

PASTEUR PERSPECTIVES

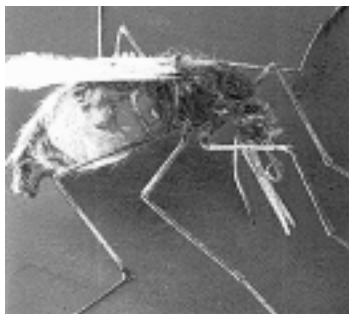
THE NEWSLETTER OF THE PASTEUR FOUNDATION DEVOTED TO THE WORLD OF THE INSTITUT PASTEUR

THE CUTTING EDGE

by Caitlin Hawke

FOCUS ON VECTORS AND MALARIA

Ticks and mosquitoes. Few readers will like the sound of those two words. Indeed, the very idea of providing the next bloodmeal for either of these two disease vectors makes most of us wince. Vectors are organisms that transmit pathological agents (viruses, bacteria, protozoa, etc.) from one host organism (a bird or a deer, for example) to another (i.e., a human). Other common vectors include lice, fleas and flies. Lyme disease (transmitted by ticks) and West Nile fever (transmitted by mos-



Anopheles gambiae,
the mosquito that transmits malaria

quitoes) are two illnesses that have unfortunately made headlines along the Eastern seaboard. There are other examples: as recently as last September, there was a Long Island case of malaria reported in *The New York Times*, and at the end of March the Federal Centers for Disease Control and Prevention reported a 70% increase in U.S. cases of the mosquito-borne tropical disease dengue fever, with New York, a primary port of entry, weighing in as the state with the highest occurrence rate. These are perfect examples of how our modern lifestyle, with its incredible ease of travel, has effectively struck down the natural barriers to the spread of disease.

A Look at West Nile Virus

While tropical vector-borne diseases still pose only a minor risk to Americans, the current appearance of West Nile virus demonstrates the reality of their threat. The New York area outbreak claimed seven lives last year and in March it was reported that up to 1,900 people in Queens, New York, were infected. Alarmingly, this outbreak is the first documented occurrence of West Nile in the Western Hemisphere. At worst, this virus can cause encephalitis, an often fatal swelling of the brain. However, more commonly

A Message from the Director General of the Institut Pasteur

Dear Readers:

Having just been appointed director general of the Institut Pasteur, I consider it a great honor to write to you—our loyal American-based friends—for the first time. Our institute has been privileged to enjoy American philanthropy since 1887, when admirers of Louis Pasteur's work, including Gordon Bennett, editor of *The New York Herald Tribune*, contributed to an international fund to establish the Institut Pasteur. The most recent example of American support is a major grant from the Florence Gould Foundation for construction of a laboratory to be completed shortly, which will be devoted to the study of highly contagious agents.



Philippe Kourilsky


Since it was founded, the Institut Pasteur has had three major vocations: biological research (focused mainly on infectious diseases but also including allergies, genetic diseases and cancer), public health applications arising from this research, and teaching. As director general, my foremost and unyielding aim shall be the pursuit of excellence in biological and, above all, microbiological research to improve the health of humanity.

Excellence in research is strictly correlated to the quality of and capacity for innovation on the part of our researchers, as well as to the technical facilities at their disposal. Your support is crucial in helping to ensure that our scientists have access to the finest equipment available in order to fulfill the mission defined by Pasteur himself.

For this, I express my hearty thanks to you.

Avec toute notre reconnaissance.

Yours sincerely,



Philippe Kourilsky
Director General



the illness is short-lived and milder, provoking flu-like symptoms and resulting in lifelong immunity.

This season, American public health officials are gearing up to combat it by way of mosquito control starting with a public awareness campaign to eliminate all sources of standing water where the insects breed. According to the *Times*, the mosquitoes that tend to carry the West Nile virus (various species of the *Culex* genus) are most active in late summer, which is when the magnitude of the problem will be determined. Understanding the lifecycle of a vector is key to combating the disease it transmits; killing larvae and reducing breeding grounds can successfully interrupt the propagation of insects. Experts feel that this season will be crucial in determining whether the West Nile virus establishes itself in this country for the long term.

Malaria

From *mal*, meaning “bad,” and *aria*, as in “air,” this mosquito-borne disease was named for the odor of stagnant water that attracts its vectors. It is endemic to Africa, where the vast majority of cases arise. A Harvard University study presented in late April analyzed the economic effect of the disease on Africa’s gross domestic product; it estimated that today’s GDP of \$300 billion would have risen to \$400 billion had malaria been eliminated in 1965.

For most Westerners, it is an all-but-forgotten tropical disease; however, during the American Civil War, there were 1.3 million cases and 10,000 deaths in the Union Army. Though it was virtually eliminated in the U.S. in the 1940s, the disease remains a major international health problem, with 2 billion people having been exposed to it worldwide and 200 to 500 million clinical cases each year resulting in 1 to 3 million deaths. Young children—particularly in sub-Saharan Africa—are its primary victims.

Chloroquine, the least expensive and most widely used treatment, is no longer effective since the malarial parasite has evolved into resistant strains. The development of resistance—not only of the parasite to such widely available drugs but also of the mosquito to insecticides—has set back control of this disease. The development of a malaria vaccine has proven elusive given the global variations of the parasite and its transmissibility.

The Three Genomic Elements of Malaria

Malaria is caused by a single-cell protozoan discovered in 1880 by Alphonse Laveran. Laveran, who later became a Pasteur scientist, was awarded the 1907 Nobel Prize in Physiology and Medicine “in recognition of his work on the role played by protozoa in causing diseases.” The most fatal and widespread species is *Plasmodium falciparum*. The parasite invades the red blood cells of vertebrate hosts (i.e., humans) and is spread from host to host by the mosquito *Anopheles gambiae*. Therefore, a full basic scientific understanding—not only of the protozoan but also of the mosquito—is necessary to best combat the disease.

Projects analyzing the human and malaria parasite genome have made significant progress. A team of Pasteur scientists in collaboration with the French Genoscope is preparing to decode the *Anopheles gambiae* genome—the third player in the transmission of the disease. It is an enormous undertaking, entailing the sequencing of 260 million nucleotide bases, isolating some 13,000 mosquito genes on three chromosomes and analyzing their functions.

Spearheaded by two young Americans, Charles Roth and Paul Brey, the Pasteur project aims to identify mosquito genes that code for the insect’s immunity to the parasite, its resistance to insecticides, its behavior, and, in general, the genes that have an effect on the ability of the malaria parasite to complete its lifecycle in the mosquito. Understanding these factors will help to curtail the vector’s capacity to spread the disease. The project will take three years to complete and will cost \$50 million.

The Role of *Anopheles gambiae* in the Parasite Lifecycle

When an infected female mosquito takes her bloodmeal from a human, she injects her saliva containing the plasmodia in their sporozoite stage, which will in turn invade the human host’s liver cells and proliferate asexually into thousands of merozoite-stage parasites that will invade the host’s red blood cells. Soon the rate of proliferation decreases and the merozoites produce gametocytes, the precursors to male and female parasites. When the next female mosquito takes a bloodmeal from this individual, the gametocytes will become male and female gametes in the mosquito’s stomach, where they will fertilize, form a zygote and subsequently proliferate into several thousand sporozoites. These organisms will then migrate back to the salivary glands of the mosquito ready to recommence the cycle and infect the next human victim.

Recently, scientists in Pasteur’s Biochemistry and Molecular Biology of Insects Laboratory, collaborating with a colleague at the London Institute of Zoology, found a correlation between the human immune response to malaria infection and the ratio of male to female parasites that are produced. This discovery may provide a means of controlling the parasite’s reproductive potential, thereby curtailing its lifecycle. (See Paul *et al* 2000 *Science*, 287, 128-131.)

In addition to its work on the basic science of this disease, the Institut Pasteur is involved in monitoring its epidemiology. The International Network of the Institut Pasteur is an exceptional observatory for studying infectious diseases such as malaria. At the Dakar Institut Pasteur, for example, scientists study individuals who have acquired an immunity to the disease.

By undertaking research on many aspects of this and other tropical diseases, the Institut Pasteur continues its commitment to improving public health in the Third World, which ultimately ensures the state of health in developed countries.

For information online: <http://bioweb.pasteur.fr/BBMI/index.html>



Caricature of Laveran fighting off mosquitoes (circa 1908)

PASTEUR INSTITUTES USA: A TURN OF THE CENTURY PHENOMENON

by Bert Hansen, Ph.D.

Circling the globe, the Pasteur Institutes established as satellites of the Institut Pasteur in Paris are justifiably world famous. Colleagues and students of Louis Pasteur created many important centers abroad as extensions of the central organization in Paris. The first was opened in Saigon by Albert Calmette in 1891. Today there are 20 institutes in the global network of the Institut Pasteur in cities such as Dakar, Athens and St. Petersburg.

While the United States has never hosted such official daughter institutes, Americans did initiate a fair number of organizations that imitated—and even anticipated—the great center in Paris. None in the U.S. was formally established by Paris, but some might have had authorization to use the founder's name.

Shortly after Louis Pasteur first publicly announced his new inoculation to prevent infection in persons bitten by rabid dogs, two groups of American physicians made plans to prepare and distribute this revolutionary remedy on our side of the Atlantic.

Independently in St. Louis and New York City, small groups of physicians announced “Pasteur Institutes” in late December 1885 and soon after the New Year. Their enthusiasm, fueled by Pasteur's report in late October 1885 of his success in July of that year, was further prompted by December's torrent of newspaper articles about four boys from Newark, New Jersey, who had traveled to Paris for treatment. The first of Pasteur's many American patients, these children had not yet returned to the U.S. when the American doctors shared their plans with the press.

When both cities used the phrase “Pasteur Institute,” they were not copying Paris; indeed, they were several months ahead. Only weeks later did Pasteur announce his ideas for a permanent institution, which in time came to bear his name. A fund-raising campaign opened in March 1886 and quickly secured major contributions from royalty and philanthropists worldwide. A splendid new facility opened its doors in November 1888, growing and thriving to the present.

In contrast, America's two earliest efforts failed to get off the ground. By March of 1886, the St. Louis endeavor had been abandoned. During the spring, Dr. Valentine Mott of New York was in Paris to learn Pasteur's new method, and on his return he first applied it to a patient in July 1886. However, his group failed to secure funding and the organization disappeared.

Five years later, a new Pasteur Institute was established in New York City by a French medical scientist, Dr. Paul Gibier, whose research on rabies had been published in a detailed doctoral thesis accepted by the Faculty of Medicine

at Paris: “Experimental Investigations on Rabies and Its Treatment” (1884). Gibier managed this facility's growth until his accidental death in 1900. It was then reduced in scale, but its work continued under the direction of his nephew, George Gibier Rambaud, educated in science in France and medicine at Columbia University in New York City. Dr. Rambaud closed the Institute in 1918, when he was commissioned overseas in the U.S. Medical Corps.

Rabies treatment efforts were organized under the name Pasteur Institute in several other cities in the U.S. Some carried out research along with the clinical treatment of rabies; some were actually agencies of state health departments, using the term Pasteur Institute or Division or Department simply to designate a focus on rabies treatment, the advance most closely associated in America with Pasteur's name in the era prior to the popularity of milk pasteurization after about 1920.

Long ignored by historians, the uneven fortunes of America's Pasteur Institutes, none of which survive today, are only now becoming known. In the interest of advancing this

knowledge—and in the hope of uncovering further documentation of their unique histories—a chronological list of American institutes bearing the Pasteur name follows.

Dr. Bert Hansen, who teaches history at Baruch College, recently published “America's First Medical Breakthrough: How Popular Excitement About a French Rabies Cure in 1885 Raised New Expectations of Medical Progress” (*American Historical Review* 103:2, April 1998, pp. 373-418) and “New Images of a New Medicine: Visual Evidence for Widespread Popularity of Therapeutic Discoveries in America After 1885” (*Bulletin of the History of Medicine* 74:4, December 1999, pp. 629-678). For copies, please contact the Pasteur Foundation.



Back cover of the Sixth Annual Report of the New York Pasteur Institute, 1896

Courtesy of Historical Collections, New York Academy of Medicine Library

REFERENCES TO U.S. PASTEUR INSTITUTES

1885	St. Louis	Plans for rabies treatment facility; abandoned
1886	New York	American Pasteur Institute; abandoned
1890	New York	New York Pasteur Institute
1890	Chicago	Chicago Pasteur Institute
1897	Baltimore	Pasteur Institute
1900	Pittsburgh	Pasteur Institute
1900	St. Louis	St. Louis Pasteur Institute
1903	Ann Arbor	Pasteur Institute
1903	Austin	Pasteur Institute
1904	Philadelphia	Possible institute established; unconfirmed
1908	Atlanta	Pasteur Department of Georgia Department of Public Health
1908	Washington, DC	Pasteur Institute
1908	Berkeley	Pasteur Division, California State Hygienic Laboratory

PASTEUR ON BROADWAY

On April 18th, the Pasteur Foundation benefited from a Broadway performance of Lincoln Center's Tony-nominated production *Contact*. Under the patronage of His Excellency the Ambassador of France to the United States and Mrs. François Bujon de l'Estang, the evening raised over \$180,000 for scientific research conducted in Pasteur laboratories.

In addition to the many generous donors listed at right, we would like to acknowledge Joseph E. Seagram & Sons, Rita and André Jammet of La Caravelle, and Jean-Georges Vongerichten of Jean Georges and Nougatine for their special in-kind contributions. Thanks also to Yves Saint Laurent Parfums, La Maison du Chocolat, Manuel Canovas and Cowtan & Tout for providing party favors.



Mrs. Mary Jaharis



Agnès and Georges Hibon



Mr. and Mrs. Pierre Valla



Dr. and Mrs. Robert Sassoon



ABOVE, L to R: Philippe Kourilsky, Mrs. Bujon de l'Estang, *Contact* stars Seán Martin Hingston and Karen Ziemba, Ambassador Bujon de l'Estang, Mrs. Anastassios Fondaras, *Contact* stars Scott Taylor and Stephanie Michels



LEFT: Restaurant Jean Georges' Tom Rice and Peter Glander, who donated their time and skill

EVENT ACKNOWLEDGEMENTS

Benefactors

The Honorable Anne Cox Chambers
Kristina and Guy Wildenstein

Patrons

CDC North America, Inc.
Mrs. Anastassios Fondaras
Merck Vaccine Division
Mr. and Mrs. John N. Rosekrans, Jr.
Mr. and Mrs. Donald E. Zilkha

Sponsors

Aventis Pasteur
BNP Paribas Group
Dr. Richard J. Coburn
Mr. Michel David-Weill
Michael and Mary Jaharis
Mr. and Mrs. Arthur Ross
Sankyo Parke Davis
Schering Plough Research Institute
Mr. and Mrs. John D. Viener
Count Arnaud de Vienne
John C. Whitehead

Patron Tickets

Mr. and Mrs. M. Bernard Aidinoff
Mr. and Mrs. Robert J. Arnold Bloomberg
Christopher H. Browne
Mr. and Mrs. Edward T. Chase
Christie's
Daniel Cohen and Leah Keith
Mrs. Elizabeth de Cuevas
Mr. and Mrs. Edgar M. Cullman, Jr.
Mr. Jonathan Farkas
Richard and Isabel Furlaud
Mr. and Mrs. Holcombe T. Green, Jr.
Frances Hayward
Mr. and Mrs. Randolph Hearst
Drue Heinz
Mr. and Mrs. Georges Hibon
Mrs. Charles O. Hoyt
Mrs. Simone Karoff
Mr. and Mrs. Stephen Kellen
Anthony C. M. Kiser
Jean-Pierre and Rachel Lehmann
Jacques Leviant
Mr. Arthur L. Loeb
Sharyn and Stephen Mann
Thierry H. Millerand
Mr. and Mrs. Laurent E. Momméja-Hermès
Barbara S. Mosbacher
Nancy B. Negley
Mrs. Barbara de Portago
Mr. and Mrs. William P. Rayner
Ambassador and Mrs. Joseph Verner Reed
David Rockefeller
Pierre-Louis and Magdeleine Roederer
Nina Rosenwald
Mrs. Nancy L. Ruwe
Judith Sulzberger, M.D.
Van Cleef & Arpels
Mr. and Mrs. Alain Wertheimer
Barbara and Al Winick
Mr. and Mrs. Ezra K. Zilkha

Sponsor Tickets

Diane L. Ackerman
Mrs. Russell B. Aitken
David W. Beer
Mrs. Marguerite de Bekessy
Estrellita and Daniel Brodsky
Dr. and Mrs. William Cahan
Dr. Daniel Carponcy
Marc A. Chiffert, P.E.
Mr. and Mrs. Rodman L. Drake
Mrs. Thomas K. Finletter
Olivia and Adam Flatto
Muffy and Xavier Flouret
Mr. and Mrs. Ralph Fraise
Mrs. and Mrs. David Granger
Richard V. Hare
Ambassador and Mrs. Arthur A. Hartman
John D. Hawke, Jr.
Marifé Hernández-Bell and Joel Bell
Lisa W. Hess
Dr. and Mrs. James M. Hester
Mr. and Mrs. Hal B. Howard
Mrs. Marjorie A. Hyman
Maria-Pilar Irisarri-Béraudière
Mrs. Marcia Israel-Curley

Mrs. Rita Jammet
Ms. Iran Khosrowshahi
Raymond Leary
Noel and Harriette Levine
Mary de Liagre
Mr. and Mrs. Michel Longchamp
Mr. and Mrs. Angus MacIver
Vicky McLoughlin
Mrs. Joseph A. Meehan
Mr. and Mrs. Michael Metz
Armenie Milliken
Mr. and Mrs. Peter O. Price
John and Eugénie Radziwill
Dr. and Mrs. Alain Roizen
Frederic Romano
Mrs. Alice Stern
Elizabeth F. Stribling and Guy Robinson
Jean-Paul and Monique Tisserre
Fanny Turschwell
Mr. and Mrs. William C. Ughetta
Mrs. Monique Uzielli
Mrs. James H. Van Alen

Donors

Edward and Marion Adelberg
Mrs. Ana Cristina Alvarado
Joan Arden
Mrs. Roone Arledge
Louis Auchincloss
Dr. Robert Austrian
Mr. and Mrs. Mathieu Baudoin
Dr. and Mrs. Lewis Berman
Mrs. Joy H. Briggs
Dr. Felix and Mrs. Leah Bronner
The Chinese Porcelain Company
Mr. and Mrs. Jonathan Churchill
Sophie Coumantaros
Madison Cox
Mrs. Gioconda M. K. Crivelli
Mrs. Sylvia de Cuevas
Mr. and Mrs. Bruno Desforgues
Beatrice Dupont
Edith Exton
Philomene A. Gates Esq.
Françoise Gilot-Salk
Dr. Jane Salmon and Dr. Jerry Gliklich
Dr. Henry P. Godfrey
Michael and Anne Golden
Mr. and Mrs. Earl G. Graves
Dr. Augusta Gross and Mr. Leslie Samuels
Mr. and Mrs. Benjamin A. Groves
George and Joan Gudefin
Polly and John Guth
Anne E. Hawke
Mr. and Mrs. Georges Hibon
Mr. and Mrs. Eric M. Javits
Dr. Edwin U. Keates
Mr. and Mrs. Christopher Kende
Mrs. Lenore Kreitman
Connie and Harvey Krueger
Flann Lippincott
Mr. Stan I. Listokin
Mr. and Mrs. Jacques Maisonrouge
Mr. and Mrs. Charles Henri Mangin
Norma Matalon
Mr. and Mrs. Arjun Mathrani
Mrs. Pierre Matisse
Mr. and Mrs. Walter Maynard, Jr.
Mr. and Mrs. George McFadden
Mrs. Mark Millard
Nina Mines
Monsieur Touton Selection, Ltd.
Princess Maita di Niscemi
Mrs. Victor and Ruth S. Nussenzeiwé
Katarina Paras
Mr. and Mrs. Samuel P. Peabody
Mr. and Mrs. Thomas P. Peardon, Jr.
Virginia S. Perrette
Gérard and Maryse Perrot
Dr. and Mrs. Stanley A. Plotkin
Priscilla and Jeffrey Potter
Mr. and Mrs. Yves Robert
Dr. and Mrs. Alain Roizen
Dr. and Mrs. Robert I. Sassoon
Joris and Elizabeth de Schepper
Janet and Frank Schwitzer
Patricia and Chaim Shimonov
Mrs. Ana Vilma de Soler
Spencer Trask Securities, Inc.
Mr. and Mrs. Michael B. Stubbs
Mr. and Mrs. Bertrand L. Taylor III
Mr. and Mrs. Edward E. Vassallo
Florence Weicker
Mr. and Mrs. Edwin L. Weisl
Bay Wellington List as of April 18, 2000



*Ambassade de France
aux Etats-Unis*

L' Ambassadeur

Dear Friends,

Washington, May 1, 2000

Louis Pasteur is perhaps the world's best-known Frenchman outside of politics. In 1887, buoyed by the international reaction to his rabies prophylaxis, he founded the Institut Pasteur, whose mission is to pursue biomedical research for the improvement of public health.

True to the wishes of its pioneering founder, the Institut Pasteur and its remarkable global network of institutes and associated structures throughout the world have never strayed from this purpose. They have worked extensively in often neglected Third World countries to understand and eradicate pathogens that threaten our well-being with widespread and emergent communicable diseases. As a result, the Institut Pasteur is now an extended Research and Development Organization playing a major role in the service of humanity.

Louis Pasteur also had the prescience to endow this institute with a private status that ensures its independence. While it has enjoyed the support of the French government over the decades, this subsidy has never exceeded fifty percent. Of course, the price of this autonomy is that the Institut Pasteur is required to raise the majority of its budget from its own activities and from the private sector.

I pay homage to you friends in the United States who understand that the Institut Pasteur is a vital international cause that concerns us all.

François Bujon de l'Estang

