



**Pan American
Health
Organization**



Regional Office of the
World Health Organization

Information on
PAHO/WHO Collaborating Centers and
National Reference Laboratories
in the Americas
that work with Dengue

Pasteur Institute, French Guiana



INSTITUT PASTEUR
DE LA GUYANE

Caribbean Subregion, Americas Region

Photo of the Institution



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Web Link to Institution

<http://www.pasteur-international.org/>

<http://www.pasteur.fr/sante/clre/cadrecnr/arboguy-index.html>

Brief Historical Outline of the Origins/Foundation of the Institution

Institut Pasteur's international initiatives in the areas of research, public health, and education are a fundamental part of its mission. Since its creation, Institut Pasteur has had an international mission. In 1887, Institut Pasteur's new laboratories in Paris allowed Louis Pasteur to build an extensive, already-international team of scientists. Thus, students and Pasteur scientists scattered across the globe to continue their work.

A unique organization, the Institut Pasteur International Network unites close to 10,000 staff from 30 institutions (including eight WHO Collaborating Centers) spread across five continents. The Network is dedicated to the surveillance, prevention and treatment of infectious diseases through biological research, education, and public-health activities.

The Institut Pasteur de la Guyane (IPG) was created in 1940 and belongs to the Institut Pasteur International Network. IPG is currently involved with the study of infectious diseases caused by parasites (e.g. malaria and leishmaniasis), bacteria (mycobacteria) or viruses (e.g. retroviruses and arboviruses).

Functions

Since 1981, the IPS Virology Laboratory has been the National Reference Center for Arboviruses and the Influenza virus, in charge of arbovirus surveillance in French Guiana and the French Antilles (West Indies). This surveillance of arboviruses is based upon laboratory diagnosis within a laboratory network. The main viruses concerned are flaviviruses and alphaviruses, all of importance in human pathology. Since 2004, this laboratory has also ensured activities involving serological and virological expertise for the laboratories located in the French Caribbean (Guadeloupe & Martinique), as well as Suriname.

The surveillance of arboviruses is also based on a syndromic surveillance system managed in collaboration with the IPG Epidemiology Unit and local and regional health authorities. The complementarity of biological and syndromic surveillance allows for a rational, specific system, the usefulness of which was highlighted during the last dengue fever outbreak in French Guiana in 2006.

Activities Developed in 2005–2006

The DENFRAME project entitled "Innovative Diagnostic Tools & Therapeutic Approaches for Dengue" is directed at the development of new diagnostic tools and therapeutic approaches for dengue fever. The main aim of the DENFRAME project is to improve the management of dengue in the human populations of Latin America and Asia. The DENFRAME Consortium, supported by the 6th Framework Programme of the European Community (FP6 – 2003- INCO – DEV2 – 517711), consists of a framework of 13 partners based in Asia (Cambodia, China and Hong Kong, Viet Nam), Europe (Belgium, France, Germany, the United Kingdom and one associated country, Israel), and Latin America (Argentina, Brazil, French Guiana, Mexico). The scientific coordination of the DENFRAME Consortium is ensured by the Institut Pasteur in Paris (France) and three regional coordinators (based in Cambodia, and French Guiana, with the National Reference Center for Arboviruses at the IPG, and the United Kingdom) supported the partners at regional level. The DENFRAME project, which began in November 2005, includes two complementary work programmes:

- The first one focuses on medical virology with the study of dengue cases among patients and members of their household. The primary objective is to standardize a collection of well-characterized sequential clinical data and biological samples from dengue patients living in Asia (Cambodia and Viet Nam) and Latin America (Brazil and French Guiana) with different dengue patterns. The secondary objectives are to
 - to standardize the procedures for current diagnostical assays through the implementation of inter-laboratory control procedures;
 - establish a bank of clinical samples to validate rapid and sensitive antigen detection and serological tests using ligand binding molecules and chemiluminescent biosensor techniques; and, at the same time,
 - establish the proportion of none or pauci-symptomatic dengue infections among household members; and
 - identify the biological prognosis markers involved in the disease severity (with estimations to be established in collaboration with WHO/TDR).
- The second work program is aimed at
 - developing an integrated approach for understanding the DV-host interaction, one which focuses on key components of innate immunity to DV infection;
 - identify potential therapeutic agents (small molecule inhibitors);
 - identify lead compounds with anti-DV activity, using two existing libraries for screening, one based in Europe and one in Asia (with compounds isolated from Chinese Traditional Medicine).

The tasks are carried out by the concerted efforts of the different groups utilizing their complementary skills and experience. This multidisciplinary strategy will establish the framework used to implement new diagnostic tools and test future therapeutic molecules. It represents a critical new collaborative approach that will underpin ongoing efforts to combat this major public-health problem. More information is available on www.denframe.org.

Research's Folder

The **National Reference Center for Arboviruses and Influenza** receives financial support from the French Ministry of Health.

Analysis of Dengue Spatial and Temporal Patterns Using a Geographic Information System: The Case of an Outbreak in Iracoubo, French Guiana, 2001: With the purpose of studying a 2001 dengue fever outbreak in Iracoubo, French Guiana, we recorded the location of all patients' homes and the date when symptoms were first observed. A geographic information system (GIS) was used to integrate patient-related information. The Knox test, a classic space-time analysis technique, was used to detect spatiotemporal clustering. Analysis of the relative-risk (RR) variations when space and time distances varied, highlighted the maximum space and time extent of a dengue transmission focus. The results show that heterogeneity in the RR variations in space and time corresponds to known entomologic and epidemiologic factors, such as the mosquito feeding cycle and host-seeking behavior. These findings demonstrate the relevance and potential of the use of GIS and spatial statistics for elaborating a dengue fever surveillance system.

Discrimination between Primary and Secondary Dengue Virus Infection by an Immunoglobulin G Avidity Test Using a Single Acute Phase Serum: For clinical and epidemiological purposes, classifying serological responses during dengue virus infection is a necessity. Thus, it is important to develop a test that can distinguish between primary and secondary serological responses. We developed an enzyme-linked immunosorbent assay (ELISA) based on changes in the avidity of immunoglobulin G (IgG) during the infectious episode. By analyzing blood samples collected between the third and seventh day of the illness, during which most clinical complications occur, the sensitivity and specificity of the test were respectively 95.1% and 80.0%. This simple rapid test appears to be an excellent alternative to the HI test for discriminating between primary and secondary dengue virus infection during the acute phase of dengue.

Re-Emergence of Dengue Virus Type 4 in the French Antilles and French Guiana in 2004–2005 After ten years of absence, dengue virus type 4 (DEN-4) has recently re-emerged in Martinique, Guadeloupe, and French Guiana. Phylogenetic analyses of the strains from 2004–2005 showed that

they all belong to the DENV-4 genotype II, but to a cluster different from the strains from 1993–1995. The French Antilles experienced a major epidemic ten months after DEN-4 re-emerged, while DEN-4 infection remained sporadic in French Guiana.

Evaluation of an Enzyme Immunoassay for Detection of the Dengue Virus NS1 Antigen in Human Serum : We evaluated a one-step sandwich-format microplate enzyme immunoassay for detecting dengue virus NS1 antigen in human serum, using Platelia™ Dengue NS1 Antigen (Ag) kits (Bio-Rad Laboratories, Marnes La Coquette, France). The sensitivity of the Platelia™ Dengue NS1 Ag was 88.7%. None of the serum samples from patients not infected with the dengue virus tested positive with the Platelia™ Dengue NS1 Ag kit. A diagnostic strategy combining Platelia™ Dengue NS1 Ag for acute-phase sera and MAC-ELISA for early convalescence-phase sera only increased sensitivity from 88.7% to 91.9%. Thus, NS1 antigen detection with the Platelia™ Dengue NS1 Ag kit could be used for first-line testing for acute dengue infection in clinical diagnostic laboratories.

Capillary Blood Samples: New Approach for Dengue Infection Diagnosis: We evaluated the use of capillary blood samples stored on filter papers for diagnosis of dengue virus. We compared the performance of standard reference methods using capillary blood samples absorbed onto filter papers versus venous blood samples. The resulting sensitivity, specificity, and positive predictive value of tests performed on filter paper compared to those performed on venous blood samples were 81.6%, 90.7%, and 92.5%. During the acute phase of dengue infection (day 1 to day 4), the tests performed on capillary blood samples had a sensitivity of 88.5% and a specificity of 93.8%. Capillary blood samples could therefore be a good alternative for the diagnosis of dengue infection in tropical areas. Indeed, these samples are convenient for storage and transport without the need for a cold chain, and simplify the collection of samples from children.

National and Regional Links

- Cellules de Veille Sanitaire (CVS) – Direction de la Santé et du Développement Social de Guyane (www.guyane.pref.gouv.fr/sante/), de la Martinique (www.martinique.sante.gouv.fr/), et de la Guadeloupe (<http://www.guadeloupe.pref.gouv.fr/>).
- Cellule Inter-Regionale d'Epidémiologie Antilles-Guyane (CIRE), Fort de France, Martinique.
- Laboratoire de Virologie-Immunologie, Centre Hospitalier Universitaire de Fort de France, Martinique.
- Laboratoire de Microbiologie, [Centre Hospitalier Universitaire des Abymes](http://www.chu-abymes.gw.fr/), Pointe à Pitre, Guadeloupe.
- Department of Arbovirology and Hemorrhagic Fevers, WHO Collaborating Center for Arbovirus Reference & Research, Instituto Evandro Chagas Secretaria de Vigilância em Saude, Ministerio da Saude, Belém, Brazil (<http://www.iec.pa.gov.br/>).
- Virology laboratory and EPI laboratory, Caribbean Epidemiology Centre ([CAREC/OPS](http://www.carec.org/)), Port of Spain - Trinidad & Tobago.
- Central Laboratory, [Bureau voor Openbare Gezondheidszorg](http://www.bog.sr.gov/) (BOG) Paramaribo, Suriname.
- Institut Pasteur, Paris: Unité d'Epidémiologie des Maladies Emergentes, Unité postulante interaction moléculaire Flavivirus-Hôtes, Département de Virologie, (<http://www.pasteur.fr/>).
- Unité de biologie des infections virales émergentes (UBIVE) et CNR des arbovirus et fièvres hémorragiques virales, [Centre de recherche Mérieux Pasteur](http://www.cmrp.pasteur.fr/), Lyon.
- Génétique et évolution des maladies infectieuses UMR CNRS-IRD 2724, Montpellier (<http://gemi.mpl.ird.fr/cepm/index.htm>).

Questionnaire for Collaborating Centers and National Reference Laboratories for Diagnosing Dengue

See form filled out by IPG at <http://www.paho.org/english/ad/dpc/cd/den-cc-ipg-ques.pdf>