

PASTEUR PERSPECTIVES

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

THE CUTTING EDGE

by Caitlin Hawke

THE RE-EMERGENCE OF PLAGUE

Plague is a disease that evokes devastating images of Medieval Europe where, from 1346 to 1350, one third of the population—25 million people—succumbed to the Black Death. The most recent major plague epidemic began in Asia in 1890 and had spread to California by the turn of the century. That epidemic took over 12 million lives.

For the past several years, cases of plague have been on the rise throughout the world, leading



Alexandre Yersin in Hong Kong, 1894

to its classification as a re-emerging disease. Although the development of antibiotics has significantly lowered the mortality rate, a recent discovery by scientists at the Institut Pasteur of Madagascar and Paris revealed a multiantibiotic-resistant strain, making the re-emergence of this

disease a potentially serious public health issue.

Historical Background

In 1890, Alexandre Yersin, a talented young researcher and teaching assistant of Émile Roux at the Institut Pasteur, left Paris for Asia to pursue his dream of becoming an explorer. In 1894, a plague epidemic broke out in southern China, threatening the French colony of Indochina. Fueled by modern means of transportation such as trains and steamships, the spread of the disease was unprecedented. When the French government turned to Yersin, who was on an expedition to the East, he went immediately to Hong Kong. Using only the modest equipment at his disposal, he isolated the plague microbe—now known as *Yersinia pestis*—from the swollen lymph nodes (buboes) of cadavers. He sent samples back to Paris, where Roux prepared the first successful anti-plague serum.

One need only read the desperate first-hand accounts of prior plague epidemics to fully understand the significance of Yersin's discovery. While

A BENEFIT EVENING AT THE THEATER

RING ROUND THE MOON

on Broadway

The Pasteur Foundation will hold a benefit evening on Wednesday, May 5th, at the Belasco Theater in New York City. Produced by the renowned Lincoln Center Theater and The Laura Pels International Foundation, the first Broadway revival of Jean Anouilh's *Ring Round the Moon* (*L'Invitation au château*) will star the incomparable three-time Tony winner Irene Worth.

A leading postwar French playwright, Jean Anouilh (1910-1987) was born in Bordeaux and studied at the Sorbonne. *Ring Round the Moon*, written in 1947, premiered in Paris and was the only play in which Brigitte Bardot has ever appeared. Its original London staging was directed by Peter Brook. The play was first seen in New York in 1950 in Christopher Fry's translation—the same one to be used in this production.

“One certainty for this spring is Ring Round the Moon, Jean Anouilh’s fantasy play about a pair of twins—one good, one evil—and a Cinderella-like ballerina.”

New York Times,
“On Stage and Off” column, January 29, 1999

Ring Round the Moon is a romantic comedy set in a French chateau, where identical twin brothers—one scheming, the other shy—compete for the attention of a beautiful ballerina as their wise aunt watches. The cast of the production, which was called “mouthwatering” by the *New York Observer*, includes the talented young British actor Toby Stephens in his Broadway debut in the dual role of the twins, Hugo and Frederic. Stephens, the son of actress Maggie Smith, appeared this past winter at the Brooklyn Academy of Music in two plays by

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explanations of previous outbreaks were sought in metaphysics, religion and the supernatural, Yersin demystified the disease by showing it to be caused by an infectious agent. The episode enticed him away from exploration and back to the laboratory. In 1895, he created the Institut Pasteur of Nha-Trang to continue his plague research. Two years ago, a museum celebrating the life and work of this great Pasteurian was built next to the Institut Pasteur in Nha-Trang.

In 1897, another Pasteurian, Paul-Louis Simond, found the plague bacillus in the stomachs of fleas taken from infected rats. Simond devised an ingenious experiment, the results of which conclusively demonstrated that fleas were responsible for transmitting plague to humans.

The Disease

Plague afflicts rodents in Asia, Africa and the Americas. In the United States, it is found in the Southwest, its human victims primarily Native Americans. Human infection usually occurs in unsanitary areas where rats and humans cohabit, often through direct contact with infected tissues of sick or dead animals. Pulmonary plague, an even more lethal form, is spread by way of respiratory droplets suspended in the air.

A few days after the onset of infection, the victim experiences flu-like symptoms, including chills, nausea and headache. The disease is also characterized by the appearance of buboes, inflammatory swellings of the lymph nodes that turn black when blood vessels break and blood dries under the skin.

In the last 15 years, the World Health Organization has recorded over 18,000 cases in 24 countries. Over half of these were in Africa. On average, up to 40 cases are reported annually in the United States, where in the last decade the disease has occurred in 13 states.

Untreated, the human mortality rate is between 50% and 90%, according to the Centers for Disease Control. However, *Yersinia pestis* has been universally responsive to antibiotics, which have reduced the mortality rate to 15%.

Until now.

Antibiotic-Resistant Plague

Experts throughout the world are concerned with the serious threat to public health posed by pathogenic bacteria that have developed resistance to traditional antibiotic treatment. As readers learned in the last issue of *Pasteur Perspectives*, the resistant tuberculosis bacillus is an ominous example of this problem in American urban centers—and the evolution of multi-resistant bacterial strains is accelerating.

Antibiotic resistance results from genetic alterations transmitted during reproductive cell division. One

scenario occurs when bacteria acquire foreign genetic information from other bacteria in the form of plasmids—small circular chromosomes that are distinct from the bacterial chromosome. These bits of DNA that code for resistance are capable of “jumping” from the plasmid to the bacterial chromosome, or vice versa. Thus, the mechanism dictating resistance has, in effect, its own infectious nature.

Thanks to advances in molecular biology and in chemical and microbiological techniques, scientists have made progress in deciphering bacterial physiology. Their findings will inevitably lead to new therapeutic possibilities, but the next generation of antibiotics will not be available for a number of years. For now, vigilant surveillance of antibiotic-resistant strains is essential in curbing their spread.

As the only WHO Collaborating Center for *Yersinia enteropathogens* and one of three international centers

for the study of plague, the *Yersinia* Laboratory at the Institut Pasteur identifies strains isolated in plague centers throughout the world and studies new therapeutic techniques. For the first time, a multi-resistant strain of *Yersinia pestis* was recently identified by Pasteur scientists working in Madagascar and Paris.

Named *Y. pestis* 17/95, this strain was isolated at the Institut Pasteur of Madagascar from a 16-year-old patient who had been diagnosed with bubonic plague. It is resistant not only to streptomycin, the standard prescription, but also to other drugs recommended by the World Health Organization for treatment of plague: chloramphenicol, tetracycline and sulfonamides. Prior to the isolation of *Y. pestis* 17/95, seven decades of epidemiological surveillance in Madagascar had not identified even a single resistant strain.

Genetics of the Resistant Strain

Genetic study of the new strain revealed the presence of a plasmid that, in laboratory cultures, readily transfers to other strains of *Y. Pestis*, suggesting the possibility that antibiotic-resistant cases of plague could proliferate in Africa. On a wider scale, the discovery of the capacity of *Y. Pestis* to acquire a multi-resistant plasmid suggests that resistant strains could also appear in other plague centers as well.

These observations are particularly alarming because the survival rate for those infected by this highly pathogenic species of bacteria is directly linked to rapid treatment with antibiotics. The emergence of this new lethal microorganism has lent increasing urgency to the work being done at the Institut Pasteur in the development of new therapies for plague and other deadly infectious diseases.

Hugues Fleury, the Pasteur press office and the museum staffs contributed significantly to this article.



18th Century garments worn by doctors during plague outbreaks

HONORING PASTEUR: THE UNITED STATES PAYS TRIBUTE

LOUIS PASTEUR ELEMENTARY SCHOOL, CHICAGO

The many schools in the United States that bear Louis Pasteur's name provide an appropriate legacy to the memory of this great scientist, who studied to be a teacher and taught junior high school in Dijon. A previous issue covered the accomplishments of a Detroit school. Here we feature a school in Chicago.

One of 485 elementary schools in the Chicago Public School System, the Louis Pasteur School ranks among the best in its region for academic achievement. With just over 900 students in kindergarten through eighth grade, the school maintains a 95% attendance rate. Principal James Gilliat and his able faculty have worked to improve the education offered at Pasteur Elementary, which has been honored for its progress and improved test scores.

This past December, a group of students from Pasteur Elementary and the Ogden School helped inaugurate our poster exposition "À la découverte de l'Institut Pasteur," hosted by the Alliance Française of Chicago. The Pasteur students sang a multilingual welcome song, and students from the Ogden School performed a skit about the life of Louis Pasteur. We congratulate them on their fine performances and thank the Alliance Française for organizing this tribute.



The Pasteur Foundation's Caitlin Hawke with Dr. Sonia Aladjem, director of the Alliance Française, at the Pasteur exposition in Chicago



Louis Pasteur Elementary students at the Alliance Française of Chicago

YOU TOO CAN HELP

Planned wisely with your attorney, a specific, percentage, contingent or residual bequest to the Pasteur Foundation could save your estate (and thereby your heirs) substantial tax payments while benefiting scientific research and enabling you to leave your personal impression on the Institut Pasteur. Many of our friends have found this the simplest way to support the Institut Pasteur. Please consult your estate advisor and/or attorney for advice on how best to achieve your goals.

For further information, contact Caitlin Hawke at the Pasteur Foundation, 212.599.2050.

OPEN HOUSE

On Saturday, May 29th, and Sunday, May 30th, the Institut Pasteur in Paris will open its doors to the general public. At the last open house, held in 1995 to commemorate the centennial of Louis Pasteur's death, 37,000 people explored the laboratories, visited the museum and attended lectures by Pasteur scientists.

If you plan to be in Paris in May, we invite you to visit.

For more information, please call the Pasteur Foundation or visit our Website: www.pasteur.fr

**MORE TO THE POINT:
BRIEF NEWS FROM PASTEUR**

HUMAN PAPILLOMAVIRUSES

Human papillomaviruses (HPVs) cause various skin diseases and cancer of the cervix, the second most common cause of death by cancer in women worldwide. The Papillomavirus Unit at the Institut Pasteur has just mapped the first chromosomal locus associated with a predisposition to papilloma infection that causes epidermodysplasia verruciformis, a rare skin disease. The identified locus is particularly interesting because it may also be involved in predisposition to psoriasis, which afflicts 2% of the population.

LISTERIA

In the third issue of *Pasteur Perspectives*, we reported on Listeria research conducted at the Institut Pasteur. While not a serious threat to healthy individuals, this bacterium can be fatal to pregnant women, their unborn children and people with suppressed immune systems. As recently as February, a winter outbreak of listeriosis in the United States caused 16 deaths and the recall of hundreds of thousands of potentially tainted food products traced to a processing plant in Zeeland, Michigan. Because early reporting leads to timely recalls, this is a reminder that to report a suspected foodborne illness, you may call the Food and Drug Administration's emergency number: 301.443.1240.

MENINGITIS

Two teams at the Institut Pasteur recently identified strains of *Neisseria meningitidis* that are strongly resistant to chloramphenicol, the antibiotic of choice in treatment of the disease. Meningococcal infections are endemic throughout the world and usually affect children under the age of five. In developed countries, 10% of cases are fatal despite appropriate antibiotic therapy. If treatment is unavailable, the mortality rate may rise above 50%, making the emergence of antibiotic-resistant strains a serious concern.

INVEST IN A HEALTHY FUTURE

One of the world's premier centers of fundamental research, the Institut Pasteur is entirely dedicated to life sciences and human health. We need your help to continue this work. Please consider making a tax-deductible contribution to the Pasteur Foundation.

PASTEUR PERSPECTIVES

A 501(c)(3) corporation, the Pasteur Foundation is the U.S. nonprofit affiliate of the Institut Pasteur. Located in New York City, the foundation works to introduce the research conducted at the Institut Pasteur to the American public, to develop exchanges between Pasteurian and U.S. scientists, and to raise funds for Pasteurian research. For more information, please contact the Pasteur Foundation.

420 Lexington Avenue, Suite 1654
New York, NY 10170
Phone: 212.599.2050
Fax: 212.599.2047
E-mail: PasteurUS@aol.com

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Caitlin M. Hawke

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PASTEUR FOUNDATION 420 LEXINGTON AVENUE, SUITE 1654, NEW YORK, NEW YORK 10170

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I want to help support the research conducted at the Institut Pasteur to improve worldwide public health.

I am enclosing a tax-deductible gift to the Pasteur Foundation in the amount of:

\$1,000 \$500 \$100 \$50 \$25 Other \$ _____

I would like more information on how to make a bequest in support of Pasteurian research.

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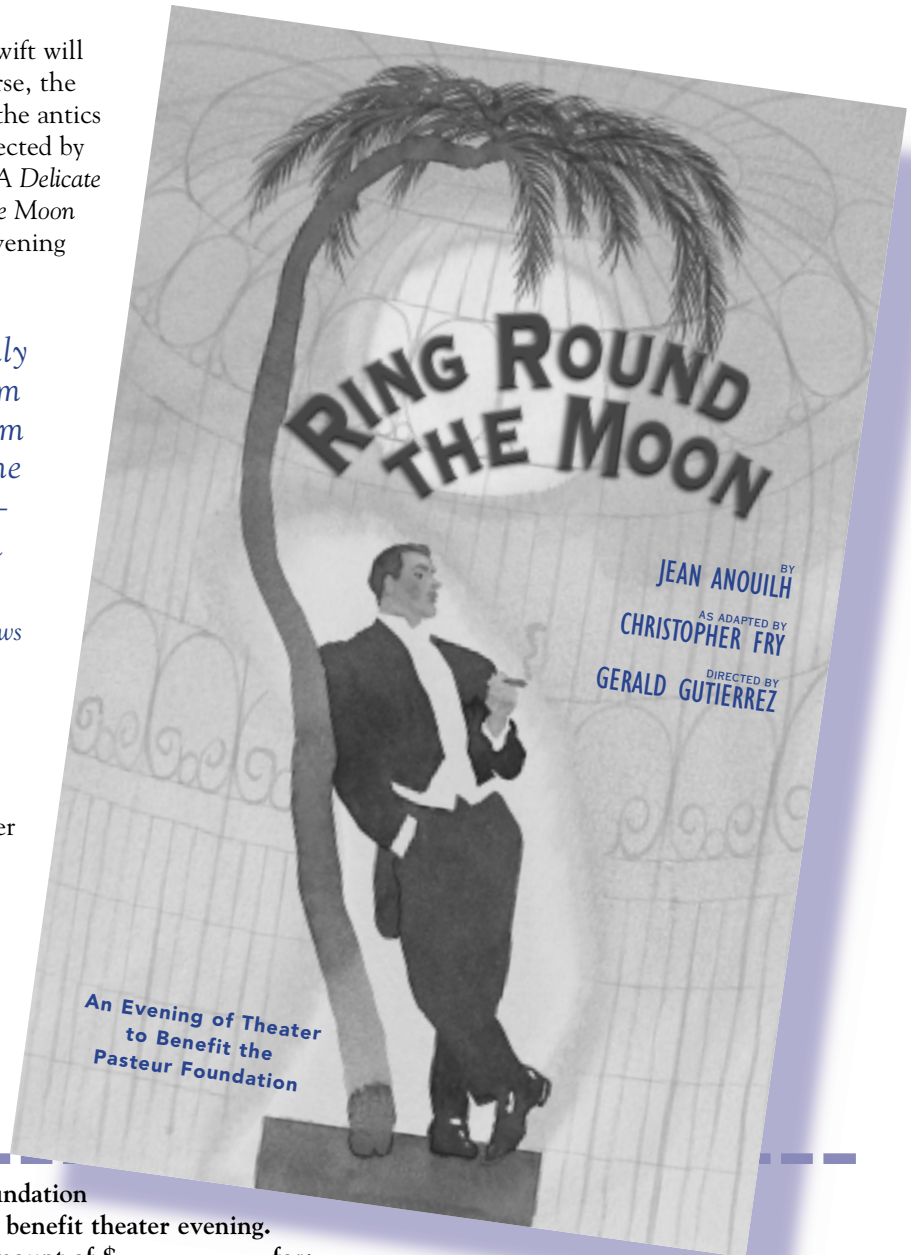
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Racine, *Phèdre* and *Britannicus*. Francie Swift will play the ballerina Isabelle. And, of course, the legendary Irene Worth will preside over the antics as the aunt, Madame Desmormotes. Directed by two-time Tony winner (*The Heiress* and *A Delicate Balance*) Gerald Gutierrez, *Ring Round the Moon* promises to be an absolutely delightful evening of theater.

“Inhabited by an array of richly drawn characters—most of whom disguise their true identities from others and conceal their genuine emotions from themselves—Ring Round the Moon is an enchanting comic tale....”

Lincoln Center Theater Member News

The Pasteur benefit performance of *Ring Round the Moon* will be held on Wednesday evening, May 5th, 1999. Benefit tickets are \$1,000 (Patrons) and \$500 (Sponsors) and include a pre-theater gala dinner at the Hudson Theater next door to the Belasco (111 West 44th Street between 6th and 7th Avenues). Donor tickets to the play alone are \$100. All tickets are tax-deductible to the extent allowed by law. For further details, please contact the Pasteur Foundation at 212.599.2050.



I would like to support the Pasteur Foundation by attending the *Ring Round the Moon* benefit theater evening.

Please find enclosed my check in the amount of \$_____ for:

- ___ Patron Ticket(s) at \$1,000 each (\$125 is not tax-deductible)
Patron ticket includes one ticket to pre-theater reception and dinner plus one preferred orchestra theater seat and Patron listing in the event program.
- ___ Sponsor Ticket(s) at \$500 each (\$125 is not tax-deductible)
Sponsor ticket includes one ticket to pre-theater reception and dinner plus one prime orchestra theater seat and Sponsor listing in the event program.
- ___ Donor Ticket(s) at \$100 each (\$55 is not tax-deductible)
Donor ticket includes one select orchestra theater seat and Donor listing in the event program.
- ___ I/We cannot attend but enclose a tax-deductible contribution of \$_____.
Contributors will be acknowledged in the event program.