Epidemiology & Public Health Unit (epi@ipc) 2011

The scientific activity report of the Epidemiology & Public Health Unit of the Institut Pasteur du Cambodge (epi@ipc) for the period January 1st to December 31st, 2011.

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This document provides a detailed overview of activities and programs conducted by the Epidemiology team of the Epidemiology and Public Health Unit of the Institut Pasteur in Cambodia for the Year 2011.

**Background**

The Institut Pasteur in Cambodia (IPC) is a Franco-Khmer, not-for-profit research organization created in 1953 to contribute to the diagnosis and study of infectious diseases and to their prevention, in close partnership with the country’s public health authorities. The epidemiology and public health unit was created in 1998 at the newly reopened Institut Pasteur du Cambodge.

Since then, the teams have dedicated themselves to research in the field of endemic and emerging or neglected infectious diseases, in close collaboration with internal (IPC laboratories) or external partners (national or international institutions).

The epidemiology and public health unit conducts descriptive or analytical studies (multivariate analyses on cross-sectional or case-control studies, prospective surveys, clinical studies and trials). In previous projects, modeling efforts have helped determine the burden of dengue or rabies in Cambodia, or dengue transmission patterns in the country. The Epidemiology unit has a long track record of collaboration with other disciplines, hosting a medical anthropologist or veterinarian PhD students and guest researchers from CIRAD or ANRS.

Over the years, research on endemic (e.g. HIV, tuberculosis, influenza, dengue…) or emerging / neglected diseases (rabies, A(H5N1), Melioidosis…) has helped assess the risk and burden for populations, evaluate the impact of intervention and guide policy or curricula. This is carried out by a dedicated team either through epidemiology-specific projects or transversal ones based on collaborations, with colleagues at IPC or external partners, both national (CDC-Cambodia, NAVRI, CNM, NCHADS) or international (Namru, WHO, NIH, US CDC, CIRAD, ESTHER, Vietnamese authorities for PAANTHER). The collaboration between human, animal and environmental health specialists will continue through several planned studies on rabies, A(H5N1), Nipah or leptospirosis, fostering a close relationship between the Institut Pasteur in Cambodia and existing and new international partners.

The Year 2011 was a year of transition for the Unit, with a new Coordinator to follow on the heritage and leadership of Dr. Sirenda Vong. In 2011, projects came to an end and were formally terminated (CAMELIA, NEA) but several others were initiated. Funding had been secured or was obtained in 2011 to initiate new research projects. These projects are summarized in Table 1 and detailed below.
### Table 1: Projects terminated or initiated in 2011 and partnerships.

<table>
<thead>
<tr>
<th>Name</th>
<th>Theme</th>
<th>Initiated</th>
<th>Status</th>
<th>Partner</th>
<th>Funding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dengue Kg Cham</strong></td>
<td>Dengue prospective study in the Cambodian rural setting</td>
<td>Jun-11</td>
<td>Ongoing analysis</td>
<td>Namru-2, CNM</td>
<td>Namru-2</td>
</tr>
<tr>
<td></td>
<td>Data analysis on discrepancies between X-ray interpretation in Cambodian hospitals</td>
<td>Apr-11</td>
<td>Complete d</td>
<td>Bourse Pierre Ledoux</td>
<td>Bourse Pierre Ledoux</td>
</tr>
<tr>
<td><strong>Stage Elodie Merlot</strong></td>
<td>Developing a diagnostic algorithm to improve the diagnosis of tuberculosis in HIV-infected children</td>
<td>Jul-11</td>
<td>Ongoing</td>
<td>ANRS, NPH</td>
<td>ANRS</td>
</tr>
<tr>
<td><strong>Paanther 12229</strong></td>
<td>Incidence and prevalence serostudy</td>
<td>Jul-11</td>
<td>Ongoing</td>
<td>IPC, WHO</td>
<td>WHO</td>
</tr>
<tr>
<td></td>
<td>Developing evidence-based national guidelines for community-acquired lower respiratory infections</td>
<td>Dec-11</td>
<td>Ongoing</td>
<td>MoH</td>
<td>SISEA</td>
</tr>
<tr>
<td><strong>Leptospirosis</strong></td>
<td>Investigating a mother and child cluster to rule out H2H transmission of A(H5N1)</td>
<td>Feb-11</td>
<td>Complete d</td>
<td>WHO</td>
<td>WHO</td>
</tr>
<tr>
<td></td>
<td>Case-control study to identify determinants of ambulatory vs. hospitalized influenza patients</td>
<td>Aug-11</td>
<td>Ongoing</td>
<td>Calmette, Takeo Hospitals</td>
<td>IMMI</td>
</tr>
<tr>
<td><strong>Cluster</strong></td>
<td>Lookback study in persons bitten by confirmed rabid dogs and documenting survival, by protocol completion.</td>
<td>Sep-11</td>
<td>Ongoing</td>
<td>CDC-Cam</td>
<td>Institut Pasteur</td>
</tr>
<tr>
<td><strong>IMMI Case-control study</strong></td>
<td>Prospective community-based study on age-specific dog bites incidence in humans</td>
<td>Jul-11</td>
<td>Analysis ongoing</td>
<td>None</td>
<td>Institut Pasteur</td>
</tr>
<tr>
<td><strong>Lookback study on rabies exposure</strong></td>
<td>Community based intervention to mitigate the spread of Zoonotic diseases in poultry and to human in South east Asia</td>
<td>Sep-09</td>
<td>Complete d Analysis ongoing</td>
<td>AVSF, Navri</td>
<td>WHO, AFD, IPC, DHHS, Cirad</td>
</tr>
</tbody>
</table>

The Epidemiology and Public Health Unit also dedicates time and effort to training in Cambodia. In 2011, IPC staff participated in a seminar on Good Clinical Practice and research ethics, organized and conducted by epidemiology staff and validated by on-line certification. Staff also contributed or participated to training programs on rabies for Cambodian clinicians, selection before mentoring of candidates to Cambodian CDC’s 2nd cohort of the Applied Epidemiology Training (AET) program, STATA training (Institut Pasteur Paris) or electronic surveillance (REDI). Epidemiology staff successfully presented
a PhD on A(H5N1) in Cambodia or a Master degree on Dengue epidemiology.

Networking with Cambodian partners has become yet closer. In the past year, staff at the Epidemiology and Public Health Unit have provided support, advice and expertise to the Ministry of Health (Technical Working Group on Zoonoses, on Infectious Diseases), to the National Dengue Control Program (elaboration of Dengue bulletin, support to develop a control strategy for Chikungunya), to the National Institute of Public Health (Epidemiology international consultative meeting on MSc. program development of the school of public health, preparation of the World Rabies Day manifestations) or NCHADS (workshop on Cambodia HIV/AIDS estimations and projections). Team members have also been invited by WHO and Cambodian authorities to help elaborate a national policy for the control of zoonoses.

Several events gave rise to epidemiological reports distributed within IPC and to National or International partners. Furthermore, the scientific excellence of the research conducted in the Epidemiology and Public Health unit was validated and recognized by numerous scientific communications at workshops, scientific conferences, in books or peer-reviewed, referenced scientific publications. These are detailed at the end of this report.

**Projects initiated**

**Prospective cohort study on Dengue in Kompong Cham villages**

This study is a prospective, community-based surveillance for febrile illness during the dengue epidemic season in 14 villages in Kampong Cham Province, Cambodia. It is conducted in collaboration with and thanks to a grant from NAMRU-2. The cohort population is subjects aged ≤30 years (around 6,000 people). The study period goes from June 2011 to June 2012 with field investigations conducted during 6 months from Jun to Nov 2011. There were two components in this study: Fever Investigation and Outbreak Investigation around confirmed dengue cases. NS1 rapid test kits were used for onsite screening of dengue infection among incident fever cases. All specimens were shipped to Institut Pasteur in Phnom Penh for testing (serology, virus detection and isolation). During the study period, more than 1000 febrile cases of which around 50 confirmed dengue cases were documented (preliminary results). Of these, 70% were asymptomatic cases. The expected outcomes are to document the incidence of dengue infection, dengue fever, and dengue hemorrhagic fever in the population ≤ 30 years old, determine the clinical/epidemiological characteristics of DF as well as the frequency and spectrum of infection caused by dengue virus infection (including asymptomatic cases). Finally, immune correlates of protection and pathogenicity are being studied.

**Investigation of a mother-and-child A(H5N1) cluster with suspected H2H transmission**

The A(H5N1) influenza virus remains a possible candidate for the emergence of a pandemic influenza strain. A mother and her child acquired fatal A(H5N1) infection in Prey Veng Province, Cambodia, in February 2011. A cluster investigation was conducted by WHO and IPC epidemiologists. Careful interviews found that there was no evidence of human-to-human transmission between the mother and her child. Blood samples were collected from the family members. Questionnaires were completed and a
family tree was drawn. All these survivors were exposed to the A(H5N1) common source but did not become infected. There was therefore no evidence in favor of the emergence of an A(H5N1) strain with enhanced interhuman transmissibility.

**IMMI case-control study on severity factors for influenza infection**

A prospective case-control study is under way to identify the epidemiological, clinical, bacteriological, virological and immunological determinants of influenza severity including A (H1N1)pdm infection in a developing country. This study is being conducted in Asia (Cambodia) and Africa (Cameroon, Madagascar, Senegal), comparing hospitalized patients to outpatients with lab--confirmed influenza.

**Leptospirosis study**

Cambodia and neighboring countries have been considered endemic for leptospirosis although surveillance does not exist and incidence data are lacking. Thanks to a grant from the World Health Organization, the study conducted anonymous, unlinked testing for antibodies to Leptospira spp and PCR on paired sera of Cambodian patients with fever illnesses. These patients were part of a cohort of villagers <20 years of age residing in urban and rural areas of Kampong Cham province, Cambodia. The serostudy conducted by IPC’s bacteriology team bore on a randomly selected subset of 2359 (33%) among the sampled subjects. Of these 2359, a total of 99 (4.20%) returned positive while they were found seronegative on an early sample. The overall estimated attack rate for symptomatic leptospirosis in Kampong Cham villages during 2007-2009 was therefore 1.4% (varying from 1.21% to 1.56%, depending on the year). Preliminary results show the importance of leptospirosis among patients with fever residing in Kampong Cham province during the years 2007-2009. These preliminary data are being further explored through detailed statistical analyses.

**Consensus guidelines for the management of community-acquired, bacterial acute lower-respiratory infection (CABALRI) in Cambodia**

The epidemiology unit at IPC played a pivotal role during the SISEA study, an Agence Française de Développement (AFD)-funded project aiming to document respiratory illness in South-East Asia between 2007 and 2009. This project helped document the epidemiology of bacterial acute lower respiratory tract infections (ALRI) in Cambodian hospitals, as well as that of HMPV or melioidosis. It also provided an opportunity to capacitate and train clinical and laboratory staff in Cambodian hospitals. Based on the data and experience accumulated at IPC and elsewhere, an AFD-funded literature review and the development of diagnostic algorithms will help develop probabilistic antibiotherapy guidelines adapted to the Cambodian situation. This effort is part of a national review of treatment guidelines in Cambodian hospitals, with an expected delivery in June 2012.

**Paanther ANRS 12229**

TB incidence is high in Cambodia, including in children. Diagnosing TB in children is difficult, and is even more so in case of HIV infection, in a situation of very high morbidity and mortality and major therapeutic and care issues. Improved diagnostic criteria are urgently needed, especially in the context of expanded access to therapies which should change the clinical presentation, and in the context of the emergence of multi and extra drug-resistant tuberculosis. Paanther is a multicentre diagnosis study conducted thanks to a grant by ANRS. It is based on a longitudinal and prospective follow-up of a cohort of 315 HIV-infected children suspect of intra-thoracic TB, diagnosed and treated according to national guidelines after
clinical, radiological and bacteriological characterization. The aim is to develop a diagnostic algorithm to improve the diagnosis of tuberculosis in HIV-infected children in the context of developing countries with high tuberculosis endemicity. The study is ongoing.

Lookback study on survival after PEP for confirmed rabid dog bites

Between 2000 and 1st November 2011, a total of 189,000 referrals were documented for type of injury, post-exposure prophylaxis (PEP) and entered in a database. Of these, over 1,300 were exposed to a confirmed rabid dog. To our knowledge, two deaths were documented, the last of which was investigated by the Unit in April 2011. Thanks to a grant from the Institut Pasteur in Paris, a retrospective epidemiological study has been undertaken to document: 1/ what became of those with a full course of PEP using i.d. Vero cell vaccine after being bitten by a confirmed rabid dog; and 2/ to compare their outcome with those who did not complete a full course. Results of this study could have direct and far-reaching implications in global public health, helping determine the number of injections that are needed to avoid rabies deaths in any setting. It could provide pragmatic and operational information on what geographic distance is a threshold beyond which exposed people find it difficult to come for successive injections. This distance is where secondary rabies sites should be created.

Women reproductive health care issues in the ANRS 12095 CIPRA kh001 CAMELIA clinical trial an anthropological approach (nov 2010-march 2012)

All HIV-infected women involved in ANRS 12095 CIPRA KH001 CAMELIA CLINICAL TRIAL were requested to use a double contraception method including condoms during the trial. Despite this strong requirement stated in the consent form, as of April 1st, 2009, 10 women enrolled in the CAMELIA trial became pregnant. Based on an ongoing ethnographical research (including in depth interviews, focus groups and observations), the aim of this study was to examine socio cultural dimensions of reproductive health (or on birth control and procreation) among women in childbearing age enrolled in the CAMELIA Clinical Trial. Results show how the clinical trial shapes various social forms of reproductive practices that are reinterpreted and negotiated locally. For example, we describe why Camelia patients do not always disclose their HIV status to their partner and the social implications of such a decision. We describe and analyze how patients dealt simultaneously with the study medical team recommendations regarding contraception and various other private issues that lead them not to follow them. This study provides knowledge on reproductive health experiences and needs of PLWH useful to design prevention and treatment activities. It also demonstrates the relevance of a multidisciplinary approach when implementing innovative medical programs.

Dogbites incidence study

This study was conducted as a baseline for a cluster-intervention canine rabies vaccine-efficacy trial. It documented the age-specific incidence of dog bites in a rural community of Siem Reap Province. Over a 6-months period, 50 bites were documented in over 400 persons, with a gross estimated incidence of approximately 0.25 bites per person-year in rural Cambodia. The results are being analyzed.
Training of epi@ipc staff

- Ith Leakhena: “Reproductive Experience For Women Living With HIV In Cambodia” Master in Socio anthropology, Royal University of Phnom Phen
- Chheng Youpheng: “Reproductive Health Needs of People Living With HIV In Cambodia Caregivers And Counselors Perspectives”. Master in Socio anthropology,Royal University of Phnom Phen
- Hun Chenda: “Perspective of Men living with HIV toward Reproductive Health: An Anthropological Approach”. Master in Socio anthropology,Royal University of Phnom Phen
- Ly Sovath. « facteurs de risques de transmission du virus d’influenza aviaire hautement pathogène a(h5n1) à l’homme ». These pour obtenir le grade de docteur en sciences. Université Montpellier II Sciences et Techniques du Languedoc en cotutelle avec l’Université des Sciences de la Santé, Cambodge, presented on 7 december 2011.
- Ly Sovath – WPRO/CDC Writing Workshop, April 4th – 8th 2011, Seoul, Korea

Training by epi@ipc staff

- GCP training of 35 IPC staff by Epidemiology & Public Health staff, 04-05/08/2011, followed by on-line validation and certification.
- Training for 20 SISEA (Kompong Cham and Takeo hospital) clinicians to interpret chest x-rays in adults (6-7/10/2011) and in children (14/11/2011)
- Several training sessions on rabies risks and prevention for clinicians
- Joint (IP Paris/IPC) Regional training on data analysis using STATA, Monday 16 May – Friday 27 May, Institut Pasteur du Cambodge, Phnom Penh (Cambodia)

Scientific workshops

- Participation and presentation of Cambodia data at Asian Rabies Experts’ Bureau (AREB), Pattaya, Thailand, 5-9 December
- Scientific Conference and 120th Anniversary Ceremony of IP HCMC in 17th -18th November, 2011.
- International symposium on «Surveillance and discovery on respiratory and other emerging infectious diseases», May 29-31, 2011. Phnom Penh, Cambodia. Several presentations and chairing of a session Présidence d’une session
- Electronic Disease Surveillance in Resource Limited Countries: The Role of Public Health Informatics, 11-13 October, 2011, Siem Reap, Cambodia. Presentation on IPC.
- Second SISEA regional workshop on encephalitis " May 5-6, 2011, Phnom Penh, Cambodia.
Other workshops

Pasteur Directors’ & Epidemiologists’ reunion, Institut Pasteur, Paris, 28-30 March 2011

Participation to IRD Chiangmai’s Strategic Orientation Committee meeting, Chiangmai, Thailand, June 23-24, 2011

National HIV/AIDS projection to 2015 workshop, 5-9 Sept 2011, Phnom Penh, Cambodia


IMMI project meeting and presentation of IPC data, Nov. 4, 2011, Paris, France.

Workshop on Australian-funded research in Vietnam and possibility for collaboration in Cambodia, Nov. 16, 2011.

The 1st Ecohealth network meeting, Koh Chang, Thailand, 29-31 January 2011


Patient-centered approach to manage tuberculosis. 5-day CENAT workshop, Phnom Penh, October 2011.

In 2011, collaborative projects, planned cooperations, scientific meetings or reunions interfaced the Epidemiology and Public Health Unit of the Institut Pasteur in Cambodia with the following partners:

National authorities
Cambodian CDC, Ministry of Health, Cambodia
Department of Hospital Services, Ministry of Health, Cambodia
NAVRI, Cambodia
NCHADS, Cambodia
NIPH, Cambodia
National partners
Angkor hospital for children
Calmette hospital
Kantha Bopha hospital
Khmero-Soviet hospital
Kompong Cham hospital
National pediatric hospital
Takeo hospital
International partners in Cambodia
FAO, Cambodia

NAMRU-2
US CDC
WHO Cambodia
International partners abroad
Amsterdam Institute for Social Science Research, Amsterdam University,
ANRS
Centre for Population Health Sciences, The University of Edinburgh
Institut Pasteur, HCMC, Vietnam
Institut Pasteur, Paris
IMMI
IRD
IRD, UMI 233
LSHTM
OIE
REDI
Communications at scientific meetings


3. P. Hancart-Petitet. Dealing with the “medically non recommended” pregnancies: Genealogies, social arrangements and jagged story-lines within the CAMELIA Clinical Trial, Cambodia.


10. S. Vong, B. Guillard, L. Borand, B. Rammaert, S. Goyet, V. Te, P. Try, S. Hem, S. Ly, P. Cavailler, C. Mayaud, P. Buchy : First data on etiologies of acute respiratory infection in Cambodia. Surveillance and Discovery in Respiratory and Other Emerging Infectious
Diseases International Workshop, 29-31May 2011, Phnom Penh, Cambodia.


Referenced, peer-reviewed publications


18. Dealing with the “medically non recommended” pregnancies: Genealogies, social arrangements and jagged story-lines within the CAMELIA Clinical Trial, Cambodia.
Pascale Hancart Petitet. Dans Hardon A. Pluralism in medical system. Special Issue Anthropology and Medecine (accepted).


**Book chapters**

1. La « pilule chinoise » au Cambodge contraception médicamenteuse en milieu informel de soins. Dans Desclaux A et Egrot M. Le Médicament à ses marges dans les pays du Sud (accepted).

For the Epidemiology and Public Health team at the Institut Pasteur du Cambodge,

Phnom Penh, 31/01/2012

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