Pasteur Institute Rebels Lose a Round

London. Scientists returning from the recent international congress of microbiology in Moscow brought back what many of them regard as distressing news from the Pasteur Institute in Paris.

The news is the failure of the institute's new council of administration to name a genuinely eminent researcher to direct the Pasteur.

Although André Lwoff, one of the three Pasteur Institute scientists to receive the Nobel prize in 1965, was a candidate for the directorship, he was turned down in late June in favor of Charles Mercier, a compromise figure. Mercier, who began his career at the Pasteur with researches on staphylococcus in the institute's production branch, had recently become secretary-general of the institute.

The rejection of Lwoff was not the result merely of internal pressures. Several top French Government scientist administrators on the board voted against Lwoff. Hence, the institute's scientists assume that the government intervened to stop his election.

As a result, the Pasteur scientists are wondering whether all their activity of the past 3 years in seeking fundamental reforms may have gone for nothing.

Without a figure of Lwoff's stature at the head of the institute, many French scientists believe, there is little chance that the institute will be reformed as it must be if it is to continue to attract top-quality researchers.

What events led to this outcome? The roots of the scientists' campaign for reform of the institute's research and manufacturing activities run far back into the Pasteur's distinguished history. Some of the difficulties, indeed, go back to the institute's founding in the aftermath of Pasteur's success in developing a treatment for rabies. At the end of a fund-raising campaign in France and abroad, the institute was inaugurated, on 14 November 1888, as a foundation recognized legally as a "public utility" under French law.

In the glow of Pasteur's great achievements, the institute received an autocratic constitution; directors after Pasteur (who served until his death in 1895) were elected for 6-year terms by the 12 members of the board of trustees, who were chosen by a "general assembly" of at least 30 members.

Under this system, turnover rarely occurred except as a result of death. There was no stipulated retirement age for director or trustees. Trustees were elected (four at a time) for 9-year terms. Elections were held every 3 years.

Furthermore, the members of the general assembly were chosen by the board of trustees. The general assembly included Establishment figures, such as Perpetual Secretaries of various French scientific academies and senior administrators of the institute itself, as well as certain of the trustees themselves.

Not only did this make the leadership of the institute a closed circle, it tended to remove all debate from the periodic meetings of the general assembly. Generally these general assembly meetings were preceded by a meeting of the trustees in the president's office. When the trustees had arranged things to their satisfaction they had only to open the door to admit a few top administrators—their own appointees—to possess a quorum.

In such a system there was little formal opportunity for debating scientific policy. The institute's scientists were scantily represented on the board of trustees and in the general assembly. Moreover, there was no scientific council of the sort that is now common in large, modern laboratories (the counterpart of a university departmental meeting) as a device for ensuring debate on policy and practical issues. Such a scientific council was formed at the Pasteur in 1964, but it does not yet operate fully.

All this mattered relatively little in the first 45 years of the institute's existence, when, it is felt, the direction was first-class. During those years the Pasteur Institute came to fill many of the research and public-health functions that are usually discharged by government agencies. Not only did the institute do research, it also operated a hospital, provided experts in all kinds of public-health emergencies, and supervised a growing number of daughter institutions in France and in France's colonies (now redefined as underdeveloped countries).

In the beginning, Pasteur was able to attract men of diverse background to head the five laboratories: two graduates of the Ecole Normale Supérieure —Duclaux and Chamberland; the Russian biologist Metchnikoff; two physicians, Grancher and E. Roux; and about ten other scientists.

Duclaux, who succeeded Pasteur in 1895 as director, was in turn succeeded by Roux, who had already assumed many of the administrative duties and established courses in microbiology. Roux was director of the institute from 1904 to his death in 1933. During most of this period the president of the board of trustees was Pasteur's son-in-law, R. Vallery-Radot,who also died in 1933, as did Calmette, deputy director since 1915 and Roux's choice as his successor.

In these years the institute's research in microbiology and allied fields expanded rapidly, supported generously by private gifts from France and abroad. Its activities in applied research and production of vaccines and antiserums expanded under the pressure of epidemics and other emergencies, when the government felt obliged to ask the Pasteur to undertake new work.

In 1894 the institute began manufacturing vaccines and antiserums. Public subscriptions enabled it to start making an antiserum to diphtheria toxin and, later, an antiserum to tetanus toxin. This was the origin of the Pasteur's production center at Garches. Some years later, private gifts enabled the Pasteur to build the first Institute of Biological Chemistry in the world, where, for many years, University of Paris courses in biological chemistry were taught. Then, a hospital annex was constructed, also with private gifts.

Meanwhile, the creation of daughter institutes had begun. Calmette founded the Pasteur Institute of Saigon in the early 1890's, and went on to become director of the first Pasteur Institute branch in France, that of Lille.

During World War I, the manufacturing activity expanded once again, in response to an outbreak of typhoid fever among soldiers fighting at Verdun. The development of diphtheria and tetanus toxoids by Pasteur Institute researcher Gaston Ramon resulted, in 1925, in further expansion of the production center at Garches.

At Lille, under Calmette's direction, the antituberculosis agent BCG was discovered. After he came to Paris, Calmette devoted much of his energy to research on the disease and to forwarding the production of BCG and tuberculin.

At the Institute of Radium, in Paris, a Pasteur Pavilion for research on the impact of radiations on tumors was established.

A notable achievement in chemotherapy was the discovery in 1935, at the Pasteur Institute, of the antimicrobial activity of *p*-aminophenylsulfamide. This was the work of Daniel Bovet and his wife and of J. and T. Tréfouel. Bovet later won the Nobel prize for work largely carried out at the Pasteur.

Many institute members had already been honored by Nobel prizes in physiology and medicine. In 1907 Pasteur researcher Alphonse Laveran received the prize for his research on the role of protozoa in causing diseases. The following year Metchnikoff shared the prize with Paul Ehrlich for research in immunology. Pasteur-trained Charles Richet received the 1913 prize for his work on anaphylaxis. In 1928 Charles Nicolle was honored for his work on typhus. In 1920 Jules Bordet of Brussels University was honored for studies of immunity that were carried out, in great part, at the Pasteur.

Thus, in the first half century of its history, many of the institute's characteristics and policies were shaped. Among the most important were the following.

1) The vital role played by private gifts, many of which allowed the institute to assume semipublic functions in the fight against disease.

2) A constant concern for the practical application of fundamental discoveries made in its laboratories.

3) Its assumption of a major role in university teaching of such subjects as microbiology, biochemistry, and immunology.

4) Its reception of a steady stream of committed researchers from abroad —vital both for the continuing youthfulness and for the influence of a research institute, but not always encouraged in European research laboratories.

5) Its readiness to give disinterested service and advice in public-health emergencies. After World War II, this led the World Health Organization to call on many Pasteur Institute researchers for help.

All of this was possible under the autocratic statutes of the institute, inherited from the patriarchal days of Pasteur himself.

But when Roux died in 1933 it was realized that something would have to be done to institutionalize and democratize the institute. The president of the trustees in 1933, A. Lacroix, made a start at rewriting the statutes, but the effort came to nothing.

The new director, Louis Martin, was a physician of no particular stature, who served until 1939, when he was succeeded by Gaston Ramon, who served briefly. In 1940, Jacques Tréfouel began a tenure of office that lasted until the end of 1964.

As Pasteur Institute scientists look back over the past 30 years they judge all three of these directors to have lacked the qualities needed to maintain the progress of earlier days. Tréfouel is judged to have been a man of great good will but quite incapable of developing or following a consistent policy in research or industrial activity. Adding to the difficulty was the traditionalist stance adopted by Louis-Joseph Pasteur Vallery-Radot, Pasteur's grandson. Vallery-Radot, who became president of the trustees in the mid-1930's, constantly emphasized the continuation of Pasteur's work—contrary, some observers say, to Pasteur's own readiness to break with precedent.

However, scientific activity did not cease merely because the director was not fully sympathetic to modern research trends. André Lwoff, who had begun his work at the institute in 1921, had risen by the late 1930's to a position where he could offer work space to Jacques Monod and other researchers.

By the end of World War II the institute was in severe financial straits. Nevertheless, in the late 1940's, the trustees rejected an offer of help from the French pension agency, Securité Sociale. They did this in part because of their political conservatism, which made them bridle at receiving help from an agency created during Léon Blum's Popular Front government of the 1930's. But there was a more important reason. Securité Sociale demanded representation on the board of trustees. This would have broken up the closed circle of administration which had existed for so long.

This attitude could not be maintained indefinitely. By about 1960 the institute's operations began to show a serious deficit. The trustees had to apply to the state for aid.

Of course the institute did this with an easy conscience, for it had given much aid to the state from its private funds in earlier days, in accordance with its idea of its obligations as the recipient of numerous gifts from the public.

The government felt that it could not give blanket aid without being represented on the board of trustees. And by now the government had developed a considerable machinery for supervising its scientific activities. There was a minister for science, who was turning for advice to panels of scientists, some of them from the Pasteur Institute, in giving out aid through the *actions concertées*. But there was no scientific council to add a third voice to the dialogue between a government which was still feeling its way in scientific matters and an institute leadership which had fallen badly out of touch with modern biological and medical science.

The Pasteur Institute scientists decided that the moment had come when they should consider independently the institute's future and take measures to insure that they would ever afterward be adequately consulted. They formed a study group which wrote a draft of a new statute for the institute. This statute provided that the institute's research and manufacturing activities should be separate, although an eminent scientist would continue to direct the institute as a whole, with the assistance of a formal scientific council. The idea was to insure that forward-looking attitudes would prevail in the research arm of the institute, and that the industrial operation would be fully modernized.

The work of the study group continued into 1965.

Meanwhile, in 1964, the science minister, Gaston Palewski, took the Pasteur scientists' part to the extent of demanding of the institute, as conditions for the receipt of government aid to meet the institute's deficits, the separation of research and manufacturing, the formation of a scientific council, and the naming of government nominees to the board of trustees.

Tréfouel found these conditions unacceptable. But Pasteur Vallery-Radot, president of the trustees, decided that they must be accepted. Consequently, Tréfouel was not reelected when his term ended in December 1964, and Charles Gernez-Rieux, director of the Lille branch of the institute, was elected director.

As it turned out, Gernez-Rieux did

not serve a full year. He resigned during the scientists' revolt of December 1965, because he found it hard to choose between the scientists and the hard-line resisters on the board of trustees.

In the meantime the scientists found that the government would go only so far in helping them. When they asked the science minister to intervene to force a dialogue between the administration and the scientists, Palewski refused. The Pasteur Institute was, after all, a private institution. To the scientists this made it clear that they had no choice but to stage a revolt on their own.

Meanwhile, the government began to give financial support to some of the institute's divisions. Subventions from the ministries of science, education, and health totaled $1 million. This amount fell far short of meeting the institute's deficits, which had mounted as high as $2.5 million a year.

In the spring of 1964 a scientific council, made up of members elected by the Pasteur scientists, began holding meetings about institute reform, but the board of trustees refused to listen. The trustees persisted in their refusal even after Gernez-Rieux joined the council as vice-chairman and endorsed such proposals as a separate industrial enterprise, the addition of scientists to the general assembly, replacement of the four members of the board of trustees up for reelection at the end of 1965, and the formation of a liaison group consisting of three members of the board of trustees.

Furthermore, during 1965 the union representing many of the Pasteur scientists (in which Monod has been very active) demanded that the institute return to the salary policy it adopted after World War II, when compensation was pegged to the levels prevailing in French universities. This policy had been suspended during the crisis over deficits. Gernez-Rieux endorsed this demand as well.

On 7 December 1965 the board of trustees rejected all these proposals and demands. On 18 December the entire scientific staff met, and Gernez-Rieux explained the situation, adding that he had resigned that morning. The staff then voted, 144 to 5, to demand the resignation of the entire council of administration. The text of their resolution was released to the press and, much to everyone's surprise, received a great deal of attention, despite the simultaneous avalanche of press coverage of the runoff presidential election, which was won by General de Gaulle.

On 23 December, 15 scientists were added to the general assembly of the institute, and on 18 January the whole board of trustees resigned. On the new board chosen at that time there were only three holdovers—former prime ministers Paul Reynaud and Antoine Pinay and a former inspector-general of finance, who had been named at the time the government began paying for some institute services.

Four scientists were named to the new board: Lwoff and Pierre Lépine of the Pasteur Institute and Etienne Wolff and Georges Champetier from outside.

Also named were Pierre Laroque, who was head of Securité Sociale when the first offer of financial help was made; Francis Perrin, High Commissioner of Atomic Energy; André Maréchal, Delegate-General of Scientific and Technical Research (head of the prime minister's scientific planning secretariat); Pierre Jacquinot, director-general of the Centre National de la Recherche Scientifique; and Gernez-Rieux.

At the same time, the scientists proposed that the board of trustees move directly to name a "director of transition" to serve for 2 years while new statutes were being put into effect.

On 22 January 1966 the scientific council suggested four possible candidates for director: Monod, Jacob, Lwoff, and Lépine. These four consulted and decided that Lwoff was the man.

Thus, last in January, it seemed that the way was clear for reform of the institute, under the sympathetic eye of some of the most powerful scientist-administrators in the government and with the support of three recent Nobel prize winners and the scientific group generally.

But it was not to be. The new trustees promptly named one of their least strong members, Champetier, president. He was more available than one of the busy officials, although he is head of the School for Physical Studies, and professor, at the University of Paris.

Champetier decided at once to delay selection of a director and the adoption of new statutes. An interim committee to administer the institute was named. It included Champetier, Lwoff, Lépine, Mercier, and two others.

A group began studying new statutes for the institute. It decided that selection of the director of the research part of the institute could be made without prior consultation with the scientific council. It also decided that the industrial center, instead of being under a scientist as overall director, would report separately to the board of trustees.

In June the general assembly met to consider these ideas, and it accepted them on the advice of the trustees. The assembly also rejected a motion by the scientists that the Pasteur Institute's director be a scientist "highly qualified" in subjects studied at the institute, although it did accept the idea that he should be a scientist.

This was a direct sign that the trustees would not agree to name Lwoff director. An even more direct sign was Champetier's surprising declaration, in May, that he himself was available as a possible director. He stated that a director "above the battle" was required, and that he stood well with government officials who would be providing money.

As time passed it was clear that there was opposition to Lwoff inside and outside the institute. It is not easy to understand this opposition, for Lwoff is a person of commanding intelligence and unique charm. But people in France note that Lwoff is also a person of uncompromising honesty and that he has often failed to use his courtly arts in powerful circles.

The idea of having Champetier as director instead of Lwoff created "a certain emotion" in the institute, because Champetier was neither a Pasteur Institute member nor a biologist. When trustee Laroque conducted informal consultations about the directorship, he found quickly that Champetier would be unacceptable.

So, when the trustees met, without Champetier and Lwoff, to choose a director, they voted 7 to 3 in favor of Charles Mercier, secretary-general of the institute since early 1965 and former director of the Pasteur Institute in Athens. The choice deeply angered a great many scientists at the Pasteur. They felt that Lwoff's appointment was highly important as a symbol of the institute's reform and determination to operate on modern lines. They asked themselves if a traditional French reaction against strong and competent personalities would prevail at the Pasteur Institute. It appeared to them that the French Government, through lack of imagination, had acted to put the future of the Pasteur Institute on ice.

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