used as a check list for criticism of grant applications by the investigator himself prior to their submission, no matter to what granting agency.

Summary

A list is given of 26 shortcomings mentioned repeatedly in study-section discussion of 605 research grant applications that were subsequently disapproved (*2*) (by vote, following the discussion). The shortcomings have to do with either (i) the conception of the research problems, or (ii) the proposed route of approach toward their solution, or (iii) the competencies to be mobilized toward prosecution of the research, or (iv) miscellaneous other matters. The percentage frequency of applications (in the total of 605) in which a given shortcoming was found is reported for each of the 26. Certain of the items in the list are discussed briefly.

Notes

1. Competitive applications are (i) applications requesting support for a new research project not previously supported by the NIH, and (ii) applications requesting *continuation* of support beyond the existing term of commitment. The "nearly 6000" applications referred to in the text consisted of 4600 proposals to initiate and 1200 to continue research; also, but not included in this analysis, there were 4500 awards of an additional year's support granted on study-section recommendations *previously* made and 650 (competitive) applications for additional funds to supplement awards already made.
2. Disapproval of an application by a study section has the force only of a recommendation to one of the National Advisory Councils. Council acceptance of the recommendation makes the disapproval official.

Charles Oberling, Research Worker on the Nature of Cancer

Charles Oberling, director of the Institute for Cancer Research Gustav Roussy of the University of Paris, was fortunate in his upbringing as scientist and man. It shaped him, as if purposely, to fight against the most challenging of diseases and to enjoy his life.

Oberling was born in 1895 in Metz, but his father—a postal clerk whom he ever remembered with admiring love—soon moved the family to Strasbourg. Here Charles was educated, gained entrance to the university, and studied medicine. But not without interruption. He joined the army in 1914, was seriously wounded twice, and only in 1920 became a doctor. Then fortune favored him again. The university had as professor of pathological anatomy the renowned cytologist Pierre Masson, inventor of revealing histological methods, who took Oberling on his staff. During eight years with Masson, Oberling received an intensive training in cytology and through this was enabled to discover new facts about the nephroses and the reticuloendothelial system, and to obtain a firsthand knowledge of tumor cells. He was assistant professor at Strasbourg when, in 1928, he was asked to become an associate professor of the Faculty of Medicine of Paris in a division dealing with histology, embryology, and pathological anatomy.

It happened that professor Gustav Roussy, who headed the division, was an experimentalist, ardently concerned with founding an institute for cancer research. Soon he had Oberling experimenting with him on the tumors of laboratory animals. In another two years he had achieved his institute, and Oberling was made its *chef de service*. Together they published a definitive atlas on the growth of the human central nervous system, but Oberling's work was now mostly experimental. He found out much about the transplantable growths of small mammals and the virus-induced tumors of fowls, and in addition he showed such ability as teacher and organizer that he was called to Strasbourg in 1937 to succeed Borrel in the chair of hygiene and microbiology.

Amédée Borrel is now a well-nigh legendary personage to French scientists concerned with the actuation of tumors. He it was who first ventured the view, in 1903, when little was sure about viruses, that they are the cause of tumors, and for this view he sought and fought throughout his later life. The times were hostile to it, for the hopes aroused in the Pasteurian epoch that tumors would prove to be due to microbes had been destroyed by tests of the newly transplanted growths of the rat and mouse: these growths yielded no other cause, on transfer, than their own living cells. Realizing through his own experimentation that this was so, Ehrlich had quit the tumor problem for others that he could solve.

Oberling's new academic duties required that he learn far more than he taught, and in strange fields. Hence, he did little on cancer before World War II began. By that time he had such a reputation as hygienist that late in 1939 he was asked by the Shah of Iran to reorganize medicine in Teheran and to try to make the city a more healthy place. Toward these ends he would be appointed dean of the Faculty of Medicine. He was working on war gases, but he was advised by the French Government to accept the offer. During two years in Iran he reformed the medical curriculum in the university, converted the city hospitals into university centers staffed with the best specialists, founded a school for nurses, and greatly improved sanitation throughout the immediate region. Then, with his task carried out, he journeyed in 1942 to the United States to undertake cancer research anew, but upon landing was again asked to come to Iran, this time to improve health throughout the country.

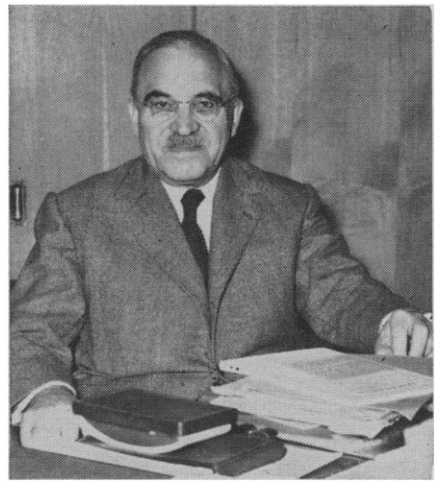
On the way back he had the first of the cardiac "strokes" which were to harass him throughout his remaining 17 years. Feeling unequal now to the task in Iran and unwilling to return to an occupied France, he brought his wife and boys to the United States and tried to enter its army. He was rejected because of his medical history, and so he became pathologist-in-chief at the Mary Imogene Bassett Hospital in Cooperstown, New York. The directors of that enlightened institution could not have known that in appointing him they acted to further cancer research even

to this day. For during his stay at Cooperstown he not only carried out his hospital tasks with engaging gusto, lecturing on war pathology in addition, but, stimulated by his environment and aided by an excellent library, he completed his book, *Le Problème du Cancer*. It was published in 1942 and was admirably translated as *The Riddle of Cancer* by William H. Woglom, previously editor of *Cancer Research*, as was also a revision in 1952. The book has since gone into several editions and has appeared in Spanish and German. It tells what is known about cancer with that limpid clarity one likes to think of as French; although written with zest for the lay scientist, it is backed by references, and specialists continue to gain from it because of the author's enterprising thought.

Oberling was still dean in Teheran University, and now the Fighting French urged him to return to Iran. He did so in 1944, ranging the whole country, inspecting local conditions and hospitals, starting medical schools in Meshed, Shiraz, Isfahan, and Tabriz, and radically bettering the situation.

In 1947 Roussy died and Oberling became his successor; for although he had done almost no laboratory research during the previous ten years, his book had been potent in stimulating it. Long before, while he was still with Roussy, he and M. Guerin had discovered that a virus producing and maintaining a transplantable leukemia in fowls would cause solid growths as well. Thus they were led to perceive not only that the leukemia studied was a neoplastic disease of blood cells but that a single virus can cause various tumors. Thus the problem presented by their diversity was simplified. On the basis of these facts, and others set forth in his book, Oberling had become convinced, even before succeeding Borrel, that viruses cause tumors in general. Since then several neoplastic viruses of unprecedented subtlety and scope had been discovered in mammals. Furthermore, the electron microscope had opened a new era in cytology, and it had actually revealed *in situ* the particles of some tumor-producing viruses. At last one could study the minute pathology of tumor cells, not only as such, but with special reference to whether they owe their state to the action of viruses. To Oberling these were the most important of tasks.

A curious situation had developed concerning the chicken tumors. Many



Charles Oberling

such growths had been induced by means of chemical agents, but from none had a causative virus been obtained, whereas every "spontaneous" fowl tumor adequately tested had yielded one. Furthermore, the spontaneous tumors propagated for years had undergone a morphological simplification (like many mammalian neoplasms of unknown cause when thus maintained). In both these respects they differed from the recent, chemically induced growths. Hence the old supposition was brought forward anew that they could not be true neoplasms. Nature had to accord with artifice, else she could not be real. But Oberling, working once more with Guerin, induced in 1950 a fowl sarcoma with 20-methylcholanthrene that not only had the morphological characters of a "spontaneous" tumor but yielded a causative virus. Other workers have recently obtained a causative virus from rat lymphomas induced by radiation.

As time went on, repeated cardiac episodes wore Oberling down; yet he could still achieve through his able and devoted young associates. Together they proved with the electron microscope that the virus particles causing fowl tumors have a form so characteristic as to be readily distinguishable from normal cell constituents. Following the intracellular cycle of these viruses electronically, they found that it takes place entirely in the cytoplasm, as does the cycle of the milk virus responsible for the nodules from which mammary mouse cancers arise. Also they saw particles characteristic of the fowl viruses scattered in certain organs of healthy chickens. Oberling came to realize that some viruses pass through a phase in which electron microscopy fails to disclose them, and he asked himself whether in many tumors they may not persist only in this form yet be responsible for the neoplastic state. His group were engaged in comparing the ultrastructure of human tumor cells with that of normal cells of the same sort throughout his last years.

Oberling served not only as director of research but as a teacher and lecturer also in the Faculty of Medicine of Paris, and in 1949 the university appointed him professor of carcinology, creating this post, with its apt title, especially for him. In 1956 he was made professor of experimental medicine in the *Collège de France*, a chair that was once Claude Bernard's. Both distinctions meant more duties, and these came while his physical powers were being lopped away. Nevertheless he labored on and even journeyed to far-off spots on occasion. To see him at the end of a grueling symposium was to feel compassion, so exhausted was he in all save mind. Yet when invited, shortly before his death, to join a gathering of virologists in New York and give an address that would render it memorable to one of their number, a personal friend, he came, and concealing how weary he was, spoke even better than had been hoped. A few days after returning to France in January 1960, he fell ill, and a few weeks later an emergency operation disclosed an unsuspected, widely distributed cancer. He died within a few hours. Had he known of his disease he might have remarked, as a spur to research, that man still walks in the shadow of cancer all his days, just as throughout his long past, though now so often rescued.

Charles Oberling was a naturalist in a widely diverse sense of the term. He delighted in phenomena, and his life had many facets. As a boy in Strasbourg he fell under the spell of the arts and was strongly inclined toward music. He had indeed the artistic temperament, yet with it an urgent sense of responsibility. The gift of admiring was his; he always saw things to enjoy. The interlude in Iran was to him a resplendent adventure because he soon came to love the people and their country. Fair-minded and humorous, comprehending and wise, his presence, wherever he went, gave personal happiness to workers against disease.

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