

EDITOR'S CORNER

The Louis Pasteur and Industry in XXIst Century Workshops/Symposium; Marnes-la-Coquette, France; September 25 to 29, 1995.

UNESCO declared 1995 as the "Year of Pasteur." What an honor for me to be invited to present a lecture at the commemoration of the 100th year anniversary of the passing of Louis Pasteur by **Institut Pasteur!** The occasion was both solemn as well as celebrative, for on the one hand we gathered at Marnes-la-Coquette where Pasteur spent the last moments of his life to remember the works of the great master and at the same time to project the influence of his work into the next century. The compound is now a first rate research and conference center.

This particular celebration involved a series of "Workshops" on many important topics in microbiology. The workshops were designed for maximum interaction between the participants and the lecturers. Typically, each workshop had about 40 scientists and lasted for the whole day. One outstanding program was the Symposium organized by Nobel Laureate Pierre Gilles de Gennes who gave a talk on "Crystals of Life" and Nobel Laureate Francis Jacob who concluded the symposium. In between, exciting topics were presented such as "From fermentation to the origins of life," "Future of biotechnologies," "Molecular genetics of silkworms," "Modern pharmaceutical industry" and "Louis Pasteur and the future of food industries." It was truly a great symposium.

Besides spending time in the meeting, Dr. Catherine Fung and I had a most enjoyable time visiting Moët & Chandon House of Champagne. Have you ever seen 5,000,000 bottles (\pm a few bottles) of champagne in 17 miles of chalk caves? The lunch with a limitless flow of the great cuvee created by Dom Perignon along with fantastic French cuisine was most unforgettable. We also visited an ultra-modern Camembert cheese factory (clean room technology) where they make the delicious soft cheese with carefully *pasteurized* milk using two stage starter culture technology so that the soft cheese (traditionally made with raw milk) is free of pathogens such as *Listeria monocytogenes* and others. The processing and packaging rooms were as clean as hospital environments. We were impressed!

One of the handouts during the meeting was a synopsis of "Pasteur Achievements." The information was so concise and educational that I obtained permission to reproduce the document *verbatim* for the readers of this *Journal*. Thus, with thanks to the courtesy of **Institut Pasteur** the following pages describe the achievements of one of the greatest scientists of all times.

DANIEL Y.C. FUNG

PASTEUR'S ACHIEVEMENTS¹

All of Pasteur's work seems to have followed a natural course of events, beginning with his studies on crystallography and ending up with his discovery of virus vaccines and the prophylaxis of rabies.

The origin of his research dates from his reading of a paper by the German physicist Mitscherlich. The latter had observed that two chemical substances, paratartrate and sodium/ammonium tartrate, had the same chemical constitution and the same crystalline form, but nonetheless had a different effect upon polarized light. Pasteur set out to discover the cause.

FIRST PERIOD FROM 1847 TO 1862 (from the age of 25 to 40)

Pasteur was basically a physicist and a chemist.

1847: Studies on Molecular Dissymmetry

After several years of research in which he combined crystallography, chemistry and optics, Pasteur established that there existed a parallelism between the outer form of a crystal, its molecular composition and its effect upon polarized light. Dissymmetrical crystals caused slanting of the polarized light, while symmetrical crystals did not.

He formulated a basic law which stated that "only those products created under the influence of life are dissymmetrical, because cosmic forces which are themselves dissymmetrical were present when they were created."

Dissymmetry is the dividing line between the organic and the mineral world. It was Pasteur's work which was at the origin of a new science called stereochemistry (or the chemistry of space).

He was also responsible for the boom in synthetic chemistry.

1855-1857: Studies on Fermentation

It was while observing paratartrate crystals that Pasteur had initially discovered molecular dissymmetry; likewise, while examining a solution of paratartronic acid,

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he noticed that, under the influence of a mould, this acid had fermented and dissociated. Only the left-hand tartaric acid remained in the fermented liquid; the right-hand tartaric acid had decomposed, or "disassembled." Indeed, a substance which was inactive with polarized light (paratartronic acid) had become active (the left-hand tartaric acid) under the influence of fermentation.

Thus, since all active substances arise from living matter, fermentation, instead of being the dead process which Liebig, the chemist, had initially assumed it to be, was, in fact, a living process, since only life can generate substances active upon polarized light. This was the first link in a logical sequence of studies which would lead Pasteur from molecular dissymmetry to fermentation and then on to contagious disease.

1857-1862:

Pasteur studied lactic and alcohol fermentation, and demonstrated that:

- all fermentation is due to the presence of a microorganism;
- to each fermentation corresponds a particular ferment.

He also noted that, in order to study fermentation, it was necessary to:

- prepare the appropriate, sterile culture medium;
- inoculate this medium with a trace of pure ferment.

With his study of the mechanism of fermentation, which led him to elucidate the role and the specificity of the microorganisms, Pasteur had become a chemist-biologist.

SECOND PERIOD FROM 1862 TO 1877

From the age of 40 to 55, Pasteur became a biologist. He elaborated the germ theory and abolished the doctrine of spontaneous generation.

1) After his initial discoveries, he sought to discover the origins of microorganisms, or agents of fermentation. Did they arise from germs similar to themselves, or did they spontaneously appear in fermenting media? The famous issue of spontaneous generation was raised.

After memorable quarrels with his detractors (Pouchet), Pasteur was able to state in his 1862 report, and on the basis of a number of varied experiments, that:

- a) atmospheric dust contains germs of "lower" organisms which can develop and multiply;
- b) even liquids which spoil most easily will remain unaltered if they are protected from contact with these germs.

"Spontaneous generation is a chimera" (Pasteur)

2) He next questioned the way in which fermentation works and how ferments act.

By studying butyric fermentation, he discovered a new class of live germs able to survive without air. He proposed the term "anaerobe" for ferments possessing the property of existing without air; the term "aerobe" was applied to microorganisms requiring the presence of free oxygen in order to develop.

Fermentation is the consequence of life without air.

Experiments on fermentation led Pasteur to apply microbiological techniques to industry and agriculture.

- He studied the formation of vinegar and the transformation of alcohol into acetic acid by the microorganism *Mycoderma aceti*, which fixes oxygen from the air on alcohol. He showed vinegar-makers how to consistently obtain high-quality vinegar.

• Wine Diseases

While studying parasitic ferments of wine, Pasteur demonstrated that each disease was due to a different ferment. By heating to 55°, it was possible to protect the wine from disease. This method, when applied to any liquid capable of being altered, is known throughout the world as pasteurization.

• Beer

Changes in beer are produced by microorganisms found in air dust. Pasteur taught the brewers how to prevent the worts from becoming contaminated and how to prevent disease by heating the beer to 55°.

• Silkworm Diseases

In 1865, the silkworm industry in France, as well as in Italy, Austria and Asia Minor, was ravaged by a disease caused pebrine.

Under the microscope, Pasteur observed that infected silkworms had shiny particles on them, which were responsible for the disease.

He demonstrated that the disease was hereditary and contagious.

He discovered another disease, flacherie, and established the notion of the presence of a "favorable environment" in order for disease to occur.

On a practical level, he was able to cure the disease by inventing the concept of cell granulation.

These findings by Pasteur were of considerable importance: indeed, for the first time, problems of heredity and contagion were solved by scientific means, and the basic guidelines of disease control were established. They were to be a prelude to his studies on contagious diseases and the germ theory.

THIRD PERIOD FROM 1877 TO 1887

From the age of 55 to 65, Pasteur applied microbiological techniques to medicine and surgery.

1877: Study of Infectious Diseases

- Discovery of the cause of boils and osteomyelitis: staphylococcus
- Discovery of the microbe responsible for puerperal infection: streptococcus
- Discovery of pneumococci

1880: Method for Attenuating Microbial Virulence

- Chicken cholera (by aging, in contact with oxygen in the air)
- Anthrax (by culture of anthrax-carrying germs at 43°, attenuated by oxygen from the air)

1881: Vaccinations

- Cholera
- Anthrax
- Swine-fever

By applying his method

- To the study of infectious diseases (microbial agents)
- To their prevention (asepsis)
- To their prophylaxis by immunization (vaccinations)

Pasteur was the founder of immunology.

1880-1885: Rabies

By this time, Pasteur had thoroughly mastered his experimental methodology. When studying rabies, he sought to isolate a microbe, but could not find it. Rabies is a disease of the nervous system. He cultured an invisible "microorganism" on rabbit spinal chord and fixed the virulence.

On July 6, 1885, the method of attenuation of virulent spinal chord was tested on a human being, Joseph Meister.

November 14, 1888:

Inauguration of the Institut Pasteur by Sadi Carnot.

BOOKS ABOUT PASTEUR

Available at the Pasteur Museum and in bookstores.

- Pasteur, une science, un style, un siècle. Bruno Latour. Ed. Perrin/Institut Pasteur, 1995
- Louis Pasteur and Germs. Steve Parker, Ed. du Sorbier, 1993
- Louis Pasteur et les microbes. Steve Parker. Ed. Le Sorbier, 1993
- Pasteur. Maurice Vallery-Radot, Ed. Perrin, 1994
- Louis Pasteur, Franc-tireur de la science. René Dubos. Ed. La Découverte, 1995
- Louis Pasteur, l'empire des microbes. Daniel Raichvarg. Ed. Découvertes Gallimard, 1995
- Pasteur, Cahiers d'un savant. Collectif CNRS. Ed. Zulma, 1995
- Sur les chemins de Pasteur. René-Charles Jaugéy. Ed. Barthelémy, 1995
- Images de la vie et de l'oeuvre de Pasteur. Louis Pasteur Vallery-Radot. Ed. Flammarion, 1956.

Out-of-stock, may be consulted in the library

- La vie de Pasteur. René Vallery-Radot. Ed. Flammarion ou Hachette
- Oeuvres de Pasteur, réunies et annotées par L. Pasteur Vallery-Radot. Paris, Masson, 1939. 7 tomes

CHRONOLOGICAL EVENTS IN THE LIFE OF LOUIS PASTEUR 1822-1895

- 1822: December 27, birth of Louis Pasteur in Dole, (Jura region), France
- 1831: Pasteur attends junior high-school in Arbois
- 1839: Louis Pasteur moves to Besançon to attend the Royal High School
- 1840: He obtains an Arts diploma in Besançon. Tutor at Besançon junior high school
- 1842: High school diploma in mathematics, Dijon
- 1843: Admitted to the "Ecole Normale Supérieure" (science faculty)
- 1845: Obtains his Bachelor of Science degree
- 1846: Appointed physics teacher in a high school in Tournon (Ardèche), but remains at the "Ecole Normale" to prepare for the aggregation
- Meets Mr. Laurent in his Balard Laboratory. Studies on crystals*
- 1847: PhD in science
- 1848: Appointed as physics teacher at Dijon high school. Substitute teacher in chemistry at the Faculty of Science, Strasbourg

Research into dimorphism. Historic paper on the dissociation of sodium paratartrate and ammonia

- 1849: Marries Marie Laurent, daughter of the rector of the University of Strasbourg
- Research on the specific properties of the two acid components racemic acid*
- 1851: Thesis by Pasteur on aspartic and malic acids
- 1852: New research on possible relationships between crystalline forms, chemical composition and direction of rotative polarization
- 1853: Pasteur is made Chevalier of the Imperial order of the "Légion d'Honneur." He receives the Société de Pharmacie de Paris prize for synthesis of racemic acid
- Memorandum on the discovery of the transformation of tartaric acid into racemic acid. Discovery of inactive tartaric acid*
- 1854: Pasteur appointed Dean of the Faculty of Science, Lille University
- 1855: *Beginning of studies on fermentation. In Lille, he presents a paper on amylic alcohol*
- 1856: *Start of research into the fermentation of alcohol.*
- 1857: Is named member of the Board of Directors of the "Ecole Normale" and Director of Scientific Studies at that school
- Thesis on lactic fermentation. Thesis on alcohol fermentation*
- 1858: Installation of his laboratory in the attic of the "Ecole Normale," rue d'Ulm, Paris
- Pasteur investigates so-called "spontaneous" generation*
- 1859: Awarded the experimental physiology prize by the "Académie des Sciences" for his work on fermentation
- 1860: *Takes air samples in Arbois in order to study the problem of "spontaneous" generation. Examines the doctrine of spontaneous generation.*
- 1861: "Jecker Award" from the "Académie des Sciences" for research on fermentation
- Publication in the journal of the Chemical Society of Paris of all results concerning vinegar*
- 1862: Election to the "Académie des Sciences" (Mineralogy Section)
- Studies on mycoderms, and the role of these plants in acetic fermentation*
- "Alhumbert Award" for research on spontaneous generation
- 1863: Emperor Napoleon III requests Pasteur to study diseases of wine

Studies on wine — and the influence of oxygen in the air on vinification

Pasteur is named Professor of Geology, Applied Physics and Chemistry at the "Ecole des Beaux Arts" (Paris)

1864: Sets up a laboratory in Arbois (Jura) for his research on wine

1865: *Practical procedure for the conservation and improvement of wines*

Studies on silkworm diseases. Work on pasteurization.

1866: *Publication of "Studies on wines." Publication of an essay on the scientific achievements of Claude Bernard*

1867: Setting up of a physiological chemistry laboratory at the "Ecole Normale." Appointed Professor of Organic Chemistry at the Sorbonne (University of Paris). Grand Prize at the Great Exhibition for his studies on wine. Resigns from his administrative functions at the "Ecole Normale."

1868: Diploma of Doctor of Medicine from the University of Bonn (Germany). Pasteur is afflicted with hemiplegia on the left side. He is promoted Commander of the Legion of Honor.

Publication of his studies on vinegar

1870: *Publication of studies on silk worm diseases*

1871: *Studies on beer*

1873: Elected member of the "Académie de Médecine"

1876: *Publication of studies on beer*

1877: *Memorandum on urine alteration. Studies on anthrax. Studies on septicemia.*

1878: Promoted Grand Officer of the Legion of Honor

Publication of the paper "The Theory of Germs and its Application to Medicine and Surgery." Memorandum on chicken cholera.

Research on gangrene, septicemia, and puerperal fever

1879: *Note on the plague. Discovery of immunization using attenuated cultures.*

1880: Appointed member of the Central Society of Veterinary Medicine

Presents his work on virulent diseases (for the first time, Pasteur makes public the principles of "virus/vaccins." The beginning of his research on rabies.

1881: Appointed "Grand-Croix" of the Legion of Honor

Anthrax vaccine. Work on yellow fever near Bordeaux

Election to the "Académie Française"

1882: *Note on contagious peripneumonia of horned animals. Studies on swine fever*

1883: *Vaccination against swine fever using attenuated virus.*

1884: *Presents his work on rabies. Lecture on pathogenic microbes and "virus/vaccins" at the Copenhagen Congress. Pasteur explains the general principle of vaccination against virulent diseases.*

1885: *First rabies vaccination of a human being*

1887: Elected Permanent Secretary of the "Académie des Sciences." Victim of a second attack of hemiplegia.

First experiments on destruction of rabbits in Australia by the chicken cholera microbe.

1888: Inauguration of the Institut Pasteur of Paris.

1895: *September 28: death of Louis Pasteur in Villeneuve-l'Étang.*