen discovery’. The objective of this project is to detect unknown pathogens in some patients hospitalised for encephalitis (and severe respiratory infection) in Cambodia and China, using a high throughput sequencing approach. Additional funds were also obtained to organize a workshop on encephalitis diagnostic standardisation in the region (Pasteur Institutes in Asia, Vietnam, WHO, etc.) in May 2011.

Publications and presentations
The preliminary result of this study was used as training report for a Master student in Public Health at École Pasteur-CNAM, France. The present results will be presented at the regional workshop on encephalitis which will be held at IPC, Phnom Penh in May 2011. A manuscript describing the results will be submitted for publication in 2011.
12. **Clinical Investigation of In-Vivo Susceptibility of P. Falciparum to Artesunate in Western Cambodia**

Formal Li Ka Shing funding finished in 2008 for the project below, but it continues to have an impact. Please see below for an update.

**Investigators**

Dr Duong Socheat, National Malaria Control Programme, Cambodia  
Dr Arjen Dondorp, University of Oxford and Mahidol University, Thailand  
Professor Nick White, University of Oxford and Mahidol University, Thailand  
Professor Nick Day, University of Oxford and Mahidol University, Thailand

**Project Update**

In the 2009 Annual Report, we presented the final report for this project, which had received a one-year grant from the Li Ka Shing Foundation. The clinical study that this funded concluded that the malaria parasite P. falciparum has in Western Cambodia become less susceptible to artesunate, the mainstay of antimalarial therapy worldwide but that this ‘artemisinin resistance’ had not yet spread to Northwestern Thailand. Since then, the full study has been published in the *New England Journal of Medicine*, and, as the most comprehensive study to date on this problem, it has massively raised the public profile of this important threat to global health. We are now part of a Bill & Melinda Gates Foundation-funded WHO-coordinated research collaboration aimed at tracking and containing artemisinin resistant malaria. The research work funded by the Li Ka Shing Foundation provided much of the rationale and stimulus for this important initiative. Artemisinin resistance is a true public health emergency, and the Li Ka Shing funding has allowed us to respond to it quickly and efficiently. No other grant source would have afforded us such flexibility.

**Funding**

The study in Pailin was funded by the Li Ka Shing Foundation. Following the initiation of this study, WHO provided funds to conduct the comparator study in Mae Sod and provided support for the Village Malaria Worker network run by CNM which identified cases for the study (grant number: WP/07/66224 CAM). As a result of the concern generated by the results of this study and of a study conducted by AFRIMS in nearby TaSanh, the Bill and Melinda Gates Foundation provided considerable financial support, through WHO, for a new Artemisinin Resistance Task Force, of which we are a part (Bill and Melinda Gates Foundation grant number: 48821). The development in malaria parasites of resistance to the artemisinin drugs, the mainstay of antimalarial treatment worldwide, is a potential global public health disaster. In 2007, we became aware of the possibility that such resistance may have developed along the Thai-Cambodian border. The Li Ka Shing funding for this project enabled us to respond rapidly to this emergency situation, set up and begin a clinical trial to confirm, or otherwise, the existence of the problem. The study we started back in 2007 yielded our 2009 New England Journal of Medicine paper, which confirmed and described the existence and clinical nature of reduced susceptibility to the artemisinins. Further funding followed for our studies but only because we were already working on the problem in the relatively remote part of Western Cambodia where it was thought to exist. This was possible only because of the rapid and timely availability of the Li Ka Shing Foundation funds; our initial funding source for what has become a major programme of research.

**New partnerships and collaborations formed**

This project led to our involvement in forming the WHO-coordinated, BMGF-funded ‘ARC3’ collaboration (Artemisinin Resistance Confirmation, Characterisation and Containment). This brings together research partners from across the region and from North America and Europe.

**Publications and presentations**

The results of this study were presented at the International Conference for Antimicrobial Agents and Chemotherapy in Washington DC in October 2008 and at the Meeting of the American Society of Tropical Medicine and Hygiene in New Orleans in December 2008.


The Responsive Fund

From 2007-2010 the Responsive Fund was used to respond to emerging health issues in Asia. The fund allocated seed funding to 10 of the original collaborative research projects, which enabled the projects to extend their research. The fund was also used to enable the start-up of a new one-year project entitled ‘Central Nervous Systems and Tuberculosis in Cambodia’ (details above).

The Responsive Fund also helped cover the cost of a full time Programme Officer, Laura Alexander, who facilitates the day-to-day management of the project and in particular is the Liaison Officer for all students and training activities supported through the University of Oxford–Li Ka Shing Global Health Programme.
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