

# EIR Science & Technology

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## The Pasteurians: building nations by means of science

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*Part II of a series by Garance Upham Phau focuses on the career of Alexandre Yersin, who discovered the bacillus for plague and introduced the rubber tree to Indochina.*

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*In Part I of this series, we met the French biologist Louis Pasteur (1822-95) in his capacity as the leader of a movement to build nations throughout the world, by means of science. The first Pasteur Institute was founded in Paris a century ago, in 1888, and then replicated in other French cities in Asia and in Africa. The first installment traced the political battle waged by Albert Calmette, a military doctor best known for his groundbreaking discovery in the fight against tuberculosis, the BCG vaccine.*

Louis Pasteur was *not* a doctor, but a chemist and crystallographer. In company with his first great associate and friend Pierre Emile Duclaux (1840-1904), to initiate the revolution in medical practice and to develop the new science of microbiology, he set out to find and recruit young doctors, medical students who would be steeped in Pasteur's method before becoming teachers themselves. Emile Roux (1853-1933), who took over the Institute at the death of Duclaux, and Alexandre Yersin (1863-1943) are exemplary of the success of Pasteur's recruitment program.

In 1883, Pasteur had already sent Roux to study cholera in Egypt, but the team was forced to come back after the death of the masterful physician Thuillier.

Upon the founding of the Institute in 1888, Pasteur said, "The Paris center shall have to train young scientists who shall go bring the method to faraway countries."

The underlying concept was that of medicine as the leading edge of the economic development of what is now called the "Third World." This concept was expressed in 1937 by one of the greatest of the Pasteurians, Dr. Charles Nicolle, as follows:

"What beneficial results would ensue from the action of civilized nations if, taking sincerely the minor people under

tutelage, those culturally rich nations would understand the nobility of their mission?

"There are only two conquerors worthy of praise: the educator and the physician. Their action is the only reason, the only excuse for the ascendancy of powerful people upon the weaker ones.

"The rest is enrichment, increase of power, pride, sports and crimes, awaiting the just return of any breach of natural law: rivalries of predator nations, depopulation and hence the ruin of the conquered nations, hatred, revolts, and diseases of the vanquished expanding upon the conquerors."

### The diphtheria serum

The newly created Pasteur Institute attracted the best minds of Europe, for example Elie Metchnikoff (1845-1916), who arrived from Odessa with the discovery of the basic functioning of the immune system, phagocytosis. Up to 40 different nationalities might be represented attending Roux's master classes in microbiology.

An all-encompassing mind, Alexandre Yersin would only tackle a difficult problem to solve it, and move on to another difficulty. He came to Paris from Switzerland to participate in the adventure of the Pasteur Institute.

After groundbreaking work on anthrax and rabies with Pasteur, Emile Roux undertook to tackle the major infant killer disease of the time: diphtheria. The bacillus had been found by Klebs and Loeffler a few years before, but the bacillus's specific activity remained a mystery. Roux thought that the paralysis of the respiratory muscle could be due to an intoxication, the effect of a poison or toxin introduced by the bacillus into the organism. Yersin and Roux were to prove this hypothesis, with a series of experiments injecting the filtrate of the bacillus culture (without bacillus) into animals,



World Health Organization Photo

A French medieval painting of the bubonic plague, which carried off one-third of the population of Europe during the Black Death of 1348-49. It was the Pasteurian Alexandre Yersin who discovered the bacillus that transmits plague, making it possible to wipe out this scourge.

and producing the disease. Diphtheria toxin diluted at 1/5,000 its volume of water will kill a guinea pig in two days. This discovery was followed by the German Emil von Behring's (1864-1917) discovery of the antitoxin produced by the organism affected with diphtheria.

It was then that Roux and Yersin made another breakthrough of extraordinary impact for mankind: They injected a diphtheria toxin weakened with iodine into a horse and took its serum, which contained antitoxins that agglutinate the bacillus and neutralize the toxins. This horse serum was then used to treat people in the early phase of the disease.

By 1895, "serotherapy" saved most infants, reducing infant mortality by 50% worldwide, as half of infant death was due to diphtheria. Beyond diphtheria, serotherapy would be found efficient in most diseases, and remained the only treatment until the discovery of antibiotics during World War II.

This discovery brought the Pasteurians into raising horses, and the construction of what remain among the best-conceived hospitals in the world, all with voluntary contributions of citizens. From then on, the Pasteurians brought to tropical countries the capacity to *treat* or *immunize* against major scourges of mankind, and piloted horse farming, soon followed by comprehensive farming.

Yersin found teaching master classes with Roux too confining, the students too plodding for his adventurous mind. So, he enlisted in the Messagerie Maritime shipping line as a doctor to go see Asia and China.

In 1902, Pasteur interceded on his behalf with the Colonial Ministry for a mission in Indochina. The government asked him to study the road from Saigon to the Moï country. Yersin wrote to Pasteur: "I must find out about the resources

of the country, study the wealth of its forests, and investigate whether there are metals that can be mined."

It was amid those explorations that he met Calmette in Saigon. Albert Calmette was the first Pasteurian sent overseas by the old man to create a Pasteur Institute in Saigon. Calmette re-recruited Yersin to the Pasteurian colonial enterprise. An epidemic of bubonic plague had broken out in Hong Kong, and Europe was trembling at the idea of a repeat of the greatest killer ever known to mankind. Since the time of the big epidemic of 1347, which decimated a third of Europe from its Chinese origin, or even since the smaller epidemics that ravaged some European cities in spite of Colbert's early 17th-century quarantine, the ships bearing disease vectors traveled much faster, moving from China to Europe in a matter of a few weeks, not months.

Calmette's assignment to Yersin was quite a challenge: find the agent of the plague. Thereupon, Yersin traveled to Hong Kong, where 100,000 people were dead or dying of the disease.

At the British hospital, the Japanese bacteriologist Shibasaburo Kitasato and his team were carrying out autopsies, and Yersin could not get any cadavers. He set up a tent on the square in front of the hospital, paid off British soldiers to bring him cadavers, and immediately hit on the idea that had escaped Kitasato: The agent might be in the bubo (the swollen lymph glands of the plague victims) and not in the blood. Yersin had a makeshift "autoclave" that did not warm culture at 37°C (human body temperature) but much less. But as luck would have it, the long stick-like bacillus he found in the bubo, would only proliferate at 27°C (the average air temperature of Hong Kong) instead of 37°C. Yersin experimented with his bacillus culture and found that it gave the

plague to mice. He also autopsied dead rats found in the streets and found them to have died of the plague.

He sent back to the Pasteur Institute two major discoveries: the agent of the plague, and the hypothesis that rat epidemics preceded human epidemics.

The connection between the rat plague and the human plague had not hitherto been known. Early Bible and other illustrations of the plague show live rats on the scene, indicating ignorance that the rat population would have been decimated before the human plague. Only an early Indian poem had hinted at an observation of the reality: "If thou see a rat fall off a roof and wander through the city as a drunken man, flee man, flee, for the plague has entered the city."

Kitasato, with his better equipment, found only an ordinary streptococcus in the blood that multiplied at 37°C, and the fact that Yersin and not Kitasato had made the discovery was established in international medical congresses. That has not, however, prevented English-language publications from speaking of the Yersin-Kitasato discovery.

The bacillus was called the *Yersinia pestis bacillus*. A serum against the plague was quickly made by Roux and Yersin, and the latter started treating people in Hong Kong. By then the plague was ravaging Bombay, and the British Indian authorities asked Yersin to come there.

But Yersin had only about 1,000 doses of the serum, so he refused and went instead to Nha Trang, a beautiful spot along the Indochina coast. There, he pulled together the resources and the horses to make serum. Shortly, 100,000 doses were available, and then Yersin left for Bombay. The serum worked only if injected at the first manifestation of the disease, minutes or at most a couple of hours after infection.

The fight to free the human race from the ravages of the plague was carried on by other Pasteurians as well. In Bombay, another Pasteurian, Simond, found out how rats transmit the plague to man: by the flea bite. Again, this was no small task: The fleas left the rat just as it died, and a rat dead for hours is not contagious at all. The fleas had to be collected and the bacillus cultivated from the fleas. Balthazar, another great Pasteurian who became the next generation's student of the plague worldwide, used to collect fleas by walking his cat on a leash amidst epidemic-stricken cities!

## Nha Trang

Yersin was an enthusiast of all science and engineering devices: An astronomer, he built a dome for astronomical studies and set up the first prism astrolabe. His observatory in Nha Trang became his home. Yersin mastered chemistry, physics, and electrical engineering, and built his own generators for his compound. He was also a lover of automobiles, buying the first one in Indochina in around 1900. He toyed with the first plane, built kites going thousands of feet into the air, with cables and pulleys, for his weather studies. But what could have filled many men's lives was only a part of his activities.

In Nha Trang, he built a pilot scientific research station,

including: an operating room for animals; a laboratory for serum production; and a library. He also began to raise horses for the serum, and also other animals for experimentation: cattle, sheep, goats, and later chickens. Horses must be fed, and so necessity—since Paris was poor and the Institute was left to find its own resources to operate—demanded farming to support the animals. From there, not only animal diseases, but also plant diseases, became of interest, as well as ways to breed better animals and new plants. Yersin's mind was ever resourceful and imaginative. Soon, he built a second pilot experimental farm in Suoi Giao of about 1,500 acres—1,150 for crops, and the rest for animals.

Yersin built four more such stations, one at high altitude (4,500 feet) to study fauna and flora peculiar to mountains.

He tried out a variety of plants: *Theobroma cacao* (the chocolate tree), *Coffea Liberica* (a coffee shrub), cola, manioc, palm oil tree, tobacco, several medicinal plants (all of which were successful). Rice, *Coffea Arabica* (another coffee shrub) and others, which were less successful, were tried and abandoned.

In 1899, fascinated by the progress of the first automobile, not to mention the success of bicycles, Yersin became interested in latex production, called *caoutchouc* in French, from the local tongue "Cao-o-chu," the crying tree.

Yersin obtained 1,000 seeds of *Hevea Brasiliiana*, or "rubber tree," to initiate cultivation, as opposed to random killing of trees in the forest as was then practiced wherever the tree was to be found. Three problems of agronomy had to be solved:

- to obtain plantation trees as vigorous as those in the wilderness;
- to find ways of bleeding the trees so as to get the maximum amount of latex without damaging the tree, which needs the latex to live;
- to improve the quality of the latex.

For all this, Yersin needed manpower. With his initial team of local people, he cleared forest land, not only for the stations, but also to offer 150 acres of land to peasants in the area to cultivate their rice, the main staple of the Annamite local diet, in return for work on the stations.

Soon his pilot Hevea plantation solved a variety of problems involved in latex production: diseases of Hevea trees, a better instrument for bleeding the trees—latex coagulation problems—choice of seeds, etc. In 1916, Yersin's Heveas produced two tons per month. In spite of a typhoon in 1926 which destroyed two-thirds of the plantation and necessitated restarting everything, by 1943 it produced enough to ensure the wealth of Indochina.

But that was not Yersin's only occupation. His main station was also a training center for any French veterinarian coming into Asia, and also for the Indochinese. There the students learned everything about the vaccination of cattle and pets, studied livestock husbandry including hygiene, and studied animal diseases. In 1930, Yersin had 1,500 cattle, 440 sheep (later 750), 40 goats (later 400), and he started a

big chicken coop.

Yersin added yet another dimension, when he endeavored to master cross-breeding two cows and a bull from France with local cattle which were more resistant to local diseases but gave poor milk and serum, and had stringy meat. From that initial experiment, he moved further to produce a new high-quality breed of cattle for the region.

Yersin worked many years on the diseases affecting Indochina's cattle, notably bovine plague, sleeping sickness of horses (which he found was transmitted to the horses by cows that carried the trypanosome parasite without clinical manifestations), pasteurella, apthoid fever, and others.

The Nha Trang compound produced vaccines and serum for a dozen major animal diseases, and in 1935, Yersin set up a new building for breeding pigs to produce serums against porcine plague.

Nha Trang also either produced or imported from the Paris Institute, and distributed to the population of Indochina, serum and vaccines against rabies, diphtheria, pneumococcus, tetanus, dysentery, bubonic plague, meningitis, cholera, and malaria. But all of that was not Yersin's only task.

In 1899, his friend and political ally, Doumer, then governor of Indochina, had asked him to train veterinarians, which he did. By 1902, Doumer had a more ambitious project, the Hanoi School of Medicine. This was to be a hospital, laboratory, and teaching center. Doumer asked Yersin to direct the project. Yersin set up the school, and then taught physics and chemistry. Unfortunately, Doumer was replaced as governor by a certain Mr. Beau, who did not share Yersin and Doumer's principles and did not want the Vietnamese to be trained as Pasteurian scientists, but only as nurses' aides. This was violently against Yersin's scientific and ethical principles, so he left the school.

But Yersin still had other interests. He initiated the cultivation of European vegetables and fruit trees, with all the imagination which he would bring to such a project. He also started the cultivation of flowers with a friend, all types of flowers, and especially, the most fantastic orchid plantation conceivable. On the side, Yersin also set up local tree plantations for reforestation purposes.

World War I brought yet another challenge: Paris stopped sending quinine to Indochina, a medicine essential for malarial countries. So, Yersin and his friend Krempk developed a cinchona tree plantation to produce quinine in Indochina. In 1931, the station produced 2.5 tons of bark, or 137,000 kg of sulfate of quinine. In 1936 production was up to 28.5 tons of quinine, yielding 2,045 kg of sulfate. Yersin died in 1943, and his tomb has been under guard ever since, a sad memory kept by the Vietnamese of what foreigners could bring of love and devotion to the science of building nations.

Perhaps, the tragedy of Vietnam after Yersin can be seen as an imperialist rage to destroy that beauty.

## The basics of epidemiology

A contemporary Pasteurian noted that the early Pasteu-

rians' era was the era of the *Médecine debout*, (standing medicine) and that later, when scientific exploration, missionary work, and terrain epidemiology ceased to be associated with medicine, came the era of *la Médecine assise*, or "armchair medicine." The conquest of the *médecine debout* involved:

- Exploring the ecology of a region: study of topology, waterways, soil, fauna and flora;
- Investigative epidemiology and research: investigation of new and old diseases, search for pathogens, experiments on pathogens; testing for diseases, census endemic or epidemic pathologies; work carried out on human, animal, and plant pathologies,
- Investigation of means of transmission vectors; entomology, parasite control;
- Cattle raising, agricultural experiments, and pilot farming;
- Water purification, draining of marshes, insect control.

In 1900, Dr. Roux sent a mission to Algeria to verify the discovery of Ronald Ross (in part inspired by the hypothesis of Charles Laveran, 1845-1922) on the role of mosquitoes in the transmission of malaria, and to bring Pasteurian methods to the area. This permanent mission was assigned to the brothers Edmond and Etienne Sergent.

In a major groundbreaking work entitled: "Réflexions sur les modalités de l'infection" (Reflections on the Modalities of Infection), the Sergent brothers were to lay the scientific bases of epidemiology.

The central concept is that of uncovering the "unapparent disease," or what is today called the "asymptomatic carrier," and fighting a disease with prophylaxis to protect the population *before* a disease breaks out. The purpose is to intervene at the point before a disease would be able to transform itself from the endemic form to the epidemic or pandemic form. It means that the pool of asymptomatic carriers will be so circumscribed as to give only a limited number of sick people, who then might be treated one by one.

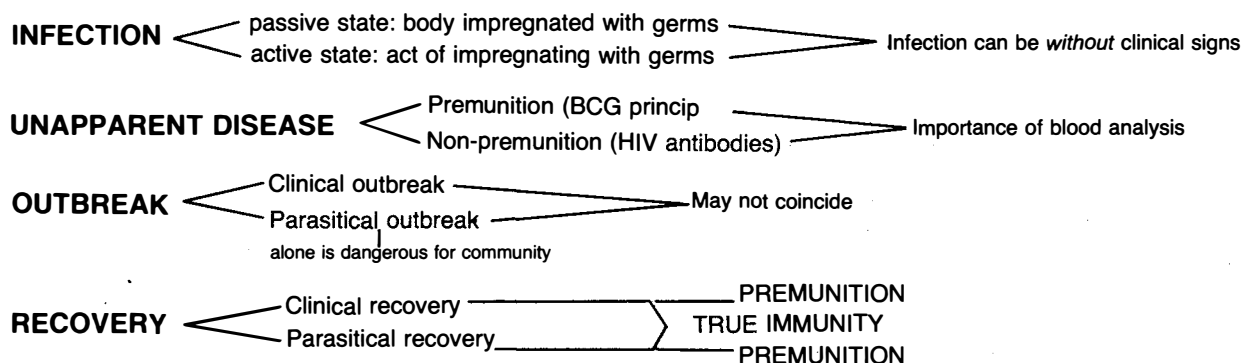
In the majority of diseases, treatment in the early phase of infection will not only save the person from developing the acute and disabling form of the disease, it will also prevent contagion to the rest of the community. For example, leprosy or tuberculosis are highly infectious in the advanced stages, but hardly so in the period preceding the acute clinical phase.

The Sergents put forth the concept of the "threshold of danger," for a given malarial area, which depends on three factors:

- the number of sick people;
- the number of carriers;
- the number of insects.

Embedded in that concept is the idea of both the vectors of transmission and the speed with which a disease can spread. That speed of transmission can mean increased virulence. If we take the plague as an example, the first transmission is rat

## Edmond Sergent, Algiers: 'Reflections on the modalities of infection'



fleas to man, the second is man's fleas to man's fleas, and once a certain threshold is reached, pulmonary aerosol transmission.

The danger of "casual transmission" exists for all diseases past a certain threshold.

The Sergents refined that notion, with their discussion of the different modes of infection in both sick and carriers.

Infection, they wrote, can be either passive or active.

*Passive* means the body is impregnated with germs.

*Active* means the act of impregnating with germs.

*Either* form of infection can be *without clinical signs*.

The active phase is what is today called viremia for viral infections.

In short: It is important, even crucial, to distinguish between the person who has antibodies to a viral infection because he has a few cells in which the virus hides, and that same person during periods of viremia when he or she will be producing millions of viral particles and hence be highly contagious.

It is also of note that today's children with HIV-induced immuno-deficiency can no longer be immunized against other diseases, and that those people who are developing immune deficiencies see the "passive" pathogen multiply and become active.

An unapparent disease can mean either *premunition* or *non-premunition*. Premunition means that as long as a person is infected with a small quantity of hematozoa (blood parasites), he or she is immune against catching a "superinfection" of malaria, but is infectious to others, even without suffering clinical symptoms.

However, once, and if, the body clears itself of all parasites, the person can catch the disease again.

Non-premunition is the case for AIDS today. In their groundbreaking studies of piroplasmosis, the Sergents adduced the following: "Experimental study of resistance to superinfections conferred by an initial infection has led us to be able to specify the notion of premunition, a form of resistance different from real immunity. An animal infected by a

piroplasm [a small parasite of the blood commonly carried by ticks], if it survives the acute crisis of invasion and comes to tolerate the virus, resists, as long as it remains a germ carrier, reinoculations of the same piroplasm (law of precedence). If it recovers from its primo-infection, it stops being protected against reinfections. One has drawn from this conception of premunition a practical conclusion: to give the cow a benign, chronic (if possible latent) infection, which will prevent it from getting a grave infection." (Virus is meant in its original sense of filtrable microbe.)

From that understanding of the successive modes of infection, the Sergents adduced the importance of *screening by blood test*, a screening as wide and comprehensive as possible, using the entire array of bacteriological and viral detection measures available to them at the time.

Systematic testing of the blood was made necessary, they said, because of the fact that the parasitical outbreak and the clinical outbreak might not coincide.

Together, clinical recovery and parasitical recovery mean separate immunity, mean *premunition*.

## Correction

In our *Science & Technology* section in the June 10, 1988 issue, "Stopping the Epidemics: The French Military Legacy," due to an editorial error, we inadvertently placed an epidemic of Chagas' disease in the African nation of Chad. The Chadian epidemic is trypanosomiasis, familiarly known as "sleeping sickness," caused by a trypanosome carried by the tse-tse fly. Chagas' disease, also caused by a trypanosome, attacks the visceral organs and occurs only in Ibero-America.

# SPETSNAZ



## SPETSNAZ

In the Pentagon's "authoritative" report on the Soviet military threat, *Soviet Military Power 1988*, the word *spetsnaz* never even appears. But *spetsnaz* are Russian "green berets." Infiltrated into Western Europe, *spetsnaz* have new weapons that can wipe out NATO'S mobility, firepower, and depth of defense, before Marshal Nikolai Ogarkov launches his general assault.

## ELECTROMAGNETIC PULSE WEAPONS

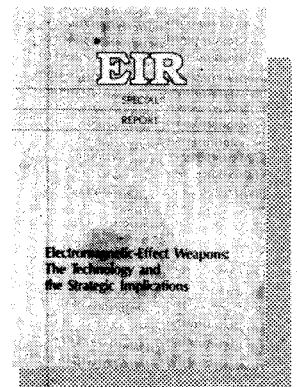
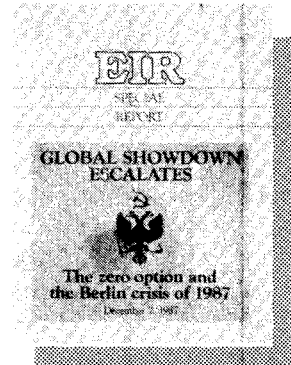
At least the Pentagon report mentions them—but only their "defensive" applications. In fact, they can be transported by *spetsnaz*, finely tuned to kill, paralyze, or disorient masses of people, or to destroy electronics and communications. With EMP, as strategic weaponry or in the hands of *spetsnaz*, the Russians won't need to fire a single nuclear missile to take Europe.

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